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神経化学

Bulletin of the Japanese Society for Neurochemistry

Vol. 47 (No. 2, 3), 2008

第51回日本神経化学会(富山)大会

抄録号

連合開催: 2nd WFSBP Asia pacific Congress and 30th Annual Meeting of JSBP

第2回 アジア・太平洋生物学的精神医学会・第30回 日本生物学的精神医学会

平成20年8月

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※今回の日本神経化学学会大会は、The 2nd Asia Pacific Congress of Biological Psychiatry・第30回日本生物学的精神医学会との連合開催です。日本神経化学学会大会の参加者は、両学会とも自由に聴講いただけます。(会場：富山国際会議場、ANAクラウンプラザホテル富山、富山県民会館ホール)

第 51 回日本神経化学学会大会
The 51st Annual Meeting of the Japanese Society for Neurochemistry

抄録号 訂正 -Corrigenda-

以下、「神経化学」抄録号 Vol.47(No.2,3), 2008 につきまして、誤りがありましたので、訂正させていただきます。

A corrigendum was found on Neurochemistry abstract book Vol.47(No.2,3), 2008.

Detail is as follows.

■ P.64 9 月 12 日 (金) 日程表 シンポジウム 8 E 会場・9:00-12:00

【誤】 座長：島 明彦 武田 雅俊 シンポジスト：田上 真次 西村 正樹 富山 貴美 柳澤 勝彦 田中 稔久 島 明彦	→	【正】 座長： <u>高島 明彦</u> 武田 雅俊 シンポジスト：田上 真次 西村 正樹 富山 貴美 柳澤 勝彦 田中 稔久 <u>高島 明彦</u>
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■ P.67 13 September (Saturday) 日程表 Symposium13 F 会場 15:20-17:20

【Incorrect】 Lopatina Olga

↓

【Correct】 Olga Lopatina

■ P.131 Educational Lecture

【Incorrect】 Shinichi Kohsaka
National Center of Neurology and Psychology

↓

【Correct】 Shinichi Kohsaka
National Institute of Neuroscience, NCNP, Tokyo, JAPAN

第51回日本神経化学会(富山)大会 抄録集

会 期：2008年9月11日(木)～13日(土)

会 場：富山国際会議場 TEL.076-424-5931

大会長：武田雅俊(大阪大学大学院医学系研究科精神医学教室)

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TEL.076-429-5708 FAX.076-428-9156
E-mail:jsn51@lni.co.jp

大会URL <http://www.lni.co.jp/jsn51>

ご挨拶

このたび富山国際会議場において第51回日本神経化学学会を担当することになりました。平成18年度は、名古屋国際会議場で日本生物学的精神医学会・日本神経精神薬理学会との合同大会であり、昨年度はパシフィコ横浜での日本神経科学学会との合同大会でありました。今回は、富山国際会議場で、Asia Pacific Congress of Biological Psychiatry と日本生物学的精神医学会との連合大会です。

今年の日本神経化学学会年会の特徴は、(1) 基礎から臨床へのトランスレーショナル研究の推進、(2) 口演重視、(3) 国際化、(4) 若手育成、の四点です。

日本神経化学学会会員の研究活動は最終的には精神神経疾患の克服という目標に向かってなされています。基礎の側からは、最新の研究手法を提供していただき、臨床の側からは疾患の特徴を同定してどのような研究手法が有効かを提示していただき、双方の研究活動が共通の目標に向かってダイナミックに統合されことを期待したいと思います。

日本神経化学学会は、伝統的に口演発表を重視してきました。今回はメインホールに加えて5つの小会場を最大限に活用したプログラムを用意しました。日本神経化学学会の伝統である「口演と討論の重視」にこだわり、応募演題約250演題のうちの4/5を口演発表にしました。一題あたりの発表時間も討論時間も今までになく長い時間をかけたプログラムとなりましたので、活発な討論を期待しています。

今回は Asia Pacific Congress of Biological Psychiatry との連合開催でありますので、発表は基本的に英語でとの方針にいたしました。特別講演、シンポジウムは、英語での発表です。一般演題についても、スライドは英語で作成していただけてできるだけ英語での口演発表をお願いしたいと思っています。

また、理事会の強いバックアップのもとに今回初めての企画「神経化学の若手研究者育成セミナー」を準備しました。現在学会をリードしている研究者と膝を交えて夜中まで懇談していただく場を提供することにより、若い人に神経化学の素晴らしさをお伝えしようという企画です。約百名の若い研究者（大学院生、ポストドク）の参加を得ましたので、熱のこもった議論を展開していただきたいと思います。

今回の日本神経化学学会は、The 2nd Asia Pacific Congress of Biological Psychiatry 第30回日本生物学的精神医学会との連合開催です。合同企画によるプログラムを用意するだけでなく、神経化学学会への参加登録者はお隣の学会にも自由に出入りすることができます。富山での3日間が会員の皆様にとって有意義な時間となることを期待しています。

第51回日本神経化学学会大会

大会長 武田雅俊（大阪大学大学院医学系研究科精神医学教室）

大会委員一覧

大会長

武田 雅俊 大阪大学大学院医学系研究科精神医学教室

組織委員会委員

五十嵐道弘	新潟大学	遠山 正彌	大阪大学
岸本 年史	奈良県立医科大学	中村 祐	香川大学
木山 博資	大阪市立大学	東田 陽博	金沢大学
切池 信夫	大阪市立大学	樋口 宗史	新潟大学
倉知 正佳	富山大学	森 則夫	浜松医科大学
高坂 新一	国立精神・神経センター	吉川 和明	大阪大学
齋藤 利和	札幌医科大学	米田 幸雄	金沢大学
佐藤 真	福井大学	渡辺 恭良	理化学研究所
仙波 純一	さいたま市立病院	渡辺 義文	山口大学
祖父江憲治	大阪大学	和中 明生	奈良県立医科大学

プログラム委員会委員

大森 哲郎	徳島大学	津田 正明	富山大学
岡野 栄之	慶應義塾大学	那波 宏之	新潟大学
小川 智	金沢大学	西川 徹	東京医科歯科大学
神庭 重信	九州大学	西澤 正豊	新潟大学
小山 司	北海道大学	橋本 均	大阪大学
佐野 輝	鹿児島大学	橋本 亮太	大阪大学
島田 昌一	名古屋市立大学	山脇 成人	広島大学

合同シンポジウム委員

池中 一裕	生理学研究所	那波 宏之	新潟大学
島田 昌一	名古屋市立大学	橋本 均	大阪大学

(五十音順)

交通案内

●東京首都圏からの交通

(JR利用の場合)

東京駅 ———— 越後湯沢駅 ———— 富山駅
 約90分 約120分
 上越新幹線とき 特急はくたか

(航空機利用の場合)

東京（羽田空港） ———— 富山空港 ———— 富山駅
 約60分 約20分
 全日空 富山地方鉄道バス

●大阪からの交通

(JR利用の場合)

大阪駅 ———— 富山駅
 約200分
 特急サンダーバード

●名古屋からの交通

(JR利用の場合)

名古屋駅 ———— 富山駅
 約210分
 特急しらさぎ

●北陸近辺からの交通

(JR特急利用の場合)

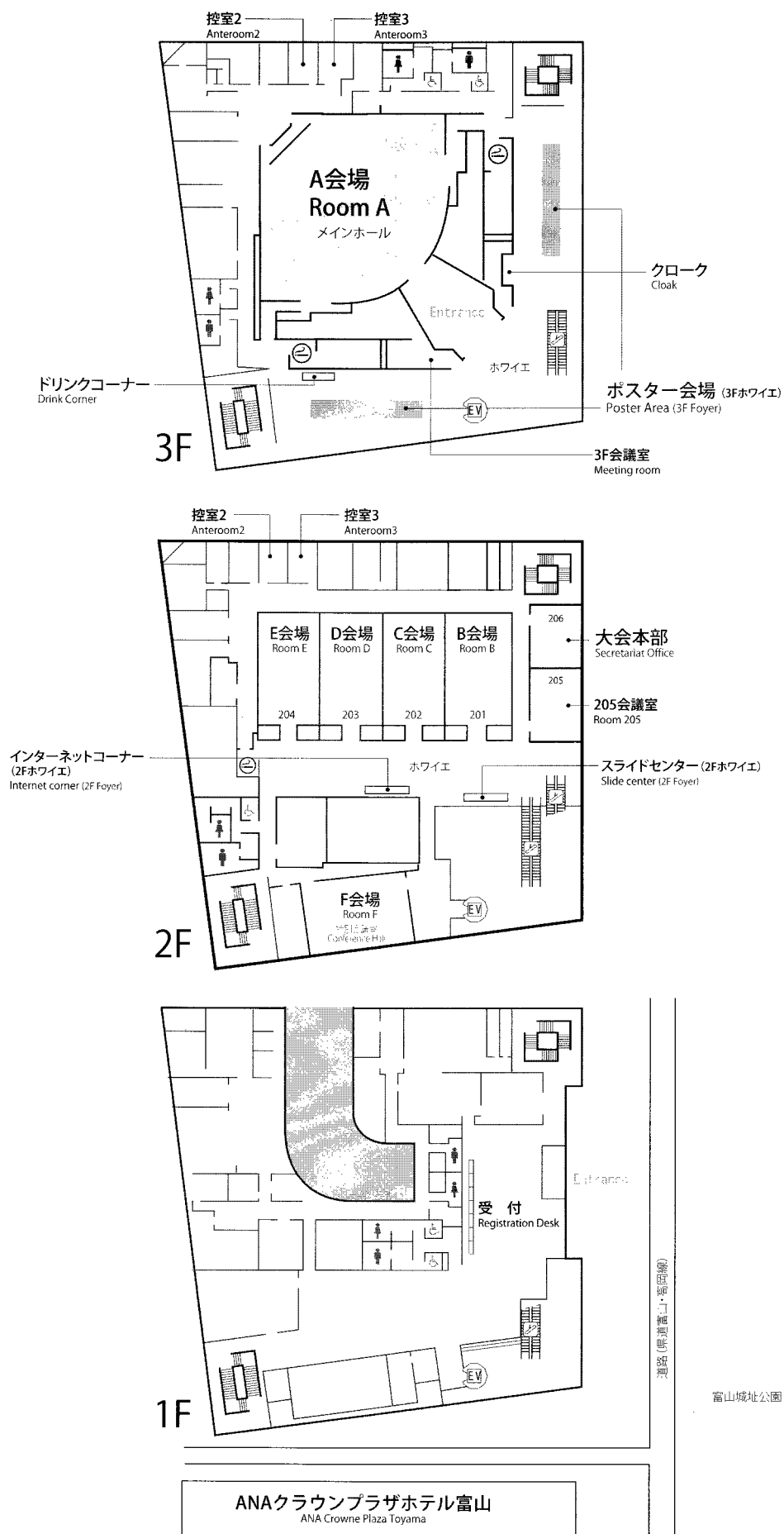
福井駅 ———— 富山駅
 約85分
 北陸本線

金沢駅 ———— 富山駅
 約30分
 北陸本線

新潟駅 ———— 富山駅
 約170分
 信越本線・北陸本線

会場案内図

■富山国際会議場 Toyama International Conference Center



大会日程概要

■第1日目 9月11日(木)

	A会場 メインホール	ポスター会場 3Fホワイエ	B会場 201号室	C会場 202号室	D会場 203号室	E会場 204号室	F会場 特別会議室
8:00							
9:00		8:30-10:00					
10:00	9:45-10:45 教育講演 EL-1 講師：高坂 新一 座長：遠山 正彌	貼 付	9:00-12:00 一般口演 O1-1～9 シナプス 座長：小池 達郎 加藤 敏夫 武田 泰生	9:00-12:00 一般口演 O2-1～9 アストロサイト 座長：津田 正明 片山 泰一 山崎 成人	9:00-12:00 一般口演 O3-1～9 神経幹・前駆細胞 座長：堀井 裕行 堀江 秀典 新谷 紀人	9:00-12:00 一般口演 O4-1～9 神経細胞死 1 座長：岡澤 均 野田 百美 堀恒 忍	9:00-12:00 一般口演 O5-1～9 統合失調症 座長：岸本 年史 車地 晴生 上野 修一
11:00	11:00-12:00 特別講演 1 SL-1 講師：Julio Licinio 座長：御子柴 克彦						
12:00							
13:00	12:15-13:15 ランチョンセミナー 1 LS-1 講師：Lester Binder 座長：辻 省次	掲 示					
14:00			13:20-14:20 若手奨励賞 シンポジウム LA 座長：米田 幸雄 木山 博賢	13:20-15:20 シンポジウム S1 神経系におけるプロテオミクス研究の新展開 座長：和中 明生 宮田 清司 シナプス：梶 正幸 青野 幸子 宮田 清司 辰巳 晃子	13:20-15:20 シンポジウム S2 動物やヒトの行動に対する遺伝子・環境相互作用 座長：堀島 俊隆 堀口 宗史 シナプス：John Waddington 東田 陽博 山田 浩文 Ramon Cabellos	13:20-15:20 シンポジウム S3 痛覚と痛み 座長：仙波 恵美子 柴田 政彦 シナプス：柴田 政彦 牛田 孝宏 柳井 雄子 仙波 恵美子	13:20-15:20 シンポジウム S4 摂食障害の生物学的研究 座長：堀島 俊隆 小牧 元 シナプス：河合 啓介 小牧 元 岩崎 進一 兒島 貴哉
15:00	14:30-16:10 第2回アジア・太平洋生物学的精神医学会・第30回日本生物学的精神医学会 シンポジウム						
16:00		15:20-16:00 ポスター討論 (P-01～25)					
17:00	16:30-18:30 理事会企画 オープンシンポジウム OS 脳皮質形成のメカニズム - 神経化学からの貢献 - 座長：東田 陽博 貝瀬 弘三 シナプス：貝瀬 弘三 山下 俊英 佐藤 真 祖父江 憲治	掲 示	16:00-18:00 一般口演 O6-1～6 神経伝達 座長：馬場 広子 太田 明	16:00-18:00 一般口演 O7-1～6 神経免疫・内分泌 座長：大西 浩史 大熊 康修	16:00-18:00 一般口演 O8-1～6 セロトニン系 座長：仙波 純一 大森 百郎	16:00-18:00 一般口演 O9-1～6 転写制御因子・細胞接着因子 座長：奥山 典生 崎村 達司	16:00-18:00 一般口演 O10-1～6 神経変性疾患 座長：佐野 勝 豊島 至
18:00							
19:00			18:30-19:00 育成セミナー オリエンテーション				
20:00			19:15-21:00 第51回日本神経化学学会大会 第2回アジア・太平洋生物学的精神医学会・ 第30回日本生物学的精神医学会 懇親会 (Welcome Reception) ～富山第一ホテルにて～				

■ 11 September (Thursday)

	Room A Main Hall	Poster Area 3F Foyer	Room B 201	Room C 202	Room D 203	Room E 204	Room F Conference Hall
8:00							
9:00		Setting Up	9:00-12:00	9:00-12:00	9:00-12:00	9:00-12:00	9:00-12:00
10:00	9:45-10:45 Educational Lecture EL-1 Speaker: Shinichi Kohsaka Chair: Masaya Tohyama		Oral Session O1-1 ~ 9 Synapse Chairs: Tatsuro Koike Fusao Kato Yasuo Takeda	Oral Session O2-1 ~ 9 Astrocyte Chairs: Masaki Tsuda Tatichi Katayama Shigeto Yamawaki	Oral Session O3-1 ~ 9 Neural stem/ Progenitor cells Chairs: Hiroyuki Fukui Hidenori Horie Norihito Shintani	Oral Session O4-1 ~ 9 Neuronal death I Chairs: Hiroshi Okazawa Mami Noda Shinobu Inagaki	Oral Session O5-1 ~ 9 Schizophrenia Chairs: Toshitomi Kishimoto Akeo Kurumaji Shu-ichi Ueno
11:00	11:00-12:00 Special Lecture 1 SL-1 Speaker: Julio Licinio Chair: Katsuhiko Mikoshiba						
12:00	12:15-13:15 Luncheon Seminar 1 LS-1 Speaker: Lester Binder Chair: Shoji Tsuji	Exhibition					
13:00			13:20-14:20 Young Scientists Lectureship Award Symposium LA Chairs: Yuki Yoneda Hiroshi Kiyama	13:20-15:20 Symposium S1 Recent advances in neurochemical research of proteoglycans Chairs: Akio Yanaka Seiji Miyata Speakers: Masayuki Masu Sachiko Aono Seiji Miyata Kouko Tatsumi	13:20-15:20 Symposium S2 Gene environmental interaction affecting animal and human behavior Chairs: Toshiyuki Nobeshima Hiroshi Higuchi Speakers: John Waddington Haruhiko Higashida Kiyofumi Yamada Ramon Carballedo	13:20-15:20 Symposium S3 Nociception and pain Chairs: Emiko Senba Masahiko Shibata Speakers: Masahiko Shibata Takahiro Ushida Masako Hosoi Emiko Senba	13:20-15:20 Symposium S4 Biology of eating disorder Chairs: Nobuo Kiriike Gen Komaki Speakers: Keisuke Kawai Gen Komaki Shinichi Iwasaki Shinya Kojima
14:00							
15:00	14:30-16:10 2nd World Federation of Societies of Biological Psychiatry Asia-Pacific Congress and 30th Annual Meeting of Japanese Society of Biological Psychiatry Symposium	15:20-16:00 Poster Presentation (P-01 ~ 25)					
16:00		Exhibition	16:00-18:00 Oral Session O6-1 ~ 6 Neurotransmission Chairs: Hiroko Baba Akira Ota	16:00-18:00 Oral Session O7-1 ~ 6 Neuroimmuno- endocrinology Chairs: Hiroshi Ohtsuki Yasunobu Okuma	16:00-18:00 Oral Session O8-1 ~ 6 Serotonin Chairs: Jun'ichi Senba Tetsuro Ohnori	16:00-18:00 Oral Session O9-1 ~ 6 Transcriptional factor/Cell adhesion factor Chairs: Tsuneo Okuyama Kenji Sakimura	16:00-18:00 Oral Session O10-1 ~ 6 Neurodegenerative disorders Chairs: Akira Sano Iaru Toyoshima
17:00	16:30-18:30 Open Symposium OS Mechanism of Corticogenesis -Contribution from Neurochemistry- Chairs: Haruhiko Higashida Kozo Kaibuchi Speakers: Kozo Kaibuchi Toshihide Yamashita Makoto Sato Kenji Sobue						
18:00							
19:00			18:30-19:00 Training Seminar Orientation				
20:00	19:15-21:00 Joint Welcome Reception (At TOYAMA DAIICHI HOTEL) with 2nd World Federation of Societies of Biological Psychiatry Asia-Pacific Congress and 30th Annual Meeting of Japanese Society of Biological Psychiatry						

■第2日目 9月12日(金)

	A会場 メインホール	ポスター会場 3Fロワイエ	B会場 201号室	C会場 202号室	D会場 203号室	E会場 204号室	F会場 特別会議室
8:00							
9:00							
10:00	10:00-11:50 第2回アジア・太平洋生物 学的精神医学会・第30回 日本生物学的精神医学会 シンポジウム		9:00-12:00 シンポジウム S5 精神神経疾患の モデル動物 —線虫からサルまで— 座長：小山 司 司会：馬場 明道 パネリスト：三谷 昌平 坂井 貴臣 沼川 剛 銅島 俊隆 中村 聡 殿家 宗孝	9:00-12:00 シンポジウム S6 社会性の病理 と脳基盤 座長：神庭 重信 和田 圭司 司会：神庭 重信 和田 圭司 パネリスト：栗田 公孝 栗田 公孝 村山 英徳 船越 洋 和田 圭司	9:00-12:00 シンポジウム S7 神経新生・ 幹細胞の生物学 座長：岡野 素之 司会：岡野 素之 和延 欽一 澤本 義孝 中島 義孝 橋本 渉 等 誠司	9:00-12:00 シンポジウム S8 アルツハイマー病 の神経化学 座長：島 明彦 司会：島 明彦 武田 雅俊 田上 真次 西村 正樹 富山 義孝 柳澤 隆彦 田中 修久 島 明彦	9:00-12:00 シンポジウム S9 精神神経疾患の リスク遺伝子 座長：吉川 武男 司会：岡崎 勉 佐々木 忠雄 谷井 久志 服巻 昌成 水川 義典 吉川 武男
11:00							
12:00	12:05-13:05 ランチョンセミナー 2 L-2 講師：Julio Licinio 座長：仲嶋 一範	掲 示		12:10-12:40 評議員会			
13:00				12:50-13:50 総 会			
14:00							
15:00	14:15-15:15 特別講演 2 SL-2 講師：Lester Binder 座長：武田 雅俊		14:05-15:45 一般口演 O11-1～ 5 神経突起伸展 座長：五十嵐道弘 上口 裕之	14:05-15:45 一般口演 O12-1～ 5 脳虚血 座長：小倉 明彦 山田 和雄	14:05-15:45 一般口演 O13-1～ 5 シグナル伝達 座長：鈴木 龍雄 橋本義孝	14:05-15:45 一般口演 O14-1～ 5 神経保護作用 座長：吉村 和広 小倉 幸生	14:05-15:45 一般口演 O15-1～ 5 疾患モデル1 座長：西澤 正豊 北山 滋雄
16:00		15:45-16:25 ポスター討論 (P-26～ 50)					
17:00	16:25-18:55 アニュアル シンポジウム AS Translational Research in Neurochemistry 統合失調症の 創薬をめざして 座長：遠山 正彌 西川 徹 司会：橋本 亮太 松崎 伸介 加藤 宏之 橋本 隆紀 清口 博之 西川 徹	掲 示	16:25-18:25 一般口演 O16-1～ 6 軸索輸送、細胞 運動、細胞骨格 座長：佐野 康 平松 緑	16:25-18:25 一般口演 O17-1～ 6 ミクログリア・ オリゴデンドロサイト 座長：宮武 正 中村 洋一	16:25-18:25 一般口演 O18-1～ 6 神経細胞分化 座長：吉川 和明 野村 雄幸	16:25-18:25 一般口演 O19-1～ 6 βアミロイド 座長：駒野 宏一 荒木 亘	16:25-18:25 一般口演 O20-1～ 6 認知症 座長：中村 重信 森 望
18:00		18:00-19:00 撤 去					
19:00			19:00-20:50 育成セミナー 講義	19:00-20:50 育成セミナー 講義	19:00-20:50 育成セミナー 講義	19:00-20:50 育成セミナー 講義	19:00-20:50 育成セミナー 講義
20:00							

■ 12 September (Friday)

	Room A Main Hall	Poster Area 3F Foyer	Room B 201	Room C 202	Room D 203	Room E 204	Room F Conference Hall
8:00							
9:00			9:00-12:00 Symposium S5	9:00-12:00 Symposium S6	9:00-12:00 Symposium S7	9:00-12:00 Symposium S8	9:00-12:00 Symposium S9
10:00	10:00-11:50 2nd World Federation of Societies of Biological Psychiatry Asia-Pacific Congress and 30th Annual Meeting of Japanese Society of Biological Psychiatry		Animal models of neuropsychiatric disorders From C. elegans to monkey	Social brain and its correlates	Neurogenesis and stem cell biology	Neurochemistry of Alzheimer disease	Risk genes in neuropsychiatric disorders
11:00	Symposium		Chairs: Tsukasa Koyama Akenishi Baba Speakers: Shohhei Mitani Takajima Saki Tsunoyoshi Miyakawa Toshitaka Nobeshima Katsuki Nakamura Munetaka Shirata	Chairs: Shigenobu Kanba Keiji Wada Speakers: Shigenobu Kanba Haruhiko Higashida Kimi Kuroda Miho Murayama Hiroshi Furukoshi Keiji Wada	Chairs: Hideyuki Okano Toshikazu Saito Speakers: Hideyuki Okano Kazunobu Sawamoto Kinichi Nakashima Yoshitaka Tatebayashi Wataru Ueki Seiji Iitoshi	Chairs: Akihiko Takashima Masatoshi Takeda Speakers: Shinji Tagami Masaki Nishimura Takami Tomiyama Katsuhiko Yamagawa Toshihisa Tanaka Akihiko Takashima	Chairs: Takeo Yoshikawa Yoji Okazaki Speakers: Tadno Arinami Hisashi Tanii Yasuyuki Fukumaki Masanari Iwakawa Takashi Morihata Takeo Yoshikawa
12:00	12:05-13:05 Luncheon Seminar 2 LS-2	Exhibition		12:10-12:40 Council Meeting			
13:00	Speaker: Julio Licinio Chair: Kazunori Nakajima			12:50-13:50 General Assembly			
14:00							
15:00	14:15-15:15 Special Lecture 2 SL-2 Speaker: Lester Binder Chair: Masatoshi Takeda		14:05-15:45 Oral Session O11-1 ~ 5 Axonal and dendritic outgrowth Chairs: Michihiro Igarashi Hiroaki Kanaguchi	14:05-15:45 Oral Session O12-1 ~ 5 Cerebral ischemia Chairs: Akihiko Ogura Kazuo Yamada	14:05-15:45 Oral Session O13-1 ~ 5 Signal transduction Chairs: Tatsuo Suzuki Mitsuko Hashii	14:05-15:45 Oral Session O14-1 ~ 5 Neuroprotection Chairs: Kazunori Yoshimura Kosei Ojika	14:05-15:45 Oral Session O15-1 ~ 5 Animal models I Chairs: Masatoshi Nishizawa Shigeo Kitayama
16:00		15:45-16:25 Poster Presentation (P-26 ~ 50)					
17:00	16:25-18:55 Annual Symposium AS Translational Research in Neurochemistry Drug development for schizophrenia Chairs: Masaya Tohyama Toru Nishikawa Speakers: Ryota Hashimoto Shinsuke Matsuzaki Hiroaki Nawa Takanori Hashimoto Hiroaki Muzuguchi Toru Nishikawa	Exhibition	16:25-18:25 Oral Session O16-1 ~ 6 Axonal transport / Cell motility / Cytoskeleton Chairs: Mamoru Sano Midori Hiramatsu	16:25-18:25 Oral Session O17-1 ~ 6 Microglia / Oligodendrocyte Chairs: Tadashi Miyatake Yoichi Nakamura	16:25-18:25 Oral Session O18-1 ~ 6 Neuronal differentiation Chairs: Kazuaki Yoshikawa Yasuyuki Nomura	16:25-18:25 Oral Session O19-1 ~ 6 β Amyloid Chairs: Hiroto Komano Wataru Araki	16:25-18:25 Oral Session O20-1 ~ 6 Dementia Chairs: Shigenobu Nakamura Nozomu Mori
18:00		18:00-19:00 Removing					
19:00			19:00-20:50 Training Seminar Lecture	19:00-20:50 Training Seminar Lecture	19:00-20:50 Training Seminar Lecture	19:00-20:50 Training Seminar Lecture	19:00-20:50 Training Seminar Lecture
20:00							

■第3日目 9月13日(土)

	A会場 メインホール	ポスター会場 3Fロワイエ	B会場 201号室	C会場 202号室	D会場 203号室	E会場 204号室	F会場 特別会議室
8:00	8:00-8:45 第2回アジア・太平洋生物学的 ・第30回日本生物学的精神医学会 Free Communication						
9:00	9:00-9:50 第2回アジア・太平洋生物学的精神医学会 ・第30回日本生物学的精神医学会 Plenary Lecture 3		9:00-12:00	9:00-12:00	9:00-12:00	9:00-12:00	9:00-12:00
10:00	10:00-10:50 第2回アジア・太平洋生物学的精神医学会 ・第30回日本生物学的精神医学会 Special Lecture 2		一般口演 O21-1～9 神経回路網形成	一般口演 O22-1～9 グリア、ミエリン	一般口演 O23-1～9 神経発達・可塑性	一般口演 O24-1～9 イオンチャンネル、 受容体	一般口演 O25-1～9 うつ・ストレス
11:00	11:00-11:50 第2回アジア・太平洋生物学的精神医学会 ・第30回日本生物学的精神医学会 Special Lecture 3		座長：武井 延之 加藤 聖 渡邊 和忠	座長：佐藤 康二 吉岡 元弘 浅井 清文	座長：濱 登希子 池田 正明 一瀬 宏	座長：野村 正彦 横山 茂 黒木 俊秀	座長：渡辺 義文 渡辺 康裕 谷口 泰造
12:00	12:15-13:15 ランチョンセミナー 3 LS-3						
13:00	講師：染矢 俊幸 座長：武田 雅俊						
14:00	13:30-14:15 日本生物学的精神医学会 General Assembly		13:20-16:00 第30回 日本生物学的精神医学会 合同シンポジウム	13:20-15:20 一般口演 O26-1～6 疾患モデル2	13:20-15:20 一般口演 O27-1～6 ドパミン系	13:20-15:20 一般口演 O28-1～6 神経細胞死2	13:20-15:20 一般口演 O29-1～6 記憶・学習 のメカニズム
15:00	14:30-16:10 第2回アジア・太平洋生物 学的精神医学会・第30回 日本生物学的精神医学会 シンポジウム		神経化学と精神医学の 融合による精神疾患病 態解明・治療法開発 座長：斎藤 利和 シゴダ：池田 一裕 尾子 篤子 鈴木 克治 有銘 慎世希 永井 拓 坪井 大輔 前川 義子	座長：仲田 義啓 丹羽 正美	座長：西尾 廣昭 五嶋 良郎	座長：櫻戸 靖 池田 横衛	座長：永田 栄一郎 田中 佐知子
16:00			15:20-17:20 シンポジウム S10 小胞体ストレス	15:20-17:20 シンポジウム S11 膜内タンパク 分解制御 (RIP) シグナル伝達	15:20-17:20 シンポジウム S12 疲労と意欲の脳科学	15:20-17:20 シンポジウム S13 発達障害の 神経化学	15:20-17:20 シンポジウム S13 発達障害の 神経化学
17:00	17:00-19:00 第30回 日本生物学的精神医学会 市民公開講座		座長：工藤 泰 今泉 和剛 シゴダ：今泉 和剛 堀 修 上原 孝 工藤 泰	座長：齋田 泰輔 大河内 正康 シゴダ：大河内 正康 森島 真帆 富田 泰輔 谷垣 健二	座長：定藤 明弘 田中 雅彰 シゴダ：田中 雅彰 倉恒 弘彦 田島 世貴 堀 翼龍	座長：松田 敏夫 成田 正明 シゴダ：ロバチナ オリガ 石濱 壽敏 田代 朋子 内野 茂夫	
18:00							
19:00							
20:00							

13 September (Saturday)

	Room A Main Hall	Poster Area 3F Foyer	Room B 201	Room C 202	Room D 203	Room E 204	Room F Conference Hall
8:00	8:00-8:45 2nd WFSBP Asia-Pacific Congress and 30th Annual Meeting of JSBP Free Communication						
9:00	9:00-9:50 2nd WFSBP Asia-Pacific Congress and 30th Annual Meeting of JSBP Plenary Lecture 3		9:00-12:00 Oral Session O21-1 ~ 9 Neural network formation Chairs: Nobuyuki Takei Satoru Kato Kazutada Watanabe	9:00-12:00 Oral Session O22-1 ~ 9 Glia/Myelin Chairs: Kohji Sato Mitsuhiro Yoshioka Kiyofumi Asai	9:00-12:00 Oral Session O23-1 ~ 9 Neural development/ Plasticity Chairs: Tokiko Hama Masaaki Ikeda Hiroshi Ichinose	9:00-12:00 Oral Session O24-1 ~ 9 Ion channels/ Receptors Chairs: Masahiko Nomura Shigeru Yokoyama Toshhide Kuroki	9:00-12:00 Oral Session O25-1 ~ 9 Depression/Stress Chairs: Yoshifumi Watanabe Yasuhiro Watanabe Taizo Taniguchi
10:00	10:00-10:50 2nd WFSBP Asia-Pacific Congress and 30th Annual Meeting of JSBP Special Lecture 2						
11:00	11:00-11:50 2nd WFSBP Asia-Pacific Congress and 30th Annual Meeting of JSBP Special Lecture 3						
12:00							
13:00	12:15-13:15 Luncheon Seminar 3 LS-3 Speaker: Toshiyuki Someya Chair: Masatoshi Takeda						
14:00	13:30-14:15 JSBP General Assembly		13:20-16:00 Joint Symposium with 30th Annual Meeting of Japanese Society of Biological Psychiatry Joint Symposium Chairs to the pathophysiology and treatment of psychiatric disorders through integrating neurochemistry and psychiatry Chairs: Toshikazu Saito Kazuhito Ikenaka Speakers: Atsuko Sugita Katsuji Suzuki Yoshifu Arima Taku Nagai Daisuke Tsuboi Motoo Maekawa	13:20-15:20 Oral Session O26-1 ~ 6 Animal models 2 Chairs: Yoshihiro Nakata Masami Niwa	13:20-15:20 Oral Session O27-1 ~ 6 Dopamine Chairs: Hiroaki Nishio Yoshio Goshima	13:20-15:20 Oral Session O28-1 ~ 6 Neuronal death 2 Chairs: Yasushi Enokido Joh-E Ikeda	13:20-15:20 Oral Session O29-1 ~ 6 Memory/ Learning mechanism Chairs: Eiichiro Nagata Sachiko Tanaka
15:00	14:30-16:10 2nd World Federation of Societies of Biological Psychiatry Asia-Pacific Congress and 30th Annual Meeting of Japanese Society of Biological Psychiatry Symposium			15:20-17:20 Symposium S10 ER stress Chairs: Takashi Kudo Kazunori Imazumi Speakers: Kazunori Imazumi Osami Hori Takashi Uehara Takashi Kudo	15:20-17:20 Symposium S11 Regulated intramembrane proteolysis signaling Chairs: Tatsuke Tomita Masayasu Okochi Speakers: Masayasu Okochi Maki Wazuhara Kowakami Tatsuke Tomita Kenji Tanigaki	15:20-17:20 Symposium S12 Brain science on fatigue and motivation Chairs: Norihiro Sadato Masaaki Tanaka Speakers: Masaaki Tanaka Hirohiko Kuratsune Seko Tajima Yilong Cui	15:20-17:20 Symposium S13 Neurochemistry of developmental disorder Chairs: Toshio Matsuda Masaaki Narita Speakers: Tziporina Olga Toshihiro Ishihama Tomoko Tashiro Shigeo Uchino
16:00							
17:00	17:00-19:00 30th Annual Meeting of Japanese Society of Biological Psychiatry						
18:00	Public Lecture						
19:00							
20:00							

学会の参加受付

1. 参加者の皆様へ

●事前参加登録がお済みの方

学会当日は、大会事務局からお送りいたしました参加証（ネームカード）に所属と氏名をご記入の上、必ずご持参ください。会期中はネームカードを必ず着用してください。万が一、お忘れになった場合は総合受付までお申し出ください。ネームカードのない方の入場はお断りいたします。

●当日参加登録される方

受付は1階ロビーにおいて、午前8時15分より開始いたします。参加費は以下の通りです。学生の方は受付に学生証を提示してください。

[当日参加登録費]

会 員（一般）	：14,000円
非会員（一般）	：16,000円
学 生（会員・非会員）	：5,000円

[懇親会（Welcome Reception）費]

会 員（一般）	：5,000円
非会員（一般）	：5,000円
学 生（会員・非会員）	：3,000円

●非会員の方

日本神経化学会に入会希望の方は、下記事務局までお問合せください。

（入会申込連絡先）

〒160-0016 東京都新宿区信濃町35 信濃町煉瓦館

（財）国際医学情報センター内 日本神経化学会事務局

TEL: 03-5361-7107 FAX: 03-5361-7091

E-mail: jsn@imic.or.jp

●単位取得について

本学会への参加は、日本精神神経学会、日本神経学会、日本小児神経学会、および日本良導絡自律神経学会の認定医研修単位の対象となります。

日本神経学会、日本小児神経学会および日本良導絡自律神経学会の詳細はそれぞれの学会に直接ご照会ください。

2. お知らせ

●会場の入退場について

富山国際会議場の開館は午前8時となっております。午前8時以前に入館はできませんのでご注意ください。また、閉館時間は午後9時となっております。

●クローク

会期中は3階にクロークを設置いたしますが、スペースに限りがございます。できるだけホテル等のクロークをご利用くださいますようお願いいたします。

(クローク開設時間)

9月11日(木) 8:00~19:00

9月12日(金) 8:00~19:15

9月13日(土) 8:00~17:45

●呼び出し・伝言

アナウンスでの参加者の呼び出し、お電話の取次ぎ等は一切いたしません。1階ロビーに伝言掲示板を設けておりますので、ご利用ください。

●宿泊・交通・観光案内

お問合せは下記までお願いいたします。

連絡先：トップツアー株式会社 富山支店

富山県富山市本町9-10 大同生命富山ビル 7F

TEL：076-431-7638

FAX：076-441-6790

E-mail：koji_kasama@toptour.co.jp

(営業時間) 平日 9:20-18:00

土曜日 9:20-12:40

日・祝祭日 休業

●大会本部

会期中は2階206号室を大会本部にいたします。

●懇親会 (Welcome Reception)

大会1日目の9月11日(木) 19時15分より、富山第一ホテル3階にて行います。

なお、この懇親会は第2回アジア・太平洋生物学的精神医学会・第30回日本生物学的精神医学会と合同で開催いたします。

●インターネットコーナー

2階ホワイエにLANケーブルをご用意いたします。ご自身のパソコンを接続し、ご利用いただけます。

●ドリンクコーナー

3階ホワイエにフリードリンクコーナーを設置いたします。ご自由にご利用ください。

3. 大会行事

●特別講演1

日時：9月11日(木) 11:00~12:00

会場：3階メインホール (A会場)

●特別講演2

日時：9月12日(金) 14:15~15:15

会場：3階メインホール (A会場)

●教育講演

日時：9月11日(木) 9:45~10:45

会場：3階メインホール (A会場)

●理事会企画オープンシンポジウム

日時：9月11日(木) 16:30~18:30

会場：3階メインホール (A会場)

●アニュアルシンポジウム

日時：9月12日(金) 16:25~18:55

会場：3階メインホール (A会場)

●日本生物学的精神医学会 合同シンポジウム

日時：9月13日(土) 13:20~16:00

会場：2階201号室 (B会場)

●若手奨励賞シンポジウム

日時：9月11日(木) 13:20~14:20

会場：2階201号室 (B会場)

4. 関連行事

●理事会

日時：9月10日(水) 13:30~17:00

会場：2階201号室 (B会場)

●評議員会

日時：9月12日(金) 12:10~12:40

会場：2階201・202号室 (B・C会場)

●総会

日時：9月12日(金) 12:50~13:50

会場：2階201・202号室 (B・C会場)

●懇親会 (Welcome Reception)

日時：9月11日(木) 19:15~21:00

会場：富山第一ホテル 3階

5. 各種委員会

●出版・広報委員会

日時：9月11日(木) 12:00~13:00

会場：2階控室 2

●将来計画委員会

日時：9月11日(木) 10:00~12:00

会場：2階205号室

●シンポジウム企画委員会

日時：9月11日(木) 11:00~13:00

会場：2階控室 3

●奨励賞選考委員会

日時：9月11日(木) 14:20~16:20

会場：2階205号室

●国際対応委員会

日時：9月11日(木) 10:00~12:00

会場：3階会議室

●脳研究推進委員会

日時：9月11日(木) 13:15~15:15

会場：3階会議室

6. 神経化学の若手研究者育成セミナー

日時：9月11日（木）

18：30～19：00 オリエンテーション

会場：2階201・202号室

（B・C会場）

19：15～21：00 懇親会（Welcome Reception）

会場：富山第一ホテル3階

21：30～23：00 フリーディスカッション

会場：ホテルよし原

日時：9月12日（金）

19：00～20：50 育成セミナー講義

会場：2階201～204号室・

特別会議室（B～F会場）

21：30～23：00 フリーディスカッション

会場：ホテルよし原

口演発表要項

1. 発表・討論、進行

- 1) 発表は英語の使用を推奨いたしますが、日本語で口演して頂いても結構です。
- 2) 各演者の発表・討論の時間はプログラムに記載されていますので、時間厳守をお願いします。
(シンポジウム：発表25分／討論5分 一般口演：発表15分／討論5分)
- 3) 進行は座長の責任において行ってください。終了時間の厳守をお願いいたします。
- 4) 演者は口演開始20分前までに、次演者席にお着きください。
- 5) 討論者は、あらかじめ会場内の討論用マイクの前でお待ちください。

2. 発表機材

本大会の発表はPCプレゼンテーションに限らせていただきます。以下の項目についてご確認ください。

- 1) USBフラッシュメモリにて発表データをお持ちください。Macintoshまたは動画を使用される方は、ご自身のPCをお持ちください。
PCをご持参いただく場合は、mini-D sub15pinの出力端子が、本体にあることをご確認ください。本体にない場合は変換ケーブルをご持参ください。また、バッテリー切れを防ぐため、必ず付属の電源アダプターをお持ちください。
※発表中にスクリーンセーバーや省電力モードにならないよう事前に設定をしてください。
- 2) 事務局でご用意するPCは以下のとおりです。
【OS】Windows XP
【アプリケーション】Power Point 2003, Power Point 2007
- 3) 発表の60分前までにスライドセンター(2Fホワイエ)にて出力チェックをしてください。
- 4) プレゼンテーションに静止画・動画・グラフ等のデータをリンクさせている場合は、データも必ず保存していただき、事前に動作確認を行ってください。
- 5) 演台上にモニター・マウス・キーボードを用意しておりますので、発表時の操作はご自身でお願いいたします。

3. 座長の方へ

- 1) ご担当セッションの開始20分前までに、次座長席にお着きいただき進行係に一声かけてくださいますようお願いいたします。
- 2) 時間厳守に留意していただき、進行をお願いいたします。

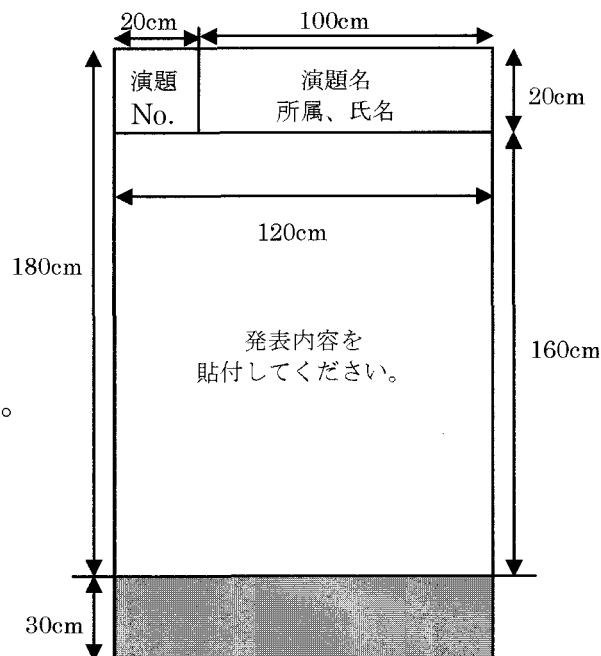
ポスター発表要項

1. 会 場

ポスター発表は、3階ホワイエにて行います。

2. 発表要項

- 1) 右図のように、縦20cm×横100cmのサイズに
演題名、著者名、所属を英日併記したものを
ご用意ください。
- 2) 発表内容は右図発表スペース
(縦160cm×横120cm)に収まるようにしてく
ださい。
- 3) ポスターの原稿はすべて英語で作成してください。
ただし、日本語のサマリーも添えてください。
- 4) 演題番号は運営事務局で用意いたします。
- 5) 押しピンは各パネルにご用意しておりますので、
のり、テープ等は使用しないでください。



3. 掲示・討論・撤去

- 1) ポスターの貼付・討論・撤去は下記の時間内に行ってください。
貼付：9月11日（木） 8：30～10：00
討論：9月11日（木） 15：20～16：00（P-01～25）
9月12日（金） 15：45～16：25（P-26～50）
撤去：9月12日（金） 18：00～19：00
- 2) 各パネルにリボンを用意しておきますので、討論の際には着用してください。
- 3) 発表開始5分前には、ポスター前で待機してください。
- 4) 発表5分、討論3分です。
- 5) 撤去時間後も掲示してあるポスター等は事務局にて撤去・処分をさせていただきますのであ
らかじめご了承ください。

4. 座長の方へ

- 1) 座長は開始5分前までに担当セッションのパネル前でスタンバイしてください。

学会からのお知らせ

1. 評議員会

日 時：9月12日（金）12時10分～12時40分

場 所：富山国際会議場 2階 B会場・C会場

議 題：日本神経化学会の発展のためにすべきこと

※ 昼食は有料となりますので、ご了承下さい。

2. 総会

日 時：9月12日（金）12時50分～13時50分

場 所：富山国際会議場 2階 B会場・C会場

- 議 題：
1. 理事長報告
 2. 庶務報告
 3. 会計報告
 4. 出版・広報報告
 5. プログラム編成報告
 6. 各種委員会報告
 - ①将来計画委員会
 - ②脳研究推進委員会
 - ③国際対応委員会
 - ④研究助成金等候補者選考委員会
 - ⑤シンポジウム企画委員会
 - ⑥連合大会委員会
 - ⑦出版・広報委員会
 7. 2008年度奨励賞選考結果報告
 8. 2007年度決算の件
 9. 同監査報告
 10. 2009年度予算の件
 11. 評議員選任の件
 12. 名誉会員選任の件
 13. 次期大会の件
 14. その他

理事会議事録

2008年度第1回理事会議事録

日 時：2008年3月7日（金）13：00-17：00

会 場：（財）国際医学情報センター 第2会議室

出 席：高坂 新一（理事長）、池中 一裕（副理事長）、米田 幸雄（庶務担当）、木山 博資（会計担当）、岡野 栄之、塩坂 貞夫、今泉 和則、神庭 重信、武田 雅俊、和田 圭司、高橋 正身（以上 理事）、和中 明生（国際対応委員会委員長）、宮本 英七（監事）、田代 朋子（第52回大会長）、橋本 亮太（武田雅俊理事代理人）

委任状：仲嶋 一範（出版・広報担当）、御子柴克彦、武田 雅俊、東田 陽博、辻 省次（以上 理事）、三木 直正（監事）

議 題

議題に先立ち、高坂新一理事長より挨拶がなされた。

【報告事項】

1. 2007年度第3回理事会議事録承認の件

高坂新一理事長より、先般持回り審査を行い、承認が得られている旨報告された。

2. 理事長報告

特になし。

3. 庶務報告

米田幸雄庶務担当理事より、庶務報告がなされた。

・会員状況について

会員数が減少している現状を踏まえ、入会勧誘方法について議論された。その結果、単なる数合わせではなく、活動的な会員の獲得・増加を目指していくため、小規模ならではの特殊性を打ち出しながら魅力ある学会作りに努め、理事・評議員等の教室員を中心にアピールしていくこととなった。

また、賛助会員の現状についても報告があり、面識のある企業への勧誘等、引き続き理事・評議員に協力を仰ぐこととした。

4. 会計報告

木山博資会計担当理事より、会計報告がなされた。

・2007年度決算及び税務申告について

決算業務及び税務申告は公認会計士と相談の上行われ、納税額が決定された。

（2007年度決算について）

一般会計に関し、2006年度決算と比べ、繰越金を約190万円増やすことができた。主な理由としては、経費節約、年会費収入の増加等が挙げられる。大会運営の補助金として計150万円を大会運営事務局へ支出したものの、大会収益の中から全額返金された。

また、特別事業積立金に関し、積立専用口座を開設し、2008年度分からはその口座で一括管理することとした。

(税務申告について)

2007年度より税務申告を行い、納税額は総額230,500円となった。

・年会費未納者数について

* 年会費未納者数について現状報告がなされた。また、3年度分以上年会費を滞納している会員に対し、除名処理を行った旨報告がなされた。今後も引き続き未納者へ適宜督促を行い、場合によっては未納者の所属長へ協力を仰ぐこととなった。

* 海外出張・留学のために支払が滞るケースが指摘され、休会制度新設のため会則変更を検討することとなった。

* 納入方法として、口座からの自動引落やクレジットカード支払等が提案されたが、手数料の観点から現時点では導入しないことと決した。

・旅費支給について

当会運営にかかる会議等に出席する場合の旅費について、支給方法が確認された。

5. 出版・広報報告

今泉和則出版・広報委員より、出版・広報委員会の活動について概要が報告された。

6. 委員会報告

(1) 将来計画委員会

米田幸雄委員長より、2007年9月10日開催の委員会について報告された。

・ 日本神経科学学会との合同大会（Neuro 大会）について、多くの情報が収集でき大変有意義であるため、従来通り3年に1回の開催が好ましい。

・ 日本神経化学会のアイデンティティーとしては、若手研究者育成に力を入れていきたい。今後も議論を重ねて、最終的な結論・提案を出したい。

(2) 出版・広報委員会

今泉和則委員より、次の通り報告された。

・ 機関誌製作の業務委託先について

株式会社六甲出版販売から有限会社シーワークスへの委託先変更について、経緯が説明された。審議の結果、提案通り変更することに決した。トラブル回避のため契約書・覚書を締結し、先1年間の経過を元に次年度の契約更新を再考することとなった。

・ 会員検索システムの変更について

会員情報検索システムの変更について経過報告された。国内外より自由にアクセスできるシステムを採用するため、全会員から改めて開示情報の各項目について掲載の同意を取り直すことが確認された。また、会員情報記入シート（案）が提示され、専門分野に関するキーワードも掲載予定とのことであった。委員会より提案されたキーワードについて、精神疾患関連のキーワードをもう少し追加してはどうかとの意見があり、引き続き検討することとなった。さらに、会員の業績に関する情報も閲覧できた方がよいとの意見が出され、引き続き検討することとなった。

・ 学会ホームページの管理・運営

英語版のホームページについて説明がなされた。かねてから検討しているが、実現できていないとのことであった。議論の結果、庶務担当理事が英語版の入会申込書を作成し、それを元に準備を進めることとなった。

また、日本語版ホームページでの第51回大会のアナウンスについて、単に大会のホームページにリンクするだけでなく、閲覧者の目を引くよう大会のキーワードを追加掲載してはどうかとの意見がなされ、今後検討することとなった。

・広報活動

ホームページ上にて「神経化学トピックス」と題し、一般向け広報活動の一環として会員の研究成果を紹介している。現在2件の論文（要旨）が掲載されており、引き続き掲載希望者・推薦者を募っているが、応募がないとのことであった。2008年度中には掲載数を4～5件に増やしたいと考えているため、各理事へ同コーナーを周知の上、適任者の推薦が要請された。

（3）シンポジウム企画委員会

東田陽博委員長欠席のため、代理として橋本亮太氏（大阪大学）より報告された。

理事会企画オープンシンポジウムとして神経経済学を取り上げる予定であるとのことであった。これに対し、複数の理事より神経経済学は学問として発展途上の領域であるため、学会の方向性を示す理事会企画オープンシンポジウムでの採用は時期尚早であるとの意見が出された。以上を踏まえ、委員会にて至急再検討することとなった。

（4）国際対応委員会

和中明生委員長より APSN biennial meeting, ISN Special Neurochemistry Conference, ISN biennial meeting について報告された。

- ・第8回 APSN biennial meeting の一般演題締切日が変更となった。（2008年3月末まで）
- ・2010年開催予定の第9回 APSN biennial meeting について、日本が有力候補地となる可能性が高く、委員会としては日本開催を視野に入れて活動していきたい。日本開催の場合、日本神経化学学会大会と合同で開催するのが理想的であるが、2010年は日本神経科学学会との合同大会（Neuro2010）が予定されているため、APSN biennial meeting との合同開催の可能性について、理事会で議論願いたい。（報告事項7.参照）
- ・2011年開催予定の ISN biennial meeting は、開催地がギリシャ・アテネとなった。
- ・APSN 理事選挙、ISN 理事選挙について、APSN では米田幸雄氏（金沢大学）の出馬が決定、ISN では白尾智明氏（群馬大学）を推薦したい。
- ・日本神経化学学会の国際化について、APSN 及び ISN の Meeting 等へこれまで以上に若手研究者を派遣し、海外経験を蓄積させることが有効ではないか。そのためには評議員レベルでの国際化に対する理解・協力が必要である。
- ・広報活動としては、日本神経化学学会ホームページへAPSN及びISN関係の情報を掲載している。今後は Meeting 参加者による体験記を機関誌へ掲載する等、APSN 及び ISN へ参加するメリットも広く周知していきたい。

また、理事より、活発に活動しているアジア諸国に対抗できるよう、日本もより積極的に国際学会へ参加すべきだとの意見があった。APSN や ISN の演題募集やトラベルアワードへ若手研究者が積極的に応募し、国際経験を積むことが重要であるとの認識の下で、評議員レベルに対し、若手研究者への働きかけ等協力を請うこととなった。

（5）研究助成金等候補者選考委員会

神庭重信委員長より、2007年10月以降の公募数及び応募数について報告された。

(財)ブレインサイエンス振興財団の第21回 海外研究者招聘助成へ日本神経化学会第51回大会事務局より応募があった旨報告された。また、推薦結果についても報告された。

応募者が少ない現状を踏まえ、奨励賞受賞者に応募を募る等、委員会で候補者の掘り起こしを行うこととなった。

(6) 脳研究推進委員会

辻省次委員長欠席により、岡野栄之委員より2007年9月10日開催の委員会について、次の通り報告された。

- ・基礎系の若手研究者と臨床系研究者の参加を喚起する魅力的な活動が必要である。両者が求めるものを両立させる方策について議論を継続していく。
- ・日本神経化学会はボトムアップ型で活動し、現状の規模だからこそできる活動にこだわっていくべきである。そのためには会員、特に若手からの意見をどのように集約していくかが重要となる。

集約した意見を元にそれに見合ったシンポジウム等を企画すれば効果的であろうとのことであった。

なお、意見の集約については、まず本年大会（第51回大会）で開催される神経化学育成セミナーが絶好の機会と考えており、今後もこのような企画を継続することが望まれる。

上記他、科研費の動向について委員会としてどのような活動が考えられるか等についても報告された。

(7) 奨励賞選考委員会

米田幸雄委員長より、次の通り報告された。

- ・選考基準について検討され、①研究業績 ②発表貢献度 ③将来性 ④総合評価 の4項目を客観的に点数化した上で、最終的な順位付けを各委員の判断に委ねることとなった。また、評価の際には、若年応募者が不利にならないよう配慮することも確認された。
- ・応募条件が「会員歴3年以上、研究歴3年以上で、本会で積極的に発表した実績を持ち、＜中略＞満40歳未満」となっているため、応募者に指導的立場の研究者と博士号取得前後の研究者が混在する。後者を対象とする賞の設置が提案され、議論の結果、従来の奨励賞に加え、ポスター賞や口頭発表優秀者の表彰等の新設を委員会で検討していくこととなった。

(8) 連合大会委員会

池中一裕委員長より、次の通り報告された。

- ・日本生物学的精神医学会と日本神経精神薬理学会に対し、ゆるやかな連合を提案しているが、日本神経精神薬理学会は日本臨床精神神経薬理学会との合併問題を抱えているため、そちらを優先したいとの意向である。合併問題が解決したのちに日本神経化学会との連合開催について検討したいとのことであった。一方、日本生物学的精神医学会では、3年に1回程度の連合開催がよいのではないかと多くの意見が多いとのことであった。
- 今後もあらゆる可能性について、委員会で検討していくこととなった。

7. 第50回（2007年度）大会及び第53回大会（2010年度：Neuro 2010）について

高坂新一理事長より、次の通り報告された。

- ・第50回（2007年度）大会

参加者約3,700名の盛会となり、内容も好評であった。日本神経科学学会と連合開催することは

意義があるため、日本神経化学学会の独自性を発揮できるよう十分調整の上、引き続き定期的な連合を続けて行きたい。

・第53回大会（2010年度：Neuro 2010）

大会長が井上和秀氏（九州大学）と決定した。9月21日～25日にパシフィコ横浜で開催したい旨、日本神経科学学会へ伝えたとのことであった。

また、APSNに関連し、①APSN biennial meeting を2012年に誘致、同時に日本神経化学学会単独大会を開催 ②大会長は池田一裕氏（APSN 理事長）との事項が提案され、理事の総意を得た。

【審議事項】

1. 評議員の退会希望について

退会を希望する評議員のうち、3名が功労会員として継続参加し、2名は退会することとなった。

2. 新評議員の推薦について

審議の結果、候補者1名の推薦が承認された。

3. 名誉会員の推薦について

審議の結果、候補者1名の推薦が承認された。

4. 功労会員新設に伴う会則変更について

米田幸雄庶務担当理事より草案が示され、議論された。

有資格者は「評議員経験者でかつ定年により現職を退いた者」、「永年、正会員として本会に貢献をした者」となり、理事会が候補者を決定の上総会へ推薦、総会での承認を得て就任することとなった。

5. 第51回（2008年度）大会について

武田雅俊第51回大会長が欠席のため、代理人 橋本亮太氏より次の通り報告された。

- ・①基礎から臨床へのトランスレーショナル研究の推進 ②口演重視 ③若手研究者の育成 を意識した内容であるとのことであり、プログラムの決定事項は次の通り。

* 特別講演

Julio Licinio 氏（University of Miami）

Christian Haass 氏（Ludwing-Maximilians-University）

* 教育講演

高坂 新一 氏（国立精神・神経センター神経研究所）

* 神経化学教育セミナー

* 日本生物学的精神医学会 合同シンポジウム

「神経化学と精神医学の融合による精神疾患病態解明・治療法開発」

* 理事会企画オープンシンポジウム

* Annual シンポジウム Translational Research in Neurochemistry

統合失調症の創薬をめざして

* 若手奨励賞シンポジウム

- ・上記他、シンポジウム12演題、一般口演（発表15分、討論5分）約200演題、ポスター発表 約100演題を予定している。
- ・若手研究者育成のため、新たに神経化学育成セミナーが企画された。学生を対象とし、合宿形式でフリーディスカッションや教育講演を催し、神経化学の魅力を伝えたいとのことであった。同セミナーを本大会の目玉企画と位置付け、積極的に広報し、より多くの参加者が集まるよう努めることとなった。
また、理事より、日本生物学的精神医学会との合同シンポジウムも若手育成を目的としているため、うまく連携させてほしいと意見が出され、合同シンポジウム参加者に対しても育成セミナーへの参加を呼びかけることとなった。
- ・2008年3月4日より演題登録が開始された。
- ・使用言語については、シンポジウムは英語、一般口演はできるだけ英語、スライド・ポスターは英語とする。
- ・複数の理事より、一般口演とシンポジウムを同時に開催すると、参加者がシンポジウムに偏る恐れがあるため、スケジュールを工夫するよう指摘があった。これを受け、昨年の総会で将来計画委員会から提案された通り、評議員に参加口演を割り振り、活発な議論となるよう協力を仰ぐ予定と説明された。
また、演題募集時に講演内容のキーワードを公開すると、参加者に対して目安になりよいのではないかと意見も出され、検討することとなった。

6. 第52回（2009年度）大会について

田代朋子第52回大会長より報告された。群馬県伊香保にて合宿形式での開催が提案され、議論の結果、2009年6月22日～24日に伊香保で開催する方向で調整することとなった。

7. その他

- ・第51回大会での抄録販売について
橋本亮太氏より第51回大会時での抄録について、価格2,000円で販売したい旨提案された。従来は6,000円で販売していることから、活発に議論されたが、木山博資会計担当理事の判断に委ねることとなった。
- ・寄付について
国際生物学オリンピックへの寄付について審議された。2口20,000円を寄付することに決した。

以上を以て予定した全ての議事を終了し、本年度第1回理事会を閉じた。

2008年8月

日本神経化学会
会員 各位

日本神経化学会
理事長 高坂新一

第51回日本神経化学会・総会の開催について

謹 啓

時下ますますご清祥のこととお慶び申し上げます。

さて、下記の通り日本神経化学会総会を開催致したくご案内申し上げます。

尚、総会に欠席される方は委任状（ハガキ）に必要事項をご記入の上、事務局宛て
ご送付下さるか、学会当日、受付までご提出下さいますようお願い申し上げます。

敬 白

記

日 時： 2008年9月12日（金） 12：50～13：50

場 所： 富山国際会議場 2階 B会場・C会場

議題(予定)：

1. 理事長報告	9. 同監査報告
2. 庶務報告	10. 2009年度予算の件
3. 会計報告	11. 評議員選任の件
4. 出版・広報報告	12. 名誉会員選任の件
5. プログラム編成報告	13. 次期大会の件
6. 各種委員会報告	14. その他
7. 2008年度奨励賞選考結果報告	
8. 2007年度決算の件	

(切り離して「投函下さい」)



2008年
日本神経化学会
総会

委任状

(ご欠席の方はご記入ください)

2008年日本神経化学会総会の議決権の行使に
関する一切の権限を

代理人 _____ に委任します。

2008年 月 日

所属

氏名



料金受取人払郵便

新宿支店承認

2724

差出有効期限
平成21年8月
9日まで
(切手不要)

郵便はがき

1608792

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東京都新宿区信濃町35番地
信濃町煉瓦館

(財) 国際医学情報センター内

日本神経化学会 行



プログラム Program

特別講演
Special Lectures

教育講演
Educational Lecture

理事会企画オープンシンポジウム
Open Symposium

日本生物学的精神医学会 合同シンポジウム
Joint Symposium with 30th Annual Meeting
of Japanese Society of Biological Psychiatry

アニュアルシンポジウム
Annual Symposium

若手奨励賞シンポジウム
Young Scientists Lectureship Award Symposium

シンポジウム
Symposia

一般口演・ポスター発表
Oral Sessions / Poster Sessions

ランチョンセミナー
Luncheon Seminars

演題番号の見方 How to read Abstract numbers

特別講演 Special Lectures

SL-1

発表日
Day

教育講演 Educational Lecture

EL-1

発表日
Day

理事会企画オープンシンポジウム Open Symposium

OS-1

発表順
Order

合同シンポジウム Joint Symposium

JS-1

発表順
Order

アニュアルシンポジウム Annual Symposium

AS-1

発表順
Order

若手奨励賞シンポジウム Young Scientists Lectureship Award Symposium

LA-1

発表順
Order

シンポジウム Symposia

S1-1

発表順
Order

セッション No.
Session No.

一般口演 Oral Sessions

O1-1

発表順
Order

セッション No.
Session No.

ポスター Poster Sessions

P-01 ~ P-50

ランチョンセミナー Luncheon Seminars

LS-1

発表日
Day

特別講演

9月11日(木)

11:00~12:00 (A会場)

SL-1

座長：御子柴克彦（理化学研究所脳科学総合研究センター）

Pharmacogenomics of Antidepressant Treatment Response

Julio Licinio

University of Miami Miller School of Medicine

9月12日(金)

14:15~15:15 (A会場)

SL-2

座長：武田 雅俊（大阪大学大学院医学系研究科精神医学教室）

The Structure and Function of Abnormal Tau in Alzheimer's Disease.

Binder, L.I.¹, Lapointe, N.E.^{1,3}, Guillozet, A.¹, Morfini, G.^{2,3}, Pignio, G.^{2,3}, and Brady, S.T.^{2,3}

¹Feinberg School of Medicine, Northwestern University, ²University of Illinois at Chicago,

³Marine Biological Laboratory

教育講演

9月11日(木)

9:45~10:45 (A会場)

EL-1

座長：遠山 正彌（大阪大学大学院医学系研究科 神経機能形態学講座）

正常と病態脳におけるミクログリアの静的および動的機能

高坂 新一

国立精神・神経センター神経研究所

理事会企画オープンシンポジウム

9月11日(木)

16:30~18:30 (A会場)

OS-1~OS-4 脳皮質形成のメカニズム-神経化学からの貢献-

座長: 東田 陽博 (金沢大学21世紀 COE 革新脳科学プログラム)

貝淵 弘三 (名古屋大学大学院医学系研究科 神経情報薬理学)

OS-1 軸索輸送と軸索形成

○貝淵 弘三¹

¹名古屋大学大学院医学系研究科 神経情報薬理学

OS-2 脳損傷後に神経回路はいかにして修復されるか?

○山下 俊英¹

¹大阪大学大学院医学系研究科分子神経科学

OS-3 細胞移動による脳構築の仕組みの解明から疾病理解への展開

○佐藤 真^{1,2}

¹福井大学医学部形態機能医科学講座組織細胞形態学・神経科学領域

²福井大学生命科学複合研究教育センター

OS-4 グルココルチコイドにより誘導される神経細胞移動障害の分子メカニズム

○祖父江憲治¹、福本健太郎¹、真柳 平¹

¹大阪大学大学院医学系研究科 神経科学 (神経細胞医科学)

日本生物学的精神医学会 合同シンポジウム

9月13日(土)

13:20~16:00 (B会場)

JS-1~JS-6 神経化学と精神医学の融合による精神疾患病態解明・治療法開発
 座長：齋藤 利和（札幌医科大学医学部神経精神医学講座）
 池中 一裕（生理学研究所 分子神経生理研究部門）

- JS-1 うつ病の病態への一酸化窒素（NO）の関与 -基礎から臨床まで-
 ○杉田 篤子¹
¹産業医科大学精神医学教室
- JS-2 双極性障害における血小板内カルシウム濃度増加反応研究の展開
 ○鈴木 克治¹
¹北海道大学大学院医学研究科精神医学分野
- JS-3 モノアミン神経伝達制御による認知機能障害に対する効果と作用機序
 ○有銘預世布¹、曾良 一郎¹
¹東北大学大学院医学系研究科 神経・感覚器病態学講座 精神・神経生物学分野
- JS-4 モルヒネ誘発性精神障害における tPA- プラスミンシステムの役割
 ○永井 拓¹、鍋島 俊隆^{1,2}、山田 清文¹
¹名古屋大学大学院医学系研究科医療薬学・附属病院薬剤部
²名城大学大学院薬学研究科薬品作用学
- JS-5 海馬神経細胞において DISC1 は IP3 受容体 mRNA の樹状突起局在を制御する
 ○坪井 大輔¹、田谷真一郎¹、篠田 友靖¹、貝淵 弘三¹
¹名古屋大院・医学系研究科・神経情報薬理学
- JS-6 アラキドン酸の海馬神経新生およびプレパルス抑制に対する効果
 ○前川 素子^{1,2,3}、高嶋 記子⁴、松股 美穂^{1,5}、池上 司郎⁶、紺谷 昌仙⁷、
 原 芳伸^{1,5}、河島 洋⁷、大和田祐二⁸、吉川 武男³、湯浅 茂樹²、
 木曾 良信⁷、井ノ口 馨⁴、大隅 典子^{1,5}
¹東北大学大学院医学系研究科 創生応用医学研究センター 形態形成解析分野、
²国立精神・神経センター 神経研究所 微細構造研究部、³独立行政法人理化学
 研究所 脳科学総合研究センター 分子精神科学研究チーム、⁴三菱化学生命科学
 研究所 記憶形成・精神疾患研究グループ、⁵CREST、⁶埼玉工業大学 人間社会
 学部 心理学科、⁷サントリー健康科学研究所、⁸山口大学大学院 医学系研究科
 器官解剖学分野

アニュアルシンポジウム

9月12日(金)

16:25~18:55 (A会場)

AS-1~AS-6

統合失調症の創薬をめざして

座長：遠山 正彌 (大阪大学大学院医学系研究科 神経機能形態学講座)

西川 徹 (東京医科歯科大学大学院 歯学総合研究科 精神行動
医科学分野)

AS-1 中間表現型を用いた統合失調症脆弱性遺伝子の同定

○橋本 亮太^{1,2}、武田 雅俊^{1,2}

¹大阪大院・医・子どものこころ、²大阪大院・医・精神医学

AS-2 Dysbindin を介した統合失調症発症の分子メカニズム解明

○松崎 伸介^{1,2}、遠山 正彌^{1,2}

¹大阪大学大学院 医学系研究科 神経機能形態学講座、²子どものこころの分子
統御機構研究センター

AS-3 ニューレグリン・EGFシグナル阻害剤が有する抗精神病活性

○那波 宏之¹、加藤 泰介¹、阿部 祐一¹、外山 英和¹、難波 寿明¹、
水野 誠¹

¹新潟大学・脳研・分子神経

AS-4 統合失調症における GABA 伝達障害：皮質領域と分子マーカー

○橋本 隆紀^{1,2}、Lewis David A.²

¹金沢大学 脳情報病態学 (精神医学)、²ピッツバーグ大学 精神医学部門

AS-5 統合失調症様認知障害モデル動物における GABAB 受容体作用薬の有効性

○溝口 博之¹、山田 清文²

¹名古屋大学環境医学研究所近未来環境シミュレーションセンター、²名古屋大学
大学院医学系研究科医療薬学附属病院薬剤部

AS-6 NMDA 受容体 -D- セリン系を標的とした新規統合失調症治療薬の可能性

○西川 徹¹

¹東京医科歯科大学大学院 歯学総合研究科 精神行動医科学分野

若手奨励賞シンポジウム

9月11日(木)

13:20~14:20 (B会場)

LA-1~LA-2

若手奨励賞シンポジウム

座長：米田 幸雄 (奨励賞選考委員長/金沢大学大学院自然科学研究科
薬物学研究室)

木山 博資 (奨励賞選考委員/大阪市立大学大学院医学研究科
機能細胞形態学)

LA-1 マウス網膜発生における個々の Rb ファミリーの役割解明

味岡 逸樹

セントジュード小児研究病院発生神経生物学部門

LA-2 精神疾患のトランスレーショナルリサーチ

橋本 亮太

大阪大学大学院医学系研究科附属子どものこころの分子統御機構研究センター、
大阪大学大学院医学系研究科情報統合医学講座精神医学教室

シンポジウム

9月11日(木)

13:20~15:20 (C会場)

S1-1~S1-4 神経系におけるプロテオグリカン研究の新展開

座長：和中 明生（奈良県立医科大学医学部 第二解剖学）

宮田 清司（京都工芸繊維大学・応用生物学部門）

S1-1 神経発生におけるヘパラン硫酸エンドスルファターゼの役割

○榊 正幸¹、岡田 拓也¹、長嶺 聖史¹、塩見 健輔¹、丹波 道子¹、
石嶺 久子¹、大戸 達之¹、國田 智²、高橋 智²、榊 和子¹

¹筑波大・院人間総合科学、²筑波大・生命科学動物資源センター

S1-2 中枢神経系におけるニューログリカンC

○青野 幸子¹

¹愛知県心身障害者コロニー発達障害研究所・周生期学部

S1-3 プロテオグリカン細胞外マトリクスより構成される Perineuronal nets

○宮田 清司¹

¹京都工芸繊維大学・応用生物学部門

S1-4 コンドロイチン硫酸プロテオグリカンが形成する脳内新規細胞外マトリックス構造-DACS-について

○辰巳 晃子¹、林 謹子²、奥田 洋明¹、和中 明生¹

¹奈良県立医科大学・医学部・第2解剖学教室、²奈良県立医科大学・医学部・寄生虫学教室

9月11日(木)

13:20~15:20 (D会場)

S2-1~S2-4 動物やヒトの行動に対する遺伝子・環境相互作用

座長：鍋島 俊隆（名城大学大学院薬学研究科臨床薬学専攻病態解析学
コース薬品作用学教室）

樋口 宗史（新潟大学大学院医歯学総合研究科 分子細胞医学
シグナル伝達遺伝子制御薬理学分野）

S2-1 Neuregulin and the pathobiology of schizophrenia: studies in 'knockout' mice

○John L. Waddington

Molecular & Cellular Therapeutics, Royal College of Surgeons in Ireland, Dublin 2, Ireland

S2-2 CD38: オキシトシン遊離調節による社会認識行動

○東田 陽博¹

¹金沢大・21世紀COE革新脳科学プログラム

S2-3 メタンフェタミン依存マウスにおける薬物探索行動：GDNF の役割

○山田 清文¹、鍋島 俊隆²¹名古屋大院・医・医療薬学、²名城大院・薬・薬品作用

S2-4 PHARMACOGENOMICS IN CNS DISORDERS

○Ramón Cacabelos

EuroEspes Biomedical Research Center, Institute for CNS Disorders and Genomic Medicine, EuroEspes Chair of Biotechnology and Genomics, Camilo José Cela University, Coruña, Spain.

9月11日(木)

13:20~15:20 (E会場)

S3-1~S3-4 痛覚と痛み

座長：仙波恵美子（和歌山県立医科大学医学部第二解剖）

柴田 政彦（大阪大学大学院医学系研究科 疼痛医学）

S3-1 難治性疼痛と脳

○柴田 政彦¹¹大阪大院・医・疼痛医学

S3-2 慢性神経因性疼痛（アロデニア）患者における中枢神経の可塑的变化：fMRI 研究

○牛田 享宏^{1,2,5}、池本 竜則^{2,5}、田中 茂樹⁴、谷口 慎一郎^{2,5}、村田 和子³¹愛知医科大学 学際的痛みセンター、²高知大学医学部整形外科教室、³高知大学医学部放射線医学教室、⁴仁愛大学心理学講座、⁵南国疼痛研究会

S3-3 失感情症と痛み体験

○細井 昌子¹¹九州大学病院 心療内科

S3-4 慢性痛による中枢の変化：脳による疼痛の制御

○仙波 恵美子¹¹和歌山県立医科大学医学部第二解剖

9月11日(木)

13:20~15:20 (F会場)

S4-1~S4-4 摂食障害の生物学的研究

座長：切池 信夫（大阪市立大学大学院医学研究科 神経精神医学）

小牧 元（国立精神・神経センター精神保健研究所心身医学研究部）

S4-1 神経性食欲不振症ならびに健常人の BMI を規定する身体的・心理的因子

○河合 啓介¹、森田 千尋¹、松原 慎¹、山中 竹春²、山下さきの¹、瀧井 正人¹、久保 千春¹¹九州大学病院心療内科、²九州がんセンター

S4-2 摂食障害の遺伝子研究

○小牧 元¹、安藤 哲也¹

¹国立精神・神経センター精神保健研究所心身医学研究部

S4-3 摂食障害の動物モデル

○岩崎 進一¹、井上 幸紀¹、切池 信夫¹

¹大阪市立大学大学院医学研究科神経精神医学教室

S4-4 摂食障害の脳画像解析

○兒島 真哉¹、浅川 明弘³、乾 明夫³、成尾 鉄朗²

¹鹿児島大学医学部・歯学部附属病院心身医療科、²司誠会野上病院 心療内科、

³鹿児島大学大学院医歯学総合研究科行動医学講座

9月12日(金)

9:00~12:00 (B会場)

S5-1~S5-6 精神神経疾患のモデル動物—線虫からサルまで

座長：小山 司(北海道大学大学院医学研究科 神経病態学講座)

馬場 明道(大阪大学大学院薬学研究科 神経薬理学分野)

S5-1 線虫をモデル生物として用いた機能ゲノミクス

○三谷 昌平¹

¹東京女子医科大学医学部第二生理学教室

S5-2 統合失調症関連遺伝子のショウジョウバエホモログはショウジョウバエの長期記憶に必要である

○坂井 貴臣¹

¹首都大・理工学研究科・生命科学

S5-3 Alpha-CaMKII ヘテロノックアウトにより引き起こされる行動異常と未成熟歯状回

○宮川 剛^{1,2}

¹藤田保健衛生大・総医研・システム医科学、²京都大院・医・先端技術センター

S5-4 大脳皮質発達時に DISC 1 を一過性にノックダウンするとドパミン作動性神経系の機能障害と統合失調症様の障害を成熟マウスに惹起する

○鍋島 俊隆^{1,2}、丹羽 美苗^{1,2}、村井 里菜^{1,2}、野田 幸裕^{1,3}、久保 健一郎⁴、神谷 篤⁵、Hanna Jaaro-Peled⁵、仲嶋 一範⁴、澤 明^{5,6,7}

¹名城大院・薬・薬品作用学、²名古屋大院・医・附属病院薬剤部・医療薬学、³名城大・薬・病態解析学、⁴慶応大院・医・解剖学、⁵ジョンズホプキンス大・医・精神医学、⁶ジョンズホプキンス大・医・神経科学、⁷ジョンズホプキンス大・医・細胞分子医学

S5-5 精神・神経疾患モデル動物としてのマーマセットの可能性

○中村 克樹^{1,2}

¹国立精神・神経センター神経研究所、²CREST, JST

S5-6 霊長類の前頭葉内側部のニューロン活動と精神疾患

○設楽 宗孝¹

¹筑波大学大学院人間総合科学研究科

9月12日(金)

9:00~12:00 (C会場)

- S6-1~S6-6 社会性の病理と脳基盤
 座長：神庭 重信（九州大学大学院医学研究院 精神病態医学分野）
 和田 圭司（国立精神・神経センター神経研究所）
- S6-1 精神疾患における心の理論の障害
 ○神庭 重信¹、山田 和男²、井上 由美子²
 ¹九州大学大学院医学研究院精神病態医学分野、²東京女子医大東医療センター精神科
- S6-2 社会認識、オキシトシンとCD38
 ○東田 陽博¹
 ¹金沢大・21世紀 COE 革新脳科学プログラム
- S6-3 養育障害を示す FosB 遺伝子改変マウスの行動学的・神経組織学的解析
 ○黒田 公美¹
 ¹理研・脳センター・黒田ユニット
- S6-4 動物の行動の背景となる遺伝子の解明
 ○村山 美穂¹
 ¹京都大学野生動物研究センター
- S6-5 Tryptophan 2,3-Dioxygenase (TDO)-ノックアウトマウスでは、神経新生の促進と不安行動の修飾が認められる
 ○船越 洋¹、金井 将昭¹、高橋 寿明¹、水野 信哉¹、松本 邦夫¹、中村 敏一¹
 ¹阪大院・医・分子再生医学
- S6-6 母子間バイオコミュニケーション：マウスに学ぶ
 ○和田 圭司^{1,2}
 ¹国立精神・神経センター神経研究所、²CREST, JST

9月12日(金)

9:00~12:00 (D会場)

- S7-1~S7-6 神経新生・幹細胞の生物学
 座長：岡野 栄之（慶應義塾大学医学部 生理学教室）
 齋藤 利和（札幌医科大学医学部 神経精神医学講座）
- S7-1 多能性幹細胞による脊髄再生
 ○岡野 栄之¹、岡田 洋平¹、熊谷玄太郎^{1,2}、中村 雅也²
 ¹慶應義塾大学医学部生理学教室、²慶應義塾大学医学部整形外科学教室

- S7-2 成体脳における新生ニューロンの移動
○澤本 和延¹
¹名古屋市立大学大学院医学研究科再生医学分野
- S7-3 REST/NRSF を介した骨形成因子 BMP による新規ニューロン分化抑制機構
神山 淳¹、高塚 絵里子¹、佐野坂 司¹、徳永 暁憲²、岡野 栄之²、
○中島 欽一¹
¹奈良先端大・バイオ・分子神経分化制御、²慶応大・医・生理
- S7-4 NG2 細胞は精神疾患の治療ターゲットになるか？
○楯林 義孝¹
¹うつ病プロジェクト、気分障害研究チーム、東京都精神医学総合研究所
- S7-5 精神疾患に対する幹細胞移植療法の可能性に関する研究
○鶴飼 渉¹、吉永 敏弘¹、石井 貴男²、橋本 恵理¹、小野 貴文¹、
館農 勝¹、渡邊 公彦¹、渡邊 一平¹、白坂 知彦¹、向 裕加¹、
齋藤 諭¹、齋藤 利和¹
¹札幌医科大学医学部神経精神医学講座、²札幌医科大学保健医療学部作業療法学科
- S7-6 成体脳の神経幹細胞と神経細胞新生：気分障害との接点を探る
○等 誠司¹
¹自然科学研究機構・生理学研究所・分子神経生理

9月12日(金)

9:00~12:00 (E会場)

- S8-1~S8-6 アルツハイマー病の神経化学
座長：高島 明彦（理化学研究所脳科学総合研究所 アルツハイマー病研究チーム）
武田 雅俊（大阪大学大学院医学系研究科 精神医学教室）

- S8-1 「アルツハイマー病の病原性物質であるAb42」を産生する仕組みには「細胞の分化に必須の Notch シグナル強度」を調節する生理作用がある-Ab42産生抑制薬の開発時に予想される問題点とその解決法の模索
○田上 真次¹、大河内 正康¹、武田 雅俊¹
¹大阪大学大学院医学系研究科精神医学教室
- S8-2 プレセニリン複合体とγセクレターゼ活性
○西村 正樹¹
¹滋賀医科大学分子神経科学研究センター
- S8-3 アルツハイマー病の原因分子を特定する
○富山 貴美¹
¹大阪市立大学大学院医学研究科脳神経科学

S8-4 $A\beta$ 重合開始の分子機構○柳澤 勝彦¹¹国立長寿医療センター 研究所

S8-5 タウ蛋白の神経変性への関与

○田中 稔久¹、Golam Sadik¹、加藤希世子¹、柳 健太郎¹、武田 雅俊¹¹大阪大学院・医・精神医学

S8-6 脳老化とアルツハイマー病

○高島 明彦¹¹理研 脳科学総合研究所 アルツハイマー病研究チーム

9月12日(金)

9:00~12:00 (F会場)

S9-1~S9-6 精神神経疾患のリスク遺伝子

座長：吉川 武男（理化学研究所脳科学総合研究センター 分子精神科学）

岡崎 祐士（東京都立松沢病院）

S9-1 統合失調症の大規模関連解析

○有波 忠雄¹、石黒 浩毅¹、古賀 農人^{1,2}、堀内 泰江¹、¹筑波大学大学院人間総合科学研究科生命システム医学専攻遺伝医学分野、²CREST

S9-2 パニック障害の疾患感受性遺伝子に関するゲノムワイド関連研究

○谷井 久志¹、佐々木 司²、音羽 健司³、加藤 忠史⁴、吉川 武男⁵、有波 忠雄⁶、功刀 浩⁷、染矢 俊幸⁸、松本 直道⁹、貝谷 久宣¹⁰、岡崎 祐士¹¹¹三重大学大学院医学系研究科・神経感覚医学講座・精神病態学分野、²東京大学保健センター、³東京大学医学部精神医学教室、⁴独立行政法人理化学研究所精神疾患動態研究チーム、⁵独立行政法人理化学研究所分子精神科学研究チーム、⁶筑波大学基礎医学系遺伝医学部門、⁷国立精神・神経センター神経研究所疾病研究第三部、⁸新潟大学医歯学総合科学研究科、⁹横浜市立大学医学研究科環境分子医科学、¹⁰医療法人 和楽会、¹¹東京都立松沢病院

S9-3 統合失調症のリスク遺伝子の探索：ゲノムおよび動物モデルからのアプローチ

○服巻 保幸¹¹九州大学生体防御医学研究所遺伝情報実験センターゲノム機能学分野

S9-4 稀な症例を出発点とした統合失調症の遺伝子研究

○糸川 昌成^{1,2,3}¹東京都精神医学総合研究所統合失調症研究チーム、²理化学研究所脳科学総合研究センター分子精神科学研究チーム、³都立松沢病院精神科

S9-5 認知症のリスク遺伝子

○森原 剛史¹、紙野 晃人²、木村 亮³、鎌形 英一郎¹、林 紀行¹、高屋 雅彦¹、横小路 美貴子¹、徳永 博正¹、数井 裕光¹、田中 稔久¹、工藤 喬¹、武田 雅俊¹

¹大阪大学・医・精神医学、²国立松籟荘病院、³大阪府立急性期総合医療センター

S9-6 脂肪酸結合タンパク遺伝子と機能性精神疾患

○吉川 武男¹

¹理研・脳センター・分子精神科学

9月13日(土)

15:20~17:20 (C会場)

S10-1~S10-4 小胞体ストレス

座長：工藤 喬 (大阪大学大学院医学系研究科 精神医学教室)
今泉 和則 (宮崎大学医学部 解剖学分子細胞生物学)

S10-1 神経系における小胞体ストレス応答の多様性

○今泉 和則¹

¹宮崎大・医・解剖学・分子細胞生物学

S10-2 小胞体におけるストレス制御と黒質神経細胞死

○堀 修¹

¹金沢大院・医・神経分子

S10-3 一酸化窒素による小胞体機能消失

○上原 孝¹

¹北海道大学大学院薬学研究院薬理学研究室

S10-4 ERストレスに基づく治療戦略

○工藤 喬¹

¹大阪大学大学院医学系研究科精神医学教室

9月13日(土)

15:20~17:20 (D会場)

S11-1~S11-4 膜内タンパク分解制御 (RIP) シグナル伝達

座長：富田 泰輔 (東京大学大学院薬学系研究科 臨床薬学教室)
大河内 正康 (大阪大学大学院医学系研究科 精神医学教室)

S11-1 アルツハイマー病診断治療薬開発の視点から見たRIPシグナル伝達の仕組み

○大河内 正康¹、田上 真次¹、武田 雅俊¹

¹大阪大院・医・精神医学

S11-2 γ セクレターゼ： β アミロイド前駆体タンパク質の膜内切断機序○森島 真帆¹¹北海道大学大学院薬学研究院 神経病理・病態生化学 (IBL)

S11-3 膜内でタンパクがどのように加水分解されるのか：膜内配列切断プロテアーゼの構造活性相関

○富田 泰輔¹¹東大・薬・臨床薬学

S11-4 神経特異的 RBP-J 欠損マウスと行動異常

○谷垣 健二¹、鳥塚 通弘^{1,3}、紀本 創兵^{1,3}、村木 一枝¹、岸本 年史³、
本庶 佑²¹滋賀成人病センター 研究所、²京大・医・免疫ゲノム、³奈良医大・精神科

9月13日(土)

15:20~17:20 (E会場)

S12-1~S12-4 疲労と意欲の脳科学

座長：定藤 規弘 (生理学研究所 大脳皮質機能研究系

心理生理学研究部門)

田中 雅彰 (大阪市立大学大学院医学研究科 COE生体情報解析学)

S12-1 疲労と意欲のニューロイメージング

○田中 雅彰^{1,2,3,4}、水野 敬^{2,3,4}、渡辺 恭良^{2,3,4,5}¹大阪市大・院・COE 生体情報解析学、²大阪市大・院・システム神経科学、³21世紀 COE プログラム疲労克服研究教育拠点、⁴独立行政法人科学技術振興機構、⁵理化学研究所分子イメージング研究プログラム

S12-2 慢性疲労症候群における脳機能異常

○倉恒 弘彦¹、渡辺 恭良³¹関西福祉科学大・健康福祉・健康科学、²大阪市立大学医学部疲労クリニカルセンター、³独立行政法人理化学研究所 分子イメージング研究プログラム

S12-3 疲労状態と自律神経機能の構造方程式モデリングの試み - 労働者の疲労に関する特定検診へ向けて

○田島 世貴¹、倉恒 大輔²、倉恒 弘彦¹、小泉 純一³¹関西福祉科学大学健康福祉学部健康科学科、²大阪市立大学大学院医学研究科生化学分子病態学、³横浜国立大学工学院

S12-4 動物モデルを用いた中枢神経疲労の分子・神経メカニズムの解析

○崔 翼龍¹、片岡 洋祐^{1,2}、渡辺 恭良^{1,2}¹(独) 理化学研究所・分子イメージング研究プログラム、²21世紀 COE プログラム・大阪市立大学大学院医学研究科

9月13日(土)

15:20~17:20 (F会場)

S13-1~S13-4 発達障害の神経化学

座長：松田 敏夫（大阪大学大学院 薬学研究科 複合薬物動態学分野）

成田 正明（三重大学大学院医学系研究科 発生再生医学）

S13-1 マウスの社会行動と血中オキシトシン濃度は母乳と視床下部のADP リボシルシクラーゼ活性の二重支配を受ける

○ロパチナ オリガ¹、劉 鴻翔¹、東田 陽博¹

¹金沢大・医薬保健学域・脳細胞遺伝子

S13-2 PACAP 遺伝子欠損マウスの異常行動発現に対する環境因子の影響

○石濱 壽紘¹、吾郷 由希夫¹、嶋田 祥子¹、新谷 紀人²、橋本 均^{2,3}、馬場 明道²、田熊 一敏¹、松田 敏夫^{1,3}

¹大阪大院・薬・複合薬物動態、²大阪大院・薬・神経薬理、³大阪大院・医・子どもこのころの分子統御機構研究センター

S13-3 胎生期サリドマイド曝露ラット大脳皮質におけるセロトニン・システムの生後発達異常

○田代 朋子¹、山村 尚志¹、鏡田 大輔¹、宮城 祐介¹、成田 正明²

¹青山学院大・理工・化学・生命科学、²三重大学大学院医学系研究科発達・再生医学

S13-4 自閉症患者におけるシナプス機能分子 SHANK3 の遺伝子解析

○内野 茂夫¹、和賀 央子¹、岡本 伸彦²、高坂 新一¹

¹国立精神神経センター・神経研究所・代謝研究部、²大阪府立母子保健総合医療センター・企画調査部

一般口演

9月11日(木)

9:00~12:00 (B会場)

O1-1~O1-9 シナプス

座長：小池 達郎 (北大生命科学院 生命システム科学分子神経研)

加藤 総夫 (慈恵医大・神経生理学)

武田 泰生 (鹿児島大学大学院 医歯学総合研究科 薬物動態制御学)

O1-1 経験依存的 AMPA 受容体シナプス移行

○宮崎 智之¹、多田 敬典¹、美津島 大¹、高橋 琢哉¹

¹横浜市立大学大学院医学研究科生理学

O1-2 シナプス前膜の年齢依存的な GM1 ganglioside 集積ドメイン形成は A β 線維化を促す

○山本 直樹^{1,2,3}、松原 輝彦⁴、湯山 耕平¹、佐藤 智典⁴、柳澤 勝彦¹

¹長寿医療セ アルツハイマー病、²日本学術振興会、³立命館大学 薬、⁴慶應大学 理工

O1-3 不飽和脂肪酸由来の HEPBA は CaMKII 経路を介して $\alpha 7$ 受容体の膜への移行を促進し海馬シナプス伝達効率を高める。

○矢口 貴博¹

¹兵庫医科大学・医・生理学講座生体情報部門

O1-4 後シナプス領域における Cdk5 と CaMKII の相互作用

○細川 智永¹、斎藤 太郎¹、浅田 明子¹、久永 眞市¹

¹首都大院・理工・生命

O1-5 タンパクメチル化酵素 Protein Arginine N-methyltransferase 3 (PRMT3) によるラット海馬神経細胞樹状突起での翻訳制御機構

○宮田 信吾¹、森 泰丈¹、遠山 正彌^{1,2}

¹大阪大院・医・神経機能形態学、²子どものこころの分子統御機構研究センター

O1-6 スパイカーによるスパイン形成はドレブリンにより阻害される。

○白尾 智明¹、山崎 博幸¹

¹群馬大学大学院医学系研究科神経薬理学

O1-7 Neuropsin 依存的, 非依存的シナプス・タギング

○石川 保幸¹、田村 英紀¹、塩坂 貞夫¹

¹奈良先端科学技術大学院大学・細胞構造学

O1-8 マウスクロマフィン細胞における開口分泌の特性

○笹川 展幸¹、松田 冬香¹、林 光紀¹、渡邊 裕美^{2,3}、五十嵐道弘^{2,3}、

崎村 建司⁴、熊倉鴻之助¹

¹上智大・理工・情報理工、²新潟大・医歯学・分子細胞機能学、³新潟大・超域研究機構、⁴新潟大・脳研・細胞神経生物学

O1-9 新規情報伝達物質8-ニトログアノシン3',5'-サイクリックモノホスフェートによる開口放出の調節

○居原 秀¹、津々木博康¹、笹川 展幸²、井田 智章¹、林 光紀²、熊倉鴻之助²、澤 智裕³、赤池 孝章³

¹大阪府立大学理学系研究科生物科学科、²上智大学生命科学研究科神経化学・神経薬理学部門、³熊本大学大学院医学薬学研究部微生物学分野

9月11日(木)

9:00~12:00 (C会場)

O2-1~O2-9 アストロサイト

座長：津田 正明(富山大学大学院医学薬学研究部(薬学))

片山 泰一(浜松医科大学・解剖学講座)

山脇 成人(広島大学大学院・精神神経医科学)

O2-1 培養アストロサイトおよびラット脳におけるアクアポリン4発現に対するエンドセリンの作用

○田中 一裕¹、小山 豊¹

¹大阪大谷大学・薬学部・薬理学講座

O2-2 アストロサイト BMP シグナリングが脳血管形成を制御する

○山田 真久¹、新家 瑠奈¹、工藤もゑこ¹、三品 裕司²

¹理化学研究所脳センター山田ユニット、²Lab. of Reproductive and Developmental Toxicology, NIH-NIEHS

O2-3 アストロサイトの部位特異性に関わる分子の同定

○青山 峰芳¹、垣田 博樹²、加藤 晋²、藤田 政隆³、祖父江和哉⁴、浅井 清文¹

¹名古屋市立大院・医・分子神経生物学、²名古屋市立大院・医・新生児・小児医学、³名古屋市立大院・医・脳神経外科学、⁴名古屋市立大院・医・麻酔・危機管理医学

O2-4 培養アストロサイトからのグリオトランスマター放出機構の解析

○李 海雄¹、Liu Hongtao²、田中 謙二¹、並木 繁行³、廣瀬 謙造³、古家 喜四夫⁴、曾我部 正博⁴、岡田 泰信²、池中 一裕¹

¹生理学研究所・分子神経生理、²生理学研究所・機能協関、³名古屋大院・医・細胞生理学、⁴名古屋大院・医・細胞生理学/イメージング生理学

O2-5 血管内皮細胞 mPGES-1 は EP3 を介してアストロサイトの Ca²⁺ 依存性グルタミン酸放出を制御する

○竹宮 孝子^{1,2}、松村 潔³、杉浦 弘子²、安田 新²、植松 智⁴、審良 静男⁴、山形 要人²

¹東京女子医大・医・総研研究部、²東京都神経研・神経薬理、³大阪工業大学・情報科学、⁴大阪大学・微研・自然免疫

- O2-6 ニコチンアミドによる PARP-1 誘発性アストロサイト細胞死抑制にはトランスポーターを介した取り込みが不可欠である
○奥田 浩人¹、鈴木 恵理¹、長澤 一樹¹、藤本 貞毅¹
¹京都薬大・衛生化学
- O2-7 アストログリア細胞に発現するグルタミントランスポーターは酸化ストレス脆弱性の決定因子である
○小椋 正人¹、福森 良¹、伊東 佑真¹、中道 範隆¹、谷浦 秀夫¹、米田 幸雄¹
¹金沢大学大学院自然科学研究科薬物学
- O2-8 培養アストロサイトへの過酸化水素によるチミジン取り込みにおける Ca²⁺-ATPase 阻害薬の効果
○田中 康一^{1,2}、佐藤 友昭²、西川 殷維²、北中 純一³、北中 順恵³、竹村 基彦³、西山 信好¹
¹兵庫医療大学薬学部医療薬学科薬理学、²鹿児島大学大学院医歯学総合研究科生体機能制御学講座歯科応用薬理学分野、³兵庫医科大学薬理学講座
- O2-9 強制運動によるマウス脳アストロサイトの動態変化
○金井 康至¹、高野 温志¹、光本 泰秀¹
¹北陸大学・薬・代替医療薬学

9月11日(木)

9:00~12:00 (D会場)

O3-1~O3-9 神経幹・前駆細胞

座長：福井 裕行（徳島大学大学院ヘルスバイオサイエンス研究部分子薬理学分野）
堀江 秀典（神奈川歯科大学 高次脳・口腔科学研）
新谷 紀人（大阪大学大学院 薬学研究科 神経薬理学分野）

- O3-1 p38MAPキナーゼによる神経幹細胞増殖の制御
○浜之上 誠¹、高松 研¹
¹東邦大学医学部生理学講座細胞生理
- O3-2 GABAシグナルによる神経系前駆細胞の増殖と分化の調節
○小澤 秀介¹、福井 正樹¹、寶田 剛志¹、谷浦 秀夫¹、中道 範隆¹、米田 幸雄¹
¹金沢大院・自然科学・薬物
- O3-3 マウス胎児海馬由来神経系前駆細胞の増殖・生存における活性酸素種の必要性
○川田 浩一¹、米山 雅紀¹、荻田 喜代一¹
¹摂南大・薬・薬理
- O3-4 成熟脳海馬神経系前駆細胞に高発現する Ifrd1 の特性
○前田紗弥香¹、渡邊 真未¹、中村有加里¹、谷浦 秀夫¹、中道 範隆¹、米田 幸雄¹
¹金沢大院・薬・薬物学

- O3-5 成体脳の新生ニューロンの移動におけるSlit-Roboシグナルの機能の解析
○金子奈穂子¹、Marin Oscar²、廣田 ゆき¹、Rubenstein John³、村上富士夫⁴、
Alvarez-Buylla Arturo³、岡野 栄之⁵、Tessier-Lavigne Marc⁶、澤本 和延¹
¹名古屋市立大学大学院医学研究科再生医学分野、²ミゲル・エルナンデス大学、
³カリフォルニア大学サンフランシスコ校、⁴大阪大学大学院生命機能研究科脳神
経工学講座、⁵慶応義塾大学医学部生理学教室、⁶ジェネンティック社
- O3-6 FACS を用いた成体海馬におけるニューロン新生の検出方法の開発
○難波 隆志¹、石 龍徳²、内野 茂夫¹、高坂 新一¹
¹国立精神・神経センター、²順天堂大学医学部解剖学第二講座
- O3-7 ニコチンの神経前駆細胞に対する作用—分化神経細胞との比較—
○新郷 明子¹、鬼頭 昭三²
¹兵庫大学健康科学部、²順心会幸生リハビリテーション病院
- O3-8 発生期マウス小脳に存在するアストロサイト前駆細胞
○蔡 娜¹、倉知 正¹、石崎 泰樹¹
¹群馬大学大学院医学系研究科分子細胞生物学
- O3-9 発生中の視床網様核における Olig2 由来 GABA 作動性ニューロンの解析
○稲村 直子¹、小野 勝彦¹、竹林 浩秀¹、池中 一裕¹
¹自然科学研究機構 生理学研究所 分子神経生理研究部門

9月11日(木)

9:00~12:00 (E会場)

O4-1~O4-9

神経細胞死 1

座長：岡澤 均（東京医科歯科大学 難治疾患研究所 神経病理学）
野田 百美（九州大学大学院薬学研究院病態生理学分野）
稲垣 忍（大阪大学医学系研究科保健学専攻神経生物学研究室）

- O4-1 大脳皮質神経細胞の NMDA 抵抗性
○神戸 悠輝¹、中道 範隆¹、川越 博文¹、清永 大輔¹、谷浦 秀夫¹、米田 幸
雄¹
¹金沢大院・自然科学・薬物
- O4-2 新規小胞体ストレス応答遺伝子OASISの脳における機能解析
○齋藤 敦¹、千原 一泰¹、村上 智彦¹、原 英彰²、和中 昭生³、今泉 和
則¹
¹宮崎大学大学院医学研究科解剖学講座分子細胞生物学分野、²岐阜薬科大学薬効
解析学研究室、³奈良県立医科大学医学部第二解剖学教室
- O4-3 HRD1 のタンパク質分解抑制は小胞体ストレスとアポトーシスを伴うアミロイド
前駆体タンパク質の蓄積と A β の産生増加を引き起こす
○金子 雅幸¹、小池 洋²、大村 友博¹、大熊 康修¹、野村 靖幸³
¹千葉科学大・薬・薬理、²北大院・薬・薬理、³横浜薬大・薬・薬物治療

- O4-4 大脳皮質ニューロンにおける Necdin の Sirt1 を介した p53アセチル化の調節
○長谷川孝一¹、吉川 和明¹
¹大阪大学 蛋白質研究所 神経発生制御研究室
- O4-5 SH-SY5Y 細胞における一酸化窒素誘発細胞死に対する Na⁺/Ca²⁺ 交換系の関与
○梨子田哲明¹、川崎 俊之¹、北尾 達哉¹、福田小夜子¹、吾郷由希夫¹、田熊 一
敏¹、松田 敏夫^{1,2}
¹大阪大院・薬・複合薬物動態、²大阪大院・医・子どものこころの分子統御機構
研究センター
- O4-6 神経細胞に発現する P2X7 受容体を介した ATP 誘発性神経細胞死分子機構の解明
○中谷 庸寿¹、奥田 浩人¹、白山 怜奈¹、中西麻由香¹、山谷 香織¹、長澤 一
樹¹、藤本 貞毅¹
¹京都薬大・衛生化学
- O4-7 表面プラズモン共鳴法を用いた異常伸長ポリグルタミンタンパク質に対する凝集
阻害分子の結合特異性の解析
○岡本 佑馬^{1,2}、永井 義隆¹、藤掛 伸宏¹、ポピエル ヘレナ明子¹、戸田 達
史¹、乾 隆²
¹大阪大学大学院医学系研究科遺伝医学講座臨床遺伝学、²大阪府立大学大学院生
命環境科学研究科応用生命科学専攻細胞情報化学講座
- O4-8 CHO 細胞と PC12 細胞においての SFAP75/Norbin の機能解析
○徳原 康哲¹、酒井 学¹、柴田 理志¹、大岡 嘉治²、稲垣 忍¹
¹大阪大院・医・保健学、²徳島文理大学香川・薬・生体防御学
- O4-9 neogenin の細胞死誘導の分子メカニズム
○藤田 幸¹、谷口 順子²、内川 昌則³、遠藤 光晴¹、羽田 克彦¹、久保 武
一²、山下 俊英^{1,2}
¹大阪大学大学院医学系研究科分子神経科学、²千葉大学大学院医学系研究院神経
生物学、³大阪大学大学院生命機能研究科形態形成学

9月11日(木)

9:00~12:00 (F会場)

O5-1~O5-9 統合失調症

座長：岸本 年史（奈良県立医科大学精神医学）

車地 暁生（東京医科歯科大学大学院 精神行動医科学分野）

上野 修一（愛媛大学大学院医学系研究科脳とこころの医学分野）

O5-1 日本人における統合失調症と疾患感受性遺伝子G72の関連研究

○大井 一高¹、橋本 亮太^{1,2}、安田 由華^{1,2}、吉田 哲彦¹、高橋 秀俊¹、井池
直美¹、岩瀬 真生¹、紙野 晃人¹、石井 良平¹、数井 裕光¹、喜多村祐里³、疇
地 道代¹、池澤 浩二¹、鎌形英一郎¹、谷向 仁¹、田上 真次¹、森原 剛史¹、
大河内正康¹、大沼 徹⁴、沼田 周助⁵、池田 匡志⁶、上野 修一⁵、福永 知子¹、
田中 稔久¹、工藤 喬^{1,2}、新井 平伊⁴、大森 哲郎⁵、岩田 伸生⁶、尾崎 紀夫⁷、
武田 雅俊^{1,2}

¹大阪大学大学院医学系研究科精神医学、²大阪大学大学院医学系研究科附属子どものこころの分子統御機構研究センター疾患関連分子解析部門、³大阪大学大学院医学系研究科生理学教室、⁴順天堂大学医学部精神医学教室、⁵徳島大学大学院医学系研究科精神医学教室、⁶藤田保健衛生大学医学部精神医学教室、⁷名古屋大学大学院医学系研究科精神医学教室

O5-2 日本人における PNPO 遺伝子と統合失調症の関連

○宋 鴻偉¹、上野 修一²、沼田 周助¹、伊賀 淳一¹、渋谷-田吉 純子¹、中瀧 理仁¹、田吉 信哉¹、山内 健¹、住谷さつき¹、友竹 正人¹、多田 友人³、棚橋としひと⁴、板倉 光夫⁴、大森 哲郎¹

¹徳島大学ヘルスバイオサイエンス研究部精神医学、²徳島大学医学部大学院ヘルスバイオサイエンス研究部、保健科学部門看護学講座、³徳島市第一病院、⁴徳島大学疾患ゲノム研究センター

O5-3 統合失調症関連遺伝子 Dysbindin の機能解析

○窪田 杏子¹、熊本奈都子¹、松崎 伸介^{1,2}、橋本 亮太^{2,3}、遠山 正彌^{1,2}

¹大阪大学大学院医学系研究科神経機能形態学、²大阪大学大学院医学系研究科附属子どものこころの分子統御機構研究センター、³大阪大学大学院医学系研究科精神医学

O5-4 新規 Dysbindin 結合分子としての AP-3 複合体の同定

○藤野 泰孝¹、匹田 貴夫¹、黒田 摂子¹、田谷真一郎¹、貝淵 弘三¹

¹名古屋大学大学院医学系研究科神経情報薬理学講座

O5-5 ERK による DISC1 のリン酸化は Kinesin-1 との結合を制御する

○黒田 啓介¹、田谷真一郎¹、浦口 淳子¹、舟橋 祐介¹、貝淵 弘三¹

¹名古屋大院・医・神経情報薬理

O5-6 新生仔期ニューレグリン 1-β1 暴露は成熟後の MK-801 感受性を増強する

○加藤 泰介¹、水野 誠^{1,2}、那波 宏之¹

¹新潟大学脳研究所分子神経生物学分野、²新潟大学超域研究機構

O5-7 新生期上皮成長因子によるドーパミンD2 受容体感受性の亢進と大脳基底核 GABA 作動性経路に対する影響

○外山 英和¹、那波 宏之¹

¹新潟大学・脳研究所・分子神経生物学

O5-8 反復投与された高用量のメタンフェタミンによって引き起こされるプレパルスインヒビション阻害のラモトリギンによる阻止

○仲唐 安哉¹、安部川智浩¹、伊藤 侯輝¹、角田 彩¹、小山 司¹

¹北海道大院・医・精神医学

O5-9 長期隔離飼育誘発プレパルスインヒビション障害におけるムスカリン性 ACh 受容体の関与

○香田 健¹、矢野 耕史¹、吾郷由希夫¹、西村 百恵¹、田熊 一敏¹、松田 敏夫^{1,2}

¹大阪大院・薬・複合薬物動態、²大阪大院・医・子どものこころの分子統御機構研究センター

9月11日(木)

16:00~18:00 (B会場)

O6-1~O6-6 神経伝達

座長：太田 明(藤田保健衛生大学医学部生理学講座I)

馬場 広子(東京薬科大学薬学部機能形態学教室)

O6-1 サイクリックADPリボースの神経細胞内Ca動員機構の解析

○アミナ サラワト¹、劉 鴻翔¹、ロパチナ オリガ¹、橋井美奈子¹、東田 陽博¹¹金沢大・医薬保健学域・脳細胞遺伝

O6-2 HPC-1/syntaxin1A ノックアウトマウスにおける HPA-axis の障害

○小藤 剛史¹、藤原 智徳²、真田ますみ²、赤川 公朗²¹杏林大・医・共研RI部門、²杏林大学・医・細胞生理

O6-3 グリア細胞における新規ニトロ化セカンドメッセンジャー 8-ニトログアノシン 3',5'-環状 1 リン酸の生成

○井田 智章¹、澤 智裕²、赤池 孝章²、居原 秀¹¹大阪府立大学理学系研究科生物科学、²熊本大学大学院医学薬学研究部微生物学分野

O6-4 セピアプテリン還元酵素ノックアウトマウスにおけるテトラヒドロピオプテリン依存性酵素量の変化

○本間 大悟¹、高澤 千智¹、藤本 健吾²、加藤 節子²、一瀬 宏¹¹東京工業大学大学院生命理工学研究科分子生命科学専攻、²明海大学歯学部

O6-5 プロスタグランジン CRTH2 受容体を介した概日リズムの光誘発位相前進調節

○新谷 紀人¹、川口ちひろ¹、中村 玲子¹、畑中 道賢¹、磯島 康史^{2,3}、土田 理恵¹、羽場 亮太¹、橋本 均^{1,4}、杉本 幸彦⁵、永井 克也²、平井 博之⁶、永田 欽也⁶、中村 正孝⁷、松岡 俊行⁸、成宮 周⁸、馬場 明道¹¹大阪大院・薬・神経薬理、²大阪大・蛋白研、³理研・ゲノム科学センター、⁴大阪大院・医附・子どものこころの研究センター、⁵京大院・薬・生体情報制御学、⁶株式会社ビー・エム・エル・先端医療開発部、⁷東京医科歯科大学・疾患遺伝子実験センター、⁸京大院・医・薬理学

O6-6 プロスタグランジン CRTH2 受容体作動薬のオープンフィールド行動に対する作用

○羽場 亮太¹、畑中 道賢¹、新谷 紀人¹、王 海波¹、橋本 均¹、馬場 明道¹¹大阪大院・薬・神経薬理

9月11日(木)

16:00~18:00(C会場)

O7-1~O7-6

神経免疫・内分泌

座長:大西 浩史(群馬大学生体調節研究所 バイオシグナル分野)

大熊 康修(千葉科学大学薬学部 薬理学教室)

O7-1 エンドトキシン活性化ミクログリアは GDNF の分泌を抑制する

○中嶋 一行^{1,2}、松下 雄一¹、遠山 陽子¹、高坂 新一²、栗原 正¹

¹創価大学工学部生命情報工学科、²国立精神・神経センター神経研究所

O7-2 線条体神経細胞におけるドーパミン受容体を介した TrkB 受容体のトランスアクティベーション

○岩倉百合子¹、那波 宏之¹、曾良 一郎²、チャオ V. モーゼス³

¹新潟大・脳研究所・分子神経生物学分野、²東北大院・医、神経・感覚器病態学講座、精神・神経生物学分野、³ニューヨーク大・スカーボール研究所・分子神経生物学分野

O7-3 イボテン酸投与統合失調症モデルラットにおけるチロシン受容体阻害剤の効果

○水野 誠¹、鄭 英君²、川村 宏樹²、渋谷 雅子²、朴 英善²、外山 英和²、江田 岳譽²、那波 宏之²

¹新潟大学・超域研究機構、²新潟大学脳研究所分子神経生物学分野

O7-4 神経成長因子は、GRP78 発現の加速上昇を介して 2-deoxyglucose による小胞体ストレス誘導型アポトーシスを抑制する

○岸 宗一郎¹、下家 浩二^{1,2}、奥村 宣明³、島田 貴史¹、藤田 裕子¹、永井 克也⁴、新家 一男⁵、池内 俊彦^{1,2}

¹関西大学大学院工学研究科、²関西大学化学生命工学部生命・生物工学科、³大阪大学蛋白質研究所、⁴株式会社ANBAS、⁵産業総合技術研究所バイオメディシナル情報研究センター

O7-5 下垂体細胞アデニル酸シクラーゼ活性化ポリペプチド PACAP により誘導される神経活動依存的な遺伝子発現カスケードに関する解析

○福地 守¹、渡邊信次郎¹、高崎 一郎²、田淵 明子¹、津田 正明¹

¹富大院・医薬・分子神経生物学、²富大・生命科学先端研究センター・遺伝子実験施設

O7-6 ATPによるアストログリア細胞の神経栄養因子発現制御

○清長 大輔¹、加藤 俊亮¹、神戸 悠輝¹、小椋 正人¹、谷浦 秀夫¹、中道 範隆¹、米田 幸雄¹

¹金沢大学院・自然科学・薬物

9月11日(木)

16:00~18:00(D会場)

O8-1~O8-6

セロトニン系

座長：仙波 純一（さいたま市立病院精神科）

大森 哲郎（徳島大学大学院ヘルスバイオサイエンス研究部精神医学分野）

- O8-1 ADHD治療薬の逆説的鎮静化作用におけるセロトニン1A受容体の関与
○土田 理恵¹、橋本 均^{1,2}、久保 勝裕¹、新谷 紀人¹、吾郷由希夫³、松田 敏夫^{2,3}、馬場 明道¹
¹大阪大院・薬・神経薬理、²大阪大院・医・子どものこころの発達研究センター、³大阪大院・薬・複合薬物動態
- O8-2 マウス海馬におけるセロトニン受容体の発現プロファイル
○田中 謙二¹、レネ ヘン²
¹生理研 分子神経生理、²コロンビア大学
- O8-3 種々のGタンパク質に共役するセロトニン受容体機能の単一解析法
○植田 高史¹、鶴川 眞也¹、石田 雄介¹、島田 昌一¹
¹名古屋市大院・医・機能組織
- O8-4 非定型抗精神病薬による前頭前野ドパミン遊離促進作用におけるD2および5-HT1A受容体の関与
○長尾奈穂子^{1,2}、黒木 俊秀²、中原 辰雄^{1,2}、本村 啓介¹、橋本喜次郎²、神庭 重信¹
¹九州大院・医・精神病態、²独立行政法人国立病院機構 肥前精神医療センター
- O8-5 [¹¹C] DASBを用いた無麻酔下マーマセット脳におけるセロトニントランスポーターのPETイメージング
○横山ちひろ¹、川崎 章弘¹、尾上 嘉代²、長田 浩子³、畑中 恵子³、土居 久志³、尾上 浩隆¹
¹理化学研究所・分子イメージング研究プログラム・分子プローブ機能評価研究チーム、²理化学研究所・分子イメージング研究プログラム・分子プローブ動態応用研究チーム、³理化学研究所・分子イメージング研究プログラム・分子プローブ設計創薬研究チーム
- O8-6 Tryptophan 2,3-Dioxygenase (TDO) ならびに Indoleamine 2,3-Dioxygenase (IDO) ノックアウトはトリプトファンとセロトニン代謝を修飾する
○金井 将昭¹、船越 洋¹、高橋 寿明¹、水野 信哉¹、松本 邦夫¹、中村 敏一¹
¹阪大院・医・分子再生医学

9月11日(木)

16:00~18:00 (E会場)

O9-1~O9-6

転写制御因子・細胞接着因子

座長：奥山 典生 (1: (株)プロテインテクノスインスティテュート
2: (財)緒方医学化学研究所)

崎村 建司 (新潟大学脳研究所細胞神経生物学分野)

O9-1 転写因子 OASIS のプロテオグリカン産生への関与

○奥田 洋明¹、辰巳 晃子¹、今泉 和則²、和中 明生¹

¹奈良県立医科大学医学部第二解剖、²宮崎大学医学部解剖学講座分子細胞生物学分野

O9-2 Foxp1 は発生過程において脊髄運動ニューロンの一部に発現している

○久岡 朋子¹、森川 吉博¹、仙波恵美子¹

¹和歌山県立医科大学 第二解剖

O9-3 Necdin は Foxo1 と相互作用して転写活性を抑制する

○川原 知浩¹、長谷川孝一¹、吉川 和明¹

¹大阪大学 蛋白質研究所 神経発生制御研究室

O9-4 視床下部における転写調節因子 AF5q31 の身体の成長やエネルギー代謝に対する役割の検討

○小森 忠祐¹、野阪 哲哉²、北村 俊雄³、仙波恵美子¹、森川 吉博¹

¹和歌山県立医科大学 第二解剖、²三重大学大学院医学系研究科 感染症制御医学分野、³東京大学医科学研究所 先端医療研究センター 細胞療法分野

O9-5 NB-3 欠損マウス小脳における平行線維-プルキンエ細胞間シナプス形成の異常

○桜井 都衣¹、豊島 学¹、松原 航太¹、武田 泰生²、霜田 靖¹、Karagoeos Domna³、渡邊 和忠¹

¹長岡技科大・生物、²鹿児島大院・医歯学総合、³クレタ大院・医

O9-6 精神疾患患者では海馬顆粒細胞における細胞接着分子 L1 の発現が減少している

○堀之内和広^{1,2,3}、泉 愛子²、遠山 正彌³、塩坂 貞夫¹、有馬 邦正⁴、功刀 浩²

¹奈良先端科学技術大学院大学バイオサイエンス研究科細胞構造学講座、²国立精神・神経センター神経研究所疾病研究第三部、³大阪大学大学院医学系研究科神経機能形態学講座、⁴国立精神・神経センター病院臨床検査部

9月11日(木)

16:00~18:00 (F会場)

O10-1~O10-6

神経変性疾患

座長：佐野 輝 (鹿児島大学大学院医歯学総合研究科精神機能病学分野)
豊島 至 (秋田大学医学部医学教育センター)

- O10-1 家族性パーキンソン病関連変異型 UCH-L1 は LAMP-2A と結合する
○株田 智弘¹、古田 晶子¹、青木 俊介¹、古田 耕²、和田 圭司¹
¹国立精神神経センター 神経研究所 疾病研究第四部、²国立がんセンター 中央病院
- O10-2 神経変性疾患に関連した変異による UCH-L1 と SOD1 の分泌変化
○紺谷 千穂¹、株田 智弘¹、衣川亜衣子¹、和田 圭司¹
¹国立精神・神経センター神経研究所疾病研究第4部
- O10-3 脱ユビキチン化酵素 UCH-L1 と脂質酸化ストレス
○長嶺 聖史¹、株田 智弘¹、山本 和弘²、高橋 明男²、和田 圭司¹
¹国立精神神経セ・疾病研究第四部、²国立精神神経セ・実験動物管理室
- O10-4 酸化修飾タンパク質はパーキンソン病の発症に関与する
○永井 雅代¹、丸山和佳子¹、直井 信²
¹国立長寿医療センター研究所老年病研究部、²岐阜県国際バイオ研究所
- O10-5 ALS および ALS with dementia におけるエンドソーム関連タンパクの染色性
○高橋 哲也¹、日地 正典²、福場 浩正¹、山下 拓史¹、郡山 達男¹、松本 昌泰¹
¹広島大院・医・脳神経内科、²ビハーラ花の里病院
- O10-6 ALS2/alsin 機能喪失は変異 SOD1^{H46R} 発現マウスの疾患症状を悪化させる
○秦野 伸二^{1,2}、大友 麻子¹、國田 竜太¹、鈴木(宇都宮) 恭子¹、尾上久一郎¹、大須賀 等¹、青木 正志³、糸山 泰人³、池田 穰衛^{1,2}
¹東海大・医・分子生命、²東海大院・医・脳神経疾患研究セ、³東北大院・医・神経内科

9月12日(金)

14:05~15:45 (B会場)

O11-1~O11-5 神経突起伸展

座長：五十嵐道弘（新潟大学医歯学系分子細胞機能学（医学部生化学第二））

上口 裕之（理化学研究所 脳科学総合研究センター 神経成長機構研究チーム）

- O11-1 軸索成長に関係する成長円錐蛋白質の網羅的同定と分布の決定
○野住 素広^{1,2}、五十嵐道弘^{1,2}
¹新潟大・医歯学・分子細胞機能学、²新潟大・超域研究機構
- O11-2 ドレブリンによる軸索成長調節
○水井 利幸^{1,2}、山崎 博幸¹、白尾 智明¹
¹群馬大学大学院医学系研究科神経薬理学、²21COE
- O11-3 異なる CaMKK-CaMKI 経路による軸索/樹状突起の特異的形成制御
○上田(石原) 奈津実¹、竹本-木村さやか¹、安達-森島 亜希¹、野中 美応¹、奥野 浩行¹、尾藤 晴彦¹
¹東京大院・医・神経生化

O11-4 神経組織培養と光照射分子機能阻害技術を用いた機能分子スクリーニング法

○竹居光太郎^{1,3}、山口めぐみ¹、佐藤 泰史^{1,2,3}、池谷 真澄¹、有江 裕子¹、五嶋良郎^{1,3}

¹横浜市大院・医・分子薬理神経、²三菱化学・生命研・脳梗塞、³科学技術振興機構・CREST

O11-5 運動ニューロン由来因子が後根神経節の発生に与える影響

○臼井 紀好^{1,2}、竹林 浩秀^{1,2}、小野 勝彦^{1,2}、池中 一裕^{1,2}

¹総合研究大学院大学生命科学研究科生理科学専攻、²自然科学研究機構生理学研究所分子神経生理部門

9月12日(金)

14:05~15:45(C会場)

O12-1~O12-5 脳虚血

座長：小倉 明彦(大阪大学大学院生命機能研究科)

山田 和雄(名古屋市立大 脳神経外科学)

O12-1 脳卒中モデル動物における細胞死と Sema4D

○稲垣 忍¹、和田 剛信²、山口 航¹、荻矢麻里子¹、上杉 紀子¹、高原 瑞恵¹、斉野 織恵³、古山 達雄⁴、古郷 幹彦²、松山 知弘³

¹大阪大・医・保健学、²大阪大院・歯・顎病因病態制御、³兵庫医大・医・先端医学研究所・神経再生研、⁴香川県立保健医療大学

O12-2 脳卒中モデル動物における神経系細胞の再生とSema4D

○和田 剛信¹、山口 航²、斉野 織恵³、谷口 佳孝¹、玉井 里枝²、阿部 真土⁴、古山 達雄⁵、松山 知弘³、稲垣 忍²、古郷 幹彦¹

¹大阪大院・歯・顎病因病態制御、²大阪大院・医・保健学・生体情報科学講座・神経生物学、³兵庫医大・医・先端医学研究所・神経再生研、⁴大阪大院・歯・口腔分化発育情報学(口腔解剖1)、⁵香川県立保健医療大学

O12-3 虚血性脳血管障害における eNOS アンカッピングの病態生理学的意義

○韓 峰¹、福永 浩司^{1,2}

¹東北大院・薬・薬理、²東北大学・21世紀 COE プログラム

O12-4 タンパク質チロシンキナーゼ阻害は一過性局所脳虚血後の血液脳関門の破綻を抑制し、梗塞巣を縮小する。

○室富 和俊¹、高木 教夫¹、竹永 悠司¹、竹尾 聡¹、田野中浩一¹

¹東京薬科大学薬学部 分子細胞病態薬理学教室

O12-5 一過性脳虚血に対する PEDF の脳保護作用

○矢部 武士¹、佐柳 友規¹、山田 陽城¹

¹北里大学・北里生命研

9月12日(金)

14:05~15:45 (D会場)

O13-1~O13-5 シグナル伝達

座長：鈴木 龍雄（信州大学 大学院医学研究科加齢適応医科学系独立専攻 神経可塑性学分野）
橋井美奈子（金沢大学・医薬保健・脳細胞遺伝）

O13-1 CaMKII と相互作用する分子種の探索と共発現データベースを用いた解析

○山田 隆文¹、岩松 明彦²、大林 武³、木下 賢吾³、大迫 俊二¹

¹東京都神経研、²プロテインリサーチネットワーク、³東大・医科研・インシリコ
分野

O13-2 ニューロプシンはサイトメガロウイルスプロモーターの活性を増大させる

○田村 英紀¹、石川 保幸¹、塩坂 貞夫¹¹奈良先端大・バイオ・細胞構造

O13-3 パルミトイル化は AATYK1A のエンドソームへの局在と Src キナーゼとの相互作用の制御する

○堤 弘次¹、友村美根子²、古市 貞市³、久永 眞市¹

¹首都大院・理・生物、²理研・脳科学総合研究センター・神経成長研究チーム、
³理研・脳科学総合研究センター・分子神経形成研究チーム

O13-4 Plexin-B1 相互作用因子 RhoGEF10 の機能解析

○茶屋 太郎¹、柴田 理志¹、大岡 嘉治²、稲垣 忍¹¹大阪大院・医・保健学、²徳島文理大学香川・薬・生体防御

O13-5 RGMa の細胞内シグナル伝達機構

○羽田 克彦¹、山下 俊英¹¹大阪大学院医学系研究科分子神経科学講座

9月12日(金)

14:05~15:45 (E会場)

O14-1~O14-5 神経保護作用

座長：吉村 和法（日本医療科学大学・リハビリテーション学科）
小鹿 幸生（名古屋市立大学大学院医学研究科 神経内科）

O14-1 メタンフェタミン神経毒性に対するインターフェロン γ の保護効果における PPAR γ の関与○浅沼 幹人¹、福岡 早紀²、穂積 宏彰²、宮崎 育子¹、北村 佳久³、千堂 年昭²、喜多 大三⁴

¹岡山大学大学院医歯薬学総合研究科神経情報学、²岡山大学大学院医歯薬学総合
研究科臨床薬剤薬理学、³岡山大学大学院医歯薬学総合研究科医薬管理学、⁴九州
栄養福祉大学大学院食物栄養学研究科薬理学研究室

