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第５４回日本神経化学会（石川）大会

抄録号

平成 23 年 9 月

かけがえのない「日常」をつなぐ新しいカタチのご提案

愛娘の成長を見守り、家族のためにがんばってきたハル子さん。
今、ハル子さんは、家族との思い出や温かい絆に支えられながら、
自分らしくあり続けるため、懸命に生きています。
イクセロンパッチは、※アルツハイマー型認知症治療剤として、
日本初のパッチ剤。
アルツハイマー型認知症の人とご家族のかけがえのない「日常」のために、
一日一回貼付の新しいカタチをご提案します。

※軽度及び中等度のアルツハイマー型認知症における認知症症状の進行抑制

NOVARTIS

新発売

アルツハイマー型認知症治療剤

薬価基準収載

イクセロン®パッチ 4.5mg/ 9mg 13.5mg/18mg

EXELON® PATCH

リバスチグミン経皮吸収型製剤

劇薬 処方せん医薬品 注意ー医師等の処方せんにより使用すること

【禁忌(次の患者には使用しないこと)】
本剤の成分又はカルバメート系誘導体に対し過敏症の既往歴のある患者

【効能又は効果】
軽度及び中等度のアルツハイマー型認知症における認知症症状の進行抑制
〈効能又は効果に関連する使用上の注意〉
(1) アルツハイマー型認知症と診断された患者にのみ使用すること。
(2) 本剤がアルツハイマー型認知症の病態そのものの進行を抑制するという成績は得られていない。
(3) アルツハイマー型認知症以外の認知症性疾患において本剤の有効性は確認されていない。
(4) 本剤の使用が適切であるか、以下に示す本剤の特性を十分に理解した上で慎重に判断すること。
1) 国内臨床試験において、本剤の貼付により高頻度に適用部位の皮膚症状が認められている。(「4. 副作用」の項参照)
2) 本剤は維持量に到達するまで12週間以上を要する。

【用法及び用量】
通常、成人にはリバスチグミンとして1日1回4.5mgから開始し、原則として4週毎に4.5mgずつ増量し、維持量として1日1回18mgを貼付する。
本剤は背部、上腕部、胸部のいずれかの正常で健康な皮膚に貼付し、24時間毎に貼り替える。
〈用法及び用量に関連する使用上の注意〉
(1) 1日18mg未満は有効用量ではなく、漸増又は一時的な減量を目的とした用量であるので、維持量である18mgまで増量すること。
(2) 本剤は、維持量に到達するまでは、1日量として18mgを超えない範囲で症状により適宜増減が可能である。消化器系障害(悪心、嘔吐等)がみられた場合は、減量するかこれらの症状が消失するまで休薬する。休薬期間が4日程度の場合は、休薬前と同じ用量又は休薬前より1段階低い用量で投与を再開する。それ以外の場合は本剤4.5mgを用いて投与を再開する。投与再開後は、再開時の用量を2週間以上投与し、忍容性が良好であることを確認した上で、減量前の用量までは2週間以上の間隔で増量する。
(3) 本剤の貼付による皮膚刺激を避けるため、貼付箇所を毎回変更すること。(「2. 重要な基本的注意」及び「8. 適用上の注意」の項参照)
(4) 原則として、1日1回につき1枚のみ貼付すること。
(5) 他のコリンエステラーゼ阻害作用を有する同効薬(ドネペジル等)と併用しないこと。
(6) 医療従事者又は介護者等の管理のもとで投与すること。

【使用上の注意】
1. 慎重投与(次の患者には慎重に使用すること)
(1) 本剤のコリン作動性作用により以下に示す患者では、症状を誘発又は悪化させるおそれがあるため慎重に投与すること。
1) 洞不全症候群又は伝導障害(洞房ブロック、房室ブロック)等の心疾患のある患者〔迷走神経刺激作用により徐脈又は不整脈が起こるおそれがある。〕
2) 胃潰瘍又は十二指腸潰瘍のある患者、あるいはこれらの既往歴のある患者、非ステロイド性消炎鎮痛剤投与中の患者〔胃酸分泌量が増加し、胃潰瘍又は十二指腸潰瘍を誘発又は悪化させるおそれがある。〕
3) 尿路閉塞のある患者又はこれを起こしやすい患者〔排尿筋を収縮させ症状を誘発又は悪化させるおそれがある。〕
4) てんかん等の痙攣性疾患又はこれらの既往歴のある患者〔痙攣閾値を低下させ痙攣発作を誘発させるおそれがある。〕
5) 気管支喘息又は閉塞性肺疾患、あるいはこれらの既往歴のある患者〔気管支平滑筋の収縮及び気管支粘液分泌の亢進により症状を悪化させるおそれがある。〕
6) 錐体外路障害(パーキンソン病、パーキンソン症候群等)のある患者〔線条体のコリン系神経を亢進することにより、症状を悪化させるおそれがある。〕
(2) 重度の肝機能障害のある患者〔血中濃度が上昇するおそれがある。〕(「2. 重要な基本的注意」の項参照)
2. 重要な基本的注意
(1) 本剤の投与により、徐脈、心ブロック等があらわれることがあるので、特に心疾患(心筋梗塞、弁膜症、心筋症等)を有する患者や電解質異常(低カリウム血症等)のある患者等では、重篤な不整脈に移行しないよう観察を十分に行うこと。(「4. 副作用(1)重大な副作用」の項参照)
(2) 他の認知症性疾患との鑑別診断に留意すること。
(3) 本剤投与で効果が認められない場合には、漫然と投与しないこと。
(4) アルツハイマー型認知症は、自動車の運転等の機械操作能力を低下させる可能性がある。また、本剤は主に投与開始時又は増量時にめまい及び傾眠を誘発することがある。このため、自動車の運転等の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。
(5) 本剤の貼付により皮膚症状があらわれることがあるため、貼付箇所を毎回変更すること。皮膚症状があらわれた場合には、ステロイド軟膏又は抗ヒスタミン外用剤等を使用するか、本剤の減量又は一時休薬、あるいは使用を中止するなど適切な処置を行うこと。
(6) 本剤を同一箇所に連日貼付・除去を繰り返した場合、皮膚角質層の剥離等が生じ、血中濃度が増加するおそれがあるため、貼付箇所を毎回変更すること。
(7) 本剤の貼り替えの際、貼付している製剤を除去せずに新たな製剤を貼付したために過量投与となり、重篤な副作用が発現した例が報告されている。貼り替えの際は先に貼付している製剤を除去したことを十分確認するよう患者及び介護者等に指導すること。(「7. 過量投与」の項参照)
(8) 嘔吐あるいは下痢の持続により脱水があらわれることがある。脱水により、重篤な転帰をたどるおそれがあるので、嘔吐あるいは下痢がみられた場合には、観察を十分に行い適切な処置を行うこと。(「4. 副作用(1)重大な副作用」の項参照)
(9) アルツハイマー型認知症患者では、体重減少が認められることがある。また、本剤を含むコリンエステラーゼ阻害剤の投与により、体重減少が報告されているので、治療中は体重の変化に注意すること。
(10) 重度の肝機能障害のある患者では、投与経験がなく、安全性が確立されていないため、治療上やむを得ないと判断される場合にのみ投与すること。
3. 相互作用
本剤は、主にエステラーゼにより加水分解され、その後硫酸抱合を受ける。本剤のチトクロームP450(CYP)による代謝はわずかである。
併用注意(併用に注意すること)
コリン作動薬：アセチルコリン、カルプロニウム、ベタネコール、アクラトニウム　コリンエステラーゼ阻害剤：アンベノニウム、ジスチグミン、ピリドスチグミン、ネオスチグミン等　抗コリン作用を有する薬剤：トリヘキシフェニジル、ピロヘプチン、マザチコール、メチキセン、ビペリデン等　アトロピン系抗コリン剤：ブチルスコポラミン、アトロピン等　サクシニルコリン系筋弛緩剤：スキサメトニウム等
4. 副作用
(1) 重大な副作用
1) 狭心症(0.2%)、心筋梗塞(0.3%)、徐脈(0.8%)、心ブロック(0.1%)、洞不全症候群(頻度不明[注])：狭心症、心筋梗塞、徐脈、心ブロック、洞不全症候群があらわれることがあるので、このような場合には直ちに投与を中止し、適切な処置を行うこと。
2) 脳血管発作(頻度不明[注])、痙攣発作(0.2%)：脳血管発作、痙攣発作があらわれることがあるので、このような場合には直ちに投与を中止し、適切な処置を行うこと。
3) 食道破裂を伴う重度の嘔吐、胃潰瘍(いずれも頻度不明[注])、十二指腸潰瘍、胃腸出血(いずれも0.1%)：食道破裂を伴う重度の嘔吐、胃潰瘍、十二指腸潰瘍、胃腸出血があらわれることがあるので、このような場合には直ちに投与を中止し、適切な処置を行うこと。
4) 肝炎(頻度不明[注])：肝炎があらわれることがあるので、このような場合には直ちに投与を中止し、適切な処置を行うこと。
5) 失神(0.1%)：失神があらわれることがあるので、このような場合には直ちに投与を中止し、適切な処置を行うこと。
6) 幻覚(0.2%)、激越、せん妄、錯乱(いずれも頻度不明[注])：幻覚、激越、せん妄、錯乱があらわれることがあるので、このような場合には減量又は休薬等の適切な処置を行うこと。
7) 脱水(0.2%)：嘔吐あるいは下痢の持続により脱水があらわれることがあるので、このような場合には、補液の実施及び本剤の減量又は投与を中止するなど適切な処置を行うこと。

【投薬期間制限医薬品に関する情報】
本剤は新医薬品であるため、厚生労働省告示第97号(平成20年3月19日付)に基づき、2012年7月末日までは、投薬期間は1回14日分を限度とされています。

● その他の使用上の注意等詳細については、製品添付文書をご参照ください。

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2011年7月作成

2011年９月

日本神経化学会
会員　各位

日本神経化学会
理事長　井上　和秀

＊第54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。

なお、欠席される方は委任状に必要事項（代理人もご指定下さい）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

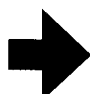
記

日　　　時：　2011年９月28日（水）　11：45～12：30

場　　　所：　瑠璃光「花離宮」（石川県加賀市山代温泉）

議題（予定）：
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
8. 2011年度奨励賞選考結果報告
9. 2010年度決算の件
10. 同監査報告
11. 2012年度予算の件
12. 評議員選任の件
13. 名誉会員推薦の件
14. 功労会員推薦の件
15. 次期大会の件
16. その他

（切り離してご投函ください）



2011年
日本神経化学会
総会

委任状

（ご欠席の方はご記入ください）

2011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。

2011年　　月　　日

所属

氏名　　　　　　　　

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日本神経化学会 行

日本神経化学会
　会員　各位

日本神経化学会
出版・広報担当理事
仲嶋　一範

E-mail配信に関するご理解・ご協力について

平素より当学会の活動に御尽力・御協力賜り、心より御礼申し上げます。

当会では、情報伝達の迅速化のため、E-mailを積極的に活用しているところでございますが、個人情報保護法に鑑み、配信に同意いただいた会員様に限りE-mailをお送りしております。E-mailは旬の情報を迅速にお届けできる利点があり、当会と致しましてはこれまで以上にE-mailでの広報活動に力を入れ、学会活動の活性化に繋げたいと考えております。

一方、E-mail配信に不同意または未回答の方々に対しては、機関誌（年４号発行）や学会ホームページ（月１回更新）での情報提供に留まっており、緊急のご連絡や〆切が近いご案内などの重要な情報をリアルタイムにご提供できない状況となっております。

つきましては、ぜひメール配信にご理解、ご同意を頂戴致したくお願い致します。
過去半年間に当会よりE-mailを受け取られていない方は、配信に同意されていない可能性がございます。これを機に同意いただけます場合には、当会事務局宛てE-mail（jsn@imic.or.jp）にてお知らせ下さいますようお願い致します。

なお、配信に同意いただいている方でも、メールアドレスの未登録や使用中止により、配信不能となっている場合がございます。配信に同意いただいているのにも関わらず過去半年間に当会よりE-mailを受け取られていない方は、配信を希望されるメールアドレスを事務局宛てにお知らせ下さい。

以上、何卒よろしくお願い致します。

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第54回 日本神経化学会（石川）大会
抄録集

会　期：２０１１年９月２６日（月）～２８日（水）
会　場：山代温泉　瑠璃光
大会長：米田　幸雄（金沢大学医薬保健研究域薬学系）

〈大会事務局〉
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〈大会URL〉
http://www.p.kanazawa-u.ac.jp/~jsn54/

ご挨拶

日本神経化学会は発足当初より、基礎系神経医学研究者と臨床系精神医学研究者が一同に会して討論する場を提供することにより、情報交換の促進と人的交流の推 進を通じて、数多くの共同研究成果と果実を生み出して参りました。特に、神経化学を標榜する学会としては世界最古の歴史を誇る我が国には稀有な学会です。今回の第54回大会においても、この従来の歴史と伝統を可能な限り尊重する所存です。本大会のプログラムは、９月26日から28日までの３日間、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などの各セッションを予定しています。さらに、2010年１月に逝去された、日本神経化学会名誉会員マーシャル・ニーレンバーグ博士（1968年ノーベル生理学・医学賞受賞者）の追悼シンポジウムも企画しており、国内外から500名以上の参加者が見込まれております。そのため、使用言語は日本語と英語の両方を予定しています。

学会の当初からの伝統である活発な議論を踏襲するために、第51回富山大会から導入された、「一般口演重視」と「若手の育成」というプログラム編成が第52回伊香保大会および第53回 神戸大会においても継続して好評を博しておりますので、本大会も引き続き、一般口演の多いプログラム編成および若手育成セミナーの企画を行う予定です。これら神経化学会大会独自の方向性を生かして、神経疾患の分子病態解明を基盤とする創薬研究展開と医薬品適正使用を通じて、生活の質改善を指向するフロンティア領域開拓に向けて、多様な学問的バックグラウンドをもつ研究者が目的を共有することで、基礎研究から臨床研究へと真のトランスレーショナル研究を育む場を提供したいと考えております。

第54回日本神経化学会大会

大会長　米田 幸雄（金沢大学医薬保健研究域薬学系）

高垣玄吉郎君を偲んで

高垣君には平成23年１月17日肺炎のため急逝されました。誠に残念でなりません。

彼とのお付き合いは60年来のもので、私にとって最も古い共同研究者であります。三鷹の仮校舎で神経化学の研究が始まりました。

当時の慶應の信濃町の基礎医学校舎は、戦災で消失し、研究の場所も資材も無い状態でした。私は、戦後直ぐ生理学教室に入室しましたが、林髞先生のお勧めで三菱化成の研究所で抗炎症薬の開発研究に携わる事になりました。これは、酵素阻害剤であり、酵素学と有機合成化学技術の勉強が必須でした。この基礎知識を持って慶應に戻りました時の、最初の共同研究者が高垣君であり、取り組んだ課題が「脳のグルタミン酸代謝の研究」でした。分析機器も無く、入手出来たのはコンウェーのアンモニア拡散測定器と滴定器、それにアミノ酸のペーパークロマトグラフィーのみでした。それでも解剖学教室のトラックをお借りして、昭和電工から液体酸素を頂き、ラットの瞬間凍結脳を作って、死後に脳で爆発的に増加するアンモニアの源を探ることでした。脳のアンモニアは、脳の興奮時にも増加することが知られており、脳機能と生化学的変化を結びつける貴重な指標でした。私どもは、朝から晩まで研究室に閉じこもり頑張りました。夜12時の終電車で帰宅するのが日課で、帰りに駅前のそば屋でラーメンを流し込みながら、翌日の研究の打ち合わせをするのも楽しみでした。その成果は「NATURE（1954）」に発表する事が出来ました。

昭和34年に私がアメリカ留学を終え、東邦大学に移った後、高垣君もコロンビア大学ウェルシュ教授のもとに留学し、同位元素を駆使した、脳のグルタミン酸代謝の研究で大きな成果を挙げられました。

その頃、日本でも脳の生化学研究が東大、大阪大、岡山大等の、精神科の若手研究者の間で関心が高まり、昭和33年には世界に先駆けて「神経化学懇話会」なる専門集団が出来、毎年討論集会が開催され「日本神経化学会」として今日まで引き継がれてきております。この研究会で発表するには、予め発表要旨を提出し、審査会で委員が集まり、激論を交しながら討論に適するか、否かを判断した上で発表のプログラムが決められると云う極めて厳しい制度が採られていました。当時、諸学会でも討論が盛んな研究会として話題となりましたが、此の折にも高垣君は最初から参加され、懇話会の「サーキュラー」の編集や発刊等を担当され、将に中心メンバーとして大いに尽力されました。

昭和40年に私が慶應大に戻りました折には、助教授として生理学教室の発展に大いに貢献して頂きました。

その後、東京都神経科学総合究所が開設されるに当たり、神経生化学部門の室長として研究に専念されて参りました。また慶応大では客員教授として学生の指導にも当たられました。

彼は、将に研究一筋に進んでこられた優れた先駆的な神経化学者だったと確信しております。また国際誌「J.Neurochemistry」の発刊に当ってはEditorの一人として、日本の神経化学研究を数多く紹介されたことも大きな功績でした。

定年退職後は、脳研究の歴史に興味をもたれ、度々「ミクロスコピア」に名文を投稿され、脳研究の歴史家としても大きな業績を残されました。その資料集めに米国や英国の医学図書館を最近まで歩き回られ、お元気そのものでした。突然の訃報に接し、惜しい人を亡くしたとしみじみ思う此の頃です。ご冥福を心からお祈り申し上げます。

平成23年4月24日

塚田 裕三

大会委員一覧

大　会　長

米田　幸雄　　金沢大学医薬保健研究域薬学系

組織委員会

組織委員長	東田　陽博	金沢大学
	加藤　　聖	金沢大学
	加藤　将夫	金沢大学
	程　　　肇	金沢大学
	三邉　義雄	金沢大学
	村本健一郎	金沢大学
	山田　正仁	金沢大学

プログラム委員会

松田　敏夫	大阪大学
伊藤　芳久	日本大学
大隅　典子	東北大学
荻田喜代一	摂南大学
小山　　豊	大阪大谷大学
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谷浦　秀夫	立命館大学
永田　浩一	愛知県心身障害者コロニー発達障害研究所
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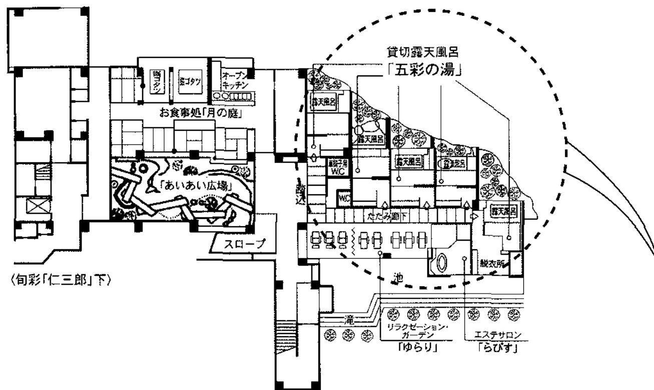
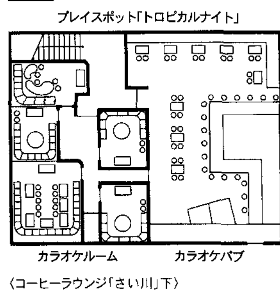
堀　　　修	金沢大学
南　　雅文	北海道大学
山田　清文	名古屋大学
山脇　成人	広島大学
和中　明生	奈良県立医科大学

会場案内図

	新・星の棟	風の棟		月の棟
6F	客室 601、602、620~622	客室 606~608、610、611		客室 652、653、655~660
5F	客室 501~503、505~507	客室 520~523、525	客室	客室 550~553、555~563、565、567、568 宴会場／山茶花
4F	客室 401~403、405~407	客室 420~423、425	客室	客室 450~453、455~463、465~468 宴会場／紫陽花
3F	客室 301~303、305~307	客室 320~323、325	プール、ジャグジー	客室 350~353、355~363、365、366 宴会場／黒百合、楓
2F	客室 201~203、205~207	宴会場／**天平**、鏡花	宴会場／**鳳凰**、犀星	宴会場／**平安**、水仙、桔梗、山吹
1F	新・星の棟専用ラウンジ 宴会場／萩	客室 122、123 大浴場／男しょうぶ・女しょうぶ 檜造り大露天風呂／月光の湯 庭園大露天岩風呂／日光の湯	旬彩「仁三郎」 あいあい広場 足湯「ささら」	フロント おみやげ処「月うさぎ」 ロビーラウンジ「さい川」 **シアター＆クラブ「能残月」** **コンベンションホール「花離宮」**
B1			お食事処「月の庭」 貸切露天風呂「五彩の湯」 リラクゼーション・ガーデン「ゆらり」 エステサロン「らびす」	プレイスポット「トロピカルナイト」 ・カラオケルーム ・カラオケパブ



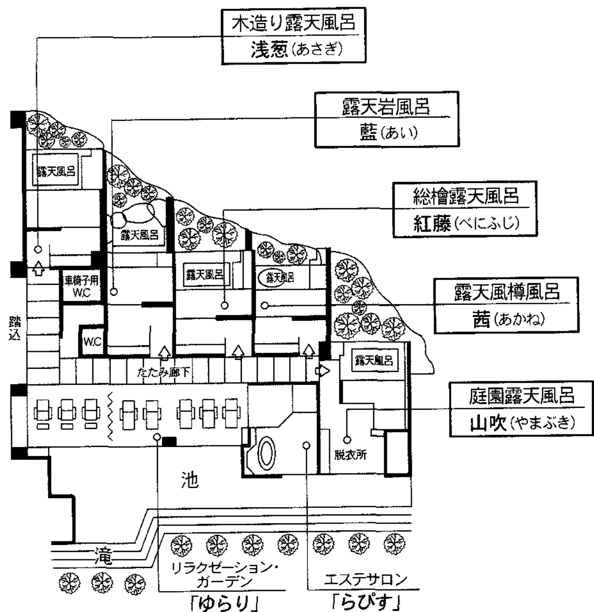
〈旬彩「仁三郎」下〉



〈コーヒーラウンジ「さい川」下〉

B1F

貸切露天風呂
「五彩の湯」

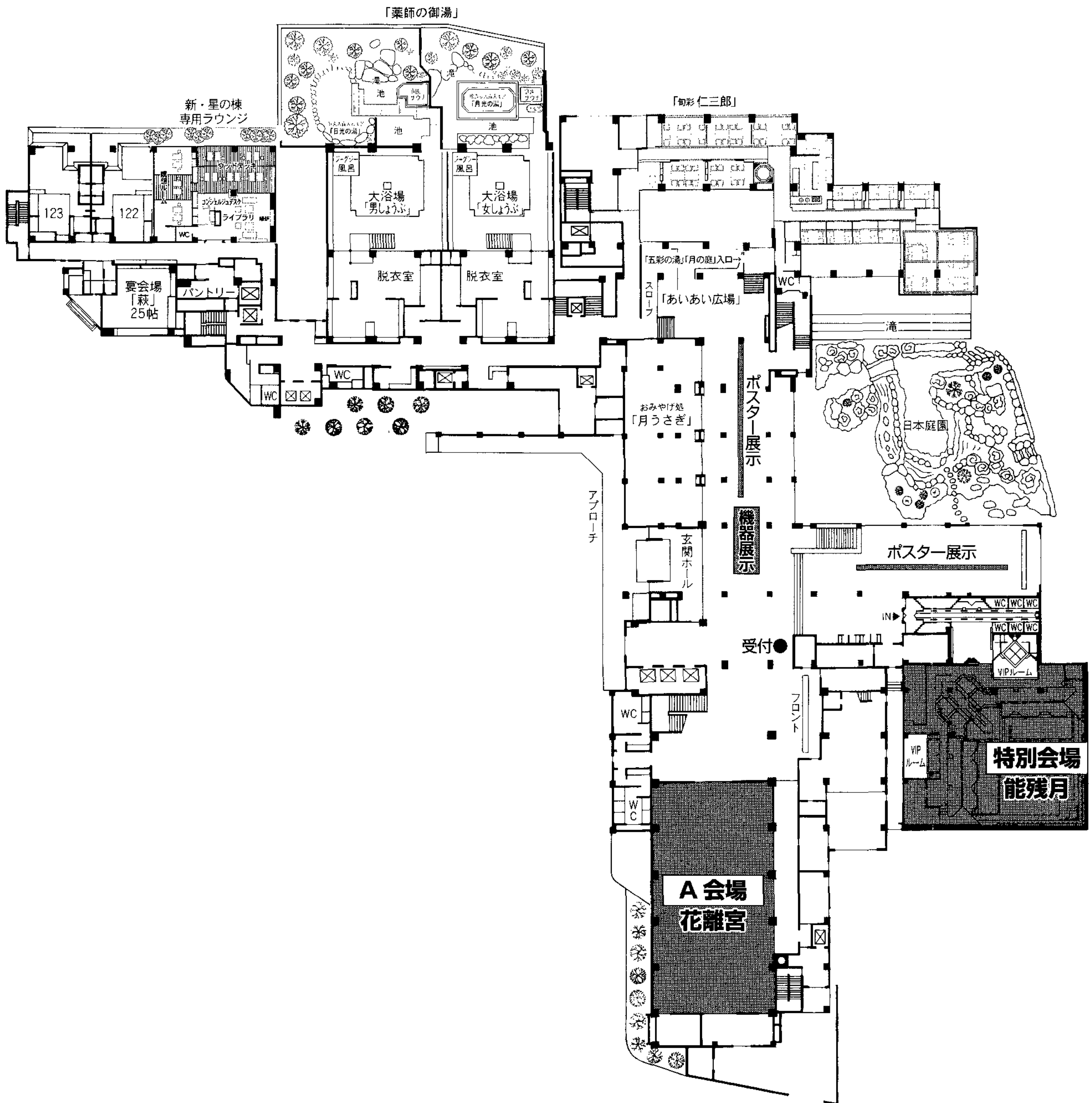


1F

A 会場・懇親会場／花離宮

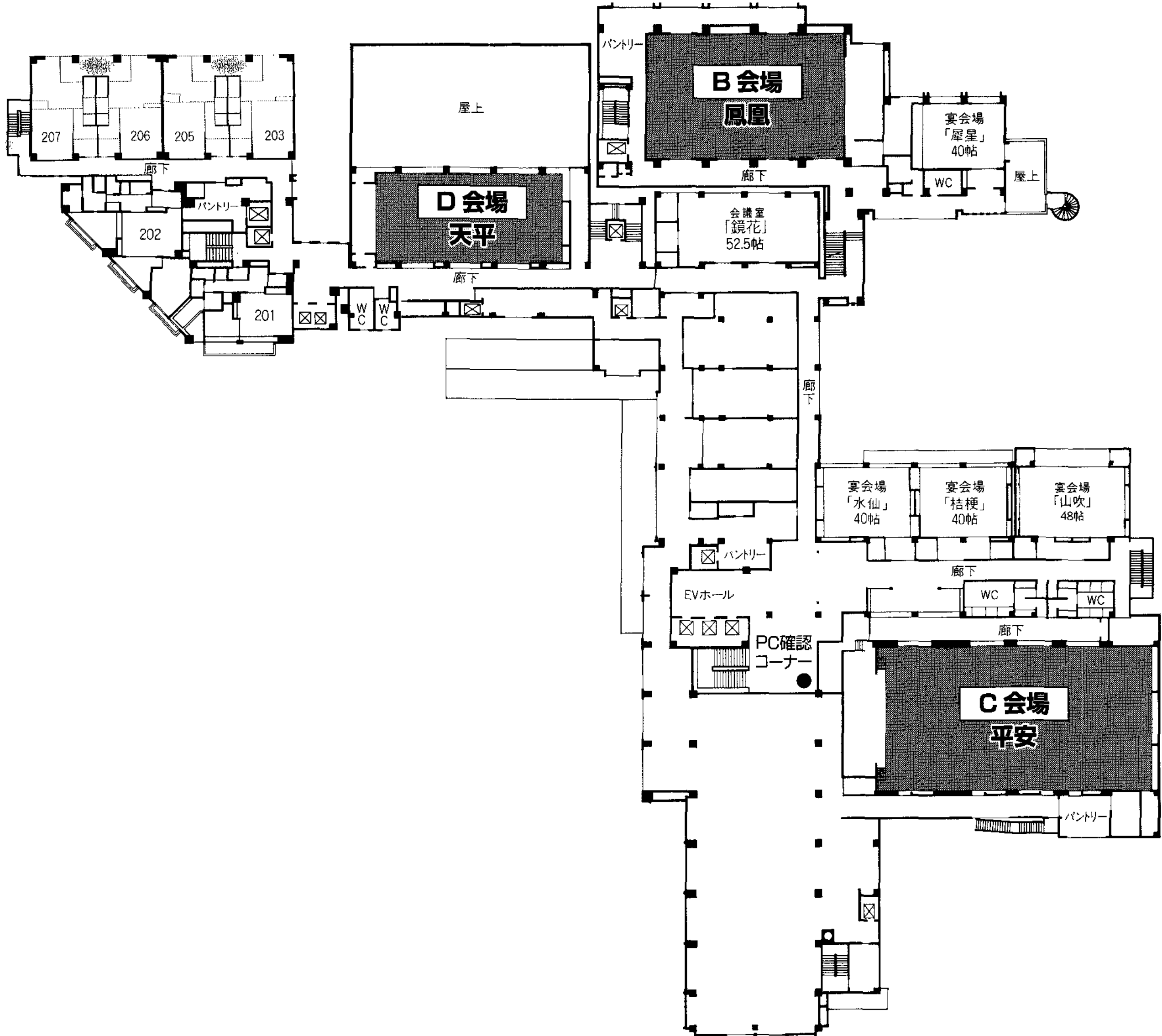
特別会場／能残月

ポスター展示会場／ロビーラウンジ

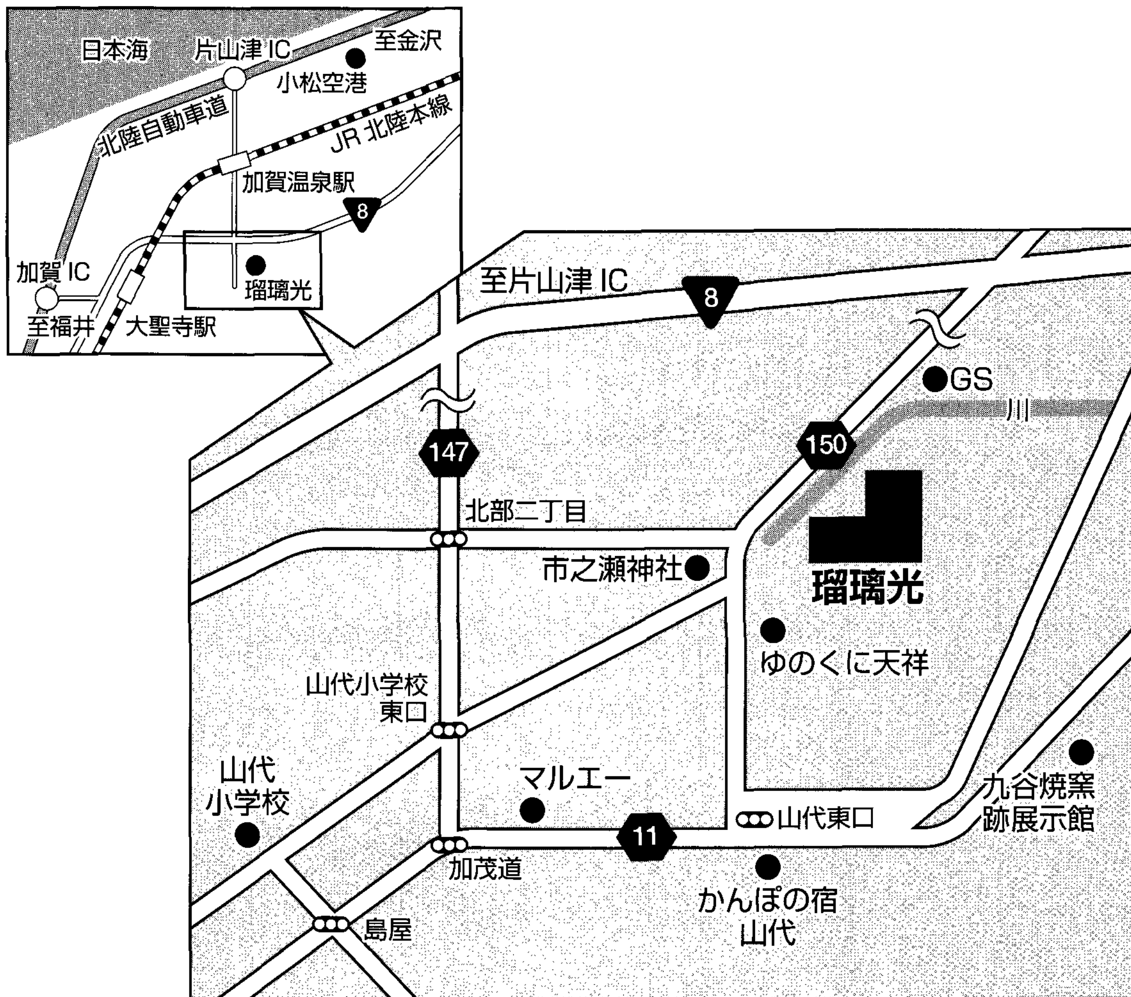


2F

B 会場／鳳凰
C 会場／平安
D 会場／天平

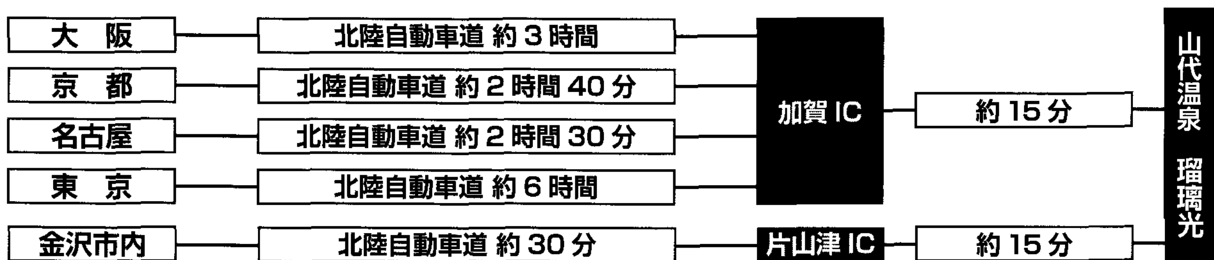


会場周辺図

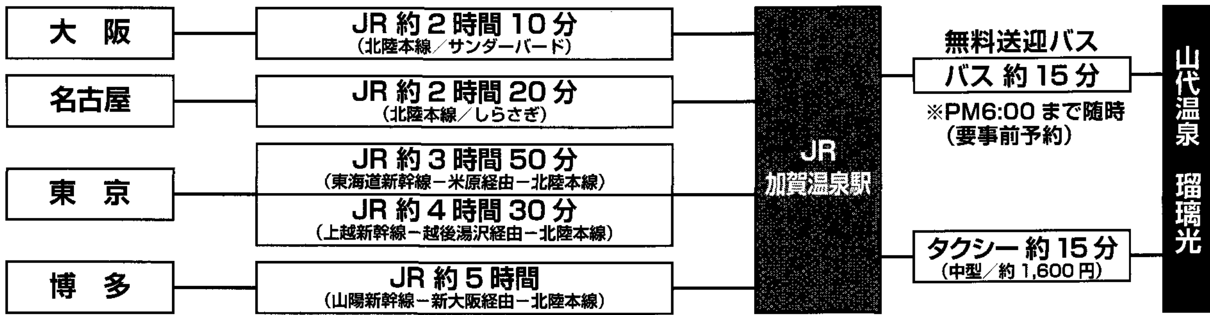


交通案内

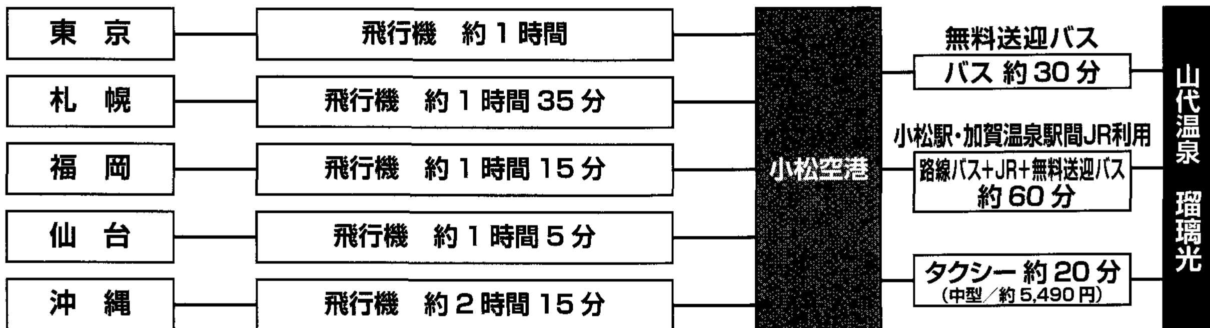
●お車をご利用の場合



●電車をご利用の場合

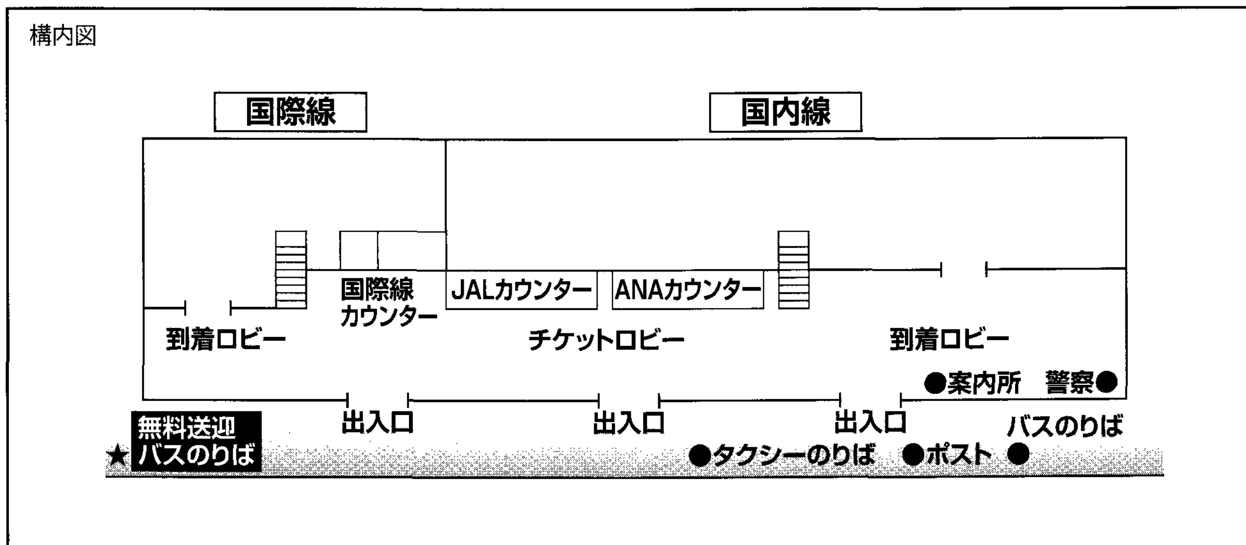


●飛行機をご利用の場合



無料送迎バス運行予定表

〈 小松空港 ⇔ 瑠璃光 〉（片道30分）



●9月25日（日）

9：30頃・11：20頃　小松空港発の2便を予定しています。

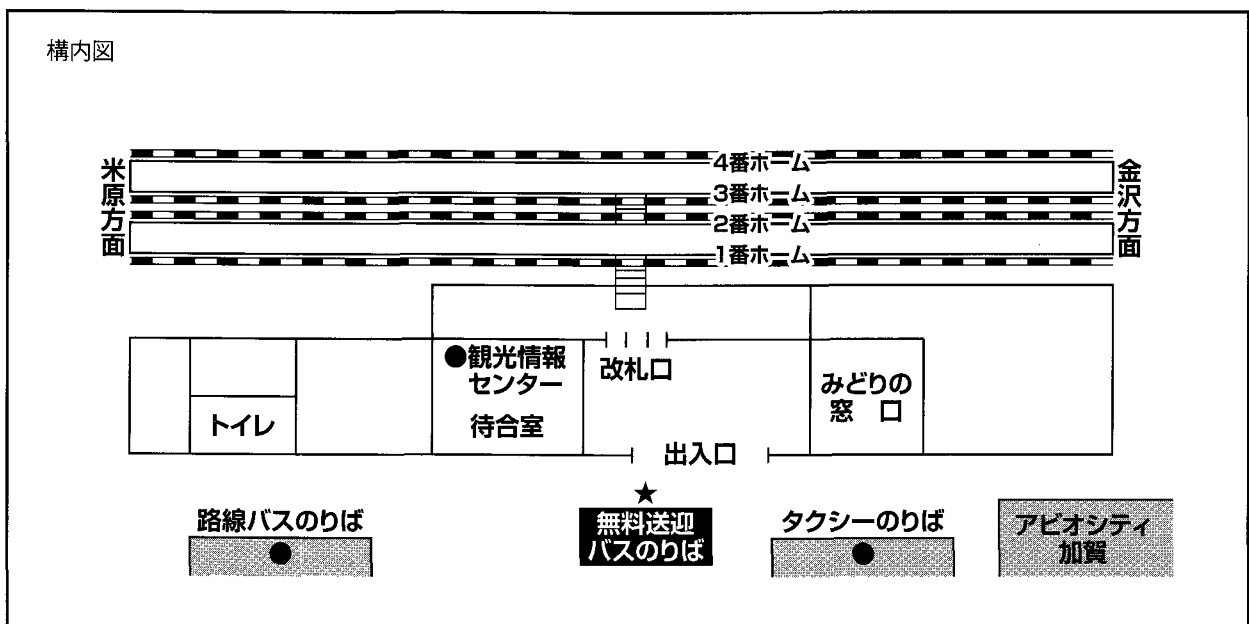
●9月26日（月）・27日（火）

9：30～21：30の間で運行します。（詳しくは大会ホームページでご確認ください。）

●9月28日（水）

お帰りの方を中心に運行します。

〈加賀温泉駅 ⇔ 瑠璃光〉（片道15分）



●9月25日（日）～28日（水）

特急発着時刻に合わせて運行します。

※上記以外の便をご利用希望の方は、瑠璃光まで事前にお電話でご相談ください。

瑠璃光　電話番号　0761−77−2323

※特に小松空港到着の方に関しましては、時間によって路線バスとJRを乗り継いで加賀温泉駅まで来ていただく場合がございますのであらかじめご了承ください。

大会日程概要

■前日　9月25日（日）

会場名	鏡花（2F）	花離宮（1F）
13:00	理事会 13:00～17:00	
14:00		神経化学カレッジ ①うつ病 竹林　実 ②アルツハイマー病 田中稔久 ③シナプス伝達 松山正剛 ④ニューロン 金子周司 ⑤グリア 小山　豊 ⑥神経幹細胞 橋本　均 14:00～17:15
17:30		評議員会 17:30～18:10

