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神経化学

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第52回日本神経化学会(伊香保)大会

抄録号

連携開催：神経組織の成長・再生・移植研究会 第24回学術集会

平成21年6月

目 次 Contents

ご挨拶 Greetings	47
大会委員一覧 Committee Members	48
交通案内 Access	49
会場周辺図 Neighboring Guide Map	49
会場案内図 Floor Guide	50
大会日程概要 Program at a glance	51
学会の参加受付 Information for Participants	58
口演発表要項 Information for Oral Sessions	61
ポスター発表要項 Information for Poster Sessions	62
学会からのお知らせ Announcements from the Society	63
理事会議事録 Minutes of the Board Meeting	64
プログラム	71
神経化学会－GRT研究会連携オープンシンポジウム・ISN シンポジウム	
日本神経化学会－日本生物学的精神医学会合同シンポジウム	
若手奨励賞シンポジウム・シンポジウム	
一般口演・ポスター発表・ランチョンセミナー	
Program	109
JSN - GRT Joint Open Symposium・ISN Symposium	
JSN - JSBP Joint Symposium	
Young Scientists Lectureship Award Symposium・Symposia	
Oral Sessions・Poster Sessions・Luncheon Seminars	
神経化学の若手研究者育成セミナー概要 Information for Training Seminar for Students	
	155
抄 録 Abstracts	161
神経化学会－GRT研究会連携オープンシンポジウム	
JSN - GRT Joint Open Symposium	163
ISN シンポジウム ISN Symposium	164
日本神経化学会－日本生物学的精神医学会合同シンポジウム	
JSN - JSBP Joint Symposium	165
シンポジウム Symposia	166
一般口演 Oral Sessions	187
ポスター発表 Poster Sessions	210
人名索引 Author Index	225
キーワード索引 Subject Index	237
学会掲示板	243
賛助会員	258
謝辞	259

2009 年 6 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 52 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： 2009 年 6 月 22 日（月） 12：40～13：30

場 所： 伊香保温泉 ホテル天坊 1 階 A 会場「キング」

議 題（予定）：

1. 理事長報告	10. 同監査報告
2. 選挙結果報告	11. 2010 年度予算の件
3. 庶務報告	12. 監事選任の件
4. 会計報告	13. 評議員選任の件
5. 出版・広報報告	14. 名誉会員選任の件
6. プログラム編成報告	15. 会則・細則変更の件
7. 各種委員会報告	16. 次期大会の件
8. 2009 年度奨励賞選考結果報告	17. その他
9. 2008 年度決算の件	

以上

（切り離して「投函ください」）



2009 年
日 本 神 經 化 学 会
総 会

委 任 状

（ご欠席の方はご記入ください）

2009 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。

2009 年 月 日

所 属

氏 名

㊞

郵便はがき

160-8792

376

(財)国際医学情報センター内

東京都新宿区信濃町35番地
信濃町煉瓦館

日本神経化学会行

料金受取人払郵便

新宿支店承認

6300

差出有効期限
平成22年4月
30日まで
(切手不要)



第 52 回 日本神経化学会(伊香保)大会 抄録集

会 期：2009年6月21日（日）～24日（水）
会 場：伊香保温泉 ホテル天坊
大会長：田代 朋子（青山学院大学理工学部 化学・生命科学科）

<大会事務局>

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TEL : 03-3496-6950 FAX : 03-3496-2150

E-mail : jsn52@gakkai.co.jp

<大会 URL > <http://www.gakkai.co.jp/jsn52>

ご挨拶

第 52 回日本神経化学会大会は、神経組織の成長再生移植研究会（GRT 研究会）第 24 回学術集会との連携のもと、群馬県伊香保温泉で開催の運びとなりました。私がかつて 10 年間を過ごしました群馬大学医学部の諸先生方の全面的なご協力により、この会が実現できましたことに深く感謝しております。

本大会では、GRT 研究会との連携オープンシンポジウム、国際神経化学会の共催による ISN シンポジウム、日本生物学的精神医学会との合同シンポジウムなどの特別シンポジウムをはじめ、会員提案によるタイムリーなシンポジウムが企画され、多数の非会員シンポジストをお迎えしております。

会員相互のコミュニケーションを大切に、「顔の見える学会」を目指す本学会の特徴の一つは、「一般口演を重視する」ことです。一演題あたり 20 分という十分な時間を取り、会場での討論を大切にしてきました。今大会では、この伝統を守るとともに、二つのことを試みました。一つは、会員からの公募提案によるシンポジウムの中に、一般演題から数題ずつ選んで組み込んでいただいたことです。二つ目は、一般演題の中で特に数が多く、内容的にも充実していた分野から、新たにシンポジウムを一つ作ったことです。時間的制約の中で、プログラム委員の皆さま、シンポジウム・オーガナイザーの皆さまの多大なご協力を得て実現したこの二つの試みにより、参加して下さる会員の方々の意向を少しでも反映することができたのではないかと考えております。

本学会のもう一つの誇るべき特徴は、「次世代の育成」に力を注いできたことにあります。現在の学会を担っておられる会員の多くは、神経化学会の口演発表で「鍛えられた」経験をお持ちだと思います。本大会でも多くの大学院生が初めての口演あるいはポスター発表を経験されることでしょう。会員の皆さまには、活発な討論を通して次世代の育成に参加していただけますようお願いします。また、本大会では、理事会のバックアップのもと、昨年年第 51 回大会で武田雅俊先生がスタートして下さった「若手育成セミナー」を引き継ぎ、育てる努力を続けております。講師を引き受けて下さった先生方、学生を送り出して下さった先生方とともに、「若手育成セミナー」が神経化学会の新たな伝統として定着できるよう、皆さまのご協力をお願い致します。

1980 年・第 23 回大会以来の温泉地での開催です。参加される皆さまには、大いに楽しみつつコミュニケーションを深め、新たな連携の芽をみつけていただけますようお願いしております。

第 52 回日本神経化学会大会

大会長 田代朋子（青山学院大学理工学部 化学・生命科学科）

大会委員一覧

大会長

田代 朋子 青山学院大学理工学部 化学・生命科学科

組織委員会

組織委員長	石崎 泰樹	群馬大学
	石川 良樹	群馬大学
	井上 順雄	首都大学東京
	熊倉鴻之助	上智大学
	児島 伸彦	群馬大学
	小濱 一弘	群馬大学
	白尾 智明	群馬大学
	高橋 正身	北里大学
	久永 眞市	首都大学東京
	三國 雅彦	群馬大学

プログラム委員会

五十嵐道弘	新潟大学
岡野 栄之	慶應義塾大学
木山 博資	大阪市立大学
小泉 修一	山梨大学
高坂 新一	国立精神・神経センター
関野 祐子	東京大学
武井 延之	新潟大学
辻 省次	東京大学
西川 徹	東京医科歯科大学
橋本 亮太	大阪大学
馬場 広子	東京薬科大学
古市 貞一	理化学研究所
和田 圭司	国立精神・神経センター
和中 明生	奈良県立医科大学

(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 ———— 高崎駅 ———— 渋川駅 ———— 見晴下バス停 下車
 約 50 分 約 20 分 約 20 分
 <上越新幹線> <上越線> <路線バス>

上野駅 ———— 渋川駅 ———— 見晴下バス停 下車
 約 105 分 約 20 分
 <上越線・特急> <路線バス>

【高速バス利用の場合】

新宿駅(新南口) ———— 伊香保温泉 見晴下バス停 下車
 約 2 時間 40 分
 <関越道高速バス 上州名湯めぐり号>

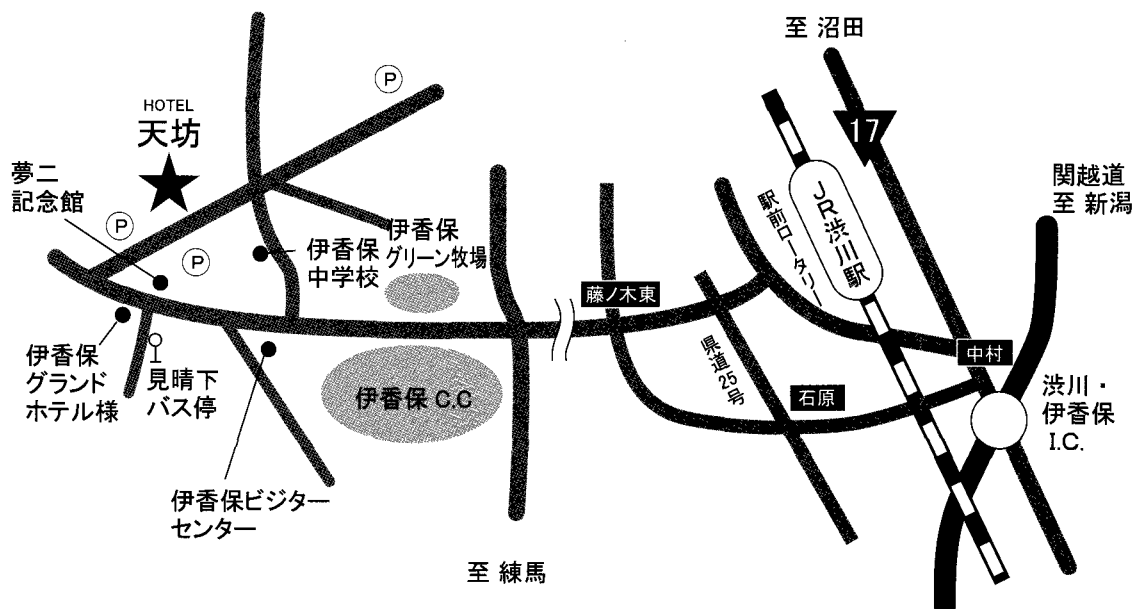
● 新潟からの交通

【ＪＲ利用の場合】

新潟駅 ———— 高崎駅 ———— 渋川駅 ———— 見晴下バス停 下車
 約 95 分 約 20 分 約 20 分
 <上越新幹線> <上越線> <路線バス>

※ 詳細については、「伊香保温泉 ホテル天坊」ホームページの「交通案内」をご参照下さい。

会場周辺図

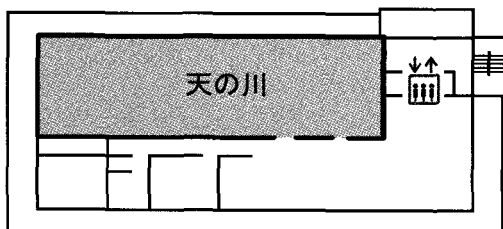


会場案内図

スカイホール「天の川」		9F		
客室 851~855	客室 801~810	8F		
客室 751~758	客室 702~713	7F	客室 715~723	7F
客室 651~658	客室 602~613	6F	客室 615~627	6F
客室 551~558	客室 502~513	5F	客室 515~527	5F
大浴場、貸切露天風呂、家族風呂、 マッサージ・エステサロン、プール、 チャペル		3F	客室 415~427	4F
バンケットホール「烏帽子」			客室 315~326 ライブラリー	3F
お食事処、宴会場	宴会場「五万石」 宴会場「谷川」	2F	宴会場 ギャラリー	2F
バンケットホール 「キング」「クイーン」 会議室「長峰」「平安」 お食事処		1F	フロント・玄関・ロビー ロビーラウンジ・ティーラウンジ バラエティーホール・売店・ 情報コーナー	1F
				BF
				岩風呂 露天風呂

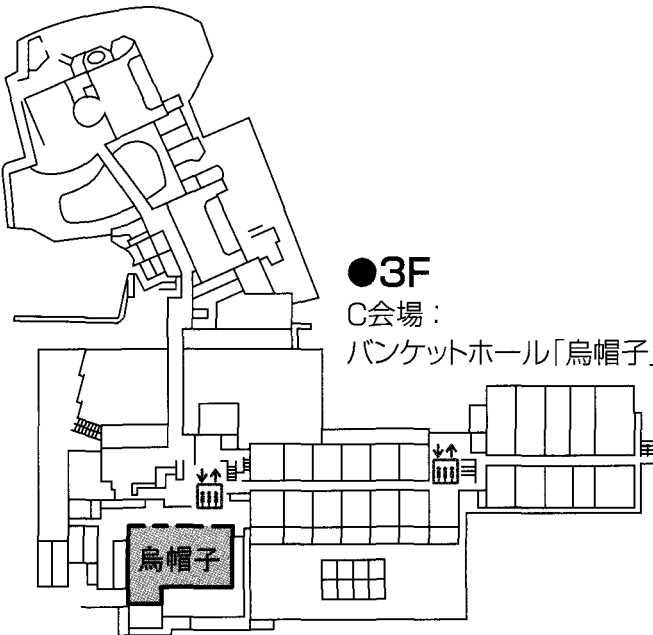
●9F

B会場：スカイホール「天の川」



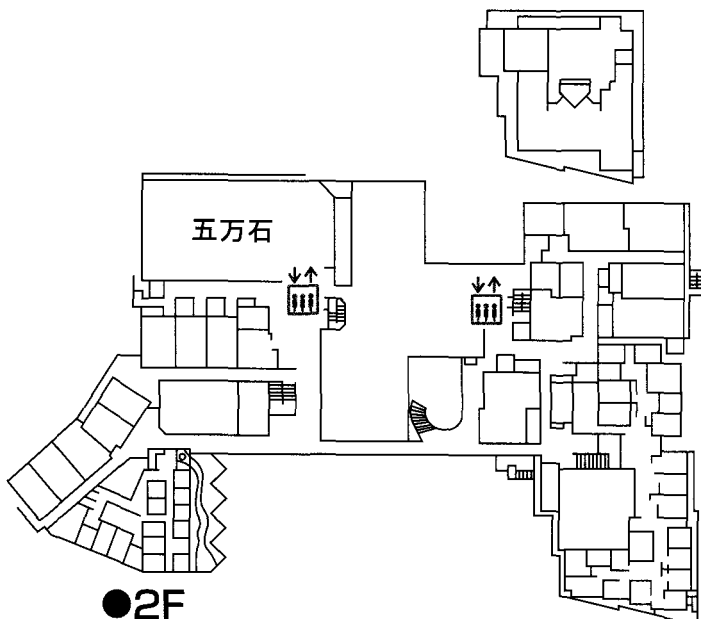
●3F

C会場：バンケットホール「烏帽子」



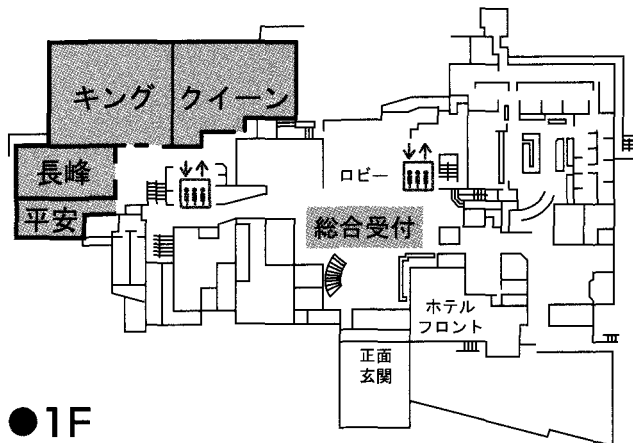
●2F

懇親会場：宴会場「五万石」



●1F

A会場：バンケットホール「キング」
ポスター会場・展示会場：バンケットホール「クイーン」
D会場：会議室「長峰」
本部：会議室「平安」



大会日程概要

■第1日目 6月21日(日)

会場名	A会場 (1F・キング)	ポスター展示会場 (1F・クイーン)
8:30		
9:00	開会の挨拶	
9:30	GRT 研究会 シンポジウム I	
10:00		
10:30	コーヒーブレイク	
11:00	GRT 研究会 シンポジウム II	
11:30		
12:00	GRT 研究会 ランチョンセミナー	
12:30		
13:00	議事総会	
13:30	GRT 研究会 特別講演	
14:00		
14:30		GRT 研究会 ポスター討論時間
15:00		
15:30		
16:00	GRT 研究会 シンポジウム III	
16:30		
17:00	開会の挨拶	
17:30	神経化学会-GRT研究会 連携オープンシンポジウム 「成体脳における神経新 生と中枢神経系の 再生戦略」 座長：岡野 栄之 板倉 徹	
18:00		
18:30		
19:00		
19:30		
20:00		
20:30		
21:00		
21:30		
22:00		
22:30		

■ 21 June (Sun)

Room	Room A (1F・King)	Poster Area (1F・Queen)
8:30		
9:00	Opening	
9:30	GRT Symposium I	
10:00		
10:30	Coffee break	
11:00	GRT Symposium II	
11:30		
12:00	GRT Luncheon Seminar	
12:30		
13:00	General Assembly	
13:30	GRT Special Lecture	
14:00		
14:30		GRT Poster Discussion
15:00		
15:30		
16:00	GRT Symposium III	
16:30		
17:00	Closing	
17:30	JSN - GRT Joint Open Symposium "Adult Neurogenesis and New Strategies for CNS Regeneration" Chairs: Hideyuki Okano Toru Itakura	
18:00		
18:30		
19:00		
19:30		
20:00		
20:30		
21:00		
21:30		
22:00		
22:30		

■第2日目 6月22日(月)

会場名	A会場 (1F・キング)	B会場 (9F・天の川)	C会場 (3F・烏帽子)	D会場 (1F・長峰)	ポスター展示会場 (1F・クイーン)
8:30 40 50					ポスター 貼付時間
9:00 10 20	開会の辞				
9:30 40 50	ISN シンポジウム (国際神経化学会共催) 「Axon Homeostasis and Diseases」 座長：木山 博資 御子柴 克彦	シンポジウム1 アストロサイトの 発生と分化 座長：石崎 泰樹 中島 欽一	シンポジウム2 エピジェネティクスか らの精神疾患解明への 挑戦 座長：福永 浩司 久保田 健夫	シンポジウム3 発達障害における基礎 研究の成果を臨床像と 照らしつつ今一度検証 する 座長：成田 正明 武田 雅俊	
10:00 10 20					
10:30 40 50					
11:00 10 20					
11:30 40 50					ポスター掲 示
12:00 10 20	評議員会				
12:30 40 50					
13:00 10 20	総会				
13:30 40 50					ポスター討論時間
14:00 10 20					
14:30 40 50	若手奨励賞 シンポジウム 座長：米田 幸雄 木山 博資	一般口演1 ミクログリア 座長：仲田 義啓 浜之上 誠	一般口演2 タンパク・リン酸化とそ の制御 座長：大西 浩史 高橋 正身	一般口演3 遺伝子発現 座長：山形 要人 渡辺 康裕	ポスター掲 示
15:00 10 20					
15:30 40 50					
16:00 10 20					
16:30 40 50	一般口演4 神経細胞死 座長：一瀬 宏 岡澤 均 武田 泰生	一般口演5 βアミロイド・認知症 座長：桑野 良三 錦島 俊隆 道川 誠	一般口演6 神経可塑性 座長：植田 弘師 塩坂 貞夫	一般口演7 細胞移動・ 軸索ガイダンス 座長：佐藤 真 東田 陽博	
17:00 10 20					
17:30 40 50					
18:00 10 20					
18:30 40 50					
19:00 10 20	懇親会 <2F・五万石にて>				
19:30 40 50					
20:00 10 20					
20:30 40 50					
21:00 10 20	育成セミナー ～ 23:00				
21:30 40 50					
22:00 10 20					
22:30 40 50					

■ 22 June (Mon)

Room	Room A (1F・King)	Room B (9F・Amanogawa)	Room C (3F・Eboshi)	Room D (1F・Nagamine)	Poster Area (1F・Queen)
8:30 40 50					
9:00 10 20 30 40 50	Opening				Poster Set up
10:00 10 20 30 40 50	ISN Symposium "Axon Homeostasis and Diseases" Chairs: Hiroshi Kiyama Katsuhiko Mikoshiba	Symposium 1 New insights into astrocytogenesis in the mammalian central nervous system Chairs: Yasuki Ishizaki Kinichi Nakashima	Symposium 2 The challenge of epigenetics to elucidate the cause of mental disorders Chairs: Kohji Fukunaga Takeo Kubota	Symposium 3 Update of autism and other developmental disorders, basic and clinic Chairs: Masaaki Narita Masatoshi Takeda	
11:00 10 20 30 40 50					Poster Exhibition
12:00 10 20 30 40 50	Council Meeting				
13:00 10 20 30 40 50	General Assembly				
14:00 10 20 30 40 50					Poster Discussion
14:30 10 20 30 40 50	Young Scientists Lectureship Award Chairs: Yukio Yoneda Hiroshi Kiyama	Oral Session 1 Microglia Chairs: Yoshihiro Nakata Makoto Hamanoue	Oral Session 2 Protein phosphorylation Chairs: Hiroshi Ohnishi Masami Takahashi	Oral Session 3 Gene expression Chairs: Kanato Yamagata Yasuhiro Watanabe	
15:00 10 20 30 40 50					
16:00 10 20 30 40 50	Oral Session 4 Neuronal death Chairs: Hiroshi Ichinose Hitoshi Okazawa Yasuo Takeda	Oral Session 5 β Amyloid/Dementia Chairs: Ryozo Kuwano Toshitaka Nabeshima Makoto Michikawa	Oral Session 6 Neural Plasticity Chairs: Hiroshi Ueda Sadao Shiosaka	Oral Session 7 Cell migration/Axon guidance Chairs: Makoto Sato Haruhiro Higashida	Poster Exhibition
17:00 10 20 30 40 50					
18:00 10 20 30 40 50					
19:00 10 20 30 40 50	Welcome Reception <at 2F/Gomangoku>				
20:00 10 20 30 40 50					
21:00 10 20 30 40 50	Training Seminar for Students ~ 23:00				
22:00 10 20 30 40 50					

■第3日目 6月23日（火）

会場名	A 会場 (1F・キング)	B 会場 (9F・天の川)	C 会場 (3F・烏帽子)	D 会場 (1F・長峰)	ポスター展示会場 (1F・クイーン)
8:30 40 50					
9:00 10 20 30 40 50	神経化学会－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」 座長：池田 一裕 齋藤 利和 三國 雅彦	シンポジウム4 シナプス可塑性・記憶 形成におけるプロテイン キナーゼの役割 －新たな展開 座長：久永 真市 喜田 聡	シンポジウム5 基礎研究と創薬を結 び付ける Translational Research 座長：小泉 信一 高坂 新一 パネリスト：塚本 尚 永井 義隆 新田 淳美	シンポジウム6 何がどのように細胞移 動と軸索ガイダンスを 制御するのか？ 座長：五嶋 良郎 仲嶋 一範	ポスター掲示
10:00 10 20 30 40 50					
11:00 10 20 30 40 50					
12:00 10 20 30 40 50	ランチョンセミナー1 座長：三國 雅彦 講演：工藤 希		ランチョンセミナー2 座長：岡田 勇彦 講演：津幡 卓一 五十嵐 道弘		
13:00 10 20 30 40 50					ポスター討論時間
14:00 10 20 30 40 50					
14:30 40 50	一般口演8 ストレス・不安 座長：車地 曉生 中村 俊	一般口演9 ミエリン・脱髄疾患 座長：阿相 皓晃 渡部 和彦	一般口演10 開口放出 座長：島田 昌一 樋口 宗史	一般口演11 シナプス形成 座長：高松 研 森 望	ポスター掲示
15:00 10 20 30 40 50					
16:00 10 20 30 40 50	シンポジウム7 精神医学と神経学の統合 的展開 座長：和田 圭司 西川 徹	シンポジウム8 蛋白質品質管理と 脳神経疾患 座長：工藤 希 今泉 和則	シンポジウム9 網羅的アプローチ (-omics) による、神経 化学の新しい世界観 座長：五十嵐 道弘 平林 義雄	シンポジウム10 神経突起先端および スパインにおける細胞 骨格、内膜系の動態と 機能 座長：石川 良樹 鈴木 龍雄	
17:00 10 20 30 40 50					
18:00 10 20 30 40 50					
19:00 10 20 30 40 50	育成セミナー 夕食会 ＜2F・五万石にて＞				ポスター掲示
19:30 40 50					
20:00 10 20 30 40 50					
21:00 10 20 30 40 50	育成セミナー ～ 23:00				
22:00 10 20 30 40 50					
22:30 40 50					

■ 23 June (Tue)

Room	Room A (1F・King)	Room B (9F・Amanogawa)	Room C (3F・Eboshi)	Room D (1F・Nagamine)	Poster Area (1F・Queen)
8:30 40 50					
9:00 10 20 30 40 50	JSN - JSBP Joint Symposium "Clues to the pathophysiology and treatment of psychiatric disorders through integrating neurochemistry and psychiatry" Chairs:Kazuhiro Ikenaka Toshikazu Saito Masahiko Mikuni	Symposium 4 Novel insights into the roles of protein kinases in synaptic plasticity and memory Chairs:Shin-ichi Hisanaga Satoshi Kida	Symposium 5 Translational research between basic science and drug discovery Chairs:Shinichi Koizumi Shinichi Kohsaka Panelists:Takashi Tsukamoto Yoshitaka Nagai Atsumi Niita	Symposium 6 Regulation of cell migration and axon guidance Chairs:Yoshio Goshima Kazunori Nakajima	Poster Exhibition
10:00 10 20 30 40 50					
10:30 40 50					
11:00 10 20 30 40 50					
12:00 10 20 30 40 50	Luncheon Seminar 1 Chair:Masahiko Mikuni Speaker: Takashi Kudo		Luncheon Seminar 2 Chair:Takehiko Okada Speakers: Takuichi Tsubata Michihiro Igarashi		
13:00 10 20 30 40 50					Poster Discussion
13:30 40 50					
14:00 10 20 30 40 50					
14:30 40 50	Oral Session 8 Stress/Anxiety Chairs:Akeo Kurumaji Shun Nakamura	Oral Session 9 Myelin/Demyelinating disease Chairs:Hiroaki Asou Kazuhiko Watabe	Oral Session 10 Exocytosis Chairs:Shoichi Shimada Hiroshi Higuchi	Oral Session 11 Synapse formation Chairs:Ken Takamatsu Nozomu Mori	Poster Exhibition
15:00 10 20 30 40 50					
16:00 10 20 30 40 50	Symposium 7 Integrative advance of neurology and psychiatry Chairs:Keiji Wada Toru Nishikawa	Symposium 8 Quality controls of proteins and neuropsychiatric diseases Chairs:Takashi Kudo Kazunori Iinazumi	Symposium 9 New vistas of neurochemistry using the large-scale genome-wide analysis : -omics approaches Chairs:Michihiro Igarashi Yoshio Hirabayashi	Symposium 10 Dynamics and functions of cytoskeletal- and membrane-proteins in neuronal growth cones and dendritic spines Chairs: Ryoki Ishikawa Tatsuo Suzuki	
17:00 10 20 30 40 50					
17:30 40 50					
18:00 10 20 30 40 50					
18:30 40 50	Dinner for Training Seminar Participants 				

■第4日目 6月24日(水)

会場名	A会場 (1F・キング)	B会場 (9F・天の川)	C会場 (3F・烏帽子)	D会場 (1F・長峰)	ポスター展示会場 (1F・クイーン)
8:30 40 50					
9:00 10 20 30 40 50	一般口演12 アストロサイト 座長：浅井 清文 榎戸 靖 松田 敏夫	一般口演13 神経幹細胞・前駆細胞 座長：井上 順雄 堀尾 嘉幸 吉川 和明	一般口演14 成長因子・栄養因子 座長：荒川 義弘 仙波 りつ子 松岡 一郎	一般口演15 精神疾患・発達障害 座長：神庭 重信 田中 稔久 森 則夫	ポスター掲示
10:00 10 20 30 40 50					
11:00 10 20 30 40 50					
12:00 10 20 30 40 50		ランチョンセミナー3 座長：三國 雅彦 講演：久住 一郎			
13:00 10 20 30 40 50					
14:00 10 20 30 40 50	シンポジウム11 ミクログリアの機能と病態 ー最近の研究動向と 将来の展望 座長：中西 博 井上 和秀	シンポジウム12 精神・神経・筋疾患の トランスレーショナル リサーチ 座長：橋本 亮太 辻 省次	シンポジウム13 薬長類を用いた精神神 経疾患モデルの現況と 展望 座長：中村 克樹 那波 宏之	シンポジウム14 ニューラルコミュニケー ションの新たな理解への チャレンジ 座長：関野 祐子 熊倉 鶴之助	
15:00 10 20 30 40 50					(15時までに ポスター撤去)
16:00 10 20 30 40 50	閉会の辞				
17:00 10 20 30 40 50					
18:00 10 20 30 40 50					
19:00 10 20 30 40 50					
20:00 10 20 30 40 50					
21:00 10 20 30 40 50					
22:00 10 20 30 40 50					

■ 24 June (Wed)

Room	Room A (1F・King)	Room B (9F・Amanogawa)	Room C (3F・Eboshi)	Room D (1F・Nagamine)	Poster Area (1F・Queen)
8:30 40 50					
9:00 10 20					
9:30 40 50	Oral Session 12 Astrocyte Chairs: Kiyofumi Asai Yasushi Enokido Toshio Matsuda	Oral Session 13 Neural stem/Progenitor cells Chairs: Nobuo Inoue Yoshiyuki Horio Kazuaki Yoshikawa	Oral Session 14 Growth factor/Trophic factor Chairs: Yoshihiro Arakawa Ritsuko Ktoh-Senba Ichiro Matsuoka	Oral Session 15 Psychiatric diseases/Developmental disorders Chairs: Shigenobu Kanba Toshihisa Tanaka Norio Mori	Poster Exhibition
10:00 10 20					
10:30 40 50					
11:00 10 20					
11:30 40 50					
12:00 10 20					
12:30 40 50		Luncheon Seminar 3 Chair: Masahiko Mikuni Speaker: Ichiro Kusumi			
13:00 10 20					
13:30 40 50	Symposium 11 Physiological and pathological functions of microglia: current knowledge and future directions Chairs: Hiroshi Nakanishi Kazuhide Inoue	Symposium 12 Translational research for psychiatric, neurological, neuromuscular diseases Chairs: Ryota Hashimoto Shoji Tsuji	Symposium 13 Recent progress and perspective of primate models for psychiatric diseases Chairs: Katsuki Nakamura Hiroyuki Nawa	Symposium 14 Frontiers in understanding neuronal communication Chairs: Yuko Sekino Konosuke Kumakura	
14:00 10 20					
14:30 40 50					
15:00 10 20					(Poster Removal ~ 15:00)
15:30 40 50					
16:00 10 20	Closing				
16:30 40 50					
17:00 10 20					
17:30 40 50					
18:00 10 20					
18:30 40 50					
19:00 10 20					
19:30 40 50					
20:00 10 20					
20:30 40 50					
21:00 10 20					
21:30 40 50					
22:00 10 20					
22:30 40 50					

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。なお、事前参加登録費の払込み手続きが完了した段階で、メールまたはFAXにてご送付いたしました「参加登録確認書」を、念のためプリントアウトしてお持ちください。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「参加登録確認書」をお持ちになり、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階ロビーにて、6月21日は11時30分から18:00まで、6月22日以降は午前8時15分より開始いたします。

参加費は以下の通りです。学部学生、及び大学院生の方は、受付に学生証を提示してください。

【当日参加登録費】

＜日本神経化学学会大会のみ参加登録＞

会 員（一般）	: 14,000 円
非 会 員（一般）	: 16,000 円
大 学 院 生（会員・非会員）	: 4,000 円

＜日本神経化学学会大会・GRT研究会の両方に参加登録＞

神 経 化 学 会 会 員（一般）	: 19,000 円
神 経 化 学 会 非 会 員（一般）	: 21,000 円
大 学 院 生（神経化学学会会員・非会員）	: 6,000 円

※ 筆頭著者発表を行わない学部学生の参加費は無料です。受付に学生証を提示してください。

【懇親会（Welcome Reception）費】

ホテル天坊に宿泊される方	: 3,000 円（宿泊費に含まれています）
ホテル天坊に宿泊されない方	: 8,000 円

● 非会員の方

日本神経化学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。

＜入会申込み連絡先＞

〒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、社団法人日本精神神経学会より精神科専門医制度における精神科専門医資格の更新に際して必要とする取得単位の対象となりますので、単位が必要な方は受付までお申し出下さい。

2. お知らせ

● クローク

会期中は1階「かもん」にクロークを設置いたします。

＜クローク開設時間＞

6月22日（月） 8：15～16：00

6月23日（火） 8：15～16：00

6月24日（水） 8：15～16：30

● 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、直接「ホテル天坊」フロントまでお願いいたします。

● 大会本部

会期中は1階「平安」を大会本部にいたします。

● 懇親会 (Welcome Reception)

6月22日（月）19：00より、2F「五万石」にて行います。

事前予約が原則ですが、当日参加希望の方は、13：00までにホテルフロントにお申し出下さい。

● インターネットコーナー

本大会では、特にインターネットコーナーとしては設置いたしません。A、B、C、D会場前のロビーでは、無線LANが使用できます。

● ドリンクコーナー

ポスター・展示会場（1F「クイーン」）内に、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。

● 会期中の昼食について

6月23日（火）・24日（水）は、ランチョンセミナーがあります。

また、6月22日（月）の昼食や、ランチョンセミナーに参加されない方のために、昼食用お弁当を1,000円にて有料販売いたします。1Fロビーの総合受付にて、販売予約券をお渡しいたしますので、お弁当を購入される方はお立寄りください。

3. 大会行事

● 神経化学会－GRT研究会連携オープンシンポジウム

日時：6月21日（日）17：00～19：00 会場：1F「キング」（A会場）

● ISN シンポジウム

日時：6月22日（月）9：00～11：40 会場：1F「キング」（A会場）

● 日本神経化学会－日本生物学的精神医学会 合同シンポジウム

日時：6月23日（火）9：00～11：40 会場：1F「キング」（A会場）

● 若手奨励賞シンポジウム

日時：6月22日（月）14：20～15：50 会場：1F「キング」（A会場）

4. 関連行事

● 理事会

日時：6月21日（日）12：50～16：50 会場：1F「平安」

● 評議員会

日時：6月22日（月）11：50～12：40 会場：1F「キング」（A会場）

● 総会

日時：6月22日（月）12：40～13：30 会場：1F「キング」（A会場）

● 懇親会（Welcome Reception）

日時：6月22日（月）19：00～21：00 会場：2F「五万石」

5. 各種委員会

● 将来計画委員会

日時：6月22日（月）9：30～11：30 会場：2F「しらかば・もみじ」

● シンポジウム企画委員会

日時：6月22日（月）9：30～11：30 会場：2F「けやき」

● 脳研究推進委員会

日時：6月22日（月）9：30～11：30 会場：2F「からまつ」

● 出版・広報委員会

日時：6月22日（月）16：00～18：00 会場：2F「けやき」

● 国際対応委員会

日時：6月22日（月）16：00～18：00 会場：2F「からまつ」

● 奨励賞選考委員会

日時：6月22日（月）16：00～18：00 会場：2F「いちよう」

6. 神経化学の若手研究者育成セミナー

日時：6月22日（月）

21：00（懇親会終了後）～22：00 オリエンテーション（A～D会場）

22：00～23：00 フリーディスカッション（B会場：天の川）

6月23日（火）

18：40～19：30 育成セミナー夕食会 （2F：五万石）

19：30～21：30 育成セミナー講義 （A～D会場）

21：30～23：00 フリーディスカッション （B会場：天の川）

口演発表要項

1. 発表・討論、進行

- 1) 発表は英語にこだわらず内容の充実を優先いたしますので、日本語で口演いただいても結構です。また英語の場合も討論は日本語可で進めてまいります。
- 2) 各演者の発表・討論時間はプログラムに掲載されていますので、時間厳守をお願いいたします。
(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) 演者は口演時間 20 分前までに、次演者席にお着きください。
- 5) 討論者は、討論用マイクがある会場においては、あらかじめ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) 口演会場に用意する PC の仕様について
 【OS】Windows XP
 【アプリケーション】Microsoft Office PowerPoint 2003
 【音声出力】不可
 - 2) 上記仕様で作成された発表データを USB フラッシュメモリーに保存し、他の PC での動作確認後、お持ち込みください。
 - 3) 動画を使用する場合は、ご自身の PC をご持参ください。
 - 4) Windows Vista、PowerPoint 2007 でデータを作成した場合は、データ保存形式を上記仕様に合わせるか、ご自身の PC をお持ち込みください。
 - 5) Macintosh で作成した場合は、上記仕様で動作確認、及び修正をしてからお持ちいただくか、ご自身の PC をお持ち込みください。
 - 6) PC をご持参いただく場合は、外部出力端子 (mini-Dsub15pin) の形状をご確認ください。上記出力端子が本体に付いていない場合は、変換アダプターをご持参ください。また、バッテリー切れを防ぐため、必ず付属の AC 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。
- 7) ウイルスチェックは必ず行ってください。
 - 8) 発表データは、各口演会場内で受付いたします。発表の 60 分前までに各口演会場内のスクリーンに向かって左前方 (演台の脇) の「PC 技師席」にお持ちください。PC 技師がデータコピー後に、試写・内容・動作確認をしていただいた後、データのみをお預かりいたします。
PC 本体をお持ち込みの場合は、発表終了後、速やかに「PC 技師席」にてご返却いたします。
 - 9) 事前にご自身でデータ確認・出力チェックをされる場合は PC 確認コーナー (1F「キング」前ロビー) をご利用ください。
 - 10) 演台上にはモニター・マウス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。PC 本体をお持ち込みの場合も、同様の操作となります。

3. 座長の方へ

- 1) ご担当セッションの開始 20 分前までに、次座長席にお着きください。
- 2) 各演者の発表・討論時間はプログラムに掲載されていますので、時間厳守に留意していただき、円滑なプログラム進行にご協力をお願いいたします。
(シンポジウム：2 時間 40 分の枠内でご自由にお使いください。一般口演：発表 15 分／討論 5 分)

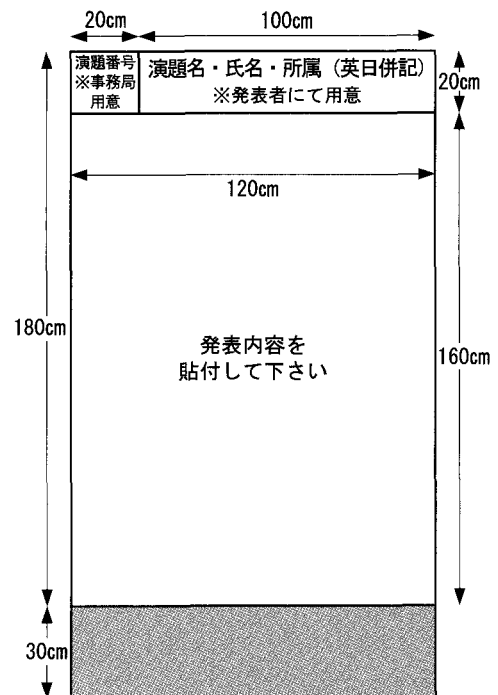
ポスター発表要項

1. 会場

ポスター発表は、1F「クイーン」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) 貼付用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：6月22日（月） 8：30～10：00

討論：6月22日（月）13：30～14：15

6月23日（火）13：10～14：10

撤去：6月24日（水）15：00 まで

- 2) ポスターは会期を通じて継続掲示しますので、発表者は上記の討論時間には、両日ともポスター前に待機してください。尚、座長を交えた発表（5分）と討論（3分）は、どちらか一方の時間帯に行います。
各パネルにリボンを用意しておきますので、討論時間には着用してください。
- 3) 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。
- 2) 各演者の発表・討論時間は、時間厳守に留意していただき、円滑なプログラム進行にご協力をお願いいたします（発表5分／討論3分）。

学会からのお知らせ

1. 評議員会

日 時：6 月 22 日（月） 11：50～12：40

場 所：伊香保温泉 ホテル天坊 1F「キング」（A 会場）

課 題：日本神経化学会と社会との接点

※ 昼食は有料となりますので、ご了承ください。

2. 総会

日 時：6 月 22 日（月） 12：40～13：30

場 所：伊香保温泉 ホテル天坊 1F「キング」（A 会場）

- 課 題：
1. 理事長報告
 2. 選挙結果報告
 3. 庶務報告
 4. 会計報告
 5. 出版・広報報告
 6. プログラム編成報告
 7. 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 出版・広報委員会
 - ⑤ 研究助成金等候補者選考委員会
 - ⑥ シンポジウム企画委員会
 - ⑦ 連合大会委員会
 8. 2009 年度奨励賞選考結果報告
 9. 2008 年度決算の件
 10. 同監査報告
 11. 2010 年度予算の件
 12. 監事選任の件
 13. 評議員選任の件
 14. 名誉会員選任の件
 15. 会則・細則変更の件
 16. 次期大会の件
 17. その他

2009 年度第 1 回理事会議事録

日 時：2009 年 3 月 9 日（月）13：30-17：30

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）、仲嶋一範（出版・広報担当）、岡野栄之、塩坂貞夫、今泉和則、和田圭司、高橋正身（以上理事）、三木直正（監事）、井上和秀（新任理事・第 53 回大会長）、榎戸靖（2009 年選挙管理委員会委員長）、遠山正彌、柳澤勝彦、島田昌一、熊倉鴻之助（以上 新任理事）、石崎泰樹（田代朋子大会長代理人）、田代朋子（第 52 回大会長）

委 任 状：御子柴克彦、神庭重信、武田雅俊、東田陽博（以上 理事）、宮本英七（監事）、和中明生（新任理事・国際対応委員会委員長）

欠 席：辻省次（理事）

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. 2008 年度第 2 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. 選挙結果報告

(1) 理事改選結果について

平成 21 年 2 月 3 日に開票された理事選挙結果について、榎戸靖選挙管理委員会委員長より報告がなされた。なお、同点の取り扱いについては、年齢の昇順とした。

(2) 科研費審査員候補者選出選挙の件

平成 21 年 2 月 3 日に開票された科研費審査委員候補者選出選挙結果について、榎戸靖選挙管理委員会委員長より報告がなされた。

3. 役職理事・委員長選出

(1) 2009 年度の理事長・副理事長選出の件

2009 年度理事（補充理事除く）9 名による投票の結果、理事長に高坂新一理事（国立精神・神経センター）、副理事長に井上和秀理事（九州大学）が選出された（任期は 2011 年 2 月末日迄）。

(2) 補充理事選任の件

得票数、専門分野および地域性等を考慮し、審議の結果、下記の通り補充理事候補者を選出した。

（敬称略：50 音順）

白尾智明（群馬大学）

田代朋子（青山学院大学）

西川徹（東京医科歯科大学）

(3) 担当理事の選出

審議の結果、各担当理事（任期は 2011 年 2 月末日迄）を以下の通り選出した。

（敬称略）

庶務担当：岡野栄之（慶應義塾大学）
会計担当：島田昌一（名古屋市立大学）
出版・広報担当：今泉和則（宮崎大学）

(4) 委員会委員長の選出

審議の結果、各委員会の委員長（任期は 2011 年 2 月末日迄）を以下の通り選出した。

（敬称略）

将来計画委員会委員長：池中一裕（自然科学研究機構 生理学研究所）
出版・広報委員会委員長：今泉和則（宮崎大学） ※出版・広報担当理事兼務
シンポジウム企画委員会委員長：柳澤勝彦（国立長寿医療センター研究所）
国際対応委員会委員長：和中明生（奈良県立医科大学）
研究助成金等候補者選考委員会委員長：神庭重信（九州大学）
脳研究推進委員会委員長：遠山正彌（大阪大学）
連合大会委員会委員長：井上和秀（九州大学） ※副理事長兼務

また、各委員長から委員の推薦を受けることと決した。

(5) 次期奨励賞選考委員会委員候補者の選出

審議の結果、次期奨励賞選考委員会委員候補者（任期は 2009 年度総会終了時～ 2013 年度総会終了時）を以下の通り選出した。

（敬称略）

塩坂貞夫（奈良先端科学技術大学院大学）
馬場広子（東京薬科大学）
柳澤勝彦（国立長寿医療センター研究所）

4. 次期監事候補者の選出

審議の結果、次期監事候補者（任期は 2009 年度総会終了時～ 2013 年度総会終了時）を以下の通り選出した。

（敬称略）

鍋島俊隆（名城大学）
野村靖幸（横浜薬科大学）

5. 理事長報告

特になし。

6. 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
会員数動向について報告がなされた。
- ・除名について
2005 年度から年会費を滞納していた会員を除名とした旨報告がなされた。
- ・評議員の退会希望について
退会の希望があった評議員の慰留状況について報告がなされた。

7. 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。

- ・年会費未納者数について
会費未納者数について現状報告がなされた。今後も引き続き未納者へ適宜督促を行うことが確認された。

- ・選挙関連経費について

選挙関連経費について、以下の3点により、2007年度実績と比べ、経費が増加した旨報告された。

ア) 封入・投函作業を委託した

イ) 封入する内袋を増やした

ウ) 作業の正確さを考慮し、委託先業者を変更した

8. 出版・広報報告

仲嶋一範出版・広報担当理事より、出版・広報報告がなされた。

- ・機関誌製作について

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後も、問題なく発行できている旨報告された。

9. 委員会報告

(1) 将来計画委員会

米田幸雄委員長より、2008年9月11日開催の委員会について報告がなされた。

- * 国際化の取り組みについて、英語発表だけが国際化ではないという意見も多く、特にプレドク学生向けの日本語セッションを設けることが提案された。

- * 若手育成セミナーを今後とも継続すべきとの意見で一致した旨報告された。

- * 女性研究者の支援について、学会ホームページ上に女性研究者による意見交換や情報提供の場を設けることが提案され、出版・広報委員会で検討されている旨報告された。

また国際化の取り組みに関連して、日本の若手研究者を海外の学会に送り込み、体験させることが大切であるため、日本神経化学会が提供するトラベラー・アワードの創設を検討してもよいのではないかと議論がなされた旨、理事長より報告された。

また、理事より次のような意見が出され、議論された。

- * 委員会よりなされた提言の実現状況を会員に分かりやすく伝えるためのロードマップを作った方がよいのではないかという意見が出された。これについて、機関誌やホームページ上での実現を検討していくとともに、機関誌に掲載している委員会議事録についても、簡潔化すべきとの意見が出された。

- * 日本神経化学会が力を入れてきた若手育成に関連して、ポスドク対策、特に企業とのマッチングを行ってはどうか、またそれが賛助会員獲得につながるのではないかと意見が出された。この意見に対して、推薦制度は有効だが、学会としてはすべての希望者に対して同等に推薦を行うことはできないので、そのルール作りも重要でかつ有効であるとの意見が出された。これについては、今後とも将来計画委員会で審議していくこととなった。

これらの意見を受けて委員長より、委員会は提言を行い、提言の実現状況について評価・追跡していくことを目標とする旨確認がなされた。

(2) 出版・広報委員会

仲嶋一範委員長より、次の通り報告された。

- ・学会ホームページについて

学会ホームページの更新状況について報告がなされた。

- ・第105回日本精神神経学会学術総会のセッション企画参加について

セッション企画参加が決定した旨報告がなされ、セッションの概要および抄録の内容について確認された。

- ・新会員情報検索システムの進捗状況について

2008年9月11日の委員会において、当面は現行システムで使用しているUMIN・PLAZAサーバーの利用を継続しつつ、並行してUMIN・OASISサーバーの進捗状況をフォローして、今後UMIN・

OASIS が本学会の希望する内容を満たすことが確認されれば、UMIN・PLAZA から UMIN・OASIS に乗り換えていくことが望ましいという結論になった旨報告され、現在の進捗状況が報告された。また本学会で希望する内容をより反映させやすい方法として、自前サーバーを導入する可能性についても委員会内で議論されている旨報告された。

これに対し、UMIN を使用した場合の個人情報の二重管理の問題が指摘されるとともに、会員情報検索システムの活用方法とニーズについて、以前の理事会で決定された方向性を再度検討し、費用対効果に基づいた議論をしていくべきであるとの意見が出された。

(3) シンポジウム企画委員会

東田陽博委員長欠席のため、2008 年 9 月 11 日開催の委員会について資料で報告された。

また、田代朋子大会長の代理として石崎泰樹氏（群馬大学）より、52 回大会中 2009 年 6 月 21 日開催予定の神経組織の成長・再生・移植研究会第 24 回学術集会との連携シンポジウムについて進捗状況が報告された。

(4) 国際対応委員会

和中明生委員長欠席のため、資料により報告された。

また、池中一裕副理事長より報告がなされた。

- * ISN 理事選挙について、白尾智明氏（群馬大学）が理事選挙の候補者となった旨報告され、白尾氏当選に向け、当会としても協力していくこととなった。

- * 第 22 回 ISN/APS N meeting について、ポスターアワード等への参加呼びかけをお願いしたいとのことであった。

- * 第 9 回 APSN ミーティングについて、2010 年 10 月 18 日～20 日にタイ・プーケット島で開催されることが決定し、プログラム委員長に和中明生氏が就任した旨報告された。また、シンポジウム、コロキウムについて 4 月以降募集を行う予定であるとのことであった。

(5) 研究助成金等候補者選考委員会

神庭重信委員長欠席のため、資料により報告された。

また候補者が少ないので若い研究者の推薦をお願いしたいとのことであった。

(6) 脳研究推進委員会

辻省次委員長欠席のため、代理として岡野栄之理事より 2008 年 9 月 11 日開催の委員会について報告された。

- * 脳研究委員会のミッションとして、(1) 脳研究の科学政策（研究費）に対する積極的な提言を行うこと、(2) 学会員に研究費に関する情報を伝えること、(3) 日本神経化学会として、積極的に推進すべき研究分野を提言すること、などが位置づけられている旨報告された。

- * 研究費の動向あるいは各省庁などの公募研究費などを学会ホームページから会員に伝えるため、出版・広報委員会の広報担当と緊密な連携をとっていきたいとのことであった。

- * 日本神経化学会として、積極的に推進すべき研究分野として、chemical neurobiology、分子イメージングなど、物質を基盤とする研究分野、疾患研究、translational research などの研究分野を積極的に取り込んでいくことが提言された。

また、将来的には提言だけでなく行動をとった委員会になっていく可能性がある旨理事長より報告され、次期委員会では他の委員会と協力しながら活動していくとのことであった。

(7) 奨励賞選考委員会

米田幸雄委員長より、2008 年 9 月 11 日に開催された第 2 回奨励賞選考委員会において、橋本亮太氏が最優秀奨励賞に選出された旨報告された。

(8) 連合大会委員会

池中一裕委員長より次のとおり報告された。

今年の第52回大会の期間中に日本生物学的精神医学会との合同シンポジウムを開催することが決定された旨報告された。両学会の若手の研究者が発表により、精神疾患をめぐる問題意識を共有し、人間関係を築いていくことを目標にしているとのことであった。

また日本生物学的精神医学会の側で同様の合同シンポジウムが開催される場合、学会から若手演者への援助を行うかどうか、議論されたいとのことであった。

10. 第51回大会(2008年度)について

武田雅俊大会長欠席のため、資料により報告された。

11. 大学評価・学位授与機構における機関別認証評価委員会専門委員候補者の推薦について

高坂新一理事長より、鍋島俊隆氏、野村正彦氏を推薦した旨報告された。

【審議事項】

1. 新評議員の推薦について

審議の結果、候補者5名の推薦が承認され、次回総会に諮ることとなった。

2. 名誉会員の推薦について

2007年第2回理事会において監事職満了時の総会にて推薦されることが決定している宮本英七氏が、2009年度総会にて推薦されることが確認された。

3. 名誉会員の規定変更について

米田幸雄庶務担当理事より草案が示され、審議の結果、変更内容が決定した。

4. 奨励賞規定・内規の変更について

米田幸雄委員長より草案が示され、審議の結果、変更内容が決定した。

5. 2008年度決算および2010年度予算について

木山博資会計担当理事より会計報告がなされ、審議の結果承認された。

・2008年度決算および税務申告について

決算業務および税務申告は税理士により行われ、納税額が決定された。納税額は159,100円となった。

(2008年度決算について)

会費収入は減少したが、次年度繰越金を増やすことができた。主な理由として、経費節約、大会運営の補助金100万円のうち大会収益から約88万円が返金されたこと、が挙げられる。また例年に比べ、会誌売上代が大幅に増加した。

なお2008年度より、特別事業積立金に関し、積立専用口座が開設され、この口座で一括管理されている。

・2010年度予算について

2008年度実績に倣い予算立てが行われた。旅費交通費について、2010年度は理事改選を行わないため、改選を行う年度に比べ予算が少ない。国際交流費、特別シンポジウム予備費について、2008年度は支出がなかったが、2010年度はNeuro2010が開催されるため予算に加えた。

6. 年会費の納入方法について

会費収入が減少傾向にあることをふまえ、年会費の納入方法について審議された。カード決済導入を検討していくこととなった。

7. 年会費の値上げについて

会費収入が減少傾向にあることをふまえ、年会費の値上げについて審議された。
カード決済導入と同時に年会費の値上げを行う方向で引き続き検討していくこととなった。

8. 休会制度の規定について

木山博資会計担当理事より草案が示され、審議された。以下の方向で引き続き検討していくこととなり、休会申込の様式等についても次期理事会で審議することとなった。

長期の海外留学等、海外居住により一時的に学会活動が困難となる場合、休会届を提出した上で休会できることとする。休会期間は当会会計年度（1 月 1 日～12 月 31 日）単位で、最長 3 年度とする。海外留学等終了後には、ただちに本会活動に復帰する旨申し出なければならない。
なお、休会中は次の通り取り扱うこととする。

- (1) 年会費は免除する
- (2) 機関誌「神経化学」は配布しない
- (3) 大会等当会主催の集会等の参加費は非会員扱いとする
- (4) 総会議決権は有しない
- (5) 役員等の選挙権及び被選挙権は有しない
- (6) 当会奨励賞の応募資格は有しない
- (7) 休会期間は会員歴に含めない
- (8) 休会開始後 3 年度を超えて復帰の届出がないときは、除名処分とする

ただし、次の場合は休会を認めない。

- (1) 年会費を滞納しているとき
 - (2) 休会中常時連絡可能な連絡先（住所・電子メールアドレス等）を申し出ないとき
 - (3) その他当会理事会にて不適当と判断されたとき
-

9. 学会ホームページにおける「女性研究者の声をまとめるコーナー」設置について

学会ホームページにおける「女性研究者の声をまとめるコーナー」設置について、将来計画委員会より提案され、出版広報委員会で審議されている旨仲嶋一範出版・広報担当理事より報告され、審議が行われた。

- *（案 1）学会ホームページに掲示板を設ける。この場合、不正な書き込みのコントロールや規則をどのようにするか等の問題がある。
- *（案 2）女性研究者に、これまでの体験談や苦労したことなどを、ホームページに（女性）研究者紹介コーナーのようなものを開設して、連載してもらう。研究室をもっている女性研究者だけでなく、留学から帰ってきたぐらいの若手の方にも書いていただくのも良いのではないか。また、ある女性研究者が、別の女性研究者の研究室を訪問して、インタビュー（取材）形式の記事に仕立てるといような企画もよいのではないか。これらの場合は、内容を順番にホームページへ掲載していくことになるので、現在のホームページ管理体制のままで対応可能と思われる。

これについて、理事より次のような意見が出された。

- * 女性研究者の問題について、男性会員からの意見も参考になるのではないか。
- * 各大学で女性研究者育成のためのプロジェクトが進んでおり、その内容は似通っているので、学会で同様のことをするよりも、採択されたプロジェクトの進展について情報提供する方が

よいのではないか。

- * 女子学生が研究を続ける割合の少ないことが問題になっており、女性研究者のためのコーナーを設置することで、研究のモデルケースを提示し、女子学生に幅を広げてもらえるのではないかな。
- * ホームページに掲示板を設けることは、問題のある書き込み等の恐れがあり、管理に消耗するのは現実的ではないのではないかな。
- * 学会にこのようなコーナーを設けることは時期尚早と思われるが、現在ホームページに掲載されている神経トピックスに類似した形で投稿してもらうのはよいのではないかな。
- * メーリングリストを設け、希望者を募ってはどうか。
- * 女性研究者の問題は一般的な問題ではあるが、学会としても女性研究者を育てていく姿勢を示すことが大切ではないかな。
- * 問題の裾野を広げるよりも、より多くの女性研究者に学会に参加してもらえるための具体策を考えたほうがよいのではないかな。

以上をふまえ、将来計画委員会で引き続き議論していくこととなった。

10. 第 52 回大会について

第 52 回大会について、田代朋子第 52 回大会長より報告された。

本年度は 2009 年 6 月 21 日（日）～ 24 日（水）の 4 日間、群馬県・伊香保温泉ホテル天坊にて開催されることとなっており、昨年同様、口演を重視した内容であるとのことであった。特別シンポジウム、シンポジウムについてプログラムおよび日程が決定し、充実した内容となっている旨報告された。また、前回に引き続き、若手育成セミナーを開催することとなり、案内を行うとのことであった。

11. 第 53 回大会について

第 53 回大会について、井上和秀第 53 回大会長より報告された。

会期は 2010 年 9 月 2 日（木）～ 9 月 4 日（土）、会場は神戸国際会議場・神戸国際展示場となった。第 52 回大会終了後にホームページでの案内を開始する予定であり、準備が整っている旨報告された。

12. 第 54 回大会長（2011 年度）及び第 55 回大会長（2012 年度）について

審議の結果、第 54 回大会長に米田幸雄氏が就任することとなり、第 55 回大会長に池田一裕氏が就任することとなった。

池田氏より第 55 回大会は APSN との合同大会とすることをねらっていくので、日本神経化学会から APSN へのプロポーザルを作製し、2009 年 6 月に開催予定の理事会で承認を得たいこと、またそのプロポーザルの案は池田氏の他、島田氏（会計担当理事）、和中氏（国際対応委員会委員長）、米田氏（APSN 理事）と作製したい旨提案があり、了承された。

13. その他

- ・ 科研費審査委員候補者について

科研費審査委員候補者について、投票で選出された上位 10 名を推薦することとなった。

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。

プログラム Program

神経化学会－GRT 研究会連携オープンシンポジウム
JSN - GRT Joint Open Symposium

ISN シンポジウム
ISN Symposium

日本神経化学会－日本生物学的精神医学会合同シンポジウム
JSN - JSBP Joint 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
Oral Sessions

ポスター発表
Poster Sessions

ランチョンセミナー
Luncheon Seminars

神経化学会－GRT研究会連携オープンシンポジウム

6 月 21 日 (日)

17:00～19:00 A会場 (1F・キング)

OS-1～OS-4 成体脳における神経新生と中枢神経系の再生戦略

座長：岡野 栄之 (慶應義塾大学医学部生理学教室)

板倉 徹 (和歌山県立医科大学脳神経外科)

OS-1 海馬ニューロン新生と神経再生戦略

○久恒 辰博

東京大院・新領域・先端生命

OS-2 成熟脳における新生ニューロンの分化段階と放射線耐性出現

○白尾 智明

群馬大学大学院医学系研究科神経薬理学

OS-3 メチル化 DNA 結合タンパク質による神経系細胞の分化・可塑性制御

○中島 欽一

奈良先端大・バイオ・分子神経分化制御

OS-4 神経新生の低下と精神疾患発症の脆弱性

○大隅 典子

東北大学大学院医学系研究科

ISNシンポジウム

6月22日(月)

9:00 ~ 11:40 A会場 (1F・キング)

ISN-1 ~ ISN-4 Axon Homeostasis and Diseases

座長：木山 博資 (大阪市立大学大学院医学研究科 機能細胞形態学)
御子柴克彦 (理化学研究所脳科学総合研究センター)

ISN-1 Molecular regulation of Wallerian degeneration of axons

○ Michael Coleman
The Babraham Institute, Cambridge, UK

ISN-2 Axon formation and polarized transport

○ Kozo Kaibuchi
Nagoya University Graduate School of Medicine

ISN-3 Control of axonal mitochondrial mobility and its impact on axonal homeostasis and degeneration

○ Zu-Hang Sheng
NINDS, NIH, USA

ISN-4 Transport and assembly dynamics of axonal neurofilaments

○ Anthony Brown
Center for Molecular Neurobiology and Department of Neuroscience, Ohio State University, Columbus, USA

日本神経化学会－日本生物学的精神医学会 合同シンポジウム

6 月 23 日 (火)

9 : 00 ~ 11 : 40 A会場 (1F・キング)

JSN-JSBP-1 ~

JSN-JSBP-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：池中 一裕 (生理学研究所分子神経生理研究部門)

齋藤 利和 (札幌医科大学医学部・神経精神医学講座)

三國 雅彦 (群馬大学大学院脳神経発達統御学講座 神経精神医学分野)

JSN-JSBP-1 末梢サイトカイン変化と精神疾患の病態について

○鶴飼 渉、小野 貴文、渡邊 公彦、橋本 恵理、吉永 敏弘、石井 貴男、
館農 勝、渡邊 一平、白坂 知彦、齋藤 利和

札幌医科大学医学部神経精神医学講座

JSN-JSBP-2 部位特異的な神経保護効果による持続的な GSK-3 β 阻害の抗うつ効果

○小俣 直人^{1,3}、村田 哲人¹、丸岡 伸行¹、PR Moya⁴、Y Leng³、CT Chiu³、Z Wang³、
P Leeds³、藤林 靖久²、和田 有司¹、DM Chuang³

¹ 福井大学医学部病態制御医学講座精神医学領域、² 福井大学高エネルギー医学研究センター、³ Molecular Neurobiology Section, NIMH, NIH、⁴ Laboratory of Clinical Science, NIMH, NIH

JSN-JSBP-3 中間表現型を用いた精神疾患脆弱性遺伝子の同定

○橋本 亮太^{1,2}、安田 由華^{1,2}、大井 一高²、福本 素由己²、高村 明孝²、
高橋 秀俊²、山森 英長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御機構研究センター、² 大阪大学大学院医学系研究科精神医学教室

JSN-JSBP-4 イボテン酸投与統合失調症モデルラットにおける EGF 受容体シグナルの関与

○水野 誠^{1,2}、鄭 英君²、外山 英和²、川村 宏樹²、阿部 佑一²、江田 岳誉²、
渋谷 雅子³、難波 寿明²、那波 宏之^{1,2}

¹ 新潟大・超域研究機構、² 新潟大・脳研・分子神経、³ 新潟大・医歯学総合・精神医学

JSN-JSBP-5 社会性の男女差と自閉症における社会性障害の脳画像研究

○山末 英典

東京大学大学院医学系研究科脳神経医学専攻精神医学分野

JSN-JSBP-6 統合失調症関連因子 PACAP による神経分化調節機構の解析

○山田 浩平¹、松崎 伸介^{1,2}、服部 剛志³、橋本 均⁴、新谷 紀人^{3,4}、馬場 明道⁴、
片山 泰一^{2,5}、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 大阪大・浜松医大・金沢大のこころの発達研究センター、³ 大阪大学大学院・医・分子精神神経学寄付講座、⁴ 大阪大学大学院・薬・神経薬理学分野、⁵ 浜松医科大学 解剖学講座

若手奨励賞シンポジウム

6月22日(月)

14:20～15:50 A会場(1F・キング)

LA-1

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 グルココルチコイド受容体およびBDNF受容体の相互作用に制御されるグルタミン酸放出

○沼川 忠広

国立精神・神経センター疾病研究第三部

シンポジウム

6 月 22 日 (月)

9 : 00 ~ 11 : 40 B会場 (9F・天の川)

S01-1 ~ S01-6 アストロサイトの発生と分化

座長 : 石崎 泰樹 (群馬大学大学院医学系研究科 脳神経発達統御学講座 分子細胞生物学分野)

中島 欽一 (奈良先端科学技術大学院大学バイオサイエンス研究科 分子神経分化制御学講座)

S01-1 成体脳における Olig2 陽性細胞の動態—アストロサイトへの分化を中心に—

○辰巳 晃子、奥田 洋明、和中 明生

奈良県立医科大学 医学部 第2解剖学教室

S01-2 BMPRIA 受容体と BMPRIIB 受容体を介した BMP シグナルは、グリア瘢痕形成に対して異なる影響を与える

○山田 真久¹、北村 尚士¹、佐藤 友美²、古市 貞一²、三品 裕司³

¹理化学研究所・脳センター・山田ユニット、²理化学研究所・脳センター・分子神経形成、³ミシガン大学

S01-3 発生期マウス小脳におけるアストロサイト前駆細胞

○倉知 正、蔡 娜、岡野一内田 孝幸、石崎 泰樹

群馬大院・医・分子細胞生物

S01-4 中枢神経系グリア細胞亜集団の細胞系譜解析

○鹿川 哲史、田賀 哲也

東京医歯大・難治研・幹細胞制御

S01-5 神経幹細胞が生み出す細胞の順番付けの仕組み

○中島 欽一

奈良先端大・バイオ・分子神経分化制御

S01-6 アストロサイトの発生分化における転写因子 Pax6 の役割

○大隅 典子

東北大学大学院医学系研究科

6 月 22 日 (月)

9 : 00 ~ 11 : 40 C会場 (3F・烏帽子)

S02-1 ~ S02-5 エピジェネティクスからの精神疾患解明への挑戦

座長 : 福永 浩司 (東北大学大学院薬学研究科)

久保田健夫 (山梨大学大学院医学工学総合研究部)

S02-1 精神疾患における DNA メチル化の意義

○加藤 忠史

- S02-2 アストロサイト特異的遺伝子 GFAP 発現制御に関与する DNA メチル化と遺伝子座核内配置
○滝沢 琢己、中島 欽一
奈良先端大・バイオ・分子神経分化制御
- S02-3 クロマチンリモデリング因子 ATRX 変異精神遅滞モデルマウスにおけるスパイン形成異常とそのメカニズム
○塩田 倫史¹、別府 秀幸²、北島 勲³、福永 浩司^{1,4}
¹東北大学大学院・薬学研究科・薬理学分野、²ハーバード大・心血管研、³富山大院・医・臨床分子病態検査、⁴東北大学 21 世紀 COE プログラム CRESCENDO
- S02-4 網膜神経細胞の分化に対するエピジェネティック因子の役割
○味岡 逸樹^{1,2,3}、仲嶋 一範²、Dyer Michael³
¹慶応大・医・咸臨丸プロジェクト、²慶応大・医・解剖学、³セントジュード小児研究病院・発生神経生物学
- S02-5 精神発達障害疾患のエピジェネティクス
○久保田 健夫、平澤 孝枝
山梨大院・医工総合・環境遺伝医学

6 月 22 日 (月)

9 : 00 ~ 11 : 40 D会場 (1F・長峰)

- S03-1 ~ S03-6 発達障害における基礎研究の成果を臨床像と照らしつつ今一度検証する
座長：成田 正明 (三重大大学大学院医学系研究科・発生再生医学)
武田 雅俊 (大阪大学大学院医学系研究科精神医学教室)

- S03-1 発達障害 (自閉症) モデル動物の現状
○成田 正明、大藪 明子、井村 誉史雄、横山 智美、鎌田 尚樹、田野 かおり、太城 康良、内田 敦子
三重大院・医・発生再生医学
- S03-2 ADHD モデルラットの脳内遺伝子・蛋白質の発現変化
○増尾 好則
産業技術総合研究所健康工学研究センター精神ストレス研究チーム
- S03-3 脳血流動態からみた発達障害 - 神経化学的アプローチに生かせるか -
○成田 奈緒子、五月女 颯之、樋口 大樹、熊倉 悠佳
文教大学教育学部特別支援教育専修
- S03-4 自閉症生物学的マーカー研究の展望
○松崎 秀夫^{1,2}
¹大阪大院・小児発達学研究科、²浜松医科大学精神神経医学講座

S03-5 ニューレグリン -1 の新生仔暴露はドーパミン機能を変化させる

○加藤 泰介、武井 延之、那波 宏之
新潟大院・医・分子神経生物

S03-6 妊娠期感染症が脳皮質神経発生に及ぼす影響

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

6 月 23 日 (火)

9 : 00 ~ 11 : 40 B会場 (9F・天の川)

S04-1 ~ S04-6 シナプス可塑性・記憶形成におけるプロテインキナーゼの役割 — 新たな展開

座長：久永 眞市 (首都大学東京 生命科学専攻 神経分子機能研究室)

喜田 聡 (東京農業大学応用生物科学部 バイオサイエンス学科)

S04-1 シナプス可塑性における神経活動依存的 CaMKII 活性化の役割

○福永 浩司
東北大院・薬 薬理学、21 世紀 COE “CRESCENDO”

S04-2 記憶形成に対する CaMKIV 情報伝達経路の役割

○喜田 聡
東京農大・バイオサイエンス

S04-3 PKA 活性の抑制による記憶促進

○堀内 純二郎
首都大学東京 理工学研究科 生命科学専攻

S04-4 学習課題における mTOR キナーゼシグナル

○武井 延之、石塚 佑太、那波 宏之
新潟大学脳研究所

S04-5 シナプス可塑性、学習と記憶における GSK3 β

○プラットナー フロリアン
ロンドン大学・神経研

S04-6 Cdk5 とシナプス可塑性

○ビブ ジェームス
テキサス大学サウスウェスタンメディカルセンター

6月23日(火)

9:00 ~ 11:40 C会場 (3F・烏帽子)

S05-1 ~ S05-3 基礎研究と創薬を結び付ける Translational Research

座長: 小泉 信一 (ラクオリア創薬株式会社)

高坂 新一 (国立精神・神経センター 神経研究所)

パネリスト: 塚本 尚 (ジョンスホプキンス大学)

永井 義隆 (国立精神・神経センター神経研究所 疾病研究第四部)

新田 淳美 (名古屋大学大学院医学系研究科 医療薬学分野)

S05-1 サイエンスを医薬候補品に結びつける創薬研究

○小泉 信一

ラクオリア創薬株式会社

S05-2 創薬シード化合物探索のための画期的な新規計算手法の紹介

○奥野 恭史、村上 竜太

京都大学大学院薬学研究科

S05-3 如何にして“化合物”を“薬”に結びつけるか

○山本 利憲

ラクオリア創薬株式会社

6月23日(火)

9:00 ~ 11:40 D会場 (1F・長峰)

S06-1 ~ S06-6 何がどのように細胞移動と軸索ガイダンスを制御するのか?

座長: 五嶋 良郎 (横浜市立大学大学院医学研究科)

仲嶋 一範 (慶應義塾大学医学部解剖学教室)

S06-1 大脳皮質形成の神経細胞移動において Abi2 は WAVE-Arp2/3 を介して重要な役割を担う

○謝 敏かく¹、八木 秀司^{1,2}、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

S06-2 Reelin-Dab1 シグナルは terminal translocation によって局所での inside-out 様式の層構造形成を制御する

○関根 克敏、川内 健史、久保 健一郎、本田 岳夫、仲嶋 一範

慶應義塾大学医学部解剖学教室

S06-3 正常脳・傷害脳における Slit-Robo シグナルの新生ニューロン移動制御

○金子 奈穂子¹、マリン オスカー²、廣田 ゆき¹、

ルービンシュタイン ジョン³、村上 富士夫⁴、アルバレスビュイラ アルトロ³、

岡野 栄之⁵、ティッシャーラビン マーク⁶、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 アリカンテ神経科学研究所、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所、⁵慶應義塾大学医学部生理学教室、⁶ジェネンテック

S06-4 新しい軸索ガイダンス分子, Draxin

○田中 英明^{1,2}、新明 洋平¹、Shahidul M Islam¹、Tatsuya Okafuji¹、Yuhong Su^{1,2}、Iftekhar Bin Naser^{1,2}、Giasuddin Ahmed^{1,2}、Sanbing Zhang^{1,2}、太田 訓正¹
¹熊本大学大学院医学薬学研究部神経分化学、²グローバル COE「細胞系譜制御」熊本大学

S06-5 新規軸索ガイダンス分子 LOTUS の細胞機能

○竹居 光太郎¹、佐藤 泰史^{1,2}、山口 めぐみ¹、池谷 真澄¹、有江 裕子¹、五嶋 良郎¹
¹横浜市大院・医・分子薬理神経、²三菱化学・生命研・脳梗塞

S06-6 膜伸展刺激活性化チャネルを介した軸索伸長の制御：新規ポジティブフィードバック機構

○柴崎 貢志^{1,2,3}、村山 奈美枝^{1,3}、小野 勝彦⁴、石崎 泰樹⁵、富永 真琴^{1,2,3}
¹岡崎統合バイオサイエンスセンター・細胞生理、²生理学研究所・細胞生理、³総合研究大学院大学・生命科学研究科、⁴京都府立医大・生物学、⁵群馬大・医・分子細胞生物学

6 月 23 日 (火)

15 : 50 ~ 18 : 30 A会場 (1F・キング)

S07-1 ~ S07-5 精神医学と神経学の統合的展開

座長：和田 圭司 (国立精神・神経センター神経研究所疾病研究第四部)
西川 徹 (東京医科歯科大学精神行動医科学分野)

S07-1 精神症状と神経症状の接点としての神経機能不全：臨床と基礎の架け橋

○澤 明
Program in Molecular Psychiatry, Departments of Psychiatry and Neuroscience, Johns Hopkins University School of Medicine

S07-2 経験依存的 AMPA 受容体シナプス移行

○高橋 琢哉
横浜市立大学大学院医学研究科生理学

S07-3 生体情報の統合器官として脳

○和田 圭司^{1,2}
¹国立精神・神経センター神経研究所、²CREST, JST

S07-4 精神医学と神経学の統合的展開—神経内科医の立場から

○村田 美穂
国立精神神経センター病院神経内科

S07-5 精神医学と神経学の統合的展開：臨床的観点（精神医学）

○佐野 輝

鹿児島大院・医歯学・精神機能病学

6月23日（火）

15:50～18:30 B会場（9F・天の川）

S08-1～S08-5 蛋白質品質管理と脳神経疾患

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 解剖学第一講座）

S08-1 小胞体ストレスと神経変性疾患、躁鬱病

○浦野 文彦

University of Massachusetts Medical School

S08-2 APP E693 Δ 変異で促進されるA β オリゴマーによる細胞障害

○富山 貴美

大阪市立大学大学院医学研究科脳神経科学

S08-3 タウ凝集による神経変性機構

○高島 明彦

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

S08-4 脳虚血後の病態におけるERストレスの関与

○原 英彰

岐阜薬科大学

S08-5 小胞体－プロテアソーム系に基づく神経変性疾患の新しい治療戦略

○工藤 喬¹、今泉 和則²

¹大阪大学大学院医学系研究科、精神医学教室、²宮崎大学医学部 解剖学講座 分子細胞生物学分野

6月23日（火）

15:50～18:30 C会場（3F・烏帽子）

S09-1～S09-5 網羅的アプローチ（-omics）による、神経化学の新しい世界観

座長：五十嵐道弘（新潟大学大学院医歯学総合研究科 分子細胞機能学）

平林 義雄（理化学研究所 脳科学総合研究センター平林研究ユニット）

S09-1 マウス小脳発達トランスクリプトーム解析：小脳神経回路発達の遺伝基盤の解明に向けて

○林 周宏¹、西部 弘純¹、佐藤 明²、古市 貞一¹

¹理化学研究所・脳科学総合研究センター・分子神経形成研究チーム、²理化学研究所 基幹研究所、応用システムバイオロジー研究所

S09-2 パルミトイル化酵素ファミリーによるシナプス機能制御

○深田 正紀^{1,2}、則竹 淳¹、深田 優子^{1,2}

¹ 生理学研究所 細胞器官研究系 生体膜研究部門、² 科学技術振興機構・さがけ

S09-3 成長円錐研究におけるプロテオミクスの導入と網羅的研究戦略

○五十嵐 道弘

新潟大・医歯学・分子細胞機能学(医・生化学第二)

S09-4 神経化学のためのリポミクス ―基盤技術と戦略―

○田口 良

東京大院・医・メタボローム

S09-5 脳内微量成分の質量分析ーリン酸化蛋白質と膜脂質

○平林 義雄、鍋谷 卓司

理研・脳センター

6 月 23 日 (火)

15:50 ~ 18:30 D会場 (1F・長峰)

S10-1 ~ S10-6 神経突起先端およびスパインにおける細胞骨格、内膜系の動態と機能

座長：石川 良樹 (群馬大学大学院医学系研究科病態薬理学分野)

鈴木 龍雄 (信州大学大学院医学系研究科神経可塑性学分野)

S10-1 神経成長円錐におけるアクチン結合タンパク質の動態観察

○加藤 薫¹、海老原 利枝¹、東ヶ崎 健¹、野住 素宏²、五十嵐 道弘²

¹ 産総研・脳神経情報、² 新潟大院・医歯学・シグナル伝達

S10-2 アクトミオシン系におけるドレブリン E を介したアクチン側からの制御の軸索成長に与える役割

○花村 健次、水井 利幸、白尾 智明

群馬大院・医・神経薬理学

S10-3 BDNF による樹状突起形成におけるコフィリンリン酸化の役割

○大橋 一正、宮島 健、斉藤 聡彦、木内 泰、赤塚 淳一、水野 健作

東北大・院・生命

S10-4 成長円錐におけるファシン、コフィリン、ドレブリン動態：精製蛋白質系より得られた知見との比較

○石川 良樹

群馬大・院医・病態薬理

S10-5 電子線トモグラフィーを用いたダイナミン1ノックアウトマウスの神経終末におけるエンドサイトーシス中間体の解析

○西野一林 美都子^{1,2}、オー' トゥール アイリーン³、ファークソン ショーン²、

デ・カミリ ピエトロ²

¹大阪大・産研・生体情報、²エール大・医・細胞生物 / ハワードヒューズ、³コロラド大・ボールダー校・分子細胞発生生物

S10-6 シナプス可塑性における微小管の役割

○光山 冬樹¹、奥谷 正人²、小出 直³

¹藤田保健衛生大学脳外科、²天寿病院、内科、³福友医学研究所

6月24日(水)

13:10 ~ 15:50 A会場 (1F・キング)

S11-1 ~ S11-5 ミクログリアの機能と病態 — 最近の研究動向と将来の展望

座長：中西 博 (九州大学大学院歯学研究院口腔常態制御学講座 口腔機能分子科学分野)
井上 和秀 (九州大学大学院薬学研究院医療薬科学部門・薬効解析学分野)

S11-1 ミクログリアの形態変化と遊走 — 細胞外 ATP による遊走と突起伸長の調節分子機構 —

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

¹国立精神・神経セ・神経研・代謝、²神戸大学院・医・脂質生化学、³九州大学院・薬・薬理学

S11-2 ミクログリアと疼痛

○津田 誠、井上 和秀

九州大学大学院薬学研究院薬理学分野

S11-3 ミクログリアによる p38 MAPK を介した変性軸索の貪食

○田中 達英、山下 俊英

大阪大院・医・分子神経科学

S11-4 脳の老化におけるミクログリア内リソソームならびにミトコンドリア由来 ROS の役割

○中西 博

九州大学院・歯・加齢口腔科学

S11-5 Alzheimer 病における末梢性ベンゾジアゼピン受容体をバイオマーカーと機能性分子とする視点からのグリア細胞の寄与

○季 斌、樋口 真人、須原 哲也

放射線医学総合研究所分子イメージングセンター分子神経イメージング研究グループ

6 月 24 日 (水)

13:10 ~ 15:50 B会場 (9F・天の川)

S12-1 ~ S12-6 精神・神経・筋疾患のトランスレーショナルリサーチ

座長：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疾患関連分子解析部門)

辻 省次 (東京大学大学院医学系研究科 神経内科学教室)

S12-1 精神疾患のトランスレーショナルリサーチ：統合失調症とディスバインジン

○橋本 亮太^{1,2}、大井 一高²、安田 由華^{1,2}、福本 素由己²、高村 明孝²、
山森 英長^{2,3}、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、³大阪大院・医・分子
精神神経学

S12-2 隔離飼育ストレス負荷 Disrupted-in-Schizophrenia-1 変異遺伝子過剰発現マウスは新規統合失調症および気分障害病態モデルマウスとして有用である

○丹羽 美苗^{1,2}、ジャロペレド ハンナ³、尾崎 紀夫¹、澤 明³、鍋島 俊隆²

¹名古屋大院・医・精神医学、²名城大院・薬・薬品作用学、³ジョンスホプキンス大・
医・精神医学

S12-3 ALS における RNA editing 異常の病因的意義

○郭 伸

東京大院・医・神経内科

S12-4 パーキンソン病モデル MPTP 誘発ドパミン神経障害における $\text{Na}^+/\text{Ca}^{2+}$ 交換系の関与

○梨子田 哲明¹、川崎 俊之¹、大槻 健弥¹、北尾 達哉¹、吾郷 由希夫¹、
田熊 一徹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

S12-5 糖鎖異常と筋ジストロフィー - 病態・治療戦略

○戸田 達史

神戸大院・医・神経内科／分子脳科学

S12-6 筋疾患のトランスレーショナルリサーチ (基礎から臨床へ)

○武田 伸一

国立精神・神経センター 神経研究所 遺伝子疾患治療研究部

6月24日(水)

13:10～15:50 C会場(3F・烏帽子)

S13-1～S13-5 霊長類を用いた精神神経疾患モデルの現況と展望

座長：中村 克樹(京都大学霊長類研究所)

那波 宏之(新潟大学脳研究所・分子神経生物学)

S13-1 霊長類における社会行動発現の神経機構

○西条 寿夫^{1,2}、堀 悦郎^{1,2}、マオ カンバン^{1,2}、小野 武年^{1,2}

¹富山大学医学薬学研究部システム情動科学、²CREST, JST

S13-2 マーモセットの行動評価法

○中村 克樹^{1,2}

¹京都大学霊長類研究所、²国立精神・神経センター神経研究所

S13-3 上皮成長因子受容体リガンドを用いた統合失調症モデル動物

○那波 宏之^{1,2}、水野 誠²、外山 英和¹、鄭 英君¹、加藤 泰介¹、阿部 佑一¹、坂井 美和子³、渋谷 雅子³、江田 岳誉¹、王 冉¹、荒木 一明¹、石塚 佑太¹、武井 延之¹、岩倉 百合子¹、難波 寿明¹

¹新潟大・脳研・分子神経、²新潟大・超域、³新潟大・医歯学総合・精神医学

S13-4 ウイルスベクターを用いた霊長類モデル作出と遺伝子治療

○高田 昌彦

京都大学霊長類研究所 分子生理研究部門 統合脳システム分野

S13-5 マーモセットの発生工学 -トランスジェニックマーモセットの作出に向けて-

○佐々木 えりか¹、岡野 栄之²

¹(財)実験動物中央研究所マーモセット研究部応用発生生物研究室、²慶應義塾大学医学部生理学教室

6月24日(水)

13:10～15:50 D会場(1F・長峰)

S14-1～S14-5 ニューラルコミュニケーションの新たな理解へのチャレンジ

座長：関野 祐子(東京大学医科学研究所基礎医科学部門 神経ネットワーク分野)

熊倉鴻之助(上智大学理工学部情報理工学科)

S14-1 トランスミッター放出マシナリータンパク複合体の分子構造基盤

○大塚 稔久

富山大院・医薬(医)・臨床分子

S14-2 扁桃体外側核の興奮・抑制シナプス応答の可視化と時間空間パターン解析

○関野 祐子¹

¹東京大・医科研・神経ネットワーク、²科学技術振興機構、CREST

S14-3 グルタミン酸センサーで可視化したグルタミン酸放出

○廣瀬 謙造

東京大学大学院医学系研究科神経生物学

S14-4 小脳神経回路発達における GABA 放出部位の変化と機能

○吉田 様子

豊橋技術科学大学 物質工学系

S14-5 BDNF の神経活動依存的遊離の可視化

○松田 尚人^{1,2}、ル フイ²、深田 優子¹、則竹 淳¹、ガオ ホンフエン²、根本 知己¹、
深田 正紀¹、プー ムーミン²

¹生理学研究所、²カリフォルニア大学バークレー校

一般口演

6月22日(月)

14:20～16:00 B会場(9F・天の川)

001-1～001-5 ミクログリア

座長：仲田 義啓(広島大学大学院医歯薬学総合研究科・薬効解析科学)
浜之上 誠(東邦大学医学部生理学・細胞生理学)

001-1 フィブロネクチン刺激ミクログリアにおける P2X₄ 受容体発現増加の翻訳および翻訳後制御

○豊満 笑加、津田 誠、齋藤 秀俊、井上 和秀
九州大学大学院薬学研究院薬理学分野

001-2 アメボイドミクログリアにおける PLD4 の解析

○大谷 嘉典¹、山口 宜秀¹、木谷 裕²、池中 一裕³、佐藤 友美⁴、古市 貞一⁴、馬場 広子¹

¹東京薬大・薬・機能形態学、²家畜センター、³生理研・分子神経生理、⁴理研・脳センター・分子神経形成

001-3 血小板由来増殖因子PDGF誘発アロディニアにおける脊髄ミクログリアの関与

○増田 潤哉、津田 誠、齋藤 秀俊、井上 和秀
九州大学大学院薬学研究院薬理学

001-4 ミクログリア細胞における時計遺伝子の機能的発現

○山本 朋未、宝田 剛志、米田 幸雄
金沢大院・自然科学(薬)・薬物学

001-5 リポポリサッカライドで生じる学習記憶障害過程におけるインターロイキン 1 の重要性

○田中 佐知子¹、神田 錦吾¹、中町 智哉²、沼沢 聡¹、塩田 清二²、吉田 武美¹

¹昭和大学・薬・毒物、²昭和大学・医・解剖

6月22日(月)

14:20～16:20 C会場(3F・烏帽子)

002-1～002-6 タンパク・リン酸化とその制御

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)
高橋 正身(北里大学 医学部生化学)

002-1 プロリン指向性プロテインキナーゼによるタウリン酸化は、サイクリック AMP 依存性プロテインキナーゼにより複雑な制御を受ける。

○橋口 美津子
東京医科大学医学部細胞生理学講座

O02-2 Phos-tag SDS-PAGE による Cdk5 活性化サブユニット p35 のリン酸化状態及び新規リン酸化サイトの解析

○細川 智永、斎藤 太郎、浅田 明子、久永 真市
首都大・理工・生命

O02-3 神経細胞に特異的なカルシウムとプロテアソームに依存した Cdk5 活性化サブユニット p35 の分解

○佐藤 亘¹、岩田 修永²、高野 二郎²、斉藤 太郎¹、浅田 明子¹、西道 隆臣²、久永 真市¹
¹首都大院・理工・生命、²理研 BSI・神経蛋白制御研究チーム

O02-4 Cdk5 の活性化サブユニット p39 と p35 の膜結合依存的な分解制御機構の解析

○嶺岸 正治、浅田 明子、瀧上 孝裕、斎藤 太郎、久永 真市
首都大学東京理工学研究科生命科学専攻神経分子機能研究室

O02-5 成体マウス嗅球のインターニューロンにおける Protein tyrosine phosphatase receptor-type O (PTPRO) の発現

○小谷 武徳、村田 陽二、大西 浩史、森 宗昌、草薙 伸也、齊藤 泰之、岡澤 秀樹、的崎 尚
群馬大学生体調節研究所バイオシグナル分野

O02-6 チロシンリン酸化シグナルによる脳のストレス応答制御

○大西 浩史¹、草薙 伸也¹、林 由里子¹、高雄 啓三²、宮川 剛²、齊藤 泰之¹、村田 陽二¹、的崎 尚¹
¹群馬大学生体調節研究所バイオシグナル分野、²藤田保健衛生大学総合医科学研究部門

6 月 22 日 (月)

14 : 20 ~ 16 : 20 D会場 (1F・長峰)

O03-1 ~ O03-6 遺伝子発現

座長：山形 要人 (東京都神経科学総合研究所神経薬理研究部門)
渡辺 康裕 (防衛医科大学校薬理学)