- O14-2 アストロサイトのニコチン性シグナルによる神経細胞保護メカニズム
○川越 博文¹、小椋 正人¹、及川 弘崇²、中道 範隆¹、米田 幸雄¹
¹金沢大学大学院自然科学研究科薬物学、²セントルイス大学医学部小児科医学遺伝学部門
- O14-3 脳損傷モデルマウスにおける脳移行性骨髄細胞の神経保護効果
○小野 健治¹、山本 奈穂¹、鈴木 弘美¹、佐藤 愛美¹、澤田 誠¹
¹名古屋大学環境医学研究所 生体適応・防御研究部門 脳機能分野
- O14-4 NMDA 神経毒性に対する ATP の保護作用
○亀島 優太¹、加藤 俊亮¹、神戸 悠輝¹、谷浦 秀夫¹、中道 範隆¹、米田 幸雄¹
¹金沢大院・自然科学・薬物
- O14-5 抑肝散のグルタミン酸誘発神経細胞死に対する保護作用
○川上 善治¹、寺脇 潔¹、菅野 仁美¹、田渕 雅宏¹、五十嵐 康¹、加瀬 義夫¹
¹株式会社ツムラ ツムラ研究所

9月12日(金)

14:05~15:45 (F会場)

O15-1~O15-5 疾患モデル1

座長：西澤 正豊（新潟大学脳研究所神経内科）

北山 滋雄（岡山大学大学院医歯薬学総合研究科歯科薬理学分野）

- O15-1 Bcl-2 ファミリーは有棘赤血球舞踏病モデルマウスの神経細胞死に関与する
○松田三恵子¹、中村 雅之¹、市場 美緒¹、加藤真依子¹、下 洋央¹、富安 昭之¹、河野 奈理¹、内之倉陽子¹、森 さつき¹、石塚 貴周¹、林 武宏¹、佐野 輝¹
¹鹿児島大学大学院医歯学総合研究科精神機能病学
- O15-2 Adducin β の発現減少は有棘赤血球舞踏病の神経変性と有棘赤血球症に関連する
○中村 雅之¹、松田三恵子¹、市場 美緒¹、加藤真衣子¹、下 洋央¹、富安 昭之¹、河野 奈理¹、内之倉陽子¹、森 さつき¹、石塚 貴周¹、林 岳宏¹、佐野 輝¹
¹鹿児島大学大学院医歯学総合研究科精神機能病学
- O15-3 DRPLA モデルマウスにおいて、nicotine 投与により最初期遺伝子蛋白は海馬での発現が低下する
○金 毅¹、鈴木 一詩¹、佐藤 俊哉²、清水 潤¹、後藤 順¹、辻 省次¹
¹東京大学附属病院 神経内科、²新潟大学 脳研究所 生命科学リソース研究センター

- O15-4 gracile axonal dystrophy (GAD) マウスにおける逆行性軸索変性分子メカニズム解析
 ○後藤 章子^{1,2}、王 玉来²、節家 理恵子²、株田 智弘²、小坂 仁²、澤明³、石浦 章一¹、和田 圭司²
¹東大院・総合文化・生命環境、²国立精神・神経センター・神経研・疾病4部、³ジョンズホプキンス大・医・精神神経医学
- O15-5 バクリタキセルによる末梢神経障害ラットの脊髄後根神経節における網羅的遺伝子発現解析
 西田健太郎¹、口岩 聡²、大磯 茂¹、二川 俊隆^{1,3}、益田 将吾¹、茂見 茜里³、藤崎 裕子³、○武田 泰生^{1,3}、山田 勝士^{1,3}
¹鹿児島大院・医歯学総合・薬物動態制御、²鹿児島大院・医歯学総合・神経解剖学、³鹿児島大病院・薬剤部

9月12日(金)

16:25~18:25 (B会場)

O16-1~O16-6 軸索輸送、細胞運動、細胞骨格

座長：佐野 護 (同志社大学、生命医科学部)

平松 緑 (東北公益文科大学)

- O16-1 マルチドメイン・アダプター蛋白質 p140Cap のプレシナプスにおける機能
 ○永田 浩一¹、伊東 秀記¹、武井 史郎²、須藤 香織¹、岩本 郁子¹、森下 理香¹、浅野 富子¹、仙波 禮治²
¹愛知県コロニー・研究所・神経制御、²愛知県コロニー・研究所・病理
- O16-2 クロマフィン細胞における分泌顆粒供給へのミオシン ATPアーゼの関与：走査電顕による検討
 ○熊倉鴻之助¹、関口 瑞季¹、リヴァ アレッサンドロ²、村上 正隆³、林 光紀¹、笹川 展幸¹
¹上智大・理工・情報理工、²カリアリ大・細胞形態学、イタリア、³生理学研究所、岡崎
- O16-3 大脳皮質形成過程においてロコモーション様式で移動する神経細胞の形態変化を制御する分子の探索
 ○西村 嘉晃^{1,2}、仲嶋 一範¹、鍋島 陽一²、星野 幹雄^{2,3}、川内 健史^{1,2}
¹慶應大・医・解剖学、²京都大院・医・腫瘍生物、³国立精神・神経センター神経研究所診断研究部
- O16-4 Abi2 は非筋肉性ミオシン IIB 型との相互作用によってラディアルマイグレーションを制御する
 ○謝 敏かく¹、八木 秀司^{1,2}、岡本 昌之¹、佐藤 真^{1,2}
¹福井大学医学部 形態機能医科学講座 組織細胞形態学・神経科学領域、²生命科学複合研究教育センター
- O16-5 神経再生時における脂質輸送関連 ABC トランスポーター A1 の発現
 ○池島(獅子王) 信江¹、中込 咲綾¹、小西 博之¹、木山 博資¹
¹大阪市立大学大学院医学研究科機能細胞形態学

O16-6 ATP 受容体 P2Y₁₂ を介したインテグリン β 1 活性化によるミクログリア突起伸長調節

○大澤 圭子¹、中村 泰子¹、入野 康宏²、鈴木 恵里¹、佐柳 友規¹、井上 和秀³、高坂 新一¹

¹国立精神・神経センター 神経研究所 代謝研究部、²神戸大学大学院医学研究科脂質生化学分野、³九州大学大学院薬学研究院 薬理学分野

9月12日(金)

16:25~18:25 (C会場)

O17-1~O17-6 ミクログリア・オリゴデンドロサイト

座長：宮武 正 (理化学研究所脳科学総合研究センター)

中村 洋一 (大阪府立大学大学院生命環境科学研究科獣医学専攻統合生理学教室)

O17-1 顔面神経切断時におけるミクログリアの増殖因子 M-CSF とその受容体 cFMS の調節について

○山本 伸一¹、中嶋 一行^{1,2}、遠山 陽子¹、高坂 新一²、栗原 正¹

¹創価大学工学部生命情報工学科、²国立精神・神経センター神経研究所

O17-2 P2X₇ 受容体を介した脳内亜鉛によるミクログリアの活性化

○東 洋一郎¹、長澤 一樹²、瀬川 将平²、奥田 浩人²、大西 美穂²、勝田 優²、渡辺 侑里子²、水島 徹¹、藤本 貞毅²

¹熊本大学大学院医学薬学研究部薬学微生物学分野、²京都薬科大学衛生化学

O17-3 ミクログリア細胞に発現する時計遺伝子群

○山本 朋未¹、宝田 剛志¹、佐原 甲一¹、橘 正毅¹、谷浦 秀夫¹、米田 幸雄¹

¹金沢大院・自然科学(薬)・薬物学

O17-4 脱髄疾患モデルマウスにおける Olig2+ 細胞の細胞系譜追跡

○清水 崇弘^{1,2}、竹林 浩秀^{1,2}、小野 勝彦^{1,2}、池中 一裕^{1,2}

¹総合研究大学院大学、²生理学研究所

O17-5 オリゴデンドロサイトの成熟に伴う MBP の局在の変化

○佐藤菜名子^{1,2}、清和 千佳²、築地 謙治¹、漆瀬 道洋¹、佐藤友理恵¹、品川 理佳³、下田 泰治³、阿相 皓晃^{1,2}、渡辺 賢治¹

¹慶應大学・医・漢方医学センター、²東京都老人総合研究所ニューロングリア研究、³小野薬品工業株式会社

O17-6 オリゴデンドロサイトにおけるセマフォリン 4D の発現

○山口 航¹、玉井 里枝¹、谷口 佳孝²、古山 達雄³、稲垣 忍¹

¹大阪大学大学院医学系研究科生体情報科学講座神経生物学、²大阪大学大学院歯学系研究科顎口腔病因病態制御学講座、³香川県立保健医療大学教養部解剖学・生理学

9月12日(金)

16:25~18:25(D会場)

O18-1~O18-6 神経細胞分化

座長:野村 靖幸(横浜薬科大学)

吉川 和明(大阪大学 蛋白質研究所 神経発生制御研究室)

O18-1 Neural Stem Sphere 法によるヒト ES 細胞の神経細胞への一方向的な分化誘導

○大津 昌弘^{1,2}、稲田 大助¹、久米 伸恵¹、祭 友昭^{1,3}、百木 智子¹、中山 孝^{1,4}、鈴木 豊⁵、近藤 靖⁵、笠井 久隆¹、井上 順雄¹¹首都大院・人間健康科学・神経再生科学、²杏林大・医・化学、³慈恵医大・整形外科、⁴横浜市立大・医・生化学、⁵田辺三菱製薬・先端研

O18-2 グループ III 型代謝調節性グルタミン酸レセプターによる神経系前駆細胞の分化制御

○MAKANGA JULIET O.¹、吉田 浩平¹、福井 正樹¹、中道 範隆¹、米田 幸雄¹¹金沢大院・薬・薬物学

O18-3 ES 細胞からの新規セロトニン神経細胞分化誘導系の確立

○嶋田 健¹、高井 良宏¹、篠原季久子¹、橋本 均^{1,2}、新谷 紀人¹、馬場 明道¹¹大阪大院・薬・神経薬理、²大阪大院・医・子どものこころの発達研究センター

O18-4 ES 細胞由来神経幹細胞の分化過程における神経特異的遺伝子 BRINP ファミリーの発現誘導と機能の解析

○寺島 理代¹、小林三和子^{2,3}、本宮 真¹、井上 順雄⁴、岩崎 倫政¹、三浪 明男¹、松岡 一郎^{2,3,5}¹北海道大学大学院 医学研究科 整形外科、²北海道大学 創成科学共同研究機構、³松山大学 薬学部 生理化学研究室、⁴首都大学東京 健康福祉学部大学院 人間健康科学研究科 フロンティアヘルスサイエンス系、⁵北海道大学 大学院薬学研究科

O18-5 網膜桿体細胞分化におけるクロマチン構造変化のダイナミクス

○味岡 逸樹¹、Donovan Stacy¹、Michael Dyer^{1,2}¹セント・ジュード小児研究病院・発生神経生物学部門、²テネシー州立大学・医学部・眼科学

O18-6 マウス胎生繊維芽細胞の培養条件が胚性幹細胞の増殖と分化に及ぼす影響

山之端万里¹、○北沢 啓子¹、久米 伸恵²、大津 昌弘^{2,3}、井上 順雄²¹創価大・工・環境共生工学・発生再生科学、²首都大学東京・院・人間健康科学・神経再生科学、³杏林大学・医・化学

9月12日(金)

16:25~18:25(E会場)

O19-1~O19-6 β アミロイド

座長:駒野 宏人(岩手医科大学 薬学部 神経科学講座)

荒木 亘(国立精神・神経センター神経研究所 疾病研究第六部)

- O19-1 アミロイド β は神経細胞においてマクロオートファジーを誘導する
○鎌形英一郎¹、工藤 喬¹、谷向 仁¹、武田 雅俊¹
¹大阪大院・医・精神医学
- O19-2 A β 繊維化に關与する GM1 ガングリオシド集積を誘導するエンドサイトーシス経路障害
○湯山 耕平¹、山本 直樹^{1,2,3}、柳澤 勝彦¹
¹長寿医療セ・アルツハイマー病、²日本学術振興会、³立命館大学・薬
- O19-3 BACE による切断の基質特異的阻害ニューレグリン1の細胞外ドメイン分離に影響を与えずにベータ切断を阻害することは可能か
○児玉 高志¹、伊藤 尚弘¹、大河内正康¹、田上 真次¹、柳田 寛太¹、中山 泰亮¹、辰巳 真一¹、姜 経緯¹、森 康治¹、西富 晃平¹、武田 雅俊¹
¹大阪大学大学院医学系研究科精神医学
- O19-4 アミロイド前駆体蛋白の膜内蛋白分解を調節する膜結合因子の特徴
○森 康治¹、大河内正康¹、田上 真次¹、児玉 高志¹、柳田 寛太¹、福森 亮雄¹、姜 経緯¹、辰巳 真一¹、西富 晃平¹、中山 泰亮¹、武田 雅俊¹
¹大阪大学・精神医学
- O19-5 アミロイド β タンパク質の神経細胞膜輸送における RAGE および p38 MAPK の役割
○田熊 一徹^{1,2}、溝口 博之^{2,3}、スターン デイビッド⁴、山田 清文^{2,3}、ヤン シェドゥー⁵
¹大阪大院・薬・複合薬物動態、²金沢大院・自然科・薬物治療、³名古屋大院・医・医療薬学、⁴シンシナティ大・医、⁵コロンビア大・医・病理
- O19-6 M-CSF 欠損マウスにおける血漿中 A β の濃度
○辰巳 真一¹、姜 経緯¹、大河内正康¹、田上 真次¹、柳田 寛太¹、中山 泰亮¹、森 康治¹、児玉 高志¹、武田 雅俊¹
¹大阪大学大学院医学系研究科精神医学

9月12日(金)

16:25~18:25 (F会場)

O20-1~O20-6 認知症

座長：中村 重信(洛和会京都治験・臨床研究支援センター)
森 望(長崎大学 医学部 神経形態学)

- O20-1 プレセニリンガンマセクレターゼ修飾薬の生理活性について
○田上 真次¹、大河内正康¹、武田 雅俊¹
¹大阪大学
- O20-2 プレセニリン1と2の比活性の違いを決定しているドメインの同定
○城谷 圭朗¹、橋本 康弘¹、畠山 鎮次²
¹福島県立医科大学・生化学講座、²北海道大学大学院医学研究科・医学専攻・生化学講座・医化学分野

- O20-3 γ -セクレターゼ阻害薬の Wnt シグナル抑制作用に Presenilin は関与しない
○中山 泰亮¹、大河内正康¹、田上 真次¹、児玉 高志¹、柳田 寛太¹、姜 経緯¹、森 康治¹、辰巳 真一¹、森原 剛史¹、橋本 亮太¹、田中 稔久¹、工藤 喬¹、武田 雅俊¹
¹大阪大学大学院医学系研究科精神医学教室
- O20-4 アルツハイマー病病理にかかわるマウスの遺伝子背景について (APP トランジェニックマウスを用いて)
○横小路美貴子¹、森原 剛史¹、林 紀行¹、田上 真次¹、武田 雅俊¹
¹大阪大院・医・精神
- O20-5 ApoE3 によるコレステロール搬出に及ぼすホモシステインの阻害作用
○源川 博久¹、Gong Jian-Sheng¹、Lund-Katz Sissel²、Phillips Michael²、斎藤 博幸³、道川 誠¹
¹国立長寿医療センター研究所・アルツハイマー病研究部、²ペンシルバニア医科大学、³神戸薬科大学
- O20-6 14-3-3 による 3 リピートおよび 4 リピートタウ蛋白の重合化の検討
○サディック ゴラム¹、田中 稔久¹、加藤希世子¹、柳 健太郎¹、武田 雅俊¹
¹大阪大院・医・精神医学

9 月 13 日 (土)

9 : 00 ~ 12 : 00 (B 会場)

O21-1 ~ O21-9 神経回路網形成

座長：武井 延之 (新潟大学・脳研究所・分子神経生物学)
加藤 聖 (金沢大学大学院医学系研究科 脳情報分子学)
渡邊 和忠 (長岡技術科学大学・生物系)

- O21-1 神経回路網形成を司る新規分子 LOTUS の同定
○佐藤 泰史^{1,2,3}、山口めぐみ¹、池谷 真澄¹、有江 裕子¹、中村 史雄¹、川崎 能彦⁴、平田たつみ⁴、五嶋 良郎^{1,3}、竹居光太郎^{1,3}
¹横浜市大院・医・分子薬理神経、²三菱化学・生命研・脳梗塞、³科学技術振興機構・CREST、⁴遺伝研・脳機能
- O21-2 神経回路網形成を司る新規分子 LOTUS の発現パターン
○池谷 真澄¹、佐藤 泰史^{1,2,3}、山口めぐみ¹、有江 裕子¹、金子一関口 晴美¹、中村 史雄¹、五嶋 良郎^{1,3}、竹居光太郎^{1,3}
¹横浜市大院・医・分子薬理神経、²三菱化学・生命研・脳梗塞、³科学技術振興機構・CREST
- O21-3 神経回路網形成を司る新規分子 LOTUS の受容体機能解析
○山口めぐみ¹、佐藤 泰史^{1,2,3}、池谷 真澄¹、有江 裕子¹、金子一関口 晴美¹、中村 史雄¹、五嶋 良郎^{1,3}、竹居光太郎^{1,3}
¹横浜市大院・医・分子薬理神経、²三菱化学・生命研・脳梗塞、³科学技術振興機構・CREST

- O21-4 神経回路網形成を司る新規分子 LOTUS と Nogo-66 受容体との結合様式
○有江 裕子^{1,2}、山口めぐみ¹、佐藤 泰史^{1,3,4}、池谷 真澄¹、金子一関口 晴美¹、
中村 史雄¹、水木 信久²、五嶋 良郎^{1,4}、竹居 光太郎^{1,4}
¹横浜市大院・医・分子薬理神経、²横浜市大院・医・視覚器病態、³三菱化学・生命研・脳梗塞、⁴科学技振興機構・CREST
- O21-5 魚類視神経再生過程における FactorXIII の発現とその機能について
○杉谷 加代¹、山下 友樹¹、加藤 聖²
¹金沢大院・医・保健学専攻、²金沢大院・医・脳情報分子
- O21-6 NB-2 欠損マウスにおける聴性脳幹反応 (ABR) の変化とグルタミン酸作動性シナプスの形成異常
○豊島 学¹、桜井 都衣¹、武田 泰生²、島崎久仁子³、霜田 靖¹、渡邊 和忠¹
¹長岡技大・生物系・神経機能工学、²鹿児島大院・医歯学総合、³自治医大・医・神経脳生理
- O21-7 プロトカドヘリンγコンディショナルターゲティングマウスに認められる異常
○糸賀 康人¹、牧野佳生子¹、平林 敬浩¹、八木 健¹
¹大阪大・院・生命機能
- O21-8 マウス前脳における Robo1 の発現様式
○権田 裕子¹、田畑 秀典²、仲嶋 一範²、内野 茂夫¹、高坂 新一¹
¹国立精神・神経センター・神経研究所・代謝、²慶応大・医・解剖
- O21-9 プルプリンはラット損傷中枢神経系のアポトーシスを保護する
○郡山 恵樹¹、松川 通¹、斉藤 淳一²、野中 真澄²、加藤 聖¹
¹金沢大院・医・脳情報分子学、²金沢大院・医・保健学専攻

9月13日(土)

9:00~12:00 (C会場)

O22-1~O22-9 グリア、ミエリン

座長：佐藤 康二 (浜松医科大学 解剖学)

吉岡 充弘 (北海道大学大学院医学研究科/薬理学講座/神経薬理学分野)

浅井 清文 (名古屋市立大学大学院医学研究科分子神経生物学分野)

- O22-1 神経幹細胞画分における細胞周期調節因子 cyclin D1 はアストロサイト分化を阻害する
○備前 典久¹、井上 俊洋¹、清水 健史²、鹿川 哲史¹、田賀 哲也¹
¹熊本大・発生研・転写制御、²理研・CDB・体軸形成研究チーム
- O22-2 BMPRII 受容体を介した BMP シグナルは、グリア細胞の分化に必須である
○石橋 智子^{1,2}、工藤もゑこ²、岸田 治夫²、カレン リオンス³、山田 真久²
¹東京薬科大学・薬学部・機能形態学、²理化学研究所・脳科学総合研究センター・山田研究ユニット、³脳科学研究所 カリフォルニア大学ロサンゼルス校

- O22-3 新規領域特異的遺伝子導入法とそれを用いたグリア細胞発生機構の解析
○後藤 仁志¹、小野 勝彦¹、竹林 浩秀¹、池中 一裕¹
¹生理学研究所 分子神経生理部門
- O22-4 骨関連遺伝子の脳内における発現
○宝田 剛志¹、黒川晋太郎¹、砺波 佑介¹、小西 志歩¹、米田 幸雄¹
¹金沢大学大学院自然科学研究科
- O22-5 生後初期マウス小脳における PLD4 発現の解析
○大谷 嘉典¹、山口 宜秀¹、吉川 文生²、佐藤 友美²、古市 貞一²、馬場 広子¹
¹東京薬科大学薬学部機能形態学教室、²理研・脳センター・分子神経形成チーム
- O22-6 アストロサイト由来 ATP による海馬神経細胞 M1 ムスカリン性アセチルコリン受容体の発現制御
○藤下加代子¹、井上 和秀²、小泉 修一¹
¹山梨大・院・医工・薬理、²九州大・院・薬・薬理
- O22-7 rotenone により引き起こされる astrocyte gap junctions/hemichannels の変動 (*in vivo, in vitro*)
○河寄 麻実¹、林 奉権²、中地 敬²、古武弥一郎¹、太田 茂¹
¹広島大学医歯薬学総合研究科 生体機能分子動態学講座、²広島放射線影響研究所
- O22-8 リゾレシチン誘導坐骨神経脱髄モデルマウスにおける Annexin2 の役割
○片伯部哲也¹、林 明子¹、馬場 広子¹
¹東京薬科大学大学院薬学研究科機能形態学
- O22-9 末梢神経系パラノーダル・ジャンクション形成異常における軸索ミトコンドリアの変化
○児玉 明子¹、立石 陽子¹、石橋 智子¹、馬場 広子¹
¹東京薬科大学・薬学部・機能形態学

9月13日(土)

9:00~12:00 (D会場)

O23-1~O23-9 神経発達・可塑性

座長：濱 登希子(特許庁審査第三部)

池田 正明(埼玉医科大学 医学部 生理学/ゲノム医学研究センター
分子時計プロジェクト)

一瀬 宏(東京工業大学 大学院生命理工学研究科)

- O23-1 X-連鎖精神遅滞モデルマウスにおける CaMKII/Rac1-GEF/PAK シグナルを介したスパイン形態異常
○塩田 倫史¹、所 崇²、別府 秀幸³、北島 勲²、福永 浩司¹
¹東北大院・薬・薬理学、²富山大院・医・臨床分子病態検査、³ハーバード大・心血管研

- O23-2 発達・精神障害関連遺伝子 CNTNAP2 がコードする Caspr2 のシナプス発達への関与
○有田 和旦¹、霜田 靖¹、酒井 優¹、植田 英寛¹、渡邊 和忠¹
¹長岡技大・生物系
- O23-3 母親の肥満は、仔の肥満および過酸化脂質の蓄積をもたらす
○戸塚 祐介^{1,2}、和田恵津子^{1,3}、和田 圭司^{1,3}
¹国立精神・神経センター神経研究所疾病研究第四部、²財団法人医療機器センター、³戦略的創造研究推進事業
- O23-4 トリブチルスズ経世代曝露による発達期脳の遺伝子発現変化
○若佐 美佳¹、今村 誠¹、吉岡 良祐¹、高橋 理貴¹、根岸 隆之¹、角田 正史²、相澤 好治²、田代 英夫³、田代 朋子¹
¹青山学院大学分子神経生物学研究室、²北里大学医学部衛生学公衆衛生学研究室、³理化学研究所分子計測工学
- O23-5 ラット脳内在性 D-serine 代謝関連遺伝子の発現、局在と発達依存性変化
○山本 直樹¹、嶋津 奈¹、兼松 宗太郎¹、谷口 豪¹、海野 麻未¹、西川 徹¹
¹東京医科歯科大・医歯学・精神行動医科学
- O23-6 後根神経節ニューロンの発生過程における mKirre の発現、およびネフリンとの関連
○森川 吉博¹、小森 忠祐¹、形部 裕昭¹、上野 博夫²、北村 俊雄³、仙波 恵美子¹
¹和歌山県立医科大学医学部第二解剖学、²スタンフォード大学医学部幹細胞再生医学研究所、³東京大学医科学研究所先端医療研究センター細胞療法分野
- O23-7 発達期視覚野における視覚入力による核内ERK活性の制御
○高村 明孝^{1,2}、一坂 吏志³、林 千尋³、牧 廣利³、畠 義郎²
¹大阪大学・院・医・精神医学、²鳥取大学・院・医・生体高次機能学、³鳥取大・医・生命・神経生物
- O23-8 可塑性関連遺伝子 Arc の活動依存的発現調節を担うゲノムエレメントの同定
○奥野 浩行¹、川島 尚之¹、安達-森島 亜希¹、岡村 理子¹、尾藤 晴彦¹
¹東京大学院・医・神経生化学
- O23-9 初代培養ラット小脳顆粒細胞における低カリウム誘発細胞死に対する内因性グルタミン酸の役割
○小柳 洸志¹、高橋 理貴¹、根岸 隆之¹、田代 朋子¹
¹青山学院大学大学院理工学研究科化学・生命科学

9月13日(土)

9:00~12:00 (E会場)

O24-1~O24-9 イオンチャンネル、受容体

座長：野村 正彦(埼玉医大 国際交流センター)

横山 茂(金沢大学大学院医学系研究科脳細胞遺伝子学)

黒木 俊秀(国立病院機構肥前精神医療センター)

O24-1 原子間力顕微鏡を用いた NMDA 受容体の一分子観察

○篠崎 陽一¹、住友 弘二¹、鳥光 慶一¹¹NTT 物性科学基礎研究所

O24-2 未分化神経系前駆細胞に発現する NMDA レセプターの機能解析

○福森 良¹、米山 雅紀¹、小椋 正人¹、中道 範隆¹、米田 幸雄¹¹金沢大院・自然科学・薬物

O24-3 グリシン感受性 NMDA 受容体による神経系前駆細胞の増殖制御

○米山 雅紀¹、後藤 由佳¹、川田 浩一¹、荻田喜代一¹¹摂南大学薬学部薬理学研究室

O24-4 中大脳動脈結紮に伴う脳内グルタメイトレセプターの発現変化

○黒川晋太郎¹、原 智也¹、小西 志歩¹、寶田 剛志¹、中道 範隆¹、米田 幸雄¹¹金沢大院・自然科学・薬物学

O24-5 RGS8 による摂食受容体 MCH1R のシグナリング調節機能

斎藤祐見子¹、齊藤 修²、○宮本真由美¹¹広島大学総合科学研究科、²長浜バイオ大学

O24-6 ヒスタミンH2受容体カルボキシ末端に結合する蛋白質の同定と機能解析

○谷内 一彦¹、徐 阿晶¹、櫻井 映子¹、倉増 敦朗¹¹東北大院・医・機能薬理

O24-7 新規相互作用蛋白質80K-H によるイノシトール3リン酸受容体のカルシウム放出活性制御

○河合 克宏^{1,2}、久恒 智博²、田代 朋子¹、御子柴克彦²¹青山学院大院・理工学・理工学、²独立行政法人理化学研究所 脳科学総合研究センター 発生神経生物研究チーム

O24-8 ジヒドロピリジン誘導体の1種であるアムロジピンによるN型カルシウムチャンネル抑制に重要な領域

○額田 敏秀¹、宮下 順子¹、古川 泰司²、亀ヶ谷悦子¹、吉井 光信³¹東京都精神医学総合研究所 神経情報伝達研究チーム、²帝京大学 医学部 内科学部門、³東京都精神医学総合研究所 神経可塑性研究チームO24-9 α CaMKII mRNA の3'-非翻訳領域に結合するタンパク質群の単離とその機能解析○森 泰丈¹、幸坂 葵¹、宮田 信吾¹、遠山 正彌¹¹大阪大院・医・神経機能形態

9月13日(土)

9:00~12:00(F会場)

O25-1~O25-9 うつ・ストレス

座長: 渡辺 義文(山口大学大学院医学系研究科高次脳機能病態学分野)

渡辺 康裕(防衛医大・薬理)

谷口 泰造(姫路独協大学 薬学部)

O25-1 ストレスによる脳の SNAP-25 のリン酸化の亢進

○菅谷 大地¹、山森 早織¹、板倉 誠¹、高橋 正身¹

¹北里大院・医療系・分子神経生物学

O25-2 母仔分離ストレス負荷ラットにおける転写抑制因子 REST/NRSF を介した遺伝子発現調節異常

○内田 周作¹、原 久美子¹、古林亜由美¹、大舘 孝治¹、渡辺 義文¹

¹山口大院・医・高次脳機能病態学

O25-3 ストレス誘発 HPA-axis 反応における中枢 PACAP の役割

○新谷 紀人¹、斎田 洋子¹、角田 享也²、築山 直弘¹、尾形 勝弥¹、橋本均^{1,2}、馬場 明道¹

¹大阪大院・薬・神経薬理、²大阪大院・医附・子どものこころの研究センター

O25-4 ラット視床下部におけるグルココルチコイド標的遺伝子の大規模解析

○佐藤 大仁¹、堀川 幸男^{2,3}、飯塚 勝美³、桜井 敬子¹、田中 毅¹、志原伸幸³、大嶋 明彦⁴、武田 純^{2,3}、三國 雅彦¹

¹群馬大学大学院医学系研究科神経精神医学分野、²岐阜大学大学院内分泌代謝病態学分野、³群馬大学生体調節研究所疾患ゲノム研究分野、⁴北里大学医学部精神科

O25-5 ジベプチド Leu-Ile は連続強制水泳によって誘導されるうつ様症状を抑制する

○日比 陽子^{1,2}、新田 淳美²、池田 武史³、森下 幸治³、鍋島 俊隆⁴、山田清文²

¹(財)長寿科学振興財団、²名古屋大・病院・薬剤部、³協和発酵・ヘルスケア商品開発センター、⁴名城大薬

O25-6 デセン酸エチルエステルは脳内 MAP キナーゼの活性化を介して抗うつ効果を示す

○古川 昭栄¹、牧野 晃久¹、伊藤 悟¹、福光 秀文¹

¹岐阜薬科大学・薬・生体機能解析学大講座・分子生物

O25-7 マウス脳海馬における PTSD 応答性ミオシン VI の発現

○橘 正毅¹、玉置 啓祐¹、伊東 佑真¹、寶田 剛志¹、谷浦 秀夫¹、中道 範隆¹、米田 幸雄¹

¹金沢大院・自然科学・薬物

O25-8 マウス脳のジヒドロプテリジン還元酵素の局在とジヒドロプテリジン還元酵素欠損マウスにおける生化学的解析

○実近 翔¹、須藤 雄介¹、山下 純平¹、本田俊一郎¹、嶋口 翔¹、小島 雅代¹、一瀬 宏¹

¹東工大院・生命理工・分子生命

O25-9 神経細胞 1 次繊毛の精神疾患への関与

○三好 耕¹、笠原 恭輔¹、宮崎 育子¹、浅沼 幹人¹

¹岡山大院・医歯薬・脳神経制御・神経情報

9月13日(土)

13:20~15:20(C会場)

O26-1~O26-6 疾患モデル2

座長: 仲田 義啓(広島大学大学院・医歯薬学総合研究科)

丹羽 正美(長崎大学大学院医歯薬学総合研究科薬理学(医))

O26-1 MuSK抗体による重症筋無力症発症の分子メカニズム

○重本 和宏¹、久保 幸穂¹、丸山 直記¹、小西 哲郎²、太田 潔江³、太田 光熙⁴

¹都老人研・バイオマーカー、²国病機構宇多野病院・神経内科、³国病機構宇多野病院・臨床研究部、⁴神戸薬大・病態生化学

O26-2 iNOS mRNA の発現を介したピロロキノリンキノンの脊髄損傷修復効果

○平川 明弘^{1,2}、清水 克時²、福光 秀文¹、古川 昭栄¹

¹岐阜薬科大学分子生物科学研究室、²岐阜大学大学院医学系研究科整形外科

O26-3 二次元電気泳動法を用いた脱髄性疾患モデルラット (dmy) の解析

○宮城 雄大¹、山口 宜秀¹、馬場 広子¹

¹東京薬科大学・薬学部・機能形態学

O26-4 FILIP 欠損による大脳皮質の異常と行動異常の検討

○八木 秀司^{1,2}、池田 弘^{2,3}、山崎 信幸⁴、宮川 剛^{4,5}、岡部 勝⁶、謝 敏かく¹、佐藤 真^{1,2}

¹福井大学・医・形態機能医科学講座・組織細胞形態学・神経科学領域、²福井大学・生命科学複合研究教育センター、³福井大学・工学部・知能システム工学科、⁴京都大院・医・先端技術センター・生体遺伝子機能、⁵藤田保健衛生大学総合医科学研究所、⁶大阪大・遺伝情報センター・遺伝子機能解析

O26-5 大脳皮質の神経発生に及ぼす妊娠期感染症の影響

○宗宮 仁美¹、福光 秀文¹、古川 昭栄¹

¹岐阜薬科大学 生体機能解析学大講座 分子生物科学研究室

O26-6 げっ歯類の眼窩前頭皮質は目的志向的行動において行動と報酬に関わる情報を並列にコードする。

○古屋敷智之¹、Ehrlich Aliza¹、Holland Peter²、Gallagher Michela²

¹京都大院・医・神経細胞薬理、²ジョーンズ・ホプキンス大・心理学

9月13日(土)

13:20~15:20(D会場)

O27-1~O27-6 ドパミン系

座長：西尾 廣昭(福山大学薬学部応用薬理学研究室)

五嶋 良郎(横浜市立大学大学院医学研究科 分子薬理神経生物学)

O27-1 ニューロメラニン(ML)はミトコンドリアの脱グルタチオン反応を介し、ドパミン神経細胞死を誘導する

○直井 信¹、丸山和佳子²、永井 雅代²

¹岐阜県国際バイオ研究所・脳神経、²国立長寿医療センター研究所

O27-2 水素水はパーキンソン病モデルマウスにおいてドパミン神経細胞死を抑制する

○藤田 慶大¹、清家 稔博¹、大野みずき²、山口 浩雄²、山田 英孝²、高木 厚司³、城戸 瑞穂⁴、中別府雄作²、野田 百美¹

¹九州大学大学院薬学研究院 病態生理学分野、²九州大学生体医学防御研究所 脳機能制御学分野、³九州大学大学院医学研究院 統合生理学分野、⁴九州大学大学院歯学研究院 硬組織構造解析学分野

O27-3 MPTP 誘発マウスドパミン神経障害に対する新規神経保護物質 T-817MA の作用

○吾郷由希夫¹、川崎 俊之¹、北尾 達哉¹、梨子田哲明¹、高木 明子²、田熊 一敏¹、松田 敏夫^{1,3}

¹大阪大院・薬・複合薬物動態、²富山化学工業(株)・総合研究所・第二研究部、

³大阪大院・医・子どものこころの発達研究センター

O27-4 L-DOPA 投与に特異的な活性化アストロサイトにおけるメタロチオネインの発現誘導

○宮崎 育子¹、吉川 友理¹、木本 直孝¹、三好 耕¹、浅沼 幹人¹

¹岡山大学大学院医歯薬学総合研究科神経情報学

O27-5 ピッコロはメタンフェタミンによるドパミントランスポーターの内在化を抑制する

○新田 淳美¹、せん きしあほ¹、衣斐 大祐¹、丹羽 美苗^{1,2}、山田 清文¹、鍋島 俊隆^{1,2}

¹名古屋大院・医療薬学・附属病院・薬剤部、²名城大学大学院薬学研究科臨床薬学専攻病態解析学コース薬品作用学教室

O27-6 新規機能分子“shati”はメタンフェタミン誘発ドパミン取り込み能低下を抑制する

○丹羽 美苗^{1,2,3}、新田 淳美²、Cen Xiaobo²、尾崎 紀夫¹、鍋島 俊隆^{2,3}

¹名大院医・精神医学、²名大院・医・医療薬学・附属病院薬剤部、³名城大院・薬・薬品作用学

9月13日(土)

13:20~15:20 (E会場)

O28-1~O28-6 神経細胞死 2

座長: 榎戸 靖 (東京医科歯科大学 難治疾患研究所)

池田 穰衛 (東海大学大学院医学研究科先端医科学/脳・神経変性疾患研究センター)

O28-1 β アミロイド前駆体蛋白質のプロセッシングに及ぼす効果は2つのシタキシン5アイソフォーム間で異なる○須賀 圭¹、齋藤 綾子¹、富山 貴美²、森 啓²、赤川 公朗¹¹杏林大・医・細胞生理、²大阪市立大・医・脳神経科学

O28-2 アルツハイマー病マウスモデル大脳皮質における calsynenin-3 の発現変化とその意味

○内田 洋子¹、五味不二也¹¹東京都老人総合研究所老年病ゲノムT

O28-3 ミトコンドリアプロテアーゼ Omi/HtrA2 の基質タンパク質の探索と解析

○鈴木 泰行¹、田中 修二¹、和田 圭司¹、高橋 良輔²¹国立精神・神経センター 神経研究所 疾病研究第四部、²京都大学大学院医学研究科 臨床神経学O28-4 マウス脳シナプトソームにおける MPP⁺ 誘発ミトコンドリア機能障害○小林 星太¹、兼城みずき¹、野村 昌平¹、松島 大章¹、室山 明子¹、光本 泰秀¹¹北陸大学・薬・代替医療薬学

O28-5 環境汚染化学物質トリブチルスズが惹起するグルタミン酸脆弱性

○古武弥一郎¹、中津 祐介¹、日野 渥子¹、瀧下 智子¹、太田 茂¹¹広島大院・医歯薬

O28-6 トリメチルスズによる海馬 glutathione S-transferase の発現増強

○佐野 尚平¹、長嶋 玲子¹、荻田喜代一¹¹摂南大学大学院薬学研究科薬理研究室

9月13日(土)

13:20~15:20 (F会場)

O29-1~O29-6 記憶・学習のメカニズム

座長: 永田栄一郎 (東海大学医学部神経内科)

田中佐知子 (昭和大学薬学部毒物学教室)

O29-1 Sominoneによる記憶促進作用および分子メカニズムの検討

○城屋敷枝里¹、東田 千尋¹¹富山大学和漢医薬学総合研究所民族薬物研究センター薬効解析部

- O29-2 ミクログリア活性化学習記憶障害モデルマウスの神経変性機構-サイトカインノックアウトマウスを用いて-
○神田 錦吾¹、田中佐知子¹、中町 智哉²、塩田 清二²、沼澤 聡¹、吉田 武美¹
¹昭和大院・薬・毒物、²昭和大・医・解剖
- O29-3 A β 処置マウス海馬でのニューロフィラメントLが過剰にニトロ化されると認知障害が誘導される
○アルカム トルソン^{1,2}、新田 淳美¹、溝口 博之¹、伊藤亜紀雄¹、山田 清文¹、鍋島 俊隆^{1,3}
¹名大大院・医・神経精神薬理、²ウイゲル伝統医・基医、³名城大院・薬・薬品作用学
- O29-4 Na⁺/Ca²⁺ 交換体 (NCX2) 欠損マウスはカルシウム/カルモデュリン依存性プロテインキナーゼ II の機能低下による認知機能不全を誘発する
○森口 茂樹¹、韓 峰¹、喜多紗斗美²、小室 一成³、岩本 隆宏²、福永 浩司¹
¹東北大院・薬・薬理、²福岡大・医・薬理、³千葉大院・医・循環病態医科学
- O29-5 文脈性恐怖記憶の消去学習における内側前頭前野の時限付き関与
○関口 正幸¹、圖子田 康¹、和田 圭司¹
¹国立精神神経センター・神経研究所・疾病研究第四部
- O29-6 KIBRA 遺伝子の遺伝子多型は日本人の健常者の記憶に関連する
○安田 由華^{1,2}、橋本 亮太^{1,2}、大井 一高²、高村 明孝²、福本 素己²、井池直美²、桐林 雅子²、吉田 哲彦²、高橋 秀俊²、森原 剛史²、田上 真次²、大河内正康²、田中 稔久²、工藤 喬²、紙野 晃人³、石井 良平²、岩瀬 真生²、数井 裕光²、武田 雅俊^{1,2}
¹大阪大学大学院医学系研究科附属子どものこころの分子統合機構研究センター疾患関連分子解析部門、²大阪大学大学院医学系研究科情報統合医学講座精神医学教室、³国立病院機構 松籟荘病院

ポスター

9月11日(木)

15:20~16:00(ポスター会場)

P-01~P-05

グリア

座長: 平 英一(岩手医科大学薬理学講座)

- P-01 apoA-I と ABCA1 相互作用を介した phospholipase Cgamma の活性化と HDL 新生促進
○伊藤 仁一¹、長安 祐子¹、横山 信治¹
¹名古屋市立大学大学院医学研究科生物化学
- P-02 ミクログリアの代謝的特徴
○金松 知幸¹、中嶋 一行²、澤 紀子¹
¹創価大学工学部環境共生工学科、²創価大学工学部生命情報工学科
- P-03 脊髄損傷によりマクログリアで PRMT8 の発現が誘導される
○幸坂 葵¹、小山 佳久¹、森 泰丈¹、遠山 正彌^{1,2}
¹大阪大院・医・神経機能形態、²大阪大院・医・子どものこころの分子統御機構研究センター
- P-04 マウス中枢神経系グリア細胞系譜の解析
○鹿川 哲史¹、清水 健史¹、荒木 喜美¹、竹田 直樹²、田賀 哲也¹
¹熊本大学発生医学研究センター、²熊本大学生命資源研究・支援センター
- P-05 視床下部における新生グリア細胞と体重増加との関わり
○山内 崇平¹、牧之段 学¹、辰巳 晃子²、奥田 洋明²、竹田 友彦¹、定松 美幸¹、岸本 年史¹、和中 明生²
¹奈良県立医科大学精神科、²奈良県立医科大学第2解剖学

9月11日(木)

15:20~16:00(ポスター会場)

P-06~P-10

神経細胞死

座長: 秋山 一文(獨協医科大学医学部精神生物学講座)

- P-06 初代培養ミクログリアの生存期間に及ぼすリポポリサッカライドの影響
○金子 葉子¹、中島 昭¹、森 啓至¹、永津 俊治²、永津 郁子³、太田 明¹
¹藤田保健衛生大・医・生理 I、²藤田保健衛生大・医・薬理、³藤田保健衛生大・医・解剖 II
- P-07 内因性終末糖化産物のアルツハイマー病進展への関与
○村松 充¹、佐藤 隆¹、竹内 正義¹
¹北陸大学 薬学部 病態生理化学

- P-08 新規インビトロ血液脳関門モデルの確立とその機能解析
○片山 貴博¹、坂口 絵美¹、南 雅文¹
¹北海道大院・薬・薬理学
- P-09 ミクログリアは神経細胞のトランスフェリン非依存性鉄輸送系を抑えることにより神経細胞死を抑制する。
○大城 聡¹、森岡 勝樹²、中嶋 一行³
¹大東大・健康・細胞生物、²東京医科歯科大学、院疾患生命、疾患生命情報学、³創価大学 工学部 神経科学
- P-10 酸化ストレス誘発性神経細胞死において、核内 GAPDH が PARP-1 を活性化する
○小野 葉子¹、居原 秀²、中嶋 秀満¹、東 泰孝¹、竹内 正吉¹
¹大阪府立大学院・生命環境科学・応用薬理、²大阪府立大学 理学部

9月11日(木)

15:20~16:00 (ポスター会場)

P-11~P-15 遺伝子発現

座長：古市 貞一 (理化学研究所 脳科学総合研究センター)

- P-11 ニューロブシン欠損マウスの炎症皮膚で発現変動する遺伝子の解析
○新垣 健太¹、谷口 学¹、松崎 伸介^{1,2}、遠山 正彌^{1,2}
¹大阪大院・医・神経機能形態、²大阪大学医学部医学系研究科子どものこころの分子制御機構研究センター
- P-12 癌転移関連糖タンパク gpnmb のラット中枢神経系における発現
○黄 健軍¹、馬 文ショウ¹、東田 陽博¹、横山 茂¹
¹金沢大学大学院医学系研究科脳細胞遺伝子学
- P-13 視神経損傷後のゼブラフィッシュ網膜における HSP70 の遺伝子発現
○藤川千恵子¹、永島 幹子²、馬渡 一浩²、加藤 聖³
¹金沢大・医・保健学、²金沢大院・医・保健学、³金沢大院・医・脳細胞分子学
- P-14 慢性社会的ストレスが行動および脳内遺伝子に与える影響
○築地 謙治¹、生井 和樹¹、漆瀬 道洋¹、皆川 紗代¹、中田 英之¹、石毛 敦¹、渡辺 賢治¹
¹慶應義塾大学医学部 漢方医学センター
- P-15 脳神経組織における MAGI-1 の性状解析
○伊東 秀記¹、森下 理香¹、須藤 香織¹、岩本 郁子¹、篠田 友靖¹、岡本 賢一¹、永田 浩一¹
¹愛知県コロニー・研・神経制御

9月11日(木)

15:20~16:00 (ポスター会場)

P-16~P-20

加齢・認知症

座長：笠井 久隆 (首都大学東京)

P-16 老化促進モデルマウス SAMP8 の学習記憶能における食餌成分およびカロリー制限の影響

○千葉 卓哉¹、小松 利光¹、山座 治義¹、山下樹三裕²、島田 厚良³、樋上 賀一⁴、デカボ ラファエル⁵、イングラム ドナルド⁶、下川 功¹¹長崎大院・医歯薬総合・探索病理、²長崎大学・環境科学部・自然環境保全講座、³愛知県心身障害者コロニー発達障害研究所・病理学部、⁴東京理科大学・薬学部・分子病理・薬物代謝、⁵米国立老化研究所、⁶ルイジアナステート大学システム

P-17 抑肝散のセロトニン1A 受容体に対するパーシャルアゴニスト作用

○寺脇 潔¹、関口 協二¹、山口 琢児¹、今村 幸子¹、菅野 仁美¹、五十嵐 康¹、加瀬 義夫¹¹株式会社ツムラ ツムラ研究所

P-18 コレステロールホメオスタシスにおけるアミロイドベータの新しい機能

○梅田 知宙¹、チェン フィ²¹大阪市立大院・医・老年研脳神経科学、²ベイラー医科大学ハフフントン老化センターP-19 Presenilin/ γ -secretase による Notch S3 切断の高感度な検出法の開発○柳田 寛太¹、大河内正康¹、田上 真次¹、西富 晃平¹、中山 泰亮¹、児玉 高志¹、姜 経緯¹、辰巳 真一¹、森 康治¹、武田 雅俊¹¹大阪大学大学院・医学系研究科・内科系臨床医学専攻・情報統合医学講座・精神医学分野P-20 A β は ATBF1 の発現を上昇させ神経細胞死を誘導する○鄭 且均¹、川口 誠²、三浦 裕³、赤津 裕康⁴、金 泰善³、道川 誠¹¹国立長寿医療センター研究所、²新潟労災病院、³名古屋市大・医研・分子神経生物、⁴福祉村病院・長寿医学研究所

9月11日(木)

15:20~16:00 (ポスター会場)

P-21~P-25

神経幹細胞

座長：荒川 義弘 (東京大学医学部附属病院臨床試験部)

P-21 PACAP による大脳皮質神経細胞の層特異的性質の決定

○福光 秀文¹、大塚 正成¹、古川 昭栄¹¹岐阜薬科大学学生体機能解析学大講座分子生物学研究室

- P-22 神経特異的 BRINP ファミリーのタンパク質相互作用の解析
○松岡 一郎¹、一色 真明³、久永 真市⁴、小林三和子^{1,2}
¹松山大学薬学部、²北海道大学創成科学共同研究機構、³北海道大学大学院薬学研究
院、⁴首都大学東京大学院理工学研究科
- P-23 マウス胚性幹細胞から神経系細胞への分化に対する塩化メチル水銀の影響
○稲田 大助¹、大津 昌弘^{1,2}、小林 肇¹、村上 拓治¹、中山 孝³、笠井
久隆¹、井上 順雄¹
¹首都大院・人間健康科学研究科・神経再生科学、²杏林大・医・化学、³横浜市大
医・生化学
- P-24 神経細胞および神経幹細胞ダメージに対する外来性神経幹細胞の効果
○小野 貴文¹、鵜飼 渉¹、石井 貴男²、吉永 敏弘¹、渡邊 公彦¹、橋本 恵
理¹、渡邊 一平¹、白坂 知彦¹、館農 勝¹、齋藤 諭¹、齋藤 利和¹
¹札幌医科大学医学部神経精神医学講座、²札幌医科大学保健医療学部作業療法学
科
- P-25 PRC1 複合体のマウス胚 cortex での発現解析
○イスラム モハマド-サハル^{1,4}、小泉 恵太^{2,4}、吉原 亨^{2,4}、浅野 雅秀^{3,4}、
東田 陽博^{1,2,4}、
¹金沢大学大学院医学系研究科脳細胞遺伝子、²金沢大学子どものこころの発達研
究センター、³金沢大学学際科学実験センター、⁴金沢大学21世紀 COE プログラム、
発達・学習・記憶と障害の革新脳科学の創成

9月12日(金)

15:45~16:25 (ポスター会場)

P-26~P-30 ミエリン、脱髄

座長：南 雅文（北海道大学大学院薬学研究院薬理学研究室）

- P-26 脱髄モデルマウスにおける神経伝導の特性
○板東 良雄¹、高草木 薫²、吉田 成孝¹
¹旭川医大・解剖学講座・機能形態学、²旭川医科大学 生理学講座
- P-27 発達段階による MBP isoforms の分布や特性の違い
○漆瀬 道洋^{1,2}、築地 謙治¹、佐藤菜名子^{1,3}、佐藤友里恵¹、石毛 敦¹、阿相
皓晃^{1,3}、深井 文雄²、渡辺 賢治¹
¹慶應義塾大学医学部漢方医学センター、²東京理科大学薬学部分子病態学研究室、
³東京都老人総合研究所グリア細胞研究グループ
- P-28 ラット前頭眼窩野と視覚野における神経突起伸展や髄鞘化に関わる分子の生後発
達変化
○一坂 吏志¹、佐野 香織²、宮原 愛美¹、山本 朱乃¹、日比野里美²、小島 一
宏²、畠 義郎^{1,2}
¹鳥取大・医・生命・神経生物、²鳥取大・院・医・生体高次機能

P-29 ミエリン画分におけるミオシン 1D の解析

○山口 宜秀¹、宮城 雄大¹、石川 詩帆¹、馬場 広子¹¹東京薬科大学・薬学部・機能形態学教室

P-30 実験的脳炎モデル (EAE) における B7-H3 および B7-H4 の役割

○板東 良雄^{1,2}、Zhu Bing²、Chitnis Tanuja²、吉田 成孝¹、Khoury Samia²¹旭川医大・解剖学講座・機能形態学、²米国ハーバード大学・ブリガム女性病院・神経変性疾患センター

9月12日 (金)

15:45~16:25 (ポスター会場)

P-31~P-35 神経発達・可塑性

座長: 中村 俊 (国立大学法人東京農工大学大学院共生科学技術研究院)

P-31 マウスでの豊かな環境によるニューロブシンへの影響

塩坂 貞夫¹, ○小暮 洋子¹、石川 保幸¹¹奈良先端科学技術大学院大学バイオサイエンス研究科細胞構造学

P-32 発生中大脳皮質におけるリーリンシグナルの役割の解析

○久保健一郎¹、本田 岳夫¹、富田 憲司¹、田畑 秀典¹、仲嶋 一範¹¹慶應義塾大学医学部解剖学

P-33 Sept14の皮質神経細胞局在化における機能

○篠田 友靖¹、伊東 秀記¹、須藤 香織¹、岡本 賢一¹、岩本 郁子¹、森下 理香¹、永田 浩一¹¹愛知県コロニー発達障害研究所・神経制御学部

P-34 結節性硬化症におけるスパイン異常のメカニズム

○杉浦 弘子¹、瀧上 周¹、安田 新¹、吉村 好之²、竹宮 孝子¹、山内 卓²、樋野 興夫³、山形 要人¹¹東京都医学研究機構・神経研、²徳島大学 HBS・薬学部・生化学研究室、³順天堂大学・医学部・病理・腫瘍学講座

P-35 マウスの父親の養育行動

○劉 鴻翔¹、ロパチナ オリガ¹、東田 陽博¹¹金沢大・医薬保健学域・脳細胞遺伝子

9月12日 (金)

15:45~16:25 (ポスター会場)

P-36~P-40 疾患モデル

座長: 山本 秀子 ((財) 東京都医学研究機構・東京都精神医学総合研究所)

P-36 ケタミン連続投与による行動感作の獲得

○山本 敏文¹、中山 朋美¹、山本 秀子²
¹横浜市大院・国際総合科学研究科、²都精神研・精神生物学分野

P-37 産褥期のストレスは仔の成長傷害を引き起こす

○中田 英之¹、西村 甲¹、高 鵬飛¹、村上 優¹、築地 謙治¹、石毛 敦¹、渡辺 賢治¹
¹慶應義塾大学医学部 漢方医学センター

P-38 シグマ受容体情報伝達と覚せい剤による常同行動

○北中 純一¹、北中 順恵¹、立田 知大²、田中 康一³、西山 信好³、守田 嘉男²、竹村 基彦¹
¹兵庫医大・薬理、²兵庫医大・精神科神経科、³兵庫医療大・薬・薬理

P-39 リコピンを摂取したスナネズミでは一過性の脳虚血後海馬の SOD 活性値が増加した

○藤田 公和¹、芳本 信子²、松本 岳³、稲熊 隆博³、加藤 寿章⁴、今田 英己¹、永田 豊¹、宮地 栄一¹
¹藤田保衛大・医・生理、²名古屋文理大学短大部・食品科学、³カゴメ株式会社、総合研究所、⁴藤田保衛大短大部・臨床検査学

P-40 止瀉薬成分の神経細胞保護作用

○中村有加里¹、松島 伸行²、森口 展明^{1,2}、柴田 仁²、神戸 悠輝¹、中道 範隆¹、米田 幸雄¹
¹金沢大院・自然科学・薬物、²大幸薬品株式会社

9月12日(金)

15:45~16:25 (ポスター会場)

P-41~P-45 遺伝子解析、他

座長：桑野 良三 (新潟大学脳研究所附属生命科学リソース研究センター)

P-41 NRG 1 遺伝子と覚醒剤使用障害患者の関連解析

○大河内 智¹、岸 太郎¹、池田 匡志¹、北島 剛司¹、木下 葉子¹、川島 邦裕¹、奥村 武則¹、角鹿 智子¹、稲田 俊哉²、山田 光彦²、内村 直尚²、伊豫雅臣²、曾良 一郎²、尾崎 紀夫²、氏家 寛²、岩田 伸生^{1,2}
¹藤田保健衛生大学精神医学教室、²多施設覚醒剤使用障害遺伝子研究グループ

P-42 日本人気分障害と CLOCK 遺伝子との関連解析

○岸 太郎¹、北島 剛司¹、池田 匡志¹、山之内芳雄¹、木下 葉子¹、川島 邦裕¹、大河内 智¹、奥村 武則¹、角鹿 智子¹、尾崎 紀夫²、岩田 伸生¹
¹藤田保健衛生大学病院医学部精神医学教室、²名古屋大学大学院医学系研究科精神医学・親と子どもの心療学分野

P-43 日本人双極性障害患者および統合失調症患者におけるセロトニン・トランスポーター遺伝子多型の解析

○光安 博志¹、後藤 玲央¹、小林 祐樹¹、織部 直弥¹、高田 篤¹、土持 諒輔²、川崎 弘昭¹、神庭 重信¹
¹九州大院・医・精神病態医学、²九州大学医学部

- P-44 オランザピン, ハロペリドール連投後のラットにおけるアリピプラゾールの影響
-運動量を用いた評価-
○広瀬 毅¹、二村 隆史¹、ジョーダン ショーン²、マックウェード ロバート³、
菊地 哲朗¹
¹大塚製薬株式会社 Qs' 研究所、²大塚メリーランドメディカルラボラトリーズ
ニューロサイエンスリサーチ、³大塚ファーマシューティカルディベロップメント
アンドコマーシャライゼーション
- P-45 UCH-L1 と UCH-L3 によるエネルギー代謝制御
○鈴木 マリ¹、節家理恵子¹、和田 圭司¹
¹国立精神・神経センター 神経研究所 疾病研究第四部

9月12日(金)

15:45~16:25 (ポスター会場)

- P-46~P-50 神経免疫・内分泌、他
座長：長池 一博 (株式会社 免疫生物研究所)
- P-46 LPS誘導末梢性炎症による脳内甲状腺ホルモンシステムの変化
○高橋 理貴^{1,2}、根岸 隆之¹、澤野恵梨香¹、田代 朋子¹
¹青山学院大学大学院理工学研究科、²日本学術振興会
- P-47 培養アストロサイトにおける LPS 誘導性のトランスグルタミナーゼ 2 の発現と
NO産生の関与
○高野 桂¹、白岩 謙介¹、森山 光章¹、中村 洋一¹
¹大阪府立大院・生命環境科学・獣医・統合生理
- P-48 緑茶成分による [³H] ゲルタミン取り込み阻害
○利波 佑介¹、角田 隆巳²、野澤 歩²、小椋 正人¹、宝田 剛志¹、檜井 栄
一¹、米田 幸雄¹
¹金沢大院・自然科学・薬物、²伊藤園中央研究所
- P-49 マウス舌におけるグルコーストランスポーターの分布
○石田 雄介¹、鶴川 真也¹、植田 高史¹、島田 昌一¹
¹名古屋市立大院・医・機能組織学
- P-50 糖尿病と海馬-臨床的および実験的研究-
○鬼頭 昭三¹、新郷 明子²
¹順心会幸生リハビリテーション病院、²兵庫大学健康科学部

ランチョンセミナー

9月11日(木)

12:15~13:15 (A会場)

LS-1

共催：エーザイ株式会社

座長：辻 省次 (東京大学大学院医学系研究科)

Modification of Tau Proteins by Nitritative Oxidation in Tauopathies.

Binder, Lester I., Reyes, Juan F., Reynolds, Matthew R., and Vana, Laurel C.

Feinberg School of Medicine, Northwestern University

9月12日(金)

12:05~13:05 (A会場)

LS-2

共催：明治製菓株式会社

座長：仲嶋 一範 (慶應義塾大学医学部)

Pharmacogenomics of Obesity and Depression

Julio Licinio

University of Miami Miller School of Medicine

9月13日(土)

12:15~13:15 (A会場)

LS-3

共催：グラクソ・スミスクライン株式会社

座長：武田 雅俊 (大阪大学大学院医学系研究科精神医学教室)

精神科薬物治療の個別化を目指して：薬理ゲノム学の現状と課題

染矢 俊幸

新潟大学大学院医歯学総合研究科精神医学分野

Special Lecture

September 11 (Thursday)

11 : 00 ~ 12 : 00 (Room A)

SL-1

Chair : Katsuhiko Mikoshiba (RIKEN Brain Science Institute)

Pharmacogenomics of Antidepressant Treatment Response

Julio Licinio

University of Miami Miller School of Medicine

September 12 (Friday)

14 : 15 ~ 15 : 15 (Room A)

SL-2

Chair : Masatoshi Takeda (Osaka University Graduate School of Medicine)

The Structure and Function of Abnormal Tau in Alzheimer's Disease

Binder, L.I.¹, Lapointe, N.E.^{1,3}, Guillozet, A.¹, Morfini, G.^{2,3}, Pignio, G.^{2,3}, and Brady, S.T.^{2,3}

¹Feinberg School of Medicine, Northwestern University, ²University of Illinois at Chicago,

³Marine Biological Laboratory

Educational Lecture

September 11 (Thursday)

9 : 45 ~ 10 : 45 (Room A)

EL-1

Chair : Masaya Tohyama (Osaka University Graduate School of Medicine)

Static and Dynamic Functions of Microglia in Health and Disease

Shinichi Kohsaka

National Center of Neurology and Psychology

Open Symposium

September 11 (Thursday)

16 : 30~18 : 30 (Room A)

OS-1~OS-4 Mechanism of Corticogenesis -Contribution from Neurochemistry-
 Chairs : Haruhiro Higashida (Kanazawa University 21st Century COE Program
 on Innovative Brain Science)
 Kozo Kaibuchi (Nagoya University Graduate School of Medicine)

- OS-1 Axon formation and axonal transport
 ○Kozo Kaibuchi¹
¹Nagoya University Graduate School of Medicine, Department of Cell Pharmacology
- OS-2 How is the neural network restored after brain injury?
 ○Toshihide Yamashita¹
¹Dept. of Mol. Neurosci., Med., Osaka Univ.
- OS-3 Microscopic migration disorder: a possible cause of some neurological/psychiatric diseases
 ○Makoto Sato^{1,2}
¹Division of Cell Biology and Neuroscience, Department of Morphological and Physiological Sciences, Faculty of Medical Sciences; ²Research and Education Program for Life Science, University of Fukui, Fukui, Japan
- OS-4 Molecular mechanism underlying glucocorticoid-induced impairment of neuronal migration
 ○Kenji Sobue¹, Kentaro Fukumoto¹, Taira Mayanagi¹
¹Osaka University Graduate School of Medicine, Department of Neuroscience

Joint Symposium with 30th Annual Meeting of Japanese Society of Biological Psychiatry

September 13 (Saturday)

13 : 20 ~ 16 : 00 (Room B)

- JS-1 ~ JS-6 Clues to the pathophysiology and treatment of psychiatric disorders through integrating neurochemistry and psychiatry
Chairs : Toshikazu Saito (Sapporo Medical University)
Kazuhiro Ikenaka (National Institute of Physiological Sciences)
- JS-1 Involvement with nitric oxide in pathophysiology of depression
○Atsuko Ikenouchi-Sugita¹
¹Department of neuropsychiatry, University of Occupational and Environmental Health
- JS-2 Platelet intracellular calcium mobilization in bipolar disorders and beyond
○Katsuji Suzuki¹
¹Department of Psychiatry, Hokkaido University Graduate School of Medicine
- JS-3 The effects of monoaminergic regulation on cognitive dysfunction and how it exerts one's action
○Yosefu Arime¹, Ichiro Sora¹
¹Department of Biological Psychiatry, Tohoku University Graduate School of Medicine
- JS-4 Role of tPA-plasmin system in neuropsychological abnormalities induced by morphine.
○Taku Nagai¹, Toshitaka Nabeshima^{1,2}, Kiyofumi Yamada¹
¹Department of Neuropsychopharmacology and Hospital Pharmacy, Nagoya University Graduate School of Medicine, ²Department of Chemical Pharmacology, Graduate School of Pharmaceutical Sciences, Meijo University, Nagoya
- JS-5 DISC1 regulates the dendritic localization of IP3R1 mRNA in hippocampal neuron
○Daisuke Tsuboi¹, Shinichiro Taya¹, Tomoyasu Shinoda¹, Kozo Kaibuchi¹
¹Department of Cell Pharmacology, Graduate School of Medicine, Nagoya University
- JS-6 Arachidonic acid increases neurogenesis and restores prepulse inhibition deficits in model rats
○Motoko Maekawa^{1,2,3}, Noriko Takashima⁴, Miho Matsumata^{1,5}, Shiro Ikegami⁶, Masanori Kontani⁷, Yoshinobu Hara^{1,5}, Hiroshi Kawashima⁷, Yuji Owada⁸, Takeo Yoshikawa³, Shigeki Yuasa², Yoshinobu Kiso⁷, Kaoru Inokuchi⁴, Noriko Osumi^{1,5}
¹Tohoku University Graduate School of Medicine, ²National Institute of Neuroscience, ³RIKEN Brain Science Institute, ⁴Mitsubishi Kagaku Institute of Life Sciences, ⁵CREST, ⁶Saitama Institute of Technology, ⁷Suntory Ltd, ⁸Yamaguchi University Graduate School of Medicine

Annual Symposium

September 12 (Friday)

16 : 25~18 : 55 (Room A)

- AS-1~AS-6** **Drug development for schizophrenia**
Chairs : Masaya Tohyama (Osaka University Graduate School of Medicine)
Toru Nishikawa (Department of Psychiatry and Behavioral Sciences, Tokyo Medical and Dental University Graduate School, Tokyo, Japan)
- AS-1** **Identification of susceptibility genes for schizophrenia using intermediate phenotype**
○Ryota Hashimoto^{1,2}, Masatoshi Takeda^{1,2}
¹The Osaka-Hamamatsu Joint Research Center For Child Mental Development, Osaka Univ. Grad. Sch. of Med., Suita, Japan, ²Dept of Psychiatry, Osaka Univ. Grad. Sch. of Med., Suita, Japan
- AS-2** **Molecular mechanism of schizophrenia via the dysfunction of Dysbindin**
○Shinsuke Matsuzaki^{1,2}, Masaya Tohyama^{1,2}
¹Department of Anatomy and Neuroscience, Graduate School of Medicine, Osaka university, Suita, Japan, ²Molecular Research Center For Child Mental Development, Graduate School of Medicine, Osaka university, Suita, Japan
- AS-3** **Antipsychotic Potential of Signal Inhibitors for Neuregulin and Epidermal Growth Factor**
○Hiroyuki Nawa¹, Taisuke Kato¹, Yuichi Abe¹, Hidekazu Sotoyama¹, Hisaaki Namba¹, Makoto Mizuno¹
¹Mol Neurobiol. Brain Res Inst. Niigata Univ
- AS-4** **Cortical GABA Neurotransmission in Schizophrenia: Regional and Molecular Phenotypes**
○Takanori Hashimoto^{1,2}, David A. Lewis²
¹Department of Psychiatry and Neurobiology, Kanazawa University, ²Department of Psychiatry, University of Pittsburgh, Pittsburgh, PA, USA
- AS-5** **Effect of GABA_B receptor agonist in animal models for schizophrenia-like cognitive impairment**
○Hiroyuki Mizoguchi¹, Kiyofumi Yamada²
¹Futuristic Environmental Simulation Center, Research Institute of Environmental Medicine, Nagoya University, Nagoya, Japan ²Department of Neuropsychopharmacology and Hospital Pharmacy, Nagoya University Graduate School of Medicine, Nagoya, Japan
- AS-6** **NMDA receptor-D-serine system-targeted treatment development for schizophrenia**
○Toru Nishikawa¹
¹Department of Psychiatry and Behavioral Sciences, Tokyo Medical and Dental University Graduate School, Tokyo, Japan

Young Scientists Lectureship Award Symposium

September 11 (Thursday)

13 : 20 ~ 14 : 20 (Room B)

LA-1 ~ LA-2 Young Scientists Lectureship Award

Chairs : Yukio Yoneda (Laboratory of Molecular Pharmacology, Kanazawa University
Graduate School of Natural Science and Technology)

Hiroshi Kiyama (Department of Anatomy & Neurobiology, Osaka City
University Graduate School of Medicine)

LA-1 The role of the individual Rb family member during mouse retinal development

Itsuki Ajioka

St. Jude Children's Research Hospital Department of Developmental Neurobiology

LA-2 Translational research in mental disorder

Ryota Hashimoto

The Osaka-Hamamatsu Joint Research Center for Child Mental Development, Osaka
University Graduate School of Medicine, Suita, Osaka, Japan.,

Psychiatry, Department of Integrated Medicine, Division of Internal Medicine, Osaka
University Graduate School of Medicine

Symposia

September 11 (Thursday)

13 : 20~15 : 20 (Room C)

S1-1~S1-4 **Recent advances in neurochemical research of proteoglycans**
Chairs : Akio Wanaka (The department of Anatomy of Nara Medical University)
Seiji Miyata (Kyoto Institute of Technology)

- S1-1** **Heparan sulfate endosulfatases are required for normal brain development**
○Masayuki Masu¹, Takuya Okada¹, Satoshi Nagamine¹, Kensuke Shiomi¹, Michiko Tamba¹, Hisako Ishimine¹, Tatsuyuki Ohto¹, Satoru Kunita², Satoru Takahashi², Kazuko Keino-Masu¹
¹Grad. Sch. Comp. Human Sci., Univ. Tsukuba, ²Lab. Animal Resource Center, Univ. Tsukuba
- S1-2** **The role of neuroglycan C, a membrane-spanning chondroitin sulfate proteoglycan, in the central nervous system**
○Sachiko Aono¹
¹Department of Perinatology, Institute for Developmental Research, Aichi Human Service Center, Aichi, Japan
- S1-3** **Perineuronal nets of proteoglycan-containing extracellular matrix**
○Seiji Miyata¹
¹Dept. of Appl. Biol., Kyoto Inst. of Technol
- S1-4** **DACS, novel matrixstructure composed of chondroitin sulfate proteoglycan in the brain**
○Kouko Tatsumi¹, Noriko Hayashi², Hiroaki Okuda¹, Akio Wanaka¹
¹Department of Anatomy, Faculty of Medicine, Nara Medical University, ²Department of Parasitology, Faculty of Medicine, Nara Medical University

September 11 (Thursday)

13 : 20~15 : 20 (Room D)

S2-1~S2-4 **Gene environmental interaction affecting animal and human behavior**
Chairs : Toshitaka Nabeshima (Department of Chemical Pharmacology, Meijo University Graduate School of Pharmaceutical Sciences)
Hiroshi Higuchi (Nigata University Graduate School of Medical and Dental Sciences)

- S2-1** **Neuregulin and the pathobiology of schizophrenia: studies in 'knockout' mice**
○John L. Waddington
Molecular & Cellular Therapeutics, Royal College of Surgeons in Ireland, Dublin 2, Ireland

- S2-2 Social behavior controlled by oxytocin release due to CD38
 ○Haruhiro Higashida¹
¹Kanazawa University 21st Century COE Program on Innovative Brain Science, Kanazawa, Japan
- S2-3 Drug-seeking behavior in methamphetamine-dependent mice: a role for GDNF
 ○Kiyofumi Yamada¹, Toshitaka Nabeshima²
¹Dept. of Neuropsychopharmacol. Hospital Pharmacy, Nagoya Univ. Grad. Sch. Med.
²Dept. of Chem. Pharmacol. Grad. Sch. of Pharmaceut. Sci., Meijo Univ.
- S2-4 PHARMACOGENOMICS IN CNS DISORDERS
 ○Ramón Cacabelos
 EuroEspes Biomedical Research Center, Institute for CNS Disorders and Genomic Medicine, EuroEspes Chair of Biotechnology and Genomics, Camilo José Cela University, Coruña, Spain.

September 11 (Thursday)

13 : 20~15 : 20 (Room E)

- S3-1~S3-4 Nociception and pain
 Chairs : Emiko Senba (Dept. of Anatomy & Neurobiology, Wakayama Medical University)
 Masahiko Shibata (Dept. of Pain Med., Univ. of Osaka)
- S3-1 Pain is perceived by the brain, pain behavior is originated from the brain
 ○Masahiko Shibata¹
¹Dept. of Pain Med., Univ. of Osaka
- S3-2 Altered cortical activations in chronic alodynic pain patients: a fMRI study
 ○Takahiro Ushida^{1,2,5}, Tatsunori Ikemoto^{2,5}, Shigeki Tanaka⁴, Shinichirou Taniguchi^{2,5}, Yoriko Murata³
¹Multidiscip. Pain Ctr., Aichi Med. Univ., Aichi, Japan, ²Dept. Orthopaedic Surg., Kochi Med. Sch., Kochi, Japan, ³Dept. Radiol., Kochi Med. Sch., Kochi, Japan, ⁴Dept. Psychol., Jin-Ai Univ, Fukui, Japan, ⁵Nankoku Pain ResearchGroup, Kochi, Japan
- S3-3 Alexithymia and pain experience
 ○Masako Hosoi¹
¹Dept. of Psychosomatic Medicine, Kyushu University Hospital, Fukuoka, Japan
- S3-4 Chronic pain and central sensitization: evidence for descending facilitation in animal models
 ○Emiko Senba¹
¹Dept. of Anatomy & Neurobiology, Wakayama Medical University, Wakayama, Japan

September 11 (Thursday)

13 : 20~15 : 20 (Room F)

S4-1~S4-4

Biology of eating disorder

Chairs : Nobuo Kiriike (Osaka City University Graduate School of Medicine)

Gen Komaki (Department of Psychosomatic Research, National Institute of Mental Health, National Center of Neurology and Psychiatry)

S4-1 Somatic and psychological factors that regulate the body mass index of patients with anorexia nervosa and normal subjects

○Keisuke Kawai¹, Chihiro Morita¹, Shin Matsubara¹, Takeharu Yamanaka², Sakino Yamashita¹, Masato Takii¹, Chiharu Kubo¹

¹Dept. of Psychosomatic Med, Kyushu University, Fukuoka, ²Institute for Clinical Research, National Kyushu Cancer Center, Fukuoka, Japan

S4-2 Genetic study of Eating Disorders

○Gen Komaki¹, Tetsuya Ando¹

¹Department of Psychosomatic Research, National Institute of Mental Health, National Center of Neurology and Psychiatry

S4-3 The animal model of eating disorders

○Shinichi Iwasaki¹, Koki Inoue¹, Nobuo Kiriike¹

¹Dept. of Neuropsychiatry, Osaka City University Medical School, Osaka, Japan

S4-4 Brain imaging on eating disorders

○Shinya Kojima¹, Akihiro Asakawa³, Akio Inui³, Tetsuro Naruo²

¹Dept. of Psychosomatic Medicine, Kagoshima Univ. Hosp., Kagoshima, Japan,

²Psychosomatic medicine, Nogami Hospital, Kagoshima, JAPAN, ³Department of Behavioral Medicine, Kagoshima University Graduate School of Medical and Dental Sciences, Kagoshima, Japan

September 12 (Friday)

9 : 00~12 : 00 (Room B)

S5-1~S5-6

Animal models of neuropsychiatric disorders - from C. elegans to monkey -

Chairs : Tsukasa Koyama (Hokkaido University Graduate School of Medicine)

Akemichi Baba (Osaka University Graduate School of Pharmaceutical Sciences)

S5-1 Functional genomics using C. elegans as a model organism

○Shohei Mitani¹

¹Department of Physiology, Tokyo Women's Medical University School of Medicine

S5-2 Drosophila homologs of schizophrenia-associated genes are required for long-term memory

○Takaomi Sakai¹

¹Department of Biological Sciences, Tokyo Metropolitan Univ.

- S5-3** Alpha-CaMKII deficiency causes dysregulated behaviors and immature dentate gyrus
 ○Tsuyoshi Miyakawa^{1,2}
¹Div. of Systems Medicine, ICMS, Fujita Health Univ. Toyoake, Japan, ²Frontier Tech Ctr, Grad. Sch. Med., Kyoto Univ., Kyoto, Japan
- S5-4** Transient knockdown of DISC1 in the developing cerebral cortex leads to dopaminergic disturbance and schizophrenia-like deficits in young adult mice
 ○Toshitaka Nabeshima^{1,2}, Minae Niwa^{1,2}, Rina Murai^{1,2}, Yukihiro Noda^{1,3}, Ken-ichiro Kubo⁴, Atsushi Kamiya⁵, Hanna Jaaro-Peled⁵, Kazunori Nakajima⁴, and Akira Sawa^{5,6,7}
¹Department of Chemical Pharmacology, Meijo University Graduate School of Pharmaceutical Sciences, Nagoya, Japan, ²Department of Neuropsychopharmacology and Hospital Pharmacy, Nagoya University Graduate School of Medicine, Nagoya, Japan. ³Division of Clinical Science in Clinical Pharmacy Practice, Management, and Research, Faculty of Pharmacy, Meijo University, Nagoya, Japan. ⁴Department of Anatomy, Keio University School of Medicine, Tokyo, Japan. ⁵Department of Psychiatry and Behavioral Sciences, ⁶Department of Neuroscience, ⁷Graduate Program in Cellular and Molecular Medicine, Johns Hopkins University School of Medicine, 600 N Wolfe Street, Baltimore, MD, USA.
- S5-5** Potential of marmosets as animal models for mental and nervous disease
 ○Katsuki Nakamura¹
¹National Institute of Neuroscience, National Center of Neurology and Psychiatry
²CREST, JST, Saitama, Japan
- S5-6** Neuronal signals in the primate medial frontal cortex and neuropsychiatric disorders
 ○Munetaka Shidara¹
¹Graduate School of Comprehensive Human Sciences, University of Tsukuba, Ibaraki, Japan

September 12 (Friday)

9 : 00 ~ 12 : 00 (Room C)

- S6-1 ~ S6-6** Social brain and its correlates
 Chairs : Shigenobu Kanba (Department of Neuropsychiatry, Kyushu University)
 Keiji Wada (Natl Inst Neurosci, NCNP)

- S6-1** Dficit of Theory of Mind in psychiatric disorders
 ○Shigenobu Kanba¹, Kazuo Yamada², Yumiko Inoue²
¹Department of Neuropsychiatry, Kyushu University, ²Department of Psychiatry, East Center, Tokyo Wemens Medical College
- S6-2** Social recognition, oxytocin and CD38
 ○Haruhiro Higashida¹
¹Kanazawa University 21st Century COE Program on Innovative Brain Science, Kanazawa, Japan

- S6-3 Neurobehavioral basis of the impaired nurturing in mice lacking the immediate early gene FosB**
○Kumi Kuroda¹
¹Kuroda Unit, BSI, RIKEN
- S6-4 Genetic polymorphism as a background of animal behavior**
○Miho Inoue-Murayama¹
¹Wildlife Research Center of Kyoto University, Kyoto, Japan
- S6-5 Promotion of Neurogenesis and Alteration of Anxiety-related Behavior in Tryptophan 2,3-Dioxygenase (TDO) Knockout Mice**
○Hiroshi Funakoshi¹, Masaaki Kanai¹, Hisaaki Takahashi¹, Shinya Mizuno¹, Kunio Matsumoto¹, Toshikazu Nakamura¹
¹Division of Molecular Regenerative Medicine, Department of Biochemistry and Molecular Biology, Osaka University Graduate School of Medicine
- S6-6 Mother-child bio-communication: lessons from mice**
○Keiji Wada^{1,2}
¹Natl Inst Neurosci, NCNP, Tokyo, Japan, ²CREST, JST, Kawaguchi, Saitama, Japan

September 12 (Friday)

9 : 00~12 : 00 (Room D)

- S7-1~S7-6 Neurogenesis and stem cell biology**
Chairs : Hideyuki Okano (Department of Physiology, Keio University School of Medicine)
Toshikazu Saito (Sapporo Medical University)
- S7-1 Cell therapy for spinal cord injury using neural stem/progenitor cells derived from pluripotent stem cells.**
○Hideyuki Okano¹, Yohei Okada¹, Gentaro Kumagai^{1,2}, Masaya Nakamura²
¹Department of Physiology, Keio University School of Medicine, Tokyo, Japan
²Department of Orthopaedic Surgery, Keio University School of Medicine, Japan.
- S7-2 Migration of new neurons in the adult brain**
○Kazunobu Sawamoto¹
¹Department of Developmental and Regenerative Biology, Institute of Molecular Medicine, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan
- S7-3 A inhibitory mechanism of neuronal differentiation mediated by BMP-induced REST/NRSF**
Jun Kohyama¹, Eriko Takatsuka¹, Tsukasa Sanosaka¹, Akinori Tokunaga², Hideyuki Okano², ○Kinichi Nakashima¹
¹Lab. Mol. Neurosci. Grad. Sch. Biol. Sci. NAIST, ²Dept. Physiol. Sch. Med. Keio Univ.
- S7-4 NG2 cells: A therapeutic target for psychiatric disorders?**
○Yoshitaka Tatebayashi
Depression project, Mood disorder research team, Tokyo Institute of Psychiatry

- S7-5 The stem cell therapy as a possible new treatment for psychiatric disorders
 ○Wataru Ukai¹, Toshihiro Yoshinaga¹, Takao Ishii², Eri Hashimoto¹, Takafumi Ono¹, Masaru Tateno¹, Kimihiko Watanabe¹, Ippei Watanabe¹, Tomohiro Sirasaka¹, Yuka Mukai¹, Satoshi Saito¹, Toshikazu Saito¹
¹Dept of Neuropsych Sapporo Medical Univ, Sapporo, ²Dept of Occupational Therapy, Sapporo Medical Univ, Sapporo
- S7-6 Neural stem cells in the adult brain: implications for the pathogenesis of mood affective disorders
 ○Seiji Hitoshi¹
¹National Institute for Physiological Sciences

September 12 (Friday)

9 : 00~12 : 00 (Room E)

- S8-1~S8-6 Neurochemistry of Alzheimer disease
 Chairs : Akihiko Takashima (Laboratory for Alzheimer's Disease, RIKEN, Brain Science Institute.)
 Masatoshi Takeda (Osaka University Graduate School of Medicine)
- S8-1 Amyloid beta42 generating process has a physiological role in regulating Notch signaling intensity.
 ○Shinji Tagami¹, Masayasu Okochi¹, Masatoshi Takeda¹
¹Department of Psychiatry, Osaka University Graduate School of Medicine
- S8-2 Presenilin complex and γ -secretase activity
 ○Masaki Nishimura¹
¹Molecular Neuroscience Research Center, Shiga University of Medical Science, Shiga, Japan
- S8-3 Fibrillar or nonfibrillar A β ? A causal molecule for Alzheimer's disease
 ○Takami Tomiyama¹
¹Department of Neuroscience, Osaka City University Graduate School of Medicine
- S8-4 Molecular mechanism underlying A β assembly
 ○Katsuhiko Yanagisawa¹
¹National Institute for Longevity Sciences, NCGG, Aichi, Japan
- S8-5 Involvement of tau protein in neurodegeneration
 Toshihisa Tanaka¹, Golam Sadik¹, Kiyoko Kato¹, Kentaro Yanagi¹, Masatoshi Takeda¹
¹Department of Clinical Neuroscience, Psychiatry, Osaka University, Graduate School of Medicine.

S8-6 Brain aging and Alzheimer's disease

○Akihiko Takashima¹

¹Laboratory for Alzheimer's Disease, RIKEN, Brain Science Institute.

September 12 (Friday)

9 : 00~12 : 00 (Room F)

S9-1~S9-6 Risk genes in neuropsychiatric disorders

Chairs : Takeo Yoshikawa (Lab. for Molecular Psychiatry, RIKEN Brain Science Institute)
Yuji Okazaki (Tokyo Metropolitan Matsuzawa Hospital)

S9-1 Large-scale genetic association study of schizophrenia

○Tadao Arinami¹, Hiroki Ishiguro¹, Minoru Koga^{1,2}, Yasue Horiuchi¹

¹Dept. of Med. Genet., Inst. Med. Sci., Uni. of Tsukuba, Tsukuba, Japan, ²CREST, Japan Science and Technology Agency, Kawaguchi-shi, Japan

S9-2 Risk genes for panic disorder: a GWAS study

○Hisashi Tani¹, Tsukasa Sasaki², Takeshi Otowa³, Tadao Kato⁴, Takeo Yoshikawa⁵, Tadao Arinami⁶, Hiroshi Kunugi⁷, Toshiyuki Someya⁸, Naomichi Matsumoto⁹, Hisanobu Kaiya¹⁰, Yuji Okazaki¹¹

¹Department of Psychiatry, Mie University Graduate School of Medicine, Mie, Japan

²Health Service Center, University of Tokyo, Tokyo, Japan, ³Department of Neuropsychiatry, Graduate School of Medicine, University of Tokyo, Tokyo, Japan,

⁴Laboratory for Molecular Dynamics of Mental Disorders, RIKEN Brain Science Institute, Saitama, Japan, ⁵Laboratory for Molecular Psychiatry, RIKEN Brain Science Institute, Saitama, Japan.

⁶Department of Medical Genetics, University of Tsukuba, Tsukuba, Japan,

⁷Department of Mental Disorder Research, National Center of Neurology and Psychiatry, Tokyo, Japan, ⁸Department of Psychiatry, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan, ⁹Department of Human Genetics, Yokohama City University Graduate School of Medicine, Yokohama, Japan, ¹⁰Warakukai Incorporated Medical Institution, Tokyo, Japan, ¹¹Tokyo Metropolitan Matsuzawa Hospital

S9-3 Genomic and animal model approaches to risk genes for schizophrenia

○Yasuyuki Fukumaki¹

¹Medical Institute of Bioregulation, Kyushu Univ., Fukuoka, Japan

S9-4 A genetic study on schizophrenia started from a rare case.

○Masanari Itokawa^{1,2,3}

¹Schizophrenia Research Team, Tokyo Institute of Psychiatry, Tokyo, ²Lab. for Molecular Psychiatry, BSI, RIKEN, ³Dep. Psychiatry, Tokyo Metropolitan Matsuzawa Hospital

S9-5 Risk Genes for Dementia

○Takashi Morihara¹, Kouzin Kamino², Ryo Kimura³, Eiichiro Kamagata¹, Noriyuki Hayashi¹, Masahiko Takaya¹, Mikiko Yokokoji¹, Hiromasa Tokunaga¹, Hiroaki Kazui¹, Toshihisa Tanaka¹, Takashi Kudo¹, Masatoshi Takeda¹

¹Department of Psychiatry Osaka University Graduate School of Medicine, Osaka, Japan,

²Shoraiso National Hospital, Koriyama, Japan, ³Osaka Prefectural Hospital Organization, Osaka, Japan

S9-6 Genes for fatty-acid binding proteins and functional psychoses

Takeo Yoshikawa¹¹Lab. for Molecular Psychiatry, RIKEN Brain Science Institute

September 13 (Saturday)

15 : 20~17 : 20 (Room C)

S10-1~S10-4 ER stress

Chairs : Takashi Kudo (Department of Psychiatry, Osaka University Graduate School of Medicine)

Kazunori Imaizumi (Div. Mol. Cell. Biol., Dept. Anatomy, Faculty of Medicine, Univ. Miyazaki.)

S10-1 Diversity of ER stress response in neurons and astrocytes

○Kazunori Imaizumi¹¹Div. Mol. Cell. Biol., Dept. Anatomy, Faculty of Medicine, Univ. Miyazaki.

S10-2 ER stress response and neuronal cell death in the substantia nigra

○Osamu Hori¹¹Department of Neuroanatomy, Kanazawa University Graduate School of Medical Science

S10-3 ER dysfunction induced by nitric oxide

○Takashi Uehara¹¹Department of Pharmacology, Graduate School of Pharmaceutical Sciences, Hokkaido University, Sapporo, Japan

S10-4 Therapeutic Strategies based on ER stress

○Takashi Kudo¹¹Department of Psychiatry, Osaka University Graduate School of Medicine

September 13 (Saturday)

15 : 20~17 : 20 (Room D)

S11-1~S11-4 Regulated intramembrane proteolysis signaling

Chairs : Taisuke Tomita (Dept Neuropathol Neurosci, Grad Sch Pharm Sci, Univ Tokyo)

Masayasu Okochi (Dept. Psy., Osaka Univ.)

S11-1 Association of RIP signaling and Alzheimer disease process indicates future therapeutic interventions.

○Masayasu Okochi¹, Shinji Tagami¹, Masatoshi Takeda¹¹Dept. Psy., Osaka Univ.

- S11-2 γ -Secretase: Intramembrane cleavage of β -amyloid precursor protein**
 ○Maho Morishima-Kawashima¹
¹Department of Molecular Neuropathology, Graduate School of Pharmaceutical Science, Hokkaido University, Sapporo, Japan
- S11-3 Structure-function relationships of the intramembrane-cleaving proteases**
 ○Taisuke Tomita¹
¹Dept Neuropathol Neurosci, Grad Sch Pharm Sci, Univ Tokyo
- S11-4 Behavioral Analysis of Neuron-specific RBP-J knockout mice**
 ○Kenji Tanigaki¹, Michihiro Toritsuka^{1,3}, Sohei Kimoto^{1,3}, Kazue Muraki¹, Toshihumi Kishimoto³, Tasuku Honjo²
¹Research Institute, Shiga Medical Center, ²Dept. of Immunology and Genomic Medicine, Kyoto. Univ. ³Dept. of Psychiat., Nara. Med. Univ.

September 13 (Saturday)

15 : 20~17 : 20 (Room E)

S12-1~S12-4 Brain science on fatigue and motivation

Chairs : Norihiro Sadato (National Institute for Physiological Sciences)
 Masaaki Tanaka (Dept. Biomark. Mol. Bioph., Osaka City Univ.)

- S12-1 Functional neuroimaging on fatigue and motivation**
 ○Masaaki Tanaka^{1,2,3,4}, Kei Mizuno^{2,3,4}, Yasuyoshi Watanabe^{2,3,4,5}
¹Dept. Biomark. Mol. Bioph., Osaka City Univ., ²Dept. Physiol. Osaka City Univ., ³The 21st Century COE Program, Base to Overcome Fatigue, ⁴RISTEX/JST, ⁵Molecular Imaging Research Program, RIKEN
- S12-2 Brain dysfunction is a key abnormality for understanding the state of chronic fatigue**
 ○Hirohiko Kuratsune¹, Yasuyoshi Watanabe³
¹Kansai Univ. of Welfare Sci. ²Clinical Center for Fatigue, Osaka City Univ. of Medical School, ³Mol. Imaging Res. Prog, RIKEN Frontier Res. System
- S12-3 Structural equation modeling between fatigue and autonomic function; Preliminary analysis to the fatigue medical checkup for labor**
 ○Seiki Tajima¹, Daisuke Kuratsune², Hirohiko Kuratsune¹, Junichi Koizumi³
¹Department of Health Sciences, Kansai University of Welfare Sciences, Kashiwara, Japan, ²Department of Biochemistry and Molecular Pathology, Osaka City University Graduate School of Medicine, Osaka, Japan, ³Yokohama National University Graduate School of Engineering, Yokohama, Japan
- S12-4 Neural mechanism of central fatigue in the animal models**
 ○Yilong Cui¹, Yosky Kataoka^{1,2}, Yasuyoshi Watanabe^{1,2}
¹Molecular Imaging Research Program, RIKEN, ²21st Century COE Program, Osaka City Univ. Grad. Sch. Med

September 13 (Saturday)

15 : 20~17 : 20 (Room F)

- S13-1~S13-4** **Neurochemistry of developmental disorder**
 Chairs : Toshio Matsuda (Lab. of Med. Pharmacol., Grad. Sch. of Pharm. Scis., Osaka Univ.)
 Masaaki Narita (Mie University, Graduate School of Medicine)
- S13-1** **Social behaviors and plasma oxytocin level are dually regulated by breast milk and hypothalamic ADP-ribosyl cyclase in infant mice**
 ○Olga Lopatina¹, HongXiang Liu¹, Haruhiro Higashida¹
¹Dept. of Biophysical Genetics. Med., Univ. of Kanazawa
- S13-2** **Effects of environmental factors on behavioral abnormalities in PACAP-KO mice**
 ○Toshihiro Ishihama¹, Yukio Ago¹, Sachiko Shimada¹, Norihito Shintani², Hitoshi Hashimoto^{2,3}, Akemichi Baba², Kazuhiro Takuma¹, Toshio Matsuda^{1,3}
¹Lab. Medicinal Pharmacol., Grad. Sch. Pharmaceut. Sci., Osaka Univ., Osaka, Japan,
²Lab. Mol. Neuropharmacol., Grad. Sch. Pharmaceut. Sci., Osaka Univ., Osaka, Japan,
³Center for Child Mental Dev., Grad. Sch. Med, Osaka Univ., Osaka, Japan
- S13-3** **Alterations in the development of the serotonergic system in the cerebral cortex of rats induced by fetal thalidomide exposure**
 ○Tomoko Tashiro¹, Naoshi Yamamura¹, Daisuke Kagamida¹, Yuusuke Miyagi¹, Masaaki Narita²
¹Dept. of Chem. & Biol. Sci., Sch. of Sci. & Engineer., Aoyama Gakuin Univ., Sagamihara, Japan, ²Dept. of Dev. & Regener. Med., Mie Univ. Grad. Sch. of Med., Tsu, Japan
- S13-4** **Mutations in *SHANK3* gene encoding the synaptic scaffolding protein possibly associated with autism spectrum disorder.**
 ○Shigeo Uchino¹, Chikako Waga¹, Nobuhiko Okamoto², Shinichi Kohsaka¹
¹Department of Neurochemistry, National Institute of Neuroscience, Tokyo, Japan,
²Department of Planning and Research, Osaka Medical Center and Research Institute for Maternal and Child Health, Osaka Japan.

Oral Sessions

September 11 (Thursday)

9 : 00 ~ 12 : 00 (Room B)

O1-1 ~ O1-9

Synapse

Chairs : Tatsuro Koike (Hokkaido University Graduate School of Life Science Molecular Neurobiol Lab.)

Fusao Kato (Lab Neurophysiol, Dept Neurosci, Jikei Univ Sch Med)

Yasuo Takeda (Department of Pharmacy and Pharmacology, Kagoshima

University Graduate School of Medical and Dental Sciences)

- O1-1 Experience dependent synaptic delivery of AMPA receptors
○Tomoyuki Miyazaki¹, Hirobumi Tada¹, Dai Mitsushima¹, Takuya Takahashi¹
¹Department of Physiology, Yokohama City University, Graduate School of Medicine
- O1-2 Age-dependent formation of GM1-ganglioside-enriched microdomain in synaptosomes induces amyloid β -protein fibrillogenesis
○Naoki Yamamoto^{1,2,3}, Teruhiko Matsubara⁴, Kohei Yuyama¹, Tashinori Sato⁴, Katsuhiko Yanagisawa¹
¹Dept. Alzheimer's Disease Res. Natl. Inst. for Longevity Sci., NCGG, ²JSPS, ³Dept. Pharmacy, Ritsumeikan Univ. ⁴Dept. Biosci. and Informatics, Keio Univ.
- O1-3 THE CIS-UNSATURATED FREE FATTY ACID DERIVATIVE HEPBA REGULATES $\alpha 7$ ACH RECEPTOR TRAFFICKING, AND SYNAPTIC PLASTICITY VIA A CAMKII PATHWAY.
○Takahiro Yaguchi¹
¹Department of Physiology, Division of Bioinformation, Hyogo College of Medicine, Hyogo, Japan
- O1-4 Crosstalk between Cdk5 and CaMKII in the postsynaptic region
○Tomohisa Hosokawa¹, Taro Saito¹, Akiko Asada¹, Shin-ichi Hisanaga¹
¹Dept. of Biol., Grad. sch. of Sci., Tokyo Metropolitan Univ.
- O1-5 PRMT3 regulates rps2 stability and activity-dependent dendritic spine maturation of hippocampal neurons
○Shingo Miyata¹, Yasutake Mori¹, Masaya Tohyama^{1,2}
¹Dept. of Anat&Neurosci. Med. Osaka Univ. ²Dept. of Clinical Disorder Res. The Osaka-Hamamatsu Joint Res. Center for Child Mental Development, Osaka.
- O1-6 Spine formation induced by Spikar is negatively regulated with drebrin.
○Tomoaki Shirao¹, Hiroyuki Yamazaki¹
¹Department of Neurobiology and Behavior, Gunma University Graduate School of Medicine

- O1-7 **Neuropsin (KLK8)-dependent and -independent Synaptic Tagging**
 ○Yasuyuki Ishikawa¹, Hideki Tamura¹, Sadao Shiosaka¹
¹Division of Structural Cell Biology, Nara Institute of Science and Technology
- O1-8 **Characterization of exocytotic events and the dynamics of secretory vesicles in single mouse chromaffin cells.**
 ○Nobuyuki Sasakawa¹, Fuyuka Matsuda¹, Mitsunori Hayashi¹, Yumi Wanabe^{2,3}, Michihiro Igarashi^{2,3}, Kenji Sakimura⁴, Konosuke Kumakura¹
¹Dept. of Information & Communication Sci., Faculty of Sci. & Technolo. Sophia Univ., Tokyo, Japan, ²Div Mol Cell Biol, Grad Sch Med Dent Sci, Niigata Univ, Niigata, ³Trans-disciplinary Res Program, Niigata Univ, Niigata, ⁴Dept Cell Neurobiol, Brain Res Institute, Niigata Univ, Niigata
- O1-9 **Modulation of exocytosis by a novel nitrated second messenger, 8-nitroguanosine 3',5'-cyclic monophosphate**
 ○Hideshi Ihara¹, Hiroyasu Tsutsuki¹, Nobuyuki Sasakawa², Tomoaki Ida¹, Mitsuki Hayashi², Konosuke Kumakura², Tomohiro Sawa³, Takaaki Akaike³
¹Department of Biological Science, Graduate School of Science, Osaka Prefecture University, ²Laboratory of Neurochemistry and Neuropharmacology, Life Science Institute, Sophia University, ³Department of Microbiology, Graduate School of Medical Sciences, Kumamoto University

September 11 (Thursday)

9 : 00 ~ 12 : 00 (Room C)

- O2-1 ~ O2-9 **Astrocyte**
 Chairs : Masaaki Tsuda (Graduate School of Innovative Life Science (Research) University of Toyama)
 Taichi Katayama (Hamamatsu University School of Medicine, Department of Anatomy & Neuroscience)
 Shigeto Yamawaki (Psychiatry and Neurosciences, Hiroshima University)
- O2-1 **Endothelin decreases aquaporin-4 expression in cultured rat astrocyte and in the rat cerebral cortex**
 ○Kazuhiro Tanaka¹, Yutaka Koyama¹
¹Lab. Pharmacology, Faculty of Pharmacy, Osaka Ohtani Univ., Osaka, Japan
- O2-2 **BMPRIA signaling in astrocytes is essential for proper cerebral angiogenesis**
 ○Masahisa Yamada¹, Runa Araya¹, Moeko Kudo¹, Yuji Mishina²
¹Yamada Unit, RIKEN-BSI, ²Lab. of Reproductive and Developmental Toxicology, NIEHS, Research Triangle Park, NC, USA.
- O2-3 **Identification of the molecules, which are responsible for astroglial heterogeneity in the central nervous system**
 ○Mineyoshi Aoyama¹, Hiroki Kakita², Shin Kato², Masataka Fujita³, Kazuya Sobue⁴, Kiyofumi Asai¹
¹Dept of Mol Neurobiology, Nagoya City Univ, Nagoya, ²Dept of Pediatrics, Nagoya City Univ, Nagoya, ³Dept of Neurosurgery, Nagoya City Univ, Nagoya, ⁴Dept of Anesthesiology and Medical Crisis Management, Nagoya City Univ, Nagoya

- O2-4 Mechanism underlying gliotransmitter release from cultured astrocytes**
 ○Hae Ung Lee¹, Hongtao Liu², Kenji Tanaka¹, Shigeyuki Namiki³, Kenzo Hirose³, Kishio Furuya⁴, Masahiro Sogabe⁴, Yasunobu Okada², Kazuhiro Ikenaka¹
¹Div of Neurobiology and bioinformatics, National Institute for Physiological Sciences.
²Dep. Cell Physiol. National Institute for Physiological Sciences, Okazaki, Japan, ³Cell physiology/Cell Pharmacology, Nagoya Univ. Grad. Med. Nagoya, Japan, ⁴Cell Biophysics/Imaging Physiology, Nagoya Univ. Grad. Med. Nagoya, Japan
- O2-5 Endothelial mPGES-1 regulates Ca²⁺-dependent glutamate release from astrocyte via EP3**
 ○Takako Takemiya^{1,2}, Kiyoshi Matsumura³, Hiroko Sugiura², Shin Yasuda², Satoshi Uematsu⁴, Shizuo Akira⁴, Kanato Yamagata²
¹Med. Res. Insti., Tokyo Women's Medical Univ. ²Dept. Neuropharmacol., Tokyo Metro. Insti. Neurosci. ³Information Sci. and Technol., Osaka Inst. Technol. ⁴Dept. of Host Defense, Res. Insti. for Microbial Dis., Osaka Univ.
- O2-6 Transporter-mediated uptake of nicotinamide is critical for its preventive effect on PARP-1-triggered astrocyte death**
 ○Hiroto Okuda¹, Eri Suzuki¹, Kazuki Nagasawa¹, Sadaki Fujimoto¹
¹Dept. of Environ. Biochem., Kyoto Pharm. Univ., Kyoto, Japan
- O2-7 Glutamine transporter is a determinant of the vulnerability to oxidative stress in cultured rat neocortical astrocytes**
 ○Masato Ogura¹, Ryo Fukumori¹, Yuma Ito¹, Noritaka Nakamichi¹, Hideo Taniura¹, Yukio Yoneda¹
¹Laboratory of Molecular Pharmacology, Kanazawa University Graduate School of Natural Science and Technology, Kanazawa, Japan
- O2-8 Effects of Ca²⁺-ATPase inhibitors on hydrogen peroxide-induced thymidine incorporation into cultured astrocytes**
 ○Koh-ichi Tanaka^{1,2}, Tomoaki Sato², Takashige Nishikawa², Junichi Kitanaka³, Nobue Kitanaka³, Motohiko Takemura³, Nobuyoshi Nishiyama¹
¹Division of Pharmacology, Department of Pharmacy, School of Pharmacy, Hyogo University of Health Sciences, Kobe, Hyogo, Japan, ²Department of Applied Pharmacology, Kagoshima University Graduate School of Medical and Dental Sciences, Kagoshima, Japan, ³Department of Pharmacology, Hyogo College of Medicine, Nishinomiya, Hyogo, Japan
- O2-9 Behavioral changes of brain astrocytes in mice after forced exercise**
 ○Yasushi Kanai¹, Atsushi Takano¹, Yasuhide Mitsumoto¹
¹Dept. of Alternative Med. and Exp. Therapeutics, Faculty of Pharmaceutical Sciences, Hokuriku University

September 11 (Thursday)

9:00~12:00 (Room D)

O3-1~O3-9

Neural stem/Progenitor cells

Chairs : Hiroyuki Fukui (Department of Molecular Pharmacology, Institute of Health Biosciences, The University of Tokushima Graduate School)
 Hidenori Horie (Research Center of Brain and Oral Science, Kanagawa Dental College)
 Norihito Shintani (Laboratory of Molecular Neuropharmacology, Graduate School of Pharmaceutical Sciences, Osaka University)

- O3-1 Regulation of neural progenitor cells proliferation by p38 MAP kinase
 ○Makoto Hamanoue¹, Ken Takamatsu¹
¹Department of Physiology, Toho University School of Medicine, Tokyo, Japan
- O3-2 Modulation of proliferation and differentiation by GABAergic signaling in murine neural progenitor cells
 ○Shusuke Ozawa¹, Masaki Fukui¹, Takeshi Takarada¹, Hideo Taniura¹, Noritaka Nakamichi¹, Yukio Yoneda¹
¹Lab Mol Pharmacol, Kanazawa Univ Grad Sch Nat Sci Tech, Kanazawa, Japan
- O3-3 Requirement of reactive oxygen species in proliferation and survival of neural progenitor cells derived from embryonic hippocampus of mice
 ○Koichi Kawada¹, Masanori Yoneyama¹, Kiyokazu Ogita¹
¹Dept. of Pharmacol., Setsunan Univ., Osaka, Japan
- O3-4 Profiles of Ifrd1 highly expressed by neural progenitor cells of adult mouse hippocampus
 ○Sayaka Maeda¹, Mami Watanabe¹, Yukary Nakamura¹, Hideo Taniura¹, Noritaka Nakamichi¹, Yukio Yoneda¹
¹Lab Mol Pharmacol, Kanazawa Univ Grad Sch Nat Sci Tech, Kanazawa, Japan
- O3-5 Slit-Robo signaling regulates neuroblast migration toward the olfactory bulb in the postnatal brain.
 ○Naoko Kaneko¹, Oscar Marin², Yuki Hirota¹, John Rubenstein³, Fujio Murakami⁴, Arturo Alvarez-Buylla³, Hideyuki Okano⁵, Marc Tessier-Lavigne⁶, Kazunobu Sawamoto¹
¹Department of Developmental and Regenerative Biology, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan, ²Instituto de Neurociencias de Alicante, Consejo Superior de Investigaciones Científicas and Universidad Miguel Hernández, Spain, ³University of California San Francisco, USA, ⁴Graduate School of Frontier Bioscience, Osaka Univ., Osaka, Japan, ⁵Department of Physiology, Keio University School of Medicine, Japan, ⁶Genentech, USA
- O3-6 A rapid method for quantitative and qualitative analysis of the adult neurogenesis by using the flow cytometry
 ○Takashi Namba¹, Tatsunori Seki², Shigeo Uchino¹, Shinichi Kohsaka¹
¹Department of Neurochemistry, National Institute of Neuroscience, ²Department of Anatomy, Juntendo University School of Medicine

- O3-7 Nicotine acts differently depending on the differentiated level of the neural cells.
○Akiko Shingo¹, Shozo Kito²
¹Hyogo University School of Health Sciences, Hyogo, Japan, ²Junshin-kai Kousei Rehabilitation Hospital, Hyogo, Japan
- O3-8 Isolation and characterization of astrocyte precursor cells from the developing mouse cerebellum
○Na Cai¹, Masashi Kurachi¹, Yasuki Ishizaki¹
¹Department of Molecular and Cellular Neurobiology, Gunma University Graduate School of Medicine
- O3-9 GABAergic neurons in the ventral thalamus are derived from Olig2+ cells in the area surrounding the zona limitans intrathalamica
○Naoko Inamura¹, Katsuhiko Ono¹, Hirohide Takebayashi¹, Kazuhiro Ikenaka¹
¹Division of Neurobiology and Bioinformatics National Institute for Physiological Sciences, Okazaki, Japan

September 11 (Thursday)

9 : 00~12 : 00 (Room E)

- O4-1~O4-9 Neuronal death 1
Chairs : Hitoshi Okazawa (Department of Neuropathology, Medical Research Institute, Tokyo Medical and Dental University)
Mami Noda (Laboratory of Pathophysiology, Graduate School of Pharmaceutical Sciences, Kyushu University)
Shinobu Inagaki (Group of Neurobiology, Division of Health Sciences, Graduate School of Medicine, Osaka University)
- O4-1 Insensitivity to NMDA in cortical neurons
○Yuki Kambe¹, Noritaka Nakamichi¹, Hirofumi Kawagoe¹, Daisuke Kiyonaga¹, Hideo Taniura¹, Yukio Yoneda¹
¹Laboratory of Molecular Pharmacology, Kanazawa University Graduate School of Natural Science and Technology, Kanazawa, Japan
- O4-2 Functional analysis of a novel ER stress transducer OASIS in brains.
○Atsushi Saito¹, Kazuyasu Chihara¹, Tomohiko Murakami¹, Hideaki Hara², Akio Wanaka³, Kazunori Imaizumi¹
¹Division of Molecular and Cellular Biology, Department of Anatomy, Faculty of Medicine, University of Miyazaki, Miyazaki, Japan, ²Department of Biofunctional Evaluation, Molecular Pharmacology, Gifu Pharmaceutical University, Gifu, Japan, ³Department of Anatomy, Nara Medical University, Nara, Japan
- O4-3 Suppression of HRD1-mediated protein degradation causes amyloid precursor protein accumulation and β -amyloid generation with endoplasmic reticulum stress and apoptosis
○Masayuki Kaneko¹, Hiroshi Koike², Tomohiro Omura¹, Yasunobu Okuma¹, Yasuyuki Nomura³

¹Department of Pharmacology, Chiba Institute of Science, Choshi, Japan, ²Department of Pharmacology, Hokkaido University, Sapporo, Japan, ³Department of Pharmacotherapeutics, Yokohama College of Pharmacy, Yokohama, Japan

- O4-4 Necdin controls p53 acetylation via Sirt1 in cortical neurons
 ○Koichi Hasegawa¹, Kazuaki Yoshikawa¹
¹Laboratory of Regulation of Neuronal Development, Institute for Protein Research, Osaka University
- O4-5 Involvement of Na⁺/Ca²⁺ exchanger in nitric oxide-induced cytotoxicity in SH-SY5Y cells.
 ○Tetsuaki Nashida¹, Toshiyuki Kawasaki¹, Tatsuya Kitao¹, Sayoko Fukuda¹, Yukio Ago¹, Kazuhiro Takuma¹, Toshio Matsuda^{1,2}
¹Lab. Medicinal Pharmacol., Grad. Sch. Pharmaceut. Sci., Osaka Univ. Osaka, Japan, ²Center For Child Mental Dev., Grad. Sch. Med., Osaka Univ. Osaka, Japan
- O4-6 Functional P2X7 receptors are expressed by cultured neurons and involved in ATP-induced neuronal death
 ○Tsunetoshi Nakatani¹, Hiroto Okuda¹, Reina Shirayama¹, Mayuka Nakanishi¹, Kaori Yamatani¹, Kazuki Nagasawa¹, Sadaki Fujimoto¹
¹Dept. of Environ. Biochem., Kyoto Pharm. Univ., Kyoto, Japan
- O4-7 Characterization of specific binding of polyglutamine aggregate inhibitors to the expanded polyglutamine stretch using surface plasmon resonance
 ○Yuma Okamoto^{1,2}, Yoshitaka Nagai¹, Nobuhiro Fujikake¹, Helena Akiko Popiel¹, Tatsushi Toda¹, Takashi Inui²
¹Div. of Clin. Genet., Dep. of Med. Genet., Osaka Univ. Grad. Sch. of Med., Suita, Japan, ²Dep. of Mol. Biol. and Cell Inform., Div. of Appl. Life Sci., Grad. Sch. of Life and Envi. Sci., Osaka Pref. Univ., Sakai, Japan
- O4-8 Functional analysis of SFAP75/Norbin in CHO and PC12 cells
 ○Yasunori Tokuhara¹, Manabu Sakai¹, Satoshi Shibata¹, Yoshiharu Ohoka², Shinobu Inagaki¹
¹School of Allied Health Science, Faculty of Medicine, Osaka University, ²Laboratory of Biodefense Research, Tokushima Bunri University Faculty of Pharmaceutical Science at Kagawa Campus, Kagawa, Japan
- O4-9 The mechanism of neogenin induced neuronal cell death
 ○Yuki Fujita¹, Junko Taniguchi², Masanori Uchikawa³, Mitsuharu Endo¹, Katsuhiko Hata¹, Takekazu Kubo², Toshihide Yamashita^{1,2}
¹Department of Molecular Neuroscience, Graduate School of Medicine, Osaka University, ²Department of Neurobiology, Graduate School of Medicine, Chiba University, ³Laboratory for Developmental Biology, Graduate School of Frontier Biosciences, Osaka University

September 11 (Thursday)

9 : 00~12 : 00 (Room F)

O5-1~O5-9

Schizophrenia

Chairs : Toshifumi Kishimoto (Department of Psychiatry, Nara Medical University)

Akeo Kurumaji (Tokyo Medical and Dental University Graduate School, Section
of Psychiatry and Behavioral Sciences)

Shu-ichi Ueno (Department of Neuropsychiatry, Neuroscience, Ehime University
Graduate School of Medicine)

O5-1 Associations of candidate gene G72 polymorphisms with schizophrenia in a Japanese population

○Kazutaka Ohi¹, Ryota Hashimoto^{1,2}, Yuka Yasuda^{1,2}, Tetsuhiko Yoshida¹, Hidetoshi Takahashi¹, Naomi Iike¹, Masao Iwase¹, Kouzin Kamino¹, Ryohei Ishii¹, Hiroaki Kazui¹, Yuri Kitamura³, Michiyo Azechi¹, Koji Ikezawa¹, Eiichiro Kamagata¹, Hitoshi Tanimukai¹, Shinji Tagami¹, Takashi Morihara¹, Masayasu Okochi¹, Tohru Ohnuma⁴, Shusuke Numata⁵, Masashi Ikeda⁶, Shuichi Ueno⁵, Tomoko Fukunaga¹, Toshihisa Tanaka¹, Takashi Kudo^{1,2}, Heii Arai⁴, Tetsuro Ohmori⁵, Nakao Iwata⁶, Norio Ozaki⁷, Masatoshi Takeda^{1,2}

¹Dept Psychiatry, Osaka Univ Grad Sch Med, ²The Osaka-Hamamatsu Joint Research Center for Child Mental Development, Osaka Univ Grad Sch Med, ³Dept Physiology, Osaka Univ Grad Sch Med, ⁴Dept Psychiatry, Juntendo Univ Sch Med, ⁵Dept Psychiatry, Tokushima Univ Grad Sch Med, ⁶Dept Psychiatry, Fujita Health Univ Sch Med ⁷Dept Psychiatry, Nagoya Univ Grad Sch Med

O5-2 Association between PNPO and schizophrenia in the Japanese population

○Hongwei Song¹, Shuichi Ueno², Shusuke Numata¹, Junichi Iga¹, Shumiko Shibuya-Tayoshi¹, Masahito Nakataki¹, Shin'Ya Tayoshi¹, Ken Yamauchi¹, Satsuki Simitani¹, Tomohito Tomotake¹, Tomohito Tada³, Toshihito Tanahasi⁴, Mitsuo Itakura⁴, Tetsuro Ohmori¹

¹Dept of Psychiatry, Institute of Health Biosciences, Univ. of Tokushima, ²Dept. of Community and Psychiatric Nursing, School of Health Sciences, Univ. of Tokushima, ³Dept. of Intern Med., Daiichi Hosp., Tokushima, ⁴Division of Genetic Infor., Institute for Genome Res., Univ. of Tokushima

O5-3 Functional analysis of Dysbindin, one of schizophrenia susceptibility genes

○Kyoko Kubota¹, Natsuko Kumamoto¹, Shinsuke Matsuzaki^{1,2}, Ryota Hashimoto^{2,3}, Masaya Tohyama^{1,2}

¹Department of Anatomy and Neuroscience, Osaka University Graduate School of Medicine, Osaka, Japan, ²The Osaka-Hamamatsu Joint Research Center For Child Mental Development, Osaka University Graduate School of Medicine, Osaka, Japan, ³Department of Psychiatry, Osaka University Graduate School of Medicine, Osaka, Japan

O5-4 Identification of the AP-3 complex as a novel Dysbindin-interacting molecule

○Yasutaka Fujino¹, Takao Hikita¹, Setsuko Kuroda¹, Shinichiro Taya¹, Kozo Kaibuchi¹

¹Department of Cell Pharmacology, Graduate School of Medicine, Nagoya University, Nagoya, Japan

- O5-5 Phosphorylation by Erk regulates interaction between DISC1 and Kinesin-1
 ○Keisuke Kuroda¹, Shinichiro Taya¹, Junko Uraguchi¹, Yusuke Funahashi¹, Kozo Kaibuchi¹
¹Dept of Cell Pharmacol., Nagoya Univ. Grad Sch. of Med., Nagoya, Japan
- O5-6 Neonatal exposure to neuregulin1- β 1 potentiates MK-801 sensitivity in locomotion and c-fos expression in adult mice
 ○Taisuke Kato¹, Makoto Mizuno^{1,2}, Hiroyuki Nawa¹
¹Mol. Neurobiol. Brain Res. Inst. Niigata Univ, ²Center for Transdisciplinary Res. Niigata Univ
- O5-7 Neonatal exposure to epidermal growth factor potentiates dopamine D2 receptor sensitivity and influences GABAergic activity in the basal ganglia
 ○Hidekazu Sotoyama¹, Hiroyuki Nawa¹
¹Dept. of Mol. Neurobiol., Niigata Univ.
- O5-8 Lamotrigine prevented neuroplastic disruption of prepulse inhibition induced by repeated administration of a high-dose of methamphetamine
 ○Yasuya Nakato¹, Tomohiro Abekawa¹, Koki Ito¹, Aya Kakuta¹, Tsukasa Koyama¹
¹Dept. of Psychiatry, Univ. of Hokkaido
- O5-9 Involvement of muscarinic acetylcholine receptor in isolation rearing-induced deficits in prepulse inhibition of the acoustic startle response in mice
 ○Ken Koda¹, Koji Yano¹, Yukio Ago¹, Momoe Nishimura¹, Kazuhiro Takuma¹, Toshio Matsuda^{1,2}
¹Lab. Medicinal. Pharmacol., Grad. Sch. Pharmaceut. Sci., Osaka Univ., Osaka, Japan ² Center For Child Mental Dev., Grad. Sch. Med., Osaka Univ., Osaka, Japan

September 11 (Thursday)

16:00~18:00 (Room B)

- O6-1~O6-6 Neurotransmission
 Chairs: Akira Ota (Department of Physiology, Fujita Health University School of Medicine)
 Hiroko Baba (Department of Molecular Neurobiology, School of Pharmacy,
 Tokyo University of Pharmacy and Life Sciences)
- O6-1 The role of cyclic ADP-ribose for calcium release in NG108-15 neuronal cells
 ○Sarwat Amina¹, HongXiang Liu¹, Olga Lopatina¹, Minako Hashii¹, Haruhiro Higashida¹
¹Dept. of Biophysical Gen., Kanazawa Univ
- O6-2 Impairment of HPA-axis in HPC-1/syntaxin1A knockout mice
 ○Takefumi Kofuji¹, Tomonori Fujiwara², Masumi Sanada², Kimio Akagawa²
¹Radioisotope Laboratory, Kyorin University School of Medicine, Mitaka, Tokyo, Japan,
²Department of Cell Physiology, Kyorin University School of Medicine, Mitaka, Tokyo, Japan

- O6-3 Formation of a novel nitrated second messenger, 8-nitroguanosine 3', 5'-cyclic monophosphate in glial cells**
○Tomoaki Ida¹, Tomohiro Sawa², Takaaki Akaike², Hideshi Ihara¹
¹Department of Biological Science, Graduate School of Science, Osaka Prefecture University, Osaka, Japan, ²Department of Microbiology, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan
- O6-4 Altered expression of tetrahydrobiopterin-dependent enzymes in sepiapterin reductase-null mice**
○Daigo Homma¹, Chisato Takazawa¹, Kengo Fujimoto², Setsuko Katoh², Hiroshi Ichinose¹
¹Graduate School of Bioscience and Bioechnology, Tokyo Institute of Technology, Yokohama, Japan, ²Meikai University School of Dentistry
- O6-5 Prostanoid CRTH2 receptor signaling regulates light-induced phase advance of circadian rhythm**
○Norihito Shintani¹, Chihiro Kawaguchi¹, Reiko Nakamura¹, Michiyoshi Hatanaka¹, Yasushi Isojima^{2,3}, Rie Tsuchida¹, Ryota Haba¹, Hitoshi Hashimoto^{1,4}, Yukihiro Sugimoto⁵, Katsuya Nagai², Hiroyuki Hirai⁶, Kinya Nagata⁶, Masataka Nakamura⁷, Toshiyuki Matsuoka⁸, Shu Narumiya⁸, Akemichi Baba¹
¹Lab. Mol. Neuropharmacol., Grad. Sch. Pharmaceut. Sci., Osaka Univ. ²Inst. Protein Res., Osaka Univ. ³Genomic Sci. Cent., RIKEN, ⁴Center Child Mental Dev., Grad. Sch. Med., Osaka Univ. ⁵Dept. Physiol. Chem., Grad. Sch. Pharmaceut. Sci., Kyoto Univ. ⁶Dept. Advanced Med. and Dev., BML, Inc., ⁷Human Gene Sci. Center, Tokyo Med. and Dent. Univ. ⁸Dept. Pharmacol., Fac. Med., Kyoto Univ.
- O6-6 Effects of intracerebroventricular injection of prostanoid CRTH2 receptor agonists on the open-field behavior in mice**
○Ryota Haba¹, Michiyoshi Hatanaka¹, Norihito Shintani¹, Hyper Wang¹, Hitoshi Hashimoto¹, Akemichi Baba¹
¹Lab. Mol. Neuropharmacol., Grad. Sch. Pharmaceut. Sci., Osaka Univ.

September 11 (Thursday)

16 : 00~18 : 00 (Room C)

O7-1~O7-6 Neuroimmuno-endocrinology

Chairs : Hiroshi Ohnishi (Laboratory of Biosignal Sciences, Institute for Molecular and Cellular Regulation, Gunma University)
Yasunobu Okuma (Department of Pharmacology, Faculty of Pharmaceutical Sciences, Chiba Institute of Science)

- O7-1 Suppression of glial cell line-derived neurotrophic factor (GDNF) secretion from microglia activated by endotoxin**
○Kazuyuki Nakajima^{1,2}, Yuichi Matsushita¹, Yoko Tohyama¹, Shinichi Kohsaka², Tadashi Kurihara¹
¹Dept. of Bioinformatics, Faculty of Engineering, Soka University, Tokyo, Japan, ²National Institute of Neuroscience, Tokyo

- O7-2 Dopamine D1 receptor-induced signaling through TrkB receptors in striatal neurons**
 ○Yuriko Iwakura¹, Hiroyuki Nawa¹, Ichiro Sora², Moses Chao V.³
¹Division of Molecular Neurobiology, Brain Research Institute, Niigata University,
²Department of Biological Psychiatry, Tohoku University Graduate School of Medicine,
³Molecular Neurobiology Program, Kimmel Center at Skirball Institute of Biomolecular Medicine, New York University School of Medicine
- O7-3 Antipsychotic effects of ErbB1 tyrosine kinase inhibitors on behavioral deficits in the neonatal hippocampal lesion model of schizophrenia**
 ○Makoto Mizuno¹, YingJun Zheng², Hiroki Kawamura², Masako Shibuya², Ying-shan Piao², Hidekazu Sotoyama², Takeyoshi Eda², Hiroyuki Nawa²
¹Center for Transdisciplinary Research, Niigata Univ. ²Dept. of Mol. Neurobiol., Brain Res. Institute, Niigata Univ.
- O7-4 Nerve growth factor attenuates 2-deoxyglucose-triggered endoplasmic reticulum stress-mediated apoptosis via enhanced induction of GRP78 expression**
 ○Soichiro Kishi¹, Koji Shimoke^{1,2}, Nobuaki Okumura³, Takafumi Shimada¹, Yuko Fujita¹, Katsuya Nagai⁴, Kazuo Shin-ya⁵, Toshihiko Ikeuchi^{1,2}
¹Grad. School of Engin., Kansai Univ., Osaka, ²Dept. of Life Sci. and Biotech., Fac. of Chem., Mat. and Bioengin., Kansai Univ., Osaka, ³Institute for Protein Research, Osaka Univ., Osaka, ⁴ANBAS Corporation, Osaka, ⁵Biomedical Information Research Center, Advanced Industrial Science & Technology, Tokyo
- O7-5 Activity-dependent cascade of gene expression regulated by pituitary adenylate cyclase-activating polypeptide (PACAP) in neurons**
 ○Mamoru Fukuchi¹, Shinjiro Watanabe¹, Ichiro Takasaki², Akiko Tabuchi¹, Masaaki Tsuda¹
¹Dept of Biol Chem, Grad Sch of Med & Pharm Sci, Univ of Toyama, ²Div of Mol Gene Res, Life Sci Res Ctr, Univ of Toyama
- O7-6 Modulation by ATP of neurotrophic factor expression in astroglia**
 ○Daisuke Kiyonaga¹, Shunsuke Kato¹, Yuki Kambe¹, Masato Ogura¹, Hideo Taniura¹, Noritaka Nakamiti¹, Yukio Yoneda¹
¹Lab Mol Pharmacol, Kanazawa Uni Grad Sch Nat Sci Tech, Kanazawa, Japan

September 11 (Thursday)

16 : 00 ~ 18 : 00 (Room D)

O8-1 ~ O8-6 Serotonin

Chairs : Jun'ichi Semba (Department of Psychiatry, Saitama City Hospital)
 Tetsuro Ohmori (Department of Psychiatry, The University of Tokushima)

- O8-1 Serotonin 1A receptor is involved in the paradoxical antihyperkinetic effect of the drugs treating ADHD**
 ○Rie Tsuchida¹, Hitoshi Hashimoto^{1,2}, Masahiro Kubo¹, Norihito Shintani¹, Yukio Ago³, Toshio Matsuda^{2,3}, Akemichi Baba¹

¹Laboratory of Lab. Mol. Neuropharmacol., Grad. Sch. Pharmaceut. Sci., Osaka Univ.
²Center for Child Mental Dev., Grad. Sch. Med, Osaka Univ. ³Lab of Medical Pharmacology, Grad Sch of Pharmaceutical Sci, Osaka Univ.