■ 25 September（Sunday）

Room	2F・Kyoka	1F・Hanarikyu
13:00	Board of Directors 13:00～17:00	
14:00		Neurochemistry College ①Depression Minoru Takebayashi ②Alzheimer's Disease Toshihisa Tanaka ③Synaptic Transmission Shogo Matsuyama ④Neurons Shuji Kaneko ⑤Glia Yutaka Koyama ⑥Neural Stem Cells Hitoshi Hashimoto 14:00～17:15
17:30		Council Meeting 17:30～18:10

■第１日目　９月26日（月）

会場名	A会場 1F・花離宮 (英語)	B会場 2F・鳳凰 (英語)	C会場 2F・平安 (日本語)	D会場 2F・天平 (日本語)	1F ロビーラウンジ ポスター展示会場	特別会場 1F・能残月 (英語)
8:30					ポスター貼付 P1 8:30〜10:00	
9:25	開会の辞					
9:30	シンポジウム S01 中枢神経障害・神経損傷に対する新規薬物治療と修復再生を目指して 座長：伊藤 芳久 荻田 喜代一 9:30〜11:45	シンポジウム S02 精神障害の新規原因分子について-最近の知見から- 座長：那波 宏之 新田 淳美 9:30〜11:45	一般口演 O1 気分障害・情報伝達 座長：齋藤 利和 木山 博資 9:30〜11:30	大学院生口演 G1 突起伸展・回路網形成 座長：田渕 明子 溝口 博之 9:30〜11:30	ポスター掲示	故ニーレンバーグ先生追悼シンポジウム M1 9:30〜11:30
12:45	神経化学会 公開シンポジウム OS (日本語) 「パーキンソン病研究の新展開 〜ミトコンドリア機能障害を中心に」 座長：和田 圭司 望月 秀樹 12:45〜15:15					
15:15	シンポジウム S03 統合失調症の最先端研究：全ゲノム解析から環境要因による神経発達障害の分子機構まで 座長：貝淵 弘三 山田 清文 15:15〜17:30	シンポジウム S04 ニューロンとグリアにおけるセプチン細胞骨格の機能解明に向けたアプローチ 座長：永田 浩一 木下 専 15:15〜17:30	一般口演 O2 神経変性・筋疾患 座長：島田 昌一 仲田 義啓 15:15〜17:15	大学院口演 G2 発達障害・転写制御因子 座長：渡部 和彦 柳澤 勝彦 15:15〜17:15		故ニーレンバーグ博士追悼シンポジウム M2 15:15〜17:15
17:30					ポスター討論時間 P1 17:30〜18:30	
18:30					ポスター撤去 18:30〜21:00	
19:00	懇親会 19:00〜20:30					
21:00		神経化学の若手研究者育成セミナー 21:00〜				

■ 26 September（Monday）

Room	Room A (1F・Hanarikyu)	Room B (2F・Hōō)	Room C (2F・Heian)	Room D (2F・Tenpyo)	1F Lobby Lounge Poster Area	Special Room (1F・No-Zangetsu)
8:30					Poster Set up P1 8:30～10:00	
9:25	Opening					
9:30	Symposium S01 Toward developing new drugs and repair and regeneration for neurological disorders and nerve injury in the CNS Chairs:Yoshihisa Ito Kiyokazu Ogita 9:30～11:45	Symposium S02 Novel molecules related to psychiatric diseases －Hot Topics－ Chairs:Hiroyuki Nawa Atsumi Nitta 9:30～11:45	Oral Session O1 Mood disorders/ Signal transduction Chairs:Toshikazu Saito Hiroshi Kiyama 9:30～11:30	Graduate Oral Session G1 Axonal and dendritic outgrowth/Network formation Chairs:Akiko Tabuchi Hiroyuki Mizoguchi 9:30～11:30		Dr. Nirenberg Memorial Symposium M1 9:30～11:30
10:00					Poster Exhibition	
12:45	JSN Open Symposium OS Parkinson's disease; Research frontline and mitochondrial dysfunction Chairs:Keiji Wada Hideki Mochizuki 12:45～15:15					
15:15	Symposium S03 The latest frontiers of schizophrenia research: from gene to environment Chairs:Kozo Kaibuchi Kiyofumi Yamada 15:15～17:30	Symposium S04 Approaches for the elucidation of septin functions in neurons and glia Chairs:Koh-ichi Nagata Makoto Kinoshita 15:15～17:30	Oral Session O2 Neurodegeneration/ Neuromuscular diseases Chairs:Shoichi Shimada Yoshihiro Nakata 15:15～17:15	Graduate Oral Session G2 Developmental disorders/Transcription factors Chairs:Kazuhiko Watabe Katsuhiko Yanagisawa 15:15～17:15		Dr. Nirenberg Memorial Symposium M2 15:15～17:15
17:30					Poster Discussion P1 17:30～18:30	
18:30					Poster Removal 18:30～21:00	
19:00	Welcome Reception 19:00～20:30					
21:00		Training Seminar for Students 21:00～				

■第2日目　9月27日（火）

時間	A会場 1F・花離宮 （英語）	B会場 2F・鳳凰 （英語）	C会場 2F・平安 （日本語）	D会場 2F・天平 （日本語）	1F ロビーラウンジ ポスター展示会場	特別会場 1F・能残月 （英語）
8:30〜10:00					ポスター貼付 P2 8:30〜10:00	
9:15〜11:30	神経化学会・ 生物学的精神医学会 合同シンポジウム JS 「うつ病の分子的基盤」 座長：神庭 重信 加藤 忠史 9:15〜11:30	シンポジウム S05 スパイン病の神経生物学と病態生理学 座長：福永 浩司 林 康紀 9:15〜11:30	一般口演 O3 薬物依存・シナプス可塑性 座長：田代 朋子 佐藤 真 9:30〜11:30	大学院生口演 G3 グリア・ミエリン 座長：加藤 [illegible] 小山 [illegible] 9:30〜11:30	ポスター掲示	故ニーレンバーグ先生 追悼シンポジウム M3 9:30〜11:30
11:30〜12:30					ポスター討論時間 P2 11:30〜12:30	
12:30〜14:45	シンポジウム S06 神経形態制御から機能へ — スペーシャルセルバイオロジーの観点から 座長：小西 慶幸 佐藤 真 12:30〜14:45	シンポジウム S07 生活環境が作り出す脳機能の多様性 座長：永井 拓 古屋敷 智之 12:30〜14:45	一般口演 O4 てんかん・神経変性疾患 座長：福永 浩司 片山 泰一 12:30〜14:30	大学院生口演 G4 神経変性疾患・疾患モデル 座長：和田 圭司 谷浦 秀夫 12:30〜14:30	ポスター掲示	故ニーレンバーグ先生 追悼シンポジウム M4 12:30〜17:00
14:30〜17:00	シンポジウム S08 行動を規定する脳基盤：こころの分子メカニズム 座長：橋本 均 橋本 亮太 14:45〜17:00	シンポジウム S09 中枢神経系と摂食・エネルギー代謝調節 座長：[illegible] 鈴木 [illegible] 14:45〜17:00	一般口演 O5 統合失調症・ジェノミクス 座長：西川 徹 [illegible] 14:30〜16:30	大学院生口演 G5 統合失調症・シナプス可塑性 座長：工藤 喬 中道 範隆 14:30〜16:30		
16:30〜18:30			大学院生口演 G6 気分障害・細胞接着因子 座長：白尾 智明 田丸 輝也 16:30〜18:30	大学院生口演 G7 不安・ストレス 座長：[illegible] 酒井 規雄 16:30〜18:30		
18:30〜21:00	夕食会 19:00〜20:30				ポスター撤去 18:30〜21:00	
21:00〜		神経化学の若手研究者育成セミナー 21:00〜				

■ 27 September (Tuesday)

Room A (1F・Hanarikyu)

- JSN-JSBP Joint Symposium JS: Molecular Basis of Depression. Chairs: Shigenobu Kanba, Tadafumi Kato. 9:15～11:30
- Symposium S06: Regulation of neuronal morphology and function. —From the perspectives of spatial cell biology. Chairs: Yoshiyuki Konishi, Makoto Sato. 12:30～14:45
- Symposium S08: Brain basis for behavior: molecular mechanism of mind. Chairs: Hitoshi Hashimoto, Ryota Hashimoto. 14:45～17:00
- Dinner. 19:00～20:30

Room B (2F・Hoo)

- Symposium S05: Neurobiology and Pathophysiology of the Spine Diseases. Chairs: Kohji Fukunaga, Yasunori Hayashi. 9:15～11:30
- Symposium S07: Diversity of brain function created by living environment. Chairs: Taku Nagai, Tomoyuki Furuyashiki. 12:30～14:45
- Symposium S09: Central nervous system and control of food intake and energy balance. Chairs: Shuichi Koda, Ryo Suzuki. 14:45～17:00

Room C (2F・Heian)

- Oral Session O3: Substance dependence/Synaptic plasticity. Chairs: Tomoko Tashiro, Makoto Sato. 9:30～11:30
- Oral Session O4: Epilepsy/Neurodegenerative disorders. Chairs: Fukunaga Kohji, Taichi Katayama. 12:30～14:30
- Oral Session O5: Schizophrenia/Genomics. Chairs: Toru Nishikawa, Akio Wanaka. 14:30～16:30
- Graduate Oral Session G6: Mood disorders/Cell adhesion factors. Chairs: Tomoaki Shirao, Teruya Tamaru. 16:30～18:30

Room D (2F・Tenpyo)

- Graduate Oral Session G3: Glia/Myelin. Chairs: Satoru Kato, Yutaka Koyama. 9:30～11:30
- Graduate Oral Session G4: Neurodegenerative disorders/Animal models. Chairs: Keiji Wada, Hideo Tamura. 12:30～14:30
- Graduate Oral Session G5: Schizophrenia/Synaptic plasticity. Chairs: Takashi Kudo, Noriaki Nakamichi. 14:30～16:30
- Graduate Oral Session G7: Anxiety/Stress. Chairs: Akira Sano, Norio Sakai. 16:30～18:30

Rooms B, C and D (combined)

- Training Seminar for Students. 21:00～

1F Lobby Lounge Poster Area

- Poster Set up P2. 8:30～10:00
- Poster Exhibition (10:00～11:30)
- Poster Discussion P2. 11:30～12:30
- Poster Exhibition (12:30～18:30)
- Poster Removal. 18:30～21:00

Special Room (1F・No-Zangetsu)

- Dr. Nirenberg Memorial Symposium M3. 9:30～11:30
- Dr. Nirenberg Memorial Symposium M4. 12:30～17:00

■第3日目　9月28日（水）

会場名	A会場 1F・花離宮 （英語）	B会場 2F・鳳凰 （英語）	C会場 2F・平安 （日本語）	D会場 2F・天平 （日本語）		特別会場 1F・能残月 （英語）
8:30						
9:00						
9:30	シンポジウム S10 イノシタイド・シグナルの多様性 座長：永田 栄一郎 三村 徹郎 9:30～11:45	シンポジウム S11 機能回復を目指した網膜・視神経の生存と再生の新規ストラテジー 座長：原 英彰 郡山 恵樹 9:30～11:45	一般口演 06 グリア・ミエリン 座長：渡辺 [illegible] 川西 [illegible] 9:30～11:30	一般口演 07 情報伝達・突起伸展 座長：石崎 泰樹 那波 宏之 9:30～11:10		故ニーレンバーグ先生 追悼シンポジウム M5 9:30～11:30
10:00						
10:30						
11:00						
11:30						
11:45	総会 11:45～12:30					
12:00						
12:30	エーザイ・ファイザー共催/ランチョンセミナー 座長：岸本 年史 講演：田中 稔久 12:30～13:30	第一三共共催/ミニランチョンセミナー 座長山田正仁 講演小野賢二郎 12:30～13:10				
13:00						
13:30	シンポジウム S12 中枢神経系における小胞体ストレス応答の重要性 座長：工藤 喬 堀 修 13:30～15:45	シンポジウム S13 ニューロン-グリア機能連関の新展開 座長：柴崎 貢志 鹿川 哲史 13:30～15:45		一般口演 08 発達障害・神経幹細胞 座長：久永 眞市 井上 敏子 13:30～15:30		
14:00						
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15:45	閉会の辞					
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22:30						

■ 28 September（Wednesday）

Room	Room A (1F・Hanarikyu)	Room B (2F・Hōō)	Room C (2F・Heian)	Room D (2F・Tenpyo)		Special Room (1F・No-Zangetsu)
9:30	Symposium S10 The diversity of inositide signaling Chairs:Eiichiro Nagata Tetsuro Mimura 9:30～11:45	Symposium S11 A novel strategy of survival and the reproduction of the retina and the optic nerve for functional recovery Chairs:Hideaki Hara Yoshiki Koriyama 9:30～11:45	Oral Session 06 Glia/Myelin Chairs:Yasuhiro Watanabe Hiroshi Nakanishi 9:30～11:30	Oral Session 07 Signal transduction/ Axonal and dendritic outgrowth Chairs:Yasuki Ishizaki Hiroyuki Nawa 9:30～11:10		Dr. Nirenberg Memorial Symposium M5 9:30～11:30
11:45	General Assembly 11:45～12:30					
12:30	Luncheon Seminar Chairs:Toshifumi Kishimoto Speaker:Toshihisa Tanaka 12:30～13:30	Luncheon Seminar Chairs:Masahito Yamada Speaker:Kenjiro Ono 12:30～13:10				
13:30	Symposium S12 The important role of ER stress response in the central nervous system Chairs:Takashi Kudo Osamu Hori 13:30～15:45	Symposium S13 New insight of functional interactions between neurons and astrocytes Chairs:Koji Shibasaki Tetsushi Kagawa 13:30～15:45		Oral Session 08 Developmental disorders/ Neuronal stem cell Chairs:Shin-ichi Hisanaga Atsuko Inoue 13:30～15:30		
15:45	Closing					

参加者へのご案内

●参加者の皆様へ

1．参加証について

参加証（ネームカード）は、当日会場受付にてお渡しします（事前参加登録者を含む）。受付にて所属と氏名をご記入の上、大会参加中はネームカードを必ず着用してください。ネームカードのない方の入場はお断りいたします。

〈受付時間〉

9／25（日）15：00～18：30
9／26（月）8：45～18：30
9／27（火）8：45～18：30
9／28（水）8：45～13：30

2．当日参加登録される方

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】

一般会員　：14,000円
一般非会員　：16,000円
大学院生／学部生（筆頭著者）：4,000円
学部学生（筆頭著者以外）：0円
同伴者（小学生以下無料）：1,000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。受付時に学生証を提示してください。

【懇親会（Welcome Reception）費】

瑠璃光に宿泊される方　：無料（宿泊費に含まれています）
瑠璃光に宿泊されない方：8,000円

3．非会員の方

日本神経化学会に入会ご希望の方は、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　日本神経化学会事務局
TEL：03-5361-7107　FAX：03-5361-7091
E-mail：jsn@imic.or.jp

4．単位取得について

日本神経化学会大会では、以下の専門医制度において資格・認定の更新に必要となる単位を取得することができます。単位が必要な方は受付までお申し出ください。

社団法人 日本精神神経学会　精神科専門医　取得単位：C群　30点
一般社団法人 日本神経学会　専門医　取得単位：2単位

●お知らせ

1．クローク

会期中は、常時１Ｆフロントにてお荷物をお預かりいたします。なお、瑠璃光に他の方と相部屋でお泊りの方は、ご希望に応じて別途貴重品をお預かりいたします。

2．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。

3．宿泊・交通・観光案内

お問合せは、直接１Ｆフロントまでお願いいたします。

4．懇親会（Welcome Reception）・表彰式

９月26日（月）19：00より、１Ｆ「花離宮」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までに受付までお申し出ください。ビュッフェ形式となります。当日の大学院優秀発表賞受賞者の発表と表彰が行われる予定です。９月27日（火）の大学院優秀発表賞受賞者の発表と表彰は、当日の夕食会にて行います。当日に瑠璃光へお泊りの方はすべて懇親会場での夕食となります。

5．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は設置いたしませんが、１Ｆロビーでは無線LANが使用できます。

6．フリードリンクコーナー

フリードリンクコーナーを設置する予定ですので、ご自由にご利用ください。

7．会期中の昼食について

９月28日（水）は、ランチョンセミナーがあります。お弁当の数に限りがありますので、整理券を当日朝８：45より受付にて、１人１枚限り、参加証の提示と引き換えに配布いたします。また９月26日（月）と27日（火）は、軽食を準備する予定ですので、ご利用ください。

8．禁止事項

・会場内での撮影・録画・録音はすべて禁止となっております。
・会場内は禁煙です。施設内の喫煙スペースは別途ご案内します。

9．神経化学カレッジ

大会前日に全希望者を対象とする「神経化学カレッジ」を開講します。下記６テーマについて、それぞれ30分ずつの基礎的内容の講義です。参加予約や登録は必要ありませんので、学生以外の方々も随時参加可能です。ただし、若手研究者育成セミナー参加者は、本カレッジへの参加が必修です。

日　程：2011年９月25日（日）　14：00～17：15
会　場：瑠璃光１Ｆ「花離宮」
世話人：松田敏夫　教授（大阪大学・大学院薬学研究科・薬物治療学分野）

神経化学カレッジ　スケジュール

（敬称略）

テーマ	講　　師
うつ病 14：00〜14：30	竹林　実　Minoru Takebayashi （国立病院機構呉医療センター・精神科・臨床研究部）
アルツハイマー病 14：30〜15：00	田中稔久　Toshihisa Tanaka （大阪大学大学院・医学系研究科・精神医学）
シナプス伝達 15：00〜15：30	松山正剛　Shogo Matsuyama （姫路獨協大学・薬学部・薬理学）
休憩	15分
ニューロン 15：45〜16：15	金子周司　Shuji Kaneko （京都大学大学院・薬学研究科・生体機能解析）
グリア 16：15〜16：45	小山　豊　Yutaka Koyama （大阪大谷大学・薬学部・薬理学）
神経幹細胞 16：45〜17：15	橋本　均　Hitoshi Hashimoto （大阪大学大学院・薬学研究科・神経薬理学）

10. 神経化学の若手研究者育成セミナー

日　程：2011年９月25日（日）〜28日（水）
会　場：瑠璃光内各宴会場
世話人：伊藤芳久　教授（日本大学・薬学部・薬理学研究室）

９月25日（日）	13：30	集合
	14：00〜17：30	神経化学カレッジ参加
	17：30〜消灯	自由行動
９月26日（月）	日中	大会参加（自由行動）
	19：00〜20：30	懇親会参加
	21：00〜22：00	グループミーティング
	22：00〜消灯	フリーディスカッション
９月27日（火）	日中	大会参加（自由行動）
	19：00〜20：30	夕食会参加
	21：00〜22：00	グループミーティング
	22：00〜消灯	フリーディスカッション
９月28日（水）		自由解散

上記日程は予定なので、参加者数次第では変更がある可能性をお含みおきください。

神経化学の若手研究者育成セミナー　講師

（敬称略）　　五十音順

講師	所属
味岡逸樹	東京医科歯科大学・脳統合機能研究センター
池中一裕	自然科学研究機構・生理学研究所
石川保幸	奈良先端科学技術大学院大学・神経機能科学
上原孝	岡山大学大学院・医歯薬学総合研究科・薬効解析学分野
榎戸靖	東京医科歯科大学・難治疾患研究所
岡野栄之	慶応義塾大学・医学部生理学教室
金子葉子	藤田保健衛生大学・医学部・生理学Ⅰ
小泉修一	山梨大学医学部薬理学・薬理学
澤本和延	名古屋市立大学大学院・医学研究科・再生医学分野
津田誠	九州大学大学院・薬学研究院・薬理学分野
津田正明	富山大学大学院・医学薬学研究部
遠山正彌	大阪大学大学院・連合小児／医学系研究科
野田百美	九州大学・大学院・薬学研究院・病態生理学分野
新田淳美	富山大学大学院・医学薬学研究部・薬物治療学
橋本均	大阪大学大学院・薬学研究科・神経薬理学分野
橋本亮太	大阪大学大学院・連合小児発達学研究科
馬場広子	東京薬科大学・薬学部・医療薬学科・機能形態学
東田千尋	富山大学・和漢医薬学総合研究所・民族薬物研究センター・薬効解析部
丸山和佳子	国立長寿医療研究センター・加齢健康脳科学研究部
南雅文	北海道大学・薬学研究院・薬理学
山田清文	名古屋大学大学院・医学系研究科・医療薬学

11. 特別シンポジウム

●日本神経化学会公開シンポジウム

日　程：2011年９月26日（月）12：45～15：15
会　場：瑠璃光１Ｆ「花離宮」
※発表は日本語です。

●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　程：2011年９月27日（火）９：15～11：30
会　場：瑠璃光１Ｆ「花離宮」
※発表は英語です。

●故ニーレンバーグ先生追悼シンポジウム〈金沢大学 子どものこころの発達研究センター 共催〉

日　程：2011年９月26日（月）～28日（水）
会　場：瑠璃光１Ｆ「能残月」
世話人：東田陽博　教授（金沢大学・医薬保健研究域医学系・脳細胞遺伝子学）

2010年１月に逝去された、日本神経化学会名誉会員　マーシャル・ニーレンバーグ先生（1968年ノーベル生理学・医学賞受賞者）の追悼シンポジウムを、国内外から約20人のシンポジストをお迎えして開催いたします。たくさんの方々のご参加をお待ちしています。
※発表は英語です。

12. 各種委員会

●将来計画委員会
日　時：９月26日（月）10：00～12：00　　会場：３Ｆ「黒百合」

●奨励賞選考委員会
日　時：９月26日（月）10：00～12：00　　会場：２Ｆ「鏡花」

●国際対応委員会
日　時：９月26日（月）16：00～18：00　　会場：３Ｆ「黒百合」

●脳研究推進委員会
日　時：９月26日（月）16：00～18：00　　会場：２Ｆ「鏡花」

●APSNプログラム委員会
日　時：９月27日（火）10：00～13：00　　会場：３Ｆ「楓」

●日本神経化学会活性化特別委員会
日　時：９月27日（火）13：00～15：00　　会場：３Ｆ「黒百合」

●研究助成金等候補者選考委員会
日　時：９月27日（火）13：00～15：00　　会場：２Ｆ「鏡花」

●シンポジウム企画委員会
日　時：９月27日（火）15：00～17：00　　会場：３Ｆ「黒百合」

●出版・広報委員会
日　時：９月28日（水）13：00～14：00　　会場：３Ｆ「黒百合」

13. 関連行事

●理事会
日　時：９月25日（日）13：00～17：00　　会場：２Ｆ「鏡花」

●評議員会
日　時：９月25日（日）17：30～18：10　　会場：１Ｆ「花離宮」

●総会
日　時：９月28日（水）11：45～12：30　　会場：１Ｆ「花離宮」

発表者へのご案内

■口演発表

1．発表・討論、進行

1）発表形式は下記の通りです。
　○一般シンポジウム・合同シンポジウム・追悼シンポジウム：英語
　○公開シンポジウム：日本語
　○一般口演：日本語
　○大学院生口演：日本語
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、時間厳守でお願いします。（一般シンポジウム：発表25分／討論５分、一般口演：発表15分／討論５分、大学院生口演：発表10分／討論10分。）
3）進行は座長にご一任します。ただ、終了時間の厳守をお願いいたします。
4）演者は口演開始時刻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（Windows）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
　　（＊Windows Vista、PowerPoint 2007/2010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。）
　【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）Macintosh PCの持ち込みはご遠慮ください。
5）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。
6）ウイルスチェックは必ず行ってください。
7）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・動作をご確認ください。その後、データのみをお預かりいたします。なお、指示がない限りは口演後にはデータを破棄いたします。
　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PC本体をご返却いたします。
8）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確認コーナーをご利用ください。
9）演台上にはモニター・マウス・キーボードを用意しておりますので、発表時の操作はご自身

でお願いいたします。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時刻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。（一般シンポジウム：発表25分／討論５分、一般口演：発表15分／討論５分、大学院生口演：10分／討論10分。）

4．大学院優秀発表賞の選考

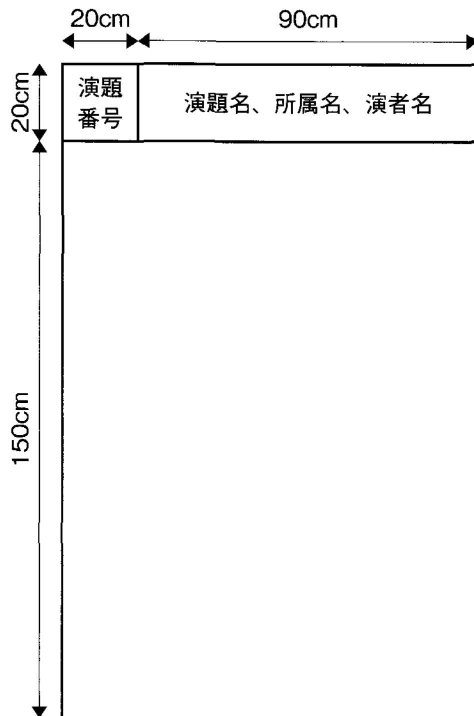
大学院生口演セッションごとに優秀発表賞該当者１名を選考する予定です。白熱した討論を期待しています。

■ポスター発表

1．会場

ポスター発表は、１Ｆロビーラウンジにて行います。

2．発表要項



1）左図のように、縦20cm×横90cmのサイズに演題名、著者名、所属を英語標記したものをご用意ください。
2）発表内容は左図発表スペース（縦150cm×横110cm）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。
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：９月26日（月）８：30～10：00
　　　９月27日（火）８：30～10：00
討論：９月26日（月）17：30～18：30
　　　９月27日（火）11：30～12：30
撤去：９月26日（月）18：30～21：00
　　　９月27日（火）18：30～21：00

2）ポスター発表討論時間は第１日目と２日目で異なりますので、ご注意ください。発表者は上記の討論時間には、ポスター前に待機してください。
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）撤去時刻終了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。

学会からのお知らせ

1．評議員会

日　時：9月25日（日）17時30分～18時10分
場　所：瑠璃光1F「花離宮」
議　題：1．大会のあり方
　　　　2．会員増の具体策
　　　　3．グローバル化への対応
　　　　※お弁当のご用意はございません。

2．総　　会

日　時：9月28日（水）11時45分～12時30分
場　所：瑠璃光1F「花離宮」
議　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出版・広報委員会
　　　　　③シンポジウム企画委員会
　　　　　④国際対応委員会
　　　　　⑤研究助成金等候補者選考委員会
　　　　　⑥脳研究推進委員会
　　　　　⑦連合大会委員会
　　　　　⑧日本神経化学会活性化特別委員会
　　　　8．2011年度奨励賞選考結果報告
　　　　9．2010年度決算の件
　　　　10．同監査報告
　　　　11．2012年度予算の件
　　　　12．評議員選任の件
　　　　13．名誉会員推薦の件
　　　　14．功労会員推薦の件
　　　　15．次期大会の件
　　　　16．その他

理事会議事録

2011年度第1回理事会議事録

日　時：2011年３月４日（金）13：30～17：30
会　場：(財) 国際医学情報センター第２会議室

出　席：髙坂新一（理事長)、井上和秀（副理事長)、島田昌一（会計担当)、今泉和則（出版・広報担当)、熊倉鴻之助、塩坂貞夫、遠山正彌、御子柴克彦、柳澤勝彦、和中明生、田代朋子、白尾智明、(以上 理事)、鍋島俊隆（監事)、池中一裕（将来計画委員会委員長)、和田圭司（奨励賞選考委員会委員長)、米田幸雄（第54回大会長)、浜之上誠（選挙管理委員会委員長)、木山博資、佐藤真、石崎泰樹（以上 新理事）
委任状：岡野栄之（庶務担当理事)、神庭重信、西川徹（以上 理事)、野村靖幸（監事)、仲嶋一範（新理事）

議　題

議事に先立ち、髙坂新一理事長より挨拶がなされた。

【報告事項】

１．2010年度第３回理事会議事録承認の件

髙坂新一理事長より、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

・理事改選結果について

2011年２月４日に開票された理事選挙結果について、浜之上誠選挙管理委員会委員長より報告された。なお、同点の取り扱いについては、年齢や生年月日の昇順とされた。

・科研費審査委員候補者選出選挙の件

2011年２月４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、浜之上誠選挙管理委員会委員長より報告された。
また、髙坂新一理事長より科研費審査委員候補者名簿に誤りがあり、現理事の名前が欠落していた旨報告され、取り扱いについて以下の通り提案された。

科研費審査委員候補者として日本学術振興会に推薦済みの者は再推薦が不要であることを踏まえ、
①選出選挙にて選出された候補者のうち、当会から推薦履歴がない者を推薦する
②名簿から名前が欠落していた者のうち、当会から推薦履歴がない者を理事会より推薦する

上記について審議され、①・②共に承認された。②については、該当者３名となった。

３．理事長・副理事長・補充理事選出

・理事長・副理事長について

2011年度理事（補充理事除く）11名による投票及び審議の結果、理事長に井上和秀理事、副理事長に池中一裕理事が選出された（任期は2013年２月末日迄)。なお、その他担当理事、委員会委員長については、次回理事会にて決定することとなった。

・補充理事選任について
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。
（50音順） 加藤忠史氏
馬場広子氏
和田圭司氏

4．理事長報告

高坂新一前理事長より理事長就任中の総括及び謝辞が述べられた。

5．庶務報告

井上和秀新理事長より、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
年会費長期未納者（未納期間：2007年度～）が報告され、2010年12月31日付けで44名に対し、除名処理を行ったことが報告された。
・評議員の退会希望について
退会を希望している評議員について、慰留結果が報告された。退会希望者３名のうち、１名は退会意志が固く慰留不能のため、退会処理済みである。もう２名は慰留に応じ、功労会員として本年総会へ推薦予定である。功労会員として当該２名を推薦することについて審議の結果、承認された。

6．会計報告

島田昌一会計担当理事より、会計報告がなされた。

・年会費未納者数について
年会費未納者数について報告され、引き続き督促を行う旨確認された。
また、評議員１名について功労会員への移行を前提として督促を行うこととなった。
・2010年度決算及び税務申告について
①2010年度決算について
2010年度決算が報告された。また、Neuro2010大会の収支決算が良好であったことについて大会長に謝意が述べられた。
②税務申告について
税務申告について法人税等計70,000円を申告済みである旨報告された。なお、2010年度の課税売上高が1,000万円を超過したため、2012年度における消費税納税義務者となったとのことであった。実際に納税の必要があるかどうかは2011年度の課税売上高によるとのことであった。

7．出版・広報報告

今泉和則出版・広報担当理事より、以下の通り報告された。

・機関誌「神経化学」の発行が順調に行われており、現在は50巻第１号発行に向け準備中である。
・会員検索システムのサーバーをXooNIpsへ移行し、ソフトがほぼ完成した。近々会員へ運用に向けアナウンス予定である。

8．委員会報告

(1) 将来計画委員会

池中一裕委員長より報告され、現在議論を進めている内容は次回理事会にて報告したいとのことであった。

(2) 出版・広報委員会
今泉和則委員長より、次の通り報告された。

・プレスリリースについて
Neuro2010にて3学会合同のプレスリリースを行い一定の効果を得たため、2011年度以降も継続することとし、大会前に社会性の高い演題を中心にマスコミへ情報発信を行いたいとのことであった。併せてプレスリリースにかかる指針が示され、異議なく承認された。

・機関誌の電子発行について
髙坂新一前理事長より、現在紙媒体で発行している機関誌「神経化学」を経費削減のため、原稿をPDFに変換した上でオンラインにて発行してはどうかと提案され、2社からの見積を取った結果、若干の経費節減が見込まれた。今後は対費用効果を加味してさらに検討を進めることとした。

・e-mail配信告知状況について
会員からのe-mail配信に対する同意状況について報告された。

・第107回日本精神神経学会学術総会への参加について
日本精神神経学会より、第107回日本精神神経学会学術総会にて行われる「関連学会からの報告」に2009年同様参加の打診があった旨報告された。
審議の結果、2009年開催時の状況を踏まえ、可能な限り理事長が参加することとなった。
また、髙坂新一前理事長より、日本学術会議から学会活動に関する原稿依頼があったため、原稿作成の上、提出済みである旨報告された。

(3) シンポジウム企画委員会
柳澤勝彦委員長より報告され、2011年度大会における日本神経化学会公開シンポジウムは「パーキンソン病研究の新展開：ミトコンドリア機能障害を中心に」(オーガナイザー 和田圭司氏) とし、9月26日 (月) 開催予定とのことであった。

(4) 国際対応委員会
和中明生委員長より、以下の通り報告された。

・2010年 APSN meeting (at Phuket) 【開催日】2010年10月18日～20日
Plenary Lecture：3
Special Lecture：2
シンポジウム：6
Young investigator colloquim：4
Poster：178
日本からの参加者は20名強であった。

・2011年 ISN/ESN meeting (at Athens) 【開催日】2011年8月28日～9月1日
当会若手海外派遣プロジェクトでtravel awardを募ったところ、2010年末までに19名の希望者があった。国際対応委員会にて応募書類の添削やチェックを行い、最終的に17名が応募した。
当初、同プロジェクトでは1研究室から1名の応募で計10名程度の規模を見込んでいたが、今回はそれよりも規模が大きく、かつ1研究室から複数の応募がある。委員会での議論の結果、awardは極力応募を受け付け、学会財政の状況を踏まえながら取り扱いを検討することとした。
また、大会会期前1週間でAdvanced School (教育プログラム) が開催され、こちらも旅費と宿泊費等の補助がある。本プログラムには上記の17名のうち、2名が重複応募している。

・2012年 APSN meeting (当会大会と合同開催) 【開催日】2012年9月29日～10月2日

神戸国際会議場にて開催予定（池中一裕大会長）。日本生物学的精神医学会と連合開催を予定している。プログラム委員長はWoong Sun氏（韓国 高麗大学）。

・2015年　ISN/APSN meeting

2010年末、APSNより2015年のmeeting開催地の立候補を募る旨連絡があった。国際対応委員会にて審議の結果、1）立候補締切日（2011年1月10日）が逼迫しており、広く大会長候補を募るのは難しい2）大規模な学会運営を要するため、世界的に知名度や業績が高い人物が大会長として立候補すべきであるとの観点から岡野栄之氏（慶應義塾大学）を大会長候補者として高坂新一前理事長へ推薦した。これを踏まえ、高坂新一前理事長から岡野氏へ打診され、岡野氏より快諾を得た。本件は2010年末に理事会にて持ち回り審議を行い、承認されたところである。

立候補は日本とオーストラリアから応募があり、オーストラリアはANS（オーストラリア神経科学学会）の執行部が代表となっているとのことである。

なお、開催地は、アテネで開かれるISN理事会における各候補地のプレゼンテーション及び投票を以って決定される。

・ISN理事選挙について

田代朋子氏の任期満了（2011年8月）を控え、ISN理事選挙が行われる予定である。

「地域別理事数分布」に基づき東アジアから理事1名を選出するため、理事候補のnomination（2011年2月15日締切）が行われた。

国際対応委員会では池中一裕氏を推薦し、2月10日時点でnominationが成立した。

今回の推薦は、池中氏がISN理事経験者であることを踏まえ、事前にISNへ多選であっても推薦可能か確認した上で進められた。

その後、池中氏本人へISN執行部より理事の多選を制限したいとの意向がメールで伝えられ、これを受けてやむを得ず立候補を辞退する事態となった。ISN執行部からの意向伝達が推薦締切直前であったため、新たな候補者を出すことができず締切を迎えた。

今回のISN執行部の行動は、ISN幹部が「推薦は個人単位で行われるべきものであり、学会等組織が関与すべきでない」との意向を持っているためと推測されるが、その旨公式に明文化されておらず、現時点では執行部の私的な意向と言わざるを得ない。また、nominationには同国人3名以内及び異国人7名以上の推薦が必要であり、nominationが成立した時点で、池中氏の推薦は当会に限った意思ではないことが明らかである。

今回の事態は極めて異例であり、国際対応委員会は強い違和感を持っている。

上記ISN理事選挙におけるISN執行部の行動に対し、理事より異議が相次いだ。また、「地域別理事数分布」にも不公平感が訴えられた。検討の結果、ISN理事である田代朋子氏、白尾智明氏から本件についてISN理事会にて事実確認を行い、多選についての明確な指針の策定を提案することになった。

(5) 研究助成金等候補者選考委員会

神庭重信委員長欠席のため、資料により報告された。

(6) 脳研究推進委員会

遠山正彌委員長より、以下の通り報告された。

・脳科学研究戦略推進プログラム（脳プロ）について、文部科学省研究振興局ライフサイエンス課の努力もあり、フェアな選考に向け状況が改善されているように見受けられるが、一部透明性を欠くものもあり、引き続き注視していきたい。

・各種大会等で発達障害を積極的に取り上げてほしい。発達障害、心理、精神科等の領域は今後重要なキーワードとして注目されていく分野であり、当会でも重要視していきたい。

(7) 奨励賞選考委員会

和田圭司委員長より報告され、2011年度奨励賞募集に向け準備を進めている。今回は応募締

切を５月27日（金）必着とする予定である。

(8) 連合大会委員会

井上和秀委員長より2013年開催予定の日本神経科学学会との合同大会について、同会会長・副会長と当会理事長・副理事長が面談の上、覚書を交わした旨報告された。覚書の内容は、2010年合同大会での運用をベースとし、新たに余剰金や赤字負担金は各学会の総会員数で按分する旨が追加されたとのことであった。

9．第53回大会（2010年度）について

井上和秀大会長より第53回大会（2010年度）について、挨拶と謝辞が述べられた。

10．その他

特になし。

【審議事項】

1．評議員の推薦候補者について

井上和秀新理事長より報告され、審議の結果、候補者２名に対し、総会への推薦が承認された。

2．名誉会員の推薦候補者について

井上和秀新理事長より報告された。適宜理事より井上和秀新理事長に適任者を推薦することとなり、年齢、貢献度等を踏まえ、次回理事会にて候補者を決定することとなった。

3．第54回（2011年度）大会について

米田幸雄大会長より、開催案について報告された。

【概要】

会　　　期：2011年９月26日（月）～28日（水）
場　　　所：瑠璃光　〒922-0295　石川県加賀市山代温泉
URL：http://www.p.kanazawa-u.ac.jp/~jsn54/
テ　ー　マ：「分子とこころ」A molecule for mind
同 時 開 催：故ニーレンバーグ博士追悼シンポジウム
事前参加登録期間：2011年５月６日（金）～７月29日（金）
演題登録期間：2011年５月６日（金）～７月１日（金）
宿泊申込期間：2011年５月６日（金）～８月26日（金）
大　会　長：米田　幸雄（金沢大学医薬保健研究域薬学系）
事 務 局 長：檜井　栄一（金沢大学医薬保健研究域薬学系准教授）
組織委員長：東田　陽博（金沢大学医薬保健研究域医学系教授）
組織委員(50音順)：加藤　　聖（金沢大学医薬保健研究域医学系教授）
加藤　将夫（金沢大学医薬保健研究域薬学系教授）
程　　　肇（金沢大学理工研究域理学系教授）
三邉　義雄（金沢大学医薬保健研究域医学系教授）
村本健一郎（金沢大学理工研究域工学系教授）
山田　正仁（金沢大学医薬保健研究域医学系教授）

【日程表】

企画名	言語	日時	内容等
神経化学カレッジ	日本語	9／25（日）14：00～17：15 30分×6テーマ（15分休憩）	①シナプス伝達 ②ニューロン ③グリア ④神経幹細胞 ⑤うつ病 ⑥アルツハイマー病
日本神経化学会公開シンポジウム	英語	9／26（月）12：45～15：15	パーキンソン病研究の新展開：ミトコンドリア機能障害を中心に
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	英語	9／27（火）9：15～11：30	
最優秀奨励賞受賞者講演	英語	9／28（水）9：30～10：00	
シンポジウム（1～13）	英語	9／26（月）～28（水） 1シンポジウム＝135分 （テーマ背景説明15分、30分×4演題）	4演題×13シンポジウム＝52演題
一般口演（1～7）	日本語	9／26（月）～28（水） 1コマ＝20分×6演題	6演題×7コマ＝42演題
大学院生口演（1～5）	日本語	9／26（月）～28（水） 1コマ＝20分×6演題	6演題×5コマ＝30演題
ポスター発表	日本語	9／26（月）～27（火） 終日展示、1時間討論	100演題×2日＝200演題
ニーレンバーグ先生追悼シンポジウム（1～7）	英語	9／26（月）～28（水） 1シンポジウム＝30分×4演題	4演題×7シンポジウム＝28演題

その他、スケジュール案、参加登録費案、宿泊料金案が報告された。
また、2011年より当会大会は、日本神経学会専門医資格更新にかかる取得単位の対象となる企画（講演会）として認定される旨確認された。

4．第55回（2012年度）大会について

池中一裕大会長より、開催案について報告された。

■APSN 11th biennial meetingと合同開催
■日本生物学的精神医学会（9／28～9／30）とゆるやかな連合開催
開催日：2012年9月29日（土）～10月2日（火）※9月29日は懇親会（get together）
シンポジウム提出期限：2011年7月31日（日）
アブストラクト提出期限：2012年3月1日（木）
プログラム委員長：Woong Sun氏（韓国 高麗大学）

・プログラム委員会はAPSN側から5名、日本側から5名となる。
・Local organizerは準備段階として現在4名決定しているが、順次増員予定である。

また、議場にて以下の点が確認された。
・大会から日本在住のシンポジストに金銭的補助は行わない。なお、海外から参加のシンポジストには平均500ドル程度の補助が行われる。
・日本生物学的精神医学会と合同でシンポジウムを行う。

5．第56回（2013年度）大会について

木山博資大会長より、以下の通り報告された。

・2010年同様、日本神経科学学会との合同大会（Neuro大会）となった。8．委員会報告の（8）連合大会委員会にて報告された覚書に沿って準備を進めていく。また、WFSBP World Congress（武田雅俊大会長）とゆるやかな連合を行うこととし、WFSBP会期前にNeuro大会を開催する予定である。
WFSBPを含め共通のテーマを設けたいが、全日程で5～6日間程度あるため、参加者数維持に工夫が必要であると考えている。