O03-1 神経細胞への新規バキュロウイルスシステムによる遺伝子導入発現法

○武内 恒成、本多 敦子、野住 素広、五十嵐 道弘
新潟大学大学院医歯学総合研究科分子細胞機能学

O03-2 脳発達過程における MAGE ファミリー遺伝子の発現調節

○大雲 剛志、蔡 宗樺、長谷川 孝一、吉川 和明
大阪大学蛋白質研究所神経発生制御研究室

O03-3 神経細胞に発現する鉄関連遺伝子

○中村 有加里、中道 範隆、宝田 剛志、米田 幸雄
金沢大院 自然科学 (薬) 薬物学

- O03-4 新規トリプトファン 2,3- ジオキシゲナーゼバリエーションの同定：予想される海馬と小脳での TDO の機能について
○金井 将昭¹、中村 敏一²、船越 洋¹
¹大阪大学大学院・医学系研究科・分子再生医学分野、²大阪大学・先端イノベーション・クリングルファーマ再生創薬共同研究部門
- O03-5 マウス脳内における runt related factor 2 の発現
○橘 正毅、宝田 剛志、米田 幸雄
金沢大院・自然科学・薬物
- O03-6 嗅球摘出マウス脳におけるシナプス可塑性関連遺伝子の発現量変化
○竹田 麗子、白尾 智明、児島 伸彦
群馬大院・医・神経薬理

6 月 22 日 (月)

16 : 10 ~ 18 : 30 A会場 (1F・キング)

O04-1 ~ O04-7 神経細胞死

座長：一瀬 宏 (東京工業大学大学院生命理工学研究科)
岡澤 均 (東京医科歯科大学難治疾患研究所 神経病理学分野)
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)

- O04-1 カイニン酸誘発てんかんラット脳における PAP I, PAP III の発現誘導
○川原 慎一¹、小西 博之¹、森野 道晴²、大畑 健治²、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、²大阪市立大学大学院医学研究科脳神経外科
- O04-2 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によるグルタミン酸神経毒性防御
○家亦 美佳、小椋 正人、谷浦 秀夫、中道 範隆、宝田 剛志、米田 幸雄
金沢大院・自然科学・薬物学
- O04-3 培養小脳顆粒細胞における低カリウム誘発細胞死に対する甲状腺ホルモン T4 の細胞保護作用
○小柳 洗志、高橋 理貴、根岸 隆之、田代 朋子
青山学院大学大学院理工学研究科理工学専攻生命科学コース
- O04-4 熱ショック転写因子 (HSF1) 活性化剤は分子シャペロン群の発現を誘導し、ポリグルタミン病の神経変性を抑制する
○永井 義隆¹、藤掛 伸宏¹、ポピエル 明子¹、山口 政光²、戸田 達史³、和田 圭司¹
¹国立精神・神経センター・神経研究所・疾病4部、²京都工繊大・繊維・応用生物、³大阪大・院医・臨床遺伝学

- O04-5 タウオパチーにより引き起こされるパーキンソン症状：SJLB マウスの検討**
 ○谷口 泰造¹、角山 圭一¹、炬口 真理子¹、西本 高明¹、千葉 俊明²、鈴木 登²、
 松本 明¹、松山 正剛¹
¹姫路獨協大学 薬学部、²聖マリアンナ医科大学 免疫学
- O04-6 小脳顆粒細胞におけるジフェニルアルシン酸による酸化ストレスと細胞死**
 ○根岸 隆之¹、高橋 理貴¹、小柳 洸志¹、大西 大空¹、平野 靖史郎²、
 田代 朋子¹
¹青山学院大学理工学部化学・生命科学科、²国立環境研究所環境リスク研究センター
- O04-7 トリメチルスズ誘発性海馬歯状回神経細胞障害におけるミネラルコルチコイド受容体の関与**
 ○杉山 千絵、首藤 誠、荻田 喜代一
 摂南大学 薬学部 薬理学研究室

6 月 22 日 (月)

16 : 10 ~ 18 : 30 B会場 (9F・天の川)

O05-1 ~ O05-7 β アミロイド・認知症

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)

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)

道川 誠 (国立長寿医療センターアルツハイマー病研究部)

O05-1 小胞体とゴルジ体での β APP のプロセッシングと細胞内輸送における Syntaxin5 アイソフォームの役割

○須賀 圭¹、齋藤 綾子¹、富山 貴美²、森 啓²、赤川 公朗¹

¹杏林大学医学部細胞生理学教室、²大阪市立大学大学院医学研究科脳神経科学教室

O05-2 アルツハイマー病における GM1 ガングリオシド誘導性アミロイド β 蛋白質重合に関与する後期エンドサイトーシス障害

○湯山 耕平、柳澤 勝彦

国立長寿医療センター研究所 アルツハイマー病研究部

O05-3 アンギオテンシン変換酵素のもつ A β 変換活性のドメイン解析

○鄒 鷗¹、前田 智司¹、大葉 龍太郎³、道川 誠²、駒野 宏人¹

¹岩手医大・薬・神経科学、²国立長寿医療センター・アルツハイマー病研究部、³(株) ビーエムエル・先端医療開発部

O05-4 インスリンによる神経膜からの A β 重合抑制

○山本 直樹、鈴木 健二

立命館大学・薬

O05-5 新規神経保護因子の β - アミロイドによる誘導

○五味 不二也、内田 洋子

O05-6 SAMP8 海馬と脈絡叢における Ttr と App の発現

○降旗 千恵¹、渡辺 貴志¹、猪狩 寛子¹、嘉山 巧¹、鴻野 貴司¹、鈴木 孝昌²、
太田 浩良³、野村 靖幸⁴、田代 朋子¹

¹青山学院大学理工学研究科生命科学、²国立医薬品食品衛生研究所、³信州大学医学部、⁴北海道大学薬学部

O05-7 Nefiracetam による興奮性および抑制性神経伝達は、ニコチン性アセチルコリン受容体により制御される

○森口 茂樹¹、檜橋 敏夫²、福永 浩司¹

¹東北大院・薬・薬理、²ノースウエスタン大・医・分子薬理

6 月 22 日 (月)

16:30 ~ 18:30 C会場 (3F・烏帽子)

O06-1 ~ O06-6 神経可塑性

座長：植田 弘師 (長崎大学大学院医歯薬学総合研究科分子薬理学)

塩坂 貞夫 (奈良先端科学技術大学院大学 バイオサイエンス研究科)

O06-1 繰り返しグルタミン酸刺激誘発性の長期神経可塑性に伴う遺伝子発現変化の解析

○河合 克宏^{1,2}、富永一吉野 恵子³、谷口 直子³、御子柴 克彦^{1,2}、小倉 明彦³、
田代 朋子⁴

¹(独) 科学技術振興機構・発展研究・ICORP-SORST・カルシウム振動プロジェクト、
²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、³大阪大学大学院・生命機能研究科、⁴青山学院大学大学院 理工学研究科

O06-2 出力先皮質を含む培養海馬切片での PKA 繰り返し活性化後の長期的シナプス強化

飯嶋 一之、大江 祐樹、江頭 良明、○富永一吉野 恵子、小倉 明彦
大阪大学大学院生命機能研究科脳神経工学講座神経可塑性生理学研究室

O06-3 培養海馬神経細胞における樹状突起スパインからシャフトへのドレブリントランスロケーションの調節メカニズム

○水井 利幸^{1,3}、白尾 智明¹、関野 祐子^{2,3}

¹群馬大学大学院医学系研究科神経薬理学、²東京大学医科学研究所神経ネットワーク、³CREST,JST

O06-4 ドレブリン A 欠失による文脈依存的恐怖条件づけの障害と NMDA 受容体の恒常性可塑性の異常

○児島 伸彦¹、青木 ちえ²、花村 健次¹、山崎 博幸¹、白尾 智明¹

¹群馬大院・医・神経薬理、²ニューヨーク大学神経科学センター

O06-5 A CaMKII mRNA の輸送機構に関与するタンパク質の同定

○森 泰丈¹、宮田 信吾^{1,2}、遠山 正彌^{1,2}

¹大阪大院・医・神経機能形態、²大阪大院・医・こどものこころの分子統御機構

O06-6 Neuropsin による領域特異的・プロセス特異的シナプスタグ形成

○石川 保幸、田村 英紀、塩坂 貞夫
奈良先端科学技術大学院大学細胞構造学講座

6 月 22 日 (月)

16:30 ~ 18:30 D会場 (1F・長峰)

O07-1 ~ O07-6 細胞移動・軸索ガイダンス

座長：佐藤 真 (福井大学医学部医学科形態機能医科学講座)

東田 陽博 (金沢大学大学院医学系研究科 脳細胞遺伝子学講座)

O07-1 Dab1 の核細胞質間シャトリングが脳皮質層形成に果たす役割の解明

○本田 岳夫¹、山崎 真弥²、長澤 寿磨²、阿部 学²、崎村 建司²

¹慶應義塾大学医学部解剖学教室、²新潟大学脳研究所基礎神経科学部門細胞神経生物学分野

O07-2 大脳皮質発生におけるセブチンの機能

篠田 友靖、伊東 秀記、須藤 香織、岩本 郁子、森下 理香、岡本 賢一、

○永田 浩一

愛知県コロニー発達障害研究所・神経制御学部

O07-3 嗅索形成における新規軸索ガイダンス分子 LOTUS の Nogo シグナリング抑制作用

○池谷 真澄¹、山口 めぐみ¹、佐藤 泰史^{1,2}、有江 裕子¹、栗原 裕司¹、中村 史雄¹、
五嶋 良郎¹、竹居 光太郎¹

¹横浜市大院・医・分子薬理神経、²三菱化学・生命研・脳梗塞

O07-4 新規軸索ガイダンス分子 LOTUS と Nogo-66 受容体との結合による神経突起伸長作用

○栗原 裕司^{1,2}、有江 裕子^{1,2}、山口 めぐみ¹、池谷 真澄¹、中村 史雄¹、
水木 信久²、五嶋 良郎¹、竹居 光太郎¹

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

O07-5 セマフォリン3A情報伝達におけるフィラミンAの役割

○中村 史雄、久米田 孝輔、山根 昌之、山下 直也、小倉 顕一、五嶋 良郎
横浜市立大学・医学部・分子薬理

O07-6 チュープリンのチロシン化修飾による軸索へのキネシン輸送制御

○小西 慶幸、瀬藤 光利

浜松医大・分子解剖

6月23日(火)

14:20 ~ 15:40 A会場 (1F・キング)

O08-1 ~ O08-4 ストレス・不安

座長: 車地 暁生 (東京医科歯科大学精神行動医科学分野)

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)

O08-1 幼若期ニューロンへのグルココルチコイド暴露は BDNF で増強されるシナプス成熟を抑制する

○熊丸 絵美、沼川 忠広、安達 直樹、泉 愛子、功刀 浩

国立精神・神経センター・神経研究所・疾病三部

O08-2 慢性ストレス負荷ラット下垂体中間葉においてドーパミンレベル低下により誘導される pancreatitis-associated protein I の発現

○小西 博之^{1,2}、小川 登紀子^{1,2}、川原 慎一¹、中込 咲綾¹、井上 浄²、遠山 正彌²、木山 博資^{1,2}

¹大阪市立大学大学院医学研究科機能細胞形態学、²21 世紀 COE プログラム「疲労克服研究教育拠点の形成」、³大阪大学大学院医学系研究科神経機能形態学講座

O08-3 社会性嗅覚刺激は mdx マウスの非条件性情動応答を減弱する

○山本 和弘¹、高橋 明男¹、和田 圭司²、関口 正幸²

¹国立精神・神経センター 神経研究所 実験動物管理室、²国立精神・神経センター 神経研究所 疾病研究第4部

O08-4 授乳期における母体摂食制限が仔の行動に与える影響

○公文 麻美¹、山本 和弘¹、高橋 明男¹、和田 恵津子^{1,2}、和田 圭司^{1,2}

¹国立精神神経センター神経研究所疾病4研究4部、²科学技術振興機構

6月23日(火)

14:20 ~ 15:40 B会場 (9F・天の川)

O09-1 ~ O09-4 ミエリン・脱髄疾患

座長: 阿相 皓晃 (慶応義塾大学医学部漢方医学センター)

渡部 和彦 (東京都神経科学総合研究所 分子神経病理研究部門)

O09-1 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の変化

○児玉 明子、石橋 智子、馬場 広子

東京薬科大学・薬学部・機能形態学

O09-2 Annexin2 によるリゾレシチン誘導坐骨神経脱髄の阻害作用

○林 明子、片伯部 哲也、木村 昂司、馬場 広子

東京薬科大学 機能形態学

O09-3 マウス多発性硬化症モデルにおける KLK6 を介した脱髄分子機序

○板東 良雄、坂田 亜衣、布村 光、村上 公一、吉田 成孝

旭川医科大学 解剖学講座 機能形態学

O09-4 多発性硬化症における誘導型プロスタグランジン E 合成酵素の役割

○竹内 千仙^{1,2,3}、松本 陽⁴、神山 邦子⁴、植松 智⁵、審良 静男⁵、山形 要人²、竹宮 孝子^{1,2}

¹東京女子医大・総研、²東京都神経研・神経薬理、³東京女子医大・神経内科、⁴東京都神経研・分子神経病理、⁵大阪大・微研・自然免疫

6 月 23 日 (火)

14:20 ~ 15:40 C会場 (3F・烏帽子)

O10-1 ~ O10-4 開口放出

座長：島田 昌一 (大阪大学大学院医学研究科 神経細胞生物学講座)

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・薬理学)

O10-1 ウシ副腎髄質クロマフィン細胞における分泌顆粒の細胞内局在、及び動態の 4 次元解析

○林 光紀、田村 和希、姜 裕貴、笹川 展幸、熊倉 鴻之助

上智大学理工学部情報理工学科

O10-2 Complexin directly binds with synaptotagmin 1.

○清水一岡部 千草¹、篠原 巧¹、阿部 輝雄²、得丸 博史¹

¹徳島文理大学 香川薬学部 薬理学、²新潟大学 脳研究所 細胞神経生物学分野

O10-3 SNAP-23 リン酸化部位の網羅的解析

○安田 圭一¹、板倉 誠¹、永田 悦子¹、山森 早織¹、居原 秀²、高橋 正身¹

¹北里大学医学部生化学、²大阪府立大学・大学院理学系研究科・生物科学専攻

O10-4 SNAP-25 のリン酸化サイトを欠失した KI マウスで見られた歯状回顆粒細胞の異常活動

○大塚 信太朗、山森 早織、内田 達也、板倉 誠、高橋 正身

北里大学医学部生化学

6 月 23 日 (火)

14:20 ~ 15:40 D会場 (1F・長峰)

O11-1 ~ O11-4 シナプス形成

座長：高松 研 (東邦大学医学部細胞生理学)

森 望 (長崎大学大学院医歯薬総合研究科 形態制御解析学)

O11-1 NB-2 欠損マウスにおける bushy neuron の投射不全とシナプス形成異常

○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

- O11-2 ドレブリン結合タンパク質 Spikar によるスパイン形成への関与及びその機能ドメインの
特定
○山崎 博幸、児島 伸彦、白尾 智明
群馬大学大学院医学系研究科神経薬理学
- O11-3 精神発達障害関連遺伝子 CNTNAP2 がコードする Caspr2 のシナプス発達における役割
○霜田 靖、植田 英寛、渡邊 和忠
長岡技術科学大学・生物系
- O11-4 ラット海馬神経細胞での局所的翻訳における rpS2 の安定化の重要性
○宮田 信吾^{1,2}、森 泰丈¹、遠山 正彌^{1,2}
¹大阪大学院・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

6月24日(水)

9:00 ~ 11:40 A会場 (1F・キング)

O12-1 ~ O12-8 アストロサイト

座長：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)
榎戸 靖 (東京医科歯科大学難治疾患研究所神経病理)
松田 敏夫 (大阪大学大学院薬学研究科複合薬物動態学)

- O12-1 発生期小脳に存在する A2B5 陽性細胞
○蔡 娜、倉知 正、岡野一内田 孝幸、石崎 泰樹
群馬大学大学院医学系研究科分子細胞生物学
- O12-2 発生期マウス小脳由来 EGF 応答性細胞のアストロサイト分化に対する Notch シグナル
の阻害効果
○岡野一内田 孝幸¹、関本 研一^{1,2}、倉知 正¹、磯 達也³、倉林 正彦³、
齋藤 繁²、石崎 泰樹¹
¹群馬大院・医・分子細胞生物学、²群馬大院・医・麻酔神経科学、³群馬大院・医・
臓器病態内科学
- O12-3 アストロサイトにおける Runt related factor-2 の機能的発現
○宝田 剛志、家亦 美佳、橘 正毅、米田 幸雄
金沢大学医薬保険研究域薬学系
- O12-4 培養アストロサイトからのグリオトランスミッター放出の空間的・時間的特徴
○李 海雄¹、並木 繁行³、古家 喜四夫^{4,5}、田中 謙二¹、Hongtao Liu²、岡田 泰信²、
曾我部 正博^{4,5}、廣瀬 謙造³、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東京大院・医・神経
生物学、⁴名古屋大院・医・細胞生理学 / イメージング生理学、⁵科学技術振興機構・
ICORP/SORST・細胞力覚プロジェクト

- O12-5 無刺激及び酸化ストレス負荷条件下での神経細胞及びアストロサイトによるアデノシン取り込み特性について
○奥田 浩人、田中 晶子、西田 健太郎、長澤 一樹、藤本 貞毅
京都薬大・衛生化学
- O12-6 ニコチン曝露アストログリアにおけるグリア由来神経栄養因子の生成促進
○川越 博文、小椋 正人、中道 範隆、宝田 剛志、米田 幸雄
金沢大院・自然科学(薬)・薬物学
- O12-7 培養アストロサイトにおける LPS 誘導性 NO 産生に対する theophylline の効果
○小川 瑞恵、高野 桂、森山 光章、中村 洋一
大阪府立大院・生命環境科学・獣医・統合生理
- O12-8 神経因性疼痛へのブシ末の鎮痛効果
○柴田 圭輔¹、菅原 健²、藤下 加代子¹、小澤 哲朗¹、松川 隆²、鈴木 勉³、小泉 修一¹
¹山梨大院・医・薬理、²山梨大院・医・麻酔科学、³星薬大院・薬・薬品毒性

6 月 24 日 (水)

9:00 ~ 11:40 B会場 (9F・天の川)

O13-1 ~ O13-8 神経幹細胞・前駆細胞

座長：井上 順雄 (首都大学東京大学院人間健康科学研究科神経再生科学)
堀尾 嘉幸 (札幌医科大学医学部薬理学講座)
吉川 和明 (大阪大学蛋白質研究所・神経発生制御)

- O13-1 領域特異的遺伝子改変法の確立ーグリア細胞の発生機能の解析
○後藤 仁志、小野 勝彦、竹林 浩秀、池中 一裕
生理学研究所・分子神経生理部門
- O13-2 マウス *glial cells missing* 遺伝子は初期胚における *Hes5* 発現を誘導する
○等 誠司¹、クマーラ アキレス¹、石野 雄吾¹、田中 謙二¹、細谷 俊彦²、堀田 凱樹³、池中 一裕¹
¹生理学研究所・分子神経生理、²理研 BSI、³情報システム研究機構
- O13-3 神経幹細胞画分における細胞周期調節因子 cyclin D1 は細胞周期調節非依存的にアストロサイト分化を阻害する
○備前 典久¹、井上 俊洋²、清水 健史³、鹿川 哲史¹、田賀 哲也¹
¹東京医科歯科大・医・幹細胞制御、²熊本大院・医・視機能病態学、³理研・CDB・体軸形成研究チーム
- O13-4 マウス脳発生過程における Apc の発現解析
○田口 紋子¹、山田 泰広^{1,2}、原 明¹
¹岐阜大・院医・腫瘍病理、²さががけ・科学技術振興機構

- O13-5 成体マウス神経幹 / 前駆細胞の細胞表面抗原ホスファチジルグルコシドの同定**
 ○金子 順^{1,2}、木下 雅美^{1,2}、町田 武生²、長塚 靖子¹、平林 義雄¹
¹理化学研究所脳科学総合研究センター平林リサーチユニット、²埼玉大学理学部生体制御学科
- O13-6 HCNP 前駆体蛋白は神経前駆細胞の分化に関与する**
 ○匂坂 尚史、金森 哲子、上松 則彦、豊田 剛成、松川 則之、小鹿 幸生
 名古屋市立大学大学院 神経内科学
- O13-7 マウス胚性幹細胞由来の神経幹細胞に対する放射線照射の生物学的影響**
 ○磯野 真由¹、大津 昌弘^{1,2}、新屋 冬美¹、大森 啓之¹、吉江 拓也¹、大谷 浩樹³、福士 政広³、中山 孝⁴、井上 順雄¹
¹首都大学東京大学院人間健康科学研究科神経再生科学、²杏林大学医学部化学、³首都大学東京大学院人間健康科学研究科放射線科学、⁴横浜市立大学医学部生化学
- O13-8 NB-3 欠損マウス小脳における顆粒細胞の発達の異常**
 ○桜井 都衣¹、豊島 学¹、武田 泰生²、霜田 靖¹、Domna Karagogeos³、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

6月24日(水)

9:00 ~ 11:40 C会場 (3F・烏帽子)

O14-1 ~ O14-8 成長因子・栄養因子

座長：荒川 義弘 (東京大学医学部附属病院臨床試験部)

仙波りつ子 (理化学研究所 脳科学総合研究センター分子神経形成研究チーム)

松岡 一郎 (松山大学薬学部生理化学)

- O14-1 ニューロトロフィン-3 の ERK1/2 シグナル活性化による大脳皮質神経前駆細胞の分裂促進**
 ○福光 秀文、大塚 正成、伊藤 光広、古川 昭栄
 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
- O14-2 感覚神経発生における運動ニューロン由来 NT-3 の役割**
 ○臼井 紀好^{1,2}、渡辺 啓介³、小野 勝彦⁴、玉巻 伸章³、池中 一裕^{1,2}、竹林 浩秀³
¹総研大・生命・生理、²生理研・分子神経生理、³熊大・医・脳回路、⁴京都府立医・医・生物
- O14-3 神経成長因子は、小胞体ストレス下でのみ GRP78 の発現を加速上昇させる**
 ○下家 浩二、中谷 陽介、岸 宗一郎、島田 貴史、入船 宏美、笹谷 晴恵、池内 俊彦
 関西大・化学生命工・生命生物

O14-4 脊髄由来の FGF-2 応答細胞は脊髄損傷後の運動機能を改善する

○河西 正樹、福光 秀文、古川 昭栄
岐阜薬科大学分子生物学区研究室

O14-5 BDNF ノックアウトマウスの脂質メタボローム解析

○鈴木 辰吾^{1,2}、清末 和之⁴、笠間 健嗣⁵、伊丹 千晶⁶、小島 正己³、
田中 光一²

¹東京医科歯科大・難治疾患研究所・MTT プログラム、²東京医科歯科大・難治疾患
研究所・分子神経科学、³産総研・セルエンジニアリング部門・バイオインターフェー
スグループ、⁴産総研・脳神経情報研究部門・脳遺伝子研究グループ、⁵東京医科歯
科大・機器分析センター、⁶埼玉医科大学・医学部・生理学教室

O14-6 中鎖脂肪酸誘導体、2- デセン酸エチルエステルの神経栄養因子様シグナリング

○古川 昭栄、牧野 晃久、伊藤 悟、福光 秀文
岐阜薬科大学学生体機能解析学大講座分子生物学

O14-7 HCNP 遺伝子組み換えマウスの中隔核では Choline acetyltransferase が増加している。

○上松 則彦¹、松川 則之¹、豊田 剛成¹、匂坂 尚文¹、金森 哲子¹、橋詰 良夫²、
小鹿 幸生¹

¹名古屋市立大院・医・神経内科、²愛知医科大学 加齢医学研究所

O14-8 絶食時の視床下部における転写因子 AF5q31 と β Klotho の発現についての検討

○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・医学部・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

6 月 24 日 (水)

9 : 00 ~ 11 : 40 D会場 (1F・長峰)

O15-1 ~ O15-8 精神疾患・発達障害

座長：神庭 重信 (九州大学大学院 医学研究院精神病態医学)

田中 稔久 (大阪大学大学院医学系研究科精神医学)

森 則夫 (浜松医科大学精神科)

O15-1 フェンサイクリジンによる大脳皮質ニューロンのシナプス減少に、BDNFの分泌阻害が関与する

○安達 直樹¹、沼川 忠広¹、熊丸 絵美¹、伊丹 千晶²、仙波 りつ子³、
トルゲン トルスン^{1,4}、功刀 浩¹

¹国立精神・神経セ 神経研 疾病三部、²埼玉医大 生理学、³理研 脳センター 分
子神経形成研究チーム、⁴東京医大 病理学

O15-2 神経新生での PACAP による突起伸展調節機構の解析

○山田 浩平¹、松崎 伸介^{1,4}、服部 剛志³、橋本 均²、新谷 紀人²、馬場 明道²、
片山 泰一⁴、遠山 正彌¹

¹大阪大院・医・神経機能形態学、²大阪大院・薬・神経薬理学分野、³大阪大院・医・

分子精神神経学寄付講座、⁴大阪大・浜松医大・金沢大の子どもたちの発達研究センター

O15-3 Dysbindin-1 による海馬神経細胞の樹状突起形態制御

○伊東 秀記、森下 理香、篠田 友靖、岩本 郁子、須藤 香織、岡本 賢一、永田 浩一

愛知県コロニー・研・神経制御

O15-4 ガランタミンのムスカリン受容体活性化を介したアポモルヒネ誘発プレパルスインヒビション障害抑制作用

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

¹大阪大学大学院薬学研究科複合薬物動態、²大阪大学大学院医学系研究科附属子どもたちの分子統御機構研究センター

O15-5 摂食うつに関連する受容体 MCH1R における RGS タンパク質の選択的作用機序

○斎藤 祐見子、宮本一松原 真由美

広島大学・総合科学研究科・行動科学講座

O15-6 マウス脳内モノアミン遊離に対するアトモキセチン、メチルフェニデートの単回および慢性投与の影響

○香田 健¹、吾郷 由希夫¹、Yana Cong¹、矢野 耕史¹、田熊 一敏¹、松田 敏夫^{1,2}

¹大阪大学大学院薬学研究科複合薬物動態学分野、²大阪大学大学院医学系研究科附属子どもたちの分子統御機構研究センター

O15-7 Tsc2 変異による神経細胞樹状突起形態異常の電子顕微鏡解析

○瀧上 周¹、安田 新¹、杉浦 弘子¹、吉村 好之²、竹宮 孝子¹、山内 卓¹、樋野 興夫³、山形 要人¹

¹東京都神経科学総合研究所・神経薬理、²徳島大学 HBS・薬・生化学、³順天堂大学・医・病理腫瘍学

O15-8 ラット脳の発達に対するトリブチルスズ曝露の影響に関する二世代トキシコジェノミック研究

○角田 正史¹、若佐 美佳²、浅川 秀雄¹、高橋 理貴²、根岸 隆之²、峽戸 孝也¹、細川 まゆ子¹、菅谷 ちえ美¹、井上 葉子¹、相澤 好治¹、田代 朋子²

¹北里大学医学部衛生学公衆衛生学、²青山学院大学理工学部生命科学科

ポスター発表

ポスター会場 (1F・クイーン)

ポスター討論時間

6 月 22 日 (月) 13:30 ~ 14:15

6 月 23 日 (火) 13:10 ~ 14:10

P-1 ~ P-6 神経幹細胞・前駆細胞

座長: 等 誠司 (生理学研究所 分子神経生理)

P-1 大脳皮質由来神経系前駆細胞の生存及び増殖における 5' -AMP-activated protein kinase の関与の可能性

○佐野 尚平、倉本 展行、米山 雅紀、長嶋 玲子、川田 浩一、荻田 喜代一
摂南大学薬学部薬理学研究室

P-2 マウス胎児海馬由来神経系前駆細胞の増殖における活性酸素種および一酸化窒素の関与

○川田 浩一、米山 雅紀、荻田 喜代一
摂南大・薬・薬理

P-3 マウス胎児大脳皮質由来培養神経系前駆細胞の増殖に対する caspase inhibitor の影響

○田中 始、川田 浩一、長嶋 玲子、米山 雅紀、荻田 喜代一
摂南大学薬学部薬理学研究室

P-4 トラウマ性ストレス応答性を示すミオシン VI による神経系前駆細胞の増殖抑制

○伊東 佑真、玉置 啓祐、中道 範隆、橘 正毅、寶田 剛志、米田 幸雄
金沢大学院・自然科学・薬物

P-5 NMDA 受容体は海馬歯状回神経細胞傷害後に出現する神経系前駆細胞の増殖を促進する

○米山 雅紀、川田 浩一、芝 達雄、荻田 喜代一
摂南大学薬学部薬理学研究室

P-6 サル胚性幹細胞由来神経幹細胞の増殖に対するメチル水銀の影響

○久米 伸恵¹、稲田 大助¹、大津 昌弘^{1,2}、小林 肇¹、吉江 拓也¹、村上 拓治¹、中山 孝³、鈴木 豊⁴、近藤 靖⁴、井上 順雄¹

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- P-7 マウス ES 細胞から分化誘導・調製した神経幹細胞の増殖・分化に対する温熱刺激の影響**
 ○大森 啓之¹、大津 昌弘^{1,2}、磯野 真由¹、久米 伸恵¹、新屋 冬美¹、吉江 拓也¹、中山 孝³、井上 順雄¹
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- P-8 マウス胚性幹細胞から神経細胞への分化に対する X 線照射の影響**
 ○新屋 冬美¹、永野 仁士¹、大津 昌弘^{1,2}、磯野 真由¹、大森 啓之¹、大谷 浩樹³、福士 政広³、中山 孝⁴、井上 順雄¹
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- P-9 GABA_B レセプターによる神経細胞分化の調節**
 ○小澤 秀介、福井 正樹、宝田 剛志、米田 幸雄
 金沢大院・自然科学・薬物
- P-10 NSS 法による ES 細胞から神経細胞への一方向的な分化におけるメチル水銀の劇的な影響の差異**
 ○大津 昌弘^{1,2}、稲田 大助²、久米 伸恵²、中山 孝³、笠井 久隆²、井上 順雄²
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- P-11 神経新生の変化における攻撃性・衝動性のメカニズム**
 ○渡邊 一平¹、鵜飼 渉¹、小野 貴文¹、渡邊 公彦¹、白坂 知彦¹、橋本 恵理¹、石井 貴男²、館農 勝¹、齋藤 利和¹
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- P-12 新規に同定した神経成長関連蛋白質 (nGAPs) の成長円錐における役割**
 ○野住 素広^{1,3}、呂 嘉²、五十嵐 道弘^{1,3}
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- P-13 シンタキシン1A-CaMKII 相互作用のシナプス小胞輸送と脳高次機能における役割**
 ○渡邊 裕美^{1,2}、伊藤 理恵子¹、多田 幸代¹、高雄 啓三^{3,4}、宮川 剛^{3,4}、崎村 建司⁵、五十嵐 道弘^{1,2}
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P-14 コンドロイチン硫酸プロテオグリカンの糖鎖生合成酵素欠損マウスの解析

○比嘉 進^{1,2}、渡邊 裕美^{1,2}、武内 恒成^{1,2}、五十嵐 道弘^{1,2}

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P-15 ~ P-19

神経細胞死

座長：吾郷 由希夫（大阪大学大学院 薬学研究科複合薬物動態学）

P-15 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 および PPAR γ アゴニストの保護効果

○浅沼 幹人¹、宮崎 育子¹、福岡 早紀²、穂積 宏彰²、辻 武史¹、北村 佳久³、千堂 年昭²、喜多 大三⁴

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P-16 シグマレセプターアゴニストSA4503は培養大脳皮質ニューロンにおいて生存維持効果を発揮する

○トルグン トルスン^{1,2}、沼川 忠広²、安達 直樹²、熊丸 絵美²、工藤 玄恵¹、功刀 浩²

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P-17 β -アミロイドによって誘導される calyntenin-3 の代謝とその神経変性への影響

○内田 洋子、五味 不二也

東京都老人総合研究所老年病ゲノムT

P-18 活性酸素消去薬は海馬歯状回神経細胞傷害後の新生細胞の生存を促進する

○芝 達雄、川田 浩一、米山 雅紀、荻田 喜代一

摂南大・薬・薬理

P-19 パーキンソン病モデル神経細胞死における Cdk5 活性化サブユニット p35 のプロテアソームによる分解

○遠藤 良¹、斉藤 太郎¹、浅田 明子¹、川原 裕之²、大島 登志男³、久永 真市¹

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P-20 ~ P-23

アストロサイト

座長：吾郷 由希夫（大阪大学大学院 薬学研究科複合薬物動態学）

P-20 アストロサイトにおける Rho kinase を介した apoA-I 誘導性コレステロール搬出機構

○伊藤 仁一、アリレザ ケイロラ、長安 祐子、横山 信治

- P-21 ジクロフェナックがサイトカイン刺激によってアストロサイトから誘導される NO 産生を増強する—インフルエンザ脳症増悪化メカニズムの解析—
○青山 峰芳¹、垣田 博樹^{1,2,3}、フセイン モハメド^{1,2}、加藤 晋^{1,2}、鈴木 悟²、伊藤 哲也²、戸荻 創²、浅井 清文¹
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- P-22 肺癌脳転移において、アストロサイトは炎症性サイトカイン（特に IL-6）を介して肺癌細胞の増殖を促進する。
○山川 裕希子¹、藤田 慶大¹、清家 稔博¹、城戸 瑞穂²、井口 東郎³、野田 百美¹
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- P-23 アストロサイトにおけるメタロチオネイン発現誘導によるドパミン神経保護
○宮崎 育子¹、吉川 友理¹、竹島 美香²、三好 耕¹、浅沼 幹人¹
¹岡山大院・医歯薬・神経情報学、²九州栄養福祉大院・食物栄養学・薬理学
- P-24 ~ P-31 受容体・イオンチャネル・輸送体
座長：斎藤 祐見子（広島大学 総合科学研究科・行動科学講座）
谷内 一彦（東北大学大学院 医学系研究科）
- P-24 G タンパク質との会合を指標にした Gi 共役型受容体アッセイ系の確立
○植田 高史¹、鶴川 眞也¹、石田 雄介¹、島田 昌一²
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- P-25 GABA_BR2 サブユニット上の serine 892 のリン酸化および脱リン酸化
○甲谷 章、倉本 展行、荻田 喜代一
摂南大学薬学部薬理学研究室
- P-26 NMDA 受容体強制発現 HEK293 細胞株の機能解析
○福森 良、中道 範隆、神戸 悠輝、谷浦 秀夫、宝田 剛志、米田 幸雄
金沢大院・自然科学・薬物学
- P-27 シグマ 1 受容体リガンドの薬理学的性質：アゴニスト選択的アップレギュレーション
○山本 敏文¹、山本 秀子²
¹横浜市大・院・生命ナノシステム・分子精神薬理、²東京都精神研・分子精神医学
- P-28 グルココルチコイド受容体およびBDNF受容体の相互作用に制御されるBDNF依存的グルタミン酸放出
○沼川 忠広、熊丸 絵美、安達 直樹、矢ヶ崎 有希、泉 愛子、功刀 浩
国立精神・神経セ 神経研 疾病三部

- P-29 マウスアストロサイトに発現する P2X7 受容体の PPAR- γ を介した活性制御について

○西田 健太朗、長澤 一樹、宮木 純、木戸 悠佳、藤本 貞毅
京都薬大・衛生化学

- P-30 GABA 神経伝達機構の発達における甲状腺ホルモンの役割

○澤野 恵梨香、高橋 理貴、船津 尚子、木村 洋人、根岸 隆之、田代 朋子
青山学院大学理工学部化学・生命科学科

- P-31 VGAT-Venus ラットを用いた、発達期小脳組織における VGAT 発現パターン

○小河 匡、上松 正和、吉田 祥子
豊橋技術科学大学 物質工学系

P-32 ~ P-39 転写因子・遺伝子発現

座長：鯉淵 典之（群馬大学大学院 医学系研究科応用生理学）

- P-32 時計遺伝子 *Bmal1* のデキサメサゾンによるリズム発現誘導は ROR レスポンスエレメントを介する

○熊谷 恵^{1,2}、中島 芳浩³、池田 正明^{1,2}

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- P-33 転写因子 OASIS によるコンドロイチン硫酸プロテオグリカンの糖鎖修飾の調節

○奥田 洋明¹、辰巳 晃子¹、今泉 和則²、和中 明生¹

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- P-34 脊髄発達過程の V1 インターニューロンにおける Foxp1 の発現

○久岡 朋子、森川 吉博、小森 忠祐、仙波 恵美子

和歌山県立医科大学・医学部・第二解剖

- P-35 発達過程の脊髄における Foxp2 の発現解析

○森川 吉博、久岡 朋子、仙波 恵美子

和歌山県立医科大学・医学部・第二解剖

- P-36 ラット迷走・舌咽神経節における TRPM8、TRPA1、TRPV1 mRNA の発現

○石田 雄介¹、本堂 亜紀^{1,2}、鵜川 眞也¹、植田 高史¹、山田 貴博¹、島田 昌一¹

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- P-37 慢性脱髄巢形成とともに起こるミクログリア特異的な遺伝子発現の変化

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- P-38 マウス脳微小血管内皮細胞によるタンパク質発現に及ぼすシロスタゾールの効果
○ファリッド アハマド^{1,2}、今井 英明¹、アリフィン モー²、プエンテス サンドラ¹、
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- P-39 N-結合型糖鎖解析の微量化
○吉村 武¹、鳥居 知宏¹、石井 章寛¹、東 幹人²、田辺 和弘²、池中 一裕¹
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P-40 ~ P-47 動物モデル

座長：齋藤 繁（群馬大学大学院医学系研究科 麻酔神経科学分野）
高山 清茂（群馬大学医学部 保健学科検査技術科学専攻）

- P-40 2型糖尿病モデル・GKラットの脳におけるホモシステイン代謝の変化
○宇野 健史、石橋 瑛、高橋 理貴、根岸 隆之、田代 朋子
青山学院大学理工学部化学生命科学科

- P-41 中大脳動脈結紮マウス脳内における Ifrd1 mRNA 発現の一過性上昇
○小西 志歩、前田 紗弥香、渡邊 真未、中道 範隆、宝田 剛志、米田 幸雄
金沢大学院・薬・薬物学

- P-42 The trial for axonal regeneration by using bFGF continuous delivery system in lacunar
infarction model of the rat
○プエンテス サンドラ¹、今井 英明¹、ファリエド アファマド¹、岡野一内田 孝幸²、
倉知 正²、石崎 泰樹²、田畑 泰彦³、好本 裕平¹
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- P-43 マウス海馬における新環境ストレスに反応する分子機構の生後発達
○車地 暁生、西川 徹
東京医科歯科大院・医歯・精神行動医科

- P-44 恐怖記憶の消去学習と再固定化の薬理学的弁別
○山田 大輔^{1,2}、和田 圭司^{1,2}、関口 正幸^{1,2}
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- P-45 筋萎縮性側索硬化症モデルマウスにおけるミクログリアと microsomal prostaglandin E
synthase-1 の役割
○宮岸 寛子¹、小菅 康弘¹、石毛 久美子¹、小野 真一²、伊藤 芳久¹
¹日本大学薬学部薬理学ユニット、²日本大学薬学部臨床医学ユニット

- P-46 強音曝露は蝸牛靱帯線維細胞の 5'-AMP-activated protein kinase/c-Jun N-terminal
kinase 経路を活性化する
○長嶋 玲子、田中 始、倉本 展行、荻田 喜代一

摂南大学薬学部薬理学研究室

P-47 ニューログリカン C の遺伝子改変マウスの行動解析

○青野 幸子¹、時田 義人¹、松井 ふみ子¹、大平 敦彦²、伊川 正人³、岡部 勝³、小野 勝彦⁴

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P-48 ~ P-51

ヒト臨床研究

座長：齋藤 繁（群馬大学大学院医学系研究科 麻酔神経科学分野）
高山 清茂（群馬大学医学部 保健学科検査技術科学専攻）

P-48 MYH9 遺伝子と統合失調症との関連解析

○渡部 雄一郎、布川 綾子、金子 尚史、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

P-49 KIBRA 遺伝子の遺伝子多型と日本人における記憶の関連について

○安田 由華^{1,2,3}、橋本 亮太^{1,2,3}、大井 一高^{2,3}、高村 孝則^{2,3}、福本 素己^{2,3}、高橋 秀俊^{2,3}、吉田 哲彦²、井池 直美^{2,4}、山森 英長^{2,5}、森原 剛史²、田上 真次²、大河内 正康²、田中 稔久²、工藤 喬^{1,2}、紙野 晃人^{2,6}、石井 良平²、岩瀬 真生²、数井 裕光²、武田 雅俊^{1,2}

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P-50 Human A β 1-38 測定系 ELISA の開発

○角田 伸人、堀越 優子、長池 一博
（株）免疫生物研究所

P-51 うつ病での血小板 BDNF の働き

○渡邊 公彦¹、橋本 恵理¹、鶴飼 渉¹、石井 貴男²、吉永 敏弘¹、小野 貴文¹、館農 勝¹、渡邊 一平¹、白坂 知彦¹、齋藤 利和¹

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ランチョンセミナー

6月23日(火)

12:00～13:00 A会場(1F・キング)

LS-1

共催: ヤンセンファーマ株式会社

座長: 三國 雅彦(群馬大学大学院脳神経発達統御学講座神経精神医学分野)

「統合失調症の病態仮説と薬物療法」

工藤 喬

大阪大学大学院医学系研究科精神医学教室

6月23日(火)

12:00～13:00 C会場(3F・烏帽子)

LS-2

共催: アプライドバイオシステムズジャパン株式会社

座長: 岡田 勇彦(アプライドバイオシステムズジャパン(株))

1. 「リン酸化タンパク質の変動解析とリン酸化部位決定のためのツールの紹介」

津幡 卓一

アプライドバイオシステムズジャパン(株)

2. 「神経成長とシナプス伝達に関与するリン酸化蛋白質の解析と意義」

五十嵐 道弘

新潟大学大学院医歯学総合研究科分子細胞機能学

6月24日(水)

12:00～13:00 B会場(9F・天の川)

LS-3

共催: 田辺三菱製薬株式会社・吉富薬品株式会社

座長: 三國 雅彦(群馬大学大学院脳神経発達統御学講座神経精神医学分野)

「作用機序から見た第二世代抗精神病薬の選択と適応」

久住 一郎

北海道大学大学院医学研究科精神医学分野

JSN - GRT Joint Open Symposium

June 21 (Sunday)

17 : 00 ~ 19 : 00 Room A (1F • King)

OS-1 ~ OS-4 **Adult Neurogenesis and New Strategies for CNS Regeneration**
Chairs : Hideyuki Okano (Department of Physiology, Keio University School of
Medicine)
Toru Itakura (Department of Neurological Surgery, Wakayama Medical
University)

- OS-1 **Hippocampal neurogenesis and neural repair**
○Tatsuhiro Hisatsune
Dept Integrated Biosciences, Univ of Tokyo
- OS-2 **Cytoskeletal maturation and radiosensitivity of newly-generated neurons in the adult brain**
○Tomoaki Shirao
Department of Neurobiology and Behavior, Gunma University Graduate School of Medicine
- OS-3 **Neural cell differentiation plasticity regulated by methyl-CpG binding proteins**
○Kinichi Nakashima
Lab. Mol. Neurosci., Grad. Sch. Biol. Sci., Nara Inst. Sci. Tech.
- OS-4 **Decreased neurogenesis as a risk factor for mental diseases**
○Noriko Osumi
Tohoku University Graduate School of Medicine

ISN Symposium

June 22 (Monday)

9 : 00 ~ 11 : 40 Room A (1F • King)

ISN-1 ~ ISN-4

Axon Homeostasis and Diseases

Chairs : Hiroshi Kiyama (Department of Anatomy & Neurobiology, Osaka City
University Graduate School of Medicine)
Katsuhiko Mikoshiba (Laboratory for Developmental Neurobiology, RIKEN
Brain Science Institute)

ISN-1 Molecular regulation of Wallerian degeneration of axons

○Michael Coleman

The Babraham Institute, Cambridge, UK

ISN-2 Axon formation and polarized transport

○Kozo Kaibuchi

Nagoya University Graduate School of Medicine

ISN-3 Control of axonal mitochondrial mobility and its impact on axonal homeostasis and degeneration

○Zu-Hang Sheng

NINDS, NIH, USA

ISN-4 Transport and assembly dynamics of axonal neurofilaments

○Anthony Brown

Center for Molecular Neurobiology and Department of Neuroscience, Ohio State
University, Columbus, USA

JSN - JSBP Joint Symposium

June 23 (Tuesday)

9 : 00 ~ 11 : 40 Room A (1F • King)

JSN-JSBP-1 ~

JSN-JSBP-6

Clues to the pathophysiology and treatment of psychiatric disorders through integrating neurochemistry and psychiatry

Chairs : Kazuhiro Ikenaka (Department of Molecular Physiology, National Institute for Physiological Sciences)

Toshikazu Saito (Department of Neuropsychiatry, School of Medicine, Sapporo Medical University)

Masahiko Mikuni (Department of Psychiatry and Human Behavior, Gunma University Graduate School of Medicine)

JSN-JSBP-1 Peripheral cytokine level change in the pathophysiology of psychiatric disorders
○ Wataru Ukai, Takafumi Ono, Kimihiko Watanabe, Eri Hashimoto, Toshihiro Yoshinaga, Takao Ishii, Masaru Tateno, Ippei Watanabe, Tomohiro Shirasaka, Toshikazu Saito
Dept. of Neuropsychiatry, Sapporo Medical University, Sapporo, Japan

JSN-JSBP-2 Antidepressive-like effect of continuous inhibition of GSK3 β through region-specific neuroprotective effect
○ Naoto Omata^{1,3}, T Murata¹, N Maruoka¹, PR Moya⁴, Y Leng³, CT Chiu³, Z Wang³, P Leeds³, Y Fujibayashi², Y Wada¹, DM Chuang³
¹Department of Neuropsychiatry, University of Fukui, Fukui, Japan, ²BIRC, University of Fukui, Fukui, Japan, ³Molecular Neurobiology Section, NIMH, NIH, Bethesda, USA, ⁴Laboratory of Clinical Science, NIMH, NIH, Bethesda, USA

JSN-JSBP-3 Identification of susceptibility genes for mental disorders using intermediate phenotype
○ Ryota Hashimoto^{1,2}, Yuka Yasuda^{1,2}, Kazutaka Ohi², Motoyuki Fukumoto², Hironori Takamura², Hidetoshi Takahashi², Hidenaga Yamamori², Masatoshi Takeda^{1,2}
¹The Osaka-Hamamatsu Joint Research Center For Child Mental Development, Osaka University Graduate School of Medicine, Suita, Japan, ²Department of Psychiatry, Osaka University Graduate School of Medicine, Suita, Japan

JSN-JSBP-4 Function of EGF receptor signaling in the neonatal hippocampal lesion model of schizophrenia
○ Makoto Mizuno^{1,2}, Yingjun Zheng², Hidekazu Sotoyama², Hiroki Kawamura², Yuichi Abe², Takeyoshi Eda², Masako Shibuya³, Hisaaki Namba², Hiroyuki Nawa^{1,2}
¹Center for Transdisciplinary Research, Niigata Univ, ²Mol Neurobiol, Brain Res Inst, Niigata Univ, ³Dept Psy, Grad Sch Med, Niigata Univ

JSN-JSBP-5 Neural correlates of sexually-dimorphic social behavior and social dysfunction in subjects with autism

○Hidenori Yamasue

Department of Neuropsychiatry, Graduate School of Medicine, The University of Tokyo, Tokyo, JAPAN

JSN-JSBP-6 PACAP regulates the neural extension in adult neurogenesis

○Kohei Yamada¹, Shinsuke Matsuzaki^{1,2}, Tsuyoshi Hattori³, Hitoshi Hashimoto⁴, Norihito Shintani^{3,4}, Akemichi Baba⁴, Taiichi Katayama^{2,5}, 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, ³Department of Molecular Neuropsychiatry Graduate School of Medicine, Osaka University, ⁴Laboratory of Molecular Neuropharmacology, Graduate School of Pharmaceutical Sciences, Osaka University, ⁵Department of Anatomy and Neuroscience, Hamamatsu University School of Medicine

Young Scientists Lectureship Award Symposium

June 22 (Monday)

14 : 20 ~ 15 : 50 Room A (1F・King)

LA-1

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 Glucocorticoid receptor interaction with TrkB promotes BDNF-triggered glutamate release

○Tadahiro Numakawa

Department of Mental Disorder Research, National Institute of Neuroscience, National
Center of Neurology and Psychiatry

Symposia

June 22 (Monday)

9 : 00 ~ 11 : 40 Room B (9F • Amanogawa)

- S01-1 ~ S01-6 New insights into astrocytogenesis in the mammalian central nervous system**
Chairs : Yasuki Ishizaki (Department of Molecular and Cellular Neurobiology, Gunma University Graduate School of Medicine)
 Kinichi Nakashima (Laboratory of Molecular Neuroscience, Graduate School of Biological Sciences, Nara Institute of Science and Technology)
- S01-1 *Olig2 progenitor cells preferentially differentiate to astrocytes in response to various stimuli in the gray matter of adult forebrain***
 ○ Kouko Tatsumi, Hiroaki Okuda, Akio Wanaka
 The Department of Anatomy, Nara Medical University, Nara, Japan
- S01-2 *BMPR1A and BMPR1B differentially regulate gliosis***
 ○ Masahisa Yamada¹, Naohito Kitamura¹, Yumi Sato², Teiichi Furuichi², Yuji Mishina³
¹RIKEN Brain Science Institute, Yamada Research Unit, ²RIKEN Brain Science Institute, Laboratory for Molecular Neurogenesis, Saitama 351-0198, Japan, ³University of Michigan, School of Dentistry, Ann Arbor, MI 48109, USA.
- S01-3 *Astrocyte precursor cells in the developing mouse cerebellum***
 ○ Masashi Kurachi, Na Cai, Takayuki Okano-Uchida, Yasuki Ishizaki
 Department of Molecular and Cellular Neurobiology, Gunma University Graduate School of Medicine, Maebashi, Japan
- S01-4 *Glial cell sub-lineages in the developing central nervous system***
 ○ Tetsushi Kagawa, Tetsuya Taga
 Dept. of stem cell regulation, Med. Res. Inst., Tokyo Med. and Dent. Univ.
- S01-5 *Mechanism in sequential differentiation of neural stem cells***
 ○ Kinichi Nakashima
 Lab. Mol. Neurosci., Grad. Sch. Biol. Sci., Nara Inst. Sci. Tech.
- S01-6 *The role of neurogenesis-regulating transcription factor Pax6 in astroglial development***
 ○ Noriko Osumi
 Tohoku University Graduate School of Medicine

June 22 (Monday)

9 : 00 ~ 11 : 40 Room C (3F • Eboshi)

S02-1 ~ S02-5 The challenge of epigenetics to elucidate the cause of mental disorders
 Chairs : Kohji Fukunaga (Graduate School of Pharmaceutical Sciences, Tohoku University)
 Takeo Kubota (Department of Epigenetic Medicine, University of Yamanashi)

S02-1 Role of DNA methylation in mental disorders
 ○Tadafumi Kato
 Laboratory for Molecular Dynamics of Mental Disorders, RIKEN Brain Science Institute

S02-2 DNA demethylation and spatial gene positioning of an astrocyte specific gene, GFAP
 ○Takumi Takizawa, Kinichi Nakashima
 Lab. of Molecular Neuroscience, Grad. School of Biological Sciences, NAIST

S02-3 The mechanism of abnormal dendritic spine formation in chromatin remodeling factor *ATRX* mutant mice
 ○Norifumi Shioda¹, Hideyuki Beppu², Isao Kitajima³, Kohji Fukunaga^{1,4}
¹Department of Pharmacology, Graduate School of Pharmaceutical Sciences, Tohoku University, Sendai, Japan, ²Cardiovascular Research Center, Massachusetts General Hospital, Harvard Medical School, Charlestown, Massachusetts 02129, U.S.A., ³Department of Clinical and Molecular Pathology, Faculty of Medicine, University of Toyama, Toyama 930-0194, Japan, ⁴Tohoku University 21st Century COE Program CRESCENDO Sendai, Japan

S02-4 The Role of Epigenetic Modifier for Neuronal Differentiation during Retinogenesis
 ○Itsuki Ajioka^{1,2,3}, Kazunori Nakajima², Dyer Michael³
¹KANRINMARU-project, Keio U Sch Med, Tokyo, Japan, ²Dept of Anatomy, Keio U Sch Med, Tokyo, Japan, ³Dept of Developmental Neurobiology, St Jude Childrens Res Hosp, Memphis, TN, USA

S02-5 Epigenetics in autistic diseases
 ○Takeo Kubota, Takae Hirasawa
 Dept. Epigenetic Med., Univ. of Yamanashi

June 22 (Monday)

9 : 00 ~ 11 : 40 Room D (1F • Nagamine)

S03-1 ~ S03-6 Update of autism and other developmental disorders, basic and clinic
Chairs : Masaaki Narita (School of Medicine, Mie University)
Masatoshi Takeda (Department of Psychiatry, Osaka University Graduate School
of Medicine)

S03-1 Update of autism model animals

○Masaaki Narita, Akiko Oyabu, Yoshio Imura, Tomomi Yokoyama, Naoki Kamada,
Kaori Tano, Yasura Tashiro, Atsuko Uchida
Mie University School of Medicine

S03-2 Alterations in the expression of gene and protein in ADHD model rats

○Yoshinori Masuo
Mental Stress Team, Health Technology Research Center, National Institute of Advanced
Industrial Science and Technology (AIST)

S03-3 Impaired prefrontal cortical response by switching stimuli in autism spectrum
disorders assessed by near-infrared spectroscopy

○Naoko Narita, Akiyuki Saotome, Hiroki Higuchi, Yuka Kumakura
Dept. of Education, Bunkyo University

S03-4 A perspective of biological marker research for Autism

○Hideo Matsuzaki ^{1,2}

¹Osaka Univ Graduate School of Child Development, Suita, Japan, ²Dept of Psychiatry
and Neurology, Hamamatsu Univ School of Med

S03-5 Neonatal exposure to excess neuregulin-1 signaling alters the dopaminergic
function

○Taisuke Kato, Nobuyuki Takei, Hiroyuki Nawa
Mol .Neurobiol. Brain Res. Inst. Niigata Univ., Niigata

S03-6 Maternal infection affects neurogenesis in the developing cerebral cortex

○Hitomi Soumiya, Hidefumi Fukumitsu, Shoei Furukawa
Laboratory of Molecular Biology, Department of Biofunctional analysis, Gifu
Pharmaceutical University, Gifu, Japan

June 23 (Tuesday)

9 : 00 ~ 11 : 40 Room B (9F • Amanogawa)

- S04-1 ~ S04-6 Novel insights into the roles of protein kinases in synaptic plasticity and memory
Chairs : Shin-ichi Hisanaga (Molecular Neuroscience Laboratory, Department of
Biological Sciences, Tokyo Metropolitan University)
Satoshi Kida (Department of Bioscience, Tokyo University of Agriculture)
- S04-1 The function of neuronal activity-dependent CaMKII activation in synaptic plasticity
○Kohji Fukunaga
Dept. Pharmacol., Tohoku Univ. Grad. Sch. Pharm. Scis. and COE program
"CRESCENDO"
- S04-2 Roles of CaMKIV Signaling Pathway in Memory Formation
○Satoshi Kida
Tokyo University of Agriculture
- S04-3 Memory improvement by inhibiting PKA in *Drosophila*
○Junjiro Horiuchi
Laboratory of Cellular Genetics, Tokyo Metropolitan University
- S04-4 mTOR kinase signaling in learning paradigm
○Nobuyuki Takei, Yuta Ishizuka, Hiroyuki Nawa
Brain Research Institute, Niigata University
- S04-5 Glycogen synthase kinase 3 (GSK3) in synaptic plasticity, learning & memory
○Florian Plattner
Institute of Neurology, University College London
- S04-6 CDK5 AND SYNAPTIC PLASTICITY
○James Bibb
Department of Psychiatry, The University of Texas Southwestern Medical Center

June 23 (Tuesday)

9 : 00 ~ 11 : 40 Room C (3F • Eboshi)

- S05-1 ~ S05-3 Translational research between basic science and drug discovery**
Chairs : Shinichi Koizumi (RaQualia Pharma Inc.)
Shinichi Kohsaka (National Institute of Neuroscience, National Center of
Neurology and Psychiatry)
Panelists : Takashi Tsukamoto (Johns Hopkins University)
Yoshitaka Nagai (Department of Degenerative Neurological Diseases, National
Institute of Neuroscience)
Atsumi Nitta (Department of Neuropsychopharmacology and Hospital
Pharmacy Nagoya University Graduate School of Medicine)
- S05-1 Drug discovery research as a translation of science to drug candidates**
○Shinichi Koizumi
RaQualia Pharma Inc. Aichi, Japan
- S05-2 A novel computational approach for drug discovery: Chemical genomics-based in
silico ligand screening**
○Yasushi Okuno, Ryuta Murakami
Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, Japan
- S05-3 How to translate "chemical compounds" into "medicines" for the use of disease
treatments**
○Toshinori Yamamoto
RaQualia Pharma Inc.

June 23 (Tuesday)

9 : 00 ~ 11 : 40 Room D (1F • Nagamine)

- S06-1 ~ S06-6 Regulation of cell migration and axon guidance**
Chairs : Yoshio Goshima (Department of Molecular Pharmacology and Neurobiology,
Graduate School of Medicine, Yokohama City University)
Kazunori Nakajima (Department of Anatomy, Keio University School of
Medicine)
- S06-1 Abi2 plays an essential role for radial migration in the developing cerebral cortex
via WAVE2-Arp 2/3 complex**
○Min-Jue Xie¹, Hideshi Yagi^{1,2}, Makoto Sato^{1,2}
¹Division of Cell Biology and Neuroscience, Department of Morphological and
Physiological Sciences, Faculty of Medical Sciences, University of Fukui, Fukui, ²
Research and Education Program for Life Science, University of Fukui

- S06-2 Reelin-Dab1 signal regulates the local inside-out lamination through terminal translocation**
 ○Katsutoshi Sekine, Takeshi Kawauchi, Ken-ichiro Kubo, Takao Honda, Kazunori Nakajima
 Department of Anatomy, Keio University School of Medicine, Tokyo, Japan
- S06-3 Slit-Robo signaling regulates migration of newly-born neurons under physiological and pathological conditions 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, ⁶Genentech
- S06-4 A novel repulsive guidance protein, Draxin**
 ○Hideaki Tanaka^{1,2}, Yohei Shinmyo¹, Shahidul M Islam¹, Tatsuya Okafuji¹, Yuhong Su^{1,2}, Iftekhar Bin Naser^{1,2}, Giasuddin Ahmed^{1,2}, Sanbing Zhang^{1,2}, Kunimasa Ohta¹
¹Division of Developmental Neurobiology, Kumamoto University, ²Global COE "Cell Fate Regulation Research and Education Unit", Kumamoto University
- S06-5 Cellular functions of a novel axon guidance molecule LOTUS**
 ○Kohtaro Takei¹, Yasufumi Sato^{1,2}, Megumi Yamaguchi¹, Masumi Iketani¹, Yuko Arie¹, Yoshio Goshima¹
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
- S06-6 Regulation of axon outgrowth by new positive feedback mechanisms through membrane stretch activated channel**
 ○Koji Shibasaki^{1,2,3}, Namie Murayama^{1,3}, Katsuhiko Ono⁴, Yasuki Ishizaki⁵, Makoto Tominaga^{1,2,3}
¹Section of Cell Signaling, Okazaki Institute for Integrative Bioscience, National Institutes of Natural Sciences, ²National Institute for Physiological Sciences, ³Department of Physiological Sciences, The Graduate University for Advanced Studies, ⁴Department of Biology, Kyoto Prefectural University of Medicine, ⁵Department of Molecular and Cellular Neurobiology, Gunma University Graduate School of Medicine

June 23 (Tuesday)

15 : 50 ~ 18 : 30 Room A (1F • King)

S07-1 ~ S07-5 Integrative advance of neurology and psychiatry

Chairs : Keiji Wada (Department of Degenerative Neurological Diseases, National
Institute of Neuroscience)
Toru Nishikawa (Section of Psychiatry and Behavioral Sciences, Tokyo Medical
and Dental University)

S07-1 Neuronal cell dysfunction as a common pathophysiology of neurological and psychiatric disorders

○Akira Sawa

Program in Molecular Psychiatry, Departments of Psychiatry and Neuroscience, Johns
Hopkins University School of Medicine

S07-2 Experience dependent synaptic delivery of AMPA receptors

○Takuya Takahashi

Dept of Physiol., Yokohama City Univ. Grad. Sch. Med., Yokohama, Japan

S07-3 The brain as the center for the integration of biological information

○Keiji Wada ^{1,2}

¹Natl Inst Neurosci, NCNP, Tokyo, Japan, ²CREST, JST, Kawaguchi, Saitama, Japan

S07-4 From a Neurologist

○Miho Murata

Dept. Neurology, National Center Hospital of Neurology & Psychiatry, Tokyo, Japan

S07-5 Integrated approaches of psychiatry and neurology; from a clinical psychiatry perspective

○Akira Sano

Department of Psychiatry, Kagoshima University Graduateschool of Medical and Dental
Sciences, Kagoshima, Japan

June 23 (Tuesday)

15 : 50 ~ 18 : 30 Room B (9F • Amanogawa)

S08-1 ~ S08-5 Quality controls of proteins and neuropsychiatric diseases

Chairs : Takashi Kudo (Department of Psychiatry, Osaka University Graduate School of
Medicine)
Kazunori Imaizumi (Division of Molecular and Cellular Biology, University of
Miyazaki)

S08-1 Role of chronic ER stress in neurodegeneration and bipolar disorder

○Fumihiko Urano

University of Massachusetts Medical School, Worcester, Massachusetts, U.S.A.

- S08-2 Cellular dysfunction associated with A β oligomers enhanced by APP E693 Δ mutation
○Takami Tomiyama
Department of Neuroscience, Osaka City University Graduate School of Medicine, Osaka, Japan
- S08-3 Mechanism of tau aggregation mediated neurodegeneration
○Akihiko Takashima
Laboratory for Alzheimer's Disease, RIKEN, Brain science Institute, Wako, Japan
- S08-4 The involvement of ER stress in pathogenesis after cerebral ischemia
○Hideaki Hara
Gifu Pharmaceutical Uni., Gifu, JAPAN
- S08-5 Novel therapeutic strategies for neurodegenerative diseases based on ER-proteasome system
○Takashi Kudo¹, Kazunori Imaizumi²
¹Department of Psychiatry, Osaka University Graduate School of Medicine, Suita, Japan, ² Division of Molecular and Cellular Biology, Department of Anatomy, Faculty of Medicine, University of Miyazaki, Miyazaki, Japan

June 23 (Tuesday)

15 : 50 ~ 18 : 30 Room C (3F • Eboshi)

- S09-1 ~ S09-5 New vistas of neurochemistry using the large-scale genome-wide analysis : -omics approaches
Chairs : Michihiro Igarashi (Graduate School of Medical and Dental Sciences, Niigata University)
Yoshio Hirabayashi (Hirabayashi Research Unit, RIKEN Brain Science Institute)
- S09-1 Cerebellar Development Transcriptome Analysis: Towards the elucidation of the genetic basis of cerebellar circuit development
○Kanehiro Hayashi¹, Hirozumi Nishibe¹, Akira Sato², Teiichi Furuichi¹
¹Lab for Molecular Neurogenesis, RIKEN BSI, ² Synthetic biology Team, RIKEN ASI
- S09-2 Synaptic function regulated by palmitoylating enzyme family
○Masaki Fukata^{1,2}, Jun Noritake¹, Yuko Fukata^{1,2}
¹Division of Membrane Physiology, National Institute for Physiological Sciences, ² PRESTO, JST
- S09-3 Strategy for the Growth Cone Research using Proteomics
○Michihiro Igarashi
Niigata Univ Grad Sch Med Dent Sci, Niigata, Japan

- S09-4 Lipidomics for neurochemistry - basic techniques and strategy
 ○Ryo Taguchi
 Dept. of Metabolome, Med, Univ. of Tokyo
- S09-5 Mass spectrometric analysis of minor components in brain -phosphorylated proteins and membrane lipids
 ○Yoshio Hirabayashi, Takuji Nabetani
 RIKEN Brain Science Institute

June 23 (Tuesday)

15 : 50 ~ 18 : 30 Room D (1F • Nagamine)

- S10-1 ~ S10-6 Dynamics and functions of cytoskeletal- and membrane-proteins in neuronal growth cones and dendritic spines
 Chairs : Ryoki Ishikawa (Department of Molecular and Cellular Pharmacology, Gunma University Graduate School of Medicine)
 Tatsuo Suzuki (Department of Neuroplasticity, Shinshu University Graduate School of Medicine)
- S10-1 Dynamics of Actin binding proteins observed in living growth cones
 ○Kaoru Katoh¹, Satoe Ebihara¹, Takeshi Tougasaki¹, Motohiro Nozumi², Michihiro Igarashi²
¹Neurosci. Res. Inst., AIST, Tsukuba, Japan, ²Niigata, Univ. Grad. Sci. Med. Dent. Sci., Dept. Sign.
- S10-2 Drebrin-mediated actin-linked control of actomyosin system at the transitional zone plays a pivotal role in axonal growth
 ○Kenji Hanamura, Toshiyuki Mizui, Tomoaki Shirao
 Dept Neurobiology and Behavior, Gunma Univ. Grad Sch of Med,
- S10-3 Role of cofilin phosphorylation in BDNF-induced dendritogenesis
 ○Kazumasa Ohashi, Ken Miyajima, Akihiko Saito, Tai Kiuchi, Junichi Akatsuka, Kensaku Mizuno
 Grad. Sch. of Life Sci., Tohoku Univ., Sendai
- S10-4 Dynamics of fascin, cofilin, and drebrin in growth cones: comparison with the results obtained by in vitro analysis
 ○Ryoki Ishikawa
 Dept. Mol. Cell. Pharmacol., Gunma Univ. Grad. Sch. Med.
- S10-5 Electron tomographic reconstruction of clathrin coated endocytic intermediates in nerve terminals that lack dynamin 1
 ○Mitsuko Hayashi-Nishino^{1,2}, Eileen O'Toole³, Shawn Ferguson², Pietro De Camilli²
¹Dept. of Cell Memb. Biol., ISIR, Osaka Univ., ²Dept. of Cell Biol./HHMI, Yale Univ. School of Med., ³Dept. of Mol. Cell. Dev. Biol, Univ. of Colorado, Boulder

S10-6 The role of microtubules for synaptic plasticity

○Fuyuki Mitsuyama¹, Masato Okuya², Tadashi Koide³

¹Dept. of Neurosurgery, Univ. of Fujita-Health Univ. Japan, ²Dept. of Internal Medicine, Tenjyu-Hospital, Japan, ³Fukuyu Medical Institute

June 24 (Wednesday)

13 : 10 ~ 15 : 50 Room A (1F • King)

S11-1 ~ S11-5 Physiological and pathological functions of microglia : current knowledge and future directions

Chairs : Hiroshi Nakanishi (Department of Aging and Pharmacological Sciences, Faculty of Dental Sciences, Kyushu University)

Kazuhide Inoue (Department of Molecular and System Pharmacology, Graduate School of Pharmaceutical Sciences, Kyushu University)

S11-1 Chemotactic response of microglia to brain injury; molecular mechanisms of microglial migration and process extension induced by extracellular ATP

○Keiko Ohsawa¹, Tomomi Sanagi¹, Yasuko Nakamura¹, Eri Suzuki¹, Yasuhiro Irino², Kazuhide Inoue³, Shinichi Kohsaka¹

¹Dept. of Neurochem., Natl. Inst. of Neurosci., ²Div. Lipid Biochem., Grad. Sch. Med. Kobe Univ., Hyogo Japan, ³Dept. Mol. System Pharmacol., Grad. Sch. Pharmac. Sci., Kyushu Univ., Fukuoka Japan

S11-2 Microglia and pathological pain

○Makoto Tsuda, Kazuhide Inoue

Department of Molecular and System Pharmacology, Graduate School of Pharmaceutical Sciences, Kyushu University, Fukuoka, Japan

S11-3 Engulfment of axon debris by microglia requires p38 MAPK activity

○Tatsuhide Tanaka, Toshihide Yamashita

Dept. of Mol. Neurosci., Grad. Sch. of Med., Osaka Univ.

S11-4 Microglia-aging: Roles of microglial lysosome- and mitochondria-derived reactive oxygen species in brain aging

○Hiroshi Nakanishi

Laboratory of Oral Aging Science, Faculty of Dental Sciences, Kyushu University

S11-5 The Involvement of Glial Reaction with Peripheral Benzodiazepine Receptor as Biomarker and Functional Molecule in Pathological Development of Alzheimers disease

○Bin Ji, Makoto Higuchi, Tetsuya Suhara

National Institute of Radiological Sciences, Chiba, Japan

June 24 (Wednesday)

13 : 10 ~ 15 : 50 Room B (9F • Amanogawa)

S12-1 ~ S12-6 **Translational research for psychiatric, neurological, neuromuscular diseases**
Chairs : Ryota Hashimoto (The Osaka-Hamamatsu Joint Research Center for Child
Mental Development, Osaka University Graduate School of Medicine)
Shoji Tsuji (Department of Neurology, Graduate School of Medicine, The
University of Tokyo)

- S12-1** **Translational research in psychiatry: dysbindin and schizophrenia**
○Ryota Hashimoto ^{1,2}, Kazutaka Ohi ², Yuka Yasuda ^{1,2}, Motoyuki Fukumoto ²,
Hironori Takamura ², Hidenaga Yamamori ^{2,3}, Masatoshi Takeda ^{1,2}
¹The Osaka-Hamamatsu Joint Research Center for Child Mental Development, Osaka
University Graduate School of Medicine, ²Department of Psychiatry, Osaka University
Graduate School of Medicine, ³Department of Molecular Neuropsychiatry, Osaka
University Graduate School of Medicine
- S12-2** **Social isolated dominant-negative Disrupted-in-Schizophrenia-1 transgenic mice is
useful for a novel animal model of schizophrenia and mood disorders**
○Minae Niwa ^{1,2}, Hanna Jaaro-Peled ³, Norio Ozaki ¹, Akira Sawa ³, Toshitaka Nabeshima ²
¹Psychiatry, Nagoya Univ Grad Sch Med, Nagoya, ²Chem Pharmacol, Meijo Univ Grad
Sch Pharmacol Sci, Nagoya, ³Psychiatry, Johns Hopkins Univ Sch Med, Baltimore, USA
- S12-3** **Aberrant A-to-I RNA editing and ALS**
○Shin Kwak
Dept. of Neurol., Grad. School. of Med., Univ. of Tokyo, Tokyo, Japan
- S12-4** **Na⁺/Ca²⁺ exchanger mediates dopaminergic neurodegeneration in the MPTP
mouse model of Parkinson's disease**
○Tetsuaki Nashida ¹, Toshiyuki Kawasaki ¹, Takeya Otsuki ¹, Tatsuya Kitao ¹, Yukio Ago ¹,
Kazuhiro Takuma ¹, 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
- S12-5** **Glycosylation abnormality and muscular dystrophy -pathomechanism and
therapeutic strategy**
○Tatsushi Toda
Div. of Neurol. & Molec. Neurosci., Kobe Univ. Grad. Schl. Med.
- S12-6** **Progress in translational research of muscular dystrophy (from lab bench to
bedside)**
○Shin'ichi Takeda
Department of Molecular Therapy, National Institute of Neuroscience, NCNP

June 24 (Wednesday)

13 : 10 ~ 15 : 50 Room C (3F • Eboshi)

S13-1 ~ S13-5 Recent progress and perspective of primate models for psychiatric diseases

Chairs : Katsuki Nakamura (Primate Research Institute, Kyoto University)

Hiroyuki Nawa (Division of Neurobiology, Brain Research Institute, Niigata University)

S13-1 Neural mechanisms of social behaviors in primates

○Hisao Nishijo^{1,2}, Etsuro Hori^{1,2}, Can Van Mao^{1,2}, Taketoshi Ono^{1,2}

¹System Emotional Science, ²CREST, JST

S13-2 Methods for assessing marmoset behavior

○Katsuki Nakamura^{1,2}

¹Primate Research Institute, Kyoto University, ²National Institute of Neuroscience, National Center of Neurology and Psychiatry

S13-3 Schizophrenia animal models established with ErbB receptor ligands

○Hiroyuki Nawa^{1,2}, Makoto Mizuno², Hidekazu Sotoyama¹, Yingjun Zheng¹, Taisuke Kato¹, Yuichi Abe¹, Miwako Sakai³, Masako Shibuya³, Takeyoshi Eda¹, Ran Wang¹, Kazuaki Araki¹, Yuta Ishizuka¹, Nobuyuki Takei¹, Yuriko Iwakura¹, Hisaaki Namba¹

¹Mol Neurobiol, Brain Res Inst, Niigata Univ, ²Trans Res, Niigata Univ, ³Dept Psy, Grad Sch Med, Niigata Univ

S13-4 Application of recombinant viral vectors to primate brain research: Gene therapy for Parkinson disease

○Masahiko Takada

Systems Neuroscience Section, Department of Cellular and Molecular Biology, Primate Research Institute, Kyoto University, Kyoto, Japan

S13-5 Towards generation of transgenic nonhuman primates

○Erika Sasaki¹, Hideyuki Okano²

¹Marmoset Research Department, Central Institute for Experimental Animals, ²Department of Physiology, Keio University School of Medicine

June 24 (Wednesday)

13 : 10 ~ 15 : 50 Room D (1F • Nagamine)

S14-1 ~ S14-5 Frontiers in understanding neuronal communication

Chairs : Yuko Sekino (Division of Neuronal Network, Institute of Medical Science,

University of Tokyo)

Konosuke Kumakura (Department of Information and Communication Sciences,

Sophia University)

S14-1 Molecular structure underlying neurotransmitter release from the active zone

○Toshihisa Ohtsuka

Dep. of Mol. Patho., Univ. of Toyama

S14-2 Imaging of excitatory and inhibitory synaptic responses in the lateral amygdala using a voltage sensitive dye

○Yuko Sekino ¹

¹ Div. of Neuronal Network, Inst.Med.Sci., University of Tokyo, Tokyo, Japan, ²CREST, JST, Saitama, Japan

S14-3 Glutamate release visualized with glutamate optical sensor

○Kenzo Hirose

Department of Neurobiology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

S14-4 GABA imaging and transient GABA distribution in the developing cerebellar cortex

○Sachiko Yoshida

Department of Material Science., Toyohashi University of Technology, Toyohashi, Japan

S14-5 Imaging Activity-Dependent Secretion of BDNF

○Naoto Matsuda ^{1,2}, Hui Lu ², Yuko Fukata ¹, Jun Noritake ¹, Hongfeng Gao ², Tomomi Nemoto ¹, Masaki Fukata ¹, Mu-ming Poo ²

¹ NIPS, ² University of California, Berkeley

Oral Sessions

June 22 (Monday)

14 : 20 ~ 16 : 00 Room B (9F • Amanogawa)

O01-1 ~ O01-5 Microglia

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

Makoto Hamanoue (Department of Physiology, Toho University)

O01-1 Transcriptional and post-transcriptional regulations of P2X₄ receptor upregulation in fibronectin-stimulated microglia

○Emika Toyomitsu, Makoto Tsuda, Hidetoshi Saitoh, Kazuhide Inoue
Dept. Mol. Syst. Pharmacol., Grad. Sch. Pharm. Sci., Kyushu Univ.

O01-2 Analysis of PLD4 in amoeboid microglia

○Yoshinori Otani¹, Yoshihide Yamaguchi¹, Hiroshi Kitani², Kazuhiro Ikenaka³,
Yumi Sato⁴, Teiichi Furuichi⁴, Hiroko Baba¹

¹Dept of Mol Neurobio, Tokyo Univ of Pharm and Life Sci, Hachioji, Japan., ²Trans Anim Res Cr, Tsukuba, Japan., ³Natl Inst for Phy Sci, Okazaki, Japan., ⁴Lab for Mol Neurogenesis, RIKEN Brain Sci Inst, Wako, Japan.

O01-3 Involvement of spinal microglia in tactile allodynia caused by intrathecal administration of PDGF

○Junya Masuda, Makoto Tsuda, Hidetoshi Tozaki-Saitoh, Kazuhide Inoue
Dept. Mol. Syst. Pharmacol., Grad. Sch. Pharm. Sci., Kyushu Univ., Fukuoka 812-8582, Japan

O01-4 Functional expression of clock genes in microglia

○Tomomi Yamamoto, Takeshi Takarada, Yukio Yoneda
Laboratory of Molecular Pharmacology, Kanazawa University Graduate School of Natural Science and Technology, Kanazawa, Japan

O01-5 Role of IL-1 in lipopolysaccharide-induced learning and memory deficits

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

¹Department of Biochemical Toxicology, School of Pharmacy, Showa University, Tokyo, Japan, ²Department of Anatomy, School of Medicine, Showa University

June 22 (Monday)

14 : 20 ~ 16 : 20 Room C (3F • Eboshi)

O02-1 ~ O02-6 Protein phosphorylation

Chairs : Hiroshi Ohnishi (Institute for Molecular and Cellular Regulation, Laboratory of Biosignal Sciences, Gunma University)
Masami Takahashi (Department of Biochemistry, Kitasato University School of Medicine)

- O02-1 Modulation of tau phosphorylation on Ser/Pro or Thr/Pro motif catalyzed by multiple proline-directed protein kinases by cyclic AMP-dependent protein kinase A
○Mitsuko Hashiguchi
Department of Physiology, Tokyo Medical University
- O02-2 Analysis of phosphorylation states and identification of a novel phosphorylation site of Cdk5 activator p35 by phos-tag SDS-PAGE
○Tomohisa Hosokawa, Taro Saito, Akiko Asada, Shin-ichi Hisanaga
Dept. of Biol., Grad. sch. of Science., Tokyo Metropolitan Univ.
- O02-3 Calcium-induced and proteasome-dependent degradation of Cdk5 activator p35
○Ko Sato¹, Nobuhisa Iwata², Jiro Takano², Taro Saito¹, Akiko Asada¹, Takaomi Saido², Shin-ichi Hisanaga¹
¹Dept of Biol. Sci., Grad.Sch. of Sci. and Engin., Tokyo Metropolitan Univ, ²Lab. for Proteolytic Neuroscience. RIKEN BSI
- O02-4 Proteolysis of Cdk5 activators p35 and p39 on membranes
○Seiji Minegishi, Akiko Asada, Takahiro Fuchigami, Taro Saito, Shinichi Hisanaga
Department of Biological Sciences, Graduate Schools of Sciences, Tokyo Metropolitan University
- O02-5 Expression of protein tyrosine phosphatase receptor-type O (PTPRO) protein in the interneurons of adult mouse olfactory bulb
○Takenori Kotani, Yoji Murata, Hiroshi Ohnishi, Munemasa Mori, Shinya Kusakari, Yasuyuki Saito, Hideki Okazawa, Takashi Matozaki
Laboratory of Biosignal Sciences, Institute for Molecular and Cellular Regulation, Gunma University
- O02-6 Regulation of stress response in the brain by tyrosine phosphorylation signal
○Hiroshi Ohnishi¹, Shinya Kusakari¹, Yuriko Hayashi¹, Keizo Takao², Tsuyoshi Miyakawa², Yasuyuki Saito¹, Yoji Murata¹, Takashi Matozaki¹
¹Laboratory of Biosignal Sciences, Institute for Molecular and Cellular Regulation, Gunma University, ²Division of System Medical Science, Institute for Comprehensive Medical Science, Fujita Health University

June 22 (Monday)

14 : 20 ~ 16 : 20 Room D (1F • Nagamine)

O03-1 ~ O03-6 Gene expression

Chairs : Kanato Yamagata (Department of Neuropharmacology, Tokyo Metropolitan
Institute for Neuroscience)
Yasuhiro Watanabe (Department of Pharmacology, National Defense Medical
College)

- O03-1 A new transfection and expression technology for neural cells - Gene expression by the BmNPV baculovirus system -**
○Kosei Takeuchi, Atsuko Honda, Motohiro Nozumi, Michihiro Igarashi
Div. of Molecular Cell Biol., Niigata University for Graduate School of Medicine, Niigata, Japan
- O03-2 Regulated expression of MAGE family genes during neural development**
○Tsuyoshi Ohkumo, Chung-Hua Tsai, Koichi Hasegawa, Kazuaki Yoshikawa
Laboratory of Regulation of Neuronal Development, Institute for Protein Research, Osaka University, Suita, Osaka
- O03-3 Iron-related genes expressed by neurons**
○Yukary Nakamura, Noritaka Nakamichi, Takeshi Takarada, Yukio Yoneda
Lab. Mol. Pharmacol., Kanazawa Univ. Grad. Sch. Nat. Sci. Tech.
- O03-4 Identification and characterization of novel variants of the tryptophan 2,3-dioxygenase gene: Possible role of TDOs in the hippocampus and cerebellum**
○Masaaki Kanai¹, Toshikazu Nakamura², Hiroshi Funakoshi¹
¹Div. Mol. Reg. Med., Dept. Biochem. and Mol. Biol., Osaka Univ. Grad. Sch. Med., Osaka, ²Kringle Pharma Joint Res. Div. for Reg. Drug. Dis., Cent. Adv. Sci. Innov., Osaka univ.
- O03-5 Expression of runt related factor-2 in murine brains**
○Masaki Tachibana, Takeshi Takarada, Yukio Yoneda
Lab Mol Pharmacol, Kanazawa Univ Grad Sch Nat Sci Tech, Kanazawa, Japan
- O03-6 Changes in the expression level of synaptic function-related molecules in the limbic system of olfactory bulbectomized mice**
○Reiko Takeda, Tomoaki Shirao, Nobuhiko Kojima
Department of Neurobiology and Behavior, Gunma University Graduate School of Medicine

June 22 (Monday)

16 : 10 ~ 18 : 30 Room A (1F • King)

O04-1 ~ O04-7 **Neuronal death**

Chairs : Hiroshi Ichinose (Graduate School of Bioscience and Biotechnology, Tokyo Institute of Technology)
Hitoshi Okazawa (Neuropathology, Medical Research Institute, Tokyo Medical and Dental University)
Yasuo Takeda (Department of Clinical Pharmacy and Pharmacology, Kagoshima University Graduate School of Medical and Dental Sciences)

- O04-1 Induction of PAP-I and PAP-III Expression in Damaged Neurons of Rat following Kainic acid-induced Seizure
○Shinichi Kawahara ¹, Hiroyuki Konishi ¹, Michiharu Morino ², Kenji Ohata ², Hiroshi Kiyama ¹
¹Department of Anatomy and Neurobiology, Osaka City University, Graduate School of Medicine, Osaka, Japan, ²Department of Neurosurgery, Osaka City University, Graduate School of Medicine, Osaka, Japan
- O04-2 Prevention by astroglial glutamine transporter overexpression against glutamate neurotoxicity
○Mika Iemata, Masato Ogura, Hideo Taniura, Noritaka Nakamichi, Takeshi Takarada, Yukio Yoneda
Lab Mol Pharmacol, Kanazawa Univ Grad Sch Nat Sci Tech, Kanazawa, Japan
- O04-3 Thyroxine (T4) protects cultured cerebellar granule cells against low KCl-induced cell death
○Koshi Oyanagi, Masaki Takahashi, Takayuki Negishi, Tomoko Tashiro
Dept. of Chem. and Biol. Sci., Grad. Sch. of Sci. and Engineer., Aoyama Gakuin Univ.
- O04-4 Pharmacological activation of heat shock transcription factor 1 (HSF1) suppresses polyglutamine-induced neurodegeneration through induction of multiple molecular chaperones
○Yoshitaka Nagai ¹, Nobuhiro Fujikake ¹, Akiko Popiel ¹, Masamitsu Yamaguchi ², Tatsushi Toda ³, Keiji Wada ¹
¹Dept Degenerative Neurological Diseases, Natl Inst Neurosci, NCNP, ²Dept Appl Biol, Kyoto Inst Tech, ³Div Clin Genet, Osaka Univ Grad Sch Med
- O04-5 Tauopathy induced Parkinsonism: analysis of SJLB mice
○Taizo Taniguchi ¹, Keiichi Kadoyama ¹, Mariko Takenokuchi ¹, Takaaki Nishimoto ¹, Shunmei Chiba ², Noboru Suzuki ², Akira Matsumoto ¹, Shogo Matsuyama ¹
¹Department of Pharmaceutical Health Care, Faculty of Pharmaceutical Sciences, Himeji Dokkyo University, ²Department of Immunology, St. Marianna University School of Medicine

O04-6 Diphenylarsinic acid induced oxidative stress and cell death in cerebellar granule cells

○Takayuki Negishi¹, Masaki Takahashi¹, Koshi Oyanagi¹, Hiroaki Ohnishi¹,
Seishiro Hirano², Tomoko Tashiro¹

¹Department of Chemistry and Biological Science, Aoyama Gakuin University, Kanagawa, Japan, ²Research Center for Environmental Risk, National Institute for Environmental Studies, Tsukuba, Japan

O04-7 Involvement of mineralocorticoid receptor on trimethyltin-induced neuronal cell damage in the dentate gyrus

○Chie Sugiyama, Makoto Shuto, Kiyokazu Ogita

Department of Pharmacology, Setsunan University, Osaka, Japan

June 22 (Monday)

16 : 10 ~ 18 : 30 Room B (9F • Amanogawa)

O05-1 ~ O05-7 β Amyloid/Dementia

Chairs : Ryozo Kuwano (Center for Bioresources, Brain Research Institute, Niigata University)

Toshitaka Nabeshima (Graduate School of Pharmaceutical Sciences, Meijo University)

Makoto Michikawa (Alzheimer Disease Research, National Center for Geriatrics and Gerontology)

O05-1 Role of Syntaxin5 isoforms on the processing and trafficking of β APP in the ER through the Golgi compartments

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

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

O05-2 Late endocytic dysfunction as a putative pathway for GM1 ganglioside-induced amyloid formation in Alzheimer's disease

○Kohei Yuyama, Katsuhiko Yanagisawa

Dept. Alzheimer's Disease Res. Natl. Inst. for Longevity Sci., NCGG

O05-3 Glycosylation-required and domain-specific A β 42-to-A β 40-converting activity of angiotensin-converting enzyme

○Kun Zou¹, Tomoji Maeda¹, Ryutaro Oba³, Makoto Michikawa², Hiroto Komano¹

¹Dept. of Neurosci., Iwate Med. Univ., ²Dept. of Alzheimer's Disease Res., Natl. Inst. of Longevity Sci., Natl. Center for Geriatrics and Gerontology, ³Dept. of Advanced Medicine and Development, BML, INC.

O05-4 Suppression of A β assembly from neuronal membrane by insulin

○Naoki Yamamoto, Kenji Suzuki

Dept. of Pharmacy, Ritsumeikan Univ., Kusatsu, Japan

- O05-5 A novel neuroprotective factor induced by beta amyloid
○Fujiya Gomi, Yoko Uchida
Gene expression research group, Research team for geriatric disorders, Tokyo Metropolitan Institute of gerontology
- O05-6 Expression of transthyretin and amyloid beta precursor protein in SAMP8 hippocampus and choroid plexus
○Chie Furihata¹, Takashi Watanabe¹, Hiroko Igari¹, Takumi Kayama¹, Takashi Kohno¹, Takayoshi Suzuki², Hiroyoshi Ota³, Yasuyuki Nomura⁴, Tomoko Tashiro¹
¹School of Science and Engineering, Aoyama Gakuin Univ., Sagami-hara, ²National Institute of Health Science, Tokyo, ³Shinshu University School of Medicine, Matsumoto, ⁴Graduate School of Pharmaceutical Sciences, Hokkaido University, Sapporo
- O05-7 Nefiracetam-induced modulation of excitatory and inhibitory synaptic transmission via stimulation of neuronal nicotinic acetylcholine receptors in rat cortical neurons
○Shigeki Moriguchi¹, Toshio Narahashi², Kohji Fukunaga¹
¹Dept. Pharmacol., Grad. Sch. Pharm. Scie., Tohoku Univ., ²Dept. Mol. Pharmacol and Biol. Chem., Northwestern Univ. Med. Sch. Chicago, U.S.A.