- O8-2 Serotonin receptor expression profiles in mouse hippocampus along the septo-temporal axis of the mouse hippocampus**
○Kenji Tanaka¹, Rene Hen²
¹Div. Neurobiol & Bioinfo, National Institute for Physiological Sciences, ²Dept of Neuroscience, Columbia University, New York, NY, USA
- O8-3 Functional analysis of a wide range of G protein-coupled serotonin receptors by a single method**
○Takashi Ueda¹, Shinya Ugawa¹, Yusuke Ishida¹, Shoichi Shimada¹
¹Dept. of Neurobiol. and Anat., Nagoya City Univ.
- O8-4 Involvement of dopamine-D² and serotonin^{1A} receptors in the ability of atypical antipsychotic drugs to induce prefrontal dopamine release**
○Naoko Nagao^{1,2}, Toshihide Kuroki², Tatsuo Nakahara^{1,2}, Keisuke Motomura¹, Kijiro Hashimoto², Shigenobu Kanba¹
¹Dept. of Neuropsychiatry Kyushu Univ. Grad. Sch. Med. Sci., Fukuoka, Japan, ²NHO Hizen Psychiatric Center, Yoshinogari, Japan
- O8-5 Brain serotonin transporter imaging by PET with [¹¹C]DASB in conscious marmosets**
○Chihiro Yokoyama¹, Akihiro Kawasaki¹, Kayo Onoe², Hiroko Nagata³, Keiko Hatanaka³, Hisashi Doi³, Hirotaka Onoe¹
¹Functional Probe Res. Lab., Mol. Imag. Res. Prog., RIKEN, Kobe, Japan, ²Mol. Probe Dynamics Lab., Mol. Imag. Res. Prog., RIKEN, Kobe, Japan, ³Mol. Probe & Drug Design Lab., Mol. Imag. Res. Prog., RIKEN, Kobe, Japan
- O8-6 Modulation of Tryptophan and Serotonin Metabolites in Tryptophan 2,3-Dioxygenase and Indoleamine 2,3-Dioxygenase Knockout Mice**
○Masaaki Kanai¹, Hiroshi Funakoshi¹, Hisaaki Takahashi¹, Shinya Mizuno¹, Kunio Matsumoto¹, Toshikazu Nakamura¹
¹Div. Mol. Regenerative Med., Dept. Biochemistry and Mol. Biology, Osaka Univ. Grad. Sch. Med., Osaka, Japan

September 11 (Thursday)

16 : 00~18 : 00 (Room E)

- O9-1~O9-6 Transcriptional factor/Cell adhesion factor**
Chairs : Tsuneo Okuyama (1 : Protein Technos Institute Ltd.
2 : Ogata Institute for Medical and Chemical Research)
Kenji Sakimura (Dept. of Cellular Neurobiology, Brain Research Institute,
Niigata University)

- O9-1** OASIS, a member of the CREB/ATF family transcription factor, is involved in CSPG production in the CNS
 ○Hiroaki Okuda¹, Kouko Tastumi¹, Kazunori Imaizumi², Akio Wanaka¹
¹Department of 2nd Anatomy, Nara medical University, Nara, Japan, ²Division of molecular and cellular biology, Dept. of Anatomy, Faculty of Medicine, Univ. of Miyazaki, Miyazaki, Japan
- O9-2** Expression of Foxp1 in a subset of spinal motor neurons during development
 ○Tomoko Hisaoka¹, Yoshihiro Morikawa¹, Emiko Senba¹
¹Department of Anatomy & Neurobiology, Wakayama Medical University, Wakayama, Japan
- O9-3** Necdin interacts with Foxo1 and represses its transcriptional activity
 ○Tomohiro Kawahara¹, Koichi Hasegawa¹, Kazuaki Yoshikawa¹
¹Laboratory of Regulation of Neuronal Development, Institute for Protein Research, Osaka University
- O9-4** Regulation of somatic growth and energy homeostasis by a putative transcription factor AF5q31 in the hypothalamus
 ○Tadasuke Komori¹, Tetsuya Nosaka², Toshio Kitamura³, Emiko Senba¹, Yoshihiro Morikawa¹
¹Department of Anatomy & Neurobiology, Wakayama Medical University, Wakayama, Japan, ²Department of Microbiology, Mie University Graduate School of Medicine, Mie, Japan, ³Division of Cellular Therapy, Advanced Clinical Research Center, The Institute of Medical Science, The University of Tokyo, Tokyo, Japan
- O9-5** Synaptogenesis between the parallel fibers and Purkinje cells of the cerebellum is perturbed in NB-3 knockout mice
 ○Kunie Sakurai¹, Manabu Toyoshima¹, Kota Matsubara¹, Yasuo Takeda², Yasushi Shimoda¹, Domna Karagogeos³, Kazutada Watanabe¹
¹Dept. Bioeng., Nagaoka Univ. Tech. ²Dept. Clinic. Pharm. & Pharmacol., Kagoshima Univ. Grad. Sch. Med. & Dent. Sci. ³Dept. Basic Sci., Crete Univ. Grad. Sch. Med.
- O9-6** L1 mRNA was decreased in the hippocampal granule cells in the patients with schizophrenia, major depression, and bipolar disorder.
 ○Kazuhiro Horinouchi^{1,2,3}, Aiko Izumi², Masaya Tohyama³, Sadao Shiosaka¹, Kunimasa Arima⁴, Hiroshi Kunugi²
¹Division of Structural Cellular Biology, Nara Institute of Science and Technology, ²Department of Mental Disorder Research, National Institute of Neuroscience (NIN), National Center of Neurology and Psychiatry (NCNP), ³Department of Anatomy and Neuroscience, Graduate School of Medicine, Osaka University, ⁴Department of Laboratory Medicine, Musashi Hospital, National Center of Neurology and Psychiatry (NCNP)

September 11 (Thursday)

16 : 00~18 : 00 (Room F)

O10-1~O10-6

Neurodegenerative disorders

Chairs : Akira Sano (Department of Psychiatry, Kagoshima University Graduate School of Medical and Dental Sciences)
Itaru Toyoshima (Medical Education Center, Akita University School of Medicine)

O10-1 Aberrant interaction between familial Parkinson's disease-associated mutant UCH-L1 and the lysosomal receptor for chaperone-mediated autophagy

○Tomohiro Kabuta¹, Akiko Furuta¹, Shunsuke Aoki¹, Koh Furuta², Keiji Wada¹

¹Department of Degenerative Neurological Diseases, National Institute of Neuroscience, National Center of Neurology and Psychiatry, Tokyo, Japan, ²Division of Clinical Laboratories, National Cancer Center Hospital, Tokyo, Japan

O10-2 Decreased secretion of UCH-L1 and SOD1 by the mutations associated with neurodegenerative diseases

○Chiho M Konya¹, Tomohiro Kabuta¹, Aiko Kinugawa¹, Keiji Wada¹

¹Department of Degenerative Neurological Diseases, National Institute of Neuroscience, National Center of Neurology and Psychiatry

O10-3 The de-ubiquitinating enzyme, UCH-L1, and lipid peroxidation

○Satoshi Nagamine¹, Tomohiro Kabuta¹, Kazuhiro Yamamoto², Akio Takahashi², Keiji Wada¹

¹Department of Degenerative Neurological Diseases, National Institute of Neuroscience, National Center of Neurology and Psychiatry, Tokyo, Japan, ²Administrative Section of Laboratory Animal Resources, National Institute of Neuroscience, National Center of Neurology and Psychiatry, Tokyo, Japan

O10-4 Involvement of oxidative-modified protein in the pathogenesis of Parkinson disease

○Masayo Nagai-Shamoto¹, wakako Maruyama¹, Makoto Naoi²

¹Dept. of Gerontology, National Institute for Geriatrics and Gerontology, Obu, Japan, ²Gifu International Institute of Biotechnology, Kakamigahara, Japan

O10-5 Immunoreactivity of endosome related proteins in ALS and ALS with dementia

○Tetsuya Takahashi¹, Masanori Hiji², Hiromasa Fukuba¹, Hiroshi Yamashita¹, Tatsuo Kohriyama¹, Masayasu Matsumoto¹

¹Dept. of Clinical Neuroscience and Therapeutics, Hiroshima Univ. ²Viha-ra Hananosato Hospital, Miyoshi City, Hiroshima, Japan

O10-6 Loss of ALS2/alsin exacerbates motor dysfunction and axonal damage in SOD1^{H46R} transgenic mice

○Shinji Hadano^{1,2}, Asako Otomo¹, Ryota Kunita¹, Kyoko Suzuki-Utsunomiya¹, Kyuichiro Onoe¹, Hitoshi Osuga¹, Masashi Aoki³, Yasuto Itoyama³, Joh-E Ikeda^{1,2}

¹Dept. of Mol. Life Sci., Tokai Univ. Sch. of Med. ²Neurodegenerative Dis. Res. Centre, Grad. Sch. of Med., Tokai Univ. ³Dept of Neurol., Tohoku Univ. Grad. Sch. of Med.

September 12 (Friday)

14 : 05~15 : 45 (Room B)

- O11-1~O11-5 Axonal and dendritic outgrowth**
 Chairs : Michihiro Igarashi (Div Mol Cell Biol, Niigata Univ Grad Sch Med Dent Sci)
 Hiroyuki Kamiguchi (Laboratory for Neuronal Growth Mechanisms RIKEN
 Brain Science Institute)
- O11-1 Systematic Identification of the growth cone proteins that are essential to axonal growth**
 ○Motohiro Nozumi^{1,2}, Michihiro Igarashi^{1,2}
¹Div Mol Cell Biol, Niigata Univ Grad Sch Med, ²Trans-deciplinary Res Progr, Niigata Univ
- O11-2 Regulation of axonal outgrowth by drebrin-mediated F-actin reorganization**
 ○Toshiyuki Mizui^{1,2}, Hiroyuki Yamazaki¹, Tomoaki Shirao¹
¹Department of Neurobiology and Behavior, Gunma University Graduate School of Medicine, Maebashi, Japan, ²21st Century COE Program, Japan
- O11-3 Differential regulation of cortical dendritic and axonal development via distinct activation of CaMKK-CaMKI pathways**
 ○Natsumi Ageta-Ishihara¹, Sayaka Takemoto-Kimura¹, Aki Adachi-Morishima¹, Mio Nonaka¹, Hiroyuki Okuno¹, Haruhiko Bito¹
¹ Dept Neurochem, Univ of Tokyo
- O11-4 Functional screen combining fluorophore-assisted light inactivation and organotypic cultures of the developing brain**
 ○Kohtaro Takei^{1,3}, Megumi Yamaguchi¹, Yasufumi Sato^{1,2,3}, Masumi Iketani¹, Yuko Arie¹, Yoshio Goshima^{1,3}
¹Department of Molecular Pharmacology and Neurobiology, Graduate School of Medicine, Yokohama City University, Yokohama, Japan, ² Stroke Research Group, Mitsubishi Kagaku Institute of Life Sciences, Tokyo, Japan, ³CREST, Japan Science and Technology Agency, Kawaguchi, Japan
- O11-5 Effects of motoneuron-derived factor(s) on dorsal root ganglia development in mouse embryos**
 ○Noriyoshi Usui^{1,2}, Hirohide Takebayashi^{1,2}, Katsuhiko Ono^{1,2}, Kazuhiro Ikenaka^{1,2}
¹Department of Physiological Sciences, The Graduate University for Advanced Studies, Hayama, Japan, ²Division of Neurobiology and Bioinformatics, National Institute for Physiological Sciences, Okazaki, Japan

September 12 (Friday)

14 : 05 ~ 15 : 45 (Room C)

O12-1 ~ O12-5

Cerebral ischemia

Chairs : Akihiko Ogura (Osaka University Graduate School of Frontier Biosciences)

Kazuo Yamada (Neurosurgery, Nagoya City University)

O12-1 Sema4D in regulation of neural cell apoptosis after stroke

○Shinobu Inagaki¹, Takenobu Wada², Wataru Yamaguchi¹, Mariko Ogiya¹, Noriko Uesugi¹, Mizue Takahara¹, Orié Saino³, Tatsuo Furuyama⁴, Mikihiro Kogo², Tomohiro Matsuyama³

¹Group of Neurobiology, Division of Health Sciences, Osaka University Graduate School of Medicine, ²Department of Pathogenesis and Control of Oral Diseases, Osaka University Graduate School of Dentistry, ³Hyogo College of Medicine, ⁴Department of Oral Anatomy and Developmental Biology, ⁵Kagawa Prefectural College of Health Sciences

O12-2 Sema4D in regulation of neural cell production after stroke

○Takenobu Wada¹, Wataru Yamaguchi², Orié Saino³, Yoshitaka Taniguchi¹, Rie Tamai², Makoto Abe⁴, Tatsuo Furuyama⁵, Tomohiro Matsuyama³, Shinobu Inagaki², Mikihiro Kogo¹

¹Department of Pathogenesis and Control of Oral Diseases, Graduate School of Dentistry, Osaka University, ²Group of Neurobiology, Division of Health Sciences, Osaka University Graduate School of Medicine, ³Laboratory of Neurogenesis and CNS Repair, Institute for Advanced Medical Sciences, Hyogo College of Medicine, ⁴Department of Oral Anatomy and Developmental Biology, Graduate School of Dentistry, ⁵Kagawa Prefectural College of Health Sciences

O12-3 Pathophysiological relevance of uncoupled endothelial nitric oxide synthase in ischemia-induced neurovascular injury

○Feng Han¹, Kohji Fukunaga^{1,2}

¹Department of Pharmacology, Tohoku University, Sendai, Japan, ²Tohoku Univ. 21st Century COE Program

O12-4 Inhibition of protein tyrosine kinase prevents disruption of blood brain barrier and attenuates infarct size after transient focal cerebral ischemia

○Kazutoshi Murotomi¹, Norio Takagi¹, Yuji Takenaga¹, Satoshi Takeo¹, Kouichi Tanonaka¹

¹Department of Molecular and Cellular Pharmacology, Tokyo University of Pharmacy and Life Sciences, Tokyo, Japan

O12-5 PEDF protects against ischemic brain injury in the rat middle cerebral artery occlusion model.

○Takeshi Yabe¹, Tomomi Sanagi¹, Haruki Yamada¹

¹Kitasato Institute for Life Sciences, Kitasato University

September 12 (Friday)

14 : 05~15 : 45 (Room D)

O13-1~O13-5

Signal transduction

Chairs : Tatsuo Suzuki (Dept. Neuroplasticity, Shinshu Univ. Grad. Sch. Med.)

Minako Hashii (Dept. Biophysical Genetics, Kanazawa Univ. School of Medicine)

- O13-1 Searching for CaMKII-interacting proteins and analysis of the functional relationship using coexpression database

○Takafumi Yamada¹, Akihiro Iwamatsu², Takeshi Obayashi³, Kengo Kinoshita³, Shunji Ohsako¹

¹Tokyo Metro. Inst. for Neurosci. ²Protein Research Network, Inc. ³Inst. of Med. Sci. Univ. of Tokyo

- O13-2 Neuropsin strongly induces cytomegalovirus major immediate-early promoter/enhancer activity in neurons

○Hideki Tamura¹, Yasuyuki Ishikawa¹, Sadao Shiosaka¹

¹Dept. of Structural Cellular Biology, NAIST

- O13-3 Regulation of endosomal localization of AATYK1A and its interaction with Src by palmitoylation

○Koji Tsutsumi¹, Mineko Tomomura², Teiichi Furuichi³, Shin-ichi Hisanaga¹

¹Dept. of Biol. Sci., Grad. Sch. of Sci., Tokyo Metro. Univ. ²RIKEN, Brain Sci. inst., Lab. Neuronal Growth Mechanisms lab, ³RIKEN, Brain Sci. inst., Lab. Molecular Neurogenesis lab.

- O13-4 Functional analysis of RhoGEF10

○Taro Chaya¹, Satoshi Shibata¹, Yoshiharu Ohoka², Shinobu Inagaki¹

¹School of Allied Health Science, Faculty of Medicine, Osaka University, ²Laboratory of Biodefense Research, Tokushima Bunri University Faculty of Pharmaceutical Science at Kagawa Campus, Kagawa, Japan

- O13-5 The intracellular signal of repulsive guidance molecule RGMa

○Katsuhiko Hata¹, Toshihide Yamashita¹

¹Department of Molecular Neuroscience, Graduate School of Medicine, Osaka University

September 12 (Friday)

14 : 05~15 : 45 (Room E)

O14-1~O14-5

Neuroprotection

Chairs : Kazunori Yoshimura (Department of Rehabilitation Nihon Institute of Medical Science)

Kosei Ojika (Department of Neurology, Graduate School of Medical Science, Nagoya City University)

- O14-1 Possible involvement of peroxisome proliferator-activated receptor- γ in protective effects of interferon- γ against methamphetamine-induced neurotoxicity

○Masato Asanuma¹, Saki Fukuoka², Hiroaki Hozumi², Ikuko Miyazaki¹, Yoshihisa Kitamura³, Toshiaki Sendo², Taizo Kita⁴

¹Dept. of Brain Sci., Okayama Univ. Grad. Sch. of Med., Dent. and Pharmaceut. Sci., Okayama, Japan, ²Dept. of Clin. Pharmacol. and Pharm., Okayama Univ. Grad. Sch. of Med., Dent. and Pharmaceut. Sci., Okayama, Japan, ³Dept. of Pharmaceut. Care and Health Sci., Okayama Univ. Grad. Sch. of Med., Dent. and Pharmaceut. Sci., Okayama, Japan, ⁴Lab. of Pharmacol., Kyushu Nutr. Welfare Univ., Grad Sch. of Food and Nutr., Kitakyushu, Japan

O14-2 Mechanisms of neuroprotection by nicotinic signaling in cultured rat cortical astrocytes

○Hirofumi Kawagoe¹, Masato Ogura¹, Hirotaka Oikawa², Noritaka Nakamichi¹, Yukio Yoneda¹

¹Laboratory of Molecular Pharmacology, Kanazawa Univ. Graduate School of Natural Science and Technology, Kanazawa, Japan, ²Division of Medical Genetics Dept. of Pediatrics School of Med. Saint Louis Univ., Saint Louis, USA

O14-3 Neuroprotection by brain-migrated immature bone marrow cells in an artificial brain injury

○Kenji Ono¹, Naho Yamamoto¹, Hiromi Suzuki¹, Emi Sato¹, Makoto Sawada¹

¹Department of Brain Functions, Division of Stress Adaptation and Protection, Research Institute of Environmental Medicine, Nagoya University

O14-4 Protection by ATP against NMDA neurotoxicity

○Yuta Kameshima¹, Shunsuke Kato¹, Yuki Kambe¹, Hideo Taniura¹, Noritaka Nakamichi¹, Yukio Yoneda¹

¹Lab Mol Pharmacol, Kanazawa Univ Grad Sch Nat Sci Tech, Kanazawa, Japan

O14-5 Protective effects of yokukansan, a traditional Japanese medicine, on glutamate-induced neuronal death

○Zenji Kawakami¹, Kiyoshi Terawaki¹, Hitomi Kanno¹, Masahiro Tabuchi¹, Yasushi Ikarashi¹, Yoshio Kase¹

¹TSUMURA Research Laboratories, TSUMURA & CO., Ibaraki, Japan

September 12 (Friday)

14 : 05~15 : 45 (Room F)

O15-1~O15-5 Animal models 1

Chairs : Masatoyo Nishizawa (Department of Neurology, Brain Research Institute, Niigata University)

Shigeo Kitayama (Department of Dental Pharmacology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences)

O15-1 Bcl-2 family proteins are involved in neuronal apoptosis in the chorea-acanthocytosis model mouse.

○Mieko Matsuda¹, Masayuki Nakamura¹, Mio Ichiba¹, Maiko Kato¹, Hirochika Simo¹, Akiyuki Tomiyasu¹, Nari Kono¹, Yoko Uchinokura¹, Satsuki Mori¹, Takanori Ishizuka¹, Takehiro Hayashi¹, Akira Sano¹

¹Department of Psychiatry, Kagoshima University, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, Japan

- O15-2** Decreased expression level of adducin β is associated with neurodegeneration and acanthocyte in chorea-acanthocytosis
 ○Masayuki Nakamura¹, Mieko Matsuda¹, Mio Ichiba¹, Maiko Kato¹, Hirochika Shimo¹, Akiyuki Tomiyasu¹, Nari Kono¹, Yoko Uchinokura¹, Satsuki Mori¹, Takanori Ishizuka¹, Takehiro Hayashi¹, Akira Sano¹
¹Department of Psychiatry, Kagoshima University Graduate School of Medical and Dental Sciences, Kagoshima, Japan
- O15-3** Immediate early gene products down-regulated by nicotine in hippocampus in DRPLA transgenic mice
 ○Yi Jin¹, Kazushi Suzuki¹, Toshiya Sato², Jun Shimizu¹, Jun Goto¹, Shoji Tsuji¹
¹Department of Neurology, Tokyo University, Tokyo, Japan ²Center for Bioresource-based Researches, Brain Research Institute, Niigata University, Niigata, Japan
- O15-4** Analysis of the molecular mechanism for 'dying-bac' type of axonal degeneration in gracile axonal dystrophy (GAD) mouse
 ○Akiko Goto^{1,2}, Yu-Lai Wang², Rieko Setsuie², Tomohiro Kabuta², Hitoshi Osaka², Akira Sawa³, Shoichi Ishiura¹, Keiji Wada²
¹Dept. of Life Sciences, Graduate School of Arts and Sciences, Univ. of Tokyo, Tokyo, Japan, ²Dept. of Degenerative Neurological Diseases, National Institute of Neuroscience, National Center of Neurology and Psychiatry, Kodaira, Tokyo, Japan, ³Dept of Neuroscience, Johns Hopkins University School of Medicine, Baltimore, MD, USA.
- O15-5** Microarray analysis in the dorsal root ganglion of rats with paclitaxel-induced neuropathy
 Kentaro Nishida¹, Satoshi Kuchiiwa², Shigeru Oiso¹, Toshitaka Futagawa^{1,3}, Shogo Masuda¹, Akari Shigemi³, Yuko Fujisaki³, ○Yasuo Takeda^{1,3}, Katsushi Yamada^{1,3}
¹Dept. of Clin. Pharm. and Pharmacol., Grad. Sch. of Med. and Dent. Sci., Kagoshima Univ. ²Dept. of Neuroanat., Grad. Sch. of Med. and Dent. Sci., Kagoshima Univ. ³Dept. of Clin. Pharm., Kagoshima Univ. Hosp.

September 12 (Friday)

16 : 25~18 : 25 (Room B)

O16-1~O16-6 Axonal transport / Cell motility / Cytoskeleton

Chairs : Mamoru Sano (Doshisha University, Department of Biomedical Engineering)
 Midori Hiramatsu (Tohoku University of Community Service and Science)

- O16-1** Possible role of a multi-domain adaptor protein, p140Cap, at the presynapse
 ○Koh-ichi Nagata¹, Hidenori Ito¹, Shiro Takei², Kaori Sudo¹, Ikuko Iwamoto¹, Rika Morishita¹, Tomiko Asano¹, Reiji Semba²
¹Dept. Mol. Neurobiol., Inst. Dev. Res., Aichi Human Service Ctr, Kasugai, Japan, ²Dept. Pathol., Inst. Dev. Res., Aichi Human Service Ctr, Kasugai, Japan
- O16-2** Possible involvement of myosin-ATPase in the vesicle recruitment for exocytosis in adrenal chromaffin cells: Studies with scanning electron microscopy.
 ○Konosuke Kumakura¹, Mizuki Sekiguti¹, Alessandro Riva², Masataka Murakami³, Mitunori Hayashi¹, Nobuyuki Sasakawa¹

¹Dept. of Information and Communication Science, Faculty of Science and Technology, Sophia University, Tokyo, Japan, ²Dept. of Cytomorphology, University of Cagliari, Italy, ³National Institute of Physiology, Okazaki, Japan

- O16-3 Chemical inhibitor screening for molecules regulating morphological changes of locomoting neurons in the developing cerebral cortex**
○Yoshiaki Nishimura^{1,2}, Kazunori Nakajima¹, Yo-ichi Nabeshima², Mikio Hoshino^{2,3}, Takeshi Kawauchi^{1,2}
¹Dept Anat, Keio Univ Sch, Tokyo, ²Dept Pathology and Tumor Biology, Grad Sch Medicine, Kyoto Univ, Kyoto, ³Dept Biochemistry and Cellular Biology, NCNP
- O16-4 Abi2 is involved in radial migration, possibly through interaction with nonmuscle myosin IIB**
○Min-Jue Xie¹, Hideshi Yagi^{1,2}, Masayuki Okamoto¹, Makoto Sato^{1,2}
¹Division of Cell Biology and Neuroscience, Department of Morphological and Physiological Sciences, Faculty of Medical Sciences, University of Fukui, Fukui, Japan, ²Research and Education Program for Life Science, University of Fukui
- O16-5 Expression of ABCA1 transporter is up-regulated in response to nerve injury**
○Nobue Ikejima-Shishioh¹, Saya Nakagomi¹, Hiroyuki Konishi¹, Hiroshi Kiyama¹
¹Department of Anatomy and Neurobiology, Osaka City University, Graduate school of Medicine, Osaka, Japan
- O16-6 Involvement of integrin β 1 activation by P2Y₁₂ receptor in the extension of microglial processes**
○Keiko Ohsawa¹, Yasuko Nakamura¹, Yasuhiro Irino², Eri Suzuki¹, Tomomi Sanagi¹, Kazuhide Inoue³, Shinichi Kohsaka¹
¹Dept. Neurochem., Natl. Inst. Neurosci., Tokyo Japan, ²Div. Lipid Biochem., Grad. Sch. Med. Kobe Univ., Hyogo Japan, ³Dept. Mol. System Pharmacol., Grad. Sch. Pharmac. Sci., Kyusyu Univ., Fukuoka Japan

September 12 (Friday)

16 : 25~18 : 25 (Room C)

O17-1~O17-6 Microglia/Oligodendrocyte

Chairs : Tadashi Miyatake (RIKEN Brain Science Institute)

Yoichi Nakamura (Department of Integrative Physiology in Veterinary Science, Osaka Prefecture University)

- O17-1 Upregulation of microglial mitogen macrophage-colony stimulating factor (M-CSF) and the receptor cFms in rat axotomized facial nucleus**
○Shinichi Yamamoto¹, Kazuyuki Nakajima^{1,2}, Yoko Tohyama¹, Shinichi Kohsaka², Tadashi Kurihara¹
¹Department of Bioinformatics, Faculty of Engineering, Soka University, Tokyo, Japan, ²Department of Neurochemistry, National Institute of Neuroscience, Tokyo, Japan

- O17-2 P2X7 receptor mediates zinc-triggered microglial activation**
 ○ Youichirou Higashi¹, Kazuki Nagasawa², Shohei Segawa², Hiroto Okuda², Miho Onishi², Yu Katsuta², Yuriko Watanabe², Tohru Mizushima¹, Sadaki Fujimoto²
¹Graduate School of Medical and Pharmaceutical Science, Kumamoto University, Kumamoto, Japan, ²Department of Environmental Biochemistry, Kyoto Pharmaceutical University
- O17-3 Clock genes expressed by microglia**
 ○ Tomomi Yamamoto¹, Takeshi Takarada¹, Koichi Sahara¹, Masaki Tachibana¹, Hideo Taniura¹, Yukio Yoneda¹
¹Lab Mol Pharmacol, Kanazawa Univ Grad Sch Nat Sci Tech, Kanazawa, Japan
- O17-4 The lineage tracing of Olig2+ cells in a murine demyelinating disease model**
 ○ Takahiro Shimizu^{1,2}, Hirohide Takebayashi^{1,2}, Katsuhiko Ono^{1,2}, Kazuhiro Ikenaka^{1,2}
¹The Graduate University of Advanced Studies, Aichi, Japan ²National Institute for Physiological Sciences, Aichi, Japan
- O17-5 Differential localization of Myelin basic protein mediated oligodendrocyte maturation.**
 ○ Nanako Sato^{1,2}, Chika Seiwa², Kenji Tsuiji¹, Michihiro Uruse¹, Yurie Sato¹, Rika Shinagawa³, Yasuhiro Shimoda³, Hiroaki Asou^{1,2}, Kenji Watanabe¹
¹Center for Kampo Medicine, Med, Univ. of Keio, Tokyo, Japan, ²Department of Neurobiology, Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan, ³Ono pharmaceutical co. ltd., Osaka
- O17-6 Sema4D expression in oligodendrocytes**
 ○ Wataru Yamaguchi¹, Rie Tamai¹, Yoshitaka Taniguchi², Tatsuo Furuyama³, Shinobu Inagaki¹
¹Group of Neurobiology, Division of Health Sciences, University of Osaka, Osaka, Japan, ²Department of Pathogenesis and Control of Oral Diseases, University of Osaka, Osaka, Japan, ³Kagawa Prefectural College of Health Sciences, Kagawa, Japan

September 12 (Friday)

16 : 25~18 : 25 (Room D)

O18-1~O18-6 Neuronal differentiation

Chairs : Yasuyuki Nomura (Yokohama College of Pharmacy)

Kazuaki Yoshikawa (Laboratory of Regulation of Neuronal Development

Institute for Protein Research, Osaka University)

O18-1 Uni-directional neural differentiation from human embryonic stem cells by Neural Stem Sphere method

○ Masahiro Otsu^{1,2}, Daisuke Inada¹, Nobue Kume¹, Tomoaki Sai^{1,3}, Tomoko Momokisoga¹, Takashi Nakayama^{1,4}, Yutaka Suzuki⁵, Yasushi Kondo⁵, Hisataka Kasai¹, Nobuo Inoue¹

¹Lab. Regener. Neurosci., Tokyo Metropol. Univ. Grad. Sch. Human Health Sci., Tokyo, Japan, ²Dept. Chem., Kyorin Univ. Sch. Med. ³Dept. Orthop. Surg., Jikei Univ. Sch. Med. ⁴Dept. Biochem., Yokohama City Univ. Sch. Med. ⁵Adv. Med. Res. Dept., Mitsubishi Tanabe Pharma Co.

- O18-2 Modulation of differentiation by group III metabotropic glutamate receptor signals in murine neural progenitor cells**
○Juliet O. Makanga¹, Kohei Yoshida¹, Masaki Fukui¹, Noritaka Nakamichi¹, Yukio Yoneda¹
¹Lab Mol Pharmacol, Kanazawa Univ Grad Sch Nat Sci Tech, Kanazawa, Japan
- O18-3 A new method to generate serotonergic neurons from ES cells**
○Takeshi Shimada¹, Yoshihiro Takai¹, Kikuko Shinohara¹, Hitoshi Hashimoto^{1,2}, Norihito Shintani¹, Akemichi Baba¹
¹Lab. Mol. Neuropharmacol., Grad. Sch. Pharmaceut. Sci., Osaka Univ. ²Center for Child Mental Dev., Grad. Sch. Med., Osaka Univ.
- O18-4 Analysis on the expression and function of BRINP family genes during neuronal differentiation of mouse embryonic stem cell-derived neural stem cells**
○Michiyo Terashima¹, Miwako Kobayashi^{2,3}, Makoto Motomiya¹, Nobuo Inoue⁴, Norimasa Iwasaki¹, Akio Minami¹, Ichiro Matsuoka^{2,3,5}
¹Dept. of Orthop. Surg., Univ. of Hokkaido, ²CRIS, ³Lab. of Physiol. Chem., Univ. of Matsuyama, ⁴Dept. of Frontier Health Sci., Univ. of Tokyo Metropolitan, ⁵Grad. Sch. of Pharm. Sci., Univ. of Hokkaido
- O18-5 The Dynamics of Chromatin Organization during Rod Photoreceptor Differentiation**
○Itsuki Ajioka¹, Stacy Donovan¹, Dyer Michael^{1,2}
¹Department of Developmental Neurobiology, St. Jude Children's Research Hospital, ²Department of Ophthalmology, College of Medicine, University of Tennessee Health Science Center, Memphis, TN, U.S.A.
- O18-6 Effects on Proliferation and Differentiation of ES Cells by culture conditions of Mouse Embryonic Fibroblast**
Banri Yamanoha¹, ○Keiko Kitazawa¹, Nobue Kume², Masahiro Otsu^{2,3}, Nobuo Inoue²
¹Dept. of Environment. Engineer. for Symbiosis., Facult. of Engineer., Soka Univ. ²Dept. of Frontier Health Sciences, Tokyo Metropolitan Univ. ³Dept. of Chemistry., Med., Kyorin Univ.

September 12 (Friday)

16 : 25~18 : 25 (Room E)

O19-1~O19-6

β Amyloid

Chairs : Hiroto Komano (Department of Neuroscience Faculty of Pharmaceutical Sciences Iwate Medical University)
Wataru Araki (Department of Demyelinating Disease and Aging, National Institute of Neuroscience, NCNP)

O19-1 β -amyloid induces macroautophagy in neuron

○Eiichiro Kamagata¹, Takashi Kudo¹, Hitoshi Tanimukai¹, Masatoshi Takeda¹
¹Department of Psychiatry, Osaka University Graduate School of Medicine

- O19-2 Characterization of GM1 ganglioside (GM1) endocytic pathways responsible for GM1-induced A β fibrillogenesis
 ○Kohei Yuyama¹, Naoki Yamamoto^{1,2,3}, Katsuhiko Yanagisawa¹
¹Dept. Alzheimer's Disease Res. Natl. Inst. for Longevity Sci., NCGG, ²JSPS, ³Dept. Pharmacy, Ritsumeikan Univ.
- O19-3 Substrate specific inhibition of BACE-mediated cleavage - Can inhibition of beta-cleavage be achieved without affecting extracellular shedding of Neuregulin1?
 ○Takashi Kodama¹, Naohiro Itoh¹, Masayasu Okochi¹, Shinji Tagami¹, Kanta Yanagida¹, Taisuke Nakayama¹, Shin-ichi Tatsumi¹, Jinwei Jiang¹, Kohji Mori¹, Kohei Nishitomi¹, Masatoshi Takeda¹
¹Department of Psychiatry, Osaka University Graduate School of Medicine, Osaka, Japan
- O19-4 Characteristics of membrane-bound factors affecting regulated intramembrane proteolysis of β APP
 ○Kohji Mori¹, Masayasu Okochi¹, Shinji Tagami¹, Takashi Kodama¹, Kanta Yanagida¹, Akio Fukumori¹, Jinwei Jiang¹, Shinichi Tatsumi¹, Kouhei Nishitomi¹, Taisuke Nakayama¹, Masatoshi Takeda¹
¹Psychiatry, Osaka University
- O19-5 Roles of receptor for advanced glycation endproducts and p38 MAPK in neuronal membrane transport of amyloid β -peptide
 ○Kazuhiro Takuma^{1,2}, Hiroyuki Mizoguchi^{2,3}, David M. Stern⁴, Kiyofumi Yamada^{2,3}, Shi Du Yan⁵
¹Lab. of Med. Pharmacol., Grad. Sch. of Pharmac. Sci., Osaka Univ., Suita, Japan, ²Lab. of Neuropsychopharmacol., Grad. Sch. of Nat. Sci. & Technol., Kanazawa Univ., Kanazawa, Japan, ³Hosp. Pharm., Nagoya Univ. Grad. Sch. of Med. ⁴Univ. of Cincinnati, Coll. of Med., Cincinnati, OH, USA, ⁵Dept. of Pathol., Columbia Univ., Coll. Phys. & Surg., New York, NY, USA
- O19-6 The level of plasma A β is lowered in M-CSF deficient mice
 ○Shin-ichi Tatsumi¹, Jinwei Jiang¹, Masayasu Okochi¹, Shinji Tagami¹, Kanta Yanagida¹, Taisuke Nakayama¹, Kohji Mori¹, Takashi Kodama¹, Masatoshi Takeda¹
¹Department of Psychiatry, Osaka University Graduate School of Medicine

September 12 (Friday)

16 : 25~18 : 25 (Room F)

O20-1~O20-6 **Dementia**
 Chairs : Shigenobu Nakamura (Kyoto Clinical Trial Center)
 Nozomu Nori (Nagasaki University School of Medicine)

- O20-1 Biological effects of Presenilin/ γ modifiers
 ○Shinji Tagami¹, Masayasu Okochi¹, Masatoshi Takeda¹
¹Department of Psychiatry, Osaka University Graduate School of Medicine

- O20-2 Characterization of the domain responsible for the different specific activity of PS1 and PS2.**
○Keiro Shirotani¹, Yasuhiro Hashimoto¹, Shigetsugu Hatakeyama²
¹Department of Biochemistry, Fukushima Medical University School of Medicine,
²Department of Biochemistry, Hokkaido University Graduate School of Medicine
- O20-3 Presenilins are independent of the inhibitory effects of γ -secretase inhibitors on Wnt signaling**
○Taisuke Nakayama¹, Masayasu Okochi¹, Shinji Tagami¹, Takashi Kodama¹, Kanta Yanagida¹, Jingwei Jiang¹, Kohji Mori¹, Shin-ichi Tatsumi¹, Takashi Morihara¹, Ryota Hashimoto¹, Toshihisa Tanaka¹, Takashi Kudo¹, Masatoshi Takeda¹
¹Department of Psychiatry, Osaka University Graduate School of Medicine
- O20-4 Impact on Abeta accumulation in APP Tg mice by genetic background**
○Mikiko Yokokoji¹, Takashi Morihara¹, Noriyuki Hayashi¹, Shinji Tagami¹, Masatoshi Takeda¹
¹Department of Psychiatry, Osaka University Graduate School of Medicine, Osaka, Japan
- O20-5 Inhibitory effect of homocysteine on ApoE3-mediated cholesterol efflux from cultured astrocytes.**
○Hirohisa Minagawa¹, Jian-Sheng Gong¹, Sissel Lund-Katz², Michael Phillips², Hiroyuki Saito³, Makoto Michikawa¹
¹Dept of Alzheimer's Dis Res, NILS, National Center for Geriatrics and Gerontology, Obu, Japan, ²University of Pennsylvania School of Medicine, Philadelphia, PA, USA, ³Kobe Pharmaceutical University, Kobe, Japan
- O20-6 14-3-3 differentially induces 3-repeat and 4-repeat tau aggregation**
○Golam Sadik¹, Toshihisa Tanaka¹, Kiyoko Kato¹, Kentaro Yanagi¹, Masatoshi Takeda¹
¹Dept. Psychiatry, Osaka University Graduate School of Medicine

September 13 (Saturday)

9 : 00~12 : 00 (Room B)

- O21-1~O21-9 Neural network formation**
Chairs : Nobuyuki Takei (Department of Molecular Neurobiology, Brain Research Institute, Niigata University)
Satoru Kato (Department of Molecular Neurobiology, Grad. Sch. Med., Kanazawa University)
Kazutada Watanabe (Nagaoka University of Technology, Department of Bioengineering)

- O21-1 Identification of LOTUS, a novel molecule serving for neural circuit formation**
○Yasufumi Sato^{1,2,3}, Megumi Yamaguchi¹, Masumi Iketani¹, Yuko Arie¹, Fumio Nakamura¹, Takahiko Kawasaki⁴, Tatsumi Hirata⁴, Yoshio Goshima^{1,3}, Kohtaro Takei^{1,3}
¹Department of Molecular Pharmacology and Neurobiology, Graduate School of Medicine, Yokohama City University, Yokohama, Japan, ²Brain Stroke Research Group, Mitsubishi Kagaku Institute of Life Sciences, Tokyo, Japan, ³CREST, Japan Science and Technology Agency, Kawaguchi, Japan, ⁴Division of Brain Function, National Institute of Genetics, Graduate School for Advanced Studies, Mishima, Japan

- O21-2 Expression pattern of LOTUS, a novel molecule serving for neural circuit formation**
 ○Masumi Iketani¹, Yasufumi Sato^{1,2,3}, Megumi Yamaguchi¹, Yuko Arie¹, Harumi Kaneko-Sekiguchi¹, Fumio Nakamura¹, Yoshio Goshima^{1,3}, Kohtaro Takei^{1,3}
¹Department of Molecular Pharmacology and Neurobiology, Graduate School of Medicine, Yokohama City University, Yokohama, Japan, ²Brain Stroke Research Group, Mitsubishi Kagaku Institute of Life Sciences, Tokyo, Japan, ³CREST, Japan Science and Technology Agency, Kawaguchi, Japan
- O21-3 Functional analysis of the receptor for LOTUS, a novel molecule serving for neural circuit formation**
 ○Megumi Yamaguchi¹, Yasufumi Sato^{1,2,3}, Masumi Iketani¹, Yuko Arie¹, Harumi Kaneko-Sekiguchi¹, Fumio Nakamura¹, Yoshio Goshima^{1,3}, Kohtaro Takei^{1,3}
¹Department of Molecular Pharmacology and Neurobiology, Graduate School of Medicine, Yokohama City University, Kanagawa, Japan, ²Brain Stroke Research Group, Mitsubishi Kagaku Institute of Life Sciences, Tokyo, Japan, ³CREST, Japan Science and Technology Agency, Tokyo, Japan
- O21-4 Characterization of LOTUS, novel molecule serving for circuit formation, with Nogo-66 receptor**
 ○Yuko Arie^{1,2}, Megumi Yamaguchi¹, Yasufumi Sato^{1,3,4}, Masumi Iketani¹, Harumi Kaneko-Sekiguchi¹, Fumio Nakamura¹, Nobuhisa Mizuki², Yoshio Goshima^{1,4}, Kohtaro Takei^{1,4}
¹Department of Molecular Pharmacology and Neurobiology, Graduate School of Medicine, Yokohama City University, Yokohama, Japan, ²Department of Ophthalmology, Graduate School of Medicine, Yokohama City University, Yokohama, Japan, ³Brain Stroke Research Group, Mitsubishi Kagaku Institute of Life Sciences, Tokyo, Japan, ⁴CREST, Japan Science and Technology Agency, Kawaguchi, Japan
- O21-5 Involvement of Factor XIII in fish optic nerve regeneration**
 ○Kayo Sugitani¹, Tomoki Yamashita¹, Satoru Kato²
¹Div. Health Sci., Grad. Sch. Med. Univ. Kanazawa, Kanazawa, Japan, ²Dept. Mol. Neurobiol., Grad. Sch. Med. Univ. Kanazawa, Kanazawa, Japan
- O21-6 Aberrant auditory brainstem response and glutamatergic synaptic formation in NB-2 knockout mice**
 ○Manabu Toyoshima¹, Kunie Sakurai¹, Yasuo Takeda², Kuniko Shimazaki³, Yasushi Shimoda¹, Kazutada Watanabe¹
¹Dept. Bioeng., Nagaoka Univ. Tech., Niigata, ²Dept. Clinic. Pharm. & Pharmacol., Kagoshima Univ., Grad. Sch. Med. & Dent., Kagoshima, ³Dept. Physiol., Jichi Med. Univ., Tochigi
- O21-7 Abnormalities of mice with conditional targeted *Pcdh-γ* allele**
 ○Yasuto Itoga¹, Kayoko Makino¹, Takahiro Hirabayashi¹, Takeshi Yagi¹
¹Grad. Sch., Front. Biosci., Osaka Univ.
- O21-8 Expression profile of Roundabout1 (Robo1) in the developing mouse neocortex**
 ○Yuko Gonda¹, Hidenori Tabata², Kazunori Nakajima², Shigeo Uchino¹, Shinichi Kohsaka¹

¹Department of Neurochemistry, National Institute of Neuroscience, Tokyo, Japan,

²Department of Anatomy, Keio University School of Medicine, Tokyo, Japan

O21-9 Purpurin protects injury-induced apoptosis in rat CNS neurons

○Yoshiki Koriyama¹, Toru Matsukawa¹, Junichi Saito², Masumi Nonaka², Satoru Kato¹

¹Dept. Mol. Neurobiol., Grad. Sch. Med., Kanazawa Univ., Kanazawa, Japan, ²Div. Health Sci., Grad. Sch. Med., Kanazawa Univ., Kanazawa, Japan

September 13 (Saturday)

9 : 00~12 : 00 (Room C)

O22-1~O22-9 Glia/Myelin

Chairs : Kohji Sato (Department of Anatomy & Neuroscience, Hamamatsu Univ. School of Medicine)

Mitsuhiro Yoshioka (Department of Neuropharmacology, Hokkaido University Graduate School of Medicine)

Kiyofumi Asai (Department of Molecular Neurobiology, Nagoya City University Graduate School of Medical Sciences)

O22-1 Cyclin D1 inhibits astrocyte differentiation in the section of neural stem cell

○Norihsa Bizen¹, toshihiro Inoue¹, Takeshi Shimizu², Tetushi Kagawa¹, Tetuya Taga¹

¹Div. of Cell Fate Mod., Insti. of Mol. Emb. and Gene., Kumamoto Univ, Kumamoto, Japan, ²Lab. for Vert. axis Form., RIKEN. CDB., Kobe, Japan

O22-2 BMP signaling through BMPRII is essential for proper terminal differentiation in glial progenitor cells

○Tomoko Ishibashi^{1,2}, Moeko Kudoh², Haruo Kishida², Lyons Karen M.³, Masahisa Yamada²

¹Dept. of Mol. Neurobiology, Tokyo Univ. of Pharmacy and Life Sciences, ²Yamada Research Unit, RIKEN BSI ³Brain Research Institute, UCLA, USA

O22-3 A novel method for domain specific gene modification, and analysis of glial development

○Hitoshi Gotoh¹, Katsuhiko Ono¹, Hirohide Takebayashi¹, Kazuhiro Ikenaka¹

¹Division of Neurobiology and Bioinformatics, National Institute for Physiological Sciences

O22-4 Osseous genes expressed in the brain

○Takeshi Takarada¹, Shintaro Kurokawa¹, Yusuke Tonami¹, Shiho Konishi¹, Yukio Yoneda¹

¹Laboratory of Molecular Pharmacology, Kanazawa University Graduate School of Natural Science and Technology

O22-5 Analysis of the Expression of PLD4 in the early postnatal mouse cerebellum

○Yoshinori Otani¹, Yoshihide Yamaguchi¹, Fumio Yoshikawa², Yumi Sato², Teiichi Furuichi², Hiroko Baba¹

¹Department of Molecular Neurobiology, Tokyo University of Pharmacy and Life Sciences, hachioji, japan, ²Laboratory for Molecular Neurogenesis, RIKEN Brain Science Institute, wako, japan

- O22-6 Involvement of astrocytic ATP in modulation of M1 muscarinic acetylcholine receptor expression in the hippocampal neurons
 ○Kayoko Fujishita¹, Kazuhide Inoue², Shuichi Koizumi¹
¹Dept. Pharmacol., Interdisciplinary Grad. Sch. Medicine and Engineering, Yamanashi Univ., Yamanashi, Japan, ²Dept. Pharmacol., Grad. Sch. Pharmaceut. Sci., Kyusyu Univ., Fukuoka, Japan
- O22-7 Modulation of gap junctions/hemichannels in astrocytes by rotenone *in vivo* and *in vitro*
 ○Asami Kawasaki¹, Tomonori Hayashi², Kei Nakachi², Yaichiro Kotake¹, Shigeru Ohta¹
¹Grad Sch. Biomed Sci., Hiroshima Univ., Hiroshima, Japan, ²Radiation Effects Res. Found., Hiroshima, Japan
- O22-8 A role of Annexin2 in the lysolecithin-induced demyelinating model mice
 ○Tetsuya Katakabe¹, Akiko Hayashi¹, Hiroko Baba¹
¹Department of Molecular Neurobiology, Tokyo University of Pharmacy and Life Sciences
- O22-9 Disruption of paranodal axo-glial junctions causes alteration of axonal mitochondria at nodes of Ranvier
 ○Akiko Kodama¹, Yoko Tateishi¹, Tomoko Ishibashi¹, Hiroko Baba¹
¹Department of Molecular Neurobiology, Tokyo University of Pharmacy and Life Sciences

September 13 (Saturday)

9 : 00 ~ 12 : 00 (Room D)

- O23-1 ~ O23-9 Neural development/Plasticity
 Chairs : Tokiko Hama (Japan Patent Office, Dept. Patent Examination)
 Masaaki Ikeda (1: Department of Physiology, and 2: Molecular Clock Project, Research Center for Genomic Medicine, Saitama Medical School)
 Hiroshi Ichinose (Tokyo Institute of Technology, Graduate School of Bioscience and Biotechnology)
- O23-1 Abnormal dendritic spine formation via CaMKII/Rac1-GEF/PAK signaling in X-linked mental retardation model mouse.
 ○Norifumi Shioda¹, Takashi Tokoro², Hideyuki Beppu³, Isao Kitajima², Kohji Fukunaga¹
¹Dept. Pharmacol., Tohoku Univ. Grad. Sch. Pharm. Sci. ²Dept. of Clinical and Molecular Pathology, Faculty of Med., Univ. of Toyama, ³Cardiovascular Research Center, Massachusetts General Hospital, Harvard Medical School
- O23-2 Caspr2 encoded by developmental and psychiatric disorder-susceptibility gene CNTNAP2 is involved in the synaptic development
 ○Kazuaki Arita¹, Yasushi Shimoda¹, Masaru Sakai¹, Hidehiro Ueda¹, Kazutada Watanabe¹
¹Department of Bioengineering, Nagaoka University of Technology

- O23-3 Diet-induced obesity in female mice leads to obesity and peroxidized lipid accumulation during early life of their offspring**
○Yusuke Tozuka^{1,2}, Etsuko Wada^{1,3}, Keiji Wada^{1,3}
¹Department of Degenerative Neurological Diseases, National Institute of Neuroscience, National Center of Neurology and Psychiatry, Tokyo, Japan, ²Japan Association for the Advancement of Medical Equipment, Tokyo, Japan, ³CREST, Japan Science and Technology Agency, Saitama, Japan
- O23-4 Toxicogenomic analysis of the effects of pre- and post-natal tributyltin exposure on the developing rat brain**
○Mika Wakasa¹, Makoto Imamura¹, Ryosuke Yoshioka¹, Masaki Takahashi¹, Takayuki Negishi¹, Masashi Tsunoda², Yoshiharu Aizawa², Hideo Tashiro³, Tomoko Tashiro¹
¹Department of Chemistry and Biological Science, Faculty of Science and Engineering, Aoyama Gakuin University, ²Department of Preventive Medicine and Public Health, Kitasato University School of Medicine, ³Sensing Technology Laboratory, Discovery Research Institute, RIKEN
- O23-5 Expression, localization and developmental changes of the D-serine-related genes in the rat central nervous system**
○Naoki Yamamoto¹, Dai Shimazu¹, Sotaro Kanematsu¹, Go Taniguchi¹, Asami Umino¹, Toru Nishikawa¹
¹Psychiatry and Behavioral Sciences, Tokyo Medical and Dental University Graduate School
- O23-6 Developmental expression pattern of mKirre in proprioceptive neurons of the dorsal root ganglia: its interaction with nephrin in the muscle spindles.**
○Yoshihiro Morikawa¹, Tadasuke Komori¹, Hiroaki Gyobu¹, Hiroo Ueno², Toshio Kitamura³, Emiko Senba¹
¹Department of Anatomy & Neurobiology, Wakayama Medical University, Wakayama, Japan, ²Institute for Stem Cell Biology and Regenerative Medicine, Stanford University School of Medicine, Stanford, CA, USA, ³Division of Cellular Therapy, Advanced Clinical Research Center, Institute of Medical Science, University of Tokyo, Tokyo
- O23-7 Visual input-dependent regulation of nuclear extracellular signal-regulated kinase in developing visual cortex**
○Hironori Takamura^{1,2}, Satoshi Ichisaka³, Chihiro Hayashi³, Hirotoshi Maki³, Yoshio Hata²
¹Dept. Psychiatry, Osaka Univ. Grad. Sch. Med. ²Div. Integrative Bioscience, Tottori Univ. Grad. Sch. Med. Sci. ³Div. Neurobiology, Sch. Life Sci., Fac. Med., Tottori Univ.
- O23-8 SARE: synaptic activity-responsive element that governs expression of the plasticity-related gene Arc**
○Hiroyuki Okuno¹, Takashi Kawashima¹, Aki Adachi-Morishima¹, Michiko Okamura¹, Haruhiko Bito¹
¹Department of Neurochemistry, University of Tokyo Graduate School of Medicine

- O23-9 Endogenous glutamic acid acts as neuroprotective agent against low potassium-induced cell death via metabotropic receptors in cultured rat cerebellar granule cells

○Koshi Oyanagi¹, Masaki Takahashi¹, Takayuki Negishi¹, Tomoko Tashiro¹

¹Department of Chemistry and Biological Science, Faculty of Science and Engineering, Aoyama Gakuin University

September 13 (Saturday)

9 : 00 ~ 12 : 00 (Room E)

O24-1 ~ O24-9 Ion channels/Receptors

Chairs : Masahiko Nomura (Saitama Medical University International Education and Training Center)

Shigeru Yokoyama (Department of Biophysical Genetics, Kanazawa University Graduate School of Medicine)

Toshihide Kuroki (NHO Hizen Psychiatric Center)

- O24-1 Single receptor imaging of NMDA receptor with atomic force microscopy

○Youichi Shinozaki¹, Koji Sumitomo¹, Keiichi Torimitsu¹

¹NTT Basic Research Labs, NTT Corporation

- O24-2 Functionality of NMDA receptors expressed by undifferentiated neural progenitor cells

○Ryo Fukumori¹, Masanori Yoneyama¹, Masato Ogura¹, Noritaka Nakamichi¹, Yukio Yoneda¹

¹Lab Mol Pharmacol, Kanazawa Univ Grad Sch Nat Sci Tech, Kanazawa, Japan

- O24-3 Glycine-sensitive NMDA receptor-mediated regulation in proliferative activity of neural progenitor cells

○Masanori Yoneyama¹, Yuka Gotoh¹, Koichi Kawada¹, Kiyokazu Ogita¹

¹Department of Pharmacology, Faculty of Pharmaceutical Sciences, Setsunan University, Osaka, Japan

- O24-4 Glutamate receptors in brains of rats with middle cerebral artery occlusion

○Shintaro Kurokawa¹, Tomoya Hara¹, Shiho Konishi¹, Takeshi Takarada¹, Noritaka Nakamichi¹, Yukio Yoneda¹

¹Lab Mol Pharmacol, Kanazawa Univ Grad Sch Nat Sci Tech, Kanazawa, Japan

- O24-5 RGS modulates signaling of the melanin-concentrating hormone receptor through the receptor third intracellular loop

Yumiko Saito¹, Osamu Saitoh², ○Mayumi Miyamoto-Matsubara¹

¹Graduate School of Integrated Arts and Sciences, Hiroshima University, ²Department of Bio-Science, Nagahama Institute of Bio-Science and Technology, Nagahama

- O24-6 Identification and functional analysis of proteins that bind to the C-terminal tail of histamine H2 receptor

○Kazuhiko Yanai¹, Ajing Xu¹, Eiko Sakurai¹, Atsuo Kuramasu¹

¹Dept. Pharmacol. Tohoku Univ. Sch, Med.

O24-7 80K-H interacts with inositol 1,4,5-trisphosphate receptors and regulates IP₃ - induced calcium release activity

○Katsuhiro Kawaai^{1,2}, Chihiro Hisatsune², Tomoko Tashiro¹, Katsuhiko Mikoshiba²

¹Dept. of Chem. and Biol. Sci., Aoyama-Gakuin Univ., Sagamihara, Kanagawa, Japan,

²Laboratory for Developmental Neurobiology, Brain Science Institute, RIKEN, Wako, Saitama, Japan

O24-8 A region of N-type Ca²⁺ channel critical for blockade by a dihydropyridine derivative amlodipine

○Toshihide Nukada¹, Yoriko Miyashita¹, Taiji Furukawa², Etsuko Kamegaya¹, Mitsunobu Yoshii³

¹Department of Neuronal Signaling, Tokyo Institute of Psychiatry, Tokyo, Japan,

²Department of Medicine, Teikyo University School of Medicine, Tokyo, Japan,

³Department of Neural Plasticity, Tokyo Institute of Psychiatry, Tokyo, Japan

O24-9 Identification and functional analysis of binding proteins to the 3'-UTR of alpha CaMKII mRNA.

○Yasutake Mori¹, Aoi Kousaka¹, Shingo Miyata¹, Masaya Tohyama¹

¹Department of Anatomy and Neuroscience, Graduate School of Medicine, Osaka University

September 13 (Saturday)

9 : 00~12 : 00 (Room F)

O25-1~O25-9 Depression/Stress

Chairs : Yoshifumi Watanabe (Division of Neuropsychiatry, Department of Neuroscience, Yamaguchi University Graduate School of Medicine)

Yasuhiro Watanabe (Department of Pharmacology National Defense Medical College)

Taizo Taniguchi (Faculty of Pharmaceutical Sciences, Himeji Dokkyo University)

O25-1 Stress-induced phosphorylation of SNAP-25 in mouse brain

○Daichi Sugaya¹, Saori Yamamori¹, Makoto Itakura¹, Masami Takahashi¹

¹Dept. of Biochem., Kitasato Univ. Sch. of Med.

O25-2 Role of REST/NRSF repressor-mediated gene regulations in the risk of developing depression-like behavior

○Shusaku Uchida¹, Kumiko Hara¹, Ayumi Kobayashi¹, Kolji Otsuki¹, Yoshifumi Watanabe¹

¹Dept. of Neurosci., Yamaguchi Univ. Med., Yamaguchi

O25-3 Central PACAP plays a stimulatory role in the stress-induced HPA-axis response

○Norihito Shintani¹, Yoko Saida¹, Michiya Kakuda², Naohiro Tsukiyama¹, Katsuya Ogata¹, Hitoshi Hashimoto^{1,2}, Akemichi Baba¹

¹Lab. Mol. Neuroparmacol., Grad. Sch. Pharmaceut. Sci., Osaka Univ. ²Center Child Mental Dev., Grad. Sch. Med., Osaka Univ.

- O25-4 Large-scale analysis of glucocorticoid target genes in rat hypothalamus**
 ○Hirohito Sato¹, Yukio Horikawa^{2,3}, Katsumi Iizuka³, Noriko Sakurai¹, Takeshi Tanaka¹, Nobuyuki Shihara³, Akihiko Oshima⁴, Jun Takeda^{2,3}, Masahiko Mikuni¹
¹Dept. of Psychiatry, Gunma Univ. Grad. Sch. of Med., Gunma, Japan, ²Dept. of Diabetes and Endocrinology, Gifu Univ. Grad. Sch. of Med., Gifu, Japan, ³Lab. of Med. Genomics, Inst. for Mol. and Cellular Regulation, Gunma, Japan, ⁴Dept. of Psychiatry, Kitasato Univ. Sch. of Med., Sagamihara, Japan
- O25-5 Anti-depressant like effect of dipeptide Leu-Ile on the chronic forced swim test**
 ○Yoko Hibi^{1,2}, Atsumi Nitta², Takeshi Ikeda³, Koji Morishita³, Toshitaka Nabeshima⁴, Kiyofumi Yamada²
¹Japan foundation for aging and health, Obu, Japan, ²Department of Neuropsychopharmacology & Hospital Pharmacy, Nagoya University Graduate School of Medicine, Nagoya, Japan, ³Healthcare Products Development Center, Kyowa Hakko Kogyo co., LTD., Tsukuba, Japan, ⁴Faculty of Pharmacy, Meijo University, Nagoya, Japan
- O25-6 Therapeutic effect of decenoic acid ethylester on depression of animal model via the activation of MAP kinase of the brain**
 ○Shoei Furukawa¹, Akihisa Makino¹, Satoru Itoh¹, Hidefumi Fukumitsu¹
¹Lab. of Mol. Biol., Dept. of Biofunctional Analysis, Gifu Pharmaceutical Univ.
- O25-7 Expression of myosin VI by PTSD in mouse hippocampus**
 ○Masaki Tachibana¹, Keisuke Tamaki¹, Yuma Ito¹, Takeshi Takarada¹, Hideo Taniura¹, Noritaka Nakamichi¹, Yukio Yoneda¹
¹Lab Mol Pharmacol, Kanazawa Univ Grad Sch Nat Sci Tech, Kanazawa, Japan
- O25-8 Localization of dihydropteridine reductase in the mouse brain and biochemical changes in dihydropteridine reductase-null mice**
 ○Sho Sanechika¹, Yusuke Sudo¹, Junpei Yamashita¹, Shun-ichiro Honda¹, Sho Shimaguchi¹, Masayo Kojima¹, Hiroshi Ichinose¹
¹Graduate School of Bioscience and Biotechnology, Tokyo Institute of Technology, Yokohama, Kanagawa, Japan
- O25-9 Involvement of neuronal primary cilia in psychiatric disorders**
 ○Ko Miyoshi¹, Kyosuke Kasahara¹, Ikuko Miyazaki¹, Masato Asanuma¹
¹Department of Brain Science, Okayama University, Okayama, Japan

September 13 (Saturday)

13 : 20~15 : 20 (Room C)

O26-1~O26-6

Animal models 2

Chairs : Yoshihiro Nakata (Department of Pharmacology, Graduate School of Biomedical Sciences, Hiroshima University)

Masami Niwa (Department of Pharmacology, Nagasaki University Graduate School of Biomedical Sciences)

- O26-1 Pathogenic roles of MuSK antibodies in myasthenia gravis**
○Kazuhiro Shigemoto¹, Sachiho Kubo¹, Naoki Maruyama¹, Tetsurou Konishi², Kiyoe Ohta³, Mitsuhiro Ohta⁴
¹Mol.Biomarkers., Tokyo Metro. Inst. of Gerontology, Tokyo, Japan, ²Dept. of Neurology., Utano Natl. Hospl. Kyoto, Japan, ³Clin.Res.Cent., Utano Natl. Hospl. Kyoto, Japan, ⁴Dep. of Med. Biochem., Kobe Pharm. Univ., Kobe, Japan
- O26-2 Pyrroloquinoline quinone enhances recovery of the locomotion activity after hemitransection of the spinal cord via attenuation of the mRNA expression of inducible nitric oxide synthase**
○Akihiro Hirakawa^{1,2}, Katsuji Shimizu², Hidefumi Fukumitsu¹, Shoei Furukawa¹
¹Laboratory of Molecular Biology, Gifu Pharmaceutical University, Gifu, Japan, ²Department of Orthopedic Surgery, Gifu University Graduate School of Medicine, Gifu, Japan
- O26-3 Analysis of the demyelination rat (dmy) using two-dimensional electrophoresis**
○Yudai Miyagi¹, Yoshihide Yamaguchi¹, Hiroko Baba¹
¹Department of Molecular Neurobiology, Tokyo University of Pharmacy and Life Sciences, Hachioji, Japan
- O26-4 FILIP knockout mice showed weak forearm strength and abnormalities in the visual cortex**
○Hideshi Yagi^{1,2}, Hiroshi Ikeda^{2,3}, Nobuyuki Yamasaki⁴, Tsuyoshi Miyakawa^{4,5}, Masaru Okabe⁶, Min-Jue Xie¹, Makoto Sato^{1,2}
¹Div. Cell Biol. & Neurosci., Dept. Morphol. & Physiol. Sci., Univ. of Fukui, Japan, ²Res. & Edu. Program Life Sci., Univ. of Fukui, Japan, ³Dept. Human & AI Systems, Univ. of Fukui, Fukui, Japan, ⁴Frontier Tech. Ctr., Grad. Sch. of Med., Kyoto Univ., Kyoto, Japan, ⁵ICMS, Fujita Health. Univ., Toyoake, Japan, ⁶GIRC, Osaka Univ., Suita, Japan
- O26-5 Maternal infection affects neurogenesis in the development of mouse cerebral cortex**
○Hitomi Soumiya¹, Hidefumi Fukumitsu¹, Shoei Furukawa¹
¹Laboratory of Molecular Biology, Department of Biofunctional analysis, Gifu Pharmaceutical University, Gifu, Japan
- O26-6 Rodent orbitofrontal cortex separately encodes response and outcome information during performance of goal-directed behavior.**
○Tomoyuki Furuyashiki¹, Aliza Ehrlich¹, Peter Holland², Michela Gallagher²
¹Dept. of Pharmacol., Kyoto Univ. Grad. Sch. of Med. ²Dept. of Psychol., Johns Hopkins Univ., Baltimore, USA

September 13 (Saturday)

13 : 20~15 : 20 (Room D)

O27-1~O27-6 Dopamine

Chairs : Hiroaki Nishio (Dept. Pharmacol., Faculty of Pharmacy and Pharmaceut. Sci.,
Fukuyama Univ.)

Yoshio Goshima (Department of Molecular Pharmacology & Neurobiology,
Yokohama City University Graduate School of Medicine)

- O27-1 Neuromelanin induces apoptosis through deglutathionylation of mitochondria**
 ○Makoto Naoi¹, Wakako Maruyama², Masayo Nagai-Shamoto²
¹Gifu International Institute of Biotechnology, Kakamigahara, Japan, ²National Institute for Geriatrics and Gerontology, Obu, Japan
- O27-2 Drinking hydrogenated water reduces dopaminergic neuronal loss in a mouse model of Parkinson's Disease**
 ○Kyota Fujita¹, Toshihiro Seike¹, Mizuki Ohno², Hiroo Yamaguchi², Hideyuki Yamada², Atsushi Takaki³, Mizuho Kido⁴, Yusaku Nakabeppu², Mami Noda¹
¹Laboratory of Pathophysiology, Graduated School of Pharmaceutical Sciences, Kyushu University, Fukuoka, Japan, ²Division of Neurofunctional Genomics, Department of Immunobiology and Neuroscience, Medical Institute of Bioregulation, Kyushu University, Fukuoka, Japan, ³Department of Integrative Physiology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan, ⁴Oral Biological Science, Graduate School of Dental Sciences, Kyushu University, Fukuoka, Japan
- O27-3 Effect of T-817MA, a novel neuroprotective agent, on MPTP-induced dopaminergic neurotoxicity in mice**
 ○Yukio Ago¹, Toshiyuki Kawasaki¹, Tatsuya Kitao¹, Tetsuaki Nashida¹, Akiko Takagi², Kazuhiro Takuma¹, Toshio Matsuda^{1,3}
¹Lab. of Medicinal Pharmacol., Grad. Sch. of Pharmaceut. Sci., Osaka Univ. ²2nd Res. Dept., Res. Lab., Toyama Chemical Co. Ltd., Toyama, ³Center for Child Mental Dev., Grad. Sch. of Med., Osaka Univ.
- O27-4 L-DOPA-specific induction of metallothionein in reactive astrocytes**
 ○Ikuko Miyazaki¹, Yuri Kikkawa¹, Naotaka Kimoto¹, Ko Miyoshi¹, Masato Asanuma¹
¹Dept. of Brain Sci., Okayama Univ. Grad. Sch. of Med., Dent. and Pharmaceut. Sci., Okayama, Japan
- O27-5 identification of piccolo as a regulator of behavioral plasticity and dopamine transporter internalization**
 ○Atsumi Nitta¹, Xiaobo Cen¹, Daisuke Ibi¹, Minae Niwa^{1,2}, Kiyofumi Yamada¹, Toshitaka Nabeshima^{1,2}
¹Dept. of Neuropsychopharmacol and Hospi Pharmacy, Nagoya, Japan, ²Department of Chemical Pharmacology, Graduate School of Pharmaceutical Sciences Meijo University, Nagoya, Japan

- O27-6** A novel molecule "shati" ameliorates the methamphetamine-induced decrease in dopamine uptake via tumor necrosis factor- α in PC12 cells

○Minae Niwa^{1,2,3}, Atsumi Nitta², Xiaobo Cen², Norio Ozaki¹, Toshitaka Nabeshima^{2,3}

¹Psychiatry, Nagoya Univ Grad Sch Med, ²Neuropsychopharmacol & Hosp Pharm, Nagoya Univ Grad Sch Med, ³Chem Pharmacol, Meijo Univ Grad Sch Pharm Sci

September 13 (Saturday)

13 : 20~15 : 20 (Room E)

O28-1~O28-6 Neuronal death 2

Chairs : Yasushi Enokido (Medical Research Institute, Tokyo Medical and Dental University)
Joh-E Ikeda (Neurodegenerative Diseases Research Centre, Tokai University Graduate School of Medicine)

- O28-1** Distinct effect of Syntaxin5 isoforms on the processing of β APP

○Kei Suga¹, Ayako Saito¹, Takami Tomiyama², Hiroshi Mori², Kimio Akagawa¹

¹The Department of Cell Physiology, Kyorin University School of Medicine, Tokyo, Japan, ²The Department of Neuroscience, Osaka City University Medical School, Osaka, Japan

- O28-2** Up-regulation of calsyntenin-3 in an Alzheimer's disease mouse model.

○Yoko Uchida¹, Fujiya Gomi¹

¹RT for Geriatric Disorders, Tokyo Metropolitan Institute of Gerontology

- O28-3** Identification and characterization of substrates for the mitochondrial protease Omi/HtrA2

○Yasuyuki Suzuki¹, Shuji Tanaka¹, Keiji Wada¹, Ryosuke Takahashi²

¹Department of Degenerative Neurological Diseases, National Institute of Neuroscience, National Center of Neurology and Psychiatry, Kodaira, Japan, ²Department of Neurology, Kyoto University Graduate School of Medicine, Kyoto, Japan

- O28-4** Mitochondrial dysfunction induced by MPP⁺ in mouse brain synaptosomes

○Shota Kobayashi¹, Mizuki Kaneshiro¹, Shohei Nomura¹, Hiroaki Matsushima¹, Akiko Muroyama¹, Yasuhide Mitsumoto¹

¹Dept. of Alternative Med. and Exp. Therapeutics, Faculty of Pharmaceutical Sciences, Hokuriku University

- O28-5** Vulnerability to glutamate induced by tributyltin, an environmental-polluting chemical

○Yaichiro Kotake¹, Yusuke Nakatsu¹, Atsuko Hino¹, Tomoko Takishita¹, Shigeru Ohta¹

¹Grad. Sch. of Biomed. Sci., Hiroshima Univ.

- O28-6** Enhanced expression of glutathione S-transferase in the hippocampus of mice after trimethyltin treatment

○Shohei Sano¹, Reiko Nagashima¹, Kiyokazu Ogita¹

¹Department of Pharmacology, Setsunan University Faculty of Pharmaceutical Sciences, Japan

September 13 (Saturday)

13 : 20~15 : 20 (Room F)

O29-1~O29-6 Memory/Learning mechanism

Chairs : Eiichiro Nagata (Department of Neurology, Tokai University School of Medicine)

Sachiko Tanaka (Department of Biochemical Toxicology, School of Pharmaceutical Sciences, Showa University)

O29-1 Effects of sominone on memory enhancement and the molecular mechanism underlying these effects

○Eri Joyashiki¹, Chihiro Tohda¹

¹Div. of Biofunctional Evaluation, Inst. of Natural Med., Univ. of Toyama

O29-2 Mechanism for activated microglia-induced learning and memory deficits in cytokine knock out mouse.

○Kingo Kanda¹, Sachiko Tanaka¹, Tomoya Nakamachi², Seiji Shioda², Satoshi Numazawa¹, Takemi Yoshida¹

¹Department of Biochemical Toxicology, Showa university, Tokyo, Japan, ²Department of Anatomy, Showa University, Tokyo, Japan

O29-3 The extensive nitration of neurofilament light chain in the hippocampus contributes to the cognitive impairment in A β -treated mice

○Tursun Alkam^{1,2}, Atsumi Nitta¹, Hiroyuki Mizoguchi¹, Akio Itoh¹, Kiyofumi Yamada¹, Toshitaka Nabeshima^{1,3}

¹Dept. Neuropsychopharm., Nagoya Univ. Grad. Sch. Med. ²Dept. of Basic Med., Col. of Traditional Uighur Med, ³Dept. Chemical Pharmacol. Grad Sch Pharm Sci. Meijo Univ

O29-4 Impairment of cognitive function via down-regulation of calcium/calmodulin-dependent protein kinase II in Na⁺/Ca²⁺ exchanger (NCX2) knock-out mice

○Shigeki Moriguchi¹, Feng Han¹, Satomi Kita², Issei Komuro³, Takahiro Iwamoto², Kohji Fukunaga¹

¹Department of Pharmacology, Graduate School of Pharmaceutical Sciences, Tohoku University, Sendai, Japan, ²Department of Pharmacology, School of Medicine, Fukuoka University, Fukuoka, Japan, ³Department of Cardiovascular Sciences and Medicine, Graduate School of Medicine, Chiba University, Chiba, Japan

O29-5 Time-limited involvement of the medial prefrontal cortex in extinction of contextual fear memory

○Masayuki Sekiguchi¹, Ko Zushida¹, Keiji Wada¹

¹Dept. Degenerative Neurological Diseases, National Institute of Neuroscience. National Center of Neurology & Psychiatry

O29-6 A genetic variation of the KIBRA gene is associated with memory performance in Japanese healthy subjects

○Yuka Yasuda^{1,2}, Ryota Hashimoto^{1,2}, Kazutaka Ohi², Hironori Takamura², Motoyuki Fukumoto², Naomi Iike², Masako Kiribayashi², Tetsuhiko Yoshida², Hidetoshi Takahashi², Takashi Morihara², Shinji Tagami², Masayasu Okochi², Toshihisa Tanaka², Takashi Kudo², Kouzin Kamino³, Ryohei Ishii², Masao Iwase², Hiroaki Kazui², Masatoshi Takeda^{1,2}

¹The Osaka-Hamamatsu Joint Research Center for Child Mental Development, Osaka University Graduate School of Medicine, Suita, Osaka, Japan. ²Department of Psychiatry, Osaka University Graduate School of Medicine, Suita, Osaka, Japan. ³Shoraiso National Hospital

Poster Sessions

September 11 (Thursday)

15 : 20 ~ 16 : 00 (Poster Area)

P-01 ~ P-05

Glia

Chair : Eiichi Taira (Department of Pharmacology, Iwate Medical School)

- P-01** Activation of phospholipase Cgamma and HDL generation through interaction between apoA-I and ABCA1
 ○ Jinichi Ito¹, Yuko Nagayasu¹, Shinji Yokoyama¹
¹Department of Biochemistry, Nagoya City University Graduate School of Medical Sciences, Nagoya
- P-02** Metabolic characteristics of microglia
 ○ Tomoyuki Kanamatsu¹, Kazuyuki Nakajima², Noriko Sawa¹
¹Dept. of Environmental Engineering for Symbiosis, Faculty of Engineering, Soka Univ., Tokyo, Japan, ²Dept. of Bioinformatics, Faculty of Engineering, Soka Univ., Tokyo, Japan
- P-03** Spinal cord injury induces expression of PRMT8 in microglia/macrophages in mouse
 ○ Aoi Kousaka¹, Yoshihisa Koyama¹, Yasutake Mori¹, Masaya Tohyama^{1,2}
¹Department of Anatomy and Neuroscience, Graduate School of Medicine, Osaka University, Osaka, Japan, ²The Osaka-Hamamatsu Joint Research Center For Child Mental Development, Graduate School of Medicine, Osaka University, Osaka, Japan
- P-04** Establishment of GFAP/Cre-reporter mouse system to analyze glial cell sub-lineages in the developing central nervous system
 ○ Tetsushi Kagawa¹, Takeshi Shimizu¹, Kimi Araki¹, Naoki Takeda², Tetsuya Taga¹
¹Institute of Molecular Embryology and Genetics, Kumamoto University, ²Center for Animal Resources and Development, Kumamoto University
- P-05** The increase of newborn glial cells in the hypothalamus might be related body weight gain
 ○ Takahira Yamauchi¹, Manabu Makinodan¹, Kouko Tatsumi², Hiroaki Okuda², Tomohiko Takeda¹, Miyuki Sadamatsu¹, Tosifumi Kisimoto¹, Akio Wanaka²
¹The Department of Psychiatry, Nara Medical University, Nara, Japan ²The Second Department of Anatomy, Nara Medical University, Nara, Japan

September 11 (Thursday)

15 : 20~16 : 00 (Poster Area)

P-06~P-10

Neuronal death

Chair : Kazufumi Akiyama (Department of Biological Psychiatry and Neuroscience,
Dokkyo Medical University School of Medicine)

- P-06** Effect of lipopolysaccharide on the life-span of primary-cultured microglia
○Yoko Kaneko¹, Akira Nakashima¹, Keiji Mori¹, Toshiharu Nagatsu², Ikuko Nagatsu³, Akira Ota¹
¹Fujita Hlth. Univ. Sch. Med., Dept. of Physiol. ²Fujita Hlth. Univ. Sch.Med., Dept. of Pharmacol. ³Fujita Hlth. Univ. Sch.Med., Dept. of Anatomy
- P-07** Involvement of endogenous advanced glycation end-products in the development of Alzheimer's disease
○Michiru Muramatsu¹, Takashi Sato¹, Masayoshi Takeuchi¹
¹Department of Pathophysiological Science, Faculty of Pharmaceutical Sciences, Hokuriku University, Kanazawa, Japan
- P-08** Development and functional analysis of a novel *in vitro* blood-brain barrier model
○Takahiro Katayama¹, Emi Sakaguchi¹, Masabumi Minami¹
¹Dept. Pharmacol., Grad. Sch. Pharm. Sci., Hokkaido Univ., Sapporo, Japan
- P-09** Microglia prevent oxidative stress-induced neuronal cell death by suppressing transferrin-independent iron uptake.
○Satoru Oshiro¹, Masaki Morioka², Kazuyuki Nakajima³
¹The Division of Cell Biology, Department of Health Science, Faculty of Sports and Health Sciences, Daito Bunka University, Japan, ²Department of Computational Biology, School of Biomedical Sciences, Tokyo Medical and Dental University, ³Department of Neurochemistry, Institute of Life Science, Soka University.
- P-10** Nuclear GAPDH activates PARP-1 in oxidative stress-induced neuronal cell death
○Yoko Ono¹, Hideshi Ihara², Hidemitsu Nakajima¹, Yasu-Taka Azuma¹, Tadayoshi Takeuchi¹
¹Lab. of Veterinary Pharmacology, Osaka Pref. Univ. ²Dep. of Biol Sci., Osaka Pref. Univ.

September 11 (Thursday)

15 : 20~16 : 00 (Poster Area)

P-11~P-15

Gene expression

Chair : Teiichi Furuichi (RIKEN BRAIN SCIENCE INSTITUTE.)

- P-11** Analysis of differential gene expression in inflamed skin of neuropeptide-deficient mice

○Kenta Shingaki¹, Manabu Taniguchi¹, Shinsuke Matsuzaki^{1,2}, Masaya Tohyama^{1,2}

¹Department of Anatomy and Neuroscience, Osaka University Graduate School of Medicine, ²The Osaka-Hamamatsu Joint Research Center for Child Mental Development, Graduate School of Medicine, Osaka University

- P-12 Expression of gpnmb, a tumor metastasis-associated glycoprotein, in the rat central nervous system

○Jian-Jun Huang¹, Wen-Jie Ma¹, Haruhiro Higashida¹, Shigeru Yokoyama¹

¹Dept. of Biophysical Genetics, Kanazawa University Graduate School of Medicine

- P-13 Expression of HSP70 in zebrafish retina after optic nerve injury

○Chieko Fujikawa¹, Mikiko Nagashima², Kazuhiro Mawatari², Satoru Kato³

¹Department of Laboratory Science, School of Medicine, Kanazawa University, ²Division of Health Sciences, Graduate School of Medicine, Kanazawa University, ³Department of Molecular Neurobiology, Graduate School of Medicine, Kanazawa University

- P-14 Effects of the chronic social defeat on behavior and gene expression in the brain

○Kenji Tsuiji¹, Kazuki Namai¹, Michihiro Uruse¹, Sayo Minagawa¹, Hideyuki Nakata¹, Atsushi Ishige¹, Kenji Watanabe¹

¹Center for Kampo Medicine, Keio University school of Medicine

- P-15 Biochemical and histological analyses of MAGI-1 in rat brain

○Hidenori Ito¹, Rika Morishita¹, Kaori Sudo¹, Ikuko Iwamoto¹, Tomoyasu Shinoda¹, Ken-ichi Okamoto¹, Koh-ichi Nagata¹

¹Dept. of Mol. Neurobiol., Inst. for Develop. Res., Aichi Human Service Center

September 11 (Thursday)

15:20~16:00 (Poster Area)

P-16~P-20

Aging/Dementia

Chair: Hisataka Kasai (Tokyo Metropolitan University)

- P-16 Manipulation of caloric content but not diet composition, attenuates the deficit in learning and memory of senescence-accelerated mouse strain P8

○Takuya Chiba¹, Toshimitsu Komatsu¹, Haruyoshi Yamaza¹, Kimihiro Yamashita², Atsuyoshi Shimada³, Yoshikazu Higami⁴, Rafael de Cabo⁵, Donald K. Ingram⁶, Isao Shimokawa¹

¹Dept. of Investigative Pathology, Nagasaki Univ. ²Dept. of Environmental Conservation, Faculty of Environmental Studies, Nagasaki Univ. ³Department of Pathology, Institute for Developmental Research, Aichi Human Service Center, ⁴Dept. of Drug Metabolism & Molecular Pathology, Faculty of Pharmaceutical Sciences, Tokyo Univ. of Science ⁵Laboratory of Experimental Gerontology, NIA, NIH, Baltimore, MD, USA ⁶Nutritional Neuroscience and Aging Laboratory, Louisiana State University System, Baton Rouge, LA, USA

- P-17 Partial agonistic effects for serotonin 1A receptors of yokukansan, a traditional Japanese medicine**
 ○Kiyoshi Terawaki¹, Kyoji Sekiguchi¹, Takuji Yamaguchi¹, Sachiko Imamura¹, Hitomi Kanno¹, Yasushi Ikarashi¹, Yoshio Kase¹
¹TSUMURA Research Laboratories, TSUMURA & CO., Ibaraki, Japan
- P-18 A novel function of amyloid beta in cholesterol homeostasis**
 ○Tomohiro Umeda¹, Hui Zheng²
¹Department of Neuroscience, Osaka City University Graduate School of Medicine,
²Huffington Center on Aging, Baylor College of Medicine
- P-19 Activity of Presenilin/ γ -secretase-mediated S3 cleavage can be efficiently measured by a newly developed Notch signaling reporter assay.**
 ○Kanta Yanagida¹, Masayasu Okochi¹, Shinji Tagami¹, Kouhei Nishitomi¹, Taisuke Nakayama¹, Takashi Kodama¹, Jingwei Jiang¹, Shin-ichi Tatsumi¹, Kohji Mori¹, Masatoshi Takeda¹
¹Psychiatry, Department of Integrated Medicine, Division of Internal Medicine, Osaka University Graduate School of Medicine
- P-20 A β enhance the ATBF1 expression responsible for the neuronal cell death**
 ○Cha-Gyun Jung¹, Makoto Kawaguchi², Yutaka Miura³, Hiroyasu Akatsu⁴, Tae-Sun Kim³, Makoto Michikawa¹
¹Dept. of Alzheimer's disease, NILS, NCGG, Obu, Aichi, Japan, ²Niigata Rosai Hosp.
³Dept. Mol. Neurobiol., Med., Nagoya City Univ., Nagoya, Japan, ⁴Choju Medical Institute, Fukushima Hospital, Toyohashi, Japan

September 11 (Thursday)

15 : 20~16 : 00 (Poster Area)

P-21~P-25 Neural stem cell

Chair : Yoshihiro Arakawa (Clinical Research Center, University of Tokyo Hospital)

- P-21 PACAP decides cortical laminar formation via PKA signaling development of mouse cerebral cortex**
 ○Hidefumi Fukumitsu¹, Masanari Ohtsuka¹, Shoei Furukawa¹
¹Lab. of Mol. Biol., Dept. of Biofunctional Analysis, Gifu Pharmaceutical University, Gifu, Japan
- P-22 Roles of BRINP and BRINP-interacting proteins in neuronal differentiation**
 ○Ichiro Matsuoka¹, Masa-aki Isshiki³, Shin-ichi Hisanaga⁴, Miwako Kobayashi^{1,2}
¹Col. of Pharm. Sci., Matsuyama Univ. ²CRIS, Hokkaido Univ., Sapporo, Japan, ³Grad. Sch. of Pharm. Sci., Hokkaido Univ., Sapporo, Japan, ⁴Dept. of Biol. Sci., Tokyo Metropolitan Univ., Tokyo, Japan

- P-23** Effects of methyl mercury chloride on neural differentiation from mouse embryonic stem cells by Neural Stem Sphere method
 ○Daisuke Inada¹, Masahiro Otsu^{1,2}, Hajime Kobayashi¹, Koji Murakami¹, Takashi Nakayama³, Hisataka Kasai¹, Nobuo Inoue¹
¹Lab. Regener. Neurosci. Grad. Sch. Human Health Sci., Tokyo Metropol. Univ., Tokyo, Japan, ²Dept. Chem., Kyorin Univ. Sch. Med., Tokyo, Japan ³Dept. Biochem., Yokohama City Univ. Sch. Med., Yokohama, Japan
- P-24** The effect of exogenous neural stem cell against the damaged neurons and neural stem cells
 ○Takafumi Ono¹, Wataru Ukai¹, Takao Ishii², Toshihiro Yoshinaga¹, Kimihiko Watanabe¹, Eri Hashimoto¹, Ippei Watanabe¹, Tomohiro Shirasaka¹, Masaru Tateno¹, Satoshi Saito¹, Toshikazu Saito¹
¹Department of Neuropsychiatry, Sapporo Medical University, Sapporo, Japan, ²Department of Occupational Therapy, Sapporo Medical University, Sapporo, Japan
- P-25** Expression profiling of PRC1 complex members in mouse embryonic cortex.
 ○Mohammad Saharul Islam^{1,4}, Keita Koizumi^{2,4}, Toru Yoshihara^{2,4}, Masahide Asano^{3,4}, Haruhiro Higashida^{1,2,4}
¹Dept of Biophysical Genetics, Kanazawa Univ, Kanazawa Japan, ²Research Center for Child Mental Development, Kanazawa Univ, Kanazawa, Japan, ³Advanced Science Research Center, Kanazawa Univ, Kanazawa, Japan, ⁴The 21st COE Program, Innovative Brain Science for Development, Learning and Memory Kanazawa Univ, Kanazawa, Japan

September 12 (Friday)

15 : 45~16 : 25 (Poster Area)

P-26~P-30

Myelin/Demyelination

Chair : Masabumi Minami (Dept. of Pharmacol., Grad. Sch. of Pharm. Sci., Hokkaido Univ.)

- P-26** Decrease in axonal conduction velocity following central nervous system demyelination in vivo.
 ○Yoshio Bando¹, Kaoru Takakusaki², Shigetaka Yoshida¹
¹Dept. of Functional Anatomy and Neurosci., Asahikawa Medical College, ²Dept. of Functional Neurophysiology, Asahikawa Medical College
- P-27** Different distributions and characteristics of myelin basic protein isoforms during the brain development
 ○Michihiro Uruse^{1,2}, Kenji Tsuiji¹, Nanako Sato^{1,3}, Yurie Sato¹, Atsushi Ishige¹, Hiroaki Asou^{1,3}, Fumio Fukai², Kenji Watanabe¹
¹Center of Kampo medicine, Keio University School of medicine, Tokyo, Japan, ²Department of Molecular Patho-Physiology, Faculty of Pharmaceutical Sciences, Tokyo university of science, Chiba, Japan, ³Department of Neuro-Glia Cell Biology, Tokyo metropolitan Institute of Gerontology, Tokyo, Japan

- P-28** Developmental changes of signaling molecules that regulate neurite outgrowth and myelination in the rat orbitofrontal cortex and visual cortex
○Satoshi Ichisaka¹, Kaori Sano², Manami Miyahara¹, Ayano Yamamoto¹, Satomi Hibino², Kojima Kazuhiro², Yoshio Hata^{1,2}
¹Div. Neurobiol., Sch. Life Sci., Fac. Med., Tottori Univ. ²Div. Integrative Biosci., Tottori Univ. Grad. Sch. of Med. Sci.
- P-29** Analysis of myosin 1D in the myelin fraction
○Yoshihide Yamaguchi¹, Yudai Miyagi¹, Shiho Ishikawa¹, Hiroko Baba¹
¹Department of Molecular Neurobiology, Tokyo University of Pharmacy and Life Sciences, Hachioji, Japan
- P-30** The regulatory function of B7-H3 and B7-H4 in Experimental Autoimmune Encephalomyelitis
○Yoshio Bando^{1,2}, Bing Zhu², Tanuja Chitnis², Shigetaka Yoshida¹, Samia Khoury²
¹Dept. of Functional Anatomy and Neurosci., Asahikawa Medical College, ²Center for Neurologic Diseases, Brigham & Women's Hospital, Harvard Medical School, USA

September 12 (Friday)

15 : 45~16 : 25 (Poster Area)

P-31~P-35

Neural development/Plasticity

Chair : Shun Nakamura (Tokyo University of Agriculture and Technology)

- P-31** Enriched environment enhances neuropsin mRNA in the hippocampus
Sadao Shiosaka¹, ○Yoko Kogure¹, Yasuyuki Ishikawa¹
¹Division of Structural Cell Biology, Nara Institute of Science and Technology (NAIST), Nara, Japan
- P-32** The analysis of the role of Reelin signalling in the developing neocortex
○Ken-ichiro Kubo¹, Takao Honda¹, Kenji Tomita¹, Hidenori Tabata¹, Kazunori Nakajima¹
¹Department of Anatomy, Keio University School of Medicine, Tokyo, Japan
- P-33** Function of Sept14 on the positioning of cortical neurons in cerebral cortex
○Tomoyasu Shinoda¹, Hidenori Ito¹, Kaori Sudo¹, Ken-ichi Okamoto¹, Ikuko Iwamoto¹, Rika Morishita¹, Koh-ichi Nagata¹
¹Dept. of Mol Neurobiology, Inst. for Dev. Res., Aichi Human Service Center
- P-34** Mechanism of dendritic spine abnormality in tuberous sclerosis.
○Hiroko Sugiura¹, Shu Takigami¹, Shin Yasuda¹, Yoshiyuki Yoshimura², Takako Takemiya¹, Takashi Yamauchi², Okio Hino³, Kanato Yamagata¹
¹Dept. Neuropharmacol., Tokyo Metropol. Insti. for Neurosci. ²Insti. Health Biosci., Gradu. School Pharma. Sci., Univ. Tokushima, ³Dept. Pathol. and Oncol., Juntendo Univ. School of Med.

- P-35 The paternal behavior in mice
 ○HongXiang Liu¹, Olga Lopatina¹, Haruhiro Higashida¹
¹Dept.of Biophysical Genetics. Med.,Univ.of Kanazawa

September 12 (Friday)

15 : 45~16 : 25 (Poster Area)

P-36~P-40

Animal models

Chair : Hideko Yamamoto (Tokyo Institute of Psychiatry)

- P-36 Development of locomotor sensitization by daily and weekly ketamine administration
 ○Toshifumi Yamamoto¹, Tomomi Nakayama¹, Hideko Yamamoto²
¹Lab. of Mol. Recognition, Grad. School of Arts and Sci., Yokohama City Univ. ²Div. of Psychobiol., Tokyo Inst. Psychiatry
- P-37 Postpartum stress on dams make their pups short statue
 ○Hideyuki Nakata¹, Ko Nishimura¹, Pengfei Gao¹, Yuu Murakami¹, Kenji Tsuiji¹, Atsushi Ishige¹, Kenji Watanabe¹
¹Center for Kampo Medicine, Keio University school of Medicine
- P-38 Sigma receptor signaling and methamphetamine-induced stereotypy
 ○Junichi Kitanaka¹, Nobue Kitanaka¹, Tomohiro Tatsuta², Koh-ichi Tanaka³, Nobuyoshi Nishiyama³, Yoshio Morita², Motohiko Takemura¹
¹Dept. Pharmacol., Hyogo Col. Med., Nishinomiya, Hyogo, Japan, ²Dept. Neuropsychiatry, Hyogo Col. Med., Nishinomiya, Hyogo, Japan, ³Div. Pharmacol., Dept. Pharm., Sch. Pharm., Hyogo Univ. Health Sci., Kobe, Hyogo, Japan
- P-39 Lycopene administration to Mongolian gerbil increase SOD activity in hippocampus after transient cerebral ischemia
 ○Kimikazu Fujita¹, Nobuko Yoshimoto², Gaku Matsumoto³, Takahiro Inakuma³, Toshiaki Kato⁴, Hideki Imada¹, Yutaka Nagata¹, Eiichi Miyachi¹
¹Department of Physiology, School of Medicine, Fujita Health University, Aichi, Japan, ²Department of Nutrition and Food Sciences, Nagoya Bunri University, College Nagoya Aichi Japan, ³Research Institute Kagome Co.Ltd Tochigi Japan, ⁴Department of Clinical Laboratory Sciences, Fujita Health University, College. Toyoake Aichi Japan
- P-40 Neuroprotection by antidiarrheic ingredients in hippocampal neurons
 ○Yukary Nakamura¹, Nobuyuki Matsushima², Nobuaki Moriguchi^{1,2}, Hitoshi Shibata², Yuki Kambe¹, Noritaka Nakamichi¹, Yukio Yoneda¹
¹Laboratory of Molecular Pharmacology, Kanazawa University Graduate School of Natural Science and Technology, ²Taiko Pharmaceutical Co, Ltd.

September 12 (Friday)

15 : 45~16 : 25 (Poster Area)

P-41~P-45

Genetic analysis/Others

Chair : Ryoza Kuwano (Center for Bioresources, Brain Research Institute, Niigata University)

- P-41 No association between NRG1 and methamphetamine use disorder in the Japanese population**
○Tomo Okochi¹, Taro Kishi¹, Masashi Ikeda¹, Tsuyoshi Kitajima¹, Yoko Kinoshita¹, Kunihiro Kawashima¹, Takenori Okumura¹, Tomoko Tsunoka¹, Toshiya Inada², Mitsuhiro Yamada², Naohisa Uchimura², Masaomi Iyo², Ichiro Sora², Norio Ozaki², Hiroshi Ujike², Nakao Iwata^{1,2}
¹Department of Psychiatry, Fujita Health University School of Medicine, Toyoake, Japan, ²Japanese Genetics Initiative for Drug Abuse (JGIDA)
- P-42 Association study of clock gene (CLOCK) and mood disorders in a Japanese population**
○Taro Kishi¹, Tsuyoshi Kitajima¹, Masashi Ikeda¹, Yoshio Yamanouchi¹, Yoko Kinoshita¹, Kunihiro Kawashima¹, Tomo Okochi¹, Takenori Okumura¹, Tomoko Tsunoka¹, Norio Ozaki², Nakao Iwata¹
¹Department of Psychiatry, Fujita Health University School of Medicine ²Department of Psychiatry, Nagoya University Graduate School of Medicine
- P-43 Serotonin transporter polymorphisms in Japanese patients with bipolar disorder and schizophrenia**
○Hiroshi Mitsuyasu¹, Leo Gotoh¹, Yuki Kobayashi¹, Naoya Oribe¹, Atsushi Takata¹, Ryosuke Tsuchimochi², Hiroaki Kawasaki¹, Shigenobu Kanba¹
¹Dept. of Neuropsychiatry, Grad. Sch of Med Sci, Kyushu Univ. ²Kyushu Univ. Medical school
- P-44 Effects of aripiprazole and apomorphine on locomotor activity after long-term treatment with olanzapine or haloperidol in rats**
○Tsuyoshi Hirose¹, Takashi Futamura¹, Shaun Jordan², Robert McQuade³, Tetsuro Kikuchi¹
¹Quests Research Institute, Otsuka Pharmaceutical Co., Ltd., Tokushima, Japan, ²Otsuka Maryland Medicinal Laboratories Inc., Neuroscience Research, Rockville, United States, ³Otsuka Pharmaceutical Development and Commercialization Inc. Princeton, United States
- P-45 Regulation of energy homeostasis by UCH-L1 and UCH-L3**
○Mari Suzuki¹, Rieko Setsuie¹, Keiji Wada¹
¹Department of Neurodegenerative Diseases, National Institute of Neuroscience, National Center of Neurology and Psychiatry

September 12 (Friday)

15 : 45~16 : 25 (Poster Area)

P-46~P-50

Neuroimmuno-endocrinology/Others

Chair : Kazuhiro Nagaike (Immuno-Biological Laboratories Co., Ltd)

- P-46 Rapid down-regulation of thyroid hormone responsive genes in the adult rat brain after peripheral administration of lipopolysaccharide
○Masaki Takahashi^{1,2}, Takayuki Negishi¹, Erika Sawano¹, Tomoko Tashiro¹
¹Department of Chemistry and Biological Science, School of Science and Engineering, Aoyama Gakuin University, ²JSPS
- P-47 LPS-induced transglutaminase 2 expression and the involvement of NO production in rat brain astrocyte
○Katsura Takano¹, Kensuke Shiraiwa¹, Mitsuaki Moriyama¹, Yoichi Nakamura¹
¹Lab. Integrative Physiology, Vet. Sci., Osaka Pref. Univ.
- P-48 Inhibition of [³H]glutamine accumulation by a green tea ingredient in rat brain neurons and astroglia
○Yusuke Tonami¹, Takumi Kakuda², Ayumu Nozawa², Masato Ogura¹, Takeshi Takarada¹, Eiichi Hinoi¹, Yukio Yoneda¹
¹Lab Mol Pharmacol, Kanazawa Univ Grad Sch Nat Sci Tech, Kanazawa, Japan, ²Central Research Institute, Itoen Ltd., Makinohara, Shizuoka, Japan
- P-49 Distribution of glucose transporters in the mouse tongue
○Yusuke Ishida¹, Shinya Ugawa¹, Takashi Ueda¹, Shoichi Shimada¹
¹Department of Neurobiology and Anatomy, Graduate School of Medical Sciences, Nagoya City University, Nagoya, Japa
- P-50 Hippocampal involvement in diabetes -Clinical and experimental studies-.
○Shozo Kito¹, Akiko Shingo²
¹Junshin-kai Kousei Rehabilitation Hospital, Hyogo, Japan, ²Hyogo University School of Health Sciences, Hyogo, Japan

Luncheon Seminar

September 11 (Thursday)

12 : 15 ~ 13 : 15 (Room A)

LS-1

Sponsor : Eisai Co., Ltd.

Chair : Shoji Tsuji (Graduate School of Medicine, The University of Tokyo)

Modification of Tau Proteins by Nitritative Oxidation in Tauopathies.

Binder, Lester I., Reyes, Juan F., Reynolds, Matthew R., and Vana, Laurel C.

Feinberg School of Medicine, Northwestern University

September 12 (Friday)

12 : 05 ~ 13 : 05 (Room A)

LS-2

Sponsor : MEIJI SEIKA KAISHA, LTD.

Chair : Kazunori Nakajima (Keio University School of Medicine)

Pharmacogenomics of Obesity and Depression

Julio Licinio

University of Miami Miller School of Medicine

September 13 (Saturday)

12 : 15 ~ 13 : 15 (Room A)

LS-3

Sponsor : Glaxo SmithKline K.K.

Chair : Masatoshi Takeda (Osaka University Graduate School of Medicine)

Current Pharmacogenomics and Personalized Medicine in Psychiatry

Toshiyuki Someya

Department of Psychiatry, Niigata University Graduate School of Medical and Dental Sciences

神経化学の若手研究者育成セミナー

A Young Researcher Training Seminar of Neurochemistry

育成セミナー講義
Training Seminar Lecture

フリーディスカッション
Free Discussion

開催趣旨

現在、神経化学会におきましては、未来を担う若手研究者を育てることが急務となっております。そこで、第51回日本神経化学会大会の開催にあたり、新たに、国内外の学生を対象とした「神経化学の若手研究者育成セミナー」を企画いたしました。

プログラムには、大会参加に加え、育成セミナー講義や宿舎でのフリーディスカッションなど、第一線で活躍する研究者と直接語り合っただけの時間をふんだんに設けました。新しい実験手法や研究内容など、神経化学の動向をじかに聞いていただき、研究の楽しさを感じてもらいたいと考えております。また、合宿のような雰囲気の中、寝食を共にしながら仲間との交流も深めていただきたいと考えております。

こうした中で、若い研究者が育ち、神経化学会全体が発展することを期待しています。

■プログラム

9月11日(木)	18:30~19:00	オリエンテーション	(富山国際会議場 2階 B~C 会場)
	19:15~21:00	懇親会	(富山第一ホテル)
	21:30~23:00	フリーディスカッション	(ホテルよし原)
9月12日(金)	19:30~20:50	育成セミナー講義	(富山国際会議場 2階 B~F 会場)
	21:30~23:00	フリーディスカッション	(ホテルよし原)

※フリーディスカッションは、飛び入り参加も歓迎です。どなたでもぜひご参加ください。

【育成セミナー講師紹介】

1. グリア細胞による中枢神経系機能制御

講師：小泉 修一先生（山梨大学医学部薬理学）

講師：津田 誠先生（九州大学大学院薬学研究院薬理学分野）

2. 脳の発達と機能を科学する

講師：塩坂 貞夫先生（奈良先端科学技術大学院大学バイオサイエンス研究科）

講師：佐藤 真先生（福井大学医学部 形態機能医科学講座）

3. 神経変性疾患とタンパク質リン酸化

講師：高島 明彦先生（理化学研究所脳科学総合研究センター）

講師：久永 真市先生（首都大学東京 理工学研究科）

4. 脳を染める・標本を読む ～神経化学研究のための脳の基礎解剖学と組織化学の手法～

講師：木山 博資先生（大阪市立大学大学院医学研究科）

講師：吉田 成孝先生（旭川医科大学解剖学講座）

5. 研究者の心技体

講師：和田 圭司先生（国立精神・神経センター神経研究所）

講師：高橋 正身先生（北里大学医学部生化学）

6. 神経幹細胞は面白い！

講師：等 誠司先生（生理学研究所・分子神経生理部門）

講師：新郷 哲郎先生（獨協医科大学 脳神経外科）

7. 足元から科学する～オリジナリティの源泉

講師：道川 誠先生（国立長寿医療センター研究所）

講師：米田 幸雄先生（金沢大学大学院自然科学研究科）

8. 神経疾患の基礎と臨床を結ぶもの

講師：丸山 和佳子先生（国立長寿医療センター研究所）

講師：古川 昭栄先生（岐阜薬科大学 生体機能解析学大講座）

9. 神経伝達機構の基礎研究と病態研究それぞれの魅力

講師：熊倉 鴻之助先生（上智大学理工学部情報理工学科）

講師：浅沼 幹人先生（岡山大学大学院医歯薬学総合研究科脳神経制御学講座）

10. 神経化学研究において形態と機能をどう結びつけるか

講師：和中 明生先生（奈良県立医科大学大学院医学系研究科）

講師：島田 昌一先生（名古屋市立大学大学院医学研究科基礎医科学講座）

1. グリア細胞による中枢神経系機能制御

講 師 1	小 泉 修 一	所 属	山梨大学医学部薬理学 (大学院医学工学総合研究部)
タイトル	グリア細胞による中枢神経系機能制御		
内 容	グリア細胞が中枢神経系の活動をダイナミックに制御していることが次々と明らかとなってきた。今後の脳研究にグリア細胞の視点を加える必要性を解説する。		
略 歴	1992年 九州大学大学院薬学研究科博士課程修了 1992年～1995年 (財) ヒューマンサイエンス振興財団 博士課程 1995年 厚生省 入省 1996年～1998年 英国ケンブリッジ大学 博士研究員 1998年 国立医薬品食品衛生研究所薬理部 研究員 2001年 同上 室長 2007年 山梨大学医学部薬理学講座 (大学院医学工学総合研究部) 教授 現在に至る。		
代表論文	Koizumi et al., Nature 2007; Koizumi et al., PNAS 2003; Koizumi et al., Neuron 1999.		
講 師 2	津 田 誠	所 属	九州大学大学院薬学研究院薬理学分野
タイトル	ミクログリアの ATP 受容体による疼痛制御		
内 容	神経因性疼痛と呼ばれる難治性疼痛の動物モデルで、ATP 受容体（細胞外 ATP の受容体）の一つである P2X4 受容体が、脊髄のミクログリアで過剰に発現する。その受容体の活性化が脳由来神経栄養因子を引き起こし、疼痛の発症維持に深く関与している。		
略 歴	1998年 3 月 星薬科大学大学院薬学研究科博士課程修了 1998年 3 月～2002年 3 月 国立医薬品食品衛生研究所（科学技術振興事業団特別研究員、医薬品機構派遣研究員） 2002年 4 月～2004年 3 月 トロント小児病院脳行動プログラム博士研究員 2004年 4 月～2005年 3 月 厚生労働省（国立医薬品食品衛生研究所） 2005年 4 月～2006年 3 月 九州大学大学院薬学研究院薬効解析学分野 助手 2006年 4 月～2007年 3 月 九州大学大学院薬学研究院薬効解析学分野 助教授 2007年 4 月～現在 九州大学大学院薬学研究院薬理学分野 准教授		
代表論文	Tsuda M, Tozaki-Saitoh H, Masuda T, Toyomitsu E, Tezuka T, Yamamoto T, Inoue K: Lyn tyrosine kinase is required for P2X4 receptor upregulation and neuropathic pain after peripheral nerve injury. <i>Glia</i> 56, 50-58 (2008) Coull JAM, Beggs S, Boudreau D, Boivin D, Tsuda M, Inoue K, Gravel C, Salter MW, De Koninck Y: BDNF from microglia causes the shift in neuronal anion gradient underlying neuropathic pain. <i>Nature</i> , 438, 1017-1021 (2005) Tsuda M, Shigemoto-Mogami Y, Koizumi S, Mizokoshi A, Kohsaka S, Salter MW Inoue, K.: P2X4 receptors induced in spinal microglia gate tactile allodynia after nerve injury. <i>Nature</i> , 424, 778-783 (2003)		

2. 脳の発達と機能を科学する

講 師 1	塩 坂 貞 夫	所 属	奈良先端科学技術大学院大学 バイオサイエンス研究科
タイトル	記憶を化学する		
内 容	シナプス接着／離反などのダイナミックスから記憶という生理現象を説明できるのかどうかを検証する。また研究方法論として生理学的方法の有用性についてもご紹介したい。		
略 歴	1977年3月 名古屋大学大学院農学研究科修了（農学修士） 1977年4月 大阪大学大学院医学研究科入学 （蛋白質研究所代謝調節学専攻） 1979年6月 大阪大学医学部助手 1986年8月 大阪大学医学部助教授 1993年4月 奈良先端科学技術大学院大学教授		
代表論文	1. Tamura, H, et al (2006) Neuropsin is essential for early processes of memory acquisition and Schaffer collateral long-term potentiation in adult mouse hippocampus in vivo. <i>J Physiol</i> , 570, 541-51. 2. Nakamura, Y, et al (2006) Role of neuropsin in formation and maturation of Schaffer-collateral L1cam-immunoreactive synaptic boutons. <i>J Cell Sci</i> , 119, 1341-9. 3. Shiosaka, S, (2004) Serine proteases regulating synaptic plasticity. <i>Anat Sci Int</i> , 79, 137-44.		
講 師 2	佐 藤 真	所 属	福井大学医学部 形態機能医科学講座 組織細胞形態学・神経科学領域
タイトル	大脳皮質の形成の仕組みとその破綻による疾患の研究		
内 容	大脳皮質は移動細胞によって構築される構造物である。大脳皮質の形成とその破綻による疾患の研究は、脳奇形を呈するヒト疾患の原因遺伝子が次々に同定され、細胞単位での遺伝子解析技術が進歩し、さらには器官培養法や子宮内遺伝子導入法により大脳皮質の形態を損なうことなく遺伝子操作を加えることが可能になり、ここ数年大きく進んだ。本セミナーでは、移動細胞により大脳皮質がつけられる仕組みに関する最新の知見とその破綻に伴う諸疾患および関連する研究手技について概説する。		
略 歴	1987.03 大阪大学医学部医学科卒業 1991.03 大阪大学医学研究科生理系専攻修了、医学博士 1991.04－1994.03 大阪大学医学部助手 （1991.06-1993.06 Salk Institute Research Associate） 1994.04－1998.01 大阪市立大学医学部助教授 1998.02－ 福井大学医学部（福井医科大学）教授		
代表論文	Nagano, T., Yoneda, T., Hatanaka, Y., Kubota, C., Murakami, F. and Sato, M. (2002) Filamin A-interacting protein (FILIP) regulates cortical cell migration out of the ventricular zone. <i>Nature Cell Biol.</i> , 4(7): 495-501 Nagano, T., Morikubo, S. and Sato, M. (2004) Filamin A and FILIP (Filamin A-interacting protein) regulate cell polarity and motility in neocortical subventricular and intermediate zones during radial migration. <i>J. Neurosci.</i> 24: 9648-9657 Yagi, H., Takamura, Y., Yoneda, T., Konno, D., Akagi, Y., Yoshida, K., and Sato, M. (2005) Vlgf1 knockout-mice show audiogenic seizure susceptibility. <i>J. Neurochem.</i> 92: 191-202		

3. 神経変性疾患とタンパク質リン酸化

講師 1	高島 明彦	所 属	理化学研究所脳科学総合研究センター アルツハイマー病研究チーム
タイトル	脳老化とアルツハイマー病		
内 容	脳の加齢変化とアルツハイマー病に至る過程を病理学的特徴の一つである神経原線維変化形成を通して解説する。		
略 歴	1981年 九州大理学部生物大学院 1987年 佐賀医大 1991年 NIH (USA) 1998年 三菱化成生命科学研究所 現在 理化学研究所脳科学総合研究センター		
代表論文	Kimura T, Yamashita S, Fukuda T, Park J-M, Murayama M, Mizoroki T, Yoshiike Y, Sahara N, and Takashima A. Hyperphosphorylated tau in parahippocampal cortex impairs place learning in aged mice expressing wild-type human tau: Analysis of brain function in a novel neurodegenerative disease model using Mn-enhanced MRI. <i>EMBO. J (in press)</i> Maeda S, Sahara N, Kim H, Saito Y, Akagi T, Miyasaka T, Hashikawa T, Murayama S, Ikai A, Takashima A: Granular tau oligomers as intermediates of tau filaments. <i>Biochemistry</i> . 2007 2;46(12):3856-61 Tatebayashi, Y. Miyasaka, T, Chui, D-H, Akagi, T., Mishima, K., Iwasaki, K., Fujiwara, M., Tanemura, K., Murayama, M., Ishiguro, K., Planel, E., Sato, S., Hashikawa, T., Takashima, A., Tau filament formation and associative memory deficit in aged mice expressing mutant (R406W) human tau <i>Proc Natl Acad Sci U S A</i> . 99, 13896-13901 (2002)		
講師 2	久永 真市	所 属	首都大学東京 理工学研究科 生命科学専攻
タイトル	神経化学におけるタンパク質のリン酸化と情報伝達		
内 容	神経細胞間の情報伝達制御および神経細胞内の様々な活性制御にタンパク質のリン酸化が使われている。リン酸化によるタンパク質活性の制御および測定法などについて情報を提供したいと考えている。		
略 歴	1982年 東京大学理学系大学院生物化学専攻博士課程修了 1982年 日本学術振興会特定領域奨励研究員 1985年 東京大学医学部解剖学教室助手 1990年 東京工業大学生命理工学部生体機構学科発生生物学講座助教授 1997年 東京都立大学理科学研究科生物科学専攻教授 2005年 首都大学東京理工学研究科生命科学専攻教授		
代表論文	Taniguchi, T., Taoka, M., Itakura, M., Asada, A., Saito, T., Kinoshita, M., Takahashi, M., Isobe, T., and Hisanaga, S. Phosphorylation of adult type sept5 (cdcl-1) by cyclin-dependent kinase 5 inhibits interaction with syntaxin-1. <i>J. Biol. Chem.</i> , 282, 7869-7876, 2007. Kamei, H., Saito, T, Ozawa, O., Fujita, Y., Asada, A., Bibb, J. A., Saido, T. C., Sorimachi, S., and Hisanaga, S. Suppression of calpain-dependent cleavage of the cdk5 activator p35 to p25 by site-specific phosphorylation. <i>J. Biol. Chem.</i> 282, 1687-1694, 2007. Sakaue, F., Saito, T., Sato, Y., Asada, A., Ishiguro, K., Hasegawa, M., and Hisanaga, S. Phosphorylation of FTDP-17 mutant tau by Cyclin-dependent kinase 5 complexed with p35, p25, or p39. <i>J. Biol. Chem.</i> 280, 31522-31529, 2005.		

4. 脳を染める・標本を読む

～神経化学研究のための脳の基礎解剖学と組織化学の手法～

講 師 1	木 山 博 資	所 属	大阪市立大学大学院医学研究科、機能細胞形態学
タイトル	脳を染める・標本を読む：神経化学研究のための脳の基礎解剖学と組織化学の手法		
内 容	実験動物の脳を使った研究をするうえで、脳のアトラスを読むことや組織染色により神経核を同定することが必要になります。このためには、基本的な脳の構造の理解と組織化学の手法について理解を深めることが必要です。そのきっかけを提供できればと企画しました。		
略 歴	1986年 大阪大学医学部・助手、高次神経研究施設神経解剖学部門 1988年 英国ケンブリッジ動物生理学遺伝学研究所 客員研究員（2年間） 1991年 大阪大学医学部・助教授、第二解剖学・神経解剖学 1997年 旭川医科大学医学部・教授、解剖学第一 2001年 大阪市立大学大学院医学研究科・教授、機能細胞形態学		
代表論文	1. 「蛋白質核酸分子の in situ 同定法」バイオマニュアルシリーズ 9、遠山正彌、塩坂貞夫、木山博資、共編（1994）羊土社 2. 木山博資（2005）損傷神経生存のバイオリジー、細胞工学、24（11）：1200－1205 3. Kiryu-Seo S, Gamo K, Tachibana T, Tanaka K, Kiyama H (2006) Unique anti-apoptotic activity of EAAC1 in injured motor neurons, <i>EMBO J</i> 25(14): 3411-3421		
講 師 2	吉 田 成 孝	所 属	旭川医科大学解剖学講座 機能形態学分野
タイトル	脳を染め組織を読む：神経化学研究のための脳の基礎解剖学と組織化学の手法		
内 容	実験動物の脳を使った研究をするうえで、脳のアトラスを読むことや組織染色により神経核を同定することが必要になります。このためには基本的な脳の構造の理解と組織化学の手法について、じっくりと話しあう機会を持ちたいと思います。		
略 歴	1990年 大阪大学医学部神経機能解剖学助手 1995年 奈良先端科学技術大学院大学 バイオサイエンス研究科助教授 2000年 兵庫医科大学 解剖学第二講座助教授 2001年 旭川医科大学 解剖学第一講座教授 （2006年より解剖学講座 機能形態学分野に名称変更）		
代表論文	Kishibe et al. Kallikrein 8 is involved in skin desquamation in cooperation with other kallikreins. <i>J Biol Chem</i> , 282, 5834-5841, 2007. Terayama et al. Neuropsin promotes oligodendrocyte death, demyelination and axonal degeneration after spinal cord injury, <i>Neuroscience</i> , 148, 175-187, 2007. Terayama et al. Involvement of neuropsin in the pathogenesis of experimental autoimmune encephalomyelitis, <i>Glia</i> 52, 108-118, 2005.		

5. 研究者の心技体

講 師 1	和田 圭司	所 属	国立精神・神経センター神経研究所
タイトル	研究者として成功するために		
内 容	私が本格的に研究を始めたのは30才を過ぎてからです。当時は研究者になりたいという夢がただ漠然としてあっただけです、人との出会いなど様々な事柄でもって今日まで育ててきてもらいました。私の経験譚を語ることで研究者をめざす皆さんがヒントを得れば幸いです。		
略 歴	1979年 大阪大学医学部卒業 1984年 大阪大学大学院修了（医学博士） 1985年～1988年 ソーク研究所ポスドク 1989年～1992年 NIH客員研究員 1992年～現在 現職（国立精神・神経センター神経研究所部長）		
代表論文	Wada, K., Ballivet, M., Boulter, J., Connolly, J., Wada, E., Deneris, E.S., Swanson, L.W., Heinemann, S. and Patrick, J., Functional expression of a new pharmacological subtype of a brain nicotinic acetylcholine receptor. Science , 240, 330-334, 1988 Saigoh, K., Wang, Y.-L., Suh, J.G., Yamanishi, T., Sakai, Y., Kiyosawa, H., Harada, T., Ichihara, N., Wakana, S., Kikuchi, T. and Wada, K., Intragenic deletion in the gene encoding ubiquitin carboxy-terminal hydrolase in gad mouse. Nature Genet. , 23, 47-51, 1999 Setsuie, R. Wada, K. The functions of UCH-L1 and its relation to neurodegenerative diseases. Neurochem. Int. , 52, 105-111, 2007. Review.		
講 師 2	高橋 正身	所 属	北里大学医学部生化学
タイトル	タンパク質の扱い方		
内 容	最近DNAは扱えるが、タンパク質の扱いが不得手な研究者が増えている。タンパク質を扱う上で陥りやすい落とし穴について、実例を交えながら説明したい。		
略 歴	昭和48年3月 大阪大学理学部生物学科卒業 昭和54年3月 大阪大学大学院理学研究科博士過程終了（理学博士） 昭和54年4月 三菱化成生命科学研究所に研究員として入所 昭和60年4月 米国ワシントン州立大学（シアトル）に留学 医学部薬理学教室 W.A.Catterall 教授 平成8年1月～平成13年3月 東京大学大学院総合文化研究科客員教授 平成8年4月～平成12年3月 三菱化成生命科学研究所プロジェクトセンター長 平成14年4月 北里大学医学部教授、同大学院医療系研究科教授		
代表論文	Shimazaki, Y., Nishiki, T., Omori, A., Sekiguchi, M., Kamata, Y., Kozaki, S., and Takahashi, M. (1996) Phosphorylation of 25-kDa synaptosome-associated protein. <i>J. Biol. Chem.</i> 271: 14548-14553. Ohnishi, H., Yamamori, S., Ono, K., Aoyagi, K., Kondo, S., and Takahashi, M. (2001) Src family tyrosine kinase inhibits neurotransmitter release from neuronal cells. <i>Proc. Natl. Acad. Sci. U.S.A.</i> 98, 10930-10935. Aoyagi K, Sugaya T, Umeda M, Yamamoto S, Terakawa S, and Takahashi M. (2005) The activation of exocytotic sites by the formation of phosphatidylinositol-4,5-bisphosphate microdomains at syntaxin clusters. <i>J. Biol. Chem.</i> , 280: 17346-17352.		

6. 神経幹細胞は面白い！

講 師 1	等 誠司	所 属	生理学研究所・分子神経生理部門
タイトル	神経幹細胞の培養法とその応用		
内 容	胎仔期の脳の発達や成体脳での神経細胞新生を研究する際に、神経幹細胞の培養は欠かせないツールです。その1つである neurosphere assay について、実際の培養法や応用の可能性、あるいはその限界などについてわかりやすく説明します。		
略 歴	1988年 東京大学医学部医学科卒業。 5年間内科および神経内科のトレーニングを受け、神経内科専門医。その後大学院に進学し、理化学研究所で糖鎖生物学を学んだ。トロント大学留学の機会を得て神経幹細胞の研究を始め、現在に至っている。臨床の知識と経験を生かした基礎研究が目標。		
代表論文	Hitoshi S, <i>et al.</i> (2007) Antidepressant drugs reverse the loss of adult neural stem cells following chronic stress. <i>J. Neurosci. Res.</i> 85, 3574-3585 Hitoshi S, <i>et al.</i> (2004) Primitive neural stem cells from the mammalian epiblast differentiate to definitive neural stem cells under the control of Notch signaling. <i>Genes & Dev.</i> 18, 1806-1811 Hitoshi S, <i>et al.</i> (2002) Notch pathway molecules are essential for the maintenance, but not for the generation, of mammalian neural stem cells. <i>Genes & Dev.</i> 16, 846-858		
講 師 2	新郷 哲郎	所 属	獨協医科大学 脳神経外科
タイトル	成体脳におけるニューロン新生の制御メカニズム		
内 容	成体脳におけるニューロン新生はさまざまな生体物質により制御されている。今回は、内因性生体ホルモンによるニューロン新生の制御メカニズムについて論じる。		
略 歴	平成5年 岡山大学医学部卒業、 平成11年～平成14年 カナダカルガリー大学 Samuel Weiss ラボに留学 それ以降 岡山大学脳神経外科を経て、現在に至る		
代表論文	Proc Natl Acad Sci USA 103: 7112-7117, 2006 J Neurosci 24:8354-8365, 2004 Science 299:117-120, 2003 J Neurosci 21:9733-43, 2001		

7. 足元から科学する～オリジナリティの源泉

講 師 1	道 川 誠	所 属	国立長寿医療センター研究所 アルツハイマー病研究部
タイトル	脂質代謝と神経変性疾患—その現状と未来への展望		
内 容	脳は最も脂質に富む臓器でありながら、脳内脂質代謝系の全貌は良く分かっていない。本講演では、特に脳内及び体循環系におけるコレステロール輸送システムの異同、神経細胞の構造的特殊性とコレステロール輸送の意義、細胞内コレステロール代謝破綻と病態、等についてアルツハイマー病やニーマンピック病との関連から解説・議論する。		
略 歴	1985年 東京医科歯科大学医学部医学科卒業後、神経内科学教室入局 1990年～1992年 カナダ・ブリティッシュコロンビア大学留学 1994年 東京医科歯科大学医学部神経内科助手 1996年～ 国立長寿医療研究センター痴呆疾患研究部室長 2005年～ 国立長寿医療センター研究所アルツハイマー病研究部長		
代表論文	Zou K, Yamaguchi H, Akatsu H, Sakamoto T, Ko M, Mizoguchi K, Gong JS, Yu W, Yamamoto T, Kosaka K, Yanagisawa K, Michikawa M. Angiotensin-converting enzyme converts amyloid β -protein1-42 ($A\beta(1-42)$) to $A\beta(1-40)$, and its inhibition enhances brain $A\beta$ deposition. <i>J Neurosci.</i> 27(32):8628-8635, 2007. Ko M, Zou K, Minagawa H, Yu W, Gong JS, Yanagisawa K, and Michikawa M. Cholesterol-mediated neurite outgrowth is differently regulated between cortical and hippocampal neurons. <i>J. Biol. Chem.</i> , 280(52):42759-42765, 2005. Yu W, Gong J-S, Ko M, Garver W. S., Yanagisawa K, Michikawa M. Altered cholesterol metabolism in Niemann-Pick Type C1 mouse brain affects mitochondria function. <i>J. Biol. Chem.</i> , 280(12): 11731-11739, 2005. Gong JS, Kobayashi M, Hayashi H, Zou K, Sawamura N, Fujita SC, Yanagisawa K, Michikawa M. Apolipoprotein E (apoE) isoform- dependent lipid release from astrocytes prepared from human-apoE3- and apoE4-knock-in mice. <i>J. Biol. Chem.</i> , 277(33): 29919-29926, 2002.		
講 師 2	米 田 幸雄	所 属	金沢大学大学院自然科学研究科薬学系薬物学研究 室（金沢大院・薬・薬物学）
タイトル	古くて新しいアミノ酸の神経化学		
内 容	グルタミン酸や GABA は脳の機能と構造の維持に必須であるが、長年の研究にもかかわらず、多くの謎が解明されないまま残されている。今回は神経細胞新生に関する成果を紹介する予定であるが、今こそ古い舟に新しい水夫が望まれる時代である。		
略 歴	1972年 大阪大学薬学部卒業 1975年 京都府立医科大学助手 1980年 シティオブホープ医学研究所研究員 1982年 京都府立医科大学講師 1984年 摂南大学薬学部助教授 1997年 同教授 1999年 金沢大学薬学部教授		
代表論文	Ogura M., Taniura H., Nakamichi N. and Yoneda Y. (2007) Upregulation of the glutamine transporter through transactivation mediated by cAMP/protein kinase A signals toward exacerbation of vulnerability to oxidative stress in rat neocortical astrocytes. <i>J. Cell. Physiol.</i> 212 , 375-385. Yoneyama M., Fukui M., Nakamichi N., Kitayama T., Taniura H. and Yoneda Y. (2007) Activation of GABAA receptors facilitates astroglial differentiation induced by ciliary neurotrophic factor in neural progenitors isolated from fetal rat brain. <i>J. Neurochem.</i> 100 , 1667-1679. Taniura H., Sanada N., Kuramoto N. and Yoneda Y. (2006) A metabotropic glutamate receptor family gene in Dictyostelium discoideum. <i>J. Biol. Chem.</i> 281 , 12336-12343.		