6．第57回（2014年度）大会について

高坂新一前理事長より、大会長として塩坂貞夫氏（奈良先端科学技術大学院大学）を推薦したい旨提案され、議場に諮ったところ、異議なく承認された。

引き続き塩坂貞夫大会長より、以下の通り報告された。

会場は奈良県新公会堂とし、開催時期を9月で検討したい。日本神経科学学会の開催も踏まえつつ、具体的な日程を考えていく。

7．その他

井上和秀新理事長、池中一裕副理事長より挨拶がなされた。

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。

第55回日本神経化学会・第11回アジア太平洋神経化学会合同大会

神戸国際会議場

2012年9月30日～10月2日

第55回日本神経化学会、第11回アジア太平洋神経化学会の合同大会が神戸国際会議場において、来年（平成24年）９月30日より10月２日にわたり開催されます。今大会は第34回生物学的精神医学会とも連携し、科学的により広範囲な会となることが期待されます。
本合同大会プログラムは、プレナリーレクチャー（４）、シンポジウム（12）、若手研究者コロキウム、一般演題（ポスター、口演）などからなり、広くアジア太平洋地域からの研究者の参加も見込まれています。日本国内外における最新の情報を得、また討論に参加するよい機会となるので、是非ご参加ください。

一般演題（ポスター、口演）発表の〆切は、平成24年３月１日です。
応募詳細その他本合同大会に関する最新の案内は、本合同大会HPに掲載されています。
http://www.congre.co.jp/jsn-apsn2012/index.html

プログラムに関するお問い合わせは、
プログラム委員長（Dr. Woong Sun）woongsun@korea.ac.kr
運営に関するお問い合わせは　jsn-apsn2012@congre.co.jp

プログラム
Program

日本神経化学会公開シンポジウム
JSN Open 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
Symposium

故ニーレンバーグ先生追悼シンポジウム
〈金沢大学 子どものこころの発達研究センター 共催〉
Dr. Nirenberg Memorial Symposium

一般口演
Oral Sessions

大学院生口演
Graduate Oral Sessions

ポスター発表
Poster Sessions

ランチョンセミナー
Luncheon Seminars

日本神経化学会公開シンポジウム

9月26日（月）

12：45〜15：15　A会場（1Ｆ・花離宮）

OS-1〜OS-5　パーキンソン病研究の新展開　〜ミトコンドリア機能障害を中心に

座長：和田　圭司（国立精神・神経医療研究センター）
望月　秀樹（北里大学医学部神経内科学）

OS-1　**パーキンソン病モデルマウスに対する水素含有飲用水の神経保護作用**

○藤田　慶大[1]、田中　喜典[2]、城戸　瑞穂[3]、片渕　俊彦[4]、中別府　雄作[5]
[1]九州大学大学院薬学研究院病態生理学分野、[2]パナソニック電工株式会社電器R&Dセンター健康科学研究室、[3]九州大学歯学研究院分子口腔解剖学分野、[4]九州大学医学研究院統合生理学分野、[5]九州大学生体防御医学研究所脳機能制御学分野

OS-2　**神経保護剤としてのミトコンドリア栄養素Coenzyme Q_{10}**

○光本　泰秀
北陸大学薬学部医療薬学講座代替医療薬学分野

OS-3　**パーキンソン病および他の神経疾患のiPS細胞技術を用いた病態解析**

○岡野　栄之
慶應義塾大学医学部生理学教室

OS-4　**MPTP誘導性パーキンソン病マウスモデルにおけるドパミン神経変性機序**

○安田　徹[1]、水野　美邦[2]、望月　秀樹[1]
[1]北里大学医学部神経内科学、[2]北里大学医学部神経再生医療学

OS-5　**パーキンソン病関連変異型UCH-L1の異常な分子性質**

○株田　智弘
国立精神・神経センター　神経研究所　疾病研究第四部

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

9月27日（火）

9：15～11：30　A会場（1F・花離宮）

JS-1～JS-4　うつ病の分子的基盤

座長：神庭　重信（九州大学精神病態医学分野）
加藤　忠史（理研脳センター）

JS-1　**うつ病におけるグリアを介した神経栄養因子・成長因子の役割**
○竹林　実
国立病院機構呉医療センター・中国がんセンター　精神科・臨床研究部

JS-2　**エピジェネティクスとストレス脆弱性、うつ病**
○山形　弘隆、内田　周作、大朏　孝治、芳原　輝之、渡邉　義文
山口大院・医・高次脳機能病態学

JS-3　**神経栄養因子BDNFとHPA系のクロストーク**
○沼川　忠広[1]、安達　直樹[1,2]、功刀　浩[1,2]
[1]（独）国立精神・神経医療研究センター・神経研・疾病三部、[2]戦略的創造研究推進事業（CREST），JST

JS-4　**うつ病の神経炎症仮説**
○門司　晃
佐賀大学医学部精神医学講座

シンポジウム

9月26日（月）

9：30～11：45　A会場（1Ｆ・花離宮）

S01-1～S01-4　**中枢神経障害・神経損傷に対する新規薬物治療と修復再生を目指して**

座長：伊藤　芳久（日本大学薬学部・薬理）
萩田喜代一（摂南大学薬学部・薬理）

S01-1　**選択的Na^+/Ca^{2+}交換系阻害はMPTP誘発パーキンソン病マウスモデルの黒質-線条体ドパミン神経障害を軽減する**

○田熊　一敞[1]、梨子田　哲明[1]、川崎　俊之[2]、吾郷　由希夫[1]、松田　敏夫[1,3]
[1]大阪大院・薬・薬物治療、[2]理研・分子イメージング研・機能評価、[3]大阪大院・連合小児発達・子どものこころセ

S01-2　**興奮毒性に対する$GABA_B$受容体の保護効果**

○倉本　展行、新原　博輝、田中　菜月、山田　健一、鷲田　水保、伊藤　槙智子、荻田　喜代一
摂南大・薬・薬理

S01-3　**化学療法薬Mithramycinの脳虚血に対する治療効果**

○小菅　康弘、石毛　久美子、伊藤　芳久
日本大学薬学部薬理学研究室

S01-4　**サカナの中枢神経再生：その分子メカニズムから哺乳類への応用まで**

○加藤　聖[1]、松川　通[1]、郡山　恵樹[1]、永島　幹子[1,2]、大貝　和裕[2]、杉谷　加代[2]
[1]金沢大院・医・脳情報分子学、[2]金沢大院・保

9月26日（月）

9：30～11：45　B会場（2Ｆ・鳳凰）

S02-1～S02-4　**精神障害の新規原因分子について―最近の知見から―**

座長：那波　宏之（新潟大学・脳研・分子神経生物）
新田　淳美（富山大学大学院医学薬学研究部（薬学）・薬物治療学研究室）

S02-1　**上皮成長因子ファミリー分子によるドーパミン過剰発達と統合失調症**

○那波　宏之、水野　誠、外山　英和
新潟大学・脳研・分子神経生物

S02-2　**舞踏病原因遺伝子VPS13A変異による精神障害発症機構**

○佐野　輝
鹿児島大院・医歯・精神機能病学

Symposium

S02-3　**新規薬物依存抑制因子shatiの機能解析**

○鳥海　和也[1]、丹羽　美苗[1]、古関　竹直[1]、永井　拓[2]、宋　梓瑜[3]、新田　淳美[4]、山田　清文[2]、福島　健[3]、鍋島　俊隆[1]
[1]名城大院・薬・薬品作用学、[2]名古屋大院・医・医療薬学、[3]東邦大・薬・薬品分析学、[4]富山大院・医学薬学研究部・薬物治療学

S02-4　**覚せい剤精神病マウス側坐核から単離された精神病関連分子について**

○新田　淳美[1]、日比　陽子[2]、宇野　恭介[1]、鍋島　俊隆[3]、宮本　嘉明[1]
[1]富山大学大学院医学薬学研究部（薬学）・薬物治療学研究室、[2]名古屋大学大学院医学系研究科・医療薬学・附属病院薬剤部、[3]名城大学比較認知科学研究所 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

Symposium

9月26日（月）

15：15～17：30　A会場（1F・花離宮）

S03-1～S03-4　**統合失調症の最先端研究：全ゲノム解析から環境要因による神経発達障害の分子機構まで**

座長：貝淵　弘三（名古屋大院・医・神経情報薬理）
山田　清文（名古屋大院・医・医療薬学）

S03-1　**統合失調症の全ゲノム解析**

○岩田　仲生
藤田保健衛生大学医学部精神神経科学講座

S03-2　**統合失調症の発症脆弱性因子DISC1の病態生理機能**

○貝淵　弘三
名古屋大院・医・神経情報薬理

S03-3　**統合失調症の候補遺伝子の神経生物学**

○橋本　亮太[1,2,3]、安田　由華[2,3]、大井　一高[2,3]、福本　素由己[2,3]、山森　英長[2,3]、梅田　知美[2]、岡田　武也[2,3]、高雄　啓三[3,4]、小林　克典[3,5]、楯林　義孝[3,6]、宮川　剛[3,4]、貝淵　弘三[3,7]、岩田　仲生[3,4]、尾崎　紀夫[3,7]、武田　雅俊[1,2]
[1]大阪大院・連合小児、[2]大阪大院・医・精神医学、[3]CREST, JST、[4]藤田保健衛生大学、[5]日本医科大学、[6]東京精神研究所、[7]名古屋大院・医

S03-4　**PolyI:C誘発性神経発達障害モデル：脳機能障害におけるIFITM3の役割**

○山田　清文
名古屋大院・医・医療薬学

9月26日（月）

15：15～17：30　B会場（2F・鳳凰）

S04-1～S04-4　ニューロンとグリアにおけるセプチン細胞骨格の機能解明に向けたアプローチ

座長：永田　浩一（愛知県コロニー発達障害研究所・神経制御学部）
木下　専（名古屋大院・理・生命理学）

S04-1　**神経突起伸長におけるセプチン依存性微小管制御メカニズムの解析**
○木下　専、上田（石原）奈津実
名古屋大院・理・生命理学

S04-2　**Cdk5のリン酸化によるSeptin5の機能制御**
○浅田　明子、谷口　誠、久永　眞市
首都大・生命

S04-3　**セプチン・モジュールによる神経細胞の形態制御**
○ヘルゲ　エバース
スイス連邦工科大学

S04-4　**大脳皮質形成におけるSeptinファミリー分子の機能**
○篠田　友靖[1]、伊東　秀記[1]、貝淵　弘三[2]、永田　浩一[1]
[1]愛知県コロニー発達障害研究所・神経制御学部、[2]名古屋大院・医・神経情報薬理

9月27日（火）

9：15～11：30　B会場（2F・鳳凰）

S05-1～S05-4　スパイン病の神経生物学と病態生理学

座長：福永　浩司（東北大学大学院・薬・薬理学分野）
林　康紀（理化学研究所脳科学総合研究センター）

S05-1　**カルモデュリンキナーゼファミリーによるスパインの形態および可塑性調節**
○ソダリング　トーマス
Vollum Institute, Oregon Health and Science University

S05-2　**Structural role of CaMKII**
○林　康紀
理化学研究所脳科学総合研究センター

S05-3　**樹状突起スパインにおけるドレブリン結合型アクチン線維の活動依存的集積度変化**
○白尾　智明
群馬大学大学院医学系研究科神経薬理学教室

Symposium

S05-4 **ATRX変異精神遅滞マウスにおけるスパイン形態異常**

○福永　浩司[1]、塩田　倫史[1]、別府　秀幸[2]、北島　勲[2]
[1]東北大学大学院・薬・薬理学分野、[2]富山大学大学院・医薬・臨床分子病態検査学講座

9月27日（火）

12：30～14：45　A会場（1Ｆ・花離宮）

S06-1～S06-4 **神経形態制御から機能へ — スペーシャルセルバイオロジーの観点から**

座長：小西　慶幸（福井大学大学院工学研究科知能システム工学専攻、福井大学生命科学複合研究教育センター）
佐藤　　真（福井大・医・形態機能、福井大学　生命科学複合研究教育センター、福井大学医学系大学院附属子どもの発達研究センター）

Symposium

S06-1 **軸索形態制御に関わる翻訳後修飾を介した細胞内分子機構：軸索伸長および軸索識別についての研究**

○小西　慶幸[1,2]
[1]福井大学大学院工学研究科知能システム工学専攻、[2]福井大学生命科学複合研究教育センター

S06-2 **大脳皮質形成時の法線方向の移動神経細胞において、樹状突起先端の成長円錐の活性は、Abl kinaseとCdk５によりWAVE2-Abi2を介し制御され、この活性化が神経細胞の多極性から双極性への形態変化、そしてラディアルグリア上の移動開始に必須である**

○佐藤　真[1,2,3]
[1]福井大・医・形態機能、[2]福井大学　生命科学複合研究教育センター、[3]福井大学医学系大学院附属子どもの発達研究センター

S06-3 **CaMKK-CaMKIカスケードによる神経細胞形態形成制御と大脳皮質構築**

○尾藤　晴彦[1,2]、鈴木　敢三[1]、上條　諭志[1]、堀金　慎一郎[1]、安達-森島　亜希[1]、竹本-木村　さやか[1]
[1]東京大院・医・神経生化、[2]CREST-JST

S06-4 **神経細胞が突起の長さを検知する仕組みと神経細胞の対称性の破れ**

○稲垣　直之
奈良先端大・バイオ・神経形態形成

9月27日（火）

12：30～14：45　B会場（2F・鳳凰）

S07-1～S07-4　生活環境が作り出す脳機能の多様性

座長：永井　拓（名古屋大学大学院医学系研究科医療薬学・医学部附属病院薬剤部）
古屋敷智之（京都大院・医・神経細胞薬理）

S07-1　神経精神発達に対する幼若期ストレスの影響

○永井　拓[1]、尹　錫在[1]、日比　陽子[1]、山田　清文[1,2]
[1]名古屋大学大学院医学系研究科医療薬学・医学部附属病院薬剤部、[2]CREST, JST

S07-2　反復社会挫折ストレスへの脆弱性におけるプロスタグランジン依存的な前頭皮質ドパミン系脱感作の役割

○古屋敷　智之、田中　昂平、北岡　志保、千歳　雄大、成宮　周
京都大院・医・神経細胞薬理

S07-3　環境因子/ストレスホルモンによるうつ様行動の発現と代謝型グルタミン酸2/3受容体

○吾郷　由希夫[1]、田熊　一敞[1]、松田　敏夫[1,2]
[1]大阪大学大学院薬学研究科薬物治療学分野、[2]大阪大学大学院大阪大学・金沢大学・浜松医科大学連合小児発達学研究科

S07-4　依存性薬物が引き起こす側坐核神経可塑性メカニズムの異常と、その機能的役割

○戸田　重誠
金沢大学附属病院神経科神経科

9月27日（火）

14：45～17：00　A会場（1F・花離宮）

S08-1～S08-4　行動を規定する脳基盤：こころの分子メカニズム

座長：橋本　均（大阪大学大学院薬学研究科神経薬理学）
橋本　亮太（大阪大院・連合小児・子どものこころ、大阪大院・医・精神医学、CREST, JST）

S08-1　精神疾患の遺伝子×環境相互作用：PACAP依存的なストレス応答と疾患の関連

○橋本　均[1]、新谷　紀人[1]、早田　敦子[2]、馬場　明道[4]
[1]大阪大学大学院薬学研究科神経薬理学、[2]大阪大学・金沢大学・浜松医科大学・連合小児発達学研究科・附属子どものこころの発達研究センター、[3]大阪大学大学院・医学系研究科・分子医薬学、[4]兵庫医療大学薬学部

S08-2　DISC1と精神疾患発症のメカニズム

○松崎　伸介[1,2,3]、服部　剛志[2,4]、伊藤　彰[4]、片山　泰一[1]、遠山　正彌[1,2,3]

Symposium

[1]大阪大学大学院・連合小児発達学研究科・こころの発達神経科学講座・分子生物遺伝学領域、[2]大阪大学大学院・連合小児発達学研究科・子どものこころ発達分子統御機構研究センター、[3]大阪大学大学院　医学系研究科　神経機能形態学講座、[4]大阪大学大学院　医学系研究科　分子精神神経学（大日本住友製薬）寄附講座

S08-3　**成長円錐における機能分子の探索**
○五十嵐　道弘
新潟大・医歯学・分子細胞機能学（医・生化学２）

S08-4　**ヒト脳表現型と分子を結ぶ新しいアプローチ：ヒト脳表現型コンソーシアム**
○橋本　亮太[1,2,3]、大井　一高[2,3]、安田　由華[2,3]、福本　素由己[2,3]、山森　英長[2,3]、梅田　知美[4]、岡田　武也[2]、岩瀬　真生[2]、数井　裕光[2]、武田　雅俊[2]
[1]大阪大院・連合小児・子どものこころ、[2]大阪大院・医・精神医学、[3]CREST, JST、[4]大阪大院・医・分子精神神経学

Symposium

９月27日（火）

14：45～17：00　Ｂ会場（２Ｆ・鳳凰）

S09-1～S09-4　**中枢神経系と摂食・エネルギー代謝調節**
座長：幸田　修一（アスビオファーマ（株）、ハーバード大学医学部 & ベスイスラエルディーコネスメディカルセンター）
鈴木　亮（東京大院・医・糖尿病・代謝内科）

S09-1　**視床下部外側野に局在する新規神経ペプチドによる摂食行動の制御**
○櫻井　武
金沢大学医薬保健研究域医学系分子神経科学・統合生理学分野

S09-2　**脂肪萎縮症を対象としたレプチン補充療法におけるfMRIを用いた摂食関連脳神経活動の解析**
○海老原　健[1]、青谷　大介[2]、澤本　伸克[3]、細田　公則[1]、福山　秀直[3]、中尾　一和[2]
[1]京都大学医学部附属病院　探索医療センター、[2]京都大学大学院医学研究科　内分泌代謝内科、[3]京都大学大学院医学研究科　高次脳機能総合研究センター

S09-3　**糖尿病が脳コレステロール代謝に与える影響**
鈴木　亮
東京大院・医・糖尿病・代謝内科

S09-4　**分子遺伝学的手法を用いた中枢神経系の摂食調節機構の解明-視床下部AgRPニューロンの急速かつ可逆的な活性化は強力な摂食行動を誘導する-**
○幸田　修一[1,2]、クライシス　マイケル[2]、イ　チャンピン[2]、ロス　ブライアン[3]、ローエル　ブラッドフォード[2]
[1]アスビオファーマ（株）、[2]ハーバード大学医学部 & ベスイスラエルディーコ

ネスメディカルセンター、[3]ノースカロライナ大学医学部

9月28日（水）

9：30～11：45　A会場（1Ｆ・花離宮）

S10-1～S10-4　イノシタイド・シグナルの多様性

座長：永田栄一郎（東海大学医学部内科学系神経内科）
三村　徹郎（神戸大院・理・生物）

S10-1　哺乳類中枢神経系におけるイノシトール6リン酸キナーゼの役割

○永田　栄一郎
東海大学

S10-2　イノシトールリン酸の植物における生理機能と網羅的測定

○三村　徹郎[1]、三橋　尚登[1]、益田　陽平[1]、田中　由祐[1]、
リチャードソン　アラン[2]、チュン　スン-キー[3]、八木澤　仁[4]
[1]神戸大院・理・生物、[2]シーエスアイアルオー　植物工場、[3]ポハン工科大学・化学科、[4]兵庫県立大学院・生命理学

S10-3　神経細胞内へのカルシウム流入はホスホリパーゼＣデルタ１の核移行と核収縮を引き起こす

○八木澤　仁、岡田　雅司
兵庫県立大院・生命理学・生体情報II

S10-4　NMDA受容体により誘導される長期抑圧において、PI(4,5)P_2産生酵素PIP5KはAMPA受容体のエンドサイトーシスに重要である

鵜木　隆光[1]、松田　信爾[2]、掛川　渉[2]、船越　祐司[1]、柚崎　通介[2]、
○長谷川　潤[1,3]、金保　安則[1]
[1]筑波大院・人間総合・生理化学、[2]慶応大・医・生理学、[3]筑波大院・人間総合・若手イニシアティブ

9月28日（水）

9：30～11：45　B会場（2Ｆ・鳳凰）

S11-1～S11-4　機能回復を目指した網膜・視神経の生存と再生の新規ストラテジー

座長：原　　英彰（岐阜薬科大学生体機能解析学大講座薬効解析学研究室）
群山　恵樹（金沢大院・医・脳情報分子学）

S11-1　視神経損傷後の新規細胞外マトリックス分子プルプリンによるラット網膜神経節細胞の生存と軸索再伸長

○郡山　恵樹、松川　通、永島　幹子、加藤　聖
金沢大院・医・脳情報分子学

Symposium

S11-2　**視中枢への新たな視神経再生－眼炎症、PTEN遺伝子欠損、cAMPアナログ併用による相乗効果についてー**
○栗本　拓治
大阪医科大学眼科学教室

S11-3　**網膜・視神経障害に伴う視路変性およびその治療戦略**
○嶋澤　雅光、原　英彰
岐阜薬科大学生体機能解析学大講座薬効解析学研究室

S11-4　**緑内障における神経保護治療**
○中澤　徹
東北大院・医・眼科

9月28日（水）

13：30～15：45　A会場（1F・花離宮）

S12-1～S12-4　**中枢神経系における小胞体ストレス応答の重要性**
座長：工藤　喬（大阪大学大学院医学系研究科精神医学教室）
堀　修（金沢大学・医・神経分子）

S12-1　**ERストレスと精神神経疾患―治療戦略への応用**
工藤　喬、光田　輝彦、近江　翼、阪上　由香子、武田　雅俊
大阪大学大学院医学系研究科精神医学教室

S12-2　**小胞体膜貫通型転写因子OASISのアストロサイト分化における役割**
○齋藤　敦[1]、佐野坂　司[2]、中島　欽一[2]、今泉　和則[1]
[1]広島大院・医・放射線ゲノム・分子細胞情報学、[2]奈良先端大・バイオ・分子神経

S12-3　**小胞体のタンパク質分解系ERADのアルツハイマー病への関与**
○金子　雅幸[1]、大熊　康修[1]、野村　靖幸[2]
[1]千葉科学大・薬・薬理、[2]横浜薬大・薬・薬物治療

S12-4　**MPTP誘導性神経障害に対する小胞体ストレス応答の役割**
○堀　修
金沢大学・医・神経分子

9月28日（水）

13：30～15：45　B会場（2F・鳳凰）

S13-1～S13-4　**ニューロン・グリア機能連関の新展開**
座長：柴崎　貢志（群馬大院・医・分子細胞生物学）
鹿川　哲史（東京医歯大・難研・幹細胞制御）

S13-1 アストロサイトが局所電場電位（LFP）に与える影響

○平瀬　肇
理化学研究所・脳科学総合研究センター

S13-2 脳内温度と神経活動の機能相関；温度センサーを発現する特殊なアストロサイト亜集団による神経機能調節

○柴崎　貢志
群馬大院・医・分子細胞生物学

S13-3 中枢神経系グリア細胞の発生分化研究の現状と展望

○鹿川　哲史[1]、備前　典久[1]、柏木　太一[1]、信久　幾夫[1]、清水　健史[2]、田賀　哲也[1]
[1]東京医歯大・難研・幹細胞制御、[2]国立シンガポール大・メカノバイオロジー研究所

S13-4 アストロサイトによる軸索を介したシナプス伝達の遠隔調節

○佐々木　拓哉
自然科学研究機構・生理学研究所・脳形態解析研究部門

Symposium

故ニーレンバーグ先生追悼シンポジウム
金沢大学 子どものこころの発達研究センター 共催

9月26日（月）

9：30～11：30　特別会場（1Ｆ・能残月）

M1-1　Marshall Warren Nirenberg, Honorary member of JSN: Nobel laureate and giant of science
○永津　俊治
藤田保健衛生大学、名古屋大学

M1-2　The potential role of ATF4 in learning and memory
○Lloyd Greene
Columbia University

M1-3　Single nucleotide polymorphisms of CD38 and oxytocin treatment for 6 subjects with autism spectrum disorders
○Yulia A. Pichugina
Krasnoyarsk Medical University

9月26日（月）

15：15～17：15　特別会場（1Ｆ・能残月）

M2-1　alpha-Synuclein in Parkinson's disease:Pathogenetic foe and therapeutic target
○M. Maral Mouradian
University of Medicine and Dentistry of New Jersey -Robert Wood Johnson Medical School

M2-2　Marshall and Medicine: impact on drug discovery
○Orest Hurko
Biologics Consulting Group, Inc.

M2-3　Regulatory approval of biopharmaceutical products
○James G. Kenimer
Biologics Consulting Group, Inc.

M2-4　A study of generations at high-risk for major depression
○Myrna M. Weissman
Columbia University

M2-5　Neuroscientists of the Future: Empirical Research on the Development and Career Decisions of Young Scientists
○Richard McGee Jr

Northwestern University

9月27日（火）

9：30～11：30　特別会場（1F・能残月）

M3-1　Bone morphogenetic proteins regulate ErbB3/GGF2 signaling to promote gliogenesis in the enteric nervous system
○Alcmène Chalazonitis
Columbia University

M3-2　Transmembrane agrin in filopodia regulation and synapse formation
○Mathew P Daniels
National Heart Lung and Blood Institute, NIH

M3-3　ECT2, an ortholog of drosophila's pebble identified from RNAi screening, regulates neuronal differentiation
○東田　知陽
金沢大学大学院医学系研究科脳細胞遺伝子学

M3-4　Neural progenitors express topographic markers
○David Trisler
University of Maryland　School of Medicine

9月27日（火）

12：30～17：00　特別会場（1F・能残月）

M4-1　Regulation of neurokine receptor signaling and trafficking
○Neil M. Nathanson
University of Washington

M4-2　Removal of adult-generated neurons and hippocampal function
○Woong Sun
Korea University

M4-3　Botulinum neurotoxin: Lethal agent or wonder drug
○Michael Adler
USAMRICD

M4-4　Therapeutic potentials of fetal neural stem cells treated with fluoxetine for Alzheimer's disease model mice
○Yoo-Hun Suh
Seoul Nat'l University

M4-5 Cholinergic therapy for Schizophrenia and Alzheimer's disease: new approaches
○Dana Hilt
Envivo Pharmaceutical

M4-6 Effects of cannabinoids on microglial and T cells: Role in an animal model of multiple sclerosis
○Zvi Vogel
Weizmann Institute of Science and the Adelson Center for Addictive Diseases Tel Aviv University

M4-7 Inhibition of myostatin activity by antibodies as a therapeutic approach to Amyotrophic Lateral Sclerosis
○Frank S Walsh
Wolfson Centre for Age Related Diseases Kings College

M4-8 Neuromodulations mediated by dextro-morphinans
○Hyoung-Chun Kim
Kangwon National University

9月28日（水）

9：30～11：30 特別会場（1Ｆ・能残月）

M5-1 Molecular analysis of central feeding regulation by neuropeptide Y (NPY) neurons with NPY receptor siRNAs
○樋口 宗史
新潟大学

M5-2 Retinovascular biology and pathophysiology
○Donald Puro
Department of Ophthalmology and Visual Science Department of Physiology

M5-3 Histamine H1 receptor functions in CNS and peripheral tissues
○福井 裕行
徳島大学大学院ヘルスバイオサイエンス研究部分子情報薬理学分野

一般口演

９月26日（月）

９：30〜11：30　Ｃ会場（２Ｆ・平安）

O1-1〜O1-6　気分障害・情報伝達
座長：齋藤　利和（札幌医科大学医学部神経精神医学講座）
木山　博資（名古屋大学大学院医学系研究科機能組織学（解剖学第二））

O1-1　電気けいれんにおけるpro-BDNFプロセッシング酵素の関与
○松本　知也[1,2]、瀬川　昌弘[1,2]、森信　繁[1,2]、淵上　学[1,2]、山脇　成人[1,2]
[1]広島大院・医歯薬・精神神経、[2]JST・CREST

O1-2　Neuropeptide Y knock outマウスはカロリー制限による寿命延長効果を示さない
○千葉　卓哉、小松　利光、森　亮一、下川　功
長崎大・院・医歯薬学総合・探索病理学

O1-3　Cdk5-p35とCdk5-p39の安定性の違いの構造基盤
○斎藤　太郎[1]、矢野　雅士[1]、河合　悠成[1]、浅田　明子[1]、土居　洋文[2]、久永　眞市[1]
[1]首都大院・理工・生命・神経分子機能、[2]セレスター・レキシコ・サイエンシズ

O1-4　新規化合物1-deoxy-nor-sominone（Denosomin）によるアストロサイトを介した脊髄損傷の改善作用
○勅使川原　匡[1]、久保山　友晴[1]、松谷　裕二[2]、東田　千尋[1]
[1]富山大・和漢薬研・薬効解析、[2]富山大・薬・薬品製造

O1-5　情動行動と前頭前野における脳由来神経栄養因子の作用の慢性拘束ストレス暴露による変化
○千葉　秀一[1,2]、沼川　忠広[2,3]、二宮　碧[2,4]、リチャーズ　ミスティ[2,5]、若林　千里[2]、氷見　敏行[1]、功刀　浩[2,3]
[1]武蔵野大学　薬学部　安全性学研究室、[2]国立精神・神経医療研究センター　神経研究所　疾病研究第三部、[3]科学技術振興機構CREST、[4]早稲田大学大学院　先進理工学研究科　薬理学研究室、[5]アルバニー医科大学　神経薬理学・神経科学センター

O1-6　Pig D-beta-アミノイソ酪酸：ピルビン酸アミノ基転移酵素配列決定および脳内分布同定
○安部　賢郎、越智　紳一郎、森　蓉子、上野　修一
愛媛大院・医・脳とこころの医学

Oral Sessions

9月26日（月）

15：15〜17：15　C会場（2Ｆ・平安）

O2-1〜O2-6　**神経変性・筋疾患**

座長：島田　昌一（大阪大学大学院医学系研究科・神経細胞生物学講座（第一解剖））
仲田　義啓（広島大学大学院医歯薬学総合研究科）

O2-1　**エンドセリンによるラット大脳でのVEGF-A産生促進とVEGF受容体の活性化**

○小山　豊[1]、永江　隆二[2]、徳山　尚吾[2]、田中　一裕[1]、道永　昌太郎[1]
[1]大阪大谷大学薬学部薬理学、[2]神戸学院大学薬学部臨床薬学

O2-2　**SOD1^{H46R}遺伝子トランスジェニックALSマウスモデルにおいてグリア線維性酸性蛋白の欠損は疾患をわずかに進行させる**

○秦野　伸二[1,2]、吉井　康裕[3]、大友　麻子[1]、潘　雷[1]、大塚　正人[1]、岩崎　泰雄[3]
[1]東海大・医・分子生命、[2]東海大院・医・脳神経疾患研究セ、[3]東邦大・医・神経内科

O2-3　**新規神経軸索誘導因子FLRT2とFLRT3によるUnc5細胞に対する反発作用**

○山岸　覚[1,2]、Hampel Falko[2]、羽田　克彦[3]、Del Toro Daniel[2]、Schwark Manuela[4,5]、Kvachnina Elena[4]、Bastmeyer Martin[6]、山下　俊英[3]、Tarabykin Victor[4,5]、Egea Joaquim[7]、Klein Ruediger[2]
[1]浜松医科大・解剖学、[2]Max-Planck 神経生物学研究所、ミュンヘン、ドイツ、[3]大阪大学・医、[4]Max-Planck 実験薬学研究所、ゲッティンゲン、ドイツ、[5]Charite-Universitaetsmedizin Berlin, ベルリン、ドイツ、[6]Universitaet Karlsruhe (TH), カールスルーエ、ドイツ、[7]Universitat de Lleida/IRBLLEIDA, イェイダ、スペイン

O2-4　**コンドロイチン硫酸合成酵素ノックアウトマウスは脊髄損傷回復が早い**

○武内　恒成[1,2]、比嘉　進[1]、吉岡　望[3]、工藤　千佳[1]、川野　仁[3]、五十嵐　道弘[1,2]
[1]新潟大院・医・分子細胞機能（生化学２）、[2]新潟大学　超域研究機構、[3]東京都医学研　神経再生

O2-5　**発生期大脳新皮質においてリーリンによって誘導される神経細胞凝集の解析**

○久保　健一郎、本田　岳夫、関根　克敏、石井　一裕、田畑　秀典、仲嶋　一範
慶應義塾大学医学部解剖学

O2-6　**トリメチルスズ誘発性神経細胞障害に対するインドメタシンの保護効果**

○中村　有加里、グエン　クィン　フォン、荻田　喜代一
摂南大・薬・薬理学

9月27日（火）

9：30～11：30　C会場（2F・平安）

O3-1～O3-6　薬物依存・シナプス可塑性

座長：田代　朋子（青山学院大学理工学部化学・生命科学科）
佐藤　　真（福井大学 医学部医学科 形態機能医科学講座 組織細胞形態学・神経化学領域）

O3-1　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アクチン骨格の再編成

○河合　克宏[1]、冨永（吉野）　恵子[2]、浦久保　知佳[2]、谷口　直子[2]、近藤　恭光[3]、田代　英夫[3]、小倉　明彦[2]、田代　朋子[4]
[1]独・理化学研究所・脳・発生神経生物研究チーム、[2]大阪大院・生命機能・脳神経工、[3]独・理化学研究所・田代計測工学、[4]青山学院大学大学院　理工学研究科

O3-2　ワサビ由来の制癌剤である6-MITCは極めて低容量でてんかんミュータントマウスの発作を抑える

○村島　善也[1]、小野瀬　敦子[1]、福家　洋子[2]
[1]首都大学東京大学院人間健康科学研究科フロンティアヘルスサイエンス学域、[2]首都大学東京大学院人間健康科学研究科ヘルスプロモーション学域

O3-3　インビトロ血液脳関門モデルを用いた骨髄間葉系幹細胞の脳実質内浸潤機構の解析

○片山　貴博[1]、松下　隆司[1,2]、木林　達也[1]、本望　修[3]、下濱　俊[2]、南　雅文[1]
[1]北海道大院・薬・薬理、[2]札幌医大・神経内科、[3]札幌医大・神経再生医学

O3-4　アクチン繊維と微小管による成長円錐の２種類の小胞輸送系

○野住　素広[1,2]、加藤　薫[3]、五十嵐　道弘[1,3]
[1]新潟大院・医歯学・分子細胞機能学、[2]新潟大・超域研究院、[3]産業技術総合研究所

O3-5　ニコチンによる海馬神経細胞スパインの形態変化

○田中　秀和、金井　好克
大阪大学大学院医学系研究科生体システム薬理学

O3-6　海馬におけるニューロプシン依存的シナプス連合性の解析

○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・神経機能科学講座

Oral Sessions

９月27日（火）

12：30〜14：30　C会場（２F・平安）

O4-1〜O4-6　てんかん・神経変性疾患

座長：福永　浩司（東北大学大学院・薬・薬理学分野）
片山　泰一（大阪大学大学院 連合小児発達学研究科 分子生物遺伝学研究領域）

O4-1　てんかん及び，情動行動における脳内成長ホルモンシグナル系の関与について

加藤　啓子[1,2]、○管野　拓[2]、平林　義雄[3]
[1]京都産大・総合生命、[2]大阪府大・生命環境、[3]理研・脳センター

O4-2　嗅球摘出マウスにおけるシグマ１受容体活性化による認知機能障害の改善

○森口　茂樹、山本　由似、福永　浩司
東北大・院薬・薬理学

O4-3　bFGF様薬理作用を有する新規化合物SUN13837のシグナルパスウェイ

○新名　芳有[1]、門嶋　大輔[1]、荻野　涼子[1]、黒田　真里子[1]、竹本　尚弘[2]、上野　新也[1]、村山　宣人[1]、井上　照好[1]
[1]アスビオファーマ株式会社・薬理第二ファカルティー、[2]アスビオファーマ株式会社・化学ファカルティー

O4-4　多系統萎縮症患者脳ではγ-tubulinが減少しており、人工的γ-tubulin 2減少モデル動物は多系統萎縮症様の神経変性と運動失調を発症する

○堤　弘次[1]、久保　亜紀子[4,14]、高木　博[4]、赤津　裕康[5]、紺野　在[1]、宮本　裕子[6]、矢尾　育子[4]、江川　潔[2]、佐藤　尚武[4]、久保　亮治[7]、安武　かおり[4]、諸根　信弘[8]、山内　大輔[6]、堀尾　哲也[11]、木村　芳滋[1]、宮川　剛[9]、福田　敦夫[2]、塚田　秀夫[10]、吉田　眞理[12]、橋詰　良夫[5]、峰雪　芳宣[6]、小西　慶幸[1]、池上　浩司[1]、瀬藤　光利[1,4]
[1]浜松医科大学・細胞生物学、[2]浜松医科大・生理学第一、[3]浜松医科大・第一内科、[4]三菱化学生命科学研究所、[5]福祉村病院・長寿医学研究所、[6]兵庫県立大院・生命理学、[7]慶応大・医・皮膚科、[8]国立精神・神経医療研究センター、[9]藤田保険衛生大・総合医学研究所・システム医科学研究部門、[10]浜松ホトニクス・中央研究所、[11]カンサス大・分子生物、[12]愛知医科大・加齢医学研究所、[13]大阪大学院・生命機能研究科、[14]慶応義塾大・医・医化学

O4-5　マトリックスメタロプロテアーゼは成熟型BDNFを増加させることでキンドリング現象に関与する

○溝口　博之[1]、佐藤　純[1]、澤田　誠[2]、鍋島　俊隆[3]、山田　清文[4]
[1]名古屋大学　環境医学研究所　近未来環境シミュレーションセンター、[2]名古屋大学環境医学研究所脳機能分野、[3]名城大学大学院薬学研究科薬品作用学教室、[4]名古屋大学大学院医学系研究科医療薬学・附属病院薬剤部

O4-6　Calsyntenin-3の細胞外ドメイン（sCst-3）は、全長Cst-3やCTFの過剰発現による神経毒性を減弱する

○内田　洋子、五味　不二也

東京都健康長寿医療センター研究所　老化制御チーム

9月27日（火）

14：30〜16：30　C会場（2Ｆ・平安）

O5-1〜O5-6　　統合失調症・ジェノミクス

座長：西川　　徹（東京医科歯科大学大学院　精神行動医科学分野）
和中　明生（奈良県立医科大学　第二解剖）

O5-1　神経発達期免疫活性化により引き起こされる脳機能障害におけるIFITM3の関与

○衣斐　大祐[1,2]、永井　拓[1]、鍋島　俊隆[2]、山田　清文[1]
[1]名古屋、[2]名城大院・薬・薬品作用

O5-2　マウス神経細胞におけるカルニチン／有機カチオントランスポーターOCTN1の機能的発現

○中道　範隆、田口　貴之、細谷　拓史、杉浦　智子、加藤　将夫
金沢大学医薬保健研究域薬学系分子薬物治療学研究室

O5-3　フェンサイクリジンによるシナプス減少にBDNFの分泌阻害が関与する

○安達　直樹[1,2]、沼川　忠広[1,2]、熊丸　絵美[1]、伊丹　千晶[3]、千葉　秀一[1]、飯島　良味[1]、リチャード　ミスティー[4]、仙波　りつ子[5]、功刀　浩[1,2]
[1]（独）国立精神・神経医療研究センター・神経研・疾病三部、[2]戦略的創造研究推進事業（CREST），JST、[3]埼玉医大・生理学、[4]アルバニー医科大学、[5]理研・脳センター

O5-4　グルタミン酸受容体結合性シナプス足場タンパク質SAP97の統合失調症における遺伝子関連解析

○山本　直樹[1]、佐藤-木村　潤子[1]、上里　彰仁[1]、嶋津　奈[1]、治徳　大介[1]、海野　真一[1]、海野　麻未[1]、車地　暁生[1]、飯嶋　良味[2]、功刀　浩[2]、岩山　佳美[3]、吉川　武男[3]、西川　徹[1]
[1]東京医科歯科大院・医歯・精神行動医科学、[2]国立精神・神経医療研究セ・神経研・疾病研究第三部、[3]理研・脳科学総合研究セ・分子精神科学

O5-5　Accell siRNAの単回脳室内投与による脳内の遺伝子サイレンシング効果

○久保　岳也[1]、中嶋　秀満[1]、瀬見　優子[1]、桑村　充[2]、井澤　武史[2]、東　泰孝[1]、竹内　正吉[1]
[1]大阪府立大院・生命環境・獣医・応用薬理、[2]大阪府立大院・生命環境・獣医・獣医病理

O5-6　新規抗体と遺伝子改変マウスを用いた統合失調症脆弱性因子DISC1の再評価

○黒田　啓介[1,2]、山田　真之亮[2,3]、田中　基樹[4]、飯塚　美知郎[1,5]、矢野　寿[1]、榎本　篤[6]、溝口　明[5]、曽我部　正博[4]、高橋　雅英[6]、山田　清文[2,3]、貝淵　弘三[1,2]
[1]名古屋大院・医・神経情報薬理、[2]JST, CREST、[3]名古屋大院・医・医療薬学、[4]名古屋大院・医・細胞生物物理、[5]三重大院・医・神経再生医学・細胞情報、

Oral Sessions

[6]名古屋大院・医・分子腫瘍

9月28日（水）

9：30～11：30　C会場（2F・平安）

06-1～06-6　グリア・ミエリン

座長：渡辺　康裕（防衛医科大学校　医学部　薬理学）
中西　博（九州大学大学院歯学研究院　口腔機能分子科学分野）

06-1　**オリゴデンドロサイト特異的なシグナル伝達機構とうつ病発症との関連**

○宮田　信吾[1,2]、小山　佳久[1]、谷口　学[1]、吉川　景子[1]、石川　淑子[1]、弓場　智雄[1]、遠山　正彌[1,2,3]
[1]大阪大院・医・神経機能形態学、[2]子どものこころの分子統御機構研究センター、[3]大阪大院・連合小児発達学・分子生物遺伝学

06-2　**PAP-III（Reg-IIIγ）はN末端切断により線維状構造を形成し軸索伸長の足場となる**

○小西　博之、松本　早紀子、木山　博資
名古屋大院・医・機能組織学

06-3　**低浸透圧ストレス負荷アストロサイトから放出された亜鉛によるミクログリアの活性化**

○長澤　一樹、瀬川　将平、中村　庄吾、大里　侑希、谷　美咲、西浦　武志、松尾　剛明、西田　健太朗
京都薬大・衛生化学

06-4　**内在性エリスロポエチンのオリゴデンドロサイト前駆細胞への細胞保護効果**

○青山　峰芳[1]、加藤　晋[1,2]、垣田　博樹[1,2]、浅井　隼人[1,2]、長屋　嘉顕[1,2]、浅井　清文[1]
[1]名古屋市立大院・医・分子神経生物学、[2]名古屋市立大院・医・新生児・小児医学