June 22 (Monday)

16 : 30 ~ 18 : 30 Room C (3F • Eboshi)

- O06-1 ~ O06-6 Neural Plasticity
Chairs : Hiroshi Ueda (Molecular Pharmacology and Neuroscience, Nagasaki University Graduate School of Biomedical Sciences)
Sadao Shiosaka (Division of Structural Cellular Biology, Nara Institute of Science and Technology)
- O06-1 Analysis of gene expression changes associated with long-lasting synaptic enhancement in hippocampal slice cultures after repetitive exposures to glutamate
○Katsuhiro Kawaai^{1,2}, Keiko Tominaga-Yoshino³, Naoko Taniguchi³, Katsuhiko Mikoshiba^{1,2}, Akihiko Ogura³, Tomoko Tashiro⁴
¹JST, ICORP-SORST, Calcium Oscillation Project, ²Lab. For Developmental Neurobiology, RIKEN Brain Science Institute, ³Department of Frontier Bioscience, Graduate School of Frontier Bioscience, University of Osaka, ⁴The Department of Science & Engineering, Graduate School of Science & Engineering, Aoyama Gakuin University
- O06-2 Long-lasting synaptic enhancement after repeated activation of PKA in the cortical region of the brain slice culture including hippocampus and entorhinal cortex
Kazuyuki Iijima, Yuki Oe, Yoshihiro Egashira, ○Keiko Tominaga-Yoshino, Akihiko Ogura
Department of Neuroscience, Osaka University Graduate School of Frontier Biosciences

- O06-3 Regulatory mechanism of drebrin translocation from dendritic spines to parent dendrites in cultured hippocampal neurons
○Toshiyuki Mizui^{1,3}, Tomoaki Shirao¹, Yuko Sekino^{2,3}
¹Department of Neurobiology and Behavior, Gunma University Graduate School of Medicine, Maebashi, Japan, ²Division of Neural Network, Institute of Medical Science, University of Tokyo, Tokyo, Japan, ³CREST,JST, Kawaguchi, Japan
- O06-4 Drebrin A knock-out impairs context-dependent fear conditioning and homeostatic plasticity of the NMDA receptor
○Nobuhiko Kojima¹, Chiye Aoki², Kenji Hanamura¹, Hiroyuki Yamazaki¹, Tomoaki Shirao¹
¹Dept. of Neurobiol. & Behav., Gunma Univ. Grad. Sch. of Med., Maebashi, Japan, ²Center for Neural Sci., New York Univ., NY, USA
- O06-5 Identification of the proteins involved in dendritic localization of A α CaMKII mRNA
○Yasutake Mori¹, Shingo Miyata^{1,2}, Masaya Tohyama^{1,2}
¹Department of Anatomy and Neuroscience, Graduate School of Medicine, Osaka University, ²Department of Clinical Disorder Research, The Osaka-Hamamatsu Joint Research Center For Child Mental Development, Osaka, Japan
- O06-6 Neuropsin (KLK8) dependent compartment specific and process specific synaptic tagging
○Yasuyuki Ishikawa, Hideki Tamura, Sadao Shiosaka
Division of Structural Cell Biology, Nara Institute of Science and Technology, Nara, Japan

June 22 (Monday)

16 : 30 ~ 18 : 30 Room D (1F • Nagamine)

- O07-1 ~ O07-6 Cell migration/Axon guidance
Chairs : Makoto Sato (Faculty of Medical Sciences, Department of Morphological and Physiological Sciences, University of Fukui)
Haruhiro Higashida (Department of Biophysical Genetics, Kanazawa University Graduate School of Medical Science)
- O07-1 Analysis of the role of Dab1-nucleocytoplasmic shuttling for layer formation of cerebral cortex
○Takao Honda¹, Maya Yamazaki², Kazuma Nagasawa², Manabu Abe², Kenji Sakimura²
¹Department of Anatomy, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo, Japan, ²Department of Cellular Neurobiology, Brain Research Institute, Niigata University
- O07-2 Roles of septin in the positioning of cortical neurons
Tomoyasu Shinoda, Hidenori Ito, Kaori Sudo, Ikuko Iwamoto, Rika Morishita, Ken-ichi Okamoto, ○Koh-ichi Nagata
Institute for Developmental Research, Aichi Human Service Center

- O07-3** LOTUS, a novel axon guidance molecule, functions as a negative regulator of Nogo signaling in LOT formation
 ○Masumi Iketani¹, Megumi Yamaguchi¹, Yasufumi Sato^{1,2}, Yuko Arie¹, Yuji Kurihara¹, Fumio Nakamura¹, Yoshio Goshima¹, Kohtaro Takei¹
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
- O07-4** Neurite outgrowth promoting effect of a novel axon guidance molecule LOTUS through binding to Nogo-66 receptor
 ○Yuji Kurihara^{1,2}, Yuko Arie^{1,2}, Megumi Yamaguchi¹, Masumi Iketani¹, Fumio Nakamura¹, Nobuhisa Mizuki², Yoshio Goshima¹, Kohtaro Takei¹
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
- O07-5** Filamin A, an actin-binding protein, participates in the Semaphorin-3A signaling through the interaction with Collapsin response mediator proteins
 ○Fumio Nakamura, Kousuke Kumeta, Masayuki Yamane, Naoya Yamashita, Ken-ichi Ogura, Yoshio Goshima
 Yokohama City Univ. Sc. Med. Dept. Pharmacol.
- O07-6** Tubulin tyrosination navigates kinesin-1 to the axon
 ○Yoshiyuki Konishi, Mitsutoshi Setou
 Dept. of Mol. Anat., Hamamatsu Univ. Sch. of Med.

June 23 (Tuesday)

14 : 20 ~ 15 : 40 Room A (1F • King)

O08-1 ~ O08-4 Stress/Anxiety

Chairs : Akeo Kurumaji (Section of Psychiatry and Behavioral Sciences, Tokyo Medical and Dental University)

Shun Nakamura (Institute of Symbiotic Science and Technology, Tokyo University of Agriculture and Technology)

- O08-1** Glucocorticoid inhibits the BDNF-mediated synaptic maturation in developing neurons via prevention of MAPK pathway
 ○Emi Kumamaru, Tadahiro Numakawa, Naoki Adachi, Aiko Izumi, Hiroshi Kunugi
 Department of Mental Disorder Research, National Center of Neurology and Psychiatry, Tokyo, Japan
- O08-2** Dopamine regulates expression of pancreatitis-associated protein I in the intermediate lobe of pituitary gland under continuous stress
 ○Hiroyuki Konishi^{1,2}, Tokiko Ogawa^{1,2}, Shinichi Kawahara¹, Saya Nakagomi¹, Kiyoshi Inoue², Masaya Tohyama², Hiroshi Kiyama^{1,2}

¹ Department of Anatomy and Neurobiology, Osaka City University, Graduate School of Medicine, Osaka, Japan, ² 21st Century COE Program "Base to Overcome Fatigue",
³ Department of Anatomy and Neuroscience, Osaka University, Graduate School of Medicine, Suita, Osaka, Japan

O08-3 Social olfactory stimulus induced the attenuation of unconditioned defensive behavior in *mdx* mice

○ Kazuhiro Yamamoto¹, Akio Takahashi¹, Keiji Wada², Masayuki Sekiguchi²

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

O08-4 Maternal dietary restriction during lactation influences postnatal behaviors in the offspring of mice

○ Mami Kumon¹, Kazuhiro Yamamoto¹, Akio Takahashi¹, Etuko Wada^{1,2}, Keiji Wada^{1,2}

¹ National Institute of Neuroscience, Tokyo, Japan, ² CREST, JST, Saitama, Japan

June 23 (Tuesday)

14 : 20 ~ 15 : 40 Room B (9F • Amanogawa)

O09-1 ~ O09-4 Myelin/Demyelinating disease

Chairs : Hiroaki Asou (Center for Kampo Medicine, Keio University)

Kazuhiko Watabe (Department of Molecular Neuropathology, Tokyo
 Metropolitan Institute for Neuroscience)

O09-1 Disruption of paranodal axo-glial junctions causes alteration of axonal transport in the PNS

○ Akiko Kodama, Tomoko Ishibashi, Hiroko Baba

Department of Molecular Neurobiology, Tokyo University of Pharmacy and Life Sciences, Tokyo, Japan

O09-2 Inhibitory effect of Annexin2 on lysolecithin-induced sciatic nerve demyelination

○ Akiko Hayashi, Tetsuya Katakabe, Kouji Kimura, Hiroko Baba

Dept. of Molecular Neurobiology, Tokyo Univ. of Pharmacy and Life Sciences, Tokyo, Japan

O09-3 Involvement of KLK6 in the pathogenesis of Experimental Autoimmune Encephalomyelitis

○ Yoshio Bando, Ai Sakata, Hikari Nunomura, Kouichi Murakami, Shigetaka Yoshida

Dept. of Functional Anatomy and Neuroscience, Asahikawa Medical College, Asahikawa, JAPAN

- O09-4 Role of microsomal prostaglandin E synthetase-1 in multiple sclerosis**
 ○Chisen Takeuchi ^{1,2,3}, Yoh Matsumoto ⁴, Kuniko Kohyama ⁴, Satoshi Uematsu ⁵,
 Shizuo Akira ⁵, Kanato Yamagata ², Takako Takemiya ^{1,2}
¹Medical Resech Inst., Tokyo Women's Med. Univ., ²Dept. Pharmacol., Tokyo Metropo.
 Inst. Neurosci., ³Dept. Neurol., Tokyo Women's Med. Univ., ⁴Dept. Mol. Neuropatho.,
 Tokyo Metropo. Inst. Neurosci., ⁵Dept. Host Defence, Reserch Inst., Microbial Dis., Osaka
 Univ.

June 23 (Tuesday)

14 : 20 ~ 15 : 40 Room C (3F • Eboshi)

O10-1 ~ O10-4 Exocytosis

Chairs : Shoichi Shimada (Department of Neurobiology and Cell Biology, Osaka
 University Graduate School of Medicine)
 Hiroshi Higuchi (Division of Pharmacology, Niigata University Graduate School
 of Medical and Dental Sciences)

- O10-1 4 dimensional characteristics of the movement and location of the secretory granules in bovine adrenal chromaffin cells**
 ○Mitsunori Hayashi, Waki Tamura, Hirotaka Kyo, Nobuyuki Sasakawa,
 Konosuke Kumakura
 Information and Communication Sciences, Science and Technology, Sophia University
- O10-2 Complexin directly binds with synaptotagmin 1**
 ○Chigusa Shimizu-Okabe ¹, Takumi Shinohara ¹, Teruo Abe ², Hiroshi Tokumaru ¹
¹Faculty of Pharmaceutial Sciences at Kagawa Tokushima Bunri University, ²Deapment
 of Cellular Neurobiology Brain Research Institute Niigara University
- O10-3 Identification of PKC-dependent phosphorylation sites of SNAP-23 in clonal glial cells**
 ○Keiichi Yasuda ¹, Makoto Itakura ¹, Etsuko Nagata ¹, Saori Yamamori ¹, Hideshi Ihara ²,
 Masami Takahashi ¹
¹Department of Biochemistry, Kitasato University School of Medicine, Sagamihara-shi,
 Japan, ²Department of Biological Science, Graduate School of Science, Osaka Prefecture
 University, Sakai-shi, Osaka 599-8531, Japan
- O10-4 Abnormal activation of dentate granule cells in phosphorylation site-deficient SNAP-25 knock-in mouse**
 ○Shintaro Otsuka, Saori Yamamori, Tatuya Uchida, Makoto Itakura, Masami Takahashi
 Department of Biochemistry, Kitasato University School of Medicine

June 23 (Tuesday)

14 : 20 ~ 15 : 40 Room D (1F • Nagamine)

O11-1 ~ O11-4 Synapse formation

Chairs : Ken Takamatsu (Department of Cellular Physiology, Toho University School of Medicine)
Nozomu Mori (Department of Anatomy and Neurobiology, Nagasaki University School of Medicine)

O11-1 Aberrant projection and synaptic formation of bushy neuron in NB-2 knockout mice

○Manabu Toyoshima¹, Kunie Sakurai¹, Yasuo Takeda², Kuniko Shimazaki³,
Yasushi Shimoda¹, Kazutada Watanabe¹

¹Department of Bioengineering, Nagaoka University of Technology, ²Department of Clinical Pharmacy and Pharmacology, Kagoshima University, ³Department of Physiology, Jichi Medical University

O11-2 The role of Spikar in cytoplasm and identification of its functional domain

○Hiroyuki Yamazaki, Nobuhiko Kojima, Tomoaki Shirao

Department of Neurobiology and Behavior, Gunma University Graduate School of Medicine, Maebashi, Japan

O11-3 A role of Caspr2 encoded by neuropsychiatric developmental disorder-susceptibility gene CNTNAP2 in synapse development

○Yasushi Shimoda, Hidehiro Ueda, Kazutada Watanabe

Department of Bioengineering, Nagaoka University of Technology

O11-4 Rps2 stability is important for activity-dependent dendritic spine maturation of hippocampal neurons

○Shingo Miyata^{1,2}, Yasutake Mori¹, Masaya Tohyama^{1,2}

¹Dept Anat & Neurosci, Grad Sch Med, Osaka Univ, Osaka, Japan, ²Dept Clinical Disorder Res, The Osaka-Hamamatsu Joint Res Center for Child Mental Development

June 24 (Wednesday)

9 : 00 ~ 11 : 40 Room A (1F • King)

O12-1 ~ O12-8 Astrocyte

Chairs : Kiyofumi Asai (Department of Molecular Neurobiology, Nagoya City University Graduate School of Medical Sciences)
Yasushi Enokido (Department of Neuropathology, Medical Research Institute, Tokyo Medical and Dental University)
Toshio Matsuda (Laboratory of Medicinal Pharmacology, Graduate School of Pharmaceutical Sciences, Osaka University)

O12-1 Characterization of A2B5-positive cells in the developing mouse cerebellum

○Na Cai, Masashi Kurachi, Takayuki Okano-Uchida, Yasuki Ishizaki

Department of Molecular and Cellular Neurobiology, Gunma University Graduate School

of Medicine, Maebashi, Japan

- O12-2 Inhibitory effect of Notch signaling on astrocyte differentiation of the EGF-responsive cells in the developing mouse cerebellum**
○Takayuki Okano-Uchida¹, Kenichi Sekimoto^{1,2}, Masashi Kurachi¹, Tatsuya Iso³, Masahiko Kurabayashi³, Shigeru Saito², Yasuki Ishizaki¹
¹Dept. of Mol. and Cell. Neurobiol., Gunma Univ. Grad. Sch. of Med., Maebashi, Japan, ²Dept. of Anesthesiol., Gunma Univ. Grad. Sch. of Med., Maebashi, Japan, ³Dept. of Med. and Biol. Sci., Gunma Univ. Grad. Sch. of Med., Maebashi, Japan
- O12-3 Functional expression of runt related factor-2 in astrocytes**
○Takeshi Takarada, Mika Iemata, Masaki Tachibana, Yukio Yoneda
Laboratory of Molecular Pharmacology, Kanazawa University Graduate School of Natural Science and Technology
- O12-4 Spatio-temporal information of gliotransmitter release from cultured astrocytes**
○Hae Ung Lee¹, Shigeyuki Namiki³, Kishio Furuya^{4,5}, Kenji Tanaka¹, Hongtao Liu², Yasunobu Okada², Masahiro Sokabe^{4,5}, Kenzo Hirose³, Kazuhiro Ikenaka¹
¹Div. of Neurobio. Bioinfo. NIPS, ²Dept. of Cell Physiology, NIPS, ³Dept. of Neurobiol. Med., Univ. of Tokyo, ⁴Cell Biophysics/Imaging Physiology, Med. Nagoya Univ., ⁵ICORP/SORST, Cell-Mechanosensing Project, Japan Science and Technology Agency
- O12-5 Transport characteristics for adenosine in neurons and astrocytes under basal and oxidative stress-loaded conditions**
○Hiroto Okuda, Akiko Tanaka, Kentaro Nishida, Kazuki Nagasawa, Sadaki Fujimoto
Dept. of Environ. Biochem., Kyoto Pharm. Univ.
- O12-6 Transactivation of glia-derived neurotrophic factor in cultured rat cortical astrocytes exposed to nicotine**
○Hirofumi Kawagoe, Masato Ogura, Noritaka Nakamichi, Takeshi Takarada, Yukio Yoneda
Laboratory of Molecular Pharmacology, Kanazawa Univ. Graduate School of Natural Science and Technology, Kanazawa, Japan
- O12-7 Effects of theophylline on LPS-induced NO production in cultured astrocytes**
○Mizue Ogawa, Katsura Takano, Mitsuaki Moriyama, Yoichi Nakamura
Lab. Integrative Physiology, Vet. Sci., Osaka Pref. Univ., Osaka, Japan
- O12-8 Analgesic effect of Bushimatsu on neuropathic pain**
○Keisuke Shibata¹, Takeshi Sugawara², Kayoko Fujishita¹, Tetsuro Ozawa¹, Takashi Matsukawa², Tsutomu Suzuki³, Schuichi Koizumi¹
¹Dept. Pharmacol., Univ. of Yamanashi, ²Dept. Anesthesiol., Univ. of Yamanashi, ³Dept. toxicol., Hoshi Univ.

June 24 (Wednesday)

9 : 00 ~ 11 : 40 Room B (9F • Amanogawa)

O13-1 ~ O13-8 Neural stem/Progenitor cells

Chairs : Nobuo Inoue (Graduate School of Human Health Sciences, Tokyo Metropolitan University)

Yoshiyuki Horio (Department of Pharmacology, Sapporo Medical University, School of Medicine)

Kazuaki Yoshikawa (Lab. Regulation of Neuronal Development, Institute for Protein Research, Osaka University)

O13-1 A novel method for region specific gene modification for the analysis of developmental origin of glial cells

○Hitoshi Goto, Katsuhiko Ono, Hirohide Takebayashi, Kazuhiro Ikenaka
Div. of Neurobiol. and Bioinfo., National Institute for Physiological Sciences

O13-2 Mammalian *glial cells missing* genes induce *Hes5* expression and definitive neural stem cells in early embryos

○Seiji Hitoshi¹, Akhilesh Kumar¹, Yugo Ishino¹, Kenji_F Tanaka¹, Toshihiko Hosoya², Yoshiki Hotta³, Kazuhiro Ikenaka¹

¹Neurobiology & Bioinformatics, NIPS, Okazaki, Japan, ²RIKEN BSI, Wako, Japan, ³Research Organization of Information and Systems, Tokyo, Japan

O13-3 Cyclin D1 inhibits astrocyte differentiation from neural stem/progenitor cells in a manner independent of cell cycle regulation

○Norihisa Bizen¹, Toshihiro Inoue², Takeshi Shimizu³, Tetsushi Kagawa¹, Tetsuya Taga¹

¹Dept. of Stem Cell Reg., Med. Res. Inst., Tokyo Med. Dent. Univ., Tokyo, Japan, ²Dept. of. Opht. Vis. sci., Grad. Sch. of. Med. Sci., Kumamoto Univ, Kumamoto, Japan, ³Lab. for. Vert. Axis Form., RIKEN. CDB., Kobe, Japan

O13-4 Expression of adenomatous polyposis coli (Apc) in the developing mouse brain

○Ayako Taguchi¹, Yasuhiro Yamada^{1,2}, Akira Hara¹

¹Gifu Univ. Grad. Sch. Med. Tumor Pathol., ²PRESTO, Japan Sci. & Tech. Agency

O13-5 Identification of Phosphatidylglucoside as cell surface antigen of adult mouse neural stem/precursor cells

○Jun Kaneko^{1,2}, Masami Kinoshita^{1,2}, Takeo Machida², Yasuko Nagatsuka¹, Yoshio Hirabayashi¹

¹Hirabayashi Research Unit, RIKEN,BSI,Saitama,Japan, ²Department of regulatory Biology, Faculty of Science, Saitama University, Saitama, Japan

O13-6 Hippocampal cholinergic neurostimulating peptide precursor protein(HCNP-pp) is involved in differentiation of neural progenitor cells

○Takafumi Sagisaka, Tetsuko Kanamori, Norihiko Uematsu, Takanari Toyoda, Noriyuki Matsukawa, Kosei Ojika

Dept Neurology, Univ of Nagoya City, Aichi

- O13-7 **Biological effects of radiation on mouse embryonic stem cell-derived neural stem cells**
 ○Mayu Isono¹, Masahiro Otsu^{1,2}, Fuyumi Shinya¹, Hiroyuki Omori¹, Takuya Yoshie¹, Hiroki Ohtani³, Masahiro Fukushi³, Takashi Nakayama⁴, Nobuo Inoue¹
¹Laboratory of Regenerative Neurosciences, Tokyo Metropolitan University Graduate School of Human Health Sciences, Tokyo, Japan, ²Department of Chemistry, Kyorin University School of Medicine, Tokyo, Japan, ³Department of Radiology Sciences, Tokyo Metropolitan University Graduate School of Human Health Sciences, Tokyo, Japan, ⁴Department of Biochemistry, Yokohama City University School of Medicine, Yokohama, Japan
- O13-8 **Aberrant development of granule cells of the cerebellum in NB-3 knockout mice**
 ○Kunie Sakurai¹, Manabu Toyoshima¹, 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.

June 24 (Wednesday)

9 : 00 ~ 11 : 40 Room C (3F • Eboshi)

O14-1 ~ O14-8 **Growth factor/Trophic factor**

Chairs : Yoshihiro Arakawa (Clinical Research Center, University of Tokyo Hospital,
 University of Tokyo)
 Ritsuko Katoh-Semba (Laboratory for Molecular Neurogenesis, RIKEN Brain
 Science Institute)
 Ichiro Matsuoka (Lab. of Physiol. Chem., College of Pharmaceutical Sciences,
 Matsuyama University)

- O14-1 **Neurotrophin-3 stimulates neurogenetic proliferation in the developing cerebral cortex, via ERK1/2-dependent signaling pathway**
 ○Hidefumi Fukumitsu, Masanari Ohtsuka, Mitsuhiro Itoh, Shoei Furukawa
 Laboratory of Molecular Biology, Department of Biofunctional Analysis, Gifu Pharmaceutical University
- O14-2 **Roles of motoneuron-derived NT-3 on sensory neuron development**
 ○Noriyoshi Usui^{1,2}, Keisuke Watanabe³, Katsuhiko Ono⁴, Nobuaki Tamamaki³, Kazuhiro Ikenaka^{1,2}, Hirohide Takebayashi³
¹Department of Physiological Sciences, The Graduate University for Advanced Studies (SOUKENDAI), Hayama, ²Division of Neurobiology and Bioinformatics, National Institute for Physiological Sciences, Okazaki, ³Department of Morphological Neural Science, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, ⁴Department of Biology, Kyoto Prefectural University of Medicine, Kyoto

- O14-3 Nerve growth factor promotes GRP78 expression only under the condition of ER stress
 ○Koji Shimoke, Yosuke Nakatani, Soichiro Kishi, Takafumi Shimada, Hiromi Irifune, Harue Sasaya, Toshihiko Ikeuchi
 Dept. Life Sci. and Biotech., Fac. Chem, Material and Bioengin., Kansai Univ.
- O14-4 Fibroblast growth factor-2-responsive and spinal cord-resident rat mesenchymal cells stimulate axonal regeneration followed by the improvement of locomotor function after complete spinal cord injury
 ○Masaki Kasai, Hidefumi Fukumitsu, Shoei Furukawa
 Laboratory of Molecular Biology, Gifu Pharmaceutical University, Gifu, Japan
- O14-5 Metabolomic analysis for brain lipids in BDNF-KO mice
 ○Shingo Suzuki^{1,2}, Kazuyuki Kiyosue⁴, Takeshi Kasama⁵, Chiaki Itami⁶, Masami Kojima³, Kouichi Tanaka²
¹MTT program, Medical Research Institute, Tokyo Medical and Dental University, ²Department of Molecular Neuroscience, Medical Research Institute, Tokyo Medical and Dental University, ³Biointerface Research Group, Research Institute for Cell engineering, AIST, ⁴Molecular Neurobiology Group, Neuroscience Research Institute, AIST, ⁵Instrumental Analysis Research Center for Life Science, Tokyo Medical and Dental University, ⁶Department of Physiology, Faculty of Medicine, Saitama Medical University
- O14-6 Neurotrophic factor-like signaling of 2-decenoic acid ethyl ester, a medium-chain fatty acid derivative
 ○Shoei Furukawa, Akihisa Makino, Satoru Itoh, Hidefumi Fukumitsu
 Lab. of Mol. Biol., Department of Biofunctional Analysis, Gifu Pharmaceutical Univ.
- O14-7 The activity of cholinacetyl transferase is increased in medial septal nucleus of HCNP precursor transgenic mouse
 ○Norihiko Uematsu¹, Noriyuki Matsukawa¹, Takanari Toyoda¹, Takafumi Sagisaka¹, Tetsuko Kanamori¹, Yoshio Hashizume², Kosei Ojika¹
¹Department of Neurology, Nagoya City University, Nagoya, Japan, ²Institute for Medical Science of Aging, Aichi Medical University, Nagakute, Japan
- O14-8 Fasting-induced expression of AF5q31, a transcription factor, and β Klotho 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

June 24 (Wednesday)

9 : 00 ~ 11 : 40 Room D (1F • Nagamine)

O15-1 ~ O15-8

Psychiatric diseases/Developmental disorders

Chairs : Shigenobu Kanba (Department of Neuropsychiatry, Kyushu University Graduate School of Medical Sciences)

Toshihisa Tanaka (Psychiatry, Osaka University Graduate School of Medicine)

Norio Mori (Department of Psychiatry, Hamamatsu University School of Medicine)

O15-1 Impairment of BDNF secretion is involved in the phencyclidine-induced synaptic loss in cortical neurons

○Naoki Adachi¹, Tadahiro Numakawa¹, Emi Kumamaru¹, Chiaki Itami², Ritsuko Senba³, Torusun Torugun^{1,4}, Hiroshi Kunugi¹

¹Dept. of Mental Disorder Research, National Institute of Neuroscience, NCNP, Tokyo, JAPAN, ²Dept. Physiol., Saitama Med. Univ., Saitama, JAPAN, ³Lab. for Mol. Neurogenesis, BSI, RIKEN, Saitama, JAPAN, ⁴Dept. Pathology., Tokyo Med. Univ., Tokyo, JAPAN

O15-2 PACAP regulates the neural extension in adult neurogenesis

○Kohei Yamada¹, Shinsuke Matsuzaki^{1,4}, Tsuyoshi Hattori³, Hitoshi Hashimoto², Norihito Shintani², Akemichi Baba², Taiichi Katayama⁴, Masaya Tohyama¹

¹Department of Anatomy and Neuroscience, Graduate School of Medicine, Osaka Univ., ²Department of Molecular Neuropharmacology, Graduate School of Pharmaceutical Sciences, Osaka Univ., ³Department of Molecular Neuropsychiatry Graduate School of Medicine, Osaka Univ., ⁴The Osaka-Hamamatsu Joint Research Center for Child Mental Development, Graduate School of Medicine, Osaka Univ.

O15-3 Dysbindin-1 regulates the dendritic morphogenesis of hippocampal neurons

○Hidenori Ito, Rika Morishita, Tomoyasu Shinoda, Ikuko Iwamoto, Kaori Sudo, Ken-ichi Okamoto, Koh-ichi Nagata

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

O15-4 Reversal by galantamine of apomorphine-induced deficits in prepulse inhibition via stimulation of muscarinic ACh receptors

○Koji Yano¹, Ken Koda¹, Yukio Ago¹, Momoe Nishimura¹, Kazuhiro Takuma¹, Toshio Matsuda^{1,2}

¹Laboratory of Medicinal Pharmacology, Graduate School of Pharmaceutical Sciences, Osaka University, ²Center For Child Mental Development, Graduate School of Medicine, Osaka University

O15-5 Selective RGS protein regulation of melanin-concentrating hormone receptor 1

○Yumiko Saito, Mayumi Miyamoto-Matsubara

Graduate School of Integrated Arts and Sciences, Hiroshima University

- O15-6 Effects of acute and chronic treatment with atomoxetine and methylphenidate on the extracellular levels of monoamine in mouse brain
○Ken Koda¹, Yukio Ago¹, Yana Cong¹, Koji Yano¹, Kazuhiro Takuma¹, Toshio Matsuda^{1,2}
¹Laboratory of Medicinal Pharmacology, Graduate School of Pharmaceutical Sciences, Osaka University, Osaka, Japan, ²Center For Child Mental Development, Graduate School of Medicine, Osaka University, Osaka, Japan
- O15-7 Electron microscopic studies on neuronal dendritic abnormality caused by TSC-2 mutation
○Shu Takigami¹, Shin Yasuda¹, Hiroko Sugiura¹, Yoshiyuki Yoshimura², Takako Takemiya¹, Takashi Yamauchi¹, Okio Hino³, Kanato Yamagata¹
¹Dept. of Neuropharmacology, Tokyo Metropolitan Institute for Neuroscience, ²Institute of Health Bioscience and Graduate School of Pharmaceutical Sciences, The University of Tokushima, ³Dept. of Pathology and Oncology, Juntendo University School of Medicine
- O15-8 Two-generation toxicogenomic study of the effects of tributyltin on the developing rat brain
○Masashi Tsunoda¹, Mika Wakasa², Hideo Asakawa¹, Masaki Takahashi², Takayuki Negishi², Takaya Kaido¹, Mayuko Hosokawa¹, Chiemi Sugaya¹, Yoko Inoue¹, Yoshiharu Aizawa¹, Tomoko Tashiro²
¹Dept. of Prev. Med. and Public Health, Kitasato Univ. School of Med., ²Dept. of Chem. and Biol. Sci., Faculty of Sci. and Engineer., Aoyama Gakuin Univ.

Poster Sessions

Poster Room (1F • Queen)

Poster Discussion

June 22 (Monday) 13:30 ~ 14:15

June 23 (Tuesday) 13:10 ~ 14:10

P-1 ~ P-6 Neural stem/Progenitor cells
Chair : Seiji Hitoshi (Neurobiology & Bioinformatics, National Institute for
Physiological Sciences)

- P-1** Possible involvement of 5'-AMP-activated protein kinase in proliferation and survival of neural stem/progenitor cells derived from the neocortex
○Shohei Sano, Nobuyuki Kuramoto, Masanori Yoneyama, Reiko Nagashima, Koichi Kawada, Kiyokazu Ogita
Department of Pharmacology, Setsunan University Faculty of Pharmaceutical Sciences, Osaka, Japan
- P-2** Participation of reactive oxygen species and nitric oxide in proliferation of neural stem/progenitor cells derived from the hippocampus of embryonic mice
○Koichi Kawada, Masanori Yoneyama, Kiyokazu Ogita
Dept. Pharmacol., Setsunan Univ.
- P-3** Effect of caspase inhibitor on proliferation of neural progenitor cells derived from embryonic neocortex of mice
○Hajime Tanaka, Koichi Kawada, Reiko Nagashima, Masanori Yoneyama, Kiyokazu Ogita
Department of Pharmacology, Setsunan University Faculty of Pharmaceutical Sciences
- P-4** Suppression by myosin VI responsive to traumatic stress of neural progenitor proliferation
○Yuma Ito, Keisuke Tamaki, Noritaka Nakamichi, Masaki Tachibana, Takeshi Takarada, Yukio Yoneda
Lab Mol Pharmacol, Kanazawa Univ Grad Sch Nat Sci Tech, Kanazawa, Japan
- P-5** NMDA receptors positively regulate proliferative activity of neural progenitor/stem cells generated after neuronal damage in the hippocampal dentate gyrus
○Masanori Yoneyama, Koichi Kawada, Tatsuo Shiba, Kiyokazu Ogita
Department of Pharmacology, Faculty of Pharmaceutical Sciences, Setsunan University
- P-6** Effects of methyl mercury on proliferation of monkey ES cell-derived neural stem cells
○Nobue Kume¹, Daisuke Inada¹, Masahiro Otsu^{1,2}, Hajime Kobayashi¹, Takuya Yoshie¹, Koji Murakami¹, Takashi Nakayama³, Yutaka Suzuki⁴, Yasushi Kondo⁴, Nobuo Inoue¹

¹Laboratory of Regenerative Neurosciences, Tokyo Metropolitan University Graduate School of Human Health Sciences, Tokyo, Japan, ²Department of Chemistry, Kyorin University School of Medicine, Tokyo, Japan, ³Department of Biochemistry, Yokohama City University School of Medicine, Yokohama, Japan, ⁴Regenerative Medicine Group, Mitsubishi Tanabe Pharma Corp.

P-7 ~ P-11

Neural differentiation

Chair : Seiji Hitoshi (Neurobiology & Bioinformatics, National Institute for Physiological Sciences)

P-7 Effects of heat shock on proliferation and differentiation of mouse ES cell-derived neural stem cells

○Hiroyuki Omori¹, Masahiro Otsu^{1,2}, Mayu Isono¹, Nobue Kume¹, Fuyumi Shinya¹, Takuya Yoshie¹, Takashi Nakayama³, Nobuo Inoue¹

¹Laboratory of Regenerative Neurosciences, Tokyo Metropolitan University Graduate School of Human Health Sciences, Tokyo, Japan, ²Department of Chemistry, Kyorin University School of Medicine, Tokyo, Japan, ³Department of Biochemistry, Yokohama City University School of Medicine, Yokohama, Japan

P-8 Effects of X-irradiation on differentiation from mouse embryonic stem cells into neuron

○Fuyumi Shinya¹, Hitoshi Nagano¹, Masahiro Otsu^{1,2}, Mayu Isono¹, Hiroyuki Omori¹, Hiroki Ohtani³, Masahiro Fukushima³, Takashi Nakayama⁴, Nobuo Inoue¹

¹Laboratory of Regenerative Neurosciences, Tokyo Metropolitan University Graduate School of Human Health Sciences, Tokyo, Japan, ²Department of Chemistry, Kyorin University School of Medicine, Tokyo, Japan, ³Department of Radiology Sciences, Tokyo Metropolitan University Graduate School of Human Health Sciences, Tokyo, Japan, ⁴Department of Biochemistry, Yokohama City University School of Medicine, Yokohama, Japan

P-9 Modulation of differentiation into neural lineages through GABA_B receptors

○Shusuke Ozawa, Masaki Fukui, Takeshi Takarada, Yukio Yoneda

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

P-10 Dramatically different effects of methyl mercury on uni-directional differentiation from embryonic stem cells into neurons by Neural Stem Sphere method

○Masahiro Otsu^{1,2}, Daisuke Inada², Nobue Kume², Takashi Nakayama³, Hisataka Kasai², Nobuo Inoue²

¹Department of Chemistry, Kyorin University School of Medicine, Tokyo, Japan, ²Laboratory of Regenerative Neurosciences, Tokyo Metropolitan University Graduate School of Human Health Sciences, Tokyo, Japan, ³Department of Biochemistry, Yokohama City University School of Medicine, Yokohama, Japan

- P-11 The mechanism of aggression and impulsivity through the change of neurogenesis
 ○Ippei Watanabe¹, Wataru Ukai¹, Takafumi Ono¹, Kimihiko Watanabe¹,
 Tomohiro Shirasaka¹, Eri Hashimoto¹, Takao Ishii², Masaru Tateno¹, Toshikazu Saito¹
¹ Department of Neuropsychiatry Sapporo Medical University School of Medicine, ²
 Department of Occupational therapy Sapporo Medical University School of Health Science

- P-12 ~ P-14 Neurite outgrowth
 Chair : Yukio Ago (Laboratory of Medicinal Pharmacology, Graduate School of
 Pharmaceutical Sciences, Osaka University)

- P-12 Roles of newly identified nerve growth-associated proteins (nGAPs) in the growth cone
 ○Motohiro Nozumi^{1,3}, Jia Lu², Michihiro Igarashi^{1,3}
¹ Div Mol Cell Biol, Niigata Univ Grad Sch Med, Niigata, JAPAN, ² Div Ophthalmol, Niigata Univ Grad Sch Med, Niigata, JAPAN, ³ Trans-disciplinary Res Progr, Niigata Univ, Niigata, JAPAN

- P-13 The significance of Syntaxin-1A-CaMKII interaction in synaptic vesicle transportation and mouse behavior
 ○Yumi Watanabe^{1,2}, Rieko Ito¹, Yukiyo Tada¹, Keizo Takao^{3,4}, Tsuyoshi Miyakawa^{3,4}, Kenji Sakimura⁵, Michihiro Igarashi^{1,2}
¹ Div. of Mol. Cell. Biol., Grad. Sch. of Med. Dent. Sci., Niigata. Univ., ² Trans-disc. Res. Prog., Niigata Univ., ³ Gen. Eng. Func. Gen. Gr., Front. Tech. Ctr., Kyoto Univ., Fac. of Med., ⁴ Div. of Sys. Med. Sci., Inst. for Comp. Med. Sci., Fujita Health Univ., ⁵ Dept. of Cell. Neurobiol., Brain. Res. Inst., Niigata Univ.

- P-14 Analyses of the knockout mice lacking in the enzymes synthesizing chondroitin sulfate
 ○Susumu Higa^{1,2}, Yumi Watanabe^{1,2}, Kosei Takeuchi^{1,2}, Michihiro Igarashi^{1,2}
¹ Division of Molecular Cell Biology, Graduate School of Medical and Dental Science, Niigata University., ² Trans-Disciplinary Research Program

- P-15 ~ P-19 Neuronal death
 Chair : Yukio Ago (Laboratory of Medicinal Pharmacology, Graduate School of
 Pharmaceutical Sciences, Osaka University)

- P-15 Protective effects of interferon- γ or peroxisome proliferator-activated receptor- γ agonist against methamphetamine-induced neurotoxicity
 ○Masato Asanuma¹, Ikuko Miyazaki¹, Saki Fukuoka², Hiroaki Hozumi², Takeshi Tsuji¹, Yoshihisa Kitamura³, Toshiaki Sendo², Taizo Kita⁴
¹ Dept. of Brain Sci., Okayama Univ. Grad. Sch. of Med., Dent. and Pharmaceut. Sci., Okayama, Japan, ² Dept. of Clin. Pharm., Okayama Univ. Grad. Sch. of Med., Dent. and Pharmaceut. Sci., Okayama, Japan, ³ Dept. of Pharmaceut. Care and Health Sci., Okayama Univ. Grad. Sch. of Med., Dent. and Pharmaceut. Sci., Okayama, Japan, ⁴ Kyushu Nutr.

Welfare Univ., Grad Sch. of Food and Nutr., Kitakyushu, Japan

- P-16 SA4503, a sigma receptor agonist, prevents cultured cortical neurons from cell death
○Torusun Torugun^{1,2}, Tadahiro Numakawa², Naoki Adachi², Emi Kumamaru², Motoshige Kudo¹, Hiroshi Kunugi²
¹Dept. Pathology, Tokyo Med. Univ., Tokyo, JAPAN, ²Department of Mental Disorder Research, National Institute of Neuroscience, NCNP, Tokyo, JAPAN
- P-17 The effect of proteolytic cleavage within calyculin-3 on the death of cerebral cortical neurons
○Yoko Uchida, Fujiya Gomi
RT for Geriatric Disorders, Tokyo Metropolitan Institute of Gerontology
- P-18 Free radical scavengers enhance the survival of cells newly generated after neuronal damage in the hippocampal dentate gyrus of mice
○Tatsuo Shiba, Koichi Kawada, Masanori Yoneyama, Kiyokazu Ogita
Dept. Pharmacol., Setsunan Univ.
- P-19 Commitment of MPP⁺-induced neuronal cell death by proteasome-mediated degradation of p35 Cdk5 activator
○Ryo Endo¹, Taro Saito¹, Akiko Asada¹, Hiroyuki Kawahara², Toshio Ohshima³, Shin-ichi Hisanaga¹
¹Laboratory of Molecular Neuroscience, Department of Biological Sciences, Tokyo Metropolitan University, ²Laboratory for Cellular Biochemistry, Department of Biological Sciences, Tokyo Metropolitan University, ³Department of Life Science and Medical Bio-Science, Waseda University
- P-20 ~ P-23 Astrocytes
Chair : Yukio Ago (Laboratory of Medicinal Pharmacology, Graduate School of Pharmaceutical Sciences, Osaka University)
- P-20 Mechanism of apoA-I-mediated cholesterol release from rat astrocytes through Rho kinase activation
○Jinichi Ito, Kheirollah Alireza, Yuko Nagayasu, Shinji Yokoyama
Biochem. Nagoya City Univ. Med. Sch.
- P-21 Diclofenac has a synergistic effect on the production of nitric oxide through NF-κB signaling in cultured astrocytes stimulated by proinflammatory cytokines
○Mineyoshi Aoyama¹, Hiroki Kakita^{1,2,3}, Mohamed Hussein^{1,2}, Shin Kato^{1,2}, Satoshi Suzuki², Tetsuya Ito², Hajime Togari², Kiyofumi Asai¹
¹Dept of Mol Neurobiology, Nagoya City Univ, Nagoya, Japan, ²Dept of Pediatrics, Nagoya City Univ, Nagoya, Japan, ³Dept of Neonatology, Aichi Human Service Center Central Hosp, Kasugai, Japan

- P-22** Astrocytes Promote the Proliferation of Lung Cancer Cells in Brain Metastases via inflammatory cytokines, especially IL-6

○Yukiko Yamakawa¹, Kyota Fujita¹, Toshihiro Seike¹, Mizuho Kido², Haruo Iguchi³, Mami Noda¹

¹Department of Pathophysiology, Graduate School of Pharmaceutical Science, Kyushu University, Maidashi, Higashi-ku, Fukuoka, Japan, ²Department of Oral Anatomy and Cell Biology, Graduate School of Dental Sciences, Kyushu University, Maidashi, Higashi-ku, Fukuoka, Japan, ³Department of Internal Medicine, National Hospital Organization Shikoku Cancer Center, Matsuyama, Ehime, Japan

- P-23** Neuroprotective properties of metallothioneins in astrocytes against dopaminergic neurotoxicity

○Ikuko Miyazaki¹, Yuri Kikkawa¹, Mika Takeshima², Ko Miyoshi¹, Masato Asanuma¹

¹Dept. of Brain Sci., Okayama Univ. Grad. Sch. of Med., Dent. and Pharmaceut. Sci., Okayama, Japan, ²Lab. of Pharmacol., Kyushu Nutr. Welfare Univ., Grad Sch. of Food and Nutr.

P-24 ~ P-31 Receptors/Ion channels/Transporters

Chairs : Yumiko Saito (Graduate School of Integrated Arts and Sciences, Hiroshima

University Laboratory for Behavioral Neuroscience)

Kazuhiko Yanai (Graduate School of Medicine, Department of Pharmacology,

Tohoku University)

- P-24** Development of Generic Calcium Imaging Assay for monitoring Gi-coupled Receptors and G protein interaction

○Takashi Ueda¹, Shinya Ugawa¹, Yusuke Ishida¹, Shoichi Shimada²

¹The Department of Neurobiology and Anatomy, Nagoya City University, Nagoya, Japan,

²Department of Neuroscience and Cell Biology, Osaka University Graduate School of Medicine, Osaka, Japan

- P-25** Phosphorylation and dephosphorylation at serine 892 on GABA_BR2 subunit

○Akira Koutani, Nobuyuki Kuramoto, Kiyokazu Ogita

Department of Pharmacology, Faculty of Pharmaceutical Sciences, Setsunan University

- P-26** Properties of acquired NMDA receptors in HEK293 cells

○Ryo Fukumori, Noritaka Nakamichi, Yuki Kanbe, Hideo Taniura, Takeshi Takarada, Yukio Yoneda

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

- P-27** Pharmacological characterization of sigma-1 receptor ligands: agonist-specific up-regulation of sigma-1 receptor

○Toshifumi Yamamoto¹, Hideko Yamamoto²

¹Lab. of Mol. Psychopharmacol. Yokohama City Univ., ²Div. of Psychobiology, Tokyo Inst. of Psychiatry

- P-28 Glucocorticoid receptor promotes BDNF-stimulated PLC γ /Ca²⁺ signaling for glutamate release via interacting with BDNF receptor TrkB
 ○Tadahiro Numakawa, Emi Kumamaru, Naoki Adachi, Yuki Yagasaki, Aiko Izumi, Hiroshi Kunugi
 Department of Mental Disorder Research, National Institute of Neuroscience, NCNP, Tokyo, JAPAN
- P-29 Possible involvement of PPAR γ in regulation of basal channel opening of P2X7 receptor in cultured mouse astrocytes
 ○Kentaro Nishida, Kazuki Nagasawa, Jun Miyaki, Yuka Kido, Sadaki Fujimoto
 Department of Environmental Biochemistry, Kyoto Pharmaceutical University
- P-30 Critical roles of thyroid hormone in the development of the GABAergic system
 ○Erika Sawano, Masaki Takahashi, Naoko Funatsu, Hirohito Kimura, Takayuki Negishi, Tomoko Tashiro
 Department of Chemistry and Biological Science, School of Science and Engineering, Aoyama Gakuin University
- P-31 VGAT-Venus expression patterns in developing cerebellar cortex *in vivo* and *in vitro*
 ○Tadashi Ogo, Masakazu Uematsu, Sachiko Yoshida
 Department of Material Science., Toyohashi University of Technology, Toyohashi, Japan
- P-32 ~ P-39 Transcription factors/Gene expression
 Chair : Noriyuki Koibuchi (Gunma University Graduate School of Medicine)
- P-32 Dexamethasone resets the circadian oscillation of *Bmal1* via ROR-response elements
 ○Megumi Kumagai^{1,2}, Yoshihiro Nakajima³, Masaaki Ikeda^{1,2}
¹Dept. of Physiol., Saitama Medical Univ., Saitama, Moroyama, Saitama, Japan, ² Molecular Clock Project, Res. Center for Genomic Med. Saitama Medical Univ. Hidaka, Saitama, Japan, ³ Cell Dynamics, Cell Engineering, AIST, Ikeda, Osaka, Japan
- P-33 OASIS, a member of the CREB/ATF family transcription factor, is involved in glycosylation of chondroitin sulphate proteoglycans
 ○Hiroaki Okuda¹, Kouko Tatsumi¹, Kazunori Imaizumi², Akio Wanaka¹
¹Dept. of Anatomy and Neuroscience, Nara medical University, Nara, Japan, ²Div. of Molecular and Cellular Biology, Dept. of Anatomy, Faculty of Medicine, Univ. of Miyazaki, Miyazaki, Japan
- P-34 Expression of Foxp1 in a subpopulation of V1 interneurons during development of the spinal cord
 ○Tomoko Hisaoka, Yoshihiro Morikawa, Tadasuke Komori, Emiko Senba
 Department of Anatomy & Neurobiology, Wakayama Medical University

- P-35 Spatio-temporal expression pattern of Foxp2 in the developing spinal cord
 ○ Yoshihiro Morikawa, Tomoko Hisaoka, Emiko Senba
 Department of Anatomy & Neurobiology, Wakayama Medical University
- P-36 Expression of TRPM8, TRPA1, and TRPV1 mRNAs in the rat nodose-petrosal ganglion complex
 ○ Yusuke Ishida¹, Aki Hondoh^{1,2}, Shinya Ugawa¹, Takashi Ueda¹, Takahiro Yamada¹, Shoichi Shimada¹
¹Department of Neurobiology and Anatomy, Graduate School of Medical Sciences, Nagoya City University, Nagoya, Japan, ²Department of Otorhinolaryngology, Graduate School of Medical Sciences, Nagoya City University, Nagoya, Japan
- P-37 Unique gene expression changes in microglia coincide with the appearance of chronic demyelinating lesions
 Jianmei Ma^{1,2}, ○Takahiro Shimizu^{1,3}, Kenji F Tanaka¹, Kazuhiro Ikenaka¹
¹Division of Neurobiology and Bioinformatics, National Institute for Physiological Science, ²Dalian Medical University, Dalian, China, ³Department of Physiological Sciences, School of Life Sciences, The Graduate University for Advanced Studies (SOKENDAI), Kanagawa 240-0193, Japan.
- P-38 Preliminary study of cilostazol effect on the protein expression changes of primary mouse brain microvessel endothelial cells
 ○ Ahmad Faried^{1,2}, Hideaki Imai¹, Moch. Arifin², Sandra Puentes¹, Masashi Kurachi³, Yuhei Yoshimoto¹, Yasuki Ishizaki³
¹Dept. Neurosurg., Gunma Univ. Grad. Sch. Med., Maebashi, Japan, ²Dept. Neurosurg., Padjadjaran Univ. Sch. Med., Bandung, Indonesia, ³Dept. Mol. Cell. Neurobiol., Gunma Univ. Grad. Sch. Med., Maebashi, Japan
- P-39 Analysis of N-glycan structure from a femtomole level of glycoprotein
 ○ Takeshi Yoshimura¹, Tomohiro Torii¹, Akihiro Ishii¹, Mikito Higashi², Kazuhiro Tanabe², Kazuhiro Ikenaka¹
¹Division of Neurobiology & Bioinformatics, NIPS, ²Analytical Services Division, Mitsubishi Chemical Science & Technology Research Center
- P-40 ~ P-47 Animal models
 Chairs : Shigeru Saito (Department of Anesthesiology, Gunma University Graduate School of Medicine)
 Kiyoshige Takayama (Department of Laboratory Sciences, Gunma University School of Health Sciences)
- P-40 Alterations in homocysteine metabolism in the brain of the Goto-Kakizaki rat, an animal model of type 2 diabetes
 ○ Takefumi Uno, Yoh Ishibashi, Masaki Takahashi, Takayuki Negishi, Tomoko Tashiro
 Department of Chemistry & Biological Science, School of Science & Engineering, Aoyama Gakuin University, Sagamihara, Japan

- P-41** A rapid but transient increase in *lfrd1* mRNA expression in brains of mice with middle cerebral artery occlusion
 ○Shiho Konishi, Sayaka Maeda, Mami Watanabe, Noritaka Nakamichi, Takeshi Takarada, Yukio Yoneda
 Lab.Mol.Pharmacol., Kanazawa Univ. Grad. Sch. Nat. Sci. Tech.
- P-42** The trial for axonal regeneration by using bFGF continuous delivery system in lacunar infarction model of the rat
 ○Sandra Puentes¹, Hideaki Imai¹, Ahmad Faried¹, Takayuki Okano-Uchida², Masashi Kurachi², Yasuki Ishizaki², Yasuhiko Tabata³, Yuhei Yoshimoto¹
¹Dept. Neurosurg, Gunma Univ. Grad. Sch. Med., Maebashi, Japan, ²Dept. Mol. and Cell. Neurobiol., Gunma Univ. Grad. Sch. Med., ³Dept. Biomaterials, Inst. Frontier Med. Sci., Kyoto Univ.
- P-43** The postnatal development of a molecular system responsive to novelty stress in the hippocampus of mice
 ○Akeo Kurumaji, Toru Nishikawa
 Sect. of Psychiatry & Behav. Sci., Tokyo Med. & Dent. Univ.
- P-44** Pharmacological discrimination of fear extinction and reconsolidation
 ○Daisuke Yamada^{1,2}, Keiji Wada^{1,2}, Masayuki Sekiguchi^{1,2}
¹Department of Degenerative Neurological Diseases, National Institute of Neuroscience, National Center of Neurology and Psychiatry, Tokyo, Japan, ²Japan Science and Technology Agency, CREST
- P-45** Pathological role of microglia and microsomal prostaglandin E synthase-1 in a mouse model for amyotrophic lateral sclerosis
 ○Hiroko Miyagishi¹, Yasuhiro Kosuge¹, Kumiko Ishige¹, Shin-ichi Ono², Yoshihisa Ito¹
¹Research Unit of Pharmacology, College of Pharmacy, Nihon University, 7-7-1 Narashinodai, Funabashi-shi, Japan, ²Research Unit of Clinical Medicine, College of Pharmacy, Nihon University, 7-7-1 Narashinodai, Funabashi-shi, Japan
- P-46** In vivo intense noise exposure activates 5'-AMP-activated protein kinase/c-Jun N-terminal kinase pathway in the cochlear spiral ligament fibrocytes of mice
 ○Reiko Nagashima, Hajime Tanaka, Nobuyuki Kuramoto, Kiyokazu Ogita
 Department of Pharmacology, Setsunan University Faculty of Pharmaceutical Sciences
- P-47** Behavioral analyses of mice which show abnormal expressions of neuroglycan C, a brain-specific chondroitin sulfate proteoglycan
 ○Sachiko Aono¹, Yoshihito Tokita¹, Fumiko Matsui¹, Atsuhiko Oohira², Masahito Ikawa³, Masaru Okabe³, Katsuhiko Ono⁴
¹Department of Perinatology, Institute for Developmental Research, Aichi Human Service Center, Kasugai, Japan, ²Research Complex of Medical Frontiers, Aichi Medical University, Aichi, Japan, ³Research Institute for Microbial Diseases, Osaka University, Osaka, Japan, ⁴Department of Biology, Kyoto Prefectural University, Kyoto, Japan

Chairs : Shigeru Saito (Department of Anesthesiology, Gunma University Graduate School of Medicine)
Kiyoshige Takayama (Department of Laboratory Sciences, Gunma University School of Health Sciences)

- P-48** A case-control association study of the MYH9 gene with schizophrenia
○Yuichiro Watanabe, Ayako Nunokawa, Naoshi Kaneko, Toshiyuki Someya
Department of Psychiatry, Niigata University Graduate School of Medical and Dental Sciences
- P-49** A genetic variation of the KIBRA gene is associated with memory performance in Japanese healthy subjects
○Yuka Yasuda ^{1,2,3}, Ryota Hashimoto ^{1,2,3}, Kazutaka Ohi ^{2,3}, Hironori Takamura ^{2,3}, Motoyuki Fukumoto ^{2,3}, Hidetoshi Takahashi ^{2,3}, Tetsuhiko Yoshida ², Naomi Iike ^{2,4}, Hidenaga Yamamori ^{2,5}, Takashi Morihara ², Shinji Tagami ², Masayasu Okochi ², Toshihisa Tanaka ², Takashi Kudo ^{1,2}, Kouzin Kamino ^{2,6}, Ryohei Ishii ², Masao Iwase ², Hiroaki Kazui ², 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, ³CREST (Core Research for Evolutionary Science and Technology), JST (Japan Science and Technology Agency), ⁴Department of Clinical Pedagogy, Osaka University Graduate School of Human Sciences, Suita, Osaka, Japan, ⁵Department of Molecular Neuropsychiatry, Osaka University Graduate School of Medicine, Suita, Osaka, Japan, ⁶Shoraiso National Hospital, Yamatokoriyama, Nara, Japan
- P-50** Construction of Human Aβ1-38 ELISA assay system
○Nobuto Kakuda, Yuko Horikoshi, Kazuhiro Nagaike
Immuno-Biological Laboratories Co., Ltd.
- P-51** The possible role of platelet brain-derived neurotrophic factor in depression
○Kimihiko Watanabe ¹, Eri Hashimoto ¹, Wataru Ukai ¹, Takao Ishii ², Toshihiro Yoshinaga ¹, Takafumi Ono ¹, Masaru Tateno ¹, Ippei Watanabe ¹, Tomohiro Shirasaka ¹, Toshikazu Saito ¹
¹Dept. of Neuropsychiatry, Sapporo Medical University, School of Medicine, ²Dept. of Occupational Therapy, Sapporo Medical University

Luncheon Seminars

June 23 (Tuesday)

12 : 00 ~ 13 : 00 Room A (1F • King)

LS-1

Sponsor: Janssen Pharmaceutical K.K.

Chair: Masahiko Mikuni, MD/PhD (Department of Psychiatry and Human Behavior,
Gunma University Graduate School of Medicine)

“Pathophysiological hypotheses and pharmacological interventions for schizophrenia”

Takashi Kudo, MD/PhD

Department of Psychiatry, Osaka University Graduate School of Medicine

June 23 (Tuesday)

12 : 00 ~ 13 : 00 Room C (3F • Eboshi)

LS-2

Sponsor : Applied Biosystems Japan Ltd.

Chair : Takehiko Okada (Applied Biosystems Japan Ltd.)

1. “Introduction of the novel tool for dynamic analysis of the phosphoproteins and
determination of their phosphorylation sites”

Takuichi Tsubata, PhD

Applied Biosystems Japan Ltd.

2. “Phosphoproteomic analysis of the growth cone and the synaptosomes:
Novel findings in neuronal growth and synaptic transmission”

Michihiro Igarashi, MD/PhD

Graduate School of Medical and Dental Sciences, Niigata University

June 24 (Wednesday)

12 : 00 ~ 13 : 00 Room B (9F • Amanogawa)

LS-3

Sponsor : Mitsubishi Tanabe Pharma Corporation

Yoshitomiyakuhin Corporation

Chair : Masahiko Mikuni, MD/PhD (Department of Psychiatry and Human
Behavior, Gunma University Graduate School of Medicine)

“How can we select the most appropriate second generation antipsychotics based on the
mechanisms of action?”

Ichiro Kusumi, MD/PhD

Department of Psychiatry, Hokkaido University Graduate School of Medicine

神経化学の若手研究者育成セミナー概要

Information for Training Seminar for Students

育成セミナー講義
Traning Seminar Lecture

フリーディスカッション
Free Discussion

開催趣旨

昨年に引き続き、神経化学分野の研究者育成を目的として、国内外の学生を対象とした育成セミナーを開催いたします。講演やフリーディスカッションを通して、新しい実験手法や研究内容、研究の方向性などを直接講師の方から聞くことができます。第一線で研究に携わる方々とじかにふれあい、神経化学の楽しさを感じてください。また、異なる大学の学生同士の交流から、神経化学会の将来を担う新しいネットワークができることを期待しています。

■プログラム

6月22日（月）

21：00（懇親会終了後）～22：00 オリエンテーション（A～D会場）

22：00～23：00 フリーディスカッション（B会場：天の川）

6月23日（火）

18：40～19：30 育成セミナー夕食会（2F：五万石）

19：30～21：30 育成セミナー講義（A～D会場）

21：30～23：00 フリーディスカッション（B会場：天の川）

*フリーディスカッションには、飛び入り参加も歓迎します。

【テーマ及び講師紹介】

統合テーマ1. 細胞骨格と神経回路形成

精製蛋白質から細胞機能を探る：アクチンミオシン系蛋白質の in vitro 解析法			
講 師	石川 良樹	所属	群馬大学大学院 医学系研究科 病態薬理学
メッセージ	混ざり物を排して蛋白質を純化し、個々の蛋白機能や相互作用を試験管内で調べる。「究極の混ざり物」である細胞現象 を探るのに、この方法で大丈夫なのか？現在も発展し続けるアクトミオシン系蛋白質の解析法を通して、その長所や限界を一緒に考えましょう。		
神経回路形成と生理活性物質の探求			
講 師	五嶋 良郎	所属	横浜市立大学大学院 医学研究科 分子薬理神経生物学
メッセージ	細胞内、細胞間のコミュニケーションは分子間相互作用に基づいている。薬理学はこのコンセプトを最初に示した学問と言える。薬理学の接点は広く、生物学の基礎的な問いかけから臨床応用につながる可能性を秘めている。私達は基礎研究と臨床における応用を切り離して考えるのではなく、自らの方向性を選択する上でも両方を同時に俯瞰できるものの見方を常日頃より養う必要があるのではないかと皆さんと一緒にこの問題について考えてみたい。		

統合テーマ2. アミノ酸と低分子化合物

神経栄養因子産生促進をする低分子化合物を用いた実用化への道 (みんなも特許をだしてみよう！)			
講 師	新田 淳美	所属	名古屋大学大学院医学研究科・医療薬学
メッセージ	神経栄養因子の産生を in vivo および in vitro で脳内で促進する低分子化合物を見つけ、それらが、薬物依存、ドーパミン神経障害、うつ様症状、認知症に効果があることを見出し、企業とタイアップして、実用化を目指しています。そのためには、まず、特許で自分の権利を主張することが必須ですので、学問的なことから、企業の方との接し方なども、お話できればと思っています。		
神経骨学の醍醐味			
講 師	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
メッセージ	アミノ酸は、タンパク質の構成成分やエネルギー源、等々、全ての細胞に普遍的な役割だけでなく、特定細胞では特殊な情報伝達の働きを発揮する低分子物質である。このアミノ酸による情報伝達をキーワードにして、神経系細胞と骨関節系細胞の相同性と相違性を紹介する。		

統合テーマ3. 神経栄養因子と長期増強

神経栄養因子研究の今後			
講 師	武井 延之	所属	新潟大学脳研究所 基礎神経科学部門 分子神経生物学分野
メッセージ	サイエンスの世界にもはやりすたりがありますが、脳・神経系の研究で神経栄養因子は大きな役割を果たしてきました。今後、どのような展開が予想されるのかを考えることで、自分の専門分野の選び方などの参考になればと思います。テーマ以外にも、皆でざっくばらんにディスカッションしましょう。		
脳切片培養を使ってできること			
講 師	小倉 明彦	所属	大阪大学大学院 生命機能研究科
メッセージ	神経科学では、細胞レベル・分子レベルの研究には培養ニューロンがしばしば用いられるが、回路レベルの研究に適用するには限界がある。といって、一足飛びに個体で解析するのは多因子すぎて困難。そんな時、回路を保存した脳切片培養という系がある。長期記憶の機構解析に切片培養を利用した講師の経験を素材にして、この方法の適用範囲を考える。		

統合テーマ4. グリア細胞

グリア細胞の神経化学			
講 師	小泉 修一	所属	山梨大学医学部薬理学
メッセージ	グリア細胞の役割が注目されるようになってきました。神経細胞だけでは、説明のつかない脳の生理機能、脳の病態等にグリア細胞が密接に関連している可能性が高いと考えられます。本育成セミナーでは、グリア細胞の新しい役割について概説するとともに、最近のグリア細胞に関する話題を皆で討議したいと思います。まだわからないことが多く、またどんな未来が待っている分野かもわかりません。新しい分野を開拓したい、と考えているチャレンジ精神旺盛なタフな皆さんと、神経化学の未来とともに語りたいと思っています。		
ミエリンと軸索の絆な関係を探る			
講 師	馬場 広子	所属	東京薬科大学薬学部
メッセージ	神経系の発達段階を含め、ミエリン形成細胞と軸索は実に密に相互作用をすることがわかってきています。また、これらの破綻は様々な疾患を生じます。知っているようで良く知らない神経細胞の迅速かつ効率的な出力の謎について紹介しながら基礎と臨床研究のつながりにも触れたいと思います。		

統合テーマ5. 神経発生と神経新生

成体脳のニューロン新生と再生医学			
講 師	澤本 和延	所属	名古屋市立大学大学院 医学研究科 再生医学分野
メッセージ	成体脳でも幹細胞が毎日多くのニューロンやグリア細胞を産生しています。そのメカニズムの解明と脳疾患の再生医療への応用を目指した研究を紹介しながら、「神経化学的」アプローチの重要性について考えたいと思います。		
神経発生研究の現状と未来展望			
講 師	鹿川 哲史	所属	東京医科歯科大学 難治疾患研究所
メッセージ	ヒト脳には約 2000 億個のニューロンがあり 1000 種類以上に分類されている。最近の遺伝子組換え動物作製技術の向上や、ゲノムプロジェクトからのフィードバックによる細胞マーカーの充実から、ニューロン・サブタイプの同定やその発生制御が明らかになりつつある。では多様な機能を持つグリア細胞にも未知のサブクラス細胞系譜があるのだろうか？ニューロンとグリア細胞の発生制御の連携は？神経発生研究の未来展望について若い方々と膝を詰めて語り合いたい。		

統合テーマ6. 目指せ、創薬

伝統薬物-based 創薬			
講 師	東田 千尋	所属	富山大学 和漢医薬学総合研究所
メッセージ	神経変性疾患からの回復に必要とされる要因に対して、ある種の伝統薬物が切れ味鋭い作用を示すという実験事実から出発し、それらの作用分子の解析によって神経回路網再構築の鍵を握る分子の解析を目指すアプローチ、「伝統薬物-based 創薬」の可能性について解説する。また、研究と子育ての両立に葛藤する女性研究者の実情に興味のある人の参加も歓迎する。		
神経変性疾患克服への挑戦 – 目的指向型研究の進め方 –			
講 師	永井 義隆	所属	国立精神神経センター 神経研究所 疾病研究第四部
メッセージ	1980 年代後半から 1990 年代にかけて分子遺伝学的解析が飛躍的に進み、多くの神経変性疾患の原因遺伝子変異が次々と明らかになった。それに続く 1990 年代後半から 2000 年代の分子生物学的解析から、実に驚くべきことに、多彩な神経変性疾患において蛋白質のミスフォールディング・凝集が共通に発症に深く関わる事が明らかになった。本セミナーでは、私たちの行っている蛋白質ミスフォールディング・凝集を標的とした神経変性疾患の治療法開発研究を紹介し、目的指向型の研究の進め方について学び、若手研究者の育成に役立てたい。		

統合テーマ7. タンパク質の科学と新しい形態学

タンパク質の扱い方			
講 師	高橋 正身	所属	北里大学医学部生化学
メッセージ	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。またタンパク質の概念の中にも修正が必要なものが出てきている。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。		

神経化学研究における形態学の有用性			
講 師	和中 明生	所属	奈良県立医科大学 大学院医学系研究科 分子機能形態学
メッセージ	形態学は単純な組織像から多重免疫染色、免疫電顕、最近では2光子励起顕微鏡に至る様々な手法を含んでいます。神経系における物質の機能を追求する上で、形態学は常に重要な役割を果たしてきました。本セミナーではこのような形態学の実例を見ていきたいと思っています。		

統合テーマ8. 脳科学の将来

脳機能を個体で解析したい：遺伝子改変マウス作成工房ができるまで			
講 師	崎村 建司	所属	新潟大学脳研究所 基礎神経科学部門 細胞神経生物学分野
メッセージ	どうしたら自分がやりたい研究ができるのか。お金が無いと研究はできないのか。プロの研究者を目指すのに必要なこととは何かを一緒に考えてみましょう。		
脳科学の発展に必要なこと：若手諸君に期待する			
講 師	和田 圭司	所属	国立精神神経センター 神経研究所 疾病研究第四部
メッセージ	脳科学は、医学・生物学だけでなく、工学、理学、さらには教育学、心理学、はたまた経済学などとも結びつく大変に幅の広い分野であります。明日の脳科学を切り拓く人材を育成するため、一人一人が持つ潜在力を見出すナビゲーターの一人として交流します。		

抄 録

Abstracts

神経化学会－GRT 研究会連携オープンシンポジウム
JSN - GRT Joint Open Symposium

ISN シンポジウム
ISN Symposium

日本神経化学会－日本生物学的精神医学会合同シンポジウム
JSN - JSBP Joint Symposium

シンポジウム
Symposia

一般口演
Oral Sessions

ポスター発表
Poster Sessions

OS-1 Hippocampal neurogenesis and neural repair

○Tatsuhiko Hisatsune

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New neurons are continuously generated in the subgranular zone of the dentate gyrus throughout life, and are involved in some form of hippocampal-dependent memory. Adult hippocampal neurogenesis is enhanced in particular physiological conditions (enriched environments, learning, and exercise) and pathological conditions (epilepsy and ischemic stroke). We studied on the activity-dependent neurogenesis, and discovered the activation of hippocampal stem/progenitor cells by hippocampal network activities. We have elucidated the biochemical mechanism responsible for this activity-dependent regulation of hippocampal neurogenesis. Since, new neurons will contribute to the memory function of hippocampal circuit; our results may help us to develop a new regenerative therapeutic strategy for neurodegenerative disorder with cognitive deficit, such as Alzheimer disease or vascular dementia.

OS-2 Cytoskeletal maturation and radiosensitivity of newly-generated neurons in the adult brain

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It is well known that adult brain keep going to generate neurons. This raised the possibility that newly-generated neurons might be used as a new strategy for CNS regeneration. It is however unknown whether maturation processes of the newly-generated neurons in the adult brain is same as those in the developing brain. In this talk I will introduce our recent findings about changes in the cytoskeletal properties and radiosensitivity of newly-generated neurons during their migration. It has been reported that drebrin E, a side-binding protein of F-actin, plays a role in the migration of melanoma cells. We have immunohistochemically demonstrated that newly-generated neurons in the adult rat brain express drebrin E during migration and that they switch the expression to a neuron-specific isoform drebrin A which is produced by changing of the splicing pattern of drebrin gene in parallel with cessation of migration. On the other hand, a microtubule-associated protein doublecortin, which also plays a role in neuronal migration, is observed in the newly-generated neurons at both of the migrating and post-migrating dendrite-growing stages. It is well-known that radiosensitivity of cells is related with their developmental stages. Although neurogenesis in adult brain is highly sensitive to x-irradiation, the radiosensitivity of newly-generated neurons in the later developing stages, such as migration and synaptogenesis stages, is not yet clarified. We have previously shown that x-irradiation induces apoptosis of neurons that do not complete the synaptogenesis. We have recently developed the method for identification of the migrating and postmigratory neurons by immunocytochemistry using drebrin antibody. By this method, we analyzed the radiosensitivity of newly-generated neurons at migration and further developed stages. Our data indicate that migrating neurons are more sensitive to x-irradiation in compared with postmigratory young neurons.

OS-3 Neural cell differentiation plasticity regulated by methyl-CpG binding proteins

○Kinichi Nakashima

Lab. Mol. Neurosci., Grad. Sch. Biol. Sci., Nara Inst. Sci. Tech.

Major CNS cell types, i.e., neurons, astrocytes and oligodendrocytes are generated from common neural progenitor cells (NPCs). It is becoming apparent that extracellular cues and intracellular epigenetic modification play critical roles in the regulation of NPC-lineage specification. However, the mechanism of how cell-type specificity in differentiated cells is regulated remains an open question. In this study, we show that a methyl-CpG binding protein, MeCP2 is a cell-intrinsic determinant regulating cellular competences to respond to astrogliogenic signals. Neurons expressing highly amount of MeCP2 did not express an astrocytic marker, GFAP, even when stimulated with astrocyte-inducing cytokine, LIF (Leukemia Inhibitory Factor). In contrast, oligodendrocytes, which do not express MeCP2, could differentiate into GFAP-positive astrocytes in response to LIF both in vivo and in vitro. Furthermore, ectopic expression of MeCP2 in oligodendrocyte inhibited LIF-induced astrocytic gene expression. A central challenge in the field of neuroscience is to understand the mechanisms whereby diverse functions of various cell-types are generated in the adult CNS. Our findings suggest a molecular basis for a part of cellular identity or plasticity and could be a first step toward unraveling the above-mentioned mechanisms.

OS-4 Decreased neurogenesis as a risk factor for mental diseases

○Noriko Osumi

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Among several endophenotypes (biological markers) of schizophrenia, deficits in prepulse inhibition (PPI) and the smaller hippocampus are reproducible ones that can be measured in patients and various animal models. From QTL analyses using two lines of mice that show different PPI performance, our group has identified FABP7 (B-FABP/BLBP), a gene encoding a fatty acid binding protein, as a responsible gene for schizophrenia. Fabp7 knockout mice also exhibit impaired neurogenesis and smaller hippocampi. Similar association is reported in knockout mice for NPAS3 and neuregulin1, and also found in Small eye rats (Pax6 ^{-/-} rats) that have a mutation in Pax6 gene, an upstream to Fabp7 and a pivotal player in neurogenesis. We thus suspect that decrease in neurogenesis may serve as a vulnerable condition not only for depression but also schizophrenia. We have tried to establish well-grounded ways to increase neurogenesis in hope for preventing and treating schizophrenia and related mental diseases. We have focused on polyunsaturated fatty acids (PUFAs) that can be bound to FABPs. At the moment, we have succeeded to increase production of new neurons via administering n-6 fatty acid, arachidonic acid (ARA), in the wild type rat pups for 4 weeks. We then raised Pax6 ^{-/-} rats with ARA-diet, and were able to prevent PPI deficits. Watanabe et al.: Fabp7 maps to a quantitative trait locus for a schizophrenia endophenotype. PLoS Biol, 5(11), e297, 2007 Osumi et al.: Concise Review: Pax6 transcription factor contributes to both embryonic and adult neurogenesis as a multifunctional regulator. Stem Cells, 26(7), 1663-1672, 2008 Mackawa et al.: Arachidonic acid drives postnatal neurogenesis and elicits a beneficial effect on prepulse inhibition, a biological trait of psychiatric illnesses. PLoS ONE, in press

ISN-1 Molecular regulation of Wallerian degeneration of axons

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The slow Wallerian degeneration protein (Wld^s) delays axon and synapse loss after injury and in some models of motor neuron disease, multiple sclerosis, Parkinson's disease and glaucoma. We identified the Wld^s gene to understand the molecular events that normally trigger Wallerian degeneration, and to manipulate them to preserve axons and synapses in disease. Extensive structure-function analysis shows that Wld^s functions in cytoplasm or axoplasm, and is present the axon itself at a low level. Its intrinsic Nmnat enzyme activity is necessary for axon protection but not sufficient.

Three fascinating and enduring questions in this field are: 'why is there a 30-40h latent phase before injured axons fragment?'; 'why is the fragmentation process directional?'; and 'how does Wld^s extend the latent phase?'. Lubinska (1977) proposed an unknown 'trophic factor' that must be constantly maintained above a threshold level by axonal transport to prevent Wallerian degeneration. We reasoned that Wld^s could mimic such a factor over an extended period. Thus, removing the putative survival factor should trigger Wallerian-like degeneration without axon injury and Wld^s should block this. It should have a half-life short enough to deplete it within the latent period of Wallerian degeneration and shorter than Wld^s, and its function and location should be similar to Wld^s.

Consistent with this model, we find that non-lethal impairment of protein synthesis in cell bodies triggers Wallerian-like degeneration. To understand the molecular events we knocked down the three Nmnat isoforms and studied the axonal response. Knockdown of the Golgi Nmnat isoform Nmnat2, but not of Nmnat 1 or 3, also triggers neurite degeneration. Wld^s can block this but endogenous levels of Nmnat1 and Nmnat3, surprisingly, cannot. Nmnat2 is the only Nmnat with a short enough half-life to account for the latent phase and Wld^s is much more stable.

Nmnat2 was previously thought not to protect axons, but its short half-life may have masked its protective capacity. Wld^s, Nmnat1 and Nmnat3 have to be overexpressed to protect axons, but Nmnat2 regulates Wallerian degeneration at its normal expression level. Its degradation is a key determinant of how well it does so, making its turnover and axonal transport important novel therapeutic targets in axonopathies

ISN-3 Control of axonal mitochondrial mobility and its impact on axonal homeostasis and degeneration

○Zu-Hang Sheng

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Proper transport and distribution of mitochondria within axons and at synapses is critical for neuronal function. While one-third of axonal mitochondria are mobile, a large proportion remains in a stationary phase in mature neurons. Mitochondrial recruitment between motile and stationary phase is a possible target of regulation by intracellular signals and synaptic activity. Our recent study elucidated a molecular mechanism for controlling axonal mitochondrial docking. Syntaphilin is newly identified neuronal specific and axonal-targeted protein and acts as a receptor for docking/retaining mitochondria through an interaction with the microtubule-based cytoskeleton. Such a mechanism enables neurons to maintain proper densities of stationary mitochondria within axons and in the proximity of synapses. We further provide cellular and genetic evidence that the mobility and density of inter-bouton mitochondria play a critical role in short-term facilitation during high frequency stimulation. Identification of syntaphilin as a docking protein for axonal mitochondria provides a unique genetic mouse model to address whether the change of axonal mitochondrial mobility has any impact on axonal homeostasis and degeneration.

ISN-2 Axon formation and polarized transport

○Kozo Kaibuchi

Nagoya University Graduate School of Medicine

During neuronal development, neurons develop two distinct neurites, axons and dendrites, and establish their polarity. Axons contain synaptic vesicles, from which they release neurotransmitters at axon terminals in response to electrical signals, whereas dendrites contain receptors for the neurotransmitters and synapse at the dendritic spines. These two neurites are structurally and functionally different, and their unique features are developed and maintained by highly specific transport of the vesicles and molecules, as well as by localized signaling events (Arimura and Kaibuchi, Nat Rev Neurosci 2007).

The neurotrophin receptor (Trk) is localized at the surface of the axon terminal and mediates key signals from brain-derived neurotrophic factor (BDNF) for diverse effects on neuronal survival, differentiation, and axon formation. Trk is sorted into axons via the anterograde transport of vesicles and then inserted into axonal plasma membranes. However, the transport mechanism remains largely unknown. We here show that the Slp1/Rab27B/CRMP-2 complex directly links TrkB to Kinesin-1 and this association is required for anterograde transport of TrkB-containing vesicles. Cytoplasmic tail of TrkB binds to Slp1 in a Rab27B-dependent manner. CRMP-2 connects Slp1 to Kinesin-1. Knockdown of these molecules by siRNA reduces the anterograde transport of TrkB and its membrane targeting to the axon surface, thereby inhibiting BDNF-induced ERK1/2 phosphorylation in axons. Our data reveal a molecular mechanism for the selective anterograde transport of TrkB in axons and show how the transport is coupled with BDNF signaling.

In this symposium, I discuss how the cargo-containing vesicles are recognized by the motor proteins, and how their interactions are regulated for better understanding of axon formation.

ISN-4 Transport and assembly dynamics of axonal neurofilaments

○Anthony Brown

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The axonal cytoskeleton consists of microtubules, microfilaments and also neurofilaments, which are the intermediate filaments of neurons. Neurofilaments are space-filling polymers with radial spoke-like side-arm projections that keep the filaments apart from each other, thereby maximizing their contribution to axonal volume. These polymers are the single most abundant structure in large myelinated axons, and as such they are the principal determinant of the size and shape of these processes. Neurofilament polymers are transported bi-directionally along axons at fast rates, but the overall rate is slow because the filaments spend most of their time pausing. The balance between the movements and pauses determines the overall rate of movement, and is likely to be a principal determinant of axonal neurofilament content. Thus we propose that neurofilament transport is a principal regulator of axonal morphology. The movement appears to be orchestrated by the coordinated actions of at least three different motor proteins, kinesin-1A, dynein and myosin-Va, which act together to convey and distribute these polymers in both the radial and longitudinal dimension of axons.

Axonal neurofilaments can be very long and are generally considered to be very stable, but little is known about how they assemble. Microtubules and microfilaments are known to lengthen and shorten by addition and loss of subunits at the polymer ends, but surprisingly this is not known for neurofilaments, or indeed for intermediate filaments in general. Using a combination of cell-cell fusion, photobleaching and photoactivation strategies in non-neuronal cells expressing fluorescent fusion proteins, we show that neurofilaments can lengthen by end-to-end joining of pre-existing polymers, and that they can also exchange subunits along their length by a mechanism which we term interstitial subunit exchange. We propose that end-to-end joining is a mechanism for neurofilament elongation in vivo and we speculate that there may be a cycle of neurofilament severing and joining that regulates the mobility and distribution of these polymers in axons.

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JSN-JSBP-1 Peripheral cytokine level change in the pathophysiology of psychiatric disorders

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Currently hypothesis focused on the progressive morphological brain change in psychiatric disorders, such as depression, schizophrenia, and alcohol-induced brain damage. Thus the promotion of maintenance and the repair of damaged neural network is a key strategy for psychiatric treatment.

In the previous study, we investigated the effects of psychotropics on the neuronal differentiation of neural stem cells (NSCs) and the survival of mature neurons in cultured cells. We have revealed the strong activation of NSC differentiation to neuron by the treatment of antidepressants. The atypical antipsychotics and mood stabilizers have shown the promotive effect of neuronal differentiation of NSCs and the survival of neurons, indicating that psychotropics-induced alteration of neurogenesis and/or survival could contribute to the neural network repair impaired in the psychiatric brain.

In the present work, we demonstrated the usefulness of intravenous transplantation of NSCs to the neurodevelopmental model rat of schizophrenia against its behavioral abnormalities, and suggested the possibility of regenerative therapy for psychiatric disease. Maternal infection during pregnancy has been associated with increased risk for schizophrenia in offspring. We have shown the potential of migration of transplanted NSCs into the brain by visualizing fluorescent cell marker and RI, and the recovery of behavioral abnormalities those were caused by the maternal injection of synthetic double strand RNA polyriboinosinic-polyribocytidilic acid (poly (I:C)) in the memory, cognition, and social interaction tasks.

In recent years, a role of brain-derived neurotrophic factor (BDNF) for the promotion of neurogenesis and protection of brain volume deficit in depression has been suggested. There are some reports demonstrated that serum BDNF level in depressive patients is lower than control subjects, and antidepressant treatment increases its serum levels in responder. However, its mechanism and biological meaning in the pathophysiology of depression have not yet understood. Here, we have revealed the induction of platelet BDNF release by the treatment of antidepressants and serum BDNF increase by intravenous treatment of antidepressant. By these results we will discuss about a role of cytokine level change and NSCs in blood focusing on the neurogenesis function change in psychiatric disorders.

JSN-JSBP-3 Identification of susceptibility genes for mental disorders 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, CHI3L1, Akt1 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.

JSN-JSBP-2 Antidepressive-like effect of continuous inhibition of GSK3 β through region-specific neuroprotective effect

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We evaluated the neuroprotective effect of chronically or acutely administered lithium against hypoxia in several brain regions. Furthermore, we investigated the contribution of glycogen synthase kinase 3 β (GSK3 β) to the neuroprotective effect of lithium. Brain slices were prepared from rats that had been treated chronically or acutely with lithium. The cerebral glucose metabolic rate (CMRglc) before and after hypoxia loading to brain slices was measured using the dynamic positron autoradiography technique with [¹⁸F]2-fluoro-2-deoxy-D-glucose. The changes of expression of GSK3 β was investigated using western blotting. After hypoxia loading, the CMRglc of the chronic lithium treatment group recovered in the frontal cortex, caudate putamen, hippocampus and cerebellum, but not in the thalamus. In contrast, the CMRglc of the acute lithium treatment group did not recover in any analyzed brain regions. After chronic lithium treatment, the expression of inactivated GSK3 β was higher than those of untreated rats in the frontal cortex, but not in the thalamus. These results demonstrated that lithium was neuroprotective against hypoxia only after chronic treatment and only in specific brain regions, and that the inhibition of GSK3 β might contribute to this effect.

Next, we examined the antidepressive-like effect of GSK3 β inhibition in the mouse dentate gyrus using lentiviral-mediated RNA interference. GSK3 β Mission® shRNA Plasmid were used to make lentiviral vector. Lentivirus was injected into each side of dentate gyrus (anti-GSK3 β animals), and after the chronic restraint stress, open field test, forced swim test and tail suspension test were tried. The inhibition of GSK3 β expression was evaluated using western blotting and immunohistochemistry. GSK3 β expression of anti-GSK3 β animals in the hippocampus was significantly reduced compared to that of control animals used scrambled shRNA plasmid, and the inhibition of GSK3 β expression was observed especially in the subgranular zone of the dentate gyrus. No significant difference was found in the locomotor activity of the open field test between control and anti-GSK3 β animals, but the immobility time of anti-GSK3 β animals was significantly shorter than that of control animals in the forced swim test and tail suspension test. From these results, it was suggested that the continuous inhibition of GSK3 β expression in the dentate gyrus might produce antidepressive-like effect.

JSN-JSBP-4 Function of EGF receptor signaling 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 pathological roles of ErbB1 signaling in the schizophrenia model rats that are established with bilateral microinjections of ibotenic acid to the ventral hippocampus as neonates. Treatment with ibotenic acid altered HB-EGF and TGF α protein levels in the forebrain regions in parallel with persistent activation of ErbB1 receptors. On postnatal week 8, rats were tested for behavioral tasks. The hippocampus-lesion significantly impaired the behavioral scores of PPI and latent learning in adults. In context fear conditioned task, memory retentions were not affected although their latent learning was significantly disrupted. We determined the antipsychotic effects of several ErbB1 tyrosine kinase receptor inhibitors in this model. The abnormalities in PPI and latent inhibition were ameliorated by icv infusion of all the ErbB1 inhibitors from an osmotic pump. These results indicate that blockade of ErbB1 signals may be a novel antipsychotic target for schizophrenia and its related disorders.

JSN-JSBP-5 Neural correlates of sexually-dimorphic social behavior and social dysfunction in subjects with autism

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Since recent literature has argued to give up a single explanation covering diverse symptom defining autism-spectrum disorder, our study focuses on deficits in social cognition as the target of phenotype in searching cause for autism-spectrum disorder. First study revealed that the gray matter volume reductions in several brain regions important for social cognition were common to monozygotic twins with Asperger's syndrome as compared with healthy matched controls. The findings suggest a contribution of shared genetic factors to underlying the structural abnormalities in autism-spectrum disorder. Second study showed that the young healthy females showed greater Cooperativeness as well as larger relative global and regional gray matter volumes than the matched males, particularly in the social-brain regions including posterior inferior frontal and anterior medial prefrontal cortices. Moreover, specifically in females, higher cooperativeness was tightly coupled with the larger relative total gray matter volume and more specifically with the regional gray matter volume in most of the regions revealing larger in female sex-dimorphism. These results suggest that sexually-dimorphic factors may affect the neurodevelopment of these "social-brain" regions, leading to higher cooperativeness in females. The findings may also have an implication for the pathophysiology of autism; characterized by severe dysfunction in social reciprocity, abnormalities in social-brain, and disproportionately low probability in females. Consistent with the implication, third study demonstrates the correlation between smaller-than normal volume of posterior inferior frontal gyrus and worse function of social communication in the males with autism.

JSN-JSBP-6 PACAP regulates the neural extension in adult neurogenesis

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Pituitary adenylate cyclase-activating polypeptide (PACAP) is a neuropeptide involved in a variety of brain function. Mice lacking the *Adcyap1* gene encoding PACAP (*Adcyap1*^{-/-}) and PACAP specific receptor, PAC1 deficient mice exhibit marked behavioral abnormalities. In order to clarify the molecular mechanism of PACAP dependent psychiatry disorders, we have first attempted to isolate the PACAP deficiency-regulated gene in the dentate gyrus of the mice using differential display (DD) method. Expression of *stathmin1* is up-regulated in the dentate gyrus both at the levels of mRNA and protein. In addition, PACAP stimulation inhibits the *stathmin1* expression in PC12 cells. In addition we have found that increased expression of *stathmin1* in the neurons of the SGC and primary cultured hippocampal neurons induces the abnormal arborization of the processes both in vivo and in vitro. Next, we elucidated the molecular pathway of *stathmin1* increase by PACAP. Present study revealed that *Ascl1* binds to E10 box to activate the *stathmin1* expression. On the other hand expression of inhibitory bHLH proteins, such as *Hes1* and *Id3*, was up-regulated rapidly by PACAP stimulation. It could be concluded that up-regulated expression of *Hes1* and *Id3* by PACAP stimulation suppress *Ascl1* expression by each functions. Furthermore, we have detected an increase expression of *stathmin1* in the brains of the schizophrenia patients. The present results show that up-regulated *stathmin1* in the dentate gyrus of the PACAP deficiency dependent psychiatric disorders may produce the abnormal neuronal circuit to cause the abnormal behavior.