8. 神経疾患の基礎と臨床を結ぶもの

講 師 1	丸山 和佳子	所 属	国立長寿医療センター 研究所 老年病研究部
タイトル	神経変性疾患の基礎と臨床を結ぶもの（パーキンソン病を例として）		
内 容	本タイトルは神経化学学会設立時の主要な課題であったにも関わらず、最近の学会ではむしろ分子生物学と臨床神経科学を総括的に語る機会は少なくなっているように思われる。講演者は自身が臨床神経医から基礎研究者に至った経緯を含め、若い研究者に“病気から見てくる神経化学”を伝えたい。		
略 歴	昭和61年 3月25日 名古屋大学医学部卒業 平成 2年 4月 1日 名古屋大学大学院医学研究科博士課程内科系神経内科学専攻入学 平成 5年 3月25日 同 修了 平成 5年 4月 1日 名古屋大学医学部研究生 平成 8年 5月14日 同 退学 昭和61年 4月 1日 名古屋第一赤十字病院常勤嘱託研修医採用 昭和63年 3月31日 同 退職 昭和63年 4月 1日 名古屋第一赤十字病院内科医採用 平成 2年 3月31日 同 退職 平成 8年 5月15日 国立療養所中部病院長寿医療センター老化機構研究部生化学・代謝室長 平成16年 3月 1日 国立長寿医療センター 老化機構研究部 代謝研究室長 平成17年 3月 1日 国立長寿医療センター 老年病研究部長		
代表論文	Shamoto-Nagai M, Maruyama W, Hashizume Y, Yoshida M, Osawa T, Riederer P, Naoi M. In parkinsonian substantia nigra, alpha-synuclein is modified by acrolein, a lipid-peroxidation product, and accumulates in the dopamine neurons with inhibition of proteasome activity. <i>J Neural Transm.</i> 2007 Aug 10; [Epub ahead of print] Youdim MB, Maruyama W, Naoi M. Neuropharmacological, neuroprotective and amyloid precursor processing properties of selective MAO-B inhibitor antiparkinsonian drug, rasagiline. <i>Drugs Today (Barc).</i> 2005 Jun;41(6):369-91. M. Shamoto-Nagai, W. Maruyama, Y. Kato, K. Isobe, M. Tanaka, M. Naoi, T. Osawa: An inhibitor of mitochondrial complex I, rotenone, inactivates proteasome by oxidative modification and induces aggregation of oxidized proteins in SH-SY5Y cells. <i>J. Neurosci. Res.</i> 74:589-97, 2003.		
講 師 2	古川 昭栄	所 属	岐阜薬科大学学生体機能解析学大講座 分子生物科学研究室
タイトル	神経栄養因子シグナルと神経疾患		
内 容	脳由来神経栄養因子（BDNF）の主要シグナルである MAP キナーゼ経路は脳の高次機能と関連が深い。そこでうつ病を例として、MAP キナーゼのリン酸化と病態形成、治療効果との関係などを調べ、その結果を新世代抗うつ薬の開発に生かす。		
略 歴	1979年 京都大学大学院薬学研究科博士課程修了 1981年 国立武蔵療養所神経センター 研究員 1986年 国立精神・神経センター神経研究所 室長 1990年 岐阜薬科大学分子生物学 助教授 1995年 同 教授		
代表論文	1. Fukumitsu H, Ohtsuka M, Murai R, Nakamura H, Itoh K, Furukawa S. Brain-derived neurotrophic factor participates in determination of neuronal laminar fate in the developing mouse cerebral cortex. <i>J Neurosci</i> 26, 13218-13230, 2006 2. 古川昭栄、古川美子. ニューロトロフィンとは両刃の剣 - プロセッシングと細胞死制御 - 神経保護・再生医療の最前線. <i>医学のあゆみ</i> , 215, 819-824, 2005 3. Hattori N, Nomoto H, Mishima S, Inagaki S, Goto M, Sako M, Furukawa S. Identification of AMP N1-oxide in royal jelly as a neurotrophic component for cultured rat pheochromocytoma PC12 cells. <i>Biosci Biotechnol Biochem</i> , 2006, 70, 897-906, 2000		

9. 神経伝達機構の基礎研究と病態研究それぞれの魅力

講 師 1	熊倉 鴻之助	所 属	上智大学生命科学研究所 (2008年4月より理工学部情報理工学科所属)
タイトル	伝達物質放出機構への神経化学的アプローチ		
内 容	私は、電気化学的測定による単一顆粒の開口現象の測定、および分泌顆粒の細胞内運動の測定解析によって、伝達物質の開口分泌機構の全体像を理解しようとしている。この研究の概要と背景を紹介して、神経化学研究の魅力を話してみたい。		
略 歴	1968年 上智大学理工学部化学科卒業 1973年～1977年 イタリア国立ミラノ大学薬理学研究所 ('73,'74年度イタリア政府留学生) 1977年 理学博士(上智大学) 1977年～1979年 アメリカ合衆国国立精神衛生研究所(N.I.M.H.)、博士研究員 1992年～ 上智大学理工学部教授(現在に至る) 2003年3月～2005年2月 日本神経化学会 副理事長		
代表論文	1. K.Kumakura, M.Ohara, G.P.Sato (1986) Real-time monitoring of the secretory function of cultured adrenal chromaffin cells. J.Neurochem. 46:1851-1858. 2. K.Kumakura, K.Sasaki, T.Sakurai, et al. (1994) "Essential role of myosin light chain kinase in the mechanism for MgATP-dependent priming of exocytosis in adrenal chromaffin cells." J. Neurosci. 14:7695-7703. 3. M.Ohara-Imaizumi, M.Fukuda, M.Niinobe, et al. (1997) Distinct roles of C2A and C2B domains of synaptotagmin in the regulation of exocytosis in adrenal chromaffin cells. Proc.Natl. Acad. Sci. U.S.A. 94:287-291. 4. K. Kumakura, N. Sasakawa, N. Murayama, and M. Ohara-Imaizumi (2004) Spatio-temporal regulation of neurotransmitter release by PKC; studies in adrenal chromaffin cells. Critical Reviews in Neurobiol., 16 (1&2), 169-175.		
講 師 2	浅沼 幹人	所 属	岡山大学大学院医歯薬学総合研究科脳神経制御学 講座神経情報学
タイトル	ドパミン神経保護に関するトランスレーショナルリサーチ		
内 容	パーキンソン病およびメタンフェタミン神経毒性でのドパミン神経障害に対する神経保護・修復に関する研究を通して、より臨床指向のトランスレーショナルリサーチ(基礎と臨床/社会医学の橋渡し研究)のおもしろさ、バタクささ、重要性について紹介したい。		
略 歴	1988年 岡山大学医学部医学科 卒業 1992年 岡山大学大学院医学研究科 修了 医学博士 1992年～1994年 岡山大学医学部分子細胞医学研究施設神経情報学部門 併任所員(財)長寿科学振興財団 リサーチレジデント 1994年～1995年 岡山大学医学部 助手 1995年～ 米国国立保健研究所(NIH)薬物濫用研究所(NIDA)分子神経精神学部門 1996年～1998年 客員研究員として留学 2000年 岡山大学医学部 助教授(分子細胞医学研究施設神経情報学部門) 2001年 岡山大学大学院医歯薬学総合研究科(脳神経制御学講座神経情報学分野) 2005年 岡山大学大学院医歯薬学総合研究科 助教授(准教授)現在に至る		
代表論文	Miyazaki, I., Asanuma, M., Diaz-Corrales, F.J., Fukuda, M., Kitaichi, K., Miyoshi, K. and Ogawa, N.: Methamphetamine-induced dopaminergic neurotoxicity is regulated by quinone formation-related molecules. FASEB J., 20: 571-573, 2006. Diaz-Corrales, F.J., Asanuma, M., Miyazaki, I., Miyoshi, K. and Ogawa, N.: Rotenone induces aggregation of gamma-tubulin protein and subsequent disorganization of the centrosome: Relevance to formation of inclusion bodies and neurodegeneration. Neuroscience, 133: 117-135, 2005. Asanuma, M., Miyazaki, I. and Ogawa, N.: Dopamine- or L-DOPA-induced neurotoxicity: the role of dopamine quinone formation and tyrosinase in a model of Parkinson's disease. Neurotox. Res., 5: 165-176, 2003. Higashi, Y., Asanuma, M., Miyazaki, I., Haque, M.E., Fujita, N., Tanaka, K. and Ogawa, N.: The p53-activated gene, PAG608, requires a zinc finger domain for nuclear localization and oxidative stress-induced apoptosis. J. Biol. Chem., 277: 42224-42232, 2002.		

10. 神経化学研究において形態と機能をどう結びつけるか

講 師 1	和中 明生	所 属	公立大学法人奈良県立医科大学 大学院医学系研究科 分子機能形態学
タイトル	神経化学研究に必要な形態学的手法について		
内 容	神経系組織はその構造、細胞種の複雑さから形態学的手法を用いることが必要不可欠である。本セミナーでは遺伝子、蛋白の可視化の重要性、及び応用方法を実際の研究例を中心に解説する。		
略 歴	1983年 大阪大学医学部卒 1988年 同上 大学院 修了（医学博士） 同年 大阪大学医学部 第二解剖 助手 1993年 同上 助教授 1995年 福島県立医科大学 生体情報伝達研究所 教授 2002年 奈良県立医科大学 第二解剖 教授		
代表論文	Hayashi N, et al. DACS, novel matrix structure composed of chondroitin sulfate proteoglycan in the brain. <i>Biochem Biophys Res Commun</i> . 2007 Dec 14;364(2):410-5. Manabe T, et al. L3/Lhx8 is involved in the determination of cholinergic or GABAergic cell fate. <i>J Neurochem</i> . 2005 Aug;94(3):723-30. Kondo S, et al. OASIS, a CREB/ATF-family member, modulates UPR signalling in astrocytes. <i>Nat Cell Biol</i> . 2005 Feb;7(2):186-94.		
講 師 2	島田 昌一	所 属	名古屋市立大学大学院医学研究科 基礎医科学講座機能組織学分野
タイトル	神経化学研究における分子局在と機能の関連性		
内 容	多種多様で複雑な細胞構築の神経系の研究を行う際に、形態学的な解析は必要不可欠である。特殊な形態から推測される機能もあれば、特殊な機能から予想される形態もある。本セミナーでは分子の局在を基盤として形態と機能をどの様に結びつけて研究を進めるかを一緒に考える。		
略 歴	昭和61年 大阪大学医学部医学科卒業 昭和63年 大阪大学医学部助手（解剖学第二講座） （平成元年～3年）（米国国立麻薬研究所客員研究員） 平成6年 大阪大学医学部講師（解剖学第二講座） 平成8年 大阪大学医学部助教授（解剖学第二講座） 平成9年 名古屋市立大学医学部教授（解剖学第二講座） 平成14年 名古屋市立大学大学院医学研究科教授（分子形態学） 平成19年 名古屋市立大学大学院医学研究科教授（機能組織学）		
代表論文	1) Shimada S, Kitayama S, Lin CL, Patel A, Nanthakumar E, Gregor P, Kuhar M, Uhl G. Cloning and expression of a cocaine-sensitive dopamine transporter complementary DNA. <i>Science</i> , 1991; 254, 576-578. 2) Ugawa S, Minami Y, Guo W, Saishin Y, Takatsuji K, Yamamoto T, Tohyama M, Shimada S. Receptor that leaves a sour taste in the mouth. <i>Nature</i> , 1998; 395, 555-556. 3) Yamamura H, Ugawa S, Ueda T, Nagao M, Shimada S. Protons activate the delta-subunit of the epithelial Na ⁺ channel in humans. <i>J Biol Chem</i> . 2004; 279:12529-34.		

抄録
Abstract

特別講演
Special Lecture

教育講演
Educational Lecture

理事会企画オープンシンポジウム
Open Symposium

日本生物学的精神医学会 合同シンポジウム
Joint Symposium with 30th Annual Meeting
of Japanese Society of Biological Psychiatry

アニュアルシンポジウム
Annual Symposium

シンポジウム
Symposium

一般口演
Oral Session

ポスター発表
Poster Session

NEUROCHEMISTRY
Neurochemistry

SL-1 Pharmacogenomics of Antidepressant Treatment Response

Julio Licinio

University of Miami Miller School of Medicine

In this presentation, we will review work on the pharmacogenomics of major depressive disorder (MDD). This is a common and complex disorder of unknown cause, for which treatment response is highly variable. Depression costs the US economy 100 billion dollars per year and it is the leading cause of suicide, which is by itself the 10th cause of death in the USA. Depression is the second cause of days lost to work in developed countries. Approximately 40% of patients do not respond to initial treatment but after multiple trials 85% of patients will respond to treatment. For this reason a key priority of contemporary psychiatry is to develop personalized strategies for antidepressant treatment. We will present existing data from 10 genes for which there are documented associations with antidepressant response: (1) serotonin transporter, (2) serotonin receptors 1A, (3) 2A, (4) 3A, (5) 3B, (6) tryptophan hydroxylase 1, (7) phosphodiesterase 11A, (8) corticotropin releasing hormone receptor 1, and (9) brain-derived neurotrophic factor, and (10) G-protein beta-3 subunit. In addition, we will present new results on the association of MDD and antidepressant response to genes important in the modulation of the hypothalamic-pituitary-adrenal axis and immune functions in Mexican Americans with major depression. We showed that single nucleotide polymorphisms (SNPs) in two genes critical for T-cell function are associated with susceptibility to MDD: PSMB4 (proteasome beta4 subunit), important for

antigen processing, and TBX21 (T bet), critical for differentiation. We also found associations of several SNPs and antidepressant response; those genes support the role of T cell (CD3E, PRKCH, PSMD9 and STAT3) and hypothalamic-pituitary-adrenal axis (UCN3) functions in treatment response. The important new area of antidepressant pharmacogenomics will provide the basis for personalized antidepressant treatment.

SL-2 The Structure and Function of Abnormal Tau in Alzheimer's Disease.

Binder, L.I.¹, Lapointe, N.E.^{1,3}, Guillozet, A.¹, Morfini, G.^{2,3}, Pignio, G.^{2,3}, and Brady, S.T.^{2,3}

¹Feinberg School of Medicine, Northwestern University, ²University of Illinois at Chicago, ³Marine Biological Laboratory

Tau proteins are microtubule associated proteins found predominantly in the nervous system. During the course of neurodegenerative diseases such as Alzheimer's disease (AD) and other tauopathies, these proteins dissociate from the microtubule and begin to aggregate. Tau filaments are thought to be toxic although the nature of this toxicity is, as yet, unknown. The tau molecule aggregates by association with its repeat region; the region of the molecule that normally mediates tau's association with microtubules. Over the past few years, we have shown that the carboxy and amino regions of the molecule constitute control elements in its aggregation with the carboxy tail region being inhibitory and the amino region being facilitative of the filament assembly process. We have been studying mechanisms by which the cell alters these regions of the tau molecule in disease. Using molecular biological, biochemical and immunological procedures, we have discovered that tau changes its conformation before and after aggregation perhaps due to truncation by enzymes such as caspases. The result of changes such as these are modeled in vitro to assess their affect on tau filament formation and assayed in situ in AD and tauopathies using appropriately targeted monoclonal antibodies. Additionally, we have used different tau isoforms and modified polymers to assess their affect on axonal transport in isolated axoplasm from the squid giant axon. Intact tau filaments and certain non-canonical isoforms of tau that contain only the amino

region of the molecule inhibit anterograde but not retrograde transport through a signal transduction cascade involving specific phosphatases and GSK3 β . Taken together, our results indicate that the amino terminal region of tau may be a primary site of toxicity in neurodegenerative disease. Aggregation of intact tau into filaments "presents" this toxic region to the cell and amino truncation and/or modification likely inhibit toxicity of tau polymers.

Supported by Grants AG14453, AG09466, AG021184, and AG021661 to LIB and by Grants NS23868 and NS41170 as well as grants from ALSA and MDA to STB.

EL-1 Static and Dynamic Functions of Microglia in Health and Disease

Shinichi Kohsaka

National Institute of Neuroscience, NCNP, Tokyo, JAPAN

Almost a century ago, Ramon Cajal described three types of cells in the central nervous system; Neurons, Astrocytes and the third element. In 1932, Del Rio-Hortega classified the third element further to oligodendrocytes and microglia, and provided the first systemic investigations on microglial cells.

In the normal adult brain, microglia ubiquitously exist in parenchyma and exhibit ramified form, which has a small cell body and long and highly branched processes. Ramified microglia are essentially considered to be quiescent cells, dormant and nonmotile, so they were called “resting microglia”. The role of resting microglia in a healthy brain has not been fully understood so far. However, recent study using two-photon laser microscopy demonstrated that the fine branches of the resting microglia are highly mobile and provide continuous surveillance of their extracellular environment like a sensor of pathology.

In pathological brain, the ramified microglia rapidly change their morphology, retract their processes, and increased their cell volume. This form is called activated microglia, which show a number of features including cell migration toward the pathological sites, proliferation and acquisition of phagocytic phenotype in case of extensive tissue damage. Activated microglia also affect surrounding cells through release of a number of either toxic or neuroprotective substances, such as inflammatory cytokines and neurotrophic factors. Therefore, the

activated microglia are thought to play important roles in the progression or repair of the pathological nervous system. In fact, accumulating lines of evidence have demonstrated that microglia are involved in many acute and chronic neurological diseases such as stroke, Alzheimer's disease, Amyotrophic Lateral Sclerosis, Multiple Sclerosis and neuropathic pain.

Recently time-lapse imaging showed that nearby microglia extend their processes rapidly toward the focal site of injury or the site of focal ATP application but they did not migrate toward the focal sites. However, we have recently shown that ATP induces chemotactic migration of microglia. Extension of cell processes or cell migration is an highly important step to function for microglia properly at the sites of normal and pathological brain. In order to investigate the molecular bases underlying the process extension and cell migration, we established novel three-dimensional (3D) culture method of microglia in collagen gels. The novel method and some of the experimental results obtained will be also presented in this lecture.

OS-1 Axon formation and axonal transport

○Kozo Kaibuchi¹

¹Nagoya University Graduate School of Medicine, Department of Cell Pharmacology

Neurons are highly polarized cells that have axons and dendrites, both of which are differentiated from common immature neurites in cultured hippocampal neurons. One of the key events for axon formation is the directional trafficking of signaling molecules including the Par complex (Par3/Par6/aPKC) and neurotrophin receptor (Trk), which play critical roles in axon formation. The anterograde transport of the vesicles and molecules into the axons is mainly mediated by microtubule-dependent, plus-end-directed motor proteins, kinesins. We previously reported that Par3 is linked to kinesin-2, and the Par complex is transported from the cell body to the axon terminal and accumulated there. We also found that collapsin response mediator protein-2 (CRMP-2) links tubulin heterodimer and Sra-1 (a Rac1 effector) to kinesin-1 and regulates their anterograde transport as a cargo receptor. Here we report that CRMP-2 links the vesicles containing TrkB to kinesin-1 through synaptotagmin-like protein 1 (Slp1) and Rab27, and regulates the anterograde transport of TrkB in growing axons. The velocity of TrkB transport is much higher in growing axons than in the immature neurites. Glycogen synthase kinase-3beta (GSK-3beta) phosphorylates CRMP-2, prevents the association of CRMP-2 with kinesin-1 and Slp1, and impairs TrkB transport and neuronal polarization. Because the activity of GSK-3beta is lower in the distal part of growing axons than in other immature neurites and cell bodies, we propose that local inactivation of GSK-3beta in growing axons promotes the complex formation of kinesin-1/CRMP-2/Slp1/Rab27 and the anterograde TrkB transport for axon formation.

In addition, we have recently found that disrupted in schizophrenia-1 (DISC1) connects the Nudel/Lis1 complex to kinesin-1 and regulates their transport into axons. I will discuss the roles of the cargo receptors including Par3, CRMP-2 and DISC1, and their axonal transport in axon formation in the symposium.

Reference

Arimura, N and Kaibuchi, K. Nat Rev Neurosci, 8, 194-205, 2007

OS-3 Microscopic migration disorder: a possible cause of some neurological/psychiatric diseases

○Makoto Sato^{1,2}

¹Division of Cell Biology and Neuroscience, Department of Morphological and Physiological Sciences, Faculty of Medical Sciences, ²Research and Education Program for Life Science, University of Fukui, Fukui 910-1193, Japan;

Most excitatory neurons are supplied and arranged through radial migration in the developing neocortex. Since neurons show global morphological changes and complicated behavior during the migration, precise regulation of cell shape and polarity as well as the migration start out of the ventricular zone, are essential for appropriate neocortical formation that is critical for its proper function. We found that Filamin A, an actin-crosslinking molecule, indispensable for cell motility, determines migrating cell behavior as well as migration starts, together with its binding partner, FILIP (Filamin A interacting protein). Moreover, our FILIP knockout mice exhibit subtly impaired cell arrangement in the upper cortical layers and mal-propagation of neuronal activities within the cortex. However, their dislocation of neuronal cells appeared to be too subtle to be recognized easily by the conventional histochemical techniques. This implies that malfunction of some genes result in subtle disarrangement of neurons due to the impairment of the radial migration (microscopic migration disorder), but lead to cortical malfunctions. In addition, we identified a molecule that regulates FILIP activities through forming a molecular cluster with Filamin A and FILIP. This machinery regulates directed cell migration/radial migration depending on the membranous phosphoinositides. Filamin A is recruited to the leading edge of the directed migrating cells, where phosphatidylinositol 3,4,5-triphosphates is accumulated, through this newly identified molecular machinery. Since F-actin is newly polymerized near the plasma membrane, it is likely that Filamin A efficiently crosslinks newly polymerized F-actin, leading to the enhanced lamellipodium formation and efficient directed cell migration. Concurrently, we recently identified two FILIP-like molecules that appear to interfere with FILIP activities.

Neuronal migration is a common event during the development of the nervous system. It has been recognized that disturbance of neuronal migration leads to some developmental as well as psychiatric disorders. Our studies, as well as other studies on molecular aspects of neuronal migration, provide us clues for better understanding the etiologies of such diseases. Details, including recent advances in this field as well as newly identified FILIP-like molecules, will be discussed in the meeting.

OS-2 How is the neural network restored after brain injury?

○Toshihide Yamashita¹

¹Dept. of Mol. Neurosci., Med., Osaka Univ.

In the adult mammalian CNS, it is well known that injured axons exhibit very limited regeneration ability. Due to this lack of appropriate axonal regeneration, a traumatic damage to the adult brain and spinal cord frequently causes permanent neuronal deficits. Several axon growth inhibitors in the CNS have been identified in the myelin. Downstream of these inhibitors, activation of RhoA and its effector Rho-kinase has been shown to be a key element for neurite growth inhibition and growth cone collapse elicited by these inhibitors. Consistent with these findings *in vitro*, inhibition of RhoA or Rho-kinase *in vivo* promotes axon growth and functional recovery after spinal cord injury. Recently, several developmental guidance proteins, including repulsive guidance molecules, semaphorin, and ephrin are suggested to be involved in axon growth inhibition after injury to the CNS. Thus, multiple axon growth inhibitors seem to contribute to inability of the injured axons to regenerate, and therapeutic strategy to block the multiple axon growth inhibitors may provide efficient tools that produce functional regeneration following injuries to the CNS. In addition, it is noted that synaptic plasticity in pre-existing pathways and the formation of new circuits through collateral sprouting of lesioned and unlesioned fibers are important components of the spontaneous recovery process. The molecular mechanism of this phenomenon is poorly understood, and elucidation of this will contribute to enhancement of functional recovery after incomplete injury to the CNS.

OS-4 Molecular mechanism underlying glucocorticoid-induced impairment of neuronal migration

○Kenji Sobue¹, Kentaro Fukumoto¹, Taira Mayanagi¹

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Glucocorticoids (GCs) are major mediators of the stress reaction. Numerous studies demonstrate that exposure to high levels of GCs triggered by stress is critically involved in the impairment of early brain development related to an increased risk of psychiatric disorders. However, the cellular and molecular mechanisms underlying the effects of GCs on the brain development, including neuronal migration, remain largely unknown. In this symposium, we will demonstrate the molecular mechanism of the GC-induced impairment of neuronal migration. We found the GC-induced retardation of neuronal migration during neocortical development, and identified the *CALD1* gene, which encodes an actin regulatory protein, caldesmon (CaD), as a main target gene of GCs. The up-regulated CaD expression was mediated by glucocorticoid receptor-dependent transcription. *In utero* electroporation experiments revealed that the overexpression of exogenous CaD retards the neuronal migration during neocortical formation *in vivo*. Thus, these results provide a novel insight into the detrimental actions of GCs on the brain development, particularly as they relate to the risk of psychiatric disorders. Further, CaD depletion by its RNAi also inhibited neuronal migration *in vivo*, suggesting the requirement of an appropriate range of CaD expression levels for normal neuronal migration during neocortical development.

JS-1 Involvement with nitric oxide in pathophysiology of depression○Atsuko Ikenouchi-Sugita¹¹Department of neuropsychiatry, University of Occupational and Environmental Health, Kitakyushu 807-8555, Japan

Nitric oxide (NO) is synthesized from L-arginine by a family of enzyme isoforms known as NO synthases (NOS). Three isoforms of NOS have been identified and cloned; a constitutive neuronal isoform (nNOS), a constitutive endothelial isoform (eNOS), and an inducible isoform (iNOS). In patients with major depression, the total amount and the density of NO synthase-immunoreactive neurons are reduced in the human paraventricular neurons, and NOS activity is decreased in the prefrontal cortex. Furthermore, neuronal type nitric oxide synthesis knock-out mouse reveals abnormal behaviors such as aggression, isolation, anxiety, fear. We consider this mouse might be a model for depression. Generally, prevalence rate for depression in patients with cardiovascular disease is higher than physically healthy subjects. Thus, we consider that NO is associated with depression as well as cardiovascular disease. In addition, prevalence rate for depression in patients with cardiovascular disease is higher than physically healthy subjects. We measured plasma levels of metabolites of NO (NOx) in depressed patients. Plasma NOx levels in depressed patients were significantly lower than those in sex- and age-matched healthy volunteers. We examined the effects of SSRI/SNRI on plasma NOx levels in depressed patients. Paroxetine, a SSRI did not change plasma NOx levels. On the other hand, milnacipran, a SNRI significantly increased plasma NOx levels at 4 weeks and 8 weeks after starting the milnacipran treatment. We investigated the effects of paroxetine/milnacipran on brain NOx levels, NOS activity and nNOS in mRNA C57 black mice. Both drugs decreased brain NOx levels and NOS activity, on the other hand these increased brain nNOS mRNA at 2 weeks after starting these drugs. There was a discrepancy between human and mice data. The reason for the discrepancy remains unknown. It may due to the drug dosage, treatment duration, types of NOS involved. Therefore, Further study is needed to explore the effects of paroxetine/milnacipran on brain NOx levels, NOS activity, NOS mRNA and plasma NOx levels in depressed model mice, which will elucidate the role of NO for depression.

JS-3 The effects of monoaminergic regulation on cognitive dysfunction and how it exerts one's action○Yosefu Arime¹, Ichiro Sora¹¹Department of Biological Psychiatry, Tohoku University Graduate School of Medicine, Sendai, Japan

Hypofrontality involved in dopamine and glutamate system is considered a possible reason of cognitive dysfunctions in schizophrenia while currently no drugs exist effectively treat them. Mesolimbic dopamine pathway has several functional roles including cognitive processes, motivation and emotion. Mesocortical dopamine pathway has a key role in cognitive functions such as working memory, executive function and inhibitory control of behavior. Dopamine transporter knockout (DAT KO) mice display hyperdopaminergic tone in nucleus accumbens (NAc) and normal levels of extracellular dopamine in PFC. DAT KO mice have several behavioral alterations such as hyperlocomotion and impairments of prepulse inhibition (PPI). PPI is considered as a reproducible phenotypic marker identified in schizophrenia. Presently, selective norepinephrine transporter (NET) blocker is approved for treatment of ADHD and is being considered with regard to cognitive impairments in schizophrenia. In a recent study, we reported that nisoxetine, a selective NET blocker, reversed PPI deficits in DAT KO mice. We examined the region-specific effects of nisoxetine on PPI deficits in DAT KO mice by microinjection of nisoxetine and how it exerts one's effect by using neural activation marker c-Fos, neuron markers and retrograde tracer fluorogold. Systemic administration of nisoxetine induced increases of the number of c-Fos positive cells in PFC, NAc shell and ventral tegmental area. Bilateral NAc infusion of nisoxetine had no effect on PPI in WT or DAT KO mice. By contrast, PFC infusion of nisoxetine increased PPI in DAT KO mice. In our preliminary data, multiple-fluorescent labeling of c-Fos, neuron markers and fluorogold revealed that glutamatergic pyramidal cells projecting to NAc in PFC were activated by nisoxetine. Extracellular dopamine in NAc is regulated by DAT but NET regulates extracellular dopamine in the PFC. In our study, administration of a selective NET blocker nisoxetine increased extracellular dopamine levels in PFC. These results suggest that the glutamatergic neurotransmission activated in cortico-subcortical pathway may underlie the amelioration of PPI in DAT KO mice.

JS-5 DISC1 regulates the dendritic localization of IP3R1 mRNA in hippocampal neuron○Daisuke Tsuboi¹, Shinichiro Taya¹, Tomoyasu Shinoda¹, Kozo Kaibuchi¹¹Department of Cell Pharmacology, Graduate School of Medicine, Nagoya University

Schizophrenia is a complex genetic disorder with fairly high heritability. Many histological studies have revealed a decrease in the number of axon terminals, distal dendrites, and dendritic spines in the postmortem brains with schizophrenic patients. These findings raise the possibility that neurodevelopmental disorders are partly involved in pathogenesis of schizophrenia. *Disrupted-In-Schizophrenia 1 (DISC1)* is a candidate gene for susceptibility to schizophrenia. We have previously reported that DISC1 accumulates at the tip of axonal processes and regulates the axonal transport of the NUDEL/LIS1/14-3-3 ϵ complex and Grb2 through Kinesin-1 in rat hippocampal neurons. Recently, we found that DISC1 distributed not only in axon but also in somatodendrites of the mature cultured hippocampal neurons. However, the molecular function of DISC1 in dendritic shafts and spines remains unclear. In this study, we identified Hematopoietic zinc finger protein (Hzf) as a novel DISC1-interacting molecule by affinity column chromatography and mass spectrometry. It has been reported that Hzf regulates the dendritic localization and translation of inositol 1, 4, 5-triphosphate receptor 1 (IP3R1) mRNA. IP3R1 acts as an IP3-gated Ca²⁺ release channel in the central nervous system, involving in synaptic plasticity in hippocampal CA1 neuron. DISC1 directly interacted with Hzf *in vitro* and *in vivo*. DISC1 partly colocalized with Hzf and IP3R1 mRNA in dendrites of hippocampal neurons. The knockdown of DISC1 by RNA interference inhibited the dendritic localization of IP3R1 mRNA. Inhibition of the interaction between DISC1 and Hzf by overexpression of Hzf fragments caused the impairment of dendritic localization of IP3R1 mRNA. Taken together, these results indicate that DISC1 regulates the dendritic localization of IP3R1 mRNA through Hzf interaction.

JS-2 Platelet intracellular calcium mobilization in bipolar disorder and beyond○Katsuji Suzuki¹¹Department of Psychiatry, Hokkaido University Graduate School of Medicine

Over 20 years ago, researchers found aberrant cortisol response to 5-hydroxytryptophan in the patients with mood disorders, which indicated hyperfunction of central 5-HT_{2A} receptors in those patients. After that, lots of laboratories including ours have been using readily accessible platelets to test 5-HT_{2A} receptor function of patients with mood disorders. Even though platelet is a peripheral organ, they have successfully reported enhanced cytosolic calcium mobilization via 5-HT_{2A} receptors in the platelets of depression or mania compared to that of control. We have found this 5-HT-induced platelet intracellular calcium response is a stable physical trait marker, and is enhanced specifically in bipolar disorders. Moreover depressed patients with enhanced calcium mobilization showed better clinical response to mood stabilizers like lithium and valproate than to antidepressants. And in a ten-year follow-up study, we reported that diagnosis of depression for the depressed patients with higher platelet intracellular calcium response to 5-HT tended to be changed into bipolar disorder. We concluded that enhanced 5-HT-induced platelet intracellular calcium response indicated some 'bipolarity' of the depressed patients.

Recently, we have focused more on the mechanism of this enhanced function of 5-HT_{2A} receptors. Because we failed to find any relation between the density of 5-HT_{2A} receptor and calcium increase after 5-HT stimulation in the platelets, in addition, some agonist independent of 5-HT_{2A} receptor such as thrombin also induced enhanced cytosolic calcium response in the platelets from bipolar disorder, it was unlikely that enhanced 5-HT-induced cytosolic calcium mobilization is merely caused by increased 5-HT_{2A} receptor number. Both 5-HT_{2A} receptor and thrombin receptor couple to G protein regulating production of inositol triphosphate (IP3). In the course of IP3 production, protein kinase C (PKC) dependent signal transduction system could be activated and regulate IP3-induced cytosolic calcium. We found inhibition of protein kinase C dependent signaling resulted in reduced agonist-induced platelet intracellular calcium mobilization in normal controls, however, this reduction was not observed in bipolar disorders, indicating increased PKC activity in bipolar disorders. On the other hand, calmodulin inhibitors evoked enhancement of agonist-induced calcium mobilization as if the response were of bipolar disorder. In addition to that, lithium normalized this enhancement of calcium mobilization produced by inhibition of calmodulin. These findings suggest that hyperfunction of PKC-dependent pathway and hypofunction of calmodulin-dependent pathway may play roles in abnormal calcium mobilization observed in the platelet of patients with bipolar disorders.

JS-4 Role of tPA-plasmin system in neuropsychological abnormalities induced by morphine.○Taku Nagai¹, Toshitaka Nabeshima², Kiyofumi Yamada¹¹Department of Neuropsychopharmacology and Hospital Pharmacy, Nagoya University Graduate School of Medicine, Nagoya 466-8560, Japan. ²Department of Chemical Pharmacology, Graduate School of Pharmaceutical Sciences, Meijo University, Nagoya 468-8503, Japan.

Drugs of abuse acutely modulate the activity of mesolimbic dopaminergic neurons, projecting from the ventral tegmental area of the midbrain to the nucleus accumbens (NAc). Recently, it has been proposed that activity-dependent synaptic plasticity and remodeling of the mesolimbic dopaminergic system play a crucial role in the development of drug dependence. Tissue plasminogen activator (tPA) is a serine protease that catalyzes the conversion of plasminogen (plg) to plasmin. The tPA-plasmin system plays a role in synaptic plasticity and remodeling. Here we show that this protease system participates in the rewarding effects of morphine. A single morphine treatment induced tPA mRNA and protein expression in a naloxone-sensitive manner, which was associated with an increase in the enzyme activity in the NAc. Morphine-induced conditioned place preference and hyperlocomotion were significantly reduced in tPA-deficient (tPA^{-/-}) and plg-deficient mice, being accompanied by a loss of morphine-induced dopamine release in the NAc. The defect of morphine-induced dopamine release and hyperlocomotion in tPA^{-/-} mice was reversed by microinjections of either exogenous tPA or plasmin into the NAc. Immunohistochemistry revealed that protease activated receptor-1 (PAR1)-immunoreactivity was localized to the nerve terminals positive for tyrosine hydroxylase in the NAc. Microinjection of a PAR1 antagonist peptide into the NAc significantly reduced morphine-induced dopamine release in the NAc and hyperlocomotion although the treatment had no effect on basal dopamine release and spontaneous locomotor activity. Furthermore, the PAR1 antagonist peptide blocked the ameliorating effect of plasmin on the defect of morphine-induced dopamine release in the NAc of tPA^{-/-} mice. Our findings suggest that targeting the tPA-plasmin-PAR1 system would provide new therapeutic approaches to the treatment of drug dependence.

JS-6 Arachidonic acid increases neurogenesis and restores prepulse inhibition deficits in model rats○Motoko Maekawa^{1,2,3}, Noriko Takashima⁴, Miho Matsumata^{1,5}, Shiro Ikegami⁶, Masanori Kontani⁷, Yoshinobu Hara^{1,5}, Hiroshi Kawashima¹, Yuji Owada⁸, Takeo Yoshikawa¹, Shigeki Yuasa², Yoshinobu Kiso⁷, Kaoru Inokuchi¹, and Noriko Osumi^{1,5}¹Tohoku University Graduate School of Medicine, ²National Institute of Neuroscience, ³RIKEN Brain Science Institute, ⁴Mitsubishi Kagaku Institute of Life Sciences, ⁵CREST, ⁶Saitama Institute of Technology, ⁷Suntory Ltd, ⁸Yamaguchi University Graduate School of Medicine

Although the precise mechanisms of schizophrenia still remain unknown, several hypotheses including "neurodevelopmental theory" have been proposed. For genetic studies of schizophrenia, the concept of "endophenotypes" is attracting attention, because they can be closer to disease etiology than clinical phenotype and can be reliable biological markers. Among them, deficits in prepulse inhibition (PPI) is known for schizophrenia. PPI can be measured not only in humans but also in experimental animals. We already reported that *FABP7/Fabp7* plays a crucial role linking neurodevelopment, schizophrenia pathology and PPI (Watanabe et al., 2007).

Here, we examined whether decreased neurogenesis may serve as vulnerable factors for PPI deficits, by using genetic (*Pax6*^{-/-} rats) and environmental (an anti-proliferative drug, methylazoxymethanol acetate, treatment) animal models. We found that the both model rats showed PPI deficits. Next, we investigated whether neurogenesis-enhancing interventions could improve PPI, in hope for establishing preventive measures for schizophrenia. Since we identified specific expressions of *Fabps* in neural progenitor cells in the developing hippocampus, we tested polyunsaturated fatty acids (PUFAs), endogenous ligands for *Fabps*, as potential neurogenesis-regulating agents. We were able to increase production of new neurons in the early postnatal stage of the wild type rats and *Pax6*^{-/-} rats by 4-week administration of arachidonic acid (ARA). In addition, we confirmed that the ARA-treated *Pax6*^{-/-} rats showed improved PPI in adulthood. Collectively, these results indicate that decreased neurogenesis in the developing brain may lead to future PPI deficits, and that ARA administration in early stages may be beneficial to ameliorate a schizophrenia endophenotype "PPI" through an augmented neurogenesis.

AS-1 Identification of susceptibility genes for schizophrenia using intermediate phenotype

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Schizophrenia, a common neuropsychiatric disorder affecting 0.5-1% of the general population worldwide, is characterized by psychosis and profound disturbances of cognition, emotion and social functioning. The pathophysiology of schizophrenia is still unclear; however, this disease is highly heritable and several intermediate phenotypes such as neurocognitive dysfunction, abnormal brain morphology, deficits in pre-pulse inhibition (PPI) of the startle response, etc. are known to be useful to identify susceptibility genes for schizophrenia. Intermediate phenotype is a neurobiological trait related to risk for schizophrenia and should have good psychometric properties; be related to the disorder and its symptoms in the general population; be stable over time; show increased expression in unaffected relatives of probands; cosegregate with the disorder in families; and have common genetic influences with the disorder. Using this approach, we present the association between the several susceptibility genes such as dysbindin, DISC1, PACAP and intermediate phenotypes, in addition to genetic association with schizophrenia. We will further present possible pathophysiological mechanisms of schizophrenia related to these susceptibility genes. Our study could be a successful example of this strategy to find susceptibility genes for complex diseases.

AS-3 Antipsychotic Potential of Signal Inhibitors for Neuregulin and Epidermal Growth Factor

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Neuregulin-1 (NRG1) and epidermal growth factor (EGF) bind to the same receptor family (ErbB) and both are implicated in schizophrenia. In agreement, neonatal exposure to NRG1 and EGF similarly perturbs behavioral and cognitive development in mice and rats. In the present study, we examined pharmacological effects of tyrosine kinase inhibitors for their receptors (ErbB). ErbB inhibitors ameliorate various behavioral impairments induced by these cytokines, hippocampal lesion and methamphetamine. This finding indicates antipsychotic potential of ErbB inhibitors.

AS-5 Effect of GABA_A receptor agonist in animal models for schizophrenia-like cognitive impairment

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Cognitive deficits including information processing are a fundamental feature of the psychopathology of schizophrenia. Deficits of prepulse inhibition (PPI) of the startle reflex, a measure of sensorimotor gating, have been well demonstrated in patients with schizophrenic and widely used as an animal model of schizophrenia. GABA is the most important inhibitory neurotransmitter in the brain, and deficits of the GABAergic system, including the reduction of the number of parvalbumin-containing GABAergic interneurons, have been documented in the prefrontal cortex of patients with schizophrenia. Reduction of GABAergic interneurons in schizophrenia is paralleled by increased GABA_A receptor binding in the prefrontal cortex, while GABA_A receptors are reduced in the hippocampus and prefrontal cortex. We have previously demonstrated that pallidotegmental GABAergic neurons play a crucial role in PPI of the startle reflex in mice through the activation of GABA_A receptors in pedunculopontine tegmental neurons (PPTg). In the present study, we examined the effects of baclofen, a GABA_B receptor agonist, on methamphetamine (METH)- and MK-801-induced PPI impairment. Furthermore, we examined the effect of baclofen on METH-induced impairment of object recognition memory. Acute treatment with METH and MK-801 significantly disrupted PPI of the startle reflex in mice. Baclofen dose-dependently ameliorated PPI impairment induced by acute treatment with METH and MK-801. Furthermore, repeated treatment with METH at a dose of 1 mg/kg for 7 days induced a long-lasting impairment of recognition memory in mice. Baclofen ameliorated the repeated METH-induced cognitive impairment, although THIP, a GABA_A receptor agonist, had no significant effect. GABA_A receptors may constitute a putative new target in treating cognitive deficits in patients suffering from schizophrenia, as well as METH psychosis.

AS-2 Molecular mechanism of schizophrenia via the dysfunction of Dysbindin

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Schizophrenia is a severe mental disorder affecting about 1% of the population worldwide. The cause of schizophrenia is thought to involve the combined effects of multiple gene components. Genetic linkage and association studies have identified potential susceptibility genes such as dysbindin, Neuregulin, Catechol-O-methyltransferase and RG4. In particular, it has been reported that chromosome 6p is one of the most susceptible regions in linkage studies of schizophrenia. Among them, genetic variants in a gene 6p22.3, dysbindin (dystrobrevin-binding protein 1; DTNBP1), which is identified as a protein interacting with dystrobrevins, has been shown to be associated strongly with schizophrenia. Many reports showed that the expression of dysbindin is down-regulated in the brain of schizophrenic patients both at the mRNA and protein levels. To elucidate the function of dysbindin, we examined the interacting partners of dysbindin using yeast two-hybrid analysis and found Dysbindin had its expected binding partners, suggesting Dysbindin involvement in neurotransmission, cell signaling, the cytoskeleton, transcription, etc. Based on the expected functions of Dysbindin, we investigated the function of Dysbindin and our data showed the possible involvement of Dysbindin in the transcription via the interaction with a transcriptional factor, resulting in the abnormal alterations such as the impaired neural transmission and the abnormal development of neurons. These findings should provide new insights into the mechanisms of neuronal development and the pathogenesis of schizophrenia via Dysbindin.

AS-4 Cortical GABA Neurotransmission in Schizophrenia: Regional and Molecular Phenotypes

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Individuals with schizophrenia exhibit disturbances in cognitive, affective, sensory and motor functions that depend on the circuitry of different cortical areas. The cognitive deficits associated with dysfunction of the dorsolateral prefrontal cortex (DLPFC) result, at least in part, from abnormalities in GABA neurotransmission as reflected in a specific pattern of altered expression of GABA-related genes. We sought to determine whether this pattern of altered gene expression is restricted to the DLPFC or could also contribute to the dysfunction of other cortical areas in the illness. Real-time quantitative polymerase chain reaction was used to assess the levels of eight GABA-related transcripts in four cortical areas (DLPFC, anterior cingulate, primary motor and primary visual cortices) from subjects with schizophrenia and matched normal comparison subjects. Expression levels of seven transcripts were lower in the subjects with schizophrenia with the magnitude of the reductions for each transcript indistinguishable across the four areas. The largest reductions were detected for the mRNAs encoding somatostatin and parvalbumin, followed by moderate decreases in mRNA expression for the 67 kD isoform of glutamate decarboxylase, the GABA membrane transporter 1, and the $\alpha 1$ and δ subunits of GABA_A receptors. In contrast, the expression of calretinin mRNA did not differ between the subject groups in any of the four areas. Because the areas examined represent the major functional domains of the cerebral cortex, our findings suggest that a conserved set of molecular alterations affecting GABA neurotransmission contributes to the pathophysiology of different clinical features of schizophrenia.

AS-6 NMDA receptor-D-serine system-targeted treatment development for schizophrenia

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Based upon the fact that phencyclidine (PCP) and other antagonists for the N-methyl-D-aspartate (NMDA) type glutamate receptor cause schizophrenia-like positive and negative symptomatology, facilitation of the NMDA receptor function has been considered to ameliorate both of the antipsychotic-responsive dopamine-related and treatment-resistant non-dopaminergic symptoms in schizophrenic patients. Indeed, we have shown that the allosteric agonists for the NMDA receptor acting at its glycine site, D-serine and/or D-alanine, inhibit PCP-induced increase in dopamine transmission in the prefrontal cortex and abnormal behavior in the rat. In agreement with these results, the two D-amino acids have been reported to improve the negative and positive symptoms and cognitive disturbances in schizophrenic patients treated with conventional antipsychotics. However, the presently available allosteric agonists have the difficult problems for the clinical use such as low permeability to the brain through the blood-brain barrier, partial agonist property, nephrotoxicity or low selectivity. Interestingly, we have demonstrated that D-serine is an endogenous substance in mammals that shows a brain-selective and NMDA receptor-related distribution, although D-amino amino acids had long been believed to be uncommon in mammalian tissues. Subsequently, we have found the synthesis, extracellular release, uptake, and degradation processes of D-serine in the brain tissues by *in vivo* experiments. Together with the observations that the stimulation of the glycine site of the NMDA receptor by an intrinsic agonist D-serine is required for the physiological activation of the NMDA receptor by glutamate in the forebrain areas, the above findings suggest that the molecular and cellular mechanisms that regulate the extracellular D-serine contents could be suitable targets for the development of a novel class of antipsychotic drugs. Thus, we have been studying these mechanisms and we here present our recent data concerning the cloning and characterization of the candidates for the molecules specifically related to the D-serine metabolism (which include dsr-1 (D-serine responsive transcript-1), dsr-2 and dsr-1 (D-serine modulator-1)), the control systems for the extracellular and intracellular D-serine contents and the cell types that contain the respective systems.

S1-1 Heparan sulfate endosulfatases are required for normal brain development

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Heparan sulfate (HS) proteoglycans play important roles in the regulation of cell differentiation and growth. These activities are mediated by the interaction between the HS attached to core proteins and signaling molecules. HS is a long unbranched sugar chain composed of the repeating disaccharide units, uronic acid and glucosamine. HS has abundant sulfation at 2-*O*-position of uronic acid and 3-*O*-, 6-*O*-, and *N*-positions of glucosamine. Because sulfation reactions do not proceed to completion, HS shows enormous structural heterogeneity. Previous biochemical studies have shown that highly sulfated regions of HS bind signaling molecules, and that sulfation pattern is an important determinant of ligand binding specificity and affinity. To date, sulfation patterns of HS are thought to be formed by specific sulfotransferases. However, recent identification of novel HS endosulfatases, SulfFP1 and SulfFP2, which remodel HS structures via 6-*O*-desulfation, necessitates the revision of this simple concept. We showed that secreted SulfFP1 and SulfFP2 selectively catalyze hydrolysis of 6-*O*-sulfate of glucosamine in trisulfated (2-*O*-, 6-*O*-, and *N*-sulfated) disaccharide units at neutral pH. Several laboratories have shown that SulfFPs activate Wnt signaling and suppresses FGF signaling, suggesting that SulfFPs modulate extracellular signaling via HS remodeling. To examine the physiological roles of *SulfFP* genes, we generated knockout mice. Single knockouts for *SulfFP1* or *SulfFP2* showed no obvious abnormalities, whereas double knockout mice die soon after birth. In these knockout mice, the sulfation profiles of HS changed as predicted from their enzymatic activities *in vitro*. In addition, they show axon guidance defect in a specific nerve tract. Taken together, these findings suggest that specific sulfation patterns generated by SulfFPs are required for normal neural network formation

S1-3 Perineuronal nets of proteoglycan-containing extracellular matrix

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More than one hundred years ago, Camillo Golgi observed incompletely impregnated envelope structure on neurons called as perineuronal nets (PNNs). Now days, they are known to be composed of several chondroitin sulfate proteoglycans (CSPGs) and hyaluronic acids and surround neuronal somata and dendrites of GABAergic neurons to form lattice-like structure. The functional significances of PNNs are not beyond the speculation, but two possibilities have been proposed. One possibility is that PNNs are associated with plasticity of neuronal connections. The chondroitinase ABC digestion restores the ocular dominance plasticity in the adult visual cortex, indicating that degradation of CSPGs around PNNs causes neurons to grow more freely into extracellular space in the absence of CSPG extracellular matrix. The other possibility is that PNNs are concerned with the neuroprotective function against the neurotoxicity of amyloid-beta protein and glutamate. We originally developed dissociated culture system for PNNs to elucidate the functions of PNNs. The PNNs in the culture system revealed a similar character to PNNs *in vivo*; the localization of PNNs was seen at somata and proximal dendrites and the components of them were CSPGs and hyaluronic acids. Moreover, it was shown that neurons themselves were able to synthesize CSPGs and constructed PNNs structure without glial cells. By using this system, we observed that CSPGs on PNNs had protective role against the neurotoxicity of amyloid peptide, indicating the direct demonstration of neuroprotective action of CSPGs.

S1-2 The role of neuroglycan C, a membrane-spanning chondroitin sulfate proteoglycan, in the central nervous system

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Neuroglycan C (NGC), a transmembrane chondroitin sulfate proteoglycan that is predominantly expressed in the brain, is a typical part-time proteoglycan that changes its structure from a proteoglycan form to a non-proteoglycan form with development of the cerebellum and retina. The chondroitin sulfate glycosylation is also regulated differently depending on cell types. The chondroitin sulfate of NGC has a higher proportion of E-unit, a highly sulfated disaccharide unit, compared with those of neurocan and phosphacan, other neural chondroitin sulfate proteoglycans. Chondroitin sulfate polysaccharides rich in the highly sulfated disaccharides have been shown to bind to several growth factors and to be involved in neurite outgrowth. NGC should function through its unique chondroitin sulfate chain in the brain. To clarify the role of NGC in development of the brain, we planned to generate NGC-gene mutant mice that show abnormal expressions of NGC by conditionally-targeted disruption of the NGC gene. Now, we have gotten NGC-knock-in mice that express NGC in non-proteoglycan form due to a mutation (S123A) at the chondroitin sulfate chain binding site, in addition to NGC-knockout mice that are completely deficient in all splice variants, NGC-knockdown mice in which the expression of NGC are down-regulated in various regions of the brain. All these mice were viable and fertile. Histochemical studies showed that these mice did not show macroscopic abnormalities in gross brain anatomy. The expression levels of neurocan and phosphacan were almost normal in these NGC mutant mice. Behavior analyses and detailed histochemical studies are on going.

Aono, S. and Oohira A. (2007) Neuroglycan C, a part-time proteoglycan, in the central nervous system. *Neural Proteoglycans* (Maeda, N., ed.), pp. 37-50. Research Signpost, Kerala.

S1-4 DACS, novel matrixstructure composed of chondroitin sulfate proteoglycan in the brain

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Chondroitin sulfate proteoglycans (CSPGs) are major components of the extracellular matrix (ECM) in the brain. During the past century, it has been known the perineuronal nets (PNNs) as exclusive ECM structures containing CSPG in the adult cerebral cortex. Here, we report a novel CSPG-containing structure distinct from PNNs in the mature mammalian cerebral cortex. An anti-chondroitin sulfate antibody CS56 delineated a structure with a unique morphology like a dandelion clock. Accordingly, we named it Dandelion Clock-like Structure (DACS) (BBRC; 364: 410-5, 2008). As the postnatal cerebral cortex matured, DACSs became visible around the end of the critical period. Immunohistochemical evidence showed that DACSs surround a group of NeuN-positive neurons. At ultrastructural level, CS56-immunoreactivities were localized in the cytoplasm and on the membrane of astrocytes. DACSs disappear when chondroitinase ABC is microinjected into the cortical parenchyma, while diffuse CSPG immunoreactivity persists in the neuropil. Interestingly, DACSs are quickly restored to the original state in a few days. This is the first report demonstrating the presence of an ECM structure DACS composed of CSPGs around a group of cortical neurons in the adult cerebral cortex. I will here introduce and discuss about the nature of DACS we elucidated so far.

S2-1 Neuregulin and the pathobiology of schizophrenia: studies in 'knockout' mice

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Neuregulin-1 (NRG1) plays a significant role in the developing brain and has been identified as a susceptibility gene for schizophrenia. In the present study the functional role of the NRG1 gene, as it relates to cognitive and social processes known to be disrupted in schizophrenia, was assessed in mice with heterozygous deletion of transmembrane (TM)-domain NRG1 in comparison with wildtypes (WT). Social affiliative behaviour was assessed using the sociability and preference for social novelty paradigm, in terms of time spent in: (i) a chamber containing an unfamiliar conspecific vs an empty chamber (sociability), or (ii) a chamber containing an unfamiliar conspecific vs a chamber containing a familiar conspecific (preference for social novelty). Social dominance and aggressive behaviour was examined in the resident-intruder paradigm. Spatial learning and memory was assessed using the Barnes maze paradigm, while spatial working memory was measured using the continuous variant of the spontaneous alternation task. Barnes maze data revealed intact spatial learning in NRG1 mutants, with elevated baseline latency to enter the escape hole in male NRG1 mutants reflecting an increase in activity level. Similarly, although a greater number of overall arm entries was found, spontaneous alternation was unaffected in NRG1 mice. Social affiliation data revealed NRG1 mutants to evidence a specific loss of WT preference for spending time with an unfamiliar as opposed to a familiar conspecific. Emotional/anxiety-related behaviour was assessed using the elevated plus-maze and the light-dark test. Social behaviour was examined further in terms of dyadic interactions between NRG1 mutants and an unfamiliar conspecific in a novel environment. There was no effect of NRG1 genotype on performance in either test of emotionality/anxiety. However, previous reports of hyperactivity in NRG1 mutants were confirmed in both paradigms. In the test of social interaction, aggressive following was increased in NRG1 mutants of both sexes, together with an increase in walkovers in female mutants. These findings elaborate the specificity of the NRG1 phenotype for the social rather than the cognitive or emotional/anxiety-related domains. They implicate NRG1 in the regulation of social novelty and in reciprocal social dominance behaviour. These data inform at a novel phenotypic level on the functional role of this gene in the context of its association with risk for schizophrenia.

S2-3 Drug-seeking behavior in methamphetamine-dependent mice: a role for GDNF

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Among the most insidious characteristics of drug addiction/dependence the recurring desire to take drugs even after many years of abstinence is a primary feature of the addiction disorder. The precise neural mechanism by which drug-associated cues induce craving and drug-seeking behavior remains poorly understood. Furthermore, while genetic factors are considered to play a role in the development and maintenance of drug dependence including vulnerability to relapse, little is known about the role of specific genes in enduring vulnerability to relapse. Bearing this in mind, we have recently succeeded to develop a typical model of drug-primed and cue-induced reinstatement of extinguished methamphetamine (METH)-seeking behavior in mice. Here we show that activation of extracellular-signal regulated kinase (ERK) in the prefrontal cortex is crucial in cue-induced reinstatement of extinguished METH-seeking behavior in mice. Thus, treatment with selective MEK inhibitors, SL327 and PD98059, attenuated cue-induced reinstatement of METH-seeking behavior without affecting METH-taking behavior. We also examined the role of glial cell line-derived neurotrophic factor (GDNF) in our mouse model of METH self-administration and relapsing behavior. Partial deletion of the GDNF expression potentiated METH self-administration, enhanced motivation to take METH, increased vulnerability to drug-primed reinstatement, and prolonged cue-induced reinstatement of extinguished METH-seeking behavior in GDNF heterozygous knockout [GDNF(+/-)] mice. In contrast, there was no significant difference in novelty responses, METH-induced hyperlocomotion and locomotor sensitization, food-reinforced instrumental behavior and motivation, or reinstatement of food-seeking behavior between GDNF(+/-) mice and wild-type littermates. These findings suggest that GDNF plays a role in enduring vulnerability to reinstatement of METH-seeking behavior.

S2-2 Social behavior controlled by oxytocin release due to CD38

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The cell surface protein CD38 is present in neurons and glia cells in the brain. However, CD38's function in the brain has remained elusive. We have now shown that CD38 is required in mice for the regulation of social behavior, including male's pair cognition and dam's nurturing behaviors of pups by regulating oxytocin, originally known as the hormone for female's uterine contraction during labor and mild ejection in lactation to babies. CD38KO dams took a long time to start to retrieve and behaved as if they were not interested in their babies, alternatively, they 'neglect' pups. They often dropped them during retrieving on the way to the nest, as if they do not remember their nest and so that pups were scattered in different places. Next, we examined in young adults of CD38^{-/-} male mice, which experienced repeated pairings with the same female mouse. Normal mice showed a significant decline in the time spent investigating a female upon subsequent presentations of the same female. In contrast, CD38KO males showed sustained high levels of investigation at each encounter with the same female and the same level of investigation, in another words, they behave as a 'stalker'. To link between CD38 and oxytocin, we measured plasma and cerebrospinal fluid oxytocin levels and found that, compared with wild-type animals, CD38KO mice had reduced oxytocin levels. In conclusion, our findings shed light on the function of CD38 in the brain and, potentially, in human diseases associated with abnormal social behavior such as pervasive developmental disorder, including autism. (Jin et al., *Nature* 446, 41-45 (2007))

S2-4 PHARMACOGENOMICS IN CNS DISORDERS

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CNS disorders represent the 3rd problem of health in developed countries behind cardiovascular disorders and cancer, and are the first cause of disability in the productive sector. Most CNS disorders are associated with multiple defects in polymorphic loci distributed across the human genome. Approximately 1,500 genes might be involved in the pathogenic processes underlying major CNS disorders (e.g., 255 genes in Alzheimer's disease, 205 in schizophrenia, 106 in depression, 107 in anxiety, 103 in stroke, 385 in ataxias, 155 in epilepsy, 83 in meningioma, 105 in glioblastoma, 37 in astrocytoma, 73 in Parkinson's disease, 7 in vascular dementia). Both prospective and retrospective studies indicate that the therapeutic response in most CNS disorders are genotype-specific. The impact of individual pharmacogenetic profiles is particularly important in major psychiatric disorders (psychosis, depression, anxiety) and dementia. Approximately, 25-30% of current drugs administered for the treatment of CNS disorders are metabolized via CYP2D6-related enzymes. Polymorphic variants of the CYP2D6 gene responsible for the genotype/phenotype of extensive (EM), intermediate (IM), poor (PM) and ultra-rapid (UM) metabolizers exhibit ethnic and geographic differences. For instance, CYP2D6 PMs are present in 5-7% of the World population (7.86% Europeans, 2.27% Middle Eastern populations, 2.09% Asians, 6.73% Africans, 2.89% Americans, 0.94% Orientals, 7.27% Polynesians). In the European population, where the mixture of ancestral cultures has occurred for centuries, the distribution of the CYP2D6 genotypes differentiates 4 major categories of CYP2D6-related metabolizer types: (i) Extensive Metabolizers (EM)(*/1, */10)(51.61%); (ii) Intermediate Metabolizers (IM)(*/3, */4, */5, */6, */7, */10, */10, */4, */10, */6, */10, */7, */10)(32.26%); (iii) Poor Metabolizers (PM)(*/4, */4, */5, */5)(9.03%); and (iv) Ultra-rapid Metabolizers (UM)(*/1xN, */1, */1xN, */4, Dupl)(7.10%). The distribution of all major genotypes is the following: */1, 47.10%; */10, 4.52%; */3, 1.95%; */4, 17.42%; */5, 3.87%; */6, 2.58%; */7, 0.65%; */10, 1.30%; */4, */10, 3.23%; */6, */10, 0.65%; */7, */10, 0.65%; */4, */4, 8.37%; */5, */5, 0.65%; */1xN, */1, 4.52%; */1xN, */4, 1.95%; and Dupl, 0.65%.

In patients with dementia there is a convergence of pharmacogenetic (CYP2D6-related) and pharmacogenomic factors (APOE-related) which accumulate in a cluster of patients (10-20%) showing a poor therapeutic response to conventional drugs (e.g., cholinesterase inhibitors). Similar findings appear in psychotic and depressive patients under treatment with neuroleptics and antidepressants. Although the field of pharmacogenetics in CNS disorders is in its infancy, it seems clear that predictive pharmacogenetic screening is a suitable strategy for therapeutic optimization.

S3-1 Pain is perceived by the brain, pain behavior is originated from the brain○Masahiko Shibata¹¹Dept. of Pain Med., Univ. of Osaka

In clinical pain setting, several unusual cases which could not be clearly explained by classical neurology nor advanced neuroscience were encountered: a case of refractory CRPS I (complex regional pain syndrome type I) after venipuncture resolved by cerebral contusion (Pain 79:313,1999), a case of sudden onset of CRPS symptom after convulsion due to brain tumor (JSPC 11:297,2004) and cases of phantom limb pain relieved by mirror visual feedback (MVF) (Rheumatology in press 2008) and motor cortex stimulation (Lancet 353:212,1999). These cases have provided us motivation to study relationship among pathological pain, emotion and motor system. We found that hyperalgesic response after nerve injury are normalized by Electro-convulsive treatment (Anesth Analg 86:584,1998) and delayed onset of anxiety and depression behavior in nerve injured mice (Anesth Analg 104:1570,2007). We focused on relation between pain and motor system and found visuospatial perception of CRPS patients are distorted (Neurology 68:152,2007) and visually induced motor imagery by MVF was more effective for reducing deep pain than superficial pain. We also started the study of pain from deep structure in human volunteer using fMRI and found that activated brain area induced by muscle and periosteum stimulation are different. Periosteum stimulation activates cont. thalamus and S2, whereas muscle stimulation activates cont. thalamus, bil S2, insula and ACC. These clinical findings and basic researches suggest that brain is hopeful target for refractory pain patients.

S3-3 Alexithymia and pain experience○Masako Hosoi¹¹Dept. of Psychosomatic Medicine, Kyushu University Hospital, Fukuoka, Japan

Alexithymia (ALEX), a lack of emotional awareness, has been recently shown to be associated with pain in patients with a number of chronic pain conditions. Moriguchi et al reported on the empathy and judging pain in a fMRI study of ALEX (Cerebral Cortex 17: 2223-2234, 2006). They found that the ALEX group showed the lower pain-rating and empathy-related scores. Furthermore, the ALEX group showed less cerebral activation in the left dorsolateral prefrontal cortex (DLPFC), the dorsal pons, the cerebellum, and the left caudal anterior cingulate cortex (ACC) within the pain matrix. The ALEX group also showed greater activation in the right insula and inferior frontal gyrus. It is important that the ALEX has the different activation pattern in the pain- and emotion-related brain areas with cognitive impairments, particularly executive and regulatory aspects, of emotional processing. These findings have brought us the question that how is the pain experience in the patients with pain disorders or somatic diseases. Following this question, we report that the effect of ALEX on the pain experience in pain disorders in Kyushu university hospital (study 1) and in neuromuscular diseases (NMD) in hospital related to University of Washington in the USA (study 2).

In the study 1, we investigated if the degree of ALEX is correlated with the pain experience in patients with pain disorder (n = 150). The patients filled original and the short-form McGill questionnaire (MPQ and SF-MPQ), Toronto ALEX scale-20 (TAS-20). The affective component of pain in the MPQ and SF-MPQ correlated with the score of TAS-20 while the sensory and evaluative component of pain did not.

In the study 2, we tested the hypotheses that ALEX is significantly associated with pain intensity, pain interference, psychological functioning, and vitality in patients with NMD (n = 129). Consistent with the study hypotheses, higher TAS total scores were significantly associated with poorer psychological functioning, higher pain intensity ratings, higher pain interference ratings and less vitality.

Thus, the ALEX has impact on the pain experience in the patients with pain disorder and NMD in clinical settings. The relationship between pain, emotion and cognition in pain experience will be discussed in relation to the pain matrix in the brain system.

S3-2 Altered cortical activations in chronic alodynic pain patients: a fMRI study○Takahiro Ushida^{1,2,3}, Tatsunori Ikemoto^{2,5}, Shigeki Tanaka⁴, Shinichirou Taniguchi^{2,5}, Yoriko Murata¹¹Multidiscip. Pain Ctr., Aichi Med. Univ., Aichi, Japan ²Dept. Orthopaedic Surg., Kochi Med. Sch., Kochi, Japan ³Dept. Radiol., Kochi Med. Sch., Kochi, Japan ⁴Dept. Psychol., Jin-Ai Univ, Fukui, Japan ⁵Nankoku Pain Research Group, Kochi, Japan

Basic pain researches revealed that neuronal sensitization and its associated plastic changes of the central nervous systems caused by noxious input from peripherals have an extremely important role in development of chronic pain conditions. CRPS is one of the typical chronic pains and usually accompanies allodynic pain. These pains have multi-dimension (sensory, cognitive, affective) and experienced in the brain subjectively. Study 1 was to investigate real pain responsive cortical area in allodynic pain patients. Mechanical painful stimuli were applied during fMRI analysis and activated cortical areas were investigated. The Patient group showed cortical activations in S1, S2, SMA and cingulate cortex. Whereas S1, S2, motor cortex, thalamus and cingulate cortex were activated in the volunteer group. (Pain Research 18 (2003) 137-144) Study 2 was to investigate whether imagination of a painful event by video viewing would evoke painful feeling and cortical activation in patients with allodynia. Since interviewing of these patients revealed that they could experience pain related discomfort when they image the painful event. As for fMRI functional task, the patients and volunteers were shown a digital video displaying tactile palm stimulation by horse hair brush. Although the volunteer group experienced no significant emotional feelings, the patient group experienced discomfort feeling by watching the task. Contrasting with the volunteer group, the patient group displayed activation of the cortical areas related to pain and emotions: prefrontal cortex and anterior cingulate cortex. (Brain topography 18 (2005) 27-35) This activation pattern was differed from volunteers imaged the painful event in the brain. (Neuroscience Lett, In press) These findings suggest that cortical mechanisms may contribute to maintenance of pain addition to spinal and peripheral mechanisms in chronic CRPS patients.

S3-4 Chronic pain and central sensitization: evidence for descending facilitation in animal models○Emiko Senba¹¹Dept. of Anatomy & Neurobiology, Wakayama Medical University, Wakayama, Japan

Spino-thalamic tract consists of two systems; lateral system participates in the discrimination of pain, and medial system mediates affective components of pain. Persistent pain induces plastic changes in cortical neurons, especially in the anterior cingulate and insular cortices. Activation of these neurons is transmitted to the periaqueductal gray and rostroventromedial medulla (RVM) (descending pain control system). This system has been considered to exert descending inhibition, but it also causes facilitation in certain pathological conditions.

Pain is a multifaceted sensation consisting of 1) nociception, 2) pain transmission, 3) pain perception and 4) pain behavior. Recent advances in basic pain research have revealed the molecular mechanisms of nociception in the periphery and dorsal horn. To elucidate the mechanisms of pain perception in the brain and subsequent descending control of pain behavior is an urgent issue. It is well known that chronic stress and depression enhance pain perception and behavior.

We demonstrated that unilateral peripheral nerve injury in rats caused bilateral and systemic hyperalgesia, which was resistant to systemic morphine treatment but attenuated by amitriptyline or gabapentin. This model well reproduces the clinical features of neuropathic pain and suggests the involvement of the CNS in the maintenance of chronic pain state.

A variety of stressful stimuli affect pain sensitivity. We demonstrated that chronic restraint stress induced thermal hyperalgesia in rats, in which phosphorylated ERK in RVM neurons and levels of tryptophan hydroxylase were increased, indicating the activation of descending serotonergic system.

Patients suffering chronic pain of deep tissues, such as temporomandibular disorder, fibromyalgia, low back pain, often complain pain and tenderness in various body parts. We injected complete Freund's adjuvant into a temporomandibular joint unilaterally, and then injected diluted formalin into the ipsilateral or contralateral masseter muscle 2 weeks later. Pain-related behavior and neuronal activation in the spinal trigeminal nucleus were enhanced on both sides compared to those in controls. Systemic hyperalgesia induced by unilateral inflammation may have been caused by the central sensitization and descending facilitation.

S4-1 Somatic and psychological factors that regulate the body mass index of patients with anorexia nervosa and normal subjects

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The central nervous system sites that control food intake in animals are the hypothalamus and brainstem. In addition, higher cortical brain function such as cognition, emotion and reward, are assumed to have been added to these brain regions in humans. In anorexia nervosa (AN) patients, leptin, which has an appetite depression action, is decreased in blood and ghrelin, which has an appetite enhancing action, is increased. However, patients with AN are at low weight. We hypothesized that psychological factors are important in AN patients, in addition to the actions of substances such as leptin and ghrelin.

We examined factors that affect body mass index (BMI) using multiple linear regression analysis of both AN and normal subjects(N). The somatic factors analyzed were daily food intake, eating regulatory substances in blood (acylated ghrelin, desacyl ghrelin, leptin), serum cortisol, and insulin. The psychological factors analyzed were depression, anxiety, EDI (Eating disorder inventory), and hunger/fullness feeling. In N, BMI was related to leptin ($\beta=0.332$), body dissatisfaction ($\beta=0.746$), and drive for thinness ($\beta=0.597$). Psychological distress was high for N whose BMI was high. In AN, appetite may be regulated by maturity fears ($\beta=-0.375$) mainly, not eating regulatory substances. Psychological distress was high for AN whose BMI was low, the opposite of N.

In addition, we examined relationship between the influence of a hypnotic image in which eating a meal gave a feeling of fullness and electrogastrogram and the eating regulatory substances of normal subjects. The fullness feeling increased significantly, but no change in the eating regulatory substances or electrogastrogram was found during hypnosis. This suggested that the fullness feeling created by the image was caused by a mechanism that did not go through the ghrelin, leptin pathway of normal subjects.

We present an appetite regulation model for normal subjects and AN and discuss the differences.

S4-3 The animal model of eating disorders

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The patients of eating disorders are increasing in number. Some neurocircuits concerning about feeding behavior might cause dysfunction in these patients with repeated exposure of disorganized eating behavior like long lasting dieting. This neuronal, or endocrinological dysfunction might be enhanced even by the psychological stress. To understand the biological bases of eating disorders is necessary to establish the effective treatment. According to the clinical feature of the patients, we have conducted some rat studies. Some of our studies about feeding behavior will be shown;

1) the model of binge eating: We have found that space restriction stress enhanced rebound hyperphagia induced by the time restricted scheduled feeding, so that we proposed the phenomenon as possible rat model of binge eating. We can assume some part of biological bases of human eating disorders, and effective prevention and treatment through such animal models.

2) maternal separation and feeding behavior: Many patients with eating disorders particularly those with bulimia nervosa have reported that they were abused in childhood. Maternal separation is one of established models of stressful experience in childhood. Postnatal maternal separation enhanced rebound hyperphagia of only female rats in later life. Postnatal maternal separation made female rats more vulnerable to the development of abnormal feeding behavior in response to food restriction in later life.

3) effects of ghrelin on feeding behavior: Ghrelin, an endogenous ligand of the growth hormone secretagogue receptor, is an acylated 28-amino acid peptide hormone first identified in rat stomach. Ghrelin is released from the stomach to stimulate food intake by hunger, and have an orexigenic effect. Ghrelin is the first peptide isolated from animal sources in which the hydroxyl group of a serine residue (Ser-3) is acylated by n-octanoic acid. Des-acyl ghrelin is generally "inactive" with respect to ingestion and indicate that acylated ghrelin centrally promotes meal initiation and may mediate a subset of ingestive responses to extended energy insufficiency. Serine residue is critical for orexigenic characteristic of ghrelin. And vaccination includes Ser-3 against the endogenous hormone ghrelin can slow weight gain in rats by decreasing feed efficiency.

S4-2 Genetic study of Eating Disorders

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Eating disorders, such as anorexia nervosa (AN) and bulimia nervosa (BN), are characterized by severe alterations in eating behavior, body shape perception, and body weight regulation. Effective treatments for AN are few and, for many, the illness runs a chronic, relapsing course. The reported mortality rate is roughly 7%, the highest of any adolescent psychiatric or psychosomatic disease in Japan. Improved understanding of the pathophysiology of eating disorders will benefit attempts to develop effective treatment interventions: Genetic approaches comprise one critical step in achieving that goal.

The purpose of this paper is to present recent findings developed in a collaborative study by the Japanese Genetic Research Group For Eating Disorders (JGRED), which consists of more than 60 facilities. We examined the association of genes related to appetite and weight regulation with eating disorders and thus found that preproghrelin gene variants were associated with BN. We have also investigated eating disorder-related psychological, anthropometric, biochemical, and endocrine measures to determine their relationship with candidate gene variants in young healthy women. Interestingly, this preproghrelin gene variant was associated with a difference in basal blood ghrelin concentration, body mass index, percent body fat, and body dissatisfaction. Recently, we performed the first ever genome wide association study for AN using micro satellite markers, and identified 11 candidate susceptibility loci. Further narrowing of the susceptibility regions with SNP markers continues. This paper is an overview of the most promising recent genetic findings to identify possibilities for future research into eating disorders and to provide new insights into their biological mechanisms.

S4-4 Brain imaging on eating disorders

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There is a general consensus that the etiology of eating disorders is multi-determined, reflecting biological, psychological and social factors that interact in a complex fashion. CT and MRI have identified structural brain abnormalities in anorexia nervosa (AN). Recently, functional imaging techniques such as PET, SPECT, and fMRI have been used to identify specific areas of abnormal brain function in patients with eating disorders. In the present study, we used SPECT to evaluate rCBF changes in AN-R patients before and after weight gain compared with normal subjects. To reveal discrete and more localized rCBF changes, we applied SPM analysis to perfusion images obtained with SPECT. We investigated changes in rCBF before and after weight gain in patients with restrictive anorexia nervosa (AN-R) in comparison with findings in normal subjects. We assessed resting rCBF using single photon emission computed tomography with technetium-99m hexamethylpropylene amine oxime in 12 AN-R patients and 11 controls. Each patient was examined at two time points, at the beginning of treatment and after weight gain. Control subjects were examined only once. Before treatment, the AN-R group had lower rCBF in the bilateral anterior lobes, including the anterior cingulate cortex (ACC), and in the right parietal lobe, the insula, and the occipital lobes. After weight gain, the patients showed significant increases in the right parietal lobe and decreases in the basal ganglia and cerebellum in accordance with significant improvement in body weight and eating attitudes. However, they showed persistent decreases in the ACC area even after weight gain compared with findings in the controls. A significant positive correlation was observed between body mass index and rCBF in the occipital lobes in the patients. These results suggest that weight gain is associated with a normalization of rCBF in a number of brain areas, but that the low level of rCBF in the ACC at baseline is unaffected by treatment in AN-R.

S5-1 Functional genomics using *C. elegans* as a model organism○Shohei Mitani¹¹Department of Physiology, Tokyo Women's Medical University School of Medicine

The nematode *C. elegans* is a small model organism used for genetic analyses including neuronal development and function. Worms grow on agar dishes fed with *E. coli* as a food source. Detailed description of morphology and cell-lineage from the fertilized egg to the adult stage have been done. Neurites and synaptic structures have been reconstituted by electron microscopic serial sections. All the chemical and gap-junction synapses have been described so that neuronal circuits of the whole animal are diagrammed.

C. elegans is the first animal whose whole genome has been sequenced. The life cycle at 20 degree is for three days and convenient for genetic manipulation such as crossing. By use of this advantage, many mutants have been isolated in the past 30 years or so. Mutants isolated by phenotypes have been used for cloning causal genes by positional cloning techniques. Now, single nucleotide polymorphisms have been described between common wild-type strain (N2) and Hawaiian variant (CB4856) and useful to clone genes from mutants isolated by phenotypes, enabling the prompt link between phenotypes and gene functions. Because the whole genome has been sequenced, researchers have been trying to isolate knock-out mutants by reverse genetics, making systematic analyses possible. Roughly, about one fourth of the genes have been knocked out by this way. Because transgenic strains are easy to make, reporter expression and functional rescue experiments are routinely conducted.

C. elegans is the animal in which the phenomenon of RNA interference has been discovered. It is remarkably useful that researchers can knock down gene expression by feeding double-stranded RNA via *E. coli* as a food. Now, *E. coli* libraries expressing double stranded RNA by IPTG induction are available for most of the known genes. Although RNAi is sometimes ineffective to nervous tissues, researchers use RNAi-hypersensitive mutants as backgrounds, and combine deletion mutants to examine the gene function. We have developed a number of technologies for mutant isolation and transgenic analyses to see the function of nervous system to understand the mechanisms of diseases.

S5-3 Alpha-CaMKII deficiency causes dysregulated behaviors and immature dentate gyrus○Tsuyoshi Miyakawa^{1,2}¹Div. of Systems Medicine, ICMS, Fujita Health Univ. Toyoake, Japan ²Frontier Tech Ctr, Grad. Sch. Med., Kyoto Univ., Kyoto, Japan

Elucidating the neural and genetic factors underlying psychiatric illness is hampered by current methods of clinical diagnosis. The identification and investigation of clinical endophenotypes may be one solution, but represents a considerable challenge in human subjects. We found that mice heterozygous for a null mutation of the alpha-isoform of calcium/calmodulin-dependent protein kinase II (alpha-CaMKII^{-/-}) have profoundly dysregulated behaviours and impaired neuronal development in the dentate gyrus (DG). The behavioural abnormalities include a severe working memory deficit and an exaggerated infradian rhythm, which are similar to symptoms seen in bipolar disorder, schizophrenia and other psychiatric disorders. Transcriptome analysis of the hippocampus of these mutants revealed that the expression levels of more than 2000 genes were significantly changed. Strikingly, among the 20 most downregulated genes, 5 had highly selective expression in the DG. Whereas BrdU incorporated cells in the mutant mouse DG was increased by more than 50 percent, the number of mature neurons in the DG was dramatically decreased. Morphological and physiological features of the DG neurons in the mutants were strikingly similar to those of immature DG neurons in normal rodents. Statistical clustering of human post-mortem brains using 10 genes differentially-expressed in the mutant mice were used to classify individuals into two clusters, one of which contained 16 of 18 schizophrenic patients. Nearly half of the differentially-expressed probes in the schizophrenia-enriched cluster encoded genes that are involved in neurogenesis or in neuronal migration/maturation. Based on these results, we propose that an "immature DG" in adulthood might induce alterations in behaviour and serve as a promising candidate endophenotype of human psychiatric disorders.

S5-5 Potential of marmosets as animal models for mental and nervous disease○Katsuki Nakamura^{1,2}¹National Institute of Neuroscience, National Center of Neurology and Psychiatry ²CREST, JST, Saitama, Japan

To understand the mechanisms of mental and nervous disease and develop the cure for the disease, animal models are indispensable. We should develop good primate models for the disease since rodents have the central nervous and immune systems very different in the structure and function from those of humans. Common marmosets (*Callithrix jacchus*) are small-bodied New World monkeys. The body weight of adult marmoset ranges 300 to 450 g. They have a social structure that revolves a stable family unit. The group ranges in size from 3 to 15 individuals including one or two breeding females and one breeding male. The ovarian cycle lasts between 24 and 30 days, but averages 28 days. Gestation lasts about five months (143 to 153 days) and soon after parturition (within 10 days), female marmosets begin to cycle again and shortly thereafter become pregnant. The interbirth interval is about five months and they give birth twice each year. Common marmosets usually give birth to twins; they also have single births and triplets. Because of this high reproductive power, common marmoset is almost one primate species suitable for developmental engineering studies. One of the extraordinary social behaviors of common marmosets is their system of cooperative breeding and infant care. The breeding adults in the group depend on the cooperation of their adult siblings and offspring to care for their new infants to ensure their survival. Such group support for developing infants is necessary among common marmosets. Twins are often 20 to 27% of the mother's total body weight; this is the equivalent of a 50-kg woman giving birth to two 6-kg babies. In their life, they show various social activity including vocal communication, parental care, etc. We believe that the high reproductive power and social ability of common marmoset is of importance as animal models especially for mental and nervous disease. In this talk, I am going to introduce common marmosets and discuss the potential of common marmosets as animal models for mental and nervous disease.

S5-2 *Drosophila* homologs of schizophrenia-associated genes are required for long-term memory○Takaomi Sakai¹¹Department of Biological Sciences, Tokyo Metropolitan Univ.

One of the most fascinating and challenging goals in neuroscience is to understand the molecular and cellular mechanisms underlying memory formation. The fruit fly, *Drosophila melanogaster*, is an excellent model organism for investigating the genetic basis of memory formation. Courtship conditioning is an associative learning paradigm in *Drosophila*, where male courtship behavior is suppressed by experience with mated unreceptive females. Previously, I determined that a transcriptional factor, *dCREB2*, and a circadian clock gene, *period* (*per*), play a key role in long-term memory (LTM) formation induced by courtship conditioning. *dCREB2* regulates transcription of the *per* gene and both *dCREB2* and *per* are involved in the generation of circadian rhythm. However, mutations in other clock genes did not affect long-term memory, suggesting that *dCREB2*-mediated *per* expression is critically involved in memory processing independently of the core oscillator of circadian clock. Interestingly, it has been reported that human CREB, Per1 and Per3 are associated with schizophrenia. This suggests the intriguing possibility that schizophrenia-associated genes may be important in long-term memory formation. To examine this possibility, I focused on two *Drosophila* homologs of schizophrenia-associated genes, *Calcineurin B2* (*CanB2*) and *Chip*. *CanB2* encodes a regulatory subunit of calcineurin. Calcineurin is a Ca²⁺/calmodulin dependent serine/threonine protein phosphatase and affects animal behavior or neuronal plasticity. On the other hand, *Chip* encodes a LIM domain binding protein regulating synapse formation in *Drosophila*. I found that null or hypomorphic mutants of both genes are disrupted for long-term memory. However, their short-lasting memory was intact. These results suggest that a subset of schizophrenia-associated genes may be involved in mechanisms of neuronal plasticity underlying various processes including memory formation.

S5-4 Transient knockdown of DISC1 in the developing cerebral cortex leads to dopaminergic disturbance and schizophrenia-like deficits in young adult miceToshitaka Nabeshima^{1,2}, Minae Niwa^{1,2}, Rina Murai^{1,2}, Yukiohro Noda^{1,3}, Ken-ichiro Kubo⁴, Atsushi Kamiya⁵, Hanna Jaaro-Peled⁶, Kazunori Nakajima⁷, and Akira Sawa^{5,6,7}¹Department of Chemical Pharmacology, Meijo University Graduate School of Pharmaceutical Sciences, Nagoya, Japan. ²Department of Neuropsychopharmacology and Hospital Pharmacy, Nagoya University Graduate School of Medicine, Nagoya, Japan. ³Division of Clinical Science in Clinical Pharmacy Practice, Management, and Research, Faculty of Pharmacy, Meijo University, Nagoya, Japan. ⁴Department of Anatomy, Keio University School of Medicine, Tokyo, Japan. ⁵Department of Psychiatry and Behavioral Sciences, ⁶Department of Neuroscience, ⁷Graduate Program in Cellular and Molecular Medicine, Johns Hopkins University School of Medicine, 600 N Wolfe Street, Baltimore, MD, USA.

Neurodevelopmental disturbances have been suggested as a key etiology underlying schizophrenia (SZ) and depression, but it remains unclear why and how such disturbances with multiple genetic and environmental factors in early neurodevelopment lead to the disease onset in young adulthood, especially that characterized by aberrant dopaminergic neurotransmission. It is also unknown which specific cells have primary roles in the overall disturbance of brain networks in SZ. Here we report the generation of mice in which selective knockdown of DISC1 is achieved in a lineage for pyramidal neurons in the frontal cortex but only during the development via *in utero* gene transfer, which leads to maturation-dependent deficits in mesocortical dopaminergic projections and associated behavioral changes relevant to schizophrenia after puberty. This strategy that allows simultaneous manipulation of multiple factors during development in a temporally and spatially specific manner could be applied generally to exploring disease pathways for major mental illnesses with developmental origins.

Key words: Neurodevelopmental disturbances, schizophrenia, genetic and environmental factors, DISC1

S5-6 Neuronal signals in the primate medial frontal cortex and neuropsychiatric disorders○Munetaka Shidara¹¹Graduate School of Comprehensive Human Sciences, University of Tsukuba, Ibaraki, Japan

During our daily life, we continually compare our current status against our expectation for reaching our goal, with feelings of anticipation or anxiety as our expectancy increases. To search for related signals we have studied neuronal activities from anterior cingulate of the medial frontal cortex of monkeys. It has been reported that the anterior cingulate resides in the so-called basal ganglia-thalamocortical loop circuit, and has roles in performance monitoring, error detection, or motor selection based on reward. Recent functional imaging studies has reported abnormally strong activation of the anterior cingulate in patients of obsessive compulsive disorder and drug abuse, or decreased activity in depressive disorders. Because one of the key processes for these disorders is thought to be disturbance of evaluating the reward availability or expectancy, we have searched for the neuronal signals in the anterior cingulate by using monkeys performing a multitrial reward schedule task. In this task, monkeys must successfully complete 1 - 4 simple visual color discrimination trials to obtain a reward. We used two conditions, cued condition and random condition. In the cued condition, the schedule progress was indicated by the cue brightness. In the random condition, the cue sequence and reward sequence were randomized so that the monkeys could not know when they would be able to obtain the reward. Behavioral errors and reaction times decreased as the monkeys approached rewarded trials in the cued condition, and those were always small and fast in the random condition. In anterior cingulate, 1/3 of the neurons showed gradually increasing or decreasing activities through the schedule in the cued condition, suggesting the role in long-term reward expectancy. In the random condition, there were two types of responses; one type showed decreased responses in any schedule in the random condition, whereas the other type showed strong response in each trial. The latter type seems as if it responded to the possibility of reward availability. Another possibility is that the latter type always respond strongly because it cannot recognize the reward availability properly, which might be the link toward the neuronal responses in the mental disorders.

S6-1 Deficit of Theory of Mind in psychiatric disorders

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Theory of mind ToM is a term used by Premack and Woodruff in 1978 in their first report Does the chimpanzee have a theory of mind. The authors defined ToM as the attribution of mental states and the prediction of other peoples behaviour on the basis of their mental state such as, purpose, intention, belief, inference and inheritance. that is, self consciousness. According to Brune in 2003, however, the term is more often used to refer to the theory of other minds, so it should be defined as the ability to infer others mental states and predict their behaviour. Since Perner et al. asserted that the understanding of others false belief means explicit representation of the minds of other people than oneself. A false belief question depends on whether one understands that person A incorrectly believes that object X exists in location Y. This is the first order false belief. On the other hand, the second order false belief is that person B incorrectly believes that person A thinks that object X exists in location Y. The ability of human beings to understand such relationships forms ones self consciousness as perceived from the point of view of others, develops representation N order beliefs, and it is essential cognition in the complex human social system. The brain regions involved in social intelligence are called the social brain. The main parts of it involve the orbit frontal cortex, superior temporal gyrus, and amygdala. Using fMRI and PET, brain imaging studies of subjects performing ToM tasks have directly shown participation of the frontal cortex ToM, which originated from evolutionary and developmental psychology, may have grave consequences of possibly elucidating psychopathology. Baron Cohen in 1985 provided evidence for a ToM deficit in autistic children, possibly accounting for their inability to pretend and communication disturbance, using a well known experiment, Sally and Ann. The ToM deficit hypothesis has also been applied to schizophrenia and depression.

S6-3 Neurobehavioral basis of the impaired nurturing in mice lacking the immediate early gene FosB

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The transcription factor FosB is induced in neurons of the medial preoptic area (MPOA) during parenting, through activation of the extracellular signal-regulated kinase (ERK). FosB mutant (-/-) postpartum mice and virgin mice that are exposed to pups show defective nurturing behavior. The FosB (-/-) MPOA fails to fully up-regulate SPRY1 and Rad, the feedback regulators of ERK and calcium signaling, respectively. Here we studied FosB function by examining the gene expression profiles and the behavioral characteristics of FosB (-/-) mice. We found that FosB (-/-) mice exhibited not only decreased parenting but also decreased infanticide compared with (+/-) littermates. We then performed gene expression analysis in the MPOA of FosB (-/-) mice compared with the wild-type littermates. We found up-regulation of glial fibrillary acidic protein (GFAP), C4, and Elal mRNA in the MPOA of FosB (-/-) mice; all of these gene products were implicated in general neuropathological conditions. Immunohistochemical analysis showed that up-regulation of GFAP was not restricted to MPOA but extended throughout the forebrain, including the cerebral cortex and striatum. Such pervasive GFAP up-regulation suggested that FosB (-/-) mice might have other behavioral abnormalities than nurturing. Indeed, these mice showed a clear alteration in emotionality, detected by the acoustic startle, elevated plus maze, and passive avoidance tests. These results suggest that FosB (-/-) mice have broader neurobehavioral dysfunctions, with which the nurturing defect might share the common mechanism.

S6-2 Social recognition, oxytocin and CD38

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CD38, a transmembrane glycoprotein with ADP-ribosyl cyclase activity, catalyzes the formation of calcium signaling molecules, but its role in the neuroendocrine system is unknown. Here we show that adult CD38 knockout (CD38KO) * female and male mice show marked defects in maternal nurturing and social behavior, respectively, with higher locomotor activity. Consistently, the plasma level of oxytocin (OT), but not vasopressin, was strongly decreased in CD38KO mice. Replacement of OT by subcutaneous injection or lentiviral vector-mediated delivery of human CD38 in the hypothalamus rescued social memory and maternal care in CD38KO mice. Depolarization-induced OT secretion and calcium elevation in oxytocinergic neurohypophyseal axon terminals were disrupted in CD38KO mice; this was mimicked by CD38 metabolite antagonists in CD38KO mice. These results reveal that CD38 is a key element for neuropeptide release, thereby playing a critical role in maternal and social behaviors, and may be a novel seat in neurodevelopmental disorders. (* Jin et al., *Nature*, 446, 41-45, 2007)

S6-4 Genetic polymorphism as a background of animal behavior

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Various studies have shown the associations between differences in human behavioral traits and genetic polymorphism of neurotransmitter-related proteins: receptor, transporter and monoamine oxidase. To clarify the genetic background of animal behavior, we analyzed corresponding regions in animals, especially in primates as the evolutionally closest animal and in dogs as the socially closest one to humans. Among primate species, great apes such as chimpanzees and gorillas had similar sequence of dopamine receptor D4 and serotonin transporter as humans compared with monkeys. On the other hand, sequence of polymorphic regions in dopamine transporter and monoamine oxidase differed greatly, indicating that functional difference of these genes might affect human evolution. In dogs, more than 400 breeds selected for different purposes show breed-specific behavior traits. Allele frequency of dopamine receptor D4 differed greatly among breeds, and a group of breeds in which long alleles were frequent tended toward higher scores in aggression-related behavioral traits than that with frequent short alleles. Long alleles were frequent in wolves, the ancestor of dog. We further evaluated individual behavior traits in chimpanzees and drug detector dogs by cooperation of keepers and trainers, and found association between scores and genotypes. The genetic polymorphism was also found in cats, chickens as well as several wild animals, and analysis of relationship with their behavior is underway.

S6-5 Promotion of Neurogenesis and Alteration of Anxiety-related Behavior in Tryptophan 2,3-Dioxygenase (TDO) Knockout Mice

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The number of studies has indicated that tryptophan (Trp) levels are associated with mood and psychiatric symptoms. Tryptophan 2,3-dioxygenase (TDO) is the initial and rate-limiting enzyme for tryptophan (Trp) metabolism, which includes the biosynthesis of serotonin (5-HT) and thus thought to be implicated in neuropsychiatric diseases. Indeed, association of several mutations in TDO has been reported but their contribution has not been elucidated. Here we generated mice deficient for *tdo* (*Tdo*^{-/-}), and assessed the role of TDO in psychiatric symptoms, including anxiety-related behavior. *Tdo*^{-/-} mice showed increased levels of Trp, 5-hydroxy-indoleacetic acid (5-HIAA: 5-HT metabolite) in plasma and elevated levels of Trp, 5-HT and 5-HIAA in the brain without modulation of *tryptophan hydroxylase 2* (*th2*: tryptophan 5-monooxygenase) mRNA level and the activity of tryptophan hydroxylase (TPH). Therefore TDO plays dominant role in serotonin metabolism in the presence of TPH *in vivo*. Double labeling with BrdU and markers for neural progenitors and neurons showed enhanced neurogenesis in *Tdo*^{-/-} mice. Elevated plus maze and open field tests revealed that anxiety-related behavior is modulated in *Tdo*^{-/-} mice. Therefore, TDO plays an essential role in the regulation of systemic and brain Trp metabolite levels and contributes to mood functions. Considering that Trp and its metabolite 5-HT levels can be modulated by dietary Trp via TDO and TDO level is regulated by glucocorticoid via glucocorticoid response elements in *tdo* gene promoter and thus affected by stress and environments, TDO might be a molecular mechanism involved in social psychiatric symptoms modulated by a variety of conditions.

S6-6 Mother-child bio-communication: lessons from mice

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It is widely accepted that maternal condition is very influential to the development of fetus and baby. Up to date, there have been many studies on harmful aspects of the maternal factors. For example, malnutrition or habits of smoking and alcohol of the mother is known to affect the development of fetus. Compared with such toxic influences, little is studied on the beneficial effects of maternal factors. In particular, molecular basis for the positive influences remains elusive. Here, we propose a hypothesis that the maternal substances support the development of the fetal brain and subsequent expression and maintenance of the higher brain function in child. We note the fact that the size of fetal or baby head is relatively larger than the other parts of its body. This indicates a possibility that the fetus and baby need to develop the head first by some reason. Both intrinsic and extrinsic factors to the fetus and baby are likely involved in the selective development of the head. Accordingly, we aimed to identify the extrinsic maternal factors/substances that contribute to the selective development. To elucidate the maternal molecules, we first analyzed the gene expression in the mouse fetal brain by housing dam in various environments. As a result, we observed that the expression of some GPCR genes was changed in the fetus. Then, we confirmed that the endogenous ligand for a particular GPCR is less expressed in the fetal brain. Infusion of the ligand to dams led some behavioral changes in her pups. These results may suggest that maternal bioactive substances could influence the brain function of the pups even after birth. We also studied the genes other than GPCRs and obtained unexpected data to support a possibility that maternal trophic factors are essential to the development of the fetus. Related to this observation, we analyzed how the nutritious condition of the mother affects the pup development at molecular level. At my presentation, the data from these ongoing projects will be shown and discussed.

S7-1 Cell therapy for spinal cord injury using neural stem/progenitor cells derived from pluripotent stem cells.○Hideyuki Okano¹, Yohei Okada¹, Gentaro Kumagai^{1,2}, Masaya Nakamura²¹Department of Physiology, Keio University School of Medicine, Tokyo, Japan²Department of Orthopaedic Surgery, Keio University School of Medicine, Japan.

Neural stem/progenitor cells (NS/PCs) are tissue stem cells that can generate a variety of neural cells and show promise for cell replacement therapy to treat various intractable central nervous system (CNS) disorders, such as Parkinson's disease, Huntington's disease and spinal cord injury (SCI). However, although previous studies demonstrated that transplanted NS/PCs differentiated into neuron, astrocyte, and oligodendrocyte and promoted functional recovery after SCI, there is still an important problem to be resolved about the differentiation potential and survival rate play a role in functional recovery after transplantation. To address this issue, we took advantage of our original *in vitro* differentiation of embryonic stem (ES) cells. We newly developed a novel *in vitro* model which allows precise and complete four-dimensional recapitulation of CNS development by taking advantage of ES cell-derived neurospheres. This method enables efficient derivation of highly neurogenic FGF-responsive NS/PCs with early temporal identities and high plasticities, which are subsequently specified to be EGF-responsive and more gliogenic during repeated passages. Here, we cultured mouse embryonic stem cell (ES) cell-derived neurogenic primary neurosphere (ES-PNS) and gliogenic secondary neurosphere (ES-SNS) *in vitro* and transplanted them into the injured spinal cord of mice. PNS- and SNS-derived cells 10-20 percent survived similarly without tumor formation and differentiated with the properties of *in vitro*. Surprisingly, transplantation of gliogenic ES-SNS, but not neurogenic ES-PNS, promoted axonal growth, remyelination, angiogenesis, and functional recovery after SCI. These findings suggested that injured spinal cord required gliogenic ES-derived neurospheres for functional recovery and gave an important cue for the establishment of the regenerative medicine for SCI using ES or induced pluripotent stem cells (iPS cells) in the near future.

S7-3 A inhibitory mechanism of neuronal differentiation mediated by BMP-induced REST/NRSFJun Kohyama¹, Eriko Takatsuka¹, Tsukasa Sanosaka¹, Akinori Tokunaga², Hideyuki Okano², ○Kinichi Nakashima¹¹Lab. Mol. Neurosci. Grad. Sch. Biol. Sci. NAIST ²Dept. Physiol. Sch. Med. Keio Univ.

Once they have differentiated, cells retain their individual character and repress genes that are specifically expressed in other cell lineages, how alternative fate choice is restricted during and/or after differentiation remains unclear. In the mammalian central nervous system (CNS), neurons, astrocytes and oligodendrocytes are generated from common tripotent neural progenitor cells (NPCs) throughout life. Bone morphogenetic proteins (BMPs) are well-known astrocyte-inducing cytokines. We show here that the expression of a transcriptional repressor, RE1 silencer of transcription (REST)/neuron-restrictive silencer factor (NRSF), is upregulated and sustained by BMP-signaling activation in the course of astrocytic differentiation of NPCs, and restricts neuronal differentiation. Expression of REST/NRSF alone was sufficient to repress neuronal differentiation, and a dominant negative form of REST/NRSF counteracted BMP2-mediated suppression of neurogenesis of NPCs. We further show that, in differentiated astrocytes, endogenous REST/NRSF associates with various neuronal genes and that disruption of its function resulted in their de-repression, thereby explaining how ectopic neuronal gene expression is prevented in cells with astrocytic traits. Taken together, our results identify REST/NRSF as a candidate molecular regulator of cellular plasticity in astrocytes.

S7-5 The stem cell therapy as a possible new treatment for psychiatric disorders○Wataru Ukai¹, Toshihiro Yoshinaga¹, Takao Ishii², Eri Hashimoto¹, Takafumi Ono¹, Masaru Tateno¹, Kimihiko Watanabe¹, Ippei Watanabe¹, Tomohiro Sirasaka¹, Yuka Mukai¹, Satoshi Saito¹, Toshikazu Saito¹¹Dept of Neuropsychiatry Sapporo Medical Univ, Sapporo ²Dept of Occupational Therapy, Sapporo Medical Univ, Sapporo

Recently, it has been elucidated that cerebral morphological change is the key mechanism of various clinical conditions of psychiatric disorders. The neurogenic and neurotrophic effects of psychotropics are considered to contribute to the prevention of reduction in brain volume. However, the precise mechanism and the way for suppression of brain morphological change have not yet cleared.

In the previous study, we have reported the relations of deficits of neural network to the psychiatric disorders such as depression, schizophrenia, and alcohol-induced brain damage. We also demonstrated the behavioral recovery of alcohol-induced brain damage and schizophrenia model rats by the NSCs transplantation, which is one of the promising new treatment strategies for treatment-resistant psychiatric disorders. We revealed that intravenously administered NSCs were detected in the damaged brain area by visualizing a fluorescent marker. We also showed that NSC transplantation ameliorated behavioral abnormalities of these model rats.

In the present study, we analyzed the differentiation of transplanted NSCs to each phenotype of cells by immunofluorescence assay. We found that transplanted NSCs had the potential to differentiate to neurons and glia. The ratio of differentiation to neurons or glia varied in different brain regions. Furthermore, we also investigated the maturation of neurons differentiated from transplanted NSCs. Furthermore, we investigated the effect of exogenous NSCs on the neuronal survival and NSC differentiation *in vitro*, and suggested the trophic factor signaling change in neurons and NSCs without cell-cell contact, which may be suggested a mechanism of contribution to the neural network repair by the NSC transplantation *in vivo*.

These results may suggest that the NSC transplantation may be a possible approach to recover the brain damage of neuronal network and CNS dysfunction in psychiatric disorders, and the intravenously transplanted NSC could contribute to the neural network repair through the functional cells and trophic effects in the brain.

S7-2 Migration of new neurons in the adult brain○Kazunobu Sawamoto¹¹Department of Developmental and Regenerative Biology, Institute of Molecular Medicine, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan

Neurons continue to be born in the subventricular zone (SVZ) of the lateral ventricles of adult animals including rodents and primates. Newborn neurons migrate through a complex network of chains within the SVZ and the rostral migratory stream (RMS) into the olfactory bulb (OB). In the OB, the new neurons differentiate into granule and periglomerular neurons. In this symposium, I will present how these new neurons migrate in normal and injured adult brain. In the SVZ the migration of these new neurons parallels the flow of cerebrospinal fluid (CSF) in the ventricle. Our data suggest that the beating of the cilia on the ependymal cells is required for directional CSF flow, the formation of chemorepulsive factors and the rostral migration of neurons. More recent study indicates that the long-distance, directional migration of neurons depends on the function of cdk5. We will also present our work on the regeneration potential of SVZ cells after stroke. Using a mouse model of middle cerebral artery occlusion in combination with cre-loxP-based cell tracing methods, we found that SVZ-derived new neurons migrate towards the damaged brain tissue along the blood vessels and regenerate mature striatal neurons in the ischemic striatum. These results highlight the role of the SVZ in neuronal regeneration and its potential as an important therapeutic target for treating various neurological diseases.

S7-4 NG2 cells: A therapeutic target for psychiatric disorders?

○Yoshitaka Tatebayashi

Depression project, Mood disorder research team, Tokyo Institute of Psychiatry

NG2 proteoglycan-expressing cells (NG2 cells) persist during central nervous system (CNS) development, and are the largest proliferating cell population throughout the adult CNS. Although NG2 cells are believed to be precursors of oligodendrocytes, they may also play roles in gliogenesis (or gliosis), neurogenesis as well as in synaptic signaling. In this symposium, I will show some evidence indicating that certain abnormalities exist in NG2 cell populations in the brains of psychiatric disorders. One of the most predictable consequences from these abnormalities may be deficits in glutamatergic and GABAergic signalings probably modulated by these cells. I will also show some *in vitro* evidence obtained from cultured adult rat NG2 cells indicating that these cells play important roles in glutamatergic pathways.

S7-6 Neural stem cells in the adult brain: implications for the pathogenesis of mood affective disorders○Seiji Hitoshi¹¹National Institute for Physiological Sciences

Neural stem cells (NSCs) have attracted considerable attention as a potential source of cells for therapeutic treatment of impaired areas of the central nervous system. However, efficient and clinically feasible strategies for expansion of the endogenous NSC pool are currently unavailable. We have recently demonstrated that mood stabilizing drugs, which are used to treat patients with bipolar disorder, enhance the self-renewal capability of mouse NSCs *in vitro* and that this enhancement is achieved at therapeutically relevant concentrations in the cerebrospinal fluid. The pharmacological effects are mediated by the activation of Notch signaling in the NSC. Treatment with mood stabilizers increased an active form of Notch receptor and upregulated its target genes in neural stem/progenitor cells, whereas co-culture with γ -secretase inhibitor or the presence of mutation in the presenilin1 gene blocked the effects of mood stabilizers. In addition, chronic administration of mood stabilizers expanded the NSC pool in the adult brain, which subsequently increased the cell supply to the olfactory bulb. We suggest that treatment with mood stabilizing drugs could be used to facilitate regeneration following insult to the central nervous system. I will discuss the possible link between adult neurogenesis and mood affective disorders based on the results of this study and our recent work, in which we showed that NSCs in the adult mouse brain were decreased after chronic stress and recovered by antidepressant treatment.

S8-1 Amyloid beta42 generating process has a physiological role in regulating Notch signaling intensity.

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Presenilin (PS) / γ -secretase degrade transmembrane domains (TM) of more than thirty proteins. Among them, β APP and Notch are considered to be important substrates because PS/ γ -secretase generates Alzheimer disease (AD)-associated amyloid-beta (A β) from β APP TM and Notch intracellular domain (NICD), an essential transcriptional factor for Notch signaling from Notch TM. An unusual characteristic of the proteolysis is that some of the cleavage sites can vary. γ -Cleavage of β APP occurs mainly at residue 40, producing A β 40, and at residue 42, producing A β 42. A small increase in the proportion of A β 42 to A β 40 is consistently observed in many familial AD-associated PS or β APP mutants. Therefore, changes in the precision of PS/ γ -secretase have a pathological importance. However, it is unclear whether such changes in the precision of PS/ γ -secretase have any biological effects. Recently, we found that S3 cleavage mediated by PS/ γ -secretase has diversity, resulting in the production of two types of NICD (NICD-S and NICD-V) with apparently distinct ability to transmit Notch signaling. We also showed that the precision of S3 cleavage can be modulated by physiological factors, which affects the intensity of Notch signaling. Taking advantage of the novel process, we tried to find conventional methods to either up- or down-regulate Notch signaling. These methods may rescue conditions in which Notch signaling is abnormally down-regulated, for example, side effects of γ -secretase inhibitors.

S8-3 Fibrillar or nonfibrillar A β ? A causal molecule for Alzheimer's disease

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Based on experimental models, soluble A β oligomers have been proposed to initiate synaptic and cognitive dysfunction in Alzheimer's disease (AD). However, there is no direct evidence in humans that this mechanism can cause AD. We identified a new type of APP mutation that lacks codon 693 (GAA) encoding glutamate-22 in the A β sequence in several Japanese pedigrees showing AD. While the secretion of total A β from cells was markedly reduced by this mutation, the mutant A β E22 Δ peptide was more resistant to degradation by neprilysin and insulin-degrading enzyme. The A β E22 Δ peptide showed a unique aggregation property of enhanced oligomerization but no fibrillization. When injected into rat cerebral ventricle (10 ng peptide/2 μ l/rat), the A β 42 E22 Δ peptide inhibited hippocampal long-term potentiation more potently than wild-type A β 42 peptide *in vivo*. In the MTT assay, wild-type A β 42 peptide showed a dose-dependent (1 nM to 1 μ M) cytotoxicity to cultured neuronal cells, whereas A β 42 E22 Δ peptide was toxic only at 1 μ M. In mouse hippocampal slices, however, A β 42 E22 Δ peptide caused a dose-dependent (0.1-10 μ M) decrease of synaptophysin, whereas wild-type A β 42 peptide was trophic at 0.1-1 μ M and toxic at 10 μ M. Thus, extracellular A β E22 Δ was shown to induce more potent synaptic dysfunction and alteration, but lower neurodegeneration, than wild-type A β probably due to its unique aggregation property. Consistent with the non-fibrillogenic property of the mutant A β , very low amyloid signal was observed in the patient's brain on positron emission tomography using Pittsburgh compound-B. These results suggest that the E693 Δ mutation causes disease by enhanced formation of synaptotoxic A β oligomers in the absence of fibril formation. Our findings may provide genetic validation in humans for the A β oligomer hypothesis.

S8-5 Involvement of tau protein in neurodegeneration

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Neurofibrillary tangles are neuropathological hallmarks of Alzheimer disease (AD) and other tauopathies including frontotemporal dementia (FTD) and corticobasal degeneration, and abnormally hyperphosphorylated tau protein is the major protein component of NFT. After finding of tau gene on chromosome 17 as a causative gene for familial FTD (FTDP-17), tau is thought to be essentially important for understanding of neurodegenerative processes in dementia. In brain of tauopathies tau is hyperphosphorylated and ubiquitinated, and self-assembles and forms filaments or aggregates, however the mechanisms of the involvement of tau in neurodegeneration are unclear.

To understand the mechanisms of self-assembly of tau, we investigated the effects of phosphorylation of tau on the process self-assembly induced by 14-3-3. Phosphorylation of tau by protein kinase A (PKA) or protein kinase B (PKB), not glycogen synthase kinase-3, enhanced the binding of tau with 14-3-3, however PKA- or PKB-phosphorylation abolished the self-assembly of tau protein. And we investigated the effects of FTDP-17 mutations of tau on the process self-assembly induced by 14-3-3. The mutant tau (P301L, V337M and R406W) had higher affinity with 14-3-3 than wild type tau, and P301L tau induced the highest self-assembly level than others in the presence of 14-3-3. Our results suggest that phosphorylation and mutations of tau might play an important role in self-assembly of tau and its involvement in the neurodegenerative processes will be discussed.

S8-2 Presenilin complex and γ -secretase activity

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γ -Secretase mediates intramembrane cleavage of type I transmembrane proteins such as amyloid β precursor protein (APP) and Notch receptor. Proteolytic processing of APP yields neurotoxic amyloid β (A β) peptides in Alzheimer's brains, whereas γ -cleavage of Notch releases the intracellular domain that is critical for the signal transduction. Presenilin-1 (PS1) and presenilin-2 (PS2) assemble with nicastrin, APH-1 and PEN-2 to form active γ -secretase complexes. These proteins are considered as core components, although additional proteins might bind with the complexes to modify the catalytic activity. Recently, it has been reported that Drosophila transmembrane protein Crumbs negatively regulates Notch signaling. Among mammalian homologues of Crumbs, CRB2 is expressed in the brain at a higher level. We investigated a modulatory role of CRB2 on γ -secretase cleavage of APP. When overexpressed in APP-expressing HEK293 cells, CRB2 suppressed secretion of A β peptides. CRB2 knock-down caused increased secretion of A β from SH-SY5Y neuroblastoma cells. Analysis using the truncation mutants indicated that the N-terminal extracellular domain of CRB2 is dispensable for inhibition of γ -secretase cleavage. Co-immunoprecipitation study suggested that CRB2 binds with PS1. Furthermore, using HEK293 cells expressing affinity tag-fused PEN-2, we have searched for proteins that interact with γ -secretase complexes. Purified complexes were separated by SDS-PAGE, and peptides from several bands were analyzed with LC-MS/MS. By this screening, we identified a membrane protein that bound with the complex. Overexpression of this protein suppressed A β secretion and increased accumulation level of immature APP, whereas the knockdown increased A β secretion as well as amount of APP-CTFs. These results suggest that there are multiple proteins involved in the regulation of γ -secretase activity.

S8-4 Molecular mechanism underlying A β assembly

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One of the fundamental questions regarding the pathogenesis of Alzheimer's disease (AD) is how the monomeric, nontoxic amyloid β -protein (A β) is converted to its toxic assemblies in the brain. We previously identified a unique A β species in an AD brain, which is characterized by its binding to the GM1 ganglioside (GM1). On the basis of the molecular characteristics of this GM1-bound A β (GA β), it was hypothesized that A β adopts an altered conformation through its binding to GM1, and GA β acts as a seed for A β fibrillogenesis in an AD brain. We have confirmed the GA β generation in AD brains and aged monkey brains using a novel monoclonal antibody specific to GA β . Furthermore, we have recently provided evidence that A β assembly initially occurs through GA β generation at presynaptic terminals following interaction with GM1-ganglioside-enriched membrane microdomains. Taken together with a previous study of other group, showing that the level of GM1 ganglioside increased in synaptosomes prepared from AD brains, our results suggest that accumulation of GM1 ganglioside at presynaptic terminal is a background to A β deposition in AD brain. In the symposium, significance of GM1 ganglioside in the pathogenesis of AD will be discussed.

S8-6 Brain aging and Alzheimer's disease

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Neurofibrillary tangles (NFTs), composed of hyperphosphorylated tau, are commonly observed pathological change in brain aging and Alzheimer disease (AD). Because NFTs reflect intraneuronal changes and because the amount of NFTs correlates with the progression of dementia, the mechanism underlying NFT formation represents a factor contributing to the memory impairment and dementia seen in brain aging and AD. During normal aging, NFTs first appear in the entorhinal cortex. As dementia progresses, however, NFTs begin to appear in neocortical and limbic areas, including the hippocampus. Individuals with NFTs in limbic regions show learning and memory difficulties. Moreover, the presence of NFTs in neocortex correlates with more severe levels of dementia (Braak and Braak, *Acta Neurol.* 165, 3-12 (1996)). Interestingly, Braak and Braak found that, in the entorhinal cortex, NFT formation is independent of A β deposition; in limbic and neocortical areas, however, NFT formation occurs only after A β deposition. Their analysis suggests that NFTs in entorhinal cortex may develop during the course of normal brain aging, only developing into limbic and neocortical areas under the AD disease state. That is, the chronology of pathological changes appears to start with NFTs developing in entorhinal cortex in the absence of A β and continues with A β deposition, which then triggers the appearance of NFTs into limbic and neocortical areas. This hypothesis implies that brain aging is characterized by NFT development in the entorhinal cortex, that the rate of brain aging is the determining factor for onset age of AD, and that A β can accelerate brain aging, resulting in AD. In this symposium, I am discussing how aging induce NFTs, and memory impairment.

S9-1 Large-scale genetic association study of schizophrenia○Tadao Arimami¹, Hiroki Ishiguro¹, Minoru Koga^{1,2}, Yasue Horiuchi¹¹Dept. of Med. Genet., Inst. Med. Sci., Uni. of Tsukuba, Tsukuba, Japan ²CREST, Japan Science and Technology Agency, Kawaguchi-shi, Japan

Genetic susceptibility genes for schizophrenia serve as rare but strong risk factors or as common but weak risk factors for its development. Dozens of risk genes of the latter group are already known and genome-wide studies (GWAS) with single nucleotide polymorphisms (SNPs), which is suitable for identifying the latter group of genes, are adding lists of risk genes for schizophrenia. On the other hand, some regions with sparse SNPs in the HapMap database may elude GWAS. Traditional candidate gene approach is still valuable, though a large sample size is crucial for candidate gene as well as genome-wide approach. Our genome-wide screening with SNPs also highlighted some genes and approximately half of them were genes that had been already reported to be associated with schizophrenia. One of the novel genes identified as associated with schizophrenia encodes a protein that plays a role in chromatin remodeling. The risk allele was indicated to impair localization in cell nuclei of the protein and reducing its gene expression significantly correlated with the direction of changes in gene expression reported in schizophrenia postmortem brains. Treatment with methamphetamine reduced and haloperidol increased the gene expression in mouse brains. Thus, some genetic risk factors may be involved in the susceptibility to schizophrenia through epigenetic mechanisms. We will also report a novel risk gene identified by candidate approaches.

S9-3 Genomic and animal model approaches to risk genes for schizophrenia○Yasuyuki Fukumaki¹¹Medical Institute of Bioregulation, Kyushu Univ., Fukuoka, Japan

Schizophrenia is a devastating neuropsychiatric disorder with a multifactorial background. To search for risk genes for schizophrenia, we have been taking three approaches as follows. I) Genome-wide approach: We conducted the case-control study using about 30,000 STR markers distributed across the entire genome. To overcome the type I error due to multiple tests, we planned three sequential steps of screening using independent pooling sample sets. After the three screening steps, 352 markers showed significant associations. Fifty-nine of them were selected for SNP typing through evaluation of reproducibility of associated alleles for each marker. Tag SNPs in the vicinity of about 200 kb from each positive marker were used for the case-control study of combined samples. Confirmatory association study for the positive SNPs using independent samples of more than 2,400 pairs showed that the significant association was replicated for one SNP. II) Candidate gene approach: Since schizophrenia-like symptoms are produced by administration of phencyclidine (PCP), a noncompetitive antagonist of N-methyl-D-aspartate (NMDA) receptors, we searched for PCP responsible genes using brain samples of rats treated with PCP as candidates for risk genes. We have successfully identified ten genes of which expression was altered at least two folds using the microarray technique followed by quantitative evaluation by real time PCR. To date six of them have been analyzed by the case-control association procedure. Haplotypes of two genes showed significant association with the disorder. III) Model animal approach: We have previously reported significant association of *GRIA4* which encodes AMPA4 glutamate receptor, GluR4, with the disorder in a systematic study of associations of glutamate receptor gene family members with schizophrenia. To evaluate functional roles of *GRIA4* in pathogenesis of schizophrenia we produced knockout mice of GluR4 and conducted behavioral analyses using 6th-generation backcross progenies. Homozygous mutant mice showed impaired prepulse inhibition (PPI) and accentuated response to MK801 in the open field test, suggesting involvement of this gene in generating schizophrenia endophenotypes. Combination of genomic and animal model approaches would elucidate risk genes for schizophrenia.

S9-5 Risk Genes for Dementia○Takashi Morihara¹, Kouzin Kamino², Ryo Kimura³, Eiichiro Kamagata¹, Noriyuki Hayashi¹, Masahiko Takaya¹, Mikiko Yokokoji¹, Hiromasa Tokunaga¹, Hiroaki Kazui¹, Toshihisa Tanaka¹, Takashi Kudo¹, Masatoshi Takeda¹¹Department of Psychiatry Osaka University Graduate School of Medicine, Tokyo, Japan ²Shoraiso National Hospital, Koriyama, Japan ³Osaka Prefectural Hospital Organization, Osaka, Japan

Alzheimer disease (AD) is most common form of dementia. In developed countries the prevalence of AD is estimated at 3-10% in 65-years-olds and expected to double every decade thereafter. After age, family history is the second greatest risk factor for AD. Genetic studies have been dramatically accelerated AD research, not only for the understanding of the disease but also the development of treatment and diagnosis. Genetic analysis showed that amyloid precursor protein (APP), presenilin1 and 2 mutations cause familial AD. Most of these mutations increase the production of Aβ42 protein and result in typical AD phenotype except earlier age of onset. These facts have greatly helped to understand the mechanisms of AD including sporadic cases, an extremely complex disease, and have been the major evidence to support "amyloid cascade hypothesis". New treatments and diagnosis methods based on this hypothesis are currently in clinical trials. The majority of AD cases occur sporadically. ε4 allele of the Apolipoprotein E (ApoE) which is closely connected to lipid metabolism is the strong genetic risk factor for late onset AD. More than 500 genes have been examined as AD risk candidate genes and 10 or more AD association studies are being published monthly. No gene except ApoE, however, has been established as AD risk gene so far, because of poor replications. In this presentation, expanding genetic information will be overviewed and new approach will be mentioned.

S9-2 Risk genes for panic disorder: a GWAS study○Hisashi Tani¹, Tsukasa Sasaki², Takeshi Otowa³, Tadaaki Kato⁴, Takeo Yoshikawa⁵, Tadao Arimami⁶, Hiroshi Kunugi⁷, Toshiyuki Someya⁸, Naomichi Matsumoto⁹, Hisanobu Kaiya¹⁰, Yuji Okazaki¹¹¹Department of Psychiatry, Mie University Graduate School of Medicine, Mie, Japan ²Health Service Center, University of Tokyo, Tokyo, Japan ³Department of Neuropsychiatry, Graduate School of Medicine, University of Tokyo, Tokyo, Japan ⁴Laboratory for Molecular Dynamics of Mental Disorders, RIKEN Brain Science Institute, Saitama, Japan ⁵Laboratory for Molecular Psychiatry, RIKEN Brain Science Institute, Saitama, Japan ⁶Department of Medical Genetics, University of Tsukuba, Tsukuba, Japan ⁷Department of Mental Disorder Research, National Center of Neurology and Psychiatry, Tokyo, Japan ⁸Department of Psychiatry, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan ⁹Department of Human Genetics, Yokohama City University Graduate School of Medicine, Yokohama, Japan ¹⁰Warakukai Incorporated Medical Institution, Tokyo, Japan ¹¹Tokyo Metropolitan Matsuzawa Hospital

Twin and family studies have provided evidence that genetic factors play a significant role in the development of panic disorder (PD). The authors are collecting DNA samples of PD in the Japanese population and conducting genome-wide association study (GWAS). More than eight hundred DNA samples of Japanese PD have been collected at the outpatient clinics specializing in anxiety disorders in Tokyo and Nagoya, Japan. The diagnosis was confirmed at the interview using the MINI (Mini-International Neuropsychiatric Interview) and by reviewing the clinical charts. Genotyping of 500,568 SNPs was conducted in the first sample consisting of 200 PD patients and the same number of the healthy controls, using the GeneChip Human Mapping 500K Array Set (Affymetrix). The genotyping calls were analyzed employing the BRLMM algorithm in the SNPs on autosomal chromosomes (n=490,032). The results were filtered by parameters including call rate (>95%), minor allele frequency (>1%) and Hardy-Weinberg Equilibrium (>0.1%), which selected 275,329 SNPs. Among the SNPs, significant difference of p < 0.00001 in the allele frequency was observed between patients and controls in 42 SNPs. We are going to analyze the 42 SNPs in the second sample consisting of 550 PD patients and the same number of the controls, using the DigiTag2 assay system. The result will be discussed at the presentation.

S9-4 A genetic study on schizophrenia started from a rare case.○Masanari Itokawa^{1,2,3}¹Schizophrenia Research Team, Tokyo Institute of Psychiatry, Tokyo ²Lab. for Molecular Psychiatry, BSI, RIKEN ³Dep. Psychiatry, Tokyo Metropolitan Matsuzawa Hospital

The prevalence of schizophrenia, a common and complex mental disorder, is approximately 1% world wide and appears unrelated to race, gender, and economic conditions. A meta-analysis of twin studies estimated the heritability of schizophrenia to approximately 80%, suggesting relative high involvement of genetic factors on developing the disease. Prominent progress of the genetic researches has not been recognized as huge amount of the genetic data are conflicting each other although intensive genetic studies have been performing since early nineties. One of the reasons for the complication in schizophrenia genetics is that the illness is a heterogeneous disorder. Recent research trend is expanding sample size to detect a small-effect common variant but increasing heterogeneous samples makes us harder to detect each variation among individuals having different genetic factors. We have been trying to detect a large-effect rare mutation based upon common disease-rare variant hypothesis, not common disease-common variant. We found a disrupted gene by a chromosomal translocation of a male with schizophrenia. The gene might contribute to neural development. A case-control association study revealed that the gene was associated with schizophrenia. We detected a rare frameshift mutation in a stress-related gene, which is an essential component for cellular metabolisms. The patient showed a 40 to 50% reduction in enzymatic activity. Seven homozygotes of missense mutation, who all suffered from schizophrenia, were also identified by resequencing using 2,000 individuals including 1,000 schizophrenia. Their enzymatic activities were reduced by approximately 20 to 30%. All schizophrenic subjects having decreased enzymatic activities showed elevated levels of plasma metabolized products.