06-5　**Interferon regulatory factor-8は、神経損傷後に見られる脊髄ミクログリアの過活動状態への移行に重要な転写因子である**

○増田　隆博[1]、津田　誠[1]、吉永　遼平[1]、齊藤　秀俊[1]、田村　智彦[2]、井上　和秀[1]
[1]九州大院・薬・薬理、[2]横浜市立大学大学院医学研究科免疫学教室

06-6　**実験的脳脊髄炎モデルを用いた脱髄および軸索変性の形態学的解析**

○板東　良雄[1]、野村　太一[1]、暮地本　宙巳[2]、甲賀　大輔[3]、渡部　剛[2]、吉田　成孝[1]
[1]旭川医科大学　解剖学講座　機能形態学分野、[2]旭川医科大学　解剖学講座　顕微解剖学分野、[3]新潟大学大学院　医歯学総合研究科　顕微解剖学分野

9月28日（水）

9：30〜11：10　D会場（2F・天平）

O7-1〜O7-5　情報伝達・突起伸展

座長：石崎　泰樹（群馬大学大学院医学系研究科分子細胞生物学）
那波　宏之（新潟大学・脳研・分子神経生物）

O7-1　機能的リン酸化プロテオミクスによる新規CaMKI基質の同定

○実吉　岳郎[1,2]、松本　雅記[3]、野崎　直人[4]、草野　秀夫[1]、家村　俊一郎[1]、中山　敬一[3]、夏目　徹[1]
[1]産業技術総合研究センター、[2]脳科学総合研究センター、理研、[3]九州大学生体防御医学研究所、[4]神奈川歯科大学

O7-2　Bリンパ球刺激因子に対する内在性Nogo受容体アンタゴニストLOTUSの拮抗作用

○西山　邦幸、栗原　裕司、池谷　真澄、伊藤　拓夢、五嶋　良郎、竹居　光太郎
横浜市大・医・分子薬理神経

O7-3　コンドロイチン硫酸プロテオグリカンによる軸索再生阻害のシグナル伝達機構

○久保山　友晴[1,2]、Silver Jerry[3]、東田　千尋[1]、上口　裕之[2]
[1]富山大・和漢研・民族薬物研究セ・薬効解析、[2]理研・脳センター・神経成長機構研究チーム、[3]Dep. of Neurosciences, School of Med., Case Western Reserve大

O7-4　マウス大脳皮質発達過程における自閉症関連分子Shank3のバリアント発現解析

○浅野　弘嗣、和賀　央子、土屋　明子、内野　茂夫、高坂　新一
独立行政法人国立精神神経医療研究センター神経研究所代謝研究部

O7-5　PACAPによる神経突起の形成過程におけるPgc1αの細胞内局在変化の関与

○神戸　悠輝、井上　和彦、栗原　崇、宮田　篤郎
鹿児島大院・医歯学総合・生体情報薬理

9月28日（水）

13：30〜15：30　D会場（2F・天平）

O8-1〜O8-6　発達障害・神経幹細胞

座長：久永　真市（首都大学東京大学院理工学研究科・生命科学専攻）
井上　敦子（福山大学薬学部薬物治療学）

O8-1　大脳皮質前駆細胞の細胞周期からの離脱と分化の協調はRbファミリーにより制御される

○味岡　逸樹、押川　未央、岡田　桂
東京医科歯科大学　脳統合機能研究センター

O8-2　マウス人工多能性幹細胞の増殖および神経前駆細胞への分化に対する神経伝達物質受容体の役割

○石塚　俊晶、渡辺　康裕
防衛医大・薬理

O8-3　Glial cells missing遺伝子によるHes5遺伝子プロモーターの脱メチル化を介する神経幹細胞の誘導

○等　誠司[1,2]、石野　雄吾[1,2]、池中　一裕[1,2]
[1]生理研・分子神経生理、[2]総研大生理科学

O8-4　ラットの多動はビスフェノールAにより惹起されるが、代謝産物では惹起されない

○増尾　好則[1]、寺崎　正紀[2]、森田　昌敏[3]、石堂　正美[3]
[1]東邦大学大学院 理学研究科生物学専攻 神経科学研究室、[2]静岡県立大学大学院 生活健康科学研究科 環境物質科学専攻 物性化研究室、[3]独立行政法人国立環境研究所 環境リスク研究センター

O8-5　低血圧マウス延髄血管運動中枢におけるニューロペプチドY受容体の発現上昇

○村瀬　真一、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　薬理学分野

O8-6　自閉症児童の血清中下垂体前葉ホルモンの動態

○松崎　秀夫、岩田　圭子、森　則夫
浜松医科大学・子どものこころの発達研究センター

大学院生口演

9月26日（月）

9：30～11：30　D会場（2Ｆ・天平）

G1-1～G1-6　突起伸展・回路網形成

座長：田渕　明子（富山大学大学院医学薬学研究部（薬学））
溝口　博之（名古屋大学環境医学研究所
近未来環境シミュレーションセンター）

G1-1　Cdk5-LMTK1/AATYK1-Rab11は軸索伸長を制御する新たなシグナル経路である

○高野　哲也[1]、友村　美根子[2]、吉岡　望[1,3]、堤　弘次[1]、寺沢　雄吉[1]、
川野　仁[3]、福田　光則[4]、久永　眞市[1]
[1]首都大学東京大学院、理工、生命科学、[2]MPL, 明海大学歯学部、[3]東京都医学総合研究所, 神経再生研究室、[4]東北大学大学院、生命科学、膜輸送解析分野

G1-2　内在性Nogo66受容体アンタゴニストLOTUSの機能ドメイン検索

○栗原　裕司[1,2]、池谷　真澄[1]、伊藤　拓夢[1]、西山　邦幸[1]、榊原　裕介[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

G1-3　LOTUS-Nogo受容体相互作用の嗅索形成における生理的役割

○池谷　真澄、栗原　裕司、伊藤　拓夢、西山　邦幸、五嶋　良郎、
竹居　光太郎
横浜市立大学大学院医学研究科分子薬理神経生物学教室

G1-4　内在性Nogo66受容体アンタゴニストLOTUSの神経突起伸長作用

○伊藤　拓夢、栗原　裕司、池谷　真澄、西山　邦幸、榊原　祐介、
中村　史雄、五嶋　良郎、竹居　光太郎
横浜市大院・医・分子薬理神経

G1-5　脳内sigma-1受容体の新規スプライスバリアントsigma-1 short受容体の発現と機能

○石川　潔、塩田　倫史、福永　浩司
東北大学大学院薬学研究科薬理学分野

G1-6　ダイナクチンノックダウン線虫を用いた孤発性ALS軸索輸送障害モデルの作成と解析

○池中　建介、河合　香里、黄　哲、蒋　月梅、勝野　雅央、田中　章景、
祖父江　元
名古屋大学大学院医学系研究科神経内科学

9月26日（月）

15：15～17：15　D会場（2F・天平）

G2-1～G2-6　発達障害・転写制御因子

座長：渡部　和彦（東京都医学総合研究所・神経変性病理プロジェクト）
柳澤　勝彦（国立長寿医療研究センター）

G2-1　ICRマウスのオスによる養育行動を制御する神経回路の解析

○アクタル　シリン、東田　知陽、梁　明坤、鐘　静、東田　陽博
金沢大学大学院医学系研究科脳細胞遺伝子学

G2-2　マウス胎仔期バルプロ酸曝露による自閉症様行動の発現および大脳皮質層構造変化におけるヒストンアセチル化の関与

○原　雄大[1]、片岡　駿介[1]、前田　優子[1]、吾郷　由希夫[1]、田熊　一敞[1]、松田　敏夫[1,2]
[1]大阪大学大学院薬学研究科薬物治療学、[2]大阪大学・金沢大学・浜松医科大学連合小児発達学研究科

G2-3　脊髄損傷の運動機能回復に関与するDenosominの軸索伸展作用

○執行　美智子[1]、長田　愛子[1]、勅使川原　匡[1]、久保山　友晴[1]、松谷　裕二[2]、東田　千尋[1]
[1]富山大・和漢薬研・薬効解析、[2]富山大・薬・薬品製造

G2-4　脱髄性疾患モデルにおけるシスタチンＦの機能解析

○清水　崇弘[1,2]、田中　謙二[1,2]、馬　堅妹[3]、池中　一裕[1,2]
[1]総合研究大学院大学、[2]生理学研究所　分子神経生理部門、[3]大連医科大学

G2-5　視床下部におけるnecdinは、甲状腺ホルモンによるエネルギー消費を制御する

○白石　千夏、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

G2-6　Necdinは哺乳類脳においてSmc5/6構成要素と多蛋白質複合体を形成する

○柏木　裕呂樹、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

9月27日（火）

9：30～11：30　D会場（2F・天平）

G3-1～G3-6　グリア・ミエリン

座長：加藤　聖（金沢大学大学院医学系研究科脳情報分子学）
小山　豊（大阪大谷大学　薬学部　薬理）

G3-1　ATPエキソサイトーシスによるミクログリアの情報発信

○井村　誉史雄[1]、森澤　陽介[1]、柴田　圭輔[1]、篠崎　陽一[1]、森山　芳則[2]、小泉　修一[1]

[1]山梨大学・院・医工・薬理学、[2]岡山大学医歯薬学総合研究科 薬学生体膜生化学

G3-2 ミクログリアにおけるtransglutaminase 2およびfactor13a発現とその変化

○河辺　憲司、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

G3-3 脳外傷後の神経再生阻害と組織修復に果たすグリアー線維性瘢痕の役割について

○吉岡　望[1,2]、阿相　皓晃[3]、木村-黒田　純子[1]、久永　眞市[2]、川野　仁[1]
[1]都医学研、[2]首都大・理工・生命、[3]慶応大・漢方医学センター

G3-4 ミクログリアの活性化に伴うPLD4発現調節機構

○大谷　嘉典[1]、山口　宜秀[1]、木谷　裕[2]、佐藤　友美[3]、古市　貞一[3,4]、馬場　広子[1]
[1]東京薬大・薬・機能形態学、[2]農業生物資源研・遺伝子組換え家畜研究センター、[3]理研・脳センター・分子神経形成、[4]東京理大・理工・応用生物

G3-5 オリゴデンドロサイトの発達と髄鞘形成に関わるSema4Dの働き

○奥野　晃司[1]、山口　航[1]、玉井　里枝[1]、蔭浦　美穂[1]、古山　達雄[2]、稲垣　忍[1]
[1]大阪大学大学院医学系研究科保健学専攻、[2]香川保健医療大学

G3-6 ヒトアストロサイトによるヒスタミン取り込み機構について

○長沼　史登、吉川　雄朗、中村　正帆、井筒　敏恵、谷内　一彦
東北大学大学院医学系研究科機能薬理学

９月27日（火）

12：30～14：30　D会場（２Ｆ・天平）

G4-1～G4-6　神経変性疾患・疾患モデル

座長：和田　圭司（国立精神・神経医療研究センター）
谷浦　秀夫（立命館大学薬学部）

G4-1 神経型一酸化窒素合成酵素阻害剤7-nitroindazoleは6-hydroxydopamine神経障害ラットにおいてL-DOPA誘発ジスキネジアの形成を抑制する

○太田　友樹[1]、田熊　一敞[1]、高橋　剛士[1]、吾郷　由希夫[1]、松田　敏夫[1,2]
[1]大阪大学大学院薬学研究科薬物治療学、[2]大阪大学・金沢大学・浜松医科大学連合小児発達学研究科

G4-2 GAPDH凝集物はアミロイドβの線維化を促進する

○瀬見　優子、中嶋　秀満、久保　岳也、板倉　正典、東　泰孝、竹内　正吉
大阪府立大・生命環境・応用薬理

G4-3 I2020T変異型LRRK2トランスジェニックマウスが示す運動機能異常と病態変化

○前川　達則[1]、森　小百合[1]、佐々木　唯[1]、宮島　任司[1]、東　貞宏[2]、

Graduate Oral Sessions

太田　悦朗[1]、小幡　文弥[1]
[1]北里大学大学院・医療系研究科・臨床免疫学、[2]北里大学・医学部・実験動物学

G4-4　**老化促進モデルマウス（SAMP8）の若齢期における局所的な甲状腺ホルモン代謝の変化：ミエリン形成遅滞および行動異常との関連**
○澤野　恵梨香、菊間　慎平、錦　美樹、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

G4-5　**ユビキチンリガーゼRNF19BおよびDorfinがアルツハイマー病原因タンパク質アミロイド-β産生に関与する可能性**
○山森　正嗣[1]、金子　雅幸[1]、小野口　雅之[1]、野村　靖幸[2]、大熊　康修[1]
[1]千葉科学大・薬・薬理、[2]横浜薬大・薬・薬物治療

G4-6　**ドネペジルのタウ蛋白リン酸化に及ぼす影響　ー細胞モデルを用いた検討ー**
○佐々木　宏仁[1]、濱野　忠則[1]、白藤　法道[1]、石田　智恵美[1]、岸谷　融[1]、Yen Shu-Hui[2]、米田　誠[1]、栗山　勝[1]、中本　安成[1]
[1]福井大学医学部第二内科、[2]メイヨークリニック・ジャクソンビル

９月27日（火）

14：30～16：30　D会場（２F・天平）

G5-1～G5-6　**統合失調症・シナプス可塑性**
座長：工藤　喬（大阪大学大学院医学系研究科精神医学教室）
中道　範隆（金沢大学医薬保健研究域薬学系分子薬物治療学研究室）

G5-1　**てんかんミュータントELマウス背側海馬へのマウスES細胞由来神経幹細胞移植**
○小野瀬　敦子[1]、村島　善也[1]、大津　昌弘[2]、大森　啓之[1]、吉江　拓也[1]、中山　孝[3]、福家　洋子[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フロンティアヘルスサイエンス学域神経再生科学分野、[2]杏林大学医学部化学、[3]横浜市立大学医学部生化学、[4]首都大学東京大学院人間健康科学研究科ヘルスプロモーションサイエンス学域

G5-2　**PACAPによる樹状突起スパインの形態調節**
○尾形　勝弥[1]、早田　敦子[1,2]、勢力　薫[1]、狭間　啓佑[1]、百崎　久恵[1]、新谷　紀人[1]、馬場　明道[3]、橋本　均[1,2,4]
[1]大阪大院・薬・神経薬理、[2]大阪大院・連合小児・子どものこころセンター、[3]兵庫医療大・薬・薬理、[4]大阪大院・医・分子医薬

G5-3　**マウス海馬におけるマトリックスメタロプロテアーゼ活性の組織学的解析**
○鈴木　春満、金河　大、塩坂　貞夫
奈良先端大・バイオ・神経機能学

G5-4　**SNAREタンパク質SNAP-25の脱リン酸化機構の解明**
○飯田　諭宜[1]、山森　早織[2]、中屋　千恵美[2]、板倉　誠[2]、宮岡　等[3]、

Graduate Oral Sessions

高橋　正身[2]
[1]北里大学大学院医療系研究科、[2]北里大学医学部生化学、[3]北里大学医学部精神科

G5-5　**統合失調症治療薬が神経幹細胞のインターニューロンへの分化に及ぼす影響について**

○金田　博雄、鵜飼　渉、橋本　恵理、吉永　敏弘、館農　勝、渡邊　公彦、白坂　知彦、五十嵐　健史、石井　貴男、齋藤　利和
札幌医科大学神経精神医学講座

G5-6　**対数増殖条件下におけるマウスES細胞由来神経幹細胞のX線照射に対する放射線感受性の測定**

○磯野　真由[1,2]、小西　輝昭[2]、大津　昌弘[3]、吉江　拓也[1]、大森　啓之[1]、塩見　尚子[2]、酢屋　徳啓[2]、小林　亜利紗[2]、中山　孝[4]、井上　順雄[1]
[1]首都大院・人間健康科学・神経再生科学、[2]放医研・研究基盤セ・研究基盤技術、[3]杏林大・医・化学、[4]横浜市大・医・生化学

9月27日（火）

16：30〜18：30　C会場（2Ｆ・平安）

G6-1〜G6-6　**気分障害・細胞接着因子**

座長：白尾　智明（群馬大学大学院医学系研究科神経薬理学教室）
田丸　輝也（東邦大学医学部生理学講座細胞生理学分野）

G6-1　**フローサイトメーターを用いた新規脳細胞解析法の確立と大うつ病患者死後脳の解析**

○林　義剛[1,2]、菊池　尚美[2]、篠崎　たき子[2]、伊東　多恵子[2]、久永　眞市[1]、楯林　義孝[2]
[1]首都大学東京大学院理工学研究科生命科学専攻神経分子機能研究室、[2]財団法人東京都医学総合研究所統合失調症うつ病プロジェクト気分障害研究部門

G6-2　**σ_1受容体と5-HT_{1A}受容体の活性化は副腎・睾丸摘出マウスの大脳皮質ドパミン遊離を促進する**

○平松　直樹[1]、矢野　耕史[1]、吾郷　由希夫[1]、田熊　一敞[1]、松田　敏夫[1,2]
[1]大阪大学大学院薬学研究科薬物治療学、[2]大阪大学・金沢大学・浜松医科大学連合小児発達学研究科

G6-3　**海馬アストロサイトにおける抗うつ薬fluoxetineのBDNF発現メカニズム**

○木下　真直、小泉　修一
山梨大学・医・薬理

G6-4　**リチウムは大脳皮質のドパミンならびにセロトニン遊離の調節を介して、メタンフェタミンによる多動、行動感作を抑制する**

○田中　辰典[1]、喜多　祐紀[1]、吾郷　由希夫[1]、田熊　一敞[1]、松田　敏夫[1,2]
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Graduate Oral Sessions

大学連合小児発達学研究科

G6-5 **神経接着分子Caspr3のマウス大脳基底核における局在**
○平田 晴菜[1]、梅森 十三[2]、小出 剛[2]、渡邉 和忠[1,3]、霜田 靖[1]
[1]長岡技術科学大学・生物系、[2]国立遺伝学研究所 マウス開発研究室、[3]長岡工業高等専門学校

G6-6 **神経認識分子NB-3と受容体型チロシンホスファターゼRPTPγの相互作用解析**
○中野 悟司[1]、平田 晴菜[1]、長田 恭平[1]、渡邉 和忠[1,2]、霜田 靖[1]
[1]長岡技術科学大学 生物系、[2]長岡工業高等専門学校

9月27日（火）

16：30〜18：30 D会場（2Ｆ・天平）

G7-1〜G7-6 不安・ストレス
座長：佐野 輝（鹿児島大学大学院医歯学総合研究科精神機能病学分野）
酒井 規雄（広島大学 医歯薬学総合 神経薬理学）

G7-1 **マウス間相互作用による長期隔離飼育マウス前頭前野の活性化とドパミン、セロトニン遊離の促進**
○荒木 良太[1]、吾郷 由希夫[1]、笹賀 あすか[1]、田熊 一敞[1]、松田 敏夫[1,2]
[1]大阪大学大学院薬学研究科薬物治療学分野、[2]大阪大学・金沢大学・浜松医科大学連合小児発達学研究科

G7-2 **マウス活動期の社会的過密環境は抗不安、抗うつ様効果をもたらす**
○北本 真理[1]、田中 辰典[1]、吾郷 由希夫[1]、田熊 一敞[1]、松田 敏夫[1,2]
[1]大阪大学大学院薬学研究科薬物治療学、[2]大阪大学・金沢大学・浜松医科大学連合小児発達学研究科

G7-3 **動物実験モデルにおける肉体的および精神的疲労のバイオマーカーの測定**
○岩沢 勇也[1]、大城 聰[1]、簗瀬 澄乃[2]、高山 成伸[3]、森岡 勝樹[4]
[1]大東文化大学大学院スポーツ健康科学研究科細胞生物学、[2]大東文化大学大学院スポーツ健康科学研究科分子生命科学、[3]大東文化大学大学院スポーツ健康科学研究科分子臨床免疫、[4]東京大学大学院循環器内科

G7-4 **メラニン凝集ホルモン受容体１におけるGi/o選択的共役部位の特定**
○濱本 明恵、斎藤 祐見子
広島大学大学院総合科学研究科

G7-5 **神経型一酸化窒素合成酵素のSer847リン酸化は神経細胞における一酸化窒素-活性酸素種シグナリングを調節する**
○笠松 真吾[1]、澤 智裕[2]、渡邊 泰男[3]、赤池 孝章[2]、居原 秀[1]
[1]大阪府大院・理・生物科学、[2]熊本大院・医・微生物、[3]昭和薬科大学 薬理学部

G7-6　マウスES細胞からの*in vitro*セロトニン神経分化の評価系の構築: I型BMP受容体キナーゼ阻害の重要性

○山崎　淳史[1]、浅野　宏治[1]、問　暁裕[1]、早田-高野　敦子[2]、新谷　紀人[1]、馬場　明道[3]、橋本　均[1,2,4]
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大学院生口演評価者（敬称略）

（五十音順）

氏　名	所　属
赤木宏行	広島国際大学・薬学部・分子細胞薬理学
浅沼幹人	岡山大学大学院・医歯薬学総合研究科・神経情報学
石毛久美子	日本大学薬学部
井上順雄	首都大学東京
大熊康修	千葉科学大学薬学部薬理学
小倉明彦	大阪大学　大学院生命機能研究科
岸本年史	奈良県立医科大学精神医学
熊倉鴻之助	上智大学理工学部情報理工学科
高坂新一	国立精神・神経医療研究センター神経研究所
﨑村建司	新潟大学脳研究所細胞神経生物学分野
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神経機能科学
高橋正身	北里大学大学院医療系研究科分子神経生物学
宝田剛志	金沢大学医薬保健研究域　薬学系　薬物学研究室
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野田幸裕	名城大学薬学部病態解析学
野村靖幸	横浜薬科大学
堀　修	金沢大学医薬保健研究域　医学系　神経分子標的学
松岡一郎	松山大学薬学部生理化学研究室
吉川和明	大阪大学蛋白質研究所

大学院優秀発表賞受賞者の選考には上記評価者にご協力いただく予定です。

ポスター発表

ポスター会場（１Ｆ・ロビーラウンジ）
ポスター討論時間

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P1-01 **新規疼痛制御ターゲットとしてのミクログリアK_{Ca}チャネルの役割**
○林　良憲[1]、河路　広大[1]、孫　麗[1]、張　馨文[1]、横山　武志[2]、高坂　新一[3]、井上　和秀[4]、中西　博[1]
[1]九大院・歯・口腔機能分子、[2]九大・歯・歯科麻酔、[3]国立精神・神経医療研究センター・代謝研究、[4]九大・薬・薬理

P1-02 **脊髄ミクログリアのinterferon regulatory factor-5は神経障害性疼痛の発現に重要な転写因子である**
○吉永　遼平[1]、津田　誠[1]、増田　隆博[1]、西本　奈央[1]、齋藤　秀俊[1]、田村　智彦[2]、井上　和秀[1]
[1]九州大学大学院薬学府薬理学分野、[2]横浜市立大学大学院医学研究科免疫学教室

P1-03 **末梢神経損傷後の末梢神経および後根神経節における浸潤マクロファージのサブタイプの検討**
○小森　忠祐、森川　吉博、稲田　剛司、久岡　朋子、仙波　恵美子
和歌山県立医科大学・第二解剖

P1-04 **初代培養ミクログリアにおけるP2Y12受容体を介したケモカインの発現制御**
○宮田　広行、齊藤　秀俊、津田　誠、井上　和秀
九大院・薬・薬理

P1-05 **ドパミンはNF-κB p65の核移行を抑制することにより活性化ミクログリアによるサイトカイン産生を抑制する**
○杉野　佑太、吉岡　靖啓、西元　和哉、山室　晶子、石丸　侑希、前田　定秋
摂南大薬・薬物治療

P1-06 **亜鉛は培養アストロサイトにおけるLPS誘導性一酸化窒素産生を増強する**
○森山　光章、藤塚　俊輔、高野　桂、中村　洋一
大阪府立大学・生命環境科学研究科・統合生理学

P1-07 **神経細胞傷害時に漏出するRNAのアストロサイト活性化への関与**
○山下　友輝、片山　貴博、田中　浩貴、五十嵐　ひかる、木林　達也、南　雅文
北海道大院・薬・薬理

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P1-08 大脳皮質由来初代培養神経細胞のシナプス形成に対する低濃度トリブチルスズの抑制作用

○小柳　洸志、田代　寛典、根岸　隆之、田代　朋子
青山学院大学大学院理工学研究科

P1-09 酸化ストレスに対するサリドマイドとそのエナンチオマーによる神経保護作用

○山田　春佳[1]、大平　浩史[1]、朝日　透[1,2]、澤村　直哉[1,2]
[1]早稲田大学 理工学術院、[2]早稲田大学 先端科学・健康医療融合研究機構（ASMeW）

P1-10 初代培養ラット皮質神経のグルタミン酸誘発神経細胞死に対する抑肝散の保護効果

○川上　善治、五十嵐　康、加瀬　義夫
株式会社ツムラ　ツムラ研究所

P1-11 N-メチル-D-アスパラギン酸受容体のGluN2Dサブユニットはフェンサイクリジンで誘導される行動，遺伝子発現及びFOS陽性細胞の増加に必要とされる

○山本　秀子[1]、亀ケ谷　悦子[1]、澤田　和可子[1]、長谷川　遼太[1]、山本　敏文[2]、萩野　洋子[1]、高松　幸雄[1]、三品　昌美[3]、池田　和隆[1]
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P1-12 複数回膜貫通タンパク質TMEM168はメタンフェタミン連続投与によりマウス側坐核において誘導される

○高山　華南子、宮本　嘉明、宇野　恭介、徐　承姫、新田　淳美
富山大学大学院医学薬学医学薬学研究部（薬学）薬物治療学研究室

P1-13 側坐核ドパミンD2受容体ノックダウンマウスにおける覚せい剤への低感受性

○宮本　嘉明[1]、村松　慎一[2]、新田　淳美[1]
[1]富山大学大学院医学薬学研究部（薬学）薬物治療学研究室、[2]自治医科大学神経内科学講座

P1-14 ニューログリカンC-KOマウスの脳タンパクに対する向精神薬の影響

○青野　幸子[1]、時田　義人[2]、松井　ふみ子[2]、米田　雅彦[3]、渡辺　英治[1]
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P1-15 神経認識分子NB-2とAPLP1の相互作用解析

○伊藤　将来[1]、長田　恭平[1]、渡邉　和忠[1,2]、霜田　靖[1]
[1]長岡技術科学大学 生物系、[2]長岡工業高等専門学校

P1-16 自閉症関連因子Marcksl1の神経ネットワーク形成機構への関与

○石川　淑子[1]、宮田　信吾[2,3]、小山　佳久[2]、松崎　伸介[1,2,3]、片山　泰一[1]、遠山　正彌[1,2,3]
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構研究センター

P1-17 **サリドマイド誘発型自閉症モデルラットにおけるMeCP2標的遺伝子群の発現変化**

○毛利　政文、沖重　愛佳、根岸　隆之、田代　朋子
青山学院大学理工学研究科

P1-18 **TSC変異モデルにみられる興奮性シナプス形成異常のメカニズム**

○安田　新[1,2]、杉浦　弘子[1,2]、瀧上　周[2]、竹宮　孝子[2,3]、今村　博臣[4]、樋野　興夫[5]、山形　要人[1,2]
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P1-19 **アルツハイマー病モデルマウスの記憶障害と軸索変性に対する加味帰脾湯の改善作用**

○中田　理恵、久保山　友晴、東田　千尋
富山大・和漢研・民族薬物センター・薬効解析

P1-20 **Aβ43変換活性におけるACEの二つ活性ドメインの役割**

○鄒　鶤[1]、劉　俊俊[1]、劉　しゅ余[1]、田邉　千晶[1]、前田　智司[1]、渡邉　淳[3]、道川　誠[2]、駒野　宏人[1]
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P1-21 **アルツハイマー病前駆体タンパク質細胞内ドメインを発現させた細胞のプロテオミクス解析**

○亀谷　富由樹、羽賀　誠一
財団法人東京都医学総合研究所　認知症・高次脳機能研究分野

P1-22 **Aβ凝集時の足場としてのCHRNA7タンパクの役割**

○琚　曄[1]、和田　丈慶[1]、朝日　透[1,2]、澤村　直哉[1,2]
[1]早稲田大学 理工学術院、[2]早稲田大学 先端科学・健康医療融合研究機構

P1-23 **ペプチジルプロリルイソメラーゼPin1はCdk5-P25によってリン酸化されたTauの脱リン酸化に影響を与える**

○木村　妙子[1]、堤　弘次[1]、斎藤　太郎[1]、田岡　万悟[2]、石黒　幸一[3]、内田　隆史[4]、長谷川　成人[5]、磯辺　俊明[2]、久永　眞市[1]
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P1-24 **アミロイド前駆タンパク質E693Δトランスジェニックマウスにおける網羅的プロテオーム解析**

○前倉　孝治[1]、鷹野　正興[1]、尾谷　三枝子[1]、佐野　圭二[1]、富山　貴美[2]、森　啓[2]、廣田　徹[3]、松山　正剛[3]
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[3]姫路獨協大・薬・薬理

P1-25　L-DOPAの初代培養ドパミン神経保護効果およびそれに対する3-OMDの抑制作用はアストロサイトを標的としている

○浅沼　幹人、村上　真樹、宮崎　育子
岡山大院・医歯薬・神経情報学

P1-26　線条体アストロサイトに取り込まれたL-DOPAの利用効率

○宮崎　育子、村上　真樹、浅沼　幹人
岡山大院・医歯薬・神経情報学

P1-27　パーキンソン病モデルマウス及び細胞におけるMagnololの神経保護効果

○室山　明子[1]、呂　程[1]、藤田　絢[1]、福山　愛保[2]、光本　泰秀[1]
[1]北陸大学　薬学部　医療薬学講座　代替医療薬学分野、[2]徳島文理大学　薬学部

P1-28　ミトコンドリア形態制御におけるTRAP1の役割

○高村　明孝[1]、宮田　信吾[2]、嶽本　香菜[2]、小山　佳久[2]、松崎　伸介[1,2]、遠山　正彌[1,2]、片山　泰一[2]
[1]大阪大・院・連合小児発達・分子生物遺伝学、[2]大阪大・院・医・神経機能形態学

P1-29　うつに関与する受容体TACR1（タキキニン受容体１）の情報伝達調節因子

○古本　有香[1]、齊藤　修[2]
[1]広島大学大学院総合科学研究科、[2]長浜バイオ大学バイオサイエンス研究科

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○永田　麻実、濱本　明恵、斎藤　祐見子
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[1]金沢大院・医・脳細胞遺伝子学、[2]北海道大院・薬学研究院・創薬有機化学講座

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[1]北里大学理学部生物科学科、[2]北里大学大学院医療系研究科、[3]北里大学医学部精神科、[4]北里大学医学部

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○小林 三和子[1]、尾崎 亮介[1]、中谷 俊幸[2]、本宮 真[3]、高雄 啓三[4]、幸田 敏明[5]、宮川 剛[6]、松岡 一郎[1]
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○ウィゼスミス　ウィライワン[1,2]、清水　崇弘[1,2]、田中　謙二[2]、池中　一裕[1,2]
[1]総合研究大学院大学生命科学研究科生理科学専攻、[2]自然科学研究機構　生理学研究所　分子神経生理部門

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○竹内　啓喜[1,2]、井上　治久[2,3]、樋口　真人[4]、高雄　啓三[5]、月田　香代子[2]、
唐津　歓子[2]、岩本　由美子[2]、宮川　剛[6]、須原　哲也[4]、高橋　良輔[1]
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○山本　未希[1]、一坂　吏志[2]、仙波　りつ子[3]、畠　義郎[1,2]
[1]鳥取大・院・医・生体高次機能、[2]鳥取大・医・生命・神経生物、[3]理研・脳センター・分子神経形成研究チーム

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○黄　健軍、馬　文ショウ、横山　茂
金沢大学大学院医学系研究科脳細胞遺伝子学

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○石崎　泰樹[1]、齋藤　朋美[2]、柴崎　貢志[1]、倉知　正[1]、
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○大野　一紀
岡山大学大学院医歯薬学総合研究科薬効解析学

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[1]首都大学東京大学院・生命科学、[2]群馬大学大学院・医学研究科・脳神経発達統御学講座

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[1]横浜市大院・生命ナノシステム・分子精神薬理、[2]東京都医学総合研究所・依存性薬物プロジェクト

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[1]大阪府立大院・理・生物科学、[2]熊本大院・医・微生物、[3]北里大・医・生化学

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○杉谷　加代[1]、大貝　和裕[1]、人見　清隆[2]、加藤　聖[3]
[1]金沢大院・医・保健学専攻、[2]名大院・生命農・応用分子生命科学、[3]金沢大院・医・脳情報分子

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○田中　英明、Hossain M、伊藤　綾子、Ahmed G、Song X、Asrafuzzaman R、新明　洋平、Naser IB、太田　訓正
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○久岡　朋子[1]、形部　裕昭[1]、小森　忠祐[1]、藤本　幸太[1]、北村　俊雄[2]、仙波　恵美子[1]、森川　吉博[1]
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[1]首都大院・人間健康科学・神経再生科学、[2]杏林大・医・化学、[3]横浜市大・医・生化学、[4]田辺三菱製薬先端医療研究所

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○川田　浩一[1]、東野　俊作[1]、藤永　直己[1]、山下　美穂[1]、佐藤　亜紗美[1]、金子　雅幸[1]、野村　靖幸[2]、大熊　康修[1]
[1]千葉科学大・薬・薬理、[2]横浜薬科大・薬・薬物治療

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[1]首都大院・人間健康科学・神経再生科学、[2]杏林大・医・化学、[3]横浜市大・医・生化学

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○後岡　克典[1]、辰巳　晃子[2]、奥田　洋明[2]、緒方　奈保子[1]、和中　明生[2]
[1]奈良県立医科大学眼科学教室、[2]奈良県立医科大学第２解剖学教室

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○西谷　真希[1]、馬渡　一浩[1]、永島　幹子[2]、大貝　和裕[1]、加藤　聖[2]
[1]金沢大学大学院医学系研究科保健学専攻、[2]金沢大学大学院医学系研究科脳情報分子学

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○石橋　智子、馬場　広子
東京薬科大学・薬学部・機能形態学

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○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・連合小児発達

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○岩田　圭子[1]、松崎　秀夫[1]、森　則夫[1,2]
[1]浜松医科大学・子どものこころの発達研究センター、[2]浜松医科大学・医学部・精神神経医学講座

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○中嶋　一行[1,2]、野田　真里子[1]、高坂　新一[2]
[1]創価大・工・生命情報、[2]国立精神・神経医療研究センター、神経研究所

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○山口　宜秀、内藤　優、永田　秋、菊川　拓弥、山崎　礼二、馬場　広子
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○山本　伸一[1]、高坂　新一[2]、中嶋　一行[1,2]
[1]創価大学工学部生命情報工学科、[2]国立精神・神経センター

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○杉尾　翔太[1]、田中　謙二[2]、渡辺　雅彦[3]、池中　一裕[1,2]
[1]総合研究大学院大学生命科学研究科生理科学専攻、[2]自然科学研究機構　生理学研究所　分子神経生理部門、[3]北海道大学大学院医学研究科　解剖発生学分野

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○大澤　圭子[1]、佐柳　友規[1]、中村　泰子[1]、鈴木　恵理[1]、井上　和秀[2]、高坂　新一[1]
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○奥田　洋明[1]、渋川　幸直[2]、是金　宏昭[3,4]、堀井　謹子[5]、辰巳　晃子[1]、和田　芳直[2]、谷口　直之[3,4]、和中　明生[1]
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P2-33　Voluntary exerciseは大脳基底核におけるOlig2細胞のアストロサイト分化を促進する

○辰巳　晃子[1]、奥田　洋明[1]、山野　眞利子[2]、和中　明生[1]
[1]奈良県立医科大学・医・解剖学第２、[2]大阪府立大学総合・リハビリテーション学部

P2-34　アストロサイトは、ミクログリアが誘導するTNFα量を促進する

○増田　寿明、中嶋　一行
創価大学工学部生命情報工学科

P2-35　中枢神経系における乳酸供給細胞としてのミクログリア

○竹澤　洋亮[1]、中嶋　一行[1,2]、高坂　新一[2]
[1]創価大学院・工・生命情報工、[2]国立精神・神経センター、神経研究所、代謝研究部

P2-36　神経傷害とミクログリアの応答性：神経栄養因子作用の解析

○本田　芳成[1]、山本　伸一[1]、高坂　新一[2]、中嶋　一行[1,2]
[1]創価大学大学院　工学研究科　生命情報工学専攻、[2]国立精神・神経センター

P2-37　UDP誘発性のミクログリアによるマクロピノサイトーシスへのPKDの関与

○上杉　歩未、片岡　彩子、齊藤　秀俊、津田　誠、井上　和秀
九州大学大学院薬学研究院医療薬科学部門薬理学分野

P2-38　グリオーマおよびグリオーマ幹細胞におけるHOXD9の機能解析

○大多　茂樹[1]、田伏　将尚[2]、大橋　陽平[3]、深谷　雷太[2]、三沢　彩[1]、吉田　一成[2]、河瀬　斌[2]、佐谷　秀行[4]、ティオロン　シェシール[5]、シュネベス　ハルベ[5]、松崎　有未[6]、岡野　栄之[6]、河上　裕[1]、戸田　正博[2]
[1]慶應大・医・先端研・細胞情報、[2]慶應大・医・脳外科、[3]東京大院・医・統合生理、[4]慶應大・医・先端研・遺伝子制御、[5]パリ・デカルト大、[6]慶應大・医・生理

P2-39　マウス脳内における新規シアル酸化糖鎖の解析

○鳴海　麻衣[1,2]、吉村　武[2]、鳥居　知宏[2]、池中　一裕[1,2]
[1]総合研究大学院大学・生命科学研究科・生理科学専攻・分子神経生理研究部門、[2]自然科学研究機構・生理学研究所

P2-40　cAMPアナログの長期処置はRN46A細胞においてセロトニントランスポーターの機能を亢進させる

○山本　光、田中　茂、秀　和泉、関　貴弘、酒井　規雄
広島大学・医歯薬学総合・神経薬理

P2-41　ケミカルシャペロンのセロトニントランスポーター機能に対する影響

○酒井　規雄、藤原　雅幸、山本　光、関　貴弘、田中　茂、秀　和泉
広島大学・院・医歯薬総合・神経薬理

P2-42　抗躁剤バルプロ酸によるCdk5-p35の活性制御

○石田　愛美、斉藤　太郎、浅田　明子、久永　眞市
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

P2-43　新生児期における母子分離経験はオープンフィールド試験における寄りかかり行動を増加させる

○一坂　吏志[1]、山本　未希[2]、井久保　樹子[1]、國石　洋[1]、畠　義郎[2]
[1]鳥取大・医・生命・神経生物、[2]鳥取大・院・医・生体高次機能

P2-44　オレキシン発現制御領域結合因子の同定

○田中　進、本多　芳子、本多　真、児玉　亨
財）東京都医学総合研究所・睡眠覚醒制御プロジェクト

P2-45　Double in situ hybridization法を用いたラット膝神経節におけるセロトニン3Aと3B遺伝子の発現の検討

○石田　雄介、中村　雪子、山田　貴博、島田　昌一
大阪大院・医・神経細胞生物学

ランチョンセミナー

９月28日（水）

12：30～13：30　A会場（１F・花離宮）

共催：エーザイ株式会社　ファイザー株式会社
座長：岸本　年史（奈良県立医科大学　精神医学）

「タウの分子病態と神経変性」

田中　稔久
大阪大学大学院医学系研究科　精神医学

９月28日（水）

12：30～13：10　B会場（２F・鳳凰）

共催：第一三共株式会社
座長：山田　正仁（金沢大学大学院　脳老化・神経病態学（神経内科））

「アルツハイマー病βアミロイド蛋白凝集機構解明から予防・治療薬開発へ」

小野　賢二郎
金沢大学大学院　脳老化・神経病態学（神経内科）

JSN Open Symposium

September 26 (Monday)

12:45～15:15 Room A (1F・Hanarikyu)

OS-1～OS-5 Parkinson's disease: Research frontline and mitochondrial dysfunction

Chairs：Keiji Wada (National Center for Neurology and Psychiatry)
Hideki Mochizuki (Kitasato University School of Medicine)

OS-1 Neuroprotective effects of hydrogen on dopaminergic neuronal loss in mice model of Parkinson's disease

○Kyota Fujita[1], Yoshinori Tanaka[2], Mizuho Kido[3], Toshihiko Katafuchi[4], Yusaku Nakabeppu[5]

[1]Laboratory of Pathophysiology, Graduate School of Pharmaceutical Science, Kyushu University, Fukuoka, Japan, [2]R&D Center, Home Appliances Manufacturing Business Unit, Panasonic Electric Works Co., Ltd., Osaka, Japan, [3]Department of Oral Anatomy and Cell Biology, Graduate School of Dental Sciences, Kyushu University, Fukuoka, Japan, [4]Department of Integrative Physiology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan, [5]Division of Neurofunctional Genomics, Medical Institute of Bioregulation, Kyushu University, Fukuoka, Japan

OS-2 Mitochondrial nutrition, Coenzyme Q_{10} as a neuroprotectant

○Yasuhide Mitsumoto

Lab. of Alternative Med. and Exp. Therapeutics, Dept. of Clinical Pharmacy. Faculty of Pharmaceutical Sciences, Hokuriku Univ.

OS-3 Modelling the pathophysiology of Parkinson's diseases and other neurodegenerative diseases using iPS cell thechnology

○Hideyuki Okano

Dept. of Physiology, Keio University School of Medicine

OS-4 Molecular mechanisms of dopaminergic cell death in MPTP mouse model of Parkinson's disease

○Toru Yasuda[1], Yoshikuni Mizuno[2], Hideki Mochizuki[1]

[1]Department of Neurology, Kitasato University School of Medicine, [2]Division of Neuroregenerative Medicine, Kitasato University School of Medicine

OS-5 Aberrant molecular properties of the Parkinson's disease-associated mutant UCH-L1

○Tomohiro Kabuta

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

JSN - JSBP Joint Symposium

September 27 (Tuesday)

9:15～11:30 Room A (1F・Hanarikyu)

JS-1～JS-4 Molecular Basis of Depression

Chairs：Shigenobu Kanba (Neuropsychiatry, Kyushu University)
Tadafumi Kato (RIKEN, Brain Science Institute)

JS-1 Role of neurotrophic/growth factor as a mediator of glia in depression

○Minoru Takebayashi
Department of Psychiatry/Institute for Clinical Research, NHO Kure Medical Center, Kure, Japan

JS-2 Epigenetic regulation of stress vulnerability and depression

○Hirotaka Yamagata, Shusaku Uchida, Koji Otsuki, Teruyuki Hobara, Yoshifumi Watanabe
Div. Neuropsy., Dept. Neurosci., Yamagichi Univ. Grad. Sch. Med.