S01-1 Olig2 progenitor cells preferentially differentiate to astrocytes in response to various stimuli in the gray matter of adult forebrain

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Recently we have reported that Olig2-expressing cells (Olig2 cells) in the adult brain proliferate in response to cryo-injury, and differentiate into astrocytes using genetic marking strategy (Tatsumi et al., J Neurosci. Res.2008). We also observed nearly all Olig2 cells in the gray matter co-expressed NG2- proteoglycan or PDGF receptor alpha in the normal adult forebrain. This finding indicates that Olig2 cells in the adult brain have progenitor-like characteristics and could be a target of various physiological and pathological stimuli. In this presentation, we introduce our data regarding the differential potential of Olig2 cells under various stimuli, e.g., cryo-injury, enriched stimuli and voluntary exercise. Our genetic tracing study targeted the *olig2* locus demonstrated that Olig2 cells favored astrogliogenesis in response to injury in the cerebral cortex. As mentioned above, majority of Olig2 lineage cells after cryo-injury in the cerebral cortex differentiated to astrocytes with strong GFAP-immunoreactivity, a hallmark of reactive astrocyte. Concurrently, these astrocytes expressed CS-A chain of chondroitin proteoglycan, which is one of the inhibitory factors to axonal regeneration. In contrast, Olig2 cells kept their progenitor-like nature in the amygdala. Under enriched environment, astrocytes derived from Olig2 cells were positive for glutamine synthetase (GS) and/or S100β, but never expressed GFAP. Likewise, after voluntary exercise, GS+/ S100β+ astrocytes dramatically increased in the subthalamic nucleus. These data suggest that Olig2 positive cells in the amygdala and subthalamic nucleus preferentially differentiate into astrocytes sensing neuronal activity. Our findings demonstrated that Olig2 cells in the adult brain have potential to differentiate to, at least, two subtypes of astrocytes depending on the stimuli and brain regions. These results may lead to the development of efficient repair strategies against various physiological and pathological stimuli.

S01-2 BMPR1A and BMPR1B differentially regulate gliosis

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Here we describe the novel and opposite functions of BMP signaling through BMP type IA receptor and BMP type IB receptor in glial scar formation upon brain cortex injury. The glial scar exerts well-known inhibitory effects on axon regeneration. On the other hand, glial proliferation in the sub-acute phase is critical for wound healing. Bone morphogenetic proteins (BMPs) are thought to play a role in glial scarring because they are highly expressed at the sites of brain injury and they potently stimulate reactive astrocytic responses. However, the mechanism by which BMP signaling regulates astrocytic responses is not well understood. *Bmpr1a* but not *Bmpr1b* is required for -astrocyte proliferation in injured mouse brain in the sub-acute phase of brain cortex injury. BMPRIA but not BMPRIB activates MAPK signaling in astrocytes via XIAP. Furthermore, *Bmpr1a*-deficient astrocytes showed enhanced nuclear accumulation of phosphorylated Smad at the sites of cortical injury in mouse brain in the sub-acute phase, and treatment with MAPK inhibitors enhanced nuclear accumulation of phosphorylated Smad in astrocytes in vitro. Therefore, BMP signaling through different type I receptors differentially regulate nuclear translocation of phosphorylated Smads to regulate cell proliferation in an opposite manner. Our finding suggest that enhancement of BMP signaling through BMPRIA-XIAP in the sub-acute phase and suppression of Smads signaling in the late phase would have a therapeutic advantage for axonal regeneration upon CNS injury.

S01-3 Astrocyte precursor cells in the developing mouse cerebellum

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It is generally considered that neural stem cells are committed to become either neuronal precursor cells or glial precursor cells before terminally differentiating into neurons or glial cells. Up to now, neuronal precursor cells and oligodendrocyte precursor cells have been identified in several areas in the murine CNS. Presence of astrocyte precursor cells (APCs), however, has been reported only rarely so far. In the murine cerebellar cortex, there are three types of astrocytes: protoplasmic astrocytes in the granule layer, fibrous astrocytes in the white matter, and Bergmann glial cells which have their cell bodies near the Purkinje cells and extend their radial processes toward the pial surface. To help understand the mechanism for the generation of these astrocytes during cerebellar development, we isolated APC candidates from developing mouse cerebellum, exploiting the expression of A2B5, a marker for glial progenitor cells, by these cells. Most of the A2B5-positive cells were positive for brain lipid-binding protein (BLBP), a marker for the astrocytic lineage, but negative for glial fibrillary acidic protein (GFAP), a marker for mature astrocytes. In the presence of both basic fibroblast growth factor (bFGF) and bone morphogenetic protein 4 (BMP4), many of these cells incorporated BrdU, and most of the BrdU-positive cells were GFAP-negative, suggesting that the combination of bFGF and BMP4 is 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 are also essential for their survival. When these cells were treated with ciliary neurotrophic factor (CNTF) or leukemia inhibitory factor (LIF), the proportion of GFAP-positive cells increased dramatically, confirming these cells are indeed APCs and their astrocytic differentiation is stimulated by these factors. We will discuss the characteristics of these APC candidates and the generation of astrocytes from these cells during cerebellar development.

S01-5 Mechanism in sequential differentiation of neural stem cells

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During mid-gestation, mammalian neural stem cells (NSCs) differentiate only into neurons. Generation of astrocytes is prevented at this stage, because astrocyte-specific gene promoters are methylated. How the subsequent switch from suppression to expression of astrocytic genes occurs is unknown. We here show that Notch ligands are expressed on committed neuronal precursors and young neurons in mid-gestational telencephalon, and that neighboring Notch-activated NSCs acquire the potential to become astrocytes. Activation of the Notch signaling pathway in mid-gestational NSCs induces expression of the transcription factor nuclear factor- κ B, which binds to astrocytic gene promoters, resulting in demethylation of astrocyte-specific genes. These findings provide a mechanistic explanation for why neurons come first: committed neuronal precursors and young neurons potentiate remaining NSCs to differentiate into the next cell lineage, astrocytes.

S01-4 Glial cell sub-lineages in the developing central nervous system

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Glial cells exhibit various functions to support neural activities: Delivery of nutrition to neurons, recycling of neurotransmitters, regulation of synaptic activity, blood-brain barrier formation, and myelin formation. When and how glial cells are specified to exhibit such diverged functions have been 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 hypothesized that the neuroepithelial domains may also contribute to glial cell diversification. To challenge this question, we have developed a new method to trace cell lineages in vivo by introducing a plasmid DNA that encoded Cre recombinase into the ROSA/Cre-reporter mouse brain in ventral- or dorsal-specific manner with in utero DNA electroporation technique. We firstly analyzed the cell lineage specification and differentiation of oligodendrocyte, which is a major class of glial cells in the central nervous system. The GFP-labeled myelinating oligodendrocytes were only detected in the adult cortex when electroporation was targeted to the ventral neuroepithelium at E12, suggesting that the most cortical oligodendrocyte lineage cells are generated from ventral neuroepithelial cells. In contrast, astrocytes that constituted another major class of glial cells were generated from both dorsal and ventral forebrain. It must be interesting if there is any functional difference between dorsal and ventral forebrain-derived astrocytes. Thus, to further investigate neuroepithelial domain-specific astrocyte sub-lineages, gene-targeted mouse lines that carry the Cre/loxP-reporter (loxP-nlacZ-loxP-GAP43GFP) construct knocked-in glial fibrillary acidic protein (GFAP) gene locus. The GFAP/Cre-reporter mouse lines were crossed with Emx1-Cre KI delta-neo mice (provided by Drs. Iwasato and Itohara) to label Emx1-positive pallial progenitors-derived astrocytes as GFP-positive cells. Most astrocytes in cortical plate were GFP-positive, while a subpopulation of midline glia that guided corpus callosum formation expressed nlacZ, suggesting that functionally different cortical astrocytes and midline glia were generated from different origins.

S01-6 The role of neurogenesis-regulating transcription factor Pax6 in astroglial development

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Astrocytes serve various important functions in the central nervous system (CNS), but the molecular mechanisms of their generation and maturation are still enigmatic. Our group has reported that Pax6 is expressed in GFAP-positive (GFAP+) neural stem/early progenitor cells in the rat hippocampal dentate gyrus, and that Pax6 regulates cell proliferation and differentiation in these cells. In the course of this study, we also found that Pax6 is expressed in GFAP+ astrocytes in the rat hippocampus. We have also noticed that Pax6 expression overlaps with GLAST, a marker for astrocytic precursors in the mouse spinal cord. Furthermore, the expression patterns of Pax6 in the Allen Brain Atlas imply that astrocytes may express Pax6 in the adult mouse CNS (<http://www.brainatlas.org/aba/>). Such evidence has prompted us to examine how Pax6 is involved in development of astrocyte progenitors and/or mature astrocytes. In this symposium, I would like to show that Pax6, a key transcription factor that controls neurogenesis, also regulates proliferation, differentiation, and migration of astrocytes in the CNS. Our group first reveal that Pax6 is expressed in astrocytes during development as well as postnatally in the wild-type mouse. Astrocytes derived from Pax6 homozygous mutants (Sey/Sey) mice exhibited aberrant proliferation together with immature differentiation, both in vivo and in vitro, with higher migration potential in scratch-wound assays in vitro. Furthermore, a larger population of Sey/Sey astrocytes expresses neural-stem-cell markers such as nestin, Sox2, and prominin-1. These phenotypes of Pax6-deficient astrocytes putatively occur via higher Akt activity. Thus, the breakdown of Pax6 function induces the retention of neural-stem-like characteristics and inhibits astrocytes maturation. Sakurai, K. and Osumi, N. The neurogenesis-controlling factor, Pax6, inhibits proliferation and promotes maturation in murine astrocytes. *J Neurosci*, 28(18), 4604-4612, 2008.

S02-1 Role of DNA methylation in mental disorders

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Mental disorders develop as a result of gene-environmental interaction. Early life stress may play a role in the development of stress vulnerability as a risk factor for depression. The epigenetic regulation of the promoter of the glucocorticoid receptor gene has been suggested as a molecular basis of such stress vulnerability. It has been suggested that clinical action of antidepressants and electroconvulsive therapy may be mediated by epigenetic modification of the BDNF (brain derived neurotrophic factor) gene. We searched for DNA methylation difference responsible for the discordant phenotypes in the monozygotic twins using methylation-specific representational differential analysis. We found that PPIEL (peptidylprolyl isomerase E-like) was hypomethylated in the twin with bipolar disorder. Hypomethylation of PPIEL was found in patients with bipolar II disorder in a case control analysis. Further studies of epigenetics in mental disorders are warranted.

S02-2 DNA demethylation and spatial gene positioning of an astrocyte specific gene, GFAP

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Astrocyte differentiation, which occurs late in brain development, is largely dependent on the activation of a transcription factor, STAT3. We show that astrocytes, as judged by glial fibrillary acidic protein (GFAP) expression, never emerge from neuroepithelial cells on embryonic day (E) 11.5 even when STAT3 is activated, in contrast to E14.5 neuroepithelial cells. A CpG dinucleotide within a STAT3 binding element in the GFAP promoter is highly methylated in E11.5 neuroepithelial cells, but is demethylated in cells responsive to the STAT3 activation signal to express GFAP. This CpG methylation leads to inaccessibility of STAT3 to the binding element. We suggest that methylation of a cell type-specific gene promoter is a pivotal event in regulating lineage specification in the developing brain. We also found that spatial positioning of the GFAP gene locus in the interphase nucleus changes from the periphery toward the center of the nucleus during astrocyte differentiation. GFAP is mostly expressed monoallelically in cultured astrocytes and its active alleles are more internally located than the inactive ones. The active allele of GFAP colocalizes to splicing factor compartment celled speckles. These results show the spatial distribution of GFAP alleles in the nucleus is highly relevant to its transcriptional activity.

S02-3 The mechanism of abnormal dendritic spine formation in chromatin remodeling factor *ATRX* mutant mice

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ATRX is an SWI/SNF-like chromatin remodeling protein that is mutated in Alpha-thalassemia X-linked mental retardation (*ATRX*) syndrome. *ATRX* syndrome reveals a severe and nonprogressive mental retardation that is frequently associated with various clinical manifestations such as severe mental retardation, genital abnormalities and epileptic seizures. We generated *ATRX* mutant mice (*ATRX*^{ΔE2}) lacking of exon 2 with mild mental retardation, which is accompanied with impaired cognitive functions. We here addressed causative mechanisms of abnormal spine formation in the medial prefrontal cortex (mPFC) observed in *ATRX*^{ΔE2} mouse brain. Consistent with other mental retardation model 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 aberrant increased calcium/calmodulin-dependent protein kinase II (CaMKII) activity was observed in the prefrontal cortex of *ATRX*^{ΔE2} mice. The increased CaMKII autophosphorylation was associated with increased phosphorylation of Rac1-guanine nucleotide exchange factors (GEFs), Tiam1 and Kalirin-7. Since Tiam1 and Kalirin-7 are known to be substrate for CaMKII, thereby activating p21-activated kinases (PAKs), we confirmed increased phosphorylation of Tiam1, Kalirin-7 and PAK1-3 in extracts from the mPFC. Furthermore, reduced protein expression and activity of protein phosphatase 1 (PP1) was evident in the mPFC from the *ATRX*^{ΔE2} mice. Taken together, aberrant CaMKII activation likely mediates abnormal spine formation in the mPFC and the elevated Rac1-GEF/PAK signaling in *ATRX*^{ΔE2} mice likely accounts for mental retardation syndrome-related abnormal spine formation.

S02-4 The Role of Epigenetic Modifier for Neuronal Differentiation during Retinogenesis

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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 to analyze gene knockout mice would be important to answer this question.

S02-5 Epigenetics in autistic diseases

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The number of autistic children is increasing during the past ten years in Japan. Although its biological cause is not known, environmental factors are suggestive, rather than genetic factors (such as higher mutation rate). Several lines of evidence have recently suggested that epigenetic gene regulation mechanism, based on DNA methylation and chromosomal histone modifications, is affected by several environmental factors, such as nutrition, toxins, and mental stress. We have previously reported that congenital neurodevelopmental diseases are not only caused by mutations of molecules associated with brain function, but also caused by failures in the epigenetic system. One of such disease is Rett syndrome, an congenital autistic disease cause by mutations in *MECP2* that encodes a methylated DNA-binding protein. To know the pathogenesis of this syndrome, we searched neuronal genes regulated by MeCP2, and identified three candidates. Out of the genes, one showed aberrant expression in the brain tissues of *Mecp2* deficient mice and those of postmortem Rett patients, and another, which showed expression in synapse junctions, exhibited increase of DNA methylation after administration of a DNA-methylation residue (S-adenosylmethionine) *in vitro*. These results suggested that not only genetic mutation but also abnormal epigenetic regulation of synaptic molecules could cause autistic diseases, and indicated that environmental factors might produce autistic children via epigenetic mechanism.

S03-1 Update of autism model animals○Masaaki Narita, Akiko Oyabu, Yoshio Imura, Tomomi Yokoyama, Naoki Kamada, Kaori Tano, Yasura Tashiro, Atsuko Uchida
Mie University School of Medicine

Autism, classified as a developmental disorder, is a behaviorally defined disorder characterized by impairment of socialization, abnormalities of communication, limited activity and curiosity. Prevalence of autism has steadily risen within these several decades, from 0.05 % to over 1 % (more than ten fold). This increased prevalence of autism cannot be readily explained by simply widening diagnostic criteria and increased public recognition or awareness. Therefore, specific factors related to these several decades including environmental factors during the embryonic period such as exposures to chemicals might be involved in this increase.

Although autism is considered as a congenital disorder, little is known regarding when and how disturbed in the embryonic period. Because even trained clinicians can not give appropriate answer to this question of patients, molecular approach is an urgent necessity. For that purpose, numerous efforts have been made to establish autism model rats including viral infection, genetic engineering, and drug-induced methods. However, since etiology of autism cannot be explained as a single factor during the embryonic period such as a single genetic factor, it is hard to reproduce autism model rats that faithfully reflect human autism, nor is it expected that results from model animals contribute to the treatment or prevention of autism.

Along these lines, I planned this symposium for the help of understanding developmental disorders including autism, and ADHD. Four speakers including Drs. Yoshinori Masuo, Naoko Narita, and Hideo Matsuzaki will review what is known and what is unknown from their point of specialties so as not to overlap with previous symposiums.

S03-2 Alterations in the expression of gene and protein in ADHD model rats

○Yoshinori Masuo

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Attention-deficit hyperactivity disorder (ADHD) is characterized as inattention, impulsivity and uncontrolled motor hyperactivity. To understand the mechanisms of behavioral hyperactivities, we examined the effect of several kinds of treatment on the behavior and the CNS in the rat. We performed intracisternal injection of 6-OHDA into five-day-old male Wistar rats after i.p. injection of desipramine. The rats showed significant increase in spontaneous motor activity during the dark phase at 4-5 weeks of age, which was attenuated by s.c. injection of methamphetamine (MAP). Congenic wiggling (Wig) rats also showed hyperactivities during the dark phase. However, MAP treatment increased motor activity levels in contrast to the 6-OHDA-lesioned rats. We also investigated the effects of intracisternal injection of environmental chemicals, such as bisphenol A, on male Wistar rats. These chemicals caused significant motor hyperactivities during the dark and light phases at 4-5 week of age. However, MAP did not clearly modify motor activities. Tyrosine hydroxylase immunoreactivity was low in the striatum and midbrain of Wig rats and rats treated with environmental chemicals, similarly to the effects of 6-OHDA.

We performed gene expression profiling using a DNA array. After 6-OHDA lesions, gene expression was increased in insulin-like growth factor binding protein 1, N-methyl-D-aspartate receptor, tachykinin 2, arrestin beta2, and calcium/calmodulin-dependent protein kinase II increased in the striatum at 4 weeks of age. In the midbrain, increased gene expression was found in the Huntington disease gene homolog, BH3 interacting domain 3, and Lyn protein non-receptor kinase. Gene expression profiles in Wig rats differed from those in 6-OHDA-lesioned rats, but both groups showed decreased expression of the GABA transporter in the striatum and midbrain. Gene expression profiles after environmental chemicals showed variation and differed from those of 6-OHDA-lesioned and Wig rats.

The present results suggest that deficient development of dopamine neurons may underlie motor hyperactivity. Additional factors may be altered in Wig rats and animals treated with environmental chemicals, which may reflect different response to MAP response.

S03-3 Impaired prefrontal cortical response by switching stimuli in autism spectrum disorders assessed by near-infrared spectroscopy

○Naoko Narita, Akiyuki Saotome, Hiroki Higuchi, Yuka Kumakura
Dept. of Education, Bunkyo University

Impairments in various kinds and degrees of higher-order cognitive processing related to prefrontal cortex (PFC) are reported in autism spectrum disorder (ASD) patients. We aim to investigate the reactive pattern of PFC in ASD upon consecutive exhibit of cognitive and less-cognitive stimulation, by using geometrical figure-memorization paradigm in which working memory requiring task (WM) and non-working memory requiring task (NWM) are alternately appeared.

FC oxygenation level was measured by NIRS during the paradigm. The task-switching paradigm was designed using randomized geometrical figures in combination of three shapes and four colors. For WM, subjects were required to memorize figures which appear one by one every 3 seconds on a PC screen, and subsequently were ordered to touch the figures in consecutive order as they memorized, from a multiple choices appeared on the screen. For NWM, all test figures are already appeared with the multiple choices so that the subjects can touch the figures while watching them. The number of figures was gradually increased up to 6. PFC oxygenation was continuously measured by NIRS during the task performance, and the oxygenated Hb level in PFC during each task was examined between control and ASD subjects. In the controls (n,14), oxygenated Hb level was increased during WM and decreased during NWM, and was gradually elevated when the number of figures is increased, suggesting that in the control PFC, shifting of signal processing was sensitively occurred according to the task switch. Additionally, laterality of right PFC was consistently observed in the controls, which is predictable from the nature of the present paradigm that requires spatial cognition. However, ASD subjects (n,11) lack the clear switching tendency of PFC oxygenation according to the WM-NWM switch, and obvious right PFC laterality was not observed. The comparison of oxy-Hb transition curve during the whole tasks were significantly different between controls and ASDs (Rt $p < 0.001$, Lt $p < 0.05$, controls vs ASDs respectively by two-way ANOVA).

The rapid and obvious response of PFC oxygenation to the incoming switching stimuli was not observed in ASD subjects, which may explain their difficulties in the daily life.

S03-5 Neonatal exposure to excess neuregulin-1 signaling alters the dopaminergic function

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Neuregulin-1 (NRG1) is identified as a susceptibility gene for schizophrenia in Iceland, and knockout studies indicate the deficiency of NRG1 signaling affects the onset of schizophrenia. Previously we reported that neonatal exposure to Ig-NRG1 $\beta 1$ disrupted various cognitive and behavioral developments in mice. In the present study, we examined the neonatal perturbation of NRG1 signaling on the development of dopaminergic neuron in mouse. In situ hybridization and immunocytochemistry revealed that ErbB4, NRG1 receptor, was intensively expressed in mouse dopaminergic neuron on neonatal stage. We subcutaneously injected Ig-NRG1 $\beta 1$ (1 mg/kg) to neonatal mice (P2-P10) to trigger ErbB4 signaling in the brain. Subchronic Ig-NRG1 $\beta 1$ treatment facilitated the phosphorylation of tyrosine-hydroxylase (TH), the rate-limiting enzyme in the catecholamine biosynthesis and increased the dopamine content in the Prefrontal cortex and striatum on neonatal stage. After development, we found increase in the contents of dopamine metabolites (DOPAC and HVA) levels, indicating an increase in dopamine turnover in the prefrontal cortex. These results suggest that perturbation of NRG1-signaling during development persistently alters the function of dopaminergic neuron in vivo.

S03-4 A perspective of biological marker research for Autism

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Autism, first identified by Kanner in 1943, is a neurodevelopmental disorder characterized by severe and sustained impairment in social interaction, deviance in communication, and patterns of behavior and interest that are restricted or stereotyped. But no one has discovered its neurobiological basis for autism, or drug to treat it. Half of individuals diagnosed with autism also are diagnosed with mental retardation. The autistic persons without complication of mental retardation are diagnosed with *high-functioning autism*. There is a clear genetic predisposition to the disease since if one twin has the disease, there is a chance the other twin will also develop autism in most cases. Although autism is present from birth, it is not diagnosed until the recognition of behavior characteristic of autism because a biological marker specific to the disorder has not been discovered since Kanner identified. To find the biological marker of autism in peripheral blood, we have compared various components in the blood of children and adults <6-26yo, all male> with high-functioning autism to that of those with no diseases in cooperation with the Asperger Society Japan. In this study, we have found some candidates as biological marker in the blood of men with high-functioning autism. In this symposium, I will review the previous studies about biological marker of autism and present results of our research. In addition, we imagine that our finding will enable diagnosis for autism at birth and eventually give a clue to cure or prevent it. Ultra-early diagnosis of autism can be a silver bullet for infants with undiagnosed autism. We think that diagnosing these children at birth will help parents intervene earlier to improve their children's quality of life. Intensive behavioral training can help autistic children communicate and socialize to a certain extent. To examine whether the candidate components we found will be biological marker at birth, we have a plan to collect cord bloods given at childbirth in 1000 pregnancy case and pursue correlation between development of the babies and their components concentration in the blood. I would also like to give an outline of this plan and future directions in this symposium.

S03-6 Maternal infection affects neurogenesis in the developing cerebral cortex

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Epidemiological studies have indicated that maternal infections during pregnancy increase the risk for neurodevelopmental disorder such as Schizophrenia and autism. Although mechanism of pathogenesis remained to be elucidated, abnormality in microstructures and connectivity of cerebral cortex are commonly found and thought to be responsible for abnormal cognitive functions of the patients. Recent studies of animal models based on the epidemiological observations revealed that prenatal exposure to polyriboinosinic-polyribocytidilic acid (Poly I:C), a synthetic analog of viral mimic double strand RNA induces activation of immune system causing behavioral abnormalities in the adult offspring. Using this model, we have previously reported that prenatal immunoactivation reduced the thickness of cortical upper layer of adult offsprings. One of the possibility is that prenatal immunochallenge might disrupt the development of the embryonic cortex, leading to the impaired formation of neuronal network associated to behavior abnormality in adulthood. To address this possibility, we intraperitoneally administered Poly I:C (20 mg/kg) or vehicle into mice bearing 9-day-old embryos (E9) and examined genesis and migration of the cortical neurons at mid- or later-stage of cortical development by investigating distribution and particular gene expression, stage specific marker for neural development, of BrdU positive cells at several time points after BrdU administration on E13 or E15, respectively. In the mid-stage of cortical development, the timing and number of generating neurons were almost identical in both treated cortex with similar migration ratio of postmitotic neurons afterward. On the other hands, comparing to control, delayed timing and reduction in number of generating neurons were found in the later-stage cortex of Poly I:C-treated mice. Since neurons distributed into deeper and upper layer were generated at mid- and later-stage, respectively, prenatal immunochallenge induced the later-stage specific alteration of neurogenesis would cause to the upper-layer thinner cortex and might be involved in the pathogenesis of neurodevelopmental disorder.

S04-1 The function of neuronal activity-dependent CaMKII activation in synaptic plasticity

○Kohji Fukunaga

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Calcium/calmodulin-dependent protein kinase II (CaMKII) is critical for change in synaptic efficacy through regulation of AMPA receptor (GluR1) recruitment into synapse in the hippocampus-dependent memory formation. Recent studies also demonstrated that CaMKII and CaMKI are important for the neuronal activity-dependent remodeling of spines during the hippocampal long-term potentiation. We first documented that the persistent elevation of CaMKI and CaMKII activities in the CA1 region following LTP induction. We here focused on the remodeling of spine formation by activity-dependent manner in the physiological or pathological event. The intracellular application of autophosphorylated CaMKII reproduced spine morphological changes and triggered filopodia growth and new spine formation. The CaMKII-dependent morphological change in the spine was associated with an increased excitatory synaptic transmission in the CA1 region. CaMKII inhibitor prevented the synaptic enhancement, the growth filopodia and formation of new spine. Interestingly, neuropsychiatric disorders are also associated with abnormal spine formation in the brain with concomitant dysregulation of CaMKII activity in the medial prefrontal cortex. X-linked α -thalassemia/mental retardation (ATR-X) syndrome induces by abnormal chromatin remodeling. ATRX model mice generated by a splicing mutation show abnormal CaMKII activity in the medial prefrontal cortex, where abnormal phosphorylation of guanine nucleotide exchange factors (GEFs) such as Tiam1 and PAK3 were also observed. Taken together, although causative mechanisms underlying abnormal CaMKII activity in the medial prefrontal cortex in ATR-X syndrome model mice are unclear, the dysregulation of CaMKII activity may trigger the abnormalities of spine morphology in the mental retardation model mice. In addition to the critical role played by CaMKII in LTP-induced morphological changes in spines, mental retardation may be associated with changes in spine morphology through dysregulation of CaMKII activity in specific brain regions. K. Fukunaga, N. Shioda, and E. Miyamoto, The function of CaM kinase II in synaptic plasticity and spine formation. *Handbook Neurochem Mol Neurobiol*. Neural signaling mechanisms. Springer (Ed. Mikoshiba K) pp163-184 (2009)

S04-3 Memory improvement by inhibiting PKA in *Drosophila*

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The cAMP/PKA pathway is known to be critical for learning and memory in organisms ranging from *Aplysia* to mammals, and much work has focused on increasing activity of this pathway to improve memory. However, we have discovered that decreasing, rather than increasing, PKA activity may improve memory in *Drosophila*. We identified single point mutations in *Drosophila* that significantly improve memory. These mutations are found in *DC0*, the gene encoding the catalytic subunit of the major PKA isoform found in *Drosophila* heads. Memory improving *DC0* mutants are heterozygous for recessive lethal *DC0* mutations and have 50% of wild-type PKA activity. *DC0* heterozygotes improve memory in two ways; they prevent or delay age-related memory impairment (AMI) in old flies and they increase memory retention in young flies. Similar to other organisms, *Drosophila* suffer AMI, which consists of a significant, age-dependent decrease in middle-term memory, a memory phase that can be measured one hour after training. Reducing PKA activity using various methods strongly ameliorates AMI, indicating that while PKA is important of memory formation, it also causes AMI. In young flies, *DC0* heterozygotes improve a specific memory phase, anesthesia-resistant memory (ARM). When memories are made, they are first formed in a labile state that can be disrupted by cold-shock anesthesia. This memory is known as anesthesia-sensitive memory (ASM). Over time, ASM is consolidated into ARM. *DC0* heterozygotes do not affect formation of early ASM or of protein synthesis-dependent long-term memory but do cause a significant increase in ARM. Expressing a PKA transgene in the mushroom bodies, brain structures critical for memory formation in *Drosophila*, both restores AMI in aged flies and restores normal ARM in young flies. Our results indicate that while PKA may be critical for learning and formation of several memory phases, it also functions to inhibit at least two memory phases.

S04-2 Roles of CaMKIV Signaling Pathway in Memory Formation

○Satoshi Kida

Tokyo University of Agriculture

Activity-dependent gene expression through activation of Ca^{2+} signal transduction pathways has been thought to play a central role in memory formation. Increases in intracellular concentration of Ca^{2+} activate CaMKIV. Activated CaMKIV phosphorylates transcription factor cAMP responsive element binding protein (CREB) at Serine 133 (S133). Phosphorylated CREB at S133 interacts with transcription coactivator CBP, resulting in the activation of CRE-mediated transcription. To understand the mechanisms of memory formation from the view of gene expression regulation, we are investigating roles of CREB signaling pathway in memory formation using conditional mutant mice. We examined whether overexpression of CaMKIV improves memory formation by generating transgenic mice overexpressing CaMKIV in forebrain. These transgenic mice showed an increase in phosphorylated CREB level in hippocampus, enhanced hippocampal LTP and enhanced consolidation of contextual fear and social memories. Similarly with the results of CaMKIV mice, transgenic mice overexpressing dominant active CREB mutant also showed the up-regulation of expression of CREB target genes, enhanced hippocampal LTP and enhancements of formation of spatial, fear and social memories. Taken together with our previous observation that inhibition of CaMKIV-CREB signaling pathway blocks memory formation, we are concluding that this signaling pathway functions as a positive molecular switch to form memory.

S04-4 mTOR kinase signaling in learning paradigm

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mTOR (mammalian target of rapamycin, also called as FRAP, RAFT1, RAPT) is the phosphoinositide kinase family protein kinase. This kinase plays crucial roles in protein synthesis and degradation. mTOR forms mTORC1 (mTOR complex 1) together with mLST8 and raptor and phosphorylates two important translation modulators, 4EBP (eukaryotic initiation factor 4E-binding protein) and p70S6 kinase. mTOR activates translation through these cascades by phosphorylating them. Recent studies indicate that novel protein synthesis is an essential step in certain types of neural plasticity such as LTP, LTD and learning. Here we present that mTOR kinase activity is up regulated in hippocampal extract by in vitro kinase assay in spatial learning. 4EBP and p70S6K are phosphorylated as well. Furthermore, actual protein synthesis is also enhanced in hippocampus. Furthermore, the inhibition of mTOR by rapamycin retards the acquisition of spatial learning. The results indicated that mTORC1 signal is activated and play crucial role in spatial learning acquisition.

S04-5 Glycogen synthase kinase 3 (GSK3) in synaptic plasticity, learning & memory

○ Florian Plattner

Institute of Neurology, University College London

Glycogen synthase kinase 3 (GSK3) is a multifunctional Ser/Thr kinase regulating diverse cellular processes including metabolism, apoptosis and transcription. GSK3 contributes to the various processes by integrating numerous intracellular signalling pathways. These pathways converge onto GSK3 and regulate the activity of GSK3 via regulatory phosphorylation. GSK3 exists in two isoforms, termed α and β and can be inhibited by phosphorylation at serine 9 in the β -isoform and serine 21 in the α -isoform, respectively. Deregulation of GSK3 activity has been associated with various human neuronal disorders including Alzheimer's disease, bipolar disorder and schizophrenia. However, little is known about neuronal functions of GSK3 and through which mechanisms GSK3 might contribute to these pathologies. In order to get insight into neuronal functions of GSK3, our recent work examined the role of GSK3 in synaptic plasticity, learning and memory. Our results show that inhibitory phosphorylation of GSK3 β at serine 9 is elevated after induction of long-term potentiation (LTP) in both hippocampal subfields, CA1 and the dentate gyrus. The increase in inhibitory serine 9 phosphorylation is robust and persists for at least one hour after LTP induction. Consistent with this result, LTP is found to be impaired in a transgenic mouse line with conditional GSK3 β overexpression, which displays elevated GSK3 activity (Hopper et al. 2007, EUN 25, 81-86). The involvement of the inhibitory GSK3 phosphorylation in learning and memory was studied in genetically-modified mice, in which the inhibitory serine phosphorylation site was mutated in both isoforms to a non-phosphorylatable alanine residue (GSK3 α Ser21Ala and GSK3 β Ser9Ala). In these mutant mice, ablation of the inhibitory serine phosphorylation of GSK3 α and β resulted in impaired hippocampus-dependent learning and memory in fear conditioning, but did not affect motor performance in the rotarod and open field tasks. Taken together, these results indicate that inhibition of GSK3 via serine phosphorylation is critically involved in synaptic plasticity and hippocampal memory formation. It is therefore conceivable that deregulation of GSK3 may induce synaptic impairments in the course of various human neuronal disorders. (Supported by the Alzheimer's Research Trust with a fellowship to F.P.)

S05-1 Drug discovery research as a translation of science to drug candidates

○ Shinichi Koizumi

RaQualia Pharma Inc. Aichi, Japan

Drug discovery research as a translation of science to drug candidates RaQualia Pharma Inc. Although there is an excellent and growing science around both pathological and physiological mechanism, the probabilities in drug discovery has not been improved so much and still many unmet medical needs are waiting for the innovative new drugs. Drug discovery research is the process to translate innovative science to innovative drug and the most critical path is identification of right compounds on the right target. Effective collaboration between basic/clinical scientists and drug discovery scientists is essential for innovative drug desired by patient. Therefore, this symposium focuses on the key processes of drug discovery research to get better understanding of basic scientists for future innovative new drugs. As an initial talk in this symposium, I will summarize the drug discovery processes for scientists. Then move to the concept of drug target. The good understanding about the criteria of drug targets and scientific challenges on the novel target are the first step to walk in the long way of the drug discovery process. The ideal drug target not only has critical roles in the pathological processes but also has no risk for normal physiology of human. The target needs to have target sites that drug will interact. Also the target has to be accessible by compounds effectively in vivo with an acceptable administration route. We have to consider desensitization, hyper sensitization, induction, and accumulation etc., so many factors. I hope this symposium will help any scientist who is interested jump in an attractive drug discovery world.

S04-6 CDK5 AND SYNAPTIC PLASTICITY

○ James Bibb

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The neuronal protein kinase Cdk5 has been implicated in a plethora of neuron functions during development, adulthood, and in neuropathology. However its role in learning and memory has only recently begun to be explored. We have found that conditional knockout of Cdk5 in the brain of adult mice resulted in superior learning and memory and enhanced synaptic plasticity in the hippocampus. Loss of Cdk5 activity also potentiates responses to rewarding stimuli and motor learning. Increased neuronal excitability underlies these effects, through mechanisms including the regulation of stability and surface expression of the NR2B subunit of the NMDA receptor and alterations in Ca^{2+} and cAMP dependent signaling cascades. These new findings reveal an important role for Cdk5 in synaptic remodeling during memory formation.

S05-2 A novel computational approach for drug discovery: Chemical genomics-based in silico ligand screening

○ Yasushi Okuno, Ryuta Murakami

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A novel computational approach for drug discovery: Chemical genomics-based in silico ligand screening Yasushi OKUNO¹, Ryuta MURAKAMI². Department of Systems Bioscience for Drug Discovery, Graduate School of Pharmaceutical Sciences, Kyoto University². Kyoto Constella Technologies Co., Ltd. Exploration into chemical space is a critical issue in chemical biology and drug discovery. There is a growing need to develop an efficient computational screening technique. There exist two widely-used approaches, ligand-based virtual screening (LBVS) and structure-based virtual screening (SBVS). In the emerging field of Chemical Genomics, large-scale biological assay data encompassing knowledge of compound-protein interaction (CPI) are being accumulated. We can expect to gain insights into the mechanism of multifarious intermolecular interactions between proteins and compounds, which may lead to the discovery of novel modes of interactions. However, such multiple relationships between ligands and proteins are too complicated to be comprehensively represented by the previous approaches. In this study, we present a fundamentally novel approach for in silico screening, Chemical Genomics-based virtual screening (CGBVS), which makes effective use of Chemical Genomics data. CGBVS can efficiently identify novel active compounds for a target protein based on the statistical machine learning of the conserved patterns of molecular recognitions extracted from comprehensive CPI data. We compared the performance of CGBVS, LBVS and SBVS by cross-validation using GPCR-ligand CPI data and also by retrospective predictions using the 3D structure of human beta2 adrenergic receptor (b2AR), showing that CGBVS achieves the best performance. Furthermore, verification experiments employing the prospectively predicted ligands for b2AR indicated that CGBVS provides not only very high prediction accuracy but also has the potential to discover novel scaffolds which were not detected by the other two approaches. CGBVS was superior to the existing methods, not only for GPCRs but also for Kinase family. We hope that this approach will lead to a more comprehensive understanding of the multifarious modes of CPIs and accelerate drug discovery processes such as identifying novel leads.

S05-3 How to translate "chemical compounds" into "medicines" for the use of disease treatments

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The process in drug research and development seems to be a long journey, which has huge risks and hurdles to be jumped over. There are few compounds that can finally mature into medicines, even though we have identified several compounds with any specific activities to target molecules. Besides, it will take a long time, normally over 10 years, to get approval as medicines. In the early 1990s, problems derived from pharmacokinetics/bioavailability were the major cause of attrition, and accounted for about 40% of all attrition. By 2000, however, remarkable cause of attrition has significantly shifted to the concerns regarding non-clinical and clinical safety accounting for about 30%, as well as lack of efficacy in human. Nevertheless, at the present time, failures due to both pharmacokinetics and toxicology still have demonstrated the needs for the development of more predictive assay methods and animal models. In order to translate "active compounds" into "medicines", many investigations should be made from the efficacy and safety points of view. Generally, they are evaluated in non-clinical studies (pharmacodynamics, pharmacokinetics, and toxicology), and human clinical trials. In the early phase of drug discovery, efficient and effective approaches allow us to extrapolate the results of animal data to humans, and to avoid further development of compounds that have no suitable profiles for medicines. In this context, we should focus on the following items: rate and type of gut absorption; first-pass effect; bioavailability; plasma protein binding; metabolic stability and enzymes involved; enzyme induction; drug-drug interaction; cardiovascular safety; genotoxicity; general toxicity in target organs; and responsible biomarkers. Recently, the applicable exploratory Investigational New Drug (IND) guidance issued by FDA enables us to conduct human trials earlier. Thus, this surely makes it possible to find potential risks of a compound being developed, and to maximize probability of success. Here, I would like to review the process of drug development, and also discuss requirements for drug candidates.

S06-1 Abi2 plays an essential role for radial migration in the developing cerebral cortex via WAVE2-Arp 2/3 complex

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Lamellipodium is important for directed cell migration. Dynamic formation of actin meshworks inside the lamellipodium works as a force to push the lamellipodium forward. Therefore, how actin meshworks are formed is critical to understand intracellular mechanisms underlying directed migration. In the developing cortex, most excitatory neurons are supplied and arranged through radial migration. However, how radial migration is controlled is not fully elucidated, especially on the intracellular cytoskeletal regulation. Actin nucleation through activated Arp2/3 complex produces branched actin networks that drive lamellipodium, and Arp2/3 is activated by one of the Wiscott-Aldrich syndrome protein family, such as WAVEs. However, significance of such cytoskeletal regulation for the radial migration and its underlying molecules remain elusive. We here demonstrate that WAVE2 is important for the radial migration among WAVE family and that Abi2 is critical for the radial migration, among the binding partners of WAVE2 that induce its activation. Presence of Abi2-WAVE2 complex in the developing cortex was observed using immunoprecipitation. We then used the method of in utero electroporation to transfer shRNA constructs into the cortex in order to knockdown genes acutely at embryonic day 14. We observed migration arrest of Abi2 or WAVE2-knockdown neurons in the intermediate zone of the cerebral cortex after 3-4 days of gene transfer. Since Abi2 is versatile, we then asked whether migration arrest of Abi2-knockdown is due to WAVE2 inactivation or not. Neurons expressing exogenous mutated WAVE2 that lacks Abi2 interacting domain, arrested in the intermediate zone. Therefore, it is likely that Abi2-WAVE2 complex plays an essential regulatory role for radial migration in the developing cerebral cortex.

S06-2 Reelin-Dab1 signal regulates the local inside-out lamination through terminal translocation

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Mammalian cerebral cortex exhibits an organized laminar structure with 6 neuronal layers. During development, excitatory neurons generated around the lateral ventricle migrate radially in a long way towards the pial surface. Later born neurons migrate past the earlier born neurons to reach beneath the marginal zone, and cortical plate is formed in inside out manner, that is, later born neurons settle superficial to earlier born neurons. In the course of this migration, neurons change their shape and migratory behavior dynamically. After starting the migration, neurons exhibit multipolar migration, and next, they transform into locomotion. Finally, near the top of cortical plate, locomoting neurons change their behavior to terminal translocation and stop their migration. Reelin is a glycoprotein secreted by the Cajal Retzius cells in the marginal zone. The mutant mice of Reelin, Reelin receptors, and adaptor molecule Dab1 exhibit remarkable outside in lamination in the cerebral cortex. This overall inversion of the laminar structure suggests that Reelin Dab1 signal is essential for the normal layer formation. Recently, it was shown that knock down of Dab1 caused terminal translocation failure in a cell autonomous manner. In order to identify the importance of terminal translocation for the normal inside out lamination, we introduced control or Dab1 knock down vector sequentially using in utero electroporation, and found that later born Dab1 knocked down neurons could not migrate past the earlier born normal neurons and disrupted the local inside out lamination. Our data suggests that Reelin Dab1 signal regulates the local, but not over all, inside out lamination at the top of the cortical plate after the preplate splitting.

S06-3 Slit-Robo signaling regulates migration of newly-born neurons under physiological and pathological conditions in the postnatal brain

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Neurons are continuously generated by stem cells in the subventricular zone (SVZ) throughout life. Newly-born neurons migrate in chain toward the olfactory bulb (OB), whereas they occasionally migrate toward the damaged region to regenerate the brain circuitry. However, the mechanisms that regulate these processes are largely unknown. Slit is a secreted protein which binds to its receptor Robo and acts as a chemorepellent in axon guidance and cell migration in the developing brain. In the adult brain, Slit1 is expressed in the newly-born neurons migrating from the SVZ toward the OB, but its functional significance remains unclear. Here, we show that Slit-Robo signaling mediates the interaction of newly-born neurons and surrounding astrocytes, which controls the migration of newly-born neurons toward the OB. We further show that this signaling is also required in the regenerative processes after cerebral infarction induced by middle cerebral artery occlusion.

S06-5 Cellular functions of a novel axon guidance molecule LOTUS

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Lateral olfactory tract usher substance (LOTUS) is a newly identified axon guidance molecule serving for the lateral olfactory tract (LOT) formation in developing mouse brain by functional screening using a modified fluorophore-assisted light inactivation (FALI) method. LOTUS was a plasma membrane surface protein of axons and expressed in several regions of mouse embryonic central nervous system such as olfactory bulb, cerebral cortex, hippocampus, thalamus, brainstem, and spinal cord. We also identified Nogo-66 receptor (NgR1) as an extracellular binding partner of LOTUS. LOTUS and NgR1 interaction induced cell-cell contact in LOTUS- and NgR1-transfected cells. Furthermore, this interaction promoted neurite extension of retinal ganglion cells (RGC) cultured on LOTUS-coated dish. Inactivation of LOTUS substrate by FALI reduced neurite outgrowth of RGC. Surprisingly, binding of NgR1 ligands such as Nogo-66 or myelin associated glycoprotein (MAG) to NgR1 was completely inhibited when LOTUS and NgR1 were co-expressed in a same cell. Over-expression of LOTUS inhibited Nogo-66-induced growth cone collapse in chick DRG neurons. These data suggest that LOTUS functions as a promoting factor of neurite outgrowth and a negative regulator of Nogo-NgR1 signaling through its binding to NgR1.

S06-4 A novel repulsive guidance protein, Draxin

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The correct wiring of the nervous system relies on the ability of axons and dendrites to locate and recognize their appropriate synaptic partners. The correct selection of axonal path toward to their target is known accomplished by extracellular guidance molecules such as the netrins, slits, semaphorins and ephrins. We have identified a novel secreted protein, draxin (dorsal repulsive axon guidance protein), which acts as a roof plate-derived chemorepellent for commissural axons in chick spinal cord. Here, we report that draxin is required for the midline crossing of forebrain commissures. draxin deficient mice showed severe defects in axonal projection of all three commissures, the corpus callosum, hippocampal commissure and anterior commissure, in the forebrain. In contrast, the habenular commissure and posterior commissure seemed intact. draxin was expressed in the regions that surround the forebrain commissures, such as the midline glial cells. draxin-alkaline phosphatase binding on sections revealed the presence of draxin receptors in the forebrain commissural axons. In addition, we showed that draxin repelled neurite outgrowth from cortical explants at E17, when corpus callosal axons are crossing the midline. Thus, we propose that draxin repulsion from the regions surround the trajectories of forebrain commissures is essential for proper guidance of forebrain commissural axons, preventing them from misprojecting before reaching the midline.

S06-6 Regulation of axon outgrowth by new positive feedback mechanisms through membrane stretch activated channel

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Thermosensitive TRP (thermo TRP) channels are well recognized for their contributions to sensory transduction, responding to a wide variety of stimuli including temperature, nociceptive stimuli, touch and osmolarity. However, the precise roles for the thermo TRP channels during development have not been determined. To explore the functional importance of thermo TRP channels during neural development, the temporal expression was determined in embryonic mice. Interestingly, TRPV2 expression was detected in spinal motor neurons in addition to the DRG sensory neurons from E10.5, although other thermo TRP channels were detected much later stages (ex. TRPV1 from E13.5 and TRPM8 from E16.5). TRPV2 was localized in axon shafts and growth cones, suggesting that the channel is important for axon outgrowth. Over-expression of wild type TRPV2 enhanced axon outgrowth, while over-expression of dominant negative TRPV2 inhibit axon out growth in developing sensory and motor neurons. We revealed that endogenous TRPV2 was activated in a membrane stretch dependent manner in developing neurons. Thus, for the first time we revealed that TRPV2 is an important regulator for axon outgrowth through its activation by membrane stretch during development. We hypothesized that axon outgrowth is regulated by the positive feedback mechanisms through membrane stretch which is related to activation of chemo-attractant receptors.

S07-1 Neuronal cell dysfunction as a common pathophysiology of neurological and psychiatric disorders

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Neurological and psychiatric disorders have been frequently studied as different conditions. However, both conditions may, at least in part, share similar pathological mechanisms with one another. At molecular levels, some susceptibility factors for neurological disorders interact with promising risk factors for psychiatric illnesses. From functional and brain circuitry viewpoints, disturbed synaptic maintenance and elimination are likely to be shared between these two conditions, especially in early stage of disorders. Preventive treatment of brain disorders (both neurological and psychiatric disorders) in their prodromal periods, hopefully preventing the later emergence of the full repertoire of disease symptoms is becoming a hot topic in translational neuroscience. By discussing schizophrenia and Alzheimer's disease in parallel, this talk will discuss on how the novel concept of "prodromal intervention for neurological and psychiatric disorders" can contribute to clinical psychiatry and neurology in near future.

S07-2 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 by disruption of experience-driven synaptic delivery of AMPA receptors.

S07-3 The brain as the center for the integration of biological information○Keiji Wada^{1,2}¹Natl Inst Neurosci, NCNP, Tokyo, Japan, ²CREST, JST, Kawaguchi, Saitama, Japan

The brain is a unique organ that integrates and processes a variety of biological information from peripheral tissues. In vertebrates, sensory information is mediated to the brain by peripheral nerves. On the other hand, vascular and autonomic nervous systems support the transfer of other peripheral information in metabolism, endocrine, immunity, dynamics and etc. Inside the brain, in addition to neurons, glial cells are now known to function to modulate neural information. As results of such integration and processing of the information, the brain controls the activity of a living body. The brain is so complicated organ, and, to explore the nature of the brain, we need to study it with a wide scientific view. Besides, we believe that our wide-angled approaches are very important to understand brain disorders as well. Here, we report our study on the environmental factors and their influences on brain function. We observed that, among various factors, oxidative stress likely influences both on neurological and psychiatric events. We found that the ubiquitin system plays an important role in the link between oxidative stress and brain disorders. We also detected that the modulation of maternal condition by oxidative stress affects the brain development in the offspring. In this symposium, we share our data with the audience and discuss the significance of our research. In addition, we would like to discuss what is important for the research of the brain toward the future.

S07-4 From a Neurologist

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Neurology and psychiatry look the different faces of the brain function. One face is motor and sensory system which is the territory of neurology and another face is emotional and mental system, that of psychiatry. Neurologist and psychiatrist analyze and treat the diseases of brain by their own skills from their own standpoints. Their objects are (1) the different disease, (2) the different stage of the same disease and (3) the same stage of the same disease. For example, (1) schizophrenia and major depression are the field of psychiatry, and amyotrophic lateral sclerosis (ALS) and spinocerebellar degeneration (SCD) are that of neurology. (2) Neurologists follows the patients of Huntington disease when their main symptom is chorea, but when psychiatric problems are growing worse, the help of the psychiatrist is indispensable. (3) Parkinson disease, whose main symptoms are motor symptoms such as tremor, rigidity, and akinesia, is mainly the territory of neurology. Recently, accompany with the progression of anti-parkinsonian drugs, non-motor symptoms have been attracted. 1) an unreasonable anxiety; it disturbs patients improvements of the symptoms, and 2) dopamine dysregulation syndrome; such as pathological gambling, and punding by dopamine dependency. From the view of the acceptance of the disease, cooperation of the psychiatrist is indispensable for the therapy of all the neurological disorders including ALS and SCD. For the improvement of quality of life of the patients with neurological disorders, the cooperation of the psychiatrist and the neurologist is more and more important, in the future.

S07-5 Integrated approaches of psychiatry and neurology; from a clinical psychiatry perspective

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Various medicines acting on the brain function are used in clinical psychiatric practice. All of the medicines have their own effects and adverse effects. If we think of antipsychotics, they cause drug-induced extrapyramidal symptoms as one of their frequent adverse effects as well as primary antipsychotic effects. In general, psychiatrists have no nose for motor symptoms and neurological evaluations are difficult for psychiatrists. On the other hand, dopamine replacement therapy for Parkinson disease is known to develop psychiatric conditions such as hallucination, delusion, sleep attacks, and self-control problems like addiction to medication, gambling, or hypersexuality. This so-called dopamine dysregulation syndrome (DDS) has only recently been seriously considered among neurologists. Parkinson disease itself causes depression besides motor symptoms in about 40 % of the patients, which induces substantial dysfunction in daily life. It is also true that many other neurological diseases or conditions cause psychiatric problems, which are ignored by neurologists or misdiagnosed by psychiatrists. Considering such facts happening in clinical practice, integrated approaches of psychiatry and neurology are needed to study, care and cure brain diseases.

S08-1 Role of chronic ER stress in neurodegeneration and bipolar disorder

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Wolfram syndrome, a rare autosomal recessive disorder characterized by diabetes mellitus, optical atrophy and neurodegeneration, was first described by Wolfram and Wager in 1938. In addition, about 60% of patients with Wolfram syndrome have some mental disturbance such as severe depression, psychosis, or organic brain syndrome, as well as impulsive verbal and physical aggression. The heterozygotes who do not have Wolfram syndrome are 26-fold more likely than non-carriers to have a psychiatric hospitalization. The relative risk of psychiatric hospitalization for depression was estimated to be 7.1 in these heterozygotes. The nuclear gene responsible for this syndrome was identified by two separate groups in 1998 and named WFS1. WFS1 is a rare disease, affecting approximately 1/100,000 in North America with higher frequency in the Middle East and East Asia. Despite the rarity of this disease, the carrier frequency is estimated at 1/100. Our group revealed that Wolfram syndrome is an endoplasmic reticulum (ER) stress-mediated form of diabetes and neurodegeneration in models of WFS1 deficiency. We discovered that WFS1 has an important function in the negative regulation of a feedback loop of the ER stress signaling network and prevents cells from dysfunction and death caused by hyperactivation of this signaling pathway. We propose that WFS1 could be a key target for prevention and/or therapy of ER stress-mediated diseases such as diabetes, neurodegenerative diseases, and bipolar disorder.

S08-2 Cellular dysfunction associated with A β oligomers enhanced by APP E693 Δ mutation

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The E693 Δ mutation in amyloid precursor protein (APP) has been suggested to cause dementia by enhanced formation of synaptotoxic amyloid β (A β) oligomers without forming amyloid plaques. However, this mutation markedly decreased A β secretion, implying the existence of an additional mechanism of neuronal dysfunction independent of extracellular A β . We therefore examined the effects of this mutation on APP processing to produce A β and on subcellular localization and accumulation of A β in transfected HEK293 and COS-7 cells. β - and γ -cleavage of the mutant APP was increased, indicating lack of inhibition in A β production. Instead, this mutation promoted A β accumulation within cells, including the endoplasmic reticulum (ER), Golgi apparatus, early endosomes, late endosomes, lysosomes, and autophagosomes, all of which have been proposed as intracellular sites of A β generation and/or degradation. This A β accumulation suggests impairment of intracellular APP/A β trafficking. Notably, the intracellular mutant A β was found to predominantly form oligomers. In parallel to the accumulation of A β oligomers, ER stress markers Grp78 and phosphorylated eIF2 α were strongly induced. Furthermore, activation of caspases-4 and -3 and DNA fragmentation were detected in these cells. These results suggest that the mutant A β induces alteration of A β trafficking and subsequent ER stress-induced apoptosis, probably via enhancement of its intracellular oligomerization. Intracellular accumulation of A β oligomers was also observed in the cerebral cortex and hippocampus of APP transgenic mice harboring the E693 Δ mutation. The mice showed a concomitant decrease of synaptophysin and impairments of hippocampal synaptic plasticity and memory. Taken together, our findings suggest that A β oligomers exhibit toxicity not only from the extracellular space but also from within cells themselves.

S08-3 Mechanism of tau aggregation mediated neurodegeneration

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Neurofibrillary tangles (NFTs), which consist of highly phosphorylated tau, are a hallmark of neurodegenerative disease including Alzheimer's disease. In neurodegenerative disease, neuronal dysfunction occurs accompanying with pathological change, such as NFT formation, neuronal loss, and synapse loss. These pathological change stem from the tau aggregation process, which consists of three distinct tau aggregations, such as hyperphosphorylated tau, granular tau, and fibrillar tau. However, it is unclear which tau aggregation involves in these pathological change. To clarify the relationship between tau and these pathological changes, the mouse expressing human tau with P301L mutation of FTDP-17, and that with human wild tau was compared on NFT formation, neuronal loss, synapse loss, and memory impairment in Morris water maze. Both mouse lines showed similar expression and distribution pattern of tau under CAMKII promoter, and did not show Gallyas silver staining positive neurons. P301L tau-Tg induced neuron loss without affecting synapse, resulting in no memory impairment, and Wtau-Tg induced synapse loss without affecting neuron number, resulting in memory impairment. WTtau-Tg showed hyperphosphorylated tau, but not formed sarcosyl insoluble tau aggregate, while P301Ltau-Tg showed less phosphorylated tau, but formed sarcosyl insoluble tau aggregate. Therefore, soluble form of hyperphosphorylated tau involves in synapse loss, and insoluble tau does in neuron loss. During neurodegeneration, tau is hyperphosphorylated, which induces synapse loss, an increase concentration of hyperphosphorylated tau forms granular tau oligomer, which does not have synaptotoxicity, and cause neuron loss. An increase concentration of granular tau forms fibrillar tau, which does not have neurotoxicity, and form NFT. The different tau aggregation species may involve in different pathological features in neurodegeneration.

S08-4 The involvement of ER stress in pathogenesis after cerebral ischemia

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Endoplasmic reticulum (ER)-stress, which is caused by an accumulation of unfolded proteins in the ER lumen, is associated with stroke and with neurodegenerative diseases such as Alzheimer disease. However, there are only a few reports regarding a role of ER stress on ischemia-induced neuronal damage. Therefore, we investigated the regional and time-dependent changes in ER stress-related markers after transient forebrain ischemia in gerbil and permanent middle cerebral artery occlusion (MCAO) in mice. We assessed the expression patterns of immunoglobulin heavy chain binding protein (BiP)/ glucose-regulated protein (GRP) 78, activating transcription factor (ATF)-4, and C/EBP homology protein (CHOP) after transient forebrain ischemia in gerbils. Double-fluorescent staining involving CHOP immunohistochemistry and the TUNEL method was performed to clarify the involvement of CHOP in cell death. Immunohistochemical and Western blot analyses of the hippocampal CA1 subfield showed that BiP expression was increased at 12 h, peaked at 3 days, then decreased. A transient increase was detected in CA3 at 1 day after ischemia, but BiP expression was unchanged in dentate gyrus and cortex. Signals for ATF-4 and CHOP were increased at 1 day and 3 days in CA1, and at 12 h in CA3. Co-localization of CHOP immunoreactivity and DNA fragmentation was detected by the TUNEL method at 3 days after ischemia in CA1, but not at 12 h in CA3. ER stress-related markers in the striatum and the cortex were investigated after permanent MCAO in mice. Using ER stress-activated indicator (ERAI) transgenic mice, which show splicing of X-box protein 1 (XBP-1) mRNA as green fluorescence, we monitored the regional changes in fluorescence after MCAO. BiP mRNA was increased in the cortex at 6 h. In immunohistochemical and/or Western blot analysis, the expressions of BiP, ATF-4, and CHOP were increased in the infarct region, more strongly in the cortex than in the striatum. ERAI fluorescence was observed in the ischemic area starting from 6 and 12 h, respectively, after MCAO, with the peaks at 1 day and the fluorescence co-localized with the 2,3,5-triphenyltetrazolium chloride-visible extension of brain infarction. These findings are consistent with ER stress playing a pivotal role in post-ischemic neuronal death in the gerbil hippocampal CA1 subfield and the mouse MCA territory.

S08-5 Novel therapeutic strategies for neurodegenerative diseases based on ER-proteasome system○Takashi Kudo¹, Kazunori Imaizumi²¹ Department of Psychiatry, Osaka University Graduate School of Medicine, Suita, Japan, ² Division of Molecular and Cellular Biology, Department of Anatomy, Faculty of Medicine, University of Miyazaki, Miyazaki, Japan

Recent reports have shown that the accumulation of abnormal proteins is a common mechanism for neurodegenerative diseases. Because the endoplasmic reticulum (ER)-proteasome system is deeply involved in the quality control of proteins, it can be a target of the therapeutic approach for them. I propose two strategies, the ER chaperone inducer and the induction of "proteasome tolerance". The 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 neurodegenerative diseases. To find the novel therapy for neurodegenerative diseases, we investigated the strategy which can activate proteasome function. We reported a phenomenon "proteasome tolerance": pretreatment with low dose of proteasome inhibitor increases proteasome activity to resist subsequent high dose of proteasome inhibitor treatment. We performed microarray analysis of global expression changes while "proteasome tolerance" was induced. Among increased messages, we focused on Nrf2, a transcription factor and studied its effect on proteasome function.

S09-1 Cerebellar Development Transcriptome Analysis: Towards the elucidation of the genetic basis of cerebellar circuit development

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A large amount of genetic information is devoted to brain development and functioning. The neural circuit of the mouse cerebellum develops through a series of cellular and morphological events (including neuronal proliferation and migration, axogenesis, dendritogenesis, synaptogenesis and myelination) all within three weeks of birth. All of these events are controlled by specific gene groups, whose temporal and spatial expression profiles must be encoded in the genome. To understand the genetic basis underlying cerebellar circuit development, we analyzed gene expression (transcriptome) during the developmental stages on a genome-wide basis. Spatio-temporal gene expression data were collected using in situ hybridization for spatial (cellular and regional) resolution and fluorescence differential display, GeneChip, microarray and RT-PCR for temporal (developmental time series) resolution, and were annotated using Gene Ontology (controlled terminology for genes and gene products) and anatomical context (cerebellar cell types and circuit structures). The annotated experimental data were integrated into a knowledge resource database, the Cerebellar Development Transcriptome Database (CDT-DB <http://www.cdtb.brain.riken.jp>), with seamless links to the relevant information at various bioinformatics database websites. The CDT-DB not only provides a unique informatics tool for mining both spatial and temporal pattern information on gene expression in developing mouse brains, but also opens up opportunities to elucidate the transcriptome for cerebellar development.

S09-3 Strategy for the Growth Cone Research using Proteomics

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The growth cone is the tip of the extending neuronal processes for the accurate synaptogenesis and is the most important structure for wiring of the neural network. There were no methods discovering the molecules involved in the growth cone functions systematically, thus, the molecular basis of the growth cone behavior is poorly understood and its molecular markers were not known except GAP-43. Here we take the strategy to identify the growth cone proteins that are important for axonal growth for combining purification of the growth cones from rat brain, proteomic analysis by multidimensional protein identification technology of the growth cone; immunostaining using antibodies against the proteins identified by proteomics; and RNAi that inhibits the axonal growth. We analyzed the growth cones isolated the developing rat forebrain and identified more than 900 proteins. We found that these identified proteins include the ones closely related to the growth cone functions, such as regulators of the cytoskeletal reorganization, or of the vesicular trafficking. We have already performed the immunocytochemistry concerning more than 200 identified proteins including cytoskeletal components, signaling molecules, receptors, and cell adhesion molecules, and all of them are positively stained in the growth cone area. Using this approach, surprisingly, we found approximately 90 proteins which are more concentrated in the growth cone area than GAP-43. We also performed the RNAi experiments against those proteins using the GFP-transgenic rat (Green rat) by co-transfection of both the target siRNA and siRNA against GFP. Among more than siRNAs against 50 proteins, those against 20 proteins were shown to inhibit the axonal growth significantly. In conclusion, our approach succeeded in effectively finding the proteins that operates the growth cone behavior.

S09-2 Synaptic function regulated by palmitoylating enzyme family

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Protein palmitoylation is a common posttranslational lipid modification and regulates the membrane targeting of proteins. The unique reversibility of palmitoylation allows proteins to shuttle between intracellular compartments. PSD-95, a major scaffolding proteins in neurons, is targeted to postsynaptic membrane through palmitoylation and anchors AMPA-type glutamate receptors (AMPA) at excitatory postsynapses. A large family of DHHC proteins has emerged as protein palmitoyl acyltransferases (PATs). Taking advantage of our developed systematic method, we recently identified a subset of DHHC proteins (DHHC2, 3, 7, and 15) as PSD-95-palmitoylating enzymes. Mechanisms that regulate these PATs in a physiological context, however, remain unknown. We found that blocking synaptic activity rapidly and specifically augments PSD-95 palmitoylation and mediates synaptic clustering of PSD-95 and associated AMPARs. By contrasting two representative PSD-95 palmitoylating enzymes, we found that DHHC3 stably localizes at the Golgi apparatus and constitutively palmitoylates numerous substrates including Gα, GluR2, and PSD-95. In contrast, dendritically localized DHHC2 senses changes in synaptic activity and rapidly translocates near postsynaptic membranes. Synaptically translocated DHHC2 induces palmitoylation and synaptic accumulation of PSD-95, and thereby AMPAR recruitment at postsynaptic sites. Thus, we first define differential regulation of DHHC-type palmitoylating enzymes in homeostatic AMPAR trafficking.

S09-4 Lipidomics for neurochemistry - basic techniques and strategy

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In lipidomics, the application of mass spectrometry has become increasing popular. To elucidate the function of lipids, it is necessary to analyze not only their classes and subclasses but also molecular species. For that reason the lipidomics approach is requested as the global and comprehensive analysis of them. For global analysis of phospholipids and glycerides, we normally select comprehensive LC-MS/MS analysis with data dependent-scanning, using high separation of UPLC combination with Orbitrap with high sensitivity of linear ion trap and high resolution of FT. On the other hand, minor important lipid metabolites such as oxidized lipids were often difficult to be detected by this comprehensive and untargeted method. In this case we normally select multiple reaction monitoring (MRM) analysis for detecting very small amounts of targeted molecules such as lipid mediators or oxidized lipid metabolites. Even in this analysis, the electrospray ionization (ESI) makes it possible to detect more than hundred molecules by a single LC run. In MRM analysis, the target molecules to be analyzed are needed to be defined in advance, but even in this method some level of comprehensive approach can be possible to expand the detecting target to probable molecular masses theoretically calculated by their structural similarities. The choice of these different kinds of methods seems to be very important for neuro-chemical research for detecting different kinds of lipid metabolites such as unknown lipid ligands, focused class of lipids, or targeted minor lipid mediators. Furthermore, analysis in lipid localization on individual tissues is also become very important. Here, I will introduce our recent approaches in localization analyses such as imaging mass spectrometry and combination of laser micro-dissection (LMD) with LC/MS. IMS is a mass spectrometry-based imaging technique to visualize distribution of various bio-molecules on the tissue section. And LMD is the equipment which is able to cut and collect the area of interest by laser from section. We are now applying these lipidomics techniques for the samples in localized tissues obtained by LMD. Some data on changes in molecular species of polyunsaturated containing phospholipids in acute myocardial infarction and sphingolipids in mouse brain were also discussed.

S09-5 Mass spectrometric analysis of minor components in brain -phosphorylated proteins and membrane lipids

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Over the past dozen years mass spectrometry has become a major analytical tool in the field of proteomics and lipidomics due to its high speed and sensitivity. The analysis of post-translational modifications such as phosphorylation, glycosidation, and lipidation as well as the changes in expressed protein levels between samples of interest has been a major topic in brain science. Analysis of phosphotyrosine using iTRAQ (isobaric tag for relative and absolute quantification) has made much progress. However, iTRAQ has seldom been used to phosphoprotein in general including serine/threonine derivatives, because this method requires multi-step sample enrichment as the post-treatment which needs a large amount of samples and the iTRAQ reagent. Our new method consists of the iTRAQ-labeling and separation/purification by Phos-tag (phosphate-binding tag) with C18 resin. This is a simple and efficient method for the phosphopeptide analysis; biphasic Phos-tag is overlaid on C18 resin held in a pipette tip, whereof binding and washing conditions of Phos-tag/C18 have been studied. Applying this method to phosphoproteomic analysis of tumor necrosis factor signaling in HeLa cell, we were able to detect the temporal alterations of over 400 phosphopeptides from a mixture of only 50 microgram proteins. Meanwhile, structural determination by mass spectrometry requires extreme caution, because the molecular structure is determined by only mass value. In this symposium, we will also show an example that mass spectrometry is a powerful tool for analysis of newly discovered glycolipid with the molecular mass identical to phosphatidylinositol.

S10-1 Dynamics of Actin binding proteins observed in living growth cones

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Growth cones play important roles for axonal pathfinding and target recognition. Their motility is regulated by actin-binding proteins. Some of us (M. N. and M.I.) identified a large number of growth cone proteins by proteomics, including actin-binding ones. We recorded the dynamics of GFP-labeled actin binding proteins in the growth cone of differentiated NG-108 cells and classified their localization and behaviors into 11 patterns. These are the following 4 patterns and the other seven: 1) in the plasma membrane of the leading edge (moving in the plasma membrane); 2) at spots below the leading edge and F-actin comets; 3) at the lamellipodia (F-actin meshwork); 4) at the filopodia (F-actin bundles), (2)-4) showed retrograde flow). By analyzing time-lapse images of FRAP experiments, we determined binding constant of several subunits (Arp2, Arp3, ArpC1, ArpC5) of Arp2/3 complex that was classified into the group 2) above. We will discuss the differences in the binding constant of the subunits of Arp2/3 complex and other proteins.

S10-2 Drebrin-mediated actin-linked control of actomyosin system at the transitional zone plays a pivotal role in axonal growth

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Drebrin is originally isolated from embryonic chick brain at early developmental stage. Although the neuron-specific isoform drebrin A, which is an adult type of drebrin, is known to be involved in the spine maturation, the role of the embryonic isoform drebrin E is not clarified. In this study, we used primary hippocampal neuronal cultures to analyze the role of drebrin E within the axonal growth cone. Immunocytochemistry showed that within axonal growth cones drebrin E specifically localized to the transitional zone, an area in which dense networks of F-actins and microtubules overlapped. Time-lapse imaging analysis on the distribution of GFP-DE in transfected cells demonstrated that retrograde movement of drebrin E within the transitional zone at the rate of 0.86 $\mu\text{m}/\text{min}$, which is similar to that of F-actin in the transitional zone.

The localization of drebrin E in the transitional zone depends on F-actin organization. Cytochalasin D treatment caused the localization of drebrin and F-actin to shift from the transitional zone to the distal edge of the growth cone. Because this treatment has been known to enable microtubules to penetrate the peripheral domain, consequently resulting in rapid axonal growth, appearance of drebrin E-bound F-actin at the peripheral edge of growth cones could facilitate axonal growth.

Drebrin E co-localizes with other cytoskeletal proteins, including myosin IIB, within the transitional zone of axonal growth cone. Over-expression of drebrin E caused drebrin E and F-actin to accumulate throughout the growth cones and facilitated axonal growth. In contrast, knockdown of drebrin E reduced drebrin E and F-actin in the growth cone and prevented axonal growth. Furthermore, inhibition of myosin II ATPase masked the promoting effects of drebrin E over-expression on axonal growth. These results suggest that drebrin E-bound F-actin plays a facilitative role in axonal growth through inhibition of actin-myosin interactions in the transitional zone of axonal growth cones.

S10-3 Role of cofilin phosphorylation in BDNF-induced dendritogenesis

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Actin cytoskeleton remodeling plays an essential role in axonal growth cone motility and dendritogenesis. Cofilin is a key regulator of actin filament dynamics by stimulating depolymerization and severance of actin filaments that has been implicated in growth cone motility and neurite extension. The activities of cofilin are inhibited by phosphorylation at Ser-3 by LIM-kinase (LIMK) and are reactivated by dephosphorylation by Slingshot (SSH) phosphatases. LIMK1 is activated by ROCK and PAK downstream of Rho family small GTPases and also activated by MAPKAPK-2 downstream of p38 MAP-kinase. Slingshot-1 is activated downstream of PI3-kinase and Ca^{2+} signaling. We have shown that knockdown of LIMK or SSH inhibited NGF-induced neurite outgrowth of PC12 cells and chick DRG neurons. LIMK1 is predominantly expressed in the central nervous system during embryogenesis. However, the regulation of actin cytoskeletal remodeling by phosphorylation of cofilin in the dendritogenesis remains to be known. In this study, we examined the role of LIMK1 in BDNF-induced dendritogenesis of rat hippocampal and cortical neurons. We showed that active LIMK1 increased the number of primary dendrites in rat hippocampal neurons, and knockdown of LIMK1 inhibited BDNF-induced dendritogenesis in rat cortical neurons. We also examined the signaling pathways of BDNF-induced dendritogenesis. We showed that LIMK1 was transiently activated by BDNF and that inhibitors for phospholipase C (PLC) and CaM-kinases inhibited the BDNF-induced LIMK1 activation and increase in the primary dendrites in cortical neurons. We also provided evidence that CaM-kinase activated LIMK1 *in vitro*. Our results suggest that LIMK1 is required for BDNF-induced dendritogenesis in cortical neurons and the activation of CaM-kinase by the elevation of Ca^{2+} through PLC induces LIMK1 activation. We previously reported that cofilin dephosphorylation by NGF in PC-12 cells depends on PLC activity. Thus, the extension of dendrites could be regulated by spatio-temporal regulation of LIMK and SSH activities through Ca^{2+} signaling.

S10-5 Electron tomographic reconstruction of clathrin coated endocytic intermediates in nerve terminals that lack dynamin 1

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Dynamin is a GTPase implicated in the fission reaction of endocytosis. Of the three dynamin genes present in mammalian genomes, the dynamin 1 gene is the one selectively expressed in neurons, where dynamin 1 represents a very abundant protein. Dynamin 1 is highly concentrated in nerve terminals where it participates in the endocytosis of synaptic vesicles. We have recently found that nerve terminals of dynamin 1 KO mice are characterized by a variable, activity-dependent, accumulation of clathrin-coated endocytic intermediates. We report here detailed 3D reconstructions of nerve terminals exhibiting a very prominent accumulation of such structures by electron tomography. The most striking feature is the presence of branched tubular networks capped by clathrin-coated buds, with only few buds originating directly from the outer profile of the plasma membrane. Some clathrin-coated buds appear to originate from deep tubular invaginations of the plasma membrane containing an evagination of the adjacent cell. These structures may derive from spinules. While an accumulation of clathrin coated intermediates was also observed in synaptotagmin 1 KO synapses, tomographic analysis of these membranes confirmed that they are all free coated vesicles, thus supporting the hypothesis that dynamin and synaptotagmin act at related, but distinct, sites in vesicle recycling. The branched tubular necks of clathrin-coated pits in dynamin 1 KO synapses emphasize the important partnership of dynamin with membrane tubulating proteins.

S10-4 Dynamics of fascin, cofilin, and drebrin in growth cones: comparison with the results obtained by *in vitro* analysis

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Growth cones contain an actin-rich cytoskeleton, and a wide variety of actin-binding proteins and motor proteins are postulated to regulate growth cone dynamics. Fascin is an actin-bundling protein in filopodia, cofilin is the principle accelerators of actin dynamics, and drebrin is a major brain protein, all of which expressed in growth cones. To explore the role of these proteins in nerve cell growth cones, we examined the dynamics and *in vitro* functions of these proteins. Transfection of mCherry-actin, EGFP-fascin, ECFP-drebrin, and cofilin-EYFP revealed that drebrin localized in the central domain of growth cones, and was distributed differently from cofilin or fascin. Fascin concentrated in filopodia, and cofilin accumulated in lamellipodia. Actin, fascin, and cofilin showed vigorous retrograde flow while drebrin did not. The dynamics of the drebrin-associated actin cytoskeleton were much slower than those of cofilin- or fascin-associated actin cytoskeleton. In purified proteins system, drebrin inhibited the actin-binding of fascin, actin-bundling activity of fascin, actin-binding of cofilin, and the cofilin-dependent actin turnover, that were confirmed by high-speed centrifugation assay, low-speed centrifugation assay, direct observation of fluorescently labeled F-actin, and the binding of 1,N6-etheno ATP to actin. Drebrin and cofilin strongly inhibited the activities of myosins while fascin did not. These findings suggest that differential distributions of drebrin, cofilin, and fascin may be caused by the competitive F-actin binding of these proteins. Drebrin may function as an actin stabilizer in neuronal growth cones through inhibiting the activities of fascin, cofilin and myosins.

S10-6 The role of microtubules for synaptic plasticity

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How the neuronal activities are performed by using only the long-lasting plasticity change of individual synapses? It is likely that the neuronal activities are performed by enhancing the plasticity of special synapses. Only the plasticity of repeatedly stimulated synapses should be enhanced. To do this, the mechanism that the plasticity-promoting molecules can be translocated only to the stimulated synapses must be present. Although microtubules are one of the good candidates of this mechanism, but it had been observed that less microtubules was present in the spines. Recently, we have reported that LTP-producing stimulation makes new microtubule track between cell body and the stimulated postsynaptic membrane in CA1 neurons. This newly produced microtubule track only to the stimulated postsynaptic membrane might be the mechanism. This lead us the hypothesis of the "endless plasticity amplifying circuit" that means gene expression-promoting molecules are translocated from postsynaptic membrane to the cell body and enter into nucleus and activate transcription factors, and gene products, which will probably promote plasticity, may be re-translocated only to the stimulated postsynaptic membrane along microtubules. The result by another group about the emergence of capture of plus-ends of microtubules in the spines by using living cultured neurons will also be discussed. Finally, I would like to propose the microtubule-instability as a possible mechanism to induce the degenerative diseases. Rotenone could induce Parkinson's disease as microtubules depolymerizer. Phosphorylation of tau, loses the MT-stabilizing effect, might cause MTs depolymerization in Alzheimer's disease. Mutation of tau gene shows Fronto-temporal dementia with parkinsonism-17. We may be able to explain these diseases as microtubule-instability by using the "endless plasticity amplifying circuit" theory.

S11-1 Chemotactic response of microglia to brain injury; molecular mechanisms of microglial migration and process extension induced by extracellular ATP○Keiko Ohsawa¹, Tomomi Sanagi¹, Yasuko Nakamura¹, Eri Suzuki¹, Yasuhiro Irino², Kazuhide Inoue³, Shinichi Kohsaka¹¹Dept. of Neurochem., Natl. Inst. of Neurosci., ²Div. Lipid Biochem., Grad. Sch. Med. Kobe Univ., Hyogo Japan, ³Dept. Mol. System Pharmacol., Grad. Sch. Pharmac. Sci., Kyusyu Univ., Fukuoka Japan

In response to pathological stimuli microglia rapidly undergo morphological change and migrate toward the lesioned site. These microglial responses are important initial steps for tissue repair of a damaged CNS. Extracellular nucleotides are released or leaked from the stimulated or injured cells and ATP is known to regulate physiological functions of microglia through ionotropic (P2XRs) or metabotropic (P2YRs) purinergic receptors. We have previously shown that ATP induces membrane ruffling and chemotactic migration of microglia through two subtypes of ATP receptors, P2Y12R and P2X4R. The ATP-induced migration requires activation of phosphatidylinositol 3-kinase (PI3K) and phospholipase C (PLC). Recent accumulating studies have demonstrated that ramified microglia protrude rapidly their processes toward the injured site in a brain and that P2Y12R is essential for the chemotactic responses. In order to investigate the signal transduction underlying the process extension, we established a novel culture system using rat primary microglia and three-dimensional (3D) collagen gels. ATP induced process extension of microglia through P2Y12 in 3D gels and the effects of PI3K and PLC inhibitors indicated that PI3K and PLC signaling pathways are involved in the process extension. We also found that P2Y12 mediated integrin $\beta 1$ activation and the integrin $\beta 1$ activation is required for the process extension. Integrin $\beta 1$ was expressed by ramified microglia and the integrin blocking peptide RGD inhibited ADP-induced process extension of microglia in a mouse brain tissue. These results indicate that ATP induces integrin $\beta 1$ activation, which is mediated by intracellular signals downstream of P2Y12, and suggest that the integrin $\beta 1$ activation is able to trigger the extension of microglial processes.

S11-3 Engulfment of axon debris by microglia requires p38 MAPK activity

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Clearance of debris after injuries to the nervous system is a critical step for restoration of the injured neural network. Microglia are thought to be involved in elimination of degenerating neurons and axons in the central nervous system (CNS), presumably restoring a favorable environment after CNS injuries. However, the mechanism underlying debris clearance remains elusive. Here, we establish an in vitro assay system to estimate phagocytosis of axon debris. We employed a Wallerian degeneration model by cutting axons of the cortical explants. The cortical explants were co-cultured with primary microglia or the MG5 microglial cell line. The cortical neurites were then transected. MG5 cells efficiently phagocytosed the debris, whereas primary microglia showed phagocytic activity only when they were activated by lipopolysaccharide or interferon- β . When MG5 cells or primary microglia were co-cultured with degenerated axons, p38 mitogen-activated protein kinase (MAPK) was activated in these cells. Engulfment of axon debris was blocked by the p38 MAPK inhibitor SB203580, indicating that p38 MAPK is required for phagocytic activity. Receptors that recognize dying cells appeared not to be involved in the process of phagocytosis of the axon debris. In addition, the axons undergoing Wallerian degeneration did not release lactate dehydrogenase, suggesting that degeneration of the severed axons and apoptosis may represent two distinct self-destruction programs. We observed regrowth of the severed neurites after axon debris was removed. This finding suggests that axon debris, in addition to myelin debris, is an inhibitory factor for axon regeneration.

S11-2 Microglia and pathological pain

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Neuropathic pain is a highly debilitating pain condition that occurs after nerve damage, such as that induced by bone compression in cancer, diabetes, or physical injury, and is generally resistant to currently available treatments. Such pain is a reflection of the aberrant excitability of dorsal horn neurons following nerve damage. Recent emerging lines of evidence indicate that the enhanced activity of dorsal horn neurons requires a communication with spinal microglia activated by nerve damage. Results of our laboratory have shown that under normal conditions spinal resident microglia express a receptor for the cytokine interferon- γ (IFN- γ R) in a cell-type specific manner and that stimulating this receptor is essential for activation of microglia after nerve injury. IFN- γ R- and nerve injury-mediated microglia activation requires expression of the Src-family tyrosine kinase Lyn in microglia. Activating Lyn causes the upregulation of the ionotropic ATP receptor subtype P2X4 receptor (P2X4R) in microglia. IFN- γ - and nerve injury-stimulated microglia show upregulated expression of P2X4R, and P2X4 deficiency blunts tactile allodynia that follows both IFN- γ administration and nerve injury. Activated microglia also express the G-protein-coupled ATP receptor subtype P2Y12R, and mice lacking the receptor display attenuated neuropathic pain. P2X4R-stimulated microglia release BDNF as a crucial factor to signal to dorsal horn neurons, causing neuronal hyperexcitability. Based on these results, we propose that signaling from microglia activated by nerve injury to dorsal horn neurons plays a fundamental role in the pathogenesis of neuropathic pain and that glial cells are new therapeutic targets.

S11-4 Microglia-aging: Roles of microglial lysosome- and mitochondria-derived reactive oxygen species in brain aging

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Microglia represent the resident mononuclear phagocyte population within the central nervous system. During aging, microglia are activated either chronically or pathologically to influence the neuronal environment. Although studies have noted the morphological and immunophenotypic changes of microglia during aging, little is known about the precise cellular basis of these age-dependent changes in microglia. Recent our studies provide evidence that mitochondrial DNA damages and autophagic dysfunction result in the excessive generation of reactive oxygen species and inflammatory molecules in microglia during aging. Microglia-aging can thus be implicated as the potential causative factor in brain aging. Therefore, the prevention of mitochondrial DNA damage and/or lysosomal-autophagic dysfunction in microglia may be a potentially effective new pharmaceutical intervention against brain aging.

S11-5 The Involvement of Glial Reaction with Peripheral Benzodiazepine Receptor as Biomarker and Functional Molecule in Pathological Development of Alzheimers disease

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Neurodegenerative pathologies-associated glial responses have multiple natures in development of neurodegenerative diseases including Alzheimers disease (AD). The roles of activated glial cells are completely not clarified in development of AD pathologies. Amyloid β protein ($A\beta$) deposits is hallmark of AD pathologies and $A\beta$ -associated glial activation had been suggested to aggravate the functional injury via excessive release of cytokines/chemokines and reactive oxygen species (ROS). However, microglial activation is also considered to contribute to removal of $A\beta$ deposits, and promotion of microglial activity was showed to attenuate the pathological $A\beta$ deposition in several studies. The try of anti-amyloid therapy decreased $A\beta$ pathologies in preclinical experiments and clinical trials via possibly microglial activation mechanism. Imaging for peripheral benzodiazepine receptor (PBR) had been widely accepted as available tool to evaluate microglial activation for long time. However, several recent studies provided evidences that activated astrocytes also expresses considerable PBR and possibly contribute to PBR imaging in vivo. These results promote us to investigate the PBR expression in subpopulations of glial cells (astrocytes and microglia) and their contribution to PBR imaging in various neurodegenerative conditions. Interestingly, PBR was found to be prominently induced in different glial subpopulation dependent on reversibility of injury. Microglial PBR was mainly induced in irreversible neurodegenerative models and astrocytic PBR was largely increased in reversible models and paralleled with the induction of neurotrophin, suggesting PBR expression in microglia and astrocytes act possibly as functional molecule to support these two glial subpopulations to eliminate and repair the injured CNS, respectively, rather than a simple symbol of glial activation. The glial reaction and its possible roles in development of pathologies in AD-like animal models and AD patients are discussed regarding PBR as index of beneficial and detrimental glial response in CNS here. The feasibility of therapeutical strategy via functional modification of glial cells is also investigated.

S12-1 Translational research in psychiatry: dysbindin and schizophrenia

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The dysbindin-1 gene (DTNBP1: dystrobrevin binding protein 1) have been identified as a susceptibility gene for schizophrenia. Recent studies showed significant associations between genetic variants in the dysbindin-1 gene and negative symptoms, IQ, and memory performance, some of which are considered to be intermediate phenotypes of schizophrenia. Dysbindin-1 play a role in glutamatergic and dopaminergic systems related to the pathophysiology of schizophrenia. Down-regulation of endogenous dysbindin-1 reduced the release of glutamate and increased the release of dopamine and surface expression of dopamine D2 receptor and blocked dopamine-induced internalization of DRD2. In studies on postmortem brain tissue, decreased expression levels of dysbindin-1 protein and mRNA were shown in patients with schizophrenia. Chronic treatment of mice with antipsychotics did not affect the expression levels of dysbindin-1 in their brains, suggesting that prior evidence of lower levels of dysbindin-1 protein and mRNA in the postmortem brains of schizophrenics is not likely to be a simple artifact of antemortem drug treatment. These data indicate that the dysbindin-1 gene may confer susceptibility to schizophrenia through reduced expression and that sandy mice lacking dysbindin-1 protein could be a unique animal model of schizophrenia. Sandy mice were less active, heightened anxiety-like response and deficits in social interaction and lower levels of dopamine, but not glutamate, in the cerebral cortex, hippocampus, and hypothalamus. These findings indicate that sandy mice display a number of behavioral abnormalities associated with schizophrenia and suggest that these abnormalities may be mediated by reductions in forebrain dopamine transmission. This new genetic mouse model for schizophrenia could shed light on the etiology of schizophrenia and lead us to new hypotheses, novel diagnostic tools, and more effective therapies for the disorder.

S12-2 Social isolated dominant-negative Disrupted-in-Schizophrenia-1 transgenic mice is useful for a novel animal model of schizophrenia and mood disorders

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There is a "two-hit" hypothesis of psychiatric disorders including schizophrenia (SZ) and mood disorders (MD): genetic vulnerability or problems in the womb set the stage for SZ and MD, after then a second event in adolescence or early adulthood leads to the development of SZ and MD. This "second hit" may be a major life event or episode of stress. DISC1 is a promising susceptibility gene for SZ and MD. The vulnerability in early life to alternations of the rearing environment, including social deprivation, is believed to play a crucial role in the etiopathology of SZ and MD with a presumed neurodevelopmental origin. In present study, we clarified whether social isolated dominant-negative DISC1 transgenic mice under the control of prion protein promoter (PrP-Tg) is useful for a novel animal model of SZ and MD. PrP-Tg mice were isolated or group-housed from 5 to 7 weeks. Isolated PrP-Tg mice placed in a novel field showed hyperlocomotion, and exhibited abnormal behaviors in social interaction, novel object recognition, prepulse inhibition and forced swimming tests, compared with those of group-housed littermate wild-type (Wt) and PrP-Tg mice. Levels of corticosterone in the plasma of isolated PrP-Tg mice were increased compared with those of group-housed Wt and PrP-Tg mice. Contents of dopamine (DA) and expression levels of tyrosine hydroxylase in the frontal cortex (Fc) of isolated PrP-Tg mice were decreased, in comparison with those of group-housed Wt and PrP-Tg mice, although expression levels of DA D2 receptors were increased. These results suggest that disturbance of DISC1 in the Fc as a genetic factor of "first hit" be potential to generate several core endophenotypes underlying SZ and MD. Moreover, the social isolation in adolescence or early adulthood as an environmental factor of "second hit" is getting more and more obvious for development of SZ and MD. We clarified that a social isolated PrP-Tg mouse, which leads to deficits in mesocortical dopaminergic projections and associated behavioral changes relevant to SZ and MD, is useful for a novel animal model of SZ and MD.