S9-6 Genes for fatty-acid binding proteins and functional psychoses○Takeo Yoshikawa¹¹Lab. for Molecular Psychiatry, RIKEN Brain Science Institute

Prepulse inhibition (PPI) is the normal suppression of a startle response when a low intensity stimulus eliciting little or no behavioral response, immediately precedes an unexpected stronger startling stimulus. Biologically, PPI is a reflection of sensory motor gating mechanisms within the central nervous system and deficits within these mechanisms are a consistent feature of neuropsychiatric illnesses including schizophrenia. As a reproducible phenotypic marker, impaired PPI is regarded as an endophenotype for schizophrenia. It is hoped that identifying genes that underpin PPI could help in deciphering the complex polygenic mechanisms that predispose to schizophrenia. To map the genetic loci determining PPI and its related behavioral profiles, we performed large-scale quantitative trait loci (QTL) analysis using selected inbred mouse strains. QTL analysis is a method of localizing chromosomal regions harboring genetic variants that affect a continuously distributed, polygenic phenotype. By analyzing 1010 F2 mice derived by crossing C57BL/6 (B6) animals that show high PPI with C3H/He (C3) animals that show low PPI, we detected 6 major loci for PPI. 6 for the acoustic startle response and 4 for latency to response peak, some of which were sex-dependent. A promising candidate on the chromosome 10-QTL was Fabp7 (fatty acid binding protein 7, brain), a gene with functional links to the NMDA receptor and expression in astrocytes. Fabp7-deficient mice showed decreased PPI and a shortened startle response latency, typical of the QTLs proposed effects. A quantitative complementation test supported Fabp7 as a potential PPI-QTL gene, particularly in male mice. Disruption of Fabp7 attenuated neurogenesis in vivo. Human FABP7 showed altered expression in schizophrenic brains and genetic association with schizophrenia, both of which were evident in males when samples were divided by sex. These results suggest that FABP7 plays a novel and crucial role, linking the NMDA, neurodevelopmental and glial theories of schizophrenia pathology and the PPI endophenotype, with larger or overt effects in males. We are now extending our study by examining other FABP genes that are expressed in the brain, using the samples from not only schizophrenia but also bipolar disorder.

S10-1 Diversity of ER stress response in neurons and astrocytes

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The endoplasmic reticulum (ER) is susceptible to various stresses that provoke the accumulation of unfolded proteins in the ER. Excessive or long-termed stresses in the ER result in apoptotic cell death. Eukaryotic cells can adapt for survival to deal with an accumulation of unfolded proteins in the ER by increasing transcription of genes encoding ER-resident chaperones such as GRP78/BiP to facilitate protein folding. The induction system is termed the unfolded protein response (UPR). Cell fate after ER stress is determined by the balance of both apoptosis and the UPR signaling. Recently, we identified a novel ER stress sensor, OASIS, which is specifically expressed in astrocytes. This protein is a transmembrane protein containing bZIP domain. The functional analyses of OASIS showed that 1) it was cleaved within the ER membrane in response to the ER stress. 2) overexpression of OASIS induced the transcription of GRP78/BiP mRNA through the activation of cyclic AMP responsive element and ER stress responsive element, 3) its stable cell lines were resistant to ER stress compared with the control cells. These results indicate that the ER-resident transcription factor OASIS may be a candidate for leading astrocytes to protect against ER stress. In addition, we found that BBF2H7, structurally homologous to OASIS, is markedly induced in neurons exposed to brain ischemia. Treatment with siRNA of BBF2H7 promoted ER stress-induced neuronal death. Taken together, our results suggest that BBF2H7 is a novel ER stress sensor and could play important roles in preventing accumulation of unfolded proteins in damaged neurons.

S10-3 ER dysfunction induced by nitric oxide

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Protein quality control functions as a pivotal system of cell homeostasis. Particularly, misfolded proteins are degraded by the ER-associated degradation (ERAD) system via ubiquitin-proteasome pathway. We have demonstrated that protein-disulfide isomerase (PDI), a thioredoxin-related ER chaperone, is S-nitrosylated in cells by treatment with NO/glutamate, and this modification was also found in brains manifesting sporadic Parkinson's or Alzheimer's disease. NO-induced S-nitrosylation of PDI attenuated the enzymatic chaperone and isomerase activities, led to accumulation of poly-ubiquitinated unfolded proteins, and consequently induced the unfolded protein response (UPR) in neurons. Thus, S-nitrosylation might contribute to the ER dysfunction via abrogation of PDI activity which is involved in protein maturation. In this symposium, we will discuss other NO targets involved in the neuronal death.

S10-2 ER stress response and neuronal cell death in the substantia nigra

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Parkinsons disease (PD) is a common neurodegenerative disease characterized pathologically by the loss of dopaminergic neurons and the presence of Lewy bodies (LB), an intraneuronal protein aggregates, in the substantia nigra pars compacta (SNpc). Accumulating evidence suggests that increased levels of oxidative stress, dysfunctions of the mitochondria and ubiquitin-proteasome system (UPS) are key players in the pathogenesis of PD. Recent studies, however, have raised the possibility that the endoplasmic reticulum (ER) also plays a role in PD. Exposure of cells to conditions such as glucose starvation, inhibition of protein glycosylation, disturbance of Ca²⁺ homeostasis and oxygen deprivation accumulates unfolded proteins in the ER (ER stress), and activates a set of pathways known as the unfolded protein response (UPR). The UPR is characterized by translational suppression, induction of the UPR-targeted genes such as molecular chaperones and folding catalysts in the ER, and ER-associated degradation (ERAD). If the protein load in the ER exceeds its folding capacity, or some defects in the ER stress response exist, cells tend to die, typically, with apoptotic features (ER stress-induced cell death). We have studied the effects of the UPR-targeted genes and the UPR-regulating compounds on the neuronal cell death in SNpc. In this symposium, I would like to demonstrate our recent results that UPR-targeted genes such as ORP150 are neuroprotective, while ERAD molecule Herp may enhance the neurotoxicity in experimental PD models.

S10-4 Therapeutic Strategies based on ER stress

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The endoplasmic reticulum (ER) stress response is a defense system for dealing with the accumulation of unfolded proteins in the ER lumen. Recent reports have shown that ER stress is involved in the pathology of some neurodegenerative diseases and cerebral ischemia. In a screen for compounds that induce the ER-mediated chaperone BiP/GRP78 (BiP), we identified BiP inducer X (BIX). BIX preferentially induced BiP with slight inductions of GRP94, calreticulin, and CHOP. The induction of BiP mRNA by BIX was mediated by activation of ER stress response elements (ERSEs) upstream of the BiP gene, through the ATF6 pathway. Pretreatment of neuroblastoma cells with BIX reduced cell death induced by ER stress. Intracerebroventricular pretreatment with BIX reduced the area of infarction due to focal cerebral ischemia in mice. In the penumbra of BIX-treated mice, ER stress-induced apoptosis was suppressed, leading to a reduction in the number of apoptotic cells. Considering these results together, it appears that BIX induces BiP to prevent neuronal death by ER stress, suggesting that it may be a potential therapeutic agent for cerebral diseases caused by ER stress.

S11-1 Association of RIP signaling and Alzheimer disease process indicates future therapeutic interventions.○Masayasu Okochi¹, Shinji Tagami¹, Masatoshi Takeda¹¹Dept. Psy., Osaka Univ.

As many symptoms of dementia are thought to reflect quantitative/qualitative impairment of synaptic functions in neural networks, there are good reasons to believe that the main aim of therapeutic intervention for Alzheimer disease should be the maintenance and enhancement of synaptic functions. However, this strategy cannot impede the neurodegenerative and pathological processes involved in Alzheimer disease. Basic research results indicate that elimination of amyloid-beta peptide (A β), a major constituent of senile plaques in Alzheimer disease, impedes these processes. The A β hypothesis makes it clear that insolubilization of A β 42 contained in secreted A β , originally produced as a soluble peptide, is the initial step in the pathological process of Alzheimer disease. The current status of research and development of therapeutic interventions will be summarized here. In the second part, many type-1 receptors undergo dual-cleavage by PS/gamma-secretase within their transmembrane regions. PS/gamma-secretase hydrolyzes betaAPP and Notch-1 near the middle of transmembrane domain (TM) at the gamma and S4 sites, respectively, and at the border of the TM and the cytosol at sites epsilon and S3, respectively. In some cases, there is diversity in the specific sites of cleavage. How this change in precision occurs has been the focus of intense study because gamma-cleavage of the betaAPP increases the production of Alzheimer disease-associated longer A β 42. We identified that N β and other A β -like peptide species are secreted. The results demonstrate that the characteristics of C-terminal elongation of N β and A β are similar. We suspect that the release of A β - or N β -like peptides is a common feature of the proteolysis during RIP signaling, and anticipate that our data may open the door to searches for surrogate markers for A β 42 production.

S11-3 Structure-function relationships of the intramembrane-cleaving proteases○Taisuke Tomita¹¹Dept Neuropathol Neurosci, Grad Sch Pharm Sci, Univ Tokyo

Intramembrane-cleaving proteases (I-CLiPs) are a family of polytopic enzymes responsible for hydrolyzing substrates within hydrophobic transmembrane domains. Various I-CLiPs have been identified so far such as site 2 protease (S2P), signal peptide peptidase (SPP), rhomboid, and γ -secretase. However, the endeavor to elucidate the unusual endoproteolytic mechanism by I-CLiPs has only begun. γ -Secretase is responsible for the generation of A β peptides and plausible molecular target for Alzheimer's disease (AD) treatment. Drugs that regulate the production of A β by inhibiting or modulating γ -secretase activity could provide a disease-modifying effect on AD. However, recent studies suggest that γ -secretase plays important roles in cellular signaling including Notch pathway. Thus, understanding the molecular mechanism whereby γ -secretase recognizes and cleaves its substrate is a critical issue for the development of compounds that specifically regulate A β -generating γ -secretase activity. We recently given biochemical evidences to prove that presenilin 1 (PS1), the catalytic subunit of γ -secretase, harbors a hydrophilic catalytic pore within the membrane. Moreover, the x-ray crystal structures of I-CLiPs, rhomboid and S2P, have been reported and shown that their active sites reside in a water filled crevice, suggesting that the endoproteolysis within the hydrophilic environment within the lipid bilayer is common structure of I-CLiPs. I will review our structural studies on the γ -secretase complex, and envision the direction for developing effective and selective γ -secretase inhibitors as therapeutics for AD.

S11-2 γ -Secretase: Intramembrane cleavage of β -amyloid precursor protein○Maho Morishima-Kawashima¹¹Department of Molecular Neuropathology, Graduate School of Pharmaceutical Science, Hokkaido University, Sapporo, Japan

Amyloid β -protein (A β) is the major component of the senile plaques and plays a pivotal role for the development of AD. A β is produced from β -amyloid precursor protein (APP), a type I membrane-spanning protein, through sequential cleavages by β - and γ -secretases. γ -Secretase is a novel type of aspartyl protease of high molecular weight multimeric protein complex, which comprises at least four distinct membrane proteins, presenilin (PS) 1 or 2, nicastrin, Aph-1, and Pen-2. The most characteristic feature of γ -secretase is the catalytic aspartic acids on PS1/2 sitting within the membrane and cleaving the intramembrane region of substrates, although the precise molecular mechanism of the intramembrane cleavage is not as yet understood. γ -Secretase cleaves the transmembrane domain of APP at least at two sites. γ -Cleavage in the middle of the transmembrane domain releases A β 40 and A β 42, and ϵ -cleavage at the cytoplasmic/membrane boundary generates predominantly APP intracellular domain (AICD) 50-99. Several studies indicate that these two cleavages are interrelated. Moreover, longer A β s, putative intermediate products, including A β 45, A β 46, and A β 48, were found within the cells and brains. The treatment of the cells with DAPT built up A β 43 and A β 46 in a dose-dependent manner, concomitantly with a decrease in A β 40. These led us to hypothesize that longer A β species generated by ϵ -cleavage is processed at every three residues from its carboxyl portion on the α -helical surface of the APP transmembrane domain, which results in A β 40/42 generation. To test this possibility, we examined whether longer A β (A β 46) is processed to A β 43 and A β 40 by γ -secretase. Incubating the A β 46-accumulating membranes in the presence of L685,458 prevented AICD generation and resulted in a large decrease in A β 46 and the concomitant appearance of A β 40 and A β 43, but not A β 42. We further identified by LC-MS/MS particular five tripeptides that should be released from the transmembrane domain of APP following the cell-free A β generation. These results strongly support the stepwise processing by γ -secretase at every three residues of the transmembrane region of APP.

S11-4 Behavioral Analysis of Neuron-specific RBP-J knockout mice○Kenji Tanigaki¹, Michihiro Toritsuka^{1,3}, Sohei Kimoto^{1,3}, Kazue Muraki¹, Toshihumi Kishimoto¹, Tasuku Honjo²¹Research Institute, Shiga Medical Center ²Dept. of Immunology and Genomic Medicine, Kyoto Univ. ³Dept. of Psychiat., Nara. Med. Univ.

Notch4 has been reported to be associated with schizophrenia. Rats with reduced γ secretase activity shows behavioral abnormalities such as increased sensitivity to apomorphine. These findings suggest the possible involvement of Notch/RBP-J signaling in schizophrenia. Notch/RBP-J signaling regulates multiple developmental processes in embryonic stages. However, its physiological roles in the brain remain to be elucidated. To elucidate the functions of Notch/RBP-J signaling in the central nervous system, we generated neuron-specific RBP-J-deficient mice. We performed behavioral analysis of neuron-specific RBP-J-deficient mice and examined their responses to dopaminergic stimulation. We would like to discuss the possible roles of Notch/RBP-J signaling in the regulation of the responsiveness to Dopamine and the pathogenesis of schizophrenia.

S12-1 Functional neuroimaging on fatigue and motivation

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Fatigue is an important biological alarm that signals the need for rest. Fatigue can be the primary symptom of a disease; this is the case in chronic fatigue syndrome (CFS), which might therefore be a good model for studying the mechanisms underlying fatigue. From neuroimaging studies, various neural deteriorations have been shown: For example, patients with CFS had reduced gray-matter volume in bilateral prefrontal cortices; reduced density of serotonin transporters in anterior cingulate; and reduced functional magnetic resonance responsiveness. Although the neural deteriorations of fatigue have mostly been studied for this specific disorder, chronic fatigue may introduce both functional and organic deteriorations among healthy population. Similar to chronic fatigue, decreased motivation has also become an object on public concern. "Motivation" and "Fatigue" have been considered to be two sides of the same coin. Therefore, we would also refer to neuroimaging studies on motivation.

S12-3 Structural equation modeling between fatigue and autonomic function; Preliminary analysis to the fatigue medical checkup for labor

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In Japan, more than 60 percent in general population felt intense fatigue prolonged more than 6 months, chronic fatigue. Chronic fatigue not only interferes with one's daily life but also makes major economic losses (more than 10 billion yen per year). Prevention is most effective treatment for pathological fatigue. Especially, a reduction of occupational fatigue is essential for preventing death from over work. The Industrial Safety and Health Law for an improvement of the industrial hygiene was revised in April 2006 for that reason. However, those medical checkups are still based on history taking. Objective biomarkers for the estimation of overwork are needed from some perspectives such as early detection of the health hazard and prevention overwork death without fatigue sensation. In this study, we performed structural equation modeling between fatigue and autonomic function. As a result, sympathetic function was changed 7 times greater and vagal function was changed 13 times greater than fatigue sensation change. In conclusion, autonomic function is not only one aspect of the tension related brain function, but also sensitive indicator of fatigue. It may show that autonomic function is the brain function projection including fatigue through the physiological window.

S12-2 Brain dysfunction is a key abnormality for understanding the state of chronic fatigue

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Concerning the pathogenesis of Chronic Fatigue Syndrome (CFS), a variety of theories such as social stress events, genetic background, virus infections, HPA axis abnormality, immune dysfunction, metabolic abnormalities, autonomous nerve unbalance have been proposed. However, it would seem that they do not grasp the whole picture of CFS. In view of these situations, its mechanism is now becoming a little clear, and brain dysfunction become a key abnormality for understanding the features of CFS. That is, regional cerebral blood flow (rCBF) study revealed that the decrease in rCBF in CFS patients correspond to those involved in various neuropsychiatric complaints including autonomic imbalance, sleep disturbance, many kinds of pain, and the loss of concentration, thinking, motivation, and short-term memory. A significant decrease was found in the cerebral uptake of [2-11C]acetyl-L- carnitine in several brain regions of the CFS group, namely, in the prefrontal and temporal cortices, anterior cingulate, and cerebellum. Anterior cingulate is deeply related to concentration, attention, and some autonomic functions. When we studied 5-HT transporter (5-HTT) density by using PET, the density of 5-HTT in the rostral subdivision of the anterior cingulate was significantly reduced in the CFS patients. In addition, the density of 5-HTT in the dorsal anterior cingulate was negatively correlated with the pain score. These loci are spatially different from the locus of the rostral subdivision of the anterior cingulate. Therefore, the reduction in the density of serotonin transporters in the rostral subdivision of the anterior cingulate might be related to the chronic fatigue itself, not to the non-specific symptom of pain. Furthermore, we recently found that CFS patients had a significant reduction in gray-matter volume in their bilateral prefrontal areas and that there was a significant negative correlation between the gray-matter volume of the right prefrontal cortex and the performance status of the CFS group. I show here several brain dysfunctions found in CFS patients, and would like to explain our hypothesis: Neuro-molecular mechanism leading to chronic fatigue.

S12-4 Neural mechanism of central fatigue in the animal models

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Central fatigue is caused by excessive brain activity such as concentrating attention or feeling stress, and is thought to be relieved by taking rest or sleep. In order to investigate the neural mechanism of central fatigue, we have developed two experimental animal models mimicking overtaxed brain function: generation of cortical spreading depression (SD), the excitatory waves of depolarization spreading throughout the cerebral cortex, and long-term intracranial self-stimulation (ICSS). We have reported that the amount of non-REM sleep, but not of REM sleep increased for several hours in the animals which underwent cortical SD. In those animals, prostaglandins including PGD₂, PGE₂ and PGF₂α, the potent sleep-wake regulators in the brain, were produced by COX-2 upregulated in depolarized neurons in the cerebral cortex. NS-398, a specific inhibitor of COX-2, completely arrested the increase of the amount of non-REM sleep, indicating that the neuronal COX-2 is a crucial regulator of the amount of non-REM sleep following excessive brain activity, and likely revivifies the brain function. The ICSS behavior was realized in rats by setting the rats to electrically stimulate the hemi-lateral medial forebrain bundle by their pressing a lever. During long-term ICSS, resting behavior for dozens of minutes was often observed a few hours after the start of ICSS. The resting behavior was not induced by muscular fatigue, since the animals in the resting period restarted ICSS again when more intensive stimulations to the ipsi-lateral medial forebrain bundle or stimulations to the contra-lateral medial forebrain bundle were applied to the animals. Furthermore, threshold in stimulation intensity for inducing ICSS behavior was gradually increased during long-term ICSS. Such induction of resting behavior and increase in ICSS threshold were suppressed in animals which underwent degeneration of serotonergic neurons in the dorsal raphe nucleus by pharmacological treatment with 5,7-dihydroxy-tryptamine. In the short-term ICSS, however, the threshold was not affected by degeneration of serotonergic neurons. These observations indicate that the dorsal raphe serotonergic nervous system is involved in fatigue sensation or weariness following overtaxing the brain.

S13-1 Social behaviors and plasma oxytocin level are dually regulated by breast milk and hypothalamic ADP-ribosyl cyclase in infant mice

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Recently brain neuropeptides have received increasing attention as regulator of behaviour under healthy and psychopathological conditions. The neuropeptide oxytocin is considered a key modulator of various social behaviours, as revealed in rodent and humans. The regulation of oxytocin release from hypothalamic neurons by CD38 has previously been demonstrated in adult mice (Jin et al., Nature 441, 41-46, 2007). However, the knowledge about this CD38-oxytocin relationship in infants (during the developmental period) is not available yet. To investigate and assess this question, we first established the means to measure by using wild-type mice. We focus on ultrasonic vocalization in infants as a criteria of capability to social interaction. Number of ultrasonic vocalization calls in 7-days old infants was increased compare with 3-day old pups. The same pattern was observed in changing of ADP-ribosyl cyclase during development period in mice. Interestingly that plasma oxytocin levels were maintained nearly at the same level from childhood to adulthood. In addition, we also found that the milk of lactating mother mice is rich in oxytocin. These results suggest that even in childhood, social behavior is develop together with some biochemical parameters like as ADP-ribosyl cyclase activity and oxytocin levels. Our data demonstrate that mother's oxytocin supplied from milk intake is an important exogenous origin for mice. This dual regulation of keeping the constant oxytocin level is an important safety mechanism which ensures neurodevelopment during infants before weaning.

S13-3 Alterations in the development of the serotonergic system in the cerebral cortex of rats induced by fetal thalidomide exposure

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Autism is a developmental disorder of the brain characterized by three major symptoms; impaired social ability, impaired communication ability, and restricted and repetitive behaviors. Previous studies suggest that although genetic factors are important, environmental factors also contribute to the etiology of autism. One of the known environmental factors is fetal exposure to thalidomide (THA) between gestational days 20-24 which results in external ear malformation with high incidence of autism. By administering THA to pregnant rats at 9 days of pregnancy which corresponds to the above period in humans, a rat model of autism was created which exhibits symptoms in common with human autism such as increases in non-exploratory behavior and in the concentration of serotonin (5-HT) in blood. In this model animal, a shift in the distribution of the serotonergic neurons in the dorsal raphe nucleus has been observed. To further explore the abnormalities of the serotonergic system in this model animal, developmental changes in 5-HT and dopamine (DA) concentration as well as expression of 5-HT and DA receptors and transporters in the cerebral cortex and hippocampus of control and THA-exposed rats were compared during postnatal development up to 40 days in the present study. In control animals, both 5-HT and DA concentrations measured at 20, 30, and 40 days increased in a stepwise manner. In THA-exposed rats, both 5-HT and DA concentrations were significantly higher than the control at 20 days and 40 days. Real-time quantitative PCR analysis of the 7 subtypes of 5-HT receptor and 5-HT transporter gene expression in the cerebral cortex revealed significant up-regulation of *HTR1A*, *HTR1B*, *HTR2A*, *HTR6*, *HTR7* and 5-HT transporter at 40 days in the THA-exposed rats compared with the control. *DRD2* and *DRD3* showed similar up-regulation in THA-exposed rats at 40 days. DA transporter gene expression was not affected by THA exposure. The results thus indicate that fetal exposure to THA significantly alters the development of the serotonergic system in the rat cerebral cortex.

S13-2 Effects of environmental factors on behavioral abnormalities in PACAP-KO mice

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Mice lacking the neuropeptide PACAP (PACAP-KO mice) display some remarkable behavioral changes, including hyperactivity and abnormal jumping behavior in a novel environment (PNAS, 2001), and deficits in prepulse inhibition (PPI) (J Neurosci, 2006). These abnormal behaviors in PACAP-KO mice are ameliorated by the atypical antipsychotic drug risperidone. A recent genetic analysis shows genetic variants of the genes encoding PACAP are associated with schizophrenia (Mol Psychiatry, 2007). These findings suggest that alterations in PACAP-signaling may contribute to the pathogenesis of psychiatric disorders, but the exact mechanism is not known. On the other hand, clinical studies show that not only genetic factors but also environmental factors play a key role in pathophysiology of many psychiatric disorders. However, there are few preclinical studies on this point. In the present study, we examined the effects of environmental factors (rearing in social isolation and enriched conditions) on behaviors in wild-type and PACAP-KO mice. Locomotor activity was quantified in plastic activity monitoring boxes for 60 min using an infrared photocell beam detection system Acti-Track. Acoustic startle responses were measured in a startle chamber using SR-LAB system. Isolation rearing for 2 weeks from 4-week-old enhanced hyperlocomotion and PPI deficits, and caused aggressive behavior in PACAP-KO mice, while it did not cause hyperlocomotion and aggressive behavior in the control mice. Rearing in enriched conditions for 4 weeks from 4-week-old attenuated the hyperactivity and jumping behavior in PACAP-KO mice, although it did not affect behaviors in the control mice. In contrast, rearing in enriched conditions for 4 weeks from 8-week-old did not affect the abnormal behaviors in PACAP-KO mice. These results suggest that abnormal behaviors in PACAP-KO mice depend on environmental factors during development.

S13-4 Mutations in *SHANK3* gene encoding the synaptic scaffolding protein possibly associated with autism spectrum disorder.

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Terminal 22q13 deletion (Phelan-McDermid syndrome, PMS) is one of diseases with submicroscopic telomere deletions. PMS is characterized by significant language delay, mental retardation, hypotonia and autistic feature. Cumulative evidence has demonstrated that haploinsufficiency of *SHANK3* gene located in 22q13.3 is the major causative factor in the neurological symptoms of PMS. Shank3, a multidomain protein containing SH3 and PDZ domains, localized in the postsynaptic density, and interacts with various synaptic molecules such as PSD-95 and glutamate receptors. The expression of Shank3 is predominantly observed during synaptogenesis. Therefore, it has been thought that Shank3 plays important roles in the formation and function of synapse in the developing brain. In this study, we analyzed the *SHANK3* gene in the autistic patients showing the similar symptoms to PMS without the terminal deletion of 22q13. We obtained blood samples from about 100 patients after informed consent, and prepared genomic DNA from blood leucocytes. We amplified all *SHANK3* exons using PCR, and analyzed the sequence by ABI 3100-avant Automated Sequencer. Then, we found several mutations within the *SHANK3* gene as follows, i) deletion of 18 bp (6 amino acids) upstream of the SH3 region (1 sample), ii) point mutation caused the exchange of amino acid in the PDZ region (1 sample), iii) deletion (1 sample) or insertion (3 samples) of 10 bp-repetitious sequence downstream of exon 11. All mutations were not detected in 228 control samples. Our findings will support the recent hypothesis that major cause of autism resides in abnormalities at the synapse. To reinforce this hypothesis, we now investigate the pathological property of the mutated Shank3. All experiments were approved by The Ethics Committee in National Institute of Neuroscience and in Osaka Medical Center and Research Institute for Maternal and Child Health.

O1-1 Experience dependent synaptic delivery of AMPA receptors

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The molecular and cellular mechanisms underlying experience-dependent plasticity of brain function are poorly understood. Recent *in vitro* studies have identified the regulated trafficking of AMPA receptors (-Rs) into synapses as a major molecular component of neural plasticity. Here we ask if experience-driven plasticity in the developing rat barrel cortex is accompanied by and/or requires AMPA-R delivery to synapses. By combining *in vivo* gene delivery with *in vitro* recordings, we show that experience drives recombinant GluR1, an AMPA-R subunit, into synapses formed between layer 4 and layer 2/3 neurons. Furthermore, expression of the GluR1 cytoplasmic tail in layer 2/3 neurons, a construct that inhibits synaptic delivery of endogenous AMPA receptors during long-term potentiation, blocks experience-driven synaptic potentiation. These studies show that synaptic delivery of AMPA-Rs contributes to plasticity driven by natural stimuli in the mammalian brain. Although social isolation early in life has been shown to alter behaviors including learning and emotion, how neonatal isolation affects synaptic connection is poorly understood. Since whisker-barrel system is involved in social interaction, we examined if social isolation changes experience-dependent synaptic delivery of AMPA receptors in the developing rat barrel cortex. We found that neonatal social isolation disrupted *in vivo* trafficking of GluR1 and GluR4 into synapses formed from layer 4 to layer 2/3 of developing rat barrel cortex. These data suggested that neonatal social isolation alters neuronal reorganization.

O1-3 THE CIS-UNSATURATED FREE FATTY ACID DERIVATIVE HEPBA REGULATES $\alpha 7$ ACH RECEPTOR TRAFFICKING, AND SYNAPTIC PLASTICITY VIA A CA MKII PATHWAY.

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The present study investigated the effect of HEPBA ($C_{17}H_{33}O_2$), a newly synthesized derivative of cis-unsaturated free fatty acid containing one double bond and one benzene ring, on responses of $\alpha 7$ nACh receptors expressed in *Xenopus* oocytes. HEPBA potentiated $\alpha 7$ nACh receptor currents, reaching 150 % of basal levels 40 min after 10-min treatment at 100 nM. In contrast, the compound depressed the currents during treatment at concentrations ranged from 1 to 30 μ M. Both the potentiation and depression were inhibited by KN-93, a selective inhibitor of CaMKII, but not by GF109203X, a selective inhibitor of PKC, or H-89, a selective inhibitor of PKA. HEPBA induced a long-lasting facilitation of neurotransmission in the CA1 region of the rat hippocampal slices, and the facilitation was inhibited by KN-93 or α -bungarotoxin, an inhibitor of $\alpha 7$ receptors. In rat hippocampal slices, HEPBA enhanced the expression of $\alpha 7$ nACh receptors on membrane. This effect was inhibited by KN-93. This effect seems to translocate $\alpha 7$ nACh receptors from cytosol to membrane. The results of present study suggest that HEPBA exerts its potentiating and depressing bidirectional actions on $\alpha 7$ nACh receptor responses, and enhances translocation of $\alpha 7$ nACh receptors to membrane via a CaMKII pathway.

O1-5 PRMT3 regulates rps2 stability and activity-dependent dendritic spine maturation of hippocampal neurons

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Protein arginine N-methyltransferase 3 (PRMT3) is a cytoplasmic enzyme that utilizes S-adenosyl-L-methionine (AdoMet) to methylate specific proteins, most of which contain GAR (arginine-glycine rich) motifs. One of the most characterized roles of PRMT3 is the proper maturation of 80S ribosome through the methylation of 40S ribosomal subunit rps2. It was demonstrated that the lowered level of methylated rps2 caused an imbalance of the ratio of 40S to 60S ribosomal subunit in fission yeast. In this study, we perturbed the expression of PRMT3 in the cultured rat hippocampal and cortical neurons by transiently introducing siRNA oligonucleotides that were arranged to hybridize with PRMT3 mRNA and examined the morphological and functional effects of the PRMT3 depletion in the neurons, particularly focusing on *de novo* protein synthesis that are operated by ribosomal proteins. The PRMT3-defective neurons showed the decreased level of BDNF-induced protein synthesis of alpha-CaMKII. As expected, PRMT3 was cosedimented with a 40S ribosomal fraction in the neuronal cells and affected the formation of 80S ribosomes to cause an accumulation of free 60S ribosomes. These findings demonstrated that PRMT3 plays a pivotal role in the proceeding of translation via methylation of a specific component of ribosomal subunit, rps2, and contributes to the translation-dependent changes in the spines of dendrites.

O1-2 Age-dependent formation of GM1-ganglioside-enriched microdomain in synaptosomes induces amyloid β -protein fibrillogenesis

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Aging is a strong risk factor for the development of Alzheimer's disease (AD). However, its pathological roles remain to be clarified. In the present study, we show that GM1 ganglioside (GM1)-enriched microdomain, which was detected by the specific binding of a novel peptide (p3), appeared selectively on synaptosomes prepared from aged mouse brains. Notably, the synaptosomes bearing the GM1-enriched microdomain showed extraordinary potency to induce A β assembly, which was suppressed by an antibody specific to GM1-bound A β , an endogenous seed for AD amyloid. Together with evidence that A β deposition starts at presynaptic terminals in the AD brain and that GM1 levels significantly increase in amyloid-positive synaptosomes prepared from the AD brain, our results suggest that aging accelerates A β assembly in the brain through formation of unique GM1-enriched microdomains in synaptic plasma membranes.

O1-4 Crosstalk between Cdk5 and CaMKII in the postsynaptic region

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Cyclin-dependent kinase 5 (Cdk5) is a proline-directed Ser/Thr protein kinase that is activated when it binds to the neuron-specific activator p35. Cdk5-p35 participates in regulation of synaptic plasticity at both pre- and post-synaptic terminus. p35 associates with postsynaptic proteins such as CaMKII and alpha-actinin-1. Furthermore, hippocampal slices obtained from p35^{-/-} mice exhibit the easier induction of long-term potentiation and impaired long-term depression (LTD). We have shown that Cdk5-p35 enriched in postsynaptic region is downregulated by NMDA-induced proteasomal degradation of postsynaptic p35. Glutamate or NMDA stimulation induces CaMKII autophosphorylation over a time course that mirrored p35 degradation process. The inhibition of Cdk5 activity by roscovitine enhances CaMKII autophosphorylation and activation in cultured neurons, and in an isolated postsynaptic-density-enriched fraction. These observations suggest a possibility that Cdk5 activity suppresses CaMKII activation in resting states, and that the downregulation of Cdk5 activity by NMDA facilitates CaMKII activation. Furthermore, to analyze how Cdk5 regulates the autophosphorylation of CaMKII, we tested whether CaMKII is directly regulated by Cdk5-p35 using purified kinases. However, Cdk5-p35 did not affect the autophosphorylation of CaMKII, suggesting that the Cdk5 regulates CaMKII activity indirectly through other unknown factors. On the other hand, treatment of the postsynaptic fraction with protein phosphatase inhibitors suppressed the enhancement of CaMKII autophosphorylation induced by roscovitine. These results suggest that Cdk5 regulates CaMKII autophosphorylation through the protein phosphatases. On the other hand, we found phosphorylation of p35 at S91 by CaMKII. Although detailed function is still unknown, this phosphorylation is likely to be important for synaptic plasticity involving Cdk5-p35.

O1-6 Spine formation induced by Spikar is negatively regulated with drebrin.

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Spikar is a drebrin-binding protein, which was isolated by yeast two-hybrid screen using drebrin as bait. Spikar is localized mainly at nucleus and dendritic spines. RNAi knockdown (KD) of Spikar in cultured neuron decreased the density of dendritic protrusions (spines and filopodia), suggesting that Spikar is involved in the spine formation. To examine whether Spikar plays a role in spine formation in nucleus or spines, we performed rescue experiments of Spikar-KD neurons with wild-type-Spikar or mutated-Spikar with impaired nuclear localization signal (mutNLS-Spikar). The decrease of spine density was rescued by each of wild-type-Spikar and mutNLS-Spikar. Additionally, overexpression of mutNLS-Spikar increased the dendritic spine density. These data suggest that extranuclear Spikar is involved in spine formation, although its effect as transcriptional coactivator in nucleus cannot be excluded. Drebrin A is a neuron-specific F-actin binding protein, and one of key proteins regulating spine function and morphology. We then examined whether the interaction of extranuclear Spikar with drebrin is necessary for dendritic spine formation. We employed C-terminal region of Spikar (C-Spikar) that deleted drebrin binding region and NLS. Overexpression of C-Spikar increased the dendritic spine density similarly to mutNLS-Spikar, suggesting that interaction of Spikar with drebrin is not necessary for dendritic spine formation. What then does the interaction between Spikar and drebrin mean? We then carried out co-transfection experiment of drebrin and Spikar mutants into cultured neurons. In co-transfection experiment of mutNLS-Spikar with drebrin, the increase of dendritic spine density was inhibited completely. In contrast, co-transfection of C-Spikar with drebrin increased the density of dendritic spine similarly to C-Spikar single transfection. Taken together, our data suggest that drebrin functions as an inhibitor of Spikar in the dendritic spine formation. This work was supported by Grant-in-Aid for Young Scientists (18700306) to HY and for Scientific Research (19200029) and those on Priority Areas- Elucidation of neural network function in the brain-(18021004, 20021002) from the MEX of Japan.

O1-7 Neuropsin (KLK8)-dependent and -independent Synaptic Tagging○Yasuyuki Ishikawa¹, Hideki Tamura¹, Sadao Shiosaka¹¹Division of Structural Cell Biology, Nara Institute of Science and Technology

Hippocampal early (E-) long-term potentiation (LTP) elicited by a weak (one or two) tetanic stimulus normally fades away within 90min. Late (L-) LTP elicited by strong (four) stimuli lasts more than 180min and requires new protein synthesis to persist. If a strong tetanus is injected once into a synapse, even a weak tetanus injected into another synapse can evoke persistent LTP. It was hypothesized that a synaptic tag enables capture of newly synthesized synaptic molecules. Here, we found two synaptic capture mechanisms for a weakly stimulated synapse to acquire persistency; i.e. neuropsin-dependent and independent. The single tetanus evokes a neuropsin-dependent form that follows downstream signaling into integrin/actin signal and L-type voltage-dependent Ca²⁺ channel (LVDC) pathway. Additionally, a neuropsin-independent form of synaptic capture is evoked by a stronger (two) tetanus than the former. Both forms converging on LVDC might serve different associative memories depending on their input strength. Our study strongly supports the hypothesis of synaptic tagging and demonstrates that neuropsin-dependent late associativity is particularly important in non-stressful associative memory.

O1-9 Modulation of exocytosis by a novel nitrated second messenger, 8-nitroguanosine 3',5'-cyclic monophosphate○Hideshi Ihara¹, Hiroyasu Tsutsuki¹, Sasakawa Nobuyuki², Tomoaki Ida¹, Mitsuki Hayashi², Konosuke Kumakura³, Tomohiro Sawa⁴, Takaaki Akaike⁵¹Department of Biological Science, Graduate School of Science, Osaka Prefecture University, ²Laboratory of Neurochemistry and Neuropharmacology, Life Science Institute, Sophia University, ³Department of Microbiology, Graduate School of Medical Sciences, Kumamoto University

The main nitric oxide (NO) pathway is mediated by soluble guanylate cyclase (sGC), leading to the production of a second messenger, guanosine 3',5'-cyclic monophosphate (cGMP). Recently, it was reported that 8-nitroguanosine 3',5'-cyclic monophosphate (8-nitro-cGMP), a novel nitrated derivative of cGMP, was formed in NO-mediated signal transduction (Nat. Chem. Biol. 2007). 8-Nitro-cGMP not only activates cGMP-dependent protein kinase (PKG) as a cGMP analog, but it also has unique chemical properties, such as redox activity, membrane permeability, resistance to phosphodiesterase, and protein S-guanylation. The aim of this study was to investigate the role of 8-nitro-cGMP in the nervous system as a novel membrane-permeable exocytosis modulator. In this study, we examined the formation of 8-nitro-cGMP in astrocytes and neurons and the effect of 8-nitro-cGMP on catecholamine release from bovine adrenal chromaffin cells.

Primary astrocytes and cerebellar granule cells were prepared from Wistar rats and bovine adrenal chromaffin cells were isolated from fresh adrenal glands. Intracellular 8-nitro-cGMP was detected by immunocytochemistry using an anti-8-nitro-cGMP monoclonal antibody. Catecholamine release from chromaffin cells was analyzed by amperometric techniques. Immunocytochemistry revealed that 8-nitro-cGMP was produced in astrocytes and neurons. Amperometric techniques showed that 8-nitro-cGMP modulated the kinetics of catecholamine release from chromaffin cells. Although the effects of synthetic cGMP analog on the release were reversed by a PKG inhibitor, the effects of 8-nitro-cGMP were not. Superoxide scavenger did not affect the modulation of exocytosis kinetics mediated by 8-nitro-cGMP. These results suggested that 8-nitro-cGMP modulated exocytosis by a different PKG-dependent mechanism. Other unique chemical properties of 8-nitro-cGMP, e.g., formation of protein S-guanylation, may be involved in the mechanism of the exocytosis modulation.

O2-2 BMPRIA signaling in astrocytes is essential for proper cerebral angiogenesis○Masahisa Yamada¹, Runa Araya¹, Moeko Kudo¹, Yuji Mishina²¹Yamada Unit, RIKEN-BSI, ²Lab. of Reproductive and Developmental Toxicology, NIEHS, Research Triangle Park, NC, USA.

Neural stem cells (NSC) are self-renewing, multipotential progenitor cells with the capacity for generating neurons and glial cells including astrocytes and oligodendrocytes. NSCs in the subventricular zone, which is formed later in embryogenesis, generate neurons, astrocytes and oligodendrocytes. Astrocytes adhere to most of the capillaries in the brain and promote formation of the blood-brain-barrier (BBB). It is recently shown that Bone morphogenetic protein (BMP) signaling through BMPRIA is important for cell fate determination in NSCs towards glial lineage, and for astrocytic maturation. Furthermore, activation of BMPs signaling is thought to play a role in regulating proliferation, differentiation, and survival on vascular cells, but its involvement in regulating endothelial-astrocyte interactions is not yet understood. The study examines the role of BMP signaling through BMP type IA receptor (BMPRIA) in early neural development using a conditional mouse knockout model, in which Bmp1a is selectively disrupted in telencephalic neural stem cells. The conditional mutant mice show a significant increase in the number of cerebral blood vessels and the level of vascular endothelial growth factor (VEGF) is significantly upregulated in the mutant astrocytes. The mutant mice also show leakage of immunoglobulin around cerebral microvessels in neonatal mice, suggesting a defect in formation of the blood-brain-barrier. Astrocytic endfeet fail to encircle cortical blood vessels in the mutant mice. These results suggest that BMPRIA signaling in astrocytes regulates expression of VEGF for proper cerebrovascular angiogenesis and has a role on formation of the BBB.

O1-8 Characterization of exocytotic events and the dynamics of secretory vesicles in single mouse chromaffin cells.○Nobuyuki Sasakawa¹, Fuyuka Matsuda¹, Mitsunori Hayashi¹, Yumi Wanabe^{2,3}¹Dept. of Information & Communication Sci., Faculty of Sci. & Technol. Sophia Univ., Tokyo, Japan, ²Div Mol Cell Biol, Grad Sch Med Dent Sci, Niigata Univ, Niigata, ³Trans-disciplinary Res Program, Niigata Univ, Niigata, ⁴Dept Cell Neurobiol, Brain Res Institute, Niigata Univ, Niigata

Chromaffin cells were enzymatically dissociated from adrenal medulla from male C57BL mice (5-7 weeks after birth). The chromaffin cells were plated onto collagen coated glass-base dishes and maintained in culture for 5 to 7 days. After 3 days in culture, chromaffin cells adhered to the bottom tightly and had 10-15 μ m in diameter. By use of amperometry, single exocytotic events were analyzed in the mouse adrenal chromaffin cells. Amperometric detection was performed with a carbon fiber microelectrode (diameter = 5 μ m, applied voltage = +650 mV). To characterize a single exocytotic event detected as a single current spike, the spike parameters and the frequency of events were analyzed. To clarify the implication of the interaction of syntaxin 1A and CaMKII in the regulation of exocytosis, we examined the kinetics of single events and the events frequency in the cells prepared from R151G syntaxin 1A knock-in mice. In the preliminary observation, the frequency of the events evoked by weak stimulation was approx. 20% less than that in the cells prepared from wild type mice. The studies are under way in order to characterize the dynamics of intracellular secretory vesicles using LSM-5Live confocal laser microscope which allows the 4-dimensional analysis in the cells prepared from R151G syntaxin 1A knock-in mice.

O2-1 Endothelin decreases aquaporin-4 expression in cultured rat astrocyte and in the rat cerebral cortex○Kazuhiro Tanaka¹, Yutaka Koyama¹¹Lab. Pharmacology, Faculty of Pharmacy, Osaka Ohtani Univ. Osaka, Japan

A number of recent studies reveal that aquaporins (AQPs) in the central nervous system are involved in edema formation. Although pharmacological modulation of aquaporins expression and function may be the leading candidate for the treatment of brain edema, the regulatory mechanism of brain AQPs expression has not been fully clarified. In this study we examined the effect of endothelin, which can participate in astrocytic functions and several encephalopathic events, on the AQPs expression in cultured rat astrocyte and in rat brain. By using quantitative RT-PCR, we detected high levels of AQP1 and AQP4 mRNAs in cultured astrocyte, while AQP3 and AQP9 mRNAs were low levels. Little expression of AQPs is found in cultured rat neuron and microglia. AQP4 mRNA levels were decreased by treatment with 100 nM endothelin-1 (ET-1) for 6 or 12 hours in cultured astrocyte, whereas AQP1 levels were unaffected by ET-1. 100nM ET-1 significantly suppressed the expression levels of AQP4 protein after 48 hours of treatment. In addition, intracerebroventricular infusion of 500 pmol/day of Ala(1,3,11,15)-ET-1, a selective ETB agonist, for 7 days decreased AQP4 mRNA in the rat cerebral cortex, but not in hippocampus and caudate-putamen, whereas there's no change of AQP9 mRNA in any regions. GFAP-positive cells had immunoreactivity for AQP4, but NeuN-positive cells didn't. These results suggest that endothelin has a role in regulating the astrocytic AQP4's expression through ETB receptors.

O2-3 Identification of the molecules, which are responsible for astroglial heterogeneity in the central nervous system○Mineyoshi Aoyama¹, Hiroki Kakita², Shin Kato², Masataka Fujita¹, Kazuya Sobue⁴, Kiyofumi Asai¹¹Dept of Mol Neurobiology, Nagoya City Univ, Nagoya, ²Dept of Pediatrics, Nagoya City Univ, Nagoya, ³Dept of Neurosurgery, Nagoya City Univ, Nagoya, ⁴Dept of Anesthesiology and Medical Crisis Management, Nagoya City Univ, Nagoya

In accordance with a high degree of spatial organization in the central nervous system, many central nervous system functions and disorders display regional specificities. Although astrocytes are supposed to make regional specificities of microenvironments around neurons, it is uncertain how astrocytes display region-specific properties. In this study, we have tried to identify the molecules, which are responsible for astroglial heterogeneity in the central nervous system. Frozen sections (6 μ m thick) were prepared from the cortex and striatum of male Wistar rats, and astrocytes were labeled using rapid immunohistochemical staining with GFAP antibodies and obtained by laser microdissection. One thousand astrocytes were dissected from cortex and striatum respectively, and then their RNAs were separately isolated and subjected to DNA microarray analysis. More than ten genes appeared to be differentially expressed by a factor greater than 2-fold between cortex and striatum. From the data of microarray analysis, we selected the several candidate genes that may be expressed higher in cortex than in striatum and tried to confirm their expression by immunohistochemical staining, RT-PCR, and in situ hybridization. A water channel protein, aquaporin 4 is one of the candidate genes, and it was also highly expressed in the cortical astrocytes using immunohistochemical staining and in vitro primary culture cells using immunocytochemical staining. These findings suggest higher expressions of aquaporin-4 may support higher excitability of neurons in cortex than that in striatum.

O2-4 Mechanism underlying gliotransmitter release from cultured astrocytes

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For much of the past century, astrocytes, the major glial cell type in the CNS, have been considered passive bystanders that merely provide support to neuronal networks. However, astrocytes are now recognized as active elements in the brain. Astrocytes sense and integrate synaptic activity and, depending on intracellular Ca^{2+} levels, release gliotransmitters (e.g. glutamate, ATP and D-serine) that have feedback actions on neurons. Recently, Jourdain et al. elucidated a pathway behind this astrocytic modulation of synapses by showing that ATP-dependent vesicular release of glutamate from astrocyte terminals acts on neuronal presynaptic NMDA receptors to increase synaptic efficacy. Although these reports provided the clues that astrocytes are the active components in the brain, they did not demonstrate the release of gliotransmitters from astrocytes directly. In other words, when the functions of astrocytes were determined, they did not consider whether astrocytes release gliotransmitters (ATP and glutamate) in modulation of synaptic strength, and no one has examined what kind of machinery is major one for releasing gliotransmitters at a certain state. Hence, it has not been clear whether astrocytes release gliotransmitters through single or multiple machineries of release at certain circumstances. To examine the release of gliotransmitters, such as ATP and glutamate, I used biosensor cells with patch-clamp technology, which can measure the release of ATP and/or glutamate from a single astrocyte. By this technology, I successfully measured ATP and/or glutamate at a single cell level. As a result, some of cultured astrocytes were shown not to release ATP after glutamate stimulation, suggesting heterogeneity in astrocyte population.

O2-6 Transporter-mediated uptake of nicotinamide is critical for its preventive effect on PARP-1-triggered astrocyte death

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[Objective] Poly(ADP-ribose) polymerase-1 (PARP-1) is a nuclear enzyme, when activated by DNA damage in brain cells following ischemia, trauma etc., that consumes nicotinamide adenine dinucleotide (NAD⁺) to form poly(ADP-ribose) (PAR) on acceptor proteins. Excessive PARP-1 activation depletes cellular NAD⁺ and eventually leads cells to death. Astrocyte death caused by PARP-1 activation was known to be prevented by addition of NAD⁺, whose extracellular levels were elevated under ischemia-like conditions. We previously reported that NAD⁺ was extensively metabolized by ecto-enzymes and taken up into cells as adenosine and/or nicotinamide. Nicotinamide is a PARP inhibitor and thus it might be an important molecule in NAD⁺-mediated prevention of cell death, but there is no available information on its transport mechanisms nevertheless its cellular incorporation is considered to be essential. The aim of this study was to investigate the characteristics for nicotinamide uptake into astrocytes, and whether its transporter-mediated uptake plays key role in preventing PARP-1-mediated astrocyte death.

[Methods] Primary cultured mouse astrocytes were cultured in EMEM and used for experiments at 20-40 DIV. Cell viability was determined with intracellular LDH activity. PAR accumulation was evaluated by immunocytochemistry. Uptake experiment for [¹⁴C]nicotinamide was performed using a HBSS as the transport buffer.

[Results & Discussion] N-methyl-N'-nitro-N-nitrosoguanidine (MNNG), an alkylating agent, triggered astrocyte death and PAR accumulation were completely inhibited by treatment of nicotinamide as the same as DPO, a representative PARP inhibitor. The uptake of nicotinamide was time-, temperature-, concentration- and pH-dependent, and was inhibited and stimulated by coadministration and pretreatment of N-methylnicotinamide, an organic cation transporter substrate, respectively. Furthermore, nicotinamide-induced prevention of astrocyte death was completely disappeared by cotreatment of N-methylnicotinamide. These findings suggest that nicotinamide has protective effect against PARP-1-induced astrocyte death and its transporter-mediated uptake via a H⁺/organic cation exchange system is critical for preventing PARP-1-triggered cell death.

O2-8 Effects of Ca^{2+} -ATPase inhibitors on hydrogen peroxide-induced thymidine incorporation into cultured astrocytes

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We previously found that hydrogen peroxide (H_2O_2) specifically incorporated thymidine, but not uridine, into morphologically differentiated cultured astrocytes pretreated with N^6 , 2'-O-dibutyryladenine 3',5'-cyclic monophosphate, a permeable analogue of cAMP, but not undifferentiated astrocytes and neurons. Because this effect was not suppressed by hydroxyurea, a replicative DNA synthesis inhibitor, it seems that it occurs for the purpose other than proliferation, including the repair of H_2O_2 -induced DNA injury. But the influence of intracellular Ca^{2+} on H_2O_2 -induced thymidine incorporation is unknown. We studied the involvement of Ca^{2+} -ATPase on H_2O_2 -induced thymidine incorporation into differentiated astrocytes.

Thymidine incorporation was measured in TCA-insoluble fraction by radioactive tracer analyses. Statistical analysis was conducted by one-way factorial ANOVA followed by contrast analysis.

H_2O_2 increased intracellular Ca^{2+} in differentiated astrocytes. H_2O_2 -induced thymidine incorporation into differentiated astrocytes was suppressed partially in the absence of extracellular Ca^{2+} . Next, we examined the effects of Ca^{2+} -ATPase inhibitors on H_2O_2 -induced thymidine incorporation into differentiated astrocytes. Thapsigargin and cyclopiazonic acid dose-dependently suppressed H_2O_2 -induced thymidine incorporation into differentiated astrocytes. And the effect of thapsigargin on H_2O_2 -induced thymidine incorporation was decreased in the absence of extracellular Ca^{2+} . On the other hand, 2,5-di-(tert-butyl)-1,4-hydroquinone caused further increase of H_2O_2 -induced thymidine incorporation into differentiated astrocytes.

These findings indicate that Ca^{2+} -ATPase inhibitors give different effects on H_2O_2 -induced thymidine incorporation into differentiated astrocytes, although the mechanisms between Ca^{2+} -ATPase inhibition and H_2O_2 -induced thymidine incorporation are unknown.

O2-5 Endothelial mPGES-1 regulates Ca^{2+} -dependent glutamate release from astrocyte via EP3

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Neuronal loss after recurrent seizures is caused by the neuronal hyperexcitation. In addition, a neuron-glia circuit has been shown to play an important role in neuronal excitotoxicity following such seizures. This study demonstrates this glia-neuron interaction is further regulated by venous endothelial cells contacting astrocytic endfeet. Kainic acid (KA) elicits repetitive seizures, and induces microsomal prostaglandin G synthase-1 (mPGES-1) in endothelia. The increase in astrocytic Ca^{2+} levels with oscillation, glutamate release and neuronal damage are shown in the hippocampal slice culture of wild type mouse after KA treatment, but significantly decreased in that of mPGES-1-deficient mouse. KA simultaneously increases the expression of PGE₂ receptor EP₃ on astrocytes, and EP₃ agonist increases the Ca^{2+} levels in astrocytes. Therefore, PGE₂ synthesized by endothelial mPGES-1 up-regulates intracellular Ca^{2+} levels in astrocytes via the EP₃ receptor, which increases glutamate release from astrocytes, leading to neuronal damage. Moreover, PGE₂ does not raise Ca^{2+} levels in neurons without astrocytes. These findings suggest that endothelial cells affect neuronal excitotoxicity by regulating Ca^{2+} -dependent glutamate release from astrocytes via inducible PGE₂.

O2-7 Glutamine transporter is a determinant of the vulnerability to oxidative stress in cultured rat neocortical astrocytes

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In the mammalian central nervous system, the excitatory amino acid neurotransmitter glutamate is supposed to be recycled through the glutamine (Gln)/glutamate cycle that involves different transporters including excitatory amino acid transporters, vesicular glutamate transporters and Gln transporter (GlnT) belonging to the system A transporter family. In addition to this prevailing scheme, we have previously shown that exposure to lipopolysaccharide (LPS) leads to marked down-regulation of the expression of GlnT responsible for the incorporation of extracellular Gln into intracellular spaces through the inhibition of its promoter activity in cultured rat neocortical astrocytes. In this study, we have attempted to elucidate the effect of down-regulation of GlnT by LPS on the vulnerability to oxidative stress in cultured astrocytes. Cultured astrocytes were at first incubated with LPS at different concentrations from 0.001 to 1 μ g/ml for 24 h, followed by exposure to hydrogen peroxide at 50 to 100 μ M for 2 h and subsequent determination of the cell viability with MTT reduction assay. Prior exposure to LPS significantly prevented astrocytes against the cytotoxicity of hydrogen peroxide in a concentration-dependent manner. Similarly significant prevention was not only seen in cells previously exposed to the GlnT inhibitor N-methylaminoisobutyric acid, but also found in cells cultured in the absence of extracellular Gln. Transient overexpression of GlnT significantly exacerbated the cytotoxicity of hydrogen peroxide in primary cultured astrocytes. In C6 glioma cells with stable overexpression of GlnT, moreover, similar exacerbation was found with the cytotoxicity of hydrogen peroxide, but not of 2,4-dinitrophenol or tunicamycin, compared to cells with the empty vector. These results suggest that GlnT may be a determinant of the vulnerability to oxidative stress through a mechanism related to the active transport of extracellular Gln across plasma membranes in cultured astrocytes.

O2-9 Behavioral changes of brain astrocytes in mice after forced exercise

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The aim of this study was to investigate whether physical exercise could induce astroglial proliferation in the striatum. Male C57BL/6 mice were studied in four experimental groups: (1) non-exercise control (housed for 3 days); (2) training control (only treadmill practice for 3 days); (3) 9 days exercise group; (4) 2 weeks exercise group. Animals were exercised on a treadmill at a speed of 5 m/min for 30 min each day, 5 days/week. Brain tissues of the exercised and non-exercised mice were processed for glial fibrillary acidic protein (GFAP) immunocytochemistry and Western blotting to evaluate regional astrocyte proliferation in the striatum and cortex. By using GFAP immunocytochemistry, we compared the density of astrocytes in the animals with or without exercise. In comparison to non-exercised animals, a significant increase in the number of astrocytes was observed in both cortex and striatum of mice exercised for 9 or 14 days. Western blotting analysis showed a significant increase in GFAP protein from striatum of exercised animals compared to the protein levels in non-exercised animals. In addition, there was no difference in both dopamine transporter and tyrosine hydroxylase protein levels in the striatum among the groups. These results indicate that physical exercise can induce astroglial proliferation in the striatum. The increased number of astroglia which play a role in inducing blood-brain-barrier properties and producing neurotrophic factors, may be coupled with angiogenesis and neurogenesis.

O3-1 Regulation of neural progenitor cells proliferation by p38 MAP kinase○Makoto Hamanoue¹, Ken Takamatsu¹¹Department of Physiology, Toho University School of Medicine, Tokyo, Japan

The p38 mitogen-activated protein kinase (MAPK) is induced in response to environmental stress. Although p38 MAPK has been implicated in diverse cellular processes, including cell proliferation, differentiation, and survival of differentiated cells in the central nervous system (CNS), the expression profile and roles of p38 MAPK in the developing brain remain largely unknown. In the present study, we demonstrate that p38 MAPK is expressed predominantly in nestin-positive cells in the cerebral cortex at embryonic day 10 (E10) brain and that expression of the protein decreases gradually during development. To investigate the roles of p38 MAPK in the embryonic brain, two selective p38 MAPK inhibitors, SB202190 and SB203580, were added to the primary neuronal cultures from E10 to E14 brains. After 7 days of exposure to these inhibitors but not SB202474, a negative analog of SB203580, numerous large neurospheres were present. MAPK inhibitors also selectively increased the growth rate of neural progenitor cells (NPCs) purified from a secondary neurosphere and the number of BrdU-positive NSCs. Furthermore, the fused protein that consist of protein transduction domain of the HIV/Tat protein and the dominant negative form of p38 MAPK was added to the culture, resulting in the increase of the number of NPCs. Thus, p38 MAPK may be an intrinsic negative regulator of NPC proliferation during early brain development.

O3-3 Requirement of reactive oxygen species in proliferation and survival of neural progenitor cells derived from embryonic hippocampus of mice○Koichi Kawada¹, Masanori Yoneyama¹, Kiyokazu Ogita¹¹Dept. of Pharmacol., Setsunan Univ., Osaka, Japan

Neural progenitor cells, defined by their ability to self-renew and differentiate into the three major cell types, neurons, astrocytes and oligodendrocytes, play an essential role in the development and maturation of the central nervous system. In this study, we evaluated the effects of scavengers for reactive oxygen species (ROS) on proliferative activity in neural progenitor cells of 15-days-old embryonic mice. Neural progenitor cells were prepared from the hippocampus of 15-days-old embryonic mice by primary culturing in DMEM/F12 medium with epidermal growth factor (EGF) and basic fibroblast growth factor (bFGF) for 9 days *in vitro* (DIV). After replating, these cells were further cultured for 6 DIV in the presence of EGF and bFGF. To evaluate the effects of ROS on proliferation in the progenitor cells, we used edaravone (brain protective agent), 4-hydroxy TEMPO (radical capture agent), apocynin (NADPH oxidase inhibitor) or (+)- α -tocopherol (antioxidant agent) during culturing neural progenitor cells for a period of 9-15 DIV. Treatments with edaravone or 4-hydroxy TEMPO resulted in a marked reduction in ROS production within the cells. MTT assay and ELISA for BrdU revealed that the reduction in ROS production by treatment with edaravone or 4-hydroxy TEMPO was markedly decreased in the surviving neurospheres cultured for 11-15 DIV. In addition, neurosphere assay revealed that edaravone and 4-hydroxy TEMPO led to a marked decrease in the number of neurospheres cultured for 11-15 DIV. Moreover, treatments with apocynin and (+)- α -tocopherol produced a decrease in the surviving neurospheres cultured for 13-15 DIV in a concentration-dependent manner. Nevertheless, LDH released into the medium was unaffected by any of these agents. Western blot analysis revealed that the levels of EGF receptor, Akt, and extracellular signal-regulated kinase had no change during cultures in the presence of any agents. These results suggest that ROS may require the proliferation and survival in neural progenitor cells of murine embryonic hippocampus.

O3-5 Slit-Robo signaling regulates neuroblast migration toward the olfactory bulb in the postnatal brain.○Naoko Kaneko¹, Oscar Marin², Yuki Hirota³, John Rubenstein³, Fujio Murakami⁴, Arturo Alvarez-Buylla⁵, Hideyuki Okano⁶, Marc Tessier-Lavigne⁶, Kazunobu Sawamoto¹¹Department of Developmental and Regenerative Biology, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan, ²Instituto de Neurociencias de Alicante, Consejo Superior de Investigaciones Científicas and Universidad Miguel Hernández, Spain, ³University of California San Francisco, USA, ⁴Graduate School of Frontier Bioscience, Osaka Univ., Osaka, Japan, ⁵Department of Physiology, Keio University School of Medicine, Japan, ⁶Genentech, USA

Neuroblasts are continuously generated by stem cells in the subventricular zone (SVZ) and migrate toward the olfactory bulb (OB) through the rostral migratory stream (RMS) throughout life. Neuroblasts migrate in elongated cell aggregates referred as chains surrounded by astrocytic processes forming glial tubes. Mechanisms regulating the directional neuroblast migration and the role of the surrounding astrocytes are largely unknown. Slit1 is a secreted protein that binds to its receptor Robo and functions as a chemorepellent in axon guidance and cell migration in the embryonic brain. In the adult brain, Slit1 is expressed in the neuroblasts in the RMS as well as in the septum, suggesting its cell-autonomous and non-cell autonomous functions in cell migration. To investigate the role of Slit-Robo signaling in migration of neuroblasts in the RMS, we used Slit1 knockout (Slit1^{-/-}) mice. Histological analyses revealed smaller OB and enlarged RMS in the Slit1^{-/-} mice. Robo2 immunoreactivity was detectable strongly in astrocytes and weakly in neuroblasts in the adult RMS, suggesting that neuroblast-derived-Slit1 could repel astrocytes. Consistently, astrocytes were frequently found intermingled with the chain of neuroblasts in the Slit1^{-/-} RMS. Time-lapse recording of neuroblasts in the RMS of the Slit1^{-/-} brain slices showed an approximately 40 % reduction in their migration speed. Similar migration defects were found in wild-type (WT) neuroblasts transplanted in the RMS of the Slit1^{-/-} brain slice and Slit1^{-/-} neuroblasts in the WT RMS. These results suggest that Slit-Robo signaling regulates the interaction between neuroblasts and astrocytes in the RMS, which contributes the fast migration of neuroblasts toward the OB.

O3-2 Modulation of proliferation and differentiation by GABAergic signaling in murine neural progenitor cells○Shusuke Ozawa¹, Masaki Fukui¹, Takeshi Takarada¹, Hideo Taniura¹, Noritaka Nakamichi¹, Yukio Yoneda¹¹Lab Mol Pharmacol, Kanazawa Univ Grad Sch Nat Sci Tech, Kanazawa, Japan

There is emerging evidence that endogenous factors regulate self-renewal capacity and multipotentiality to generate different neural lineages including neurons, astroglia and oligodendroglia in neural progenitor cells expressed in the developing and matured brains. In the present study, we have attempted to demonstrate the possible modulation by signals mediated by GABA receptors (GABAR) of cellular proliferation and differentiation in neural progenitor cells prepared from embryonic mice. Cells were collected from the lower cell layer after percoll density gradient centrifugation, followed by culturing in DMEM/F12 medium containing epidermal growth factor (EGF) for 10 days. The lower cell layer preparations were immunoreactive to the neural progenitor marker protein nestin, but neither to the neuronal marker protein MAP2 nor the astroglial marker protein GFAP, while *in vitro* culture of these cells resulted in the formation of round spheres with similar immunoreactivities within 10 days. Cells before culture expressed mRNA for α 1-5, β 1-3, γ 2,3 and δ subunits of ionotropic GABA_AR and for metabotropic GABA_B R1 and GABA_B R2 subunits, but not for α 6 and γ 1 subunits of GABA_AR. In undifferentiated cells cultured for 10 days, mRNA expression was seen for α 2-5, β 1,3 and γ 1-3 subunits of GABA_AR in addition to GABA_BR1 and GABA_BR2 subunits, but not for other GABA_AR subunits. A significant increase was induced in the size of neurospheres and MTT reduction in cells exposed to the GABA_AR agonist muscimol at 100 μ M for 10 consecutive days. The removal of EGF led to the initiation of spontaneous differentiation, whereas prior exposure to muscimol led a significant increase in the number of cells immunoreactive to GFAP with a concomitant decrease in that to MAP2 when determined 4 days after the removal of EGF. These results suggest that GABA_AR may be functionally expressed by undifferentiated neural progenitors to modulate proliferation for self-replication and differentiation into neuronal and astroglial lineages.

O3-4 Profiles of Irf1 highly expressed by neural progenitor cells of adult mouse hippocampus○Sayaka Maeda¹, Mami Watanabe¹, Yukary Nakamura¹, Hideo Taniura¹, Noritaka Nakamichi¹, Yukio Yoneda¹¹Lab Mol Pharmacol, Kanazawa Univ Grad Sch Nat Sci Tech, Kanazawa, Japan

The prevailing view is that adult neurogenesis occurs in the hippocampal dentate gyrus and subventricular zone even in matured brains. In our previous studies, neurospheres are similarly formed by clusters of neural progenitor cells under proliferation between hippocampi of adult and embryonic mice, whereas astroglial differentiation predominates over neuronal differentiation in neural progenitors of adult mouse hippocampus compared to those of embryonic mouse hippocampus. We have identified the gene differentially expressed in neurospheres between adult and embryonic mouse hippocampi as interferon-related developmental regulator-1 (Irf1). In this study, therefore, we have attempted to demonstrate the functionality of Irf1 in neural progenitor cells. In neurospheres of adult mouse hippocampus, more than 7-fold higher expression was seen for Irf1 mRNA than in embryonic mouse hippocampus on semi-quantitative RT-PCR analysis. To analyze the functionality of Irf1, we used the mouse embryonic carcinoma P19 cells endowed to differentiate into neuronal and astroglial cells when cultured in the presence of ATRA. Cells were cultured in α MEM containing 5% FBS with 0.5 μ M ATRA for 4 days, followed by further culture in the absence of ATRA for an additional 12 days. Marked but transient expression was seen in MAP2 mRNA on Day 6 to 8, while expression of Irf1 mRNA was drastically increased in line with GFAP mRNA expression on Day 8 to 10. Cells were then cultured in the presence of ATRA for 4 days, followed by transfection with the Irf1 expression vector using the calcium phosphate method. In these P19 cells with transient overexpression of Irf1, a significant decrease was seen in MAP2 mRNA expression and numbers of cells immunoreactive for MAP2. These results suggest that spontaneous cellular differentiation would undergo into astroglia rather than neurons through a mechanism relevant to constitutive expression of Irf1 in hippocampal neural progenitor cells during neurogenesis in adult mouse brains.

O3-6 A rapid method for quantitative and qualitative analysis of the adult neurogenesis by using the flow cytometry○Takashi Namba¹, Tatsunori Seki², Shigeo Uchino¹, Shinichi Kohsaka¹¹Department of Neurochemistry, National Institute of Neuroscience, ²Department of Anatomy, Juntendo University School of Medicine

Neurogenesis in adult brain occurs in various mammalian species including human. In hippocampus, neurogenesis persists throughout life and plays an important role in the hippocampal cognitive functions including spatial learning and memory. Neurogenesis is usually quantified by BrdU labeling and subsequent immunohistochemical analysis using various cell-type specific antibodies. To evaluate neurogenesis more easily and rapidly, we developed a novel method using a fluorescent activated cell sorting (FACS). Recently, we found that neurogenesis was enhanced by memantine, an uncompetitive NMDA receptor antagonist and clinically used for Alzheimer's disease. We intraperitoneally injected with memantine (50 mg/kg body weight) in 3 months old mice. At 10 days after the injection we dissected the hippocampus and dissociated the cells using liberase (dispase/collagenase cocktail), and the newly generated immature neurons expressing polysialylated neural cell adhesion molecule (PSA-NCAM) were isolated and quantified by FACS using anti-PSA-NCAM antibody. Our results clearly showed that the number of the PSA-NCAM-positive immature neurons in the memantine-treated mice increased by 2.6-fold compared with that in the control mice. This value is almost similar to that obtained from the count of the PSA-NCAM-positive cells in the hippocampus using the immunohistochemical method. Furthermore, using RT-PCR and immunocytochemistry we confirmed the expression of the marker genes of the immature neurons such as NeuroD, Doublecortin and Neurogenin 2 in the isolated PSA-NCAM-positive cells. These results indicate that the method using FACS and anti-PSA-NCAM antibody will facilitate the quantitative evaluation of neurogenesis and allow us to investigate the expression profile of genes in the isolated cells.

O3-7 Nicotine acts differently depending on the differentiated level of the neural cells.

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Effects of nicotine on undifferentiated hippocampal neural cells were studied with use of HC2S2 cells to compare with the results obtained from our previous experiments on differentiated HC2S2 cells. Cells were stimulated with 0.5 or 1 μM nicotine, 1 nM estradiol, 1 μM nicotine + 1 nM estradiol or 100 ng/ml IGF-1. Then, expressions of nicotinic receptor alpha7 subunit and IGF-1 mRNAs were examined by the real time PCR assay. There was slight alpha7 mRNA up-regulation by only higher concentration of nicotine, being different from the results in differentiated cells. The up-regulation of alpha7 subunit by estradiol was remained at the same level to the differentiated cells, while there was no IGF-1-induced alpha7 up-regulation. As for the effect of these stimulations on IGF-1 mRNA expression, nicotine not only failed to induce the expression, but also inhibited the slight increase of estrogen-induced IGF-1 expression. IGF-1-induced increase of IGF-1 mRNA was definitely observed in undifferentiated cells as in differentiated ones. Effects of these stimulations on the cell death rate were also compared between differentiated and undifferentiated HC2S2 cells. It was concluded that nicotine acts differently depending on the differentiated level of the neural cells.

O3-9 GABAergic neurons in the ventral thalamus are derived from Olig2+ cells in the area surrounding the zona limitans intrathalamica

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The adult ventral thalamus is mostly composed of GABAergic neurons while the dorsal thalamus is composed of excitatory neurons in the rodent diencephalon, with a few exceptions. The mechanisms that regulate this segregation is totally unknown. In order to understand this mechanism, we investigated developmental profiles of the dorsal and ventral thalamus in the mouse. BrdU pulse-labeling study demonstrated that most of the neurons in the ventral thalamus undergo final division at E10.5 or E11.5 whereas those in the dorsal thalamus are generated at E12.5 or E13.5 (or later). We next performed lineage tracing study by using Olig3-LacZ and Olig2-CreER knockin mice. Olig3-LacZ knockin mice can be used for short-term lineage tracing as LacZ has a relatively long half life. LacZ+ cells were distributed in the dorsal thalamus but no or few in the ventral thalamus in the knockin mice. Olig2 was expressed in the ventricular zone surrounding the zona limitans intrathalamica at middle fetal stages such as E10.5 to E12.5. Olig2-CreER mice were crossed to Z/EG or Rosa26-EGFP reporter mice and tamoxifen was administered to pregnant dams to induce Cre-mediated recombination. Olig2 lineage EGFP+ cells were widely distributed in ventral thalamus at the E17.5 while EGFP+ cells were localized near the ventricular side at E14.5, following E10.5 tamoxifen treatment. A few reporter-expressing cells were observed in the caudal dorsal thalamus. Most of EGFP+ cells in the ventral thalamus expressing GAD65/67 mRNA and therefore Olig2 lineage ventral thalamic cells are inhibitory neurons. The present study suggested that ventral thalamic neurons were generated in the Olig2 expressing domain near the ZLI and migrated laterally to populate their destinations. In addition, place and timing of neuron generation of the ventral thalamus were mostly separated from those of the dorsal thalamus. These differences may be involved in mechanisms regulating the neuron segregation in this area.

O4-2 Functional analysis of a novel ER stress transducer OASIS in brains.

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Various stresses disturb Endoplasmic Reticulum (ER) function and provoke the accumulation of unfolded proteins in the ER lumen. This condition is termed ER stress. The three major ER stress transducers IRE1, PERK, and ATF6 activate during ER stress and transduce Unfolded Protein Response (UPR). We previously identified OASIS (Old Astrocyte Specifically Induced Substance), a novel ER stress transducer and structurally homologous to ATF6, expresses in cultured astrocytes and prevents from cell death induced by ER stress. OASIS is bZIP transcription factor of the CREB/ATF family with a transmembrane domain that allows it to associate with the ER. The molecule is cleaved at the membrane in response to ER stress and its cleaved N-terminal cytoplasmic domain, which contains the bZIP domain, translocates into the nucleus and activates the transcription of target genes. We generated OASIS deficient mice to analyze in vivo functions of OASIS. OASIS^{-/-} mice were born at the expected Mendelian ratios, viable, and had no histological evidence of internal organs dysfunctions, but exhibited growth retardation. In the brain, the cell number of GFAP-positive astrocytes and MAPII-positive neurons were almost equal to those in WT mice, and abnormal morphological changes were not observed, indicating that brain development is not affected in OASIS^{-/-} mice. We next investigated the sensitivities to brain damages by ischemia in OASIS^{-/-} mice. The left middle cerebral artery (MCA) was occluded, and after 24 h, brain sections were stained with TTC. The infarction area observed in OASIS^{-/-} mice was larger than those in WT mice. When cultured cells from OASIS^{-/-} were exposed to ER stress, cell death was accelerated compared with cultured WT cells. These results suggest that deletion of OASIS gene leads to vulnerability to brain damages induced by ER stress. Currently, we are trying to clarify the molecular mechanisms of the vulnerability in OASIS^{-/-} cells including the identification of OASIS target genes.

O3-8 Isolation and characterization of astrocyte precursor cells from the developing mouse cerebellum

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There are three types of astrocytes in the murine cerebellar cortex. One is the protoplasmic astrocyte in the granule layer, one is the fibrous astrocyte in the white matter, and the other is the Bergmann glia which has its cell body near the Purkinje cells and extends its radial processes towards the surface of the cerebellum. It remains unclear how these astrocytes are generated during development. Here we report the isolation of astrocyte precursor cells (APCs) from the developing mouse cerebellum. Cerebella from early postnatal mice were digested with papain, and the dissociated cells were fractionated by a step gradient of 35% and 60% Percoll. The small cell fraction was comprised mainly of granule cell precursors, while the large cell fraction contained the GFAP-positive cells and the GFAP-weakly-positive cells. We collected the large cell fraction and then removed the microglial cells by negative selection with the anti-mouse macrophage antibodies. We then removed the GFAP-positive cells and collected the GFAP-weakly-positive cells by positive selection with the A2B5 antibodies, as most of the GFAP-positive cells didn't adhere to the A2B5 panning dish. Most (> 95%) of the cells thus obtained were GFAP-weakly-positive. To determine what signals induce these cells to proliferate, we tried various signaling molecules under serum-free conditions. In the presence of both basic fibroblast growth factor (bFGF) and bone morphogenetic protein 4 (BMP4), many cells incorporated BrdU, and most of these BrdU-positive cells were GFAP weakly-positive, suggesting that the combination of bFGF and BMP4 was essential for their proliferation and the maintenance of their undifferentiated state. When BMP4 or bFGF was withdrawn from the culture, many of these cells underwent apoptosis, suggesting these factors were also essential for their survival. When these cells were treated with ciliary neurotrophic factor (CNTF) or leukemia factor (LIF), the proportion of GFAP-positive cells increased dramatically, suggesting these factors induce these cells to differentiate into GFAP-positive astrocytes. These cells (APCs) may be useful for the elucidation of the mechanism for the generation of various astrocytes during cerebellar development.

O4-1 Insensitivity to NMDA in cortical neurons

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Although the excitatory neurotransmitter glutamate (Glu) is ubiquitously distributed in the mammalian central nervous system, Glu could elicit different actions on the functionality and integrity of discrete brain structures in a particular situation. In this study, we have attempted to elucidate the mechanisms underlying signaling processes of Glu in cultured neurons derived from discrete brain structures. Rat neocortical and hippocampal neurons were individually cultured for 9 days in vitro (DIV), followed by washing and exposure to N-methyl-D-aspartate (NMDA), H2O2 or A23187 for 1 h and determination of cellular viability by MTT reduction or LDH release assay 24 h later. Cells were also exposed to 2,4-dinitrophenol or tunicamycin for 24 h for immediate determination of the viability. Exposure to NMDA significantly decreased the number of living cells in hippocampal neurons, without affecting that in cortical neurons. However, all other cytotoxins used induced similarly severe neuronal death in a manner irrespective of brain structures. Neurons cultured for 9 DIV were exposed to NMDA for 1 h, followed by staining with propidium iodide (PI) and Hoechst 33342 for DNA at different time windows. The number of cells with aggregated nuclei was significantly increased from 7 to 24 h after the exposure to NMDA with a concomitant increase in PI-positive cells at 24 h in cultured hippocampal neurons, but NMDA failed to significantly affect the cell viability in cortical neurons. Cells were loaded with rhodamine 123, followed by exposure to NMDA and subsequent fluorescence imaging to determine mitochondrial depolarization on confocal microscopy. Fluorescence intensity of rhodamine 123 was significantly increased in hippocampal neurons exposed to NMDA, while no marked increase was seen in the fluorescence intensity in cortical neurons. Our data cited above suggest that cortical neurons may be selectively less sensitive to the cytotoxicity of NMDA than hippocampal neurons through a mechanism relevant to the destruction of mitochondrial membrane potentials.

O4-3 Suppression of HRD1-mediated protein degradation causes amyloid precursor protein accumulation and β-amyloid generation with endoplasmic reticulum stress and apoptosis

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Endoplasmic reticulum-associated degradation (ERAD) is a mechanism by which proteins synthesized in the ER are retrotranslocated from the ER to the cytosol and degraded by the ubiquitin-proteasome pathway. We have identified human HRD1, which acts as a ubiquitin ligase in ERAD. Amyloid precursor protein (APP) is processed to β-amyloid (Aβ) peptides, which are deposited in the brain in Alzheimer's disease. In the present study, we found that HRD1 was colocalized with APP in brain neurons. HRD1 interacted with APP through the proline-rich region of HRD1 and promoted ubiquitination and degradation of APP, resulting in decreased generation of Aβ. Furthermore, suppression of HRD1 expression induced the accumulation of APP, which led to increased production of Aβ with ER stress and apoptosis. Immunohistochemical analysis revealed that HRD1 was involved in the aggregates formation of APP. These results suggest that HRD1 prevents APP accumulation causing Aβ generation and ER stress in the ER and promotes proteasomal degradation and aggregates formation through ERAD.

O4-4 Necdin controls p53 acetylation via Sirt1 in cortical neurons○Koichi Hasegawa¹, Kazuaki Yoshikawa¹¹Laboratory of Regulation of Neuronal Development, Institute for Protein Research, Osaka University

The NAD-dependent protein deacetylase Sirt1 is essential for stress control in various cells. The tumor suppressor protein p53 induces neuronal apoptosis under various kinds of stresses, and its function is regulated through posttranslational modifications such as phosphorylation and acetylation. Sirt1 deacetylates p53 and attenuates p53-mediated transcription of genes that are involved in apoptosis. The acetylation status of p53 is mainly regulated by Sirt1, which plays a pivotal role in lifespan extension and cell survival. However, little is known about the regulation of p53 acetylation by Sirt1 in neurons. Necdin is expressed in postmitotic neurons and regulates neuronal differentiation and survival. Necdin interacts with p53 and represses p53-dependent apoptosis. Here we demonstrate that necdin modulates p53 deacetylation through its interaction with Sirt1 to suppress neuronal apoptosis. Immunohistochemical analysis revealed that necdin was coexpressed with Sirt1 in neurons of mouse embryonic forebrain. Coimmunoprecipitation analysis demonstrated that necdin formed a ternary complex with p53 and Sirt1. The acetylation status of p53 regulated by Sirt1 in cDNA-transfected cells lysates was analyzed by Western blotting with anti-acetyl lysine antibody. When necdin was coexpressed with Sirt1 and p53, necdin increased the amount of Sirt1 coprecipitated with p53 and potentiated its deacetylation. A necdin binding-defective p53 mutant that maintains the Sirt1 binding activity showed no such potentiation, indicating that necdin enhances the accessibility of Sirt1 to p53. In primary cortical neurons prepared from necdin-deficient mouse embryos, the number of apoptotic cells and acetylated p53 levels were significantly increased in response to DNA damage. Resveratrol, a Sirt1 activator, reduced acetylated p53 levels and apoptosis in wild-type neurons, but not in necdin-deficient neurons. RNAi-induced knockdown of Sirt1 increased acetylated p53 levels and apoptosis in wild-type neurons, but these were not affected in necdin-deficient neurons. These results indicate that necdin represses neuronal apoptosis by potentiating Sirt1-mediated p53 deacetylation.

O4-6 Functional P2X7 receptors are expressed by cultured neurons and involved in ATP-induced neuronal death○Tsunetoshi Nakatani¹, Hiroto Okuda¹, Reina Shirayama¹, Mayuka Nakanishi¹, Kaori Yamatani¹, Kazuki Nagasawa¹, Sadaki Fujimoto¹¹Dept. of Environ. Biochem., Kyoto Pharm. Univ., Kyoto, Japan

[Objective] ATP and zinc are important neurotransmitters. Under pathological conditions, such as ischemia, trauma etc., however, excess amount of them were released from dead cells or by channel/transporter and eventually induce neuronal death. Generally, ATP-induced neuronal death is considered to result from oxidative stress caused by activation of P2X7 receptors (P2X7Rs) expressed by glial cells. Nevertheless neurons are reported to express P2X7Rs or P2X7R-like proteins, their functional role in ATP-induced neuronal death is unknown. Zinc, on the other hand, killed neurons by activation of neuronal ROS generation system NADPH oxidase, and thus there is a possibility that zinc might be involved in ATP-induced neuronal death. The aim of this study was to clarify whether cultured neurons expressed functional P2X7R, and its activation and zinc played role in ATP-induced neuronal death using pure neuron cultures.

[Methods] Primary cultured rat cortical neurons were cultured in B-27-supplemented EMEM and their purity was 90 or more %. Cell viability was determined by an LDH assay. mRNA and protein expressions of P2X7R were confirmed by RT-PCR or real time-PCR and western blot, respectively. P2X7R function was evaluated by YO-PRO-1 uptake.

[Results & Discussion] Administration of ATP and BzATP caused neuronal death, and IC₅₀ of the former was about 30-fold greater than that of the latter. The ATP-induced death was prevented by treatment with apyrase, but not ARL67156, an apyrase inhibitor, and was completely abolished by a selective P2X7R antagonist, oxATP. P2X7R expression in neurons was confirmed at mRNA and protein level, and ATP-treated neurons showed oxATP-inhibitable YO-PRO-1 uptake. Treatment with N-acetyl-L-cysteine, an antioxidant, prevented ATP-induced neuronal death, but neither NADPH oxidase inhibitors (apocynin and AEBSP) nor zinc chelators (TPEN and CaEDTA) had any effect. Together, these findings provide the first evidence that cultured rat neurons express functional P2X7R and its activation induces neuronal death accompanied with ROS generation, and suggest that zinc and NADPH oxidase have no or negligible roles in this cascade.

O4-8 Functional analysis of SFAP75/Norbin in CHO and PC12 cells○Yasunori Tokuhara¹, Manabu Sakai¹, Satoshi Shibata¹, Yoshiharu Ohoka², Shinobu Inagaki¹¹School of Allied Health Science, Faculty of Medicine, Osaka University,²Laboratory of Biodefense Research, Tokushima Bunri University Faculty of Pharmaceutical Science at Kagawa Campus, Kagawa, Japan

Our laboratory has identified Semaphorin 4C (previously called M-SemaF) and Semaphorin 4D (previously called M-SemaG) from mouse brain. Semaphorin 4C (Sema 4C) is specifically expressed in both embryonic and adult neuronal tissue, suggesting that Sema4C function such as directing axon pathfinding, synapse formation or synapse maintenance. In other times, we identified SFAP75 as an associating protein with a cytoplasmic domain of Sema 4C. SFAP75 is especially enriched in adult brain rather than immature one. SFAP75 is especially turned out to be the same as a Norbin, which was identified in rat hippocampal slices in screen for genes related to tetraethyl ammonium-long term potentiation and shown to promote neurite extension in Neur2a cells. Moreover, SFAP75/Norbin appear to be same as Neurocondrin, which is identified as a molecule relating chondrocyte differentiation. In late years, further research have been reported that Neurocondrin is a negative regulator of Ca²⁺/calmodulin-dependent protein kinase II phosphorylation and involved in spatial learning process and epileptic seizure but not for differentiation or neurite outgrowth of the neuron. In this way, SFAP75/Norbin may play an important role in neuronal function but is still unknown about the detailed molecular mechanisms and physiological role. Now, in order to clarify the mode of action of SFAP75/Norbin, we have established SFAP75/Norbin stable expressing CHO(Chinese hamster ovary) cell line and characterized the function of SFAP75/Norbin. When we examined cellular proliferative potential and adhesive capacity, conspicuous difference was not observed between CHO/SFAP75 and control CHO cells. Overexpression of SFAP75/Norbin protected cells from apoptosis induced by serum depletion or H₂O₂ treatment. Furthermore we performed specific knockdown of SFAP75/Norbin by RNA interference (RNAi) in PC 12 cells, and found that apoptosis in these cells occurred more effectively than control cells. These results suggested that SFAP75/Norbin function as anti-apoptotic regulatory factor in neuronal cells.

O4-5 Involvement of Na⁺/Ca²⁺ exchanger in nitric oxide-induced cytotoxicity in SH-SY5Y cells.○Tetsuaki Nashida¹, Toshiyuki Kawasaki¹, Tatsuya Kitao¹, Sayoko Fukuda¹, Yukio Ago¹, Kazuhiro Takuma¹, Toshio Matsuda^{1,2}¹Lab. Medicinal Pharmacol., Grad. Sch. Pharmaceut. Sci., Osaka Univ. Osaka, Japan,²Center For Child Mental Dev., Grad. Sch. Med., Osaka Univ. Osaka, Japan

The Na⁺/Ca²⁺ exchanger (NCX) is involved in regulation of intracellular calcium concentration by two different ion transport modes such as the forward mode calcium extrusion or the reverse mode calcium influx. Previous studies show that nitric oxide (NO) and cyclic GMP stimulate NCX activity in neuronal preparations and cultured astrocytes, and that NCX is involved in NO-induced cytotoxicity in microglia. Although NO is known to play a physiological role in neuronal cell signaling, it at higher concentrations may cause neuronal cell death, related to neurodegenerative disorders such as ischemia, Parkinson's disease and Alzheimer disease. Based on our hypothesis that NCX may be involved in NO-related pathology, the present study examined the role of NCX in NO-induced dopaminergic cell injury. We used human neuroblastoma SH-SY5Y cells, which are often used for pathophysiological studies of Parkinson's disease. The NO donor, sodium nitroprusside (SNP) induced reactive oxygen species (ROS) production and apoptosis-like cell death. These effects were attenuated by SEA0400, a specific NCX inhibitor. SNP-induced ROS production and cell death also inhibited by ERK and p38 MAP kinase inhibitors, suggesting the crucial roles of these MAP kinases in this injury. SEA0400 inhibited SNP-induced phosphorylation of ERK and p38 MAP kinase. This finding suggests that NCX act as a regulator of NO-induced cytotoxicity, at least, an upstream signal to NO-induced MAPK phosphorylation. BAPTA-AM, a membrane-permeable Ca²⁺ chelator, and removal of extracellular Ca²⁺ attenuated SNP-induced production of ROS, activation of ERK and p38 MAP kinase, and cell death. SNP increased the intracellular Ca²⁺ levels, and this effect was blocked by SEA0400. These results suggest that Ca²⁺ influx via NCX plays a key role in NO-induced cytotoxicity in SH-SY5Y cells.

O4-7 Characterization of specific binding of polyglutamine aggregate inhibitors to the expanded polyglutamine stretch using surface plasmon resonance○Yuma Okamoto^{1,2}, Yoshitaka Nagai¹, Nobuhiro Fujikake¹, Helena Akiko Popiel¹,Tatsushi Toda¹, Takashi Inui²¹Div. of Clin. Genet., Dep. of Med. Genet., Osaka Univ. Grad. Sch. of Med., Suita,²Dep. of Mol. Biol. and Cell Inform., Div. of Appl. Life Sci., Grad. Sch. of Life and Envi. Sci., Osaka Pref. Univ., Sakai, Japan

The polyglutamine (polyQ) diseases are a class of inherited neurodegenerative diseases including Huntington's disease and various types of spinocerebellar ataxia, which are caused by abnormal expansions of the polyQ stretch within various proteins. The expanded polyQ proteins are prone to change their conformations and to aggregate, and eventually cause neurodegeneration. Although screening for polyQ aggregation inhibitor chemicals is extensively being performed so far, common false-positive hits derived from various chemical screenings have also been reported to inhibit protein aggregation. Therefore, it is indispensable to exclude such non-specific inhibitors for developing therapies for the polyQ diseases. In this study, we employed surface plasmon resonance (SPR) to characterize binding specificity of polyQ aggregate inhibitors to the expanded polyQ stretch. SPR analysis detected the specific binding of polyQ binding peptide 1 (QBP1) to the expanded polyQ stretch (K_D = 5.7 μM), and the non-specific binding of Congo red to the polyQ proteins regardless of the polyQ-length. Furthermore, QBP1 inhibits the toxic conformational transition of the expanded polyQ protein, while Congo red does not. These results imply that specific binding to the expanded polyQ stretch plays a crucial role for inhibition of its toxic conformational transition. We also show that binding affinity of polyQ aggregate inhibitors to the expanded polyQ stretch correlates with their inhibitory effects on polyQ aggregation. We therefore conclude that SPR is a useful technique for screening for specific polyQ aggregate inhibitors as promising therapeutic candidates for the currently untreatable polyQ diseases.

O4-9 The mechanism of neogenin induced neuronal cell death○Yuki Fujita¹, Junko Taniguchi², Masanori Uchikawa¹, Mitsuharu Endo¹, Katsuhiko Hata¹, Takekazu Kubo¹, Toshihide Yamashita^{1,2}¹Department of Molecular Neuroscience, Graduate School of Medicine, OsakaUniversity, ²Department of Neurobiology, Graduate School of Medicine, ChibaUniversity, ³Laboratory for Developmental Biology, Graduate School of Frontier Biosciences, Osaka University

The repulsive guidance molecule (RGM) is originally identified as a membrane-bound protein that does not share significant homology with any other known proteins. RGM is involved in both repulsive properties and the ability to induce collapse of the growth cone in the chick retinotectal system. Recently, neogenin was identified as an RGM receptor. In the ligand-free state, neogenin induces apoptosis. However the signal transduction mechanism is not completely understood. In this study, we identified the serine/threonine kinase death associated protein kinase (DAP-kinase) to be an interactor of neogenin. DAP-kinase is a crucial intracellular protein that mediates cell death via its serine/threonine kinase activity. Here we show that DAP-kinase is required for the proapoptotic activity of neogenin in vitro and in vivo. To examine whether DAP-kinase is involved in neogenin-induced cell death, we analyzed cell death in neural tubes of chick embryos. We electroporated neogenin expression vectors with or without dominant negative form of DAP-kinase (DAPK-d/n) in HH stage 10 chick embryos. In the neogenin electroporated side, there was an increase in the number of TUNEL-positive cells whereas in the neogenin and DAP-kinase co-electroporated side, resulted in the decrease of the TUNEL-positive cells. Furthermore, we examined RGM functions as a cell survival factor to counteract neogenin proapoptotic activity. When RGM was reduced by RGM siRNA, the number of TUNEL-positive cells was increased in the chick neural tube. Then we examined whether DAP-kinase is associated with the apoptosis-inducing effect of the RGM silencing, the number of the TUNEL-positive cells in the RGM siRNA and DAPK-d/n co-electroporated side was decreased. These results suggest that the activity of DAP-kinase is required for neogenin induced cell death in the developing chick neural tube.

O5-1 Associations of candidate gene G72 polymorphisms with schizophrenia in a Japanese population

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Recent reports indicate that G72 is one of the most-replicated genes implicated in susceptibility to schizophrenia. Abnormalities of neurotransmission, glutamatergic systems via N-methyl-D-aspartate (NMDA) receptor, have been involved as the pathogenesis of schizophrenia. The modulation of NMDA function has been considered to be mediated by D-amino acid oxidase (DAO), which oxidizes D-serine. As G72 acts as activator of the DAO, G72 is referred to as D-amino acid oxidase activator (DAOA). The aim of this study is to investigate association between G72 and schizophrenia using eight single nucleotide polymorphisms, which have obtained significant associations in previous studies, between 1774 patients with schizophrenia and 2094 healthy controls in a Japanese population. We revealed significant association of each allele, M22/rs778293, M23/rs3918342 and M24/rs1421292, and genotype of M22/rs778293 with schizophrenia. Our results indicate that the minor alleles in these SNP could increase the risk of schizophrenia. There were no associations of allele or genotype in other five SNPs, while some haplotype with the minor allele at M15/rs2391191 and the major allele at M19/rs778294 indicate the possibility of a protective role in the etiology of schizophrenia. We replicated the association between G72 and schizophrenia in a Japanese population. Thus, G72 is likely to be related to the development of schizophrenia in various ethnics.

O5-3 Functional analysis of Dysbindin, one of schizophrenia susceptibility genes

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Dysbindin has been reported as one of the most promising susceptibility genes for schizophrenia in several independent linkage studies. Recent research indicates that the expression level of the dysbindin gene is reduced in the brains of patients with schizophrenia. Furthermore, *in vitro* assay, it has been reported that Dysbindin is linked to the PI3K-Akt signaling pathway. Here we report that Dysbindin is likely to participate in other intracellular signal transduction pathway too. These results give rise to the possibility that Dysbindin may play a role in the onset of schizophrenia via a modulation of signal transduction cascades.

O5-5 Phosphorylation by Erk regulates interaction between DISC1 and Kinesin-1

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Schizophrenia is a severe psychiatric disorder with lifelong disability. Although the causes of schizophrenia remain essentially unknown, it has been widely reported that schizophrenia has high inheritance, indicating the existence of genetic risk factors. *Disrupted-In-Schizophrenia 1* (DISC1) is a candidate gene for susceptibility to schizophrenia. We have previously found that DISC1 links Kinesin-1 to NUDEL/LIS1/14-3-3 complex or Grb2 and regulates their transport to axon as a cargo receptor (Taya et al., 2007, Shinoda et al., 2007). However, it remains unclear how the association between DISC1 and its interacting molecules are regulated. Here, we found that DISC1 was phosphorylated by ERK. The phosphorylation of DISC1 disrupted its interaction with Kinesin-1. We propose that ERK inhibits the DISC1/Kinesin-1 complex formation presumably through the phosphorylation of DISC1, and thereby releases the cargo molecules from Kinesin-1.

O5-2 Association between PNPO and schizophrenia in the Japanese population

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Backgrounds: Accumulating evidence suggests that both homocysteine metabolism and monoaminergic neurotransmitter systems are important in schizophrenia pathology. We hypothesized that the gene PNPO (pyridoxine 5'-phosphatase oxidase gene) might be a candidate for susceptibility to schizophrenia because PNPO encodes pyridoxamine 5'-phosphate oxidase (EC 1.4.3.5), a rate-limiting enzyme in pyridoxal 5'-phosphate (PLP, vitaminB₆ synthesis. PLP is metabolically-active form of vitamin B6 and thus, is required as a co-factor for enzymes involved in both homocysteine metabolism and synthesis of neurotransmitters such as catecholamine. **Methods:** We examined 8 single nucleotide polymorphisms (SNPs) in PNPO and its 5'-flanking regions in 359 schizophrenia patients diagnosed with DSM-IV criteria (228 males and 131 females, mean age; 51.1 ± 13.6 years, clinical symptoms evaluated using Brief Psychiatric Rating Scale scores, BPRS; mean 39.1 ± 10.3, mean age at onset; 25.3 ± 7.5 years, and mean medication equivalent to chlorpromazine; 751.1 ± 523.4 mg/day) and 582 control subjects (332 males and 250 females, mean age; 49.9 ± 12.3 years). The genetic association studies were approved by institutional ethics committees and written informed consent to participate in those studies was obtained from all participating subjects. **Results:** Four marker regions of PNPO showed significant levels of allelic associations with schizophrenia (the highest was rs2325751, P = 0.004). In addition, the haplotype case-control study revealed a significant association (permutation P < 0.00001) between PNPO and schizophrenia. No correlations were detected between PNPO genotypes and BPRS scores, chlorpromazine equivalent amounts of antipsychotics. **Conclusion:** These findings suggest that variations in PNPO may contribute to overall genetic risk for schizophrenia in the Japanese population.

O5-4 Identification of the AP-3 complex as a novel Dysbindin-interacting molecule

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Schizophrenia is a complex mental disorder with fairly high heritability. Dysbindin (DTNBP1: dystrobrevin binding protein 1) gene is a susceptibility gene for schizophrenia that was identified by family-based association analysis. Recent studies revealed that dysbindin is a subunit of the biogenesis of lysosome-related organelles complex-1 (BLOC-1) and is required to transport specific proteins from endosome to lysosome related organelles (LROs). However the molecular functions of dysbindin are largely unknown. To investigate the functions of dysbindin, we isolated dysbindin-interacting molecules from rat brain lysate by affinity column chromatography, and determined their molecular identity by MALDI-TOF MS and/or a combination of HPLC and tandem mass spectrometry (LC-MS/MS). Several proteins involved in membrane budding and fusion, including the AP-3 complex, were identified as dysbindin-interacting proteins. Dysbindin formed complex with the AP-3 complex *in vivo*. Dysbindin directly interacted with μ subunit of the AP-3 complex *in vitro*. In primary cultured rat hippocampal neurons, dysbindin was partially co-localized with the AP-3 complex in pre-synaptic terminal and axonal growth cones. These results suggest that dysbindin participates in the protein transport pathway via the direct interaction with μ subunit of the AP-3 complex.

O5-6 Neonatal exposure to neuregulin-1 β 1 potentiates MK-801 sensitivity in locomotion and c-fos expression in adult mice

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Neuregulin-1 (NRG1) is identified as a susceptibility gene for schizophrenia and knockout mouse studies indicate the deficiency of NRG1 signaling is associated with schizophrenia pathology. NRG1 β 1 is the isoform mainly expressed in the central nervous system. Using a recombinant protein for the EGF-like domain of NRG1 β 1 (referred as "rNRG1 β 1"), we attempted to establish a model animal for schizophrenia. We subcutaneously injected rNRG1 β 1 (1 mg/kg) to neonatal mice (P2-P10) to trigger ErbB4 signaling in the brain and examined behavioral and neurochemical consequences at the adult stage. As NRG1/ErbB4 signaling is implicated in glutamatergic synapse development, we assessed the sensitivity of rNRG1 β 1-treated mice to an NMDA receptor blocker, MK-801. Following MK-801 administration, induction of locomotor activity and c-fos expression was compared between rNRG1 β 1-treated and vehicle-treated mice. rNRG1 β 1-treated mice showed a greater response in locomotor activity. An increase in c-fos expression was also marked in medial prefrontal cortex and nucleus accumbens of rNRG1 β 1-treated mice. In contrast, NRG1 β 1-treated mice exhibited a normal reactivity to methamphetamine in locomotor induction. Thus, these results suggest that perturbation of NRG1-signaling during development persistently alters NMDA receptor function *in vivo*.

O5-7 Neonatal exposure to epidermal growth factor potentiates dopamine D2 receptor sensitivity and influences GABAergic activity in the basal ganglia○Hidekazu Sotoyama¹, Hiroyuki Nawa¹¹Dept. of Mol. Neurobiol., Niigata Univ.

Epidermal growth factor (EGF) and its structurally related peptides bind to EGF receptor (ErbB1) and regulate development of dopaminergic neurons. Previously, we found abnormalities in EGF and ErbB1 levels in the forebrain of schizophrenia patients, suggesting EGF-ErbB1 signaling may play a key role in the pathology of schizophrenia. In the agreement, neonatal exposure to EGF induces abnormal behavior phenotypes, such as deficits in prepulse inhibition and impaired social interaction in the adults. In the present report, we investigated dopamine sensitivity and GABAergic function of this animal model for schizophrenia. The threshold dose of D2 receptor agonist to alter prepulse inhibition was lowered in the EGF model whereas dose response of D1 receptor agonist was not changed. In parallel, downstream signaling of D2 receptors, such as Erk and CREB, were sensitized in the striatum of the EGF model. Therefore, presumably neonatal exposure to EGF persistently enhances D2 receptor sensitivity. Further, we investigated extracellular GABA levels in the substantia nigra in order to investigate output from the striatum. We found that extracellular GABA levels in the nigra were much higher in the EGF model than control animal. The increase in GABA release was extinguished by lesion of globus pallidus, suggesting the increased GABA release are presumably originated from the globus pallidus. These results may support the hypothesis that neonatal exposure to EGF may trigger hyper-action of striatal D2 receptor-mediated indirect pathway.

O5-9 Involvement of muscarinic acetylcholine receptor in isolation rearing-induced deficits in prepulse inhibition of the acoustic startle response in mice○Ken Koda¹, Koji Yano¹, Yukio Ago¹, Momoe Nishimura¹, Kazuhiro Takuma¹, Toshio Matsuda^{1,2}¹Lab. Medicinal Pharmacol., Grad. Sch. Pharmaceut. Sci., Osaka Univ., Osaka, Japan, ²Center For Child Mental Dev., Grad. Sch. Med., Osaka Univ., Osaka, Japan

Postmortem studies have shown that alterations in acetylcholine (ACh) receptor subtypes, such as M1 and nicotinic ACh receptors, may contribute to the cognitive impairment observed in schizophrenia. In addition, choline acetyltransferase activity in the parietal cortex is negatively correlated with the severity of cognitive impairment. These observations suggest that cholinergic transmission is linked to the development of cognitive dysfunctions in schizophrenia. Recently, we have reported that the weak acetylcholinesterase inhibitor galantamine reversed isolation rearing-induced deficits of prepulse inhibition (PPI) in mice, and this effect was not blocked by nicotinic ACh receptor antagonists (Koda et al., Psychopharmacology 2008). In this study, we examined the involvement of the muscarinic ACh receptor in isolation rearing-induced deficits in PPI of the acoustic startle response in mice. Three-week-old male ddY mice were housed either in groups of 5 or 6 per cage or isolated cages of the same size for more than 6 weeks before the initiation of experiments. PPI tests were conducted using SR-LAB system. The locomotor activity of mice was measured using a digital counter system with an infrared sensor. Non-selective muscarinic ACh receptor antagonist, scopolamine blocked the effect of galantamine on PPI deficits in isolation-reared mice. The M1 ACh receptor antagonist telenzepine also blocked the effect of galantamine. On the other hand, the non-selective muscarinic ACh receptor agonist oxotremorine and the M1 ACh receptor agonist N-desmethyloclozapine reversed PPI deficits in isolation reared mice. Muscarinic agonists decrease spontaneous locomotor activity in mice. The effect of oxotremorine on locomotion was significantly lower in isolation-reared mice than in the control. These results suggest that galantamine reverses PPI deficits in isolation reared mice, possibly via an activation of the muscarinic ACh receptor, and implies that the abnormal muscarinic receptor function may be responsible for PPI deficits in isolation-reared mice.

O6-2 Impairment of HPA-axis in HPC-1/syntaxin1A knockout mice○Takefumi Kofuji¹, Tomonori Fujiwara², Masumi Sanada², Kimio Akagawa²¹Radioisotope Laboratory, Kyorin University School of Medicine, Mitaka, Tokyo, Japan, ²Department of Cell Physiology, Kyorin University School of Medicine, Mitaka, Tokyo, Japan

HPC-1/syntaxin1A is believed to regulate the exocytosis of synaptic vesicles. Previously, we have produced HPC-1/syntaxin1A knockout mice. Although the null mutant mice revealed almost normal development, the mice exhibited neuropsychological abnormalities which resembled autistic like behavioral deficit. In addition, these behavioral abnormalities were improved by administration of 5-HTergic psychotomimetics, implicating disturbance of 5-HTergic transmission. We have also observed that pancreatic beta cell derived from null mutant mice displayed impairment of insulin release properties. In this study, we have examined if neuroendocrine system was impaired in HPC-1/syntaxin1A knockout mice. Interestingly, plasma corticosterone and ACTH contents decreased in resting condition, but OXT and AVP was almost normal. These results suggested that HPA-axis was impaired in HPC-1/syntaxin1A knockout mice. Since it was known that HPA-axis was modulated by 5-HTergic system, we have examined 5-HT release and 5-HT induced CRH release using hypothalamic slice. Implication of neuroendocrine abnormalities in HPC-1/syntaxin1A knockout mice will be discussed.

O5-8 Lamotrigine prevented neuroplastic disruption of prepulse inhibition induced by repeated administration of a high-dose of methamphetamine○Yasuya Nakato¹, Tomohiro Abekawa¹, Koki Ito¹, Aya Kakuta¹, Tsukasa Koyama¹¹Dept. of Psychiatry, Univ. of Hokkaido

Abstract: Disruption of prepulse inhibition (PPI) is evaluated as a model for endophenotype of schizophrenia. Our group has recently shown that repeated administration of a high dose of methamphetamine (METH), the dose of which increases extracellular levels of glutamate in the medial prefrontal cortex, induced PPI deficit without a challenge injection of METH. Furthermore, we have shown that a sufficient dose of olanzapine, risperidone inhibited the development of this sensory-motor deficit. Lamotrigine (LTG) has a broad-spectrum anticonvulsant that is known to block sodium channels and inhibit excessive glutamatergic neurotransmission. The present study examined whether LTG would inhibit the PPI disruption that was induced by repeated administration of a high dose of METH (2.5 mg/kg). We injected LTG (30 mg/kg) at 120 min after each METH administration (2.5 mg/kg, five times at once every other day and five times on everyday, total of ten times) and measured PPI by using SR-LAB system after sufficient withdrawal from the treatment. Repeated LTG co-administration with METH prevented the repeated-administered METH-induced PPI deficit. This result suggests that LTG may be useful for blocking progressive deterioration of neurocognitive function.

O6-1 The role of cyclic ADP-ribose for calcium release in NG108-15 neuronal cells○Sarwat Amina¹, Hong Xiang Liu¹, Olga Lopatina¹, Minako Hashii¹, Haruhiko Higashida¹¹Dept. of Biophysical Gen., Kanazawa Univ

Cyclic ADP Ribose (cADPR), which is a calcium mobilizing second messenger, is a co-activator of calcium-induced calcium release (CICR) in variable cells, i.e. such as pancreatic beta cells and T cells. In neuronal cells, we have found that CD38-dependent cADPR-sensitive Ca mobilization from the ryanodine receptor in microsome has a key role in oxytocin release. However the precise mechanism how cADPR acts on neuronal cells is not fully understood. The purpose of this study is to measure the increase in intracellular calcium concentration in NG108-15 (mouse neuroblastoma - rat glioma hybrid) neuronal cells due to the effect of cADPR. Our technique involves Ca indicator oregon green and membrane permeabilizing agent digitonin in different temperature conditions. Our results demonstrate that in the permeabilized condition the increase in intracellular calcium which was induced by cADPR was prevented by the prior application of high concentration of ryanodine. Also the cADPR induced intracellular calcium release was enhanced by the application of caffeine. In intact NG108-15 cells the extracellular application of cADPR caused rapid and strong increase in Ca under the condition of 40°C whereas such phenomenon was not observed in 35°C, suggesting that a temperature- and cADPR-sensitive Ca influx pathway may exist. Our result is very similar to what was previously demonstrated in cADPR mediated Ca influx in TRPM2-expressing pancreatic cells.

O6-3 Formation of a novel nitrated second messenger, 8-nitroguanosine 3',5'-cyclic monophosphate in glial cells○Tomoko Ida¹, Tomohiro Sawa², Takaaki Akaike², Hideshi Ihara¹¹Department of Biological Science, Graduate School of Science, Osaka Prefecture University, Osaka, Japan, ²Department of Microbiology, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan

[Background] Nitric oxide (NO) is a common messenger in biological systems. NO generally exerts its signaling effects by activating soluble guanylate cyclase (sGC), which synthesizes guanosine 3',5'-cyclic monophosphate (cGMP). Recently, Sawa et al reported the formation of a nitrated derivative of cGMP, 8-nitroguanosine 3',5'-cyclic monophosphate (8-nitro-cGMP), in NO-mediated signal transduction in mouse peritoneal exudate macrophages and RAW 264.7 cells (Nat. Chem. Biol. 2007). 8-Nitro-cGMP not only behaves as a mimic of cGMP, which can activate standard cGMP signaling pathways, but it also exhibits additional unique chemical properties such as redox activity, membrane permeability, resistance to phosphodiesterase, and protein S-guanylation. In the central nervous system (CNS), the NO-cGMP signaling pathway is involved in a variety of physiological and pathological functions. To date, however, no information is available on the formation of 8-nitro-cGMP in the CNS. The present study aimed to examine the formation of 8-nitro-cGMP in rat cerebral cortex astrocytes and C6 glioma cells. [Methods] 8-Nitro-cGMP was synthesized via a two-step reaction (introduction of the bromo group at C8 position and replication of the bromo group with the nitro group). Mouse monoclonal antibodies were generated by immunizing mice with 8-nitro-cGMP-conjugated BSA. The production of 8-nitro-cGMP in rat cerebral cortex astrocytes and C6 glioma cells was analyzed by immunocytochemistry using a monoclonal anti-8-nitro-cGMP antibody and by LC-MS/MS using a triple quadrupole mass spectrometer.

[Results and discussions] The production of 8-nitro-cGMP was mediated by an exogenous NO donor and endogenous NO produced by inducible nitric oxide synthase (iNOS) induced by cytokines. The production of 8-nitro-cGMP by endogenous NO was inhibited by a NOS and sGC inhibitor. These results show that the formation of 8-nitro-cGMP is mediated by NOS and sGC in glial cells. Because of the unique chemical properties of 8-nitro-cGMP, it can function as an inter- and/or intracellular signaling molecule.

O6-4 Altered expression of tetrahydrobiopterin-dependent enzymes in sepiapterin reductase-null mice

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Tetrahydrobiopterin (BH4) is an essential cofactor for tyrosine hydroxylase (TH), tryptophan hydroxylase (TPH), phenylalanine hydroxylase (PAH), and nitric oxide synthase (NOS). TH and TPH are the rate-limiting enzymes for the production of dopamine and serotonin, respectively. Sepiapterin reductase (SPR) catalyzes the final reaction of BH4 biosynthesis. In SPR null mice, which were produced by Lexicon Genetics Inc., showed severe growth retardation, accumulated phenylalanine, and abnormal metabolisms of pterins and monoamine neurotransmitters, and most of them died by 4 weeks. In this study, we examined the effect of BH4 depletion on expression of BH4-dependent enzymes in CNS and peripheral tissues. Western blotting analysis showed brain-specific decrease of TH protein in SPR-null mice, whereas the expression levels of TH in adrenal gland, neuronal NOS in brain and PAH in liver were not altered. To further investigate the TH-decrease, immunohistochemical study was performed and revealed that TH-immunoreactivity (TH-ir) in striatum was significantly declined in SPR null mice. TH-ir in nigral dopaminergic cells and Aromatic amino acid decarboxylase-ir in striatum were comparable to those in wild-type mice, suggesting that dopaminergic cells in substantia nigra projected their axons to striatum properly but the amount of TH protein was decreased in their terminals. Next we attempted to rescue SPR-null mice by oral administration of BH4 and precursor of monoamine neurotransmitters. This administration did not perfectly recover the growth retardation, but enabled SPR-null mice to survive beyond 10 weeks. We examined the TH protein level in the brains of the rescued mice, because dopamine is well known to stabilize TH protein. We found that the TH protein in the striatum was not recovered in the rescued mice in spite of administration of large amount of dopamine. This suggests that BH4 or some other factor(s) are required for maintenance of the TH protein in striatum.

O6-6 Effects of intracerebroventricular injection of prostanoïd CRTH2 receptor agonists on the open-field behavior in mice

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In the central nervous system (CNS), prostaglandins (PGs) are involved in the variety of brain functions. For example, PGD₂, known as the most abundant prostanoïd in the brain, plays crucial roles in the regulation of sleep and neuronal protection via acting on DP1 receptor. Recently, a second receptor for PGD₂, known as CRTH2 (chemoattractant receptor-homologous molecule expressed on Th2 lymphocytes) or DP2, has been identified and shown to mediate allergic responses in peripheral organs. However, the role of CRTH2 in the CNS remained to be elucidated, although its expression in cerebral cortex, hippocampus and thalamus has been recently demonstrated. In this study, we examined the effects of prostanoïd CRTH2 receptor agonists on the open-field behavior in mice. Intracerebroventricular (i.c.v.) injection of CRTH2 selective agonist, DK-PGD₂, caused a reduction of spontaneous locomotor activity in a dose dependent manner, and 10 pmol of DK-PGD₂ significantly decreased locomotor activity (61% reduction compared to vehicle for 60 min session). I.c.v. injection of another CRTH2 agonist, 15d-PGJ₂, also caused hypoactivity dose-dependently and the effect was most significant at a dose of 10 pmol (48% reduction compared to vehicle for 60 min session). These agonists also tended to decrease the time spent in the center region of the open-field in a dose dependent manner (10 pmol DK-PGD₂; 56% reduction, 10 pmol 15d-PGJ₂; 73% reduction compared to vehicle for 60 minutes), indicating a possible anxiogenic effect of CRTH2 agonists. On the other hand, we did not observe significant effects on the rectal temperature following 2 hours after i.c.v. injection of agonists. These results suggest that CRTH2 activation regulates psychomotor activity in mice.

O7-2 Dopamine D1 receptor-induced signaling through TrkB receptors in striatal neurons

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Dopaminergic neurotransmission plays an important role in the striatum through dopamine-dopamine receptor signaling. In addition to its role as a neurotransmitter, it has been reported that dopamine signaling can influence neurite outgrowth and regulate neuronal polarity in developing neurons. To investigate neuronal differentiation triggered by dopamine in striatal neurons, we focused upon signal transduction induced by dopamine. We found that Trk neurotrophin receptors were activated by a D1 receptor agonist, SKF38393, in cultured striatal neurons. However, a D2 receptor agonist quinpirole failed to phosphorylate Trk receptors. K-252a, a Trk tyrosine kinase inhibitor, and a dopamine D1 receptor antagonist SCH23390 attenuated the TrkB receptors phosphorylation by SKF38393. The effect of D1 receptor activation on TrkB receptors was also confirmed in HEK293 cells expressing TrkB receptors and D1 receptors. Induction of TrkB receptors activity by SKF38393 was accompanied by the phosphorylation of several Trk signaling proteins, including PLCγ, Akt and MAP kinase. The increase in TrkB phosphorylation was not the result of increased neurotrophin production. Biotinylation experiments indicated that the transactivation of TrkB resulted in an increase in levels of cell surface TrkB receptors. This increase of TrkB expression in cell surface was dependent upon an increase in intracellular calcium. Our result suggest that D1 receptors can mediate part of its signaling through TrkB receptors, and that striatal neurons can depend upon transactivation mechanisms.

O6-5 Prostanoid CRTH2 receptor signaling regulates light-induced phase advance of circadian rhythm

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Light-induced phase shift (photoentrainment) of behavioral circadian rhythm is controlled by the specific genes expression in the suprachiasmatic nucleus (SCN) by light. By using of the SCN-specific microarray analysis, we recently found marked reduction in the number of responsive genes to phase advance-inductive light (20 lx, 30 min) in PACAP-deficient mice (KO) exhibiting attenuated light-induced phase advance with normal phase delay of circadian rhythm. In the present study, we showed that, out of about 22000 genes, lipocalin-type prostaglandin D₂ synthase (L-Ptgs) was one of the genes in the SCN that was induced in wild-types but not in KO by phase advance-inductive light, and was not increased by phase delay-inductive light. Whereas light-induced phase advance was normally observed in prostanoïd DP1-deficient mice, that was significantly attenuated in CRTH2 (DP2)-deficient mice. In addition, the phase advance in wild-type mice was significantly attenuated by the i.c.v. injection of CRTH2 antagonist (CAY10471). These results suggest for the first time that L-Ptgs-PGD₂-CRTH2 signaling is a novel signaling cascade specifically involved in light-induced phase advance of circadian rhythm.

O7-1 Suppression of glial cell line-derived neurotrophic factor (GDNF) secretion from microglia activated by endotoxin

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The ability of microglia to produce/secrete glial cell line-derived neurotrophic factor (GDNF) in vitro was examined. Immunoblotting analysis revealed that nonstimulated microglia release limited amounts of GDNF with molecular sizes of 14 and 17 kDa. However, the secreted amounts significantly decreased when the microglia were activated with the endotoxin lipopolysaccharide (LPS). Comparison of the amounts of GDNF in the cells and the conditioned medium (CM) between the nonstimulated microglia and LPS-stimulated microglia clarified that the secretion of GDNF, but not its production, is strongly suppressed when the microglia are activated with LPS. The inhibitor experiments suggested that the GDNF secretion is depressed by a signaling cascade associated with protein kinase C α (PKCα) and/or mitogen-activated protein kinases (MAPKs). NFκB inhibitor did not affect the secretion. As expected from the above results, a PKC activator suppressed the secretion of GDNF in nonstimulated microglia. Taken together, these results demonstrated that microglia have the ability to produce and secrete GDNF in vitro, and that the secretion is suppressed by stimulation with endotoxin, probably due to a signaling mechanism involving PKCα and/or MAPKs.

O7-3 Antipsychotic effects of ErbB1 tyrosine kinase inhibitors on behavioral deficits in the neonatal hippocampal lesion model of schizophrenia

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There are EGF and EGF receptor (ErbB1) abnormalities in brain tissues and blood of schizophrenic patients. Here we examined ErbB1 signaling in the schizophrenia model rats that is established with bilateral microinjections of ibotenic acid to the ventral hippocampus as neonates (postnatal day 7). Treatment with ibotenic acid increased EGF protein levels in the striatum and hypothalamus, suggesting activation of ErbB1 receptor as neonates. On postnatal week 8, rats were tested for behavioral tasks; startle response, PPI, the context fear conditioning, and latent inhibition of the learning task. The ventral hippocampus-lesion significantly impaired the behavioral scores of PPI and latent learning in adults. Startle response was increased and PPI was decreased. In context fear conditioned task, however, memory retentions were normal in ibotenic acid-injected rats while their latent learning was disrupted. We also determined the antipsychotic effects of several ErbB1 tyrosine kinase receptor inhibitors in the above model. The abnormalities in PPI and latent inhibition were ameliorated by icv infusion of ErbB1 tyrosine kinase receptor inhibitors, ZD1835 (12 μg/day), OSI-774 (12 μg/day) and PD 153035 (12 μg/day) from an osmotic pump. These results indicate that blockade of ErbB1 signals may be a novel antipsychotic target for schizophrenia and its related disorders.

O7-4 Nerve growth factor attenuates 2-deoxyglucose-triggered endoplasmic reticulum stress-mediated apoptosis via enhanced induction of GRP78 expression

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2-deoxyglucose (2DG) is an analog of glucose and induces glucose depletion in cells. It is known that the inhibition of glycosylation by glucose depletion triggered by 2DG causes endoplasmic reticulum (ER) stress and then ER stress-mediated apoptosis. Glucose-regulated protein 78 (GRP78) is a molecular chaperon acting in the ER, and the GRP78 expression is induced as an unfolded protein response (UPR) during ER stress. We found that nerve growth factor (NGF) prevented 2DG-triggered ER stress-mediated apoptosis but did not prevent the induction of GRP78 expression in PC12 cells. Surprisingly, we discovered that the expression of GRP78 was further up-regulated when NGF was added to 2DG-treated PC12 cells. Then, we added LY294002, a specific inhibitor of phosphatidylinositol 3-kinase (PI3-K), to 2DG plus NGF-treated cells. LY294002 diminished both NGF effects on 2DG-induced apoptosis and the enhancement of GRP78 expression. These results suggest that GRP78 has an ability to promote the cell survival and that the NGF-activated PI3-K signaling pathway plays a role in protection against ER stress-mediated apoptosis via enhanced induction of GRP78 expression in PC12 cells.

O7-6 Modulation by ATP of neurotrophic factor expression in astroglia

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The view that extracellular ATP plays a role as a signal mediator through ionotropic P2X receptors and metabotropic P2Y receptors expressed in cellular surfaces in the brain is prevailing. In the present study, we have attempted to demonstrate the possible modulation by ATP signals of the functionality and integrity in astroglia. Astroglia were prepared from the hippocampus of embryonic rats, followed by repetition of culturing and replating, and subsequent culture for an additional 2 days. An RT-PCR analysis revealed the expression of mRNA for P2X1, P2X2, P2X3, P2X4, P2X5, P2X6, P2X7, P2Y1, P2Y2, P2Y4, P2Y6, P2Y12, P2Y13 and P2Y14 isoforms, in addition to A1, A2a, A2b and A3 isoforms of P1 receptors for adenosine, in cultured astroglia. Almost similar expression profiles were seen for these purinergic receptor isoforms in the rat glioma cell line C6 cells. Astroglia were loaded with the Ca²⁺-sensitive dye fluo-3 AM, followed by exposure to ATP at concentrations of 0.1 μM to 1 mM for 5 min and subsequent addition of the calcium ionophore A23187 for quantification of the fluorescence intensity using a confocal microscope. A marked but transient increase was seen in the fluorescence in cells exposed to ATP at a concentration over 1 μM, while 1 mM ATP significantly increased the fluorescence intensity to the level of 60% of the maximal value obtained with A23187. Cells were exposed to 1 mM ATP for different periods from 1 to 24 h, followed by determination of mRNA expression of a variety of neurotrophic factors. A significant but transient increase was found in mRNA expression of GDNF, BDNF and NGF, but not of FGF-2, EGF, CNTF, NT-3, NT-4/5 or GFAP, in cultured hippocampal astroglia exposed to 1 mM ATP for 1 h. A similarly significant increase was induced in mRNA expression of GDNF, but not of BDNF, NGF, FGF-2 or GFAP, in C6 glioma cells exposed to 1 mM ATP for 1 h. Luciferase activity was significantly increased by 1 mM ATP in C6 glioma cells transfected with GDNF promoter linked to the luciferase reporter plasmid. These results suggest that ATP may play a role in the mechanism underlying the neuroprotection through transactivation of BDNF expression in astroglia.