JS-3 Crosstalk between neurotrophin BDNF and hypothalamic-pituitary-adrenal (HPA) axis

○Tadahiro Numakawa[1], Naoki Adachi[1,2], Hiroshi Kunugi[1,2]
[1]Dept. of Mental Disorder Research, National Institute of Neuroscience, NCNP, [2]CREST, JST, Japan

JS-4 The neuroinflammation hypothesis of depression

○Akira Monji
Department of Psychiatry, Faculty of Medicine, Saga University

Symposium

September 26 (Monday)

9:30〜11:45 Room A (1F・Hanarikyu)

S01-1〜S01-4 Toward developing new drugs and repair and regeneration for neurological disorders and nerve injury in the CNS

Chairs : Yoshihisa Ito (Department of Pharmacy, Nihon University)
Kiyokazu Ogita (Dept. of Pharmacol., Setsunan Univ.)

S01-1 Specific Na^{+}/Ca^{2+} exchange inhibition attenuates MPTP-mediated nigrostriatal dopaminergic dysfunction in the subacute mouse model of Parkinson's disease

○Kazuhiro Takuma[1], Tetsuaki Nashida[1], Toshiyuki Kawasaki[2], Yukio Ago[1], Toshio Matsuda[1,3]
[1]Lab. Medicinal Pharmacol., Grad. Sch. Pharmaceut. Sci., Osaka Univ., Suita, Japan, [2]Func. Probe Res. Lab., RIKEN Ctr. Mol. Imaging Sci., Kobe, Japan, [3]Mol. Res. Ctr. Child Mental Dev., Unit. Grad. Grad. Sch. Child Dev., Osaka Univ., Kanazawa Univ., Hamamatsu Univ. Sch. of Med., Suita, Japan

S01-2 Possible neuroprotective effect of $GABA_B$ receptor on excitotoxicity

○Nobuyuki Kuramoto, Hiroki Niihara, Natsuki Tanaka, Ken-ichi Yamada, Miho Washida, Machiko Ito, Kiyokazu Ogita
Dept. of Pharmacol., Setsunan Univ.

S01-3 Therapeutic potential of mithramycin, one of the chemotherapy drugs, in brain ischemia

○Yasuhiro Kosuge, Kumiko Ishige, Yoshihisa Ito
Laboratory of Pharmacology, School of Pharmacy, Nihon University, Funabashi, Japan

S01-4 CNS regeneration in fish : a molecular mechanism to an application for mammals

○Satoru Kato[1], Toru Matsukawa[1], Yoshiki Koriyama[1], Mikiko Nagashima[1,2], Kazuhiro Ogai[2], Kayo Sugitani[2]
[1]Dept. Mol. Neurobiol., Grad. Sch. Med., Kanazawa Univ., [2]Div. Health Sci., Grad. Sch. Med., Kanazawa Univ. Kanazawa, Kanazawa, Japan

September 26 (Monday)

9:30～11:45 Room B (2F・Hōō)

S02-1～S02-4 Novel molecules related to psychiatric diseases －Hot Topics－

Chairs：Hiroyuki Nawa (Mol Neurobiol., Brain Res Inst, Niigata Univ.)
Atsumi Nitta (Depart. of Pharmaceutical Thera. & Neuropharmacol., Fac. of Pharmaceutical Sci., Grad. Sch. of Med. and Pharmaceutical Sci, Univ of Toyama)

S02-1 Hyperdopaminergic innervation triggered by epidermal growth factor; Implication in Schizophrenia

○Hiroyuki Nawa, Makoto Mizuno, Hidekazu Sotoyama
Mol Neurobiol., Brain Res Inst, Niigata Univ.

S02-2 Molecular mechanism of psychiatric condition by loss of function mutations in the VPS13A gene

○Akira Sano
Dept. of Psychiat. Kagoshima Univ.

S02-3 Functional analysis of a novel drug dependence-inhibitory factor "shati"

○Kazuya Toriumi[1], Minae Niwa[1], Takenao Koseki[1], Taku Nagai[2], Ziyu Song[3], Atsumi Nitta[4], Kiyofumi Yamada[2], Takeshi Fukushima[3], Toshitaka Nabeshima[1]
[1]Dept. of Chem. Pharmacol., Meijo Univ. Grad. Sch. of Pharmaceutical Sci., [2]Dept. of Neuropsychopharmacol. and Hospital Pharmacy, Nagoya Univ. Grad. Sch. of Med., [3]Dept. of Anal. Chem., Faculty of Pharmaceutical Sci., Toho Univ., [4]Dept of Pharm. Ther. and Neuropharmacol., Grad. Sch. of Med. and Pharm. Sci., Univ. of Toyama

S02-4 Three new molecules related to psychiatric diseases

○Atsumi Nitta[1], Yoko Furukawa-Hibi[2], Kyosuke Uno[1], Toshitaka Nabeshima[3], Yoshiaki Miyamoto[1]
[1]Depart. of Pharmaceutical Thera. & Neuropharmacol., Fac. of Pharmaceutical Sci., Grad. Sch. of Med. and Pharmaceutical Sci, Univ of Toyama, Toyama 930-0197, Japan, [2]Dept of Neuropsyachopharmacol and Hosp Pharm Nagoya Univ Grad Sch of Medi, Nagoya 460-8556, Japan, [3]Dept of Chemical Pharmacology, Grad Sch. Pharmaceutical Sci. Meijo University, Nagoya 468-8503, Japan

September 26 (Monday)

15:15～17:30 Room A (1F・Hanarikyu)

S03-1～S03-4 The latest frontiers of schizophrenia research: from gene to environment

Chairs：Kozo Kaibuchi (Dept. of Cell Pharmacol., Nagoya Univ. Grad. School. Med.)
Kiyofumi Yamada (Dept. of Neuropsychopharmacol. Hosp. Pharmcy, Nagoya Univ. Grad. Sch. Med.)

S03-1 Whole genome analysis for shcizophrenia

○Nakao Iwata

Department of Psychiatry, Fujita Health University School of Medicine, Toyoake, Aichi Japan

S03-2 DISC1 acts as a cargo adapter for neuronal transport of specific proteins and mRNAs

○Kozo Kaibuchi

Dept. of Cell Pharmacol., Nagoya Univ. Grad. School. Med.

S03-3 Neurobiology of candidate genes of schizophrenia

○Ryota Hashimoto[1,2,3], Yuka Yasuda[2,3], Kazutaka Ohi[2,3], Motoyuki Fukumoto[2,3], Hidenaga Yamamori[2,3], Satomi Umeda-Yano[2], Takeya Okada[2,3], Keizo Takao[3,4], Katsumori Kobayashi[3,5], Yoshitaka Tatebayashi[3,6], Tsuyoshi Miyakawa[3,4], Kozo Kaibuchi[3,7], Nakao Iwata[3,4], Norio Ozaki[3,7], Masatoshi Takeda[1,2]

[1]United Graduate School of Child Development, Osaka University, Osaka, Japan, [2]Osaka University Graduate School of Medicine, Suita, Osaka, Japan, [3]CREST, JST, Kawaguchi, Japan, [4]Fujita Health University, Toyoake, Japan, [5]Nippon Medical School, Tokyo, Japan, [6]Tokyo Institute of Psychiatry, Tokyo, Japan, [7]Graduate School of Medicine, Nagoya University, Nagoya, Japan

S03-4 PolyI:C-induced neurodevelopmental model of schizophrenia: role for IFITM3 in brain dysfunction

○Kiyofumi Yamada

Dept. of Neuropsychopharmacol. Hosp. Pharmcy, Nagoya Univ. Grad. Sch. Med.

September 26 (Monday)

15:15～17:30 Room B (2F・Hōō)

S04-1～S04-4 Approaches for the elucidation of septin functions in neurons and glia

Chairs：Koh-ichi Nagata (Dept. of Molecular Neurobiology, Inst. for Developmental Research, Aichi Human Service Center)
Makoto Kinoshita (Dept. of Mol. Biol., Div. of Biol. Sci., Nagoya Univ. Grad. Sch.of Sci.)

S04-1 Septin-mediated microtubule regulation during neurite extension

○Makoto Kinoshita, Natsumi Ageta-Ishihara
Dept. of Mol. Biol., Div. of Biol. Sci., Nagoya Univ. Grad. Sch.of Sci.

S04-2 Regulation of Sept5 function by phosphorylation with Cdk5

○Akiko Asada, Makoto Taniguchi, Shin-ichi Hisanaga
Dept Biol Sci, Tokyo Metropolitan Univ

S04-3 A modular septin complex regulates neuronal morphogenesis

○Ewers Helge
Lab. of Phys. Chem., ETH Zurich

S04-4 Molecular mechanism of septin-mediated neuronal migration

○Tomoyasu Shinoda[1], Hidenori Ito[1], Kozo Kaibuchi[2], Koh-ichi Nagata[1]
[1]Dept. of Molecular Neurobiology, Inst. for Developmental Research, Aichi Human Service Center, [2]Dept. Cell Pharmacology, Nagoya Univ. Graduate School of Medicine

Symposium

September 27 (Tuesday)

9:15～11:30 Room B (2F・Hōō)

S05-1～S05-4 Neurobiology and pathophysiology of the spine diseases

Chairs：Kohji Fukunaga (Dept. Pharmacology, Tohoku University Grad. Sch. Pharm. Scis.)
Yasunori Hayashi (RIKEN Brain Science Institute)

S05-1 Regulation of spine formation, morphology and plasticity by CaM-kinases

○Thomas R Soderling
Vollum Institute, Oregon Health and Science University

S05-2 Structural role of CaMKII

○Yasunori Hayashi
RIKEN Brain Science Institute

S05-3 Activity-dependent accumulation change of drebrin-bound actin filaments in dendritic spines

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

S05-4 Dysregulation of spine morphology in ATRX-mutated mental retardation mice

○Kohji Fukunaga[1], Norifumi Shioda[1], Hideyuki Beppu[2], Isao Kitajima[2]
[1]Dept. Pharmacology, Tohoku University Grad. Sch. Pharm. Scis., [2]Department of Clinical and Molecular Pathology, Faculty of Medicine, University of Toyama

September 27 (Tuesday)

12:30～14:45 Room A (1F・Hanarikyu)

S06-1～S06-4 Regulation of neuronal morphology and function. —From the perspectives of spatial cell biology

Chairs：Yoshiyuki Konishi
(Department of Human and Artificial Intelligence Systems, Graduate School of Engineering, University of Fukui,
Research and Education Program for Life Science, University of Fukui)
Makoto Sato
(Div Cell Biol Neurosci., Univ of Fukui,
Research and Education Program for Life Science, Univ Fukui, Fukui, Japan,
Child Development Research Center, Graduate School of Medicine, Univ Fukui, Fukui, Japan)

Symposium

S06-1 Cell intrinsic regulation of axonal morphogenesis mediated by posttranslational modifications: molecular systems for axonal growth regulation and axon-dendrite discrimination

○Yoshiyuki Konishi [1,2]
[1] Department of Human and Artificial Intelligence Systems, Graduate School of Engineering, University of Fukui, [2] Research and Education Program for Life Science, University of Fukui

S06-2 Dendritic growth cone activity regulated by Abl kinase and Cdk5 via WAVE2-Abi2 is essential for completing the multipolar-bipolar transition and initiating glia-guided locomotion

○Makoto Sato [1,2,3]
[1] Div Cell Biol Neurosci., Univ of Fukui, [2] Research and Education Program for Life Science, Univ Fukui, Fukui, Japan, [3] Child Development Research Center, Graduate School of Medicine, Univ Fukui, Fukui, Japan

S06-3 Regulation of neuronal morphogenesis and corticogenesis via CaMKK-CaMKI cascades

○Haruhiko Bito [1,2], Kanzo Suzuki [1], Satoshi Kamijo [1], Shinichiro Horigane [1], Aki Adachi-Morishima [1], Sayaka Takemoto-Kimura [1]
[1] Dept. of Neurochem. Univ. of Tokyo Grad. Sch, Med., Tokyo, Japan, [2] CREST-JST, Kawaguchi, Japan

S06-4 A positive feedback between neurite length-sensing and neurite outgrowth involved in neuronal symmetry breaking

○Naoyuki Inagaki
Grad Sch Biol Sci, Nara Inst Sci & Technol

September 27 (Tuesday)

12:30～14:45 Room B (2F・Hōō)

S07-1～S07-4 Diversity of brain function created by living environment

Chairs：Taku Nagai (Department of Neuropsychopharmacology and Hospital Pharmacy, Nagoya University Graduate School of Medicine)
Tomoyuki Furuyashiki (Dept. of Pharmacol. Med., Kyoto Univ.)

S07-1 Impact of stressful events during juvenile periods on neuropsychological development

○Taku Nagai[1], Jaesk Yun[1], Yoko Hibi[1], Kiyofumi Yamada[1,2]
[1] Department of Neuropsychopharmacology and Hospital Pharmacy, Nagoya University Graduate School of Medicine, Nagoya, Japan, [2] CREST, JST, Japan

S07-2 Prostaglandin E_2-mediated desensitization of prefrontal dopaminergic activity is critical for susceptibility to repeated social defeat

○Tomoyuki Furuyashiki, Kohei Tanaka, Shiho Kitaoka, Yuta Senzai, Shuh Narumiya
Dept. of Pharmacol. Med., Kyoto Univ.

S07-3 Roles of metabotropic glutamate 2/3 receptors in environmental stress- or stress hormones-induced depression-like behaviors in mice

○Yukio Ago[1], Kazuhiro Takuma[1], Toshio Matsuda[1,2]
[1] Laboratory of Medicinal Pharmacology, Graduate School of Pharmaceutical Sciences, Osaka University, Osaka, Japan, [2] United Graduate School of Child Development, Osaka University, Kanazawa University and Hamamatsu University School of Medicine, Osaka University, Osaka, Japan

S07-4 How do drugs of addiction alter the neuronal functions in the nucleus accumbens?: implications of oxidative stress

○Shigenobu Toda
Dept. of Psychiatry and Neurobiology, Kanazawa Univ. School of Med.

September 27 (Tuesday)

14:45～17:00 Room A (1F・Hanarikyu)

S08-1～S08-4 **Brain basis for behavior: molecular mechanism of mind**

Chairs：Hitoshi Hashimoto (Lab of Mol Neuropharmacol, Grad Sch of Pharmaceut Sci, Osaka Univ.)

Ryota Hashimoto
(Molecular Research Center for Children's Mental Development, United Graduate School of Child Development, Osaka University, Osaka, Japan,
Department of Psychiatry, Osaka University Graduate School of Medicine, Osaka, Japan,
CREST, JST, Kawaguchi, Japan)

Symposium

S08-1 **Gene-environment interactions in the etiology of psychiatric disorders: pathophysiological implications of PACAP-dependent stress responses**

○Hitoshi Hashimoto [1], Norihito Shintani [1], Atsuko Hayata-Takano [2], Akemichi Baba [4]
[1] Lab of Mol Neuropharmacol, Grad Sch of Pharmaceut Sci, Osaka Univ., [2] Center for Child Mental Dev, United Grad Sch of Child Dev, Osaka Univ, Kanazawa Univ and Hamamatsu Univ Sch of Med, [3] Dept of Mol Pharmaceutic Sci, Osaka Univ Grad Sch of Med, [4] Sch of Pharmacy, Hyogo Univ Health Sci

S08-2 **Functional involvement of DISC1 in pathogenesis of psychiatric diseases**

○Shinsuke Matsuzaki [1,2,3], Tuyoshi Hattori [2,4], Akira Ito [4], Taiichi Katayama [1], Masaya Tohyama [1,2,3]
[1] Dept. of Child Develop. & Mol. Brain Sci., United Grad. Sch. of Child Develop., Osaka Univ., [2] The Joint Research Center for Child Mental Develop., United Grad. Sch. of Child Develop., Osaka Univ., [3] Department of Anatomy and Neuroscience, Graduate School of Medicine, Osaka University, Suita, Osaka, Japan, [4] Department of Molecular Neuropsychiatry, Graduate School of Medicine, Osaka University, Suita, Osaka, Japan.

S08-3 **Searching for functional molecules in growth cones**

○Michihiro Igarashi
Div Mol Cell Biol, Niigata Univ Grad Sch Med Dent.

S08-4 **New approach bridging between mind and molecules: application of Human Brain Phenotype Consortium**

○Ryota Hashimoto [1,2,3], Kazutaka Ohi [2,3], Yuka Yasuda [2,3], Motoyuki Fukumoto [2,3], Hidenaga Yamamori [2,3], Satomi Umeda-Yano [4], Takeya Okada [2], Masao Iwase [2], Hiroaki Kazui [2], Masatoshi Takeda [2]
[1] Molecular Research Center for Children's Mental Development, United Graduate School of Child Development, Osaka University, Osaka, Japan, [2] Department of Psychiatry, Osaka University Graduate School of Medicine, Osaka, Japan, [3] CREST, JST, Kawaguchi, Japan, [4] Department of Neuropsychiatry, Osaka University Graduate School of Medicine, Osaka, Japan

September 27 (Tuesday)

14:45～17:00 Room B (2F・Hōō)

S09-1～S09-4 Central nervous system and control of food intake and energy balance

Chairs：Shuichi Koda (Asubio Pharma Co., Ltd., Harvard Medical School & Beth Israel Deaconess Medical Center)
Ryo Suzuki (Dept. of Diabetes and Metabolic Diseases, The Univ. of Tokyo)

S09-1 Roles of novel lateral hypothalamic peptides in regulation of feeding behavior

○Takeshi Sakurai
Dept of Molecular Neurosci & Integrative Physiology, Faculty of Medicine, Kanazawa University

S09-2 Analyses of food-related brain neural activity by functional magnetic resonance imaging in lipodystrophy with leptin-replacement therapy

○Ken Ebihara[1], Daisuke Aotani[2], Nobukatsu Sawamoto[3], Kiminori Hosoda[1], Hidenao Fukuyama[3], Kazuwa Nakao[2]
[1]Translational Research Center, Kyoto University Hospital, Kyoto, Japan, [2]Department of Medicine and Clinical Science, Kyoto University Graduate School of Medicine, [3]Human Brain Research Center, Kyoto University Graduate School of Medicine

S09-3 Diabetes affects brain cholesterol metabolism

○Ryo Suzuki
Dept. of Diabetes and Metabolic Diseases, The Univ. of Tokyo

S09-4 Molecular genetic dissecting neuronal pathway controling feeding behavior- Rapid, reversible activation of AgRP neurons potently drives feeding behavior-

○Shuichi Koda[1,2], Michael Krashes[2], ChianPing Ye[2], Bryan Roth[3], Bradford Lowell[2]
[1]Asubio Pharma Co., Ltd., [2]Harvard Medical School & Beth Israel Deaconess Medical Center, [3]University of North Carolina School of Medicine

September 28 (Wednesday)

9:30～11:45 Room A (1F・Hanarikyu)

S10-1～S10-4 The diversity of inositide signaling

Chairs：Eiichiro Nagata (Department of Neurology, Tokai University School of Medicine)
Tetsuro Mimura (Department of Biology, Graduate School of Science, Kobe University)

S10-1 The role of inositol hexakisphosphate kinases on central nerve system in the mammals

○Eiichiro Nagata
Department of Neurology, Tokai University School of Medicine

S10-2 Measurement of inositol polyphosphates by ion chromatography and their physiological status in higher plants

○Tetsuro Mimura[1], Naoto Mitsuhashi[1], Yohei Masuda[1], Yusuke Tanaka[1], Alan Richardson[2], Sung-Kee Chung[3], Hitoshi Yagisawa[4]
[1]Department of Biology, Graduate School of Science, Kobe University, [2]CSIRO Plant Industry, Canberra, ACT, 2601, Australia, [3]Department of Chemistry, Pohang University of Science and Technology, Pohang, Korea, [4]Graduate School of Life Science, University of Hyogo, Ako-gun, Hyogo, Japan

S10-3 Calcium fluxes cause nuclear shrinkage and the translocation of phospholipase C-δ1 into the nucleus

○Hitoshi Yagisawa, Masashi Okada
Graduate School of Life Science, University of Hyogo, Hyogo, Japan

S10-4 NMDA receptor-mediated activation of $PI(4,5)P_2$-producing enzyme PIP5K is essential for AMPA receptor endocytosis during long-term depression

Takamitsu Unoki[1], Shinji Matsuda[2], Wataru Kakegawa[2], Yuji Funakoshi[1], Michisuke Yuzaki[2], ○Hiroshi Hasegawa[1,3], Yasunori Kanaho[1]
[1]Dept. of Physiol. Chem., Inst. of Basic Med. Sci., Univ. of Tsukuba, [2]Dept. of Physiol., Sch. of Med., Keio Univ., [3]Initiative for the Promotion of Young Scientists' Independent Research, Univ. of Tsukuba

September 28 (Wednesday)

9:30～11:45 Room B (2F・Hōō)

S11-1～S11-4 A novel strategy of survival and the reproduction of the retina and the optic nerve for functionl recovery

Chairs：Hideaki Hara (Molecular Pharmacology, Department of Biofunctional Evaluation, Gifu Pharmaceutical University)
Yoshiki Koriyama (Dept. Mol. Neurobiol, Grad. Sch. Med. Kanazawa Univ.)

S11-1 Cell survival and axonal regeneration in rat retinal ganglion cells by purpurin, a novel extracellular matrix molecule after optic nerve injury

○Yoshiki Koriyama, Toru Matsukawa, Mikiko Nagashima, Satoru Kato
Dept. Mol. Neurobiol, Grad. Sch. Med. Kanazawa Univ.

S11-2 Long-distance axonal regeneration in mature mouse optic nerve: combined effects of intraocular inflammation, cAMP, and PTEN deletion

○Takuji Kurimoto
The Department of Ophthalmology, Osaka Medical School, Osaka, Japan

S11-3 Degeneration in the visual pathway accompanying retinal and optic nerve injuries and its therapeutic strategy

○Masamitsu Shimazawa, Hideaki Hara
Molecular Pharmacology, Department of Biofunctional Evaluation, Gifu

Pharmaceutical University, Gifu, Japan

S11-4 The neuroprotective treatment for glaucoma

○Toru Nakazawa
Dept. of Ophthalmol, Univ. of Tohoku

September 28 (Wednesday)

13:30～15:45 Room A (1F・Hanarikyu)

S12-1～S12-4 The important role of ER stress response in the central nervous system

Chairs：Takashi Kudo (Dept. of Psychiatry, Osaka University Graduate School of Medicine)
Osamu Hori (Dept. of Neuroanatomy, Kanazawa Univ.)

S12-1 ER stress and neuropsychiatric disorders-Implications for therapeutic strategies

○Takashi Kudo, Teruhiko Mitsuda, Tsubasa Oumi, Yukako Sakagami, Masatoshi Takeda
Dept. of Psychiatry, Osaka University Graduate School of Medicine

S12-2 The role of an ER-resident transmembrane transcription factor OASIS in astrocyte differentiation

○Atsushi Saito[1], Tsukasa Sanosaka[2], Kinichi Nakashima[2], Kazunori Imaizumi[1]
[1]Dept. Biochem. Div. Genome Radiobiol. Med. Sci. Grad. Sch. Biomed. Sci. Univ. Hiroshima, Hiroshima, Japan, [2]Lab. Mol. Neurosci. Grad. Sch. Biol. Sci. NAIST, Nara, Japan

S12-3 Possible involvement of endoplasmic reticulum protein degradation in Alzheimer's disease

○Masayuki Kaneko[1], Yasunobu Okuma[1], Yasuyuki Nomura[2]
[1]Dept. of Pharmacol., Fac. of Pharmaceut. Sci., Chiba Inst. of Sci., [2]Lab. of Pharmacother., Yokohama Col. of Pharm.

S12-4 Roles of the unfolded protein response (UPR) in MPTP-induced neurotoxicity

○Osamu Hori
Dept. of Neuroanatomy, Kanazawa Univ.

September 28 (Wednesday)

13:30～15:45 Room B (2F・Hōō)

S13-1～S13-4 New insight of functional interactions between neurons and astrocytes

Chairs：Koji Shibasaki (Dept. of Mol.Cell. Neurobiology, Gunma Univ. Grad. Sch. of Med.)

Tetsushi Kagawa (Dept. Stem Cell Reg., Med. Res. Inst., Tokyo Med. Dent. Univ.)

S13-1 Astrocytic modulation of local field potential

○Hajime Hirase

RIKEN - BSI, Saitama, Japan

S13-2 Interaction between brain temperature and neuronal excitability; A specific subtype of astrocyte is classified by a thermo-sensor expression

○Koji Shibasaki

Dept. of Mol.Cell. Neurobiology, Gunma Univ. Grad. Sch.of Med.

S13-3 Specification of glial cell types in the developing central nervous system

○Tetsushi Kagawa[1], Norihisa Bizen[1], Taichi Kashiwagi[1], Ikuo Nobuhisa[1], Takeshi Shimizu[2], Tetsuya Taga[1]

[1] Dept. Stem Cell Reg., Med. Res. Inst., Tokyo Med. Dent. Univ., Tokyo, [2] MechanoBiol. Inst., Natl. Univ. of Singapore

S13-4 Astrocytes regulate neurotransmission at distant synapses through axonal modulation

○Takuya Sasaki

Department of Cerebral Structure, National INstitute of Physiological Sciences

Symposium

Symposium of Kanazawa University Research Center for Child Mental Development and the 54th Annual Meeting of the Japanese Society for Neurochemistry 'Genetic and Molecular Basis of Synapses, Circuits, Memory, Behavior, and Psychological Disorders' In Memory of Dr. Marshall Nirenberg (Brain Memory 2011)

September 26 (Monday)

9:30～11:30 Special Room (1F・No - Zangetsu)

M1-1 Marshall Warren Nirenberg, Honorary member of JSN: Nobel laureate and giant of science

○Toshiharu Nagatsu
Fujita Health Univeristy, Nagoya University

M1-2 The potential role of ATF4 in learning and memory

○Lloyd Greene
Columbia University

M1-3 Single nucleotide polymorphisms of CD38 and oxytocin treatment for 6 subjects with autism spectrum disorders

○Yulia A. Pichugina
Krasnoyarsk Medical University

September 26 (Monday)

15:15～17:15 Special Room (1F・No - Zangetsu)

M2-1 alpha-Synuclein in Parkinson's disease:Pathogenetic foe and therapeutic target

○M. Maral Mouradian
University of Medicine and Dentistry of New Jersey -Robert Wood Johnson Medical School

M2-2 Marshall and Medicine: impact on drug discovery

○Orest Hurko
Biologics Consulting Group, Inc.

M2-3 Regulatory approval of biopharmaceutical products

○James G. Kenimer
Biologics Consulting Group, Inc.

M2-4 A study of generations at high-risk for major depression
○Myrna M. Weissman
Columbia University

M2-5 Neuroscientists of the Future: Empirical Research on the Development and Career Decisions of Young Scientists
○Richard McGee Jr
Northwestern University

September 27 (Tuesday)

9:30~11:30 Special Room (1F・No - Zangetsu)

M3-1 Bone morphogenetic proteins regulate ErbB3/GGF2 signaling to promote gliogenesis in the enteric nervous system
○Alcmène Chalazonitis
Columbia University

M3-2 Transmembrane agrin in filopodia regulation and synapse formation
○Mathew P Daniels
National Heart Lung and Blood Institute, NIH

M3-3 ECT2, an ortholog of drosophila's pebble identified from RNAi screening, regulates neuronal differentiation
○Chiharu Higashida
Kanazawa University

M3-4 Neural progenitors express topographic markers
○David Trisler
University of Maryland School of Medicine

September 27 (Tuesday)

12:30~17:00 Special Room (1F・No - Zangetsu)

M4-1 Regulation of neurokine receptor signaling and trafficking
○Neil M. Nathanson
University of Washington

M4-2 Removal of adult-generated neurons and hippocampal function
○Woong Sun
Korea University

M4-3 Botulinum neurotoxin: Lethal agent or wonder drug
○Michael Adler
USAMRICD

M4-4 Therapeutic potentials of fetal neural stem cells treated with fluoxetine for alzheimer's disease model mice
○Yoo-Hun Suh
Seoul Nat'l University

M4-5 Cholinergic therapy for Schizophrenia and Alzheimer's disease: new approaches
○Dana Hilt
Envivo Pharmaceutical

M4-6 Effects of cannabinoids on microglial and T cells: Role in an animal model of multiple sclerosis
○Zvi Vogel
Weizmann Institute of Science and the Adelson Center for Addictive Diseases Tel Aviv University

M4-7 Inhibition of myostatin activity by antibodies as a therapeutic approach to Amyotrophic Lateral Sclerosis
○Frank S Walsh
Wolfson Centre for Age Related Diseases Kings College

M4-8 Neuromodulations mediated by dextro-morphinans
○Hyoung-Chun Kim
Kangwon National University

September 28 (Wednesday)

9:30～11:30 Special Room (1F・No - Zangetsu)

M5-1 Molecular analysis of central feeding regulation by neuropeptide Y (NPY) neurons with NPY receptor siRNAs
○Hiroshi Higuchi
Niigata University

M5-2 Retinovascular biology and pathophysiology
○Donald Puro
Department of Ophthalmology and Visual Science Department of Physiology

M5-3 Histamine H1 receptor functions in CNS and peripheral tissues
○Hiroyuki Fukui
Department of Molecular Pharmacology, Institute of Health Biosciences, University of Tokushima Graduate School

Oral Sessions

September 26 (Monday)

9:30～11:30 Room C (2F・Heian)

O1-1～O1-6 **Mood disorders/Signal transduction**

Chairs：Toshikazu Saito (Sapporo Medical University, School of Medicine)
Hiroshi Kiyama (Dept. of Funct. Anat. and Neurosci., Nagoya Univ. Grad. Sch. of Med.)

O1-1 **Enzymes involved in pro-BDNF processing may be involved in antidepressive effects of electroconvulsive seizure in the rat hippocampus**

○Tomoya Matsumoto[1,2], Masahiro Segawa[1,2], Shigeru Morinobu[1,2], Manabu Fuchikami[1,2], Shigeto Yamawaki[1,2]
[1]Dept. of Psychiatry and Neurosciences, Hiroshima Univ., Hiroshima, JAPAN, [2]CREST, JST, Tokyo, JAPAN

O1-2 **Deletion of neuropeptide Y gene weakens stress resistance and shortens lifespan in calorie-restricted mice**

○Takuya Chiba, Toshimitsu Komatsu, Ryoichi Mori, Isao Shimokawa
Dept. of Investigative Pathology, Nagasaki Univ. Sch. of Med.

O1-3 **Structural basis for the different stability of Cdk5-p35 and Cdk5-p39**

○Taro Saito[1], Masashi Yano[1], Yusei Kawai[1], Akiko Asada[1], Hirofumi Doi[2], Shin-ichi Hisanaga[1]
[1]Dept Biol Sci, Tokyo Metropolitan Univ, Tokyo, Japan, [2]Celestar Lexico-Sciences, Chiba, Japan

O1-4 **1-Deoxy-nor-sominone (Denosomin) improves hindlimb dysfunction in spinal cord injury and promotes neurite outgrowth through astroglia-mediated signalling**

○Kiyoshi Teshigawara[1], Tomoharu Kuboyama[1], Yuji Matsuya[2], Chihiro Tohda[1]
[1]Div. of Biofunctional Evaluation, Res. Center for Ethnomed., Inst. of Natural Med., Univ. of Toyama, [2]Lab. of Organochem. Design and Synthesis, Fac. of Pharmaceutical Sci., Univ. of Toyama

O1-5 **Changes in emotional behaviors and the action of brain-derived neurotrophic factor in the prefrontal cortex after exposure to chronic restraint stress**

○Shuichi Chiba[1,2], Tadahiro Numakawa[2,3], Midori Ninomiya[2,4], Misty Richards[2,5], Chisato Wakabayashi[2], Toshiyuki Himi[1], Hiroshi Kunugi[2,3]
[1]Faculty of Pharmacy and Research Institute of Pharmaceutical Science, Musashino University, Tokyo, Japan, [2]Department of Mental Disorder Research, National Institute of Neuroscience, National Center of Neurology and Psychiatry, Tokyo, Japan, [3]CREST of Japan Science and Technology Corporation, Saitama, Japan, [4]Department of Pharmacology, Graduate School of Advanced Science and Engineering, Waseda

University, Tokyo, Japan, [5] Center for Neuropharmacology and Neuroscience, Albany Medical College, Albany, New York, United States of America

O1-6 **Sequence and distribution decision of D-beta-amino isobutyric acid(D-BAIB): pyruvate aminotransaminase(AT) in the pig brain**

○Masao Abe, Shinichirou Ochi, Youko Mori, Shu-ichi Ueno
Dept. of Neuropsychiatry, Ehime Graduate School of medicine

September 26 (Monday)

15:15～17:15 Room C (2F・Heian)

O2-1～O2-6 Neurodegeneration/Neuromuscular diseases

Chairs：Shoichi Shimada (Department of Neuroscience and Cell Biology, Osaka University)
Yoshihiro Nakata (Dept. of Pharmacology, Grad. Sch of Biomed Sci., Hiroshima University)

O2-1 **Endothelin stimulates VEGF-A production and activates VEGF receptors in the rat cerebrum**

○Yutaka Koyama [1], Ryuji Nagae [2], Shogo Tokuyama [2], Kazuhiro Tanaka [1], Shotaro Michinaga [1]
[1] Laboratory of Pharmacology, Faculty of Pharmacy, Osaka Ohtani University, Tondabayashi, Japan., [2] Department of Clinical Pharmacy, School of Pharmaceutical Sciences, Kobe Gakuin University, Kobe, Japan

O2-2 **Loss of glial fibrillary acidic protein marginally accelerates disease progression in a SOD1^{H46R} transgenic mouse model of ALS**

○Shinji Hadano [1,2], Yasuhiro Yoshii [3], Asako Otomo [1], Lei Pan [1], Masato Ohtsuka [1], Yasuo Iwasaki [3]
[1] Dept Mol Life Sci, Tokai Univ Sch of Med, Kanagawa, [2] Res Center Brain & Nervous Dis, Tokai Univ Grad Sch Med, [3] Dept Neurol, Toho Univ Omori Med Center

O2-3 **FLRT2 and FLRT3 act as repulsive guidance cues for Unc5-positive neurons**

○Satoru Yamagishi [1,2], Falko Hampel [2], Katsuhiko Hata [3], Daniel Del Toro [2], Manuela Schwark [4,5], Elena Kvachnina [4], Martin Bastmeyer [6], Toshihide Yamashita [3], Victor Tarabykin [4,5], Joaquim Egea [7], Ruediger Klein [2]
[1] Dept. of Anatomy and Neuroscience, Hamamatsu University of Medicine, [2] Max-Planck Institute of Neurobiology, Munich, Germany, [3] Osaka University Graduate School of Medicine, Osaka, [4] Max-Planck Institute of Experimental Medicine, Goettingen, Germany, [5] Charite-Universitaetsmedizin Berlin, Berlin, Germany, [6] Universitaet Karlsruhe (TH), Karlsruhe, Germany, [7] Universitat de Lleida/ IRBLLEIDA, Spain

Oral Sessions

O2-4 **Mice lacking in an enzyme involved in chondroitin sulfate synthesis shows better recovery from spinal cord injury**

○Kosei Takeuchi[1,2], Susumu Higa[1], Nozomu Yoshioka[3], Chika Kudo[1], Hitoshi Kawano[3], Michihiro Igarashi[1,2]
[1] Div. of Mol. & Cell Biol., Med., Niigata Uinv., [2] Trans-deciplinary Res Program, Niigata Univ., [3] Lab. of Neuro Regeneration, Tokyo Metro. Inst. of Medical Sci.

O2-5 **The analyses of Reelin-induced neuronal aggregation in the developing neocortex**

○Ken-ichiro Kubo, Takao Honda, Katsutoshi Sekine, Kazuhiro Ishii, Hidenori Tabata, Kazunori Nakajima
Dep. of Anatomy, Keio Univ. Sch. of Med., Tokyo, Japan

O2-6 **Protective effect of indomethacin against neuronal degeneration induced by trimethyltin in mice**

○Yukary Nakamura, Huong Nguyen Quynh, Kiyokazu Ogita
Dept. Pharmacol., Setsunan Univ. Fac. Pharm. Sci., Osaka, Japan

September 27 (Tuesday)

9:30～11:30 Room C (2F・Heian)

O3-1～O3-6 **Substance dependence/Synaptic plasticity**

Chairs：Tomoko Tashiro (Department of Chemistry and Biological Science, Aoyama Gakuin University)
Makoto Sato (Div. Cell Biol. Neurosci., Dept. Morphol. Physiol., Fac. Med. Sci., Univ. Fukui)

O3-1 **Coordinately gene expression changes of actin dynamics regulator associated with long-lasting synaptic enhancement in hippocampal slice cultures after repetitive exposures to glutamate**

○Katsuhiro Kawaai[1], Keiko Tominaga-Yoshino[2], Tomoyoshi Urakubo[2], Naoko Taniguchi[2], Yasumitsu Kondoh[3], Hideo Tashiro[3], Akihiko Ogura[2], Tomoko Tashiro[4]
[1] Lab. For Developmental Neurobiology, RIKEN Brain Science Institute, Wako, Japan, [2] Dept. Neurosci., Osaka Univ., Grad. Sch. of Frontier Biosci., Osaka, Japan , [3] Sensing Technology Laboratory, Discovery Research Institute, RIKEN, Wako, Saitama, Japan, [4] Dept. Science & Engineering, Graduate School of Science & Engineering, Aoyama Gakuin University

O3-2 **Anticancer agent 6-MITC derived from wasabi control seizures in epileptic mutant EL mice at extremely low dosage**

○Yoshiya L. Murashima[1], Atsuko Onose[1], Yoko Fuke[2]
[1] Dept Fronteer Health Sci Tokyo Metropolitan Univ Graduate School of Human Health Sci, Tokyo, Japan, [2] Dept Health Promotion Sci Tokyo Metropolitan Univ Graduate School of Human Health Sci, Tokyo, Japan

O3-3 Mesenchymal stem cells transmigrate across brain microvascular endothelial cell monolayers through transiently formed interendothelial gaps

○Takahiro Katayama[1], Takashi Matsushita[1,2], Tatsuya Kibayashi[1], Osamu Honmou[3], Shun Shimohama[2], Masabumi Minami[1]

[1]Dept. Pharmacol., Grad. Sch. Pharm. Sci., Hokkaido Univ., Sapporo, Japan, [2]Dept. Neurol., Sch. Med., Sapporo Med. Univ., Sapporo, Japan, [3]Dept. Neural Rep. and Ther., Sch. Med., Sapporo Med. Univ., Sapporo, Japan

O3-4 Two different ways of vesicle transport are mediated by actin cytoskeleton and microtubules in the growth cone

○Motohiro Nozumi[1,2], Kaoru Kato[3], Michihiro Igarashi[1,3]

[1]Div Mol Cell Biol, Niigata Univ Grad Sch Med, [2]Trans-disciplinary Res Progr, Niigata Univ, [3]National Institute of Advanced Industrial Science and Technology

O3-5 Nicotine induces dendritic spine remodeling in cultured hippocampal neurons

○Hidekazu Tanaka, Yoshikatsu Kanai

Department of Pharmacology, Osaka University School of Medicine, Osaka, Japan

O3-6 Diversity of Neuropsin-dependent Synaptic Associativity in the Hippocampal Pyramidal Neuron

○Yasuyuki Ishikawa, Hideki Tamura, Sadao Shiosaka

Laboratory of Functional Neuroscience, Nara Institute of Science and Technology

September 27 (Tuesday)

12:30～14:30 Room C (2F・Heian)

O4-1～O4-6 Epilepsy/Neurodegenerative disorder

Chairs：Kohji Fukunaga (Dept. Pharmacology, Tohoku University Grad.Sch.Pharm. Scis.)

Taiichi Katayama (Div. of Mol. Brain Sci., United Graduate School of Child Development, Osaka Univ. Kanazawa Univ. Hamamatsu Univ. sch. Med.)

O4-1 Growth hormone-related molecular system that regulates both epilepsy progression and emotional symptoms

Keiko Kato[1,2], ○Hiroki Kanno[2], Yoshio Hirabayashi[3]

[1]Fact. of Life Sci., Kyoto Sangyo Univ., Kyoto,Japan, [2]Osaka Pref. Univ., Osaka, Japan, [3]RIKEN, BSI, Saitama, Japan

O4-2 Sigma-1 receptor stimulation with dehydroepiandrosterone ameliorates cognitive deficits in olfactory bulbectomized mice

○Shigeki Moriguchi, Yui Yamamoto, Kohji Fukunaga

Dept. Pharmacol., Grad. Sch. of Pharmaceut. Sci., Tohoku Univ. Sendai, Japan

O4-3 Signaling pathway of SUN13837, a novel compound mimicking the pharmacological actions of bFGF

○Yoshiari Shimmyo[1], Taisuke Kadoshima[1], Ryoko Ogino[1], Mariko Kuroda[1], Naohiro Takemoto[2], Shinya Ueno[1], Norihito Murayama[1], Teruyoshi Inoue[1]
[1]Faculty of Pharmacology II, ASUBIO PHARMA CO., LTD., [2]Faculty of Chemistry, ASUBIO PHARMA CO., LTD.