S12-3 Aberrant A-to-I RNA editing and ALS

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GluR2, a subunit of AMPA receptors, determines their Ca^{2+} -permeability after adenosine to inosine (A-to-I) conversion at its Q/R site. Deficient GluR2 Q/R site-editing is the disease-specific dysfunction found in the dying motor neurons of sporadic ALS patients, but not in those of patients with familial ALS associated with SOD1 mutation. Thus, this molecular abnormality is likely relevant to pathogenesis of sporadic ALS. A-to-I conversion at this site is catalyzed by the enzyme called adenosine deaminase acting on RNA 2 (ADAR2). Low ADAR2 activity in motor neurons of patients suggests the pathogenic role of ADAR2 underactivity in sporadic ALS. However, whether ADAR2 under-activity induces neuronal death or not has not been demonstrated. To explore this *in vivo*, we generated genetically modified mice in which the ADAR2 gene was conditionally targeted in motor neurons using the Cre-loxP system. These mutant mice displayed progressive motor dysfunction with death of ADAR2-deficient neurons, which expressed only Q/R site-unedited GluR2. In contrast, ADAR2-expressing motor neurons did not decrease in number when the mutant mice died at the age of more than 1 year. Our results indicate that failure of GluR2 Q/R site-editing by ADAR2 is a cause of slow death of motor neurons, and is likely a target for specific therapy for sporadic ALS.

S12-4 $\text{Na}^+/\text{Ca}^{2+}$ exchanger mediates dopaminergic neurodegeneration in the MPTP mouse model of Parkinson's disease○Tetsuaki Nashida¹, Toshiyuki Kawasaki¹, Takeya Otsuki¹, Tatsuya Kitao¹, Yukio Ago¹, Kazuhiro Takuma¹, Toshio Matsuda^{1,2}¹ Lab. Medicinal Pharmacol., Grad. Sch. Pharmaceut. Sci., Osaka Univ, Osaka, Japan, ² Center for Child Mental Dev., Grad. Sch. Med. Osaka Univ, Osaka, Japan

1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) causes dopaminergic neurotoxicity and behavioral impairment in rodents as seen in Parkinson's disease. This toxicity is suggested to be mediated by mitochondrial dysfunction which is accompanied with nitric oxide (NO) and reactive oxygen species (ROS) production via microglial activation (Kawasaki et al., J Pharmacol Exp Ther, 2007; Neuropharmacology, 2008). $\text{Na}^+/\text{Ca}^{2+}$ exchanger (NCX) plays an important role in the regulation of intracellular Ca^{2+} concentrations. We have previously shown that SEA0400, a specific NCX inhibitor, attenuates NO-induced cytotoxicity in neuroblastoma SH-SY5Y cells. Based on our hypothesis that NCX may be involved in oxidative stress, the present study examined the effect of SEA0400 on MPTP-induced dopaminergic neurotoxicity in C57BL/6J mice. MPTP treatment (10 mg/kg x 4 at 2-h intervals) decreased dopamine levels and tyrosine hydroxylase immunoreactivity in the substantia nigra pars compacta, accompanied by the induction of microglial activation and lipid peroxidation. Pretreatment with SEA0400 significantly attenuated MPTP-induced dopaminergic neurotoxicity and lipid peroxidation, but did not affect microglial activation. Furthermore, behavioral analysis showed that SEA0400 improved MPTP-induced loss of motor coordination. In SH-SY5Y cells, an NO donor sodium nitroprusside induced increases in intracellular Ca^{2+} concentrations, ROS production, and apoptosis-like cell death. These effects were inhibited by SEA0400. On the other hand, SEA0400 could not protect against the toxicity of MPP⁺, an active metabolite of MPTP. These results suggest that SEA0400 has an anti-Parkinsonian-like effect and NO-stimulated Ca^{2+} influx via NCX activation induces ROS production, leading to cell death. Thus, the present finding indicates that the regulation of Ca^{2+} homeostasis by NCX may be involved in MPTP-induced neurotoxicity.

S12-5 Glycosylation abnormality and muscular dystrophy -pathomechanism and therapeutic strategy

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Muscular dystrophies are hereditary diseases characterized by the progressive degeneration of skeletal muscle. To date more than 40 genes have been identified whose mutations cause muscular dystrophies. Hypoglycosylation and reduced laminin-binding activity of α -dystroglycan are common characteristics of dystroglycanopathy, which is a group of congenital and limb-girdle muscular dystrophies. We previously identified the genes for Fukuyama congenital muscular dystrophy (FCMD) and muscle-eye-brain disease (MEB), the fukutin protein and the protein POMGnT1, respectively. FCMD, caused by a mutation in the fukutin gene, is a severe form of dystroglycanopathy. A retrotransposon insertion in fukutin is seen in almost all cases of FCMD. We show positive interactions between fukutin and POMGnT1. Fukutin mutations cause mislocalization or reduced activity of POMGnT1. Fukutin may form a protein complex with POMGnT1 and modulate POMGnT1's enzymatic activity. In this talk, pathomechanism and therapeutic strategy for dystroglycanopathies are discussed.

S12-6 Progress in translational research of muscular dystrophy (from lab bench to bedside)

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Duchenne muscular dystrophy (DMD) is a lethal muscle disorder caused by mutations of the DMD gene, which codes a 427 kDa spectrin-like cytoskeletal protein, dystrophin. Dystrophin is localized just beneath the sarcolemma, and binds F-actin via its N-terminal domain and beta-dystroglycan via its cysteine-rich domain, forming a vital link between the actin cytoskeleton and extracellular matrix in skeletal and cardiac muscle. The lack of dystrophin, accompanied by loss of dystrophin-binding proteins, weakens the muscle membrane, leading to degeneration of myofibers. There is no effective treatment for the disease at present, but exon skipping by antisense oligonucleotides is a novel method to restore the reading frame of the mutated DMD gene, and rescue dystrophin expression. We recently reported that systemic delivery of Morpholino antisense oligonucleotides targeting exon 6 and 8 of the canine DMD gene, efficiently recovered functional dystrophin at the sarcolemma of dystrophic dogs, CXMDJ and improved motor ability of affected dogs without serious side effects (Yokota et al, Ann Neurol, in press). To optimize therapeutic antisense Morpholinos for more frequent mutations of the DMD gene, we designed 14 kinds of antisense Morpholinos targeting exon 51 of the mouse DMD gene, and injected them separately or in combination into the muscles of mdx52 mice, in which exon 52 has been deleted by a gene targeting technique. A combination of two Morpholinos showed an excellent restoration of sarcolemmal dystrophin in injected muscle. We, therefore, intravenously injected them into mdx52 mice at 7 times weekly. Two weeks after the final injection, dystrophin was expressed at the sarcolemma throughout the body, with an average of about 10-50% of normal levels. This was accompanied by amelioration of dystrophic pathology, and improvement of contractile force of EDL, grip power test, and treadmill performance. This study provides a proof of concept for exon 51 skipping in the DMD animal model and that can be applicable to up to 15% of DMD deletion patients.

S13-1 Neural mechanisms of social behaviors in primates

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Schizophrenic patients display various behavioral impairments; disturbances in social skills (e.g., avoiding social contact, neglecting a surrounding environment, social isolation) are the most pervasive aspects of schizophrenic patients. However, neural mechanisms of these social deficits in schizophrenia are still unclear. To establish a primate animal model of schizophrenia with negative symptoms, behavioral effects of chronic phencyclidine (PCP) and additional acute methamphetamine (MAP) administration were investigated using 6 monkeys. The monkeys were divided into 2 groups; control (n=3) and PCP groups (n=3). The PCP group received chronic PCP treatment (0.3 mg/kg/day, i.m.) for more than 7 months. The PCP monkeys occasionally received additional acute MAP treatment (2.0 mg/kg, i.m.) (PCP+MAP group, n=3) only on the day for the behavioral tests. For a behavioral analysis, 3 linked cages (300 cm long, 130 cm wide, 160 cm high) were used. The monkeys were individually put in the side cages, and were left in the cage for 10 min. Then, the 2 partitions between the monkeys were removed for 60 min. The social behaviors of the monkeys were recorded by the CCD camera on the ceiling, and the video images were automatically analyzed online using a computer. The results indicated that chronic PCP treatment induced a significant decrease in all categories of the social behaviors, and that the chronic PCP monkeys also spent less time in proximity to other monkeys than the control monkeys. Acute MAP injection to the chronic PCP monkeys exacerbated behavioral effects of PCP. The results suggest that these monkeys can be used as a primate animal model of schizophrenia with negative symptoms.

S13-3 Schizophrenia animal models established with ErbB receptor ligands

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Epidermal growth factor (EGF) and neuregulins bind to ErbB1-4 receptors and regulate placenta and brain development. When the blood brain barrier is not established, circulating factors permeate immature brain and perturb its development. Our latest studies on rodents indicate that neonatal exposure to EGF or neuregulin sensitizes ErbB signaling and impairs neuronal development, leading to neurobehavioral deficits. In agreement, intraventricular injection of EGF mimicked the neonatal treatment whereas ErbB inhibitors ameliorate behavioral deficits of this model and other models for schizophrenia. Similarly, administering EGF to a cynomolgus monkey neonate in 2002 led to various abnormal behaviors after adolescence in 2008. These findings suggest that endogenous EGF or neuregulins circulating in the pre- and peri-natal periphery has significant impact on later behavioral development of primates.

S13-2 Methods for assessing marmoset behavior

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To understand the mechanisms of mental and nervous disease and develop the cure for the disease, primate models are indispensable. Because of this high reproductive power, common marmoset (*Callithrix jacchus*) is almost one primate species suitable for developmental engineering studies. Therefore, we can develop marmoset models for mental and nervous disease using developmental engineering techniques. On the other hand, so far there is no good battery of testing various abilities of marmosets, including motor, perceptual, and cognitive abilities. To assess their abilities, we should develop special equipment suitable for marmosets. In addition, unlike macaque monkeys, marmosets are so nervous that we need a long time for them to get used to new environments, such as an experimental room, a cage, an apparatus, etc. We believe that we should assess their abilities in their home cages if we would like to get behavioral data effectively. In this talk, I introduce our new attempts to assess these abilities of marmosets.

S13-4 Application of recombinant viral vectors to primate brain research: Gene therapy for Parkinson disease

○Masahiko Takada

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Recently, we have made an attempt to develop genetically manipulated monkeys by injecting a recombinant viral vector into a given brain region. For example, the use of viral vectors is essential for the establishment of gene therapy for neurological disorders. In this talk, data will be presented concerning the gene therapy for Parkinson disease. It is well known that Parkinson disease is caused by progressive loss of nigrostriatal dopamine neurons. A subpopulation of dopaminergic cells that resides in the dorsal tier of the substantia nigra pars compacta is known to express calbindin (Cb), a calcium-binding protein. It has been considered that these Cb-containing dopaminergic cells are selectively less vulnerable to degeneration in Parkinson disease. In the present study, we tested the hypothesis that parkinsonian motor signs may be prevented by recruitment of Cb into nigral dopaminergic cells that do not normally contain it. Two types of recombinant viral vectors expressing Cb were prepared for gene delivery. An adenoviral vector was injected unilaterally into the striatum of macaque monkeys to be delivered to the dopaminergic cells via retrograde axonal transport, while an HIV-1-based lentiviral vector was injected into the nigra directly. After 2-3 weeks postinjection periods, the Parkinson disease-inducing agent, MPTP, was systemically administered to the monkeys. Our behavioral analysis showed that a battery of motor impairments occurred primarily in the limbs ipsilateral to Cb recruitment when a cumulative dose of MPTP exceeded threshold for their bilateral onset. Furthermore, our immunohistochemical analysis revealed that the expression level of tyrosine hydroxylase in the nigrostriatal system was preserved to some extent on the Cb-recruited side, whereas alpha-synuclein was preferentially expressed in dopaminergic cells on the control side. The present results indicate that Cb recruitment into nigral dopaminergic cells by gene delivery with recombinant viral vectors may provide an effective therapeutic approach to Parkinson disease.

S13-5 Towards generation of transgenic nonhuman primates○Erika Sasaki¹, Hideyuki Okano²¹ Marmoset Research Department, Central Institute for Experimental Animals, ² Department of Physiology, Keio University School of Medicine

Since human embryonic stem (ES) cell lines and human induced pluripotent stem (iPS) cell lines were established, both cell lines have shown their multipotency in vitro and offered much hope by promising to greatly extend the numbers and range of patients who could benefit from transplants. Before differentiated these stem cells can be used in clinical applications, the short-term and long-term safety and efficacy of the stem cells therapy must be thoroughly examined. However, in vivo experiments are not appropriate for human from the ethical standpoint. Thus, it is clear that nonhuman primate experimental animals that mimic the human being in various aspects are essential for further advances in biomedical research. The common marmoset (*Callithrix jacchus*) is a new world primate species with reproductive characteristics that are appropriate for ES cell studies. More specifically, these animals are small (weighing about 350-400 g), they have a short gestation period (about 144 days), and reach sexual maturity at 12-18 months. Since 2005, we have established several CMES cell lines and these cell lines showed cellular biological and biochemical characteristics similar to those of human ES cells. A lot of invaluable information concerning the function of gene products and regulatory gene networks has been obtained at the in vivo level by taking advantage of genetically modified mice such as transgenic or gene-targeted mice. However, to assess the safety and efficacy of regenerative medicine using stem cells or gene therapy, genetically modified primates would be a more powerful human disease model for preclinical research. Toward a generation transgenic marmoset, we establish several techniques of reproductive technologies and research tools. Transgenic primates would be a powerful tool for developing new animal models for the assessment of the mechanisms of human diseases and the development of new stem cell therapies.

S14-1 Molecular structure underlying neurotransmitter release from the active zone

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The active zone (AZ), a slightly electron-dense region just beneath the presynaptic plasma membrane, is a specialized site where neurotransmitter release occurs in a precisely-regulated manner. The protein component of the AZ includes CAST/ERC2 and its family member ELKS, Bassoon, Piccolo/Aezonin, RIM1, and Munc13-1. Notably, CAST directly interacts with CAST itself, ELKS, RIM1, Bassoon, and Piccolo, forming a large molecular complex. Recently, we have reported that SAD kinase, associated with synaptic vesicles and the cytomatrix at the AZ, directly phosphorylates RIM1 implicated in neurotransmitter release. Here, in addition to RIM1, we identify Bassoon and Piccolo as potential substrates for SAD. Both the proteins contain at least three potential phosphorylation sites by SAD. Moreover, we find that SAD directly phosphorylates CAST in vitro and in vivo. I will present a phosphorylation network among the AZ proteins mediated by SAD, and discuss its impact on molecular mechanisms underlying the AZ structure and function.

S14-2 Imaging of excitatory and inhibitory synaptic responses in the lateral amygdala using a voltage sensitive dye○Yuko Sekino¹¹ Div. of Neuronal Network, Inst. Med. Sci., University of Tokyo, Tokyo, Japan, ² CREST, JST, Saitama, Japan

Membrane potential changes of neurons result from processing of information by various extra- and intracellular signaling molecules. To understand the principles of information processing in the brain, simultaneous monitoring of chemical signaling and electrical activity with high temporal and spatial resolution is required. Optical recording of membrane potential changes using voltage-sensitive dyes overcomes the lack of spatial information in conventional electrophysiological measurements. I used a voltage sensitive dye, Di-ANEPPS, to monitor membrane potential changes in amygdala slice preparation of mice in response to stimulation of the external capsule inputs from the cortex. Long-lasting hyperpolarizations (>400 ms; LLH signals) were observed to follow depolarizing synaptic responses in the lateral amygdala. Amplitudes of LLH signals depended on stimulus intensity. LLH signals were completely blocked by a GABA_B receptor antagonist. Analysis of the spatial and temporal patterns of optical signals reveals how excitation and inhibition connections work in the lateral amygdala. Optical recording of membrane potentials is a powerful tool for simultaneous monitoring of chemical and electrical signaling in brain tissue.

S14-3 Glutamate release visualized with glutamate optical sensor

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Glutamate is a major excitatory neurotransmitter in central nervous system. To understand how glutamate is released from presynaptic terminals of excitatory central synapses, we have developed an imaging technique for directly visualizing glutamate release. The technique relies on a fluorescent probe named EOS (glutamate optical sensor) which is a hybrid type fluorescent sensor consisting of two components: a glutamate binding protein derived from AMPA type glutamate receptor subunit, GluR1, and a small fluorescent dye. So far we have systematically tested hundreds of candidate probes by virtue of a powerful high-throughput screening system to obtain high performance probes. With one of the best probes, EOS3, we successfully imaged glutamate released from individual single synaptic terminals. The single synapse glutamate imaging combined with a binomial statistics based on Katz's quantal hypothesis unveiled nature of vesicular release at individual presynaptic terminals. Contrary to a popular belief that a small synapse typically found in central nervous system releases only one vesicle in response to a single action potential, we found that the individual synapses can release multiple vesicles at a time. We also found that the "readily releasable" vesicle pool, which is defined as a fraction of vesicle pools immediately released by a brief application of trains of high frequency stimuli, is not actually release ready; the maximal number of vesicles released upon a single action potential was estimated to be smaller than the number of readily releasable vesicles. Analysis of glutamate release upon paired pulse stimuli with a short interstimulus interval suggests that the apparent unwillingness of a part of "release ready" vesicles is not due to heterogeneity in intrinsic release probability of the vesicles. Rather we propose a new model for presynaptic vesicular release mechanism: a single presynaptic terminal has a limited number of "laughing pads" for vesicle release and the "readily releasable" vesicles immediately compete for the launching pads. This mechanism may exert modulatory effects on individual synapses by changing the efficiency of synaptic transmission in response to temporal firing patterns.

S14-4 GABA imaging and transient GABA distribution in the developing cerebellar cortex

○Sachiko Yoshida

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GABA (γ -amino butyric acid) and glutamate are known to play important roles as modulators in the survival and development of cerebellar neurons. In the developing cerebellar cortex, GABA acts as an excitatory neurotransmitter, and could induce cell proliferation and differentiation, although GABAergic neurons are not developed yet.

Recently we developed a new system for released GABA detection using the enzyme-linked assay of GABase, GABA disassembly enzyme, and evanescent light excitation by UV-LED. This method was useful for specifically observation of spatio-temporal GABA release without confusion of stored transmitters and UV damage. This imaging technique was used to monitor the reaction between GABase and NADP⁺ (nicotinamide adenine diphosphonucleotide), because the enzyme oxydizes released GABA, generating one NADPH molecule from one GABA, respectively. NADPH emit 480 nm fluorescence after excitation at 365 nm.

GABA was released from the developing cerebellar cortex, and the level of GABA release in the first postnatal week was higher than after 2 weeks or later. After postnatal day 8, GABA distribution was observed in the layers of GAD-expressing neurons. It was distributed in both the molecular layer containing many GABAergic neurons, and the upper the internal granular layer (IGL) corresponding to Golgi cells. In contrast, during the first postnatal week GABA distribution was observed even in the EGL. In the EGL, there were only a few GAD-expressing neurons, but many Bergmann glia develop. GABA release in the EGL was eliminated after P7. GABA might be transported in the developing EGL.

Glutamate release from granule cells in the pre-migratory zone was increased with 100 μ M GABA application. This GABA-induced glutamate release (GIGR) was observed from P4 to P6, although it was eliminated after P7. GIGR was depended not by [Ca²⁺] condition, but [Na⁺] condition. Transient GABA would be required granule cell excitation and differentiation.

S14-5 Imaging Activity-Dependent Secretion of BDNF

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Brain-derived neurotrophic factor (BDNF) plays important regulatory functions in synapse development and plasticity. Although BDNF acts on both pre- and postsynaptic cells, whether neuronal activity can trigger BDNF secretion from axons and dendrites with equal efficacy is unclear. Using BDNF fused with pH-sensitive green fluorescent protein (pHluorin) to visualize BDNF secretion, we found that BDNF-containing vesicles exhibited markedly different activity-dependent fusion properties at the axon and dendrite of cultured hippocampal neurons. Brief spiking activity triggered partial fusion and retrieval of vesicles with rare BDNF secretion at the axon but full vesicle fusion and substantial BDNF secretion at the dendrite, although prolonged high-frequency or burst spiking activities could induce full fusion and BDNF secretion at the axon. Thus activity-dependent axonal secretion of BDNF is highly restricted, and normal neural activity predominantly induces BDNF secretion from dendrites, consistent with the BDNF function as a retrograde factor. BDNF fused with pHluorin serves as an excellent reporter for real-time monitoring of exocytic events of BDNF-containing vesicles in neurons.

O01-1 Transcriptional and post-transcriptional regulations of P2X₄ receptor upregulation in fibronectin-stimulated microglia

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Microglia are resident immune cells in the CNS that become activated and produce pro-inflammatory and neurotrophic factors upon activation of various cell-surface receptors. The P2X₄ receptor (P2X₄R) is a subtype of the purinergic ion-channel receptors expressed in microglia. P2X₄R expression is upregulated under inflammatory or neurodegenerative conditions and this upregulation is implicated in disease pathology. However, the molecular mechanism underlying upregulation of P2X₄R in microglia remains unknown. In the present study, we investigated the intracellular signal transduction pathway that promotes P2X₄R expression in microglia in response to fibronectin, an extracellular matrix protein that has previously been shown to stimulate P2X₄R expression. We found that in fibronectin-stimulated microglia, activation of phosphatidylinositol 3-kinase (PI3K)-Akt and mitogen-activated protein kinase kinase (MAPK kinase, MEK)-extracellular signal-regulated kinase (ERK) signaling cascades occurred divergently downstream of Src-family kinases (SFKs). Pharmacological interference of PI3K-Akt signaling inhibited fibronectin-induced P2X₄R gene expression. Activation of PI3K-Akt signaling resulted in a decrease in the protein level of the transcription factor p53 via mouse double minute 2 (MDM2), an effect that was prevented by MG-132, an inhibitor of the proteasome. In microglia pretreated with MG-132, fibronectin failed to upregulate P2X₄R expression. Conversely, an inhibitor of p53 caused increased expression of P2X₄R, implying a negative regulatory role of p53. On the other hand, inhibiting MEK-ERK signaling activated by fibronectin suppressed an increase in P2X₄R protein but, interestingly, did not affect the level of P2X₄R mRNA. We also found that fibronectin stimulation resulted in the activation of the translational factor eIF4E via MAPK-interacting protein kinase-1 (MNK1) in a MEK-ERK signaling-dependent manner, and an MNK1 inhibitor attenuated the increase in P2X₄R protein. Together, these results suggest that the PI3K-Akt and MEK-ERK signaling cascades have distinct roles in the upregulation of P2X₄R expression in microglia at transcriptional and post-transcriptional levels, respectively.

O01-3 Involvement of spinal microglia in tactile allodynia caused by intrathecal administration of PDGF

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Tactile allodynia is pain hypersensitivity evoked by innocuous stimuli that occurs after peripheral nerve injury and is a hallmark symptom of neuropathic pain. Underlying mechanism of such abnormal pain sensation remains to be fully elucidated. Recent accumulating evidence indicates that spinal microglia become activated after peripheral nerve injury and play a crucial role in the pathogenesis of tactile allodynia. However, a signaling molecule from damaged neurons to microglia involved in this pain has yet not been determined. In the present study, we found that in naive rats intrathecal delivery of platelet-derived growth factor (PDGF), a factor that has been reported to be expressed in dorsal horn neurons, induced a long-lasting allodynic behavior. Following PDGF administration, the immunofluorescence of phosphorylated PDGF receptor β (p-PDGFR β) was markedly increased in the dorsal horn compared with vehicle controls, and, interestingly, almost all p-PDGFR β -positive cells were double-labeled with the microglia marker OX-42. Furthermore, intrathecally administered PDGF transformed microglia into modest activated form, and the PDGF induced tactile allodynia was attenuated by intrathecal administration of minocycline. These indicate that spinal microglia critically contribute to PDGF-induced tactile allodynia. In the dorsal horn of an animal model of neuropathic pain, the enhanced immunofluorescence of p-PDGFR β was also observed exclusively in microglia in the ipsilateral side of nerve injury. Together, our findings suggest that PDGF may be a signaling molecule from dorsal horn neurons to microglia and that microglial PDGF signaling may be involved in the pathogenesis of neuropathic pain.

O01-2 Analysis of PLD4 in amoeboid microglia

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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. Previously, we reported that a new member of PLD superfamily, called PLD4, is expressed in amoeboid microglia in the early postnatal mouse cerebellar white matter. PLD4-positive amoeboid microglia appears around postnatal day 0 (P0). The number of amoeboid microglia peaks at P7 and decreases to a very low level until P21 in the cerebellar white matter. During this period, myelination starts to become active with the development of cerebellum. At present, the role of amoeboid microglia in the developing white matter is unclear and the function of PLD4 is totally unknown. In this study, to clarify the function of PLD4 in the amoeboid microglia, we analyzed the expression of PLD4 in situ and in vitro. The immunohistochemical analysis of PLD4 in the cerebellum of the demyelinating model mice, myelin proteolipid protein (PLP)-transgenic mice, revealed that PLD4 was expressed in the amoeboid microglia in the pathological conditions as well as in the developmental stages. In the analysis using cultured microglial cell line (MG6), the expression of PLD4 was upregulated in the MG6 activated by lipopolysaccharide (LPS). PLD4 was primarily detected in the nucleoplasm of MG6. Furthermore, in the analysis of phagocytosis of LPS-stimulated MG6 adding BioParticles, PLD4 were colocalized with phagosomes containing BioParticles. These results suggest that the increased PLD4 in activation process may be involved in phagocytosis of amoeboid microglia in the developmental stages and the pathological conditions of white matter.

O01-4 Functional expression of clock genes in microglia

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Recent studies have demonstrated the possible functional expression of several clock genes in peripheral tissues. We have attempted to demonstrate the possible expression of particular clock genes in microglial cells in this study. Microglial cells were prepared from whole brains of 1-day-old ddY mice, followed by culture in DMEM/F12 medium containing FBS for 2 weeks with medium change twice a week and subsequent aspiration of culture medium containing detached cells with trypsin DMEM/F12 (1:4) solution. In primary cultured microglia cells highly positive to isolectin-b4 staining, no marked expression was seen for immunoreactive MAP2 or GFAP on immunohistochemistry. Reverse transcription polymerase chain reaction analysis revealed mRNA expression of different clock genes. These included Per1, Per2, Per3, Cry1, Cry2, Dec1, Dec2, DBP, Bmal1, NPAS2 and Clock. In primary microglia exposed to 1 mM ATP for a period up to 6 h, a significant increase was transiently seen in Per1 mRNA expression at 3 h of exposure. In the mouse microglial cell line BV-2 cells, transfection with both Bmal1 and NPAS2 expression vectors led to a significant increase in IL-6 mRNA expression, but not in mRNA for TNF α , IL-1 β , BDNF, TGF β or iNOS. However, further transfection with a Per1 expression vector significantly prevented the increase in IL-6 mRNA expression by both Bmal1 and NPAS2 in BV-2 cells. These results suggest that clock genes may be functionally expressed by microglial cells to modulate IL-6 mRNA expression.

001-5 Role of IL-1 in lipopolysaccharide-induced learning and memory deficits

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We have designed an animal model of learning and memory impairment based on the activation of microglia. Injection of lipopolysaccharide (LPS) into the CA1 region of the mouse hippocampus resulted in the increased production of inflammatory cytokines, such as interleukin (IL)-1 β . Immunostaining for IL-1 β revealed an increase in the signal 6 hr after LPS injection. Immunopositive cells for IL-1 β were co-localized with those immunopositive for CD11b or Iba1. In wild-type mice, subacute LPS treatment daily for 5 days caused the long-term activation of microglia and resulted in learning and memory deficits, as evaluated a step-through passive avoidance test and novel object recognition test. Gene expression of NMDA receptor NR1 and NR2A subunits was also decreased by the LPS treatment. In contrast, activation of microglia, with resultant behavioral deficits, was not observed when knockout mice lacking IL-1 α and β received subacute LPS treatment. Moreover, there was little, if any, change in gene expression of NR1 and NR2A subunits in these mice. TNF α knockout mice and IL-6 knockout mice, however, gave similar results to wild-type animals. These findings suggest that the expression of IL-1 plays an important role in the activation of microglia, which in turn leads to functional deficits in learning and memory.

002-1 Modulation of tau phosphorylation on Ser/Pro or Thr/Pro motif catalyzed by multiple proline-directed protein kinases by cyclic AMP-dependent protein kinase A

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Microtubule (MT) associating protein tau stabilizes MT, and tau-MT interaction is controlled by phosphorylation of tau. Two major tau kinases, glycogen synthase kinase-3 β (GSK3 β) and cyclin-dependent kinase 5 (CDK5), co-localize with MT. Tau, MT-associated kinases and adaptor proteins such as 14-3-3 are known to regulate MT remodeling as a tau phosphorylation protein complex (TPPC). In contrast, cyclic AMP-dependent protein kinase A (PKA) resides in cytosolic compartment, and phosphorylates tau causing an inhibition of MT-assembly and stimulation of assembly of paired helical filaments assembly.

To clarify physiological regulation of tau phosphorylation by TPPC, we set up the an *in-vitro* kinase assay by CDK5, GSK3 β and PKA using the longest isoform of human tau (htau40) and recombinant p35-CDK5 and recombinant human GSK3 β . Phosphorylation was analyzed by Western blot. We found preincubation of PKA for long term incubation evoked striking enhancement of tau phosphorylation catalyzed by GSK3 β at the most of the Ser/Pro or Thr/Pro site of the proline-rich domain (195-209), except for Ser202, while activity of p35-CDK5 was inhibited by preincubation of PKA. Differential modulatory action of PKA preincubation on TPPC may play physiological roles in MT remodeling.

002-2 Analysis of phosphorylation states and identification of a novel phosphorylation site of Cdk5 activator p35 by phos-tag SDS-PAGE

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Phosphorylation is a major post-translational modification widely used in regulation of many cellular processes. Therefore, phosphorylation has been an extensively studied research subject. Cdk5 is a proline-directed serine/threonine kinase regulating various neuronal activities such as neuronal migration, neuronal cell death, spine formation and synaptic activity. Cdk5 is activated by activation subunit p35 and the Cdk5 activity is regulated by proteolysis of p35. Phosphorylation of p35 regulates its proteolysis, degradation by proteasome and cleavage by calpain, indicating that phosphorylation of p35 is critical for regulation of the Cdk5 activity. Phosphorylation site-specific antibodies are often used to know the phosphorylation states of proteins. However, to see the total phosphorylation states we have to use a combination of antibodies to respective phosphorylation sites. Here we report the use of phos-tag SDS-PAGE to reveal the phosphorylation states of p35. Phos-tag is dinuclear metal complex and acts as a phosphate binding tag. By applying phos-tag to polyacrylamide gel, electrophoretic mobility of phosphorylated proteins was delayed in a phosphorylation site-specific manner by being trapped in gel. When p35 was expressed in Cos-7 cells, coexpression with Cdk5 shifted p35 upward, confirming that p35 is phosphorylated by Cdk5. Analysis with alanine mutants turned out usefulness of this method to analyze the phosphorylation states in neuronal cells. Using this method, we found a novel phosphorylation site at Ser91 and the phosphorylation was increased in neurons by treatment of NMDA. The fact that CAMKII phosphorylated Ser91 suggests involvement of Ser91 phosphorylation in NMDA-evoked synaptic activity. These results demonstrate that phos-tag SDS-PAGE is the useful technique to analyze the phosphorylation states of p35, and could be applied to other phospho-proteins.

O02-3 Calcium-induced and proteasome-dependent degradation of Cdk5 activator p35

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Cyclin-dependent kinase 5 (Cdk5) is a brain specific serine/threonine kinase activated by binding to its activation subunit p35 or p39. p35 is a quite unstable protein in neurons, degraded by ubiquitin/proteasome pathway under physiological conditions. The degradation of p35 is involved in synaptic plasticity such as long term potentiation and long term depression. On the other hand, p35 is cleaved to p25, a more stable fragment of p35, by calcium-dependent cysteine protease calpain under pathological conditions. As a result of the cleavage, Cdk5 is hyperactivated and is thought to induce neuronal cell death. Thus the regulation of p35 proteolysis is quite important to elucidate the physiological and pathological functions of Cdk5 in neurons. We used calpastatin transgenic (Tg) or knockout (KO) mice brain extracts to study the cleavage of p35 to p25 by calpain. Calpastatin is an endogenous inhibitor specific for calpain. We found that the cleavage of p35 to p25 proceeded more rapidly in the KO brain extract than wild type (WT) brain extract in the presence of Ca^{2+} . In contrast, there was no cleavage of p35 in Tg. These results suggest that the cleavage of p35 to p25 by calpain is controlled by the amount of calpastatin in neurons. Interestingly, p35 was degraded without the cleavage to p25 in the Tg mouse brain extract when the extracts were incubated in the presence of Ca^{2+} . This degradation was suppressed by proteasome inhibitors MG132 and epoxomicin but not other protease inhibitors including calpain inhibitor 1 or 4, protease inhibitor cocktail, z-VAD-FMK, chloroquine or puromycin, suggesting that there is a Ca^{2+} -activated degradation of p35 in the brain extract. The Ca^{2+} -dependent proteasomal degradation of p35 was observed in primary neurons when neurons were treated with Ca^{2+} -ionophore in the presence of calpain inhibitor. We are now studying how Ca^{2+} stimulates the proteasome-dependent degradation of p35.

O02-4 Proteolysis of Cdk5 activators p35 and p39 on membranes

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Cyclin-dependent kinases (Cdk5) are proline-directed Ser/Thr protein kinases that regulate cell-cycle progression in proliferating cells. Cdk5 is a member of the Cdk family but unique in its expression in postmitotic neurons. Cdk5 is activated when it binds to a neuron-specific activator p35 or p39, and functions in a variety of neuronal activities unrelated to cell cycle progression. p35 and p39 are short life proteins degraded by proteasome in healthy neurons but cleaved to p25 and p29, respectively, by calpain in pathological neurons. Thus, their metabolism is an important determinant for neuronal functions and survival. However, how their proteolysis is regulated in cells is not fully understood. Further, compared to p35/Cdk5, only a little is known for kinase activity and function of p39/Cdk5. Here, we studied the intracellular places where p35 and p39 are degraded or cleaved. First, we asked for degradation of p35 and p39 in neurons. We found that p39 was degraded slower than p35 in cerebellar granule neurons although p39 was degraded by proteasome as was p35. p35 and p39 are myristoylated proteins bound to membranes. To see whether the membrane binding affects the degradation of p35 and p39, we examined the degradation of their non-myristoylation mutant (G2A) in HEK293 cells. G2A mutants were expressed more and degraded slower than wild type p35 or p39. These results suggest that membrane-association promotes the rapid turnover of p35 and p39. p25 and p29, the C-terminal two-thirds of p35 and p39, are stable fragments. To determine which of myristoylation or the N-terminal p10 region is more important for rapid degradation, we constructed N7-p25 and N7-p29, in which the N-terminal seven amino acids of p35 and p39 containing the myristoylation consensus sequence were tagged to p29 and p25, respectively. In contrast to p25 or p29, N7-p25 or N7-p29 was degraded rapidly, indicating that myristoylation is a primary factor conferring the short life to p35 and p39. These results indicate that the proteolysis of p35 and p39 is regulated by their association on membranes.

O02-5 Expression of protein tyrosine phosphatase receptor-type O (PTPRO) protein in the interneurons of adult mouse olfactory bulb

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PTPRO is one of the type III receptor tyrosine phosphatases that have a single catalytic domain in their cytoplasmic region and fibronectin type III-like domains in their extracellular region. Previous studies have shown that its mRNA is expressed in the brain, peripheral nerve and renal glomeruli in mice. However, expression of PTPRO protein during development of mammalian brain has not been examined in detail. To clarify its expression, we generated a monoclonal antibody against the extracellular region of mouse PTPRO and examined the distribution of mouse PTPRO protein in brain by immunohistochemistry. In embryonic and newborn mice, PTPRO protein was expressed in various regions of brain, including olfactory bulb, cerebral cortex, hippocampus and tectum. Postnatal week 2, its expression was reduced except in olfactory bulb, olfactory tubercle and hippocampus. In adult mice, high expression of PTPRO protein was observed only in olfactory bulb and olfactory tubercle. In olfactory bulb of adult mice, PTPRO protein was expressed in GAD67-, tyrosine hydroxylase- or calretinin-positive olfactory interneurons, while its expression was undetectable in mitral cells and glial cells. In addition, PTPRO protein was predominantly localized to dendrites and was partly localized to synapses of olfactory interneurons. Our results suggest that PTPRO is expressed in the interneurons of the adult mice olfactory bulb. PTPRO might participate in regulation of development and function of interneurons in olfactory bulb.

O02-6 Regulation of stress response in the brain by tyrosine phosphorylation signal

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Exposure to severe stress often results in neuronal changes that are implicated in stress-related disorders such as depression. The molecular mechanisms underlying the response of the brain to stress remain largely unknown. SHPS-1 is a transmembrane protein predominantly expressed in neurons. The cytoplasmic region of SHPS-1, which is tyrosine-phosphorylated by ligand-activated receptor tyrosine kinases or Src family kinases, binds and activates a tyrosine phosphatase, SHP-2. We found that mice bearing mutant SHPS-1, that lacks most of its cytoplasmic region, manifested increased immobility in forced swim test (FST). Furthermore, FST induced marked tyrosine phosphorylation of SHPS-1 and its association with SHP-2 in the hippocampus of wild-type mice. We also found that CD47, a ligand for SHPS-1, is essential for FST-induced tyrosine phosphorylation of SHPS-1, while CD47-deficient mice manifested increased immobility in the FST. Our results suggest that the tyrosine phosphorylation signal is a novel molecular mechanism, which regulates the stress response in the brain.

O03-1 A new transfection and expression technology for neural cells - Gene expression by the BmNPV baculovirus system -

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The transfection of post-mitotic cells, especially primary cortical and hippocampal neurons, has proven for the most part to be inefficient. Methods such as electroporation, cationic lipids and micro-injection are often toxic to the cell and rarely give a enough transfection efficiency. Virus transfection methods using modified viruses such as adenovirus and lentivirus have been shown to be more efficient but the procedures need the complicated formalities and the safety process for infections. The insect virus (baculovirus) system, particularly "silkworm-virus", BmNPV (*Bombix mori* polyhedrosis virus) is well known as the most effective protein-expression techniques. Baculovirus is non-cytopathic and safe, but provides a robust cellular delivery in a wide range of cells, including many neuronal cells. Expression levels can be easily adjusted by changing the dose of virus. We utilized and evaluated this newly modified virus infection systems. We made many fluorescent proteins fusion constructs to analyze dynamic cellular processes with precise spatial and temporal resolution. In this study, we also show that the one of our applications of this technology to analyze the membrane glycoprotein M6a. M6a is a member of the proteolipid protein (PLP) family of tetraspan membrane proteins and mainly expressed in neurons. Overexpression of M6a in cultured neurons promoted neurite outgrowth and the formation of filopodial protrusions. However, the mechanisms of this protein are unknown. The various constructs of M6a were expressed by the BmNPV techniques in the undercoated membrane regions. Cross-linking and aggregation of these M6a-intracellular domains from the extracellular mechanical signaling showed the role of scaffold-formation activities.

O03-3 Iron-related genes expressed by neurons

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Iron is believed to play a dual role as an active center of the electron transfer system in mitochondria and as a cytotoxin through generation of reactive oxygen radicals in different eukaryotic cells. In recent studies, iron has been shown to be drastically accumulated in particular brain regions in patients suffering from a variety of neurodegenerative diseases such as Parkinsons disease. In this study, we have evaluated expression profiles of different genes related to iron mobilization across plasma membranes in neurons. RT-PCR analysis clearly revealed marked expression of mRNA for ferritin, transferrin (Tf) and transferrin receptor-1 (TfR1), but not for hepcidin, ferroportin or TfR2, in fetal mouse neocortical neurons cultured for 8 days. In the neuronal cell line Neuro2A cells cultured with retinoic acid (RA), neurite outgrowth was clearly seen together with a significant increase in mRNA expression of TfR1. On immunocytochemistry a number of cells were immunoreactive for TfR1 in Neuro2A cells treated with RA. In mouse embryonal carcinoma P19 cells endowed to proliferate for self-replication and differentiate into neurons and astroglia, exposure to RA led to neurite outgrowth toward neuronal differentiation along with a significant increase in TfR1 mRNA expression within 8 days in culture. However, TfR1 mRNA expression was significantly decreased in response to subsequent differentiation into an astroglial lineage in P19 cells previously cultured in the presence of RA within 16 days. These results suggest that TfR1 mRNA would be highly expressed in neurons rather than astroglia in the brain.

O03-2 Regulated expression of MAGE family genes during neural development

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Necdin is a MAGE (melanoma antigen) family protein that contributes to neuronal differentiation and survival. In contrast to mammals that have >30 MAGE family members, non-mammalian species such as *Drosophila* and chicken have only one MAGE gene, which encodes a protein that is functionally similar to necdin. MAGE family genes are divided into two groups (types I and II) based on their sequence similarities. Type I MAGE genes including MAGE-A, B, and C subfamilies, which encode tumor-rejection antigens, are expressed only in male germ cells and various cancer cells, whereas type II MAGE genes (e.g., necdin, necdin-like 2, MAGE-D1) are expressed in differentiated neurons. Although type II MAGE proteins are likely to be involved in neuronal life-and-death decisions, the roles of type I MAGE family in neuronal development remain unknown. In the present study, we examined the expression profiles of type I MAGE family genes during mouse brain development by RT-PCR-based analyses. Necdin was expressed abundantly in the brain at embryonic days (E) 12.5 and 14.5, whereas most of the type I MAGE (MAGE-a and b subfamilies) genes were expressed only at E12.5, suggesting that type I MAGE genes are expressed in neural stem cells at early stages of brain development. MAGE-a subfamily mRNAs were also detected in cultured neural stem cells prepared from the ganglionic eminences. Remarkably, expression of MAGE-a subfamily genes was drastically increased in necdin-deficient mice. Because the sequences of MAGE-a subfamily members (a1-8) show striking similarities, we constructed cDNA libraries using primers common to MAGE-a1-8 and quantified the colony populations. This analysis revealed that all of the MAGE-a subfamily genes were expressed at E14.5 in necdin-deficient mouse brain. These results suggest that expression of type I MAGE genes is regulated by endogenous necdin during neuronal differentiation.

O03-4 Identification and characterization of novel variants of the tryptophan 2,3-dioxygenase gene: Possible role of TDOs in the hippocampus and cerebellum

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Tryptophan (Trp) and its metabolites, such as neurotransmitter serotonin (5-HT) and kynurenines (Kyns), play an important role in multiple brain functions. Although the role of central 5-HT in modulating mood has been relatively known, the important physiological and behavioral consequences of Kyn synthesis in the brain have been only recently studied. Altered Kyn metabolism has been implicated in neurodegenerative and psychiatric disorders such as Huntington's disease and depression. However, the molecular mechanisms regulating Kyn metabolism in the brain are not well understood, except the notion that indoleamine 2,3-dioxygenase, an initial and rate-limiting enzyme for the Kyn pathway, play a role in the immune response in the nervous system. Tryptophan 2,3-dioxygenase (TDO), another initial and rate-limiting enzyme for the kyn pathway, is thought to play an important role in systemic Trp metabolism as well as in emotional and psychiatric status. In contrast to its predominant expression in the liver, expression of TDO in the brain is poorly understood. Here, we show that *tdo* mRNA is expressed in various nervous tissues, including the hippocampus, cerebellum, striatum and brainstem using Northern blot analyses and quantitative real-time RT-PCR. During development, *tdo* mRNA was differentially regulated in brain tissues. Further, we identified two novel variants of the *tdo* gene, termed *tdo* variant1 and variant2. Similar tetramer formation and enzymatic activity were obtained when these forms were expressed in wheat germ and COS-7 cells, respectively. Quantitative real-time RT-PCR revealed that *tdo* variants were expressed in various nervous tissues, with high expression in the cerebellum and hippocampus, followed by the midbrain. *tdo* variant2 was the only variant expressed in the cerebellum from postnatal day 4 (P4) to P7, suggesting a unique role for this variant during early postnatal development. Our findings indicate that *tdo* and its novel variants may play a critical role in not only the liver but also in local areas in developing and adult brain, such as hippocampus and cerebellum.

003-5 Expression of runt related factor-2 in murine brains

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We have previously shown the possible expression of molecular machineries required for glutamatergic and GABAergic signaling in osseous cells. Runt related factor-2 (runx2) is the master regulator of osteoblast differentiation with ability to accelerate differentiation of mesenchymal stem cells into osteoblasts. In this study, we have investigated the possible expression of runx2 in the murine brain. Adult male mice were deeply anesthetized with diethyl ether, followed by perfusion with a saline solution and 4% paraformaldehyde. Brains were removed, post-fixed in the same fixative and then cryoprotected. Sagittal sections were dissected at a thickness of 20 μ m and used for in situ hybridization using a DIG-labeled cRNA probe to analyze mRNA distribution profiles. Runx2 mRNA signals were increased in proportion to increasing antisense probe concentrations throughout sections, while no signals were detected in negative control sections reacted with a runx2 sense cRNA probe. In sagittal sections, runx2 mRNA was highly expressed in the hippocampal pyramidal cell layer, hippocampal dentate gyrus granular cell layer and cerebellar granular cell layer, respectively. Although distribution of mRNA for NSE, one of the neuronal markers, was similar to that of mRNA for runx2 in hippocampal sections, distribution of mRNA for the astroglia marker GFAP was different from that of mRNA for runx2. These results suggest that runx2, a master regulator of osteoblast differentiation, is preferentially expressed in particular neuronal cell layers in the murine brain.

003-6 Changes in the expression level of synaptic function-related molecules in the limbic system of olfactory bulbectomized mice

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Bilateral Olfactory bulbectomy (OBX) in rodents causes behavioral alterations and is thought to be an animal model of depression. It has been reported that removal of olfactory bulb bilaterally results in a number of behavioral changes, such as motor hyperactivity in a stressful novel environment, increased irritation and aggressive behavior, decreased sexual behavior and cognitive and memory impairments. It has also been known that several neurotransmitter systems in the limbic system are changed after OBX. In this study to clarify the molecular nature of the synaptic alteration after OBX, we examined changes in the expression levels of synaptic function-related genes in the OBX mouse brain. OBX mice exhibited higher locomotor activity as reported previously in rat. Two weeks after OBX the brain was removed and several brain regions including the frontal cortex, hippocampus and the complex of amygdala/piriform cortex were dissected out on ice. Total RNA was isolated from the tissue samples and converted into cDNA by reverse transcriptase with random primer. The cDNA was used as a template and for quantification of target mRNA, quantitative PCR was performed using TaqMan Gene Expression assays of Applied Biosystems 7500. We measured the mRNA levels of the genes including BDNF, synapsin I, drebrin A, 5-HT receptors 1A and 2A, NMDA receptor subunit 1, GABA_A receptor α 1 and GABA_B receptor α 1. The data values were normalized with the level of GAPDH and compared to the level of sham-operated control. We observed a slight but significant decrease in the levels of 5-HT receptor 1A and drebrin A mRNAs in the amygdala/piriform cortex and prefrontal cortex after OBX. On the other hand, the levels of BDNF and synapsin I mRNAs were significantly increased in the amygdala/piriform cortex. Thus, bidirectional changes of synaptic function-related molecules occur, in particular, in the primary target brain area of the olfactory bulb. These molecular changes in the synapses of the limbic structure may cause morphological changes in synapses and affect emotional behavior.

004-1 Induction of PAP-I and PAP-III Expression in Damaged Neurons of Rat following Kainic acid-induced Seizure

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Pancreatitis-associated protein (PAP) -I and -III are small secretory proteins belong to the Regenerating gene (Reg) family, which is structurally classified as calcium-dependant type (c-type) lectin. They were reported to be induced following peripheral nervous system (PNS) injury and play significant roles in nerve regeneration. On the contrary their expressions and functions remain unclear in the central nervous system (CNS). The present study aimed to reveal whether PAP-I and -III would be induced in damaged neurons in the CNS by evaluating the rat brain following kainic acid (KA)-induced seizure. RT-PCR study demonstrated the increase of mRNAs for PAP-I and -III in rat hippocampus and cerebral cortex with a maximal increase at 1 day after KA-induced seizure. In situ hybridization using antisense probes demonstrated accumulations of hybridization signal on cells in cerebral cortex, especially in the perirhinal, entorhinal and amygdalohippocampal areas. In addition the prominent positive signals were observed on cells in dentate gyrus of hippocampus, but not in the CA fields. Immunohistochemical staining using the specific polyclonal antibodies showed the positive cells in the same areas as observed in in situ hybridization 1 day after KA-induced seizure. Double immunofluorescence labeling showed these PAP- I or -III-immunopositive cells coexpressed the neuron marker NeuN, but neither the astrocyte marker GFAP nor the microglia marker OX42, suggesting PAP-I and PAP-III positive cells were neurons. In addition both PAP-I and -III positive neurons were negative to a GABAergic neuron marker GAD67, suggesting that the PAP-I or -III-immunopositive neurons were glutamatergic neurons. These results suggest, the expressions of PAP-I and -III are inducible in CNS neurons as seen in the PNS in response to neuronal damages. PAPs may be mediators among damaged neurons by seizure to protect the neurons, because a neuron protective function of PAP-I was demonstrated in motor neuron survival.

004-2 Prevention by astroglial glutamine transporter overexpression against glutamate neurotoxicity

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In glutamatergic neurons, the neurotransmitter glutamate is supposed to be recycled through the glutamine (Gln)/glutamate cycle that involves Gln transporter (GlnT) responsible for the incorporation of extracellular Gln. In our previous studies, we have for the first time shown the functional expression of GlnT by astroglial and microglial cells prepared from rat brains. In this study, we attempted to evaluate the possible role of astroglial GlnT in glutamate neurotoxicity in cultured hippocampal neurons. For this purpose, rat C6 glioma cells were stably transfected with GlnT expression vector. Stable overexpression of GlnT mRNA was confirmed by Northern blotting, while HPLC analysis clearly revealed a drastic increase in the intracellular levels of Gln, but not of glutamate, in C6 glioma cells stably overexpressing GlnT. Cultured rat hippocampal neurons were then exposed to glutamate at different concentrations from 1 μ M to 1 mM for 1 h, followed by further culture in either the presence or absence of conditioned medium from C6 glioma cells for 24 h and subsequent determination of cell viability with MTT reduction. Brief exposure to glutamate led to a significant decrease in MTT reduction in a concentration-dependent manner in cultured hippocampal neurons. The decreased viability by glutamate was significantly prevented in hippocampal neurons cultured with conditioned medium from C6 glioma cells, whereas the prevention was more evident in hippocampal neurons cultured with conditioned medium from stable transfectants of GlnT in C6 glioma cells. In these GlnT stable transfectants, moreover, a significant increase was seen in mRNA expression of particular neurotrophic factors such as neurotrophin-4/5 on RT-PCR analysis. These results suggest that GlnT may be a determinant of the vulnerability to glutamate neurotoxicity through promotion of particular neurotrophic factor expression for subsequent release to rescue adjacent neurons in astrocytes, in addition to fueling the neurotransmitter pool of glutamate in neurons.

004-3 Thyroxine (T4) protects cultured cerebellar granule cells against low KCl-induced cell death

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Thyroid hormone (TH) is essential for the proper development of the mammalian CNS. In the neonatal cerebellum, TH deficiency has been shown to cause defects in cell survival, differentiation, and migration. Cerebellar granule cells (CGCs) differentiate in the external granular layer (EGL) and migrate inward past the Purkinje cell layer to form the internal granular layer (IGL). During this neonatal period, CGCs contact and receive synaptic inputs from mossy fibers originating in pontine nuclei, which is essential to their survival. Primary cultures of CGCs require chronic depolarization in a medium with high KCl concentration (25 mM), reflecting the activity-dependant cell survival observed *in vivo*. When cultured under usual low KCl conditions (5 mM) for 24 - 48h, CGCs undergo apoptotic cell death. In the present study, we report the effect of thyroid hormones, T3 and T4, on the death of CGCs induced by low KCl. CGCs obtained from postnatal day 6 (P6) or day 1 (P1) rat cerebellum were cultured in D-MEM/F-12 containing 10% fetal bovine serum and 25 mM KCl for 48 h, and then transferred to serum-free medium containing 5 mM KCl with or without L-thyroxine (T4) or 3,3',5-L-triiodothyronine (T3). Cell death was quantitatively evaluated by measuring lactate dehydrogenase activity released into the culture medium and by counting the number of cells with pyknotic nuclei visualized with Hoechst 33258 dye. Apoptotic cell death was observed extensively in P6 cells cultured in low-KCl medium, but not in P1 cells under the same condition. Though both T3 and T4 induced up-regulation of TH-dependent genes in CGCs, only T4 was effective in inhibiting low KCl-induced cell death of P6-CGCs. TH exerts physiological effects through (i) genomic action, by binding to nuclear TH receptors and regulating gene expression, or (ii) non-genomic action, by directly affecting ion channels, G-protein coupled receptors, or mitochondria. Since genomic action of TH is known to be carried out by T3, the results of the present study suggest that T4 protects CGCs from low KCl-induced cell death through non-genomic action.

004-5 Tauopathy induced Parkinsonism: analysis of SJLB mice

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Frontotemporal dementia and Parkinsonism linked to chromosome 17 (FTDP-17) is an inherited dementia caused by tauopathy. Abnormally phosphorylated tau and/or tangle formation are observed in the patient brain, therefore it is treated as one of Alzheimer related diseases. Mice expressing the disease causing mutant tau have been generated and contributed to the studies of Alzheimer type of dementia. On the other hand, patients of FTDP also show severe Parkinsonism, although the mechanisms of which remain poorly understood. Recently, we have established N279K mutant tau transgenic mice, SJLB. SJLB show cognitive dysfunction with accumulation of phosphorylated tau in the brain. In the present study, we have studied whether SJLB mice show Parkinsonism. SJLB mice showed shortened stride length in the footprint test and movement disorder in the pole test. Furthermore they showed decreased dopamine (DA) neurons and DA targeting cells in the brain. These results indicate that SJLB mice show Parkinsonism and they are of usefulness not only for the study of Alzheimer disease but also for the study of tauopathy induced Parkinsonism.

004-4 Pharmacological activation of heat shock transcription factor 1 (HSF1) suppresses polyglutamine-induced neurodegeneration through induction of multiple molecular chaperones

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Most neurodegenerative diseases including Alzheimer, Parkinson, and the polyglutamine (polyQ) diseases are thought to be commonly caused by misfolding and aggregation of various proteins. The polyQ diseases, including Huntington disease (HD) and spinocerebellar ataxias (SCAs), are caused by an expansion of the polyQ stretch (>40 repeats) in each unrelated disease-causing protein. The expanded polyQ stretch is thought to trigger misfolding of these mutant proteins, leading to their aggregation and deposition as inclusion bodies in affected neurons, eventually resulting in neurodegeneration. Although genetic expression of molecular chaperones such as Hsp70 and Hsp40 has been shown to synergistically suppress polyQ protein misfolding and neurodegeneration, toward developing a therapy, it is ideal to induce multiple endogenous molecular chaperones by chemical administration. In this study, we tested whether pharmacological activation of heat shock transcription factor 1 (HSF1), which regulates the expression of molecular chaperones, suppresses polyQ-induced neurodegeneration *in vivo*. We treated a *Drosophila* model of SCA3 expressing an expanded polyQ protein with various HSF1-activating compounds, and found that oral administration of 17-(Allylamino)-17-demethoxygeldanamycin (17-AAG) markedly suppresses compound eye degeneration and inclusion body formation through induction of molecular chaperones, Hsp70, Hsp40, and Hsp90. 17-AAG treatment also dramatically rescued the lethality of the SCA3 model (74.1% rescue), and suppressed neurodegeneration in a HD model (46.3% rescue), indicating that 17-AAG is widely effective against various polyQ diseases. Furthermore, RNAi-mediated knockdown of HSF1 abolished the induction of molecular chaperones and therapeutic effect of 17-AAG treatment, indicating that its therapeutic effects depend on HSF1 activation. We therefore conclude that induction of multiple molecular chaperones by HSF1-activating compounds is a promising therapeutic approach for a wide range of polyQ diseases, and possibly other neurodegenerative diseases.

004-6 Diphenylarsinic acid induced oxidative stress and cell death in cerebellar granule cells

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Diphenylarsinic acid (DPAA) was detected in the well water in Kamisu, Ibaraki, Japan in 2003, which was released accidentally from a wasted concrete lump in underground, and some individuals drinking DPAA-containing water in this area complained of cerebellar symptom. In the present study, we investigated the influence of DPAA on primary cultured cerebellar granule cells prepared from postnatal day 2 Wistar rats. After 2 days in culture, cells were exposed to DPAA in serum-free medium. DPAA at 12.5 μ M or more significantly induced cell death of granule cells after 48 hr, and at 100.0 μ M induced complete cell death. On the other hand, with neuroblastoma (Neuro2a) cells, only 30% of cells died by exposure to DPAA at 100.0 μ M for 48 hrs. An anti-oxidant, N-acetylcysteine, at 2.0 mM completely inhibited the cytotoxicity of 50.0 μ M DPAA observed after 48 hr in granule cells, which suggests that the death of granule cells induced by high-level DPAA exposure is due to oxidative stress. In cultured granule cells, DPAA at 50.0 μ M or more significantly induced cell death within 24 hr, and at 12.5 μ M or more within 48 hr. Although DPAA at 10.0 μ M induced no significant cell death after 24 hr, it significantly increased mRNA expression of superoxide dismutase 1 (*sod1*), which suggests that, even at relatively low doses, DPAA induced oxidative stress in cerebellar granule cells. We are now trying to reveal how oxidative stress induced by relatively low doses of DPAA (0.4, 2.0, and 10.0 μ M) influences mRNA expression of genes related to neuronal function using DNA microarrays, which would contribute to the understanding of the etiology of the cerebellar symptom in DPAA-exposed individuals.

004-7 Involvement of mineralocorticoid receptor on trimethyltin-induced neuronal cell damage in the dentate gyrus

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The systemic administration of trimethyltin (TMT) is known to induce granule cell death in the dentate gyrus of mice. We have previously shown that the neuronal damage induced by TMT at the dose of 2.0 mg/kg was enhanced by adrenalectomy (ADX), with glucocorticoid receptor (GR) agonist dexamethasone being capable of abolishing this enhancement by ADX. However, little has been known about the role of mineralocorticoid receptor (MR) in the TMT-induced neuronal death. In this study, we examined the effects of MR agonist and antagonist on TMT-induced damage in the dentate granule neurons. Male mice at age of 4-5 weeks were anesthetized and then the dorsal skin was cut and fascia opened to reveal the kidney. The adrenal gland was removed and sutured. ADX and sham-operated animals were given TMT on day 7 after surgery. TMT-induced neuronal damage was assessed by the immunohistochemical analysis of single-stranded DNA (ssDNA). ADX and sham-operated animals were given MR agonist aldosterone (0.1 mg/kg, s.c.) every 12 h for 2 day (4 time) after TMT injection. Aldosterone enhanced neuronal damage induced by TMT in the dentate gyrus of both ADX and sham-operated animals. GR antagonist mifepristone had the ability to enhance TMT-induced neuronal damage, whereas MR antagonist spironolactone was effective in protecting against the neuronal damage. We next examined the effect of ADX and TMT treatment on the level of GR and MR in the hippocampus. GR level was significantly elevated by ADX, whereas TMT treatment decreased GR level in both ADX and sham-operated animals. However, the level of MR was not affected in the hippocampus by any treatment. These results suggest that the activation of MR positively regulates TMT-induced neuronal damage in the dentate gyrus.

005-1 Role of Syntaxin5 isoforms on the processing and trafficking of β APP in the ER through the Golgi compartments

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Syntaxins (Syx) are involved in trafficking of various membrane proteins between specific intracellular compartments. Syx5 is thought to function in transporting vesicles between the endoplasmic reticulum (ER) and the Golgi apparatus. We have previously shown that, among Syxs, Syx5 isoforms specifically interact with presenilin (PS) holoproteins via their cytoplasmic and transmembrane regions. 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 ($A\beta$ peptide). Like Syx5, another Syx5 isoform (designated as Syx5L) that has an extra N-terminal extension containing a di-arginine ER-retrieval motif also bound to PS1 holoprotein but not to its N- or C-terminal fragments. In contrast, unlike Syx5, Syx5L overexpression did not exhibit marked accumulation of intracellular β APP holoprotein, and did not inhibit $A\beta$ peptide secretion. Analyses using deletion and substituted mutants of Syx5L revealed that, in addition to the difference in the localization between the isoforms, presence of the N-terminal extension of Syx5L is critical for the loss of its inhibition of β APP processing. In order to further strengthen the role of Syx5 isoforms on the processing and trafficking of β APP in the early secretory compartments, we examined the effects of overexpression and down regulation of Syx5 isoforms, and inhibitor of ER-Golgi transport on the processing and trafficking of wild-type and Swedish mutant of β APP. We present here the importance of Syx5 isoforms present in the ER and the Golgi compartment, and discuss the role of Syx5 isoforms in the β APP metabolism in the early secretory pathways.

005-2 Late endocytic dysfunction as a putative pathway for GM1 ganglioside-induced amyloid formation in Alzheimer's disease

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Morphological alternations of endocytic compartments or perturbations of endocytic trafficking and function have been described as the earliest known pathological changes in the neurons of Alzheimer's disease (AD). In the previous study, we found that the treatment of differentiated PC12 cells with chloroquine, an endocytosis disrupting agent, accelerated the assembly of exogenously added amyloid- β protein ($A\beta$) through the formation of GM1 ganglioside (GM1)-bound $A\beta$ (GA β), endogenous seed for AD amyloid. The assembly of $A\beta$ to amyloid fibrils is a critical event in AD. In this study, we characterized the endocytic pathway responsible for GA β -induced amyloid formation in PC12 cells. Blocking the early endocytic transport using siRNA specific to Rab5 induced GM1 accumulation at cell surface of the cells. However, amyloid fibril formation from soluble $A\beta$ did not occur in the Rab5 siRNA-transfected cells. In contrast, blocking the late endocytic pathway by siRNA-induced suppression of Rab7 markedly increased GM1 at cell surface and accelerated the assembly of $A\beta$. Importantly, the level of insoluble $A\beta$ significantly decreased in the presence of cholera toxin B subunit, which specifically bind to GM1, or 4396C, an antibody specific to GA β . Furthermore, in the immunohistochemical analysis of Rab7 siRNA-transfected cells, enlarged early endosomes were observed, which was consistent with previous findings in the neurons of sporadic AD. Our results suggest that late but not early endocytic dysfunction contributes to the amyloid fibril formation by facilitating the generation of amyloid seed in the Alzheimer's brain.

O05-3 Glycosylation-required and domain-specific A β 42-to-A β 40-converting activity of angiotensin-converting enzyme

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The amyloid β -protein 1-42 (A β 42) has been suggested to play a central role in the pathogenesis of Alzheimer's disease (AD). We have reported that angiotensin-converting enzyme (ACE) converts A β 42 to A β 40 (Zou et al. J Neurosci, 2007). A β 40 is the predominant secreted form of A β and recent studies have suggested that A β 40 has neuroprotective effects and inhibits amyloid deposition in brain. ACE is a glycoprotein and contains two functional active domains. Here we determined the sugar modification type of human ACE and found that N-linked glycosylation of ACE was essential for converting A β 42 to A β 40 and for its angiotensin-converting activity. In addition, purified human ACE was rapidly degraded after deglycosylation, suggesting that the glycosylation of ACE is important for maintaining its stability and enzymatic activity. We also determined the ACE domain which is responsible for A β 42-to-A β 40-converting activity. Interestingly, the A β 42-to-A β 40-converting and the angiotensin-converting activities were located in different domains of ACE. Our results suggest that the glycosylation of ACE may be involved in A β metabolism and the domain-specific ACE activities can be regulated independently.

O05-5 A novel neuroprotective factor induced by beta amyloid

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A β is a causative factor in Alzheimer's disease. However the precise mechanism of A β neurotoxicity is not elucidated. To explore the mechanism of A β neurotoxicity, the effect of A β on gene expression of neuron was examined comprehensively. There were 23 candidate genes out of about 22,000 genes were supposed to be induced in cortical neurons by 5 μ M of A β for 16 hours. One candidate gene was confirmed to be 2.8 fold increased with Northern hybridization. Overexpression experiment indicated neurons expressing this gene were protected from 50% oxygen neurotoxicity. We are going to also examine the induction of this gene by 50% oxygen and whether it possesses the neuroprotective effect against other stimuli or not.

O05-4 Suppression of A β assembly from neuronal membrane by insulin

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Type 2 diabetes is a risk factor for late-onset Alzheimer's disease. However, the underlying causes remain unknown. In this study, we observed that insulin increased GM1 ganglioside (GM1) expression in detergent resistant membrane microdomains (DRMs). In addition, phosphatidylinositol 3-kinase inhibitor (LY294002), but not extracellular signal-regulated kinase inhibitor (PD98059), blocked the induction of GM1 expression in DRMs by insulin. Moreover, insulin failed to induced formation of fibril from soluble amyloid A β protein (A β), and to accelerate GM1 or A β seed-induced fibril formation. A markedly A β assembly in the culture of nerve growth factor-treated PC12 cells was significantly decreased by insulin. These results suggest that insulin suppress the A β assembly through the decrease of GM1 expression in DRMs of neuronal membranes.

O05-6 Expression of transthyretin and amyloid beta precursor protein in SAMP8 hippocampus and choroid plexus

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The senescence-accelerated mouse (SAM) is an accelerated aging model: SAMP8 shows age-related defects of learning and memory. Clarifying causative genes would be helpful to understand human age-related defects of learning and memory. Transthyretin was reported to be a protein sequestering beta-amyloid (A β) and helping to prevent the Alzheimer's disease. Remarkable down-regulation of transthyretin (*Ttr*) in 8-month-old SAMP8 hippocampus was revealed by GeneChip (unpublished). We confirmed the result by absolute quantitative real-time PCR (qPCR) in the present study. Total RNA was extracted from pooled hippocampus of five male SAMP8 and SAMR1 mice at the age of 1-, 3-, 6-, 8- and 12-months and gene expression was analyzed by qPCR. cDNAs of *Ttr*, *App* and *Gapdh* (housekeeping gene) were prepared from SAMR1 hippocampus total RNA and cloned into T-vector for preparing a standard curve in qPCR. Gene expression of *Ttr* in SAMP8 hippocampus was 564x10², 88.8x10², 14.6x10², 16.5x10² and 159x10² copies/ng total RNA at 1-, 3-, 6-, 8- and 12-months, while *Ttr* in SAMR1 was 1240x10², 115x10², 5.35x10², 403x10² and 137x10² copies/ng total RNA. *Ttr* expression level was 1/24.4 at 8-months in SAMP8 compared to SAMR1. Gene expression of *App* in SAMP8 was 558x10², 463x10², 477x10², 376x10², 158x10² copies/ng total RNA at 1-, 3-, 6-, 8- and 12-months, while *App* in SAMR1 was 426x10², 306x10², 371x10², 490x10² and 111x10² copies/ng total RNA. Ratio of *App/Ttr* was 0.989, 5.21, 32.7, 22.8 and 0.994 at 1- to 12-months in SAMP8 hippocampus and 0.344, 2.66, 69.3, 1.22 and 0.810 at 1- to 12-months in SAMR1 hippocampus. Immunohistochemical staining showed that *Ttr* protein decreased in choroid plexus, the main source of *Ttr* in brain, in four of five 8-month-old SAMP8 mice. The present results suggest that down-regulation of *Ttr* in choroid plexus and hippocampus plays a role in age-related defects of learning and memory in SAMP8.

O05-7 Nefiracetam-induced modulation of excitatory and inhibitory synaptic transmission via stimulation of neuronal nicotinic acetylcholine receptors in rat cortical neurons

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The cholinergic and glutamatergic systems are known to be down-regulated in the brain of Alzheimer's disease patients. Galantamine and nefiracetam have been shown to potentiate the phasic activity of nicotinic acetylcholine receptors (nAChRs) in the brain. Stimulation of nAChRs is also known to cause release of various neurotransmitters including glutamate and γ -aminobutyric acid (GABA). We have previously reported that nefiracetam and galantamine potentiate the activity of nAChRs. Therefore, nefiracetam and galantamine are hypothesized to affect the release of glutamate and/or GABA via stimulation of nAChRs. The present study was set out to test this hypothesis by measuring the effects of these drugs on spontaneous miniature excitatory postsynaptic currents (mEPSCs) and spontaneous miniature inhibitory postsynaptic currents (mIPSCs) recorded by whole-cell patch clamp technique from rat cortical neurons in primary cultures. ACh at 30 nM generated a steady inward current and increased the frequency of mEPSCs and mIPSCs. Nefiracetam at 10 nM plus 30 nM ACh increased the frequency of mEPSCs and mIPSCs beyond the levels increased by ACh alone. The potentiating action of nefiracetam was abolished by dihydro- β -erythroidine. None of these treatments affected the amplitude of mEPSCs or mIPSCs. Galantamine at 1 μ M plus ACh did not significantly potentiate the frequency. Nefiracetam at 10 nM alone had no effect on mEPSCs and mIPSCs. It was concluded that nefiracetam stimulates glutamate release via stimulation of the $\alpha 4\beta 2$ nAChRs.

O06-1 Analysis of gene expression changes associated with long-lasting synaptic enhancement in hippocampal slice cultures after repetitive exposures to glutamate

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We have previously shown that repetitive exposures to glutamate (100 μ M, 3min, 3 times at 24h intervals) induced a long-lasting synaptic enhancement accompanied by synaptogenesis in rat hippocampal slice cultures. To investigate the molecular mechanisms underlying this phenomenon, we first analyzed the time course of gene expression changes between 4h and 12d after repetitive stimulation using original oligonucleotide microarray "Synptoarray". Alterations in the expression of genes related to synaptic function occurred in two time phases after the 3rd stimulation; an early phase of 24h~96h and a late phase of 6d~12d. Comprehensive screening with commercially available high-density microarrays was thus carried out at 48h after the last stimulation to identify genes differentially expressed by the 2nd and the 3rd stimulation. From real-time PCR analysis of these and related genes, 2 categories of genes were identified; 1) genes previously reported to be induced by physiological as well as epileptic activity, 2) genes involved in cofilin-based regulation of actin filament dynamics. In particular, a large and progressive up-regulation by the 2nd and the 3rd stimulation was observed with genes for brain-derived neurotrophic factor, synaptotagmin 4, and 14-3-3 ζ . While genes in the second group were coordinately regulated to increase actin dynamics after the 2nd stimulation, they were regulated to decrease actin dynamics and stabilize the actin cytoskeleton after the 3rd stimulation.

O06-2 Long-lasting synaptic enhancement after repeated activation of PKA in the cortical region of the brain slice culture including hippocampus and entorhinal cortex

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We reported previously that the repeated induction of LTP by means of the application of glutamate or forskolin in the stable slice culture of the rat hippocampus causes the slowly-developing long-lasting enhancement of synaptic strength accompanied by the formation of new synapses. We designated this phenomenon RISE (Repetitive-LTP-Induced Synaptic Enhancement) to distinguish it from the single conventional LTP and proposed it as an in vitro model system suitable for the analysis of long-term memory. However, the hippocampus is not supposed to be the final storage site of memory so that the stored information should be transferred to the cortical regions in the downstream of the hippocampus. To know whether such information transfer would be reproducible in the above model system, we constructed an expanded slice culture that included the hippocampus and the entorhinal cortex. Voltage-sensitive dye monitoring of neuronal excitation coupled with electrical stimulation revealed that both cortico-hippocampal and hippocampo-cortical pathways were preserved/reconstituted in the expanded slice culture. The staining of axons with lipophilic dye supported this notion anatomically. Three repeated applications of forskolin to the expanded slice culture (the stimulation equivalent to provoke RISE in the hippocampal slice culture) resulted in the enhancement of synaptic strength in the deep layer of the entorhinal cortex receiving output from the hippocampus. In contrast, the hippocampal CA1 region did not show the enhanced synaptic response at the same time. These results suggest that information is stored in the cortex if the pathway in the downstream of the hippocampus is supplied to the brain slice culture system and that the cellular processes of memory transfer would be analyzed using this system.

O06-3 Regulatory mechanism of drebrin translocation from dendritic spines to parent dendrites in cultured hippocampal neurons

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Drebrin is one of F-actin binding proteins in the brain. We have previously shown in cultured hippocampal neurons that application of glutamate translocates drebrin and F-actin from dendritic spines to parent dendrites, resulting in morphological changes of dendritic spines. In the present study, we analyzed regulatory mechanisms of the glutamate-induced drebrin translocation. We prepared the low density cultures of rat hippocampal neurons from 18 days embryo using Banker methods. All experiments were done at 21 days in vitro. Neurons were treated with glutamate (100 μ M) for 10 min or high potassium (90 mM) for 5 min after pharmacological pretreatments with several inhibitors of candidates which were thought to be responsible for the translocation. After glutamate stimulation, we immunostained neurons with an antibody against drebrin, and analyzed the location of drebrin with MetaMorph software. An NMDA-receptor-antagonist (D-APV; 100 μ M) and an extracellular Ca^{2+} -chelator (EGTA; 20 mM) inhibited the drebrin translocation, but an L-type voltage-gated Ca^{2+} -channel-blocker (nifedipine; 20 μ M) did not. An intracellular Ca^{2+} -chelator (BAPTA-AM; 50 μ M) increased the level of drebrin contents in dendritic spines under the pretreatment condition, but did not inhibit the glutamate-induced decrease of drebrin contents in the spine. Further, a specific nonmuscle myosin II ATPase inhibitor (blebbistatin; 100 μ M) blocked the translocation, but a myosin light chain kinase inhibitor (ML-7; 10 μ M) did not. The drebrin translocation was also induced by high potassium stimulation, and inhibited by D-APV as well. Taken together, it is suggested that the drebrin accumulation into dendritic spines is regulated by concentration of intracellular Ca^{2+} within the spine and that the glutamate-induced drebrin translocation is regulated by the local elevation of intracellular Ca^{2+} concentration through NMDA receptor activation, and myosin II ATPase which is activated by the calcium influx via activation of NMDA receptor.

O06-5 Identification of the proteins involved in dendritic localization of ACaMKII mRNA

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Among dendritic mRNAs, ACaMKII is the most intensively studied one that is transported to the distal regions of hippocampal dendrites. The dendritic transport of ACaMKII mRNA is mediated by recognition of the cis-acting motif that resides in its own 3'-untranslated region (3'-UTR) with 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) recognizing the cis-element, we affinity-purified proteins that bound to the strepto-tagged 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, ACaMKII 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 ACaMKII mRNA in hippocampal neurons.

O06-4 Drebrin A knock-out impairs context-dependent fear conditioning and homeostatic plasticity of the NMDA receptor

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Dendritic spine is a postsynaptic structure in excitatory synapse, and has important roles in synaptic transmission and plasticity. Motility and functions of dendritic spine are regulated by actin-based cytoskeleton. Drebrin A, an adult form of drebrin, is one of actin-binding proteins in dendritic spine. To know the role of drebrin A in brain functions, we generated knockout mice in which a drebrin A-specific exon was deleted from the drebrin gene. In these drebrin A-specific knockout (DA-KO) mice drebrin A was substituted by drebrin E an embryonic form of drebrin. While drebrin existed only as an F-actin-bound form in the adult wild-type brain, it existed as both cytosolic and F-actin-bound forms in the adult DA-KO brain. These mice were viable, fertile and exhibited no obvious external defects. Gross morphology of the brain and spine morphology was normal in DA-KO mice, except for a small increase in perforated synapses. These observations indicate that the role of drebrin A in spine morphogenesis can be substituted by drebrin E. In spite of the absence of any profound deficits in general behavior, DA-KO mice exhibited impairment of context-dependent fear response after conditioning. Finally, we found that homeostatic increase of NR2A-labelled spines by 30-min exposure of the NMDA receptor antagonist APV was diminished in the DA-KO brain. Thus, drebrin A may have some modulatory role on fear learning through the homeostatic regulation of the NMDA receptor recruitment to the synapses.

O06-6 Neuropsin (KLK8) dependent compartment specific and process specific synaptic tagging

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Long-term potentiation (LTP) and long-term depression (LTD) are considered as cellular models for memory. LTP/LTD are characterized by temporal phases (early and late phase). Early-LTP/LTD, lasting less than 2 h can be dissociated from late-LTP/LTD by blockers of protein synthesis. It was hypothesized that a synaptic tag enables capture of newly synthesized plasticity-related proteins. Previously, we found that serine protease, neuropsin involved in formation of the synaptic tag in apical CA1 dendrites. Here, we show that in addition to apical CA1 dendrites, neuropsin-dependent synaptic tagging also takes place within basal CA1 dendritic compartments after LTP induction. Furthermore our findings demonstrate that neuropsin is involved in the LTP process-specific synaptic tag, whereas it is not involved in LTD tag.

O07-1 Analysis of the role of Dab1-nucleocytoplasmic shuttling for layer formation of cerebral cortex○Takao Honda¹, Maya Yamazaki², Kazuma Nagasawa², Manabu Abe², Kenji Sakimura²¹ Department of Anatomy, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo, Japan, ² Department of Cellular Neurobiology, Brain Research Institute, Niigata University

Formation of highly organized neocortical structure depends on the correct placement of the appropriate number and types of neurons. Reelin is a large glycoprotein secreted from neurons of various regions, including Cajal-Retzius cells in the cortical marginal zone. Disruption of the *reeler* gene causes neuroanatomical abnormalities such as a defect in the preplate splitting and inverted cortical lamination. Dab1 is a cytoplasmic adaptor protein and interacts with at least two Reelin receptors, VLDLR and ApoER2, through the N-terminal phosphotyrosine-binding (PTB) domain. The absence of *dab1* causes an almost exact neuroanatomical phenocopy of the *reeler* (*reeler* mutant mice). So far, Dab1 has been considered a cytoplasmic protein. Recently we showed that Dab1 is subject to nucleocytoplasmic shuttling. In its steady state, Dab1 is mainly located in the cytoplasm. However, treatment with leptomycin B, a specific inhibitor of the CRM1 (chromosomal region maintenance 1)-RanGTP-dependent nuclear export, resulted in nuclear accumulation of Dab1. By using deletion or substitutional mutants of Dab1 fused with enhanced green fluorescent protein, we have mapped a bipartite nuclear localization signal and two CRM1-dependent nuclear export signals. However, physiological meaning of the nucleocytoplasmic shuttling of Dab1 for Reelin-Dab1 signaling pathway is still unclear. To reveal the physiological function of nucleocytoplasmic shuttling of Dab1 in developing brain, we have developed an assay system that can mimic the *reeler*-like phenotype. Using this assay system, we are trying to reveal the physiological meaning of Dab1 nucleocytoplasmic shuttling.

O07-3 LOTUS, a novel axon guidance molecule, functions as a negative regulator of Nogo signaling in LOT formation○Masumi Iketani¹, Megumi Yamaguchi¹, Yasufumi Sato^{1,2}, Yuko Arie¹, Yuji Kurihara¹, Fumio Nakamura¹, Yoshio Goshima¹, Kohtaro Takei¹¹ Department of Molecular Pharmacology and Neurobiology, Graduate School of Medicine, Yokohama City University, Yokohama, Japan, ² Brain Stroke Research Group, Mitsubishi Kagaku Institute of Life Sciences, Tokyo, Japan

We discovered a novel axon guidance molecule LOTUS that serves for lateral olfactory tract (LOT) formation of mouse telencephalon, and identified Nogo-66 receptor (NgR1) as its binding partner. The molecular interaction between LOTUS and NgR1 induced cell-cell contact in the transfected cells. 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 of ED 12-13. Fluorophore-assisted light inactivation (FALI) of LOTUS and/or NgR1 resulted in defasciculation of LOT axonal bundles. Furthermore, as a dominant-negative effect of NgR1 or LOTUS, exposure of truncated soluble form of NgR1 or LOTUS to the organotypic culture for 24 hours at ED12-13 caused LOT to defasciculate. These results suggest that molecular interaction between LOTUS and NgR1 serves for LOT axonal bundling. Surprisingly, binding of NgR1 ligands such as Nogo-66 or myelin associated glycoprotein (MAG) to NgR1 was completely inhibited when LOTUS and NgR1 were co-expressed in Cos7 cells. Immunocytochemistry revealed that Nogo-A, a ligand of NgR1 which is known to inhibit neurite extension, is also expressed in LOT at ED 12-13. Exposure of a Nogo-66 antagonist NEPI-40 rescued FALI of LOTUS-induced defasciculation of LOT axonal bundle. This suggests that LOTUS may protect LOT formation from Nogo-66-induced defasciculation of axonal bundle. Thus, LOTUS may function as a fasciculation inducing factor and a negative regulator of Nogo/NgR1 signaling and in LOT formation.

O07-2 Roles of septin in the positioning of cortical neuronsTomoyasu Shinoda, Hidenori Ito, Kaori Sudo, Ikuko Iwamoto, Rika Morishita, Ken-ichi Okamoto, ○Koh-ichi Nagata
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Septins are a conserved family of GTP/GDP-binding proteins, and mammals have 14 genes (SEPT1~SEPT14). It has been reported that some septins are highly expressed in neuronal tissues, which raises the possibility that septins are functionally involved in neuronal development. We focused on Sept14 and examined the expression patterns in embryonic and postnatal mice. Expression of Sept14 was not detected in forebrain before E13, however, strong expression was detected in E15 cerebral cortex, when the generation and migration of cortical pyramidal neurons frequently occur. We next examined the function of Sept14 in the positioning of cortical neurons. Knockdown of Sept14 in neuroepithelial cells by in utero electroporation resulted in defective positioning of cortical pyramidal neurons. The defective localization observed was rescued by the expression of RNAi-resistant Sept14. To examine the molecular basis of the involvement of Sept14 in the neuronal positioning, we screened Sept14-interacting molecules and identified Sept4 as a candidate. Sept4 interacted with Sept14 in the cellular context. Knockdown of Sept4 in neuroepithelial cells also resulted in the defective positioning of cortical neurons, which was very similar to that of Sept14-deficient cells. These results suggest novel functions of septins during the neuronal development.

O07-4 Neurite outgrowth promoting effect of a novel axon guidance molecule LOTUS through binding to Nogo-66 receptor○Yuji Kurihara^{1,2}, Yuko Arie^{1,2}, Megumi Yamaguchi¹, Masumi Iketani¹, Fumio Nakamura¹, Nobuhisa Mizuki², Yoshio Goshima¹, Kohtaro Takei¹¹ Department of Molecular Pharmacology and Neurobiology, Graduate School of Medicine, Yokohama City University, Yokohama, Japan, ² Department of Ophthalmology, Graduate School of Medicine, Yokohama City University, Yokohama, Japan

Lateral olfactory tract usher substance (LOTUS) is a newly identified, key molecule serving for the formation of 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 each 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. Furthermore, LOTUS and NgR1 interaction induced cell-cell contact in LOTUS- and NgR1-transfected cells. We next examined if LOTUS-NgR1 binding is participated in other cellular functions. We found that neurite extension of retinal ganglion cells (RGC) cultured on LOTUS-coated dish was dramatically promoted. The promotion of neurite extension was also observed in RGC grown on C-terminal domains of LOTUS substrate. Phosphatidylinositol-specific phospholipase C (PI-PLC) reduced the neurite extension of RGC on LOTUS substrate, thus suggesting that GPI-anchored proteins expressed in RGC including NgR1 was involved in the neurite outgrowth. Fluorophore-assisted light inactivation of LOTUS substrate also reduced the neurite outgrowth, suggesting specific involvement of LOTUS in the neurite outgrowth. These data suggest that the molecular interaction between LOTUS and NgR1 promotes neurite outgrowth of RGC. Surprisingly, binding of NgR1 ligands such as Nogo-66 or myelin associated glycoprotein (MAG) to NgR1 was completely inhibited when LOTUS and NgR1 were co-expressed in Cos7 cells. Collectively, LOTUS may function as a neurite promoting factor and a negative regulator of Nogo/NgR1 signaling.

O07-5 Filamin A, an actin-binding protein, participates in the Semaphorin-3A signaling through the interaction with Collapsin response mediator proteins

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Semaphorin-3A (Sema3A) is one of potent repulsive guidance molecules. Sema3A binds to Neuropilin-1 and induces the reorganization of cytoskeleton in the growth cones. It has been shown that the signaling pathway from Sema3A to tubulin is mediated by Collapsin Response Mediator Proteins (CRMPs). However, the signal transduction to actin cytoskeleton via CRMPs is poorly understood. We found that *C. elegans* Filamin A, an actin binding protein, interacts with UNC-33, a *C. elegans* homologue of CRMPs. Mammalian Filamin A is also co-immunoprecipitated with CRMPs from rat brain. Filamin A consists of an actin binding domain and 24 repeats of immunoglobulin like domain. Using a series of truncated mutants of Filamin A, we found that the immunoglobulin repeats interacts with CRMP2. To investigate the role of Filamin A in Sema3A signaling, we have performed dominant-negative study using the truncated mutants of Filamin A. Introduction of deletion mutants lacking the actin binding domain of Filamin A in dorsal root ganglion (DRG) neurons attenuated Sema3A-induced collapse, while the overexpression of full-length Filamin A did not alter the response. RNA interference against Filamin A also suppressed the Sema3A response in DRG neurons. Filamin A full-length or ABD and Ig repeats conjugated Filamin A mutants rescued Sema3A-induced growth cone collapse in Filamin A knockdown DRG neurons. Furthermore, Filamin A RNAi suppressed the spontaneous growth cone collapse of DRG neurons introduced a phosphomimic form mutant of CRMP1, where Ser522 was substituted with Asp. These results suggest that Filamin A interacts with CRMPs and mediates Sema3A signaling in the nervous system.

O08-1 Glucocorticoid inhibits the BDNF-mediated synaptic maturation in developing neurons via prevention of MAPK pathway

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Chronic elevation of glucocorticoid level in serum due to dysfunction of HPA axis may cause neuronal damage and result in depressive disorder. The involvement of BDNF in the antidepressive effect has also been suggested. Thus, here, we investigated the effect of glucocorticoid (Dexamethasone, DEX) on synaptic maturation enhanced by BDNF in developing neurons. In the immature stage, BDNF increased the outgrowth of dendrites and the expression of synaptic proteins including glutamate receptors and presynaptic proteins. As expected, DEX pretreatment significantly inhibited the BDNF-dependent up-regulation of dendritic outgrowth and synaptic proteins. Interestingly, DEX reduced the sustained activation of MAPK pathway elicited by BDNF, which is a required intracellular signaling for the BDNF- increased synaptic proteins. Furthermore, we examined possible involvement of phosphatase, Shp2, which has important roles in maintaining the activation of MAPK pathway and found that Shp2 influenced the neuronal response to BDNF after DEX pretreatment in cultured neurons.