O8-2 Serotonin receptor expression profiles in mouse hippocampus along the septo-temporal axis of the mouse hippocampus

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Selective serotonin reuptake inhibitors have been shown to stimulate hippocampal neurogenesis. However, since there have been no comprehensive studies describing serotonin receptor (Htr) expression in the hippocampus at the cellular level, it is not clear which Htrs are responsible in modulating neurogenesis. Here we describe for the first time Htrs expression profiles using *in situ* hybridization, in which all Htr cRNA probes, excluding Htr6, were used. Htr mRNA expression was examined in regions that may affect neurogenesis directly (i.e. dentate subgranular zone) and indirectly (i.e. dentate granule cell layer, hilus, and entorhinal cortex). Htr1d, 2b, and 3b mRNA were not detected throughout the hippocampus. In the dentate subgranular zone and the hilar region, Htr1a, 1b, 2a, 3a, 5a, and 7 were expressed. Individual cells positive for these receptors, excluding Htr1a, were identifiable, since the signals were scattered. In the dentate granule cell layer, Htr1a was intensely expressed; Htr1b, 2a, 4, and 5a were weakly expressed; and Htr1f, 2c, 3a, and 5b were not expressed at all. In the entorhinal cortex, Htr1a, 2a, and 7 were strongly expressed, and Htr1b and 5a were weakly expressed. Furthermore, we predicted that if neural stem/progenitor cells expressed Htr mRNA, their expression would be absent in irradiated brains. Htr1b, 2a, 3a, 5a, and 7 mRNA signals in the subgranular zone were still present after irradiation, suggesting that these Htrs are not expressed in neural stem/progenitor cells but rather in basket cells or in stellate cells. However, we were not able to confirm whether neural stem/progenitor cells expressed Htr1a mRNA since the anticipated elimination of the signal after irradiation was masked by intense Htr1a expression in the granule cell layer. These data show that various Htrs are expressed throughout the dentate gyrus and the entorhinal cortex. Further studies will be necessary to determine if Htr1a is expressed in neural stem/progenitor cells.

O7-5 Activity-dependent cascade of gene expression regulated by pituitary adenylate cyclase-activating polypeptide (PACAP) in neurons

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PACAP is a neuropeptide which is widely expressed in the CNS and contributes to expressing a variety of neuronal functions, such as neuronal survival and plasticity. Although it has been reported that PACAP induces the expression of c-fos and brain-derived neurotrophic factor (BDNF) gene by activating NMDA receptors, we found that a number of genes (nearly 100 genes) were activated by PACAP through the NMDA receptor-derived calcium signal. Either inhibitor of protein kinase A or protein kinase C repressed the induction. Moreover, forskolin and TPA, potent activators of protein kinase A and protein kinase C, respectively, also induced gene expression through activation of NMDA receptors, indicating an involvement of Gs/protein kinase A and Gq/protein kinase C in the PACAP-induced NMDA receptor activation. Using a reporter assay system, we found that PACAP activated BDNF gene promoter IV through the CRE-dependent transcription, which is induced by calcium signals. On the other hand, the treatment with either PACAP or BDNF did not increase the expression of PACAP mRNA, but that with both PACAP and BDNF increased the expression of BDNF mRNA. The PACAP mRNA was degraded by activation of protein kinase A or protein kinase C, and its degradation was prevented by calcium signals. These results strongly suggest that one-way expression pathway from PACAP to BDNF in neurons. Thus, PACAP induces a cascade of activity-dependent gene expression, possibly leading to a selective modulation of neuronal circuits in the PACAPergic system in the brain.

O8-1 Serotonin 1A receptor is involved in the paradoxical antihyperkinetic effect of the drugs treating ADHD

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The medications most commonly used for attention-deficit hyperactivity disorder (ADHD) are the psychostimulants, including amphetamine (AMPH), methylphenidate (MPH), and methamphetamine (METH). However, the mechanism underlying this paradoxical effect of psychostimulants has been poorly understood. We previously reported that the novelty-induced hyperactivity observed in the pituitary adenylate cyclase-activating polypeptide (PACAP)-deficient mice can be attenuated by AMPH and that this AMPH action is blocked by the serotonin (5-HT) 1A receptor antagonist WAY-100635. In addition, co-administration of AMPH and the 5-HT_{1A} receptor agonist 8-OH-DPAT produced a calming effect in wild-type mice. In this study, we investigated whether METH, MPH, and atomoxetine, an recently developed non-stimulant medication of ADHD, produce the similar effect when co-administered with 5-HT_{1A} receptor agonist in wild-type mice. Here we used the 5-HT_{1A} receptor-selective agonist osetozotan. Co-administration of METH with osetozotan produced a calming effect. MPH with osetozotan produced antihyperkinetic effect, but only partially. Atomoxetine did not induce hyperactivity per se, but when co-administered with osetozotan, it produced a calming effect. To address the underlying mechanisms, we also examined c-Fos expression, a marker of neuronal activation, in medial prefrontal cortex, striatum, and nucleus accumbens. In medial prefrontal cortex, but not in the other two regions, pretreatment of the 5-HT_{1A} receptor agonist decreased the number of c-Fos-positive neurons in the psychostimulant-treated mice. These results provide evidence to support our idea that 5-HT_{1A}-receptor-mediated pathways are implicated in the antihyperkinetic effect of ADHD drugs and suggest that neurons expressing the 5-HT_{1A} receptor in medial prefrontal cortex might be involved in this paradoxical effect.

O8-3 Functional analysis of a wide range of G protein-coupled serotonin receptors by a single method

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G protein-coupled receptors (GPCRs) are seven transmembrane domain receptors that comprise a large protein family important as therapeutic targets for drug discovery. Depending on their coupling specificities, GPCRs are subdivided into three types; Gq-, Gs-, and Gi/o-coupled GPCRs. To integrate the GPCRs with different specificities, promiscuous G proteins, such as human G16 and its murine homolog, G15 have been used, but these G proteins cannot be considered as a true universal adaptor for GPCRs (Mody et al., 2000). In addition, G16/z chimera that has been devised to improve the ability of G16 to Gi/o-coupled receptors, did not couple to some Gi-coupled receptors as well (Ueda et al., 2003).

It is obvious that serotonin (5-HT) is an important neurotransmitter in the brain. It acts through numerous receptor types, which are GPCRs except for HT3 receptor; 5-HT1A - 1F are Gi/o-coupled, 5-HT2A - 2C are Gq-linked, and 5-HT4 - 7 are Gs-coupled. However, many researchers separately examine these receptor properties except for binding assay, but it cannot distinguish between agonist and antagonist.

In the present study, we established a calcium imaging system using novel G protein chimeras, and evaluated the system for the ability to translate activations of some serotonin receptors (5-HT1A, 2A, and 2C receptors) into calcium mobilization. For 5-HT1A receptors, which are Gi/o-coupled receptors, we transiently transfected with a G16/o chimera and the receptors into HEK293T cells, so as to convert the activation-induced signal into PLC/IP3 pathways. In our assay system, 5-HT activated all the receptors examined in a concentration-dependent manner. The EC₅₀ values were 1.0 ± 0.5 nM (HT1A), 5.5 ± 2.0 nM (HT2A) and 50 ± 20 nM (HT2C) and were comparable with those obtained from the other *in vitro* assays. In addition, we examined the effect of a 5-HT1A antagonist, spiperone in our assay system. As a result, spiperone dose-dependently inhibited calcium mobilization via 5-HT1A receptors caused by 10 nM 5-HT. The present assay is adaptable enough for high throughput screening, and could be useful to analyze a wide range of GPCR that contains Gq-, Gs-, and Gi/o-coupled receptors all together.

O8-4 Involvement of dopamine-D₂ and serotonin-1A receptors in the ability of atypical antipsychotic drugs to induce prefrontal dopamine release

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Most atypical antipsychotic drugs, including clozapine, risperidone, perospirone and aripiprazole, have been demonstrated to facilitate dopamine (DA) release in the prefrontal cortex and hippocampus of both rodent and primates. The prefrontal dopaminergic activation induced by atypical antipsychotic drugs has been thought to be the basis for the neurocognitive effect of these drugs on schizophrenia. This study investigated the mechanisms underlying the ability of atypical antipsychotic drugs to increase DA release in the medial prefrontal cortex (mPFC), using microdialysis with dual probe implantation of awake, freely moving rats. When applied locally into the ventral tegmental area (VTA), the DA partial agonist aripiprazole, like the full D₂ agonist quinpirole, decreased extracellular DA levels in the mPFC. By contrast, local application into the VTA with perospirone, an atypical antipsychotic with high affinity for both D₂ and serotonin (5-HT)_{1A} receptors, as well as raclopride, a selective D₂ antagonist, increased extracellular mPFC DA levels. Interestingly, clozapine, a prototype agent of atypical antipsychotics, had no effect on extracellular mPFC DA levels. Thus, depending on the manner of binding to presynaptic D₂ autoreceptors, different types of atypical antipsychotic drugs may have distinct effects on the activity of VTA DA neurons. When applied directly into the mPFC, aripiprazole and clozapine, but not perospirone or risperidone, increased extracellular DA levels. These effects were attenuated by pretreatment with WAY100,635, a 5-HT_{1A} antagonist. The ability of clozapine to induce mPFC DA release was also attenuated by co-perfusion with the selective D₂ antagonist. Taken together with distinct receptor binding profiles of each drug, the interaction between weak D₂ antagonism and potent 5-HT_{1A} agonism in the local circuitry of the mPFC may contribute to the ability of clozapine and aripiprazole to enhance prefrontal DA release. However, it may not be true for risperidone or perospirone because they display strong binding potency to D₂ receptors in the mPFC. KAKENHI17591219

O8-6 Modulation of Tryptophan and Serotonin Metabolites in Tryptophan 2,3-Dioxygenase and Indoleamine 2,3-Dioxygenase Knockout Mice

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Tryptophan (Trp) and its metabolites, such as neurotransmitter serotonin (5-HT), play an important role in multiple brain functions. Recently, it was reported that the abnormality of tryptophan hydroxylase (TPH: known as the rate-limiting enzyme for 5-HT biosynthesis) was related to depression, and the regulation of 5-HT biosynthesis is thought to be a key modulator of emotion. Tryptophan 2,3-dioxygenase (TDO: dominantly expressed in the liver) and indoleamine 2,3-dioxygenase (IDO: expressed in extra-hepatic tissues), both of which convert Trp to N-formylkynurenine, are the initial and rate-limiting enzymes for Trp metabolism. However, the contributions of TDO and IDO to the regulation of systemic and brain Trp metabolism and physiological brain functions are not well established *in vivo*. Here, we examined systemic and brain Trp and 5-HT metabolites in TDO- and IDO-knockout (KO) mice, and compared these mice with wild-type (WT) mice. Biochemical analyses using HPLC-FD systems showed that plasma levels of Trp and 5-hydroxyindoleacetic acid (5-HIAA) in TDO-KO mice were markedly modulated compared to WT mice, while those in IDO-KO mice were slightly changed. In contrast, the downstream of Trp metabolite in plasma was significantly altered in both IDO- and TDO-KO mice. Furthermore, TDO-KO mice showed increased levels of brain Trp, 5-HT, and 5-HIAA, while these levels in IDO-KO mice were little modified even IDO is expressed in the brain. Real-time RT-PCR and enzymatic assay for TPH of brainstem revealed that both mRNA levels and enzymatic activities of TPH were not modified by tdo deletion. These results suggested that, under the physiological condition, TDO plays an essential role in regulating systemic and brain Trp metabolites rather than IDO, and functions as a dominant regulator of the serotonergic pathway even in the presence of intact TPH. Further examination of IDO-KO mice, under the pathophysiological condition, should be useful to better clarify the role of IDO. In summary, TDO might be implicated in psychiatric diseases, such as depression and anxiety, via regulation of Trp and 5-HT metabolisms.

O9-2 Expression of Foxp1 in a subset of spinal motor neurons during development

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The Fox family of transcription factors play important roles in the regulation of gene expression during development of various organs, including brain, lung, heart, and liver. A member of Foxp subfamily, Foxp1, is expressed in the developing and adult central nervous system. Although it has been reported that Foxp1 mRNA is expressed in the developing spinal cord, detailed expression pattern of Foxp1 and its role in the developing spinal cord remains unclear. In the present study, we investigated a detailed expression pattern of Foxp1 in the embryonic mouse spinal cord using *in situ* hybridization and immunohistochemistry. From embryonic day (E) 9.5 to E17.5, expression of Foxp1 mRNA and protein were detected in the ventral spinal cord where motor neurons (MNs) and four classes of interneurons exist. From E10.5 to E13.5, Foxp1 was highly expressed in the ventral horn of brachial and lumbar levels of the spinal cord, but not in cervical and thoracic levels. At brachial and lumbar levels of the spinal cord, MNs that innervate limb muscles settle in a lateral position in the spinal cord and form the lateral motor column (LMC). In contrast, MNs in the medial motor column (MMC) are distributed in a medial position at all levels of the spinal cord and project to body wall muscles. Therefore, Foxp1-expressing cells in the ventral horn were supposed to be LMC neurons. Double-immunofluorescence staining for Foxp1 and Isl2 (Isl2) revealed that Foxp1 was expressed in a subset of Isl2-positive MNs at E11.5. Expression of Foxp1 was not observed in Lhx3-positive MMC neurons at E10.5 and E11.5. These findings suggest that Foxp1 expressed in LMC neurons may be involved in the development of LMC neurons, such as the specification of LMC identity and axon growth of LMC neurons.

O8-5 Brain serotonin transporter imaging by PET with [¹¹C]DASB in conscious marmosets

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In vivo imaging of brain serotonin transporter (SERT) is of interest because of its potential role in the pathophysiology of a range of psychiatric conditions, including depression, obsessive-compulsive disorder, autism, and anxiety disorders. SERT plays a critical role in the 5-HT neurotransmission and in the site of action of antidepressant drugs, SSRIs. The common marmoset (*Callithrix jacchus*) is characterized by strong socio-emotional attachment in pairs and by co-operative infant care on a family basis, which is resemble to human. Therefore, the marmoset has been lately focused as valuable animal model for studying human psychiatric disorders that is involved in social disturbance. In the present study, we performed positron emission tomography (PET) imaging of brain SERT using highly selective radioligand, [¹¹C]DASB in marmosets. To avoid the anesthetic effect on SERT, PET scans have been done under conscious condition. The *in vivo* distribution of [¹¹C]DASB was consistent with *in vitro* immunohistochemical distribution of SERT, with high uptakes of radioactivity in the midbrain, pons, thalamus, hypothalamus, amygdala, ventral striatum, intermediate levels in the dorsal striatum, anterior cingulate, orbitofrontal cortices, and modest to low levels in the neocortex and cerebellum. Parametric images of [¹¹C]DASB with binding potential (BP) values were successfully generated in all individuals (n=11), and mean regional SERT BP values ranged from 0.56 ± 0.22 in the frontal cortex to 2.43 ± 0.48 in the dorsal raphe nucleus. The quantitative *in vivo* PET imaging of brain SERT using [¹¹C]DASB in conscious marmosets will lead us to investigate elucidation of serotonergic system relevant to behavioral characteristics in normal and psychiatric conditions.

O9-1 OASIS, a member of the CREB/ATF family transcription factor, is involved in CSPG production in the CNS

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OASIS, a basic leucine zipper (bZIP) transcription factor of the CREB/ATF family, is induced in cell-culture models of gliosis and in gliotic tissues *in vivo*. Recent study had demonstrated that OASIS could have important roles in endoplasmic reticulum (ER) stress response or ER protein quality control in particular tissue or cells. OASIS was induced at the transcriptional level during ER stress and has a transmembrane domain that allows it to associate with the ER. The molecule is cleaved at the membrane in response to ER stress, and its cleaved amino-terminal cytoplasmic domain, which contains the bZIP domain, translocates into the nucleus where it activates the transcription of target genes that are mediated by ER stress-responsive and cyclic AMP-responsive elements. In this study, we focus on the potential role of OASIS in astrocytosis. In the central nerve system, the failure of axonal regeneration is partly attributed to the glia scar. Reactive astrocytes, which constitute a major cellular component of the glia scar, may produce anti-regenerative molecules such as chondroitin sulphate proteoglycans (CSPGs). Both mRNA and protein levels of OASIS were elevated in the injured cortex, and correlate closely with those of GFAP. We demonstrated the participation of OASIS in production of CSPGs through the use of OASIS knock out mice. We will discuss about the pathological role of OASIS.

O9-3 Necdin interacts with Foxo1 and represses its transcriptional activity

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Necdin is a multifunctional protein that promotes neuronal differentiation and survival. Necdin interacts with many regulatory proteins such as neuronal apoptosis-inducing transcription factors (e.g., E2F1, p53) and neurotrophin receptors (e.g., TrkA, p75NTR). It has recently been reported that necdin modulates the insulin signal pathway involved in adipogenesis. The forkhead box transcription factor Foxo1 is involved in the regulation of genes that control the insulin/IGF signal transduction, which is essential for the support of neuronal survival. Foxo1 also controls the expression of many genes involved in cell metabolism, apoptosis, cell cycle, and oxidative stress resistance. However, little is known about the regulatory mechanism of Foxo1 activities in neurons. In the present study, we examined the physical and functional interactions between necdin and Foxo1. We first analyzed the distribution patterns of necdin and Foxo1 in mouse brain at embryonic day 16.5 by immunohistochemistry, and found that necdin and Foxo1 are coexpressed in subpopulations of neurons in the hippocampus and hypothalamus. The physical interaction between necdin and Foxo1 was detected by a coimmunoprecipitation assay using cDNA-transfected cells. A transcription assay using the insulin-related substrate (IRS) gene promoter revealed that necdin repressed Foxo1-stimulated activity in a dose-dependent manner. Foxo1 is acetylated by CBP/p300 histone acetyltransferase and deacetylated by NAD-dependent protein deacetylase Sirt1, and the acetylation status of Foxo1 potentiates its transcriptional activities. We have recently found that necdin interacts with Sirt1. Thus, it is possible that the acetylation status of Foxo1 in neurons is regulated by necdin via Sirt1 and changes its subcellular distribution. We are currently investigating the effects of necdin on the function and localization of Foxo1 in primary neurons prepared from necdin-deficient mice.

O9-4 Regulation of somatic growth and energy homeostasis by a putative transcription factor AF5q31 in the hypothalamus○Tadasuke Komori¹, Tetsuya Nosaka², Toshio Kitamura³, Emiko Senba¹, Yoshihiro Morikawa¹¹Department of Anatomy & Neurobiology, Wakayama Medical University, Wakayama, Japan, ²Department of Microbiology, Mie University Graduate School of Medicine, Mie, Japan, ³Division of Cellular Therapy, Advanced Clinical Research Center, The Institute of Medical Science, The University of Tokyo, Tokyo, Japan

AF5q31 (also called ALF4 or MCEF) was identified by its involvement in chromosomal translocation with the gene mixed-lineage leukemia, and acts as a repressor of RNA polymerase II transcription. By cDNA microarray analysis, AF5q31 was increased in the hypothalamus of fasted mice compared to that of mice fed ad libitum (Li et al., J Biol Chem 277; 9069-9076, 2002). In addition, we generated AF5q31-deficient mice, which increase body weights compared to those of wild-type mice (Urano et al., Mol Cell Biol 25; 6834-6845, 2005).

In the present study, we analyzed heterozygous AF5q31-deficient mice to examine the role of hypothalamic AF5q31 in the regulation of energy homeostasis, and somatic growth, because most homozygous AF5q31-deficient mice died in utero and neonatally. In heterozygous AF5q31-deficient mice, body lengths were increased compared to those of wild-type mice as well as body weights, whereas there were no significant differences in body mass index between heterozygous AF5q31-deficient mice and wild-type mice. These results indicate that somatic growth is enhanced in heterozygous AF5q31-deficient mice. In addition, serum growth hormone (GH) and insulin-like growth factor (IGF)-1 levels were significantly elevated in heterozygous AF5q31-deficient mice. A stomach-derived hormone, ghrelin, stimulates the secretion of GH by the induction of growth hormone-releasing hormone through the growth hormone secretagogue receptor (GHS-R) in the hypothalamus. In heterozygous AF5q31-deficient mice, the expression of GHS-R was significantly increased in the hypothalamus. It is well-known that GH-IGF-1 axis regulates somatic growth and energy homeostasis. From these findings, AF5q31 may regulate somatic growth and energy homeostasis by repressing the expression of GHS-R in the hypothalamus.

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O9-6 L1 mRNA was decreased in the hippocampal granule cells in the patients with schizophrenia, major depression, and bipolar disorder.○Kazuhiro Horinouchi^{1,2,3}, Aiko Izumi², Masaya Tohyama³, Sadao Shiosaka¹, Kunimasa Arima¹, Hiroshi Kunugi²¹Division of Structural Cellular Biology, Nara Institute of Science and Technology, ²Department of Mental Disorder Research, National Institute of Neuroscience (NIN), National Center of Neurology and Psychiatry (NCNP), ³Department of Anatomy and Neuroscience, Graduate School of Medicine, Osaka University, ⁴Department of Laboratory Medicine, Musashi Hospital, National Center of Neurology and Psychiatry (NCNP)

Converging lines of evidences indicated that neural plastic events are fundamental processes to cognitive functions. Cognitive impairments are core features of some type of psychiatric disorders such as schizophrenia, bipolar disorder, and major depression, and it is thought that prefrontal cortex, hippocampus, and amygdala might be a part of focuses for these diseases. However, it remains to clear what are the fundamentally causal factors of these disorders? L1 is a multifunctional neuronal cell adhesion molecule belonging to the immunoglobulin superfamily. L1 involved neurite outgrowth, cell migration, and neural networking in immature brain and to neural plasticity such as long-term potentiation, memory, and learning in the adult brain. Additionally, it is documented that expression of L1 mRNA was altered in prefrontal cortex in the patients with schizophrenia and bipolar disorder. Together with our hypothesis and these reports, it is thought that L1 might be involved in pathogenesis of the some type of mental disorders. In present study, we performed in situ hybridization histochemistry using human prefrontal cortex, hippocampus, and amygdala slices of the patients to elucidate which cells express L1 mRNA and how altered the L1 mRNA expression level in those cells. Firstly, we observed unique expression pattern of L1 mRNA in the human hippocampus. L1 mRNA was expressed in granule cells and pyramidal cells in the hippocampus, although we detected only in the pyramidal cells in the mouse hippocampus. Secondly, we revealed L1 mRNA was decreased in the hippocampal granule cells in the patients with schizophrenia, major depression, and bipolar disorder. Therefore, it is thought that L1 in the granule cells might have critical role in the pathogenesis of bipolar disorder, schizophrenia, and major depression.

O10-2 Decreased secretion of UCH-L1 and SOD1 by the mutations associated with neurodegenerative diseases○Chiho M Konya¹, Tomohiro Kabuta¹, Aiko Kinugawa¹, Keiji Wada¹¹Department of Degenerative Neurological Diseases, National Institute of Neuroscience, National Center of Neurology and Psychiatry

Ubiquitin C-terminal hydrolase L1 (UCH-L1/PGP 9.5) is expressed predominantly in neurons. The I93M mutation in UCH-L1 is associated with familial Parkinson's disease. Previous report showed that UCH-L1 is secreted outside cells, although its physiological meaning has not been clarified. Since UCH-L1 does not contain a secretion signal, it is suggested that this protein is not secreted by the classical ER-Golgi pathway. Wild-type SOD1 and familial amyotrophic lateral sclerosis (ALS)-linked mutant SOD1 are also known to be secreted by non-classical pathway(s), while the mechanism of non-classical secretion pathway(s) has not been elucidated. We supposed that there is an interaction between the secretion of UCH-L1 and the neurodegenerative diseases. Therefore in this study, we investigated the secretion of UCH-L1 and SOD1. We measured the levels of secreted wild-type and mutant UCH-L1 or SOD1 using COS-7 cells. As a result, the levels of secreted mutant I93M UCH-L1 was reduced as compared with that of wild-type UCH-L1. The secretion of mutant A4V SOD1, which is linked to familial ALS, was hardly detected, whereas the secretion of wild-type SOD1 was observed. We then tried to identify the proteins interacted with mutant UCH-L1 and mutant SOD using co-immunoprecipitation assays and subsequent mass-spectrometry analyses. We identified ER chaperone protein, GRP78/BiP as a novel interacting protein of mutant UCH-L1 and mutant SOD1. The levels of interaction between wild-type UCH-L1 and BiP were lower than that of I93M UCH-L1, and wild-type SOD1 did not interact with BiP.

These results suggest that the interaction between BiP and mutant proteins may contribute to neurodegenerative diseases. It is possible that the impaired secretion of the disease associated proteins might directly induce the alteration of the extracellular ubiquitin system or indirectly affect the secretion of another secreted proteins such as GDNF or another cytokines. We also discuss the possible involvement of BiP in the secretion of proteins in neurodegenerative diseases.

O9-5 Synaptogenesis between the parallel fibers and Purkinje cells of the cerebellum is perturbed in NB-3 knockout mice○Kunio Sakurai¹, Manabu Toyoshima¹, Kota Matsubara¹, Yasuo Takeda², Yasushi Shimoda³, Domna Karagogeas³, Kazutada Watanabe¹¹Dept. Bioeng., Nagaoka Univ. Tech. ²Dept. Clinic. Pharm. & Pharmacol., Kagoshima Univ. Grad. Sch. Med. & Dent. Sci. ³Dept. Basic Sci., Crete Univ. Grad. Sch. Med.

The neural cell recognition molecule NB-3, which belongs to the contactin subgroup of the immunoglobulin superfamily is expressed exclusively in the nervous system. Its expression is prominently up-regulated during postnatal development of the nervous system. We demonstrated previously that NB-3 knockout (KO) mice are impaired in motor coordination. Although behavioral analyses suggested that NB-3 plays the important roles in development and function of the cerebellum, the function of NB-3 at molecular level remains elusive. In this study, we investigated the localization of NB-3 in the developing mouse cerebellum in detail using the monoclonal antibody against NB-3. To analyze the expression and localization of NB-3, we compared the immunoreactivity of NB-3 with those of TAG-1 and L1, both of which are cell adhesion molecules expressed radially migrating granule cells and parallel fibers. The postmitotic granule cells sequentially express TAG-1, L1 and then NB-3 during radial migration, suggesting that these three molecules are expressed in the developing granule cells in a stage specific manner. At P5, both TAG-1 and L1 immunopositive zones were expanded to the deeper part of cerebellum in NB-3 KO mice as compared with the wild-type mice, indicating that the development of granule cells was perturbed in NB-3 KO mice. Double labeling immunofluorescence studies revealed that signals of NB-3 were partially colocalized with those of vesicular glutamate transporter 1 at the parallel fiber terminals, which is the presynaptic marker for a subset of glutamatergic neurons. The number of synapses between parallel fibers and Purkinje cells in NB-3 knockout mice was fewer than those in wild-type mice during development of the cerebellum. Thus, NB-3 is implicated in the synaptogenesis between the parallel fibers and Purkinje cells as well as development of granule cells.

O10-1 Aberrant interaction between familial Parkinson's disease-associated mutant UCH-L1 and the lysosomal receptor for chaperone-mediated autophagy○Tomohiro Kabuta¹, Akiko Furuta¹, Shunsuke Aoki¹, Koh Furuta², Keiji Wada¹¹Department of Degenerative Neurological Diseases, National Institute of Neuroscience, National Center of Neurology and Psychiatry, Tokyo, Japan, ²Division of Clinical Laboratories, National Cancer Center Hospital, Tokyo, Japan

Parkinson's disease (PD) is the most common neurodegenerative movement disorder characterized by progressive degeneration confined mostly to dopaminergic neurons in the substantia nigra pars compacta. Although the majority of PD cases occur sporadically, nine genes have been reported to be associated with familial forms of PD. Duplication and triplication of the alpha-synuclein gene were shown to cause familial PD or parkinsonism, indicating that increases in the levels of alpha-synuclein proteins could constitute a cause of PD. Alpha-synuclein has been reported to be degraded at least partly by chaperone-mediated autophagy (CMA). A missense mutation in the ubiquitin C-terminal hydrolase L1 (UCH-L1) gene, leading to an I93M substitution at the protein level, has been reported in a German family with dominantly inherited PD. However, the relationship between alpha-synuclein and UCH-L1 proteins in the pathogenesis of PD has remained largely unclear. In this study, we found that UCH-L1 physically interacts with lysosome-associated membrane protein type 2A (LAMP-2A), the lysosomal receptor for CMA, and heat shock cognate protein 70 (Hsc70) and heat shock protein 90 (Hsp90), both of which can function as components of the CMA pathway. These interactions were abnormally enhanced by the I93M mutation, and were independent of the monoubiquitin-binding of UCH-L1. In a cell-free system, UCH-L1 directly interacted with the cytosolic region of LAMP-2A. Expression of I93M UCH-L1 in cells induced the CMA inhibition-associated increase in the amount of alpha-synuclein. Carbonyl-modified UCH-L1, which has been found in sporadic PD brains, also aberrantly interacted with LAMP-2A, Hsc70 and Hsp90. Our findings may provide novel insights into the links between familial and sporadic PD, and suggest that aberrant interactions of UCH-L1 variants with CMA machinery, at least partly, underlie the pathogenesis of PD associated with I93M UCH-L1, and possibly of sporadic PD.

O10-3 The de-ubiquitinating enzyme, UCH-L1, and lipid peroxidation○Satoshi Nagamine¹, Tomohiro Kabuta¹, Kazuhiro Yamamoto², Akio Takahashi², Keiji Wada¹¹Department of Degenerative Neurological Diseases, National Institute of Neuroscience, National Center of Neurology and Psychiatry, Tokyo, Japan, ²Administrative Section of Laboratory Animal Resources, National Institute of Neuroscience, National Center of Neurology and Psychiatry, Tokyo, Japan

The naturally occurred mutant mouse, gracile axonal dystrophy (*gad*), exhibits progressive sensory ataxia in hindlimbs due to the retrograde degeneration of axons in the gracile fasciculus. This mouse genetically lacks the de-ubiquitinating enzyme, ubiquitin C-terminal hydrolase-L1 (UCH-L1), suggesting the importance of the ubiquitin system in the pathology of the neurodegenerative diseases. However, the precise mechanism of the degeneration in the *gad* mouse remains elusive. Since the α -tocopherol (vitamin E) transfer protein-deficient mouse, which lacks vitamin E in the brain and is sensitive to lipid peroxidation, exhibits similar degeneration in the gracile fasciculus, we hypothesized that UCH-L1 may be involved in the defense system against lipid peroxidation.

Histologically, auto-fluorescent aggregations positive for the markers of lipid peroxidation were observed in the gracile fasciculus of the *gad* mouse from the early stage. Western blot analysis revealed the increase in oxidatively modified proteins in the gracile fasciculus of the *gad* mouse. When the *gad* mouse was fed with vitamin E-deficient diet, the sensory ataxia of the *gad* mouse was exacerbated, while that of wild-type mouse was not affected. When neurons of dorsal root ganglions were cultured in the medium lacking anti-oxidants, more apoptotic neuronal cell death was observed in the *gad* mouse. Supplementation of vitamin E to the medium rescued the vulnerability of the *gad* neurons. These results suggest that the lack of UCH-L1 leads to the decreased resistance to the lipid peroxidation.

O10-4 Involvement of oxidative-modified protein in the pathogenesis of Parkinson disease

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Selective degeneration of dopamine (DA) neurons and accumulation of Lewy bodies (LB) in the substantia nigra are characteristic pathological features in Parkinson disease (PD). Oxidative stress, dysfunctions of mitochondria and proteasome, and apoptotic signal activation have been proposed as the pathogenesis of PD. This paper presents our recent results to show the possible link of these pathogenic factors. The substantia nigra from PD patients and control were subjected to immuno-histochemical observation for alpha-synuclein (α -Syn), a LB component, and acrolein, a most reactive aldehyde product of lipid peroxidation with respective antibodies. α -Syn was confirmed to be modified with acrolein in DA neurons of PD patients, but not control. The relation to cell death was clarified by *in vitro* studies, that acrolein modification induced aggregation of α -Syn. In addition, acrolein reduced the enzymatic activity of 20S proteasome by direct modification of proteasome proteins, and inhibition of enzymic activity by acrolein modified α -Syn. Rotenone-induced mitochondrial dysfunction increased production of reactive oxygen and nitrogen species (ROS-RNS) with proteasomal dysfunction in a similar way. In addition, neuromelanin, a characteristic pigment in DA neurons of the substantia nigra, was prepared from human brains and the cytotoxicity was examined. Neuromelanin increased ROS-RNS levels in mitochondria through release of iron and inhibited 26S proteasome. These results clearly present that increased production of ROS-RNS in mitochondria enhances lipid peroxidation, generates cytotoxic lipid aldehydes, impairs the ubiquitin-proteasome system, accumulates modified proteins and finally induces cell death in DA neurons containing neuromelanin in PD. Considering the reduction of anti-oxidative function in PD brains, the anti-oxidative reagents, including phytochemicals might intervene this cell death process and protect DA neurons from progressive degeneration.

O10-6 Loss of ALS2/alsin exacerbates motor dysfunction and axonal damage in SOD1^{H46R} transgenic mice

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ALS2 mutations account for a number of juvenile motor neuron diseases (MNDs), including a juvenile recessive form of ALS (ALS2), a rare juvenile recessive form of primary lateral sclerosis (PLS), and an infantile-onset ascending hereditary spastic paralysis (IAHSP). Thus, its gene product ALS2 (or alsin) may play an important role in maintenance and/or survival of motor neurons. Recently, it has been shown that overexpression of ALS2/alsin protects cultured motor neuronal cells from toxicity induced by mutant SOD1, suggesting a possible neuroprotective function of ALS2/alsin. To examine whether ALS2/alsin plays a role in the onset and/or progression of MND that is associated with mutant SOD1 *in vivo*, we generated SOD1^{H46R} transgenic mice on an *Als2*^{-/-} background by crossing *Als2*^{-/-} mice with the SOD1^{H46R} mouse line expressing familial ALS-linked human SOD1^{H46R} under the control of the inherent SOD1 promoter. SOD1^{H46R} and *Als2*^{-/-};SOD1^{H46R} mice both exhibited progressive motor dysfunction and paralysis, leading to death. Remarkably, *Als2*^{-/-};SOD1^{H46R} mice showed a much earlier motor dysfunction as well as a shorter life span than SOD1^{H46R} or *Als2*^{-/-};SOD1^{H46R} mice. Axonal degeneration in the spinal tracts, which preceded motor neuronal loss, was evident from an early symptomatic stage in *Als2*^{-/-};SOD1^{H46R} mice. *Als2*^{-/-};SOD1^{H46R} mice, when compared with SOD1^{H46R} or *Als2*^{-/-};SOD1^{H46R} mice, showed the increased levels of insoluble mutant SOD1 and the ubiquitin-/LC3-binding protein "p62/SQSTM1" in the spinal cord at an earlier than 8-12 weeks of age, suggesting that ALS2/alsin deficiency hinders protein degradation and/or accelerates the accumulation of the SOD1/p62-containing aggregates in SOD1^{H46R} mice. Collectively, ALS2/alsin plays a role in the onset and/or progression of MND that is associated with H46R mutant SOD1 *in vivo*. Further characterization of these mice will clarify the implication of the ALS2/alsin-mediated functions in mutant SOD1-linked ALS *in vivo*.

O11-2 Regulation of axonal outgrowth by drebrin-mediated F-actin reorganization

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During neuronal development, an axonal growth cones plays an important role for the axonal outgrowth from the cell body to its appropriate target. We have previously shown that various actin-binding proteins are differentially localized in axonal growth cones, suggesting the role of actin-binding proteins in the axonal outgrowth. Drebrin E is expressed in early developmental stages of the neuron and is concentrated in the actin arc in the growth cone. To address the role of drebrin E in the axonal outgrowth, we examined the effects of the RNAi knockdown and the overexpression of drebrin on axonal outgrowth. We prepared the low density primary cultures of rat hippocampi from 18-days embryo using Banker Methods. Neurons were co-transfected with GFP expressing vector and the siRNA oligonucleotide against drebrin before seeding for RNAi knockdown experiments. For overexpression experiments, GFP-drebrin E expression vector was transfected. The transfection was carried out by electroporation using Amaxa Nucleofector Device. In some cases, after 48 hours of transfection, the cells were treated with Sema 3A (0.5 μ g/ml) for 0.5 to 30 min. Then, the cells were fixed and analyzed by immunofluorescence staining. Overexpression of drebrin E increased the axonal length and the number of dendrites. In contrast, knockdown of drebrin decreased the axonal length. Then we compared the effect on the axonal growth cone of between Sema 3A treatment and drebrin siRNA treatment. Sema 3A reduced the area of drebrin rich zone and F-actin intensity in the growth cones by 30 seconds stimulation, when the growth cone was not yet affected morphologically. On the other hand, down-regulation of drebrin reduced the size of the growth cone and its F-actin intensity. These data suggested that drebrin contributed to the rearrangement of F-actin in the process of Sema 3A-induced growth cone collapse. However, an occlusion type experiment showed that drebrin knockdown and Sema 3A have an additive effect on the growth cone size. In conclusion, it is suggested that drebrin-mediated F-actin reorganization is involved in the regulatory mechanism of axonal growth, which is distinct from the Sema 3A signaling pathways in the growth cone collapse.

O10-5 Immunoreactivity of endosome related proteins in ALS and ALS with dementia

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Purpose: Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disorder, neuronal loss confined to upper and lower motor neurons, however, is often associated with dementia (ALS-D). In light of immunoreactivity for TDP-43, ALS and ALS-D are shown to share the pathological feature, and this fact supports the view that these diseases represent a spectrum of neurodegenerative disorder linked mechanistically to pathological TDP-43. However, pathological difference between ALS and ALS-D remains elusive. Recently, genes coding for endosome related proteins such as CHMP2B (charged multivesicular body protein 2B) have been identified as causative genes for familial case of ALS. In an attempt to elucidate the disease specific marker for TDP-43 proteinopathy, we investigated the immunoreactivity of endosome related proteins in patients with ALS and ALS-D.

Methods : Paraffin-embedded brain and spinal specimens from 5 patients with ALS and 8 patients with ALS-D were examined. The frontal white matter and the anterior horn were immunolabeled with anti-transferrin, anti-transferrin receptor, or anti CHMP2B antibodies.

Results : Only a fraction of oligodendrocytes was immunoreactive for transferrin in patients with ALS-D. By contrast, in patients with ALS, transferrin was positive in almost all oligodendrocytes and localized around perinuclear region. In case of ALS-D, transferrin distributed diffusely along the oligodendrocyte processes. Skein like inclusions and round inclusions were immunopositive for CHMP2B in both ALS and ALS-D. In all specimens, spheroids were intensely labeled with anti-transferrin receptor antibody.

Conclusion: The pattern of immunoreactivity of an endosome related protein was pathologically discrete between ALS and ALS-D. Dysregulation of endosome pathway might be involved in the pathogenesis of motor neuron disease, and its mode of dysregulation might be reflected by the distribution of lesions detected immunocytochemically.

O11-1 Systematic Identification of the growth cone proteins that are essential to axonal growth

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The growth cone is a motile tip formed at the developing and the regenerating neuronal processes, and functions for accurate axon pathfinding and synaptogenesis. We recently identified 945 proteins in growth cones using proteomics. As a result of the systematic immunostaining, 98 proteins of them were more concentrated in the growth cone than GAP-43. We performed the RNAi experiments against those proteins and found the siRNAs against 20 proteins significantly inhibited axonal growth. These proteins were categorized into four classes based upon their localizations. The growth cone is divided into two distinct areas; i.e., peripheral (P) region where F-actin is enriched, and central (C) region where microtubule bundles and vesicle are concentrated. We identified four proteins localized in P region, and one protein was concentrated in C region. The eight other proteins were dominantly distributed in the C region, but the remaining seven species were concentrated both in the P-region and in the C-region. We conclude that these molecules may be involved in the main machinery for axonal growth.

O11-3 Differential regulation of cortical dendritic and axonal development via distinct activation of CaMKK-CaMKI pathways

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The specialized architectures observed in axons and dendrites are cellular bases for establishment of neuronal network. Calcium signaling seems to regulate both axonal and dendritic development, but downstream signaling events, which underlie differential regulation of each process, is poorly understood. The multifunctional Ca²⁺/calmodulin-dependent protein kinases (CaMKI, CaMKII and CaMKIV) are logical candidate effectors downstream of Ca²⁺ elevation, as their contribution in versatile cytoskeletal regulations has been gradually elucidated. Here we show that inhibition of CaMKKs, which are upstream kinases of CaMKI and CaMKIV, impaired both dendritic and axonal development in early cortical neurons. We further found that individual activation and inhibition of CaMKI isoforms bidirectionally regulated dendritogenesis and axonogenesis. Among CaMKI isoforms, overexpression and knockdown of CaMKI α /CL3 facilitated and impaired dendritic growth, respectively, while they had no effect on axonal growth. By clear contrast, manipulations of the CaMKI α activity specifically affected on axonal events, presumably by complementary mechanisms including distinct activation processes, respective kinase localizations and also substrate specificities. Thus we demonstrated the existence of clearly segregated Ca²⁺-dependent signaling pathways in axonal and dendritic outgrowth of cortical neurons, which may also control precise network formation during cortical development.

O11-4 Functional screen combining fluorophore-assisted light inactivation and organotypic cultures of the developing brain○Kohtaro Takei^{1,3}, Megumi Yamaguchi¹, Yasufumi Sato^{1,2,3}, Masumi Iketani¹, Yuko Arie¹, Yoshio Goshima^{1,3}¹Department of Molecular Pharmacology and Neurobiology, Graduate School of Medicine, Yokohama City University, Yokohama, Japan, ²Stroke Research Group, Mitsubishi Kagaku Institute of Life Sciences, Tokyo, Japan, ³CREST, Japan Science and Technology Agency, Kawaguchi, Japan

To exploit advances in methodology for analysis of protein function, direct target validation of proteins in living tissue is the most useful approaches. We characterized fluorophore-assisted light inactivation (FALI) that uses coherent light and fluorescein-conjugated antibody. We developed a simple and easy FALI-based protein ablation method (SELT-FALI). FALI of Neuropilin-2 (Np2), a receptor for Semaphorin-3F (Sema3F) resulted in a complete reduction of Sema3F affinity in Np2-expressed COS7 cells. The FALI-mediated damage of Np2 was dependent on the quantity of light energy. We applied it to organotypic culture of the developing mouse telencephalon. FALI of Np2 for 24 hours in culture resulted in a reduction of Sema3F affinity in Np2-expressed neurons. Thus, we established a novel strategy of protein function analysis in the cultured developing brain. By using this methodology, we performed functional screen for searching for key molecules involved in lateral olfactory tract (LOT) development with monoclonal antibodies raised against LOT protein extract. FALI with H24G11 monoclonal antibody showed defasciculation of LOT axonal bundles, and the antigen of this antibody was identified as a novel membrane surface molecule serving for LOT formation. We designated this protein as LOT usher substance (LOTUS). While FALI of LOTUS for 24 hours at embryonic day (ED) 12 resulted in defasciculation of LOT axonal bundles, FALI of LOTUS for 24 hours at ED13 showed no significant perturbation of LOT development. These observation suggest that LOTUS may function in LOT development for only 24 hours from ED12 to ED13. Thus, this methodology can provide a new approach for functional analysis of the molecule acting in a narrow time window in the developing brain.

O12-1 Sema4D in regulation of neural cell apoptosis after stroke○Shinobu Inagaki¹, Takenobu Wada², Wataru Yamaguchi¹, Mariko Ogiya¹, Noriko Uesugi¹, Mizue Takahara¹, Oriie Saino³, Tatsuo Furuyama⁴, Mikihiko Kogo², Tomohiro Matsuyama¹¹Group of Neurobiology, Division of Health Sciences, Osaka University Graduate School of Medicine, ²Department of Pathogenesis and Control of Oral Diseases, Osaka University Graduate School of Dentistry, ³Hyogo College of Medicine, ⁴Department of Oral Anatomy and Developmental Biology, Kagawa Prefectural College of Health Sciences

Sema4D, a transmembrane semaphorin, is expressed in the central nervous system (CNS) during development and in adulthood as well as in the immune system. In the adult brain, it is localized in oligodendrocytes but its roles are still equivocal. In Sema4D-mutant mice labeled by an inserted lacZ, a number of lacZ expressing cells were myelin associated glycoprotein (MAG)-positive and GSTpi-positive oligodendrocytes. This result was well in agreement with the previous studies indicating Sema4D-expression localized in mature oligodendrocytes. To investigate whether Sema4D is involved in cell death in the injured brain, the effects of Sema4D-deficiency were examined on neural cell-injury following transient focal cerebral ischemia. After cerebral ischemia produced by transient occlusion of middle cerebral artery (MCAO), apoptosis was enhanced in the Sema4D-deficient mice. We further examine how Sema4D-deficiency influences post-ischemic apoptotic cells at late stage of ischemic injury.

O12-3 Pathophysiological relevance of uncoupled endothelial nitric oxide synthase in ischemia-induced neurovascular injury○Feng Han¹, Kohji Fukunaga²¹Department of Pharmacology, Tohoku University, Sendai, Japan, ²Tohoku Univ. 21st Century COE Program

Neurodegenerative diseases including brain ischemia are in part mediated by oxidative stress, in which superoxide generation through NADPH oxidase, mitochondrial pathway and cyclooxygenase account for neurodegeneration. However, pathophysiological role of endothelial nitric oxide synthase (eNOS) in brain ischemia-induced neurovascular injury remains unclear. We previously documented that microsphere embolism (ME)-induced ischemia up-regulated eNOS expression in brain microvessels, thereby leading to blood-brain barrier disruption (1) and beta-amyloid accumulation in the microvessels (2). We here demonstrated that up-regulated eNOS in part mediates superoxide generation through eNOS uncoupling in brain microvessels. We also confirmed that superoxide generation in microvessels by uncoupled eNOS is inhibited by a novel calmodulin inhibitor, DY-9836. Taken together, superoxide generation by uncoupled eNOS following brain ischemia likely mediates neurovascular injury and inhibition of uncoupled eNOS by DY-9836 is novel therapeutic strategy for neurovascular protection in brain ischemia. 1. Han F., Fukunaga K. et al., J Neurochem. 2006; 99:97-106. 2. Han F., Fukunaga K. et al., Neuroscience 2008; 153:414-427

O11-5 Effects of motoneuron-derived factor(s) on dorsal root ganglia development in mouse embryos○Noriyoshi Usui^{1,2}, Hirohide Takebayashi^{1,2}, Katsuhiko Ono^{1,2}, Kazuhiro Ikenaka^{1,2}¹Department of Physiological Sciences, The Graduate University for Advanced Studies, Hayama, Japan, ²Division of Neurobiology and Bioinformatics, National Institute for Physiological Sciences, Okazaki, Japan

Execution of motor behaviors depends on circuitries effectively integrating immediate sensory feedback to motor pathways controlling muscle activity. Motor and sensory circuitries are thought to interact during development, however, the molecular mechanisms are not fully understood. To investigate effects of motoneuron-derived factor(s) on early dorsal root ganglia (DRG) development, we analyzed DRG phenotype of Olig2 knockout embryos, which have no motoneuron in the spinal cord. In the E10.5 DRG of Olig2 knockout mice, increased number of apoptotic cells was observed. Furthermore, abnormal axon guidance of sensory neurons was also observed in Olig2 knockout mice at E10.5 and E12.5. These data suggest that motoneuron-derived factor(s) may modulate sensory neuron survival and axon guidance. Among neurotrophic factors, we focused on neurotrophin-3 (NT-3), because NT-3 is known as a survival factor for sensory neuron and chemoattractant role for sensory axons. Using *in situ* hybridization, we confirmed NT-3 mRNA expression in motoneurons in wild type and Olig2 heterozygous mice at E10.5, and E13.5, but no expression in Olig2 knockout mice at corresponding stages. NT-3 mRNA expression outside of spinal cord became stronger at later stage. These data suggest that motoneuron-derived NT-3 is an essential factor for the survival and axon guidance of sensory neurons at early developmental stage.

O12-2 Sema4D in regulation of neural cell production after stroke○Takenobu Wada¹, Wataru Yamaguchi², Oriie Saino³, Yoshitaka Taniguchi¹, Rie Tamai¹, Makoto Abe¹, Tatsuo Furuyama⁴, Tomohiro Matsuyama¹, Shinobu Inagaki¹, Mikihiko Kogo²¹Department of Pathogenesis and Control of Oral Diseases, Graduate School of Dentistry, Osaka University, ²Group of Neurobiology, Division of Health Sciences, Osaka University Graduate School of Medicine, ³Laboratory of Neurogenesis and CNS Repair, Institute for Advanced Medical Sciences, Hyogo College of Medicine, ⁴Department of Oral Anatomy and Developmental Biology, Graduate School of Dentistry, Kagawa Prefectural College of Health Sciences

Sema4D, a transmembrane semaphorin, is expressed in the central nervous system (CNS) during development and in adulthood as well as in the immune system. In the adult brain, it is localized in oligodendrocytes but its roles are still equivocal. To investigate whether Sema4D is involved in cell death and proliferation in the injured brain, the effects of Sema4D-deficiency were examined on neural cell-injury following transient focal cerebral ischemia. In Sema4D-mutant mice labeled by an inserted lacZ, a number of lacZ expressing cells were myelin associated glycoprotein (MAG)-positive and GSTpi-positive oligodendrocytes. This result was well in agreement with the previous studies indicating Sema4D-expression localized in mature oligodendrocytes. After cerebral ischemia produced by transient occlusion of middle cerebral artery (MCAO), oligodendrocytes were markedly increased in number in injured cortex at 7 and 14 days of reperfusion in Sema4D-deficient mice but not in wild-type mice. A number of oligodendrocytes simultaneously incorporated BrdU in Sema4D-deficient mice. To investigate whether this increase in injured brain of Sema4D deficient mice might be caused by reduced cell death, ischemia-induced apoptosis was examined in the wild-type and the mutant mice. Terminal deoxynucleotidyl transferase (TdT)-mediated biotin-dUTP nick end labeling (TUNEL)-positive apoptotic cells were much more numerous in Sema4D-deficient mice than in wild-type mice. These data indicated that the lack of Sema4D enhanced oligodendrogenesis after cerebral ischemia.

O12-4 Inhibition of protein tyrosine kinase prevents disruption of blood brain barrier and attenuates infarct size after transient focal cerebral ischemia○Kazutoshi Murotomi¹, Norio Takagi¹, Yuji Takenaga¹, Satoshi Takeo¹, Kouichi Tanonaka¹¹Department of Molecular and Cellular Pharmacology, Tokyo University of Pharmacy and Life Sciences, Tokyo, Japan

Cerebral ischemia provokes disruption of the blood-brain barrier (BBB), which can be initiating factors for the development of cerebral infarctions. Although the molecular structure of tight junctional complexes in the BBB has been identified, little is known about pathophysiological alterations of tight junctional proteins after cerebral ischemia and reperfusion. In the present study, we investigated alterations of tight junctional proteins, such as occludin, in isolated brain capillaries after transient (90-min) middle cerebral artery occlusion in the rat. We demonstrated that tyrosine phosphorylation of occludin was increased, which might have been caused by an increased activity of tyrosine kinase Src after cerebral ischemia and reperfusion. The intravenous administration of a Src inhibitor PP2 (30 µg/kg, i.v.) attenuated the increase in the tyrosine phosphorylation of occludin in isolated brain capillaries after cerebral ischemia and reperfusion. BBB leakage, which was determined by injecting FITC-albumin into the carotid arteries, was augmented after cerebral ischemia and reperfusion. The administration of PP2 inhibited BBB leakage and reduced the volume of cerebral infarction. These results suggest that an increase in tyrosine phosphorylation of occludin may play a pivotal role in the disruption of endothelial tight junction in the brain, which may lead to dysfunction of the BBB after cerebral ischemia and reperfusion.

O12-5 PEDF protects against ischemic brain injury in the rat middle cerebral artery occlusion model.

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Pigment epithelium-derived factor (PEDF) is a 50-kDa glycoprotein that protects various types of cultured neurons against neurotoxic stimuli, but its precise role in the CNS is not fully understood. In this study, we used rats whose brains were transfected to overexpress human PEDF to elucidate the neuroprotective effect of PEDF after transient middle cerebral artery occlusion (MCAO). A replication-defective adenoviral vector containing the human PEDF gene (Ad.PEDF) or E.coli β -galactosidase (Ad.LacZ) was directly injected into the right striatum at 7 days prior to 70 min of MCAO in rats. Infarct volume and degree of edema of the Ad.PEDF-treated group at 24 h after MCAO were significantly reduced compared with the Ad.LacZ-treated group. Degeneration of neurons, astrocytes and oligodendrocytes caused by MCAO were attenuated by overexpression of PEDF. The up-regulation of pro-inflammatory genes (TNF α , IL-1 β , IL-6, COX-2, and iNOS) and water channel AQP4 after MCAO was significantly reduced in Ad.PEDF-injected striatum. In conclusion, the results from this study provide the first in vivo evidence that PEDF is as effective in protecting CNS neurons from ischemic insult, suggesting that PEDF may have a role as an endogenous neurotrophic factor in the CNS.

O13-2 Neuropilin strongly induces cytomegalovirus major immediate-early promoter/enhancer activity in neurons

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Proteolysis system is thought to play a crucial role in modulation of signal transduction via degradation or proteins shedding of cytoskeleton, kinases, receptors, matrix and membrane proteins. Recently, it has been suggested that neuropilin (NP), a serine protease, is associated with synaptogenesis, long-term potentiation, and working memory; however, little is known about the molecular mechanism. Here, we report that NP strongly induces cytomegalovirus (CMV) major immediate-early promoter/enhancer activity in cultured neurons. We infected neurons with CMV-green fluorescent protein (GFP) promoter/reporter constructs and measured transgene expression by quantifying GFP fluorescence. When the active form of recombinant NP added to the neurons, the promoter activity is dramatically up-regulated. The present results suggest that outside-in signaling by NP is implicated in modulation of gene expression.

O13-4 Functional analysis of RhoGEF10

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Semaphorins are axon guidance molecules that signal through the plexin family of receptors. Semaphorins also play a role in other processes such as immune regulation and tumorigenesis. Semaphorin 4D is the ligand for the plexin-B1 receptor and stimulation of the plexin-B1 activates the small GTPase RhoA. Plexin-B1 interacts with various Rho-specific guanine nucleotide exchange factors (RhoGEFs) and stimulates Rho activation and induces cytoskeletal reorganization. Previously we isolated Rho guanine nucleotide exchange factor 10 (RhoGEF10) as a novel plexin-B1-specific interacting protein using yeast two-hybrid screening. RhoGEF10 contains only Dbl-homology (DH) domain. Verhoeven et al. previously described that a single, non-silent point mutation in RhoGEF10 (an amino acid substitution of threonine to isoleucine at codon 332 (T332I)) co-segregates with slowed nerve conduction velocities and thin myelination of peripheral nerves. These data suggest that plexin-B1/RhoGEF10 signaling plays a pivotal role especially in developmental myelination of peripheral nerves. To demonstrate a role for plexin-B1/RhoGEF10 signaling, we analyzed function of RhoGEF10 using various RhoGEF10 mutants.

When expressed in HEK293T cells, RhoGEF10-T332I, Δ N, which is a mutant that is truncated at the N-terminal but contains the DH domain, induced cellular rounded-morphology. This rounded morphology was dependent on DH domain and inhibited by treatment with Y-27632, which is RhoA effector, ROCK inhibitor. Further experiments revealed that the expression of RhoGEF10- Δ N induced activation of RhoA. These data indicated that N-terminal domain of RhoGEF10 downregulates GEF activity of RhoGEF10. The pull-down assay demonstrated that both N-terminus and DH domain of RhoGEF10 interacted with intracellular domain of plexin-B1. RhoGEF10-N-terminus also interacted with RhoGEF10-C-terminus. Our data suggested that RhoGEF10-N-terminus interacts with intracellular domain of plexin-B1 and RhoGEF10-C-terminus, thereby regulating its GEF activity.

O13-1 Searching for CaMKII-interacting proteins and analysis of the functional relationship using coexpression database

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To molecularly understand neural plasticity with CaMKII, we undertook probing interaction proteins directly or indirectly bound to the key enzyme of *Drosophila melanogaster* using a monoclonal antibody. The proteins immunopurified from late embryonic extracts were separated on SDS-PAGE and identified by peptide mass fingerprinting. Most of the obtained 74 proteins have not been known as the CaMKII-interacting proteins to date, but were interesting proteins such as membrane trafficking and cytoskeleton proteins associated with synaptic transmission. Also 50% and 20% of the identified proteins had been found as postsynaptic density proteins and synaptic vesicle's proteins in proteome analyses, respectively, suggesting that identified proteins were related to CaMKII signaling in synaptic plasticity. The interactions between CaMKII and respective 30 proteins were not detected by immunoprecipitations in a mammalian expression system. From an idea on the requirement of multiple factors for the interaction, although simultaneous expression in the same cell and reconstitution experiments of several proteins were performed, the interactions were not detected in the proteins we tested. The protein complex with CaMKII is thought to be unstable or require unidentified factor(s). In addition, we analyzed functional relationship between CaMKII interacting proteins in silico by applying human orthologs. We have constructed coexpression database (db) of human genes which derived from publicly available GeneChip data and provides coexpressed gene lists and networks. Now we developed it by introducing independent protein-protein interaction and coexpression similarity into the same platform. Coexpression interactions in the identified proteins were extracted using the db. We will discuss about relationship between CaMKII and identified proteins from protein-protein and coexpression interaction.

O13-3 Regulation of endosomal localization of AATYK1A and its interaction with Src by palmitoylation

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Apoptosis-associated tyrosine kinase 1 (AATYK1), also named LMTK1, was previously isolated as an apoptosis-related gene from 32Dcl3 myeloid precursor cells, but its precise function remains unknown. AATYK1A, an isoform without a transmembrane domain, is highly expressed in neurons. We identified palmitoylation of AATYK1A at three N-terminal cysteine residues in cortical cultured neurons and COS-7 cells and found that palmitoylation determined localization of AATYK1A to the transferrin receptor-positive recycling endosomes. Further, we identified the tyrosine kinase Src as a novel AATYK1A-interacting protein. Fyn and Src phosphorylated AATYK1A at tyrosines 25 and 46 in a palmitoylation-dependent manner. The binding of AATYK1A with Src in endosomes was also palmitoylation dependent. These data suggest that palmitoylation is a critical factor regulating not only the subcellular localization of AATYK1A but also its interaction with Src.

O13-5 The intracellular signal of repulsive guidance molecule RGMa

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Repulsive guidance molecule (RGMa) is a potent inhibitor of axon regeneration in the adult central nervous system. RGMa inhibits mammalian CNS neurite outgrowth by a mechanism dependent on activation of the Rho/Rho-kinase pathway. Intrathecal administration of the RGMa-neutralizing antibody to rats with spinal cord injury results in significant axon growth of the corticospinal tract, and improves functional recovery. Here we present the ongoing study on the intracellular signal of RGMa. Understanding of the molecular mechanism of RGMa may be useful for developing methods to overcome the inhibitory signals.

O14-1 Possible involvement of peroxisome proliferator-activated receptor- γ in protective effects of interferon- γ against methamphetamine-induced neurotoxicity

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Repeated injections of methamphetamine (METH) cause degeneration of striatal dopaminergic nerve terminals representing by the reduction of dopamine transporter (DAT). Regarding the mechanism responsible for METH-induced neurotoxicity, various hypotheses have been proposed, including glutamate release, reactive oxygen/nitrogen species, dopamine quinone, apoptosis-related molecules and inflammatory molecular and/or cellular events. Recently, we reported that the intraperitoneal or intracerebroventricular injections of interferon- γ (IFN- γ) adjunct to METH injections significantly prevented METH-induced reduction of striatal DAT-positive signals and suggested IFN- γ injected systemically or its related molecule protects against METH-induced neurotoxicity through intracerebral molecular pathways (Hozumi et al., Toxicol. Lett., 177: 123-129, 2008). The peroxisome proliferator-activated receptor- γ (PPAR- γ) is an inhibitory transcription factor that inhibits gene expression of inflammatory cytokines such as IL-1 β , IL-6 and TNF- α . IFN- γ is known to activate PPAR- γ . In the present study, therefore, we examined the changes in nuclear PPAR- γ induction in the METH-induced striatal neurotoxicity and effects of IFN- γ injections, to clarify the mechanism of protective effects of IFN- γ against METH-induced neurotoxicity. The cell number and the signal density of nuclear PPAR- γ expression in the striatum were decreased 3 days after METH injections (4 mg/kg $\times$ 4, i.p. with 2 h-interval). These reductions of nuclear PPAR- γ expression were attenuated by systemic injection of IFN- γ prior to repeated METH injections. These results imply that the IFN- γ -induced PPAR- γ activation in the striatum may be involved in its protective effects against METH-induced neurotoxicity.

O14-3 Neuroprotection by brain-migrated immature bone marrow cells in an artificial brain injury

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A certain part of immature bone marrow cells (BMCs) migrate into the brain parenchyma at early stage of bone marrow transplantation and stay there for several months. It has previously been clarified that BMCs were activated and accumulated around injury sites, and most of them were differentiated into microglia-like cells in a short term after a brain injury, however, roles of BMCs at injury sites are not clear. In this study, we examined properties of BMCs and BMCs-derived cells for neural damages in short and long term after the brain injury using GFP-expressing bone marrow chimera mice (BMT mice). The injury was clearly detected on 3 days by MRI. Site of injury was gradually expanded from 2 weeks to 10 weeks in the brains of control mice, whereas that in the brains of BMT mice decreased. Immunohistochemical analysis confirmed the protective effect of BMT on neurons. Real time PCR analysis indicated increased expression of neurotrophic factors such as BDNF and GDNF in BMT mice. BMCs and BMCs-derived cells at the injury sites were partially positive for BDNF and GDNF in immunohistochemical analysis. These suggested that exogenous BMCs which migrated into the injured brain, might display neuroprotective effects via production neurotrophic factors such as BDNF and GDNF consequently.

O14-5 Protective effects of yokukansan, a traditional Japanese medicine, on glutamate-induced neuronal death

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Yokukansan, which is a traditional Japanese medicine, has been reported to improve behavioral and psychological symptoms of dementia in patients with dementia. However, the mechanism is still unclear. In various animal models used for research in the pathogenesis and therapy of dementia, the increase in the extracellular level of glutamate in the brain has been reported. Recently, we also demonstrated that the increase in extracellular level of glutamate and degenerations of neuronal and astroglial cells were observed in the brain of thiamine-deficient rats. Yokukansan inhibited not only the thiamine-deficient-induced increase in extracellular level of glutamate but also the degeneration of cerebral neurocytes and astrocytes in the rats. These results suggest that one of mechanisms underlying the effects of yokukansan may be closely related to improvement of glutamate excitatory neurotoxicity. In order to clarify this hypothesis, in the present study, we first investigated the effects of yokukansan on glutamate uptake in cultured rat cortical astrocytes. In thiamine-deficient condition, the uptake of glutamate into astrocytes and expressions of GLAST and GLT-1 mRNAs of astrocytes significantly decreased. These decreases were improved by treatment with yokukansan (100-700 μ g/ml), in a dose-dependent manner. The improvement of glutamate uptake with yokukansan was completely blocked by a glutamate transporter inhibitor, DL-threo- β -hydroxyaspartic acid. We next examined the effects of yokukansan on glutamate-induced neuronal death using cultured PC12 cells as a model for neuron. Addition of glutamate to the medium in the cultured cells induced an approximately 50% neuronal death as evaluated by the MTT assay. Yokukansan (1-1000 μ g/ml) inhibited the neuronal death, in a dose-dependent manner. Furthermore, competitive binding assay to glutamate receptors showed that yokukansan possessed a potent binding to NMDA receptor, in particular, its glutamate and glycine recognition sites. These results suggest that yokukansan may possess a protective effect against the glutamate-induced excitatory neurotoxicity not only by amelioration of dysfunction of astrocytes but also by protection of neuronal death.

O14-2 Mechanisms of neuroprotection by nicotinic signaling in cultured rat cortical astrocytes

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Activation of the nicotinic acetylcholine receptors (nAChRs) would lead to rapid opening of an ion channel permeable to Na⁺, K⁺ or Ca²⁺ ions across cell membranes, followed by facilitation of the release of various neurotransmitters and subsequent signaling cascade from the cytoplasm to the nucleus for consolidation of a transient extracellular signal carried by acetylcholine in the brain. This study was aimed at the investigation of the mechanisms underlying signaling mediated by nAChRs in cultured rat cortical astrocytes. The nAChRs are composed of heteromeric assemblies of at least eight α subunits (α 2- α 9) and three β subunits (β 2- β 4), while α 8 subunit is absent from mammals. RT-PCR analysis revealed the constitutive expression of ten different subunits in cultured rat cortical astrocytes. Cortical astrocytes were incubated with fluo-3 AM for determination of intracellular free Ca²⁺ ions on fluorescence image analysis. Exposure to nicotine led to an increase in the number of cells with high fluorescence intensity in cortical astrocytes. This increase by nicotine was significantly decreased by the addition of the α 4 β 2 heteromeric subtype specific antagonist dihydro- β -erythroidine and the α 7 homomeric subtype specific antagonist methyllycaconitine, respectively. Nicotine induced the expression of mRNA for various neurotrophic factors including GDNF in cultured cortical astrocytes, while MTT reduction activity was increased by the culture with conditioned medium from astrocytes previously incubated with nicotine in cortical neurons. *In silico* analysis revealed the existence of NF- κ B, CREB and AP-1 like binding elements on the GDNF gene promoter. Exposure to nicotine significantly increased the luciferase activity in cortical astrocytes transfected with the reporter plasmid of NF- κ B, but not that of CREB or AP-1. These results suggest that nAChRs may be functionally expressed by rat cortical astrocytes to induce mRNA expression of different neurotrophic factors including GDNF through the facilitation of its promoter activity at the NF- κ B-like site toward neuroprotection.

O14-4 Protection by ATP against NMDA neurotoxicity

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Extracellular ATP is now believed to play a role as a signal mediator through activation of ionotropic P2X receptors and metabotropic P2Y receptors in the brain. In the present study, we have attempted to demonstrate the possible modulation by ATP signals of the neurotoxicity of N-methyl-D-aspartate (NMDA). For this purpose, neurons were prepared from the hippocampus of embryonic 18-day-old rats. An RT-PCR analysis revealed the expression of mRNA for P2X2, P2X3, P2X4, P2X6, P2X7, P2Y1, P2Y2, P2Y4, P2Y6, P2Y12 and P2Y14 isoforms, in addition to A1, A2a and A2b isoforms of P1 receptors for adenosine, in neurons cultured for 8 days. However, mRNA expression was not seen for P2X1, P2X5, P2Y13 or A3 isoforms. A significant decrease was seen in MTT reduction in neurons briefly exposed to glutamate (Glu) at 10 to 500 μ M for 1 h when determined 24 h and 48 h after the exposure, whereas prior and sustained exposure to 1 mM ATP significantly prevented the decrease by Glu irrespective of the determination timing. Hoechst22242 staining confirmed the protection by sustained exposure to ATP against the neurotoxicity of Glu. Similarly significant protection was induced by UTP and ADP, in addition to ATP, against the decrease in MTT reduction in neurons exposed to NMDA at 50 to 100 μ M for 1 h. Hippocampal neurons were loaded with the Ca²⁺-sensitive dye fluo-3 AM, followed by exposure to 10 μ M Glu or 100 μ M NMDA in either the presence or absence of 1 mM ATP for 10 min and subsequent addition of the calcium ionophore A23187 for quantification of the fluorescence intensity using a confocal microscope. A marked increase was seen in the fluorescence in neuronal cells exposed to Glu or NMDA, while ATP at 1 mM significantly attenuated the increase by Glu and NMDA. However, ATP did not significantly prevent the decrease in MTT reduction in neurons exposed to hydrogen peroxide, 2,4-dinitrophenol, A23187 or tunicamycin. These results suggest that ATP may predominantly protect neurons from the cytotoxicity of NMDA through a mechanism relevant to intracellular free Ca²⁺ levels in cultured hippocampal neurons.

O15-1 Bcl-2 family proteins are involved in neuronal apoptosis in the chorea-acanthocytosis model mouse.

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Chorea-acanthocytosis (ChAc) is a hereditary neurodegenerative disorder caused by loss of function mutations in the VPS13A gene encoding chorein. Recently, we produced a ChAc model mouse using a gene targeting technique to delete exons 60-61 that corresponds to a human disease mutation. Selective neuronal degeneration was observed in striatum of the ChAc-model mouse. Previously, we reported that proteomic analysis of striatal protein in the ChAc model mouse revealed an increased protein level of DARPP-32. DARPP-32, which regulates ion channels and receptors functions acting as an inhibitor of protein phosphatase-1 (PP1) at striatum, is a pivotal integrator of dopamine signals. PP1 and protein phosphatase 2A (PP2A) dephosphorylate Bcl-2 family proteins and regulate apoptosis. In the present study, we performed immunoblot and immunohistochemical analyses to detect alterations in protein expression levels of Bcl-2 family related with apoptosis in striatum, cerebral cortex, and hippocampus of in comparison between ChAc-model mice and wild-types. The expression levels of PP2A and Caspase-3 tend to be increased in the striatum and the hippocampus and Caspase-3 expression levels increase significantly in the hippocampus of the ChAc-model mouse. Our preliminary results suggest that Bcl-2 family proteins are involved in the ChAc brain pathology.

O15-2 Decreased expression level of adducin β is associated with neurodegeneration and acanthocytosis in chorea-acanthocytosis

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Chorea-acanthocytosis (ChAc) is an autosomal recessive disorder characterized by striatal degeneration and erythrocyte acanthocytosis. Loss of function mutations in VPS13A gene coding a large protein, chorein, cause ChAc. In the present study, to understand protein expression alterations mediated by a chorein deficiency, we performed a parallel proteomic analysis of protein expression in erythrocyte membrane of a ChAc patient. We found an decreased protein level of adducin β protein which is involved in the assembly of spectrin-actin network in erythrocyte. Recently, we produced a ChAc model mouse which shows the striatal neurodegeneration. Subsequently, we performed immunoblot and immunohistochemical analyses in the striatum of the ChAc model mouse. Consistently, adducin β immunoreactivity was lower in the striatum. Our results suggest that decreased adducin β is related to both the brain pathology and acanthocytosis of ChAc.

O15-4 Analysis of the molecular mechanism for 'dying-back' type of axonal degeneration in gracile axonal dystrophy (GAD) mouse

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Local axonal degeneration is a common pathological feature of peripheral neuropathies and neurodegenerative disorders in the CNS, including Alzheimer's disease (AD), Parkinson's disease (PD) and the stroke. However, its underlying molecular mechanism is not clear yet. Here, we analyzed the gracile axonal dystrophy (gad) mouse that displays 'dying-back' type of axonal degeneration in sensory neurons to find the molecules involved in the mechanism of axonal degeneration. The gad mouse is analogous to null mutant of ubiquitin carboxyl-terminal hydrolase L1 (UCH-L1), a deubiquitinating enzyme expressed in neurons and testis/ovary. We compared protein expression in sciatic nerves between gad and wild-type mice at 2 and 12 weeks of age, using two-dimensional difference gel electrophoresis. As a result, we found age-dependent accumulations of several proteins including glyceraldehyde-3-phosphate dehydrogenase (GAPDH) and 14-3-3. In the wild-type mouse, GAPDH and 14-3-3 were localized throughout axons, however the gad mouse showed uneven localization of GAPDH along axons. Though GAPDH has been shown as a classic glycolytic enzyme, recent findings suggest that it functions as a multi-functional protein. Our findings may provide important information to understand the mechanisms of axonal degeneration, and to find a new function of GAPDH in the neurodegeneration.

O16-1 Possible role of a multi-domain adaptor protein, p140Cap, at the presynapse

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p140Cap is an adaptor protein considered to play pivotal roles in cell adhesion, growth and Src tyrosine kinase-related signaling in non-neuronal cells. It is also reported to interact with a presynaptic membrane protein, SNAP-25, and may participate in neuronal secretion. However, properties and precise functions of p140Cap in neuronal cells are almost unknown. Here we show, using biochemical analyses, that p140Cap is expressed in rat brain, in a developmental stage-dependent manner, and is relatively abundant in the synaptic plasma membrane fraction in adults. Immunohistochemistry showed localization of p140Cap in the neuropil in rat brain and immunofluorescent analyses detected p140Cap at synapses of primary cultured rat hippocampal neurons. Electron microscopy further revealed localization at presynapses along plasma membranes. Screening of p140Cap-binding proteins identified a multi-domain adaptor protein, vinexin, whose third SH3 domain interacts with the C-terminal Pro-rich motif of p140Cap. Immunocomplexes between the two proteins were confirmed in COS7 and rat brain. We also clarified that a presynaptic protein, synaptophysin, interacts with p140Cap. These results strongly suggest that p140Cap is involved in neurotransmitter release, and synapse formation/maintenance and signaling.

O15-3 Immediate early gene products down-regulated by nicotine in hippocampus in DRPLA transgenic mice

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Purpose: In previous studies we have shown that intranuclear accumulation of mutant proteins with expanded polyglutamine stretches plays essential roles in neurodegeneration in polyglutamine diseases. To investigate the effects of intranuclear accumulation of mutant proteins on the nuclear functions, we have analyzed activation of immediate early genes (IEGs) in brain of DRPLA transgenic mice induced by nicotine administration. **Methods:** DRPLA transgenic male mice (12-week-old 113 (Q113) or 8-week-old 129 (Q129) repeats) were used in this study. Animals were given intraperitoneally nicotine (1, 2, 3 or 4 mg/kg) or 0.3ml of saline, and all mice were transcardially perfused at 2 hours, and post-fixed overnight. Free floating sections were stained by immunohistochemistry. Expressions of c-Fos protein in hippocampus were quantified by Lumina Vision software. Statistical analysis was performed by the one-way or two-way analysis of variance (ANOVA). **Results:** 1. Expression levels of c-Fos were very low and did not show significant increase after administration of saline in DRPLA transgenic mice or in non-transgenic mice. 2. Expression of c-Fos was up-regulated by nicotine administration in cerebral cortex and amygdala even at low dose, and increased in hippocampus when the dose of nicotine was increased in 8-week-old male C57BL/6 mice. 3. Expression of c-Fos in DRPLA transgenic and non-transgenic mouse brain was low when administered saline or low dosage of nicotine. Importantly, expressions of c-Fos increased significantly post administration of 3 or 4 mg/kg nicotine in DRPLA non-transgenic mice, but not transgenic mice, and the degrees were dependent on the nicotine dosage. **Conclusion:** We demonstrated that expressions of IEGs products showed lower level in transgenic mice compared with non-transgenic mice. These findings suggest that suppressed activation of IEGs is involved in the nuclear dysfunctions as the results of intranuclear accumulation of mutant DRPLA protein.

O15-5 Microarray analysis in the dorsal root ganglion of rats with paclitaxel-induced neuropathy

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Paclitaxel-induced painful peripheral neuropathy is a major dose-limiting factor. Recently, it has been reported that macrophages accumulated in the dorsal root ganglion of paclitaxel-treated rats, and their activation is suggested to contribute for generation and development of the neuropathy. However, the mechanism for macrophage activation is still unknown. In this study, to explore candidate genes involved in the mechanism for macrophage activation in the dorsal root ganglion of paclitaxel-treated rats, we developed model rats for paclitaxel-induced neuropathic pain and performed a microarray assay to analyze the changes of gene expressions in the dorsal root ganglion. Among the genes with changed expression levels, we focused on matrix metalloproteinase-3 (MMP-3, stromelysin-1) and CD163, a macrophage marker. By RT-PCR, the expression levels of MMP-3 and CD163 were markedly up-regulated in paclitaxel-treated dorsal root ganglion. As a result of immunohistochemical study, large ganglion neurons, but neither Schwann cells nor macrophages, predominantly expressed MMP-3. This MMP-3 up-regulation occurred prior to macrophage accumulation in the dorsal root ganglion. In addition, recombinant MMP-3 led to the activation of RAW264 macrophages in vitro. Taken together, we suggested that the up-regulation of MMP-3 and following macrophage activation caused in the dorsal root ganglion might be a significant event to trigger a series of reactions developing paclitaxel-induced peripheral neuropathic pain.

O16-2 Possible involvement of myosin-ATPase in the vesicle recruitment for exocytosis in adrenal chromaffin cells: Studies with scanning electron microscopy

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Reorganization of actin cytoskeleton and actin-myosin interaction seem essential for the vesicle recruitment for exocytosis in adrenal chromaffin cells (1). The role of myosin II in vesicle transport was also suggested recently by Gutiérrez and his colleagues (2). In order to further clarify the involvement of myosin ATPase in the mechanism of vesicle recruitment, we examined the effects of 2,3-butanedione monoxime (BDM), an inhibitor of myosin ATPase, on the secretory events detected by amperometry and on the vesicle dynamics. Examination of exocytotic events evoked by high K⁺ and by sucrose suggested that myosin ATPase is required for the recruitment of the vesicles from the reserve pool to the releasable pool in adrenal chromaffin cells. In this study, three-dimensional (3D) structure of the interior of bovine adrenal chromaffin cells was examined by scanning electron microscopy (SEM) with a novel maceration technique (3) for further understanding of the spatio-temporal regulation of the vesicle recruitment through myosin-ATPase. The secretory vesicles are distributed adjacently to the plasma membrane with a variety of micro components such as filamentous structures. The population of the vesicles diminished after sucrose stimulation, and recovered within 3min. The recovery of the vesicle population was smaller in the BDM-treated cells without effects on the filamentous structures. These 3D structures seem to suggest that the vesicles are recruited to the releasable pool along the actin filaments where myosin-ATPase play a role for motor function of myosin. References (1) Sasakawa, N. et al. (2002) Ann. N.Y.Acad.Sci., 971:273-274. (2) Neco, P. et al. (2002) Biochem. J. 368:405-413. (3) Riva A, et al. Scanning Microsc. 13:111-122, 1999

O16-3 Chemical inhibitor screening for molecules regulating morphological changes of locomoting neurons in the developing cerebral cortex

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Cortical neurons, generated near the ventricle, migrate toward the pial surface to form the 6-layered cerebral cortex. This migration is known to be a pivotal step for normal brain functions as defects of neuronal migration cause several neurological disorders such as lissencephaly and epilepsy in human. During migration, a major population of postmitotic neurons first displays a multipolar morphology and subsequently transform into bipolar morphology with a leading process. These bipolar-shaped neurons are called "locomoting neurons". We previously reported that Cdk5-p27^{kip1} pathway regulates the multipolar cell morphology and that Rac1-JNK pathway is involved in the leading process formation. After the formation of a leading process, locomoting neurons move over a long distance with continuous changes of their morphology. However, the molecular pathways regulating the morphological changes of locomoting neurons are largely unknown. To address this issue, we added several chemical inhibitors into the slice culture of EGFP-electroporated mouse cerebral cortices to examine their effects on time-dependent morphological changes of locomoting neurons. Time-lapse imaging revealed that inhibitors for PKA, PKC and Src family kinases as well as JNK and Cdk5, but not PKG, suppressed the migration rates of locomoting neurons. Inhibitors for JNK, Cdk5 and PKC also affected the morphology of locomoting neurons. Furthermore, the neuronal morphology in each cortical slice treated with inhibitor for Cdk5 or JNK was different, suggesting that Cdk5 and JNK may regulate distinct steps in morphological changes of migrating neurons. Additional results from RNA interference or dominant negative experiments for the target molecules of these inhibitors will be presented.

O16-5 Expression of ABCA1 transporter is up-regulated in response to nerve injury

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Nerve fiber elongation requires large amounts of lipids for expansion of axonal membrane, and thus alterations of lipid dynamics in regenerating neurons are very likely. We here screened expression of lipid metabolism associated genes, particularly cholesterol homeostasis related genes, during nerve regeneration using rat hypoglossal nerve injury model. In this screening, we identified that mRNA for the ATP binding cassette transporter A1 (ABCA1), but neither ABCG1 nor ABCG4 was dramatically increased in nerve injured hypoglossal motor neurons. ABCA1 is multi transmembrane protein involved in cholesterol efflux. The mRNA level of ABCA1 in injured hypoglossal motor neuron was first increased at 12hrs after nerve injury and most abundant at 7days after axotomy by 5-fold. The up-regulation of ABCA1 mRNA was not observed in glial cells such as astrocyte and microglia. An immunohistochemical study revealed that ABCA1 immunoreactivity was seen on plasma membrane of cell bodies and axons. In vitro, ABCA1 protein level was increased in PC12 cells by NGF application and strikingly the ABCA1 protein abundantly localized at tips of neurites. In addition over-expression of ABCA1 in N1E-115 cells demonstrated a morphological changes of the cells in which a lot of microspike-like structures appeared, and ABCA1 localized at the tip of microspike-like processes. These results indicate a possibility that expression and accumulation of ABCA1 in neurite tips that reorganizes cholesterol dynamics in neurons may play a crucial role in neurite elongation as well as axon regeneration.

O17-1 Upregulation of microglial mitogen macrophage-colony stimulating factor (M-CSF) and the receptor cFms in rat axotomized facial nucleus

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Transection of rat facial nerve leads to an increase of microglial cell number in the ipsilateral facial nucleus. However, little is known how the levels of mitogen for microglia and the specific receptor are regulated in the nucleus. In the present study, we analyzed a possible mitogen macrophage-colony stimulating factor (M-CSF) and the receptor cFms. Simultaneously, a S-phase specific marker proliferating cell nuclear antigen (PCNA) and a microglial marker ionized Ca²⁺-binding adapter molecule 1 (Iba1) were determined. A limited amount of M-CSF was detected in the control nucleus, and the amount in the axotomized nucleus increased during 3-7 days after transection. A potential source for enhanced amount of M-CSF was thought to be activated microglia. On the other hand, cFms was not detected in the control nucleus, but rapidly induced in the ipsilateral nucleus at 3 day after injury and the level was sustained for over 7 days. The cFms was demonstrated to be expressed in microglia. PCNA was identified in microglia, and the level peaked at 3 days after transection. These results suggest that both upregulation of mitogen (M-CSF) and induction of the receptor (cFms) are closely associated with the microglial proliferation observed in the transected facial nucleus.

O16-4 Abi2 is involved in radial migration, possibly through interaction with nonmuscle myosin IIB

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In the developing cortex, most excitatory neurons are supplied and arranged through radial migration. Previous studies using knockout mice demonstrate that Abi2-deficiency results in defective cell migration, aberrant dendritic spine morphogenesis, and deficits in learning and memory. However, how Abi2-deficiency leads to such phenotypes remains open. We then searched for Abi2-interacting molecule to address this question, especially on how Abi2 regulates the migration during the development of cerebral cortex. Using a MALDI-ToF mass-spectrometry in extracts from the developing mouse cerebral cortices, we found that Abi2 interacts with nonmuscle myosin IIB, an actin-binding protein that is shown to play a role for migration and cell adhesion. Immunoprecipitation experiments with brain extracts further showed that Abi2 and myosin IIB interact *in vivo*. Our immunohistochemical study revealed that Abi2 and Myosin IIB are colocalized in the apical membrane of the ventricular surfaces of developing cortex. In the ventricular cells, Abi2 and Myosin IIB localized in the apical surfaces and lateral sides, especially near the apical surfaces. Such subcellular distribution of Abi2 and Myosin IIB was similar to that of F-actin, N-cadherin and beta-catenin. These results imply that Abi2 regulates actin dynamics and cell adhesion through Myosin IIB. In order to elucidate the biological significance of Abi2, we used the method of *in utero* electroporation to transfer shRNA constructs into the cortex in order to knockdown Abi2 acutely at embryonic day 14. Then we observed migration arrest of Abi2-knockdown neurons in the intermediate zone of the cerebral cortex after 3-4 days of gene transfer. Interestingly, Knockdown of myosin IIB expression resulted in the migration arrest, similar to those of Abi2-knockdown neurons. Therefore, it is likely that Abi2 regulates initial stages of radial migration together with Myosin IIB, and that Abi2-deficiency results in defective in cell migration because of the impairment of actin dynamics and/or cell adhesion there.

O16-6 Involvement of integrin $\beta 1$ activation by P2Y12 receptor in the extension of microglial processes

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In response to pathological stimuli microglia rapidly cause morphological change and migrate toward the lesioned site. These microglial responses are crucial for tissue repair of a damaged CNS. We have previously shown that ATP induces membrane ruffling and chemotactic migration of microglia through two subtypes of ATP receptors, P2Y12 and P2X4. Recently ATP has been reported to induce the extension of microglial processes through P2Y12 in response to neuronal death in the brain. In order to investigate the signal transduction underlying the process extension, we established an *in vitro* culture system using rat primary microglia and three-dimensional (3D) collagen gels. In this study, we showed that ATP activates integrin $\beta 1$ through P2Y12 and the integrin $\beta 1$ activation is involved in the extension of microglial processes. Microglia in 3D gels extended their processes toward higher concentration of ATP. We found that microglia adhered weakly on collagen gels and ATP significantly promoted the microglial cell adhesion. Experiments with agonists and antagonists against P2Y12 confirmed that P2Y12 mediates the process extension and the increase in the cell adhesion to collagen gels. The treatment of microglia with arginine-glycine-aspartate (RGD)-containing peptide, which interferes with ECM-integrin interaction, blocked the process extension and the cell adhesion. Functional-blocking studies using anti-integrin antibodies showed that both the process extension and the cell adhesion are mediated by integrin $\beta 1$. Immunoprecipitation analysis using an antibody against activated integrin $\beta 1$ showed that activation of integrin $\beta 1$ was induced by ATP in P2Y12-expressing cells. These results indicate that ATP induces integrin $\beta 1$ activation, which is mediated by intracellular signals downstream of P2Y12, and strongly suggest that the integrin $\beta 1$ activation is able to trigger the extension of microglial processes.

O17-2 P2X7 receptor mediates zinc-triggered microglial activation

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Free zinc stored in a subset of glutamatergic axon terminals throughout the mammalian forebrain has been recognized as a key toxin in the excitotoxic neuronal injury, and is released under severe disease conditions, such as ischemia, trauma and hypoglycemia. Excitotoxic neuronal injury is also associated with inflammatory responses, driven by microglial activation. We, previously, showed that zinc induced poly(ADP-ribose) (PAR) formation, apparent morphological changes and release of nitric oxide, which were blocked by the PARP-1 or NADPH oxidase inhibition, and that microglial activation following transient global ischemia was prevented by intracerebroventricular injection of an extracellular zinc chelator. However, it remains how zinc causes to PARP-1 activation through NADPH oxidase pathway to induce microglial activation. In this study, we confirmed expressions of mRNAs for P2X4 and 7 receptors, both of which have been reported to play an important role in microglial activation, and demonstrated a selective P2X7 receptor antagonist oxidized ATP attenuated zinc-induced microglial morphological changes, PAR accumulation and superoxide generation in microglia, implicating that P2X7 receptor activation is associated with zinc-induced microglial activation, and is upstream of NADPH oxidase activation in microglia. Furthermore, to determine whether ATP was released from microglia in response to zinc stimulation, microglia were treated with zinc in presence of representative inhibitors for pannexin hemichannel, anion channel or CFTR, which contribute ATP release from cells into extracellular space. Inhibition of pannexin hemichannel, but not anion channel and CFTR, blocked zinc-induced microglial morphological changes. These results suggest that zinc stimulates ATP release from microglia via pannexin hemichannel to activate P2X7 receptor, which leads to microglial activation through NADPH oxidase and PARP-1 pathway.

O17-3 Clock genes expressed by microglia

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Clock genes are shown to play a pivotal role in the mechanism associated with the oscillatory regulation of circadian rhythm in the suprachiasmatic nucleus in the mammalian brain, whereas recent studies have demonstrated the possible functional expression of several clock genes in peripheral tissues including bone. In order to evaluate expression profiles of clock genes by different cells other than neurons in the brain, we have attempted to demonstrate the possible expression of particular clock genes in microglial cells in this study. In the mouse microglial cell line BV-2 cells highly positive to isolectin-b4 staining, marked mRNA expression was seen for inducible nitric oxide after sustained exposure to 100 ng/ml lipopolysaccharide (LPS) for 3 to 24 h. In these microglial BV-2 cells, marked expression was for the first time found with mRNA for a variety of clock genes on RT-PCR analysis. These included Per1, Per2, Per3, Cry1, Cry2, Dec1, Dec2, DBP, Bmal1 and NPAS2, but not Clock. In primary cultured rat microglia, similarly marked expression was seen with Per1 mRNA. In HEK293 cells transfected with Per1 promoter linked to the luciferase reporter plasmid, introduction of either Bmal1 or NPAS2 expression vector alone did not significantly affect the luciferase activity. Co-introduction of both Bmal1 and NPAS2 expression vectors led to a more than 8-fold increase in the luciferase activity, however, while further transfection with an expression vector of Per1 or Cry1 significantly prevented the increase by both Bmal1 and NPAS2 in HEK293 cells. In BV-2 cells exposed to 100 ng/ml LPS for a period up to 24 h, no significant change was seen in mRNA expression of all clock genes expressed. By contrast, ATP induced a significant but transient increase in Per1 mRNA expression at 1 mM, without significantly affecting mRNA expression of other clock genes, in BV-2 cells. These results suggest that clock genes may be functionally expressed by the microglial cell line BV-2 cells in terms of the responsiveness of Per1 to extracellular ATP.

O17-5 Differential localization of Myelin basic protein mediated oligodendrocyte maturation.

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Myelin basic protein (MBP) isoforms are known to have different expression patterns. In order to distinguish the different localization, we have developed a method for generating homogeneous populations of oligodendrocyte precursor cells and oligodendrocyte lineage cells from primary culture of embryonic day 17 mouse forebrain. With maturation of oligodendrocytes in vitro, MBP expression increased and/or there was a striking shift in intracellular localization from cell soma to the cell processes for differentiation of oligodendrocytes after contact with astrocytes, resulting in the expression of 18.5 kDa isoform that have membrane distribution in immature oligodendrocytes. While the other isoforms (17.0 and 21.5 kDa) are distributed diffusely through the cytoplasm and often accumulate in the nuclei of early stage-immature oligodendrocyte. However, the expression of MBP mRNA (both with and without exon 2 and both with and without exon 5-7) did not change during oligodendrocyte maturation. Those results suggest a regulation of this MBP gene not at the transcriptional but at the posttranslational level, indicating the point of occurrence of both the unique patterns of the isoforms expression and the shift in intracellular localization of MBPs with maturation of oligodendrocyte.

O18-1 Uni-directional neural differentiation from human embryonic stem cells by Neural Stem Sphere method

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We have previously demonstrated that mouse and monkey embryonic stem (ES) cell can be efficiently differentiated into neural cells by Neural Stem Sphere (NSS) method. In the first stage of the method, the NSS is formed from a colony of ES cells by culture in astrocyte-conditioned medium (ACM) under free-floating conditions. In the next stage, NSSs are transferred onto matrigel-coated dishes to induce differentiation into neurons. The ES cells unidirectionally differentiate into neurons via neuroectodermal cells and neural stem cells during culture by the method. Here, we applied the method to human ES cells. Colonies of human ES cells separated enzymatically from feeder cells were cultured in ACM for 20 days. Changes in gene expression during the formation of NSSs from human ES cells were analyzed by quantitative RT-PCR. Gene expression of ES cell markers, Oct-3/4 and Nanog was down-regulated during culture and became very low at day 7. In contrast, expression of neuroectodermal marker, Sox1 and neural stem cell markers, nestin became marked from day 12 and that of neuronal markers MAP2 from day 20. However, expression of an astroglial marker GFAP and an oligodendroglial marker MBP did not increase. Expression of an early mesoderm marker Brachyury, a primitive endodermal marker GATA4 and an epidermal marker Cytokeratin-17 was very low and did not significantly increase throughout culture. By attachment of the formed NSSs on adhesive dishes and culture in ACM, many cells migrated from the NSSs. Immunofluorescence analysis showed that the migrated cells were MAP2-positive cells, suggesting that the ES cells differentiated into neurons. These results demonstrate that human ES cells can directly differentiate into neurons via neuroectodermal cells and neural stem cells by the NSS method. This work was partly supported by Grants-in-Aid for Scientific Research from JSPS and Selective Research Fund of Tokyo Metropolitan University.

O17-4 The lineage tracing of Olig2+ cells in a murine demyelinating disease model

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In chronic demyelinated brain, it is suggested that oligodendrocyte differentiation is interfered in spite of the presence of abundant oligodendrocyte progenitor cells (OPCs). In this study, we analyzed lineage and turnover of Olig2+ progenitors, which are thought to be OPCs, in chronic demyelinated brain.

Heterozygous (plp^{+/−}) transgenic mice, over-expressing proteolipid protein gene (Plp), are chronic demyelinating disease model mice. In this Plp transgenic mice brain, normal appearing myelin is formed until 2 months (2M) of age with no sign of myelin degeneration. Shortly thereafter, myelin degeneration becomes apparent. After 6M of age, remyelination is severely affected, resulting in numerous naked axons in these mice. At 8M of age, oligodendrocyte differentiation seems to be arrested at premigrating state, because there is increased number of Olig2+ OPC-like cells in the demyelinating brain. However, the lineage and turnover of Olig2+ progenitors in demyelinating lesions are not well understood. Thus we performed lineage tracing experiment on the Olig2+ cells in demyelinating disease model at various disease stages. For this purpose, we employed tamoxifen-induced Cre/loxP system and Z/EG reporter mice, which express enhanced green fluorescent protein after Cre recombination. We generated triple heterozygous (Plp; Olig2-CreER; Z/EG) mice and double heterozygous (Olig2-CreER; Z/EG) mice. To label Olig2+ progenitors in the demyelinating brain, we intraperitoneally injected tamoxifen into triple heterozygous mice at the age of 2M, 4M or 5M and then sacrificed them one month later, respectively. We observed many myelinating oligodendrocyte cells and clusters of the labeled cells at 2M, suggesting proliferation of Olig2+ progenitors. In accordance with these results, we also observed more Ki67+ proliferating cells at 4M than at 2M and 5M. In contrast, we observed not only the decrease in the number of myelinating oligodendrocytes, but also many labeled cells with short processes and small number of processes. Moreover, we also observed less number of recombined bushy astrocyte-like cells in demyelinating brain compared with normal brain, which is tamoxifen-injected double heterozygous brain.

O17-6 Sema4D expression in oligodendrocytes

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Oligodendrocytes are specialized glial cells of the central nervous system (CNS) that ensheath and insulate neuronal axons, thereby allowing efficient transmission of the electrical signal throughout the nervous system. Sema4D, a transmembrane semaphorin, is expressed in the CNS during development and in adulthood as well as in the immune system. In Sema4D-mutant mice labeled by an inserted lacZ, a number of lacZ-expressing cells were myelin associated glycoprotein (MAG)-positive and GST π -positive oligodendrocytes. This result was well in agreement with the previous studies indicating Sema4D-expression localized in mature oligodendrocytes. To investigate whether Sema4D is involved in myelin formation, we examined expression of myelin basic protein (MBP) as a marker of myelin in cerebral cortex during development. In Sema4D-deficient mice, MBP expression was higher than in wild-type mice. We further examined myelination in Sema4D-deficient mice.

O18-2 Modulation of differentiation by group III metabotropic glutamate receptor signals in murine neural progenitor cells

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Glutamate is a major excitatory neurotransmitter in the mammalian central nervous system. Although glutamate receptors have been found to be expressed by undifferentiated neural progenitor cells (NPCs), their function remains unclear. Our previous studies showed that activation of group III metabotropic glutamate receptors (group III mGluR) decreases proliferation in NPCs through the modulation of cellular cAMP levels and cyclinD1 expression. In this study we evaluate the possibility of regulation of cellular differentiation by group III mGluR in murine NPCs. Round spheres were formed by clustered cells during the culture of NPCs prepared from embryonic mouse neocortex with EGF under floating conditions, whereas cells were immunoreactive for nestin, but not for MAP2 or GFAP, with similar results after 10 days of culture. Neurospheres were then dispersed and cultured for an additional 4 days in the absence of EGF under adherent conditions for differentiation. Sustained exposure to the group III mGluR agonist, L-AP4, significantly decreased the size of neurospheres formed during culture for 10 days. Prior exposure to L-AP4 led to a significant increase in GFAP-positive cells along with decreased MAP2-positive cells upon spontaneous and induced differentiation, which occurred in a manner sensitive to a group III mGluR antagonist. Moreover, we used the mouse embryonic carcinoma cell line P19 cells endowed to differentiate into neuronal and astroglial cells. Indeed, marked but transient expression was seen for MAP2 mRNA in P19 cells cultured with retinoic acid, followed by a marked increase in GFAP mRNA expression. Forskolin significantly increased the luciferase activity in P19 cells transfected with cyclinD1 promoter linked to the luciferase reporter plasmid, but L-AP4 was effective in significantly preventing the increase by forskolin in an antagonist-sensitive fashion. These results suggest that group III mGluR signals not only decrease proliferation in NPCs, but also promote their differentiation to astroglial lineage with concomitant suppression of the differentiation to neuronal lineage.

O18-3 A new method to generate serotonergic neurons from ES cells

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Recent pharmacological studies have shown that serotonin (5-HT) can modulate a number of developmental events, including cell division, neuronal migration, cell differentiation, and synaptogenesis. In addition, as it has been shown that change in 5-HT homeostasis may lead to psychiatric disorders, study on the mechanism of serotonergic differentiation will be crucial to our understanding of the development of mental disorders. However, differentiation methods reported so far require further scrutiny of the efficiency and the mechanism of differentiation. In the present study, we therefore aimed to establish a novel method to induce neurons from mouse embryonic stem (ES) cells and then we have modified this method to increase the efficiency of the serotonergic differentiation. Based on the concept that interaction of ES cells with some components of basement membranes may trigger neuronal differentiation, we examined the effect of several cell culture substrates with different composition and coating and found that Matrigel, a solubilized basement membrane preparation, effectively promotes neuronal differentiation of ES cells. When ES cells were simply grown on Matrigel, they formed colonies, more than 80% of which extended neuritis and expressed neural markers such as nestin and β -tubulin III at day 12. However, 5-HT neurons were poorly observed in these cultures. As specific regional phenotypes of neurons have been suggested to result from local inductive cues, we examined the effect of Shh, FGF4 and FGF8, regional factors known to be involved in serotonergic differentiation, but the three factors, either alone or in combinations, showed only subtle effects, if any. However, we unexpectedly found that noggin significantly induce serotonergic differentiation. The present study proposes a simple method to generate 5-HT neurons differentiated from ES cells. As this culturing system employs neither co-culture nor fetal calf serum (FCS), it will help to examine the mechanisms for serotonergic differentiation and to provide insights into the molecular basis of psychiatric disorders.

O18-5 The Dynamics of Chromatin Organization during Rod Photoreceptor Differentiation

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Chromatin organization during development is believed to be crucial to control gene expressions. During mouse retinal development, the Rb tumor suppressor protein is required for rod photoreceptor differentiation and regulates gene expressions essential for the differentiation. One of the most dramatic morphological changes that occur in developing rods involves chromatin condensation. Although it is not known why rods are the only neuronal type in the retina that undergo chromatin condensation, one intriguing hypothesis is that rods must organize their genomic DNA to efficiently express high levels of genes required for phototransduction. Interestingly, Rb-deficient rods fail to condense their chromatin in a cell-autonomous manner, demonstrating that Rb regulates both rod-gene expression and chromatin condensation during rods differentiation. However, it is not known if rods fail to condense their chromatin because of the uncontrolled rod-gene expression or if rods fail to express rod-gene because of the uncontrolled chromatin condensation. To begin to address this question, we have characterized the expression of genes involved in chromatin organization in the developing mouse retina. We have found some genes are specifically expressed in rods under the control of Rb molecules and regulate histone modification during the chromatin condensation. Current efforts focusing on knockdown these genes would be important to answer this question.

O19-1 β -amyloid induces macroautophagy in neuron

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Previous data shows, by EM analysis, that autophagosomes and other AVs, which are rarely seen in normal brain, appear in neurons in the Alzheimer disease (AD) brain and accumulate markedly within dystrophic neurites (Nixon et al., 2005). Moreover, another study shows that macroautophagy is induced in PS1/APP mouse (Yu et al., 2005). These data suggest that macroautophagy could relate to AD pathology. According to the amyloid cascade hypothesis, the accumulation of β -amyloid ($A\beta$) is a critical step of AD pathology. Therefore, in this study, we investigate the effect of $A\beta$ on macroautophagy. We treat SK cells with $A\beta$, and detect light chain 3-II, which is the marker protein of macroautophagy, by Western blotting. It showed that light chain 3-II is increased dose-dependently by $A\beta$ exposure. This data suggests that $A\beta$ induce macroautophagy. Macroautophagy in AD brain may be associated in amyloid cascade hypothesis.

O18-4 Analysis on the expression and function of BRINP family genes during neuronal differentiation of mouse embryonic stem cell-derived neural stem cells

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Once differentiated from stem cells, neurons no longer proliferate. Although various molecules that inhibit progression of the cell-cycle in proliferating cells have been identified, the mechanism suppressing the neuronal cell-division is not fully understood and relevant molecules specifically involved in that mechanism are not identified.

We have previously identified a novel family of genes, BRINP1, 2, and 3, which are predominantly and widely expressed in both the central and peripheral nervous systems. When over-expressed in proliferating cells, all three BRINP family proteins suppressed the cell cycle progression suggesting their involvement in the mechanism of cessation of cell proliferation in the postmitotic neurons. In this context, regulation of BRINP gene expressions during stem cell differentiation should give us further insights over this mechanism.

In the present study, we analyzed the expression pattern of three BRINP genes during differentiation of mouse embryonic stem (ES) cell-derived neural stem cells (NSCs) and their effects on the cell-cycle regulation of NSCs. While any of three BRINP-mRNAs was not expressed significantly in mouse ES cells, BRINP 1 and 2-mRNAs were expressed at high levels in the ES cell-derived neural stem cells. Upon differentiation into neuronal cells in the presence of retinoic acid and BDNF, all three BRINP-mRNAs were induced with a similar time course peaking at three days of the treatment. Upon differentiation into astroglial cells in the presence of fetal calf serum, BRINP1-mRNA was slightly up-regulated, while the levels of BRINP2- and BRINP3-mRNAs did not change significantly.

While a population of exponentially growing NSCs contained $32.9 \pm 1.3\%$ of cells in G2 and S phases, over-expression of any of three BRINP genes completely suppressed the cells in G2 and S phase without producing apoptotic cells. Based on these results, physiological roles of the BRINPs in the cell-cycle suppression of terminally differentiated postmitotic neurons were discussed.

O18-6 Effects on Proliferation and Differentiation of ES Cells by culture conditions of Mouse Embryonic Fibroblast

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In a co-culture system of inactivated mouse embryonic fibroblast (MEF) and ES cells, ES cell surfaces are closely associated with the surface of inactivated MEF. Undifferentiating of ES colonies can be maintained their capacity for proliferation on a feeder-layer of inactivated MEF (stage 0). These interactions would be concerned with intercellular and tropic molecules, and permitted cellular functions for ES cells. Efficiency of the large size that is affected growth of ES colony, and the number of colony formations. These are affected on the micro environmental state. It would be come about the difference of capacity for differentiation into neural stem cells and neuron (stage1). ES cells culturing in optimal conditions are dependent on quality of feeder cells, MEF treated mitomycin-C derived from mouse. The present study evaluates the criteria of inactivated MEF under the feeder cells on the stage 0. Cell suspensions which are prepared for a feeder-layer are derived from tissue in mouse embryonic day13 except bone and intestines. The cells are plated into dishes to expanding cell number and require stabilization for cell functions, and inactivated in mitomycin-C. The other side, we have established a light scattering method for flow cytometer (LS-FCM) that individual cells are able to discriminate against cellular properties base on cell size and structure of the inner cells. To better define the quality to feeder-layers, inactivated cells are sorted from the cell suspensions by dual parameter of LS-FCM. Cell clusters are displayed on distinguishable each other, and sorted them for source of the co-culture. To defined cell properties in cluster, cells are cultured in ES medium. Typical morphology of the cells are two, dual-sharp and widespread types on dish substratum. ES cells in clonally density are co-culture with the former type cells, give arise spheres, 300-500 μ m in diameter, whereas 100 μ m and less in the others. We describe also on frequency of differentiated neural stem spheres in floating conditions using cells come from two different types.

O19-2 Characterization of GM1 ganglioside (GM1) endocytic pathways responsible for GM1-induced $A\beta$ fibrillogenesis

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Gangliosides, sialic acid-containing glycosphingolipids, are localized in the outer leaflet of the cell membranes of vertebrates and particularly abundant in the nervous system. The metabolism of GM1 ganglioside (GM1), one of the ganglioside species, is closely associated with the pathology of Alzheimer's disease (AD). We previously found that the treatment of PC12 cells with chloroquine, an endocytosis disrupting agent, induced GM1 accumulation at cell surface and accelerated the extracellular assembly of amyloid- β protein ($A\beta$) through the formation of GM1-bound $A\beta$ ($GA\beta$), endogenous seed for AD amyloid. The extracellular assemblies and deposition of $A\beta$ are pathological hallmark of AD. In this study, we characterized the endocytic pathway responsible for the GM1 accumulation at cell surface of PC12 cells. Following the blockade of GM1 endocytic entry with cholesterol depletion or Rho family GTPase inactivation, increase occurred. However, the $A\beta$ amyloidogenesis from endogenous soluble $A\beta$ was not induced. In contrast, GM1 accumulation which was induced by knockdown of Rab7, a regulator of intracellular endosomal trafficking from early endosomes to late endosomes, leads to the $A\beta$ fibrillogenesis together with GM1 accumulation on the cell surface. Moreover, Rab7 siRNA treatment induced accumulation of GM1 in enlarged early endosomes which have been reported by the studies of AD brains. These results suggest the significance of the endocytic pathway impairment for GM1-induced $A\beta$ assembly in AD brains.

O19-3 Substrate specific inhibition of BACE-mediated cleavage - Can inhibition of beta-cleavage be achieved without affecting extracellular shedding of Neuregulin1?

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Aβ is generated in the process of sequential endoproteolysis of βAPP. β- and γ-secretase are involved in the process. Inhibition of β-secretase (BACE) activities is an attractive approach to inhibit Aβ generation. However, it may cause unexpected side effects since Neuregulin1, which is associated with peripheral nerve myelination undergoes proteolysis by BACE. In this study, we tried to obtain compounds which inhibit Aβ generation by inhibiting β-cleavage but less affect Neuregulin1 shedding. We performed screening to find such compounds. We also conducted secreted alkaline phosphatase (SEAP) assay by which the level of extracellular shedding of Neuregulin1 can be measured. We will show whether there are such compounds which can reduce Aβ generation by inhibiting β-cleavage of βAPP without affecting extracellular shedding of Neuregulin1.

O19-5 Roles of receptor for advanced glycation endproducts and p38 MAPK in neuronal membrane transport of amyloid β-peptide

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Alzheimer's disease (AD) is a progressive neurodegenerative disease that is characterized by senile plaques, neurofibrillary tangles, and neuronal loss. A pathological hallmark of AD is the deposition of amyloid β-peptide (Aβ), a 39-43-amino acid peptides derived from the transmembrane amyloid precursor protein (APP). The fibrillar Aβ deposits are found in the extracellular senile plaque cores and associated with neurodegeneration in AD. In contrast, recent studies suggest that the accumulation of intraneuronal Aβ may be an early event in the pathogenesis of AD. However, the mechanisms of the neuronal membrane Aβ transport system are unknown while Aβ is predominantly produced at the plasma membrane and released into the extracellular spaces. In this study, we demonstrate that receptor for advanced glycation endproducts (RAGE) contributes to transport of Aβ from the cell surface to the intracellular space. Mouse cortical neurons exposed to extracellular human Aβ₁₋₄₂ and Aβ₁₋₄₀ subsequently showed detectable peptide intracellularly in the cytosol and mitochondria. Pretreatment of cultured neurons from wild-type mice with neutralizing antibody to RAGE and neurons from RAGE null mice displayed decreased Aβ uptake and Aβ-mediated mitochondrial dysfunction. Aβ activated p38 MAPK, but not ERK1/2 and SAPK/JNK, and then stimulated intracellular uptake of Aβ. Immunoblotting with anti-RAGE IgG demonstrated >8-fold more RAGE antigen had been immunoprecipitated from cells exposed to Aβ, compared with non-treated control. Similar intraneuronal co-localization of Aβ and RAGE was observed in the hippocampus of transgenic mice overexpressing mutant APP. These findings indicate that RAGE-dependent activation of p38 MAPK pathway contributes to mechanisms involved in the translocation of Aβ from the extracellular to the intracellular space, thereby enhancing Aβ cytotoxicity.

O20-1 Biological effects of Presenilin/β modifiers

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Presenilin (PS) γ-secretase degrade transmembrane domains of βAPP and Notch generating Alzheimer disease (AD)-associated amyloid-beta (Aβ) and Notch intracellular domains (NICD), essential transcriptional factors for Notch signaling. Notch signaling is a type of local-cell signaling that play many physiological roles including development, neurogenesis, and maintenance of stem cells. Down-regulation of Notch-1,2 and 3 signaling may cause severe genetic diseases, while abnormally up-regulated Notch signaling cause malignancies. Thus correction of abnormally down- or up-regulated Notch signaling is an important therapeutic approach against such diseases. It is well known that precision of β-cleavage of βAPP is altered by PS/γ-secretase modifiers, which up- or down-regulate generation of pathogenic Aβ42. Recently, we have discovered that PS/γ-secretase-mediated cleavage at S3 (S3 cleavage) of Notch-1 has also diversity, resulting in the production of two different types of NICD. NICD-V with Val at the N-terminus transmits relatively strong Notch signaling, while NICD-S with Ser at the N-terminus transmits relatively weak signaling. Importantly, changes in their relative ratio alter the Notch signaling intensity. In this study, we will investigate whether PS/γ-secretase modifiers also affect precision of S3 cleavage and Notch signaling intensity.

O19-4 Characteristics of membrane-bound factors affecting regulated intramembrane proteolysis of βAPP

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Background: Change in Aβ42 production ratio is important for the pathogenesis of Alzheimer Disease. However, it is not known how Aβ42 production ratio is physiologically regulated. Methods: Here, we studied if there are any physiological substances which alter the cleavage precision of PS/γ-secretase. We fractionated the membrane-bound substances from pig brains or cultured cells, and added each fraction to the cell-free assay system which can measure the cleavage precision of PS/γ-secretase in vitro. Results: We found that there are physiological substances which dramatically change the ε-cleavage precision of βAPP. The membrane-bound substances obtained from pig brains or cultured cells increase the generation ratio of shorter AICDε51(S2-99) to longer AICDε49(S0-99). Discussion: Our data suggests that the change in the precision of the intramembrane proteolysis induced by PS/γ-secretase is regulated in vivo. The change in Aβ42 production through the mechanism might be associated with pathogenesis of Alzheimer Disease.

O19-6 The level of plasma Aβ is lowered in M-CSF deficient mice

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Aβ is a major component of senile plaques and accumulated in Alzheimer disease brain. Concentration of plasma Aβ is approximately 5% of that of CSF Aβ. Therefore, Aβ efflux from cerebrospinal fluid (CSF) to peripheral blood via blood brain barrier (BBB) may play an important role in clearance of Aβ from brain. So far, several molecules such as RAGE, low-density lipoprotein receptor-related protein (LRP1), P-glycoprotein (P-gp) and IGF-1 have been shown to be involved in the Aβ efflux across BBB. Recently, it has been reported that the level of Macrophage Colony-Stimulating Factor (M-CSF) in plasma of Alzheimer disease patients is decreased. In order to examine the role of M-CSF in the pathogenesis of Alzheimer disease, we obtained M-CSF knock out mice and performed several biochemical and immunohistochemical studies. Surprisingly, compared to wild type mice, the level of plasma Aβ is ~50% lowered in M-CSF -/- mice, while the level of Aβ in brain of the mice is unchanged. In this study, we will investigate how this reduction is brought about.

O20-2 Characterization of the domain responsible for the different specific activity of PS1 and PS2.

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γ-Secretase is an aspartyl protease composed of four protein components (Presenilin, Nicastrin, Aph-1 and Pen-2) and catalyzes the final cleavage step of the β-amyloid precursor protein (APP) to release the amyloid β protein which is implicated in Alzheimer's disease pathogenesis. Two homologues of Presenilin, PS1 and PS2, are the catalytic center of the γ-secretase complex and they form distinct γ-secretase complexes. Although PS1 and PS2 have high amino acid sequence homology (64% identity, 86% similarity), PS1 γ-secretase complex displays greater specific activity than the PS2 γ-secretase complex. We aim to identify the domain which determines the different specific activity of PS1 and PS2.

O20-3 Presenilins are independent of the inhibitory effects of γ -secretase inhibitors on Wnt signaling

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To inhibit A β production is a major therapeutic target for Alzheimer's disease. γ -Secretase inhibitors suppress intramembrane proteolysis producing A β . However, γ -secretase blocking activity causes serious side-effects, since they usually inhibit sequential endoproteolysis of Notch receptors. Wnt, as well as Notch, is a crucial signaling pathway for differentiation. Both Notch and Wnt signaling cooperatively regulate differentiation of squamous cells in small intestine. In addition, γ -secretase inhibitor is known to affect the differentiation. Therefore, we asked direct effect of γ -secretase inhibitor on Wnt signaling. We reported at Neuro2007 meeting that γ -secretase inhibitors, DAPT and L-685,458, significantly reduced Wnt signaling in cultured cells. The inhibitory effects of γ -secretase inhibitors on Wnt signaling were also observed in the cells expressing dominant negative form of presenilin which had no γ -secretase activity. To clarify the involvement of presenilins in Wnt signaling, we tested the effects of γ -secretase inhibitors on Wnt signaling in cells genetically deficient in presenilin 1 and 2. Wnt signaling was assessed by modified luciferase reporter genes. Presenilins-null cells transiently transfected with reporter genes were treated with γ -secretase inhibitors and then measured luciferase activity of the cell lysate. Surprisingly, DAPT and L-685,458 significantly reduced Wnt signaling in presenilins-null cells. These results suggest that Wnt signaling was reduced with γ -secretase inhibitors acting somewhere on Wnt signaling pathway, not on presenilins.

O20-5 Inhibitory effect of homocysteine on ApoE3-mediated cholesterol efflux from cultured astrocytes.

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Apolipoprotein (Apo) E4 is the strong risk factor for Alzheimer's disease (AD). It is also known that homocysteinemia is another risk factor for AD. Homocysteine (HC) has very similar structure of cysteine harboring a thiol group. However, the molecular mechanism, by which homocysteinemia cause AD remains unknown. We previously reported that ApoE3 dimers enhanced the ability of ApoE3 to release cholesterol (CH). We hypothesized that HC may bind to thiol group of ApoE3 to impair ApoE3 function. In this study, we noted whether the HC inhibits CH efflux from cultured astrocytes induced by ApoE3. We examined that the ability of ApoE3 pre-incubated with HC to release CH. We prepared ApoE3 pre-incubated with HC then it was dialyzed against PBS to remove free HC. HC treatment reduced the level of ApoE3 dimers, and the level of CH efflux induced by ApoE3 pre-incubated with HC is lower than that induced by ApoE3. These results indicate that HC inhibits the ability of ApoE3 to release CH by inhibiting dimerization of ApoE3. We further determined whether the amount of ApoE3 dimers decrease in human CSF from patients with high serum HC. The level of ApoE3 dimers in human CSF from patients with high serum HC is significantly lower than that in human CSF from patients with normal serum HC. These results suggest that high HC may inhibit dimerization of ApoE3 in human CSF. In conclusion, it is possible that two different risk factors, ApoE4 and hyperhomocysteinemia, for AD development may share a common mechanism, by which lower level of ApoE dimer result in lower ability of ApoE to generate HDL leading to lower HDL-cholesterol supply to neurons and A β clearance from the brain.

O21-1 Identification of LOTUS, a novel molecule serving for neural circuit formation

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Mouse lateral olfactory tract (LOT) consisted of olfactory bulb (OB) neuron axons is one of the good experimental systems for analysis of neural circuit formation, because the developmental process of LOT formation can be observed in telencephalon organotypic culture. We attempted to search for a key molecule involved in the LOT formation by functional screening combining telencephalon organotypic culture and a modified fluorophore-assisted light inactivation (FALI) method by which targeted proteins can be selectively inactivated for a long time in culture. We found that inactivation of a certain protein resulted in defasciculation of LOT in telencephalon organotypic culture. This protein was a novel molecule serving for neural circuit formation in mouse central nervous system and we designated it as LOT usher substance (LOTUS). Expression of LOTUS mRNA was clearly detected in the mitral cell layer of the medioventral OB in embryonic day (ED) 12-14 mouse embryos. LOTUS was immunocytochemically found on the plasma membrane surface of cultured OB axons. Soluble form of LOTUS was bound to LOT in whole brain and distal part of cultured OB axons, indicating the binding partner of LOTUS may exist in the OB. Therefore, we attempted to identify the protein binding to LOTUS by screening with expression library from mouse embryonic OB. Surprisingly, the LOTUS binding protein was identified as Nogo-66 receptor (NgR1). Immunohistochemistry revealed that NgR1 was expressed on LOT and olfactory cortex at ED 12-14. These results suggest that LOTUS serves for LOT formation by binding to NgR1.

O20-4 Impact on Abeta accumulation in APP Tg mice by genetic background

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Though a great deal of effort has been made on the searching for the risk genes of Alzheimer disease (AD), there is little success, except ApoE. Animal model has many advantages (strict control of environmental factors, direct measurement of amyloid pathology, etc) compared to human studies. APP Tg mice (Tg2576) which are usually maintained by B6/SJL hybrid mice were crossed onto C57BL/6J, SJL/J and DBA/2J inbred strains. The shortened life span were observed in APP Tg mice with B6 rich genetic background (B6 75%, SJL 25%), which was similar to previous report (Carlson Hum Mol Genet 1997). No significant life span change, however, was observed in the mice with either SJL or DBA rich genetic background. The levels of Abeta40 and Abeta42 in Triton and GuHCl fraction from cortex were measured by ELISA. Analysis of 59 APP Tg mice at the age of 12 months showed that lower Abeta accumulation in mice with DBA rich genetic background compared to SJL or B6 rich genetic background. For example, significant difference ($p < 0.01$, Turkey-Kramer) were observed in Abeta40 (-82%) and Abeta42 (-68%) levels in Triton fraction between SJL 84% B6 16% mice and DBA 75% B6 16% SJL 9% mice. Drastic difference ($p < 0.01$, Turkey-Kramer) were observed in Abeta40 and Abeta42 levels also from GuHCl fraction between SJL 69% B6 31% and DBA 75% B6 16% SJL 9% mice (-85% and -68%) and between SJL 69% B6 31% and DBA 50% B6 31% SJL 19% mice (-75% and -50%). We focus on SJL and DBA, because the difference of Abeta accumulation was most drastic and both genetic backgrounds have no impact on life span. More animals are being analyzed and amyloid pathology modifier candidate genes will be searched using arrays.

O20-6 14-3-3 differentially induces 3-repeat and 4-repeat tau aggregation

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14-3-3 protein is a abundant cytosolic protein involved in diverse cellular functions such as intracellular signal transduction, the cell cycle, apoptosis, and cytoskeletal organization. 14-3-3 has been found to colocalize with neurofibrillary tangles (NFT) found in Alzheimer disease (AD). Recently, 14-3-3 has been demonstrated to bind tau and facilitate its aggregation or its formation of filament. To understand the mechanism of tau aggregation we analyzed the 14-3-3-induced aggregation of both 3R- and 4R-tau employing sodium dodecyl sulphate-polyacrylamide gel electrophoresis (SDS-PAGE), transmission electron microscopy (TEM) and fluorescence spectroscopy. In vitro aggregation assay employing fluorescence spectroscopy showed that 14-3-3 significantly induces the formation of thioflavine S fluorescent aggregates of 3R-tau than 4R-tau. Analysis of tau aggregates by TEM showed that 14-3-3 generated more filaments from 3R-tau than 4R-tau. SDS-PAGE analysis demonstrated that 14-3-3 induced 3R-tau for the formation of dimer predominantly, as the driving form for tau-assembly, whereas 14-3-3 induced 4R-tau for the formation of dimer, trimer, tetramer and higher order oligomers. Taken together, our results suggest that 14-3-3 differentially induces 3R- and 4R-tau aggregation and indicated that 14-3-3 might play an important role in the generation of 3R-tau-predominant NFT in AD and the related tauopathies characterized by 3R-tau.

O21-2 Expression pattern of LOTUS, a novel molecule serving for neural circuit formation

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We discovered a novel molecule LOTUS which serves for lateral olfactory tract (LOT) formation of mouse telencephalon, and identified its receptor as Nogo-66 receptor (NgR1). Molecular interaction between LOTUS and NgR1 induced cell-cell contract in their transfected cells. Fluorophore-assisted light inactivation (FALI) of LOTUS resulted in defasciculation of LOT axonal bundles, suggesting that LOTUS may function LOT axonal bundle formation through binding to NgR1. As a step in elucidating biological functions of this molecular interaction, we first examined expression pattern of LOTUS and NgR1 in developing mouse brain. In situ hybridization analysis revealed that LOTUS mRNA was clearly detected in several regions of mouse embryonic central nervous system (CNS) at embryonic day (ED) 15.5, such as olfactory bulb (OB), cerebral cortex, hippocampus, thalamus, brainstem, and spinal cord. In particular, LOTUS mRNA was highly expressed in the mitral cell layer of the ventromedial OB, suggesting that LOTUS is expressed on a part of LOT. The immunochemical data showed that LOTUS was predominantly found in growth cones and distal neurite shafts of cultured OB neurons and also in the ventral LOT in whole-mount brain. We next examined the expression pattern of NgR1 mRNA in the developing brain. NgR1 mRNA was diffusely detected in some regions of the CNS of ED13.5 and 15.5 mouse embryos, such as the OB, cerebral cortex, thalamic nuclei, brainstem, cerebellum, and spinal cord. In the OB, NgR1 mRNA was predominantly detected in the mitral cell layer of the OB and the mRNA expression in the OB was validated by immunohistochemistry in whole-mount brain. Thus, the expression patterns of LOTUS were basically consistent with those of NgR1 in the developing mouse brain. The data suggest that LOTUS may interact with NgR1 in several region of the developing CNS and may function in the neural development.

O21-3 Functional analysis of the receptor for LOTUS, a novel molecule serving for neural circuit formation

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We discovered a novel molecule LOTUS that serves for lateral olfactory tract (LOT) formation of mouse telencephalon, and identified its receptor as Nogo-66 receptor (NgR1). Molecular interaction between LOTUS and NgR1 was involved in cell-cell contact in their transfected cells. Fluorophore-assisted light inactivation (FALI) of LOTUS resulted in defasciculation of LOT axonal bundles, suggesting that LOTUS may function LOT axonal bundle formation through binding to NgR1. As a step in elucidating biological functions of this molecular interaction, we examined expression pattern of LOTUS and NgR1 in developing mouse brain. Immunohistochemistry revealed that LOTUS and NgR1 were expressed in the predicted projection route prior to LOT formation at embryonic day (ED) 12 and thereafter in the membrane surface of LOT axonal bundles during axonal elongation stage at ED 12-13. Next, we examined if abnormality in the LOT development is found when NgR1 is inactivated by FALI method that can selectively inactivate for a long time in culture. FALI of NgR1 for 24 hours at ED12-13 in telencephalon organotypic culture resulted in defasciculation of LOT axonal bundles in a similar manner to FALI of LOTUS. Simultaneous FALI of LOTUS and NgR1 showed a similar perturbation of LOT development. Furthermore, exposure of truncated soluble form of NgR1 to the organotypic culture for 24 hours at ED12-13 caused LOT to defasciculate and showed a similar perturbation of LOT development seen as a dominant-negative effect of NgR1. These results suggest that molecular interaction between LOTUS and NgR1 serves for LOT axonal bundling. We also provide a new insight of NgR1 function in the developing central nervous system.