O4-4 γ-Tubulins are decreased in the MSA patient brains and γ-tubulin 2-deficient mouse displays MSA-like neurodegeneration and ataxia

○Koji Tsutsumi[1], Akiko Yuba-Kubo[4,14], Hiroshi Takagi[4], Hiroyasu Akatsu[5], Alu Konno[1], Yuko Miyamoto[6], Ikuko Yao[4], Kiyoshi Egawa[2], Showbu Sato[4], Akiharu Kubo[7], Kaori Yasutake[4], Nobuhiro Morone[8], Daisuke Yamauchi[6], Tetsuya Horio[11], Yoshishige Kimura[1], Tsuyoshi Miyakawa[9], Atsuo Fukuda[2], Hideo Tsukada[10], Mari Yoshida[12], Yoshio Hashizume[5], Yoshinobu Mineyuki[6], Yoshiyuki Konishi[1], Koji Ikegami[1], Mitsutoshi Setou[1,4]
[1]Dept. Cell Biol., Hamamatsu Univ. Sch. Med., [2]Dept. Physiol., Hamamatsu Univ. Sch. Med., [3]1st Dept. Med., Hamamatsu Univ. Sch. Med., [4]Mitsubishi Kagaku Inst. Life Sci., [5]Choju Medical Inst., Fukushimura Hospital, [6]Dept. Life Sci., Grad. Sch. Life Sci., Univ. Hyogo, [7]Dept. Dermatology, Keio Univ. Sch. Med., [8]National Inst. Neurosci., NCNP, [9]Div. Systems Medical Sci., ICMS, Fujita Health Univ., [10]Central Research Lab., Hamamatsu Photonics K.K, [11]Dept. Molecular Biosci., Univ. of Kansas, [12]Inst. for Medical Sci. Aging, Aichi Medical Univ., [13]Grad. Sch. Front. Biosciences., Osaka Univ., [14]Dept. Biochem., Keio University

O4-5 Matrix metalloproteinase-9 contributes to kindled seizure development in pentylenetetrazole-treated mice by converting pro-BDNF to mature BDNF in the hippocampus

○Hiroyuki Mizoguchi[1], Jun Sato[1], Makoto Sawada[2], Toshitaka Nabeshima[3], Kiyofumi Yamada[4]
[1]Futuristic Environmental Simulation Center, Research Institute of Environmental Medicine, Nagoya University, [2]Department of Brain Functions, Division of Stress Adaptation and Protection, Research Institute of Environmental Medicine, Nagoya University, [3]Department of Chemical Pharmacology, Graduate School of Pharmaceutical Sciences Meijo University, [4]Department of Neuropsychopharmacology and Hospital Pharmacy, Nagoya University Graduate School of Medicine

O4-6 The secreted ectodomain of calsyntenin-3 (sCst-3) attenuates neuronal death of cortical neurons overexpressing full-length and CTF of Cst-3

○Yoko Uchida, Fujiya Gomi
RT for Functional Biogerontology, Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan

September 27 (Tuesday)

14:30～16:30 Room C (2F・Heian)

O5-1～O5-6 Schizophrenia/Genomics

Chairs：Toru Nishikawa (Department of Psychiatry and Behavioral Sciences, Tokyo Medical and Dental University Graduate School)
Akio Wanaka (Department of Anatomy and Neuroscience, Nara Medical University)

O5-1 Involvement of IFITM3 in brain dysfunction caused by immune activation during neurodevelopment

○Daisuke Ibi[1,2], Taku Nagai[1], Toshitaka Nabeshima[2], Kiyofumi Yamada[1]
[1]Dept. Neuropsychopharmacol. & Hosp pharm., Nagoya Univ. Grad. Sch. Med., [2]Dept. Chem. Pharmacol., Meijo Univ. Grad. Sch. of Pharm. Sci.

O5-2 Functional expression of carnitine/organic cation transporter OCTN1 (SLC22A4) in murine neurons

○Noritaka Nakamichi, Takayuki Taguchi, Hiroshi Hosotani, Tomoko Sugiura, Yukio Kato
Faculty of Pharmacy, Kanazawa University, Kanazawa 920-1192, Japan

O5-3 Suppression of BDNF secretion contributes to the phencyclidine-induced synaptic dysfunction

○Naoki Adachi[1,2], Tadahiro Numakawa[1,2], Emi Kumamaru[1], Chiaki Itami[3], Shuichi Chiba[1], Yoshimi Iijima[1], Misty Richards[4], Ritsuko Katoh-Semba[5], Hiroshi Kunugi[1,2]
[1]Dept. of Mental Disorder Research, National Institute of Neuroscience, NCNP, Tokyo, Japan, [2]CREST, JST, Japan, [3]Dept. of Physiology, Faculty of Medicine, Saitama Med Univ, Saitama, Japan, [4]Laboratory for Molecular Neurogenesis, Albany Medical College, Albany, NY 12208, USA, [5]RIKEN Brain Science Institute, Saitama, Japan

O5-4 Genetic association study of synapse-associated protein 97 (SAP97) and schizophrenia

○Naoki Yamamoto[1], Junko Sato-Kimura[1], Akihito Uezato[1], Dai Shimazu[1], Daisuke Jitoku[1], Masakazu Umino[1], Asami Umino[1], Akeo Kurumaji[1], Yoshimi Iijima[2], Hiroshi Kunugi[2], Yoshimi Iwayama[3], Takeo Yoshikawa[3], Toru Nishikawa[1]
[1]Section of Psychiatry and Behavioral Sciences, Tokyo Medical and Dental University Graduate School, Tokyo, Japan, [2]Department of Mental Disorder Research, National Institute of Neuroscience, NCNP, Kodaira, Tokyo, Japan, [3]Laboratory for Molecular Psychiatry, RIKEN Brain Science Institute, Wako, Saitama, Japan

O5-5 A conventional and quick gene silencing method in adult rat brain: a single intracerebroventricular injection of Accell siRNA

○Takeya Kubo[1], Hidemitsu Nakajima[1], Yuko Semi[1], Mitsuru Kuwamura[2], Takeshi Izawa[2], Yasu-Taka Azuma[1], Tadayoshi Takeuchi[1]

[1] Lab. of Veterinary Pharmacology, Osaka Pref. Univ., [2] Lab. of veterinary pathology, Osaka Pref. Univ.

O5-6 Re-evaluation of DISC1 using its new antibodies and mice with targeted disruption of exons 2 and 3 of the DISC1 gene

○Keisuke Kuroda[1,2], Shinnosuke Yamada[2,3], Motoki Tanaka[4], Michiro Iizuka[1,5], Hisashi Yano[1], Atsushi Enomoto[6], Akira Mizoguchi[5], Masahiro Sokabe[4], Masahide Takahashi[6], Kiyofumi Yamada[2,3], Kozo Kaibuchi[1,2]

[1] Dept of Cell Pharmacol, Nagoya Univ Grad Sch of Med, Nagoya, Japan, [2] JST, CREST, Nagoya, Japan, [3] Dept of Neuropsychopharmacol and Hospital Phar, Nagoya Univ Grad Sch of Med, Nagoya, Japan, [4] Dept of Physiol, Nagoya Univ Grad Sch of Med, Nagoya, Japan, [5] Dept of Neural Regener and Cell Commu, Mie Univ Grad Sch of Med, Tsu, Japan., [6] Dept of Pathol, Nagoya Univ Grad Sch of Med, Nagoya, Japan

September 28 (Wednesday)

9:30～11:30 Room C (2F・Heian)

O6-1～O6-6 Glia/Myelin

Chairs：Yasuhiro Watanabe (Dept. Pharmacol. Natl. Def. Med. Col.)
Hiroshi Nakanishi (Department of Aging Science and Pharmacology, Kyushu University)

O6-1 Analysis of the intercellular signaling cascade induced by chronic stress exposure in oligodendrocytes in corpus callosum

○Shingo Miyata[1,2], Yoshihisa Koyama[1], Manabu Taniguchi[1], Keiko Yoshikawa[1], Toshiko Ishikawa[1], Tomo-o Yuba[1], Masaya Tohyama[1,2,3]

[1] Dept. of Anat&Neurosci. Med. Osaka Univ., [2] Dept. of Clinical Disorder Res. The Osaka-Hamamatsu Joint Res. Center for Child Mental Develop. Osaka Univ., [3] Dept. of Child Develop. and Mol. Brain Sci. United Child Develop. Osaka Univ.

O6-2 N-terminus cleaved PAP-III (Reg-IIIγ) forms fibrillar structure and provides axons with a platform for adhesion and elongation

○Hiroyuki Konishi, Sakiko Matsumoto, Hiroshi Kiyama

Dept. of Funct. Anat. and Neurosci., Nagoya Univ. Grad. Sch. of Med.

O6-3 Microglial activation by zinc released from hypoosmotic stress-loaded astrocytes

○Kazuki Nagasawa, Shohei Segawa, Shogo Nakamura, Yuki Ohsato, Misaki Tani, Takeshi Nishiura, Takaaki Matsuo, Kentaro Nishida

Dept. of Environ. Biochem., Kyoto Pharm. Univ.

O6-4 The protective effect of endogenous erythropoietin released from astrocyte to the oligodendrocyte precursor cell against hypoxic and reoxygenation injury

○Mineyoshi Aoyama[1], Shin Kato[1,2], Hiroki Kakita[1,2], Hayato Asai[1,2], Yoshiaki Nagaya[1,2], Kiyofumi Asai[1]

Oral Sessions

[1] Dept. Mol Neurobiol., Nagoya City Univ., Sch. Med., [2] Dept of Pediatrics, Nagoya City Univ, Nagoya, Japan

O6-5 Interferon regulatory factor-8 in spinal microglia is a transcription factor crucial for switching to a reactive phenotype after nerve injury

○Takahiro Masuda[1], Makoto Tsuda[1], Ryohei Yoshinaga[1], Hidetoshi Saitoh[1], Tomohiko Tamura[2], Kazuhide Inoue[1]
[1] Dept. Mol. Syst. Pharmacol., Grad. Sch. Pharm. Sci., Kyushu Univ., [2] Dept. Immunol., Grad. Sch. Med., Yokohama City Univ., Yokohama, Japan

O6-6 Morphological changes of myelin and axons in experimental autoimmune encephalomyelitis

○Yoshio Bando[1], Taichi Nomura[1], Hiroki Bichimoto[2], Daisuke Kouga[3], Tsuyoshi Watanabe[2], Shigetaka Yoshida[1]
[1] Dept. of Functional Anatomy and Neuroscience, Asahikawa Medical University, Asahikawa, Japan, [2] Dept. of Microscopic Anatomy and Cell biology, Asahikawa Medical University, Asahikawa, Japan, [3] Division of Microscopic Anatomy, Grad. Sch. of Medical and Dental Sci., Niigata Univ., Niigata, Japan

September 28 (Wednesday)

9:30～11:10 Room D (2F・Tenpyo)

O7-1～O7-5 Signal transduction/Axonal and dendritic outgrowth

Chairs：Yasuki Ishizaki (Mol. Cell. Neurobiol., Gunma Univ. Grad. Sch. Med)
Hiroyuki Nawa (Mol Neurobiol., Brain Res Inst, Niigata Univ.)

O7-1 Functional phospho-proteomics analysis of cellular substrates for calcium/calmodulin-dependent protein kinase I

○Takeo Saneyoshi[1,2], Masaki Matsumoto[3], Naohito Nozaki[4], Hidewo Kusano[1], Shunichiro Iemura[1], Keiichi Nakayama[3], Tohru Natsume[1]
[1] National Institute of Advanced Science and Technology, Tokyo, Japan, [2] Brain Science Institute, RIKEN, [3] Medical Institute of Bioregulation, Kyushu Univ., Fukuoka, Japan., [4] Kanagawa Dental College, Yokosuka, Japan

O7-2 Antagonism of an endogenous Nogo receptor antagonist LOTUS to B-lymphocyte stimulator-induced axon growth inhibition

○Kuniyuki Nishiyama, Yuji Kurihara, Masumi Iketani, Hiromu Ito, Yoshio Goshima, Kohtaro Takei
Dept. of Mol. Pharmacol. & Neurobiol., Yokohama City Univ. Sch. of Med., Yokohama, Japan

O7-3 Signal transduction underlying chondroitin sulfate proteoglycan-mediated inhibition of axon regeneration

○Tomoharu Kuboyama[1,2], Jerry Silver[3], Chihiro Tohda[1], Hiroyuki Kamiguchi[2]
[1] Div. of Biofunctional Evaluation, Res. Center for Ethnomed., Inst. of Natural Med.,

Oral Sessions

Univ. of Toyama, [2]Lab. for Neuronal Growth Mechanisms, RIKEN Brain Science Institute, [3]Dep. of Neurosciences, School of Med., Case Western Reserve Univ., USA

O7-4 **Expression analysis of Shank3 variants possibly associated with autism spectrum disorders in the developing mouse neocoetex**

○Hirotsugu Asano, Chikako Waga, Akiko Tsuchiya, Shigeo Uchino, Shinichi Kohsaka
Department of Neurochemistry, National Institute of Neuroscience, Tokyo, Japan

O7-5 **Intra-cellular translocation of Pgc1 α is involved in PACAP induced neurite outgrowth in neuronal cells**

○Yuki Kambe, Kazuhiko Inoue, Takashi Kurihara, Atsuro Miyata
Grad. Sch. of Med. and Dent. Sci., Kagoshima Univ., Kagoshima

September 28 (Wednesday)

13:30～15:30 Room D (2F・Tenpyo)

O8-1～O8-6 **Developmental disorders/Neuronal stem cell**

Chairs : Shin-ichi Hisanaga (Department of Biological Sciences, Tokyo Metropolitan University)
Atsuko Inoue (Department of Pharmacotherapeutics, Faculty of Pharmacy and Pharmaceutical Sciences, Fukuyama University)

O8-1 **The coordination of the cell cycle exit and the differentiation of cerebral cortical progenitors is regulated by Rb family**

○Itsuki Ajioka, Mio Oshikawa, Kei Okada
Center for Brain Integration Research, Tokyo Medical Dental U, Tokyo, Japan

O8-2 **Effects of neurotransmitter receptors on proliferation and differentiation into neural progenitor cells in mouse induced pluripotent stem cells**

○Toshiaki Ishizuka, Yasuhiro Watanabe
Dept. Pharmacol. Natl. Def. Med. Col.

O8-3 **Mammalian glial cells missing genes induce Hes5 expression by active DNA demethylation and induce neural stem cells**

○Seiji Hitoshi [1,2], Yugo Ishino [1,2], Kazuhiro Ikenaka [1,2]
[1]Neurobiology & Bioinformatics, NIPS, Okazaki, [2]Dept. Physiol., Graduate Univ. Advanced Studies, Okazaki

O8-4 **Behavioral hyperactivity in the rat by bisphenol A, but not by its derivatives, 3-hydroxybisphenol A or bisphenol A 3,4-quinone**

○Yoshinori Masuo [1], Masanori Terasaki [2], Masatoshi Morita [3], Masami Ishido [3]
[1]Laboratory of Neuroscience, Department of Biology, Faculty of Science, Toho University, Funabashi, Japan, [2]Laboratory of Physical Chemnistry, Institute for Environmental Sciences, University of Shizuoka, Shizuoka, Japan, [3]Center for Environmental Risk Research, National Institute for Environmental Studies, Tsukuba,

Japan

O8-5 Up-regulation of neuropeptide Y receptors in hypotensive mouse vasomotor center

○Shin-ichi Murase, Hiroshi Higuchi
Division of Pharmacology, Molecular and Cellular Medicine, Niigata University, Graduate School of Medical and Dental Sciences

O8-6 Serum levels of anterior pituitary hormones in children with autism

○Hideo Matsuzaki, Keiko Iwata, Norio Mori
Research Center for Child Mental Development, Hamamatsu University School of Medicine, Hamamatsu, Japan

Graduate Oral Sessions

September 26 (Monday)

9:30～11:30 RoomD (2F・Tenpyo)

G1-1～G1-6 **Axonal and dendritic outgrowth/Network formation**

Chairs：Akiko Tabuchi (Graduate School of Medicine and Pharmaceutical Sciences, University of Toyama, Japan)
Hiroyuki Mizoguchi (Futuristic Environmental Simulation Center, Research Institute of Environmental Medicine, Nagoya University)

G1-1 **The Cdk5-LMTK1/AATYK1-Rab11 pathway, a novel cascade regulating axon outgrowth**

○Tetsuya Takano[1], Mineko Tomomura[2], Nozomu Yoshioka[1,3], Koji Tsutsumi[1], Yukichi Terasawa[1], Hitoshi Kawano[3], Mitsunori Fukuda[4], Shin-ichi Hisanaga[1]
[1]Department of Biological Sciences, Tokyo Metropolitan University,Tokyo, Japan, [2]MPL, Meikai University School of Dentistry, Saitama, Japan, [3]Laboratory of Neural regeneration, Tokyo Metropolitan Institute of Medical Science, Tokyo, Japan, [4]Department of Developmental Biology and Neurosciences, Graduate School of Life Sciences, Tohoku University, Miyagi, Japan

G1-2 **Functional domain of LOTUS serving as endogenous Nogo66 receptor antagonist**

○Yuji Kurihara[1,2], Masumi Iketani[1], Hiromu Ito[1], Kuniyuki Nishiyama[1], Yusuke Sakakibara[1], Fumio Nakamura[1], Nobuhisa Mizuki[2], Yoshio Goshima[1], Kohtaro Takei[1]
[1]Dept. of Mol. Pharmacol. & Neurobiol., Grad. Sch. of Med., Yokohama City Univ., Yokohama, Japan, [2]Dept. of Ophthalmol., Grad. Sch. of Med., Yokohama City Univ., Yokohama, Japan

G1-3 **Physiological roles of molecular interaction between LOTUS and Nogo receptor in lateral olfactory tract formation**

○Masumi Iketani, Yuji Kurihara, Hiromu Ito, Kuniyuki Nishiyama, Yoshio Goshima, Kohtaro Takei
Department of Molecular Pharmacology and Neurobiology, Graduate School of Medicine, Yokohama City University, Yokohama, Japan

G1-4 **Promoting action of an endogenous Nogo66 receptor antagonist LOTUS on neurite outgrowth**

○Hiromu Ito, Yuji Kurihara, Masumi Iketani, Kuniyuki Nishiyama, Yusuke Sakakibara, Fumio Nakamura, Yoshio Goshima, Kohtaro Takei
Dept. of Mol. Pharmacol. & Neurobiol, Grad. Sch. of Med., Yokohama City Univ.

G1-5 The function and expression of sigma-1 short receptor, a novel splice variant in the brain

○Kiyoshi Ishikawa, Norifumi Shioda, Kohji Fukunaga
Department of Pharmacology, Grad. Sch. Pharm. Scis., Tohoku University, Sendai

G1-6 Dynactin-1 knock-down C.elegans is a novel sporadic amyotrophic lateral sclerosis (SALS) model simulating axonal transport defect and motor neuron degeneration

○Kensuke Ikenaka, Kaori Kawai, Zhe Huang, Yue-mei Jiang, Masahisa Katsuno, Fumiaki Tanaka, Gen Sobue
Department of Neurology, Nagoya University Graduate School of Medicine, Nagoya, Japan

September 26 (Monday)

15:15～17:15 RoomD (2F・Tenpyo)

G2-1～G2-6 Developmental disorders/Transcription factors

Chairs：Kazuhiko Watabe (ALS/Neuropathy Project, Tokyo Metropolitan Institute of Medical Science)
Katsuhiko Yanagisawa (Director, Center for Development of Advanced Medicine for Dementia National Center for Geriatrics and Gerontology)

G2-1 Neural circuits in controlling paternal parental behavior in male ICR mice

○Shirin Akther, Chiharu Higashida, Ming Kun liang, Jin Zhong, Haruhiro Higashida
Department of Biophysical Genetics, Graduate School of Medical Science, Kanazawa University

G2-2 Involvement of transient inhibition of histone deacetylase in valproic acid-induced autisitic-like behaviors and cortical pathology in mice

○Yuta Hara [1], Shunsuke Kataoka [1], Yuko Maeda [1], Yukio Ago [1], Kazuhiro Takuma [1], Toshio Matsuda [1,2]
[1] Laboratory of Medicinal Pharmacology, Graduate School of Pharmaceutical Sciences, Osaka University, Suita, Japan, [2] United Graduate School of Child Development, Osaka University, Kanazawa University and Hamamatsu University School of Medicine, Suita, Japan

G2-3 Denosomin enhances axonal regrowth associated with motor function recovery in spinal cord injury

○Michiko Shigyo [1], Aiko Nagata [1], Kiyoshi Teshigawara [1], Tomoharu Kuboyama [1], Yuji Matsuya [2], Chihiro Tohda [1]
[1] Div. of Biofunction Evaluation, Res. Center for Ethnomed., Inst. of natural Med., Univ. of Toyama, [2] Lab. of Organochem. Design and Synthesis, Fac. of Pharmaceutical Sci., Univ. of Toyama

G2-4 **Exploring the role of cystatin F in demyelination disease**

○Takahiro Shimizu[1,2], F. Kenji Tanaka[1,2], Jianmei Ma[3], Kazuhiro Ikenaka[1,2]
[1]The Graduate University for Advanced Studies, [2]National Institute for Physiological Sciences, [3]Dalian Medical University

G2-5 **Hypothalamic necdin regulates thyroid hormone-mediated energy expenditure**

○Chinatsu Shiraishi, Kouichi Hasegawa, Kazuaki Yoshikawa
Laboratory of Regulation of Neuronal Development, Institute for Protein Research, Osaka University

G2-6 **Necdin forms multiprotein complexes with Smc5/6 components in mammalian brain**

○Hiroki Kashiwagi, Kouichi Hasegawa, Kazuaki Yoshikawa
Laboratory of Regulation of Neuronal Development, Institute for Protein Research, Osaka University

September 27 (Tuesday)

9:30～11:30 Room D (2F・Tenpyo)

G3-1～G3-6 **Glia/Myelin**

Chairs：Satoru Kato (Dept. Mol. Neurobiol, Grad. Sch. Med. Kanazawa Univ.)
Yutaka Koyama (Laboratory of Pharmacology, Faculty of Pharmacy, Osaka Ohtani University)

G3-1 **Microglia release ATP by a mechanism of exocytosis**

○Yoshio Imura[1], Yousuke Morizawa[1], Keisuke Shibata[1], Youichi Shinozaki[1], Yoshinori Moriyama[2], Schuichi Koizumi[1]
[1]Faculty of Medicine, Department of Pharmacology, University of Yamanashi, [2]Membrane Biochemistry, Okayama Univ. Sch. Med. Den. Pharmaceutocal. Sci.

G3-2 **Expression of Transglutaminase 2 and Factor XIII-A in Microglia**

○Kenji Kawabe, Katsura Takano, Mitsuaki Moriyama, Yoichi Nakamura
Lab. Integrative Physiology, Vet. Sci., Osaka Pref. Univ.

G3-3 **Role of glial and fibrotic scars in inhibition of axonal regeneration and tissue healing after traumatic injury of the brain**

○Nozomu Yoshioka[1,2], Hiroaki Asou[3], Junko Kimura-Kuroda[1], Shin-ichi Hisanaga[2], Hitoshi Kawano[1]
[1]Tokyo Met Inst of Med Sci, [2]Tokyo Metro Univ, [3]Keio Univ.

G3-4 **Regulation of PLD4 expression under microglial activation**

○Yoshinori Otani[1], Yoshihide Yamaguchi[1], Hiroshi Kitani[2], Yumi Sato[3], Teiichi Furuichi[3,4], Hiroko Baba[1]
[1]Dept of Mol Neurobio, Tokyo Univ of Pharm and Life Sci, Hachioji, Japan., [2]Trans Anim Res Cr, Natl Inst of Agrobio Sci, Tsukuba, Japan., [3]Lab for Mol Neurogenesis,

RIKEN Brain Sci Inst., [4] Dept of sci and eng, Tokyo Univ of Sci, Noda , Japan.

G3-5 Sema4D Promotes Oligodendrocyte Differentiation and Myelin Formation

○Kouji Okuno[1], Wataru Yamaguchi[1], Rie Tamai[1], Miho Kageura[1], Tatsuo Fruyama[2], Shinobu Inagaki[1]
[1] Group of Neurobiology, Division of Health Sciences, Graduate School Of Medicine, Osaka University, Osaka, Japan , [2] Kagawa Prefectural University of Health Science, Kagawa, Japan

G3-6 Important role of plasma membrane monoamine transporters in histamine uptake by human astrocytes

○Fumito Naganuma, Takeo Yoshikawa, Tadaho Nakamura, Tashie Idutu, Kazuhiko Yanai
The Department of Pharmacology, Tohoku uiversity, Sendai, Japan

September 27 (Tuesday)

12:30～14:30 Room D (2F・Tenpyo)

G4-1～G4-6 Neurodegenerative disorders/Animal models

Chairs：Keiji Wada (National Center for Neurology and Psychiatry)
Hideo Taniura (Department of Pharmacy, College of Pharmaceutical Sciences, Ritsumeikan University)

G4-1 7-Nitroindazole, a neuronal nitric oxide synthase inhibitor, attenuates the development of L-DOPA-induced dyskinesia in 6-hydroxydopamine-lesioned rats

○Yuki Ota[1], Kazuhiro Takuma[1], Tsuyoshi Takahashi[1], Yukio Ago[1], Toshio Matsuda[1,2]
[1] Laboratory of Medicinal Pharmacology, Graduate School of Pharmaceutical Sciences, Osaka University, Suita, Japan, [2] United Graduate School of Child Development, Osaka University, Kanazawa University and Hamamatsu University School of Medicine, Suita, Japan

G4-2 GAPDH aggregate accelerates fibrillation of amyloid-β

○Yuko Semi, Hidemitsu Nakajima, Takeya Kubo, Masanori Itakura, Yasu-Taka Azuma, Tadayoshi Takeuchi
The Laboratory of Veterinary Pharmacology, Graduate School of Life and Environmental Science, Osaka Prefecture University

G4-3 The I2020T LRRK2 transgenic mouse exhibits impaired locomotive ability accompanied by characteristic features of dopaminergic neurons

○T Maekawa[1], S Mori[1], Y Sasaki[1], T Miyajima[1], S Azuma[2], E Ohta[1], F Obata[1]
[1] Kitasato Univ. Grad. Scl. Medicine, Clin. Immunol., [2] Lab. Animal Sci.

G4-4 Alterations in local thyroid hormone metabolism in the young senescence-accelerated SAMP8 mice: association with delayed myelination and behavioral abnormalities

○Erika Sawano, Shinpei Kikuma, Miki Nishiki, Takayuki Negishi, Tomoko Tashiro
Department of Chemistry and Biological Science, Aoyama Gakuin University

G4-5 Possible involvement of ubiquitin ligase RNF19B and Dorfin in amyloid-β production

○Masashi Yamamori[1], Masayuki Kaneko[1], Masayuki Onoguchi[1], Yasuyuki Nomura[2], Yasunobu Okuma[1]
[1]Dept. of Pharmacol., Fac. of Pharmaceut. Sci., Chiba Inst. of Sci., [2]Lab. of Pharmacother., Yokohama Col. of Pharm.

G4-6 Donepezil reduces phosphorylation levels of tau protein in cellular model of tauopathy

○Hirohito Sadaki[1], Tadanori Hamano[1], Norimichi Shirafuji[1], Chiemi Ishida[1], Toru Kishitani[1], Shu-Hui Yen[2], Makoto Yoneda[1], Masaru Kuriyama[1], Yasunari Nakamoto[1]
[1]2nd Dept. of Intern. Med., Faculty of Medical Sciences, Unviersity of Fukui, [2]Mayo Clinic Jacksonville

September 27 (Tuesday)

14:30～16:30 Room D (2F・Tenpyo)

G5-1～G5-6 Schizophrenia/Synaptic plasticity

Chairs：Takashi Kudo (Department of Psychiatry, Osaka University Graduate School of Medicine)
Noritaka Nakamichi (Laboratory of Molecular Pharmacotherapeutics, Faculty of Pharmacy, Kanazawa University)

G5-1 Transplantation of mouse neural stem cells derived from ES cells to dorsal hippocampus of epileptic mutant EL mice

○Atsuko Onose[1], Yoshiya L. Murashima[1], Masahiro Otsu[2], Hiroyuki Omori[1], Takuya Yoshie[1], Takashi Nakayama[3], Yoko Fuke[4], Nobuo Inoue[1]
[1]Lab Regenerative Neurosci, Dept Frontier Health Sci, Tokyo Metropolitan Univ, Tokyo, Japan, [2]Dept health promotion sci Tokyo Metropolitan Univ, Tokyo, Japan, [3]Dept Biochem, Yokohama City Univ School of Medicine, Yokohama, Japan, [4]Dept health promotion sci Tokyo Metropolitan Univ Graduate School of Human Health Sci, Tokyo, Japan

G5-2 PACAP regulates dendritic spine morphology

○Katsuya Ogata[1], Atsuko Hayata[1,2], Kaoru Seiriki[1], Keisuke Hazama[1], Hisae Momosaki[1], Norihito Shintani[1], Akemichi Baba[3], Hitoshi Hashimoto[1,2,4]
[1]Lab of Mol Neuropharmacol, Grad Sch of Pharmaceut Sci, Osaka Univ., [2]Center Child Mental Dev., Unit. Grad. Sch. Child Dev., Osaka Univ., [3]Div. Pharmacol., Dept.

Pharm., Sch. Pharm., Hyogo Univ. Health Sci, [4]Dep. Mol. Phaemaceut. Sci., Osaka Univ Grad. Sch. Med

G5-3 Histological profile of synaptic matrix metalloproteinase activity in the mouse hippocampus

○Harumitsu Suzuki, Dai Kanagawa, Sadao Shiosaka
Division of Functional Neuroscience, Grad. of Biological Sciences, NAIST, Nara, Japan

G5-4 The molecular mechanism of SNAP-25 dephosphorylation in mouse brain

○Yuuki Iida[1], Saori Yamamori[2], Chiemi Nakaya[2], Makoto Itakura[2], Hitoshi Miyaoka[3], Masami Takahashi[2]
[1]Kitasato University Graduate School of Med, Knagawa, [2]Department of Biochemistry Kitasato University School of Medicine, [3]Department of Psychiatry Kitasato University School of Medicine

G5-5 The effect of antipsychotics on interneurogenesis of adult neural stem cells

○Hiroo Kaneta, Wataru Ukai, Eri Hashimoto, Toshihiro Yoshinaga, Masaru Tateno, Kimihiko Watanabe, Tomohiro Shirasaka, Takeshi Igarashi, Takao Ishii, Toshikazu Saito
Dept. of Neuropsychiatry, Sapporo Medical University, Scholl of medicine, Sapporo, Japan

G5-6 Radiosensitivity of X-irradiated neural stem cells in logarithmic growth phase: Proliferation, cell cycle regulation, apoptosis, and DNA repair

○Mayu Isono[1,2], Teruaki Konishi[2], Masahiro Otsu[3], Takuya Yoshie[1], Hiroyuki Omori[1], Naoko Shiomi[2], Noriyoshi Suya[2], Alisa Kobayashi[2], Takashi Nakayama[4], Nobuo Inoue[1]
[1]Lab. Regener. Neurosci., Grad. Sch. Human Health Sci., Tokyo Metropolitan Univ., Tokyo, Japan, [2]Dept. Tech. Sup. and Dev., Res. Dev. and Sup. centr., Natl. Inst. Radiol. Sci., Chiba, Japan, [3]Dept. Chem., Kyorin Univ. Sch. Med., Tokyo, Japan, [4]Dept. Biochem., Yokohama City Univ. Sch. Med., Yokohama, Japan

September 27 (Tuesday)

16:30～18:30 Room C (2F・Heian)

G6-1～G6-6 Mood disorders/Cell adhesion factors

Chairs：Tomoaki Shirao (Department of Neurobiology and Behavior, Gunma University Graduate School of Medicine)
Teruya Tamaru (Department of Physiology, Toho University School of Medicine)

G6-1 A novel method to quantify brain cells using flow cytometer and a study of the postmortem brains from patients with major depressive disorder

○Yoshitaka Hayashi[1,2], Naomi Kikuchi[2], Takiko Shinozaki[2], Taeko Itou[2],

Shin-ichi Hisanaga[1], Yoshitaka Tatebayashi[2]
[1]Department of Biological Sciences, Graduate School of Science, Tokyo Metropolitan University, Tokyo, Japan, [2]Affective Disorders Research Project, Tokyo Metropolitan Institute of Medical Science, Tokyo, Japan

G6-2 Activation of both σ_1 and 5-HT_{1A} receptors enhances prefrontal dopamine release in adrenalectomized/castrated mice

○Naoki Hiramatsu[1], Koji Yano[1], Yukio Ago[1], Kazuhiro Takuma[1], Toshio Matsuda[1,2]
[1]Laboratory of Medicinal Pharmacology, Graduate School of Pharmaceutical Sciences, Osaka University, Suita, Japan, [2]United Graduate School of Child Development, Osaka University, Kanazawa University and Hamamatsu University School of Medicine, Suita, Japan

G6-3 Mechanisms underlying fluoxetine-evoked increase in BDNF in hippocampal astrocytes

○Manao Kinoshita, Schuichi Koizumi
Dept. Neuropharmacol., Univ. Yamanashi, Facul. Med., 1110 Shimokato, Chuo, Yamanashi 409-3898, Japan

G6-4 Lithium inhibits methamphetamine-induced hyperactivity and behavioral sensitization via modulation of prefrontal dopamine and serotonin release in mice

○Tatsunori Tanaka[1], Yuki Kita[1], Yukio Ago[1], Kazuhiro Takuma[1], Toshio Matsuda[1,2]
[1]Laboratory of Medicinal Pharmacology, Graduate School of Pharmaceutical Sciences, Osaka University, Osaka, Japan, [2]United Graduate School of Child Development, Osaka University, Kanazawa University and Hamamatsu University School of Medicine, Osaka University, Osaka, Japan

G6-5 Localization of neural cell adhesion molecule Caspr3 at the basal ganglia in mice

○Haruna Hirata[1], Juzoh Umemori[2], Tsuyoshi Koide[2], Kazutada Watanabe[1,3], Yasushi Shimoda[1]
[1]Department of Bioengineering, Nagaoka University of Technology, Nagaoka, Japan, [2]Mouse Genomics Resource Laboratory, National Institute of Genetics, Mishima, Japan, [3]Nagaoka National College of Technology, Nagaoka, Japan

G6-6 Analysis of the interaction between neural recognition molecule NB-3 and receptor protein tyrosine phosphatase γ

○Satoshi Nakano[1], Haruna Hirata[1], Kyohei Osada[1], Kazutada Watanabe[1,2], Yasushi Shimoda[1]
[1]Department of Bioengineering, Nagaoka University of Technology, Nagaoka, Japan, [2]Nagaoka National College of Technology, Nagaoka, Japan

September 27 (Tuesday)

16:30～18:30 Room D (2F・Tenpyo)

G7-1～G7-6 Anxiety/Stress

Chairs：Akira Sano (Dept. of Psychiat. Kagoshima Univ.)
Norio Sakai (Department of Pharmacological Neuroscience Graduate School of Biomedical Sciences, Hiroshima University)

G7-1 Encounter with an unfamiliar mouse increases prefrontal neuronal activity with dopamine and serotonin release in isolation-reared mice

○Ryota Araki[1], Yukio Ago[1], Asuka Sasaga[1], Kazuhiro Takuma[1], Toshio Matsuda[1,2]
[1]Laboratory of Medicinal Pharmacology, Graduate School of Pharmaceutical Sciences, Osaka University, Osaka, Japan, [2]United Graduate School of Child Development, Osaka University, Kanazawa University and Hamamatsu University School of Medicine, Osaka, Japan

G7-2 Social crowding during the nocturnal period produces anxiolytic- and antidepressant-like effects in mice

○Mari Kitamoto[1], Tatsunori Tanaka[1], Yukio Ago[1], Kazuhiro Takuma[1], Toshio Matsuda[1,2]
[1]Laboratory of Medicinal Pharmacology, Graduate School of Pharmaceutical Science, Osaka University, Suita, [2]United Graduate School of Child Development, Osaka University, Kanazawa University and Hamamatsu University School of Medicine, Suita

G7-3 Measurement of biomarkers for physical and mental fatigue in animal model

○Yuya Iwasawa[1], Satoru Oshiro[1], Sumino Yanase[2], Shigenobu Takayama[3], Katuki Morioka[4]
[1]Division of Cell Biology, Health Science, Graduate School of Sports and Health Sciences, Daito Bunka University, [2]Division of Molecular Life Science, Health Science, Graduate School of Sports and Health Sciences, Daito Bunka University, [3]Division of Molecular Medical Immunology, Health Science, Graduate School of Sports and Health Sciences, Daito Bunka University, [4]Department of Cardiovascular Medicine, The University of Tokyo Graduate School of Medicine

G7-4 Identification of the determinant sites of Gi/o coupling by rat melanin-concentrating hormone receptor 1

○Akie Hamamoto, Yumiko Saito
Graduate School of Integrated Arts and Sciences, Hiroshima University, Hiroshima, Japan

G7-5 Phosphorylation at Ser847 of nNOS regulates NO-ROS signaling in neurons

○Shingo Kasamatsu[1], Tomohiro Sawa[2], Yasuo Watanabe[3], Takaaki Akaike[2], Hideshi Ihara[1]
[1]Dept. of Biol. Sci., Grad. Sch. of Sci., Osaka Pref. Univ., [2]Dept. of Microbiol., Grad. Sch. of Med. Sci., Kumamoto Univ., [3]Dept. of Pharmacol., Showa Pharm. Univ.

G7-6 Development of a feasible method to assess serotonergic differentiation from mouse embryonic stem (ES) cells: implication of inhibition of bone morphogenetic protein (BMP) type I receptor kinases

○Atsushi Yamasaki [1], Koji Asano [1], Akihiro Toi [1], Atsuko Hayata-Takano [2], Norihito Shintani [1], Akemichi Baba [3], Hitoshi Hashimoto [1,2,4]

[1] Lab of Mol Neuropharmacol, Grad Sch of Pharmaceut Sci, Osaka Univ, [2] United Grad Sch of Child Dev, Osaka Univ, [3] Sch of Pharmacy, Hyogo Univ Health Sci, [4] Dep of Mol Pharmaceutic Sci, Osaka Univ Grad Sch of Med.

Poster Sessions

Poster Room (Lobby Lounge)
Poster Discussion

September 26 (Monday) 17:30～18:30

P1-1～P1-46

P1-01 Ca^{2+}-activated K^+ (K_{Ca}) channels as potential novel molecular targets for pain control

○Yoshinori Hayashi[1], Kodai Kawaji[1], Li Sun[1], Xinwen Zhang[1], Takeshi Yokoyama[2], Shinichi Kohsaka[3], Kazuhide Inoue[4], Hiroshi Nakanishi[1]
[1]Dept. Aging Sci. and Pharmacol., Facul. of Dent. Sci., Kyushu Univ, Japan, [2]Dept.of Dent. Anesthesiol., Facul. of Dent. Sci., Kyushu Univ, Japan, [3]Dept. of Neurochem., National Insti. of Neurosci., Japan, [4]Dept. of Mol. and System Pharmacol., Grad. Sch. of Pharmaceu. Sci., Kyushu Univ., Japan

P1-02 Interferon regulatory factor-5 in spinal microglia is a crucial transcription factor for the development of neuropathic pain

○Ryohei Yoshinaga[1], Makoto Tsuda[1], Takahiro Masuda[1], Nao Nishimoto[1], Hidetoshi Tozaki-Saitoh[1], Tomohiko Tamura[2], Kazuhide Inoue[1]
[1]Dept. Mol. Syst. Pharmacol., Grad. Sch. Pharm. Sci., Kyushu Univ., Fukuoka 812-8582, Japan, [2]Dept. Immunol., Grad. Sch. Med., Yokohama City Univ., Yokohama 236-0004, Japan

P1-03 Subtypes of macrophages in the peripheral nerve and dorsal root ganglia after the peripheral nerve injury

○Tadasuke Komori, Yoshihiro Morikawa, Takeshi Inada, Tomoko Hisaoka, Emiko Senba
Department of Anatomy and Neurobiology, Wakayama Medical University, Wakayama, Japan

P1-04 P2Y12 receptors mediate chemokines expression in primary rat microglia

○Hiroyuki Miyata, Hidetoshi Tozaki-Saitoh, Makoto Tsuda, Kazuhide Inoue
Dept. Mol. Sys. Phamacol., Grad. Sch. Pharmceut. Sci., Kyushu Univ. 3-1-1, Maidashi, Higashi, Fukuoka

P1-05 Dopamine attenuates LPS-induced cytokine expression by inhibiting the nuclear translocation of NF-κB p65 in microglial cells

○Yuta Sugino, Yasuhiro Yoshioka, Kazuya Nishimoto, Akiko Yamamuro, Yuki Ishimaru, Sadaaki Maeda
Dept. Pharmacotherap., Faculty Pharmaceut. Sci., Setsunan Univ., Osaka 573-0101, Japan

P1-06 **Zinc enhances LPS-induced nitric oxide production in cultured astrocytes**

○Mitsuaki Moriyama, Shunsuke Fijitsuka, Katsura Takano, Yoichi Nakamura
Laboratory of Integrative Physiology in Veterinary Sciences, Osaka Prefecture University

P1-07 **Role of extracellular RNA in neuronal injury-induced astrocyte activation**

○Yuuki Yamashita, Takahiro Katayama, Hiroki Tanaka, Hikaru Igarashi, Tatsuya Kibayashi, Masabumi Minami
Dept. Pharmacol., Grad. Sch. Pharm. Sci., Hokkaido Univ. of Sapporo, Japan

P1-08 **Inhibitory effect of tributyltin on neurite formation and synatpogenesis in cultured cortical cells**

○Koshi Oyanagi, Hironori Tashiro, Takayuki Negishi, Tomoko Tashiro
Dept. of Chem. and Biol. Sci., Grad. Sch. of Sci. and Engineer., Aoyama Gakuin Univ. Sagamihara, Japan

P1-09 **Neuroprotective effect of thalidomide and its enantiomers against oxidative stress**

○Haruka Yamada [1], Hiroshi Ohira [1], Toru Asahi [1,2], Naoya Sawamura [1,2]
[1] Faculty of Science and Engineering, Waseda Univiversity, [2] Consolidated Research Institute for Advanced Science and Medical Care (ASMeW), Waseda University

P1-10 **Protective effect of *kampo* medicine yokukansan on glutamate-induced neuronal death in primary cultured rat cortical neurons**

○Zenji Kawakami, Yasushi Ikarashi, Yoshio Kase
TSUMURA Research Laboratories, TSUMURA & CO., Ibaraki, Japan

P1-11 **GluN2D subunit of the N-methyl-D-aspartate receptor is required for phencyclidine-induced behavior, gene expressions and FOS-positive cell increases**

○Hideko Yamamoto [1], Etsuko Kamegaya [1], Wakako Sawada [1], Ryouta Hasegawa [1], Toshifumi Yamamoto [2], Yoko Hagino [1], Yukio Takamatsu [1], Masayoshi Mishina [3], Kazutaka Ikeda [1]
[1] Res. Project for Addictive Subst., Tokyo Metro. Inst. Med. Sci., [2] Mol. Psychopharm., Grad. Sch. of Nanosci., Yokohama City Univ., [3] Dept. of Mol. Neurobio. Pharm., Grad. Sch. of Med., Univ. of Tokyo

P1-12 **A multi-pass membrane protein, TMEM168, is induced in the nucleus accumbens by repeated treatment of methamphetamine in mice**

○Kanako Takayama, Yoshiaki Miyamoto, Kyosuke Uno, Seunghee Seo, Atsumi Nitta
Department of Pharmaceutical Therapy and Neuropharmacology, Faculty of Pharmaceutical Sciences, Graduate School of Medicine and Pharmaceutical Sciences, University of Toyama

P1-13 Lower sensitivity to methamphetamine in accumbal dopamine D2 receptor knockdown mice

○Yoshiaki Miyamoto[1], Shin-ichi Muramatsu[2], Atsumi Nitta[1]
[1] Department of Pharmaceutical Therapy and Neuropharmacology, Faculty of Pharmaceutical Sciences, Graduate School of Medicine and Pharmaceutical Sciences, University of Toyama, Toyama, JAPAN, [2] Division of Neurology, Department of Medicine, Jichi Medical University, Shimotsuke, JAPAN

P1-14 Effect of psychotropic drugs on cerebral proteins of mice deficient neuroglycan C , a brain-specific chondroitin sulfate proteoglycan

○Sachiko Aono[1], Yoshihito Tokita[2], Fumiko Matsui[2], Masahiko Yoneda[3], Eiji Watanabe[1]
[1] Laboratory of Neurophysiology, National Institute for Basic Biology, [2] Developmental Research, Aichi Human Service Center, [3] School of Nursing & Health, Aichi Prefectural University

P1-15 Analysis of the interaction of neural recognition molecule NB-2 with amyloid precursor-like protein 1

○Masaki Itoh[1], Kyohei Osada[1], Kazutada Watanabe[1,2], Yasushi Shimoda[1]
[1] Department of Bioengineering, Nagaoka University of Technology, Nagaoka, Japan, [2] Nagaoka National College of Technology, Nagaoka, Japan

P1-16 Involvement of autism-related factor MARCKSL1 in Neural network formation

○Toshiko Ishikawa[1], Shingo Miyata[2,3], Yoshihisa Koyama[2], Shinsuke Matsuzaki[1,2,3], Taiichi Katayama[1], Masaya Tohyama[1,2,3]
[1] Dept. Molecular Brain Sci., United Graduate School of Child Development, Osaka Univ., Kanazawa Univ. and Hamamatsu Univ. School of Medicine, Osaka, Japan, [2] Dept. of Anatomy and Neuroscience, Graduate School of Medicine, Osaka Univ., Osaka, Japan, [3] Molecular Reseach Center for Children's Mental Development, Osaka Univ., Osaka, Japan

P1-17 Possible involvement of MeCP2-dependent regulation of gene expression in the autism-like developmental disorder induced by fetal thalidomide exposure in rats

○Masafumi Mouri, Aika Okishige, Takayuki Negishi, Tomoko Tashiro
Department of Chemistry & Biological Science, School of Science & Engineering, Aoyama Gakuin University, Sagamihara, Knagawa, Japan

P1-18 TSC2 mutation upregulates dendritic mitochondria and shaft synapse formation in an mTOR-dependent manner

○Shin Yasuda[1,2], Hiroko Sugiura[1,2], Shu Takigami[2], Takako Takemiya[2,3], Hiromi Imamura[4], Okio Hino[5], Kanato Yamagata[1,2]
[1] Neural Plasticity Project, Tokyo Metro. Inst. Med. Sci., Tokyo, Japan, [2] Dept. Neuropharmacol., Tokyo Metro. Inst. Neurosci., Fuchu, Japan, [3] Med. Res. Inst., Tokyo Women's Med. Univ., Tokyo, Japan, [4] Inst. Sci. Indust. Res., Osaka Univ., Ibaraki, Japan, [5] Dept. Pathol. Oncol., Juntendo Univ. Sch. Med., Tokyo, Japan

P1-19 Kamikihi-to improves memory impairment and axon degeneration in a mouse model of Alzheimer's disease, 5XFAD

○Rie Nakada, Tomoharu Kuboyama, Chihiro Tohda
Div. of Biofunctional Evaluation, Res. Center for Ethnomed., Inst. of Natural Med., Univ. of Toyama.