O07-6 Tubulin tyrosination navigates kinesin-1 to the axon

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Neurons form distinctive axonal and dendritic compartments that are important for directional signalling. The mechanisms that discriminate axons from dendrites remain elusive. The fact that the microtubule motor Kinesin-1 can recognize axons even prior to polarization is a remarkable key for the identification of spatial cues involved in axon-dendrite differentiation. Here, we found that amino acid substitutions in the sheet beta5-loop8 region transform truncated Kinesin-1 from the uni-destination (i.e. axon specific) to the bi-destination (i.e. axon and dendrites) state. Further, we demonstrated that tyrosinated tubulins that are abundant in somatodendrites prevent the wild-type Kinesin-1 from binding to microtubules, while the bi-destination-type Kinesin-1 overcomes this inhibition; this suggests that tubulin tyrosination sequesters Kinesin-1 from somatodendrites via beta5-loop8. Consistently, by inhibiting tubulin tyrosin ligase (Ttl) in hippocampal neurons, Kinesin-1 accumulated both axon and dendrites. Our study provides the first specification of amino acids within Kinesin-1 that discriminate the axonal microtubules from somatodendritic microtubules and a novel linkage between tubulin modification and polarized trafficking in neurons

O08-2 Dopamine regulates expression of pancreatitis-associated protein I in the intermediate lobe of pituitary gland under continuous stress

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Accumulated fatigue often causes various defects in homeostasis; however the molecular events occurred under the condition remain unclear. Using continuous stress (CS) model of rat we previously demonstrated significant changes in the intermediate lobe (IL) of pituitary gland. In CS rats, dopamine (DA) level in the IL decreased and this caused hyperactivation and subsequent cell death of melanotrophs. In the present study, to further analyze the molecular changes, we performed a microarray analysis and compared gene expressions in the pituitary gland between normal and CS condition. Among molecules derived in the gene screening, we have focused on a lectin-like secretory protein, pancreatitis-associated protein I (PAP-I), because its induction was prominent. *In situ* hybridization and immunohistochemical analysis clearly demonstrated increase of PAP-I expression in melanotrophs in the IL of CS rats. In addition an injection of DA agonist prevented PAP-I induction in CS rats, contrary DA antagonist induced PAP-I expression in normal rats. These results suggest that induction of PAP-I expression in CS rats is associated with decrease of DA function in the IL. Since the stress due to hyperactivation of melanotroph continues under CS condition, PAP-I may be a stress-responsive factor to protect melanotrophs as demonstrated in motor neurons.

O08-3 Social olfactory stimulus induced the attenuation of unconditioned defensive behavior in *mdx* mice

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Purpose: Duchenne muscular dystrophy (DMD) is a serious muscular disorder, which is caused by a deficit of dystrophin protein. DMD is accompanied by cognitive deficits and psychiatric symptoms. *Mdx* mouse is an animal model of DMD. We have previously reported that *mdx* mice consistently showed potent unconditioned defensive freezing responses to a brief restraint that never induced such responses in the wild-type mice. The purpose of this present study is to further characterize the abnormality of emotional responses in *mdx* mice.

Method: For this purpose, we investigated the effects of a social olfactory stimulus upon defensive freezing response in *mdx* mice.

Results and Discussion: Brief restraint induced a potent freezing response only in *mdx* mice when they were released in a new cage, as we reported previously. The freezing response was outstandingly reduced when they were released in the cage with the odor of other mice. This means that restraint-induced freezing response is interfered with the stimulus that attracts mouse's attention. Since the odor of other mice is an olfactory cue for social interaction, social buffering effects may be involved in the odor-induced reduction of restraint-induced freezing in *mdx* mice. This result suggests that enhanced defensive freezing response in *mdx* mice is attributed to the abnormal information processing in the brain.

O09-1 Disruption of paranodal axo-glial junctions causes alteration of axonal transport in the PNS

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Paranodal axo-glial junctions play a critical role in the organization and maintenance of molecular domains in myelinated axons. Previously we reported that 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. We also presented the possibility that these aberrant mitochondria remain functional in CST-deficient mouse PNS. In this study, we focused on the axonal transport in these mice.

Microtubules serve as tracks for either anterograde transport or retrograde transport of mitochondria along axons. ATP-dependent motor proteins that move mitochondria along microtubules include kinesins (anterograde transport) and dynein complex (retrograde). Therefore, to evaluate the state of axonal transport in the PNS of CST-deficient mice, we quantified the levels of the heavy chain subunit of kinesin, dynein intermediate chain, and dynactin p50 using whole sciatic nerve homogenate from age matched CST-deficient mice as well as control mice. We found that the levels of proteins we quantified were significantly decreased in CST-deficient mice. The levels of kinesin, dynein, and dynactin p50 showed reductions (approximately 54%, 61%, and 53%, respectively) in the sciatic nerves from CST-deficient mice. However the levels of these proteins showed no significant changes in brains between CST-deficient mice and the control mice. The aberrant mitochondria were also only observed in the nodal axons of sciatic nerves in these mice. Thus, the disruption of the proper axonal transport may be involved in the mitochondrial abnormality in the CST-deficient PNS.

O08-4 Maternal dietary restriction during lactation influences postnatal behaviors in the offspring of mice

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It is well known that maternal nutritional status is important for fetal development. In rodents, maternal caloric restriction throughout gestation is shown to produce subsequent permanent hypertension, impaired glucose metabolism, and insulin resistance in later offspring life. In this study, we examined the effect of maternal food restriction during lactation on the mouse offspring. From postnatal day 1 (P 1) to the weaning at P 21, control dams (CD) were fed with regular amount of daily food consumption, whereas dietary restricted dams (RD) were fed with 70% of daily food consumption. Though body weight of RD was not different from that of CD after weaning, body weight of the offspring from RD (RD offspring) was significantly lower than that of the offspring from CD (CD offspring). The difference was detectable until 9 weeks of age. Body length and brain weight of CD offspring at 3-4 weeks of age were lower than those of RD offspring. Plasma glucose, triglyceride, cholesterol, corticosterone, growth hormone and thyroxine concentrations were not different between the two groups. In the open field test, total distance was significantly decreased in RD offspring compared with CD offspring. In the hole-board test, head dip latency was increased and number of head-dip was decreased significantly in RD offspring. In the elevated plus maze test, total distance and the number of entry into open arms were significantly decreased in RD offspring. There was no difference between the two groups in the rota-rod test. These results suggest that maternal dietary restriction during lactation may affect their growth, locomotor activity, and anxiety behavior but not motor function in the offspring of mice.

O09-2 Inhibitory effect of Annexin2 on lysolecithin-induced sciatic nerve demyelination

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Annexin2 (AX2) is known as a modulator of the pathological processes through inhibition of cytosolic phospholipase A2 (cPLA2) or promotion of local fibrinolysis. Previously, we reported that AX2 was localized in the paranodal regions and Schmidt-Lanterman incisures in the PNS myelin. AX2 and cPLA2 in these regions were markedly increased in the cerebroside sulfotransferase-deficient mice, in which paranodal axo-glial junctions were disrupted. The expression of both AX2 and cPLA2 were also increased in the lysolecithin treated sciatic nerves, especially in normal-appearing myelin surrounding demyelinated region, suggesting that AX2 has some role in pathological conditions of myelin. To determine the role of AX2, we performed the suppression of AX2 by siRNA and the induction of demyelination by lysolecithin at the same time in the present study. AX2 siRNA and Lysolecithin were injected intraneurally in the left sciatic nerve of each 8-week-old ICR mouse. Lysolecithin-injected nerves and vehicle-injected nerves were used as controls. The sciatic nerves were removed at 3 and 7 days after injection for immunohistological or western blot analysis. Demyelinating conditions were evaluated by myelin basic protein (MBP) staining and the area of non- and demyelinated regions was measured by semi-thin sliced sections stained with toluidin blue. Injection of siRNA successfully suppressed AX2 upregulation during demyelination. In comparison with controls, demyelinating area was significantly enlarged in the AX2 siRNA treated groups ($P < 0.05$). By immunofluorescence staining, the enhanced intensities of cPLA2 and phosphorylated cPLA2 (activated type) were observed. These data suggest that AX2 is involved in inhibition of lesion expansion during lysolecithin-induced demyelination through regulation of cPLA2. Thus, AX2 plays an important role in the inflammation process of the PNS, and regulation of this protein may be useful for demyelinating polyneuropathies.

009-3 Involvement of KLK6 in the pathogenesis of Experimental Autoimmune Encephalomyelitis

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Multiple Sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system (CNS). However, molecular mechanism of demyelination has not been well understood. Kalikrein 6 (KLK6) is a kalikrein-like serine protease that is distributed exclusively in oligodendrocytes in the CNS. To investigate the role of KLK6 in demyelination, we examined the expression of KLK6 in myelin oligodendrocyte glycoprotein (MOG) induced experimental autoimmune encephalomyelitis (EAE). In wild-type mice, KLK6 is induced in the spinal cord of mice with EAE. KLK6 knock out (KO) mice exhibited an altered EAE progression characterized by delayed onset and progression of clinical symptoms as compared to wild-type mice. These observations suggest that KLK6 is involved in the pathogenesis of EAE mediated by demyelination.

010-1 4 dimensional characteristics of the movement and location of the secretory granules in bovine adrenal chromaffin cells

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To characterize spatio-temporal movement of the secretory granules underlying the secretory events in adrenal chromaffin cells, we analyzed the track motion of LysoTrackerGreen DND26 -labeled granules using LSM-5Live confocal laser microscope. Our previous studies on the effects of mycalolide B (MB) which disrupts of F-actin and TPA which activates protein kinase C (PKC) on the kinetics of exocytotic events and movement of granules suggested that actin-myosin interaction and PKC are implicated in the spatio-temporal regulation of vesicle recruitment for exocytosis. In this study, we examined the effects of MB and TPA on the velocity, track straightness, track displacement and location of the granules during each 2 min of resting, depolarizing stimulation, and post-stimulation. TPA-treatment increased the population of vesicles with faster track speed, higher straight movement and wider track motion during the stimulation phase, while MB-treatment decreased the spatial movement of vesicles in all phases. These results indicate the spatial movement of the vesicles is functionally linked to vesicle recruitment for exocytosis. The location of the granules in these conditions is under characterization.

009-4 Role of microsomal prostaglandin E synthetase-1 in multiple sclerosis

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PGE₂ is a potent mediator of fever, pain and inflammation. Microsomal prostaglandin synthetase-1 (mPGES-1) is an inducible terminal enzyme for PGE₂ biosynthesis, however, the effect of mPGES-1 remains unclear on the exacerbation of multiple sclerosis (MS), the inflammatory demyelinating disease of the CNS. In this study, we examined the *in vivo* role of mPGES-1 in experimental allergic encephalomyelitis (EAE), the animal model of MS. EAE were induced in mPGES-1 deficient mice (*mPGES-1*^{-/-}) and wild type mice (WT) by immunization of myelin oligodendrocyte glycoprotein peptide (MOG). Severity of EAE, time course of progression and histopathology were compared between *mPGES-1*^{-/-} and WT. EAE symptoms were scored by 6-point scale, and recorded by video monitoring system having a quantitative behavioral analysis. Histopathological analysis was examined using lumbar spinal cord at 35 days after MOG immunization, and the expression of mPGES-1 was investigated by immunohistochemistry at 19 days following immunization.

Here we show that there was no difference in EAE incidence between *mPGES-1*^{-/-} and WT, however, the maximum EAE score of *mPGES-1*^{-/-} was significantly reduced, and the duration of peak symptoms of *mPGES-1*^{-/-} was markedly shortened compared with those of WT. The quantitative analysis revealed that *mPGES-1*^{-/-} EAE showed significantly increase in locomotor activity. In histopathological examination, inflammatory lesions in the spinal cord of WT EAE were extensive in white matter, whereas the changes in that of *mPGES-1*^{-/-} EAE were much less severe. In addition, the inflammatory area in *mPGES-1*^{-/-} EAE was significantly smaller than that in WT EAE. Moreover, mPGES-1 protein was expressed in inflammatory lesions in WT EAE. These results suggest that *mPGES-1*^{-/-} was resistant to the progression of EAE compared with WT, and PGE₂ derived from mPGES-1 may enhance the inflammation and aggravate EAE symptoms. In conclusion, mPGES-1 facilitates the progress of EAE, and inhibition of mPGES-1 may be useful for treatment of human MS.

010-2 Complexin directly binds with synaptotagmin 1

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Complexins (also called synaphin) are small, soluble proteins. Complexin interacts with the soluble N-ethylmaleimide-sensitive factor attachment protein receptor (SNARE) complex via its central region is critical for neurotransmitter release. But the role of complexin remains unclear. Here, we show that complexin directly associates with synaptotagmin 1. Synaptotagmin 1 is a major calcium sensor for fast neurotransmitter release. The mapping of the complexin site involved in synaptotagmin 1 binding revealed that the C-terminal region is essential for the binding. The binding was sensitive to ionic strength, suggesting the involvement of charged residues in the C-terminus region. Mutation of the seven consecutive glutamic acid residues (residues 108-114) at the C-terminal region of complexin to alanines or glutamines resulted in a dramatic reduction in synaptotagmin 1 binding activity. Furthermore, the complexin C-terminal peptide blocked the binding of synaptotagmin 1 to complexin, while the same C-terminal peptide with mutation of all the consecutive glutamic acid residues to alanine had no effect on the binding. Immunoprecipitation experiments with the brain membrane extract showed the presence of a complex of complexin /synaptotagmin 1/SNAREs. We propose that complexin recruits synaptotagmin 1 to fusion machinery and synergistically functions with synaptotagmin 1 in mediating fast synaptic vesicle exocytosis. Supported by grant (to C. S-O, T. A. and H. T.) from Ministry of Education, Culture, Sports, Science, and Technology, Japan and from the Takeda Science Foundation.

O10-3 Identification of PKC-dependent phosphorylation sites of SNAP-23 in clonal glial cells

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It is generally accepted that glial cells release neurotransmitters such as glutamate and ATP, and various bioactive substances via exocytotic pathway, and these activities may play important roles in regulation and modulation of brain functions. Previously, we found that Ca^{2+} -dependent exocytosis was negatively regulated by a protein kinase C (PKC)-dependent mechanism in cultured mouse brain astrocytes and in cultured C6 glioma cells. We also found that synaptosomal-associated protein 23 (SNAP-23), one of the soluble *N*-ethylmaleimide-sensitive factor attachment protein receptor (SNARE) proteins essential for exocytosis of non-neuronal cells, was possibly phosphorylated by the activation of PKC. Here, we identified PKC-dependent phosphorylation sites of SNAP-23 in C6 glioma cells. To determine the phosphorylation sites, we purified SNAP-23 from phorbol 12-myristate 13-acetate (PMA)-pretreated C6 glioma cells by a specific immunoprecipitation method. The affinity purified SNAP-23 was digested with trypsin and analyzed by LC-MS/MS. Eventually, more than 95% amino acid sequence of SNAP-23 was detected and Thr²⁴, Ser⁹⁵, Ser¹²⁰ and Ser¹⁶⁰ were found to be phosphorylated in PMA-treated C6 cells. To further confirm the SNAP-23 phosphorylation in living C6 cells, currently we generated phosphorylation-specific antibodies for Ser⁹⁵ and for Ser¹²⁰. We also generated anti-phosphorylated SNAP-23 antibody for Ser¹¹⁰, which was not identified in C6 cells but was previously reported to be phosphorylated in nonneuronal tissues. Immunoblotting analysis using these antibodies clearly showed that Ser⁹⁵ and Ser¹²⁰ were phosphorylated in living C6 cells in PKC-dependent manner. In a striking contrast, Ser¹¹⁰ was phosphorylated in naive cells, and was dephosphorylated after the activation of PKC. These results suggested that the function of SNAP-23 could be regulated by several mechanisms through PKC-dependent multiple phosphorylation sites.

O10-4 Abnormal activation of dentate granule cells in phosphorylation site-deficient SNAP-25 knock-in mouse

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SNAP-25 is a t-SNARE protein essential for neurotransmitter release from nerve terminals. The function of SNAP-25 is regulated through a protein kinase C-mediated phosphorylation of Ser¹⁸⁷. To know the functional importance of SNAP-25 phosphorylation, we generated a mutant mouse having a single amino acid substitution of Ser¹⁸⁷ with Ala. In a series of experiments, we found that the homozygous mutant mice exhibited various interesting phenotypes including behavioral and emotional abnormalities, an elevation of neuropeptide Y expression, and an activation of astroglial cells. In order to know why the single amino acid substitution at the phosphorylation site of SNAP-25 causes these multiple profound phenotypes, we examined the expression of various proteins in the brain during postnatal period. At first, we quantified the expression level of glial fibrillary acidic protein (GFAP), a molecular marker of reactive astrocytosis, by immunoblotting. Although there was no significant difference in the expression level of GFAP between the wild type and the homozygous mice at three weeks after birth, the expression of GFAP increased remarkably thereafter, and 2.3-fold higher expression was observed in the hippocampus of the homozygous mouse at ten weeks after birth. In accordance with these changes, wet weight of hippocampus of the homozygous mouse increased remarkably in these period, and 1.5-fold difference was observed at fifteen weeks after birth. Interestingly, the expression of brain-derived neurotrophic factor (BDNF) was also increased in the hippocampus of the homozygous mouse, however the onset of the increase was earlier than that of GFAP, and a big difference was already observed at 3 weeks after birth. To further clarify the molecular events occurred in the brain of homozygous mouse, we examined the expression of c-fos by immunohistochemistry and found that a quite restricted expression of c-fos was observed around three weeks after birth in the granule cells of dentate gyrus of the homozygous mouse. Thus, these results raise a possibility that at least some phenotypes of SNAP-25 mutant mouse may arise from an abnormal neuronal activity of granule cells in dentate gyrus in postnatal period.

O11-1 Aberrant projection and synaptic formation of bushy neuron in NB-2 knockout mice

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NB-2 which is a neural cell recognition molecule belonging to contactin subgroup is expressed prominently in the central auditory system, especially in the ventral cochlea nucleus (VCN), superior olivary complex (SOC), ventrolateral lemniscus (VNL) and central inferior colliculus. NB-2 is localized at the neuropils and synapse of the glutamatergic neurons of these nuclei. NB-2 knockout (KO) mice exhibit a lower incidence of wild running than the wild-type littermates in the audiogenic seizure test.

Here, we identified the neurons expressing NB-2 in the VCN and examined the abnormality in the auditory pathways of NB-2 KO mice. *In situ* hybridization combined with immunohistochemistry demonstrated that NB-2 was expressed in the bushy neurons in the VCN. The bushy neurons project to the bilateral SOC via the bundle of glutamatergic axons termed the ventral acoustic stria (VAS). We compared the number of axons in the VAS projecting to the contralateral SOC between NB-2 KO mice and wild type mice. The number of axons in the VAS of NB-2 KO mice was reduced relative to that in wild-type mice. These results suggested that the reduced number of projection from VCN to medial nucleus of the trapezoid body (MNTB) might affect the number of glutamatergic synapses and neurons in MNTB. Then, we counted the number of glutamatergic synapses and neurons in the MNTB. The number of glutamatergic synapses and neurons in the MNTB was significantly reduced in NB-2 KO mice as compared with the wild-type mice. Next, we examined auditory brain stem function by the auditory brainstem response (ABR) test. The waveform reflects combined afferent activity of the auditory brain stem. The wave III to IV interpeak latency was significantly augmented in NB-2KO mice. Since the waves III and IV are responses from the SOC, lateral lemniscus and IC in the auditory brain stem, the results of ABR test indicate that the function of these nuclei is impaired in NB-2 KO mice. Together, we demonstrated that NB-2 plays a key role in the projection and synaptic formation of bushy neuron in the auditory brainstem.

O11-2 The role of Spikar in cytoplasm and identification of its functional domain

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Spikar was isolated as a drebrin-binding protein by yeast two-hybrid screen. In cultured neurons, Spikar is localized mainly at nucleus and dendritic spines. Luciferase reporter assay demonstrated that Spikar functions as a transcriptional coactivator for nuclear receptors. Morphological study showed that RNAi knockdown (KD) of Spikar decreased the number of dendritic protrusions (spines and filopodia), suggesting that Spikar is involved in the spine formation. However, it is unclear how Spikar plays a role in spine formation. In this study, we investigated the functional domain of Spikar for spine formation and molecular interaction between drebrin and Spikar. To examine whether Spikar plays a role in spine formation in cytoplasm, we performed rescue experiments of Spikar-KD neurons using wild-type-Spikar or mutated-Spikar with impaired nuclear localization signal (mutNLS-Spikar). A decrease of spine density by Spikar-KD was rescued by both wild-type-Spikar and mutNLS-Spikar. Additionally, overexpression of mutNLS-Spikar increased the number of dendritic protrusion. These results indicate that cytoplasmic-Spikar is involved in spine formation, although the possibility that the role of Spikar in nucleus influences the spine formation cannot be excluded. Since drebrin is one of key protein regulating spine morphology, we examined whether the interaction of cytoplasmic-Spikar with drebrin is necessary for dendritic spine formation. We noticed C-terminal region of Spikar (Spikar-CR), which does not contain other functional domains related to gene transcription and drebrin binding region. Immature cultured neurons (DIV8) were transfected with Spikar-CR and observed in DIV16. Although Spikar-CR cannot interact with drebrin, its overexpression induced a higher density of dendritic protrusions than those of control neurons. Taken together, our data suggest that the functional domain of Spikar for spine formation is contained in c-terminal region and the interaction of Spikar with drebrin is not necessary for spine formation.

O11-3 A role of Caspr2 encoded by neuropsychiatric developmental disorder-susceptibility gene CNTNAP2 in synapse development

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It was recently reported that the human CNTNAP2 gene encoding contactin-associated protein-like 2 (Caspr2) is associated with neuropsychiatric developmental disorders, such as autism and schizophrenia. Caspr2 is a cell recognition molecule belonging to the neurexin family and 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. It has been reported that neurexins play important roles in the synaptic formation and function and that disruption of neurexin 1 gene is associated with autism and schizophrenia, leading us to hypothesize that Caspr2 contributes to formation and/or function of the synapse. To examine whether Caspr2 is localized at the synaptic site, firstly, we performed Western blot analysis of fractions prepared from the mouse cerebral cortex, revealing that Caspr2 was enriched in the synaptosomal fraction. Secondly, immunofluorescent staining for Caspr2 was carried out on the cultured hippocampal neurons. Caspr2 immunoreactivity was detected as punctate signals on the dendrites and partially overlapped with synaptophysin, a synaptic vesicle protein. Caspr2 was also partially colocalized with both excitatory and inhibitory synaptic markers. Furthermore, overexpression of Caspr2 in the cultured hippocampal neurons and Neuro2a cells resulted in increase of the density of protrusions on the neurite. To examine which domains of Caspr2 are involved in the induction of protrusion formation, we measured numbers of protrusions on the neurites of Neuro2a cells when transfected with one of deletion mutants of Caspr2, revealing that the induction of protrusions does not require the intracellular domain, but the N-terminal fragment of the extracellular domain of Caspr2. Our data indicate that Caspr2 is present at the synaptic sites and suggest that the extracellular interaction of Caspr2 with its unidentified receptor may be involved in the synaptic development.

O11-4 Rps2 stability is important for 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.

O12-1 Characterization of A2B5-positive cells in the developing mouse cerebellum

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Introduction: Neural stem cells are committed to become either neuronal precursor cells or glial precursor cells before terminally differentiating into neurons or glial cells. Up to now, neuronal precursor cells and oligodendrocyte precursor cells have been identified in several areas in the murine CNS. Presence of astrocyte precursor cells (APCs), however, has been reported only rarely so far. In this study, we report isolation of A2B5-positive cells, candidates for APCs, from the developing mouse cerebellum. **Methods:** Cerebella from early postnatal mice were digested with papain and fractionated by a step gradient centrifuge of Percoll. We collected the large cell fraction and removed microglial cells from this fraction by immunopanning with an anti-mouse macrophage antibody. Many cells in this fraction didn't express glial fibrillary acidic protein (GFAP), a marker for mature astrocytes. A few cells, however, were GFAP-positive. To remove these GFAP-positive cells, the cells were subjected to immunopanning with the A2B5 antibody, as most of the GFAP-negative cells were A2B5-positive, while most of the GFAP-positive cells were A2B5-negative. **Results:** The cells thus obtained expressed neither GFAP nor S100-β, another marker for mature astrocytes. In contrast, they expressed brain-lipid binding protein (BLBP), a marker for radial glia. In the presence of both basic fibroblast growth factor (bFGF) and bone morphogenetic protein 4 (BMP4), many cells incorporated BrdU, and most of the BrdU-positive cells remained GFAP-negative, suggesting that the combination of bFGF and BMP4 is 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 are also essential for their survival. When these cells were treated with ciliary neurotrophic factor (CNTF) or leukemia inhibitory factor (LIF), the proportion of GFAP-positive cells increased dramatically, suggesting these factors are inducers of their astrocytic differentiation. These cells may be useful for the elucidation of the mechanism for the generation of various astrocytes during cerebellar development.

O12-2 Inhibitory effect of Notch signaling on astrocyte differentiation of the EGF-responsive cells in the developing mouse cerebellum

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In the developing CNS, it is generally accepted that Notch signaling maintains the progenitor pools and inhibits both neurogenesis and oligodendrocyte differentiation. On the other hand, it has been postulated that Notch promotes astrocyte differentiation of the neural stem cells. In this study, we examined the role of Notch signaling on astrocyte differentiation of the epidermal growth factor (EGF)-responsive proliferating cells in the developing mouse cerebellum. The EGF-responsive cells were enriched in the prominin-1-positive cell fraction and showed the cardinal characteristics of neural stem cells, self-renewal and multipotency. These cells stopped dividing and differentiated into GFAP-positive astrocytes in response to ciliary neurotrophic factor (CNTF) or bone morphogenetic protein 2 (BMP2). Overexpression of Notch intracellular domain (NICD) in these cells suppressed their GFAP expression induced by CNTF or BMP2, and kept their nestin expression in the presence of these gliogenic factors. Most of the NICD-overexpressing cells incorporated BrdU even in the presence of CNTF or BMP2. These cells expressed the mRNA of *Hes5*, a basic helix-loop-helix (bHLH) gene, in the presence of EGF, and CNTF or BMP2 treatment decreased this mRNA expression. Overexpression of NICD increased *Hes5* mRNA expression in these cells and kept it at an elevated level even in the presence of CNTF or BMP2. These findings suggest that persistent activation of Notch signaling inhibits astrocyte differentiation of the EGF-responsive cells induced by CNTF and BMP2 and maintains these cells in the undifferentiated, proliferative state, and that this inhibitory effect is mediated by the increased expression of *Hes5*.

O12-3 Functional expression of runt related factor-2 in astrocytes

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Runx2 related factor-2 (Runx2) is the master regulator of osteoblast differentiation with ability to accelerate differentiation of mesenchymal stem cells into osteoblasts. We have previously shown the expression of mRNA and corresponding protein for Runx2 in cultured rat astrocytes and C6 glioma cells. In this study, we have investigated the possible functional changes in astrocytes transiently transfected with Runx2 and C6 glioma cells stably overexpressing the dominant negative Runx2 (dnRunx2). Cultured astrocytes isolated from cerebral neocortex of 18-day-old Wistar rats were transiently transfected with expression vector of Runx2, followed by extraction of total RNA and subsequent synthesis of amino allyl amplified RNA (aRNA) labeled with Cy5 or Cy3, respectively. Panorama Micro Array was hybridized with each labeled aRNA, followed by washing and subsequent scanning with a G2505B microarray scanner. Among a variety of genes scanned, marked upregulation was seen for Runx2 (4.8 fold) and its target genes, such as osteopontin (OPN) (3.7 fold) and matrix metalloproteinase 13 (MMP13) (3.0 fold), whereas downregulation was found for particular astrocyte- and reactive astrocyte-related genes, including glial fibrillary acidic protein (GFAP) (36% decrease), excitatory amino acid transporter-1 (EAAT1) (30% decrease), vimentin (71% decrease) and glypican (72% decrease). These alterations were confirmed by quantitative RT-PCR analysis. In C6 glioma cells stably overexpressing dnRunx2, moreover, a significant decrease was found in luciferase activity for the wild type reporter containing 6 tandem copies of Runx2 binding element linked to the luciferase reporter plasmid. In these stable transfectants, a significant decrease was seen in mRNA expression of both OPN and MMP13, with significantly increased mRNA expression of GFAP and EAAT1. These results suggest that Runx2 may be functionally expressed by astrocytes in terms of transcriptional regulation of particular astrocyte-related genes.

O12-4 Spatio-temporal information of gliotransmitter release from cultured astrocytes

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Astrocytes, the major glial cell type in the CNS, have been considered to be passive bystanders that merely provide support to neuronal networks. However astrocyte is now recognized as one of the active elements that directly modulate brain functions. 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. Although these reports provided clues that astrocytes are the active components in the brain, they did not analyze the temporal and spatial pattern of gliotransmitters release from astrocytes. To observe the release of gliotransmitters, such as ATP and glutamate, we applied imaging techniques visualizing ATP and glutamate released from astrocytes. Luciferin-luciferase solution was applied to the extracellular fluid of astrocytes to visualize ATP release. To visualize glutamate release, glutamate optic sensor was applied. This specific probe for detecting glutamate is a hybrid molecule consisting of glutamate-binding protein and a small-molecule fluorescent dye. We successfully observed ATP or glutamate release from astrocytes and applied these technologies to observe spatial and temporal pattern of gliotransmitters release. By ATP (1 μ M or higher) stimulation, intracellular calcium elevation was observed in all astrocytes. However, under the same condition, only a few astrocytes (ca. 3~7%) released glutamate. A similar phenomenon was observed in glutamate-evoked ATP release from astrocytes; even though all astrocytes showed increased intracellular calcium levels, a small proportion of astrocytes released ATP by glutamate stimulation (ca. 1%). Our experiments using cultured astrocytes revealed that intracellular calcium elevation was not sufficient to evoke gliotransmitter release. For the first time, gliotransmitter release was successfully visualized and the mechanisms of gliotransmitter release were revealed through these imaging technologies.

O12-5 Transport characteristics for adenosine in neurons and astrocytes under basal and oxidative stress-loaded conditions

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[Objective] Adenosine exerts neuroprotective effect against hypoxia/ischemia conditions via activation of adenosine receptors. It is reported that extracellular adenosine concentrations in the brain is elevated under such oxidative stress-loaded conditions. Extracellular adenosine levels are suggested to be regulated by nucleoside transporters (NTs), but there is no information on transport characteristics of adenosine in neurons and astrocytes under such conditions. In the present study, therefore, we first clarified the dominant NT-mediated clearance pathway for adenosine, and then examined whether its transport characteristics were altered under basal and oxidative stress-loaded conditions.

[Methods] Primary cultured rat cortical neurons and astrocytes were cultured in B-27- and FBS-supplemented EMEM, respectively. Uptake experiments for [³H]adenosine were performed by an inhibitor-stop method. Oxidative stress was loaded to cells with SIN-1 in BSS. Cell viability and accumulation of nitrotyrosine were evaluated by an LDH assay and immunocytochemistry, respectively.

[Results & Discussion] Under basal conditions, adenosine uptake by neurons and astrocytes exhibited Na^{+} -independent saturation kinetics, and NBMPR, a representative equilibrative NT (ENT) inhibitor, decreased the uptake and its inhibition at nanomolar concentrations was less than that at micromolar ones. Cellular clearance of adenosine by astrocytes was greater than that by neurons. Thus, ENT2 expressed by astrocytes is demonstrated to have a predominant role in regulating extracellular adenosine levels. Of treatment conditions of astrocytes with SIN-1, 0.5 mM of it for 3 h induced nitrotyrosine accumulation with no change in their viability. Under this condition, adenosine uptake was significantly decreased, and this was suggested to be due to disappearance of the ENT1-mediated uptake. Although ENT1 expression was not altered, the K_m value for adenosine uptake was increased in the SIN-1-treated astrocytes without any change in the V_{max} value. Therefore, adenosine clearance by astrocytes was diminished under oxidative stress-loaded conditions, and this was resulted from decreased transport activity of ENT1, a minor component in adenosine clearance.

O12-6 Transactivation of glia-derived neurotrophic factor in cultured rat cortical astrocytes exposed to nicotine

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Activation of nicotinic acetylcholine receptors (nAChRs) is believed to lead to rapid opening of an ion channel permeable to Na^{+} , K^{+} or Ca^{2+} ions across cell membranes, followed by promotion of the release of a variety of neurotransmitters and subsequent signaling cascade from the cytoplasm to the nucleus for consolidation of a transient extracellular signal carried by acetylcholine in the brain. We have previously shown the possible functional expression of nAChRs in cultured rat cortical astrocytes. nAChRs are composed of heteromeric assemblies of at least eight α subunits ($\alpha 2$ - $\alpha 9$) and three β subunits ($\beta 2$ - $\beta 4$), while $\alpha 8$ subunit is absent from mammals. RT-PCR analysis revealed constitutive expression of ten different subunits in cultured rat cortical astrocytes. Exposure to 10 μ M nicotine for 8 h led to a selective and significant increase in mRNA expression of glia-derived neurotrophic factor (GDNF) amongst different neurotrophic factors tested in cultured rat cortical astrocytes, while MTT reduction was significantly increased in rat cortical neurons cultured with conditioned medium from astrocytes previously exposed to nicotine at 0.1 to 1 mM. The GDNF promoter region was cloned and linked to the luciferase reporter plasmid for determination of transactivation of GDNF gene. In cultured astrocytes transfected with the reporter plasmid, nicotine significantly increased luciferase activity at 0.1 to 1 mM in a concentration-dependent manner. In silico analysis revealed the presence of three different responsive elements, including NF- κ B, AP1 and CRE, -1376 upstream on the GDNF promoter region. In cultured cortical astrocytes transfected with the luciferase reporter plasmid linked to tandem copies of NF- κ B, AP1 or CRE site, moreover, nicotine selectively increased luciferase activity of the NF- κ B reporter, without significantly affecting that of AP1 or CRE reporter, at 1 mM. These results suggest that nAChRs may be functionally expressed by rat cortical astrocytes to predominantly induce mRNA expression of GDNF through gene transactivation at NF- κ B site toward neuroprotection.

O12-7 Effects of theophylline on LPS-induced NO production in cultured astrocytes

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Elucidation of the functions of astrocytes is important for understanding of the pathogenic mechanism of various neurodegenerative diseases. Theophylline is a common drug for bronchial asthma and occasionally develops side-effects, such as acute encephalopathy, due to its narrow range of toxic and therapeutic concentrations. However, the pathogenic mechanism of the side-effects is unknown. The lipopolysaccharide (LPS)-induced NO production is generally used for an index of the activation of astrocyte *in vitro*. In this study, in order to elucidate the effect of theophylline on the astrocytic functions, we examined the LPS-induced NO production and the expression of iNOS protein in cultured rat cortex astrocytes. Theophylline alone could not induce the NO production; however, NO production induced by LPS was enhanced by theophylline in a dose-dependent manner. The theophylline enhancement of NO production was further increased by dibutyl cyclic AMP, a cell membrane-permeable cAMP analog. In addition, the theophylline enhancement was also increased by forskolin, an adenylate cyclase activator, and by isobutylmethylxanthine (IBMX), a phosphodiesterase inhibitor. When the cells were preincubated with Rp-8-Br-cAMP, an inhibitor of protein kinase A, the theophylline enhancement of LPS-induced NO production was decreased. None of the reagents used above showed any significant effect on the cell viability. The extent of iNOS protein expression induced by LPS was enhanced by theophylline or IBMX. The expression of iNOS protein was not detected by the incubation with solely theophylline or IBMX. For xanthine derivatives, such as theophylline and caffeine, at least three mechanisms of action are known; inhibiting phosphodiesterase, antagonizing adenosine receptors, and inducing Ca^{2+} -mobilization from intracellular store. Among these, it is likely that phosphodiesterase inhibition is a major action mechanism for the theophylline enhancement of LPS-induced NO production in astrocytes. Theophylline-induced acute encephalopathy might be due to the hyper-activation of astrocytes via cAMP signaling to produce excess amount of NO.

O13-1 A novel method for region specific gene modification for the analysis of developmental origin of glial cells

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Neural cells, including astrocytes and oligodendrocytes develop from regionalized progenitor cells that are characterized by the expression of various transcription factors. For example, in the neural tube different classes of neurons generate from different domain structure defined by the expression of transcription factors. Recently, it was reported that these transcription factors that define positional identity also regulate subtype-specific development of astrocytes. However, the mechanism that governs glial cell development largely remains unknown as compared with those for neuron. It is difficult to analyze glial lineage or the effect of overexpression or down regulation of a certain gene in a specific cell, because of the limitation of methodology. Thus, we are trying to establish a novel method to introduce genes into chick embryo in a lineage-specific manner. This method is composed of two steps, first is to introduce murine cationic aminoacid transporter (CAT1), which is a receptor for murine retrovirus by electroporation, and second is to introduce murine retrovirus. When we introduced CAT1 vectors into the neural tube of chick embryo under the regulation of ubiquitous promoter, we successfully introduced EGFP genes into chick *in vivo*. We next tried to introduce CAT1 in a specific domain of the spinal cord. CAT1 expression driven by nkx 2.2 enhancer enables lineage tracing from p3 domain, that is characterized by the expression of Nkx2.2. These data suggest that this method is useful to analyze cell lineage and lineage-specific gain-of-function or loss-of-function studies. In this study, we will present recent progress in establishment of this method and its future application.

O12-8 Analgesic effect of Bushimatsu on neuropathic pain

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Bushimatsu (TJ3023 Tsumura Shuchi-Bushi Ethical Dispensing), a processed aconiti tuber, has a very strong analgesic effect and is used as an antinociceptive drug. However, there is little experimental evidence that Bushimatsu is effective for neuropathic pain, or much less about its molecular mechanism(s). Here, we show analgesic effects of Bushimatsu on neuropathic pain using the Seltzer model mice. We performed the thermal hyperalgesia and mechanical allodynia tests, and found that single administration of Bushimatsu dramatically suppressed both the pain behaviors in a concentration-dependent manner. This effect, however, disappeared 24 hr after the administration. On the other hand, when Bushimatsu was administered chronically for 2 weeks, the effects lasted much longer, which, interestingly, were observed 2 weeks after the withdrawal. These results suggest that Bushimatsu has a potential ability to cure neuropathic pain. We will also discuss a mechanism(s) underlying the analgesic effects of Bushimatsu against neuropathic pain.

O13-2 Mammalian glial cells missing genes induce *Hes5* expression and definitive neural stem cells in early embryos

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Notch signaling plays pivotal roles in early development of mammalian embryos and in the generation and maintenance of stem cell populations. Based largely on studies of *Drosophila* and *C. elegans*, a Notch receptor-mediated lateral inhibition model has been proposed, in which cells that are initially equivalent but eventually express ligands more than others send signal to neighboring cells. The cells that receive ligand stimuli activate canonical Notch pathway to upregulate effector genes, *Hes1* and *5*, which in turn suppress the expression of ligand genes. The lateral inhibition model may be valid to explain how neural stem cells in developing mammalian brains are kept undifferentiated; neural stem cells receive signal from their progeny that differentiate and express ligands, *Dll1* and *Jagged*. However, molecular mechanisms how Notch pathway is initially activated in stem-producing cells in the early embryo remain unknown. In this study, we show that products of Glial cells missing (*Gcm*) genes, mammalian orthologues of *Drosophila gcm*, bind to the promoter region of *Hes5* and induce its expression in *Neuro2a* cells, which requires the presence of RBP-J. Analysis of mutant embryos for *Gcm1* and *2* revealed that *Hes5* expression is reduced in *Gcm2*^{-/-} and more severely in *Gcm1/2*^{-/-} mutants at 8-12 somite stages. Due to the early lethality of *Gcm1/2*^{-/-} mutants before the induction of neural stem cells *in vivo*, we employed an *in vitro* culture system to induce basic fibroblast growth factor-responsive definitive neural stem cells from epiblasts and found that the generation of neural stem cells and subsequent differentiation of astrocytes from the neural stem cell are impaired in *Gcm1/2*^{-/-} embryos. Our results suggest that, in contrast to *Drosophila gcm*, mammalian *Gcms* are required for the initial activation of Notch signaling.

O13-3 Cyclin D1 inhibits astrocyte differentiation from neural stem/progenitor cells in a manner independent of cell cycle regulation○Norihiisa Bizen¹, Toshihiro Inoue², Takeshi Shimizu³, Tetsushi Kagawa¹, Tetsuya Taga¹¹Dept. of. Stem Cell Reg., Med. Res. Inst., Tokyo Med. Dent. Univ., Tokyo, Japan, ²Dept. of. Opt. Vis. sci., Grad. Sch. of. Med. Sci., Kumamoto Univ, Kumamoto, Japan, ³Lab. for. Vert. Axis Form., RIKEN. CDB., Kobe, Japan

Proliferation of neural stem/progenitor cells (NSCs) is intimately linked to the inhibition of neuronal and glial differentiation. However, the molecular link between induction of cell cycle progression and inhibition of cell differentiation in NSCs has been poorly understood. We recently reported that FGF2 and Wnts promoted the proliferation of NSCs/NPCs through the common signaling pathway: GSK3B, B-catenin, LEF/TCFs, and cyclin D1 (Shimizu, T. et al. MCB 2008). We also found that the cells expressing cyclin D1, a common target for FGF2 and Wnt signaling, rarely co-expressed GFAP, an astrocyte marker. Astrocyte differentiation from NSCs is synergistically induced by combination of LIF and BMP2, which activate transcriptional factors, STAT3 and Smad1 (Nakashima, K et al. Science 1999), respectively. Since a 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 (Bienvenu F, et al. J Biol Chem 2001), we hypothesized that cyclin D1 might suppress astrocyte differentiation via inactivation of STAT3-mediated transcription of astrocyte-specific genes. Forced expression of cyclin D1 in NSCs cultured with LIF and BMP2 decreased the number of GFAP expressing astrocytes by approximately 50%. Forced expression of cyclin D1 increased the number of neurospheres and their sphere-sizes. CDK4 inhibitor hardly recovered the GFAP expressing cells in number, indicating that cyclin D1 inhibited astrocyte differentiation in a manner independent of cell cycle. Co-immunoprecipitation assay demonstrated that cyclin D1 could directly bind to STAT3 and p300. Cyclin D1 suppressed GFAP promoter activation induced by LIF and BMP2. These data suggested that cyclin D1 disturbed STAT3/p300-mediated transcription of astrocyte-specific genes, and, thus, inhibited astrocyte differentiation.

O13-5 Identification of Phosphatidylglucoside as cell surface antigen of adult mouse neural stem/precursor cells○Jun Kaneko^{1,2}, Masami Kinoshita^{1,2}, Takeo Machida², Yasuko Nagatsuka¹, Yoshio Hirabayashi¹¹Hirabayashi Research Unit, RIKEN, BSI, Saitama, Japan, ²Department of regulatory Biology, Faculty of Science, Saitama University, Saitama, Japan

We have shown that phosphatidylglucoside (PtdGlc) is a cell surface antigen of embryonic neural stem/precursor cells (NSCs/NPCs) of mice (Kinoshita et al., Biochem J. 2009), and the same glycolipid is also expressed in a subset of hematopoietic stem cells (Oka et al., in submission). Our data suggest that PtdGlc plays a unique role in stem cells. PtdGlc is a type of glycosphospholipid localized in the outer leaflet of the plasma membrane. Owing to PtdGlc's unique fatty acid composition, exclusively composed of C_{18:0} at sn-1 and C_{20:0} at sn-2 of the glycerol backbone, it tends to form PtdGlc-enriched lipid rafts (PGLRs). However, the detailed expression profile and function of PtdGlc remains to be elucidated. Here, we examined the expression of PtdGlc in adult NSCs/NPCs in a postnatal neurogenic region, subventricular zone (SVZ). Immunostaining using brain sections from 8, 20 and 40-week-old mice demonstrated that PtdGlc was highly expressed in the SVZ NSCs. The expression ratio in the NSCs of PtdGlc reached 80% maximally. Very interestingly, the PtdGlc-positive cells co-expressed GFAP, adult NSC marker (Doetsch F., 2003), and both expression levels synchronously increased between 8 and 20 weeks. Next, we isolated PtdGlc-positive cells from the adult SVZ, hippocampus and olfactory bulb respectively by using flow cytometry (FACS) with anti-PtdGlc monoclonal antibody. A subset of PtdGlc-positive cells collected formed neurospheres, in which cells could differentiate into neurons and glia cells, indicating that PtdGlc-positive cell population included the NSCs/NPCs. These results suggested that PtdGlc is a promising marker of adult NSCs and the lipid may play a significant role in maintenance or self-renewal of NSCs.

O13-4 Expression of adenomatous polyposis coli (Apc) in the developing mouse brain○Ayako Taguchi¹, Yasuhiro Yamada^{1,2}, Akira Hara¹¹Gifu Univ. Grad. Sch. Med. Tumor Pathol., ²PRESTO, Japan Sci. & Tech. Agency

The Apc (adenomatous polyposis coli) protein plays an important role in the normal developmental process including neuronal network formation. The importance of Apc protein has been implicated in cell growth, cell differentiation, cell death and cell migration. In neural development, transient expression of Apc is reported at the late fetal and neonatal stage. However, little is known with regard to the precise expression patterns and the role of the Apc protein in the normal brain development. This study was aimed to analyze the expression of the Apc gene and protein, and to clarify the functional roles of the Apc in the course of the normal brain development using Apc-IRES-GFP transgenic mouse. We constructed a knock-in targeting vector that contains HA- and Flag-tags followed by IRES-GFP sequences at 3'UTR of the Apc gene. After targeting ES cells with the vector, the knock-in mice were generated by injecting the targeted ES cells into blastocysts. First, we analyzed expression of the Apc in teratomas generated by transplanting the targeted ES cells into SCID mice. Expressions of the Apc were detectable in the neural tissue in teratomas, suggesting that Apc expression is associated with neural differentiation. In the knock-in mice, higher expression of Apc gene and protein was observed at the brain and spinal cord of the mouse embryos. The expression starts at E9.5 and decreases at neonatal stage. In the adult brain, persistent expression of the Apc was observed in a small number of cells in addition to most cells at olfactory bulbs. In order to investigate the role of Apc in neural cells, we separated Apc-high neural cells from Apc-low cells by cell sorter, and analyzed the ability of neurosphere formation in each developing stage of mice. The Apc-high cells formed neurospheres more efficiently than Apc-low cells in both neonatal and adult brain. Thus a part of Apc-expressing cells are recognized to have the potential for neural stem cells. Immunohistochemical analysis for GFP revealed that a small number of cells at subventricular zone (SVZ), which possibly contains neuronal stem cells, express Apc protein in the neonatal brain. Taken together, our findings suggest that Apc-expressing cells in the adult brain contain some neural stem cells.

O13-6 Hippocampal cholinergic neurostimulating peptide precursor protein(HCNP-pp) is involved in differentiation of neural progenitor cells○Takafumi Sagisaka, Tetsuko Kanamori, Norihiko Uematsu, Takanari Toyoda, Noriyuki Matsukawa, Kosei Ojika
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Hippocampal cholinergic neurostimulating peptide (HCNP), originally purified from young rat hippocampus, have been known to promote the differentiation of septo-hippocampal cholinergic neurons. Recently, the precursor protein of HCNP (HCNP-pp) is also focused since it plays a role as a multifunctional factor, such as serin protease inhibitor and a binding protein with phosphatidylethanolamine (PEBP), ATP and Raf-1 kinase (known as Raf-1 kinase inhibitory protein). HCNP-pp is thought to be important in regulating proliferation and differentiation of neuronal cells in vitro and in vivo by modification of mitogen-activated protein kinase (MAPK) cascade. While HCNP-pp expresses in adult rat hippocampal progenitor cells(AHPs), we have previously demonstrated that HCNP-related molecules exist in neurons and oligodendrocytes, but not in astrocytes of adult rat brains. To clarify the involvement of HCNP-pp in neural differentiation, we investigated the alternation of HCNP-pp expression, relating some lineage markers, during the differentiation of cultured AHPs. Reduction rate of fluorescence intensity of HCNP-pp with differentiation had correlation with increase of GFAP fluorescence intensity. Then to examine whether the reduction of the HCNP-pp expression have some meaning in their differentiation to GFAP-positive astrocytes or not, we suppressed the HCNP-pp expression adapted the siRNA system in the cultured AHPs. AHPs which were treated with siRNA had dominant differentiation to the GFAP-positive astrocytes compared with control dishes. These results might suggest that HCNP-pp involves, directly or indirectly, in the neural differentiation of AHPs.

O13-7 Biological effects of radiation on mouse embryonic stem cell-derived neural stem cells

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The neural stem cells increase in number and differentiate into neurons, astrocytes and oligodendrocytes in developmental brain during fetal period. Radiation exposure during the fetal period leads to disturbances in development of the brain and can induce microcephaly or anencephalia. Here we investigated biological effects of the X-irradiation on the neural stem cells, prepared from mouse embryonic stem (ES) cells by the Neural Stem Sphere (NSS) method. Cultured with mitogen fibroblast growth factor-2, the neural stem cells proliferated exponentially. When the neural stem cells were exposed to various doses (1, 5, 10 and 30 Gy) of X-ray, the proliferation of the neural stem cells was dose-dependently inhibited by X-irradiation and almost completely stopped by 5 Gy-radiation. Morphology of the multipolar neural stem cells was affected by the radiation, and the surviving cells after radiation were bipolar and larger than the neural stem cells. However, immunofluorescent study showed that the surviving bipolar cells were positive for nestin, and gene expression of nestin and musashi-1 was also demonstrated in the cells by RT-PCR study. These results suggested that radiation inhibits proliferation of the neural stem cells but the surviving cells after radiation maintain basic properties of the neural stem cells. This work was partly supported by a grant of LRI by JCIA and Selective Research Fund of Tokyo Metropolitan University.

O14-1 Neurotrophin-3 stimulates neurogenetic proliferation in the developing cerebral cortex, via ERK1/2-dependent signaling pathway

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Diverse neurons composing the neuronal layers of the cerebral cortex are sequentially generated from common cortical progenitors, and the postmitotic neurons then migrate to their destinations within the cortical plate. Although recent investigations have clarified important roles of intrinsic factors such as transcription factors and regulators of the cell cycle for the maturation of cortical progenitors, growth factors and neurotrophic factors environmentally supplied by the cerebral cortex are thought to regulate proliferation and neural development, and determine neuronal differentiation, in the cerebral cortex. To test the possible involvement of neurotrophin-3 (NT3) in this process, we investigated the effects of NT3 on cortical neurogenesis by directly administered into the telencephalic ventricular space of 13.5-day-old mouse embryos. 5-Bromo-2'-deoxyuridine (BrdU) was injected into pregnant mice 3 h after the NT3 administration to label the neural progenitor cells. NT3 increased the number of BrdU-positive cells without altering their distribution. The increment of the BrdU-positive cells 24 h after the BrdU injection was attributed to Pax6-/BrdU-positive cells (neural stem cells), which increase was followed by a significant elevation of the number of Tuj1-/BrdU-positive cells (neurons) 36 or 48 h after the BrdU injection, suggesting that NT3 facilitated neurogenesis by acting in 2 sequential steps, *i.e.*, causing proliferation of neural stem cells and generation of neurons from these progenitors. NT3 stimulated phosphorylation of extracellular signal-regulated kinase (ERK)1/2 in the cortical progenitors, and the effects of NT3 on the increase in total BrdU-positive cells and Pax6-/BrdU-positive cells were diminished by a MEK inhibitor, suggesting the involvement of ERK1/2 signal transduction in the NT3 actions.

O13-8 Aberrant development of granule cells of the cerebellum in NB-3 knockout mice

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The neural cell recognition molecule NB-3, which belongs to the contactin subgroup, is expressed in the developing nervous system after birth and its deficiency causes impairment in motor coordination. In this study, we investigated the contribution of NB-3 to cerebellar development, focusing on lobule 3 to avoid deviations in the developmental time course of the different lobules. NB-3 was expressed in radially migrating granule cells and parallel fibers of lobule 3 but not in Purkinje cells. In the developing cerebellum, the neural cell recognition molecules TAG-1, L1 and NB-3 formed distinct expression zones from the deep layer of the external granule cell layer to the internal granule cell layer (IGL), respectively. The NB-3-immunoreactive zone did not overlap with the TAG-1-immunoreactive zones. By contrast, the L1-immunoreactive zone overlapped with both the TAG-1- and NB-3-immunoreactive zones. The double-immunostaining with NB-3 and vesicular glutamate transporter 1 or 2 (VGLUT1 or VGLUT2), which are presynaptic markers of glutamatergic synapses, demonstrated that NB-3 is present in the presynaptic terminals of parallel fibers and absent in those of climbing-fibers. We compared the development of granule cells between NB-3 knockout (KO) and wild type mice. At postnatal day (P) 5, dot or short fiber-like L1 immunoreactivity was abundant in the IGL of NB-3 KO mice, but was sparse in wild-type mice. These suggest that granule cells expressing L1 in the IGL of NB-3 KO mouse might be delayed or fail to form synapses with Purkinje cells, because L1 is known to be localized in developing parallel fibers, but not synaptic sites and decrease after synapse formation. The number of parallel fiber presynaptic terminals was reduced in NB-3 KO mice relative to wild-type mice at P5 and P10. These differences lessened toward adulthood. Collectively, our results indicate that NB-3 deficiency affects the postnatal development of granule cells in the cerebellum.

O14-2 Roles of motoneuron-derived NT-3 on sensory neuron development

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Execution of motor and sensory 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 motor and sensory interaction, we analyzed dorsal root ganglia (DRG) of Olig2 knockout (KO) embryos, which have no motoneuron in the spinal cord (SC). Olig2 KO mouse is a good tool for this study. In the E10.5 DRG of Olig2 KO mice, increased number of apoptotic cells was observed. Furthermore, abnormal axon projection of sensory neurons was also observed in Olig2 KO mice at E10.5 and E12.5. These data suggest that motoneuron-derived factor(s) modulate sensory neuron survival and axon projection. Among neurotrophic factors, we focused on neurotrophin-3 (NT-3), because NT-3 is known as a survival factor for sensory neuron and chemoattractant factor for sensory neuron axons *in vitro*. Using *in situ* hybridization, we confirmed NT-3 mRNA expression in motoneurons in wild type and Olig2 heterozygous SC at E10.5 and E13.5, but almost no expression in Olig2 KO mice SC at the same stages. NT-3 mRNA expression outside of SC became stronger at later stages. These data suggest that motoneuron-derived NT-3 is one of the essential factors for survival and axon guidance of sensory neurons at an early developmental stage.

O14-3 Nerve growth factor promotes GRP78 expression only under the condition of ER stress

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Glucose-regulated protein 78 (GRP78) is a molecular chaperon acting in the endoplasmic reticulum (ER), and the GRP78 expression is induced during ER stress. Transcription of the GRP78 gene is induced via three ER stress response elements (ERSEs) that reside upstream of the GRP78 promoter. We found that nerve growth factor (NGF) prevented ER stress-mediated apoptosis but did not prevent the induction of GRP78 expression in PC12 cells. We discovered that the expression of GRP78 was further up-regulated when NGF was added during ER stress although the expression did not occur with NGF alone. Then, we analyzed the transcriptional mechanism of the hyper-induction of GRP78 during ER stress, and discovered that all three ERSEs partially contribute to the NGF-mediated hyper-induction of GRP78 expression during ER stress. These results suggest that there exists an additional mechanism for the induction of the GRP78 gene through NGF-triggered PI3-K-mediated signaling in PC12 cells.

O14-4 Fibroblast growth factor-2-responsive and spinal cord-resident rat mesenchymal cells stimulate axonal regeneration followed by the improvement of locomotor function after complete spinal cord injury

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The adult CNS has only a limited capacity for axonal regeneration. In this study, basic fibroblast growth factor (FGF-2) was injected only once into the spinal cord tissue around the injury site immediately after complete spinal cord injury in rats. Surprisingly, this treatment markedly improved locomotor function of the animals. Histological analysis demonstrated that a massive tissue composed of FGF-2-induced fibronectin-positive cells (FIFs) appeared and filled large cystic cavities, in which numerous axons with neurofilament-M immunoreactivity penetrated and ran. Invading meningeal cells generally produce a fibroblastic scar after damage to the spinal cord, which scar forms an absolute barrier to axonal regeneration. It is very important to investigate the cell properties of the FIFs at the molecular level for understanding the mechanisms underlying this functional recovery by contrast with the meninx-derived fibronectin-positive cells (MDFs). To compare these cells, the FIFs were cultured by explanting tissues of the FGF-2-treated injured spinal cord, and found to have spindle-shaped morphology. RT-PCR analysis revealed that the expression level of N-cadherin and neurotrophic factors was significantly higher in FIFs than in MDFs, suggesting important roles of FIFs in axonal regeneration. Therefore, we transplanted FIFs into the transection site and found that the grafts could survive well, and the locomotor activity of the hosts markedly recovered and it came to be able to walk by moving the joints of their hindlimbs. Retrograde axonal transport of fluorescent reagent beyond the transection site into red nucleus suggested regenerative axonal growth of the rubrospinal tract. However, MDFs were not effective in improvement of locomotor activity after spinal cord injury. These observations strongly support the idea that the FIFs enhance recovery of the injury-evoked locomotor dysfunction by forming a microenvironment permissive and advantageous for axonal regrowth, and encourage us autologous transplantation of the FIFs as a novel and promising therapeutic tool for treatment of spinal cord injury.

O14-5 Metabolomic analysis for brain lipids in BDNF-KO mice

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Brain-derived neurotrophic factor (BDNF) exerts multiple functions in the CNS. Although BDNF can control transcription and protein synthesis, it still remains unclear whether BDNF controls neuronal lipid homeostasis in brain. Our previous study indicated that BDNF induced cholesterol biosynthesis in cultured CNS neurons, which seems to be important for synapse development. However its effects on cholesterol metabolism in vivo or on other lipid species are not fully investigated. To better understand them, we investigated the metabolomic analysis of neuronal lipids using Gas Chromatography-Mass Spectrometry (GC/MS), and profiled the brain lipids in neonatal BDNF-KO mice. Our result indicated that cholesterol precursors, that were rich in neurons, are specifically reduced in the brain of BDNF-KO mice, indicating the impairment of cholesterol biosynthesis in neuron in BDNF-KO mice. In addition, it was shown that neuron-specific cholesterol metabolite was specifically decreased, indicating a possibility that BDNF induces both cholesterol biosynthesis and metabolism during synapse development. Furthermore, impairment of fatty acid homeostasis was also detected in the brain of BDNF-KO mice. These results suggest that BDNF not only controls transcription and protein synthesis, but also regulates the lipid homeostasis in brain.

O14-6 Neurotrophic factor-like signaling of 2-decenoic acid ethyl ester, a medium-chain fatty acid derivative

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Biological activities of straight medium-chain fatty acids on central nervous system have not yet been clarified, although the medium-chain fatty acids reported to induce neurites from cultured rat pheochromocytoma PC12 cells. In this study, we examined the effects of medium-chain fatty acids and their derivatives on the activation of extracellular signal-regulated protein kinases 1 and 2 (ERK1/2), members of the mitogen-activated protein kinase (MAPK) super family, using neurons cultured from 18-day-old embryonic rat cortical neurons. Octanoic acid with 8 carbons, 2- and 9-decenoic acid and decanoic acid with 10 carbons, and lauric acid with 12 carbons activated MAPK. 2-Decenoic acid most potently activated MAPK, and the entyl-esterification of fatty acids was more beneficial, demonstrating that the 2-decenoic acid ethyl ester (DAEE) was the most potent derivative of medium-chain fatty acids tested. DAEE stimulated MAPK phosphorylation via MEK activation as low as 1 μ g/ml, and the activity lasted for 8 hr. DAEE subsequently activated cAMP responsive element binding protein (CREB), a downstream transcription factor of MAPK pathway, and also facilitated phosphorylation of Akt and phosphatidylinositol 3 kinase (PI3K) but did not p38 MAPK, calmodulin kinase II or protein kinase A, demonstrating that both MAPK/CREB and PI3K/Akt pathway are involved in the DAEE intracellular signaling. An inhibitor of tyrosine kinase, genistein, suppressed DAEE-induced MAPK activation, suggesting that DAEE activates a putative tyrosine kinase(s) followed by transduction of MAPK and PI3K pathways. However, Trk family tyrosine kinases might be excluded, because of a lack of inhibitory effects of K252a. p38 MAPK or calmodulin kinase II was not involved in DAEE actions. These observations suggest action mechanisms of DAEE supporting our previous findings that administration of DAEE i.p. ameliorates stress-induced reduction of MAPK in the hippocampus. The tyrosine kinase-mediated activation of MAPK/CREB and PI3K/Akt pathways suggests that DAEE is a promising neurotrophic molecule to show therapeutic effect on depression and particular neurodegenerative diseases.

O14-7 The activity of cholinacetyl transferase is increased in medial septal nucleus of HCNP precursor transgenic mouse

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The cholinergic neuronal system of septo-hippocampus is known to play a crucial role in memory. The reduction of acetylcholine, due to the inactivation of choline acetyltransferase (ChAT), was ascertained in this cholinergic system in animal models of dementia and in patients with Alzheimer's disease (AD). However, it remains unclear, why the number of cholinergic neurons in Mynelt nucleus is declined from early phase of AD. We have previously demonstrated that hippocampal cholinergic neurostimulating peptide (HCNP) and/or its precursor protein (HCNPPp/RKIP: Raf kinase inhibitor protein) induce acetylcholine synthesis, and involve in the disorder of memory in Alzheimer and model mouse of memory dysfunction. To examine directly the involvement of HCNP and HCNPPp/RKIP in memory formation, we generated the conditional transgenic mouse of HCNPPp/RKIP, driven by a subunit of Ca²⁺ calmodulin-dependent protein kinase II (α CaMKII) promoter. We obtained 5 established germ line, identified them as genetically modified model by southern blot, in situ hybridization, western blot. We find the increased expression of ChAT in medial septal nucleus by immunohistochemistry. This result suggests that HCNP and HCNPPp/RKIP associate with acetylcholine synthesis *in vivo*.

O15-1 Impairment of BDNF secretion is involved in the phencyclidine-induced synaptic loss in cortical neurons

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Phencyclidine (PCP), a non-competitive NMDA (N-methyl-D-aspartate) receptor blocker, has been used as an anesthetic agent and a dissociative drug. Chronic administration of PCP generates schizophrenia-like symptoms (positive and negative symptoms) in human and rodents. PCP-induced behavioral and gene/protein expression changes in rodents have been reported, however, little is known about the molecular mechanisms underlying the effect of PCP on neuronal dysfunction. In cultured cortical neuron, we found that PCP administration caused robustly increased expression of intracellular brain-derived neurotrophic factor (BDNF) within 3 hours. In contrast to the up-regulation of BDNF, decreased Trk (receptor for BDNF) activation and intracellular signaling (MAPK/ERK and PI3K/Akt) activation was observed. Forty-eight hours after PCP treatment, the number of synaptic sites and expression of synaptic proteins were decreased without any impact on cell viability. Generally, synaptic connections and Trk-dependent signaling pathways are positively regulated by BDNF. To resolve the paradoxical phenomenon caused by PCP, we determined the amount of endogenous BDNF secretion during PCP treatment and found that secretion of BDNF from cortical neurons was significantly decreased. Taken together, it is possible that the impairment of BDNF secretion is responsible for the loss of synaptic connections induced by PCP.

O14-8 Fasting-induced expression of AF5q31, a transcription factor, and β Klotho in the hypothalamus

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A member of AF4 transcription factors, AF5q31, is involved in the development of acute lymphoblastic leukemia. In the adult mice, AF5q31 is strongly expressed in the testis, and weakly in the heart, skeletal muscle, pancreas, and brain. It has been reported that fasting induces the expression of AF5q31 in the hypothalamus by cDNA microarray analysis. However, the roles of AF5q31 in the hypothalamus remain unclear. To gain insights into the hypothalamic function of AF5q31, we characterized AF5q31-positive cells in the hypothalamus. During fasting, both mRNA and protein expression of AF5q31 were increased in the neurons of the arcuate nucleus. In the hypothalamus of ob/ob mice, an animal model of obesity, the expression of AF5q31 was also abundant in the arcuate nucleus compared to that of lean mice. Fibroblast growth factor 21 (FGF21), a metabolic regulator predominantly expressed in the liver, was increased in the serum of both fasted mice and ob/ob mice. FGF21 exerts its effects through the receptor complex, β klotho and FGF receptor (FGFR). Coexpression of β klotho with FGFR1 or FGFR4 was observed in the neurons of the arcuate nucleus of fasted mice. Phosphorylated extracellular signal-regulated kinase 1/2 was increased and colocalized with β klotho in the arcuate nucleus of fasted mice. In addition, many AF5q31-positive cells expressed β klotho. These results suggest that AF5q31 is induced by FGF21 in the arcuate nucleus during fasting. To investigate the targets of AF5q31, we examined the colocalization of AF5q31 with some molecules expressed in the arcuate nucleus. Some AF5q31-positive cells were colocalized with neuropeptide Y, but not with proopiomelanocortin. Almost all of AF5q31-positive cells expressed growth hormone secretagogue receptor (GHS-R), a receptor for ghrelin in the arcuate nucleus. From these findings, FGF21 may exert its effect via the hypothalamus partly through the induction of AF5q31 mainly in GHS-R-positive neurons.

O15-2 PACAP regulates the neural extension in adult neurogenesis

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Pituitary adenylate cyclase-activating polypeptide (PACAP) is a neuropeptide involved in a variety of brain function. Mice lacking the *Adcyap1* gene encoding PACAP (*Adcyap1*^{-/-}) and PACAP specific receptor, PAC1 deficient mice exhibit marked behavioral abnormalities. In order to clarify the molecular mechanism of PACAP dependent psychiatric disorders, we have first attempted to isolate the PACAP deficiency-regulated gene in the dentate gyrus of the mice using differential display (DD) method. Expression of stathmin1 is up-regulated in the dentate gyrus both at the levels of mRNA and protein. In addition, PACAP stimulation inhibits the stathmin1 expression in PC12 cells. In addition we have found that increased expression of stathmin1 in the neurons of the SGC and primary cultured hippocampal neurons induces the abnormal arborization of the processes both *in vivo* and *in vitro*. Next, we elucidated the molecular pathway of stathmin1 increase by PACAP. Present study revealed that *Ascl1* binds to E10 box to activate the stathmin1 expression. On the other hand expression of inhibitory bHLH proteins, such as *Hes1* and *Id3*, was up-regulated rapidly by PACAP stimulation. It could be concluded that up-regulated expression of *Hes1* and *Id3* by PACAP stimulation suppress *Ascl1* expression by each functions. Furthermore, we have detected an increase expression of stathmin1 in the brains of the schizophrenia patients. The present results show that up-regulated stathmin1 in the dentate gyrus of the PACAP deficiency dependent psychiatric disorders may produce the abnormal neuronal circuit to cause the abnormal behavior.

O15-3 Dysbindin-1 regulates the dendritic morphogenesis of hippocampal neurons

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Genetic variations in dysbindin-1 (dystrobrevin-binding protein-1, DTNBP1) are one of the most commonly reported variations associated with schizophrenia. Schizophrenia is now considered as a neurodevelopmental disorder resulting from abnormalities of synaptic connectivity. However, the physiological role of dysbindin-1 in the neuronal development is uncertain. In this study, we attempted to clarify the function of dysbindin-1 in neuronal tissues. We examined the developmental change of dysbindin-1 in rat brain by Western blot analysis using a specific antibody for dysbindin-1 and found that a 50 kDa isoform is highly expressed during the embryonic stage while a 40 kDa isoform appeared at postnatal day 11 and increased thereafter. Immunohistochemistry revealed the localization of dysbindin-1 at soma and dendrites in cortical neurons and Purkinje cells, and immunofluorescent analyses detected dysbindin-1 at the spine-like structure of primary cultured rat hippocampal neurons. We identified WAVE2, but not N-WASP, as a binding partner for dysbindin-1. We also found that Abi-1, a binding molecule for WAVE2 involved in the spine morphogenesis, interacts with dysbindin-1. Dysbindin-1 caused the enhancement of the binding of WAVE2 to Abi-1. To explore the physiological role of dysbindin-1 in the neuronal development, RNA interference of dysbindin-1 expression was done in hippocampal neurons, and density and length of dendritic protrusions were measured. We found that knockdown of dysbindin-1 leads to the generation of abnormally elongated immature dendritic protrusions. These results suggest that dysbindin-1, WAVE2 and Abi-1 form a functional complex and coordinately regulate the spine morphogenesis in developing neurons.

O15-5 Selective RGS protein regulation of melanin-concentrating hormone receptor 1

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Melanin-concentrating hormone receptor 1 (MCH1R) is a G protein coupled receptor (GPCR) which is highly expressed in brain including hippocampus, nucleus accumbens shell, septum and amygdala. Extensive studies of genetically engineered animals and selective antagonists revealed an important role of MCH1R in the regulation of mood and stress, as well as in positive reward aspects of feeding and satiety. GPCR signaling pathway can be regulated by multiple interactions with proteins. Among these, Regulators of G-protein signaling (RGS) are negative modulators which regulate the GPCR mediated signaling by acting as GTPase-activating proteins, thereby terminating the G protein activation cycle. Previously, we elucidated that RGS8, which is highly expressed in nucleus accumbens shell, drastically inhibited the actions of both Gαq- and Gαi/o-mediated MCH1R signaling. RGS2, which is highly expressed in hippocampus, has been reported to be involved in anxiety and aggressive behavior. We therefore hypothesized that RGS2 also functionally interacts with MCH1R. Here we provide the evidence that RGS2 significantly inhibited the MCH1R-induced signaling in dose dependent manner. From the results of calcium mobilization assay with the treatment of PTX, RGS2 act on MCH1R signaling mediated by extensively Gαq-dependent pathway. We further performed the functional assay using a variety of MCH1R mutants to identify a structurally important receptor site for interaction with RGS2. Our data suggest that RGS2 and RGS8 differentially associate with MCH1R and it might represent two distinct modes of signaling modulation.

O15-4 Reversal by galantamine of apomorphine-induced deficits in prepulse inhibition via stimulation of muscarinic ACh receptors

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Schizophrenic patients show decreased levels of nicotinic ACh receptors (nAChRs) and M₁/M₄ muscarinic ACh receptors (mAChRs). In addition, atypical antipsychotic drugs preferentially increase ACh concentrations in the prefrontal cortex. These observations may provide a rationale for pharmacological approaches directed at cholinergic targets to enhance the cognitive abilities of patients with schizophrenia. Recently, we have reported in mice that acetylcholinesterase (AChE) inhibitors, galantamine and donepezil, reversed apomorphine-induced deficits of prepulse inhibition (PPI) (Koda et al., Psychopharmacology 2008). Galantamine also acts as a potentiator of nAChRs, although nAChR antagonists do not block its ability to modulate PPI deficits. In this study, we examined the role of mAChRs in the effect of galantamine, and studied the mechanism of galantamine-induced increases in prefrontal ACh levels in mice. Apomorphine (1 mg/kg) was administered to male ddY mice (9-10 weeks old) to create a PPI deficit model. Extracellular ACh concentrations in the prefrontal cortex were measured using *in vivo* microdialysis. Galantamine- and donepezil-mediated improvements in apomorphine-induced PPI deficits were blocked by the preferential M₁ mAChR antagonist telenzepine. The mAChR agonist oxotremorine also improved apomorphine-induced PPI deficits. Galantamine, like donepezil, increased extracellular ACh concentrations in the prefrontal cortex. Galantamine-induced increases in prefrontal ACh levels were partially blocked by the dopamine-D₁ receptor antagonist SCH23390, but not by antagonists of mAChRs (telenzepine) and nAChRs (mecamylamine). Galantamine increased dopamine, but not 5-HT, release in the prefrontal cortex. These results suggest that galantamine improves apomorphine-induced PPI deficits by stimulating mAChRs through increasing brain ACh levels via a dopamine-D₁ receptor-dependent mechanism and AChE inhibition.

O15-6 Effects of acute and chronic treatment with atomoxetine and methylphenidate on the extracellular levels of monoamine in mouse brain

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Atomoxetine and methylphenidate are widely used in the treatment of attention-deficit/hyperactivity disorder (ADHD). Despite the fact that patients suffering from ADHD are medicated with these drugs for relatively long periods, it is not known about the long-term effects of exposure to the drug on extracellular concentrations of monoamine neurotransmitters. In addition, neurochemical effects of atomoxetine and methylphenidate have not been studied in mice. Thus, the present study investigated, using *in vivo* microdialysis technique, the effects of acute and chronic treatment with these ADHD drugs on the extracellular levels of norepinephrine (NE), dopamine (DA) and serotonin (5-HT) in the prefrontal cortex and striatum of adolescent mice. Dialysate NE and DA levels in the prefrontal cortex were increased to the same extent by either 1 or 3 mg/kg of acute atomoxetine treatment. However, none of these monoamine levels in the striatum were changed. On the other hand, acute treatment with methylphenidate (3 and 10 mg/kg) dose-dependently increased NE and DA levels in the prefrontal cortex and striatum, but it did not affect 5-HT levels in both brain regions. Atomoxetine (1 mg/kg)- and methylphenidate (3 mg/kg)-induced increases in NE, but not DA, levels in the prefrontal cortex were markedly reduced in mice pretreated chronically with atomoxetine and methylphenidate, respectively. Furthermore, methylphenidate (3 mg/kg) significantly increased NE and DA levels in the striatum of chronic methylphenidate-treated mice. These observations suggest that ADHD drugs-induced increases in prefrontal NE and DA levels were suppressed and maintained, respectively, after chronic treatment without affecting basal extracellular levels. On the other hand, chronic treatment with methylphenidate leads to sensitize striatal NE and DA neurons. Thus, these neurochemical phenomena may be involved in therapeutic efficacy and/or adverse effect of long-term exposure to atomoxetine and methylphenidate.

O15-7 Electron microscopic studies on neuronal dendritic abnormality caused by TSC-2 mutation

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Disruption of regulatory machinery for neuronal dendritic spines has been thought to contribute to abnormal brain functions in various pediatric, neurological, and psychiatric disorders. Mutations in either *tsc2* (tuberous sclerosis complex-2) or *tsc1* gene cause TSC (tuberous sclerosis complex), which is a hereditary autistic disorder. Its characteristic symptoms are severe epilepsy, mental retardation and autism. However, the mechanistic relationship between these neurological symptoms and TSC signaling pathway remains unclear. TSC2 has GAP activity towards the Ras family small GTPase Rheb (Ras homologue enriched in brain), thereby Rheb-GTP is changed to Rheb-GDP, and then mTOR signaling pathway is suppressed. In TSC patients, TSC2 mutation sequentially activates Rheb and mTOR. To clarify the regulatory mechanism of dendritic spine development by this TSC2-Rheb-mTOR signaling pathway, we examined neuronal dendrites from Eker rats that are heterozygous for a mutation in the *tsc2*. Cultured neurons from Eker rats exhibited an increase in dendritic protrusion length and density, and a decrease in head width. Rapamycin, a specific mTOR inhibitor, in part recovered these changes. Electron microscopic analyses revealed that cultured hippocampal neurons had numerous filopodia-like dendritic protrusions with many branch and fewer spines with synapses. Furthermore, we found that mitochondria in dendritic shafts of Eker neurons were significantly larger and longer than those of wild type. In addition, proteomic study defining protein diversity in synaptosomal fraction identified some mitochondrial proteins were increased in Eker synaptosomes. Thus, perturbations of TSC pathway may change mitochondria-related gene expression accompanying mitochondrial abnormality, leading to a delay in dendritic spine development in TSC patients.

P-1 Possible involvement of 5'-AMP-activated protein kinase in proliferation and survival of neural stem/progenitor cells derived from the neocortex

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Neural stem/progenitor cells (NPCs), which are defined by their ability to self-renew and differentiate into the three major cell types, neurons, astrocytes, and oligodendrocytes, play a key role in the development and maturation of the central nervous system. 5'-AMP-activated protein kinase (AMPK) is activated in response to an increase in the ratio of AMP to ATP within the cell and therefore acts as an efficient sensor for cellular energy state. To elucidate roles of AMPK in proliferation of NPCs, in this study, we evaluated the effect of an activator and inhibitor for AMPK on proliferative activity in NPCs derived from the neocortex of embryonic mice. Neurospheres were prepared from the neocortex of 15-days-old embryonic mice by primary culturing in DMEM/F12 medium with epidermal growth factor and basic fibroblast growth factor for 9 days in vitro (DIV). After replating, the cells were further cultured for 6 DIV under the same condition in the absence or presence of metformin (AMPK activator) and compound C (AMPK inhibitor). Immunoblot analysis revealed that the level of phospho-AMPK (p-AMPK), but not AMPK, was progressively increased in a culture time-dependent manner. MTT assay and ELISA of 5'-brom-2'-deoxyuridine revealed that treatment with metformin produced enhancement of the proliferative activity and survival of neurospheres during culture, as well as an increase in the level of p-AMPK. In contrast, treatments with compound C produced a decrease in the proliferative activity and survival of neurospheres during culture. In addition, compound C was the ability to facilitate cell damage during culture. These results suggest that the activation of AMPK may positively regulate the proliferation and survival in NPCs of embryonic mouse neocortex.

O15-8 Two-generation toxicogenomic study of the effects of tributyltin on the developing rat brain

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Tributyltin (TBT) compounds which have been used as antifouling agents are reported to have neurotoxicity in mammals. The mechanism of neurotoxicity remains to be elucidated. In this study, we investigated the effect of TBT on the developing rat brain by a two-generation toxicogenomic analysis using custom DNA microarrays followed by biochemical and immunohistochemical analyses. F1 rats were exposed to TBT in utero and postnatally by feeding their mothers chow containing 25ppm or 125ppm TBT chloride. After 3w postnatally, the pups were fed normal chow free of TBT. As microarray targets, amplified and fluorescently labeled cRNA obtained from the cerebral cortex and midbrain of control and TBT-exposed animals at postnatal 1w, 2w, 3w and 6w were used. The competitive hybridizations revealed that TBT affected gene expression in the midbrain more severely than that in the cerebral cortex. Expression of several genes in the midbrain remained altered after withdrawal of TBT for 3w. Further analysis by realtime PCR confirmed following changes in gene expression 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 the genes involved in cellular calcium homeostasis, *chromogranin b* (*chgb*) and *slc8a2* at all time points including 6w. TBT exposure may reversibly affect mitochondrial function at 3w when cumulative amount of TBT intake was maximal, however, 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, *slc8a2*. Further analysis carried out in the midbrain revealed a decrease in chromogranin B at the protein level in the 125 ppm group at 6w. In addition, TBT caused a transient but significant decrease in tyrosine hydroxylase at 1w. The exposures to exogenous compounds like TBT during development may cause prolonged influences in the brain even after its withdrawal.

P-2 Participation of reactive oxygen species and nitric oxide in proliferation of neural stem/progenitor cells derived from the hippocampus of embryonic mice

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To elucidate participation of reactive oxygen species (ROS) and nitric oxide (NO) in proliferation of neural stem/progenitor cells (NPCs), in this study, we evaluated the effects of ROS scavengers and NO synthase inhibitor on proliferative activity in the NPCs of the hippocampus in embryonic mice. Neurosphere was 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 for 9 days in vitro (DIV). After replating, the cells were cultured for 6 DIV under the same conditions in the absence or presence of edaravone (brain protective agent), 4-hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl (tempol, radical capture agent), apocynin (NADPH oxidase inhibitor), N^G-nitro-L-arginine methyl ester hydrochloride (L-NAME, NO synthase inhibitor), 1H-[1,2,4]oxadiazolo[4,3-a]quinoxalin-1-one (ODQ, NO-dependent soluble guanylyl cyclase inhibitor), 8-Bromo-cyclic GMP (8-Br-cGMP, cGMP analogue) or KT5823 (protein kinase G inhibitor) for a period of 9-15 DIV. Treatments with edaravone, tempol or L-NAME resulted in a marked reduction in ROS production in the cells. Additionally, treatment with L-NAME significantly led to decrease of NO₂ level in the culture medium and intracellular cGMP level 24 h after the treatment. MTT assay and ELISA of 5'-bromo-2'-deoxyuridine (BrdU) revealed that a marked decrease in surviving neurospheres and the proliferative activity was seen by edaravone and tempol. Moreover, treatment with apocynin, L-NAME, ODQ, and KT5823 led to a decrease in the surviving neurospheres and the proliferative activity. 8-Br-cGMP partially abolished the decrease in BrdU incorporation by L-NAME. In addition, L-NAME suppressed the activation of Akt signals, without affecting EGF receptor and ERK. These results suggest that ROS and NO would positively regulate proliferative activity through the activation of Akt signals in NPCs of embryonic mouse hippocampus.

P-3 Effect of caspase inhibitor on proliferation of neural progenitor cells derived from embryonic neocortex of mice

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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 involvement of caspase-3 on proliferative activity in neural progenitor cells of 15-days-old embryonic mice. Neural progenitor cells were prepared from the neocortex 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. Immunoblot assay reveals that the level of α -Fodrin and its degradation products and phosphor-JNK (p-JNK) in neural progenitor cells cultured for 11-15 DIV. Moreover, to determine the levels of active caspase-3, we performed an immunoblot analyses and immunocytochemistry. In addition, supernatant of cells in neural progenitor cells cultured for 11-15 DIV was assayed for LDH released, to evaluate cytotoxicity. The degradation products at 120 kDa, which is cleaved by activated caspase-3, were progressively increased in a culture time-dependent manner, but not 145/150 kDa which is cleaved by activated calpains. Expression of p-JNK was decreased in culture for 11-15 DIV. Expression of active caspase-3 was significantly increased at 15 DIV. In addition, active caspase-3 was expressed in nestin positive cells. However, LDH release doesn't shown change. After replating, the cells were cultured for 6 DIV under the same conditions in the absence or presence of caspase inhibitor z-VAD-FMK for a period of 9-15 DIV. MTT assay revealed that a marked decrease in surviving neurospheres and the proliferative activity was seen by treatment with z-VAD-FNK. In addition, constitution of neurosphere was inhibited by treatment of z-VAD-FMK. These results suggest that caspase-3 would positively regulate proliferative activity in NPCs of embryonic mouse cortex.

P-5 NMDA receptors positively regulate proliferative activity of neural progenitor/stem cells generated after neuronal damage in the hippocampal dentate gyrus

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Numerous studies indicate that NMDA receptors play an important role in neural development by influencing the proliferation of neural stem/progenitor cells in vivo and in vitro. To elucidate mechanisms underlying the modulation of the neurogenesis by glutamate signals, in this study, we evaluated the effects of the NMDA receptor antagonists on the proliferative activity of neural progenitor/stem cells generated after neuronal damage induced by trimethyltin chloride (TMT) in the hippocampal dentate gyrus. In vivo experiments, TMT-treated mice were given either MK-801, SM31900 or ifenprodil with 5-bromo-2'-deoxyuridine (BrdU) every 12 h for 2 days from day 2 to day 4, and then decapitated to determine BrdU-positive cells in various subregions of the hippocampus at 12 h after the final injection of drugs. TMT treatment led to neuronal loss in the granule cells of the hippocampus on day 2 post-treatment, with being followed by a marked increase in BrdU-positive cells in the dentate gyrus on day 3 to 7 post-treatment. TMT-induced increase in BrdU-positive cells was significantly attenuated in the subgranular zone and granule cell layer by NMDA receptor antagonists such as MK-801, ifenprodil, and glycine antagonist. In vitro experiments, hippocampi were isolated from mice day 3 after injection of TMT, and then cell suspensions were maintained in DMEM/F-12 supplemented with epidermal growth factor (EGF) and basic fibroblast growth factor (bFGF). Cells were cultured in DMEM/F-12 medium containing EGF/bFGF resulted in the formation of round spheres immunoreactive to nestin at 27 days in vitro (DIV). Compared with the number of neurospheres derived from naive animals, dramatically more neurospheres were seen in those derived from TMT-treated animals. Additionally, the neurospheres cultured for 27 DIV were differentiated into neuronal cells and astrocytes. In vitro neurosphere assay revealed that MK-801 and glycine antagonist markedly decreased the number of neurospheres. Our results suggest that NMDA receptors positively regulate proliferative activity of neural progenitor/stem cells generated after neuronal damage in the hippocampal dentate gyrus.

P-4 Suppression by myosin VI responsive to traumatic stress of neural progenitor proliferation

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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 fatal traumatic stress experiences. We have previously shown that symptoms relevant to PTSD are invariably seen in mice with the extremely traumatic experience, water-immersion restraint stress (WIRS). In this study, we evaluated the underlying mechanisms for PTSD from a viewpoint of adult neurogenesis in mice. Both mRNA and corresponding protein for Myosin VI (Myo6) were selectively expressed in the murine hippocampus within 24 h after WIRS, prior to a drastic but transient decrease in proliferation activity determined by the incorporation of the thymidine analog 5-bromo-2-deoxyuridine of neural progenitor cells expressed in the dentate gyrus. Western blotting analysis clearly revealed a significant increase in the expression of Myo6 protein in the murine hippocampus within 24 h after the flashback experience by forced swimming in mice previously exposed to WIRS, but not in mice without previous exposure to WIRS. Although Myo6 protein was ubiquitously distributed in discrete mouse brain regions with exceptional condensation in the olfactory bulb, Myo6 protein was also expressed in cultured rat astroglia and neurons, in addition to cultured neural progenitor cells isolated from embryonic mouse brains. In mouse embryonal carcinoma P19 cells endowed to proliferate for self-replication and differentiate into neurons and astroglia, Myo6 protein was highly expressed in consistency with the expression of a marker protein of astroglia, but not of neurons. Transient overexpression of Myo6 led to a significant decrease in the size of clustered aggregates without affecting cell viability in P19 cells cultured with retinoic acid under floating conditions. These results suggest that Myo6 may play a pivotal role in the mechanism underlying the suppression of adult neurogenesis relevant to hippocampal atrophy seen in patients with PTSD.

P-6 Effects of methyl mercury on proliferation of monkey ES cell-derived neural stem cells

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Proliferation of the neural stem cells is essential for supplying a vast number of neurons and glia which support normal brain functions. Methylmercury (MeHg), which caused Minamata disease, acts as a neurotoxic agent during the brain development. MeHg is reported to produce microcephaly in addition to various syndromes characterized by mental retardation and motor dysfunction. In this study, the effects of MeHg on the neural stem cells, prepared from monkey embryonic stem (ES) cells by the Neural Stem Sphere (NSS) method, were investigated. Cultured with mitogen fibroblast growth factor-2, the neural stem cells proliferated exponentially up to 4 days. When the neural stem cells were exposed to MeHg (from 10 nM to 1 μ M) and cultured for 4 days, the proliferation of the cells was dose-dependently inhibited by MeHg and almost completely inhibited at 1 μ M. TUNNEL analysis demonstrated that MeHg induced apoptosis of the cells. These results were similar to those obtained for the neural stem cells prepared from mouse ES cells by the Neural Stem Sphere (NSS) method. The monkey neural stem cell was slightly more resistant to the MeHg than the mouse neural stem cell. These results suggest that MeHg inhibits proliferation of the monkey and mouse neural stem cells via apoptosis and consequently causes neurotoxic effects in the development of central nervous system including microcephaly. This work was partly supported by Grants-in-Aid for Scientific Research from JSPS and Selective Research Fund of Tokyo Metropolitan University.

P-7 Effects of heat shock on proliferation and differentiation of mouse ES cell-derived neural stem cells

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Physical therapists have use of hot pack, paraffin bath, Microwave therapy, therapeutic ultrasound, infrared therapy and low-frequency therapy. In particular, heat shock due to thermotherapy was frequently used for clinical treatment. To evaluate a clinical response of heat shock, it is important to examine the effects of heat shock on cultured neural cells. Embryonic stem (ES) cells can be efficiently induced to differentiate into neural cells by Neural Stem Sphere (NSS) method, and a large number of multipotent and self-renewing neural stem cells can be prepared. In this study, to investigate effects of heat shock on proliferation and differentiation of the neural stem cells, neural stem cells prepared from mouse ES cells were exposed to heat shock and cultured with fibroblast growth factor-2 for 4 days. After exposure to heat shock at not over 42°C, the neural stem cells could proliferate. However, when the cells were exposed to heat shock at 43°C and above, the proliferation was temperature-dependently inhibited. It suggests that heat shock may have effects on proliferation of the neural stem cells at high temperature. Gene expression of the neural stem cells cultured at not over 43°C was analyzed by real-time RT-PCR to evaluate effects of heat shock on differentiation of the cells. The gene expression of Nestin and Musashi-1, makers of neural stem cells, was demonstrated to be high. In contrast, the expression of middle molecular-mass neurofilament, a marker of neurons, glial fibrillary acidic protein, a marker of astrocytes, and myelin basic protein, a marker of oligodendrocytes, were demonstrated to be low in the cells. The expression pattern of the markers of neural stem cells was not affected by the heat-shock exposure. These results suggest that the neural stem cells maintained its cellular properties after heat-shock exposure.