O21-5 Involvement of Factor XIII in fish optic nerve regeneration

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Fish CNS neurons can repair their axons following nerve injury, while mammalian CNS neurons lose this capacity. After fish optic nerve transection, the regenerating optic axons can reinnervate the tectum by 3-5 weeks. We have investigated these regeneration mechanisms using fish visual system. Factor XIII is well known as a plasma transglutaminase that catalyzes the formation of covalent cross-linking reactions in polymerized fibrin to yield the mature clots. In addition to this, the important role of Factor XIII in wound healing has been recently reported. Using the well-established fish model, the present study has investigated the role of Factor XIII on optic nerve regeneration after injury. Using molecular cloning techniques, we identified the cDNA of goldfish Factor XIII encoded 735 amino acid residues. Analysis by RT-PCR showed that level of Factor XIII mRNA started to increase within a few hours in damaged optic nerves. In situ hybridization revealed that a lot of Factor XIII positive cells could be detected in the injured site of optic nerve. To elucidate molecular involvement of Factor XIII, we estimated the effect of recombinant Factor XIII protein on neurite outgrowth in retinal explant culture system. Recombinant Factor XIII protein clearly induced neurite outgrowth from adult goldfish retina. These effects were observed only both in the naïve retinas and in the retinas with their optic nerve lesion 1-2 days previously. These data suggest that upregulation of Factor XIII is an important event for an early stage of regenerating optic axons.

O21-7 Abnormalities of mice with conditional targeted *Pcdh-γ* allele

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The clustered protocadherin (*Pcdh*) family, which is the largest subgroup of the diverse cadherin superfamily, consists of three gene clusters, *Pcdh-α*, *Pcdh-β*, and *Pcdh-γ*. This family consists of more than 50 variable exons in mammals. Each variable exon encodes six typical extracellular domains that contain cadherin repeat motif, a transmembrane domain, and a short cytoplasmic domain. According to the single-cell RT-PCR in Purkinje cells, the expression of several *Pcdh-α* and *Pcdh-γ* mRNAs are regulated monoallelically, leading to the combinatorial expression of distinct variable exons. Therefore, the clustered *Pcdh* family has thought to be a key molecule for generating neural diversity and organization. Among this family, *Pcdh-γ* family has been suggested to contribute to the organization of specific neuronal connections in the central nervous system much more than other clustered *Pcdh* family, because *Pcdh-γ* proteins are localized in growth cones and at synapses, and they have homophilic binding activity, while *Pcdh-α* proteins have no- or very weak homophilic binding activity. In recent years, it was reported that mice homozygous for deletion of the *Pcdh-γ* locus were born alive but died within 12 hours and showed extensive apoptosis of interneurons in the spinal cord. But the function of *Pcdh-γ* family *in vivo* in adult is still unknown.

To answer the question, we have taken a strategy that allows spatiotemporal control of gene disruption. For producing conditional gene targeted mice, we have inserted loxP sites around first constant region exon (CR1) of *Pcdh-γ* cluster. In addition to deleting CR1, loss of this exon is predicted to yield premature termination codon of protein translation early in second constant region exon (CR2), due to a frameshift, and this abnormal mRNA is expected to be degraded by nonsense mediated mRNA decay (NMD). At present, we have succeeded in yielding *Pcdh-γ* floxed/homozygous mice that had CaMK2-Cre gene, which expressed Cre recombinase especially in the telencephalon after birth. These mice have lower body weights compared with littermates and show behavioral abnormalities. Here, we will show the results of analysis in these mice.

O21-4 Characterization of LOTUS, novel molecule serving for circuit formation, with Nogo-66 receptor

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LOT usher substance (LOTUS) is newly identified, a key molecule serving for the formation of lateral olfactory tract (LOT) in mouse telencephalon. We also identified Nogo-66 receptor (NgR1) as a LOTUS binding protein. To better define how LOTUS binds to NgR1, we generated several deletion mutants consisted of a single domain of LOTUS and analyzed their binding properties for NgR1. We found that two C-terminal domains of LOTUS bound to NgR1, while the mutant containing both domains interacted with LOTUS stronger. This suggests that C-terminal domains of LOTUS may bind to NgR1 with hinge-like structure. One of the domains was predicted to be the calcium binding site by amino acid sequence information. As expected, we found that LOTUS-NgR1 binding was calcium-dependent. Furthermore, LOTUS and NgR1 interaction was involved in cell-cell contact in transfected cells in a calcium dependent manner. This suggests that the calcium-dependent cell adhesion activity may be regulated by the calcium binding site of LOTUS. On the other hand, NgR1 is the founding member of the three NgR family, we also examined binding affinity for the other NgR family members, such as NgR2 and NgR3. NgR2 and NgR3 did not interact with LOTUS. The results indicate that LOTUS binds NgR1 specifically. We next attempt to examine if the LOTUS-NgR1 binding is participated in other cellular functions, such as axonal growth.

O21-6 Aberrant auditory brainstem response and glutamatergic synaptic formation in NB-2 knockout mice

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NB-2 which is a neural cell recognition molecule belonging to contactin subgroup of the immunoglobulin superfamily is expressed prominently in the central auditory system. We reported previously that NB-2 knockout (KO) mice exhibit a lower incidence of wild running than the wild-type in the audiogenic seizure test. NB-2 expression was prominent in the ventral cochlear nucleus (VCN), superior olivary complex (SOC), ventrolateral lemniscus (VLL) and central inferior colliculus in the rat auditory pathways. NB-2 was localized at the neuropils of the glutamatergic neurons in the lateral superior olivary complex and VLL, and the calyces of Held in the medial nucleus of the trapezoid body (MNTB). The expression of NB-2 in the SOC was recognized at P2, reached maximum level at P7, and declined thereafter. Here, we compared the auditory brainstem response (ABR) and projection of glutamatergic neurons in the VAS between the wild-type and NB-2 KO mice to elucidate the function of NB-2 in the auditory system. In NB-2 KO mice, the ABR thresholds depending on sound frequency (8-40 kHz) were normal. However, NB-2 KO mice exhibited delay of ABR waves IV and III-IV interpeak latency at low frequencies (8-12 kHz) as compared with wild-type mice. The waves III-IV are responses from the SOC, lateral lemniscus (LL) and IC in the auditory brain stem. Thus, the function of the SOC, LL and IC are impaired in NB-2 KO mice. Then, we examined projection of glutamatergic neurons, which express NB-2 and play essential roles in the brainstem. Among the glutamatergic neurons, the ventral acoustic stria (VAS) is the bundle of glutamatergic axons projecting from the VCN to the bilateral SOC. The VAS projecting to the contralateral SOC traverse the midline in NB-2 KO mice contained less number of axons than that in the wild-type mice. In addition, NB-2 KO mice displayed a significant decrease of glutamatergic synapses in the MNTB as compared with the wild-type mice. Together, we demonstrated that NB-2 plays a key role in the projection and synaptic formation of glutamatergic neurons in the auditory brainstem.

O21-8 Expression profile of Roundabout1 (Robo1) in the developing mouse neocortex

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It has been well known that the chemorepulsive ligand Slit and its receptor Robo mediating axon guidance are involved in the formation of midline commissures. Recent reports showed that the reduced expression of *Robo1* was associated with developmental disorders such as autism and dyslexia, suggesting that expression level of *Robo1* will be crucial for the neuronal development and higher brain function. However, the expression profile of *Robo1* in the developing brain has not been fully understood. In this study, we investigated the expression of *Robo1* in developing mouse neocortex using in situ hybridization and immunohistochemical methods. At embryonic day 15 (E15), the expression of *Robo1* mRNA was observed throughout the cortical plate, but not in the ventricular zone and the intermediate zone. After E16, however, the expression of *Robo1* mRNA was observed in the restricted regions. Strong signal of *Robo1* mRNA was closely matched with that of ER81 (the marker gene of the layer V), indicating that *Robo1* was mainly expressed in the layer V. After birth the expression of *Robo1* mRNA gradually decreased, and finally the very faint signal was seen in the layer V. Interestingly, the expression of *Robo1* mRNA failed to detect in the piriform cortex throughout the developmental stages. In contrast, *Robo1* protein was highly expressed along the axons in corpus callosum in the embryonic brain. These results suggest that *Robo1* may function in the layer V neurons projecting their axons to the contralateral hemisphere in the developing brain. To reveal the molecular mechanism regulating the restricted expression of *Robo1*, further studies are in progress.

O21-9 Purpurin protects injury-induced apoptosis in rat CNS neurons○Yoshiki Koriyama¹, Toru Matsukawa¹, Junichi Saito², Masumi Nonaka², Satoru Kato¹¹Dept. Mol. Neurobiol., Grad. Sch. Med., Kanazawa Univ., Kanazawa, Japan, ²Div. Health Sci., Grad. Sch. Med., Kanazawa Univ., Kanazawa, Japan

The retinal ganglion cells (RGCs) in mammals cannot regrow their axons and induce apoptotic cell death after optic nerve injury. However, goldfish RGCs can prevent from apoptosis and regenerate optic axons after injury. We attempt to block the cell death and thereby accelerate axonal outgrowth of rat RGCs by using molecules derived from regenerating goldfish retina. Therefore, we constructed a cDNA library from axotomized goldfish retina. We cloned purpurin, a secretory retinol binding protein as an upregulated molecule during early stage of optic nerve regeneration. The purpurin mRNA was significantly increased in the photoreceptor cells by 2 days and the protein was secreted to the RGCs. In goldfish retinal explant culture, purpurin induced axonal elongation. On the other hand, in rat, purpurin was expressed in RGCs in intact retina and diminished from ganglion cell layers by 2 days after nerve injury. Supply of purpurin could protect RGCs and hippocampal neurons from injury-induced and NMDA-induced apoptosis through a mechanism of focal adhesion kinase and Akt activation. Furthermore, purpurin had adhesive effect on rat neurons from culture study with purpurin-coated dishes. We are now in progress to investigate axonal elongation of rat RGCs by recombinant purpurin and overexpression of purpurin gene. These results shed a light on the regeneration-associated molecules against CNS degenerative disease.

O22-2 BMP signaling through BMPRII is essential for proper terminal differentiation in glial progenitor cells○Tomoko Ishibashi^{1,2}, Moeko Kudoh², Haruo Kishida², Lyons Karen M.³, Masahisa Yamada²¹Dept. of Mol. Neurobiology, Tokyo Univ. of Pharmacy and Life Sciences, ²Yamada Research Unit, RIKEN BSI, ³Brain Research Institute, UCLA, USA

Neural stem cells (NSC) are self-renewing, multipotential progenitor cells with the capacity for generating neurons and glial cells including astrocytes and oligodendrocytes. Bone morphogenetic protein (BMP) signaling is involved in differentiation of neural precursor cells into astrocytes, but its contribution to oligodendrocyte development is not well understood. BMPs bind to heteromeric receptors formed by type I (BMPRI, BMPRII, ALK2) and type II (BMPRII) subunits. It is recently shown that BMP signaling through BMPRII is important for cell fate determination in NSCs towards glial lineage (Samanta et al., 2007). In this study, we examined the optic nerves from mice lacking BMPRII during neural development. We found that an abnormal cell mass appeared in the central region along the entire optic nerves from the retina chribose to the chiasmatal region. To identify these cells, we used immunofluorescence analysis with antibodies against Neurofilament 200, MBP, NG2, GFAP, and Pax2. We found that the abnormally proliferating cells were not stained with any of these antibodies until postnatal day 7 (P7). At P10, they became MBP- and/or NG2- positive oligodendrocyte progenitor cells (OPCs). On P14 most of these cell mass had disappeared from the nerves in mice lacking BMPRII. Our findings show that loss of *Bmpr1b* gene function leads to an increase in the number of immature oligodendrocytes. These results suggest that BMP signaling may contribute in this critical period in the glial developmental process.

O22-4 Osseous genes expressed in the brain○Takeshi Takarada¹, Shintaro Kurokawa¹, Yusuke Tonami¹, Shihō Konishi¹, Yukio Yoneda¹¹Laboratory of Molecular Pharmacology, Kanazawa University Graduate School of Natural Science and Technology

We have previously shown the possible functional expression of molecular machineries required for glutamatergic signaling in osseous cells including osteoblast, osteoclast and chondrocyte. This study was thus aimed at the elucidation of possible expression of osseous genes in the mammalian brain. In embryonic and adult mouse brains, marked mRNA expression was seen for runt related factor-2 (*runx2*), core binding factor- β , *osterix*, collagen I, osteopontin, matrix metalloproteinase 13 (*MMP13*), *sox9*, indian hedgehog, calcitonin receptor and cathepsin K, but not for osteocalcin, collagen II, collagen X, parathyroid hormone (PTH)/PTH related peptide receptor, receptor activator of NF- κ B (RANK), RANK ligand or tartrate-resistant acid phosphatase on RT-PCR analysis. The master regulator of osteoblast differentiation, *runx2*, was also expressed in cultured rat cortical astrocytes and C6 glioma cells, but not in cultured rat cortical neurons and neuro2a cells. Luciferase activity was significantly higher in C6 glioma cells transfected with a construct containing 6 tandem copies of *runx2* binding element (CCAACAAC) linked to the luciferase reporter plasmid than in cells with mutated *runx2* binding site (CCAAGAAC). In C6 glioma cells stably overexpressing the dominant negative *runx2* (Δ *runx2*), moreover, significant inhibition was found with the luciferase activity for the wild type reporter plasmid, in addition to decreased mRNA expression of both osteopontin and *MMP13*, without significant changes in mRNA expression of *runx2*, epidermal growth factor, brain derived neurotrophic factor, nerve growth factor and fibroblast growth factor. Transient overexpression of *runx2* led to an increase in mRNA expression of both osteopontin and *MMP13* in cultured rat cortical astrocytes. These results suggest that several osseous genes, such as *runx2*, may be functionally expressed by rat brain astrocytes in terms of transactivation of particular target genes.

O22-1 Cyclin D1 inhibits astrocyte differentiation in the section of neural stem cell○Norihisa Bizen¹, Toshihiro Inoue¹, Takeshi Shimizu², Tetushi Kagawa¹, Tetuya Taga¹¹Div. of Cell Fate Mod., Insti. of Mol. Emb. and Gene., Kumamoto Univ, Kumamoto, Japan, ²Lab. for Vert. axis Form., RIKEN. CDB, Kobe, Japan

Neurons, astrocytes, and oligodendrocytes in the central nervous system are generated from a common progenitor, neural stem cell (NSC). The maintenance of undifferentiated state of NSCs is intimately linked to the inhibition of neural and glial differentiation. However, the molecular link between induction of cell cycle progression and inhibition of cell differentiation in NSCs is poorly understood. Astrocyte differentiation from NSC is synergistically induced by combination of LIF (leukemia inhibitory factor) and BMP2 (bone morphogenetic protein-2), which activate transcriptional factors, STAT3 (signal transducers and activators of transcription-3) and Smad1 (Nakashima, K et al. Science 1999), respectively. Recent study using a hepatoma cell line demonstrated that cyclin D1, a key regulator of G1 to S phase progression of the cell cycle, repressed LIF-induced transactivation of STAT3 (Bievenue F, et al. J Biol Chem 2001). Thus, we hypothesized that cyclin D1 suppresses astrocyte differentiation via inactivation of STAT3-mediated transcription of astrocyte-specific genes. To investigate this possibility, neuroepithelial cells from embryonic day 14.5 mouse telencephalon were cultured with FGF2 (fibroblast growth factor-2) for 4 days to enrich NSCs, and then treated with LIF and BMP2 for 24 hours. Cells that showed immunoreactivity to GFAP (glial fibrillary acidic protein), an astrocyte marker, did not express cyclin D1. Forced expression of cyclin D1 in NSCs cultured with LIF and BMP2 decreased the number of GFAP expressing astrocytes by approximately 20%. CDK4 inhibitor hardly recovered the GFAP expressing cells in number, indicating that cyclin D1 inhibits astrocyte differentiation in a manner independent of CDK4. Interestingly, the effect of cyclin D1 to suppress astrocyte differentiation was dramatically abolished by histone deacetylase (HDAC) inhibitor, Trichostatin A, suggesting that cyclin D1 represses astrocyte differentiation by down-regulating the histone acetylation in astrocyte specific gene promoter regions.

O22-3 A novel method for domain specific gene modification, and analysis of glial development○Hitoshi Gotoh¹, Katsuhiko Ono¹, Hirohide Takebayashi¹, Kazuhiro Ikenaka¹¹Division of Neurobiology and Bioinformatics, National Institute for Physiological Sciences

Glial cells are abundant in the central nervous system, and the ratio of glial cells to neurons is much higher in higher vertebrates than in lower organisms. Astrocytes and oligodendrocytes are two major component of glial cells, and the former supports neuronal function through supplement of nutrition, whereas the latter forms myelin around the axonal trajectory. Functional or morphological features of these cells are highly heterogeneous but their ontogeny is not fully understood. Recently, several researches suggest that the reason of this heterogeneity is partially caused by the location of their origin. Because glial cells develop after neuronal production is ceased, there are methodological limitations for analyzing these correlations between location of origin and their function. In order to resolve this, we are trying to establish novel method to introduce genes depending on their location. Murine retrovirus is widely used for lineage tracing analysis during development in rodent because retroviral genome can integrate into the chromosome of proliferating cells, resulting in permanent gene modification. Murine retrovirus does not have ability to infect chick cells. So, we thought that by ectopic expression of mCAT1, which is a receptor for retrovirus, in a region specific manner, it would be possible to transduce retrovirus in a region specific manner. In our preliminary study, we introduced mCAT1 into one side of neural tube by electroporation followed by injection of retrovirus. Murine retroviral vector successfully transduced into progenitor cells in the electroporated side, but not into contralateral side of neural tube. These observation suggest that electroporation of mCAT1 into specific area, such as ventral or dorsal part of brain, lineage tracing analysis could be done in chick embryo. In order to restrict the region of mCAT1, we are now trying several methods using specific promoter/enhancer or BAC (Bacterial Artificial Chromosome). In this presentation, we would like to present about these method and analysis of glial origin.

O22-5 Analysis of the Expression of PLD4 in the early postnatal mouse cerebellum○Yoshinori Otani¹, Yoshihide Yamaguchi¹, Fumio Yoshikawa², Yumi Sato², Teiichi Furuichi², Hiroko Baba¹¹Department of Molecular Neurobiology, Tokyo University of Pharmacy and Life Sciences, Hachioji, Japan, ²Laboratory for Molecular Neurogenesis, RIKEN Brain Science Institute, Wako, Japan

Phospholipase D (PLD) is a ubiquitous enzyme to hydrolyze phosphatidylcholine to phosphatidic acid and choline, and is involved in various cellular functions including membrane trafficking, secretion and mitogenesis. Recently, we identified a new member of PLD superfamily, called PLD4, in the course of the cerebellar development transcriptome database (CDT-DB) project. Unlike other conventional PLDs, PLD4 has a transmembrane domain but have no authentic PLD activity. At present, the function of PLD4 is totally unknown. The in situ hybridization (ISH) and RT-PCR data deposited in the CDT-DB showed that the expression of PLD4 mRNA peaks at postnatal day 7 (P7) of mouse cerebellum and predominates in the corpus callosum and the cerebellar white matter. At P7 consists of three kinds of glial cells (astrocyte, oligodendrocyte and microglia), a few minor cell-types, and input (climbing and mossy fibers) and output (Purkinje cell axons undergoing myelination) fibers. In this study, in order to clarify the expressing cells and the function of PLD4, we focused on the developmental process of the cerebellar white matter. We performed immunohistochemical analysis of this process using antibodies against each glial cell markers and double labeling analysis with ISH and immunostaining. GFAP-positive astrocytes were detected all over the white matter at P3 and increased with age. MBP-positive oligodendrocytes appeared in the central deep white matter at P3 and increased and moved to apical region with age. The myelination was greatly increased after P10. Iba1-positive microglia were also detected from P3 and moved to apical region ahead of MBP-positive cells. The number of Iba1-positive cells peaked around P7-10. PLD4 ISH positive signals were only detected in Iba1-positive cells and their shapes were looked as amoeboid (activated) type. Amoeboid microglia can release many humoral factors interacting with other cells. Therefore, these results suggest that the expression of PLD4 may be involved in the activation of microglia and/or interaction with other cells in the beginning of myelination.

O22-6 Involvement of astrocytic ATP in modulation of M1 muscarinic acetylcholine receptor expression in the hippocampal neurons

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Astrocytes modulate neuronal activity in an extremely dynamic and transient fashion by releasing so-called "gliotransmitter" ATP in response to neurotransmitters or even spontaneously. On the other hand, some studies suggest astrocytic involvement in more gradual and long-lasting responses such as regulation of protein expression in neurons. In the present study, we focused on the sustained effect of astrocytic ATP on the expression of M1 muscarinic acetylcholine (ACh) receptors in the hippocampal neurons in cultures. From pharmacological characterization using Ca^{2+} -imaging technique (fura-2 method), we found that the high population of hippocampal neurons possesses functional M1 ACh receptors (52.1 %), about half of which co-expressed functional P2Y₁ receptors. These findings suggest that there exist a signaling cross-talk between M1 ACh receptors and P2Y₁ receptors in the neurons. An exogenously applied 2MeSADP, a selective P2Y₁ receptor agonist, caused a significant increase in expression of the M1 ACh receptor-mediated Ca^{2+} response in hippocampal neurons in a concentration-dependent fashion, which was concomitant with upregulation of mRNA and proteins of M1 ACh receptors. We also found that the ATP-degrading enzyme apyrase or P2 receptor antagonists alone decreased M1 ACh receptor-mediated responses, showing that ATP/P2 receptor-mediated signals would tonically regulate M1 ACh receptor expression. It should be noted that this inhibitory effect by apyrase alone could be observed only in neuron-astrocyte co-cultures but not in neuron-rich cultures, indicating that astrocytes could be the source of extracellular ATP. All these findings suggest that constitutive release of ATP from astrocytes is a key event that controls expression of M1 ACh receptors in adjacent neurons, and that there might be plastic and dynamic regulatory mechanism of neuronal function by astrocytes.

O22-8 A role of Annexin2 in the lysolecithin-induced demyelinating model mice

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Annexin2 (AX2) is a calcium-dependent actin- and phospholipid-binding protein implicated in numerous intracellular functions, including signal transduction, membrane trafficking, and mRNA transport, as well as in the regulation of membrane/cytoskeleton contacts and extracellular functions. AX2 also modulate pathological processes through inhibition of cytosolic phospholipase A2 (cPLA2) or promotion of local fibrinolysis. In the central nervous system (CNS), the expression of AX2 is upregulated in some pathological conditions, however, roles of this protein in the peripheral nervous system (PNS) in normal and pathological conditions are still uncertain. Previously, we reported that AX2 was localized in the paranodal regions and Schmidt-Lanterman incisures (SLI) in the PNS (Hayashi et al., 2007). AX2 in these regions was markedly increased in the cerebroside sulfotransferase (CST)-deficient mice, in which paranodal axo-glial junctions were disrupted. cPLA2 was also accumulated in the same paranodal regions in this mutant, suggesting that AX2 may protect myelin by inhibition of cPLA2. To determine the role of AX2 in the PNS demyelination, we examined the lysolecithin-induced demyelination model mice in the present study. Lysolecithin was injected intraneurally in one sciatic nerve of each 8-week-old ICR mouse. Contralateral intact nerves and vehicle-injected nerves were used as controls. The lysolecithin-injected and control sciatic nerves were removed at 3, 5, 7, 9 and 14 days after injection for immunohistological or western blot analysis. Demyelinating conditions were evaluated by myelin basic protein (MBP) staining and electrophysiological analysis. In comparison with controls, AX2 was upregulated in the lysolecithin-injected nerves, and its distribution patterns were similar to cPLA2. From these results, AX2 may have role for anti-inflammatory effects in the PNS, and regulation of this protein may be useful for demyelinating polyneuropathies.

O23-1 Abnormal dendritic spine formation via CaMKII/Rac1-GEF/PAK signaling in X-linked mental retardation model mouse.

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Alpha-thalassemia X-linked mental retardation (ATRX) syndrome is a severe, nonprogressive form of X-linked mental retardation that is frequently associated with various clinical manifestations including severe mental retardation, genital abnormalities and epileptic seizures. We generated the ATRX mutant mice with mild mental retardation by removing exon 2 of ATRX gene. We then performed neurochemical and anatomical studies to understand biochemical mechanisms underlying generation of abnormal spines in the medial prefrontal cortex (mPFC) observed in ATRX mutant mice. The mutant mice showed remarkable morphological changes in the dendritic spines that are long and thin without change in the number of spine on the dendrites. Interestingly, an increased calcium/calmodulin-dependent protein kinase II (CaMKII) activity was observed in the postsynaptic density fraction in the ATRX mutant mouse brain. The increased CaMKII autophosphorylation was associated with an increased phosphorylation of Rac1-guanine nucleotide exchange factors (GEFs) including Tiam1 and Kalirin-7. Tiam1 and Kalirin-7 are known to be phosphorylated by CaMKII, thereby activating p21-activated kinases (PAKs) that is a downstream target of Rac1. Taken together, abnormal elevation of CaMKII activity likely elicits remarkable changes in the spine structure in the mPFC and the dysregulation of CaMKII/Rac1-GEF/PAK signaling by ATRX mutation accounts for abnormal spine formation associated with mental retardation syndrome.

O22-7 Modulation of gap junctions/hemichannels in astrocytes by rotenone *in vivo* and *in vitro*

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Dopaminergic neurons of the substantia-striatum are particularly vulnerable to oxidative stress and inflammatory attack. Such processes may play a crucial role in the etiology of Parkinson disease (PD). Since glia is the main generators of these processes, the possibility that PD may be caused by glial dysfunction needs to be considered. However, the involvements of astroglial activation in PD onset are poorly understood. It has been reported that partial inhibition of mitochondrial respiratory complex I by rotenone reproduces aspects of PD in rodents. In this study, we examined the effects of rotenone on gap junctions/hemichannels as a downstream target of parkinsonism inducing substances. *In vivo* study, the levels of the astrocytic gap junction protein, connexin43 (Cx43) and its activated phosphorylation form (P2) were selectively enhanced in striatum with astrocyte activation after chronic rotenone treatment. In striatum, increased levels of Cx43 and its activated phosphorylation form (P2) were detected during 1 to 4 weeks after rotenone treatment. *In vitro* study with primarily cultured astrocytes, we found that rotenone induced levels of Cx43 and its activated phosphorylation form (P2) without increasing of Cx43 mRNA expression. Functional gap junctions/ hemichannels were evaluated using fluorescence-recovery-after-photobleaching (FRAP) technique and measurement of ATP release, respectively. Gap junctions/ hemichannels were enhanced with increased Cx43 levels by rotenone treatment. Moreover, rotenone-induced levels of Cx43 and its activated phosphorylation form (P2) were completely suppressed by protein kinase A inhibitor H89 in cultured astrocytes. These results suggest that astrocytes respond to rotenone stimulation by reorganizing their gap junctions/hemichannels, that the qualitative nature of their response contributes to damaging chronic inflammation, and that a pool of Cx43 may contribute to the rotenone-induced elevations of this protein via cAMP-PKA pathway.

O22-9 Disruption of paranodal axo-glial junctions causes alteration of axonal mitochondria at nodes of Ranvier

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Previously we have reported that paranodal axo-glial junctions are important for ion channel clustering on the myelinated axons (Ishibashi et al., 2002). Using electron microscopic analysis, we found more recently that the mitochondria in the nodal axons of the peripheral nervous system (PNS) were aberrantly large and swollen in cerebroside sulfotransferase (CST)-deficient mice, which show the disruption of the paranodal junctions (Hoshi et al., 2007). These results suggested that myelin, especially the paranodal axo-glial junction, may have a crucial role for regulating the inside of axons as well as their surface. Therefore, in the present study we examined the axonal mitochondria in CST-deficient mouse PNS using immunofluorescence analysis to better understand how the lack of paranodal junctions affects their distribution and state. Mitochondria and other organelles are often amassed in the nodes and paranodes of peripheral myelinated axons. However, our results demonstrated that the pervasiveness of such accumulations of axonal mitochondria was strongly increased in the nodal regions in sciatic nerves of CST-deficient mice in comparison to the control nerves. We used anti-cytochrome c oxidase Complex IV (COXIV) antibody as mitochondria marker to stain the sciatic nerves from 8-week-old mice, and found that the percentage of COXIV cluster-containing nodes was dramatically increased in CST-deficient mice (63.4 ± 10.6%) compared with the control mice (10.2 ± 6.1%). The state of these mitochondria was examined by staining with antibodies against manganese superoxide dismutase (MnSOD), cytochrome c, and COXV. All proteins were concentrated at the nodes of Ranvier and were colocalized with COXIV in CST-deficient mice, suggesting that these aberrant mitochondria remain functional. Thus, our data provide insight into the role of paranodal axo-glial junctions in axonal homeostasis.

O23-2 Caspr2 encoded by developmental and psychiatric disorder-susceptibility gene CNTNAP2 is involved in the synaptic development

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Contactin-associated protein-like 2 (Caspr2) is a cell recognition molecule belonging to the neuroligin family. It has been reported that Caspr2 is localized at the juxtaparanodal regions of myelinated axon, where Caspr2 interacts with TAG-1, a GPI-anchored cell recognition molecule in the immunoglobulin superfamily, and thereby accumulates K⁺ channels in these regions. Recently, disruption or mutation of the human CNTNAP2 gene encoding Caspr2 has been associated with developmental and psychiatric disorders, such as Tourette syndrome, epilepsy, mental retardation, autism and schizophrenia. It has been reported that neuroligins play important roles in the synaptic development and that disruption of neuroligin 1 gene is associated with autism. Then, we hypothesized that Caspr2 contributes to formation and/or function of the synapse as well as the molecular organization of juxtaparanodal region. Here, we show that Caspr2 is localized at the synaptic site. We prepared the synaptosomal fraction from the mouse cerebral cortex and examined whether Caspr2 is detected in the fraction. Western blot analysis showed that Caspr2 was enriched in the synaptosomal fraction as well as PSD-95, a synaptic marker protein. Next, we investigated the detailed localization of Caspr2 using primary cultures of mouse hippocampal neurons. At early stages of synaptogenesis, clusters of Caspr2 detected in dendritic shafts were partially overlapped with those of synaptic marker proteins. To explore the function of Caspr2, cultured hippocampal neurons and Neuro2a cells were transfected with Caspr2-expressing plasmids. Overexpression of Caspr2 promoted neurite outgrowth and increased the density of dendritic filopodia-like protrusions on the neurite. Deletion mutant analysis revealed that N-terminal fragment of the extracellular domain of Caspr2 is indispensable to formation of the protrusions in Neuro2a cells. Our observations suggest that Caspr2 may play important roles in the synaptic development.

O23-3 Diet-induced obesity in female mice leads to obesity and peroxidized lipid accumulation during early life of their offspring○Yusuke Tozuka^{1,2}, Etsuko Wada^{1,3}, Keiji Wada^{1,3}¹Department of Degenerative Neurological Diseases, National Institute of Neuroscience, National Center of Neurology and Psychiatry, Tokyo, Japan, ²Japan Association for the Advancement of Medical Equipment, Tokyo, Japan, ³CREST, Japan Science and Technology Agency, Saitama, Japan

Obesity is considered as a major worldwide health issue, and the dramatic increase in the prevalence of obesity among children and adults has been attributed to increased dietary intake of high-energy, high-fat foods and reduced physical activity. Obesity is associated with an increased risk of diabetes, cardiovascular disease, neurological diseases and many other chronic diseases. Besides obesity in childbearing age are associated with increased risk of infertility, menstrual abnormalities and pregnancy complications. Maternal obesity is increasingly prevalent and may affect the long-term child developments. However, there is little information about the effect of maternal obesity on the offspring brain development and neurological diseases.

In the present study, we investigated the effects of maternal diet-induced obesity in mice on the metabolic function and brain development of their offspring. Adult female mice were fed either a control normal diet (4% fat) or a high fat diet (32% fat) for 6 weeks before mating and throughout pregnancy and lactation. There were no differences in the body weight gain and serum lipid concentrations between normal diet offspring and high fat diet offspring during gestational period. However, high fat diet offspring developed adiposity and hyperlipidemia during lactation. Additionally, peroxidized lipid accumulations were observed in serum and brain, suggesting that the oxidative stress may be accelerated in these obese offspring.

O23-5 Expression, localization and developmental changes of the D-serine-related genes in the rat central nervous system○Naoki Yamamoto¹, Dai Shimazu¹, Sotaro Kanematsu¹, Go Taniguchi¹, Asami Umino¹, Toru Nishikawa¹¹Psychiatry and Behavioral Sciences, Tokyo Medical and Dental University Graduate School

D-Serine is an endogenous co-agonist of NMDA type glutamate receptors in the mammalian brain. The precise mechanisms of the regulation of D-serine signaling and metabolism are not well understood yet. Accordingly, in this study we have examined the distribution of the D-serine-related gene products in the rat. Using functional cloning technique, we isolated the D-serine modulator (*dsm-1*) gene from the rat brain, which encoded a molecule modulating the cellular release of D-serine. The expression of *dsm-1* mRNA was predominant in brain and liver in the adult rat. Its expression within the brain indicated the similar distribution with that of endogenous D-serine. From the developmental point of view, the change of D-serine tissue content is also of worth noticeable: the amount of endogenous D-serine decreases drastically in the cerebellum with the individual development. This change is reciprocal to the expression and the activity of D-amino acid oxidase (DAO). Furthermore, the regulation of synthesis, degradation and cellular transportation of D-serine is thought to show mutual correlation with the metabolism of glycine and L-serine in the mammalian brain *in vivo*. We further discuss the expression of the enzymes involved in the metabolism of these amino acids.

O23-7 Visual input-dependent regulation of nuclear extracellular signal-regulated kinase in developing visual cortex○Hironori Takamura^{1,2}, Satoshi Ichisaka¹, Chihito Hayashi³, Hiroto Maki¹, Yoshio Hata¹¹Dept. Psychiatry, Osaka Univ. Grad. Sch. Med. ²Div. Integrative Bioscience, Tottori Univ. Grad. Sch. Med. Sci. ³Div. Neurobiology, Sch. Life Sci., Fac. Med., Tottori Univ.

Monocular deprivation (MD) induces significant plasticity in the primary visual cortex (V1) during a short period of postnatal development called critical period. In this period, cortical cells lose their responses to the deprived eye by MD. Previous reports revealed that activity of extracellular signal-regulated kinase (ERK) is necessary for the ocular dominance plasticity, but it remains to be elucidated how the ERK activity is regulated by MD. To answer the question, we examined effects of MD on ERK activity in rat V1. During attempts to examine the phosphorylation status of ERK in the cortex immunohistochemically, we determined whether deep anesthesia for euthanasia disturbs the ERK phosphorylation, because the anesthesia might influence activity-dependent phosphorylation of ERK. We found that long anesthesia (> 10 min) drastically reduced the density of phosphorylated ERK immunopositive cells to about 15 % of the short anesthesia condition (< 5 min). Thus, we carefully kept the duration of anesthesia shorter than 5 min. In addition, we reduced possible variation of pERK immunopositive cell density in V1 by normalizing the values to the density in the nonvisual area in the entorhinal cortex. Activated (phosphorylated) ERK (pERK) was mainly observed in layer II/III and VI, and we found that the amount of pERK decreased significantly in layer II/III receiving deprived eye inputs following 24-hr MD in both young and adult rats. On the other hand, the amount of pERK did not change in layer VI even after 1-week MD. As to the subcellular localization, we found a significant increase of pERK in nuclei following MD only in young rats. While MD for 12 hours did not increase nuclear pERK, 24-hr MD induced the strongest increase. The increase has declined in 3-day MD rats and was not observed after 1-week MD. These results suggest that nuclear signaling of ERK transiently upregulated following MD in young rats, and the signaling might play an important role in the ocular dominance plasticity.

O23-4 Toxicogenomic analysis of the effects of pre- and post-natal tributyltin exposure on the developing rat brain○Mika Wakasa¹, Makoto Imamura¹, Ryosuke Yoshioka¹, Masaki Takahashi¹, Takayuki Negishi¹, Masashi Tsunoda², Yoshiharu Aizawa², Hideo Tashiro³, Tomoko Tashiro¹¹Department of Chemistry and Biological Science, Faculty of Science and Engineering, Aoyama Gakuin University, ²Department of Preventive Medicine and Public Health, Kitasato University School of Medicine, ³Sensing Technology Laboratory, Discovery Research Institute, RIKEN

Tributyltin (TBT) compounds which have been widely used as antifouling agents are reported to have neurotoxicity in mammals in addition to the endocrine-disrupting effects on aquatic animals. The mechanism of neurotoxicity, however, remains to be elucidated. In the present study, we investigated the effect of TBT on the developing rat brain by a two-generation toxicogenomic analysis using custom DNA microarrays focused mainly on genes involved in synaptic structure and activity. Neonatal rats were exposed to TBT *in utero* and postnatally by feeding their mothers chow containing 25ppm or 125ppm tributyltin chloride. After 3w postnatally, the pups were fed normal chow free of TBT chloride. Comparison of cDNAs obtained from the cerebral cortex and midbrain of control and TBT-exposed animals at postnatal 1w, 2w, 3w and 6w by competitive hybridization revealed that TBT affected gene expression in the midbrain more severely than that in the cerebral cortex. As observed at 6w, expression of several genes remained altered even after withdrawal of TBT for 3w. Further analysis by realtime quantitative PCR confirmed that significant changes in the expression of the following genes were induced by TBT exposure: (1) up-regulation of the genes for mitochondrial cytochrome oxidase complex (electron transport complex IV), *cox6c* and *cox7a3*, at 3w, (2) dose-dependent up-regulation of chromogranin b gene (*chgb*) at all time points including 6w, (3) up-regulation at all time points of *slc8a2* gene coding for the Na⁺-driven Ca²⁺-exchanger. The results suggest that while TBT exposure may reversibly affect mitochondrial function, it exerts a more sustained effect on the cellular calcium homeostasis by affecting the expression of *chgb* which regulates the activity of the IP3 receptor-Ca²⁺-channel and the Na⁺-driven Ca²⁺-exchanger at the cytoplasmic membrane, *slc8a2*.

O23-6 Developmental expression pattern of mKirre in proprioceptive neurons of the dorsal root ganglia: its interaction with nephrin in the muscle spindles.○Yoshihiro Morikawa¹, Tadasuke Komori¹, Hiroaki Gyobu¹, Hiroo Ueno², Toshio Kitamura¹, Emiko Senba¹¹Department of Anatomy & Neurobiology, Wakayama Medical University, Wakayama, Japan, ²Institute for Stem Cell Biology and Regenerative Medicine, Stanford University School of Medicine, Stanford, CA, USA, ³Division of Cellular Therapy, Advanced Clinical Research Center, Institute of Medical Science, University of Tokyo, Tokyo

A mammalian homologue of the *kirre* gene of *Drosophila melanogaster*, mKirre, belongs to the immunoglobulin superfamily. Previously, we have isolated mKirre from mouse bone marrow stroma cell line OP9 (Ueno *et al.*, Nat Immunol, 4: 457-463, 2003). In addition, we have reported that mKirre is expressed in the developing and adult central nervous system (Tamura *et al.*, Neuroscience, 133: 615-624, 2005). However, the expression of mKirre in the peripheral nervous system remains unclear. In the present study, we investigated the expression of mKirre in the mouse dorsal root ganglia (DRGs). In the adult DRGs, mKirre mRNA was detected in 21.5 ± 2.3% of total dorsal root ganglion (DRG) neurons. Size frequency analysis revealed that mKirre mRNA was mainly expressed in the medium- and large-sized neurons. In addition, mKirre mRNA predominantly colocalized with tyrosine kinase receptor (Trk) C-immunoreactivity, suggesting that mKirre is expressed in the proprioceptive DRG neurons. In the developing DRGs, mKirre mRNA was first detected in a few cells at embryonic day (E) 11.5, gradually increased, and reached the adult level at E17.5. During the development, mKirre was expressed in most of TrkC-positive DRG neurons. The expression of mKirre was observed in TrkC-positive nerve fibers around neurotrophin 3 (NT3)-positive intrafusal muscle fibers of the muscle spindle at E17.5. Furthermore, nephrin was expressed in the NT3-positive intrafusal muscle fibers and was in close apposition with mKirre-immunoreactivity. Coimmunoprecipitation assay revealed that nephrin interacted with mKirre in the developing muscles. These results suggest that mKirre plays important roles in the differentiation of muscle spindle through the interaction with nephrin.

O23-8 SARE: synaptic activity-responsive element that governs expression of the plasticity-related gene Arc○Hiroyuki Okuno¹, Takashi Kawashima¹, Aki Adachi-Morishima¹, Michiko Okamura¹, Haruhiko Bito¹¹Department of Neurochemistry, University of Tokyo Graduate School of Medicine

The neuronal immediate early gene *Arc* is implicated in long-term synaptic plasticity and is widely used as one of the most reliable molecular marker for intense synaptic activity *in vivo*. However, the *cis*-acting elements responsible for such neuronal activity-dependence have not been firmly identified. We here combined luciferase reporter assays in cultured cortical neurons and comparative genome mapping to identify the critical synaptic activity-responsive elements (SARE) of the *Arc* gene. We first identified the extent of the genomic region of the mouse *Arc* promoter that was sufficient to replicate the transcriptional regulation of endogenous *Arc*. By rational deletion/mutation analyses, we then successfully isolated a major SARE within the promoter as a unique short (approximately 100 bp) element. This single element, when positioned immediately upstream of a minimal promoter, was necessary and sufficient to replicate crucial properties of endogenous *Arc*'s transcriptional regulation, including rapid onset of synaptic activity-triggered transcriptional activity and maintenance of low basal expression during synaptic inactivity. Mutations of the SARE in the context of the full-length *Arc* promoter resulted in dramatic reduction of the transcriptional regulation ability. Electrophoretic mobility-shift assays (EMSA) suggested existence of several distinct transcription factor binding sites in the SARE; the candidate trans-activators are now being scrutinized. Furthermore, pharmacological experiments have demonstrated involvement of both MEK and CaMK pathways in synaptic activity-dependent transcriptional activation via the SARE. Taken together, our study has uncovered a novel *cis*-acting component that may mediate the synapse-to-nucleus signaling in ensembles of Arc-positive activated neurons.

O23-9 Endogenous glutamic acid acts as neuroprotective agent against low potassium-induced cell death via metabotropic receptors in cultured rat cerebellar granule cells

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During brain development, endogenous glutamate acts as an essential trophic factor as well as excitatory neurotransmitter during central nervous development. Glutamate exerts its potencies via specific receptors, which are classified as ionotropic receptors such as NMDA receptors and metabotropic glutamate receptors (mGluR). These mGluRs are G protein-coupled receptors, which modulate neuronal excitability and synaptic transmission. Glutamate signals via mGluR play various roles in brain development including proliferation, differentiation, migration, and programmed cell death. In the present study, we investigated the role of endogenous glutamate in low potassium-induced cell death in cultured rat cerebellar granule cells. Cerebellar granule cells required relatively high concentration (25 mM) of potassium in culture medium for their survival, and they would be endangered when medium is replaced with normal potassium concentration (5 mM), which is considered as cell death model induced by low neuronal activities. Cerebellar granule cells from neonatal rats at postnatal day 1 were cultured in DMEM/F-12 containing 10% FBS supplemented with 25 mM KCl for 3 days. After 3 days in culture, medium was replaced with serum-free medium supplemented with 25 mM (High KCl) or 4 mM KCl (Low KCl). Low KCl weakly induced cell death after 48 hours. Although concomitant treatment with MK-801, a highly potent and selective non-competitive NMDA receptor antagonist, during 48 hours did not affect low KCl-induced cell death, treatment with 2-Amino-3-phosphonopropionic acid (AP3), a potent mGluR antagonist, significantly enhanced low KCl-induced cell death. These results suggest that glutamate have a protective effect against low activity-induced neuronal cell death via mGluR in cerebellar granule cells during brain development.

O24-2 Functionality of NMDA receptors expressed by undifferentiated neural progenitor cells

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We have previously shown that an intraperitoneal injection of N-methyl-D-aspartate (NMDA) leads to a significant decrease in the proliferation of neural progenitor cells expressed in the hippocampal dentate gyrus of adult mice. In this study, we have attempted to evaluate the possible functionality of NMDA receptor (NMDAR) channels expressed by undifferentiated neuronal progenitors isolated from 18-day-old embryonic rats. Cells were collected from the lower cell layer obtained after percoll density gradient centrifugation, followed by culturing with basic fibroblast growth factor (bFGF) for 12 days under floating conditions. Round spheres were formed within 2 to 4 days by clustered cells with immunoreactivity to the neural progenitor marker protein nestin, but not to MAP-2 or GFAP, for a culture period of up to 12 days. Removal of bFGF led to marked expression of both MAP-2 and GFAP with concomitant elimination of nestin in cells cultured thereafter under adherent conditions for an additional 6 days. An RT-PCR analysis revealed transient mRNA expression of NR1 subunit essential for the heteromeric assembly to the functional NMDAR channels permeable to Ca²⁺, but constitutive expression of NR2A to NR2D subunits in these neurospheres. In consistency with the transient expression of NR1 subunit, exposure to NMDA markedly increased the fluorescence intensity for intracellular free Ca²⁺ in neurospheres cultured for 2 to 6 days, but not in those cultured for 8 to 12 days. A similarly potent increase was seen in the fluorescence after brief exposure to NMDA in cells cultured after the removal of bFGF for an additional 6 days. Moreover, sustained exposure to NMDA not only inhibited the formation of neurospheres, but also facilitated the subsequent expression of MAP-2 with concomitant suppression of GFAP expression. These results suggest that NMDA signals may play a crucial role in the mechanisms relevant to the commitment and/or differentiation to neural lineages in neural progenitor cells.

O24-4 Glutamate receptors in brains of rats with middle cerebral artery occlusion

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Adult male Wistar rats were subjected to middle cerebral artery occlusion (MCAO) for different periods, followed by decapitation 24 h after reperfusion and subsequent dissection of coronal sections for vital staining with 2,3,5-triphenyltetrazolium chloride (TTC). Regional cerebral blood flow was occasionally monitored by a laser-Doppler flow meter, while neurological symptoms were scored after MCAO according to specific postures and behaviors evaluated by posture and rotation tests. Further experiments were done using animals displaying some postural and behavioral changes after reperfusion. Marked vital damages were seen in the ipsilateral cerebral hemispheres of animals subjected to MCAO with a severity dependent on the duration of occlusion from 1 to 8 h, but not in the contralateral cerebral hemispheres, on TTC staining assays. Animals were subjected to MCAO for 2 h, followed by decapitation 1 and 7 days after reperfusion and subsequent dissection of ipsilateral and contralateral cerebral hemispheres from forebrains for Western blotting using specific antibodies against MAP-2, GFAP and CD11b. A significant decrease was seen in the expression of MAP-2, but not GFAP, in ipsilateral hemispheres dissected 1 and 7 days after reperfusion, while MCAO for 2 h led to a transient increase in the expression of CD11b in ipsilateral hemispheres dissected 1 day after reperfusion. Moreover, MCAO for 2 h resulted in a significant decrease in the expression of NR1, NR2A and NR2B subunits of the ionotropic glutamate receptor subtype sensitive to N-methyl-D-aspartate (NMDA) in ipsilateral hemispheres dissected 7 days, but not 1 day, after reperfusion on Western blotting. However, no significant changes were seen in the expression of GluR1, GluR2 and GluR6 subunits of ionotropic non-NMDA receptors in ipsilateral hemispheres dissected 1 and 7 days after reperfusion. These results suggest that MCAO would lead to the disturbed and abnormal functionality and integrity related to multifunctions of NMDA receptors rather than non-NMDA receptors of different ionotropic glutamate receptor subtypes in rat brain.

O24-1 Single receptor imaging of NMDA receptor with atomic force microscopy

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Glutamate is one of the most important neurotransmitter which mediates fast excitatory synaptic transmission via ionotropic glutamate receptors (iGluRs) in the central nervous system (CNS). Among iGluRs, N-methyl-D-aspartate receptor (NMDAR) is involved in learning and memory and also implicated in a number of disease and injury states. Despite its functional importance, little is known about the whole structure of NMDAR. Here, we demonstrate the structure of single NMDAR under the liquid condition as determined by atomic force microscopy (AFM). AFM image of NMDAR showed a diagnostic structure highly correspondent to it of α -amino-3-hydroxy-5-methyl-4-isoxazole propionic acid receptor (AMPA) which had been previously determined by electron microscopy. In the control, two N-terminal domain (NTD) dimers of NMDAR stayed in close to each other. Stimulation of NMDAR by glutamate/glycine markedly altered its conformation with larger separation of two NTD dimers. Whereas, selective antagonists for NMDAR MK801 and AP-5 prevented the agonist-induced separation of NTDs. Additionally, we succeeded in time-lapse imaging of conformational changes of the single NMDAR. Our present data implicate that such NTDs movement is an important action connected to the ion channel pore opening in NMDAR.

O24-3 Glycine-sensitive NMDA receptor-mediated regulation in proliferative activity of neural progenitor cells

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Numerous studies indicate that NMDA receptor plays an important role in neural development by influencing the proliferation of neural stem/progenitor cells. To elucidate mechanisms underlying glutamate signals-mediated modulation of the neurogenesis, in this study, we examined the effects of NMDA receptor antagonists on proliferation in neural progenitor cells. Neural progenitor cells were prepared from the hippocampus of 15-day-old embryonic mice by primary culturing in DMEM/F12 medium with epidermal growth factor (EGF) and basic fibroblast growth factor (bFGF) for 9 days in vitro (DIV). After replating, these cells were further cultured for 6 DIV in the presence of EGF and bFGF. To evaluate glycine-sensitive NMDA receptor-mediated regulation in proliferation in the hippocampal neural progenitor cells, we used MK-801 (NMDA channel blocker), ifenprodil and Ro25-6981 (antagonist for NR2B receptor) or 5,7-dichlorokynureic acid (DCKA) and SM31900 (antagonist for the glycine site) during culturing neural progenitor cells for a period of 9-15 DIV. Cells were harvested for subsequent replating on dishes that had been previously coated with poly-L-lysine and cultured in DMEM/F12 medium containing bFGF and EGF for 1 h, followed by double-immunostaining of nestin (neural stem/progenitor cells marker) and NMDA receptor subunits (NR1, NR2A, NR2B, NR2C, and NR2D). All subunits were present in nestin-positive cells. MTT assay revealed that proliferation of the neural progenitor cells was dramatically attenuated by MK-801, ifenprodil, Ro25-6981, DCKA, and SM31900. In addition to MTT assay, neurosphere assay revealed that SM31900 markedly decreased the number of neurospheres at the size of more than 50 μ m. The attenuation induced by SM31900 was completely abolished by D-serine. Moreover, SM31900 was effective in significantly decreasing the level of phospho-extracellular signal-related kinase. These results suggest that the glycine-sensitive NMDA (NR2B) receptor positively regulates proliferation in the hippocampal neural progenitor cells of embryonic mice.

O24-5 RGS modulates signaling of the melanin-concentrating hormone receptor through the receptor third intracellular loop

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Melanin-concentrating hormone (MCH) is a hypothalamic neuropeptide that plays a central role in food intake. It acts through two G-protein-coupled receptor (GPCR) MCH1R and MCH2R, of which MCH1R is known to be regulator of feeding. Little is known about the MCH1R-binding molecules which functionally regulate receptor activity. Here we report the novel finding that RGS8, one of regulators of G-protein signaling (RGS), functions as a negative modulator of the Gq- and Gi/o-mediated MCH1R signaling. By using GST-fusion proteins and His-RGS8 protein, we first found that RGS8 selectively and directly binds to the third intracellular (i3) loop of the MCH1R. When expressed in HEK293T cells, RGS8 and MCH1R co-localize to the plasma membrane, and RGS8 potentially inhibit MCH1R-mediated calcium mobilization with a dose-dependent manner. This interaction is mediated by the region of RGS8 outside of the RGS domain, and the distal end of i3 loop was found to comprise a structurally important site for the functional interaction with RGS8. These findings demonstrate that specific RGS protein interacts directly with preferred GPCRs and that this interaction is critical for controlling RGS specificity and function.

O24-6 Identification and functional analysis of proteins that bind to the C-terminal tail of histamine H2 receptor

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Histamine H2 receptor (H2R) is a member of a superfamily of seven transmembrane domain G-protein coupled receptors (GPCRs). It plays important roles in the regulation of multiple physiological events extending from gastric acid secretion to neuronal functions. Exposure of H2R to agonist results in rapid receptor desensitization and receptor internalization. C-terminal tail of H2R can be involved in these processes. To understand the role of H2R C-terminal tail and its binding proteins at molecular level, we identified 12 proteins that interact with C-terminal tail of H2R by proteomic approach. Among them, we focused on a GTPase protein dynamin, which has been known to play a role in endocytosis of GPCRs. Dynamin could associate with H2R in vitro and in vivo. Functional analyses using dominant-negative form of dynamin (K44E-dynamin), which lost its GTPase activity, revealed that an acute response of cAMP production and following desensitization were independent of dynamin. However, the agonist-stimulated receptor internalization was inhibited by co-expression of K44E-dynamin. Furthermore, activation of extracellular-signal regulated kinases ERK1/2 in response to H2R agonist dimaprit was attenuated by K44E-dynamin. H2R with truncation of 51 amino acids at its C-terminal tail that does not internalize after agonist stimulation could still activate ERK1/2 but the degree of activation was less than that of wild-type receptor. Finally, K44E dynamin did not affect the activation of ERK1/2 via this H2R internalization-deficient truncation. These results suggest that the agonist-stimulated H2R internalization and ERK1/2 activation are dynamin-dependent. Furthermore, ERK1/2 activation via H2R is likely dependent of the endocytotic process (dynamin-dependent) rather than dynamin itself.

O24-8 A region of N-type Ca²⁺ channel critical for blockade by a dihydropyridine derivative amlodipine

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Amlodipine, a dihydropyridine (DHP) derivative, has been shown to block not only L-type but also N- and P/Q-type Ca²⁺ channels. Aiming to understand the mechanism underlying such a selective blockade of N- and P/Q-type Ca²⁺ channels by amlodipine, the present study was designed to obtain evidence for the interaction site of amlodipine on N-type (Cav2.2) Ca²⁺ channels in *Xenopus* oocyte expression system using the two-microelectrode voltage-clamp technique and the binding assay with [³H] amlodipine and oocyte membranes. When expressed as the $\alpha 1\text{Ba}2/\delta 1\beta 1\text{a}$ combination, N-type channels formed a high affinity binding site for [³H]amlodipine and were profoundly blocked by amlodipine. By contrast, R-type ($\alpha 1\text{Ea}2/\delta 1\beta 1\text{a}$) channels did not possess a high affinity binding site for [³H] amlodipine and their channel activities were not influenced by amlodipine. The transmembrane regions IIIS5, IIIS6 and IVS6 of $\alpha 1$ subunits are involved in DHP binding in L-type channels. Therefore, amino acid residues at the aligned position in these transmembrane regions were substituted between $\alpha 1\text{B}$ and $\alpha 1\text{E}$ subunits. Amino acid substitutions in IIIS5 of $\alpha 1\text{E}$ conferred a high affinity binding site for amlodipine and a high level of sensitivity to amlodipine on R-type. In N-type, reversely, amino acid substitutions in IIIS5 of $\alpha 1\text{B}$ deprived a high affinity binding site for amlodipine and reduced the channel blockade by amlodipine. The results indicate that the region IIIS5 of $\alpha 1\text{B}$ is critical for amlodipine to efficiently bind and block the N-type Ca²⁺ channel.

O25-1 Stress-induced phosphorylation of SNAP-25 in mouse brain

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Neurotransmitter is released from presynaptic nerve terminals by an exocytosis of synaptic vesicles, which involves docking and fusion of synaptic vesicle membrane with presynaptic plasma membrane. It is now generally accepted that so called SNARE proteins play a critical role in the membrane fusion, and VAMP-2/syntaxin 2 in synaptic vesicle membrane and syntaxin 1 and SNAP-25 in plasma membrane participate in neuronal synapse. Neurotransmitter release is regulated both positively and negatively by various protein kinases as well as by lipid kinases, and these regulations are believed to be essential for the various brain functions. Previously, we showed that phorbol ester treatment induced phosphorylation of SNAP-25 at Ser187 and a potentiation of Ca²⁺-induced dopamine and acetylcholine release from clonal rat pheochromocytoma PC12 cells. Recently, we showed that the phosphorylation of SNAP-25 was changed in rat hippocampus after inducing seizure by kainic acid. However, the physiological roles of SNAP-25 phosphorylation in brain function are still poorly understood. To answer this question, we examined the phosphorylation of SNAP-25 in mouse brain under stress. P2 membrane fractions of forebrain, hippocampus, hypothalamus, and cerebellum were prepared from 8 to 12-week-old C57BL/6 mice with or without having restraint stress in cold water (18 ± 1°C), and were analyzed by immunoblotting with an anti-phospho-SNAP-25 antibody. The phosphorylation level of SNAP-25 was markedly elevated in a time-dependent manner and reached a maximal level around 30 min after the stress. The phosphorylation of SNAP-25 was observed in various brain regions tested. By contrast, the phosphorylation of GAP-43 was scarcely changed in these conditions. These results suggest that the phosphorylation of SNAP-25 is involved in stress response in mouse brain.

O24-7 80K-H interacts with inositol 1,4,5-trisphosphate receptors and regulates IP₃-induced calcium release activity

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Inositol 1,4,5-trisphosphate receptors (IP₃Rs) are intracellular channel proteins that mediate Ca²⁺ release from the endoplasmic reticulum (ER) and are involved in many biological processes (e.g. fertilization, secretion, and synaptic plasticity). Recent reports show that the IP₃R activity is strictly regulated by several interacting molecules (e.g. IRBIT, ERp44) and perturbation of these regulation cause several diseases (e.g. Huntington's disease). In this study, we identified protein kinase C substrate 80K-H (80K-H) as a novel interacting molecule with the COOH-terminal tail of IP₃Rs using yeast two-hybrid screening. Immunocytochemical and immunohistochemical staining revealed that 80K-H co-localized with IP₃R1 in COS-7 cells, pyramidal cell layer of hippocampus CA1 region, and hippocampal dissociated culture neurons. We also showed that the purified recombinant 80K-H protein enhanced the IP₃-induced calcium release (IICR) activity in a Ca²⁺ release assay using mouse cerebellar microsomes. Moreover, we found that over-expression and knock-down of 80K-H by the short interference RNA enhanced and reduced IICR activity in COS-7 cells, respectively. Thus, our results suggested that 80K-H is a novel IP₃R-regulator in hippocampal neurons and may contribute to neuronal functions.

O24-9 Identification and functional analysis of binding proteins to the 3'-UTR of alpha CaMKII mRNA.

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Among dendritic mRNAs, alpha CaMKII is the most intensively studied one that is transported to the distal regions of hippocampal dendrites. The dendritic transport of alpha CaMKII mRNA is mediated by recognition of the cis-acting motif on its own 3'-untranslated region (3'-UTR) with some putative trans-acting factor(s). We previously mapped the cis-acting element for dendritic transport to the 30-40nt region that resides near the 5'-end of the 3'-UTR. To identify trans-acting factor(s) on the cis-element, we affinity-purified proteins that bound to the streptotagged RNA harbouring cis-acting element and determined their partial sequences using MALDI-TOF mass. In this study, we identified some RNA-binding proteins, hnRNP K and Y-box protein 1 (YB-1). By RT-PCR, alpha CaMKII gene was specifically amplified from cDNA synthesized from immunoprecipitated RNAs with both anti-hnRNP K and YB-1 antibodies. Gel mobility shift assay demonstrated that antibody against hnRNP K induced the lag of migration of the radiolabeled RNA binding complex. We further analysed the involvement of hnRNP K-containing complex with the dendritic transport of alpha CaMKII mRNA in hippocampal neurons.

O25-2 Role of REST/NRSF repressor-mediated gene regulations in the risk of developing depression-like behavior

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Early life stress in human enhances the risk of developing psychiatric disorders, including depression. In rodents, maternal separation is a potent early life stressor including long-lasting changes in neuroendocrine and molecular responsiveness to stress, associated with depression- and anxiety-like symptoms. However, little is known about the involvement of early life events in the susceptibility to subsequent repeated stress exposure during adulthood in rodents. The present study characterized the effects of maternal separation on the neuroendocrine and behavioral responses to repeated restraint stress in the adult rats. Rat pups were separated from the dams for 15 (HMS15) or 180 min (HMS180) per day from postnatal day 1 through 14, and they were repeatedly restrained for 14-days during adulthood. We found that non-restrained HMS180 rats showed the increased HPA axis response to stress and the increased anxiety behavior in the novelty-suppressed feeding test, compared to HMS15 and non-handling (NH) rats. However, depression-like behaviors in non-restrained HMS180 rats were comparable to that observed in HMS15 and NH rats. Importantly, repeatedly restrained HMS180 rats showed the increased depression-like behavior and anhedonic response compared with the non-restrained HMS180 rats. Further, we found the aberrant expression of transcriptional repressor REST/NRSF protein and its target genes (e.g. CRH, alphaCaMKII, microRNAs) in the medial prefrontal cortex of HMS180 rats. Thus, the aberrant REST/NRSF-mediated gene regulations in the HMS180 rats might be involved in the vulnerability to stressful situations.

O25-3 Central PACAP plays a stimulatory role in the stress-induced HPA-axis response

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Pituitary adenylate cyclase-activating polypeptide (PACAP) is a neuropeptide widely expressed in the central and peripheral tissues including medial prefrontal cortex (mPFC), medial amygdala (MeA), paraventricular nucleus of hypothalamus (PVN), pituitary and adrenal medulla. This distribution of PACAP indicates its involvement in the hypothalamic-pituitary-adrenal (HPA) axis; however, lack of PACAP antagonists has hampered the functional characterization of PACAP. In this study, we examined endogenous roles of PACAP in the stress-induced HPA-axis response by using of PACAP-deficient (KO) mice. Immobilization (tube-restraint) stress was performed by enclosing the mice in a polypropylene tube. Plasma corticosterone levels were determined by a radioimmunoassay. The expression of c-Fos, a marker for neuronal activation, was analyzed by immunohistochemistry. A two hours immobilization stress induced a marked increase in plasma corticosterone levels and c-Fos expression in the PVN in wild-type mice. In contrast, both of these response were significantly reduced in PACAP-KO mice, whereas peripheral administrations of corticotropin releasing factor (CRF) or adrenocorticotrophic hormone (ACTH) caused a similar magnitude of increase in plasma corticosterone levels in PACAP-KO mice and their wild-type littermates. In addition, we found that stress-induced c-Fos expression in MeA but not in mPFC, was significantly reduced in PACAP-KO mice. As MeA is known to play a prominent role in promoting stress responses to psychogenic stressors, impairment of stress-induced PVN/HPA-axis response in these mice may be partially resulted from the reduced neural activation in MeA. Taken together, these results suggest that central PACAP plays an important stimulatory role in the stress-induced HPA axis response.

O25-5 Anti-depressant like effect of dipeptide Leu-Ile on the chronic forced swim test

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At recently, a lot of people are troubled with depression. Increase of the patient is one of the serious problems of today. Analysis of the brain showed that the size of hippocampus of depression patients was decrease. In the present study, degeneration of the neuronal cells and decrease of neurogenesis are suggested as one of the factor of the depression. And also, brain-derived neurotrophic factor, BDNF, is noticed as an important factor for recover from depression. Previously, we have demonstrated that hydrophobic dipeptide Leu-Ile induced BDNF in the cultured neuronal cells, and also showed that protective effect on the natural cell death. So, we expected that Leu-Ile has an anti-depressant effect. To be clear the expectation, effect of Leu-Ile was examined by the model of depression, the chronic forced swim test (FST). ICR mice were forced to swim for 6-min in the cylinder (15 cm of diameter and 18.5 cm of height) which contained water once a day for two weeks. After the first 1-min the total duration of immobility was measured during 5-min test. Leu-Ile was treated by p.o. after each FST. Chronic FST enhanced immobility time day by day. However, Leu-Ile treatment reduced this enhancement, although locomotion of Leu-Ile treated-mice was not difference from control mice. Moreover, real time RT-PCR showed that Leu-Ile treatment after daily FST induced BDNF expression remarkably. Probably BDNF might be an important role to this effect of Leu-Ile. Next, we checked the cell proliferation level in the hippocampus by BrdU uptake to the cells. Chronic FST remarkably reduced the number of BrdU positive cells in the hippocampal dentate gyrus. However, surprisingly, Leu-Ile treatment recovered the number of BrdU positive cells in that area. These results suggest that Leu-Ile has an anti-depressant effect through the support of cell proliferation, and this effect may depend on the BDNF signaling pathway.

O25-7 Expression of myosin VI by PTSD in mouse hippocampus

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Posttraumatic stress disorder (PTSD) is characterized by recurrent recalls of bad memories, insomnia with nightmares and emotional withdrawal, all of which are long-lasting after initial traumatic stress experiences. In this study, we have evaluated the underlying mechanisms for PTSD from a viewpoint of adult neurogenesis in mice. Adult male mice were subjected to restraint stress in a metallic cage immersed in water up to the individual clavicle for 3 h as a traumatic experience (WIRS), followed by various behavioral tests 14 days later. Stressed mice showed increased spontaneous locomotor activities, in addition to exhibiting freezing behaviors in response to a recall flashback signal on the tone fear-conditioning task and forced swimming test, respectively. A marked but transient decrease was seen in the incorporation of the thymidine analog 5-bromo-2'-deoxyuridine (BrdU) into the hippocampal dentate gyrus 5 days after WIRS, while a similarly significant decrease was seen in BrdU incorporation in the dentate gyrus 5 days after flashback signals given 9 days after WIRS. Chronic treatment with imipramine significantly improved those abnormalities in the animal behavior and neurogenesis. Moreover, we carried out differential display analysis to profile gene expression changes in the hippocampus obtained 1 day after WIRS. Myosin VI (Myo6), one of myosin superfamily members, was identified as a gene upregulated in response to traumatic stress in the murine hippocampus. Real-time PCR and Western blot analyses clearly revealed that WIRS led to a significant but transient increase in the expression of mRNA and corresponding protein for Myo6 in the hippocampus 1 day later. Transient overexpression of Myo6 led to a marked decrease in the size of clustered cells in the murine embryonic carcinoma cell P19 cells with abilities to proliferate for self-renewal and to differentiate into neuronal and astroglial lineages. These results suggest that Myo6 could play a pivotal role in the mechanism underlying the decreased neurogenesis in the hippocampal dentate gyrus in mice with traumatic stress.

O25-4 Large-scale analysis of glucocorticoid target genes in rat hypothalamus

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Insufficient glucocorticoid (GC) signaling is frequently observed in major depressive disorder (MDD). Since emotional and behavioral symptoms are often accompanied by disturbances in hypothalamic systems, GC insufficiency in this region is regarded as important in the pathogenesis of MDD. In this study, 22 early GC-responsive genes comprising 15 upregulated and 7 downregulated genes in rat hypothalamus were identified as being regulated at least 2-fold by dexamethasone (DEX) using microarray with 22,599 unique transcripts. Simultaneously, 11,092 ESTs were obtained from rat hypothalamus to comprehensively identify the early GC-responsive genes, which were then clustered into 2,777 known genes, of which 2,498 were also detected by the microarray. Among these 22 genes, 5 of which are novel GC-responsive genes, the expression patterns of *sgk*, *bcl6*, *pdkt4*, and *plekhhf1* were examined *in vitro* in detail, and GC-responsive regions were identified only within the promoter of *sgk*. This suggests that GRE-independent pathways also play a critical role in early GC-response in hypothalamus. Considering that a number of these GC-responsive genes are candidate neuronal regulators, this gene list should be useful in clarifying the relationship between GC insufficiency and the pathogenesis of MDD.

O25-6 Therapeutic effect of decenoic acid ethylester on depression of animal model via the activation of MAP kinase of the brain

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We have recently found that the phosphorylation level of mitogen-activated protein kinase (MAPK, ERK1/2) significantly decreased in the cerebral cortex and hippocampus of the mice exposed to the chronic mild stress (CMS), and this decrease correlated well to the degree of the depression symptom, suggesting that the activation of MAPK in the brain may be protective against depression. Therefore, we examined the effect of ethyl ester of decenoic acid (DAEE), a medium-chain fatty acid, on the animal model of depression, because DAEE activated MAPK of the cultured cortical neurons. Male mice (dy strain, 7 weeks old) were forced to swim for 15 min, and kept in the leaning, drenching and rotated cages within 1-2 days for 3 weeks, and the depression symptom was evaluated by the tail suspension test, and the symptom of anxiety was evaluated according to the length of stay time in the open arm of the elevated plus maze. The mice exposed to the stress actually showed a plain depression symptom and the symptom of anxiety. Therefore, DAEE was administered to the animals i.p. once a day for 3 weeks during stress exposure (protective treatment), or for 2 weeks after the stress load (therapeutic treatment). The level of MAPK phosphorylation was evaluated with Western immunoblot assay. Fluvoxamine, a SSRI drug for depression currently used, was also examined and the results were compared with those of DAEE. A significant extension of the time in the open arm of the elevated plus maze test, or a significant shortening of the time of immobility in the tail suspension test was observed in both protective and therapeutic treatments with DAEE. Moreover, the stress-induced decrease in the level of MAPK phosphorylation of the hippocampus was ameliorated by the administration of DAEE. Two weeks were needed for fluvoxamine to elicit therapeutic effect, but the shorter time, for DAEE, and fluvoxamine did not show any activity to enhance the phosphorylation of MAPK. These results suggest that DAEE is a promising compound to have therapeutic effect on depression through activation of MAPK pathway, which is the action mechanism different from that of fluvoxamine.

O25-8 Localization of dihydropteridine reductase in the mouse brain and biochemical changes in dihydropteridine reductase-null mice

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Dihydropteridine reductase (DPR) is an enzyme catalyzing the recycling pathway of tetrahydrobiopterin (BH4). BH4 is an essential cofactor for the biosynthesis of monoamine neurotransmitters, such as dopamine, noradrenaline, and serotonin. BH4 is oxidized to BH4-4a-carbinolamine through the reaction with tyrosine hydroxylase or tryptophan hydroxylase, the rate-limiting enzymes for monoamine-synthesis. BH4-4a-carbinolamine is dehydrated to quinonoid-dihydrobiopterin by pterin-4a-carbinolamine dehydratase, and q-BH2 is reduced back to BH4 by DPR. BH4 can be synthesized de novo from guanosine triphosphate (GTP) through three enzymatic reactions. In the present study, we examined biochemical and immunohistochemical alterations in DPR-null mice to investigate physiological significance of DPR in the brain. First we immunohistochemically analyzed the distribution of DPR in the wild-type mouse brain with anti-DPR antibody. Unexpectedly, we found that anti-DPR immunoreactivity was mainly localized in oligodendrocytes. We could not detect apparent immunoreactive signals in the nuclei of monoaminergic neurons including substantia nigra and raphe nucleus. DPR-null mice were born according to the Mendelian law and grew up normally. Disappearance of the DPR protein was confirmed by Western blotting and immunohistochemistry. Immunoreactive signals in oligodendrocytes observed in wild-type mice disappeared in DPR-null mice. We examined biochemical alterations in the DPR mutant mice. There was no significant difference in the BH4 contents both in the brain and liver, probably due to increased synthesis of BH4 from the de novo pathway. Although BH4 contents in the brain were not decreased in DPR-null mice, we found that serotonin contents in DPR-null mice were decreased to 25% of wild-type. Dopamine and noradrenaline contents in the brain of DPR-null mice were 70% and 55% of wild-type, respectively. To our knowledge, this is the first report concerning DPR-null mouse. Our results suggest that deficiency of DPR affected differently to monoaminergic neurons and that serotonergic neurons were most vulnerable to deficiency of DPR.

O25-9 Involvement of neuronal primary cilia in psychiatric disorders

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Almost all vertebrate cells have an immotile primary cilium that singly extends like an antenna into the environment surrounding the cell and transduces sensory stimuli to the cell body. Adenylyl cyclase III and G protein-coupled receptors such as somatostatin receptor 3 and melanin-concentrating hormone receptor 1 have been revealed to be localized to CNS neuronal primary cilia, allowing antibodies raised to these ciliary transmembrane signaling molecules to label specifically neuronal cilia in the immunofluorescent staining of brain sections. In this study, a possible involvement of signaling via neuronal primary cilia in psychiatric disorders was investigated by characterizing the effects of psychotropic drugs and a hypomorphic mutation of the pericentrin gene on neuronal primary cilia in the mouse brain. Administration of some psychotropic drugs to mice altered the architecture of the neuronal cilia in several brain regions. The pericentrin mutant mice displayed a shortened time of immobility in the forced swimming test and the tail suspension test as well as disturbed localization of cilia-related components. These results suggest that cilia-dependent signaling may play a role in neurobiological mechanisms underlying psychiatric disorders.

O26-2 Pyrroloquinoline quinone enhances recovery of the locomotion activity after hemitransection of the spinal cord via attenuation of the mRNA expression of inducible nitric oxide synthase

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Pyrroloquinoline quinone (PQQ) is a naturally occurring redox cofactor that acts as an essential nutrient, antioxidant, and redox modulator. PQQ has been demonstrated to oxidize the redox modulatory site of NMDA receptors, and protect against NMDA- or glutamate-mediated cell injury in cultured neurons. Such agents are well known to be protective in experimental stroke models. Therefore, we examined the effect of PQQ on spinal cord injury in adult rats. PQQ was effective in promoting functional recovery after hemi-transected spinal cord injury and attenuated the expression of inducible nitric oxide (NO) synthase (iNOS) mRNA in the injured spinal cord region. NO is involved in the secondary detrimental mechanisms that aggravate the primary physical injury to the central nervous system (CNS) and implicated in NMDA receptor-mediated neurotoxicity. Seven days after hemi-transection injury, PQQ-treated animals had smaller lesions than vehicle-treated animals, suggesting that PQQ reduced secondary damage to the spinal cord, which is caused by NO, following the primary physical injury.

O26-4 FILIP knockout mice showed weak forearm strength and abnormalities in the visual cortex

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FILIP binds to Filamin A and enhances its degradation. While the decrease of Filamin A induced by the overexpression of FILIP in the embryonic brain resulted in the disturbance of the radial migration, *in vivo* function of FILIP remains elusive. In order to investigate *in vivo* function of FILIP, we made *FILIP* knockout mice. The major part of *FILIP* exon was replaced to the beta-Galactosidase cassette in the *FILIP* knockout mice. We observed the expression of the beta-Galactosidase expression in the brain, eyes and heart of the *FILIP* knockout mice at the embryonic day 11 at almost the same region that the expression of *FILIP* was observed by *in situ* hybridization. We carried out the behavior analyses. Weaker forearm strength and lower responses to the foot-shock were observed in the *FILIP* knockout mice compared to their normal littermates. As *FILIP* was expressed in the developing brain, we examined whether there exist abnormalities in the brain of the *FILIP* knockout mice or not. We examined how neuronal activities propagate in the visual cortices by stimulating the white matter where the thalamocortical inputs are contained. The decreased responses, in terms of the extent and strength, were recognized in the upper layers of the *FILIP* knockout mice compared to their littermates. We then studied the cortex of *FILIP* knockout mice by retrograde tracing method and found the abnormalities in the visual cortex of *FILIP* knockout mice.

O26-1 Pathogenic roles of MuSK antibodies in myasthenia gravis

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We have provided the evidence that active immunization with MuSK protein reproduces myasthenia gravis in animals. Next we focus on how MuSK antibodies cause MG. The pathogenic roles of MuSK antibodies in MG have been questioned as the number of AChRs is not reduced and complement is not deposited at the NMJ of biceps brachii muscles MuSK-positive patients with MG. The mechanisms of MG caused by AChR antibodies are well delineated, but the revealed mechanisms are not able to simply apply to MG with MuSK antibodies. MuSK antibodies have been identified as predominantly IgG4 subclass, which does not activate complement. We found that agrin-induced clustering of AChR was strongly blocked in the presence of MuSK antibodies, whereas absorption of the antibodies with purified MuSK products prevented this blocking effect. These results showed that the MuSK antibodies effectively inhibited the formation of agrin-induced AChR clustering. Intriguingly, the monovalent Fab fragments of MuSK antibodies from rabbits with EAMG also inhibited AChR clustering by agrin on C2C12 cells, indicating that complement-mediated mechanisms are not necessarily required for such inhibition. We then examined the reduced expression of AChR at NMJ in soleus muscles of paretic and normal rabbits by fluorescence microscopy. In addition, the structure of NMJ in our paretic rabbits, as well as the size and branching of the motor terminals, were significantly reduced. Electron microscopic observations of NMJ in rabbits with EAMG induced by injection of MuSK protein demonstrated a significant loss of complexity of convoluted synaptic folds but no destruction, and EAMG model cited here resembles the phenotype of humans with MG and MuSK antibodies. Our results showed that MuSK antibodies inhibit both anterograde and retrograde signals required for maintaining the synaptic structures in mature NMJ.

O26-3 Analysis of the demyelination rat (dmy) using two-dimensional electrophoresis

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The analysis of proteins in damaged myelin is crucial to clarify the mechanism of dys- and demyelination. One key approach for this strategy is a proteomic analysis of the myelin using two-dimensional electrophoresis (2-DE) methods. Previously, we reported that the combination of standard isoelectric-focusing 2-DE and 2-DE using cationic detergents is effective technique for the analysis of myelin proteins. In this study, we applied these 2-DE methods to analyze a demyelinating model mutant rat; demyelination rat (dmy). This unique recessive mutant exhibits severe demyelination in the CNS after 6 weeks of age. We isolated the cytosolic and membrane fractions from the spinal cord of 3, 4, and 7-week-old dmy mutant and wild type rats. In the comparison of the silver stained 2-DE gels among these fractions, eighteen spots were clearly detected differentially in the cytosolic fractions. There was no difference of the patterns of protein spots in the membrane fractions. Two of eighteen spots were identified as Aha1 (activator of HSP90 ATPase) and TDPOZ3 (a zinc finger protein) by mass spectrometry analysis. Aha1 was upregulated in 3-week-old dmy rat, which did not exhibit visibly pathological changes. This upregulation of Aha1 indicated that the signal transduction in the chaperon pathway might be activated in this age and be related to the early stage of the demyelination. On the other hand, the transcription factor TDPOZ3 was downregulated in 4 and 7-week-old dmy rat. This downregulation may be related to the severe demyelination. These results suggest that 2-DE technique is very effective to reveal the pathological changes including invisible changes in the demyelination.

O26-5 Maternal infection affects neurogenesis in the development of mouse cerebral cortex

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Maternal viral infections during pregnancy represent a risk factor in several neuropsychiatric disorders with a presumed neurodevelopmental origin, including schizophrenia, autism and mental retardation. Although mechanism of pathogenesis remained to be elucidated, abnormality in microstructures and connectivity of cerebral cortex are found and thought to be involved in the mechanism. Recently, it has been reported that the mice show behavior abnormalities related to autism (spatial exploration, social interaction, etc.), and schizophrenia (prepulse inhibition), when received prenatal infection induced by viral mimic polyriboinosinic-polyribocytidilic acid (Poly I:C), a synthetic analog of double strand RNA. The histological study revealed that atrophy was found in several brain areas including the cerebral cortex. However, it is poorly understood how prenatal immunochallenge affects the cortical organization. To address this issue, we intraperitoneally administered Poly I:C (20 mg/kg) into mice bearing 9-day-old embryos. The pups delivered normally were killed at postnatal 10 days and processed for histological analysis. We found that the cerebral cortex of the Poly I:C-treated animals was slightly thinner than that of vehicle-treated mice, and that the number of neurons composed of upper cortical layers and positive with Cux1 (orthologue of the *Drosophila* cut gene; layer II-IV) was decreased without changing the number of neurons of deeper layers that are positive with Tbr1 (T box brain1; layer III, V-IV), Ctbp2 (COUP-TF1 interacting protein; layer V), or Foxp2 (Forkhead box p2; layer IV). Therefore, it is suggested that the maternal immunochallenge induced by Poly I:C causes neuronal cell death in the upper cortical layers or suppresses neurogenesis for upper layer neurons. The decrease of cortical upper neurons would result in the cortico-cortical connections followed by behavior abnormality.

O26-6 Rodent orbitofrontal cortex separately encodes response and outcome information during performance of goal-directed behavior.

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The orbitofrontal cortex (OFC) has been implicated in behavioral guidance based on expected outcomes. OFC neurons were shown to encode the incentive value of expected outcomes. However, how the value of expected outcomes is used to guide behavior remains unknown. Here we recorded single units from rodent OFC during a four-odor discrimination task in which the encoding of expected outcomes could be isolated from the behavioral response in obtaining it. We found concurrent encoding of the behavioral response and the expected outcome in largely separate population of OFC neurons. Outcome encoding was maintained from the time of odor sampling until reward delivery. In contrast, response encoding, which was prominent after response initiation, was typically transient and closely synchronized to behavioral events in task performance. Thus rodent OFC encodes the expected outcome and the behavioral response in separate neuronal populations with distinct temporal profiles.

O27-2 Drinking hydrogenated water reduces dopaminergic neuronal loss in a mouse model of Parkinson's Disease

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It has been reported that molecular hydrogen (H₂) selectively reduces the hydroxyl radical, the most cytotoxic of reactive oxygen species (ROS), and can thereby effectively protect cells. Thus, inhalation of H₂ gas strongly suppressed ischemic and reperfusion brain injury by buffering the effects of oxidative stress. Oxidative stress damage to the brain is also induced in Parkinson's disease (PD). 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-treated mice have been widely used as an animal model of PD. MPTP is converted into MPP⁺ within nondopaminergic cells, such as glial cells and serotonergic neurons, and taken up into dopaminergic neurons via the dopamine transporter (DAT). Inside the neuron, MPP⁺ inhibits mitochondrial complex I, inducing neuronal apoptosis. We show here that H₂ in drinking water significantly reduced loss of dopaminergic neurons in PD model mice using both acute and chronic administration of MPTP. MPTP-induced production of super oxide (O₂⁻) detected by intravascular injection of hydroethidine, formation of nitrite/nitrate (NO₂/NO₃⁻) in midbrain, and accumulation of 8-oxoG in cellular DNA in striatum, were significantly decreased in mice drinking H₂-containing water. Thus drinking H₂-containing water may be useful in daily life to prevent or minimize acute and chronic oxidative stress.

O27-4 L-DOPA-specific induction of metallothionein in reactive astrocytes

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Dopamine quinone, which conjugates with cysteine residues of functional proteins to form quinoproteins, has been recently focused as dopamine neuron-specific oxidative stress in Parkinson's disease. Metallothioneins (MTs) are a family of low molecular weight, cysteine-rich (30% of the protein), ubiquitous, and inducible intracellular proteins that bind to heavy metals such as zinc, copper, and cadmium, participating in metal homeostasis and detoxification. In the previous report, we demonstrated the protective effects of MT against dopamine quinone neurotoxicity: MT quenched dopamine semiquinones generated in vitro and pretreatment with MT-inducer zinc ameliorated quinone formation and neurotoxicity induced by dopamine exposure in dopaminergic cells. Furthermore, MT exerted protective effects against the excess L-DOPA treatment-induced dopamine quinone neurotoxicity in parkinsonian model mice (Miyazaki et al., FEBS Lett, 581: 5003-8, 2007). Recently, extracellular MTs have been reported to play a role in the astrocyte-neuron response in the brain injury. In this study, we examined the effects of L-DOPA treatment on MT expression in the striatal astrocytes in hemiparkinsonian mice. Reactive astrocytes were accumulated in the parkinsonian side, not in the control side. Further marked activation of astrocytes was induced with the repeated L-DOPA treatment. MT expression was markedly elevated specifically in the reactive astrocytes in parkinsonian striatum after repeated L-DOPA administrations. On the other hand, L-DOPA-induced accumulation of reactive astrocytes was not observed in the parkinsonian side of MT-knockout mice. Taken together with the previously reported data, these results suggest that the activation of astrocytes and MT induction in the reactive astrocytes may play an important role to protect dopaminergic neuron by its quinone-quenching property through their pivotal interaction.

O27-1 Neuromelanin induces apoptosis through deglutathionylation of mitochondria

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The selective degeneration of dopamine neurons containing neuromelanin (NM) was observed in the substantia nigra in Parkinson disease (PD). This paper reports the induction of apoptosis by NM and the mechanism, using NM prepared from human substantia nigra and cultured dopaminergic SH-SY5Y cells. NM is composed of a mixture of black eumelanin and brown pheomelanin, protein, lipid and trace metals. To examine the involvement of NM components in the cytotoxicity, melanin was synthesized from dopamine in the absence (DAM) or presence of L-cysteine (cystenyldopamine melanin, Cys-DAM), as models of eum- or pheo-melanin. In addition, NM was treated protease K to remove the protein component (PK-NM). Among these melanin classes, only NM significantly induced apoptosis in the cells. Apoptosis was mediated by mitochondrial cascade: mitochondrial permeability transition, release of cytochrome c and activation of caspase 3. NM significantly increased sulfhydryl (SH) residues in mitochondria, whereas P-K did not and DAM reduced SH levels. NM-dependent reduction of SH residues was mediated by reactive oxygen and nitrogen species. In addition, NM was confirmed to contain free SH groups, which protease K treatment reduced to one fifth. In mitochondria, S-glutathionylated proteins were detected under control conditions, and some of them were identified as components of complex I and III. NM treatment markedly reduced glutathionylated protein and complex I proteins were dissociated into smaller units, as observed under non-reducing conditions. However, mild reduction of sample showed the reversibility of the NM-induced dissociation of higher structure of complex I. These results indicate that NM may induce cell death in dopamine neurons through perturbation of SH status in mitochondria and activation of apoptotic cascade. The cytotoxicity of NM depends absolutely on its protein component, and possibility to prevent the NM-dependent apoptosis with antioxidants is suggested.

O27-3 Effect of T-817MA, a novel neuroprotective agent, on MPTP-induced dopaminergic neurotoxicity in mice

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T-817MA (1-{3-[2-(1-benzothiophen-5-yl)ethoxy]propyl}azetidin-3-ol maleate) is a candidate therapeutic agents for treatment of Alzheimer's disease. Previous studies show that T-817MA inhibits oxidative stress and nitric oxide-induced neurotoxicity and it acts as a neurotrophic factor (Fukushima et al., 2006). On the other hand, we have recently shown that edaravone, a radical scavenger, prevents 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced dopaminergic neurotoxicity in the substantia nigra (SNc) and behavioral impairment similar to the features of Parkinson's disease (Kawasaki et al., 2007). These findings suggest that oxidative stress plays a key role in MPTP-induced dopaminergic neurotoxicity. Thus, the present study examines the effect of T-817MA on MPTP-induced model of Parkinson's disease. MPTP treatment (10 mg/kg × 4 with 2-h intervals) caused impairment of rotarod performance and the behavioral change was improved by T-817MA. MPTP treatment also decreased dopamine levels and tyrosine hydroxylase immunostaining in the SNc and striatum. Pretreatment with T-817MA (10 and 30 mg/kg as T-817) attenuated MPTP-induced decreases in dopamine levels and tyrosine hydroxylase immunoreactivity in the SNc and striatum, although it did not affect the levels of 1-methyl-4-phenylpyridinium ion, an active metabolite of MPTP in the brain. The protective effect was almost complete in the SNc, but partial in the striatum. MPTP increased lipid peroxidation product thiobarbituric acid reactive substance in the midbrain, but not the striatum. T-817MA blocked MPTP-induced increase in thiobarbituric acid reactive substance levels in the midbrain. An immunohistochemical study showed that MPTP caused microglial activation both in the SNc and striatum, but T-817MA did not affect the activation of microglia. These results suggest that T-817MA protects against MPTP-induced neurotoxicity by blocking lipid peroxidation in the SNc, and imply that this reagent may be useful for treatment of oxidative stress-related neurodegenerative disorders such as Parkinson's disease.

O27-5 identification of piccolo as a regulator of behavioral plasticity and dopamine transporter internalization

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Dopamine transporter (DAT) internalization is a mechanism underlying the decreased dopamine reuptake caused by addictive drugs like methamphetamine (METH). We found that Piccolo, a presynaptic scaffolding protein, was overexpressed in the nucleus accumbens (NAc) of the mice repeatedly administrated with METH. Piccolo downexpression by antisense technique augmented METH-induced behavioral sensitization, conditioned reward and synaptic dopamine accumulation in NAc. Expression of Piccolo C2A domain attenuated METH-induced inhibition of dopamine uptake in PC12 cells expressing human DAT. Consistent with this, it slowed down the accelerated DAT internalization induced by METH, thus maintaining the presentation of plasmalemmal DAT. In immunostaining and structural modeling Piccolo C2A domain displays an unusual feature of sequestering membranephosphatidylinositol 4,5-bisphosphate, which may underlie its role in modulating DAT internalization. Together, our results indicate that Piccolo upregulation induced by METH represents a homeostatic response in the NAc to excessive dopaminergic transmission. Piccolo C2A domain may act as a cytoskeletal regulator for plasmalemmal DAT internalization, which may underlie its contributions in behavioral plasticity.

O27-6 A novel molecule "shati" ameliorates the methamphetamine-induced decrease in dopamine uptake via tumor necrosis factor- α in PC12 cells

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The abuse of drugs has become a significant social and public health concern worldwide. The psychostimulatory properties of methamphetamine (METH), which is one of the most commonly abused drugs in Asia, are associated with an increase in extracellular dopamine (DA) levels in the brain, by facilitating the release of DA from presynaptic nerve terminals and inhibiting reuptake through the DA transporter. Recently, we have identified a novel molecule "shati" from the nucleus accumbens of mice treated with METH. Moreover, blockage of shati mRNA by shati-antisense oligonucleotide potentiates the METH-induced increase in extracellular DA levels and enhanced the METH-induced decrease in synaptosomal and vesicular DA uptake in the nucleus accumbens, resulting in potentiating the METH-induced hyperlocomotion, sensitization, and conditioned place preference. These results suggest that shati is involved in the development of METH-induced dependence. PC12 cells are useful as a model for neuronal system and have DA transporters. In the present study, we established a PC12 cell line which was transfected the vector containing shati cDNA to examine the effects of shati on DA uptake more clearly. Moreover, we examined the relationship among shati and tumor necrosis factor- α (TNF- α), which also increases DA uptake and inhibits the METH-induced dependence. We prepared antibodies against shati and confirmed that the PC12 cells transfected with the vector containing shati cDNA were immunopositive for these antibodies. Shati was expressed in TNF- α -immunopositive cells. Transfection of the vector containing shati cDNA, dramatically induced the expressions of shati mRNA, shati, TNF- α mRNA, and TNF- α , accelerated DA uptake and inhibited the METH-induced decrease in DA uptake. These results suggest that the functional roles of shati in METH-regulated behavioral alternations are mediated by its inhibitory effects via the induction of TNF- α expression on the METH-induced decrease in DA uptake. Targeting the shati-TNF- α system would provide new therapeutic approaches to the treatment of METH-induced dependence.

O28-2 Up-regulation of calyntenin-3 in an Alzheimer's disease mouse model.

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Beta-amyloid (A β) may play an important role in pathogenesis of Alzheimer's disease, but molecular mechanisms of A β actions, which are responsible for neurotoxicity, are not fully understood. We have previously identified calyntenin-3 as a A β -induced molecule. The calyntenin family, Cst-1, Cst-2 and Cst-3, is the postsynaptic membrane protein in excitatory synapses. Northern blot or QRT-PCR analyses revealed up-regulation of Cst-3, down-regulation of Cst-2 and no alteration of Cst-1 in A β 1-42 treated cortical neurons, indicating that A β differentially regulates calyntenin genes. In this study, we investigated whether Cst-3 protein up-regulates in neocortex from an Alzheimer's disease mouse model (PrP-APP^{sw}, Tg2576) by using immunoblotting and immunohistochemistry. The level of Cst-3 protein increased in neocortex from middle-aged PrP-APP^{sw} mice, which had numerous A β plaques. Previously we also found that overexpression of Cst-3 in cultured cortical neurons resulted in the acceleration of neuronal death. Cst-3 undergoes cleavage as does APP. Then to investigate whether transient overexpression or accumulation of Cst-3 in neurons is responsible for neuronal death, co-transfection experiments with myc-tagged Cst-3 and EYFP were carried out. Myc-immunoreactivity was disappeared in about 70 % of EYFP-labeled neurons 24 hours after transfection, indicating cleavage of Cst-3 in cortical neurons. Cortical neurons expressing myc-tag showed a significantly higher level of neuronal death than those of myc-negative neurons, suggesting that the accumulation of Cst-3 in neurons may be responsible for neuronal death.

O28-4 Mitochondrial dysfunction induced by MPP⁺ in mouse brain synaptosomes

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Mitochondrial dysfunction is the main biochemical feature of Parkinson's disease (PD). 1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) is a mitochondrial toxin that causes selective nigral dopaminergic lesions, resulting in PD in humans and primates. The neurotoxin has been widely used to generate animal model of PD. But the precise mechanism underlying 1-methyl-4-phenylpyridinium (MPP⁺), the toxic metabolite of MPTP, -induced dopaminergic neurodegeneration is not fully understood. As dopaminergic nerve terminals are a major target of MPP⁺, we tried to develop an *in vitro* model in which MPP⁺ is used to explore pathogenic role of the release of the apoptogenic molecule cytochrome *c* (cyt *c*) from the defective mitochondria in mouse brain synaptosomes. Mitochondrial oxidation-reduction (REDOX) activity as measured by Alamar blue fluorescence was inhibited by MPP⁺ in a dose-dependent manner in synaptosomes prepared from either frontal cortex or striatum. The selective dopamine uptake inhibitor, GBR-12909 partially attenuated the reduction of REDOX activity by MPP⁺ in synaptosomes. To evaluate whether MPP⁺-induced reduction of REDOX activity causes release of cyt *c*, we prepared mitochondria and cytosolic fractions from freeze-thawed synaptosomes. Cyt *c* was detected in the cytosolic fraction from MPP⁺-treated synaptosomes, but not from control synaptosomes. Our results indicate that MPP⁺-treated synaptosomes can be used as an *in vitro* model to study the mechanisms action of mitochondrial toxins and the evaluation of mitochondria-targeted agents which are expected to have neuroprotective effect.

O28-1 Distinct effect of Syntaxin5 isoforms on the processing of β APP

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Syntaxins (Syx) are involved in trafficking of various membrane proteins. Among them, mammalian Syx5 is unique since Syx5 has two isoforms (42 and 35 kDa) that are generated by the use of alternative initiator codons in Syx5 messenger RNA. The 42 kDa form of Syx5 (designated Syx5L) has extra N-terminal extension containing di-arginine ER-retrieval motif. We have previously shown that, Syx5 overexpression resulted in the accumulation of β -amyloid precursor protein (β APP) in the ER to cis-Golgi compartment, an attenuation of the amount of the C-terminal fragment (APP-CTF) of β APP, and a reduction in the secretion of β -amyloid peptide (A β peptide). In addition, Syx5 and Syx5L specifically interacted with presenilin (PS) holoproteins. In order to better understand the mechanism of Syx5 function underlying the processing and trafficking of PSs and β APP, we examined whether Syx5L have similar effect on the processing of β APP, and the secretion of A β peptides as in Syx5. We found that, in contrast to Syx5, marked accumulation of intracellular β APP holoproteins were not observed in Syx5L overexpressed cells. Concomitantly, overexpression of Syx5L did not result in the inhibition of A β peptide secretion. Syx5L deletion mutants, but not a mutant that lacked ER-retrieval motif, showed inhibitory activity on β APP processing. These results indicate that, Syx5 and Syx5L may have distinct function in modulating the metabolism and trafficking of β APP in the early secretory compartment. We discuss the molecular bases of these two isoforms for the modification of β APP processing.

O28-3 Identification and characterization of substrates for the mitochondrial protease Omi/HtrA2

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Omi/HtrA2 is a mitochondrial serine protease that is released into the cytosol during apoptosis and promotes cytochrome *c*-dependent caspase activation by neutralizing inhibitor of apoptosis proteins (IAPs) via its IAP-binding motif. The protease activity of Omi/HtrA2 also contributes to the progression of both apoptosis and caspase-independent cell death. Omi/HtrA2 is also reported to be a causative gene for Parkinson disease-13. In this study, we searched for substrates for Omi/HtrA2 using a small pool expression cloning strategy. We identified several proteins cleaved by recombinant Omi/HtrA2 protease and investigated the effect of these substrates on apoptosis. As a result, we identified an uncharacterized gene, AMOR, which showed significant anti-apoptotic activity when expressed in HeLa cells. AMOR protein was ubiquitously expressed in mouse tissues and was present in the nuclear and membrane fractions from HeLa cells. Gene silencing experiments confirmed that AMOR regulates the susceptibility to stress-mediated cytotoxicity. These results suggest that Omi/HtrA2 cleaves and inactivates several anti-apoptotic proteins, such as IAPs and AMOR, to induce apoptosis.

O28-5 Vulnerability to glutamate induced by tributyltin, an environmental-polluting chemical

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Tributyltin (TBT) has been widely used as antifouling paints. One feature of TBT is reported to be neurotoxic. Glutamate works as major neurotransmitter, but its excessive release causes neuronal death. In this study, we investigated acute and chronic glutamate-related neurotoxicity of TBT in cultured rat cortical neurons.

TBT (500 nM) for 24 h induced glutamate release and subsequent neuronal death. Though it is known that TBT decreases intracellular ATP levels, its downstream mechanism remains unknown. Therefore, we examined the involvement of AMP-activated protein kinase (AMPK) in TBT-induced cell death. AMPK is well-conserved heterotrimeric protein kinase that senses energy state. AMPK was activated by TBT, and compound C, an AMPK inhibitor, decreased glutamate release and cell death caused by TBT. These results suggest that TBT induces glutamate release and the following cell death via AMPK phosphorylation.

Next, cortical neurons were chronically exposed to 1-20 nM TBT for 9 days from DIV2 to DIV10. Neurons became susceptible to glutamate toxicity by chronic exposure of TBT. At this time, both mRNA and protein expression of GluR2 were decreased. Because AMPA receptor lacking GluR2 has calcium permeability, we measured intracellular calcium concentration by Fura-2. As a result, calcium influx by glutamate was increased in TBT-treated neurons. Thus, chronic exposure of low concentrations of TBT induced glutamate vulnerability probably due to GluR2 downregulation.

O28-6 Enhanced expression of glutathione S-transferase in the hippocampus of mice after trimethyltin treatment

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Trimethyltin chloride (TMT) is a kind of organotin derivatives that are known to induce behavioral changes and neuronal damage in human and rodent. In mice, this damage exclusively occurs in granule neurons of the dentate gyrus 2 days later. Our previous reports have demonstrated that TMT-induced neuronal damage is caused by activation of cell death signals induced at least in part by oxidative stress. However, the mechanisms underlying neuronal damage induced by TMT is not well understood. In this study, we evaluated if *in vivo* acute treatment with TMT induces the change in glutathione and glutathione-related enzymes in the hippocampus of mice. The level of total glutathione (GSH+GSSG) in the hippocampus was determined at various time points after the TMT treatment by a mean of glutathione reductase-5, 5-dithiobis-2-nitrobenzoate recycling method. A systemic injection of TMT produced a significant decrease in total glutathione level on days 1 to 7 after treatment. Next we examined activity of glutathione-S-transferase (GST) and glutathione peroxidase (GPx). TMT was effective in significantly increasing the activity of GST in the hippocampus, as well as in all regions of the brain, day 1 to 7 after treatment. However, the activity of GPx in the hippocampus was not affected at any time tested after TMT treatment. To examine the changes in the expression of glutathione-related enzymes, we carried out PCR using primers specific for the GST Ya/Yc and glutamate-cysteine ligase (GCL) and templates of mRNA prepared from the hippocampus at various time points after TMT treatment. TMT treatment led to elevated expression of GST Ya/Yc subunit mRNA in the hippocampus 24 h afterward. However, the expression of GCL mRNA was not significantly affected after TMT treatment. Taken together, our results suggest that an acute treatment with TMT produces enhanced expression of GST in the hippocampus. The enhancement of GST may cause oxidative stress through the reduction in glutathione in the hippocampus.

O29-2 mechanism for activated microglia-induced learning and memory deficits in cytokine knock out mouse.

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We have designed the animal model of learning and memory deficits with the activation of microglia. Lipopolysaccharide (LPS) when injected into the mouse hippocampus CA1 region resulted in the production of inflammatory cytokines such as IL-1 β and TNF α . Immunohistochemical analysis revealed that there was no IL-1 β but slight Iba1 immunoreactivity in the tissue sections from wild type mice treated with PBS. IL-1 β immunopositive cells were increased at 6hr after LPS injection and co-localized with immunostaining for Iba1. This phenomenon was also observed in TNF α KO mice and IL-6 KO mice. However, activation of microglia was not observed in LPS-treated IL-1 β KO mice. Subacute treatment of mice with LPS for 5 days induced learning and memory deficits when examined by a step-through passive avoidance test. Gene expression of NMDA receptor NR1 and NR2 subunit was also decreased by LPS treatment. In case of IL-1 β KO mice received subacute treatment with LPS, learning and memory deficits were not observed. Moreover, there was no change in gene expression of NR1 and NR2 subunit in these mice. On the other hand, we observed learning and memory deficits and decreased gene expression in TNF α KO mice. These results suggest that the expression of IL-1 plays an important role in the activation of microglia, thus leading to learning and memory deficits.

O29-4 Impairment of cognitive function via down-regulation of calcium/calmodulin-dependent protein kinase II in Na⁺/Ca²⁺ exchanger (NCX2) knock-out mice

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Na⁺/Ca²⁺ exchanger (NCX) is mainly expressed in the plasma membrane and mediates electrogenic of exchange one Ca²⁺ for three Na⁺, depending on the electrochemical gradients across the plasma membrane. NCX has three different isoforms (NCX1, NCX2, NCX3) encoded by distinct genes in mammals. We here report that mutant mice lacking neural NCX2 (NCX2-KO) exhibit impaired memory. NCX2-KO mice showed significantly impairment of learning and memory-related behaviors measured by Y-maze, novel object recognition and passive avoidance tasks. NCX2-KO mice were significantly impaired long-term potentiation (LTP) in hippocampal CA1 region. In immunoblot analysis, autophosphorylation of calcium/calmodulin-dependent protein kinase II (CaMKII) significantly decreased in the hippocampal CA1 region of NCX2-KO mice compared to wild mice. Enhancement of CaMKII autophosphorylation following LTP was also impaired in NCX2-KO mice. Furthermore, the impairment of CaMKII autophosphorylation was closely associated with reduced pGluR1 (Ser-831) phosphorylation, without change in synapsin I (site3) phosphorylation in the hippocampal CA1 region of NCX2-KO mice. Taken together, decreased CaMKII activity with concomitant LTP impairment accounts for the learning disability observed in NCX2-KO mice.

O29-1 Effects of sominone on memory enhancement and the molecular mechanism underlying these effects

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We previously showed that orally administered withanone IV (WS4; an compound isolated from the roots of *Withania somnifera*) improved memory deficits in A β (25-35)-induced Alzheimer's disease model mice as well as hind limb movement in spinal cord injury mice. Axons, dendrites, synapses and myelination were restored by WS4 in those models. Sominone, an aglycone of WS4, was further identified as the metabolite after oral administration of WS4, and was found to be an active component.

In the present study, we investigated the effects of sominone on memory improvement and the signal cascades of sominone in neurons. After single intraperitoneal injection of sominone (10 μ mol/kg) into normal mice (male ddY mice, 6 weeks old), an object recognition test and an object location test were carried out. Each test session was performed 24 hours after a training session. Mice given sominone were better able to distinguish a novel object and memorize scenery information compared with those abilities in control mice. To identify receptors or associated molecules of sominone, phosphorylation levels of 71 molecules were compared between control and sominone-stimulated (1 μ M, 60 min) cortical cultured cells. Phosphorylation of RET (receptor for GDNF) was increased in neurons and microglia 15 min after treatment with sominone (1 μ M). However, expression levels of RET and GFR α (GDNF family receptor) were not changed by sominone stimulation. In cortical cultured cells, only very small numbers (less than 0.02%) of macrophages expressed GDNF. Although administration of sominone (1 μ M) elicited significant outgrowths of axons and dendrites in cortical neurons, GDNF (1 and 100 ng/ml) showed lower effects on the extensions. When RET was knocked down in cortical cells using siRNAs, the level of phosphorylated RET was decreased and dendrite extension by sominone was cancelled. Phosphorylation of ACK1 (activated Cdc-42-associated tyrosine kinase) was also increased in cortical neurons 15 min after treatment with sominone (1 μ M). Knock-down of ACK1 by siRNAs also cancelled the sominone (1 μ M)-induced dendrite extension. In conclusion, sominone potentially improves memory, and the molecular mechanism of sominone may be mediated by phosphorylation of at least RET and ACK1.

O29-3 The extensive nitration of neurofilament light chain in the hippocampus contributes to the cognitive impairment in A β -treated mice

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Tyrosine nitration of proteins at an extensive level is widely associated with cognitive pathology induced by Amyloid beta (A β). The precise identity and the explicit consequences of the protein nitration, however, have scarcely been addressed. In this study, we examined the detectable nitration of proteins in the hippocampus of mice with cognitive impairment (Day 5) induced by the *i.c.v.*-injection of A β ₂₅₋₃₅ (Day 0). The intensity of nitration of proteins was inversely associated with the level of recognition memory in mice. The detectable tyrosine nitrations were revealed in proteins with a single size of approximately 70 kDa. The specific nitrated proteins at this size were identified utilizing the liquid chromatography / mass spectrometry / mass spectrometry analysis and immunodetection methods. Neurofilament light chain (NFL) was found intensely nitrated. Increased nitration of NFL was associated with its serine hyperphosphorylation and weak interaction with the nuclear distribution element-like (NUDEL), an essential protein for the stable assembly of neurofilaments. No changes in cell numbers in the hippocampus were found (Day 5) in A β ₂₅₋₃₅-injected mice. These findings suggested that extensive nitration of NFL contributes to the A β -induced impairment of recognition memory in mice.

O29-5 Time-limited involvement of the medial prefrontal cortex in extinction of contextual fear memory

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The conditioned response formed by contextual fear conditioning in mice is attenuated when the mice are repetitively exposed to the context, a phenomenon known as extinction. Previous findings established that the medial prefrontal cortex (mPFC) plays an essential role in the extinction of recently formed fear memory. However, the involvement of the mPFC in extinction of remote fear memory has not been assessed. Because longitudinal studies of trauma victims indicate the case of delayed-onset post-traumatic stress disorder (PTSD), and because extinction is thought to be a process underlying cognitive behavioral therapy for anxiety-related disorders such as PTSD, studies that focus on extinction of remote fear memory are significant. Here, we report that the mPFC is not involved in extinction of remote contextual fear memory in mice. Extinction of remote contextual fear memory, acquired 21 days before extinction training, was insensitive to 4-[2-(phenylsulfonylamino)ethylthio]-2,6-difluorophenoxyacetamide (PEPA), a drug that facilitates the extinction of recent fear memory by acting mainly on the mPFC, or to focal inactivation of mPFC with lidocaine. The lidocaine insensitivity was observed in both acquisition/consolidation and retrieval of extinction memory for remote fear. In agreement with previous reports, extinction of recent contextual fear memory, acquired one day before extinction training, was sensitive to PEPA and to focal inactivation of mPFC with lidocaine. D-cycloserine, a drug that is thought to facilitate extinction learning by acting on the amygdala, facilitates extinction of both recent and remote fear memory, suggesting that the amygdala is involved in extinction of both memory types. These results suggest that, in mice, brain regions that are involved in extinction of recent and remote fear memory overlap but are not identical. Time-limited role of the hippocampus in retrieval of contextual fear memory may participate in the above-mentioned time-limited involvement of the mPFC in extinction of the fear memory. Understanding the effective time window for extinction-facilitating drugs is necessary for their successful clinical application.

P029-6 A genetic variation of the KIBRA gene is associated with memory performance in Japanese healthy subjects

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The association between a genetic variation of the KIBRA gene, a single nucleotide polymorphism (SNP: rs17070145), and human memory performance has been initially reported in healthy subjects in Caucasian population. Since then, two replication studies supported the association with the memory performance in healthy elderly and elderly including mild cognitive impairment (MCI). However, one study did not replicate the association in healthy subjects. Another study found the association in different way in subjective memory complaints. As the previous studies are examined in Caucasian populations, we attempted to replicate the association between the SNP in the KIBRA gene and memory performance using the Wechsler Memory Scale-Revised (WMS-R) in 118 healthy subjects in a Japanese population. Genotype distribution of the SNP was in Hardy Weinberg equilibrium (CC: 6, CT: 32, TT: 80). Delayed recall of the WMS-R in CC subjects was significantly lower than that in T allele carriers consistent to the initial study. However, there was no significant difference in the other WMS-R indices (verbal memory, visual memory or attention) between the two groups. As the CC genotype frequency of the SNP is very low in Japanese (allele frequency in Japanese: 18.6%, in Caucasian: 74.5%), we next compared the scores of delayed recall in C allele carriers to those in TT subjects and found lower memory performance in C allele carriers than that in TT subjects. We found that the frequency of the C allele of the KIBRA gene was significantly lower than that in the Caucasians. However, the current study reveals that the SNP of the KIBRA gene had a similar effect on the human memory performance in an Asian population.

P-02 Metabolic characteristics of microglia

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To elucidate the metabolic characteristics of microglia, primary cultures of astrocytes, neurons and microglia were incubated with [1, 6-¹³C] glucose (Glc) or [3-¹³C] lactate (Lact) for 24 hours. ¹³C-NMR spectroscopy was performed on acid extracts of three types of cells or on mediums collected from the cultures. When all types of cells were incubated with [1, 6-¹³C] Glc, spectra of acid extracts of neurons revealed that ¹³C was incorporated into aspartate (Asp), glutamate (Glu), Lact and alanine, and those of astrocytes revealed that ¹³C was dominantly incorporated into Gln and Lact, however those of microglia showed only a peak of ¹³C-Glc. When three types of cells were incubated with [3-¹³C] Lact, spectra of acid extracts of neurons revealed that ¹³C was incorporated into Glu, Gln and Asp, and those of astrocytes showed a high labeling of Gln and an uptake of large amount of Lact, however those of microglia showed no significant peak of ¹³C. These results suggest that the metabolic characteristics of microglia differ from those of neurons and also those of astrocytes.

P-04 Establishment of GFAP/Cre-reporter mouse system to analyze glial cell sub-lineages in the developing central nervous system

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Astrocytes, the major glial cell type in the central nervous system, exhibit various functions to support neural activities: maintenance of local homeostasis, delivery of nutrition to neurons, and recycling of neurotransmitters. In addition to these classical roles, recent studies have suggested that astrocytes can integrate synaptic activity by releasing gliotransmitters, such as ATP and glutamate. When and how astrocytes are specified to have such diverged functions is poorly understood. Since the different neuroepithelial domains defined by the combinatorial expressions of transcription factors give rise to different classes of neuronal cell types during neurogenesis, we hypothesize that the neuroepithelial domains may be also correlated with astrocyte diversification during gliogenesis. To challenge this question, we established gene-targeted mouse lines that carry the Cre/loxP-reporter (loxP-nlacZ-loxP-GAP43GFP) construct knocked-in glial fibrillary acidic protein (GFAP) gene locus. As a first step to examine the recombination efficiency of Cre/loxP system, GFAP/Cre-reporter mouse lines were crossbred with Emx1-Cre K1 delta-neo mice (provided by Drs. Iwasato and Itohara; Genesis, 38, 130-138, 2004). Emx1-positive pallial progenitors generated cortical astrocytes that were GFP-positive and beta-galactosidase-negative, while Emx1-negative subpallial progenitors generated beta-galactosidase-positive astrocytes, confirming the efficient Cre/loxP recombination.

P-01 Activation of phospholipase Cgamma and HDL generation through interaction between apoA-I and ABCA1

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The ABCA1 prepared from membrane fraction of rat astrocytes was associated with the apoA-I-immobilized Affi-Gel 15. ApoA-I was also bound to the ABCA1 immuno-isolated by anti-ABCA1 antibody-bound protein G-Sepharose. Not only both the cellular ABCA1 level and association of apoA-I with ABCA1 but also the apoA-I-mediated lipid release were enhanced by a LXR agonist, T0901317, in rat astrocytoma GA-1/Mock cells which have a lowered expression level of ABCA1, suggesting that apoA-I-mediated cholesterol release is sufficiently dependent on the interaction between apoA-I and ABCA1 of astrocytes in the central nervous system like peripheral cells. Phospholipase Cgamma (PL-Cgamma) was co-isolated by apoA-I-immobilized Affi-Gel 15 and co-immunoprecipitated by anti-ABCA1 antibody along with ABCA1 from the solubilized membrane fraction of rat astrocytes. The SiRNA of ABCA1 suppressed the tyrosine phosphorylation of PL-Cg. A PL-Cgamma inhibitor, U73122, prevented apoA-I-mediated HDL generation of rat astrocytes. These findings show that the HDL generation of astrocytes is enhanced by apoA-I through the binding of apoA-I to ABCA1 and then the tyrosine phosphorylation and activation of ABCA1-associated PL-Cgamma.

P-03 Spinal cord injury induces expression of PRMT8 in microglia/macrophages in mouse

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Arginine methylation is a common post-translational modification that is mediated by the protein arginine methyltransferases (PRMTs). One of the family members, PRMT8, shows a close homology with PRMT1 that was first discovered as PRMT and is expressed specifically in the CNS, ranging from the brain to the spinal cord. We raised an antiserum against the peptide sequence that can discriminate PRMT8 from PRMT1. By immunohistochemistry, the expression pattern of PRMT8 is neuron-specific, suggesting that it is involved in some brain functions. However, the biological function of PRMT8 has not been elucidated. When we immunostained the sections of experimentally injured spinal cord, a subpopulation of the immunopositive cells that appeared around the injured region were cosained with anti-CD11b antibody, a marker for microglia and/or invading peripheral macrophages. Activated microglia were showed in lesion site 1 day after spinal cord injury (SCI), increased at 7d after SCI. PRMT8 expression in microglia were increased at 7d after SCI, but not showed at 1d after SCI. These data suggested that PRMT8 were expressed in a subset of activated microglia, but not initiated microglial activation.

P-05 The increase of newborn glial cells in the hypothalamus might be related body weight gain

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Unwanted weight gain is frequently observed in schizophrenic patients who continuously take atypical antipsychotic drugs such as olanzapine. It was six weeks after the onset of olanzapine-treatment until the body weight of olanzapine-treated mice became significantly heavier than that of control mice and that the number of BrdU-positive cells, which co-express glial cell marker, in the hypothalamus was greater in olanzapine-treated mice than in control mice. Given these results, we hypothesized that the newborn glial cells in the hypothalamus could be involved in controlling body weight. To test this hypothesis, we infused the anti-mitotic agent Cytosine-beta-D-arabinofuranoside (Ara-C) into the lateral ventricle of olanzapine-treated mice and controls from 4th week to 6th week after the onset of olanzapine-treatment with the view to reduce possible effects of olanzapine-induced glial cell proliferation in the hypothalamus. Although the olanzapine-induced weight gain was not inhibited by Ara-C administration for 2 weeks, the body weight and BrdU-positive cells in the hypothalamus was increased 2 weeks after cessation of Ara-C administration. This result might imply that the proliferating state of glial cells in the hypothalamus has some effects on body weight control.

P-06 Effect of lipopolysaccharide on the life-span of primary-cultured microglia

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Microglia play many important roles in the physiology and pathophysiology of the CNS. Although activated microglia have been implicated in the recognition and phagocytic removal of degenerating neurons, such activation should be tightly regulated, since prolonged activation could damage normal neurons. Based on our data we report that mouse primary-cultured microglia, which are destined to die within a few days under ordinary culture conditions, are able to live for more than 1 month when kept activated by lipopolysaccharide (LPS) treatment. Primary-cultured microglia treated with sub-lethal doses of LPS remained viable without any measurable increase in apoptotic or necrotic cell death. LPS-treated microglia living more than 1 month showed a ramified shape with enlarged somas and thickened cell bodies. Although the amount of intracellular ATP in these microglia was reduced by 2 h after the start of LPS treatment, this reduction had no effect on the viability of the cells. LPS treatment of microglia stimulated the transcription of the antiapoptotic factor Bcl-xL at 8 h and enhanced its protein level at 1 day. Although the treatment also increased the mRNA expression level of proapoptotic factor BAX, the level of BAX protein was not affected at all. Furthermore, microtubule-associated light chain 3, a marker protein of autophagy, decreased at 3 h after the exposure to LPS. These data indicate that the optimal dose of LPS can suppress the induction of both apoptosis and autophagy in primary-cultured microglia, allowing them to stay alive for more than 1 month. Since long-lived microglia may play critical roles in the exacerbation of neurodegeneration, the present findings suggest that bringing the active microglia into a resting stage would be a new and promising strategy to inhibit the exacerbation in neurodegenerative disease.

P-08 Development and functional analysis of a novel *in vitro* blood-brain barrier model

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Blood-brain barrier (BBB) is a physical barrier formed by tight junctions (TJs) between brain microvessel endothelial cells (BMEC), and serves to maintain the homeostasis of the brain microenvironment. In addition, it has been demonstrated that direct and indirect crosstalk between BMEC and other CNS cells, such as astrocytes and neurons, is important for maintaining the integrity of BBB. However, the cellular and molecular mechanisms underlying such a crosstalk are still unclear. To assess this issue, we first attempted to develop a novel *in vitro* BBB model composed of rat BMEC and astroglia-neuronal co-culture. BMEC culture and astroglia-neuronal co-culture were separately prepared from the cerebral cortex of 4-week-old rats and fetal rats (17-19 days of gestation), respectively. Dissociated mixed neural cells were seeded on the underside of Transwell filter (Costar Corning Inc.) to make astroglia-neuronal co-culture. After 15 days of cultivation, BMECs were harvested and seeded on the upper side of Transwell filter to make a BBB model. The barrier function was evaluated by transendothelial electrical resistance (TEER) and permeability of FITC-dextran (m.w. 4,000). This BBB model showed significantly higher TEER values and lower permeability than BBB models composed of BMEC and astrocyte cultures or BMEC alone. NMDA treatment, which causes severe neuronal injury, decreased TEER and increased permeability of FITC-dextran (m.w. 40,000) at 48 and 72 h after NMDA treatment. Immunoblot and immunohistochemical analyses revealed that these functional changes were accompanied by alterations in the subcellular localization of TJ proteins, such as occludin, claudin-5 and ZO-1. These results suggest that this BBB model could be useful to investigate the molecular and cellular mechanisms for neuro-glio-vascular interaction under various physiological and pathological conditions.

P-10 Nuclear GAPDH activates PARP-1 in oxidative stress-induced neuronal cell death

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Nuclear glyceraldehydes-3-phosphate dehydrogenase (GAPDH) is involved in neuronal cell death triggered by oxidative stress. However oxidized GAPDH augments interaction of Siah1, an E3-ubiquitin ligase, and leads to its nuclear translocation, molecular mechanisms following the nuclear translocation are not clarified. In the present study, we found that nuclear GAPDH interacts with a nuclear enzyme poly(ADP-ribose) polymerase-1 (PARP-1) and augments the enzymatic activity during oxidative stress-induced neuronal cell death. To search some molecules specifically interacting with GAPDH by oxidative stresses, we prepared Tet-inducible (Tet-On), GAPDH-overexpressing SH-SH5Y neuroblastoma cells. Proteomic analysis (TOF-MS/MS) revealed PARP-1 as a GAPDH-interactor. Thus, we checked these interactions by both co-immunoprecipitation and immunohistochemical analyses. Finally we assessed that the substantial interaction of nuclear GAPDH with PARP-1 augments the PARP-1 activity both *in vitro* and *in vivo*. These data suggest that oxidative stress-induced GAPDH nuclear translocation mediates neuronal cell death via PARP-1 activation.

P-07 Involvement of endogenous advanced glycation end-products in the development of Alzheimer's disease

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Advanced glycation end-products (AGEs) are protein adducts produced from glucose and aldehydes through a non-enzymatic reaction, and known to be increased under hyperglycemic condition. It has been reported that diabetic patients have high incidence of Alzheimer's disease (AD), showing a decrease in amyloid beta peptide 42 (Aβ42) levels and an increase in tau protein in cerebrospinal fluid. To investigate whether endogenous AGEs are associated with the onset of AD, SH-SY5Y neuroblastoma cells were exposed to various concentrations (0-1mM) of glyceraldehyde, a constituent of AGEs, for 24h. Aβ42 and total tau levels in the culture medium were measured by enzyme linked immunosorbent assay (ELISA). AGE concentrations were also examined. By the addition of glyceraldehyde, concentrations of Aβ42 in the culture medium were significantly decreased, whereas total tau protein secretion was significantly increased. These results suggest that, in the presence of glyceraldehydes, neuroblastoma cells showed AD-like characteristics, indicating the involvement of glyceraldehyde-derived AGEs in neurodegenerative pathophysiology.

P-09 Microglia prevent oxidative stress-induced neuronal cell death by suppressing transferrin-independent iron uptake.

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To understand mechanism of altered iron metabolism in brain cells in aceruloplasminemia, using neuron-microglia (MG-N) co-cultures treated with iron, we examined how MG protect neurons from oxidative stress. When each solely purified cell was treated with non-transferrin (Tf) iron, cell death occurred in N and MG. MG take up more iron but more resistant to iron stress than N. However, when co-cultured with MG, N were remarkably resistant to the oxidative stresses. In this way, we hoped to reproduce *in vitro* the iron deposition in MG observed in aceruloplasminemia. To examine how N/MG co-cultures suppress Tf-independent iron uptake, we focused on the relationship between iron metabolism and neuronal cell death. Heme oxygenase 1 (HO1), a microsomal heme-degrading enzyme involved in iron metabolism prevents cell death by regulating cellular iron metabolism. The Nramp1, Divalent metal transporter 1 (DMT1, an isoform of Nramp 1) and other DMTs are expressed on neurons as well as MG. The analysis of gene expressions of HO1 and DMTs in co-cultures using DNA microarray are in progress.

P-11 Analysis of differential gene expression in inflamed skin of neuropsin-deficient mice

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Neuropsin / kallikrein 8 is a trypsin-type serine protease that strongly induced in inflamed skin. It is shown that neuropsin is involved in recovery of skin by promoting epithelial desquamation and proliferation. To clarify the mechanism of wound healing in which neuropsin took part, we compared the gene expression profiles of inflamed skin treated with sodium dodecyl sulfate between wild-type and neuropsin-deficient mice. As a result, the difference was seen in the expression of the transcription factor which controls proliferation and differentiation of epidermal keratinocyte. It is suggested that neuropsin controls the transcription factor, and widely influences the formation of the epidermis.