P1-20 Aβ43-converting activity requires two active domains of ACE

○Kun Zou[1], Junjun Liu[1], Shuyu Liu[1], Chiaki Tanabe[1], Tomoji Maeda[1], Atsushi Watanabe[3], Makoto Michikawa[2], Hiroto Komano[1]
[1]Department of Neuroscience, School of Pharmacy, Iwate Medical University, [2]Department of Alzheimer's Disease Research, National Center for Geriatrics and Gerontology, [3]Laboratory of Research Advancement, National Center for Geriatrics and Gerontology

P1-21 Proteomic analysis of cultured cells expressing APP intracellular domain

○Fuyuki Kametani, Seiichi Haga
Department of Demetia and Higher Brain Function Research, Tokyo Metropolitan Institute of Medical Science

P1-22 CHRNA7 as scaffold molecule for Aβ aggregation

○Ye Ju[1], Takeyoshi Wada[1], Toru Asahi[1,2], Naoya Sawamura[1,2]
[1]Faculty of Science and Engineering, Waseda University, [2]Consolidated Research Institute for Advanced Science and Medical Care (ASMeW), Waseda University

P1-23 Peptidyl-prolyl isomerase Pin1 stimulates dephosphorylation of Tau phosphorylated by Cdk5-p25

○Taeko Kimura[1], Koji Tsutsumi[1], Taro Sito[1], Masato Taoka[2], Koichi Ishiguro[3], Takafumi Uchida[4], Masato Hasegawa[5], Toshiaki Isobe[2], Shin-ichi Hisanaga[1]
[1]Dept. of Biol., Grad. sch. of sci. and Eng., Tokyo Metropolitan Univ., [2]Dept. of Biol., Grad. sch. of chem., Tokyo Metropolitan Univ., [3]Mitsubishi Kagaku Iustitute of Life Science, [4]Dept. of Biol., Grad. Sch.of Sci, Tohoku Univ., [5]Tokyo Inst. Psych.

P1-24 Proteomics analysis of hippocampus and cortex under the influence of amyloid β oligomers using mutant APPE693Δ-transgenic mice

○Kouji Maekura[1], Masaoki Takano[1], Mieko Otani[1], Keiji Sano[1], Takami Tomiyama[2], Hiroshi Mori[2], Tooru Nakamura-Hirota[3], Shogo Matsuyama[3]
[1]Lab. Mol. Cell. Biol., Kobe Gakuin Univ. Sch. Pharm., [2]Depart. Neurosci. Grad. Sch. Med., Osaka City Univ., [3]Fac. Pharm. Sci., Himeji Dokkyo Univ.

P1-25 Dopaminergic neuroprotective effects of L-DOPA and inhibition by 3-OMD target astrocytes

○Masato Asanuma, Shinki Murakami, Ikuko Miyazaki
Dept. of Brain Sci., Okayama Univ. Grad. Sch. of Med., Dent. & Pharmaceut. Sci., Okayama, Japan

P1-26 Availability of L-DOPA uptaken into striatal astrocytes

○Ikuko Miyazaki, Shinki Murakami, Masato Asanuma
Dept. of Brain Sci., Okayama Univ. Grad. Sch. of Med., Dent. & Pharmaceut. Sci., Okayama, Japan

P1-27 Neuroprotective effect of magnolol *in vitro* and *in vivo* models of Parkinson's disease

○Akiko Muroyama[1], Cheng Lv[1], Aya Fujita[1], Yoshiyasu Fukuyama[2], Yasuhide Mitsumoto[1]
[1]Laboratory of Alternative Med. and Exp. Therapeutics, Department of Clinical Pharmacy, Faculty of Pharmaceutical Sciences, Hokuriku University, Kanazawa, Japan, [2]Faculty of Pharmaceutical Sciences, Tokushima Bunri University, Tokushima, Japan.

P1-28 Involvement of TRAP1 in regulation of mitochondrial morphology

○Hironori Takamura[1], Shingo Miyata[2], Kana Takemoto[2], Yoshihisa Koyama[2], Shinsuke Matsuzaki[1,2], Masaya Tohyama[1,2], Taiichi Katayama[2]
[1]Department of Child Development and Molecular Brain Science, United Grad. Sch. Child Development, Osaka Univ., Suita, Osaka, Japan, [2]Dept. Anatomy and Neurosci., Grad. Sch. Med., Osaka Univ., Suita, Osaka, Japan

P1-29 Regulation of tachykinin receptor 1 signaling by regulator of G protein signaling-8 (RSG8)

○Yuka Furumoto[1], Osamu Saitoh[2]
[1]Graduate School of Integrated Arts and Sciences, Hiroshima University, [2]Department of Bio-Science, Nagahama Institute of Bio-Science and Technology, Nagahama, Shiga

P1-30 Identification of cilialy targeting sequence of MCHR1 to primary cilia

○Asami Nagata, Akie Hamamoto, Yumiko Saito
Graduate School of Integrated Arts and Sciences, Hiroshima University, Hiroshima, Japan

P1-31 Reduced activation of Na^+, K^+-ATPase through enhancement of oxidative stress in noise-induced hearing loss

○Reiko Nagashima, Taro Yamaguchi, Kiyokazu Ogita
Dept. Pharmacol. Univ. of Setsunan

P1-32 Neurite outgrowth regulated by carnitine/organic cation transporter OCTN1 (SLC22A4)

○Hiroshi Hosotani, Noritaka Nakamichi, Takayuki Taguchi, Tomoko Sugiura, Yukio Kato
Faculty of Pharmacy, Kanazawa University, Kanazawa 920-1192, Japan

P1-33 Intracellular calcium channels regulate proliferative activity in neural stem/progenitor cells derived from subventricular zone of adult mice

○Tatsuo Shiba, Masanori Yoneyama, Kiyokazu Ogita
Dept. Pharmacol., Setsunan Univ.

P1-34 **Metformin suppresses proliferation coincident with reduction in intracellular potassium level in P19 cells**

○Ken-ichi Yamada, Tomohide Taniguchi, Nobuyuki Kuramoto, Kiyokazu Ogita
Dept. of Pharmacol, Setsunan Univ.

P1-35 **Anticancer drug irinotecan inhibits the response of 5-HT3A receptor**

○Yukiko Nakamura, Yusuke Ishida, Takahiro Yamada, Shoichi Shimada
Department of Neuroscience and Cell Biology, Osaka University Graduate School of Medicine, Osaka, Japan

P1-36 **Effects of synthetic N1-ribose-modified analogues of cyclic ADP-carbocyclic ribose on depolarization-induced cytosolic Ca^{2+} elevation in NG108-15 neuronal cells**

○Minako Hashii[1], Satoshi Shuto[2], Haruhiro Higashida[1]
[1]Dept. of Biophysical Genetics, Kanazawa Univ. Graduate School of Medicine, Kanazawa Japan, [2]Graduate School of Pharmaceutical Sciences, Hokkaido Univ., Sapporo Japan

P1-37 **Neuropsin-dependent synaptic plasticity in the hippocampal CA1 field of freely moving mice**

○Haruna Yamashita, Yasuyuki Ishikawa, Sadao Shiosaka
Laboratory of Functional Neuroscience, Nara Institute of Science and Technology

P1-38 **Involvement of BDNF release in the long-lasting synaptic enhancement in cultured slices**

○Shigeo Sakuragi, Keiko Tominaga-Yoshino, Akihiko Ogura
Osaka University Graduate School of Frontier Biosciences, Osaka, Japan

P1-39 **Filip play a role in cortical development and spine morphology**

○Hideshi Yagi[1,2], Min-Jue Xie[1,2], Hiroshi Ikeda[2,3], Munekazu Komada[1,2], Tokuichi Iguchi[1,2], Kazuki Kuroda[1,2], Masaru Okabe[5], Makoto Sato[1,2,4]
[1]Div. Cell Biol. Neurosci., Dept. Morphol. Physiol., Fac. Med. Sci., Univ. Fukui, Fukui, Japan, [2]Research and Education Program for Life Science, University of Fukui, Fukui, Japan, [3]Dept. Human & AI Systems, Univ. of Fukui, Fukui, Japan, [4]Child Dev Res Cntr, Univ. Fukui, Fukui, Japan, [5]GIRC, Osaka Univ, Osaka, Japan

P1-40 **Possible in-vitro reproduction of hippocampus-mediated memory consolidation in the cerebral cortex**

○Takuhiro Kawakami, Akihiko Ogura, Keiko Tominaga-Yoshino
Graduate School of Frontier Biosciences, Osaka University, Suita, Japan

P1-41 **Possible involvement of BDNF in expression of anxiety-likebehavior**

○Taro Ohkido[1], Takeru Iiduka[1], Makoto Itakura[4], Shintaro Ohtsuka[2], Takatsugu Watanabe[2], Saori Yamamori[4], Shigeru Watanabe[3], Hitoshi Miyaoka[3], Masami Takahashi[4]
[1]Department of Biosciences, Kitasato University School of Science, [2]Department of

Biochemistry, Kitasato University Graduate school of Medical Sciences, [3] Department of Psychiatry Kitasato University School of Medicine, [4] Department of Biochemistry, Kitasato University school of Medicine

P1-42 Lack of BRINP1 in mice causes increase of hippocampal adult neurogenesis and abnormal behavior

○Miwako Kobayashi [1], Ryosuke Ozaki [1], Toshiyuki Nakatani [2], Makoto Motomiya [3], Keizo Takao [4], Toshiaki Koda [5], Tsuyoshi Miyakawa [6], Ichiro Matsuoka [1]
[1] Col. of Pharm. Sci., Matsuyama Univ., Matsuyama Japan, [2] Grad. Sch. of Phram. Sci., Hokkaido Univ., [3] Grad. Sch. of Med., Hokkaido Univ., [4] Ctr for Genetic Analysis of Behavior, NIPS, [5] Grad. Sch. of Life Sci., Hokkaido Univ., [6] Div. of Systems Med. Sci., ICMS, Fujita Health Univ.

P1-43 Systemic treatment of SUN13837, a novel small molecular compound mimicking the pharmacological actions of bFGF, enhances functional recovery after spinal cord injury in rats

○Ryoko Ogino [1], Mariko Kuroda [1], Yukiko Iwaki [1], Shiro Imagama [2], Ryoji Tauchi [2], Yoshiari Shimmyo [1], Naohiro Takemoto [1], Yasuhiro Morita [3], Shinya Ueno [1], Norihito Murayama [1], Teruyoshi Inoue [1]
[1] Faculty of Pharmacology 2, Asubio Phrama Co. Ltd., Kobe, Japan, [2] Orthopaedic Surg., Nagoya Univ. Grad. Sch. of Med., Nagoya, Japan, [3] Physiol. Morphol., Yasuda Women's Univ. Pharmacy, Hiroshima, Japan

P1-44 Manipulation of cathepsin c gene expression in mouse

○Wilaiwan Wisessmith [1,2], Takahiro Shimizu [1,2], Kenji Tanaka [2], Kazuhiro Ikenaka [1,2]
[1] Dept. of Physiol Sci., SOKENDAI., Hayama, Japan, [2] Div. Neurobio Bioinfo., NIPS., Okazaki., Japan

P1-45 Decreased microvessel density and altered astrocyte morphology in the hippocampus of diabetic Goto-Kakizaki rats

○Yuki Matsunaga, Miki Nishiki, Takefumi Uno, Takayuki Negishi, Tomoko Tashiro
Department of Chemistry & Biological Science, School of Science & Engineering, Aoyama Gakuin University

P1-46 P301S mutant human Tau transgenic mice show early symptoms of human tauopathies with dementia and altered sensorimotor gating

○Hiroki Takeuchi [1,2], Haruhisa Inoue [2,3], Makoto Higuchi [4], Keizo Takao [5], Kayoko Tsukita [2], Yoshiko Karatsu [2], Yumiko Iwamoto [2], Tsuyoshi Miyakawa [6], Tetsuya Suhara [4], Ryosuke Takahashi [1]
[1] Dept. of Neurol. Faculty of Med. Kyoto Univ., [2] Center for iPS cell Research and Application(CiRA), Kyoto Univ., [3] CREST, JST Agency, Kawaguchi, Japan, [4] Molecular Imaging Center, NIRS, Japan, [5] Center for Genetic Analysis of Behavior, NIPS, Japan, [6] Division of Systems Med. Sci., Institute for Comprehensive Med. Sci., Fujita Health Univ.

September 27 (Tuesday) 11:30～12:30

P2-1～P2-45

P2-01 Inhibition of PKA or neuronal activity alters BDNF level with a change in the level of MeCP2 reversely, but not p-CREB, in the rat visual cortex

○Miki Yamamoto [1], Satoshi Ichisaka [2], Ritsuko Katoh-Semba [3], Yoshio Hata [1,2]
[1] Div. Integrative Biosci., Tottori Univ. Grad. Sch. Med. Sci., [2] Div. Neurobiol., Fac. Med., Tottori Univ., [3] Lab. Mol. Neurogenesis, BSI, RIKEN

P2-02 Distinct receptor affinities of neuregulin-1 splicing variants to ErbB3 and ErbB4

○Ran Wang, Yuriko Iwakura, Nobuyuki Takei, Hiroyuki Nawa
Mol. Neurobiol. Brain Res. Inst. Niigata Univ, Niigata

P2-03 Expression and cellular localization of Gpnmb, a glioma-associated glycoprotein, in the rat central nervous system

○Jianjun Huang, Wenjie Ma, Shigeru Yokoyama
Department of Biophysical Genetics, Kanazawa University Graduate School of Medicine

P2-04 Localization of VEGF in the neurovascular unit of adult mouse brain

○Yasuki Ishizaki [1], Tomomi Saito [2], Koji Shibasaki [1], Masashi Kurachi [1], Sandra Puentes [3], Masahiko Mikuni [2]
[1] Mol. Cell. Neurobiol., Gunma Univ. Grad. Sch. Med., Maebashi, Japan, [2] Psychiatry and Human Behavior, Gunma Univ. Grad. Sch. Med., Maebashi, Japan, [3] Neurosurgery, Gunma Univ. Grad. Sch. Med., Maebashi, Japan

P2-05 Isolation of S-nitrosylated proteins from the epileptic brains in rats

○Kazuki Ohno
Department of Medicinal Pharmacology, Graduate school of Medicine, Dentistry and Pharmaceutical Sciences, Okayama University

P2-06 Expression of ecto-nucleo6tidases and equilibrative nucleoside transporter in the rat circumvallate papillae

○Kentaro Nishida, Jyunki Kato, Yukari Dohi, Teruyo Kubota, Saki Matsumoto, Mai Miyata, Yuri Yamanaka, Takaaki Matsuo, Kazuki Nagasawa
Dept. of Environ. Biochem., Kyoto Pharm. Univ.

P2-07 Role of mitochondrial c-Src in respiratory functions

○Masato Ogura, Junko Yamaki, Miwako Homma, Yoshimi Homma
Dep. of Biomol. Sci., Fukushima Med. Univ. Sch. of Med.

P2-08 Cdk5-dependent phosphorylation of Drebrin

○Kazuya Tanabe [1], Hiroyuki Yamazaki [2], Akiko Asada [1], Taro Saito [1], Tomoaki Shirao [2], Shin-ichi Hisanaga [1]
[1] Department of Biological Sciences, Tokyo Metropolitan University, Tokyo, Japan,

[2] Department of Neurobiology and Behavior, Gunma University Graduate School of Medicine, Gunma, Japan

P2-09 Sigma-1 receptor agonists enhance K^+-evoked dopamine release from PC12 cells

Toshifumi Yamamoto [1,2], ○Jun Hasegawa [1], Hideko Yamamoto [2]
[1] Lab. of Mol. Psychopharmacol., Grad. Sch. Nanosci., Yokohama City Univ., Yokohama, Japan, [2] Res. Project for Addictive Substances, Tokyo Metr. Inst. of Med. Sci., Tokyo, Japan

P2-10 The effect of 8-nitro-cGMP on proteins in synaptosomes

○Tatsuya Uchino [1], Tomohiro Sawa [2], Takaaki Akaike [2], Makoto Itakura [3], Masami Takahashi [3], Hideshi Ihara [1]
[1] Dept. of Biol. Sci., Grad. Sch. of Sci., Osaka Pref. Univ., [2] Dept. of Microbiol., Grad. Sch. of Med. Sci., Kumamoto Univ., [3] Dept. of Biochem., Sch. of Med., Kitasato Univ.

P2-11 Brain response to environmental change: Odor-evoked induction of activity-dependent gene expression in mouse brain

○Hirohide Takebayashi [1,2], Asim Bepari [1], Masahiro Yamaguchi [3], Nobuaki Tamamaki [1]
[1] Dept of Morphol Neural Sci, Kumamoto Univ, [2] PREST, JST, [3] Dept of Physiol, Univ of Tokyo

P2-12 Formation of 8-nitro-cGMP and S-guanylation of SNARE proteins in neural cells

○Kouhei Kunieda [1], Tomoaki Ida [1], Tomohiro Sawa [2], Takaaki Akaike [2], Makoto Itakura [3], Masami Takahashi [3], Hideshi Ihara [1]
[1] Dept. of Biol. Sci., Grad. Sch. of Sci., Osaka Pref. Univ., Osaka, Japan, [2] Dept. of MicroBiol., Grad. Sch. of Med. Sci., Kumamoto Univ., Kumamoto, Japan, [3] Dept. of Biochem., Kitasato univ. Sch. of Med., Kanagawa, Japan

P2-13 Analysis of the nucleocytoplasmic shuttling of Dab1 required for cortical structure formation

○Takao Honda, Kazunori Nakajima
Department of Anatomy, School of Medicine, Keio University

P2-14 Neural network formation with RNA binding protein Musashi2

○Shinsuke Shibata, Hideyuki Okano
Keio Univ, Sch Med, Dept Physiol.

P2-15 Role of the transglutaminase family on optic nerve regeneration in fish

○Kayo Sugitani [1], Kazuhiro Ogai [1], Kiyotaka Hitomi [2], Satoru Kato [3]
[1] Div. Health Sci. , Grad. Sch. Med., Kanazawa Univ., [2] Dept. Appl Mol Biosci, Grad. Sch. Bioagric. Sci., Nagoya Univ., [3] Dept. Mol. Neurobiol., Grad. Sch. Med., Kanazawa Univ.

P2-16 Genetic and cellular interaction analyses of a repulsive axonal guidance cue, draxin

○Hideaki Tanaka, M Hossain, A Ito, G Ahmed, X Song, R Asrafuzzaman, Y Shinmyo, IB Naser, K Ohta
Dev. Neurobiol. Kumamoto University

P2-17 Expression pattern of kirrel3 in the central nervous system of adult mice

○Tomoko Hisaoka [1], Hiroaki Gyobu [1], Tadasuke Komori [1], Kouta Fujimoto [1], Toshio Kitamura [2], Emiko Senba [1], Yoshihiro Morikawa [1]
[1] Anatomy & Neurobiology, Wakayama Medical University, Wakayama, Japan, [2] Division of Cellular Therapy, Advanced Clinical Research Center, The Institute of Medical Science, The University of Tokyo, Tokyo, Japan.

P2-18 Expression of kirrel3 in the dorsal root ganglia during development

○Yoshihiro Morikawa [1], Hiroaki Gyobu [1], Tomoko Hisaoka [1], Tadasuke Komori [1], Toshio Kitamura [2], Emiko Senba [1]
[1] Dept. of Anat. & Neurobiol., Wakayama Med. Univ., Wakayama, Japan, [2] Div. of Cell. Ther., Adv. Clin. Res. Cent., The Inst. of Med. Sci., The Univ. of Tokyo, Tokyo, Japan.

P2-19 Effects of heat shock on proliferation of primate ES cell-derived neural stem cells

○Hiroyuki Omori [1], Masahiro Otsu [2], Mayu Isono [1], Takuya Yoshie [1], Masayoshi Shibata [1], Takashi Nakayama [3], Yutaka Suzuki [4], Yasushi Kondo [4], Nobuo Inoue [1]
[1] Lab. of Regener. Neurosci., Grad. Sch. of Human Health Sci., Tokyo Metropolitan Univ., Tokyo, Japan, [2] Dept. of Chem., Kyorin Univ. Sch. of Med., Tokyo, Japan, [3] Dept. of Biochem., Yokohama City Univ. Sch. of Med., Yokohama, Japan, [4] Advanced Med. Res. Lab., Mitsubishi Tanabe Pharma Corp., Osaka, Japan

P2-20 Influence on neuronal differentiation; enhancement by tunicamycin-induced ER stress: role of ubiquitin ligase HRD1

○Koichi Kawada [1], Shunsaku Tono [1], Naoki Fujinaga [1], Miho Yamashita [1], Asami Sato [1], Masayuki Kaneko [1], Yasuyuki Nomura [2], Yasunobu Okuma [1]
[1] Dept. Pharmacol., Chiba Institute of Sci., [2] Laboratory of Pharmacotherapeutics, Yokohama College of Pharmacy

P2-21 Effects of ultrasound on mouse neural stem cells derived from embryonic stem cells

○Shingo Kakehi [1], Hiroyuki Omori [1], Masahiro Otsu [2], Takuya Yoshie [1], Mayu Isono [1], Atsuko Onose [1], Masayoshi Shibata [1], Takashi Nakayama [3], Nobuo Inoue [1]
[1] Lab. of Regener. Neurosci.,Grad. Sch. of Human Health Sci.,Tokyo Metropolitan Univ., Tokyo, Japan , [2] Dept. of Chem., Kyourin Univ. Sch. of Med., Tokyo, Japan, [3] Dept. of Biocem., Yokohama City Univ. Sch. of Med., Yokohama, Japan

P2-22 Olig2 expression pattern in the retina of adult mouse

○Katsunori Nochioka [1], Kouko Tatsumi [2], Hiroaki Okuda [2], Nahoko Ogata [1],

Akio Wanaka[2]
[1] Department of Ophthalmology, Nara Medical University, Nara, Japan, [2] Department of Anatomy and Neuroscience, Nara Medical University, Nara, Japan

P2-23 Yamanaka factors expressions in the zebrafish retina during optic nerve regeneration

○Maki Nishitani[1], Kazuhiro Mawatari[1], Mikiko Nagashima[2], Kazuhiro Ogai[1], Satoru Kato[2]
[1] Division of Health Sciences, Graduate School of Medicine, Kanazawa University, [2] Department of Molecular Neurobiology, Graduate School of Medicine, Kanazawa University

P2-24 Disruption of axo-glial interaction causes focal axonal damage in cerebellar Purkinje neurons

○Tomoko Ishibashi, Hiroko Baba
Department of Molecular Neurobiology, Tokyo University of Pharmacy and Life Sciences

P2-25 Protein arginine N-methyltransferase 8 (PRMT8) is expressed in activated microglial cells after spinal cord injury

○Yasutake Mori[1], Shingo Miyata[1,2], Masaya Tohyama[1,2]
[1] Dept. of Anatomy and Neurosci. Med. Univ. of Osaka, [2] United Graduate School of Child Development,, Univ. of Osaka

P2-26 Alteration of the expression balance of hnRNP C1 and C2 changes the expression of myelination-related genes in the human neuroblastoma cell line

○Keiko Iwata[1], Hideo Matsuzaki[1], Norio Mori[1,2]
[1] Research Center for Child Mental Development, Hamamatsu University School of Medicine, Hamamatsu, Japan, [2] Department of Psychiatry and Neurology, Hamamatsu University School of Medicine, Shizuoka, Japan

P2-27 Ability of microglia to eliminate glutamate toxicity in the axotomized rat facial nucleus

○Kazuyuki Nakajima[1,2], Mariko Noda[1], Shinichi Kohsaka[2]
[1] Dept Bioinfo, Fac Engineering, Soka Univ, Tokyo, [2] National Institute of Neuroscience, Tokyo, Japan

P2-28 A neuropathy-associated 36K isoform of myelin P0, L-MPZ, is produced by the stop codon readthrough mechanism

○Yoshihide Yamaguchi, Yu Naito, Aki Nagata, Takuya Kikukawa, Reiji Yamazaki, Hiroko Baba
Dept. of Mol. Neurobio., Tokyo Univ. of Pharm. & Life Sci., Hachioji, Japan

P2-29 Molecular mechanism by which microgla proliferate in the transected rat facial nucleus

○Shinichi Yamamoto[1], Shinichi Kohsaka[2], Kazuyuki Nakajima[1,2]

[1] Dept. of Bioinformatics, Faculty of Engineering, Soka University, Tokyo, [2] Dept. of Neurochemistry, National Institute of Neuroscience, Tokyo

P2-30 The role of Bergmann glia in cerebellar development

○Shouta Sugio[1], Kenji Tanaka[2], Masahiko Watanabe[3], Kazuhiro Ikenaka[1,2]
[1] Dept. of Physiol Sci., SOKENDAI., Hayama, Japan, [2] Div. Neurobio Bioinfo., NIPS., Okazaki, Japan, [3] Dept. of Anat., Univ of Hokkaido., Sapporo, Japan

P2-31 Involvement of adenosine A3 receptor in microglial process extension

○Keiko Ohsawa[1], Tomomi Sanagi[1], Yasuko Nakamura[1], Eri Suzuki[1], Kazuhide Inoue[2], Shinichi Kohsaka[1]
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P2-32 Identification of CSPG constituting DACS, a novel brain extracellular matrix

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P2-33 Voluntary exercise promotes astrogliogenesis from Olig2 cells in some nuclei of the basal ganglia of adult mouse

○Kouko Tatsumi[1], Hiroaki Okuda[1], Mariko Yamano[2], Akio Wanaka[1]
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P2-34 Astrocyte-derived factor leads to upregulation of tumor necrosis factor alpha (TNF α) induced in microglia

○Toshiaki Masuda, Kazuyuki Nakajima
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P2-35 Microglia as a member of lactate supplier in the CNS

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P2-36 Attenuation of microglial activation/proliferation in axotomized facial nucleus by administration of GDNF

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P2-37 Involvement of protein kinase D in UDP-stimulated microglial macropinocytosis

○Ayumi Uesugi, Ayako Kataoka, Hidetoshi Tozaki-Saitoh, Makoto Tsuda, Kazuhide Inoue
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P2-38 Functional analysis of HOXD9 in human gliomas and glioma cancer-initiating cells

○Shigeki Ohta [1], Masanao Tabuse [2], Yohei Ohashi [3], Raita Fukaya [2], Aya Misawa [1], Kazunari Yosida [2], Takeshi Kawase [2], Hideyuki Saya [4], Cécile Thirant [5], Hérve Chneiweiss [5], Yumi Matsuzaki [6], Hideyuki Okano [6], Yutaka Kawakami [1], Masahiro Toda [2]
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P2-39 Analysis of the novel sialylated N-glycan expressed in the mouse brain

○Mai Narumi [1,2], Takeshi Yoshimura [2], Tomohiro Torii [2], Kazuhiro Ikenaka [1,2]
[1] Department of Physiological Sciences, SOKENDAI, [2] Division of Neurobiology and Bioinformatics, NIPS

P2-40 Long-term treatment of RN46A cells with cAMP analog upregulates the function of serotonin transporter (SERT)

○Hikaru Yamamoto, Shigeru Tanaka, Izumi Hide, Takahiro Seki, Norio Sakai
Dept. of Mol. and Pharmacol. Neurosci., Hiroshima Univ.

P2-41 Effects of chemical chaperons on the serotonin transporter functions

○Norio Sakai, Masayuki Fujiwara, Hikaru Yamamoto, Takahiro Seki, Shigeru Tanaka, Izumi Hide
Dept. of Mol. and Pharmacol. Neurosci., Grad. Sch. of Biomed. Sci., Hiroshima Univ.

P2-42 Down-regulation of cyclin-dependent kinase 5 activity by mood stabiliozer valproic acid

○Manami Ishida, Taro Saito, Akiko Asada, Shin-ichi Hisanaga
Dept. of Science and Technology, Tokyo Metropolitan University, Tokyo, Japan

P2-43 Neonatal maternal separation increases leaning-against-wall behavior in open field test

○Satoshi Ichisaka [1], Miki Yamamoto [2], Natsuko Ikubo [1], Hiroshi Kuniishi [1], Yoshio Hata [2]
[1] Div. Neurobiol., Fac. Med., Tottori Univ., [2] Div. Integrative Biosci., Tottori Univ. Grad. Sch. Med. Sci.

P2-44 Identification of orexin regulatory element 1-binding proteins

○Susumu Tanaka, Yoshiko Honda, Makoto Honda, Toru Kodama
Sleep Control PJ., Tokyo Metropolitan Institute of Medical Science

P2-45 Double in situ hybridization analyses of serotonin 3A and 3B receptor in the rat geniculate ganglion

○Yusuke Ishida, Yukiko Nakamura, Takahiro Yamada, Shoichi Shimada
Department of Neuroscience and Cell Biology, Graduate School of Medicine, Osaka University

Luncheon Seminars

September 28 (Wednesday)

12：30～13：30 Room A (1F・Hanarikyu)

Sponsor：Eisai Co., Ltd. Pfizer Japan Inc.
Chair：Toshifumi Kishimoto (Nara Medical University Department of Psychiatry)

"Molecular pathology of tau in neurodegeneration"

Toshihisa Tanaka
Osaka University Graduate School of Medicine, Department of Psychiatry

September 28 (Wednesday)

12：30～13：10 Room B (2F・Hōō)

Sponsor：Daiichi Sankyo Company, Limited
Chair：Masahito Yamada (Department of Neurology and Neurobiology of Aging, Kanazawa University, Graduate School of Medical Science.)

"The development of preventives and therapeutics for Alzheimer's disease that inhibit β-amyloid protein aggregation"

Kenjiro Ono
Department of Neurology and Neurobiology of Aging, Kanazawa University, Graduate School of Medical Science.

抄　録
Abstracts

日本神経化学会公開シンポジウム
JSN Open 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
Symposium

故ニーレンバーグ先生追悼シンポジウム
〈金沢大学 子どものこころの発達研究センター 共催〉
Dr. Nirenberg Memorial Symposium

一般口演
Oral Sessions

大学院生口演
Graduate Oral Sessions

ポスター発表
Poster Sessions

OS-1 Neuroprotective effects of hydrogen on dopaminergic neuronal loss in mice model of Parkinson's disease

○Kyota Fujita[1], Yoshinori Tanaka[2], Mizuho Kido[3], Toshihiko Katafuchi[4], Yusaku Nakabeppu[5]

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Reactive oxygen species (ROS)-induced damage is closely related to the onset and the progression of Parkinson's disease (PD). MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine)-treated mice have been widely used as an animal model of PD. It has also been reported that molecular hydrogen selectively reduces hydroxyl radicals, the most cytotoxic ROS, and can thereby effectively protect cells. Thus, inhalation of hydrogen gas strongly suppressed ischemic and reperfusion brain injury by buffering the effects of oxidative stress. We have previously reported that hydrogen in drinking water (hydrogen water) reduced dopaminergic neuronal loss by buffering ROS both in substantia nigra and in striatum. In the present study, giving hydrogen water prior to MPTP administration showed less decrease of dopaminergic neurons in substantia nigra and dopaminergic fibers projected to striatum. Since acute inhalation of hydrogen did not remain for no more than 10 min in brain tissue, these results may imply that pre-application of hydrogen brought resistance to neuronal loss in nigrostriatal pathway. Hydrogen also attenuated activation of microglia and astrocyte in substantia nigra 7 days after MPTP administration. The neuroprotective effects of hydrogen could be achieved by continuous drinking of hydrogen water for 7 days, and lasted for several days after the stop of hydrogen consumption. In this symposium, a new aspect and the mechanism on the neuroprotective effects of hydrogen will be shown and open to discussion.

OS-2 Mitochondrial nutrition, Coenzyme Q_{10} as a neuroprotectant

○Yasuhide Mitsumoto

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The cause of Parkinson's disease (PD) remains unknown, but our understanding of mechanisms of nigral dopaminergic neuronal death was advanced by the discovery of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), a neurotoxin that selectively damages the nigrostriatal dopaminergic system and cause a parkinsonian syndrome in humans, monkeys and mice. The discovery that MPTP acts through inhibition of complex I of the electron transport chain stimulated study of mitochondrial function in the brains from patients with PD. The studies indicated that mitochondria could be an important target for neuroprotection even if the destruction of neuron occurs by appearing as apoptotic, necrotic, or intermediate between the two extremes. Coenzyme Q_{10} (CoQ_{10}) is well known as the electron acceptor for complex I and II of mitochondrial respiratory chain and also ubiquitously acts as a powerful anti-oxidant in mitochondria and lipid membrane. The neuroprotective effect of CoQ_{10} on dopaminergic neurons shown by several *in vitro* and *in vivo* studies raises the possibility for neuroprotective therapies for PD. On the other hand, neuropathological studies of PD indicate that loss of dopaminergic nerve terminals in the striatum precedes the loss of cell bodies in the substantia nigra pars compacta. This is also seen in MPTP-treated animals. It is important, therefore, to evaluate neuroprotective effect at dopaminergic nerve terminals in the striatum. In the present study, we evaluated the neuroprotective effect of CoQ_{10} in MPTP-treated C57BL/6N mice by using immunoisolation technique for striatal dopaminergic synaptosomes. Our results clearly demonstrated that oral administration of CoQ_{10} significantly attenuated the loss of dopaminergic nerve terminals induced by MPTP treatment. Furthermore, oral administration of CoQ_{10} prevented the mitochondrial cytochrome c release in the 1-methyl-4-phenylpyridinium ion (MPP^+)-treated mouse forebrain synaptosomes. In addition, CoQ_{10} did not affect the MPP^+-induced decrease in mitochondrial oxidation-reduction activity and membrane potential in mouse forebrain synaptosomes. These results indicate that the nerve terminals are a site for the action of CoQ_{10} against the MPTP-induced dopaminergic neurodegeneration.

OS-3 Modelling the pathophysiology of Parkinson's diseases and other neurodegenerative diseases using iPS cell thechnology

○Hideyuki Okano

Dept. of Physiology, Keio University School of Medicine

Pathophysiological investigations of neurodegenerative disorders had been difficult based on the following reasons; i)Postmortem brain tissue samples from patients of neurodegenerative disorders are rarely available for testing, and ii)animal models frequently do not recapitulate all features of a specific disorder. To overcome these situations, there is an increasing interest in the induced pluripotent stem cells (iPS cells) technology, which might be used to fill the gaps in modelling of pathophysiology of human neurological diseases by creating a novel approach known as "disease in a dish" (Reviewed by Matts and Svendsen, Lancet Neurology, 2011). Parkinson's disease (PD) involves degeneration of the dopaminergic neurons within the substantia nigra, followed by other degenerative changes throughout the brain. Some of the PDs are caused familiarly by genetic mutations including SNCA, PARK2, UCHL1, LRRK2, PARK7, PINK1, GBA, and SNCAIP, although more than 90% of PD cases are sporadic. However, the dysfunctions of mitochondria and abnormal alpha-synuclein accumulation as well as Lewy Body (LB) formation are the proposed to be the common mechanisms of familial and sporadic Parkinson's diseases. Recently, we generated iPS cells from several PD patients and showed pathological changes in PD iPS cells-derived neurons in comparison with the postmortem brain of the same patient. In the present lecture, I am going to talk about the advantage of iPS cells-technology to study the pathophysiology of PD in comparison with transgenic mouse models. These new models not only revealing the mechanistic insights of PD pathophysiology, but also help us to clarify novel targets of drug screening and modifying therapies of PDs.

OS-4 Molecular mechanisms of dopaminergic cell death in MPTP mouse model of Parkinson's disease

○Toru Yasuda[1], Yoshikuni Mizuno[2], Hideki Mochizuki[1]

[1]Department of Neurology, Kitasato University School of Medicine, [2]Division of Neuroregenerative Medicine, Kitasato University School of Medicine

Parkinson's disease (PD) is clinically characterized by typical motor abnormalities. A major pathological hallmark is marked loss of dopaminergic (DA) neurons in the substantia nigra (SN). Several animal models have been generated to understand the molecular mechanisms that underlie DA neurodegeneration in PD. 1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) is most frequently used neurotoxin, of which active metabolite MPP^+ is selectively concentrated into DA neurons and inhibits electron transport in mitochondria, whereby induce DA neuronal death. Mitochondrial damage is considered to be crucial pathogenic event in PD. Accordingly, MPTP animal model has been accepted as well recapitulating DA cell death in PD. We have previously reported that distinct mechanisms are involved in MPTP-induced DA cell death, which depend on regimen of MPTP administration in mice. Acute administration of MPTP (20 mg/kg, 4 times at 2-hr intervals) caused microglial activation and inflammation-related non-cell-autonomous DA cell death, whereas sub-acute MPTP (30 mg/kg, once daily for 5 consecutive days) promoted mitochondrial apoptotic cascade. Adeno-associated viral (AAV) vector-mediated transduction of dominant-negative form of Apaf-1 prevented DA neuronal loss in sub-acute MPTP mice, supporting the idea for apoptotic death of DA cells. On the other hand, osmotic minipump-mediated high-dose and long-term MPTP administration (50 or 100 mg/kg for 28 days) was manifested by DA neurodegeneration with accumulation of mitochondria in SN DA cells. AAV-parkin delivery significantly prevented DA cell loss through maintaining Akt activity in MPTP-minipump mice. However, overexpressed parkin seemed not to affect the clearance of mitochondria that were damaged with chronic MPTP treatment. Mitochondrial dysfunction leads to overproduction of reactive oxygen species, which in turn damage chromosomal DNA. In response to DNA damage, DNA repair reactions, or alternatively, apoptotic cascade is induced through the actions of E2F1 and p53. We recently found that regulation of these two molecules was effective for protection of DA neurons in MPTP mice.

OS-5 Aberrant molecular properties of the Parkinson's disease-associated mutant UCH-L1

○Tomohiro Kabuta
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Ubiquitin C-terminal hydrolase L1 (UCH-L1) is expressed abundantly in neurons and has been reported to be a major target of oxidative/ carbonyl damage associated with sporadic Parkinson's disease (PD). The I93M mutation in UCH-L1 was reported in a German family with dominantly inherited PD. We have shown that I93M UCH-L1-transgenic mice exhibit dopaminergic cell loss. We have also developed an I93M UCH-L1-transgenic Drosophila, which displays progressive climbing deficits, indicating that the I93M mutation in UCH-L1 at least partly plays a causative role in PD. We found that UCH-L1 physically interacts with LAMP-2A, the lysosomal receptor for CMA, and Hsc70 and Hsp90, which can function as components of the CMA pathway, and α / β -tubulin. These interactions were abnormally enhanced by the I93M mutation. Expression of I93M UCH-L1 in cells induced the CMA inhibition-associated increase in the amount of α -synuclein. We observed that aberrant interaction of I93M UCH-L1 with tubulin modulates tubulin polymerization. These findings may underlie the toxic gain of function by I93M UCH-L1 in familial PD. In addition, we show that I93M UCH-L1 and carbonyl-modified UCH-L1 display shared aberrant properties. Our results suggest that the carbonyl modification of UCH-1 plays a toxic role in the neurodegenerative process in sporadic PD.