P-9 Modulation of differentiation into neural lineages through GABA_B receptors

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There is emerging evidence that endogenous factors regulate self-renewal capacity and multi-potentiality to generate different neural lineages including neurons, astroglia and oligodendroglia in neural progenitor cells expressed in the developing and matured brains. We have previously shown that tonic activation of metabotropic GABA_B receptors (GABA_BR) leads to the increased proliferation activity for self-renewal along with the promoted differentiation into a neuronal lineage in neural progenitor cells isolated from embryonic mouse brains *in vitro*. In the present study, we have further attempted to evaluate the possible importance of signal inputs mediated by GABA_BR in differentiation into the neural lineage *in vivo*. In brains of GABA_BR1-deficient mice which are lacking of all biochemical and electrophysiological GABA_B responses, a significant decrease was similarly seen in expression levels of immunoreactive GABA_BR2 subunit, but not for corresponding mRNA, when determined 1 and 7 days after birth. In brains of these neonatal GABA_BR1-deficient mice, however, no significant changes were found in expression of mRNA for other GABAergic signaling machineries. These included mGAT1, mGAT2, mGAT3, VGAT, GAD65 and GAD67. Moreover, a significant decrease was seen in expression of mRNA and corresponding protein for MAP2, but not for NSE, GAP43, NeuN, GFAP or CD11b, in brains of neonatal GABA_BR1-deficient mice. These results suggest that GABA_BR1 subunit may modulate endogenous levels of the partner protein GABA_BR2 subunit responsible for the orchestration of functional GABA_BR through a mechanism not related to gene transactivation at an early postnatal developmental stage in murine brains *in vivo*.

P-8 Effects of X-irradiation on differentiation from mouse embryonic stem cells into neuron

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Radiation exposure during the gestation period causes disturbances in development of the brain. In this study, we investigated the effects of X-irradiation on differentiation from embryonic stem (ES) cells into neurons by Neural Stem Sphere (NSS) method, where ES cells can be induced to differentiate unidirectionally into neurons via epiblast, neuroectoderm, and neural stem cells. The colonies of mouse ES cells or NSSs formed from the colonies were exposed to various doses of X-rays at floating culture day 0, 2 or 4 and cultured up to day 6. Growth of the NSSs exposed to X-ray was dose-dependently inhibited, and morphology of the NSSs was also affected. TUNEL analysis demonstrated that cell death via apoptosis was induced dose-dependently by X-ray irradiation. ES cells, epiblast and neural stem cells differed in their radio-sensitivity, and the neural stem cells were most sensitive to X-ray. These results suggest that X-ray irradiation induced retardation of cell division and cell death via apoptosis during the differentiation. Gene expression and immunofluorescent analysis of the NSSs demonstrated that the inhibition and retardation of cell differentiation were also caused by X-ray. This work was partly supported by a grant of LRI by JCIA and Selective Research Fund of Tokyo Metropolitan University.

P-10 Dramatically different effects of methyl mercury on uni-directional differentiation from embryonic stem cells into neurons by Neural Stem Sphere method

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We previously showed that ES cells uni-directionally differentiate neurons via epiblast, neuroectodermal cells and neural stem cells by Neural Stem Sphere method. Therefore, we considered that differentiation process of ES cells by the method mimics that of neurogenesis *in vivo*. Here, we analyzed effects of methyl mercury chloride (MeHg) on differentiation process from ES cells into neurons. Colonies of ES cells cultured into Astrocyte-conditioned medium (ACM) for 4 days under free-floating condition were exposed to MeHg (0.1, 1, 10 μM) for various periods of time. The colonies exposed to MeHg for 4 days had unstable structure and did not form NSSs which were composed of a vast number of neural stem cells and neurons. Interestingly, gene expression analysis showed that NSSs exposed to MeHg from day 2 comparably resembled normal NSSs. These results suggest that there are some cells during neural differentiation of ES cells by NSS method display the different sensitivity to MeHg, raising the possibility that this culture method provides a newly *in vitro* system to assess the effects of chemical substances on early neurogenesis. This work was partly supported by a Research Grant for long-range research initiative from JCIA and Selective Research Fund of Tokyo Metropolitan University.

P-11 The mechanism of aggression and impulsivity through the change of neurogenesis

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In the clinics of psychiatry, loss of control of aggression and impulsivity is one of the major problems causing troubles such as adjustment difficulty to society. But their biological mechanism and effective treatment method have not yet clarified. Recently, neuroimaging studies have revealed the progressive volume change in the course of various psychiatric diseases, and it is reported that the abnormal brain morphological change is related to the neurogenesis dysfunction and neural network disruption. TLX is the orphan nuclear receptor with restricted function as a transcription factor. Recent reports suggest that the TLX expression change severely affects on the neurogenesis function in the brain. TLX knock out mouse have revealed to show the reduction of neural stem cell (NSC) proliferation and decrease in volume of SVZ, and abnormal aggressive behaviors. In the present study, we investigate the effect of TLX expression change in cultured cells to elucidate its precise cellular mechanism of TLX on the NSC function which may induce behavioral abnormalities. Primary cultures of NSCs were prepared from E13.5 rat embryo. We treated small interfering RNA (siRNA) for TLX to NSCs with lipofectamin in the Optimem medium. 24 or 48 hours after the treatment, we assessed expression of TLX change by western blotting, and checked cell survival by MTT method. Then, we evaluated the proliferation, migration, differentiation changes of NSCs by the methods of BrdU-ELISA, boyden chamber, and Tuj-1 (MAP2)-ELISA, respectively. The functions of NSCs were significantly influenced by the treatment of TLX-siRNA. We will further discuss about the TLX dysfunction *in vivo* using this TLX-siRNA model focusing on the aggression and impulsive behaviors. The results indicated expression of TLX in NSCs decreased depending on the concentration of newly synthesized TLX-siRNAs.

P-12 Roles of newly identified nerve growth-associated proteins (nGAPs) in the growth cone

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The growth cone is the most important structure for the neural wiring, synapse formation and axonal regeneration. The growth cone continuously moves and guides axons in the accurate direction. Currently, identification of molecules involved in these functions is not enough to explain the mechanisms of the roles. We previously reported that approximately 100 proteins were more concentrated in the growth cone than GAP-43, a sole well-established marker protein of growth cones, using systematic immunocytochemistry based on our proteomic data. RNAi experiments revealed that the reduced expression of at least 20 species of proteins significantly inhibited the axonal growth. In addition, we also found that the reduced expression of several proteins promoted the axonal growth by RNAi, in contrast to the above 20 species. We called these proteins as "nGAPs, neuronal growth-associated proteins". In order to determine whether nGAPs are essential to growth cone morphogenesis, we observed distributions of microtubules and F-actin in the growth cone after RNAi treatment, and examined the effects on the growth cone area and morphology by RNAi against nGAPs. At this meeting, we will report and discuss about roles of identified nGAPs in the growth cone function and morphology.

P-13 The significance of Syntaxin-1A-CaMKII interaction in synaptic vesicle transportation and mouse behavior

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Exocytotic synaptic vesicle recycling is regulated at several steps by different concentrations of Ca^{2+} . In particular, submicromolar Ca^{2+} is believed to be important for the vesicle translocation/tethering and docking, however, the molecular mechanisms underlying these processes are poorly understood now. We previously found that the autophosphorylated CaMKII interacts with syntaxin-1A, a t-SNARE operating the vesicle docking and fusion, in the presence of submicromolar Ca^{2+} , and demonstrated at the cellular level that this binding modulates the frequency of exocytosis. This interaction is strongly dependent upon R151 of syntaxin-1A, a highly conserved residue localized in the linker domain of syntaxin-1A, and R151G syntaxin-1A completely lost the activities both binding to CaMKII *in vitro*. To understand the significance of this interaction more in detail, we made the knock-in mice having R151G syntaxin-1A from the C57/BL6-derived ES cells.

The homozygous mice with this mutation are developing without large defect. We have examined the comprehensive behavioral test battery on this mutant. The homozygote showed increase in motility and decrease in anxiety-like behavior. Although the mutants behaved normally in typical memory tests, some results indicated the mice might have some defects in short-term memory.

In the primary hippocampal culture from the mutant, we found the uptake of styryl-FM dye was low with 90mM KCl. Currently we are working on further characterization of the synaptic vesicle transportation of this mutant.

P-14 Analyses of the knockout mice lacking in the enzymes synthesizing chondroitin sulfate

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Chondroitin sulfate proteoglycans (CSPGs) are mainly found not only in the extracellular matrix (ECM) of the cartilage as aggrecan, but also are abundantly expressed in the mammalian central nervous system (CNS), as neurocan, brevican, NG2, and so on. The biosynthesis of CS initiates by the transfer of a N-acetylglucosamine (GalNAc) residue to the linkage region of a glucuronic acid (GlcUA)- β 1,3-galactose- β 1,3-galactose- β 1,4-xylose tetrasaccharide primer attached to a serine residue of the core protein. Then, the chain elongation occurs by the alternate addition of GalNAc and GlcUA residues catalyzed by chondroitin sulfate N-acetylglucosaminyltransferase e-2 (GT-2). On the other hand, N-acetylglucosaminyltransferase-1 (GT-1) mediates the initiation of CSPG chain elongation.

CSPGs are the most important molecule that inhibits axonal regeneration after CNS injury, and its inhibitory activity on synaptogenesis is shown to be physiologically involved in the synaptic plasticity of ocular dominance. To clarify the role of CSPG in the CNS and peripheral nerve system (PNS), we have tried and succeeded in producing the mice lacking in GT-1 and GT-2 enzymes, by the deletion of exon 4, which contains the DXD motif conserved in many glycosyltransferases and known as the key sequence for divalent cations binding such as Mn²⁺. Northern blot analysis revealed that the expression level of mRNA in GT-1 mice brain was decreased. Histological studies also revealed the reduced cortical thickness in GT-1 KO mice. Since GT-1 and GT-2 KO mice are viable, we are continuously trying to produce double KO mice lacking in both enzymes.

P-15 Protective effects of interferon- γ or peroxisome proliferator-activated receptor- γ agonist against methamphetamine-induced neurotoxicity

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Recently, we reported that the intraperitoneal or intracerebroventricular injections of interferon- γ (IFN- γ) adjunct to methamphetamine (METH) injections significantly prevented METH-induced reduction of striatal dopamine transporter (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., 2008). An inhibitory transcription factor, peroxisome proliferator-activated receptor- γ (PPAR- γ), inhibits AP-1, NF- κ B, and NF-AT which activated by METH injection. IFN- γ is known to activate PPAR- γ . More recently, we reported METH injections-induced reduction of PPAR- γ expression and neuroprotective effects of a PPAR- γ ligand, ibuprofen against METH neurotoxicity (Tsuji et al., 2009). In the present study, therefore, we examined the effects of IFN- γ or PPAR- γ agonist against METH-induced changes in expression of PPAR- γ and NF- κ B, and glial cell activation. Systemic injections of IFN- γ prior to repeated METH injections attenuated the reduction of nuclear PPAR- γ expression and increasing tendency of NF- κ B expression in the striatum after METH injections (4 mg/kg X4, i.p. with 2 h-interval). IFN- γ injections also enhanced METH-induced activation of striatal astrocytes. Although the treatment of an intrinsic PPAR- γ ligand 15d-PG J2 also attenuated METH-induced striatal DAT reduction, PGJ2 inhibited METH-induced activation of striatal astrocytes. These results imply that the IFN- γ indirectly induces PPAR- γ activation and NF- κ B inhibition in the striatum through astrocyte activation to exert its protective effect against METH-induced neurotoxicity, in contrast to direct PPAR- γ activation of 15d-PG J2.

P-16 SA4503, a sigma receptor agonist, prevents cultured cortical neurons from cell death

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Many antidepressant functions as a neuroprotective agent in central nervous system. However, the underlying mechanism of effects of antidepressants has not been fully elucidated. Here, we investigated the influence of SA4503 (a kind gift from M's Science Corporation) pretreatment, which is a sigma receptor agonist and a candidate for novel antidepressant, on cultured cortical neurons. Exposure of the neurons to H₂O₂ significantly induced an over-activation of p44/42 mitogen-activated protein kinase (MAPK), and resulted in apoptotic-like cell death. Pretreatment with SA4503 decreased the MAPK activation and the neuronal cell death. Interestingly, SA4503 application caused the significant down-regulation of ionotropic glutamate receptors. We previously reported that over-activation of MAPK and Ca²⁺ entry through ionotropic glutamate receptors were involved in the oxidative stress-induced cell death (Numakawa et al., 2007 *Endocrinology*). Taking these findings together, it is possible that SA4503 blocks the cell death in the oxidative stress via down-regulation of MAPK signaling activation and ionotropic glutamate receptors.

P-17 The effect of proteolytic cleavage within calsynenin-3 on the death of cerebral cortical neurons

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Beta-amyloid ($A\beta$) may play an important role in pathogenesis of Alzheimer's disease, but molecular mechanisms of $A\beta$ actions, which are responsible for neurotoxicity, are not fully understood. We have previously identified calsynenin-3 as a $A\beta$ -induced molecule. The calsynenin 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 $A\beta$ 1-42 treated cortical neurons, indicating that $A\beta$ differentially regulates calsynenin genes. We also found that Cst-3 is accumulated in dystrophic neuritis around $A\beta$ plaques in cerebral cortex of an Alzheimer's disease mouse model Tg2576. The accumulation of Cst-3 in cultured cortical neurons resulted in the acceleration of neuronal death. Cst-3 is cleaved into extracellular N-terminal and intracellular C-terminal fragments. In this study, we investigated cleavage site of Cst-3 protein and whether the accumulation of full length Cst-3 or that of the C-terminal fragment is responsible for the acceleration of neuronal death. C-terminal fragment of Cst-3 (Cst3-CTF) was purified by a combination of Ni Sepharose column chromatography, SDS-PAGE and blotting on PVDF. The analysis of N-terminal amino acid sequence of Cst3-CTF showed HVXXX. Based on the molecular weight (30 kDa) of Cst3-CTF and the effects of amino acid substitution neighboring ^{813} H on the generation of Cst3-CTF, the cleavage site of Cst-3 was deduced. Then, overexpression experiments of Cst3-CTF in cultured cortical neurons were carried out to investigate the relationship between proteolytic processing of Cst-3 and the death of cerebral cortical neurons.

P-18 Free radical scavengers enhance the survival of cells newly generated after neuronal damage in the hippocampal dentate gyrus of mice

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Several lines of evidence indicate that reactive oxygen species (ROS) participate in a diverse array of biochemical processes, including induction and maintenance of the transformed state, programmed cell death, and cellular senescence. Further studies have shown that change in redox state is critical in regulating cell survival and proliferation. It is now clear that there is a continual turnover of the hippocampal neurons throughout life even in adult. Our previous study indicated that trimethyltin chloride (TMT) causes neuronal degeneration in the hippocampal dentate gyrus selectively 2 days later, with regeneration of the dentate granule cell layer 14 days afterward. To elucidate mechanisms underlying the modulation of the neurogenesis by cell proliferation and/or cell survival, in this study, we evaluated the effect of the free radical scavenger edaravone on the survival of newly generated cells in the hippocampal dentate gyrus after the damage induced by TMT. Mice were given TMT (2.8 mg/kg, i.p.). Edaravone (50 mg/kg, i.p.) was injected for consecutive 2 or 7 days every 12 h from day 2 after TMT treatment. To label mitotic cells, we gave mice a single series of 4 injections of 5-bromo-2-deoxyuridine (BrdU, 50 mg/kg, i.p.) every 12 h from day 2 after TMT treatment. In addition, immunostaining for proliferating nuclear antigen (PCNA) was performed for determination of proliferating cells. A marked increase in the number of BrdU- and PCNA-positive cells was seen in the hippocampal dentate gyrus on day 4 after TMT treatment. These positive cells dramatically disappeared on day 9 after TMT treatment in control animals. In edaravone-treated animals, the large number of BrdU-positive cells existed even on day 9 after TMT treatment. However, the number of PCNA-positive cells had no significant change between control and edaravone-treated animals. In the subventricular zone, edaravone did not affect the number of BrdU- and PCNA-positive cells on days 4 and 9 after TMT treatment. These results suggest that the free radical scavenger contributes to the survival of newly generated cells in the hippocampal dentate gyrus after the damage induced by TMT.

P-19 Commitment of MPP⁺-induced neuronal cell death by proteasome-mediated degradation of p35 Cdk5 activator○Ryo Endo¹, Taro Saito¹, Akiko Asada¹, Hiroyuki Kawahara², Toshio Ohshima³, Shin-ichi Hisanaga¹¹Laboratory of Molecular Neuroscience, Department of Biological Sciences, Tokyo Metropolitan University, ²Laboratory for Cellular Biochemistry, Department of Biological Sciences, Tokyo Metropolitan University, ³Department of Life Science and Medical Bio-Science, Waseda University

Parkinson disease (PD) is the second most common neurodegenerative disease. The dysfunction of proteasomes and mitochondria has been implicated in the pathogenesis of Parkinson disease, but the mechanism by which this dysfunction causes neuronal cell death is unknown. The 1-methyl-4-phenylpyridinium ion (MPP⁺), a toxic metabolite of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), is a neurotoxin widely used to induce neuronal cell death in *in vitro* models of PD. Cyclin-dependent kinase 5 (Cdk5), a member of the cyclin-dependent kinase family, is a neuron specific serine/threonine kinase activated by p35 or p39. Cdk5 plays a role in a variety of neuronal activities including neuronal migration, synaptic activity, and neuronal cell death. p35, a major determinant of Cdk5 activity, is a short-life protein degraded by the ubiquitin-proteasome pathway. However, in stressed neurons, the calcium-activated protease calpain cleaves p35 to p25, more stable and active form of p35, leading to hyper-activation of Cdk5. Hyper-activated Cdk5/p25 has been implicated in the pathogenesis of numerous neurodegenerative disorders including PD. However, how p35 metabolism is altered in PD-model neurons has not been examined yet. Here, we studied the metabolism and role of p35 in the cell death of neurons treated with MPP⁺. We found that p35 was proteolysed in cultured neurons by either calpain or proteasomes, depending on the concentration of MPP⁺ used. The MPP⁺-induced proteasomal degradation of p35 occurred earlier and at lower MPP⁺ concentrations than did its cleavage by calpain. MPP⁺ up-regulated the overall proteasome activity in the neurons by impairing the mitochondrial protein import system. A brief MPP⁺ treatment, for up to ~3 h, was sufficient to induce delayed cell death at 24 h, and the overexpression of p35 suppressed this MPP⁺-induced cell death. Together, these results implicate a role for Cdk5/p35 as a survival factor in MPP⁺-treated neurons.

P-20 Mechanism of apoA-I-mediated cholesterol release from rat astrocytes through Rho kinase activation

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Apolipoprotein A-I (apoA-I) increased GTP-binding of cdc42 and activity of Rho kinase in rat astrocytes. siRNA of ATP-binding cassette transporter A1 (ABCA1) suppressed both apoA-I-induced GTP-binding of cdc42 and Rho kinase activation. siRNA of cdc42 reduced apoA-I-mediated Rho kinase activation also, suggesting that apoA-I activates Rho kinase in the manner to depend on cdc42 activation through the interaction between apoA-I and ABCA1. A Rho kinase inhibitor, Y27632, suppressed both intracellular transport of newly synthesized cholesterol to plasma membrane and apoA-I-mediated cholesterol release. Y27632 inhibited the association with the reconstituted microtubules of CLPP-related proteins such as protein kinase C and caveolin-1 and CLPP-related lipids such as cholesterol, phosphatidylcholine and sphingomyelin. These findings suggest that ApoA-I stimulated intracellular transport of cholesterol for cholesterol release through the regulation by Rho kinase of the interaction of CLPP with microtubules.

P-22 Astrocytes Promote the Proliferation of Lung Cancer Cells in Brain Metastases via inflammatory cytokines, especially IL-6

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The role of glial cells in the brain metastases of tumor cells is largely unknown. As the interaction between tumor cells and organ microenvironment regulate the progression of metastases, the brain environment may play a specific role in the proliferation, invasion and angiogenesis of metastatic tumor cells. Astrocytes are present abundantly in the brain and may play important roles in brain metastases, producing many cytokines and growth factors that can modulate tumor cell proliferation, tumor angiogenesis or tissue damage. We therefore established an animal model for brain metastasis using human lung cancer-derived cells (HARA-B) in nude mice. Activated astrocytes aggregated around the brain metastatic region in cortex and lead to astrogliosis; the amount of astrogliosis was correlated with the size of tumor. Astrocytes promoted the proliferation of cancer cells by releasing several cytokines. Among them, IL-6 may play the most important role. The expression of IL-6 receptors (IL-6R) on cancer cells was up-regulated when they were cultured with astrocytes. Addition of neutralizing antibody against IL-6 significantly attenuated the proliferation of cancer cells cultured with astrocytes. Our finding suggests that the inflammatory response by activation of astrocytes plays an important role in the development of brain metastases. Therefore, specific inflammatory cytokine released from astrocytes and its receptor might be potential targets for anti-cancer metastasis in the brain.

P-21 Diclofenac has a synergistic effect on the production of nitric oxide through NF- κ B signaling in cultured astrocytes stimulated by proinflammatory cytokines

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Recently, the number of reports of encephalitis/encephalopathy associated with influenza virus has increased. In addition, the use of a non-steroidal anti-inflammatory drug, diclofenac sodium (DCF), is associated with a significant increase in the mortality rate of influenza-associated encephalopathy. Activated astrocytes are a source of nitric oxide (NO), which is largely produced by inducible NO synthase (iNOS) in response to proinflammatory cytokines. Therefore, we investigated whether DCF enhances nitric oxide production in astrocytes stimulated with proinflammatory cytokines. We stimulated cultured rat astrocytes with three cytokines, interleukin-1 β , tumor necrosis factor- α and interferon- γ , and then treated the astrocytes with DCF or acetaminophen (N-acetyl-p-aminophenol: APAP). iNOS and NO production in astrocyte cultures were induced by proinflammatory cytokines. The addition of DCF augmented NO production, but the addition of APAP did not. NF- κ B inhibitors SN50 and MG132 inhibited iNOS gene expression in astrocytes treated with DCF and cytokines or cytokines alone, whereas a p38MAPK inhibitor SB203580, a PKA inhibitor KT5720 and a PKC inhibitor chelerythrine did not. LDH activity and DAPI staining showed that DCF induces cell damage in cytokine-stimulated astrocytes. An iNOS inhibitor, L-NMMA, inhibited the cytokine- and DCF-induced cell damage. In conclusion, this study demonstrates that iNOS and NO are induced in astrocyte cultures by proinflammatory cytokines. Addition of DCF further augments NO production. This effect is mediated via NF- κ B signaling and leads to cell damage. The enhancement of DCF on NO production may explain the significant increase in the mortality rate of influenza-associated encephalopathy in patients treated with DCF.

P-23 Neuroprotective properties of metallothioneins in astrocytes against dopaminergic neurotoxicity

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Metallothioneins (MTs) are a family of low molecular weight, cysteine-rich, ubiquitous, and inducible intracellular proteins that bind to heavy metals such as zinc, copper, and cadmium, participating in metal homeostasis and detoxification. Dopamine (DA) quinone, which conjugates with cysteine residues of functional proteins to form quinoproteins, has been recently focused as DA neuron-specific oxidative stress in Parkinson's disease. We previously demonstrated the protective effects of MT against DA quinone neurotoxicity: MT-1, 2 exerted protective effects against the excess DA/L-DOPA-induced DA quinone neurotoxicity in dopaminergic cells and parkinsonian model mice through its DA quinone-quenching activity (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 changes in MT-1, 2 expression after L-DOPA/DA exposure using 6-OHDA-injected hemi-parkinsonian mice and primary cultured mesencephalic neurons and striatal astrocytes. MT-1, 2 expression was markedly elevated specifically in the reactive astrocytes in lesioned striatum after repeated L-DOPA administration. Excess DA exposure dramatically produced MT-1, 2 induction in striatal cultured astrocytes but not in mesencephalic neurons. Reduction of mesencephalic DA neurons after DA exposure was ameliorated by pre-incubation with conditioned media from striatal astrocytes, especially DA-treated astrocytes. These protective effects of conditioned media from DA-treated astrocytes were cancelled by neutralization with anti-MT-1, 2 antibody. These results suggest that induction and secretion of MT-1, 2 in/from the reactive astrocytes may play an important role to protect dopaminergic neuron by its quinone-quenching or free radical scavenging property.

P-24 Development of Generic Calcium Imaging Assay for monitoring Gi-coupled Receptors and G protein interaction○Takashi Ueda¹, Shinya Ugawa¹, Yusuke Ishida¹, Shoichi Shimada²¹ The Department of Neurobiology and Anatomy, Nagoya City University, Nagoya, Japan, ² Department of Neuroscience and Cell Biology, Osaka University Graduate School of Medicine, Osaka, Japan

G protein-coupled receptors (GPCRs) are important therapeutic targets for many areas of drug research and development. Although chimeric $G_{\alpha_{16}}$ proteins are valuable tools for detecting the activation of Gi-coupled receptors, it is unknown whether these $G_{\alpha_{16}}$ chimeras could be used to elucidate details of GPCR pharmacology. Both dopamine D_2 and serotonin 5-HT_{1A} receptors are considered key target Gi-coupled GPCRs for antipsychotic drugs. Here we introduce a series of chimeras that combine both $G_{\alpha_{16}}$ and $G_{\alpha_{i/o}}$ ($G_{\alpha_{16/o}}$, $G_{\alpha_{16/i2}}$ and $G_{\alpha_{16/i3}}$) into a well-established transient expression system to examine the ability of these chimeras to interact with D_2 long-form (D_{2L}) dopamine and 5-HT_{1A} serotonin receptors. The pEC₅₀ data obtained for known agonists were similar to results from previous studies that used other cell-based assays, thus indicating sufficient sensitivity for our assay. Moreover, quinpirole exhibited similar intrinsic activity to dopamine at the D_{2L} receptor, whereas S-(-)-3-PPP displayed partial activity of dopamine and quinpirole in the presence of the $G_{\alpha_{16/o}}$ chimera. The potency of dopamine for D_{2L} receptors was similar among $G_{\alpha_{16/o}}$, $G_{\alpha_{16/i2}}$ and $G_{\alpha_{16/i3}}$. In contrast, the 5-HT_{1A} receptor exhibited a significantly preferential coupling for $G_{\alpha_{16/i3}}$ compared with $G_{\alpha_{16/i2}}$ when serotonin was used as ligand. This finding was in close agreement with the results of previous reports. The present system could therefore be used as a rapid functional assay for high-throughput screening (HTS) to discover novel antipsychotic drugs.

P-26 Properties of acquired NMDA receptors in HEK293 cells

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Glutamate neurotoxicity is believed to be mainly mediated by excessive influx of Ca^{2+} into neurons through activation of N-methyl-D-aspartate (NMDA) receptors (NMDAR). Calcium entry through extrasynaptic NMDAR containing an NR2B subunit is toxic to neurons, however, whereas Ca^{2+} influx through synaptic NMDAR containing an NR2A subunit is anti-apoptotic. In the present study, we evaluated properties of acquired NMDAR channels artificially orchestrated in human embryonic kidney (HEK) 293 cells. For this purpose, HEK293 cells were transfected with either an NR2A or NR2B expression vector, together with the expression vector of NR1 subunit essentially required for the assembly to functional NMDAR. Although transfection efficiency was $24.0 \pm 3.4\%$ as measured by pEGFP-C2 vector with cloned EGFP, immunocytochemical analysis clearly confirmed marked expression of different NR subunits by cells with nuclei stained with Hoechst33342 at 48 h after transfection. Exposure to 0.1 mM NMDA similarly increased the percentages of cells stained with propidium iodide (PI) over Hoechst33342-positive cells in a manner sensitive to blockade by the NMDAR antagonist MK-801 in HEK293 cells with acquired expression of NMDAR composed of NR1/NR2A and NR1/NR2B subunits. Further introduction of NR3A subunit, however, led to a significant decrease in the percentage of PI-positive cells in HEK293 cells with NR1/NR2A, but not NR1/NR2B, subunits. These results suggest that NR3A subunit may play a role as a determinant of glutamate neurotoxicity mediated by NMDAR in a particular situation.

P-25 Phosphorylation and dephosphorylation at serine 892 on GABA_BR2 subunit

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GABA_B receptors mediate slow and prolonged synaptic inhibition in the brain, and are members of the G protein-coupled receptor (GPCR) superfamily. To date, 2 subunits of GABA_B receptor have been identified as GABA_BR1 and GABA_BR2 (R2). Unlike other members of the GPCR superfamily, functional GABA_B receptors are heterodimers formed between these 2 subunits. It is also emerging that GABA_B receptors utilize unique modes of cellular regulation compared to other monomeric GPCRs. Specifically, GABA_B receptors are very stable entities on neuronal plasma membranes, and do not undergo agonist-induced phosphorylation or internalization. Therefore, we have analyzed the regulatory mechanisms of these critical inhibitory receptors. In vitro kinase analysis reproduced R2 phosphorylation at serine 892 (p892) by protein kinase A as previously reported. While R2 and p892 were strongly detected in cerebral cortex, hippocampus and cerebellum among brain regions of mice, relative phosphorylation of p892 against total R2 was significantly higher in cerebellum than other regions. In cultured cortical neuron, the phosphorylation was increased by forskolin and okadaic acid, but not by cyclosporine and orthovanadate. In vitro dephosphorylation analysis revealed that p892 dephosphorylated by PP1 α and PP2A, but not by PP2B and PP2C. Moreover, p892 decreased by tetrodotoxin treatment in cultured neurons. It is thus suggested that those 2 phosphatases vary GABA_B receptors function by sensing the neuronal activity.

P-27 Pharmacological characterization of sigma-1 receptor ligands: agonist-specific up-regulation of sigma-1 receptor○Toshifumi Yamamoto¹, Hideko Yamamoto²¹ Lab. of Mol. Psychopharmacol. Yokohama City Univ., ² Div. of Psychobiology, Tokyo Inst. of Psychiatry

Sigma-1 receptor (Sig1R) is a putative target for several drugs, including antipsychotics and antidepressants. However, the molecular actions of the Sig1R ligands are still not clear. Recent studies suggest an increase of Sig1R by treatment with an antidepressant, fluvoxamine in vitro. In the present study, we investigate the effect of Sig1R ligands on Sig1R expression in PC12 cells by using immunoblot analysis. Sig1R agonists, fluvoxamine and SA4503, but not antagonists, NE100 and haloperidol, dose- and time-dependently caused the increase in the protein levels of Sig1R expression assessed by anti-Sig1R antibody. These increase in the level of Sig1R expression by fluvoxamine or SA4503 was significantly attenuated by concurrently treatment with the antagonist, NE100. These results clearly confirmed that Sig1R expressions were specifically up-regulated by Sig1R agonists. Using this nature of the up-regulation by Sig1R agonists on the Sig1R expression, we have proposed a convenient and reliable method for determine the pharmacological characterization of Sig1R-related ligands as an agonist or an antagonist.

P-28 Glucocorticoid receptor promotes BDNF-stimulated PLC γ /Ca²⁺ signaling for glutamate release via interacting with BDNF receptor TrkB

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An increased level of glucocorticoid and down-regulation of BDNF (brain-derived neurotrophic factor) are supposed to be involved in the pathophysiology of depressive disorders. However, possible crosstalk between glucocorticoid- and BDNF-mediated neuronal functions in the central nervous system (CNS) has not been elucidated. Here, we examined whether chronic glucocorticoid exposure influences BDNF-triggered intracellular signaling for glutamate release. Chronic exposure to dexamethasone (DEX, a synthetic glucocorticoid) suppressed BDNF-induced glutamate release via weakening the activation of the PLC γ (phospholipase C γ)/Ca²⁺ system in cultured cortical neurons. We demonstrated that the GR (glucocorticoid receptor) interacts with TrkB (receptor tyrosine kinase for BDNF). Following DEX treatment, TrkB-GR interaction was reduced due to the decline in GR expression. Interestingly, BDNF-dependent binding of PLC- γ to TrkB was diminished by DEX. siRNA transfection for decrease in endogenous GR mimicked the inhibitory action of DEX. Conversely, DEX-inhibited BDNF-activated PLC γ signaling for glutamate release was recovered by GR overexpression. We propose that the decrease in TrkB-GR interaction caused by chronic exposure to glucocorticoid results in the suppression of BDNF-mediated neurotransmitter release.

P-29 Possible involvement of PPAR γ in regulation of basal channel opening of P2X7 receptor in cultured mouse astrocytes

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Recently, we demonstrated that cultured mouse astrocytes exhibited basal channel opening of P2X7 receptor (P2X7) in the absence of any exogenous ligands, but its regulatory mechanism was not clear. Since our preliminary experiments suggested possible involvement of peroxisome proliferator-activated receptor (PPAR) γ in its regulation, we examined whether PPAR γ regulated P2X7 basal channel opening in mouse astrocytes. P2X7R channel opening was assessed by uptake of a maker dye, YO-PRO-1 (YP), in the presence or absence of agonists and antagonist for PPAR γ with a fluorescence microscope. Expression of PPAR γ was evaluated by western blot and immunocytochemistry. NSAIDs such as a PPAR γ agonist, showed enhanced and inhibitory effects on YP uptake at low and high concentrations, respectively, and the enhanced uptake was abolished by periodate-oxidized ATP (oxATP), a selective P2X7R antagonist. The PPAR γ agonists, 15-deoxy-delta12,14-prostaglandin J₂ and ciglitazone, decreased the basal and FFA-enhanced YP uptake, while the antagonist, GW9662, increased YP uptake, this effect being blocked by the agonist and also by oxATP. PPAR γ was distributed in the nucleus and the cytosolic/membrane fractions of cultured mouse astrocytes. These findings indicate that basal channel opening of P2X7R in mouse astrocytes is at least in part regulated by PPAR γ .

P-30 Critical roles of thyroid hormone in the development of the GABAergic system

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Thyroid hormone (TH) plays crucial roles in proper brain development. Several recent studies on adult rodents have shown reductions in the concentration of γ -aminobutyric acid (GABA), the activity of glutamic acid decarboxylase (GAD), and the number of parvalbumin (PV)-positive neurons as a result of prolonged hypothyroidism. Here we evaluated the effect of TH status on the expression of genes involved in the GABAergic system in the developing rat hippocampus, a region highly sensitive to TH, from postnatal day (P) 4 to 28 to elucidate the primary targets of TH action. When 3 groups of newborn rats, hypothyroid (rendered hypothyroid by administering 0.025% (wt/vol) MMI in drinking water to their mothers from the 15th day of conception), hypothyroid with postnatal T4 replacement, and control, were compared, the protein expression of *gad* was positively dependent on TH at all ages examined, while mRNA expression was not. Immunohistochemical examinations revealed that numbers of GAD65-positive cells and PV-positive cells in the hippocampus were positively correlated with TH status at P15 and P28. In addition, mRNA expression of the major GABA_A receptor subunits, *gabral* and *gabrg2*, and the postsynaptic scaffold gephyrin (*gphn*) was correlated with TH status only at P28, suggesting decreased GABA release at this later stage. In the development of GABAergic system, another key event is the switching in the action of GABA from excitatory to inhibitory through reduction of intracellular Cl⁻ concentration, which takes place around the 2nd postnatal week in rats. The neuron-specific K-Cl cotransporter, *kcc2*, and the ubiquitously expressed *kcc3* are responsible for excluding intracellular Cl⁻ and establishing low intracellular Cl⁻ concentration. Expression of mRNA of both genes was positively regulated by TH status from P4, prior to increases in mRNA expression of GABARs. Interestingly, transient increase of *kcc2* and *kcc3* expression in control rats with a peak at P10 was suppressed completely by TH deficiency. Thus, one of the primary targets of TH as a transcriptional regulator in the development of the GABAergic system seems to be the K-Cl cotransporter, *kcc2* and *kcc3*.

P-31 VGAT-Venus expression patterns in developing cerebellar cortex *in vivo* and *in vitro*

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GABA (γ -amino butyric acid) is known to play important roles as a modulator in the survival and development of cerebellar cortex. To assist an advance in the observation of GABAergic neurons, we produced some vesicular GABA transporter (VGAT)-Venus (VGAT-Venus) transgenic rat. In cerebellar cortex in VGAT-Venus rat, many GABAergic neurons involving Golgi cells, Basket cells and Stellate cells were positive for Venus, whereas almost Purkinje cells were very weak. In developing cerebellum, on the other hand, many Venus positive cells were observed both in the layer under Purkinje layer and in the external granular layer (EGL). Although no GABAergic neurons distributed in the developing EGL, some fibrous glial cells expressed VGAT during first week after birth. After then, VGAT-Venus in the glial cells was eliminated. This ectopic and transient VGAT distribution in the glial cells was confirmed by immunohistochemistry. Pharmacological studies suggested this VGAT in the glial cells might correlate to redistribute GABA in the EGL from under Purkinje layer. In order to investigate the dynamics of VGAT expression in developing cerebellar cortex, we used *in vitro* cerebellar developing culture system. Previously we reported neonatal cerebellar cortex was developed *in vitro* with the treatment of both 10⁻⁸M colcemid, a synchronizer at M phase, and 200nM K252a, a multipotential kinase blocker. This conditioning induced immature granule cells to migrate to the deep layer and express several receptor proteins, and Purkinje cells to elongate their dendrites to the molecular layer within 3 days after birth. Using this culture system, we could control the developing level of cerebellar cortex *in vitro*. In the cultured cerebellar cortex of VGAT-Venus rats with colcemid and K252a treatment, VGAT-Venus was observed both in the EGL and under Purkinje layer reticulately and fibrously. The fibrous VGAT positive glia would support granule cell division and migration. We would report the role and elimination process of glial VGAT.

P-32 Dexamethasone resets the circadian oscillation of *Bmal1* via ROR-response elements○Megumi Kumagai^{1,2}, Yoshihiro Nakajima³, Masaaki Ikeda^{1,2}¹Dept. of Physiol., Saitama Medical Univ., Saitama, Moroyama, Saitama, Japan, ²Molecular Clock Project, Res. Center for Genomic Med. Saitama Medical Univ. Hidaka, Saitama, Japan, ³Cell Dynamics, Cell Engineering, AIST, Ikeda, Osaka, Japan

A single exposure of fibroblast cultures to a glucocorticoid agonist resets rhythmic but asynchronous cells to a common circadian phase and resets the circadian expression of clock genes. It has been suggested that the presence of glucocorticoid response elements (GREs) in the regulatory regions of core clock components is a likely mechanism for the resetting of the circadian expression of these components by glucocorticoids. However, the molecular mechanism that accounts for the resetting of the circadian clock remains to be elucidated. This study explores the underlying mechanism of the resetting of the circadian phase in cultured fibroblast cells by glucocorticoid by means of a promoter analysis of clock genes. The luciferase reporter assay showed that dexamethasone (DEX) enhanced *Bmal1* promoter activity in a dose-dependent manner. In addition, the glucocorticoid antagonist mifepristone attenuated the enhancement caused by DEX. Real-time monitoring of the *Bmal1* promoter activity in NIH3T3 cells revealed that application of DEX modulated the activity and circadian oscillation of the promoter. Mutation of a putative GRE in the mouse *Bmal1* promoter minimized the effect of DEX stimulation on *Bmal1* transcription. By contrast, mutation of two ROR alpha binding sites (ROR-RE) located upstream from the transcription start site of the *Bmal1* gene essentially abolished the induction of the promoter activity. Deletion of one of the ROR-REs in the *Bmal1* promoter attenuated the response to DEX treatment on the first day of the real-time analysis of promoter activity. These results indicate that DEX regulates the resetting of *Bmal1* expression mainly via ROR-RE, and not via GRE.

P-34 Expression of Foxp1 in a subpopulation of V1 interneurons during development of the spinal cord

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During embryogenesis, transcription factor Foxp1 is expressed in the central nervous system, including the striatum, cortex, cerebellum, and spinal cord. Previously, we have reported that Foxp1 is highly expressed in motor neurons of the lateral motor column and preganglionic motor column in the spinal cord from embryonic day (E) 10.25 to E17.5. In addition, Foxp1 was weakly expressed in the ventral interneurons from E12.5 to E17.5. In the present study, we characterized Foxp1-expressing interneurons in the ventral spinal cord. At E12.5, Foxp1-expressing cells were observed in intermediate regions of the ventral spinal cord at all levels. In the ventral spinal cord, there are at least four subtypes of postmitotic interneurons, which express different homeodomain proteins, Evx1 (V0), En1 (V1), Lhx3 (V2), and Sim1 (V3). Recently, V2 interneurons are further subdivided into V2a and V2b, which express Chx10 and Gata3, respectively. Double-immunofluorescence staining of Foxp1 with these homeodomain proteins revealed that Foxp1 was exclusively expressed in a subpopulation of En1-positive V1 interneurons at E12.5. Because we found that Foxp2 is also expressed in interneurons between E11.0 to E17.5, we compared the expression pattern of Foxp1 with that of Foxp2. No colocalization of Foxp1 with Foxp2 was observed in the developing spinal cord at E12.5, E13.5, and E15.5. From the complementary expression pattern of Foxp1 to Lhx3 in both motor neurons and interneurons, we examined whether Foxp1 suppresses the expression of Lhx3. In a neuroendocrine cell line, GH3, which expresses Lhx3 endogenously, overexpression of Foxp1 reduced the expression of Lhx3. Therefore, Foxp1 may regulate the differentiation of motor neurons as well as V1 interneurons probably through suppression of Lhx3 expression in the developing spinal cord.

P-33 OASIS, a member of the CREB/ATF family transcription factor, is involved in glycosylation of chondroitin sulphate proteoglycans○Hiroaki Okuda¹, Kouko Tatsumi¹, Kazunori Imaizumi², Akio Wanaka¹¹Dept. of Anatomy and Neuroscience, Nara medical University, Nara, Japan, ²Div. of Molecular and Cellular Biology, Dept. of Anatomy, Faculty of Medicine, Univ. of Miyazaki, Miyazaki, Japan

We identified OASIS (old astrocyte specifically induced substance) as a basic leucine zipper (bZIP) transcription factor of the CREB/ATF family. OASIS 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 and sequentially cleaved at the transmembrane region in response to ER stress. This releases the OASIS fragment, which translocates to the nucleus, bind to ER stress-responsive and cyclic AMP-responsive elements. In this study, we focus on the potential role of OASIS in astrogliosis. In the central nerve system, ER stress is implicated in a wide range of disorders including ischemic injury and neurodegenerative disorder. Both mRNA and protein levels of OASIS were elevated in the injured cortex and correlated closely with those of reactive astrocyte. Reactive astrocytes, which constitute a major cellular component of glial scar, may produce anti-regenerative molecules such as chondroitin sulphate proteoglycans (CSPGs). CSPGs are up-regulated in the central nerve system after injury and inhibit axon regeneration mainly through their glycosaminoglycan (CS-GAG) chains. We have analyzed the mRNA levels of the CS-GAG synthesizing enzymes using OASIS knockout mice. Expression of chondroitin 6-sulfotransferase 1 (C6ST1) is increased in cortical stab injury in wild type mice, but is not in OASIS knock out mice. These results suggest that OASIS may be involved in CSPG production through the transcription of C6ST1 in astrocytes

P-35 Spatio-temporal expression pattern of Foxp2 in the developing spinal cord

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A member of winged-helix/forkhead transcription factor family, Foxp2, is expressed in the developing central nervous system, such as the striatum, cerebral cortex, cerebellum, and spinal cord. It has been reported that Foxp2 plays important roles in the development of motor-skill learning in mice. Although Foxp2 mRNA is expressed in the developing spinal cord of mice, its roles have yet to be assigned. To understand the potential roles of Foxp2 in the development of spinal cord, we examined its expression pattern in the mouse embryos from embryonic day (E) 10.5 to E17.5 and characterized Foxp2-expressing cells using immunohistochemistry. The expression of Foxp2 was first detected at E11.0 in a cluster of cells located in the ventral spinal cord. All Foxp2-expressing cells were Pax6/Is12/neuron-specific class III β -tubulin⁺ postmitotic interneurons. Double-immunofluorescence staining for Foxp2 and some markers of subtypes of interneurons in the ventral spinal cord revealed that Foxp2 was expressed in a subpopulation of En1⁺ V1 interneurons at E11.0 and E11.5. En1⁺ V1 interneurons are subdivided into two subpopulations, Renshaw and non-Renshaw cells, and the former cells are differentiated earlier than the latter and express calbindin by E11.5. At E11.5, Foxp2 was expressed in En1⁺/calbindin⁻ non-Renshaw cells. Therefore, Foxp2 may be involved in the development of a subpopulation of V1 interneurons, probably as a fate determinant of non-Renshaw cells. Furthermore, the expression of Foxp2 was also observed in some cells of the dorsal spinal cord at E11.5 and E12.0. From E12.0 to E15.5, Foxp2 expression was also observed in medial and lateral part of the ventral spinal cord. Double-immunofluorescence staining of Foxp2 with Lhx1/5, Pax2, or En1 showed that Foxp2 was expressed in Lhx1/5⁺/Pax2⁻ d12 interneurons as well as Lhx1/5⁺/Pax2⁺/En1⁺ V1 interneurons. Unique expression patterns of Foxp2 in the developing spinal cord suggest that Foxp2 may be involved in some developmental events of V1 and d12 interneurons, such as fate determination, neuronal migration, and/or synaptogenesis.

P-36 Expression of TRPM8, TRPA1, and TRPV1 mRNAs in the rat nodose-petrosal ganglion complex

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The glossopharyngeal nerve joins the vagus nerve (cranial nerve X) and forms a complex that includes the nodose, petrosal, and jugular ganglia (NG, PG, and JG, respectively) from the peripheral side. Visceral sensory neurons (including gustatory neurons innervating the larynx and pharynx) of the vagus nerve are located in the NG, while the gustatory and somatosensory neurons (innervating the posterior part of the tongue and oropharynx) of the glossopharyngeal nerve are located in the PG. The cell bodies of somatosensory neurons of the glossopharyngeal (innervating the posterior part of ear) and vagus nerves are present in the JG. Recently, significant progress has been made with the cloning of temperature-activated ion channels, for example, members of the transient receptor potential family TRPM8 and TRPA1 are transducers that can be activated by cold stimuli, while TRPV1 is a non-selective cation channel that is activated by heat stimuli. However, little is known about the expression of thermo-sensitive TRPs in nodose-petrosal ganglion complex. In this study, we examined the expression of TRPM8, TRPA1, and TRPV1 mRNAs in the rat nodose-petrosal ganglion complex using *in situ* hybridization analysis. Moreover, we characterized the precise distribution of the ion channels in the rat vagal and glossopharyngeal sensory ganglia using immunohistochemistry and retrograde neuronal tracing by Fast Blue. In this conference, we show the results and discuss the expression pattern difference among TRPM8, TRPA1, and TRPV1 mRNAs in the rat nodose-petrosal ganglion complex.

P-38 Preliminary study of cilostazol effect on the protein expression changes of primary mouse brain microvessel endothelial cells

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Introduction: *In vitro* models are useful when they closely mimic *in vivo* situations. Establishment of the blood brain barrier (BBB) model implies the importance of brain microvessel endothelial cells (BMVECs) and the use of primary BMVECs as one of the options to study the drug delivery and its biomolecular event in BMVECs.

Materials and methods: C57/Bl6 mice were purchased from Japan SLC. Approval for the animal experiments was obtained from Animal Care and Experimentation Committee, Graduate School of Medicine, Gunma University. Cilostazol (6-[4-(1-cyclohexyl-1H-tetrazol-5-yl)butoxy]-3,4-dihydro-2-(1H)-quinolinone) was provided as pure powder from Otsuka Pharm. Co., Ltd.

Results: Expression pattern of the tight junction protein, ZO-1, showed that BMVECs formed a tightly packed, non-overlapping monolayer, consisting of contact-inhibited cells, as expected for a vessel wall endothelium. BMVEC identity was confirmed by acetylated LDL uptake, and the presence of von Willebrand factor and CD31. Contaminating pericytes could be removed by puromycin treatment. Various signaling proteins associated with brain microvessel endothelial injury were found to be differentially expressed by cilostazol-treated and untreated BMVECs.

Conclusion: We succeeded in isolating primary mouse BMVECs, which form an endothelium-like monolayer and are capable of tube formation in a few days. The protein expression patterns by BMVECs were drastically changed when they were treated with cilostazol. Further studies are in progress to assess a comprehensive comparison of protein expression changes of cilostazol-treated BMVECs using solution-based proteomics approach, isobaric tagging for relative and absolute quantitation (iTRAQTM) method.

P-37 Unique gene expression changes in microglia coincide with the appearance of chronic demyelinating lesions

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To study the causes of oligodendrocyte maturation arrest in chronic demyelinating lesions, we recently analyzed the hemizygous PLP transgenic mouse strain 4c (plptg^{-/-}) by cDNA microarray analysis. Those studies led to the present report in which we investigated expression of cystatin F. Cystatin F belongs to the cystatin superfamily, papain-like lysosomal cysteine proteinase inhibitors. The expression of cystatin F in demyelinated lesions of the central nervous system had not been previously examined. We found that cystatin F expression was completely absent in the normal brain and its induction in microglia was dependent on phagocytosis of compact myelin membranes in either plptg^{-/-} mice or in a cuprizone-induced demyelinating mouse model. *In vitro* analysis demonstrated that the expression of cystatin F in microglia was not induced after phagocytosis of non-myelin membranes. Its expression was mostly absent in brains of dysmyelinating jimpy and shiverer mutant mice, where there is no or very little compact myelin membrane even though microglia are activated in these brains. This strongly suggests that microglia can be activated in a specific manner when they phagocytize degenerated compact myelin membrane. At a later stage of demyelination in plptg^{-/-} mice and cuprizone-fed mice, the level of cystatin F expression decreased when remyelinating ability was lost. This demonstrates that gene expression of activated microglia is not constant *in vivo* during the course of demyelination, and this change coincides with the appearance of chronic demyelinating lesions.

P-39 Analysis of N-glycan structure from a femtomole level of glycoprotein

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Glycosylation is one of the most sophisticated posttranslational modifications of proteins. Sugar chains are crucial for the folding, intracellular transport, stability, and secretion of glycoproteins. Sugar chains on cell surface glycoproteins are involved in various cellular functions including cell-cell and cell-matrix interactions. Thus determination of sugar chain structure attached to a protein is very important. In spite of recent progress in sugar chain structure determination by mass spectrometry, it still requires a large amount of sample to determine isomeric structure. Structure determination of sugar chains using high-performance liquid chromatography (HPLC) after pyridylamination has been used frequently by researchers including us. However, this method also requires a picomole level of sample. We have developed an analytical method to detect a trace amount of N-linked sugar chains using two-dimensional HPLC. In this study, we present the data showing that N-linked sugar chain structures of glycoproteins separated on two dimensional gel electrophoresis or from human biopsy samples can be determined effectively by our method.

P-40 Alterations in homocysteine metabolism in the brain of the Goto-Kakizaki rat, an animal model of type 2 diabetes

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Type 2 diabetes mellitus is a systemic metabolic abnormality characterized by insulin deficiency and insulin resistance. The Goto-Kakizaki (GK) rat, obtained by selective inbreeding of Wistar rats showing impaired glucose tolerance, is considered as a polygenic model of type 2 diabetes. GK rats show hyperglycemia around postnatal day 8, and they become diabetic around 4 weeks of age. In our previous study on isolated pancreatic islets, we found that the expression of the 3 enzymes involved in homocysteine (Hcy) metabolism, betain-Hcy methyltransferase (bhmt), S-adenosylhydrolase (adcy), and cystathionine gamma-lyase (cbs), was significantly reduced in GK rat islets at 3w, resulting in an accumulation of Hcy in islet β -cells at 5 and 10w. In the present study, the effect of sustained hyperglycemia on the brain was investigated by comparing the gene expression of these 3 enzymes in the brain of GK and Wistar rats between 5-20 weeks of age. In the hippocampus, midbrain, and cerebellum, significant differences in the expression of bhmt, adcy, and cbs between GK and control rats were detected. Gene expression analyses and visualizations of brain Hcy by immunohistochemistry revealed following results. In the cerebellum of GK rats, up-regulation of cbs was seen already at 5 weeks of age, which was followed by up-regulation of adcy and the appearance of Hcy-positive Purkinje cells at later time points. Hcy-positive granule cells were also detected in the hippocampus where cbs was up-regulated at 20w. Cbs catalyzes the synthesis of cysteine from Hcy, thus serving as the starting point to synthesize the cysteine-containing peptide glutathione. Up-regulation of glutathione-S-transferase was also detected in the hippocampus of GK rats. The results thus suggest that glutathione synthesis is enhanced in the brain of GK rats to cope with the higher demand for glutathione. Accumulation of Hcy also generates increased oxidative stress through self-oxidation. These results clearly indicate that sustained hyperglycemia affects the brain of GK rats through increased oxidative stress and altered Hcy metabolism.

P-42 The trial for axonal regeneration by using bFGF continuous delivery system in lacunar infarction model of the rat

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Lacunar infarction that compromises exclusively white matter damage including axonal and myelin disruption compromises motor function. Principally, axonal regeneration is the promising treatment for the recover. To support the axonal regeneration process, we have chosen a continuous delivery system consistent in gelatin microspheres attaching bFGF to increase the nourishment into the glial scar and stimulate neuronal sprouting to establish axonal regeneration and remyelination of the damaged structures in lacunar infarction model developed in rats. Seven days after ET-1 injection into the internal capsule, gelatin microspheres (diameter 32-75 μ m) attaching bFGF or vehicle was injected using the same stereotactic technique. Fourteen days after ET-1 injection, animals were sacrificed and immunohistochemistry was performed to assess neuronal sprouting, glial components, vascular structures and chondroitin sulphate proteoglycans (ChSPGs). Microspheres was localized in the middle of the infarcted zone and surrounded by GFAP-positive astrocytes which was present in all the injured tissue. Neurofilament staining showed several neuronal sprouting across the affected place without pass through the limits of the glial scar. Also the sprouting does not follow any boundary shape and tends to avoid the place where gelatin was injected. The staining for ChSPGs showed a strong signal filling the entire injured zone and adjacent to the injected microspheres without any difference compared with the vehicle group. bFGF treatment may promote axonal sprouting. ChSPGs staining showed the glial scar constructing a barrier of reactive astrocytes, avoiding that axonal sprouted branches can go out to the glial scar. We consider that to use one kind of factor to support the brain healing process is not enough. For future research we are planning to add Chondroitinase ABC to decrease the mechanical and chemical negative signal that ChSPGs exert on the axonal regeneration process. Also we consider that longer trials must be performed.

P-41 A rapid but transient increase in Ifrd1 mRNA expression in brains of mice with middle cerebral artery occlusion

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Accumulating evidence that neurogenesis occurs in the hippocampal dentate gyrus and subventricular zone even in matured brains, in addition to developing brains, is now available in the literature. In our previous studies, we have identified interferon-related developmental regulator-1 (Ifrd1) as the gene responsible for predominant astroglial differentiation of adult hippocampal neural progenitor cells *in vitro*. In this study, we attempted to demonstrate the physiological and pathological significance of Ifrd1 in neural progenitor cells. In the mouse embryonic carcinoma P19 cells endowed to differentiate into neuronal and astroglial cells when cultured in the presence of all-trans retinoic acid (ATRA), expression of Ifrd1 mRNA was drastically increased in line with mRNA expression of GFAP, but not of MAP2. Cells were cultured with ATRA for 4 days, followed by transfection with the Ifrd1 expression vector. In these P19 cells with transient overexpression of Ifrd1, a significant decrease was seen in MAP2 mRNA expression and numbers of cells immunoreactive for MAP2. Adult male mice 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 TTC. Marked vital damages were found in the ipsilateral cerebral hemispheres of animals subjected to MCAO with severity proportional to the duration of occlusion from 90 to 150 min, but not in the contralateral cerebral hemispheres, on TTC staining assays. No significant changes were seen in mRNA expression of MAP2, NSE, GFAP or CD11b in ipsilateral hemispheres dissected 0 to 24 h after reperfusion, while MCAO led to a rapid but transient increase in Ifrd1 mRNA expression immediately after reperfusion, with delayed increases in mRNA levels of HO-1, xCT and nestin within 24 h after reperfusion. These results suggest that Ifrd1 may promote astroglial differentiation of neural progenitors with a role in mechanisms associated with the pathogenesis of ischemic brain damage at an early pathological stage.

P-43 The postnatal development of a molecular system responsive to novelty stress in the hippocampus of mice

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Exposure to novelty, a mild psychological stressor, induces a variety of changes in neural transmission (e.g., GABA and Ach) in the hippocampus of rodents, which may play an important role in stress-related adaptation, learning and memory. However, the novelty stress-induced alteration in the gene expression of the hippocampus is poorly investigated. We have previously reported stress-responsive genes in the mouse brain, i.e., Fos, Btg2, Cyr61, Gem and Nr4a1 (A. Kurumaji et al., Neurosci Res, 2008). The present study examined the novelty stress-produced changes in the gene expression of the hippocampus of young adult aged mice (8 week), 21 postnatal day (before weaning) and 15 postnatal day, using a quantitative RT-PCR method. For the stress paradigm, male mice (C57BL/6) were individually placed in a clean cage similar to their home cage for various times (15 ~ 120 min), while the control animals remained in their home cage. For the young adult aged mice, the gene expressions of the five genes were significantly activated by the exposure to the stress, which were transient and returned to the control levels after 120 min of exposure. The 30 min-stress produced the largest increase in the mRNA of Fos (+227 %) and Cyr (+82 %), whereas the enhancement of Btg2 peaked after a 15 min-stress (+190 %). The gene expressions of Gem and Nr4a1 gradually increased and showed a peak after 60 min of stress: Gem (+46%) and Nr4a1 (+66%). Moreover, whereas the pattern of the changed gene expressions after the novelty stress at 21 postnatal day was similar to that of the young adult aged mice, the molecular response to the stress was less pronounced at 15 postnatal day; there was no change in the gene expression of Gem or Cyr61 throughout the stress exposure for 120 min and the amounts of the increase in Fos, Btg2 and Nr4a1 were reduced to 84 %, 24 % and 30 %, respectively. The novelty stress for 60 min induced a significant increase in the level of the serum corticosterone for each postnatal stage. These results suggest that there is a characteristic molecular system responsive to novelty stress in the hippocampus. The immature responsive system in new-born mice may develop until weaning age, thus showing a delayed accomplishment compared to the stress response of the HPA axis.

P-44 Pharmacological discrimination of fear extinction and reconsolidation

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Conditioned fear memory, once formed through fear conditioning, is modulated by re-exposure of individuals to a conditioned stimulus. The re-exposure reactivates the fear memory, which induces reconsolidation of the memory first, and then extinction of the fear response. Both attenuating the former and facilitating the latter are effective in reducing the fear response, and these findings are potentially translatable to the enhancement of exposure therapy for complex anxiety disorders. Currently, no drug is known to selectively modulate either of reconsolidation or extinction, which are thought to be independent processes. Here, we report that an extinction-facilitating AMPA potentiator, PEPA, does not act on the reconsolidation of fear memory formed by contextual fear conditioning in mice. The freezing rates observed in contextually conditioned mice following short re-exposure (3 min) to the context were not influenced by intraperitoneal administration of PEPA. Similar short re-exposure to the context enhanced freezing responses of mice that were similarly administered D-Cycloserine (DCS), a drug that facilitates both extinction and reconsolidation. These results suggest that PEPA, unlike DCS, does not act on reconsolidation. In the same doses used in the short re-exposure experiments, PEPA and DCS facilitated extinction of the fear response, and exerted similar actions during behavioral tests that estimate reinstatement and re-extinction of fear. These results suggest that fear reconsolidation and extinction are independent processes that can be pharmacologically discriminated.

P-46 In vivo intense noise exposure activates 5'-AMP-activated protein kinase/c-Jun N-terminal kinase pathway in the cochlear spiral ligament fibrocytes of mice

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5'-AMP-activated protein kinase (AMPK) is a serine/threonine kinase activated by metabolic stress and by an increase in the AMP/ATP ratio. AMPK orchestrates intracellular events to suppress ATP-consuming anabolic pathways and enhance ATP-producing catabolic pathways. Inner ear disorders are known to be elicited by mitochondrial dysfunction, which ATP-producing is going to decrease in the inner ear. Several lines of evidence indicate that AMPK activates c-Jun N-terminal kinase (JNK) signals. In this study, we investigated AMPK/JNK pathway in the cochlear spiral ligament fibrocytes (SLF) after intense noise exposure. Std-ddY mice were exposed to 8 kHz octave band noise of 120 dB sound pressure level (SPL) for 2 h. The threshold shift of the auditory brainstem response (ABR) and hair cell loss were determined on day 14 after exposure. To determine the levels of AMPK, phospho-AMPK (p-AMPK), phospho-JNK (p-JNK), phospho-c-Jun (p-c-Jun), and phospho-ATF-2 (p-ATF-2), we performed an immunohistochemical and immunoblot analyses. ATP content in the SLF determined by bioluminescent assay at immediately after exposure. The noise exposure produced marked outer hair cell loss in the organ of Corti, as well as a dramatic threshold shift at frequencies of 4, 12, and 20 kHz. Under these experimental conditions, the noise exposure produced the expression of p-AMPK in the SLF immediately and 12 h later, without affecting the expression of AMPK. At 2 to 12 h after noise exposure, the expression of p-JNK, p-c-Jun and p-ATF-2 was enhanced in the SLF. However, ATP content in the SLF was no significant change after exposure. Taken together, our data suggest that the intense noise exposure activates AMPK/JNK pathway without the consumption of ATP in the SLF. The activation of AMPK/JNK pathway in the SLF may be involved in hearing loss induced by intense noise exposure.

P-45 Pathological role of microglia and microsomal prostaglandin E synthase-1 in a mouse model for amyotrophic lateral sclerosis

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Amyotrophic lateral sclerosis (ALS) is an adult-onset neurodegenerative disease characterized by selective degenerations of upper and lower motor neurons. Some cases of familial ALS (FALS) are associated with a point mutation in the gene encoding Cu/Zn-superoxide dismutase (SOD-1), and mice carrying a transgene for human SOD-1 with mutation of G93A (G93A mice) have been shown to develop the ALS-like disease. Activation of microglia in the spinal cord has been shown in ALS patients and the G93A mice. However, roles of the microglial activation in the pathological processes in ALS have not been clarified yet. In this study, experiments were performed to investigate the pathological role of microglial activation in G93A mice. Behavioral studies showed that disturbance of motor function appeared in 17 week-old and older mice. In accordance with this impairment, the expression of SMI32, a neurofilament marker, decreased in the spinal cord. Furthermore, in the spinal cord, Iba-1, a marker of microglial activation, was expressed, and microsomal prostaglandin E synthase (mPGES)-1, an inducible PGES by microglial activation, was elevated in an age-dependent manner (9 to 15 week-old) in these mice. However, neither Iba-1 nor mPGES-1 was detected in age-matched wild-type (WT) mice. In contrast to mPGES-1, there was no difference in the levels of cytosolic PGES (cPGES) and mPGES-2, constitutively expressed forms of PGESs, between WT and G93A mice. Dexamethasone (DEX), which has been shown to suppress disease progression and to improve survival in G93A mice, suppressed an increase in mPGES-1 expression in spinal cord in G93A mice, whereas expressions of mPGES-2 and cPGES, and Iba-1 were not affected. These results suggest that mPGES-1 induced by microglial activation was markedly elevated prior to disturbance of motor function, and that elevation of mPGES-1 level contributes to the disease onset and progression of motor neurons degeneration in the G93A mice.

P-47 Behavioral analyses of mice which show abnormal expressions of neuroglycan C, a brain-specific chondroitin sulfate proteoglycan

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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 without chondroitin sulfate during the development of the cerebellum and retina. The chondroitin sulfate glycosylation is also regulated differently depending on cell types. To clarify the roles 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 four strains of mice; 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, NGC-knockin mice that express NGC in non-proteoglycan form due to a mutation (S123A) at the chondroitin sulfate chain binding site, and mice that have both properties of NGC-knockdown and -knockin mice. All these mice were viable and fertile. Histochemical studies showed that these mice did not show macroscopic abnormalities in gross brain anatomy. To examine their behavioral phenotypes, these mice were subjected to several kinds of behavioral tests including the open field test. In this meeting, we have reported the results and discussed about the significance.

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.

P-48 A case-control association study of the MYH9 gene with schizophrenia

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[Purpose] Several genome-wide linkage studies have suggested linkage between markers on the long arm of chromosome 22 and schizophrenia. It has also been reported that 22q11.2 deletions increased the risk of schizophrenia. Our previous study using 13 microsatellite markers on 22q demonstrated associations of AFM309WD5 (D22S1174) and AFM262VH5 (D22S283) with schizophrenia, suggesting that there are susceptibility loci for schizophrenia near these two markers. The *myosin, heavy chain 9, non-muscle (MYH9)* gene, where AFM262VH5 is located, has recently reported to be associated with the subgroup of schizophrenia without deficits in sustained attention. Considering these findings together, *MYH9* is a potential candidate susceptibility gene for schizophrenia. To assess whether *MYH9* could be implicated in vulnerability to schizophrenia, we conducted a case-control association study.

[Methods] The present study was approved by the Ethics Committee on Genetics of the Niigata University School of Medicine, and written informed consent was obtained from each participant. All participants were unrelated Japanese subjects. The study population consisted of 534 patients with schizophrenia (281 men and 253 women; mean age, 40.1 [SD 14.2] years) diagnosed according to DSM-IV and 559 control subjects (297 men and 262 women; mean age, 37.3 [SD 10.1] years). We examined 25 tagging single nucleotide polymorphisms (SNPs) in *MYH9*, which were selected from the HapMap database. All SNPs were genotyped using the TaqMan 5'-exonuclease assay.

[Results] There were nominally significant allelic associations of rs5756154 and rs739096 with schizophrenia (uncorrected $p = 0.034$ and 0.038 , respectively).

[Conclusion] We found potential associations of two SNPs in *MYH9* with schizophrenia using moderate-scale sample and 25 tagging SNPs, although these associations were not significant after correction for multiple testing. To confirm potential associations obtained in the present study, further studies using large-scale independent samples will be needed.

P-50 Construction of Human A β 1-38 ELISA assay system

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Senile plaques, one of the neuropathological hallmarks of Alzheimer's disease (AD), are composed of a small, ~40-residue protein called amyloid β protein (A β). A β 40 is the most predominant species with a longer but minor species, A β 42. However, this minor form is indeed initially deposited in the brain and predominates in diffuse and mature plaques. These A β s are produced by sequential proteolytic cleavages of the amyloid β precursor protein (APP) by β - and γ -secretases. Recent studies have shown interest in the generation of shorter A β species, particularly A β 38. Modulators of γ -secretase activity, non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen or sulindac sulfide, selectively reduce the production of A β 42. Concomitantly, they increase A β 38 production. However, this generative correlation is unknown. Previous reports show that the existence of A β 38 has been mainly confirmed by mass spectrometry analysis. To detect and determine A β 38 more simply, we cloned a C-terminal specific anti-A β 38 antibody, namely 3B1, which was not cross reactive with A β 37, A β 40 or A β 42. By combining 3B1 and 82E1, highly specific for Asp-1 of human A β , we constructed an A β 1-38 ELISA assay system. Using an A β 1-38 assay kit and an A β 1-42 assay kit (IBL cat. NO.27712), we measured the behavior of A β 38 and A β 42 on NSAIDs treatment conditioned media. Our results suggested that these 3B1 antibody and ELISA assay kits could be useful for searching for the generative mechanism of A β 38/A β 42 and selective A β 42 lowering inhibitors. This work was supported by the New Energy and Industrial Technology Development Organization (NEDO).

P-49 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 the healthy elderly and the elderly including mild cognitive impairment (MCI). However, one study did not replicate the association in healthy subjects. Another study found the association in a 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 188 healthy subjects in a Japanese population. Genotype distribution of the SNP was in Hardy Weinberg equilibrium (CC: 7, CT: 57, TT: 124). Delayed recall and verbal memory of the WMS-R in CC subjects were significantly lower than that in T allele carriers consistently to the initial study ($p=0.0021$, $p=0.021$). However, there was no significant difference in the other WMS-R indices between the two groups (visual memory and attention). 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-51 The possible role of platelet brain-derived neurotrophic factor in depression

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Many studies suggest that the stressful events possibly promote neurochemical changes in the brain that may be involved in the pathogenesis of depressive disorder. Although the evidence was shown that depression and chronic stress reduce levels of growth factors, including brain-derived neurotrophic factor (BDNF) and Insulin-like growth factor 1 (IGF-1), but increase in peripheral blood and brain, amenable to antidepressants, the action of antidepressants on the regulation of growth factor levels in peripheral blood as well as brain are largely unknown. Previously, we have indicated that antidepressants promote the platelet neurotrophic factor release which could relate to their increase in serum levels. We also suggested that the change of platelet neurotrophic factors might be a biological marker of depressive state. To examine the mechanism of their release from platelets, we tried to study the change of the platelet BDNF release and serum its level with addition of antidepressants, and the expression of TrkB receptor (tyrosine kinase B, the family of BDNF-specific receptors) on the platelets using the depression model rats. The change of platelet BDNF release and serum levels was evaluated by the BDNF-ELISA methods in the washing platelets samples and serum samples prepared from depressive model rats made by chronic administration of corticosterone. We detected the change of BDNF release from platelet with antidepressants and TrkB receptor expression on the platelets in the depression model compared with control. The results suggested that platelet BDNF release could be affected by depressive state, and be association with the change of TrkB receptor expression on the platelets. The meaning between the BDNF release and TrkB receptor expression on the platelets will be discussed.

人名索引

演題番号 (太字は筆頭演者)

氏名	演題番号	氏名	演題番号	氏名	演題番号	氏名	演題番号
あ		池内 俊彦	O14-3	伊藤 芳久	P-45	え	
相澤 好治	O15-8	池谷 真澄	S06-5	伊藤 理恵子	P-13	江頭 良明	O06-2
青木 ちえ	O06-4		O07-3	稲田 大助	P-6	江田 岳誉	JSN-JSBP-4
青野 幸子	P-47		O07-4		P-10		S13-3
青山 峰芳	P-21	池田 正明	P-32	井上 和秀	S11-1	海老原 利枝	S10-1
赤川 公朗	O05-1	池中 一裕	O01-2		S11-2	遠藤 良	P-19
赤塚 淳一	S10-3		O12-4		O01-1		
Ahmed Giasuddin	S06-4		O13-1		O01-3	お	
審良 静男	O09-4		O13-2	井上 浄	O08-2	オー' トゥール アイリーン	S10-5
吾郷 由希夫	S12-4		O14-2	井上 俊洋	O13-3	大井 一高	JSN-JSBP-3
	O15-4		P-37	井上 順雄	O13-7		S12-1
	O15-6		P-39		P-6		P-49
浅井 清文	P-21	Islam Shahidul M	S06-4		P-7	大江 祐樹	O06-2
浅川 秀雄	O15-8	石井 章寛	P-39		P-8	大雲 剛志	O03-2
浅田 明子	O02-2	石井 貴男	JSN-JSBP-1		P-10	大河内 正康	P-49
	O02-3		P-11	井上 葉子	O15-8	大澤 圭子	S11-1
	O02-4		P-51	居原 秀	O10-3	大島 登志男	P-19
	P-19	石井 良平	P-49	今泉 和則	S08-5	大隅 典子	OS-4
浅沼 幹人	P-15	石川 保幸	O06-6		P-33		S01-6
	P-23	石川 良樹	S10-4	今井 英明	P-38	太田 訓正	S06-4
味岡 逸樹	S02-4	石毛 久美子	P-45		P-42	大谷 浩樹	O13-7
安達 直樹	O08-1	石崎 泰樹	S01-3	井村 誉史雄	S03-1		P-8
	O15-1		S06-6	入野 康宏	S11-1	大谷 嘉典	O01-2
	P-16		O12-1	入船 宏美	O14-3	太田 浩良	O05-6
	P-28		O12-2	岩倉 百合子	S13-3	大塚 信太朗	O10-4
阿部 輝雄	O10-2		P-38	岩瀬 真生	P-49	大塚 稔久	S14-1
阿部 学	O07-1		P-42	岩田 修永	O02-3	大塚 正成	O14-1
阿部 佑一	JSN-JSBP-4	石塚 佑太	S04-4	岩本 郁子	O07-2	大槻 健弥	S12-4
	S13-3		S13-3		O15-3	大津 昌弘	O13-7
荒木 一明	S13-3	石田 雄介	P-24	う			P-6
有江 裕子	S06-5		P-36	植田 高史	P-24		P-7
	O07-3	石野 雄吾	O13-2		P-36		P-8
	O07-4	石橋 智子	O09-1	植田 英寛	O11-3	大西 大空	O04-6
アリフィン モー	P-38	石橋 瑛	P-40	植松 智	O09-4	大西 浩史	O02-5
アリレザ ケイロラ	P-20	泉 愛子	O08-1	上松 則彦	O13-6		O02-6
アルバレスビュイラ アルトロ	S06-3		P-28		O14-7	大橋 一正	S10-3
い		磯 達也	O12-2	上松 正和	P-31	大畑 健治	O04-1
井池 直美	P-49	磯野 真由	O13-7	鵜飼 渉	JSN-JSBP-1	大葉 龍太郎	O05-3
飯嶋 一之	O06-2		P-7		P-11	大平 敦彦	P-47
家亦 美佳	O04-2	板倉 誠	O10-3		P-51	大森 啓之	O13-7
	O12-3		O10-4	鵜川 眞也	P-24		P-7
五十嵐 道弘	S09-3	伊丹 千晶	O14-5		P-36		P-8
	S10-1		O15-1	臼井 紀好	O14-2	大藪 明子	S03-1
	O03-1	伊藤 悟	O14-6	内田 敦子	S03-1	岡澤 秀樹	O02-5
	P-12	伊藤 仁一	P-20	内田 達也	O10-4	岡田 泰信	O12-4
	P-13	伊藤 哲也	P-21	内田 洋子	O05-5	岡野一内田 孝幸	S01-3
	P-14	伊東 秀記	O07-2		P-17		O12-1
猪狩 寛子	O05-6		O15-3	宇野 健史	P-40		O12-2
伊川 正人	P-47	伊藤 光広	O14-1	浦野 文彦	S08-1		P-42
井口 東郎	P-22	伊東 佑真	P-4			岡野 栄之	S06-3

氏名	演題番号	氏名	演題番号	氏名	演題番号	氏名	演題番号
	S13-5	河西 正樹	O14-4	木村 昂司	O09-2	鴻野 貴司	O05-6
Okafuji Tatsuya	S06-4	笠間 健嗣	O14-5	木村 洋人	P-30	神山 邦子	O09-4
岡部 勝	P-47	数井 裕光	P-49	木山 博資	O04-1	児島 伸彦	O03-6
岡本 賢一	O07-2	片伯部 哲也	O09-2		O08-2		O06-4
	O15-3	片山 泰一	JSN-JSBP-6	姜 裕貴	O10-1		O11-2
小川 登紀子	O08-2		O15-2	清末 和之	O14-5	小島 正己	O14-5
小川 瑞恵	O12-7	加藤 薫	S10-1			五嶋 良郎	S06-5
荻田 喜代一	O04-7	加藤 晋	P-21				O07-3
	P-1	加藤 泰介	S03-5	草苺 伸也	O02-5		O07-4
	P-2		S13-3		O02-6		O07-5
	P-3	加藤 忠史	S02-1	工藤 喬	S08-5	小菅 康弘	P-45
	P-5	角山 圭一	O04-5		P-49	小谷 武徳	O02-5
	P-18	金井 将昭	O03-4	工藤 玄恵	P-16	児玉 明子	O09-1
	P-25	金森 哲子	O13-6	功刀 浩	O08-1	後藤 仁志	O13-1
	P-46		O14-7		O15-1	小西 志歩	P-41
奥田 洋明	S01-1	金子 順	O13-5		P-16	小西 博之	O04-1
	P-33	金子 奈穂子	S06-3		P-28		O08-2
奥田 浩人	O12-5	金子 尚史	P-48	久保 健一郎	S06-2	小西 慶幸	O07-6
奥野 恭史	S05-2	鎌田 尚樹	S03-1	久保田 健夫	S02-5	小林 肇	P-6
奥谷 正人	S10-6	紙野 晃人	P-49	クマール アキレッシュ	O13-2	駒野 宏人	O05-3
小倉 明彦	O06-1	嘉山 巧	O05-6	熊谷 恵	P-32	五味 不二也	O05-5
	O06-2	Karagogeos Domna	O13-8	熊倉 鴻之助	O10-1		P-17
小倉 颯一	O07-5	河合 克宏	O06-1	熊倉 悠佳	S03-3	小森 忠祐	O14-8
小椋 正人	O04-2	川内 健史	S06-2	熊丸 絵美	O08-1		P-34
	O12-6	川越 博文	O12-6		O15-1	近藤 靖	P-6
小河 匡	P-31	川崎 俊之	S12-4		P-16		
尾崎 紀夫	S12-2	川田 浩一	P-1		P-28		さ
小澤 秀介	P-9		P-2	久米田 孝輔	O07-5	斎藤 聡彦	S10-3
小澤 哲朗	O12-8		P-3	久米 伸恵	P-6	齋藤 綾子	O05-1
小鹿 幸生	O13-6		P-5		P-7	齋藤 繁	O12-2
	O14-7		P-18		P-10	西道 隆臣	O02-3
小野 勝彦	S06-6	川原 慎一	O04-1	公文 麻美	O08-4	斎藤 太郎	O02-2
	O13-1		O08-2	倉知 正	S01-3		O02-3
	O14-2	川原 裕之	P-19		O12-1		O02-4
	P-47	川村 宏樹	JSN-JSBP-4		O12-2		P-19
小野 真一	P-45	神田 錦吾	O01-5		P-38	齋藤 利和	JSN-JSBP-1
小野 貴文	JSN-JSBP-1	神戸 悠輝	P-26		P-42		P-11
	P-11			倉林 正彦	O12-2		P-51
	P-51		き	倉本 展行	P-1	齊藤 秀俊	O01-1
小野 武年	S13-1	木内 泰	S10-3		P-25		O01-3
小俣 直人	JSN-JSBP-2	岸 宗一郎	O14-3		P-46	齊藤 泰之	O02-5
小柳 洸志	O04-3	北尾 達哉	S12-4	栗原 裕司	O07-3		O02-6
	O04-6	喜田 聡	S04-2		O07-4	斎藤 祐見子	O15-5
		北島 勲	S02-3	車地 暁生	P-43	蔡 娜	S01-3
		喜多 大三	P-15				O12-1
		木谷 裕	O01-2			五月女 颯之	S03-3
峽戸 孝也	O15-8	北村 俊雄	O14-8	Coleman Michael	ISN-1	坂井 美和子	S13-3
Kaibuchi Kozo	ISN-2	北村 尚士	S01-2	小泉 修一	O12-8	坂田 亜衣	O09-3
ガオ ホンフエン	S14-5	北村 佳久	P-15	小泉 信一	S05-1	匂坂 尚史	O13-6
鹿川 哲史	S01-4	吉川 友理	P-23	小出 直	S10-6		O14-7
	O13-3	城戸 瑞穂	P-22	高坂 新一	S11-1	崎村 建司	O07-1
垣田 博樹	P-21	木戸 悠佳	P-29	香田 健	O15-4		P-13
郭 伸	S12-3	木下 雅美	O13-5		O15-6	桜井 都衣	O11-1
角田 伸人	P-50	季 斌	S11-5	甲谷 章	P-25		O13-8
笠井 久隆	P-10						

氏名	演題番号	氏名	演題番号	氏名	演題番号	氏名	演題番号
Zhang Sanbing	S06-4		P-11		P-13	武田 泰生	O11-1
笹川 展幸	O10-1		P-51	高島 明彦	S08-3		O13-8
佐々木 えりか	S13-5	新谷 紀人	JSN-JSBP-6	高田 昌彦	S13-4	竹田 麗子	O03-6
笹谷 晴恵	O14-3		O15-2	田賀 哲也	S01-4	炬口 真理子	O04-5
佐藤 明	S09-1	新明 洋平	S06-4		O13-3	竹林 浩秀	O13-1
佐藤 亘	O02-3	新屋 冬美	O13-7	高野 桂	O12-7		O14-2
佐藤 真	S06-1		P-7	高野 二郎	O02-3	竹宮 孝子	O09-4
佐藤 泰史	S06-5		P-8	高橋 明男	O08-3		O15-7
	O07-3				O08-4	田代 朋子	O04-3
佐藤 友美	S01-2	す		高橋 琢哉	S07-2		O04-6
	O01-2	須賀 圭	O05-1	高橋 秀俊	JSN-JSBP-3		O05-6
佐柳 友規	S11-1	菅谷 ちえ美	O15-8		P-49		O06-1
佐野 輝	S07-5	菅原 健	O12-8	高橋 理貴	O04-3		O15-8
佐野 尚平	P-1	杉浦 弘子	O15-7		O04-6		P-30
澤 明	S07-1	杉山 千絵	O04-7		O15-8		P-40
	S12-2	鈴木 恵里	S11-1		P-30	太城 康良	S03-1
澤野 恵梨香	P-30	鈴木 健二	O05-4		P-40	多田 幸代	P-13
澤本 和延	S06-3	鈴木 悟	P-21	高橋 正身	O10-3	橘 正毅	O03-5
		鈴木 辰吾	O14-5		O10-4		O12-3
し		鈴木 孝昌	O05-6	田上 真次	P-49		P-4
塩坂 貞夫	O06-6	鈴木 勉	O12-8	高村 孝則	P-49	辰巳 晃子	S01-1
塩田 清二	O01-5	鈴木 登	O04-5	高村 明孝	JSN-JSBP-3		P-33
塩田 倫史	S02-3	鈴木 豊	P-6		S12-1	館農 勝	JSN-JSBP-1
Sheng Zu-Hang	ISN-3	須藤 香織	O07-2	宝田 剛志	O01-4		P-11
篠田 友靖	O07-2		O15-3		O03-3		P-51
	O15-3	須原 哲也	S11-5		O03-5	田中 晶子	O12-5
篠原 巧	O10-2	Su Yuhong	S06-4		O04-2	田中 謙二	O12-4
柴崎 貢志	S06-6				O12-3		O13-2
柴田 圭輔	O12-8	せ			O12-6		P-37
芝 達雄	P-5	清家 稔博	P-22		P-4	田中 光一	O14-5
	P-18	関口 正幸	O08-3		P-9	田中 佐知子	O01-5
渋谷 雅子	JSN-JSBP-4		P-44		P-26	田中 達英	S11-3
	S13-3	関根 克敏	S06-2		P-41	田中 稔久	P-49
島崎 久仁子	O11-1	関野 祐子	S14-2	瀧上 周	O15-7	田中 始	P-3
島田 昌一	P-24		O06-3	滝沢 琢己	S02-2		P-46
	P-36	関本 研一	O12-2	田口 紋子	O13-4	田中 英明	S06-4
島田 貴史	O14-3	瀬藤 光利	O07-6	田口 良	S09-4	田辺 和弘	P-39
清水-岡部 千草	O10-2	千堂 年昭	P-15	田熊 一敏	S12-4	谷浦 秀夫	O04-2
清水 崇弘	P-37	仙波 恵美子	O14-8		O15-4		P-26
清水 健史	O13-3		P-34		O15-6	谷口 泰造	O04-5
下家 浩二	O14-3		P-35	竹居 光太郎	S06-5	谷口 直子	O06-1
霜田 靖	O11-1	仙波 りつ子	O15-1		O07-3	田野 かおり	S03-1
	O11-3				O07-4	田畑 泰彦	P-42
	O13-8	そ		武井 延之	S03-5	玉置 啓祐	P-4
謝 敏かく	S06-1	Cong Yana	O15-6		S04-4	玉巻 伸章	O14-2
ジャロペレド ハンナ	S12-2	鄒 鶴	O05-3		S13-3	田村 英紀	O06-6
首藤 誠	O04-7	宗宮 仁美	S03-6	武内 恒成	O03-1	田村 和希	O10-1
白尾 智明	O8-2	曾我部 正博	O12-4		P-14		
	S10-2	外山 英和	JSN-JSBP-4	竹内 千仙	O09-4	ち	
	O03-6		S13-3	竹島 美香	P-23	Chiu CT	JSN-JSBP-2
	O06-3	染矢 俊幸	P-48	武田 伸一	S12-6	千葉 俊明	O04-5
	O06-4			武田 雅俊	JSN-JSBP-3	Chuang DM	JSN-JSBP-2
	O11-2	た			S12-1		
白坂 知彦	JSN-JSBP-1	高雄 啓三	O02-6		P-49		

氏名	演題番号	氏名	演題番号	氏名	演題番号	氏名	演題番号
つ		長嶋 玲子	P-1	丹羽 美苗	S12-2	林 由里子	O02-6
蔡 宗樺	O03-2		P-3			原 明	O13-4
辻 武史	P-15		P-46	ぬ		原 英彰	S08-4
津田 誠	S11-2	永田 悦子	O10-3	布川 綾子	P-48	板東 良雄	O09-3
	O01-1	永田 浩一	O07-2	布村 光	O09-3		
	O01-3		O15-3	沼川 忠広	LA-1	ひ	
角田 正史	O15-8	中谷 陽介	O14-3		O08-1	東 幹人	P-39
て		長塚 靖子	O13-5		O15-1	比嘉 進	P-14
鄭 英君	JSN-JSBP-4	中西 博	S11-4		P-16	樋口 大樹	S03-3
	S13-3	永野 仁士	P-8		P-28	樋口 真人	S11-5
ティッシャーラビン マーク	S06-3	中町 智哉	O01-5	沼沢 聡	O01-5	久岡 朋子	P-34
デ・カミリ ビエトロ	S10-5	中道 範隆	O03-3				P-35
			O04-2	ね		久恒 辰博	O8-1
			O12-6	根岸 隆之	O04-3	久永 眞市	O02-2
と			P-4		O04-6		O02-3
東ヶ崎 健	S10-1		P-26		O15-8		O02-4
遠山 正彌	JSN-JSBP-6		P-41		P-30		P-19
	O06-5	中村 克樹	S13-2		P-40	備前 典久	O13-3
	O08-2	中村 敏一	O03-4	根本 知己	S14-5	等 誠司	O13-2
	O11-4	中村 史雄	O07-3			樋野 興夫	O15-7
	O15-2		O07-4	の		ビブ ジェームス	S04-6
戸蒔 創	P-21		O07-5	野阪 哲哉	O14-8	平澤 孝枝	S02-5
時田 義人	P-47	中村 泰子	S11-1	野住 素広	S10-1	平野 靖史郎	O04-6
得丸 博史	O10-2	中村 有加里	O03-3		O03-1	平林 義雄	S09-5
戸田 達史	S12-5	中村 洋一	O12-7		P-12		O13-5
	O04-4	長安 祐子	P-20	野田 百美	P-22	廣瀬 謙造	S14-3
富永 真琴	S06-6	中山 孝	O13-7	野村 靖幸	O05-6		O12-4
富永一吉野 恵子	O06-1		P-6	則竹 淳	S09-2	廣田 ゆき	S06-3
	O06-2		P-7		S14-5		
富山 貴美	S08-2		P-8			ふ	
	O05-1		P-10	は		ブー ムーミン	S14-5
豊島 学	O11-1	梨子田 哲明	S12-4	橋口 美津子	O02-1	ファークソン ショーン	S10-5
	O13-8	鍋島 俊隆	S12-2	橋詰 良夫	O14-7	ファリッド アハマド	P-38
豊田 剛成	O13-6	鍋谷 卓司	S09-5	橋本 恵理	JSN-JSBP-1		P-42
	O14-7	並木 繁行	O12-4		P-11	ブエンテス サンドラ	P-38
豊満 笑加	O01-1	檜橋 敏夫	O05-7		P-51		P-42
鳥居 知宏	P-39	成田 奈緒子	S03-3	橋本 均	JSN-JSBP-6	深田 正紀	S09-2
トルグン トルスン	O15-1	成田 正明	S03-1		O15-2		S14-5
	P-16	那波 宏之	JSN-JSBP-4	橋本 亮太	JSN-JSBP-3	深田 優子	S09-2
			S03-5		S12-1		S14-5
			S04-4		P-49	福井 正樹	P-9
な			S13-3	長谷川 孝一	O03-2	福岡 早紀	P-15
Naser Iftekhhar Bin	S06-4	難波 寿明	JSN-JSBP-4	服部 剛志	JSN-JSBP-6	福士 政広	O13-7
長池 一博	P-50		S13-3		O15-2		P-8
永井 義隆	O04-4	に		花村 健次	S10-2	福永 浩司	S02-3
中込 咲綾	O08-2				O06-4		S04-1
長澤 一樹	O12-5	西川 徹	P-43	馬場 明道	JSN-JSBP-6		O05-7
	P-29	西条 寿夫	S13-1		O15-2	福光 秀文	S03-6
長澤 寿磨	O07-1	西田 健太郎	O12-5	馬場 広子	O01-2		O14-1
仲嶋 一範	S02-4		P-29		O09-1		O14-4
	S06-2	西野一林 美都子	S10-5		O09-2		O14-6
中島 欽一	O8-3	西部 弘純	S09-1	林 明子	O09-2	福本 素由己	JSN-JSBP-3
	S01-5	西村 百恵	O15-4	林 周宏	S09-1		S12-1
	S02-2	西本 高明	O04-5	林 光紀	O10-1		P-49
中島 芳浩	P-32						