P-12 Expression of gpnmb, a tumor metastasis-associated glycoprotein, in the rat central nervous system

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The glycoprotein nmb (gpnmb), also referred to as osteoactivin in rats, is a type-I transmembrane protein that contains several motifs common to melanosomal proteins. Since the initial identification in human non-metastatic malignant melanoma cells, gpnmb has been known to be expressed in tumor cells including melanoma and glioma. However, physiological neural function(s) of gpnmb remain to be unknown. In this study, we examined whether or not gpnmb was expressed in the normal central nervous system of rats. Reverse transcription-polymerase chain reaction analysis revealed that mRNA for gpnmb is present in the cerebrum, cerebellum, and brain stem of normal adult rats. We next raised antibodies against rat gpnmb by immunizing rabbits with the carboxy-terminal portion of the protein. Immunoblot analysis using the resulting antibodies detected a major band of ~60 kD in COS-7 cells transfected with gpnmb cDNA; but not at all in mock-transfected and untransfected COS-7 cells. The antibodies also recognized a major band of ~100 kD in C6 glioma cells. In immunofluorescent staining, immunoreactivity (IR) for gpnmb was localized to large lysosome-like vesicular structures in the cDNA-transfected COS-7 cells, but not in mock-transfected and untransfected cells. Immunoperoxidase staining of adult brain revealed that gpnmb-IR was prominent in ependymal cells surrounding the third and fourth ventricles. Weak gpnmb-IR was also observed in cells adjacent to cerebellar Purkinje cells. In neonatal rats, gpnmb-IR was intensely observed in cells with large nuclei in the cerebral and cerebellar cortex. These results suggest that gpnmb plays important roles in ependyma, choroid plexus, and developing cerebral and cerebellar cortex.

P-14 Effects of the chronic social defeat on behavior and gene expression in the brain

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Chronic social stress has been one of the major problems in human society. Recently, a lot of social stress related studies have been carried out. The animal models have been used in the investigation of stress effect. In humans, chronic stress events may be repeated in a day and for a long period. But it is difficult to develop an animal model for appropriate situations in human stressful life. Human chronic stress may cause the different reaction that has been reported. In this study, we developed an animal model for chronic social stress, using EI mice, which deteriorate memory and cognitive abilities, for the aggressor, and we exposed a social defeat stress in a long time and period. This chronic stress for tested ICR mice was 1 hour daily exposure to the highly aggressive EI mice. In order to continue the aggression of EI mice and administer a constant stress to each test mouse, the aggressor mice had attacked different mice daily for 1 week or 4 weeks. We tested behavioral analysis (Tail suspension test; TST and Contextual fear condition; CFC) for one day after each stress. We collected hippocampus for two days after behavioral analysis, and analysis for alteration in gene expression (GR and BDNF). Compared to control mice, chronically stressed (4 weeks stressed) mice showed up-regulation of glucocorticoid receptor (GR) mRNA and brain-derived neurotrophic factor (BDNF) related mRNA in hippocampus ($P < 0.05$). And also they showed acquisition of fear memory, anxiety-related behavior (CFC and TST, $P < 0.05$). Our results suggest that chronic social stress may induce posttraumatic stress disorder associated with anxiety. Now the mechanism and treatment of PTSD are still developing, thus our results may be a key to solve these problems.

P-16 Manipulation of caloric content but not diet composition, attenuates the deficit in learning and memory of senescence-accelerated mouse strain P8

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Calorie restriction (CR) is an experimental intervention in laboratory animals that attenuates age-associated increases in morbidity, mortality, and functional impairment. It is characterized by mild ketosis, hypoinsulinemia and hypoglycemia. In this study, we examined whether metabolic simulation of CR by a diet of isocaloric ketogenic or hypoinsulinemic diets ameliorated the learning and memory deficit in a strain of senescence-accelerated prone mice (SAMP8), a mouse model of age-dependent impairments in learning and memory. Male SAMP8 mice were fed high carbohydrate (CHO), high fat (FAT), or high protein (PRO) diets after weaning, and caloric intake was adjusted to 95% (sub ad libitum, sAL) or 70% (CR) of the mean caloric intake of control mice. At 28 weeks of age, we found CR ameliorated the performance deficits of SAMP8 mice in a passive avoidance task. Neither FAT nor PRO diets affected performance of the task when fed sAL level, although a diet of these compositions partially mimicked the serum parameters of CR mice. These results suggest restriction of caloric intake is important for the prevention of learning and memory deficits, and that the simulation of serum changes induced by CR is not sufficient to prevent the cognitive deficits of SAMP8 mice.

P-13 Expression of HSP70 in zebrafish retina after optic nerve injury

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Heat shock proteins (HSPs) play an important role for cell protection by various environmental stresses, such as heat, heavy metals, and reactive oxygen. Following stresses, HSPs are rapidly induced to function cell survival and maintenance. HSP gene are highly conservative throughout E.coli to humans. Fish CNS neurons can survive and regenerate their axons after nerve lesion. Study of fish optic nerve regeneration is the best model for CNS repair after injury. Although many factors are involved in the fish optic nerve regeneration process, there is no report describing HSPs in the fish retina during nerve regeneration. In the present study, we compared the expression of HSPs after nerve injury and heat shock condition. In normal adult zebrafish retina, HSP70 mRNA was hardly expressed. After 37 °C heat shock for 30 min, HSP70 mRNA drastically increased in zebrafish retina at 30-60 min, and then returned to control value by 180 min. This increased expression of HSP70 mRNA was detected in all retinal layers. In contrast, the level of HSP70 mRNA after nerve injury was rapidly elevated in zebrafish retina at 30 min and the elevation continued for 24 hours and then return to the control value at 3 days. The increased expression of HSP70 mRNA was limited only to the ganglion cell layer. HSP was transactivated by heat shock factors (HSFs). HSFs normally exist in cytoplasm, and it is translocated to nucleus under stress. After heating, the levels of HSF1 and HSF2 mRNA were not changed. Whereas, HSF1 and HSF2 mRNAs were significantly increased in zebrafish retina 30 min to 24 hours after optic nerve lesion. These results indicate that activation of the transient increase (30-60 min) of HSP mRNA, induced by heat shock, is ascribed to only translocation of HSF, whereas the continuous increase (30 min to 24 hours) of HSP, induced by optic nerve injury, is ascribed to both activation of translocation and transcription of HSF.

P-15 Biochemical and histological analyses of MAGI-1 in rat brain

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The membrane-associated guanylate kinase with inverted organization (MAGI) proteins consist of three members, MAGI-1, MAGI-2/S-SCAM and MAGI-3. MAGI proteins belong to a subfamily of protein known as membrane-associated guanylate kinases (MAGUKs) and usually harbor six PSD-95/Discs large/ZO-1 (PDZ), a guanylate kinase and two WW domains. MAGI-2/S-SCAM is a synaptic protein and the molecular feature of this protein in neuronal tissue is well characterized. In contrast, the function of MAGI-1 in neuronal tissues is yet obscure. In this study, we performed biochemical and histological analyses of MAGI-1 in rat brain. We firstly raised the antibody against full length MAGI-1 and performed affinity purification from the antiserum (anti-MAGI-1-FL). This antibody recognized all three MAGI family proteins transiently expressed in HEK293 cells. We next performed the affinity purification from the antiserum against GST-MAGI-1 (194-295) and found that anti-MAGI-1 (194-295) selectively recognized MAGI-1. We tried to determine the tissue distribution in rat by western blot analysis and found that MAGI-1 was enriched in brain and muscle tissues. When the expression pattern of MAGI-1 in twelve brain regions was analyzed, we found that this protein was enriched in cerebellum and olfactory bulb. Immunohistochemistry of rat cerebellum showed the localization of MAGI-1 in Purkinje cells. To further analyze the function of MAGI-1 in neuronal tissues, we are now trying to identify the binding partner for MAGI-1 using yeast two-hybrid screening.

P-17 Partial agonistic effects for serotonin 1A receptors of yokukansan, a traditional Japanese medicine

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Recently, the improving effect of yokukansan, a traditional Japanese medicine, on behavioral and psychological symptoms of dementia (BPSD) in patients with dementia has been reported. There are many evidences that serotonergic system may contribute to BPSD. In fact, we demonstrated that yokukansan improved p-chloroamphetamine (serotonergic neurotoxin)-induced aggression as well as a serotonin (5-HT)_{1A} agonist or 2A antagonist did. These results suggest the possibility that yokukansan has an agonistic effect for 5-HT_{1A} receptors or an antagonistic effect for 5-HT_{2A} receptors. In the present study, in order to clarify the hypothesis, the effects of yokukansan and its seven constituent herbs on 5-HT receptors were evaluated using membranes of CHO cells which expressed the 1A or 2A receptors. Specific binding of these substances to the receptors were measured by a competitive binding assay using [³H]-OH-DPAT for 5-HT_{1A} or [³H] ketanserin for 5-HT_{2A} receptors. 5-HT_{1A} receptor agonist/antagonist activity of the substances was evaluated by [³S]GTPγS binding assay using the CHO cells membrane.

Yokukansan (6.25-400 μg/ml) and *Uncaria Hook* (3.125-200 μg/ml), one of constituent herbs, inhibited [³H]-OH-DPAT binding to 5-HT_{1A} receptors, in a concentration-dependent manner, suggesting that these substances bound to 5-HT_{1A} receptors. The [³S]GTPγS binding to the 5-HT_{1A} receptors was increased by yokukansan or *Uncaria Hook*. However, the binding rates of [³S]GTPγS of both substances were approximately 50% of that of a full agonist, 5-HT (300 nM), suggesting that yokukansan and *Uncaria Hook* are partial agonists for 5-HT_{1A} receptors. In the experiments using yokukansan without *Uncaria Hook*, inhibition of [³H]-OH-DPAT binding or increase in [³S]GTPγS binding to 5-HT_{1A} receptors were not observed. On the other hand, the binding of [³H]ketanserin to 5-HT_{2A} receptors were hardly influenced by yokukansan or seven constituent herbs. These results suggest that partial agonistic effects for 5-HT_{1A} receptors of yokukansan may be mainly due to the effects of *Uncaria Hook*. The partial agonistic effects may be closely related to the ameliorative effects of aggressive behaviors.

P-18 A novel function of amyloid beta in cholesterol homeostasis

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Amyloid beta (Aβ) peptide is produced from amyloid precursor protein (APP), but its physiological function is not well known. Here we show that APP-expressing cells rapidly excreted the excess cellular cholesterol into medium in response to cholesterol-loading, depending on their Aβ production and secretion of Aβ-containing lipoprotein-like particles. Furthermore, when injected into the cerebral ventricle of APP-knockout mice, Aβ-containing lipoproteins were excreted more efficiently from the brain into peripheral tissues than control lipoproteins without Aβ. Based on these results, we propose a novel, apolipoprotein-like function of Aβ to maintain cellular and cerebral homeostasis of cholesterol.

P-20 Aβ enhance the ATBF1 expression responsible for the neuronal cell death

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ATBF1 (AT-motif binding factor 1), a 404-kDa transcription factor that contains 4 homeodomains and 23 zinc finger motifs, regulates gene transcription including α -fetoprotein and p21. We have demonstrated that ATBF1 is highly expressed in the nucleus of postmitotic neurons and it induces cell cycle arrest associated with neuronal differentiation in the developing brain. Furthermore, the subcellular localization of ATBF1 is regulated by PI3 kinase including Ataxia telangiectasia mutated (ATM). Recently, we found that ATBF1 is highly expressed in the Alzheimer's disease (AD) brain and APP transgenic mice compared with age-matched control. The aim of this study is to investigate whether ATBF1 plays any role in the pathogenesis of AD brain. We hypothesize that up-regulated expression of ATBF1 in AD brain is a response to DNA damage induced by Aβ, which causes oxidative DNA damage in AD brain and cultured cortical neurons. We found that ATBF1 expression was up-regulated in the cultured rat cortical neurons treated with different genotoxic compounds (etoposide, homocysteine, and Aβ (1-42)) and in the SH-SY5Y cells treated with etoposide. It has been reported that these genotoxic agents involved in pathogenesis of AD and induce apoptosis in cultured cortical neurons. Apoptosis induced by Aβ and etoposide in cultured neurons was attenuated by small interfering RNA-mediated knockdown of ATBF1. We also found that ionizing irradiation and etoposide induce phosphorylation of ATBF1 and that ATBF1 binds to ATM to activate ATM signaling pathways leading to apoptosis caused by DNA damage. Our data suggest that ATBF1 expression is enhanced by increased level of Aβ in AD brain and APP transgenic mouse brain, and enhanced level of ATBF1, in turn, activates ATM signaling pathways responsible for the neuronal cell death.

P-22 Roles of BRINP and BRINP-interacting proteins in neuronal differentiation

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Once differentiated from stem cells, neurons no longer proliferate, but extend nerve fibers to form neural circuitry. Although various molecules that inhibit the cell-cycle progression in proliferating cells have been identified, the mechanism suppressing the neuronal cell-division is not fully understood and the relevant molecules that are specific to the terminally differentiated neurons are not identified. On the other hand, we have previously identified a novel family of neuron-specific proteins, BRINP family (BRINP1, 2, 3) that retains no similarity with other known proteins but possesses abilities to suppress the cell-cycle progression and causes cell death in proliferating cells. Emergence of three BRINPs during mammalian development indeed coincides with the period of neurogenesis in both the CNS and PNS and they continue to be expressed into adulthood. In the present study, to further clarify the physiological roles of BRINP family proteins in neuronal cells, we analyzed the interaction of BRINPs with proteins we identified with the two-hybrid system such as Cyclin-dependent kinase 5 (CDK5) and Rab family of small GTP binding proteins. Immunoprecipitation (IP)-Western blotting experiment on BRINP-expressed 3T3 cells confirmed that all three BRINPs are able to bind to expressed CDK5. However, strength of the binding varied with different BRINPs, i.e. BRINP3 > BRINP2 > BRINP1. The experiment with BRINP3-deletion mutants showed that an internal domain of BRINP3 is responsible for the interaction with CDK5. Interestingly, this domain closely overlapped with the BRINP3 cell-cycle suppression domain. On the other hand, Rab3 and Rab11 are also able to bind to all three BRINPs in a GTP-dependent manner with slightly different preference, i.e. BRINP2 > BRINP3 > BRINP1. On the basis of these findings, physiological roles of BRINPs in neuronal differentiation will be discussed.

P-19 Activity of Presenilin/γ-secretase-mediated S3 cleavage can be efficiently measured by a newly developed Notch signaling reporter assay.

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Followed by extracellular shedding, Presenilin (PS) /γ-secretase degrade transmembrane domains of βAPP and Notch generating Alzheimer disease (AD)-associated amyloid-beta (Aβ) and Notch intracellular domains (NICD). In research of pathological process of AD, highly sensitive assay to measure the level of Aβ is a very important tool and conventional ELISA systems have been developed and widely used. However, currently available Notch signaling assay, which reflects activity of PS/γ-secretase-mediated S3 cleavage, is not as sensitive as Aβ ELISA system. Therefore, to measure the Notch signaling intensity in cultured cells, overexpression of Notch or Notch derivative constructs are necessary. In this study, we will show a newly developed Hes-1 promoter assay which can evaluate endogenous Notch signaling. We expect that the construct will be a useful tool in research of regulation of Notch signaling as well as biological effects of PS/γ-secretase.

P-21 PACAP decides cortical laminar formation via PKA signaling development of mouse cerebral cortex

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Laminar formation in the developing cerebral cortex requires the precisely regulated generation of phenotype-specified neurons. To test the possible involvement of pituitary adenylate cyclase-activating polypeptide (PACAP) in this formation, we investigated the effects of PACAP administered into the telencephalic ventricular space of 13.5-day-old mouse embryos. Within 5 min after PACAP administration (10 pmol/embryo), c-AMP responsive element binding protein (CREB) was phosphorylated in the nuclei of the cortical cells, which lasted for 1h after administration. PACAP partially inhibited the proliferation of cortical progenitors and altered the position and gene-expression profiles of newly generated neurons otherwise expected for layer IV to those of neurons for the deeper layers, V and VI, of the cerebral cortex. The former and latter effects were seen only when the parent progenitor cells were exposed to PACAP in the later and in earlier G1 phase, respectively; and these effects were suppressed by co-treatment with a protein kinase A (PKA) inhibitor, H89. Moreover, single administration of PKA inhibitor affected on the cortical progenitor cells in the opposite way to those of PACAP. That is, H89 stimulated the proliferation of cortical progenitor cells and altered the laminar fate of neurons to migrate into upper layer. Here, in previous study, we have shown that brain-derived neurotrophic factor (BDNF), a member of neurotrophin family-neurotrophic factor, similarly altered newly-generated cortical neurons with their localization and gene-expression profiles. Although PACAP are known to stimulate BDNF gene expression, the effects of PACAP were not suppressed by co-treatment with anti-BDNF antibody. These observations suggest that PACAP participates in the processes forming the neuronal laminas in the developing cortex via the intracellular PKA pathway, and that BDNF was not involved in the PACAP action.

P-23 Effects of methyl mercury chloride on neural differentiation from mouse embryonic stem cells by Neural Stem Sphere method

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We have established Neural Stem Sphere (NSS) method, which can efficiently induce differentiation of embryonic stem (ES) cells into neural cells, and demonstrated that ES cells unidirectionally differentiate into neurons via epiblast, neuroectodermal cells and neural stem cells by the method. Here, we analyzed effects of methyl mercury (MeHg), which caused Minamata disease, on the differentiation pathway from mouse ES cells into neurons by the method, to elucidate the neurotoxic action of MeHg during brain development. Cultured in astrocyte-conditioned medium (ACM) for 4 days under free-floating conditions in the absence of MeHg, colonies of mouse ES cells formed spheres of cells. The spheres grew during culture and gave rise to NSSs that mainly consist of neural stem cells. Expression of the ES cell marker was down-regulated during culture, in contrast, expression of the neural stem/progenitor cell marker and subsequently neuronal marker were up-regulated. When the colonies were exposed to MeHg (from 1 nM to 10 μM) from the start of culture for 4 days, formation of the NSSs was affected dose-dependently. Growth of the NSSs was suppressed and shapes of the spheres became ambiguous. Gene expression analysis of the spheres clearly demonstrated that MeHg inhibited the neural differentiation during culture. In contrast, when the spheres were exposed to MeHg from day 2 to day 4 in culture, effects of MeHg on the neural differentiation during culture were modest. These results suggest that there are some differences in the sensitivity to MeHg between the cells which were generated during neural differentiation of ES cells by the NSS method and also that this method offers a good model system to analyze effects of neurotoxin, such as MeHg, on neural differentiation. This work was partly supported by a Research Grant for long-range research initiative from JICA and Selective Research Fund of Tokyo Metropolitan University. (2331)

P-24 The effect of exogenous neural stem cell against the damaged neurons and neural stem cells

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Recent Neuroimaging studies have revealed the progressive volume change in the course of schizophrenia. The neurogenetic and neurotrophic effects of antipsychotics are considered to contribute to the prevention of reduction in brain volume. However, the precise mechanism for suppression of brain morphological change by antipsychotics has not yet cleared. Previously, we demonstrated the different effects of typical/atypical antipsychotics on the neuronal survival and neural stem cell (NSC) differentiation, and behavioral recovery of schizophrenia model rat by the intravenous transplantation of NSCs, which is one of the promising new treatment strategies for schizophrenia. In the present study, we investigate the effect of exogenous NSC on the neuronal survival and NSC differentiation in vitro, to clarify the possibility of stem cell therapy for schizophrenia. Primary cultures of neurons and NSCs were prepared from E18 and E14 rat embryo, respectively. The neuronal survival and NSC differentiation were assessed by the methods of MTT, LDH, MAP2 positive cell counting. The trophic factor signaling change in neurons and NSCs were analyzed by western blotting. The results indicate the protective effect of NSCs on the matured neurons and NSCs damaged by the trophic factor deprivation without cell-cell contact. The mechanism of neuroprotection and promotion of NSC differentiation by exogenous NSCs which may contribute to the efficacy of cell transplantation as a new therapy for schizophrenia will be discussed.

P-26 Decrease in axonal conduction velocity following central nervous system demyelination in vivo.

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Transgenic and knockout mice have been used to investigate the molecular mechanisms of demyelinating diseases. However, less attention has been given to elucidate the changes of nerve conduction in these mice. Treatment of cuprizone induces oligodendroglial loss and demyelination in the corpus callosum. In this model, remyelination is initiated by returning the mice to a normal diet. Here, we established an experimental system to measure latency of cortical neurons and report the changes in nerve conduction in cuprizone induced demyelinating mice and myelin basic protein (MBP)-deficient shiverer mice. Stimulating and recording electrodes were placed in the right and left sensorimotor cortices. Electrical stimulation applied to the right cortex evoked antidromic responses of left cortical neurons with a latency of 9.38 ± 0.31 ms ($N=107$; Mean $\pm$ SEM). While latency was delayed in mice at 7 days of cuprizone treatment (12.35 ± 0.35 ms; $N=102$; $p<0.01$ vs control, ANOVA followed by post-hoc test), latency at 7 days after removal of cuprizone was slightly restored (10.72 ± 0.45 ms; $N=106$; $p<0.05$ vs control). Consistent with these observations, electron microscopy also showed cuprizone induced demyelination in the corpus callosum and removal of cuprizone promotes remyelination. These results indicate that axonal conduction velocity following central nervous system demyelination is decreased. We further examined whether abnormality of myelin did affect to latency in shiverer mice. Latency of 9.83 ± 0.24 ms ($N=103$) in shiverer mice showed no significant difference compared with wild type mice (9.33 ± 0.22 ms; $N=112$). These results indicate that there might be another mechanism to maintain nerve conduction in shiverer mice. This electrophysiological assessment may provide us new insights to understand the pathophysiology in demyelinating animal models in the central nervous system.

P-28 Developmental changes of signaling molecules that regulate neurite outgrowth and myelination in the rat orbitofrontal cortex and visual cortex

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Neural circuits in the primary visual cortex (V1) exhibit experience-dependent plasticity during the critical period of postnatal development. Growing evidences suggest that the structural dynamics of synapses and myelination may play a crucial role in the plasticity of V1. To determine whether similar age-specific plasticity operates in the development and plasticity of the orbitofrontal cortex (OFC) which contributes to personality, we compared developmental changes of the molecules that regulate neurite outgrowth and myelination between the two areas. We measured the amount and activity of the following proteins by western blot analysis in Long-Evans rats at various postnatal ages: Erk and Cdk5, which are downstream effectors of neurotrophin, induce oligodendrocyte differentiation, axon elongation and dendritic spine outgrowth; RhoA, which is a downstream effector of NgR, EphA and CSPG, inhibits oligodendrocyte differentiation and axon elongation. In the V1, Cdk5 level was high during the critical period (P30) and decreased significantly in adults. RhoA activity was lowest at the critical period. On the other hand, the level of p-Erk and Cdk5 was maintained at high level until adulthood (P100) in the OFC. These results suggest that the remodeling of axons and spines would be most active during the critical period in V1, but the OFC might preserve the ability to add new neuronal circuits in adulthood.

P-25 Expression profiling of PRC1 complex members in mouse embryonic cortex.

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To identify genes involved in the nervous system development and responsible for human developmental disorders, genome-wide RNAi screening of Drosophila genes is underway. So far, 211 genes were identified among more than 8000 genes. In these Drosophila 211 genes, 161 genes have mammalian homologues and 79 genes locate on putative autistic locus. Now we started studying of these mammalian homologues by using the mouse as a model animal.

We are especially interested in genes required for epigenetic transcriptional regulation and, here, present genes expression profiling of PRC1 complex members that are in the list of our screened genes. A number of papers indicate the PRC1 complex has a critical role in the neural development, including differentiation from stem cells. Recent studies indicate ubiquitin ligase activity of PRC1 is critical for neural stem cell differentiation. However, study of each PRC1 complex member is not enough.

Here, we try to figure out which members of the PRC1 complex are expressed and critical during the nervous system development in the mouse cortex. For this purpose, RT-PCR analysis of each PRC1 member is currently undergoing. We found mRNA levels of several PRC1 members increase following neuronal differentiation stages while others are ubiquitous. Some of PRC1 member expression is much less than other members. These data suggest distinct roles of PRC1 complex members during the neuronal development.

P-27 Different distributions and characteristics of myelin basic protein isoforms during the brain development

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Myelin basic protein (MBP) is the structural protein found to be essential for formation of CNS myelin. In mice and rats, four mRNA of MBP are most abundant and encode polypeptide of 14.0, 17.0, 18.5, 21.5 kDa, and they are phosphorylated under physiological conditions. The phosphorylation state of MBP has been assumed to regulate myelin sheath integrity.

To investigate this, we analyzed phosphorylated and total MBPs by western blot of myelin sheath isolated from the corpus callosum of early (10-day-old), young (3-month-old), and adult (12-month-old), and aged (24-month-old) mice.

Though the aged mouse brains showed increase of demyelination, significant decreases in total MBPs were not observed. However, 21.5 kDa of phosphorylated MBP (pMBP) dramatically decreased in the aged brain. Furthermore, in the aged mice (31-month-old) whose many paranodal loops were retracted, MBP was decreased relative to other myelin proteins and 21.5 kDa isoform of MBP was almost completely absent.

Next we investigated whether these different isoforms localize to different regions of the myelin sheath on developing mouse brains, by detergent extraction. Then 21.5 kDa and 17 kDa isoforms were present in Triton X-100 insoluble fraction (extracted as lipid-free MBP) at early development of mouse brain (10-day-old). As a result of examination in lipid compositions of myelin in this stage, galactosylceramide (Galc) and sulfatide were not contained. On the other hand, in young mouse brains (3-month-old), 17.0 kDa isoform was also present in Triton X-100 insoluble fraction as early stage, but 21.5 kDa isoform was found in the soluble fraction with Galc and sulfatide.

These results suggest that the 21.5 kDa isoform which is present in different fractions can interact with different constituents and form complexes in myelin.

P-29 Analysis of myosin 1D in the myelin fraction

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Myosins are actin-based motors that are involved in a variety of cellular functions. The myosin superfamily consists of at least 18 distinct families. All type of myosin is composed of actin-activated ATPase head, neck, and tail domains. Unlike conventional muscle type Class II myosins with long coiled-coil tail, Class I myosins have highly basic tail that mediates interactions with acidic phospholipids and act as a monomer. Previously using two-dimensional electrophoresis with a cationic detergent and mass spectrometry, we revealed that myosin 1D (Myo1D), a member of Class I, was clearly enriched in the rat CNS myelin fraction. Myelin is a unique structure that consists of multiple membrane layers around axons and known to act as an electric insulator for action potential transmitted through neuronal axons. At present, Myo1D is thought to be expressed only in the neuron in the CNS and its function is still unclear. In this study, to clarify the function of Myo1D in the CNS, we focused the relationship between Myo1D and the myelin. First, to clarify whether the purified myelin contains neuronal components or not, we analyzed the compositions of the myelin fraction by western blotting. Proteins of compact myelin and paranodal loop were enriched in the purified myelin fraction, and also neuronal proteins of axolemma except proteins of node of Ranvier were included. In addition, neuronal components in axoplasm were not apparent in this fraction. In the developmental analysis of myelin fraction by western blotting, Myo1D was detected from 3 weeks of age and increased with age in the same way as major myelin proteins (PLP, DM-20, MBP, CNP). Myelinogenesis is very active in 3-4-week-old rat CNS. Proteins up-regulated in 3-4-week-old rat brain myelin fraction are possibly involved in the maturation of myelinated fibers. Further, in the immunostaining of Myo1D in the adult rat cerebellum, positive signal in the white matter was similar to that of MBP. These results suggest that Myo1D may be distributed in myelin or near axolemma covered by myelin. Since Myo1D is known to be related to the membrane trafficking along the recycling pathway, this myosin may be involved in the membrane dynamics of the myelinated fibers.

P-30 The regulatory function of B7-H3 and B7-H4 in Experimental Autoimmune Encephalomyelitis

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The proliferation and differentiation of T cells require signals provided by molecules on antigen presenting cells (APCs), called costimulators, in addition to antigen-induced signals. The best defined costimulators for T cells are the B7 family of molecules on APCs that bind to members of the CD28 family of receptors on T cells. Thus, costimulatory pathways play a critical role in regulating T cell immunity. B7-H3 and B7-H4 are newer members of the B7 family. These proteins can be considered negative regulators of T cells by inhibiting T cell proliferation and cytokine production. However, it remains unknown the role of B7-H3 and B7-H4. In this study, we observed that blockade of B7-H3 and B7-H4 by antibody treatment significantly worsened disease and CNS inflammation in experimental autoimmune encephalomyelitis (EAE) and accelerated disease onset in adoptive transfer EAE. B7-H3 and B7-H4 blockade markedly increased pro-inflammatory cytokine production and significantly increased the frequencies of antigen-specific CD4 T cells in the CNS. Interestingly, B7-H3 and B7-H4 expression was predominantly upregulated by CNS astrocytes, microglia/macrophages and dendritic cells during the course of EAE. These observations indicate that B7-H3 and B7-H4 function as negative costimulatory pathways in EAE model, and highlight the specific role of B7-H3 and B7-H4 in regulating effector T cells within the target tissue parenchyma.

P-32 The analysis of the role of Reelin signaling in the developing neocortex

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During neocortical development in mammals, neurons are born mainly in the ventricular zone along the ventricle and migrate radially towards the pial surface to be aligned in defined patterns in the cortical plate. These precise patterns of neuronal alignment are regulated by an extracellular matrix protein, Reelin, which is secreted from Cajal-Retzius neurons in the marginal zone of the neocortex. When Reelin binds to its receptors, tyrosine phosphorylation of the intracellular adaptor protein Disabled 1 (Dab1) is induced. Although the molecular cascade of Reelin signaling is being uncovered, the biological response of cortical neurons to the Reelin signal remains uncertain. To elucidate the biological role of Reelin molecule in the developing neocortex, we used the *in utero* electroporation system. Reelin was expressed ectopically in the developing neocortex and the effect on migrating neurons was analyzed.

P-34 Mechanism of dendritic spine abnormality in tuberous sclerosis.

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Tuberous sclerosis complex (TSC) is a hereditary autistic disorder caused by mutations in *tsc2* gene. *TSC2* has GAP activity towards small GTPase Rheb, and *TSC2* antagonizes mTOR pathway by stimulation of GTP hydrolysis of Rheb. We used Eker rats heterozygous for a mutation in the *tsc2* to examine an involvement of TSC pathway in synaptogenesis. *TSC2* mutation exhibited an increase in spine length and density, and a decrease in head width. Rapamycin reversed these changes, suggesting the effects of *TSC2* mutation were mediated via mTOR. As enhanced synaptic protein synthesis may be associated with abnormal spine morphology in Eker, we performed proteomic study to define protein diversity in synaptosomal fraction between wild and Eker rats, and identified some mitochondrial proteins were increased in the synaptosomal fraction from Eker rats. Thus, perturbations of TSC pathway may cause autistic symptoms of TSC by changing mitochondrial gene expression.

P-31 Enriched environment enhances neuropsin mRNA in the hippocampus

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Environmental enrichment is known to induce neural development and plasticity change in the hippocampus of rodent. However, the molecular mechanism of plasticity change in the hippocampus is not yet known. Here, we report how environmental enrichment influence the mRNA expression level of serine protease group (neuropsin, neurotrypsin, tPA) and cell adhesion molecule group (L1CAM, NCAM, N-cadherine). It is known that extracellular serine protease and cell adhesion molecules play a pivotal role in neural plasticity. As a result, neuropsin mRNA increased significantly in the hippocampus of enriched mouse. This result suggests that neuropsin involve in adaptation to environmental change.

P-33 Function of Sept14 on the positioning of cortical neurons in cerebral cortex

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Correct cortical neuronal generation, migration and positioning during cortical development are essential for proper brain functions. Septins are conserved family of GTP/GDP-binding proteins. There are 14 septin members (Sept1~Sept14) in mammals. It has been reported that some member of septin family highly expressed specifically in developing neuronal tissues, which raise the possibility that septins are functionally involved in neuronal development. We focused on Sept14 and examined the expression patterns in embryonic and postnatal mice. Strong expression of Sept14 in cerebral cortex was detected from E13 to P6. We next examined the function of Sept14 against the positioning of cortical neurons. Knockdown of Sept14 in neuroepithelial cells by *in utero* electroporation resulted in defective positioning of cortical neuron. We also screened the interacting molecules of Sept14 and found that Sept5 and Sept7 interacted with Sept14 in a physiological condition. These results suggest a novel function of septins on neuronal development.

P-35 The paternal behavior in mice

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Parental behavior is a set of behavioral and mental capacities that are crucial for reproductive and this period is associated with intense parental preoccupations in humans. Parental care in animals is defined as the collection of behaviors such as nesting, nursing and retrieving, that can increase offspring survival. Compare with well-known maternal behavior, paternal care is relatively uncommon in mammals and is found predominantly among rodents, carnivores, primates and human. Litter is known about proximate mechanisms underlying paternal behavior, although some researches indicated that prolactin and progesterone, both are female hormones, play the important role in it. Based on our previous research of CD38 on the secretion of oxytocin which is another female hormone and maternal behavior, we want to challenge the mechanism of paternal care and to further study the relationship between oxytocin and paternal behavior. Here we report our preliminary experiment about paternal behavior by using a laboratory strain of male mice.

P-36 Development of locomotor sensitization by daily and weekly ketamine administration○Toshifumi Yamamoto¹, Tomomi Nakayama¹, Hideko Yamamoto²¹Lab. of Mol. Recognition, Grad. School of Arts and Sci., Yokohama City Univ.²Div. of Psychobiol., Tokyo Inst. Psychiatry

Although ketamine has been widely used as a dissociative anaesthetic, low-doses ketamine produces several psychological abnormalities associated with schizophrenia. Ketamine is closely related to psychoactive drug, phencyclidine (PCP). These drugs act as noncompetitive open-channel blocker of the N-methyl-D-aspartate (NMDA) receptor. In the present study, we investigated the ketamine-induced locomotor sensitization in the mice. Single subanaesthetic doses of ketamine (25 mg/kg, sc) caused increased locomotor activity. Mice were then treated with same doses of ketamine daily or weekly intervals. In both consecutive and intermittent administration, locomotor sensitization already developed at second ketamine administration at 24h and 1-week after first administration. Those increased sensitization response to ketamine were maximum at the third administration. Furthermore, one month withdrawal of ketamine after repeated daily and weekly administration returned to basal behavioural condition. These results suggest that low dose of ketamine develops behavioural sensitization readily and also restore behaviour to the normal condition after withdrawal.

P-38 Sigma receptor signaling and methamphetamine-induced stereotypy○Junichi Kitanaka¹, Nobue Kitanaka¹, Tomohiro Tatsuta², Koh-ichi Tanaka³, Nobuyoshi Nishiyama³, Yoshio Morita³, Motohiko Takemura³¹Dept. Pharmacol., Hyogo Col. Med., Nishinomiya, Hyogo, Japan, ²Dept. Neuropsychiatry, Hyogo Col. Med., Nishinomiya, Hyogo, Japan, ³Div. Pharmacol., Dept. Pharm., Sch. Pharm., Hyogo Univ. Health Sci., Kobe, Hyogo, Japan

The administration of methamphetamine (METH, 10 mg/kg, i.p.) to male ddY mice induced stereotyped behavior consisting of nail and/or wood chip biting (90.1%), continuous sniffing (4.2%), head bobbing (4.1%), and circling (1.7%) during the observation period of 1 h. Pretreatment of the mice with BMJ 14802 (1, 5, and 10 mg/kg, i.p.), a general sigma receptor antagonist, significantly increased and decreased METH-induced continuous sniffing (19.2, 30.5, and 43.8%) and nail and/or wood chip biting (76.6, 66.9, and 49.3%), respectively, in a dose-dependent manner. This response was completely abolished by SKF 10047 (4 mg/kg, i.p.), a putative sigma₁ receptor agonist, and partially by PB 28 (1 mg/kg, i.v.), a putative sigma₂ receptor agonist. The BMJ 14802 action on METH-induced stereotypy was mimicked by BD 1047 (10 mg/kg, i.p.), a putative sigma₁ receptor antagonist, but not by SM-21 (1 mg/kg, i.p.), a putative sigma₂ receptor antagonist, and the BD 1047 action on METH-induced stereotypy was also abolished completely by SKF 10047 and partially by PB 28. The frequency of the expression of METH-induced total stereotypic patterns was unchanged with these sigma receptor ligands. The BMJ 14802 action on METH-induced stereotypy was not affected by pretreatment with centrally acting histamine H₁ receptor antagonists (pyrilamine and ketotifen, each used at 10 mg/kg, i.p.), while similar effects of histamine N-methyltransferase inhibitors were blocked by these agents. These results suggest that blockade of central sigma₁ receptors may switch the expression pattern of METH-induced stereotypy from biting to sniffing via a mechanism independent of histamine H₁ receptor signaling system.

P-40 Neuroprotection by antidiarrhetic ingredients in hippocampal neurons○Yukary Nakamura¹, Nobuyuki Matsushima², Nobuaki Moriguchi^{1,2}, Hitoshi Shibata¹, Yuki Kambe¹, Noritaka Nakamichi¹, Yukio Yoneda¹¹Laboratory of Molecular Pharmacology, Kanazawa University Graduate School of Natural Science and Technology, ²Taiko Pharmaceutical Co. Ltd.

We have previously shown that particular phenolic antidiarrhetic ingredients, including 2-methoxyphenol (2MP), 2-methoxy-4-methylphenol (2M4MP) and 2-methoxy-4-ethylphenol (2M4EP), significantly prevent cell death by hydrogen peroxide (H₂O₂) in cultured rat calvarial osteoblasts *in vivo*. In the present study, we have evaluated the pharmacological actions of these three phenolic antidiarrhetic ingredients on ischemic neuronal damage in brains of rats with middle cerebral artery occlusion (MCAO) *in vivo*. In the ipsilateral cerebral hemisphere of rats with MCAO, a significant decrease was seen in the neuronal marker protein level on Western blotting analysis. A significant decrease was seen in the infarct volume with an increased level of MAP2 in the ipsilateral hemisphere of MCAO rats with prior daily oral administration of 2M4MP for 7 days, but not 2MP or 2M4EP. In rat hippocampal neurons cultured for 9 days *in vivo*, exposure to H₂O₂ or glutamate (Glu) prominently reduced the cell viability estimated by MTT reduction, whereas simultaneous addition of 2MP, 2M4MP and 2M4EP resulted in significant protection against the loss of cellular viability by both H₂O₂ and Glu. Exposure to H₂O₂ markedly increased intracellular reactive oxygen species (ROS) levels determined with the ROS sensitive fluorescent indicator DCFH-DA, while Glu drastically elevated concentrations of intracellular free Ca²⁺ ions determined with the Ca²⁺ sensitive fluorescent indicator fluo-3 AM. These intracellular events were significantly prevented by all phenolic ingredients examined. These results suggest that the three phenolic antidiarrhetic ingredients may lead to cytoprotection against the cytotoxicity of oxidative stress as well as the excitotoxicity of Glu through different plural mechanisms in cultured rat hippocampal neurons. Conflict of interest : N.M., N.M. and H.S. are employees of Taiko Pharmaceutical Co. Ltd., Japan. All other authors have no conflicts of interest.

P-37 Postpartum stress on dams make their pups short statue○Hideyuki Nakata¹, Ko Nishimura¹, Pengfei Gao¹, Yuu Murakami¹, Kenji Tsuiji¹, Atsushi Ishige¹, Kenji Watanabe¹¹Center for Kambo Medicine, Keio University school of Medicine

Early neonatal environmental factors such as change in bedding, litter removal, odor of strange male, physical isolation and other new environments enhance anxiety-related behaviors in offspring and appear to have powerful and long-lasting influence on the pups' physiology. But few reports explain the maternal stress and its effect on offspring. We introduced immobilize stress on postpartum dam and checked the effects on both dams and offspring. ICR mice were used in this study. Within 24hrs from delivery, immobilized stress on dams was started. Dams were immobilized from postpartum 1-21 day, 3hrs 9:00 to 12:00 everyday. Tail suspension test and locomotor activity test were done on postpartum day 22. Dams were sacrificed on postpartum day 23 and hippocampus tissue were collected to check the molecular change. At the same time, pups' serum IGF-1 were checked and GHRH stimulation test were done. Immobilize stress on dams arise no behavioral change of dams but serious growth impairment of the offspring. The pups' serum IGF-1 decreased significantly and pituitary were significantly poor response to GHRH stimulation. We report for the first time that maternal stress arise pups' physical change. Our mouse model may bring us a new insight for those short statue.

P-39 Lycopene administration to Mongolian gerbil increase SOD activity in hippocampus after transient cerebral ischemia○Kimikazu Fujita¹, Nobuko Yoshimoto², Gaku Matsumoto³, Takahiro Inakuma³, Toshiaki Kato⁴, Hideki Imada¹, Yutaka Nagata¹, Eiichi Miyachi¹¹Department of Physiology, School of Medicine, Fujita Health University, Aichi, Japan, ²Department of Nutrition and Food Sciences, Nagoya Bunri University, College Nagoya Aichi Japan, ³Research Institute Kagome Co.Ltd Tochigi Japan, ⁴Department of Clinical Laboratory Sciences, Fujita Health University, College. Toyooka Aichi Japan

Cytotoxic reactive oxygen species (ROS), which trigger neuronal apoptosis, are produced mainly in mitochondria after application of transient cerebral ischemia/recirculation in Mongolian gerbil. Some antioxidant molecules such as superoxide dismutase (SOD), catalase, glutathione peroxidase are naturally found in animal tissues and act to eliminate or delay the effect of oxidative damage. Lycopene of plant origin acts as an antioxidant agent by per oral administration to the experimental animals. After weaning at 21st day after birth, the animals were fed on lycopene containing animal food (250 mg/100g) freely. And after having grown up to body weight of 60-70g (about 2.5 months of age), the animals were given transient cerebral ischemia for 10 min. We took out brain on 3 hour, 1,3 and 7th day after operation and analyzed SOD activity using a assay kit. SOD activity in hippocampus of non-operated control group was kept high level (3.37±0.33 U/mg protein). In normal (non-lycopene) food uptake group, the enzymatic activity decreased at 3 hour after ischemic insult (1.84±0.57 U/mg protein). SOD activity of lycopene uptake group was 2.67±0.24 U/mg protein after 3 hour of the operation, then the activity gradually increased to the control level. Between lycopene uptake group and non-lycopene uptake group, statistical significant difference was found (p<0.05). These results suggest that lycopene acts to increase the antioxidant enzymatic activity to prevent tissue damage.

P-41 No association between NRG1 and methamphetamine use disorder in the Japanese population○Tomo Okochi¹, Taro Kishi¹, Masashi Ikeda¹, Tsuyoshi Kitajima¹, Yoko Kinoshita¹, Kunihiro Kawashima¹, Takenori Okumura¹, Tomoko Tsunoka¹, Toshiya Inada¹, Mitsuhiko Yamada¹, Naohisa Uchimura², Masao Iyo², Ichiro Sora², Norio Ozaki², Hiroshi Ujike², Nakao Iwata^{1,2}¹Department of Psychiatry, Fujita Health University School of Medicine, Toyooka, Japan, ²Japanese Genetics Initiative for Drug Abuse (JGIDA)

Neuregulin1 gene (NRG1) had been identified as a candidate gene for schizophrenia by linkage study in the Icelandic population, and recent evidences suggested that it might contribute to neurodevelopmental hypothesis and glutamate hypothesis of schizophrenia. Because the symptomatology of methamphetamine (METH) use disorder is similar to that of patient with schizophrenia, NRG1 is a good candidate gene for METH use disorder. Therefore, we conducted a case-control association study between NRG1 and METH use disorder in a Japanese population (213 with METH use disorder and 534 controls). Written informed consent was obtained from each subject. This study was approved by the Ethics Committee at Fujita Health University School of Medicine, Nagoya University Graduate School of Medicine and each participating institute of the Japanese Genetics Initiative for Drug Abuse (JGIDA). We selected four SNPs (SNP8NRG221533, SNP8NRG241930, rs699492, rs3924999) in the NRG1 gene from previous reports. All SNPs were genotyped by TaqMan assay. Marker-trait association was evaluated with chi-square test and the log-likelihood test. No significant allele/genotype-wise or haplotype-wise association was found between NRG1 and METH use disorder. We suggest that NRG1 might not contribute to the risk of METH use disorder in the Japanese population.

P-42 Association study of clock gene (CLOCK) and mood disorders in a Japanese population

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Several investigations have been suggested dysregulation of circadian rhythm for pathophysiology of mood disorders. Some genetic studies have been reported that clock gene (CLOCK) associated with bipolar disorder and major depressive disorder. Therefore, we used Japanese patients diagnosed with 149 bipolar disorder (BP) and 324 major depressive disorder (MDD) based 795 Japanese controls to investigate the association between the six tagging SNPs in CLOCK and the risk of mood disorders. Written informed consent was obtained from each subject. This study was approved by the ethics committees at Fujita Health University, Nagoya University Graduate School of Medicine. No significant associations between all tag SNPs in CLOCK and Japanese BP and MDD in the allele/genotype-wise analysis or haplotype-wise analysis were detected. In conclusion, we suggest that CLOCK may not play a major role of pathophysiology of mood disorders a Japanese population.

P-44 Effects of aripiprazole and apomorphine on locomotor activity after long-term treatment with olanzapine or haloperidol in rats

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Background: Aripiprazole is a next generation antipsychotic, having a favorable safety profile with low potential for extrapyramidal symptoms (EPS), hyperprolactinemia and weight gain. These clinical findings may be associated with the partial agonist properties of D2 receptors of this drug. Recently, we revealed that the intrinsic activities of partial agonists for hD2 receptors are dependent on the receptor density and the concentration of endogenous ligand. In the present study, we intended to clarify whether or not aripiprazole could influence the dopaminergic hyperactivity of rats whose dopamine D2 receptors were supersensitized after chronic treatment with the dopamine D2 antagonists, olanzapine or haloperidol. **Method:** Olanzapine (7.5 mg/kg/day) or haloperidol (0.25 mg/kg/day), and vehicle were administered using ALZET osmotic mini-pumps for 21 days. Three and seven days after the removal of the mini-pumps, rats in each group were analyzed to determine the influence on locomotor activity by treatment with apomorphine (0, 0.1 mg/kg, SC) or aripiprazole (0, 10, 30 mg/kg, PO). We also evaluated the receptor binding properties of striatal D2 receptors of rats in each of three long-term treatment groups. **Results:** Low dose of apomorphine, a D2 receptor full agonist, significantly increased the locomotor activity in olanzapine and haloperidol treatment groups as compared with long-term vehicle treated group. These results suggest that long-term treatment of D2 antagonists led to the supersensitization of post-synaptic D2 receptors in rat brains. In contrast, no doses of aripiprazole increased the locomotor activity in any of the drug-treatment groups; rather a significant decrease in locomotor activity was seen by the treatment with aripiprazole. **Conclusion:** These results suggest that aripiprazole have no stimulating effect at supersensitized D2 receptors in our behavioral evaluation after the long-term treatment of olanzapine or haloperidol having D2 receptor antagonistic activity.

P-46 Rapid down-regulation of thyroid hormone responsive genes in the adult rat brain after peripheral administration of lipopolysaccharide

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Since thyroid hormone plays essential roles in the developing as well as mature brain, perturbations of the thyroid hormone system by exogenous factors may adversely affect the normal functioning of the brain. Recent studies have revealed that activation of the innate immune system leads to major changes in the hypothalamus-pituitary-thyroid axis by altering the local thyroid hormone metabolism in the hypothalamus. However, little is known about the effect of peripheral inflammation on the thyroid hormone-dependent systems in other brain regions. In the present study, we investigated the effect of lipopolysaccharide (LPS)-induced peripheral inflammation on the expression of thyroid hormone-related genes in six brain regions (cerebral cortex, hippocampus, striatum, thalamus, midbrain and cerebellum). Expression of inflammatory cytokines (IL1b and TNFa) was significantly increased in 5 out of 6 regions 4h after intraperitoneal injection of LPS (100µg/kg), with more than ten-fold increases in IL1b mRNA in the cerebral cortex, hippocampus, and the cerebellum where the basal expression levels were low. Expression of type 2 deiodinase which converts thyroxine (T4) into bioactive triiodothyronine (T3) was significantly up-regulated by LPS in the hippocampus, thalamus, and the cerebellum. Type 3 deiodinase which inactivates T3 was up-regulated in the hippocampus and the midbrain. Two genes known to be directly regulated by thyroid hormone, hairless and rc3/neurogranin, were both down-regulated by LPS in all the regions except thalamus, suggesting decreases in the local level of T3 in these regions. The results show that there are regional differences in sensitivity towards peripheral inflammation, with hippocampus being the most sensitive. The results suggest that peripheral inflammation could participate in the impairment of diverse CNS function through perturbations of the local thyroid hormone system.

P-43 Serotonin transporter polymorphisms in Japanese patients with bipolar disorder and schizophrenia

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Differences in serotonin transporter (SERT) expression and function produced by gene polymorphisms are associated with several psychiatric diseases; unipolar depression, bipolar disorder (BD) and schizophrenia (SZ). There are two polymorphic regions of SERT gene: a 44-base-pair (bp) insertion/deletion polymorphism in the promoter region (SERTPR/5HTT-LPR), and variable number of tandem repeats (VNTR) in second intron (SERT-in2/5HTT-VNTR) have been characterized. VNTR has been reported to be associated with unipolar depression, bipolar depression, SZ, and anxiety disorders and LPR with unipolar and bipolar depression. But the results are inconsistent. In this study, we investigated the frequency distribution of polymorphic variants of short (S, in2.9) and long (L, in2.12) alleles, genotypes and haplotypes of SERTPR, and SERTin2, in patients with BD, SZ and compared the data with results obtained from the Japanese normal controls (NC). Twenty-four BD patients and 191 SZ patients diagnosed using the Structured Clinical Interview for DSM-IV (SCID) and 77 healthy volunteers were included in the study. Each chromosomal region including SERT-in2 and SERTPR was amplified by polymerase chain reaction. Allele sizes were determined by electrophoresis. Association analysis of each polymorphism was performed with BD, SZ and NC. In genotype frequency, SERTPR indicated statistically significant difference between BP and NC. There is also significant difference between SZ and NC. In allele type frequency, there is significant difference between BP and NC, whereas SERT-in2 showed no differences. We are now carrying out further analysis. All subjects were given informed consent before blood collection strictly based on the ethical regulations of Kyushu University.

P-45 Regulation of energy homeostasis by UCH-L1 and UCH-L3

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Precise control of the ubiquitin system is crucial for the physiological regulation of many cellular processes. Impairment of this system has been indicated in many human diseases. The enzymes that remove ubiquitin from proteins are called de-ubiquitinating enzymes (DUBs); these modulate the process of protein ubiquitination. Despite the importance of DUBs, knowledge of their physiological functions is scant. Among the DUBs, UCH-L1 and UCH-L3 constitute two members of the ubiquitin carboxy terminal hydrolase (UCH) subclass with about 40% identity and distinct expression patterns; UCH-L1 is restricted to brain and testis/ovary and UCH-L3 is ubiquitous. Our previous studies indicate that both enzymes are crucial in the homeostasis of the brain function. *gad* mice, which lack UCH-L1 expression, and UCH-L3 knockout mice show neurodegeneration in the distinct area. Recently, caloric restriction was shown to delay the neurodegeneration in various rodent models of neurodegenerative diseases, indicating the close link between the metabolic regulation and neural function. However, little is known about the underlying mechanisms of the link. Here we show that UCH-L1 and UCH-L3 unexpectedly contribute to the regulation of the energy metabolism. Both UCH-L3 knockout mice and *gad* mice displayed a reduced percentage of adipose tissue mass associated with the increase in the glucose clearance in selected peripheral tissues. To gain insight into the molecular mechanisms of the phenotypes seen in these mice, we focused on two major pathways, which are responsible for the regulation of the energy metabolism: Insulin/IGF-1 signaling pathways and AMP-activated protein kinase pathway. We found that molecules regarding these pathways are altered in some tissues of UCH-L3 knockout mice. We are also looking into the changes of these pathways in the brain of *gad* mice. Our approach should provide important information to reveal neural and metabolic connection.

P-47 LPS-induced transglutaminase 2 expression and the involvement of NO production in rat brain astrocyte

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Activation of glia has been observed in neurodegenerative diseases such as Parkinson's disease (PD), Alzheimer's disease (AD) and multiple sclerosis. Excessive production of nitric oxide (NO), as a consequence of increased inducible nitric oxide synthase (iNOS) in glia, contributes to neurodegeneration. Transglutaminase 2 (TGase 2) is a cross-linking enzyme, which is activated in neurodegenerative diseases such as AD, PD and Huntington's diseases. However, mechanisms contributing to the increased TGase activity in neurodegenerative diseases remain to be clarified. In the present study, we examined the expression of TGase 2 in cultured rat cortex astrocytes activated with lipopolysaccharide (LPS). We found that expression of TGase 2 mRNA and protein were increased by LPS-stimulation. On the other hand, LPS-induced NO production was inhibited by monodansylcadaverine and cystamine, (inhibitors of TGase 2) in a dose-dependent manner. Furthermore, LPS-induced TGase 2 expression, as well as NO production were diminished by ammonium pyrrolidine-1-carbodithioate (NF-κB inhibitor) and ethyl pyruvate (antioxidant; stable derivative of pyruvate). These results suggest that NF-κB and oxidative stress are involved in LPS-induced TGase 2 expression in cultured astrocytes and that TGase 2 induction in the activated astrocytes may associate with NO production.

P-48 Inhibition of [³H]glutamine accumulation by a green tea ingredient in rat brain neurons and astroglia○Yusuke Tonami¹, Takumi Kakuda², Ayumu Nozawa², Masato Ogura¹, Takeshi Takarada¹, Eiichi Hinoi¹, Yukio Yoneda¹¹Lab Mol Pharmacol, Kanazawa Univ Grad Sch Nat Sci Tech, Kanazawa, Japan,²Central Research Institute, Itoen Ltd., Makinohara, Shizuoka, Japan

The fact that the structural evaluation clearly reveals higher similarity of the green tea ingredient theanine (≡γ-glutamylethylamide) to glutamine (Gln) than to glutamate, which is also a structural analog of theanine, suggests that theanine could elicit its pharmacological actions through particular mechanisms relevant to Gln rather than to glutamate in the brain. The neurotransmitter pool of glutamate is thought to be fueled by the entry of the structural analog Gln and subsequent cleavage by glutaminase. In this study, therefore, we have determined the incorporation of [³H]glutamate, [³H]Gln and [³H]theanine in order to evaluate the possible action site of theanine in the brain. Although theanine did not inhibit [³H]glutamate accumulation, [³H]theanine was actively accumulated in a temperature-dependent and saturable manner in rat brain synaptosomal fractions. The accumulation of [³H]theanine was markedly inhibited by Gln in a concentration-dependent manner, while [³H]Gln accumulation was inhibited by theanine vice versa. Both [³H]theanine and [³H]Gln accumulations were decreased after the replacement of sodium chloride with choline chloride along with similarly high distribution profiles in telencephalic structures. A similar equilibrium was seen within 30 min at 30°C for the accumulations of both [³H]theanine and [³H]Gln in cultured rat neocortical astroglia as well as neurons, whereas theanine inhibited [³H]Gln accumulation in a concentration-dependent manner at 0.1 to 10 mM. Furthermore, sustained exposure to 10 mM theanine led to a significant decrease in the level of extracellular glutamate released from cultured neurons. These results suggest that the green tea ingredient theanine would be an inhibitor of different transporters capable of transporting Gln across plasma membranes toward the modulation of the glutamate/Gln cycle required for fueling the neurotransmitter pool of glutamate in neurons.

P-49 Distribution of glucose transporters in the mouse tongue○Yusuke Ishida¹, Shinya Ugawa¹, Takashi Ueda¹, Shoichi Shimada¹¹Department of Neurobiology and Anatomy, Graduate School of Medical Sciences, Nagoya City University, Nagoya, Japan

A major source of metabolic energy for mammalian cells is the oxidation of glucose, and the cellular uptake of sugar is achieved by membrane-associated carrier proteins. Two classes of glucose carriers have been known in mammalian cells: the facilitative glucose transporters (GLUT) and the sodium- and energy-dependent glucose transporters (SGLT). On the other hand, it has been reported that SGLT3 is not a sodium-glucose cotransporter but instead a glucose sensor in the plasma membrane of cholinergic neurons, skeletal muscle, and other tissue. Perhaps, there is a possibility that SGLT3 or the other sugar transporters function as sweet receptors in the tongue. However, the distribution of sugar transporters in the tongue remains to be carried out. We investigated here details of the expression of GLUT1-3 and SGLT1-3 in the mouse tongue using reverse transcriptase-polymerase chain reaction (RT-PCR) and in situ hybridization analysis. In this conference, we show the results and discuss the functional significance of sugar transporters in the tongue.

P-50 Hippocampal involvement in diabetes -Clinical and experimental studies-○Shozo Kito¹, Akiko Shingo²¹Junshin-kai Kousei Rehabilitation Hospital, Hyogo, Japan ²Hyogo University School of Health Sciences, Hyogo, Japan

It has been established that diabetes mellitus type2 (DM2) patients have an increased risk of developing Alzheimer's disease (AD). Clinically, we analyzed hippocampal and extrahippocampal morphology of 61 cases of DM2 aged 33 to 75 years by voxel-based morphometry using MRI. As the results, 50% of examined cases showed selective atrophy of the parahippocampal gyrus. The degree of the atrophy was more marked in cases with impaired insulin reactivity.

Experimentally, working memory studies with use of 8 radial maze were performed on STZ-induced diabetic rats and DM2 model GK rats. In diabetic rats, there were working memory impairments which were improved by estrogen administration. After sacrificing, in situ hybridization for IDE (insulin degrading enzyme) mRNA was performed on the hippocampal slices. It was revealed that the expression of IDE mRNA was reduced in the hippocampus of GK rats as compared to controls. The expression of IDE mRNA in the hippocampus was compared between estradiol-treated and untreated GK rats.

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人名索引

演題番号 (太字は筆頭著者)

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ZEBRA FISH	P-13
ZINC	O4-6
	O17-2

Others

5-HTT	S12-2
α 7 NACH RECEPTOR	O1-3
8-NITRO-CGMP	O1-9

学会掲示板

【助成・褒章案内】

第40回（2008年度）内藤記念科学振興賞候補者推薦要領

趣旨：

人類の健康の増進に寄与する自然科学の基礎的領域において進歩発展に顕著な功績のあった研究者に対してほう賞を授与するものである。

候補資格：

1. 人類の健康の増進に寄与する自然科学の基礎的研究において独創的テーマに取り組み、進歩発展に顕著な功績を挙げた研究者。
2. 候補者は単独とするが、異なる研究グループによる共同研究の場合には、連名であっても良い。
3. 候補者の再度の推薦は差支えない。

推薦者：

1. 下記27学会の代表者

高分子学会	日本獣医学会	日本農芸化学会
日本遺伝学会	日本植物生理学学会	日本発生生物学会
日本ウイルス学会	日本神経科学学会	日本ビタミン学会
日本栄養・食糧学会	日本神経化学会	日本病理学会
日本解剖学会	日本生化学会	日本物理学会
日本化学会	日本生物工学会	日本分子生物学会
日本癌学会	日本生物物理学会	日本免疫学会
日本細菌学会	日本生理学会	日本薬学会
日本細胞生物学会	日本動物学会	日本薬理学会

2. 内藤記念科学振興財団の理事・監事および評議員

※推薦件数は、1推薦者につき1件

推薦方法：

所定の用紙（候補者推薦書、宛名シール）に必要事項を記入し、内藤記念科学振興財団宛て郵送する。あわせて必要事項を記入した候補者推薦書などを電子メールで同財団宛てに送付する。
日本神経化学学会の推薦をご希望の方は、当会研究助成金等候補者選考委員会宛てにご送付下さい。
同委員会では選考の上、推薦候補者を決定致します。

締切日：

2008年10月1日（水）（内藤記念科学振興財団必着）

日本神経化学学会の推薦をご希望の方は、2008年9月1日（月）必着。

選考方法：

内藤記念科学振興財団選考委員会で審査し、評議員会の同意を得て、理事会で決定する。
本年度は同財団の40周年にあたり、記念事業としての1件を追加し、計2件採択する。
採否の結果は、2009年2月に候補者および推薦者に通知する。

授賞式・顕彰：

授賞式は受賞者夫妻を招いて2009年3月17日（火）に行う。

受賞者には内藤記念科学振興賞（正賞：金メダル、副賞：1,000万円（従来は500万円））を贈呈する。

その他：

1. 候補者推薦書は、内藤記念科学振興財団ホームページ（<http://www.naito-f.or.jp/>）よりダウンロードし、ご記入下さい。
2. 推薦書用紙は必ず両面印刷で、宛名シールはシール用紙に印刷して下さい。
3. 学会推薦の場合は、学会の公印を捺印下さい。

第40回（2008年度）内藤記念海外学者招へい助成金（前期・後期）申請要領

趣旨：

人類の健康の増進に寄与する自然科学の基礎的研究を行う外国の研究者を招へいする際の費用を補助するものである。

申請者資格：

1. 人類の健康の増進に寄与する自然科学の基礎的研究に独創的・意欲的に取り組み、国際的に高い評価を得ている外国の研究者を招へいする際の当該学術集会組織委員長。
2. 同一年度の同一学術集会に招へいする場合の申請は1件とする。
3. 招へい時期が下記の期間内であること。

招へい時期	申請区分
2009年1月1日～2009年6月30日	前期
2009年7月1日～2009年12月31日	後期

4. 助成が決定した後、申請招へい学者が来日中止の場合は助成を辞退していただきます。
5. 内藤記念科学振興財団の選考委員と同一の教室（講座）に所属する者は申請することができない。

推薦者：

1. 大学関係…大学院：研究科長 学部：学部長 研究所：研究所長
大学共通組織（研究センター、研究施設等）：学長
ただし医学研究科・医学部がある場合などは、どちらか一方の推薦者とする。
注）センター長、施設長、病院長は推薦者となることができない。
2. 大学以外の研究機関…内藤記念科学振興財団の理事会が承認した基礎研究機関の代表責任者
3. 内藤記念科学振興財団の理事・監事および評議員
4. 内藤記念科学振興財団の指定した学術集会の代表者

※ 推薦件数：1推薦者につき1件（前期・後期 各々1件）

申請方法：

希望者 ⇒ 大学・研究機関事務 ⇒ 内藤記念科学振興財団

所定の用紙（申請書、宛名シール）に必要事項を記入し、内藤記念科学振興財団宛て送付する。

推薦が決まった方は、あわせて必要事項を記入した申請書などを電子メールで内藤記念科学振興財団宛てに送付する。

日本神経化学会の推薦をご希望の方は、当会研究助成金等候補者選考委員会宛てにご送付下さい。同委員会で選考の上、推薦候補者を決定致します。

締切日：

＜前期＞2008年6月2日（月） ＜後期＞2008年10月1日（水）

（いずれも内藤記念科学振興財団必着）

日本神経化学会の推薦をご希望の方は ＜後期＞2008年9月1日（月）必着。

選考方法・採択件数：

内藤記念科学振興財団選考委員会で審査し、評議員会の同意を得て、理事会で決定する。

採択件数は 前期・後期各10件以内（予算範囲内）

採否の結果は ＜前期＞2008年10月 ＜後期＞2009年2月に申請者および推薦者に通知する。

助成額：

エ リ ア	助成額（万円）
中東・アフリカ	80
米国・カナダ（西海岸除く）、ヨーロッパ	60
米国・カナダ西海岸、オーストラリア、ニュージーランド	50
東南アジア、インド	30
中国、台湾、韓国	20

送金時期：

＜前期＞2008年12月 ＜後期＞2009年3月

所定用紙の注意事項：

1. 申請書は内藤記念科学振興財団ホームページ（<http://www.naito-f.or.jp/>）よりダウンロードし、ご記入下さい。
2. 申請書用紙は必ず両面印刷して下さい。宛名シールはシール用紙に印刷して下さい。

報告の義務：

1. スポンサーについて 当該学術集会で海外学者による招待講演が行われる場合は、プログラム等に内藤記念科学振興財団（英文：The Naito Foundation）の助成によるものであることを明記する。なお、プログラム等を一部送付下さい。
2. 研究結果報告について 組織委員長は招へい終了1ヶ月以内に所定用紙にて報告する。
3. 来日中止の場合について 申請招へい学者が来日中止の場合は辞退していただきますので連絡下さい。

財団法人 井上科学振興財団
第25回（平成20年度）井上学術賞受賞候補者推薦要綱

候補者の対象：

自然科学の基礎的研究で特に顕著な業績をあげた研究者。
但し、年齢が平成20年9月20日現在で50歳未満の研究者に限ります。

学術賞：

＜本賞＞賞状及び金メダル ＜副賞＞ 200万円

授賞件数は5件以内とします。

（注）受賞者は、原則として1件につき1人とします。特に複数であることを必要とするときは、それらの研究者の寄与が同等であることを示して下さい。但し、この場合においても1件として取り扱います。

推薦依頼先：

下記の34学会、並びに井上科学振興財団の理事・評議員等に推薦を依頼します。

推薦件数：

各推薦学会または各推薦者から、原則としてそれぞれ1件とします。

提出方法：

所定の推薦書用紙（井上科学振興財団ホームページに掲載）に必要事項を記載し、井上科学振興財団宛てに提出願います。

締切期日：

平成20年9月20日（土）（井上科学振興財団必着）

選考：

井上科学振興財団選考委員会において選考し、理事会において決定します。
選考の結果は、平成20年12月中旬に推薦者に通知します。

学術賞の贈呈：

平成21年2月4日（水）午後4時から 東京で開催の予定。

推薦書提出先及び連絡先：

財団法人 井上科学振興財団

〒150-0036 東京都渋谷区南平台町15-15 南平台今井ビル601

電 話 ： 03-3477-2738

F A X ： 03-3477-2747

E-mail ： inoue01@inoue-zaidan.or.jp

日本数学会	日本遺伝学会	有機合成化学協会
日本応用数理学会	日本発生生物学会	日本セラミックス協会
日本物理学会	日本分子生物学会	日本農芸化学会
日本生物物理学会	日本地震学会	日本解剖学会
日本天文学会	地球電磁気・地球惑星圏学会	日本神経科学学会
日本化学会	日本気象学会	日本神経化学会
日本分析化学会	日本海洋学会	日本生化学会
触媒学会	応用物理学会	日本免疫学会
日本動物学会	電子情報通信学会	日本癌学会
日本植物学会	日本金属学会	日本薬学会
日本植物生理学会	電気化学会	
日本細胞生物学会	高分子学会	

財団法人 井上科学振興財団
第25回（平成20年度）井上研究奨励賞受賞候補者推薦要綱

推薦の対象：

平成17年4月1日～20年3月31日（平成17年度～19年度）の過去3年間に、理学・工学・医学・薬学・農学等の分野で博士の学位を取得した35歳未満（平成20年9月20日現在。ただし医学、歯学、又は獣医学の学位取得者については37歳未満。）の研究者で、自然科学の基礎的研究において新しい領域を開拓する可能性のある優れた博士論文を提出した研究者。

授賞件数及び研究奨励金：

授賞予定件数は30件。受賞者には、賞状、メダル及び1件当たり50万円の井上研究奨励金を贈呈します。

推薦者：

原則として、博士論文の作成を指導した研究者とします。

（博士論文指導研究者によることが困難な場合は、準ずる役割の研究者の推薦とします。）

提出手続：

- （1）推薦者（博士論文指導研究者）は、所定の推薦書用紙に必要事項を記入し、候補者が博士の学位を取得した大学の学長に提出願います。
- （2）（1）により推薦書の提出を受けた学長は、井上科学振興財団から学長にあてた推薦依頼文書に示された推薦件数枠の範囲内で推薦書を取りまとめの上、学長名の文書を添えて、所定の提出書類とともに井上科学振興財団へ一括して提出願います。

提出書類：

- （1）推薦書 本文……………1部
※全4ページ。所定の様式による。用紙は井上科学振興財団ホームページよりダウンロード可
- （2）同上 写し……………2部
- （3）博士論文の概要……………2部
※形式自由。A4版で1～2ページ。冒頭に、論文題目と大学・研究科・氏名を記入
※この「概要」は、「（1）推薦書」（4ページ）とは別です。ご注意下さい。

(4) 博士論文……………2部

※審査終了後、返却します。写しでも可

締切期日：

平成20年9月20日（土）（必着）

選考：

井上科学振興財団の選考委員会において選考し、理事会において決定します。選考結果は、平成20年12月中旬に推薦大学の学長に通知します。

研究奨励賞贈呈式：

平成21年2月4日（水）午後4時から 東京で開催の予定。

推薦書提出先及び連絡先：

財団法人 井上科学振興財団

〒150-0036 東京都渋谷区南平台町15-15南平台今井ビル 601

電 話： 03-3477-2738

F A X： 03-3477-2747

E-mail： inoue01@inoue-zaidan.or.jp

URL： <http://www.inoue-zaidan.or.jp/jigyoo/jigyoo01.html>

2009年度 女性科学者に明るい未来をの会 猿橋賞候補者推薦要綱

対象：

推薦締切日に50才未満で、自然科学の分野で、顕著な研究業績を収めている女性科学者

表彰内容：

賞状、副賞として賞金30万円、1件（1名）

応募方法：

所定の用紙（当会のホームページからダウンロード）に、推薦者（個人・団体、自薦も可）・受賞候補者の略歴、推薦対象となる研究題目・推薦理由(800字程度)、及び主な業績リスト（指定は1頁です。やむを得ない場合でも追加は1頁までです）を記入して、主な論文別刷10編程度（2部ずつ、コピーも可）を添え、下記推薦書類送付先までお送り下さい。

日本神経化学会の推薦をご希望の方は、当会研究助成金等候補者選考委員会宛てにご送付下さい。同委員会で選考の上、推薦候補者を決定致します。

締切日：

2008年11月30日

日本神経化学会の推薦をご希望の方は 2008年10月24日（金）必着。

推薦書類送付先：

〒247-0022 横浜市栄区庄戸 5-14-3

女性科学者に明るい未来をの会

（封筒には、「猿橋賞推薦書類」と明記して下さい。書類は、猿橋賞選考のためにのみ選考委員会などで用いられます。書類は返却致しませんのでご了承下さい）

なお、この件についての問い合わせは、下記に電子メールでお願い致します。

女性科学者に明るい未来をの会： saruhashi2008@saruhashi.net

第49回（平成20年度）東レ科学技術賞候補者推薦要領**候補者の対象：**

日本神経化学会が関与する分野で、下記のいずれかに該当するもの

- (1) 学術上の業績が顕著な方
- (2) 学術上重要な発見をした方
- (3) 効果が大きい重要な発明をした方
- (4) 技術上重要な問題を解決して、技術の進歩に大きく貢献した方

年齢は問いません。

科学技術賞：

1件につき、賞状、金メダルおよび賞金500万円（2件前後の予定）

推薦者：

東レ科学振興会指定の学協会の代表者および東レ科学振興会の推薦委員（非公開）

候補者推薦件数：

1学協会から2件以内および1推薦委員から1件以内

推薦手続：

所定の推薦書用紙に選考に必要な事項を正確に記載し、東レ科学振興会あて1部ご送付願います。

日本神経化学会の推薦をご希望の方は、当会研究助成金等候補者選考委員会宛てにご送付下さい。

同委員会で選考の上、推薦候補者を決定致します。

推薦締切期日：

平成20年10月10日（金）必着

日本神経化学会の推薦をご希望の方は 平成20年9月1日（月）必着。

選考方法：

下記委員からなる選考委員会において選考し、評議員会において受賞者を決定します。

選考委員 末松 安晴（委員長） 浅島 誠 新宮 秀夫 清水 孝雄
本河 光博 奈良坂紘一 竹縄 忠臣 本島 修 松本洋一郎

選考結果は平成21年2月下旬に推薦者（学協会の代表者および東レ科学振興会の推薦委員）に通知します。

科学技術賞の贈呈：

平成21年3月の予定

- (注) a. 推薦を受けた候補者は、その年度および次の年度にわたって選考の対象としております。
したがって平成19年度に推薦された候補者については、平成20年度候補者として再度推薦の必要はありません。ただし平成19年度の推薦以降において、追加すべき顕著な業績又は発表や受賞があり加筆が必要な場合は、再提出いただいても結構です。
- b. 受賞者は、原則として1件1人としします。特に複数であることを必要とするときはそれらの研究者の寄与が同等であることを示して下さい。ただし、この場合でも1件として取り扱います。
- c. この科学技術賞は、所得税法（第9条第1項第13号二）の規定により非課税となっています。
- d. 推薦書の用紙は、下記ホームページからダウンロードできます。
財団法人 東レ科学振興会 <http://www.toray.co.jp/tsf/index.html>

第49回（平成20年度）東レ科学技術研究助成候補者推薦要領

候補者の対象：

日本神経化学会が関与する分野で国内の研究機関において自らのアイディアで萌芽的研究に従事しており、今後の研究の成果が科学技術の進歩、発展に貢献するところが大きいと考えられる若手研究者（原則として推薦時45才以下）従来の研究の多くが海外で行われていても差し支えありません。

研究助成金：

総額1億3千万円。1件3千万円程度まで10件程度とします。

推薦者：

東レ科学振興会指定の学協会の代表者および東レ科学振興会の推薦委員（非公開）

候補者推薦件数：

1学協会から2件以内および1推薦委員から1件以内

推薦手続：

所定の推薦書用紙に、選考に必要な事項を正確に記載し、東レ科学振興会あて1部ご送付願います。

日本神経化学会の推薦をご希望の方は、当会研究助成金等候補者選考委員会宛てにご送付下さい。
同委員会にて選考の上、推薦候補者を決定致します。

推薦締切期日：

平成20年10月10日（金）必着

日本神経化学会の推薦をご希望の方は 平成20年9月1日（月）必着。

選考方法：

下記委員からなる選考委員会において、提出された書類により一次選考を行い、さらに面接による二次選考を経て、評議員会において決定します。なお、二次選考対象の助成候補者の方は、平成20年12月下旬に面接をさせていただきます。

選考委員 末松 安晴（委員長） 浅島 誠 新宮 秀夫 清水 孝雄
本河 光博 奈良坂紘一 竹縄 忠臣 本島 修 松本洋一郎

選考結果は平成21年2月下旬に推薦者（学協会の代表者および東レ科学振興会の推薦委員）に通知します。

研究助成金の贈呈：

平成20年3月の予定

- （注） a. 東レ科学振興会では専門分野の異なる選考委員全員が選考に関与します。したがって、日本神経化学会内での選考過程で用いられた推薦書の内容が異なる分野の研究者にわかりにくいと感じられる場合は、候補者が、被推薦決定後に日本神経化学会代表者の了解を得て、推薦書の表現を手直しされても結構です。
- b. この研究助成は、研究目的を達成するために有効に使用されるものであれば、どのような使途で申請されても結構です。ただし、原則として間接経費、管理経費、共通経費は助成の対象になりません。また、助成金受領決定後、その使途を変更される場合は、事前に東レ科学振興会の承諾を得ていただきます。
- 助成研究の期間は、特別の事情がない限り助成金受領決定の次年度から3年以内とします。
- c. 助成金の受領者は、研究終了時まで毎年「助成研究年次報告書」を、また研究終了時に、「助成研究終了報告書」を提出していただきます。
- d. この助成金は、所得税法（第9条第1項第13号ニ）の規定により非課税となっています。
- e. 推薦書の用紙は、下記ホームページからダウンロードできます。
- 財団法人 東レ科学振興会 <http://www.toray.so.jp/tsf/index.html>

（財）ブレインサイエンス振興財団
第23回塚原仲晃記念賞受賞候補者推薦要領

趣旨：

生命科学の分野において優れた独創的研究を行っている45歳以下の研究者（国内外を問わない）に対して塚原仲晃記念賞を贈呈します。

褒賞金：

贈呈件数は原則として1件とし、賞碑ならびに副賞（100万円）を贈呈します。

推薦締切日：

平成20年10月17日（金）とします。

日本神経化学会の推薦をご希望の方は、平成20年9月12日（金）当会研究助成金等候補者選考委員会宛てにご送付下さい。同委員会では選考の上、推薦候補者を決定致します。

推薦者：

候補者の業績についてよく知る人。(1 推薦者から1件に限ります。)

推薦方法：

所定の推薦書に必要事項を記入し、ブレインサイエンス振興財団に提出して下さい。

推薦書はブレインサイエンス振興財団のHPから取り出せます。

URL：http://www.bs-f.jp/

審査方法：

ブレインサイエンス振興財団の選考委員会において審査選考し、理事会において決定します。

審査結果の通知：

平成21年3月末までに推薦者および受賞者あて通知します。

賞碑ならびに副賞の贈呈：

贈呈決定者に対して別途通知します。

推薦書提出先および連絡先

財団法人 ブレインサイエンス振興財団

〒104-0028 東京都中央区八重洲 2-6-20

電話 (03) 3273-2565 (直通)

(財) ブレインサイエンス振興財団 第23回研究助成候補者応募要領

趣旨：

ブレインサイエンスの広い分野における研究に対して助成を行いますが、特に、下記の各項について、脳のメカニズムを解明する独創的な研究計画の助成に重点をおきます。

研究分野は実験研究のみならず、理論、モデリング研究をも含みます。

- (1) 神経化学の基礎研究
- (2) 脳への工学からのアプローチ
- (3) 脳への物理学からのアプローチ

研究助成額：

助成額は1件100万円、助成件数は8～12件とします。

応募締切日：

平成20年10月17日(金)とします。

日本神経化学会の推薦をご希望の方は、平成20年9月12日(金)までに当会研究助成金等候補者選考委員会宛てにご送付下さい。同委員会で選考の上、推薦候補者を決定致します。

応募方法：

所定の応募用紙に必要事項を記入し、ブレインサイエンス振興財団に提出して下さい。

(研究についての問い合わせ可能な所属長名を明記して下さい。)

応募用紙：

応募用紙はブレインサイエンス振興財団HPから取り出せます。

URL：http://www.bs-f.jp/

審査方法：

ブレインサイエンス振興財団の選考委員会において審査選考し、理事会において決定します。

採否の通知：

平成21年3月末日までに応募者あて採否を通知します。

助成金の交付：

平成21年6月末日までに助成決定者の指定口座に振り込みます。

助成金の使途：

助成金は応募用紙記載の通り使用することを原則とします。なお、経理報告書を平成22年5月末日までに提出して下さい。

成果の報告：

平成22年5月末日までに、研究成果報告書を提出して下さい。また、助成金による研究を専門誌に載せる場合には、「財団法人ブレインサイエンス振興財団（英文＝Brain Science Foundation）の助成による」旨を書き添えて下さい。

応募用紙提出先および連絡先：

財団法人 ブレインサイエンス振興財団
〒104-0028 東京都中央区八重洲 2-6-20
電話（03）3273-2565（直通）

（財）ブレインサイエンス振興財団 第22回海外派遣研究助成候補者応募要領**趣旨：**

我が国におけるブレインサイエンスの研究の促進を図るため、国際学会、シンポジウム等への参加、あるいは短期間（6ヶ月以内）の共同研究のための研究者の海外派遣を助成します。但し、平成21年4月から平成22年3月の間に出発できるものに限りします。

助成予定額：

1件あたりの助成額は往復の航空運賃を主とし、30万円までを限度として必要額を若干件数助成します。

応募締切日：

平成21年1月16日（金）とします。

日本神経化学会の推薦をご希望の方は、平成20年12月5日（金）までに当会研究助成金等候補者選考委員会宛てにご送付下さい。同委員会にて選考の上、推薦候補者を決定致します。

応募方法：

所定の応募用紙に必要事項を記入し、ブレインサイエンス振興財団に提出して下さい。

○学会、シンポジウム等の問い合わせ可能な所属長の名前を明記して下さい。

○受入先の承諾書を添付して下さい。

(学会、シンポジウム等参加の場合は参加証明書または招待状の写し。短期の共同研究の場合は受入機関または共同研究者の手紙の写し。)

応募用紙：

応募用紙はブレインサイエンス振興財団のHPから取り出せます。

URL：<http://www.bs-f.jp/>

審査方法：

ブレインサイエンス振興財団の選考委員会において審査選考し、理事会において決定します。

採否の通知：

平成21年3月末日までに応募者あて採否を通知します。

助成金の交付：

平成21年4月以降出発時期に応じて助成決定者の指定口座に振り込みます。

助成金の使途：

助成金は応募用紙記載のとおり使用することを原則とします。

成果の報告：

帰国後2ヶ月以内に派遣の成果についての報告書及び派遣助成金の使途内訳を提出して下さい。

応募用紙提出先および連絡先：

財団法人ブレインサイエンス振興財団

〒104-0028 東京都中央区八重洲 2-6-20

電話 (03) 3273-2565 (直通)

(財)ブレインサイエンス振興財団 第22回海外研究者招聘助成候補者申込要領

趣旨：

ブレインサイエンス研究分野において、独創的テーマに意欲的に取り組んでいる外国人研究者の短期間(3ヶ月以内)の招聘を助成します。

ただし、平成21年4月1日から平成22年3月31日の間に招聘するものとします。

また、助成金は招聘する受入責任者に交付します。

招聘助成予定額：

1件あたりの助成額は往復の航空運賃を主とし、30万円までを限度として必要額を若干件数助成します。

申込締切日：

平成21年1月16日（金）とします。

日本神経化学会の推薦をご希望の方は、平成20年12月5日（金）までに当会研究助成金等候補者選考委員会宛てにご送付下さい。同委員会にて選考の上、推薦候補者を決定致します。

申込方法：

所定の申込書に必要事項を記入し、ブレインサイエンス振興財団に提出して下さい。

申込書はブレインサイエンス振興財団 HP から取り出せます。

URL：http://www.bs-f.jp/

審査方法：

ブレインサイエンス振興財団の選考委員会において審査選考し、理事会において決定します。

採否の通知：

平成21年3月末日までに申込者あて採否を通知します。

助成金の交付：

平成21年4月から必要に応じて受入責任者あて指定口座に振り込みます。

助成金の使途：

助成金は申込書記載のとおり使用することを原則とします。

成果の報告：

招聘後2ヶ月以内に、招聘の成果報告書及び招聘助成金の使途内訳を提出して下さい。

申込書提出先および連絡先：

財団法人ブレインサイエンス振興財団

〒104-0028 東京都中央区八重洲 2-6-20

電話（03）3273-2565（直通）

【セミナー・講習会】**千里ライフサイエンスセミナー****「機能的 non-coding RNA - 古典的なセントラルドグマへの挑戦」**

日 時： 平成20年11月11日（火）10:00～17:00

場 所： 千里ライフサイエンスセンタービル 5階ライフホール

主 催： 財団法人千里ライフサイエンス振興財団

着眼点： 生物の複雑さを生み出す仕組みは蛋白質の種類や数にあるのではないことが明らかになってきた。では、複雑さを生み出す仕組みとはなにか？私達のゲノムの大半は転写され非蛋白質コード領域に由来する様々な RNA (non-coding RNA) が生み出されている。このようなRNAが蛋白質の発現を複雑に制御し連携させることで

高度な回路の形成を可能にし、これこそが生物の複雑さを生み出しているという新しいコンセプトが誕生した。

コーディネータ：慶應義塾大学医学部分子生物学教室 塩見 春彦
産業技術総合研究所バイオメディシナル情報研究センター 廣瀬 哲郎

プログラム： 1. はじめに
慶應義塾大学医学部分子生物学教室 教授 塩見 春彦
2. 哺乳類 non-coding RNA の細胞内動態と機能
産業技術総合研究所バイオメディシナル情報研究センター 研究チーム長 廣瀬 哲郎
3. 機能性 RNA の配列情報解析
東京大学大学院新領域創成科学研究科 教授 浅井 潔
4. 小分子 non-coding RNA による転移因子の抑制
慶應義塾大学医学部分子生物学教室 教授 塩見 春彦
5. 代謝制御と小分子 RNA
名古屋大学大学院理学研究科 教授 饗場 弘二
6. 小分子 RNA による染色体機能制御
久留米大学分子生命科学研究所 講師 石井浩二郎
7. 小分子 RNA と植物の発生
東京大学大学院総合文化研究科 教授 渡辺雄一郎
8. おわりに
産業技術総合研究所バイオメディシナル情報研究センター 廣瀬 哲郎

参加費： 無料

定 員： 300名

申込方法： 氏名、勤務先、〒所在地、所属、電話及び FAX 番号を明記の上、郵便、FAX または E-mail で下記宛にお申込み下さい。セミナー事務局より参加証を返送致します。参加証はセミナー当日、受付で提示下さい。

申込先： (財)千里ライフサイエンス振興財団 セミナーY2係
〒560-0082 大阪府豊中市新千里東町 1-4-2
千里ライフサイエンスセンタービル8階
TEL：06-6873-2001
FAX：06-6873-2002
E-mail：tnb@senri-life.or.jp

千里ライフサイエンス技術講習会 第49回
「組み換え蛋白質生産のための細胞培養と精製技術」

日 時： 平成20年11月17日（月）午前9時から午後5時30分まで

場 所： 午前⇒千里ライフサイエンスセンタービル9階（903-905号室にて講演）
 午後⇒和研薬株式会社・大阪センター（大阪府箕面市船場東 1-12-8）

ねらい： 大腸菌を用いた組み換え発現による蛋白質の生産は、構造や機能解析のために無く
 てはならない技術だが、いわゆる難発現性蛋白質やヒト蛋白質の中には高等生物の
 発現系の採用を要求するものが多い。しかし高等生物の発現系を用いた蛋白質生産
 は、コスト、時間、ノウハウの面で初めての研究者には敷居の高いものとなっている。
 本講習会では、高等生物（動物及び昆虫）発現系を用いた生産と精製に関する
 講義と、それらを行う際に重要となる培養技術についての実地講習を中心に、大学
 や企業でのラボスケールの蛋白質生産力を高めたい研究者の役に立つ情報を提供致
 します。

コーディネータ： 高木 淳一 大阪大学蛋白質研究所 教授

プログラム：

講演（午前）

9:00 森 肇（京都工業繊維大）

バキュロ昆虫細胞系によるタンパク質発現

9:45 前仲勝美（九大生体防医研）

カイコ成虫を使った構造解析品質の蛋白質生産

10:30 加藤博章（京大薬）

動物細胞一過性発現系を用いた組み換え蛋白質の迅速・大量生産

11:15 高木淳一（阪大蛋白研）

動物細胞安定発現株の作製、培養と精製技術

12:00～13:30 昼食

実習（午後） 技術解説と実技演習 ※13:30より60分間ずつの実習を4つ行います

実習 1 バキュロウイルスを用いたタンパク質発現と大量培養

実習 2 バイオリアクター及び Bell Cell システムを用いた動物細胞の生産
 培養

実習 3 ファーマンターを用いた大腸菌の高密度培養

実習 4 アフィニティータグ抗体カラムを用いた蛋白質精製

参加費： 1日参加⇒5,000円、午前のみ参加⇒3,000円

定 員： 午前60名、午後15名

参加資格： 細胞培養・タンパク質発現に関する基礎知識を有していること。

申込方法： 参加申込みは以下の手順にしたがって行って下さい。

- ① 氏名、勤務先、所属、役職名、〒、所在地、電話、FAX 番号を明記の上、郵便、FAX または E-mail で下記宛お申し込み下さい。1日参加か午前のみのかを明示して下さい。

- ② 講習会事務局より受付の通知を返送致しますので、そこに記載した振込先口座に参加費をお振込み下さい。
- ③ 入金を確認後、通常1週間以内に領収書兼参加証をお届け致します。

申込締切： 平成20年10月24日（財団必着）
但し、定員を超過した場合は参加者の調整を行う場合があります。

主 催： 財団法人千里ライフサイエンス振興財団

協 賛： 和研薬株式会社

申込先： （財）千里ライフサイエンス振興財団 技術講習会 G49係
〒560-0082 大阪府豊中市新千里東町 1-4-2
千里ライフサイエンスセンタービル8階
TEL：06-6873-2001
FAX：06-6873-2002
E-mail：tnb@senri-life.or.jp

【ポスドク募集】

ポスドク募集 林 康紀研究室

研究内容：

海馬、大脳皮質神経回路網可塑性の分子機構の分子生物学、イメージング、電気生理学を組み合わせた解明

勤務地：

理化学研究所脳科学総合研究センター（埼玉県和光市、現在研究室はマサチューセッツ工科大学内に有りますので、一時そちらに来て頂く可能性もあります）

赴任時期：

相談可能です。

給与：

理化学研究所の規定によります。

応募方法：

履歴書と業績リスト、他適宜参考になる情報を電子メールにて御送り下さい。様式は自由です。また参照できる方3人の（博士論文指導者など）の連絡先を御知らせ下さい。

選考方法：

書類審査と推薦書により候補者を選んだ上で、セミナーをしていただき決定します。

連絡先：

yhayashi@mit.edu

参考：

- Okamoto, K., Nagai, T., Miyawaki, A. & Hayashi, Y. (2004) **Nat Neurosci** 7, 1104-1112
- Nakagawa, T., Futai, K., Lashuel, H.A., Lo, I., Okamoto, K., Walz, T., Hayashi, Y., & Sheng, M. **Neuron**. 44, 453-467
- Takao, K., Okamoto, K., Nakagawa, T., Neve, R. L., Nagai, T., Miyawaki, A., Hashikawa, T., Kobayashi, S., & Hayashi, Y. (2005). **J Neurosci** 25, 3107-3112
- Hayashi, M.K., Ames, H., & Hayashi, Y. (2006) **J. Neurosci.** 23, 8492-8501
- Futai, K., Kim, KJ., Hashikawa, T., Scheiffele, M., Sheng, M., & Hayashi, Y. (2007) **Nat. Neurosci.** 10, 186-195
- Okamoto, K., Narayanan, R., Lee, S.-H., Murata, K., & Hayashi, Y. (2007) **Proc. Natl. Acad. Sci.** 104, 6418-6423

日本神経化学会 賛助会員 (50音順)

旭化成ファーマ株式会社

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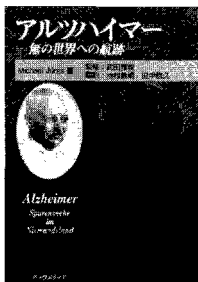
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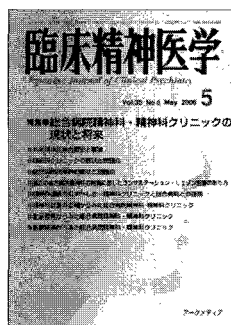
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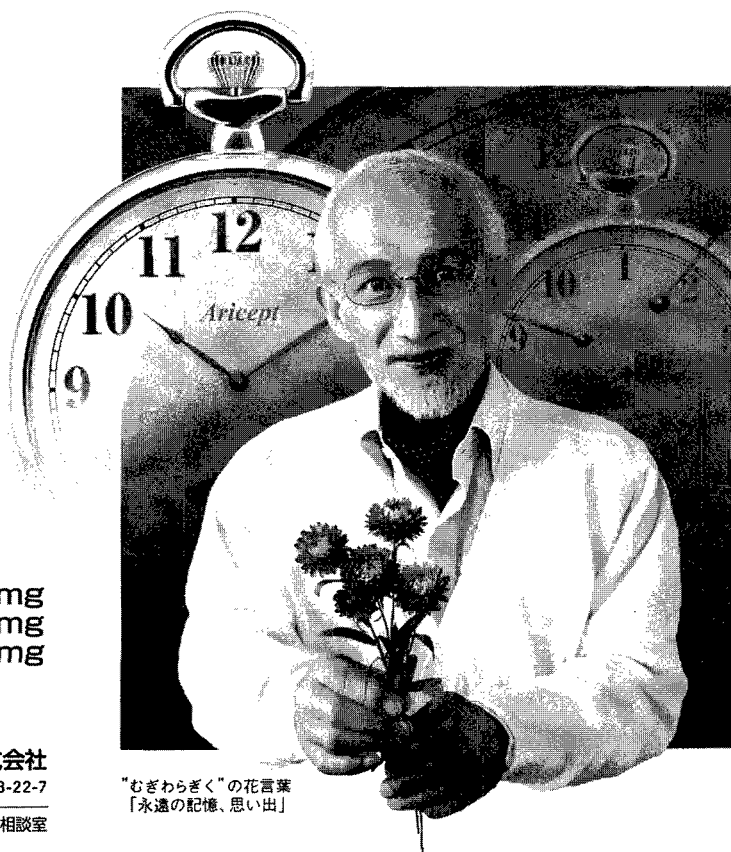


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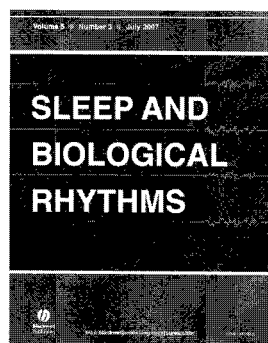
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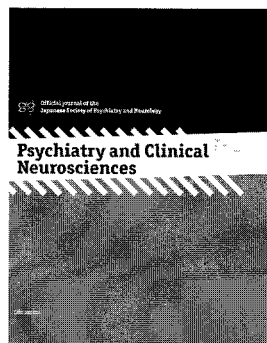
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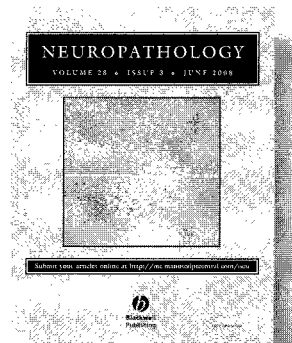
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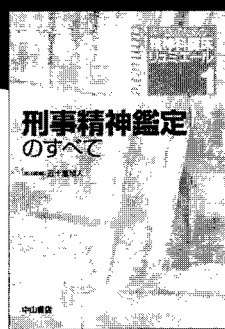
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2007年11月作成

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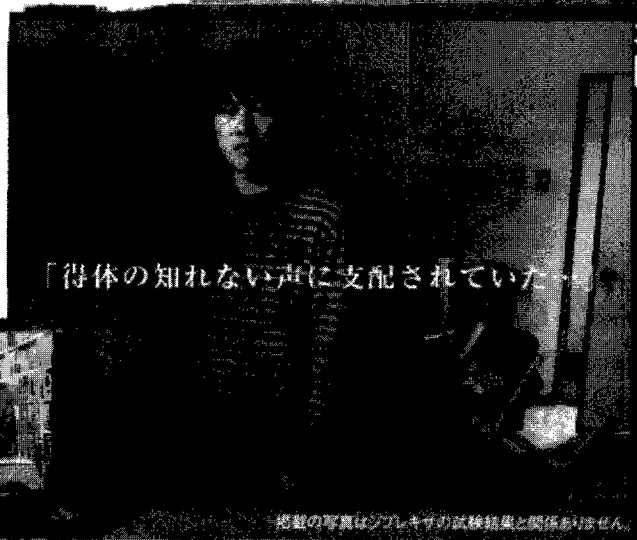
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薬価基準収載



発売〔資料請求先〕

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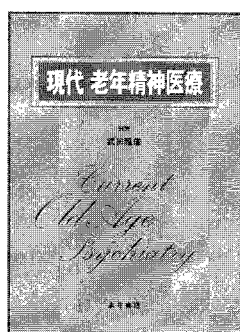
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MGA42 2008.02



高齢者医療に携わる方々の必携書

現代 老年精神医療

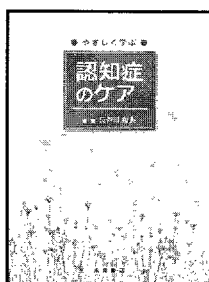
編集：武田 雅俊

大阪大学大学院医学系研究科
情報統合医学講座精神医学 教授

定価 13,650円 (本体 13,000円+税5%)

B5判 650頁 図253 表250

精神疾患はもちろん高齢者に多発する疾患をすべての診療科にわたって取り上げる。これまでの精神医学の教科書の枠組を超越した、650頁に及ぶ現代老年医療の決定版。臨床医学の各項目についてはほとんどすべての診療科の専門家に執筆を依頼。基礎研究者から臨床家、医療従事者から介護・福祉の専門家まで、執筆者は各領域を代表する多彩な顔ぶれで、読み応えのある最新知見を網羅する。



やさしく学ぶ 認知症のケア

編著：長谷川 和夫

浴風会認知症介護研究・
研修東京センター センター長・
聖マリアンナ医科大学 名誉教授定価 3,150円
(本体 3,000円+税5%)
B5判・190頁・図58・表35

実際に認知症の人々に向き合い多様な問題に直面している方々を対象に、医師・ケアマネジャー・社会福祉士などの専門家が、認知症の医療はもちろんのこと、認知症のケアの実際について大局的に捉えた実践的テキスト。一人ひとりの個別のかかわり(個人の物語)を重視する「認知症ケア」を真に理解し、どう支えて行けばよいかを、12の章を設け、わかりやすく懇切に教えてくれる。



名医に学ぶ 認知症診療のこれまでとこれから

著 長谷川 和夫

浴風会 認知症介護研究・
研修東京センター センター長定価 2,940円
(本体 2,800円+税5%)
A5判・142頁・図32・表28

「長谷川式スケール」の考案者である著者が、長年の臨床経験に基づき「認知症」のすべてを披露!「なぜ?」「どうして?」「どうすれば?」の答えがこの1冊に凝縮。臨床医・研究医、ケア専門職、そして家族の方々にとっても必読の書。

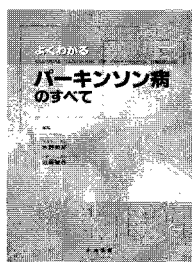


よくわかる アルツハイマー病

実際にかかわる人のために

編集 中野 今治 自治医科大学 教授
水澤 英洋 東京医科歯科大学 教授定価 7,140円
(本体 6,800円+税5%)
B5判・396頁・図106・表98

臨床像の克明な解説と危険因子を探索する医療の現状、また薬物療法の先進知見や治療法、リハビリ、ターミナルケアへの対応、さらに行政・法律関係者による社会的取り組みなど、アルツハイマー病のすべてを網羅。



よくわかる パーキンソン病のすべて

編集 水野 美邦 順天堂大学名誉教授
近藤 智善 和歌山県立医科大学 教授定価 6,930円
(本体 6,600円+税5%)
B5判・346頁・図63・表68

パーキンソン病治療の専門医はもちろん、専門家でない方々にも、特徴的な神経症状、診断法、治療法の実態を、詳しい中にも要点を強調した、わかりやすい記述によってすぐに把握できるよう工夫。この一書で、パーキンソン病に関する最新知識がわかる。



永井書店

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精神科専門医・研修医待望のアドバンスクラスレベルの教科書

Advanced Psychiatry

脳と心の精神医学

大阪大学大学院教授 自治医科大学教授 九州大学大学院教授
著 武田雅俊・加藤 敏・神庭重信

NBM と EBM が統合されたわが国独自の精神医学の確立をゴールにすえて、内外の重要誌 (AGP, AJP, BJP, 精神誌等) の最新の知見に目を通した上でのオリジナリティあふれる書下ろし。

A5変型判・440頁 定価 7,140円 (本体6,800円+税5%)

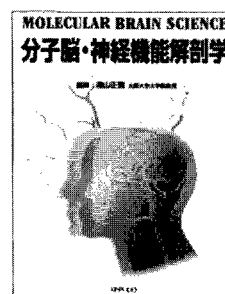


分子脳・神経機能解剖学

編集 遠山正彌 大阪大学大学院教授

若い研究者に分子レベルの観点から「脳・神経研究の化学的基本的知識」をわかりやすく提供。また「脳・神経研究の最先端と今後の展望」を第一線の国際的研究者によって示しており、今後の研究の道しるべとすることができる。

A4変型判・692頁 定価 10,500円 (本体10,000円+税5%)



季刊誌『脳21』

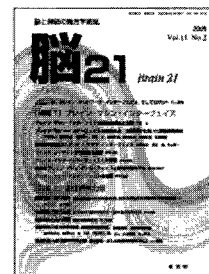
基礎から臨床まで広範囲な脳科学を統括！
立体的・総合的把握のために！！

編集委員 (五十音順)

木山博資, 久保 武, 佐古田三郎, 塩坂貞夫, 重永凱男, 武田雅俊,
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俣野彰三, 山下俊英, 吉峰俊樹

発行: 年4回 (1月, 4月, 7月, 10月)

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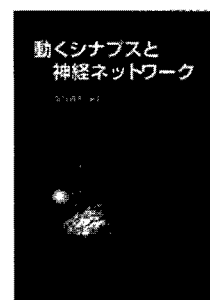


動くシナプスと 神経ネットワーク

編集 塩坂貞夫 奈良先端科学技術大学院大学

分子動態, 形態動態解析のための新しいアプローチ, 時々刻々と変化するミクロ, ナノレベルの構造変化を観るための理論と方法. シナプスの動きの科学を分かりやすく解説。

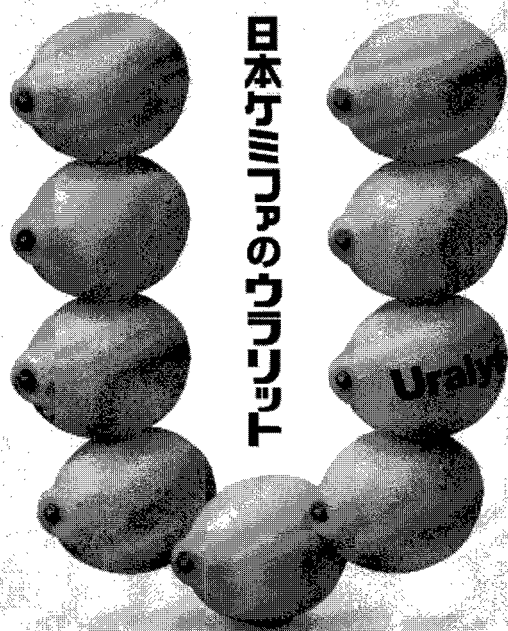
B5判・192頁 定価 7,560円 (本体7,200円+税5%)



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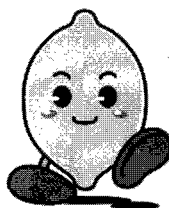
アルカリ化療法剤—酸性尿・アシドーシス改善—
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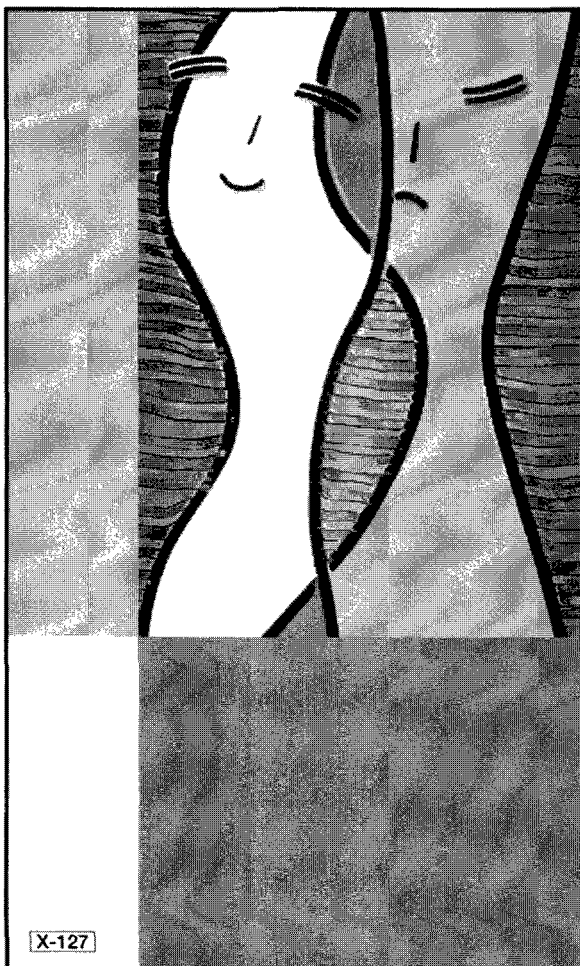
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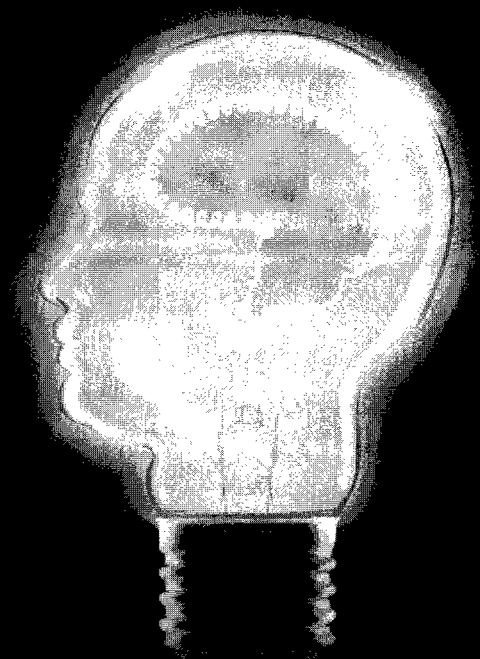
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ニセルゴリンとして、通常成人1日量15mgを3回に分けて(参考:1日量剤形換算)
経口投与する。なお、年齢、症状により適宜増減する。

	成人1日量(15mg)
サアミオン錠5mg	3錠
サアミオン散1%	1.5g

用法・用量に関連する使用上の注意

本剤の投与期間は、臨床効果及び副作用の程度を考慮しながら慎重に決定するが、投与12週で効果が認められない場合には投与を中止すること。

使用上の注意

1.副作用 臨床試験(治験):総症例1,017例中、副作用が報告されたのは28例(2.75%)で、主な副作用は食欲不振(0.39%)、下痢(0.39%)、便秘(0.29%)等であった。使用成績調査(1988年6月～1994年3月):総症例11,939例中、副作用が報告されたのは56例(0.47%)で、主な副作用は悪心(0.08%)、発疹(0.06%)、頭痛(0.05%)、AST(GOT)・ALT(GPT)の上昇(0.05%)、食欲不振(0.03%)、便秘(0.03%)、腹痛(0.03%)等であった。副作用が認められた場合には、投与を中止するなど適切な処置を行うこと。消化器 0.1%未満:食欲不振、下痢、便秘、悪心、腹痛、口渇 肝臓 頻度不明:肝機能障害 循環器 0.1%未満:めまい、立ちくらみ、動悸、はてり 精神神経系 0.1%未満:眠気、倦怠感、頭痛、耳鳴、不眠 過敏症 0.1%未満:発疹、蕁麻疹、そう痒 2.高齢者への投与 一般に高齢者では生理機能が低下しているので減量するなど注意すること。3.妊婦、産婦、授乳婦等への投与 1)妊婦又は妊娠している可能性のある婦人には、治療上の有益性が危険性を上まわると判断される場合にのみ投与すること。〔動物実験(ラット)で次世代の発育抑制が報告されている。〕2)授乳中の婦人への投与は避けることが望ましいが、やむを得ず投与する場合は授乳を避けさせること。〔動物実験(ラット)で乳汁中へ移行することが報告されている。〕4.小児等への投与 小児等に対する安全性は確立していない(使用経験がない)。

●使用上の注意については、添付文書をご参照ください。

●使用上の注意の改訂に十分ご注意ください。

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田辺三菱製薬株式会社
大阪市中央区道修町3-2-10

2008年2月作成

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2008年2月作成

あなたは血管性認知症をどのようにとらえていますか？

血管性認知症

遂行機能と社会適応能力の障害

本体(3,400円)+税／B5判 232頁

東北大学教授
目黒謙一 著

認知症を語るとき、血管性認知症を知らなければ何も語れないことは専門家ならば自明の理である。Bio
ならば ...

その重要と言われている血管性認知症について専門的に記された著書が不思議なことにいままで一冊もなかった ...
だからこそ本書が「誕生」したのである。

血管性認知症の理解には局在論的な発想ではなく脳全体をみるダイナミックな思考が必要である。

本書は、認知症の概念から、疫学、神経基盤、神経心理症候学、代表的な症例、包括的システム、さらに軽度認知障害の問題までを、内外の最新知見を取り入れて詳解している。

新刊!!



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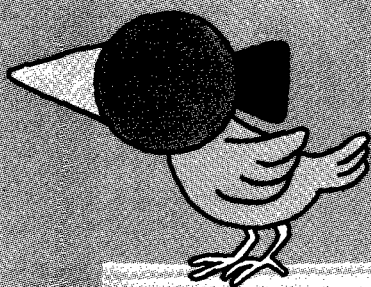
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<http://glaxosmithkline.co.jp>
<http://paxil.jp>

プロモーション提携

吉富薬品株式会社

大阪市中央区淡路町 2-5-6

2008年1月作成



抗精神病剤 薬価基準収載
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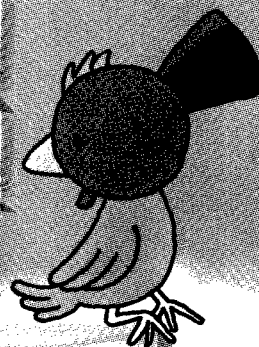
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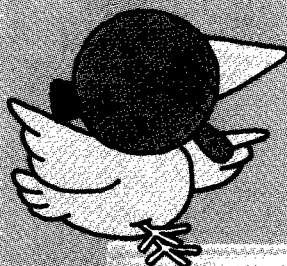
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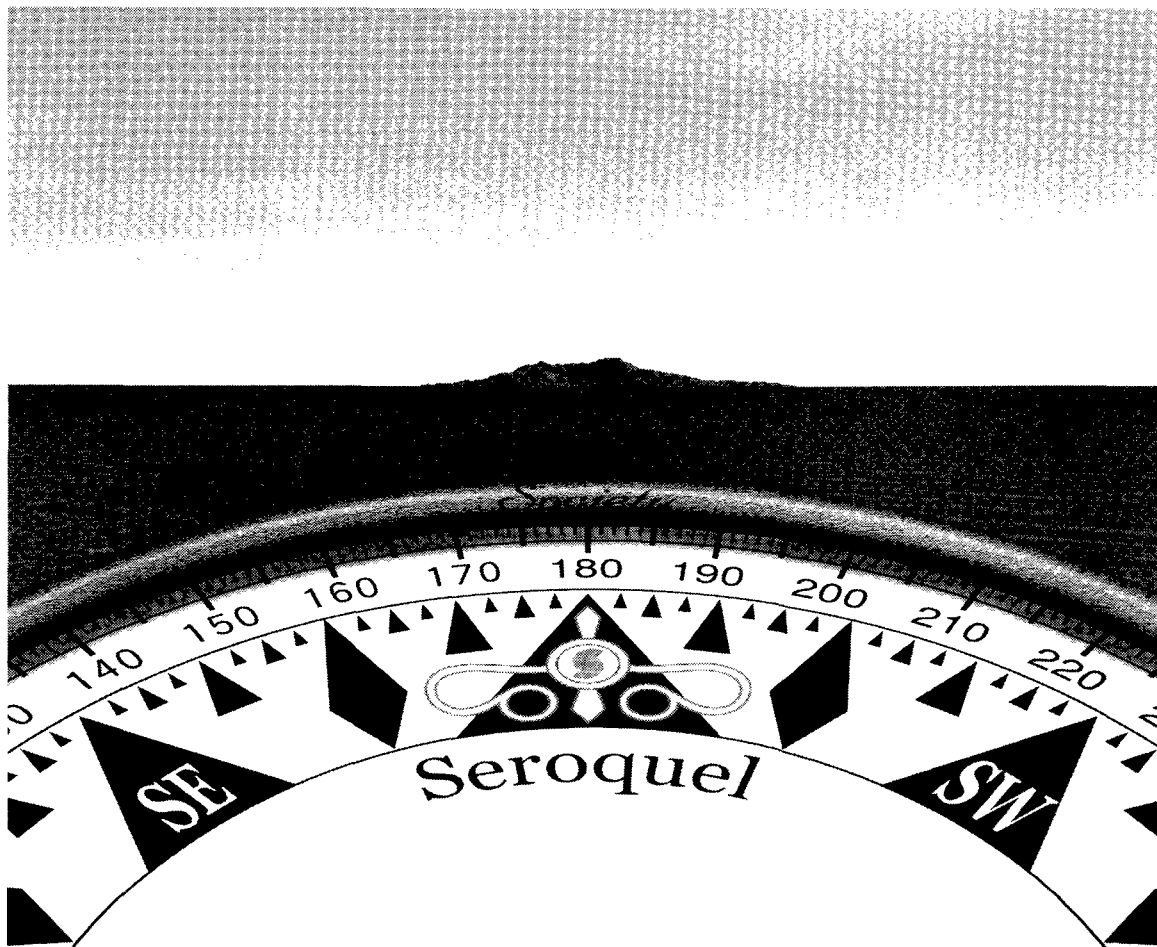
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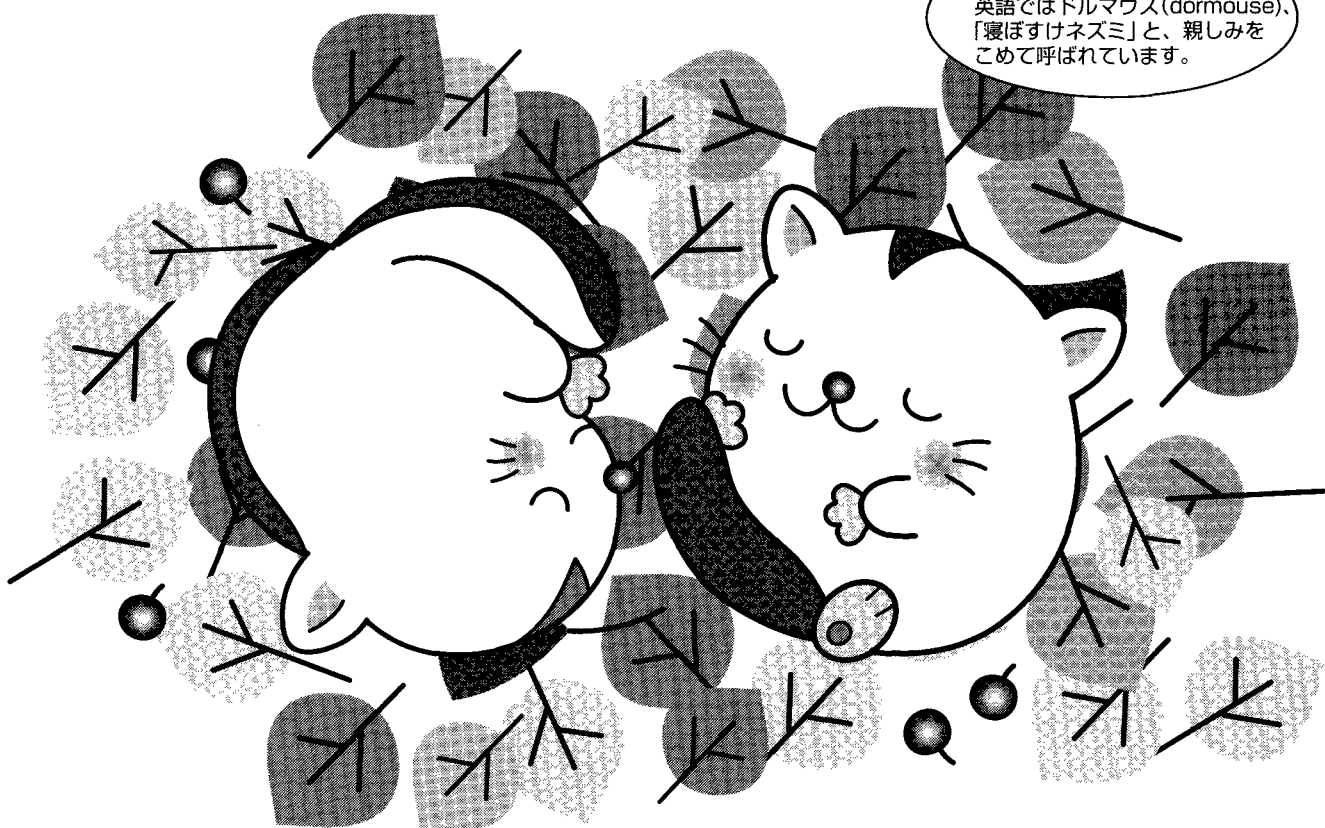
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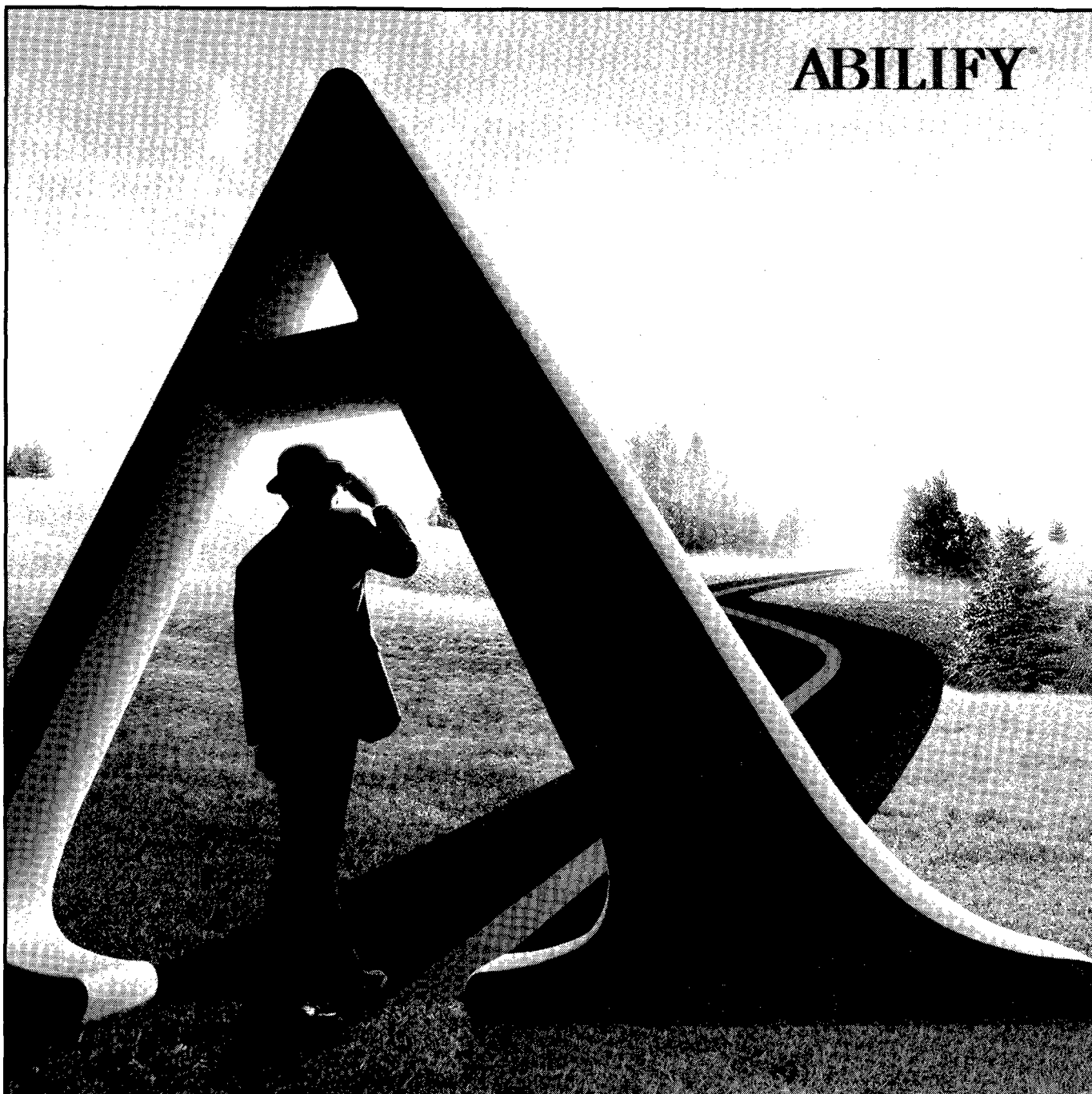


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医学・医療のあらゆる分野を網羅した医学書院「医学書院 医学大辞典」を業界初収録*しています。また、ほぼすべての市販薬を網羅した「治療薬マニュアル」、2008年2月に6年ぶりの改訂版となりましたメジカルビュー社「ステッドマン医学大辞典 改訂第6版」を収録している、医学スペシャリストのための電子辞書です。

文字や図版・表がはっきり見やすい「くつきリアル®液晶」を搭載し、「医学書院 医学大辞典」から約2,300点「ステッドマン医学大辞典」から約550点の図版や表を収録しています。

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ネイティブ発音箇所も充実しており、「ステッドマン医学大辞典」の医学用語約56,000語、「ジーニアス英和大辞典」の一般英単語約60,000語を発音します。

新版改訂となった「広辞苑第六版」、世界で高い評価を得ている「ブリタニカ国際大百科電子辞書対応小項目版」など、電子辞書の基本的なコンテンツも充実しており、普段の生活にも役立ちます。

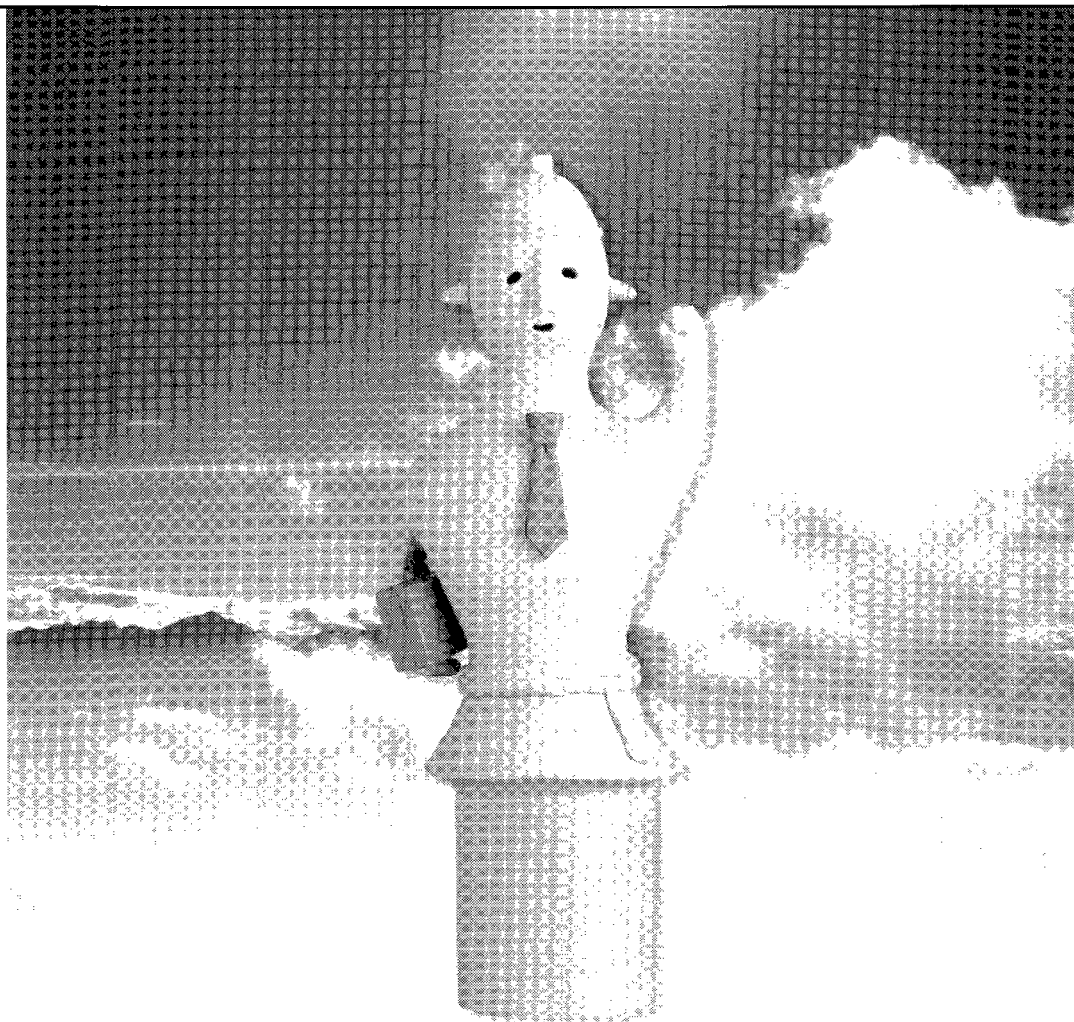
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