氏名	演題番号	氏名	演題番号	氏名	演題番号	氏名	演題番号
福森 良	P-26		O14-7		P-34		O10-4
藤掛 伸宏	O04-4	松崎 伸介	JSN-JSBP-6		P-35	山森 英長	JSN-JSBP-3
藤下 加代子	O12-8		O15-2	森口 茂樹	O05-7		S12-1
藤田 慶大	P-22	松崎 秀夫	S03-4	森下 理香	O07-2		P-49
藤林 靖久	JSN-JSBP-2	松田 敏夫	S12-4		O15-3		
藤本 貞毅	O12-5		O15-4	森野 道晴	O04-1	ゆ	
	P-29		O15-6	森原 剛史	P-49	湯山 耕平	O05-2
フセイイン モハメド	P-21	松田 尚人	S14-5	森 啓	O05-1		
洲上 孝裕	O02-4	松本 明	O04-5	森 宗昌	O02-5	よ	
船越 洋	O03-4	松本 陽	O09-4	森 泰文	O06-5	横山 信治	P-20
船津 尚子	P-30	松山 正剛	O04-5		O11-4	横山 智美	S03-1
Brown Anthony	ISN-4	的崎 尚	O02-5	森山 光章	O12-7	吉江 拓也	O13-7
プラットナー フロリアン	S04-5		O02-6				P-6
降旗 千恵	O05-6	マリン オスカー	S06-3	や			P-7
古市 貞一	S01-2	丸岡 伸行	JSN-JSBP-2	矢ヶ崎 有希	P-28	吉川 和明	O03-2
	S09-1			八木 秀司	S06-1	吉田 祥子	S14-4
	O01-2	み		安田 圭一	O10-3		P-31
古川 昭栄	S03-6	御子柴 克彦	O06-1	安田 新	O15-7	吉田 成孝	O09-3
	O14-1	三品 裕司	S01-2	安田 由華	JSN-JSBP-3	吉田 武美	O01-5
	O14-4	水井 利幸	S10-2		S12-1	吉田 哲彦	P-49
	O14-6		O06-3		P-49	吉永 敏弘	JSN-JSBP-1
古家 喜四夫	O12-4	水木 信久	O07-4	柳澤 勝彦	O05-2		P-51
		水野 健作	S10-3	矢野 耕史	O15-4	吉村 武	P-39
へ		水野 誠	JSN-JSBP-4		O15-6	吉村 好之	O15-7
別府 秀幸	S02-3		S13-3	山内 卓	O15-7	好本 裕平	P-38
		道川 誠	O05-3	山形 要人	O09-4		P-42
ほ		光山 冬樹	S10-6		O15-7	米田 幸雄	O01-4
穂積 宏彰	P-15	嶺岸 正治	O02-4	山川 裕希子	P-22		O03-3
細川 智永	O02-2	宮川 剛	O02-6	山口 政光	O04-4		O03-5
細川 まゆ子	O15-8		P-13	山口 めぐみ	S06-5		O04-2
細谷 俊彦	O13-2	宮岸 寛子	P-45		O07-3		O12-3
堀田 凱樹	O13-2	宮木 純	P-29		O07-4		O12-6
ポピエル 明子	O04-4	宮崎 育子	P-15	山口 宜秀	O01-2		P-4
堀内 純二郎	S04-3		P-23	山崎 博幸	O06-4		P-9
堀 悦郎	S13-1	宮島 健	S10-3		O11-2		P-26
堀越 優子	P-50	宮田 信吾	O06-5	山崎 真弥	O07-1		P-41
本多 敦子	O03-1		O11-4	山下 俊英	S11-3	米山 雅紀	P-1
本田 岳夫	S06-2	宮本ー松原 真由美	O15-5	山下 直也	O07-5		P-2
	O07-1	三好 耕	P-23	山末 英典	JSN-JSBP-5		P-3
本堂 亜紀	P-36			山田 浩平	JSN-JSBP-6		P-5
		む			O15-2		P-18
ま		村上 公一	O09-3	山田 大輔	P-44		
Michael Dyer	S02-4	村上 拡治	P-6	山田 貴博	P-36	り	
前田 紗弥香	P-41	村上 富士夫	S06-3	山田 真久	S01-2	Leeds P	JSN-JSBP-2
前田 智司	O05-3	村上 竜太	S05-2	山田 泰広	O13-4	李 海雄	O12-4
マオ カンバン	S13-1	村田 哲人	JSN-JSBP-2	山根 昌之	O07-5	Liu Hongtao	O12-4
牧野 晃久	O14-6	村田 美穂	S07-4	山本 和弘	O08-3		
馬 堅妹	P-37	村田 陽二	O02-5		O08-4	る	
増尾 好則	S03-2		O02-6	山本 利憲	S05-3	ルービンシュタイン ジョン	S06-3
増田 潤哉	O01-3	村山 奈美枝	S06-6	山本 敏文	P-27	ル フイ	S14-5
町田 武生	O13-5			山本 朋未	O01-4		
松井 ふみ子	P-47	も		山本 直樹	O05-4	れ	
松川 隆	O12-8	Moya PR	JSN-JSBP-2	山本 秀子	P-27	Leng Y	JSN-JSBP-2
松川 則之	O13-6	森川 吉博	O14-8	山森 早織	O10-3		

氏名	演題番号	氏名	演題番号	氏名	演題番号	氏名	演題番号
ろ							
呂 嘉	P-12						
わ							
若佐 美佳	O15-8						
和田 恵津子	O08-4						
和田 圭司	S07-3						
	O04-4						
	O08-3						
	O08-4						
	P-44						
渡邊 一平	JSN-JSBP-1						
	P-11						
	P-51						
渡邊 和忠	O11-1						
	O11-3						
	O13-8						
渡邊 公彦	JSN-JSBP-1						
	P-11						
	P-51						
渡辺 啓介	O14-2						
渡辺 貴志	O05-6						
渡邊 真未	P-41						
渡部 雄一郎	P-48						
渡邊 裕美	P-13						
	P-14						
和田 有司	JSN-JSBP-2						
和中 明生	S01-1						
	P-33						
Wang Z	JSN-JSBP-2						
王 冉	S13-3						

Author Index

演題番号 (太字は筆頭演者)

氏名	演題番号	氏名	演題番号	氏名	演題番号	氏名	演題番号
A			012-1		S09-1		O12-4
Abe Manabu	O07-1	Chiba Shunmei	O04-5		O01-2	Hirota Yuki	S06-3
Abe Teruo	O10-2	Chiu CT	JSN-JSBP-2	Furukawa Shoei	S03-6	Hisanaga Shin-ichi	O02-2
Abe Yuichi	JSN-JSBP-4	Chuang DM	JSN-JSBP-2		O14-1		O02-3
	S13-3	Coleman Michael	ISN-1		O14-4		O02-4
Adachi Naoki	O08-1	Cong Yana	O15-6		O14-6		P-19
	O15-1			Furuya Kishio	O12-4	Hisaoka Tomoko	P-34
	P-16	D					P-35
	P-28	De Camilli Pietro	S10-5	G		Hisatsune Tatsuhiko	OS-1
Ago Yukio	S12-4			Gao Hongfeng	S14-5	Hitoshi Seiji	O13-2
	O15-4	E		Gomi Fujiya	O05-5	Honda Atsuko	O03-1
	O15-6	Ebihara Satoe	S10-1		P-17	Honda Takao	S06-2
Ahmed Giasuddin	S06-4	Eda Takeyoshi	JSN-JSBP-4	Goshima Yoshio	S06-5		O07-1
Aizawa Yoshiharu	O15-8		S13-3		O07-3	Hondoh Aki	P-36
Ajoka Itsuki	S02-4	Egashira Yoshihiro	O06-2		O07-4	Hori Etsuro	S13-1
Akagawa Kimio	O05-1	Endo Ryo	P-19		O07-5	Horikoshi Yuko	P-50
Akatsuka Junichi	S10-3			Goto Hitoshi	O13-1	Horiuchi Junjiro	S04-3
Akira Shizuo	O09-4	F				Hosokawa Mayuko	O15-8
Alireza Kheirollah	P-20	Faried Ahmad	P-38	H		Hosokawa Tomohisa	O02-2
Alvarez-Buylla Arturo	S06-3		P-42	Hanamura Kenji	S10-2	Hosoya Toshihiko	O13-2
Aoki Chiye	O06-4	Ferguson Shawn	S10-5		O06-4	Hotta Yoshiki	O13-2
Aono Sachiko	P-47	Fuchigami Takahiro	O02-4	Hara Akira	O13-4	Hozumi Hiroaki	P-15
Aoyama Mineyoshi	P-21	Fujibayashi Y	JSN-JSBP-2	Hara Hideaki	S08-4	Hussein Mohamed	P-21
Araki Kazuaki	S13-3	Fujikake Nobuhiro	O04-4	Hasegawa Koichi	O03-2		
Arie Yuko	S06-5	Fujimoto Sadaki	O12-5	Hashiguchi Mitsuko	O02-1	I	
	O07-3		P-29	Hashimoto Eri	JSN-JSBP-1	Iemata Mika	O04-2
	O07-4	Fujishita Kayoko	O12-8		P-11		O12-3
Arifin Moch.	P-38	Fujita Kyota	P-22		P-51	Igarashi Michihiro	S09-3
Asada Akiko	O02-2	Fukata Masaki	S09-2	Hashimoto Hitoshi	JSN-JSBP-6		S10-1
	O02-3		S14-5		O15-2		O03-1
	O02-4	Fukata Yuko	S09-2	Hashimoto Ryota	JSN-JSBP-3		P-12
	P-19		S14-5		S12-1		P-13
Asai Kiyofumi	P-21	Fukui Masaki	P-9		P-49		P-14
Asakawa Hideo	O15-8	Fukumitsu Hidefumi	S03-6	Hashizume Yoshio	O14-7	Igari Hiroko	O05-6
Asanuma Masato	P-15		O14-1	Hattori Tsuyoshi	JSN-JSBP-6	Iguchi Haruo	P-22
	P-23		O14-4		O15-2	Ihara Hideshi	O10-3
			O14-6	Hayashi Akiko	O09-2	Iijima Kazuyuki	O06-2
B		Fukumori Ryo	P-26	Hayashi Kanehiro	S09-1	Iike Naomi	P-49
Baba Akemichi	JSN-JSBP-6	Fukumoto Motoyuki	JSN-JSBP-3	Hayashi Mitsunori	O10-1	Ikawa Masahito	P-47
	O15-2		S12-1	Hayashi Yuriko	O02-6	Ikeda Masaaki	P-32
Baba Hiroko	O01-2		P-49	Hayashi-Nishino Mitsuko	S10-5	Ikenaka Kazuhiro	O01-2
	O09-1	Fukunaga Kohji	S02-3	Higa Susumu	P-14		O12-4
	O09-2		S04-1	Higashi Mikito	P-39		O13-1
Bando Yoshio	O09-3		O05-7	Higuchi Hiroki	S03-3		O13-2
Beppu Hideyuki	S02-3	Fukuoka Saki	P-15	Higuchi Makoto	S11-5		O14-2
Bibb James	S04-6	Fukushi Masahiro	O13-7	Hino Okio	O15-7		P-37
Bizen Norihisa	O13-3		P-8	Hirabayashi Yoshio	S09-5		P-39
Brown Anthony	ISN-4	Funakoshi Hiroshi	O03-4		O13-5	Iketani Masumi	S06-5
		Funatsu Naoko	P-30	Hirano Seishiro	O04-6		O07-3
C		Furihata Chie	O05-6	Hirasawa Takae	S02-5		O07-4
Cai Na	S01-3	Furuichi Teiichi	S01-2	Hirose Kenzo	S14-3	Ikeuchi Toshihiko	O14-3

氏名	演題番号	氏名	演題番号	氏名	演題番号	氏名	演題番号
Imai Hideaki	P-38	Ito Rieko	P-13	Kawagoe Hirofumi	O12-6	Kubota Takeo	S02-5
	P-42	Ito Tetsuya	P-21	Kawahara Hiroyuki	P-19	Kudo Motoshige	P-16
Imaizumi Kazunori	S08-5	Ito Yoshihisa	P-45	Kawahara Shinichi	O04-1	Kudo Takashi	S08-5
	P-33	Ito Yuma	P-4		O08-2		P-49
Imura Yoshio	S03-1	Itoh Mitsuhiro	O14-1	Kawamura Hiroki	JSN-JSBP-4	Kumagai Megumi	P-32
Inada Daisuke	P-6	Itoh Satoru	O14-6	Kawasaki Toshiyuki	S12-4	Kumakura Konosuke	O10-1
	P-10	Iwakura Yuriko	S13-3	Kawauchi Takeshi	S06-2	Kumakura Yuka	S03-3
Inoue Kazuhide	S11-1	Iwamoto Ikuko	O07-2	Kayama Takumi	O05-6	Kumamaru Emi	O08-1
	S11-2		O15-3	Kazui Hiroaki	P-49		O15-1
	O01-1	Iwase Masao	P-49	Kida Satoshi	S04-2		P-16
	O01-3	Iwata Nobuhisa	O02-3	Kido Mizuho	P-22		P-28
Inoue Kiyoshi	O08-2	Izumi Aiko	O08-1	Kido Yuka	P-29	Kumar Akhilesh	O13-2
Inoue Nobuo	O13-7		P-28	Kikkawa Yuri	P-23	Kume Nobue	P-6
	P-6			Kimura Hirohito	P-30		P-7
	P-7	J		Kimura Kouji	O09-2		P-10
	P-8	Jaaro-Peled Hanna	S12-2	Kinoshita Masami	O13-5	Kumeta Kousuke	O07-5
	P-10	Ji Bin	S11-5	Kishi Soichiro	O14-3	Kumon Mami	O08-4
Inoue Toshihiro	O13-3			Kita Taizo	P-15	Kunugi Hiroshi	O08-1
Inoue Yoko	O15-8	K		Kitajima Isao	S02-3		O15-1
Irifune Hiromi	O14-3	Kadoyama Keiichi	O04-5	Kitamura Naohito	S01-2		P-16
Irino Yasuhiro	S11-1	Kagawa Tetsushi	S01-4	Kitamura Toshio	O14-8		P-28
Ishibashi Tomoko	O09-1		O13-3	Kitamura Yoshihisa	P-15	Kurabayashi Masahiko	O12-2
Ishibashi Yoh	P-40	Kaibuchi Kozo	ISN-2	Kitani Hiroshi	O01-2	Kurachi Masashi	S01-3
Ishida Yusuke	P-24	Kaido Takaya	O15-8	Kitao Tatsuya	S12-4		O12-1
	P-36	Kakita Hiroki	P-21	Kiuchi Tai	S10-3		O12-2
Ishige Kumiko	P-45	Kakuda Nobuto	P-50	Kiyama Hiroshi	O04-1		P-38
Ishii Akihiro	P-39	Kamada Naoki	S03-1		O08-2		P-42
Ishii Ryohei	P-49	Kamino Kouzin	P-49	Kiyosue Kazuyuki	O14-5	Kuramoto Nobuyuki	P-1
Ishii Takao	JSN-JSBP-1	Kanai Masaaki	O03-4	Kobayashi Hajime	P-6		P-25
	P-11	Kanamori Tetsuko	O13-6	Koda Ken	O15-4		P-46
	P-51		O14-7		O15-6	Kurihara Yuji	O07-3
Ishikawa Ryoki	S10-4	Kanbe Yuki	P-26	Kodama Akiko	O09-1		O07-4
Ishikawa Yasuyuki	O06-6	Kanda Kingo	O01-5	Kohno Takashi	O05-6	Kurumaji Akeo	P-43
Ishino Yugo	O13-2	Kaneko Jun	O13-5	Kohsaka Shinichi	S11-1	Kusakari Shinya	O02-5
Ishizaki Yasuki	S01-3	Kaneko Naoko	S06-3	Kohyama Kuniko	O09-4		O02-6
	S06-6	Kaneko Naoshi	P-48	Koide Tadashi	S10-6	Kwak Shin	S12-3
	O12-1	Karagogeos Domna	O13-8	Koizumi Schuichi	O12-8	Kyo Hirotaka	O10-1
	O12-2	Kasai Hisataka	P-10	Koizumi Shinichi	S05-1		
	P-38	Kasai Masaki	O14-4	Kojima Masami	O14-5	L	
	P-42	Kasama Takeshi	O14-5	Kojima Nobuhiko	O03-6	Lee Hae Ung	O12-4
Ishizuka Yuta	S04-4	Katakabe Tetsuya	O09-2		O06-4	Leeds P	JSN-JSBP-2
	S13-3	Katayama Taiichi	JSN-JSBP-6		O11-2	Leng Y	JSN-JSBP-2
Islam Shahidul M	S06-4		O15-2	Komano Hiroto	O05-3	Liu Hongtao	O12-4
Iso Tatsuya	O12-2	Kato Shin	P-21	Komori Tadasuke	O14-8	Lu Hui	S14-5
Isono Mayu	O13-7	Kato Tadafumi	S02-1		P-34	Lu Jia	P-12
	P-7	Kato Taisuke	S03-5	Kondo Yasushi	P-6		
	P-8		S13-3	Konishi Hiroyuki	O04-1	M	
Itakura Makoto	O10-3	Katoh Kaoru	S10-1		O08-2	Ma Jianmei	P-37
	O10-4	Kawaai Katsuhiko	O06-1	Konishi Shiho	P-41	Machida Takeo	O13-5
Itami Chiaki	O14-5	Kawada Koichi	P-1	Konishi Yoshiyuki	O07-6	Maeda Sayaka	P-41
	O15-1		P-2	Kosuge Yasuhiro	P-45	Maeda Tomoji	O05-3
Ito Hidenori	O07-2		P-3	Kotani Takenori	O02-5	Makino Akihisa	O14-6
	O15-3		P-5	Koutani Akira	P-25	Mao Can Van	S13-1
Ito Jinichi	P-20		P-18	Kubo Ken-ichiro	S06-2	Marin Oscar	S06-3

第 52 回 日本神経化学会大会抄録集

氏名	演題番号	氏名	演題番号	氏名	演題番号	氏名	演題番号
Maruoka N	JSN-JSBP-2		O15-3	Nakayama Takashi	O13-7	Ogita Kiyokazu	O04-7
Masuda Junya	O01-3	Moriyama Mitsuki	O12-7		P-6		P-1
Masuo Yoshinori	S03-2	Moya PR	JSN-JSBP-2		P-7		P-2
Matozaki Takashi	O02-5	Murakami Fujio	S06-3		P-8		P-3
	O02-6	Murakami Koji	P-6		P-10		P-5
Matsuda Naoto	S14-5	Murakami Kouichi	O09-3	Namba Hisaaki	JSN-JSBP-4		P-18
Matsuda Toshio	S12-4	Murakami Ryuta	S05-2		S13-3		P-25
	O15-4	Murata Miho	S07-4	Namiki Shigeyuki	O12-4		P-46
	O15-6	Murata T	JSN-JSBP-2	Narahashi Toshio	O05-7	Ogo Tadashi	P-31
Matsui Fumiko	P-47	Murata Yoji	O02-5	Narita Masaaki	S03-1	Ogura Akihiko	O06-1
Matsukawa Noriyuki	O13-6		O02-6	Narita Naoko	S03-3		O06-2
	O14-7	Murayama Namie	S06-6	Naser Iftkhar Bin	S06-4	Ogura Ken-ichi	O07-5
Matsukawa Takashi	O12-8			Nashida Tetsuaki	S12-4	Ogura Masato	O04-2
Matsumoto Akira	O04-5	N		Nawa Hiroyuki	JSN-JSBP-4		O12-6
Matsumoto Yoh	O09-4	Nabeshima Toshitaka	S12-2		S03-5	Ohashi Kazumasa	S10-3
Matsuyama Shogo	O04-5	Nabetani Takuji	S09-5		S04-4	Ohata Kenji	O04-1
Matsuzaki Hideo	S03-4	Nagai Yoshitaka	O04-4		S13-3	Ohi Kazutaka	JSN-JSBP-3
Matsuzaki Shinsuke	JSN-JSBP-6	Nagaike Kazuhiro	P-50	Negishi Takayuki	O04-3		S12-1
	O15-2	Nagano Hitoshi	P-8		O04-6		P-49
Michael Dyer	S02-4	Nagasawa Kazuki	O12-5		O15-8	Ohkumo Tsuyoshi	O03-2
Michikawa Makoto	O05-3		P-29		P-30	Ohnishi Hiroaki	O04-6
Mikoshiba Katsuhiko	O06-1	Nagasawa Kazuma	O07-1		P-40	Ohnishi Hiroshi	O02-5
Minegishi Seiji	O02-4	Nagashima Reiko	P-1	Nemoto Tomomi	S14-5		O02-6
Mishina Yuji	S01-2		P-3	Nishibe Hirozumi	S09-1	Ohsawa Keiko	S11-1
Mitsuyama Fuyuki	S10-6		P-46	Nishida Kentaro	O12-5	Ohshima Toshio	P-19
Miyagishi Hiroko	P-45	Nagata Etsuko	O10-3		P-29	Ohta Kunimasa	S06-4
Miyajima Ken	S10-3	Nagata Koh-ichi	O07-2	Nishijo Hisao	S13-1	Ohtani Hiroki	O13-7
Miyakawa Tsuyoshi	O02-6		O15-3	Nishikwa Toru	P-43		P-8
	P-13	Nagatsuka Yasuko	O13-5	Nishimoto Takaaki	O04-5	Ohtsuka Masanari	O14-1
Miyaki Jun	P-29	Nagayasu Yuko	P-20	Nishimura Momoe	O15-4	Ohtsuka Toshihisa	S14-1
Miyamoto-Matsubara Mayumi		Nakagomi Saya	O08-2	Niwa Minae	S12-2	Ojika Kosei	O13-6
	O15-5	Nakajima Kazunori	S02-4	Noda Mami	P-22		O14-7
Miyata Shingo	O06-5		S06-2	Nomura Yasuyuki	O05-6	Okabe Masaru	P-47
	O11-4	Nakajima Yoshihiro	P-32	Noritake Jun	S09-2	Okada Yasunobu	O12-4
Miyazaki Ikuko	P-15	Nakamachi Tomoya	O01-5		S14-5	Okafuji Tatsuya	S06-4
	P-23	Nakamichi Noritaka	O03-3	Nosaka Tetsuya	O14-8	Okamoto Ken-ichi	O07-2
Miyoshi Ko	P-23		O04-2	Nozumi Motohiro	S10-1		O15-3
Mizui Toshiyuki	S10-2		O12-6		O03-1	Okano Hideyuki	S06-3
	O06-3		P-4		P-12		S13-5
Mizuki Nobuhisa	O07-4		P-26	Numakawa Tadahiro	LA-1	Okano-Uchida Takayuki	S01-3
Mizuno Kensaku	S10-3		P-41		O08-1		O12-1
Mizuno Makoto	JSN-JSBP-4	Nakamura Fumio	O07-3		O15-1		O12-2
	S13-3		O07-4		P-16		P-42
Mori Hiroshi	O05-1		O07-5		P-28	Okazawa Hideki	O02-5
Mori Munemasa	O02-5	Nakamura Katsuki	S13-2	Numazawa Satoshi	O01-5	Okochi Masayasu	P-49
Mori Yasutake	O06-5	Nakamura Toshikazu	O03-4	Nunokawa Ayako	P-48	Okuda Hiroaki	S01-1
	O11-4	Nakamura Yasuko	S11-1	Nunomura Hikari	O09-3		P-33
Moriguchi Shigeki	O05-7	Nakamura Yoichi	O12-7			Okuda Hiroto	O12-5
Morihara Takashi	P-49	Nakamura Yukary	O03-3	O		Okuno Yasushi	S05-2
Morikawa Yoshihiro	O14-8	Nakanishi Hiroshi	S11-4	O'Toole Eileen	S10-5	Okuya Masato	S10-6
	P-34	Nakashima Kinichi	O8-3	Oba Ryutaro	O05-3	Omata Naoto	JSN-JSBP-2
	P-35		S01-5	Oe Yuki	O06-2	Omori Hiroyuki	O13-7
Morino Michiharu	O04-1		S02-2	Ogawa Mizue	O12-7		P-7
Morishita Rika	O07-2	Nakatani Yosuke	O14-3	Ogawa Tokiko	O08-2		P-8

氏名	演題番号	氏名	演題番号	氏名	演題番号	氏名	演題番号
Ono Katsuhiko	S06-6	Saito Yumiko	O15-5		O11-3	Taga Tetsuya	S01-4
	O13-1	Saitoh Hidetoshi	O01-1		O13-8		O13-3
	O14-2	Sakai Miwako	S13-3	Shimoike Koji	O14-3	Tagami Shinji	P-49
	P-47	Sakata Ai	O09-3	Shinmyo Yohei	S06-4	Taguchi Ayako	O13-4
Ono Shin-ichi	P-45	Sakimura Kenji	O07-1	Shinoda Tomoyasu	O07-2	Taguchi Ryo	S09-4
Ono Takafumi	JSN-JSBP-1		P-13		O15-3	Takada Masahiko	S13-4
	P-11	Sakurai Kunie	O11-1	Shinohara Takumi	O10-2	Takahashi Akio	O08-3
	P-51		O13-8	Shintani Norihito	JSN-JSBP-6		O08-4
Ono Taketoshi	S13-1	Sanagi Tomomi	S11-1		O15-2	Takahashi Hidetoshi	JSN-JSBP-3
Oohira Atsuhiko	P-47	Sano Akira	S07-5	Shinya Fuyumi	O13-7		P-49
Osumi Noriko	OS-4	Sano Shohei	P-1		P-7	Takahashi Masaki	O04-3
	S01-6	Saotome Akiyuki	S03-3		P-8		O04-6
Ota Hiroyoshi	O05-6	Sasakawa Nobuyuki	O10-1	Shioda Norifumi	S02-3		O15-8
Otani Yoshinori	O01-2	Sasaki Erika	S13-5	Shioda Seiji	O01-5		P-30
Otsu Masahiro	O13-7	Sasaya Harue	O14-3	Shiosaka Sadao	O06-6		P-40
	P-6	Sato Akira	S09-1	Shirao Tomoaki	OS-2	Takahashi Masami	O10-3
	P-7	Sato Ko	O02-3		S10-2		O10-4
	P-8	Sato Makoto	S06-1		O03-6	Takahashi Takuya	S07-2
	P-10	Sato Yasufumi	S06-5		O06-3	Takamura Hironori	JSN-JSBP-3
Otsuka Shintaro	O10-4		O07-3		O06-4		S12-1
Otsuki Takeya	S12-4	Sato Yumi	S01-2		O11-2		P-49
Oyabu Akiko	S03-1		O01-2	Shirasaka Tomohiro	JSN-JSBP-1	Takano Jiro	O02-3
Oyanagi Koshi	O04-3	Sawa Akira	S07-1		P-11	Takano Katsura	O12-7
	O04-6		S12-2		P-51	Takao Keizo	O02-6
Ozaki Norio	S12-2	Sawamoto Kazunobu	S06-3	Shuto Makoto	O04-7		P-13
Ozawa Shusuke	P-9	Sawano Erika	P-30	Sokabe Masahiro	O12-4	Takarada Takeshi	O01-4
Ozawa Tetsuro	O12-8	Seike Toshihiro	P-22	Someya Toshiyuki	P-48		O03-3
		Sekiguchi Masayuki	O08-3	Sotoyama Hidekazu	JSN-JSBP-4		O03-5
	P		P-44		S13-3		O04-2
Plattner Florian	S04-5	Sekimoto Kenichi	O12-2	Soumiya Hitomi	S03-6		O12-3
Poo Mu-ming	S14-5	Sekine Katsutoshi	S06-2	Su Yuhong	S06-4		O12-6
Popiel Akiko	O04-4	Sekino Yuko	S14-2	Sudo Kaori	O07-2		P-4
Puentes Sandra	P-38		O06-3		O15-3		P-9
	P-42	Senba Emiko	O14-8	Suga Kei	O05-1		P-26
			P-34	Sugawara Takeshi	O12-8		P-41
	R		P-35	Sugaya Chiemi	O15-8	Takashima Akihiko	S08-3
Rubenstein John	S06-3	Senba Ritsuko	O15-1	Sugiura Hiroko	O15-7	Takebayashi Hirohide	O13-1
		Sendo Toshiaki	P-15	Sugiyama Chie	O04-7		O14-2
	S	Setou Mitsutoshi	O07-6	Suhara Tetsuya	S11-5	Takeda Masatoshi	JSN-JSBP-3
Sagisaka Takafumi	O13-6	Sheng Zu-Hang	ISN-3	Suzuki Eri	S11-1		S12-1
	O14-7	Shiba Tatsuo	P-5	Suzuki Kenji	O05-4		P-49
Saido Takaomi	O02-3		P-18	Suzuki Noboru	O04-5	Takeda Reiko	O03-6
Saito Akihiko	S10-3	Shibasaki Koji	S06-6	Suzuki Satoshi	P-21	Takeda Shin'ichi	S12-6
Saito Ayako	O05-1	Shibata Keisuke	O12-8	Suzuki Shingo	O14-5	Takeda Yasuo	O11-1
Saito Shigeru	O12-2	Shibuya Masako	JSN-JSBP-4	Suzuki Takayoshi	O05-6		O13-8
Saito Taro	O02-2		S13-3	Suzuki Tsutomu	O12-8	Takei Kohtarō	S06-5
	O02-3	Shimada Shoichi	P-24	Suzuki Yutaka	P-6		O07-3
	O02-4		P-36				O07-4
	P-19	Shimada Takafumi	O14-3		T	Takei Nobuyuki	S03-5
Saito Toshikazu	JSN-JSBP-1	Shimazaki Kuniko	O11-1	Tabata Yasuhiko	P-42		S04-4
	P-11	Shimizu Takahiro	P-37	Tachibana Masaki	O03-5		S13-3
	P-51	Shimizu Takeshi	O13-3		O12-3	Takemiya Takako	O09-4
Saito Yasuyuki	O02-5	Shimizu-Okabe Chigusa	O10-2		P-4		O15-7
	O02-6	Shimoda Yasushi	O11-1	Tada Yukiyo	P-13	Takenokuchi Mariko	O04-5

氏名	演題番号	氏名	演題番号	氏名	演題番号	氏名	演題番号
Takeshima Mika	P-23	Tominaga Makoto	S06-6	Wang Ran	S13-3	Yamauchi Takashi	O15-7
Takeuchi Chisen	O09-4	Tominaga-Yoshino Keiko	O06-1	Wang Z	JSN-JSBP-2	Yamazaki Hiroyuki	O06-4
Takeuchi Kosei	O03-1		O06-2	Watanabe Ippei	JSN-JSBP-1		O11-2
	P-14	Tomiyama Takami	S08-2		P-11	Yamazaki Maya	O07-1
Takigami Shu	O15-7		O05-1		P-51	Yanagisawa Katsuhiko	O05-2
Takizawa Takumi	S02-2	Torii Tomohiro	P-39	Watanabe Kazutada	O11-1	Yano Koji	O15-4
Takuma Kazuhiro	S12-4	Torugun Torusun	O15-1		O11-3		O15-6
	O15-4		P-16		O13-8	Yasuda Keiichi	O10-3
	O15-6	Tougasaki Takeshi	S10-1	Watanabe Keisuke	O14-2	Yasuda Shin	O15-7
Tamaki Keisuke	P-4	Toyoda Takanari	O13-6	Watanabe Kimihiko	JSN-JSBP-1	Yasuda Yuka	JSN-JSBP-3
Tamamaki Nobuaki	O14-2		O14-7		P-11		S12-1
Tamura Hideki	O06-6	Toyomitsu Emika	O01-1		P-51		P-49
Tamura Waki	O10-1	Toyoshima Manabu	O11-1	Watanabe Mami	P-41	Yokoyama Shinji	P-20
Tanabe Kazuhiro	P-39		O13-8	Watanabe Takashi	O05-6	Yokoyama Tomomi	S03-1
Tanaka Akiko	O12-5	Tozaki-Saitoh Hidetoshi	O01-3	Watanabe Yuichiro	P-48	Yoneda Yukio	O01-4
Tanaka Hajime	P-3	Tsai Chung-Hua	O03-2	Watanabe Yumi	P-13		O03-3
	P-46	Tsuda Makoto	S11-2		P-14		O03-5
Tanaka Hideaki	S06-4		O01-1				O04-2
Tanaka Kenji F	O12-4		O01-3		X		O12-3
	O13-2	Tsuji Takeshi	P-15	Xie Min-Jue	S06-1		O12-6
	P-37	Tsunoda Masashi	O15-8				P-4
Tanaka Kouichi	O14-5				Y		P-9
Tanaka Sachiko	O01-5		U	Yagasaki Yuki	P-28		P-26
Tanaka Tatsuhide	S11-3	Uchida Atsuko	S03-1	Yagi Hideshi	S06-1		P-41
Tanaka Toshihisa	P-49	Uchida Tatuya	O10-4	Yamada Daisuke	P-44	Yoneyama Masanori	P-1
Taniguchi Naoko	O06-1	Uchida Yoko	O05-5	Yamada Kohei	JSN-JSBP-6		P-2
Taniguchi Taizo	O04-5		P-17		O15-2		P-3
Taniura Hideo	O04-2	Ueda Hidehiro	O11-3	Yamada Masahisa	S01-2		P-5
	P-26	Ueda Takashi	P-24	Yamada Takahiro	P-36		P-18
Tano Kaori	S03-1		P-36	Yamada Yasuhiro	O13-4	Yoshida Sachiko	S14-4
Tashiro Tomoko	O04-3	Uematsu Masakazu	P-31	Yamagata Kanato	O09-4		P-31
	O04-6	Uematsu Norihiko	O13-6		O15-7	Yoshida Shigetaka	O09-3
	O05-6		O14-7	Yamaguchi Masamitsu	O04-4	Yoshida Takemi	O01-5
	O06-1	Uematsu Satoshi	O09-4	Yamaguchi Megumi	S06-5	Yoshida Tetsuhiko	P-49
	O15-8	Ugawa Shinya	P-24		O07-3	Yoshie Takuya	O13-7
	P-30		P-36		O07-4		P-6
	P-40	Ukai Wataru	JSN-JSBP-1	Yamaguchi Yoshihide	O01-2		P-7
Tashiro Yasura	S03-1		P-11	Yamakawa Yukiko	P-22	Yoshikawa Kazuaki	O03-2
Tateno Masaru	JSN-JSBP-1		P-51	Yamamori Hidenaga	JSN-JSBP-3	Yoshimoto Yuhei	P-38
	P-11	Uno Takefumi	P-40		S12-1		P-42
	P-51	Urano Fumihiko	S08-1		P-49	Yoshimura Takeshi	P-39
Tatsumi Kouko	S01-1	Usui Noriyoshi	O14-2	Yamamori Saori	O10-3	Yoshimura Yoshiyuki	O15-7
	P-33				O10-4	Yoshinaga Toshihiro	JSN-JSBP-1
Tessier-Lavigne Marc	S06-3		W	Yamamoto Hideko	P-27		P-51
Toda Tatsushi	S12-5	Wada Etuko	O08-4	Yamamoto Kazuhiro	O08-3	Yuyama Kohei	O05-2
	O04-4	Wada Keiji	S07-3		O08-4		
Togari Hajime	P-21		O04-4	Yamamoto Naoki	O05-4		Z
Tohyama Masaya	JSN-JSBP-6		O08-3	Yamamoto Tomomi	O01-4	Zhang Sanbing	S06-4
	O06-5		O08-4	Yamamoto Toshifumi	P-27	Zheng Yingjun	JSN-JSBP-4
	O08-2		P-44	Yamamoto Toshinori	S05-3		S13-3
	O11-4	Wada Y	JSN-JSBP-2	Yamane Masayuki	O07-5	Zou Kun	O05-3
	O15-2	Wakasa Mika	O15-8	Yamashita Naoya	O07-5		
Tokita Yoshihito	P-47	Wanaka Akio	S01-1	Yamashita Toshihide	S11-3		
Tokumaru Hiroshi	O10-2		P-33	Yamasue Hidenori	JSN-JSBP-5		

キーワード索引

A					
ABI2	S06-1	ANTERIOR CINGULATE	S13-1	AXONOGENESIS	S06-6
ACETYLCHOLINE[ACH]	O15-4	ANTIDEPRESSANT	JSN-JSBP-2		
ACETYLCHOLINESTERASE[ACHE]	O15-4		P-16		
ACTIN	OS-2	ANTIGEN	O13-5		
	S10-1	ANTIPSYCHOTIC	P-24		
	S10-2	APOLIPOPROTEIN A-I	P-20		
	S10-3	APOMORPHINE	O15-4		
	S10-4	APOPTOSIS	S08-2		
	O06-3		O04-3		
	O07-5		O14-3		
	O11-2		P-6		
			P-8		
ACTIVATION	S11-1	ARCUATE	O14-8		
ACTIVE ZONE	S14-1	ARP2/3	S06-1		
ADAPTATION	P-43	ASSOCIATION	P-48		
ADENOSINE	O12-5	ASSOCIATIVE MEMORY	S04-3		
ADHESION	S06-5	ASTROCYTE	S01-1		
	O07-3		S01-2		
ADRENALECTOMY	O04-7		S01-5		
AGGRESSION	P-11		S01-6		
AGING	S11-4		O04-2		
	O05-6		O10-3		
AGONIST	P-27		O12-4		
ALLODYNIA	O01-3		O12-5		
ALS	P-45		O12-8		
ALS [AMYOTROPHIC LATERAL SCLEROSIS]	S12-3		P-20		
ALZHEIMER	OS-1		P-21		
	S08-2		P-22		
	S08-5		P-33		
	S11-5	ASTROCYTE [ASTROGLIA]	S01-3		
	O05-1		S01-4		
	O05-2		S02-2		
	O05-3		S06-3		
	O05-4		O12-1		
	O05-6		O12-2		
	O05-7		O12-3		
	P-50		O12-6		
ALZHEIMER'S DISEASE	S07-1		O12-7		
AMPA	S07-2		O13-3		
	S12-3		P-23		
	P-44	ATP	O12-4		
AMPA RECEPTOR	S09-2	ATP [ADENOSINE TRIPHOSPHATE]	S11-1		
AMYGDALA	S01-1		O01-1		
	S14-2		P-29		
AMYLOID	O05-2	AUDITORY	O11-1		
	O05-3		P-46		
	O05-5	AXON	S06-4		
	P-50		S10-2		
AMYLOID A β PROTEIN	O05-4		S11-3		
ANALGESIA	O12-8		O07-6		
ANALYSIS	S14-4	AXONAL REGENERATION	P-42		
ANTAGONIST	P-27	AXONAL TRANSPORT	O09-1		

B

BARREL	S07-2
BASAL GANGLIA	S13-4
BDNF	S04-4
	S14-5
	O14-5
BDNF [BRAIN DERIVED NEUROTROPHIC FACTOR]	S10-3
	O03-6
	O10-4
	O15-1
	P-28
	P-51
BEHAVIOR	JSN-JSBP-5
	S13-2
	O08-4
	O09-4
	P-13
	P-47
β -AMYLOID	P-17
BETA-AMYLOID	S08-2
	O05-1
BFGF	P-42
BINDING	O07-4
BIPOLAR	S08-1
BLOOD-BRAIN	S07-3
BRAIN	JSN-JSBP-1
	S03-2
	S07-3
	S07-5
	S09-4
	O03-3
	P-22
	P-40
BULB	O02-5

C

CALCIUM	S04-2
	O02-3
CALCIUM [CA]	S02-3
	S12-4
CALMODULIN	S04-1
	S04-2
CALSYNTENIN	P-17
CASPASE	P-3
CDC42	P-20
CDK	S04-6
	O02-2
	O02-3
CELL MIGRATION	S06-1
CEREBELLAR	O14-1

CEREBELLUM	S01-3	DEMYELINATION	O09-3		O04-4
	S09-1		P-37	DNA	S02-1
	O04-3	DENDRITE	S10-3	DOMAIN	O05-3
	O04-6		O11-4	DOPAMINE	S03-5
	O12-1		O15-7		S07-4
	O12-2	DENDRITIC	O06-3		S12-1
	O13-8		O06-5		O08-2
CEREBRAL	S03-6	DENTATE	OS-1		O15-6
CEREBRAL CORTEX	S06-1	DEPRESSION	JSN-JSBP-1		P-15
CHANNEL	S06-6		O02-6		P-23
CHOLESTEROL	O14-5		O03-6		P-24
CHOLESTEROL EFFLUX	P-20		O15-5	DOPAMINERGIC	O04-5
CHOLINE ACETYL TRANSFERASE	O14-7		P-16		P-23
CHRONIC	JSN-JSBP-2		P-28	DREBRIN	OS-2
CIRCADIAN	P-32		P-51		S10-2
CIRCUIT	S09-1	DEVELOPMENT	S01-3		O03-6
	O06-2		S01-4		O06-3
CLOCK	O01-4		S02-4		O06-4
	P-32		S03-2		O11-2
CNS	O09-3		S03-4	DROSOPHILA	S04-3
	O15-8		S03-6		O04-4
COCHLEA	P-46		S05-3	DRUG	S05-1
COFILIN	S10-3		S06-6		S05-2
COGNITION	JSN-JSBP-3		S09-1		S05-3
COGNITIVE	S13-2		S14-4		P-24
COMMISSURE	S06-4		O03-4		P-38
COMPOUND	S05-3		O07-2	DYNAMIN	S10-5
CONDITIONED	O06-4		O12-1	DYSTROPHIC	S12-5
CORD	P-34		O13-1		S12-6
	P-35		O13-4		
CORTEX	O04-1		O13-8	E	
	P-44		O15-3	EGF	JSN-JSBP-4
CORTICOGENESIS	O07-2		O15-8		S13-3
CREB	S04-2		P-3	ELECTRON BEAM TOMOGRAPHY	S10-5
CRMP	O07-5		P-30	ELECTROPORATION	S06-2
CULTURE	O03-1		P-31	EMOTION	O08-3
	O15-7		P-34	ENDOCYTOSIS	P-13
CYCLIC AMP [CAMP,C-AMP]	O12-7		P-35	ENDORPHIN	OS-4
CYNOMOLGUS MONKEY	S13-3	DEXAMETHASONE	P-45	ENDOTHELIAL	P-38
CYSTATIN F	P-37	DIABETES	P-40	ENTORHINAL	O06-2
CYTOKINE	JSN-JSBP-1	DIFFERENTIATION	S01-3	ENVIRONMENTAL	S01-1
	S11-2		S01-4		S07-3
	P-21		S01-5		O04-6
	P-22		S02-2		O15-8
CYTOSKELETON	O07-6		S02-4	ENZYME	S09-2
D			O12-1		O05-3
DANTATE GYRUS	O04-1		O12-2	EPIGENETICS	OS-3
DEAFFERENTATION	O13-3		O13-6	EPILEPSY	O04-1
DEATH	O04-6		O13-7	ER [ENDOPLASMIC RETICULUM]	S08-1
	O05-5		P-8		S08-2
			P-9		S08-4
DEGENERATION	S10-6	DIFFERENTIATION PLASTICITY	OS-3		S08-5
	S11-3	DISC1	S12-2		O14-3
	O04-4	DISEASE	S02-1	ERBB	S13-3
DEMENTIA	O04-5		S05-3	ERBB1	JSN-JSBP-4

EXOCYTOSIS	S14-3	GLYCOPROTEIN	S12-5		P-15
	O10-1		P-39	INFORMATION	S07-3
	O10-2	GLYCOSYLTRANSFERASE	S12-5	INJURY	S01-2
	O10-3	GM1 GANGLIOSIDE	O05-4	INSULIN	O05-4
	P-13	GPROTEIN	O15-5	INTEGRATION	S07-5
EXPRESSION	O03-1		P-24	INTERFERON	P-15
	P-38	GRANULE CELL	O13-8	INTERLEUKIN	O01-4
EXTINCTION	P-44	GROWTH CONE	S09-3		O01-5
			S10-1		P-22
F			S10-2	INTERNEURON	O02-5
FASCICULATION	O07-3		S10-4		P-34
FATIGUE	O08-2		O07-5		P-35
FATTY ACID	O14-6		P-12	INTERVENTION	S07-1
FEAR	P-44	GROWTH FACTOR	O01-3	INTRATHECAL	O01-3
FEEDING	O15-5		O14-8	ISCHEMIA	S08-4
FORMATION	O11-1	GUIDANCE	S06-4		S08-5
FREE RADICALS	P-18		S06-5		P-41
			O07-3	ISOLATION	S07-2
G			O07-4		
GABA	P-25			K	
GABA [GAMMA-AMINOBTYRIC]	S14-2	H		KAINIC ACID	O04-1
	S14-4	HEAT	P-7	KINASE	S04-1
	O05-7	HIPPOCAMPAL SLICE	O06-1		S05-2
	P-9	HIPPOCAMPUS	JSN-JSBP-2	KINESIN	O07-6
	P-30		JSN-JSBP-6	KNOCK-IN	P-47
	P-31		O05-6	KNOCKOUT	S06-4
GANGLION	P-36		O06-2		O01-5
GANGLIOSIDE	O05-2		O10-4		O06-4
GDNF	O12-6		P-4		O13-2
GENE	JSN-JSBP-3		P-18		P-14
	S02-5		P-30		P-47
	S03-2		P-43		
	S09-1	HIPPOCUMPUS LEGION	JSN-JSBP-4	L	
	P-48	HPLC	P-39	LACUNAR INFARCITION MODEL	P-42
	P-49	HUNTINGTON	O04-4	LEARNING	S02-3
GENOME	S02-5	HYBRIDIZATION	P-36		S04-4
GFAP[GLIAL FIBRILLARY ACIDIC PROTEIN]	S02-2	HYPERACTIVITY	S03-2		S04-5
	O10-4	HYPERTENSION	O05-3	LECTIN	O08-2
	O12-3	HYPOTHALAMUS	O14-8	LIMBIC	S07-4
GFP	S10-1				O03-6
GLIA	S11-5	I		LIMBIC SYSTEM	S13-1
	O13-1	IMAGING	JSN-JSBP-5	LINEAGE	S01-4
	P-31		S09-4	LIPID	S09-4
GLUCOCORTICOID	O08-1		S10-1		O14-5
	P-28		S11-5	LITHIUM	JSN-JSBP-2
GLUR	S12-3		S14-2	LOCAL	O06-5
GLUTAMATE	S12-1		O03-1		O11-4
	S14-3		O10-1	LTD	O06-6
	S14-4		O12-4	LTP	S04-1
	O05-7	IMMUNOBLOT	P-27		O06-6
	O06-1	IMMUNOHISTOCHEMISTRY	O03-5	LYSOSOME	S11-4
	O11-1	IN VITRO	O03-1		
	O12-4	INFLAMMATION	S09-4	M	
GLYCOLIPID	S09-5		S11-5	MAGE FAMILY	O03-2
	O13-5		O09-4	MAP KINASE	O08-1

	O14-1	MONKEY	S13-2	JSN-JSBP-6
	P-16		S13-4	S03-6
	P-46	MOOD DISORDERS	S12-2	S06-3
MARMOSSET	S13-2	MORPHOLOGY	O15-7	O14-1
MASS SPECTROMETRY	S09-5		P-11	O15-2
MATURATION	S01-6	MOTILITY	S11-1	P-5
MECP2	OS-3	MOTONEURON	O14-2	P-10
MEMORY	S02-3		P-45	P-11
	S04-2	MOTONEURON [MOTOR NEURON]	S12-3	NEUROLOGY
	S04-5	MOTOR	S07-4	NEURON
	S04-6	MOTOR NEURON	S06-6	O03-3
	S10-6	MOUSE	S06-4	O12-5
	S12-1		O04-5	O15-3
	O01-5		O08-3	NEURONAL
	O05-7		O14-8	P-19
	O14-7		P-13	NEURONAL DEATH
	P-44	MOVEMENT	O10-1	NEUROPATHY
	P-49	MPTP	S12-4	O01-1
MENTAL	S02-3	MRI [MAGNETIC RESONANCEIMAGING]		NEUROPEPTIDE
	S02-5		JSN-JSBP-3	O14-7
METABOLISM	S07-3		JSN-JSBP-5	O15-2
	O03-4	MRNA	O06-5	NEUROPSIN
	O05-2		P-43	NEUROTOXICITY
	P-40	MULTIPLE SCLEROSIS	O09-3	O04-7
METALLOTHIONEIN	P-23		O09-4	P-6
METHAMPHETAMINE	P-15	MUSCARINIC	O15-4	P-10
METHYLATION	S02-2	MUSCLE	S12-5	P-15
	S02-5		S12-6	NEUROTROPHIC
	O11-4	MUTATION	S08-2	O14-6
MICRODIALYSIS	O15-6	MYELIN	O09-1	NEUROTROPHIN
MICROGLIA	S11-1		O09-2	NGF[NERVE GROWTH FACTOR]
	S11-2		P-37	NITRIC OXIDE
	S11-3	MYOSIN	S10-2	O12-7
	S11-4		P-4	P-2
	O01-1			P-21
	O01-2	N	NMDA	O06-4
	O01-3	NECDIN	O03-2	NMDA[N-METHYL-D-ASPARTATE]
	O01-4	NEONATAL	S03-5	P-26
	O01-5	NERVE TERMINAL	S10-5	NODOSE
	P-37	NEURAL	O13-6	NOREPINEPHRINE[NORADRENALINE]
	P-45		O13-7	NOTCH
MICROSCOPY	S10-1		P-6	O12-2
MICROTUBULE	S10-6		P-7	O13-2
	O07-6		P-8	NT-3
MIGRATION	OS-2	NEURAL DEVELOPMENT	O03-2	O14-2
	S06-3	NEURAL STEM CELL	S09-5	NUCLEOLUS
	S11-1		O13-3	NUCLEUS
	S12-5	NEURAL STEM CELLS	OS-3	
	O07-1	NEURAL TUBE[NEURALCREST,NEURAL PLATE]	O13-2	O
MINERALOCORTICOID[ALDOSTERONE]	O04-7	NEURITE	S06-5	ODOR
MITOCHONDRIA	S11-4		O03-3	OLFACTORY
	O09-1	NEUROBLASTOMA	O04-6	OLIG2/NG2
	O15-7	NEUROGENESIS	OS-1	OLIGODENDROCYTE
MODEL	S03-1		OS-4	OLIGODENDROCYTE[OLIGODENDROGLIA]
	S12-6		JSN-JSBP-1	OUTGROWTH

OXIDATION	S09-4	PROLIFERATION	O13-3	RNA	S12-3
	O04-2		O13-7	ROD	S02-4
	P-40		P-1		
OXYGENASE	O03-4		P-2	S	
OXYTOCIN	JSN-JSBP-5		P-3	SCHIZOPHRENIA	JSN-JSBP-1
			P-5		JSN-JSBP-3
P			P-6		JSN-JSBP-4
P38 MAPK	S11-3		P-7		JSN-JSBP-6
PAIN	S11-2		P-8		S07-1
	O01-3	PROSTAGLANDIN	O09-4		S12-1
	O12-8		P-45		S12-2
PALMITOYLATION	S09-2	PROTEASE	O02-3		S13-1
PARKINSON	S13-4		O09-3		S13-3
	O04-5	PROTEIN	S03-2		O15-3
	P-19		P-38		P-48
	P-23	PROTEIN KINASE	S04-3	SCHWANN CELL	O09-2
PC12	O14-3		S04-4	SECRETION	S14-5
PET[POSITRON EMISSION TOMOGRAPHY]	S11-5		S04-5		O15-1
PHENCYCLIDINE	O15-1		O02-1	SEMAPHORIN	O07-5
PHENOTYPE	JSN-JSBP-3		O02-3	SENSORY NEURONS	S06-6
PHLUORIN	S14-5	PROTEIN SYNTHESIS	S04-4		O14-2
PHOSPHATASE	O02-5		O11-4	SEPTIN	O07-2
	O02-6	PROTEIN TARGETING	S09-2	SEPTUM	O14-7
PHOSPHOLIPASE	O01-2	PROTEOGLYCAN	P-33	SEROTONIN	S03-3
PHOSPHORINATION	P-25		P-47		O03-4
PHOSPHORYLATION	S09-5	PROTEOLYSIS	O02-3		O15-6
	S10-3		O02-4		P-24
	O02-1		P-19	SERUM	S03-4
	O02-2	PSYCHIATRY	S07-5	SEXUAL DIMORPHISM	JSN-JSBP-5
	O02-6	PURINERGIC	S11-2	SHOCK	P-7
	O10-3	PURKINJE CELL	O13-8	SIGNAL	O14-3
	O10-4				O14-6
PITUITARY	O08-2	Q		SNARE	O10-3
PKC	O10-3	QUANTAL	S14-3		O10-4
PLASTICITY	S10-6			SOCIAL BEHAVIOR	S13-1
	O06-1	R		SPINAL	S11-2
	O06-2	RAT	O04-1		O14-4
	O06-4		O15-8		P-34
	O12-8	RECEPTER	P-25		P-35
PLATELET	P-51	RECEPTOR	S05-2	SPINAL CORD	O09-4
POLYGLUTAMINE	O04-4		P-5	SPINE	S02-3
POSTNATAL	P-43		P-27		S04-1
PREFRONTAL	S03-3	REELER	O07-1		O06-3
PRESENILIN	O05-1	REELIN	S06-2		O11-2
PRESYNAPSE	O10-2		O07-1		O15-3
PRIMATES	S13-5	REGENERATION	OS-1		O15-7
PRODROMAL	S07-1		S06-3		P-47
PROGENITOR	S01-1		S06-5	STEM CELL	S01-5
	S01-3		S11-3		S06-3
	O12-1		O07-4		O12-2
	O13-6	REMYELINATION	P-37		O13-2
	P-3	RETINA	S02-4		O13-5
	P-5	RETINAL GANGLION CELL	O07-4		O13-7
PROJECTION	O11-1	RHO KINASE	P-20		P-2
	O14-2	RHYTHM	P-32		P-5

	P-6	P-33
	P-7	P-34
	P-9	P-35
	P-10	TRANSGENIC O14-7
	P-11	TRANSMISSION P-28
STRESS	S08-5	TRANSPORT O07-1
	O04-2	O07-6
	O04-6	TRANSPORTER O04-2
	O08-2	O12-3
	O12-5	O12-5
	P-4	O15-6
	P-43	P-31
STROKE	OS-1	TRIMETHYLTIN O04-7
	S08-5	TRYPTOPHAN O03-4
SURVIVAL	O14-2	TUBULIN OS-2
	P-16	TUMOR P-22
	P-18	TYROSINE O02-5
SYNAPSE	S02-5	
	S04-5	V
	S04-6	VAGUS P-36
	S07-2	VECTOR JSN-JSBP-2
	S09-2	S13-4
	S10-5	VIRUS O03-1
	S10-6	VOLTAGE SENSITIVE DYE S14-2
	S14-1	
	S14-3	W
	O02-2	WAVE2 COMPLEX S06-1
	O03-6	
	O06-2	X
	O06-6	X-IRRADIATION O13-7
	O08-1	X-IRRADIATION[X-RAY] P-8
	O11-3	
	O13-8	
	O15-1	
SYNAPTIC	O11-1	
	T	
TAGGING	O06-6	
TARGET	S05-1	
TAU	S08-3	
	O02-1	
	O04-5	
THEOPHYLLINE	O12-7	
THYROXINE	O04-3	
	P-30	
TIRF	S14-5	
TNF	O01-5	
TRACER	P-36	
TRANSCRIPTION	S01-6	
	S02-2	
	S02-4	
	O11-2	
	O14-8	
	P-11	
	P-32	

学会掲示板

【助成・褒章案内】

財団法人 内藤記念科学振興財団

第 41 回（2009 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：

内藤記念科学振興財団ホームページ「助成金事業」に記載の手順に従い推薦する。

締切日：

2009 年 10 月 1 日（木）（内藤記念科学振興財団必着）

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。
採否の結果は、2010 年 2 月に候補者および推薦者に通知する。

贈呈式・顕彰：

受賞者夫妻は 2010 年 3 月 18 日（木）に行う贈呈式に出席いただきます。
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）を贈呈する。

その他：

1. 学会推薦の場合は、学会の公印を捺印する。
2. 内藤記念科学振興財団の理事、監事または評議員推薦の場合は、私印を捺印する。

問い合わせ先：

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財団法人 内藤記念科学振興財団**第 41 回（2009 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。

候補者資格：

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（ただし内藤記念科学振興財団の理事、監事、評議員、選考委員は申請できない）。
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
2010 年 1 月 1 日～2010 年 6 月 30 日	前期
2010 年 7 月 1 日～2010 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（科学振興賞と同じ 27 学会）の代表者

※推薦件数は 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
内藤記念科学振興財団ホームページの「助成金事業」に記載の手順に従い申請する。

締切日：

<前期> 2009 年 6 月 1 日（月） <後期> 2009 年 10 月 1 日（木）
（いずれも内藤記念科学振興財団必着）

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。

採択件数：

前期・後期各 10 件以内（予算範囲以内）

助成額：

招へいエリアによる（20 万円～ 80 万円）
（ホームページ参照 URL：<http://www.naito-f.or.jp>）

問い合わせ先：

財団法人 内藤記念科学振興財団
〒 113-0033 東京都文京区本郷 3-42-6 NKD ビル 8 階
TEL：03-3813-3005
FAX：03-3811-2917
URL：<http://www.naito-f.or.jp>
E-mail：naitofound@naito-f.or.jp

財団法人 井上科学振興財団

第 26 回（2009 年度）井上學術賞受賞候補者推薦要項

1. 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 2009 年 9 月 20 日現在で 50 歳未満の研究者に限ります。

2. 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。

3. 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。

4. 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。

5. 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。なお、提出書類の返却はいたしません。

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。

6. 締切期日：

2009 年 9 月 20 日（日）（井上科学振興財団必着）

日本神経化学会の推薦をご希望の方は 2009 年 8 月 14 日（金）必着。

7. 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、2009 年 12 月中旬に推薦者に通知します。

8. 学術賞の贈呈：

2010 年 2 月 4 日（木）午後 4 時から 東京で開催の予定。

9. 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

FAX : 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 26 回 (2009 年度) 井上研究奨励賞受賞候補者推薦要項

1. 推薦の対象 :

2006 年 4 月 1 日～2009 年 3 月 31 日 (2006 年度～2008 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 (2009 年 9 月 20 日現在。ただし医学、歯学、また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。

2. 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。

3. 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。

4. 提出手続 :

- (1) 推薦者 (博士論文指導者) 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。

5. 提出書類：

- (1) 推薦書 本文 ……………1 部

※ 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

※写しでも可

なお、提出書類の返却はいたしません。

6. 締切期日：

2009 年 9 月 20 日（日）（井上科学振興財団必着）

7. 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。選考の結果は、2009 年 12 月中旬に推薦大学の学長に通知します。

8. 研究奨励賞贈呈式：

2010 年 2 月 4 日（木）午後 4 時から 東京で開催の予定。

9. 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

FAX：03-3477-2747

E-mail：inoue01@inoue-zaidan.or.jp

財団法人 井上科学振興財団

井上リサーチアワード 第 2 回（2010 年度）募集要項

1. 趣旨：

自然科学の基礎的研究で優れた業績を挙げ、さらに開拓的発展を目指す若手研究者の独創性と自立を支援する目的で、研究を助成します。研究者が、これまでの成果を踏まえ、単独でまたは

共同研究者の協力を得て行う、将来性豊かな研究計画を対象とします。

2. 対象分野：

自然科学の全分野

3. 応募資格：

自然科学の基礎的研究で博士の学位を取得した研究者で、博士の学位取得後 9 年未満（2010 年 3 月 31 日現在）の国公立大学並びに大学共同利用機関に所属または所属予定の研究者。ただし、出産又は子の養育のために、やむを得ず研究活動を中断した場合には、その中断期間は学位取得後の年限には含めないものとします。年齢は問いません。

4. 助成金の額と期間：

助成金の額は一人当たり 1,000 万円とし、期間は 2 年とします。なお助成金の使途は本研究推進に直接寄与する経費（共同研究員を雇用するための経費を含む）に限り、間接経費等機関の共通経費には使用できません。

5. 採択予定数：

3 名以内。うち、1 名以上を女性研究者とします。

6. 応募方法：

自薦とします。また、応募研究者についての意見を求めることができる研究者 2 名を付記することとします。

7. 提出書類：

所定の申請書（井上科学振興財団のホームページ <http://www.inoue-zaidan.or.jp/> からダウンロードできます。）に必要事項を記載し、所属機関長の承認を得て、井上科学振興財団あてに申請書 1 部および主要論文別刷 1 部を提出してください。また、申請書は E-mail（inoue01@inoue-zaidan.or.jp）でもお送りください。

提出書類の返却はいたしません。

8. 締切期日：

2009 年 7 月 31 日（金）（井上科学振興財団必着）

9. 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。

結果は、2009 年 12 月中旬に応募者に通知します。採択通知を受けた研究者は、通知受領後、実施計画書（2010 ～ 2011 年度）を作成し、所属機関長の承認を得て、井上科学振興財団に提出していただきます。

10. アワードの贈呈：

2010 年 2 月 4 日（木）午後 4 時から 東京で開催の予定

11. 応募書類提出先及び連絡先：

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

FAX：03-3477-2747

E-mail：inoue01@inoue-zaidan.or.jp

財団法人 藤原科学財団

2010 年～2011 年開催 藤原セミナー募集要項

趣旨：

藤原科学財団は、科学技術の振興に寄与することを目的として、2010 年～2011 年の間に「藤原セミナー」の開催を希望する研究者から、下記募集要項に基づいて申請を受け付けます。申請された案件について選考を行い、採択されたものに対してセミナー開催に必要な経費を援助いたします。

藤原セミナーの選考委員は次の通りです。

杉村隆（委員長）、井口洋夫、西村暹、末松安晴、山崎敏光（敬称略、順不同）

又、必要に応じて専門委員を委嘱することがあります。

1. 対象分野

自然科学の全分野

2. 応募資格

わが国の大学等学術研究機関に所属する常勤の研究者

3. 開催件数

2 件以内

4. 開催費用援助額

1 件につき 12,000 千円以内（総額 24,000 千円以内）

5. セミナーの要件

(1) セミナーは、国際的にも学問的水準の高いものとし、そのテーマはなるべく基礎的なもので、関連分野を含めた発展に寄与するものであること。

但し二国間会議、定期的に行われる国際会議、およびその準備会議、サテライト会議は対象としない。

(2) 参加者は、50 ～ 100 人程度とし、外国人研究者が参加者の 5 分の 1 程度含まれること。

なお、国内外の優れた研究実績を有する若い専門研究者の参加を奨励する。

- (3) セミナーの開催対象期間は、2010 年 1 月 1 日～2011 年 12 月 31 日
- (4) セミナーの開催地は日本国内であること。（原則として北海道苫小牧市で開催）
- (5) セミナー開催日数は 2～4 日以内とする。
- (6) 参加者が、セミナー開催期間中、起居を共にすることを原則とし、計画された講演・討論のほか、個人的な討論など自由な雰囲気です学問的な交流と人間的接触を深め、永続する協力の基盤を作るようなものであること。

6. 申請受付期間

2009 年（平成 21 年）4 月 1 日（水）～同年 7 月 31 日（金）（藤原科学財団必着）

7. 藤原科学財団が支給する経費

セミナー開催に直接必要な経費として藤原科学財団が認めたもので、その費目は次のとおりとする。

(1) 準備費

準備費は、セミナー開催の準備のために必要な国内外旅費、印刷製本費、通信運搬費、会議費、賃金、消耗品費、雑役務費等とする。

(2) 海外参加者旅費

海外からの参加者旅費は、航空費、滞在費及び必要な場合は交通費とし、次の基準により援助することができる。

- ① セミナー参加を特に要請する者については、旅費全額
- ② その他の参加者のうち必要な者については、旅費の一部

(3) 国内参加者旅費

国内参加者旅費は、交通費（出発地から開催地までの往復鉄道賃等）、日当及び宿泊料とし、次の基準により援助することができる。

- ① セミナー参加を特に要請する者については、旅費全額
- ② その他の参加者のうち必要な者については、旅費の一部

(4) セミナー経費

セミナー経費は、セミナー開催期間中に必要な組織責任者等の旅費、印刷製本費、通信運搬費、会議費、レセプション経費、賃金、消耗品費、雑役務費等とする。

8. 申請の方法

セミナー開催希望者は「藤原セミナー開催申請書」（1 通）を、所属組織長を経由して藤原科学財団に提出すること。尚、著名な参加予定者については、セミナーのテーマに関する主要論文（5 名以内 1 人につき 1 篇、コピーで可）を添付のこと。

9. 選考及び通知

藤原科学財団の藤原セミナー委員会（前記の選考委員で構成）で選考のうえ、その結果を 2009 年（平成 21 年）9 月中旬に申請者ならびに所属組織長に通知する。

10. 開催責任者とその義務

申請が採択された場合は、申請者がセミナー開催責任者となる。セミナー開催責任者は、セミナーを企画し、運営し、次の事項を処理するとともに藤原科学財団との連絡に当たる。

- (1) 実施計画書の提出・・・・・・・・・・・・・・・・（セミナー開催日の2ヶ月前迄）
- (2) 実施報告書及び収支決算報告書の提出・・・（セミナー終了後3ヶ月以内）
- (3) 準備から終了に至るセミナー開催に関するすべての事項

11. 申請書提出先・連絡先

〒104-0061 東京都中央区銀座3-7-12

財団法人 藤原科学財団

TEL (03)3561-7736

FAX (03)3561-7860

HP <http://www.fujizai.or.jp>

※尚ホームページ上に開催申請書がPDFにて掲載されています。

※本セミナーは原則として北海道の苫小牧市で開催する事とする。開催にあたっては下記ホテルでの会議場、宿泊などを藤原科学財団で斡旋します。

苫小牧市・・・グランドホテルニュー王子

【セミナー・講習会】

千里ライフサイエンスセミナー

「臨床に繋がる癌幹細胞研究」

日 時： 平成21年8月25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

着眼点： 癌幹細胞は、悪性腫瘍の発生、治療抵抗性、再発、転移等に重要な役割を果たす。臨床応用に直結する可能性を秘めた癌幹細胞研究は造血器腫瘍が先行する形で進み、固形腫瘍でも精力的に検証が進んでいるのが現状である。本セミナーでは、主に固形腫瘍の癌幹細胞研究の動向をまとめ、近未来の臨床応用に繋がる内容として、特に若手研究者のスキルアップを目指したい。

コーディネータ：大阪大学大学院医学系研究科
東京医科歯科大学難治疾患研究所

森 正 樹
田賀 哲也

- プログラム：
1. 消化器癌における癌幹細胞
大阪大学大学院医学系研究科 石井 秀始、森 正 樹
 2. 肝胆膵領域における癌幹細胞研究の動向
横浜市立大学大学院医学研究科 谷口 英樹
 3. グリオーマ幹細胞の性状解析
理化学研究所発生・再生科学総合研究センター 近 藤 亨
 4. 神経幹細胞の増殖能と多分化能の分子基盤から癌細胞制御を探索
東京医科歯科大学難治疾患研究所 田賀 哲也
 5. 癌幹細胞のエピジェネティクスとポリコーム遺伝子の機能
千葉大学大学院医学研究院 岩間 厚志
 6. 幹細胞とがん幹細胞の異同
慶應義塾大学医学部 須田 年生

定 員： 300 名

参加費： 無料

- 申込方法：
- 1) 氏名、勤務先、〒所在地、所属、電話および FAX 番号を明記の上、郵便、FAX または E-mail で下記宛にお申し込み下さい。
 - 2) 事務局より参加証を送付します。
 - 3) 参加証は、セミナー開催当日、受付で提示ください。

申 込 先： (財) 千里ライフサイエンス振興財団セミナー Z 3事務局
〒 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 20 階
TEL 06-6873-2001
FAX 06-6873-2002
E-mail tkd@senri-life.or.jp

千里ライフサイエンスセミナー

「ユビキチン研究の新展開：病態生理学的観点から」

日 時： 平成 21 年 9 月 7 日 (月) 10:00 ～ 16:10

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 : エネルギー依存性タンパク質分解系の一部として発見されたユビキチン系は、その異常がガンや神経変性疾患などの原因になることや、ユビキチン化タンパク質を分解するプロテアソームの阻害剤が抗ガン剤として認可されているなど、関与しない生命現象が存在しないと考えられるほどに私達の身体で重要な役割を演じています。しかも、ユビキチン系はタンパク質分解の枠組みを凌駕し、多彩な様式でタンパク質の機能制御を司っていることも解ってきました。
本セミナーでは、日本のユビキチン-プロテアソーム研究のトップランナーにユビキチン研究の最前線を紹介していただきます。

コーディネータ : 東京都臨床医学総合研究所 所長代行 田中 啓二
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プログラム : 1. はじめに
東京都臨床医学総合研究所 所長代行 田中 啓二
2. 直鎖状ポリユビキチン化 : NF- κ B 活性化に必須な新たなユビキチン修飾系
大阪大学大学院生命機能研究科 教授 岩井 一宏
3. 脂溶性生理活性物質によるユビキチン化制御機構
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4. がんの進展とタンパク質分解
筑波大学大学院生命環境科学研究科 教授 柳澤 純
5. 超分子複合体タンパク質分解酵素プロテアソームによる生体制御
東京大学大学院薬学系研究科 教授 村田 茂穂
6. プロテオミクスが拓くユビキチン研究の新地平 : 酵素-基質関係の網羅的解明にむけて
九州大学生体防御医学研究所 教授 中山 敬一
7. おわりに
大阪大学大学院生命機能研究科 教授 岩井 一宏

定 員 : 300 名

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日米セミナー・第 2 回 Cdk5 国際シンポジウム

神経の機能と変性を制御する多機能性プロテインキナーゼ Cdk5

Cdk5, a multifunctional protein kinase in nervous system function and neurodegeneration

日 時 : 2009 年 6 月 26 日 (金) 27 日 (土)

会 場 : 首都大学東京 南大沢キャンパス 国際交流会館 大会議室

組織委員会 : 久永眞市 (首都大)、大島登志男 (早大)、五嶋良郎 (横市大)、富澤一仁 (熊大)

講演予定者 : A. Almeida (Spain), JA. Bibb (UTSW, USA), A. Cole (Univ. Melbourne, Australia), K. Duff (Columbia Univ., USA), Y. Goshima (Yokohama City Univ. Japan), S. Humbert (CNRS, France), K. Herrup (Rutgers Univ., USA), S. Hisanaga (TMU, Japan), N. Ip (HKUST, HK), S. Jessberger (ETH, Switzerland), P. Juo (Tufts Univ., USA), T. Kawauchi (Keio Univ, Japan), KT Kim (Postech., Korea), Y. Kim (Rockefeller Univ, USA), A. Kulkarni (NIH, USA), D. Lagace (Univ. Ottawa, Canada), K-Y. Lee (Univ. Calgary, Canada), Z. Mao (Emory Univ., USA), T. Ohshima (Waseda Univ. Japan), HC.Pant (NIH, USA), R. Qi (HKUST, HK), D. Qu (Univ. Ottawa, Canada), K. Shah (Purdue Univ. USA), V. Tan (NUS, Singapore), K. Tomizawa (Kumamoto Univ. Japan), L-H. Tsai (MIT, USA), Y. Wang (Peking Univ, China), J. Yamauchi (NCH, Japan)

参加費 : 無料

ポスター発表 : ポスター発表も行います。Cdk5 に関連するものでしたら、既に発表されたものでも結構です。Cdk5 の研究者が集まっています。いろいろな角度から discussion できることと思います。発表を希望される方は参加申し込み時にポスター希望としてご連絡ください。

懇親会 : 6 月 26 日 (金) 18 : 30 より 懇親会費 3000 円

参加申し込み : 会場の収容人数が 120 名です。参加希望の方は下記までお名前、所属、連絡

先、懇親会への出席をご連絡ください。

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第13回活性アミンに関するワークショップ年会

- 日時： 2009年8月28日（金）9時（または10時）～17時頃
- 会場： 三重大学医学部・先端医科学教育研究棟3階講義室
（津市江戸橋2-174；近鉄名古屋線江戸橋駅下車徒歩10分、あるいは津駅下車タクシー5分）
- 世話人代表： 成田正明（三重大学大学院医学系研究科・発生再生医学）
- 事務局： 只野武、中川西修（東北薬科大学薬理学教室）
- プログラム： 特別講演1 福井義浩先生
（徳島大学大学院ヘルスバイオサイエンス研究部・発生発達医学講座・機能解剖学分野 教授）
特別講演2 角田和彦先生
（かくたこども&アレルギークリニック院長）
☆口演並びにポスターによる一般演題
- 演題応募締切：2009年7月10日（金）
セロトニン、ドパミン、ノルアドレナリンなど活性アミンに関する研究を広く募集します。
- 参加費： 5,000円（学生1,000円）、懇親会3,000円（学生無料）
- 事前参加手続きをお願いします：
事前参加の締め切りは7月24日（金）です。
振込先や参加登録の詳細は当研究会のホームページ
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本大会を開催するにあたり、下記の企業および団体から多大なご援助を頂きました。
ここに衷心より感謝の意を表します。

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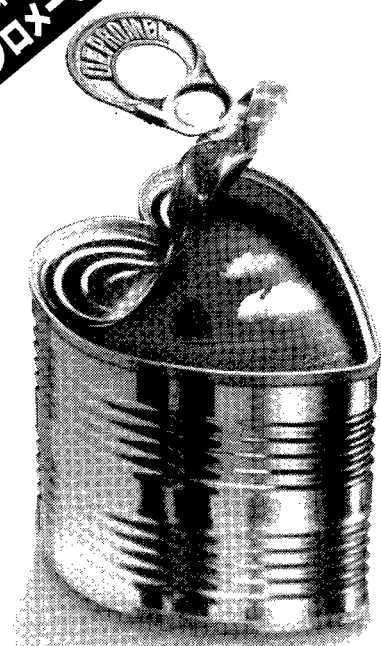
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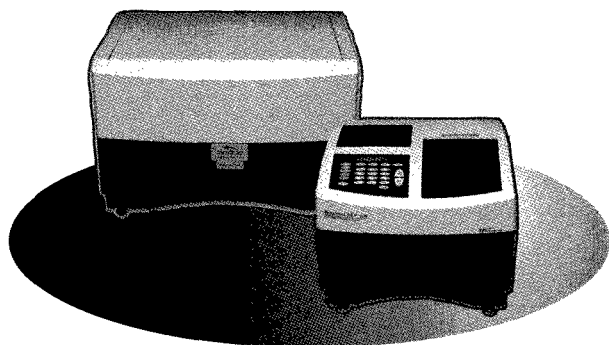
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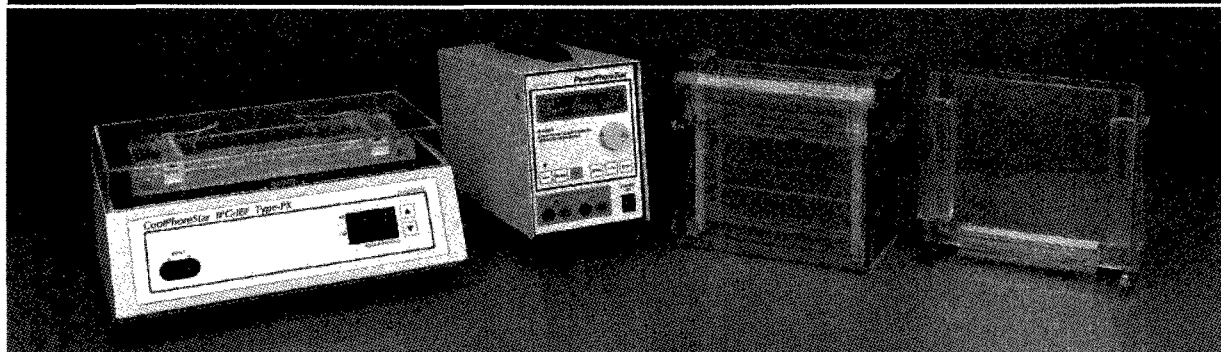
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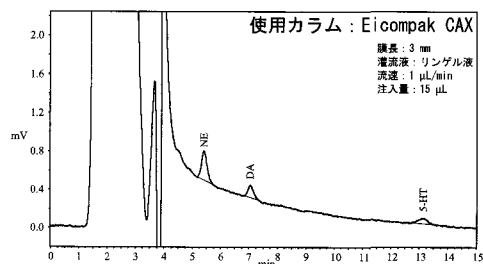
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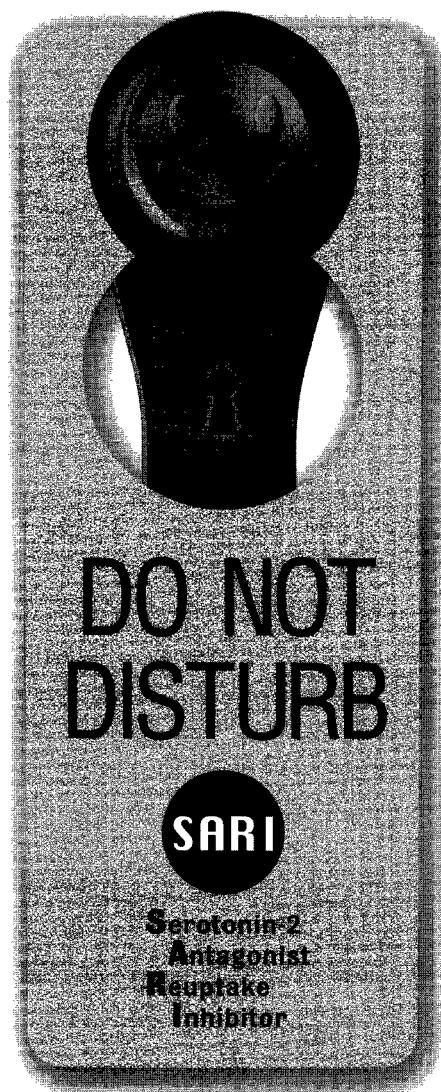
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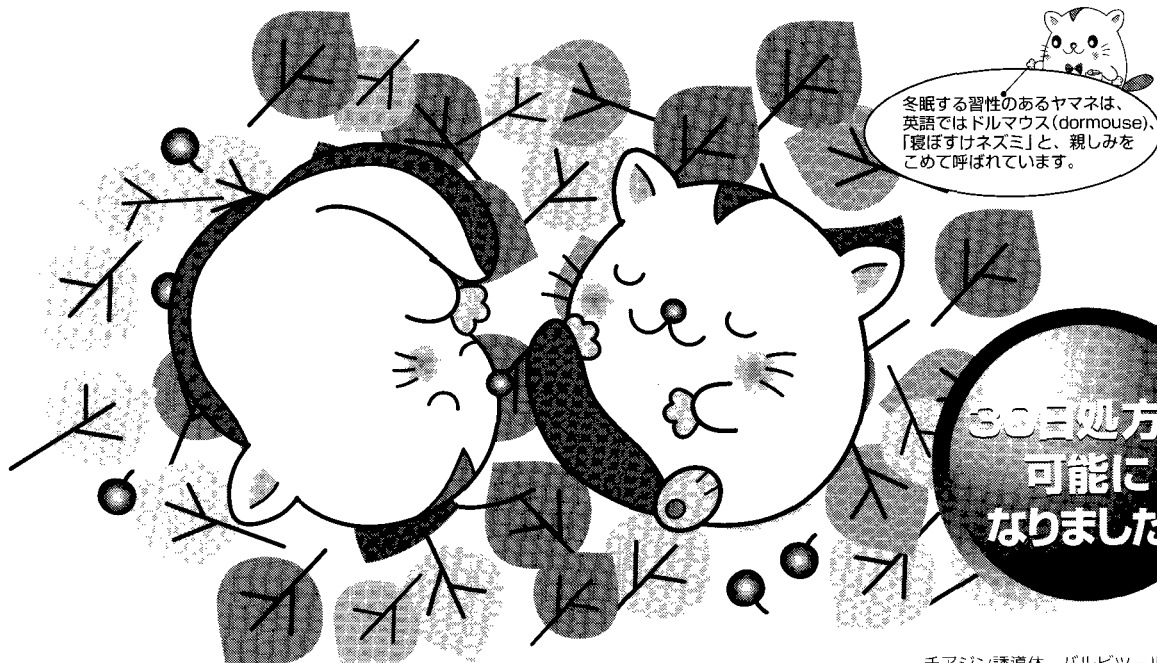
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チアジン誘導体、バルビツール酸誘導体等)、MAO阻害剤、シメチジン

睡眠障害改善剤 ドラール錠 15・20

クアゼパム錠 向精神薬、習慣性医薬品^{注1)}、指定医薬品、処方せん医薬品^{注2)}
DORAL[®] TABLETS 注1) 注意—習慣性あり 注2) 注意—医師等の処方せんにより使用すること 薬価基準収載

【禁忌】(次の患者には投与しないこと)

- (1) 本剤の成分に対し過敏症の既往歴のある患者
- (2) 急性閉塞隅角緑内障のある患者〔眼圧を上昇させるおそれがある。〕
- (3) 重症筋無力症のある患者〔重症筋無力症の症状を悪化させるおそれがある。〕
- (4) 睡眠時無呼吸症候群の患者〔呼吸障害を悪化させるおそれがある。〕
- (5) リトナビルを投与中の患者

【原則禁忌】(次の患者には投与しないことを原則とするが、特に必要とする場合には慎重に投与すること)

肺性心、肺気腫、気管支喘息及び脳血管障害の急性期等で呼吸機能が高度に低下している場合〔炭酸ガスナルコーシスを起こしやすい。〕

【効能・効果】

1. 不眠症
2. 麻酔前投薬

【用法・用量】

1. 不眠症
通常、成人にはクアゼパムとして1回20mgを就寝前に経口投与する。なお、年齢、症状、疾患により適宜増減するが、1日最高量は30mgとする。
2. 麻酔前投薬
手術前夜：通常、成人にはクアゼパムとして1回15～30mgを就寝前に経口投与する。なお、年齢、症状、疾患により適宜増減するが、1日最高量は30mgとする。

【用法・用量に関連する使用上の注意】

不眠症には、就寝の直前に服用させること。また、服用して就寝した後、睡眠途中において一時的に起床して仕事等をする可能性があるときは服用させないこと。

【使用上の注意】

1. 慎重投与(次の患者には慎重に投与すること)
 - (1) 衰弱患者〔作用が強くなりおそれがある。〕
 - (2) 高齢者
 - (3) 心障害のある患者〔心障害が悪化するおそれがある。〕
 - (4) 肝障害、腎障害のある患者〔肝障害、腎障害のある患者では一般に排泄が遅延する傾向があるので、薬物の体内蓄積による副作用の発現に注意すること。〕
 - (5) 脳に器質的障害のある患者〔作用が強くなりおそれがある。〕
 - (6) 統合失調症等の精神障害者
 - (7) 妊婦又は妊娠している可能性のある患者
 - (8) 小児等
2. 重要な基本的注意
 - (1) 食後の服用を避けること。
 - (2) 本剤の影響が翌朝以後に及び、眠気、注意力・集中力・反射運動能力等の低下が起こることがあるので、自動車の運転等危険を伴う機械の操作に従事させないよう注意すること。
 - (3) 本剤を投与する場合、反応に個人差があるため少量から投与を開始すること。やむを得ず増量する場合は観察を十分に行いながら慎重に行うこと。ただし、30mgを超えないこととし、症状の改善に伴って減量に努めること。
 - (4) 不眠症に対して投与する場合は、継続投与を避け、短期間にとどめること。やむを得ず継続投与を行う場合には、定期的に患者の状態、症状等の異常の有無を十分確認のうえ慎重に行うこと。
3. 相互作用
本剤は、主として肝代謝酵素CYP2C9、CYP3A4で代謝される。
 - (1) 併用禁忌(併用しないこと)
食物、リトナビル(ノービーア)
 - (2) 併用注意(併用に注意すること)
アルコール(飲酒)、中枢神経抑制剤(フェノ

4. 副作用

495例中副作用が報告されたのは52例(10.5%)で、その主なものは眠気・傾眠30件(6.1%)、ふらつき18件(3.6%)、頭重感7件(1.4%)、倦怠感5件(1.0%)等であった。(承認時)

(1) 重大な副作用

- 1) 依存性(頻度不明)：大量連用により薬物依存を生じることがあるので、観察を十分に行い、用量を超えないよう慎重に投与すること。また、大量投与又は連用中における投与量の急激な減少ないし投与中止により、痙攣発作、譫妄、振戦、不眠、不安、幻覚、妄想等の離脱症状があらわれることがあるので、投与を中止する場合には、徐々に減量するなど慎重に行うこと。
- 2) 刺激興奮、錯乱(いずれも頻度不明)：統合失調症等の精神障害者に投与すると逆に刺激興奮、錯乱等があらわれることがある。
- 3) 呼吸抑制、炭酸ガスナルコーシス(いずれも頻度不明)：呼吸抑制があらわれることがある。また、呼吸機能が高度に低下している患者に投与した場合、炭酸ガスナルコーシスを起こすことがあるので、このような場合には気道を確保し、換気を図るなど適切な処置を講ずること。
- 4) 精神症状(幻覚、妄想等)、意識障害、思考異常、勃起障害、興奮、運動失調、運動機能低下、錯乱、協調異常、言語障害、振戦(いずれも頻度不明)：あらわれたとの報告があるので、異常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。
- 5) 一過性前向性健忘、もうろう状態(いずれも頻度不明)：一過性前向性健忘、また、もうろう状態があらわれることがあるので、本剤を投与する場合には少量から開始するなど、慎重に行うこと。なお、十分に覚醒しないまま、車の運転、食事等を行い、その出来事を記憶していないとの報告がある。異常が認められた場合には投与を中止すること。

※その他の使用上の注意等については、製品添付文書をご参照ください。



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