JS-1 Role of neurotrophic/growth factor as a mediator of glia in depression

○Minoru Takebayashi
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Neurotrophic/growth factors have common potential roles such as cellular proliferation, differentiation, protection, and anti-inflammatory actions. Glia, especially astrocytes as well as neurons, synthesize and release different trophic factors such as BDNF, FGF-2, GDNF, and VEGF, most of which are implicated in the ethiology and treatment of depression. This indicates that several neurotrophic/growth factors may be comprehensively involved in depression-related cellular plasticity. Interestingly, astrocytes could produce these neurotrophic/ growth factors in both a monoamine-independent (antidepressant-specific) and a monoamine-dependent manner, while neurons do so only in a monoamine-dependent manner. Data indicate a possible direct linkage between glia and neurons via neurotrophic/growth factors in the antidepressant effect. It has been recently suggested that depression can be characterized by neuronal and glial pathology, as reported by postmortem findings. Thus, it is important to focus on regulation of the neuron-glia network in the search for an underlying cellular pathology and a novel treatment of depression.

JS-2 Epigenetic regulation of stress vulnerability and depression

○Hirotaka Yamagata, Shusaku Uchida, Koji Otsuki, Teruyuki Hobara, Yoshifumi Watanabe
Div. Neuropsy., Dept. Neurosci., Yamagichi Univ. Grad. Sch. Med.

Recent studies have suggested that the epigenetic regulation of genes, such as DNA methylation and histone modification, can trigger the development of stress vulnerability and predisposition to depression. However, the involvement of the epigenetic gene regulation in the susceptibility and adaptation to chronic stress is largely unknown. In this symposium, we show recent evidence demonstrating the epigenetic mechanisms underlying susceptibility and adaptation to stress and antidepressant response in mice. Two genetically distinct mouse strains, BALB/c (BALB) and C57BL/6 (B6), exhibited different behavioral responses to chronic stress: BALB mice showed depression-like behavior with stressful stimuli, while B6 mice could adapt to the same stressor. In the ventral striatum, the expression of the glial cell-derived neurotrophic factor (GDNF) decreased in BALB mice, but increased in B6 mice. Chronic antidepressant treatment improved the depression-like behavior and decreased GDNF expression in BALB mice. We found that in chronic stress conditions, the MeCP2-HDAC2 complex is recruited to the methylated GDNF promoter in BALB mice, whereas the MeCP2-CREB complex was recruited to GDNF promoter in B6 mice. These results indicate the crucial role of histone modification and DNA methylation in controlling GDNF expression and subsequent behavioral responses to chronic stress. We have also found the important role of epigenetic gene regulation in antidepressant action. Subchronic treatment (5 days) with a histone deacetylase (HDAC) inhibitor (suberoylanilide hydroxamic acid; SAHA) reversed the increased depression-like behavior in stressed BALB mice, as observed in mice receiving chronic antidepressant treatment (3 weeks). We found that SAHA enhanced calcium/calmodulin-dependent protein kinase II β (CaMKII β) expression in the hippocampus. The viral-mediated overexpression of CaMKII β in the hippocampus suppressed the depression-like behavior in stressed BALB mice. In addition, dendrite growth was stimulated by subchronic treatment with SAHA in the hippocampus. These data suggest that the HDAC inhibitor induced CaMKII β expression and facilitated structural plasticity in the hippocampus, resulting in an improvement in depression-like behavior.

JS-3 Crosstalk between neurotrophin BDNF and hypothalamic-pituitary-adrenal (HPA) axis

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Increased glucocorticoid due to the hyperactivity of HPA axis is suggested to be involved in the pathophysiology of depressive disorder. Chronic upregulation of glucocorticoid levels may cause brain damage and result in the onset of depression. On the other hand, dynamics of brain-derived neurotrophic factor, BDNF, may be also associated with depressive disorder as it is well-known that BDNF is critical for many neuronal aspects including neuronal plasticity in the central nervous system (CNS). Therefore, possible interaction between glucocorticoid and BDNF function is very interesting. In *in vitro* system using cultured CNS neurons, we found that pretreatment with glucocorticoids reduced BDNF function such as synapse establishment and neurotransmitter release. Following glucocorticoid exposure, significant decrease in expression of glucocorticoid receptor (GR) was observed. Interestingly, overexpression of GR enhanced release of excitatory neurotransmitter glutamate stimulated by BDNF application. Reversely, GR downregulation by RNAi technique diminished the BDNF-induced glutamate release, suggesting that GR protein has essential role in the BDNF action. Generally, glucocorticoid exerts its effect via GR-mediated transcriptional activity. In our system, immunoprecipitation approach revealed that GR binds to TrkB (receptor for BDNF), and the GR-TrkB interaction is important for the BDNF-dependent glutamate release. In addition to transcriptional activity, glucocorticoid/GR may directly contribute to intracellular signalings in CNS neurons.

JS-4 The neuroinflammation hypothesis of depression

○Akira Monji
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The etiology of depression remains unclear while, in many aspects, its pathophysiology has recently been reported to be closely associated with neuroinflammation. Despite the fact that microglia comprise only <10% of the total brain cells, microglia respond rapidly to even minor pathological changes in the brain and may contribute directly to the neuroinflammation by producing various pro-inflammatory cytokines and free radicals. We and other researchers have recently shown the inhibitory effects of some antidepressants as well as some typical/atypical antipsychotics on the release of inflammatory cytokines and free radicals from activated microglia, both of which have recently been known to cause the synaptic pathology, a decrease in neurogenesis, and white matter abnormalities found in the brains of patients with depression. Microglial activation may not be the primary cause of depression but it may be closely related to the pathology of acute stage of depression. The neuroinflammation hypothesis of depression may shed new light on the therapeutic strategy for depression.

S01-1 Specific Na^+/Ca^{2+} exchange inhibition attenuates MPTP-mediated nigrostriatal dopaminergic dysfunction in the subacute mouse model of Parkinson's disease

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The Na^+/Ca^{2+} exchanger (NCX) plays a role in the regulation of intracellular Ca^{2+} levels, and nitric oxide (NO) may be involved in the pathology of neurodegenerative disorders. The previous finding that NO stimulates the activity of NCX suggests that NCX-mediated Ca^{2+} alteration is involved in NO-related pathology. To address this point, we recently examined the effects of the specific NCX inhibitor SEA0400 on NO-induced injury in neuroblastoma SH-SY5Y cells and 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-treated mice, a model of Parkinson's disease. The NO donor sodium nitroprusside (SNP)-induced cytotoxicity was blocked by the mitogen-activated protein (MAP)/extracellular signal-regulated kinase (ERK) kinase inhibitor U0126 and the p38 MAP kinase inhibitor SB203580 in SH-SY5Y cells. SNP increased Ca^{2+} influx in an NCX-mediated manner, and SNP increased ERK and p38 MAPK phosphorylation and production of reactive oxygen species (ROS) in an extracellular Ca^{2+}-dependent manner. This Ca^{2+}-dependent cytotoxicity was prevented by SEA0400. Moreover, SNP-induced increase in intracellular Ca^{2+} levels, ROS production and decrease in cell viability were blocked by a cGMP-dependent protein kinase inhibitor. In an *in vivo* study, repeated MPTP caused dopaminergic neurotoxicity and the effect was blocked by the neuronal NO synthase inhibitor 7-nitroindazole in mice. Moreover, MPTP increased ERK phosphorylation and lipid peroxidation in the midbrain. A systemic administration of SEA0400 attenuated MPTP-induced nigral dopaminergic neurotoxicity including ERK activation and lipid peroxidation in the midbrain and dysfunction of motor coordination. Based on these findings, the present review discusses the role of NCX as a novel pharmacological target for the prevention of Parkinson's disease.

S01-2 Possible neuroprotective effect of $GABA_B$ receptor on excitotoxicity

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GABAB receptors are members of the G protein-coupled receptor (GPCR) superfamily and mediate slow and prolonged synaptic inhibition in the brain. Unlike other members of the GPCR superfamily, functional GABAB receptors are heterodimers formed by 2 subunits identified as GABABR1(R1) and GABABR2 (R2). R2 is highly phosphorylated at serine 892 (S892) by protein kinase A. In addition to protein kinase A, 5'-AMP-activated protein kinase (AMPK) phosphorylates another residue serine 783 (S783). Phosphorylation of both sites suppresses desensitization of GABAB receptors. To date, however, it is difficult to distinguish the importance and timing of the phosphorylation in these sites. Therefore, we tried to elucidate functional significance and regulation of phosphorylation in these sites. Of mouse discrete brain structures including the olfactory bulb, cerebellum, medulla-pons, hypothalamus, striatum, midbrain, hippocampus, and cerebral cortex, the hippocampus and cerebral cortex had the highest expression of R2 with phosphorylation of both sites (p892 and p783). Relative phosphorylation of p892 to total R2 was almost even among these brain regions, whereas that of p783 was uneven among these brain regions. In the acute hippocampal slices, the level of p892 was decreased during the incubation with the artificial cerebrospinal fluid (aCSF) with being blocked by okadaic acid. In addition, the level of p892 was decreased by tetrodotoxin in cultures of the hippocampal neurons. In the acute hippocampal slices, the level of p783 was decreased immediately during the incubation with aCSF, coincident with the decrease in the AMPK activity. Phosphorylation status of S783 was easily disappeared during the preparative procedures of immunoprecipitation *in vitro*, suggesting that endogenous serine/threonine phosphatases dephosphorylate the p783. However, exogenously added phosphatases were ineffective in dephosphorylating the p783. These results suggest that in the central nervous system, S892 is highly phosphorylated during neuronal excitation process, with being dephosphorylated by okadaic acid-sensitive phosphatases. Phosphorylation of S783 may be promptly regulated by AMPK and/or undefined phosphatase in response to cellular signals.

S01-3 Therapeutic potential of mithramycin, one of the chemotherapy drugs, in brain ischemia

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Laboratory of Pharmacology, School of Pharmacy, Nihon University, Funabashi, Japan

Ischemic injury elicits a delayed neuronal death in the mammalian brain. In survivors of cardiac arrest, transient global ischemia causes selective neuronal death in area CA1 of the hippocampus, resulting in impairment of cognitive and memory functions within days after ischemia/reperfusion. Mithramycin (MTM) is an antibiotic that binds to DNA to regulate transcription. Recent research shows that it is helpful in treating motor symptoms and prolonging life in a mouse model of Huntington's disease. Recently, we have demonstrated that MTM reduced the neuronal death induced by tunicamycin, a potent inducer of endoplasmic reticulum (ER) stress, and that this neuroprotective property of MTM is attributable, at least in part, to the attenuation of C/EBP homologous protein (CHOP), a key transcription factor for ER stress-induced neuronal death, expression in rat cultured hippocampal neurons and organotypic hippocampal slice cultures. In the present study, the neuroprotective effect of MTM against ischemia/reperfusion-induced neuronal injury was evaluated in the hippocampus in the mice. Neuronal damage was apparent in area CA1 of the hippocampus after transient global ischemia/reperfusion. The expression of CHOP showed a pronounced increase in area CA1 in the mice. Treatment of the mice with MTM significantly decreased both the expression level of CHOP and the number of neurons stained with Fluoro-Jade B (FJB) in this region. In contrast, MTM did not affect the increase of 78-kDa glucose-regulated protein (GRP78) induced by ischemia/reperfusion. MTM restored the ischemia/reperfusion-induced impairment of long-term potentiation (LTP) in area CA1 of the hippocampus. These results suggest that administration of MTM protects neurons in area CA1 of the hippocampus against injury induced by transient global ischemia/reperfusion through attenuation of ER stress-associated signals in the hippocampus. MTM appears to have more promise as a therapeutic drug for ischemic brain disease than other drugs tested hitherto, and could be potentially useful for development of new treatments.

S01-4 CNS regeneration in fish : a molecular mechanism to an application for mammals

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Unlike mammals, fish optic nerve and spinal cord can survive, and regrow their axons and finally restore their function even after nerve transection. In zebrafish, visual function completely recovers by 90-100 days after optic nerve lesion, whereas fish can freely swim by 8-10 weeks after spinal cord transection as revealed by with behavioral analyses. To investigate molecular mechanism for CNS regeneration in zebrafish, we screened upregulated genes from zebrafish retinas previously axotomized for 0-30 days with molecular cloning techniques. The genes screened were as follows, heat-shock-protein 70 (HSP70), insulin-like growth factor-1 (IGF-1), purpurin (a retinol-binding protein), sox2, coagulation factor XIIIA (FXIIIA), neural nitric oxide synthetase (nNOS), retinoic acid signaling molecules (RALDH, Cyp26a1, CRABP1, RAR α 1) and tissue transglutaminase. As a temporal change of gene expression, HSP70 mRNA increased at 0.5-24 h, IGF-1 mRNA increased at 1-3 days, purpurin mRNA increased at 2-5 days, sox2 mRNA increased at 3-5 days, FXIIIA, retinoic acid signaling molecules and nNOS mRNAs increased at 5-10 days, and tissue transglutaminase mRNA increased at 10-30 days after optic nerve injury. The cellular localization of these transcriptions was all at retinal ganglion cells (RGCs) but except for purpurin. The purpurin mRNA was transcripted at photoreceptors. We further characterized gain and loss of function of these genes with gene transfer and knock-down experiments. From these results, we concluded that (i) HSP70 and IGF-1 work as a promoting factor for cell survival, (ii) purpurin and sox2 work as a preparative molecule for axonal elongation, (iii) retinoic acid signaling molecules, FXIIIA and nNOS work as an early axonal elongation factor, and (iv) tissue transglutaminase works as a late axonal elongation factor to the injured RGCs. Therefore, understanding the molecular mechanism of fish CNS regeneration is very useful to construct a reliable therapeutic tool for rescuing mammalian CNS degenerative neurons. Certainly, purpurin, IGF-1 retinoic acid signaling molecules, nNOS and tissue transglutaminase could regrow rat optic nerve *in vitro* and *in vivo*.

S02-1 Hyperdopaminergic innervation triggered by epidermal growth factor; Implication in Schizophrenia

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Epidermal growth factor (EGF) is one of ErbB receptor ligands that are implicated in schizophrenia neuropathology and neurotrophic regulation of midbrain dopaminergic neurons. EGF is highly enriched in human amniotic fluid and involved in unfavorable uterine contractions and pre-term labor. To evaluate the impact of prenatal and perinatal ErbB hypersignaling on neurobehavioral development, EGF was subcutaneously administered to rat neonates as the neurodevelopmental period of rodent perinatal stage that matches the second trimester of human fetus having immature blood-brain barrier and the initiation of glial proliferation. We found that EGF can penetrate the immature blood-brain barrier and reach brain neurons, later resulting in various behavioral impairments associated with schizophrenia endophenotypes at the post-pubertal stage; acoustic prepulse inhibition (PPI), latent inhibition of learning, social interaction, and methamphetamine hypersensitivity. To elucidate the neuropathological mechanism of this schizophrenia model, we studied dopaminergic states and pharmacology of this model and their behavioral correlates. EGF-treated rats exhibited increases in tyrosine hydroxylase levels and dopamine content in the brain. In parallel, local dopamine releases were elevated and exhibited inverse correlations with prepulse inhibition scores. Moreover, administration of a D2-like receptor antagonist (raclopride) ameliorated PPI deficits without inducing catalepsy. These findings suggest that endogenous EGF circulating in the pre- and peri-natal periphery has significant impact on later behavioral development and contributes to schizophrenia vulnerability.

S02-2 Molecular mechanism of psychiatric condition by loss of function mutations in the VPS13A gene

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Chorea-acanthocytosis (ChAc) is a rare hereditary neurodegenerative disorder characterized by adult-onset chorea and peripheral acanthocytes. Loss of function mutations in the VPS13A gene, encoding a protein named chorein, have been identified in ChAc patients. ChAc patients exhibit various clinical symptoms such as psychiatric features, epilepsy, peripheral neuropathy, and myopathy. The neuropsychiatric symptoms include delirium, cognitive disturbances, personality change, obsessive-compulsive symptoms, schizophrenia-like symptoms, depression and anxiety. Cognitive disturbances that consist typically of slowness in thinking, behavior and forgetfulness, and neuropsychiatric symptoms such as personality change and obsessive-compulsive symptoms or sterotypies can be attributable to dysfunction of frontosubcortical circuits because of the primary degeneration of striatum. There is a high incidence of mood disorder among ChAc patients. We hypothesized that the VPS13A gene might be associated with susceptibility to mood disorder. We performed a comprehensive mutation screen of VPS13A in mood disorder subjects. We also performed copy number variation (CNV) analysis in mood disorder subjects. We identified several non-synonymous, synonymous and six intron variants in mood disorder subjects and a novel GAT triplet repeat polymorphism in VPS13A. By CNV analysis, we identified a heterozygous exons deletion in VPS13A in one mood disorder subject. The presence of a pathogenic mutation or a potentially functional variant in mood disorder or schizophrenia subjects suggests that VPS13A genes might be involved in the mood disorder. We performed a comprehensive mutation screen, including sequencing and copy number variation (CNV) analysis, of the VPS13A gene in ChAc patients. All 73 exons and flanking regions of VPS13A were sequenced in 35 patients diagnosed with ChAc. We identified 36 pathogenic mutations, 20 of which were previously unreported, including two novel CNVs. In addition, we investigated the expression of chorein in 16 patients by western blotting of erythrocyte ghosts. This demonstrated the complete absence of chorein in patients with pathogenic mutations.

S02-3 Functional analysis of a novel drug dependence-inhibitory factor "shati"

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Repeated exposure to addictive drugs causes cellular adaptations in specific neuronal populations that ultimately can lead to a state of addiction. We have identified a novel molecule "shati" from the nucleus accumbens (NAc) of mice treated with methamphetamine (METH), one of the most abused drugs all over the world, using the PCR-select complementary DNA subtraction method. Treatment with the shati antisense oligonucleotide (shati-AS), which significantly inhibited the expression of shati mRNA, enhanced the acute METH response, METH-induced behavioral sensitization, and conditioned place preference (CPP). Moreover, blockage of shati mRNA by shati-AS potentiated the METH-induced increase of DA overflow in the NAc and the METH-induced decrease in synaptosomal and vesicular DA uptake in the midbrain. These results suggest that the functional roles of shati in METH-regulated behavioral changes are mediated through inhibition of the METH-induced decrease in DA uptake.Recently, shati has been reported to be aspartate N-acetyl transferase which synthesizes N-acetylaspartate (NAA) from L-aspartate and acetyl-CoA. NAA is an abundant compound in brain specifically and occurs almost exclusively in neurons. However, METH-treatment did not increase NAA in any brain region, suggesting the possibility that shati has other functions to inhibit METH dependence. Thus, to clarify the novel functions of shati, we tried to identify shati-binding proteins by GST-pull down and mass spectrometry. As the result, shati was associated with tubulin and components of AP-2 complex, suggesting that shati might be involved in microtubule dynamics and/or endocytotic event.In this session, we will introduce the physiological function of a novel drug dependence-inhibitory molecule "shati" in our recent findings, and discuss about possibility of clinical application of shati to drug addiction.

S02-4 Three new molecules related to psychiatric diseases

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The abuse of substance has become a significant social and public health concern worldwide. Methamphetamine (METH) has significantly psychiatric consequences, including psychosis, dependence, overdose and even death. To clearly the mechanism of establishment of drug dependence, we have identified there new molecules shati, piccolo and TMEM168 from the nucleus accumbens (NAc) of mice treated with METH, using the polymerase chain reaction-select complementary DNA subtraction method. Shati can inhibit the establishment of the addiction of METH and morphine. This protein can protect the inactivation of the dopamine transporter (DAT) by METH, and then be involved in the development of METH-induced hyperlocomotion, sensitization, and conditioned place preference. The functional roles of shati in METH-regulated behavioral alternations are likely to be mediated by its inhibitory effects on the METH-induced increase of DA overflow in the NAc and the METH-induced decrease in DA uptake in the midbrain. Next, piccolo C2A domain displays an unusual feature of sequestering membrane phosphatidylinositol 4,5-bisphosphate, which may underlie its role in modulating DAT internalization. Piccolo upregulation induced by METH represents a homeostatic response in the NAc to excessive dopaminergic transmission. Piccolo C2A domain may act as a cytoskeletal regulator for plasmalemmal DAT internalization, which may underlie its contributions in behavioral plasticity. In the last, TMEM 168 is proposed as a ten-transmembrane protein following the amino-acid sequence. TMEM168 is also respondent to over flow of dopamine. The three new molecules are suggested that certain psychiatric diseases, which related to dopamine systems.

S03-1 Whole genome analysis for shcizophrenia

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Because the high heritability for schizophrenia, it is anticipated to bring out the pathophysiology of the disease by genetic research. Candidate gene approach based on certain hypothesis or the linkage analysis using the family sample was carried out, but does not reach clear associated molecules identification till now. Genome wide association study (GWAS) to analyze the SNP which extended over whole genomes came to be performed using Europe and US mainly Caucasian sample and showed some susceptible variants these days. However, it was recognized that effect size of these SNPs frequency was very small and is hard to have come to explain the whole heritability by only these SNPs. A result was provided including our group in GWAS using the Japanese sample, but does not reach genome wide association at present. I report the present conditions of the schizophrenia genomics in this symposium and discuss it about the future prospects.

S03-2 DISC1 acts as a cargo adapter for neuronal transport of specific proteins and mRNAs

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Schizophrenia is a severe psychiatric disorder with lifelong disability. Although the causes of schizophrenia remain largely unknown, it has been widely reported that schizophrenia has high inheritance, indicating the existence of genetical risk factors (Owen et al., 2004; Craddock et al., 2005; Harrison and Weinberger, 2005). Disrupted-In-Schizophrenia 1 (DISC1) is a candidate gene for susceptibility to schizophrenia. Accumulating evidence suggests that DISC1 participates in neurodevelopment such neurogenesis, neuronal migration and axon/dendrite formation through the interaction with NUDEL/LIS1, FEZ1 and GSK3beta. We also found that DISC1 accumulates at the tip of axons and regulates the axonal transport of NUDEL/LIS1/14-3-3 epsilon complex (Taya et al., 2007), Grb2 (Shinoda et al., 2007) and Girdin (Enomoto et al., 2009) through Kinesin-1 in rat hippocampal neurons. However, its modes of action remain largely unknown. Here, we comprehensively screened for DISC1-interacting proteins by proteomic analysis and identified many RNA-binding proteins including Hematopoietic zinc finger (HZF), which acts as a component of RNA-transporting granules and participates in the dendritic localization of inositol 1,4,5-trisphosphate receptor type 1 (IP3R1) mRNA. DISC1 co-localizes with HZF and RNA-transporting granules in hippocampal dendrites. DISC1 directly associates with IP3R1 mRNA and is co-transported into dendrites. Impairment of DISC1 function prohibits both the dendritic transport and BDNF-induced local translation of IP3R1 mRNA. Because Kinesin-1 also interacts with DISC1 and mediates the transport of DISC1 and IP3R1 mRNA along microtubules, we propose that DISC1 with HZF binds IP3R1 mRNA and thereby regulates its dendritic transport as a cargo adaptor for the local translation.

S03-3 Neurobiology of candidate genes of schizophrenia

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Several candidate genes of schizophrenia reported in recent 10 years has been transferred into neurochemistry in these days. These candidate genes include DISC1, dysbindin, neuregulin1, COMT, G72, PACAP, etc. This talk focuses in neurobiology of dysbindin, a risk gene for schizophrenia firstly reported in 2002 and repeatedly replicated the association with schizophrenia in many studies. Postmortem brain analysis revealed decreased expression levels of dysbindin-1 in patients with schizophrenia, suggesting that sandy mice lacking dysbindin-1 protein could be a unique animal model of schizophrenia. Sandy mice were less active, had heightened anxiety-like response and demonstrated deficits in social interaction. Sandy mouse also showed impaired long-term memory retention and working memory. Sandy mouse demonstrated lower levels of dopamine, but not glutamate, in restricted brain regions including hippocampus. Reduced rate of neurogenesis in hippocampus and correlated alterations in dopaminergic and serotonergic modulations at the hippocampal mossy fiber synapse were observed in sandy mouse. Since genetic variation in dysbindin is associated with both schizophrenia and memory function, and memory function is compromised in patients with schizophrenia, the alterations in neurotransmitter systems in hippocampus in sandy mouse may be related to the neurobiological mechanisms of memory dysfunction in the disorder. In cellular and molecular analysis revealed that dysbindin might regulates to neurotransmitter release such as glutamate and dopamine via interaction with synaptic vesicle proteins. These findings could shed light on the etiology of schizophrenia and lead us to new hypotheses, novel diagnostic tools, and more effective therapies for the disorder.

S03-4 PolyI:C-induced neurodevelopmental model of schizophrenia: role for IFITM3 in brain dysfunction

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Viral infection during neurodevelopment is a major environmental risk for schizophrenia, and gene-environment interactions may play a role in the pathogenesis of schizophrenia. Perinatal injections of polyriboinosinic-polyribocytidylic acid (polyI:C), which mimics innate immune responses elicited by viral infection, lead to schizophrenia-like behavioral alteration in rodents after puberty. Furthermore, neonatal polyI:C treatment in dominant-negative DISC1 transgenic mice results in synergistic effects on some behavioral and histological phenotypes in adulthood. Here we discuss the mechanism underlying the polyI:C-induced brain dysfunction. Cultured astrocytes isolated from the cortices and hippocampi of mice were activated by polyI:C treatment *in vitro*, leading to an increase in mRNA levels of interferon-induced transmembrane protein 3 (IFITM3) as well as various inflammatory cytokines. PolyI:C-induced expression of IFITM3 mRNA was blocked by treatment with neutralizing anti-interferon-β (IFN-β) antibody while treatment with IFN-β protein increased IFITM3 expression in astrocytes. Immunocytochemistry revealed that IFITM3 proteins are specifically localized in early endosomes in astrocytes following polyI:C treatment. Overexpression of IFITM3 in COS7 cells resulted in a significant reduction of the activity of endocytosis. When primary cultured neurons were treated with the conditioned medium of astrocytes (ACM) treated with polyI:C (polyI:C-ACM), neurite outgrowth and spine formation were diminished. The neurodevelopmental abnormalities of cultured neurons induced by polyI:C-ACM were significantly alleviated when astrocytes were prepared from IFITM3-KO mice. Furthermore, aberrant reduction of cerebral MAP2 levels as well as memory impairment was evident in polyI:C-treated wild-type mice, but such neurodevelopmental and behavioral abnormalities were not observed in polyI:C-treated IFITM3-KO mice. These results suggest a role for IFITM3 in polyI:C-induced neurodevelopmental abnormality.

S04-1 Septin-mediated microtubule regulation during neurite extension

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Microtubule and actin cytoskeleton play pleiotropic roles in neurogenesis, whereas roles for another nucleotide-binding polymers of septins remain to be elucidated, despite their abundance in metazoan nervous systems, implications in neurito/synapto/spinogenesis, a hereditary neuropathy and neuropsychiatric disorders in humans. In this study, we probed the role of septins in neuritogenesis in primary cultured neurons and developing mouse cerebral cortex. Our rigorous morphometric analysis revealed that short hairpin RNA-mediated depletion of the nonredundant septin subunit SEPT7 significantly inhibited the extension of both axons and dendrites of primary cultured cortical neurons, which was rescued by co-expression of an RNAi-resistant conservative mutant of SEPT7. The short neurite phenotype was recapitulated in axons projecting from neurons at the layer 2/3 of somatosensory areas (S1 and S2) to the contralateral areas (*in utero* electroporation of shRNA expression vector was done in collaboration with Dr. Takaki Miyata at Nagoya Univ). To explore the molecular mechanism underlying the phenotype, we examined the status of microtubules, the principal determinant of neurite length. Both *in vitro* and *in vivo*, septin-depletion increased the amount of acetylated α-tubulin at Lysine 40. Since hyperacetylation is known to hyperstabilize microtubules by slowing the depolymerization rate, the aberrant modification seems to retard neurite extension by reducing the growth speed of microtubule. We are currently investigating the role of septins in the regulation of acetylation/deacetylation of α-tubulin by genetic, biochemical and small molecule approaches.

S04-2 Regulation of Sept5 function by phosphorylation with Cdk5

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Septin 5 (Sept5) is a member of the Septin GTPase family, which is predominantly expressed in mammalian brains. Sept5 is localized in presynaptic terminals where it associates physically with synaptic vesicles and other membranes. However, a role of Sept5 was not known yet. During searching for the Cdk5 substrates in synaptosomal fractions, we identified Sept5 as one of Cdk5-phosphorylated proteins. Cdk5 is a family of cyclin-dependent kinases, whose kinase activities specifically expressed in postmitotic neurons. Cdk5 suppresses neurotransmitter release by phosphorylating dynamin I and amphiphysin I. Further, we demonstrate that Cdk5 is a factor determining threshold of excitation at the synaptic region. However, how Cdk5 regulates the synaptic activity is not understood. We thought that Sept5 phosphorylation by Cdk5 might play a role in the regulation of synaptic activity. We would like to show the expression of Sept5 in mouse brains, Cdk5 phosphorylation site in Sept5 and the effect of phosphorylation on the interaction with syntaxin I. As many other Septin proteins, Sept5 is alternatively spliced in rat and human brains, producing long (Sept5_v1) and short (Sept5_v2) isoforms. However, expressions of these two isoforms were not clear in mouse brains. First, we decided to determine which isoforms were expressed in mouse brains. We isolated Sept5_v1 cDNA from mouse brain total RNA by PCR. Mouse Sept5_v1 cDNA showed a high degree of homology to the corresponding isoform of rat and human Sept5. Sept5_v1, as well as Sept5_v2, were expressed mainly in brain and testis at the mRNA level, but protein expression was restricted to brains. Sept5_v2 expression increased gradually from E17 to P30, but expression of Sept5_v1 was delayed until P10. We identified Ser17 of Sept5_v1 as a major Cdk5 phosphorylation site *in vivo* and *in vitro*. Sept5 bound to Syntaxin 1, v-SNARE protein mainly associated with presynaptic membranes. Phosphorylation of Sept5_v1 by Cdk5 decreased its binding to syntaxin-1. These results indicate that the interaction of Sept5 with syntaxin-1 is regulated by phosphorylation of Sept5_v1 at Ser17 by Cdk5. Since Ser17 is a unique site present only in Sept5_v1, Cdk5 may regulate the interaction between Sept5_v1 and Syntaxin-1 in an isoform-specific manner.

S04-3 A modular septin complex regulates neuronal morphogenesis

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The septins are a conserved family of GTPases which are involved in a number of processes at the interface of membranes and the cytoskeleton. The 13 mammalian septins are classified into 4 homology groups and heteromeric septin complexes were found to be assembled from several combinations of members of different groups. The complexes can assemble into filaments and septins are redundant within groups *in vitro*, but the rules governing septin complex and filament assembly in cells are unclear. Several septins are expressed highly in the brain, some exclusively there and septins are found in plaques in Alzheimer's and levy-bodies in Parkinson's disease. In the light of these findings it is of great importance to understand how neuronal septins assemble into complexes and filaments.We have now investigated at the example of the septin 5,7 and 11 complex at the base of dendritic spines if septins from a homology-group can indeed replace one another in functional complexes in neurons. To do so, we downregulated septin5 expression by RNA-interference and simultaneously overexpressed septin 2-group isomers labeled with GFP. In these neurons, septin 2-GFP and septin 4-GFP localized to dendritic branching points and spine necks and colocalized with endogenous septin 7. In contrast to this, septin 1-GFP showed a diffusive localization with almost no colocalization with endogenous septin 7.When we quantified the amount of septin5 detected by immunofluorescence in septin 5-shRNA treated cells, we found that septin5 downregulation negatively affected the expression level of septin7. However, overexpression of septin2 or septin4 rescued septin7 expression to wild type levels. Detailed analysis of the morphological development of these neurons revealed that dendritic branching was reduced in septin-5-downregulated neurons, but the overexpression of septin 2 restored normal morphology. Our results demonstrate that septin 2 can functionally replace septin 5 in septin complexes required for morphological development, but that septinl cannot. We conclude, that septins within homology-groups are not entirely redundant.

S04-4 Molecular mechanism of septin-mediated neuronal migration

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The coordinated migration of neurons is essential for functional and architectural formation of cerebral cortex. During corticogenesis, postmitotic excitatory neurons generated in the ventricular zone move through the intermediate zone and radially migrate to the superficial layers of the cortical plate. Although proper regulation of cytoskeletal molecules has been proposed to be indispensable for the radial migration, the underlying molecular mechanisms still remain to be elucidated. Recent reports suggest that several members of septin family molecules specifically express in developing cerebral cortex. The molecular function of septin on cortical development, however, is largely unknown. We have found that Sept4 and Sept14 is functionally involved in the migration of excitatory neurons. Knockdown of Sept4 or Sept14 by RNAi with in utero electroporation impaired proper positioning of neurons in the cortical plate. Sept4 and Sept14 formed a molecular complex in physiological condition and the interaction of these septin molecules was required for proper neuronal migration. Moreover, Sept4- or Sept14- knockdown neurons had abnormal leading processes. To investigate the molecular basis of septin-mediated neuronal migration, we screened Sept4- or Sept14-interacting molecules by proteomic approach and identified several cytoskeletal regulator proteins as candidates. These results suggest that Sept4 together with Sept14 play important roles in neuronal migration by regulating cytoskeletal dynamics.

Symposium

S05-1 Regulation of spine formation, morphology and plasticity by CaM-kinases

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Intracellular free calcium ion is highly regulated in cells such as neurons where it plays a major role in multiple aspects of neuronal development, functions and pathologies. Key targets of Ca^{2+} include protein kinases that are activated by the Ca^{2+}/CaM complex (CaM-kinases or CaMKs). Previous studies from numerous laboratories have established important neuronal functions, such as synaptic plasticity (LTP), for CaMKII (Nat. Rev. Neurosci. 8, 101-13). Over the past decade we and others have demonstrated that CaMKK and its downstream targets CaMKI, CaMKIV, PKB/Akt, and AMP-kinase are important in multiple aspects of neuronal development (e.g., axon and dendrite formation, spine formation) and activity-dependent synaptic plasticity (e.g., recruit of Ca^{2+} permeable AMPA-receptors and enlarged spine head morphology). Roles of these CaMKs have been established using multiple, independent approaches including pharmacological inhibitors, transfected dominant-negative and constitutively active constructs, and suppression of endogenous proteins using RNAi (Wayman et al. Cell Calcium April 28, 2011). Multiple signaling pathways, such as activation of the Rac/Pak/actin pathway, cross-talk with MEK/Erk/CREB-dependent transcription pathway, including multi-protein complexes are involved. Reviews: Curr. Opin. Neurobiol. 20, 108-15; Neuron 59. 914-31.

S05-2 Structural role of CaMKII

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Dendritic spines are tiny protrusions where most of the excitatory synapses reside. Spines are dynamic structure which changes their connectivity and strength in response to neuronal activity, and this property is believed to be the fundamentals of brain circuit formation and learning and memory. CaMKII and actin are two essential molecules involved in this process. While the importance of CaMKII activity in LTP is well accepted, there has been a mystery of CaMKII; it constitutes 1~2% of total brain protein, and 10~30% of the postsynaptic density (PSD), which is much more abundant than any other signaling molecule and comparable to the structural proteins such as actin. Recent evidence indicates CaMKII has structural roles in addition to well-known enzymatic roles via direct interaction with F-actin. In this study, we investigate the structural aspect of CaMKII during the structural plasticity of dendritic spine.CaMKII β has F-actin binding domain between Ca^{2+}/ *calmodulin binding domain* and association domain, and we identified many serines and threonines in this domain as putative phosphorylation sites in response to LTP induction using mass spectrometry. We found that CaMKII stabilizes F-actin by bundling and activation of CaMKII and autophosphorylation detaches CaMKII from F-actin and unbundles it. This CaMKII β -mediated F-actin bundling was shown to inhibit the access and action of actin regulating proteins *in vitro*. Phosphorylation of this domain also affects spine localization and turnover of CaMKII β. These observations made CaMKII a unique F-actin bundling protein that is negatively regulated by Ca^{2+}, and we speculate that CaMKII acts as a gate of structural plasticity.

S05-3 Activity-dependent accumulation change of drebrin-bound actin filaments in dendritic spines

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Drebrin is a side-binding protein of actin filaments. Drebrin A is a neuron-specific isoform, most of which are tightly bound to actin filaments *in vivo*. Drebrin-bound actin filaments (DB-actin) are highly concentrated in dendritic spines of mature neurons, but they disappear in the Alzheimer's disease brain. Drebrin A knockout eliminates the rapid form of homeostatic NMDA receptor accumulation at dendritic spines. Moreover, drebrin A expression levels are related to the synaptic strength in synapses of cultured neurons. These data suggest that drebrin is involved in synaptic function. In this talk, we first introduce the effect of chronic inhibition of glutamate receptor activity on drebrin localization at dendritic spines by fluorescence recovery after photobleaching (FRAP) analysis. The activation of AMPA-type glutamate receptors is necessary for DB-actin accumulation at dendritic spines. Although NMDA-type glutamate receptors are involved in the DB-actin turnover rate, but are not necessary for DB-actin accumulation in dendritic spines. On the other hand, NMDA-type glutamate receptor activation is known to induce swift DB-actin dislocation from dendritic spines. So we next show recent studies about the molecular mechanism of acute effect of NMDA-type glutamate receptor activation on DB-actin localization in dendritic spines. Acute inhibition of NMDA-type glutamate receptor activity facilitates the accumulation of DB-actin in dendritic spines, and also completely blocks the swift drebrin dislocation. Comparison of the effect of various sources of Ca^{2+} influx on DB-actin dislocation suggests that the basal accumulation of DB-actin in dendritic spines are regulated by intracellular Ca^{2+} concentration as a whole, but the swift dislocation of DB-actins was specifically regulated by local Ca^{2+} microdomain near NMDA receptors. Finally, we will discuss the molecular mechanism how local Ca^{2+} microdomain regulates the swift DB-actin dislocation.

S05-4 Dysregulation of spine morphology in ATRX-mutated mental retardation mice

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Alpha-thalassemia X-linked mental retardation (ATRX) syndrome is a severe, non-progressive mental retardation. We generated ATRX mutant mice ($ATRX^{\Delta E2}$) lacking of exon 2 with impaired cognitive functions without changes in emotional behavior and locomotor activity (Hippocampus 2011;21:678-687; J Neurosci. 2011;31:346-358). Interestingly, in the medial prefrontal cortex (mPFC) of $ATRX^{\Delta E2}$ 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. As a causative biochemical mechanism, an aberrant increased calcium/calmodulin-dependent protein kinase II (CaMKII) and decreased protein phosphatase 1 (PP1) activities were observed in the prefrontal cortex of $ATRX^{\Delta E2}$ mice without changes in CaMKI and CaMKIV phosphorylation. 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 phosphorylated by CaMKII, thereby activating p21-activated kinases (PAKs), we confirmed increased phosphorylation of Tiam1, Kalirin-7 and PAK1-3 in extracts from the mPFC. Taken together, the dysregulation of CaMKII and PP1 activities in part mediates abnormal spine formation in the mPFC through elevated Rac1-GEF/PAK signaling in $ATRX^{\Delta E2}$ mice.

S06-1 Cell intrinsic regulation of axonal morphogenesis mediated by posttranslational modifications: molecular systems for axonal growth regulation and axon-dendrite discrimination

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Neurons are capable to extend the axon and establish polarized morphology without particular cell extrinsic cues. Molecular systems that control this process remain to be elucidated. Previously, we demonstrated that E3 ubiquitin ligase complex, Cdh1/APC mediate inhibition of transcription factor SnoN, thereby control the growth of axons. Mechanisms by which this signaling pathway specifically affects on the axon, but not on the dendrites has not been clarified. We hypothesized that another cellular system that discriminate the axon from dendrites may contribute to this process. Recently, we identified that one of the posttranslational modification of tubulins acts as an intracellular cue to discriminate the axon from dendrites by navigating kinesin-1 motor into the axon. In addition, our studies suggest that this mechanism is required to maintain the polarized neuronal morphology. Further functions of tubulin modifications in the control of neuronal structure as well as possible molecular link between the two distinct processes (i.e. axonal growth and axon-dendrite discrimination) will be discussed.

S06-2 Dendritic growth cone activity regulated by Abl kinase and Cdk5 via WAVE2-Abi2 is essential for completing the multipolar-bipolar transition and initiating glia-guided locomotion

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Glia-guided locomotion during radial migration is a characteristic yet unique mode of migration. In this process, the directionality of migration is predetermined by glial processes and not by growth cones. Prior to the initiation of locomotion, migrating neurons transform from multipolar to bipolar, but the molecular mechanisms underlying this multipolar-bipolar transition and the commencement of glia-guided locomotion are not fully understood. Here, we demonstrate that the multipolar-bipolar transition is not solely a cell autonomous event; instead, the interaction of growth cones with glial processes plays an essential role. Time-lapse imaging with lattice assays reveals the importance of vigorously active growth cones in searching for appropriate glial scaffolds, completing the transition and initiating glia-guided locomotion. These growth cone activities are regulated by Abl kinase and Cdk5 via WAVE2-Abi2 through the phosphorylation of tyrosine 150 and serine 137 of WAVE2. Neurons that do not display such growth cone activities are located in a more superficial location in the neocortex regardless of their birthdates, suggesting the significance of growth cones for the final location of the neurons. This process occurs in spite of the 'inside-out' principle in which later-born neurons are situated more superficially.

S06-3 Regulation of neuronal morphogenesis and corticogenesis via CaMKK-CaMKI cascades

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We previously identified a CaMKI isoform that contained a C-terminal lipid modification motif. This novel membrane-anchored CaMK (CLICK-III/CaMKIgamma) was highly expressed in the cortical plate of the developing cerebral cortex. We found that prenylation and activity-dependent palmitoylation of CaMKIgamma enabled its proper sorting into lipid rafts enriched in dendrite membranes of immature cortical neurons. Furthermore, CaMKIgamma specifically regulated Rac-mediated actin remodeling that was required for BDNF-stimulated dendrite growth. In contrast, CaMKIalpha, a related kinase expressed in the cytoplasm, mediated GABA-stimulated axonal growth and activity-dependent fine tuning of axon terminal growth of callosal projections into contralateral hemispheres. Thus, CaMKK-CaMKI cascades may significantly influence spontaneous activity-regulated growth of dendrites and axons during an early developmental period that precedes the massive arrival of sensory inputs in the cerebral cortex.

S06-4 A positive feedback between neurite length-sensing and neurite outgrowth involved in neuronal symmetry breaking

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Previous studies suggest that polarizing cultured hippocampal neurons can sense neurite length, identify the longest neurite, and induce its subsequent outgrowth for axonogenesis. We found that shootin1, a key regulator of axon outgrowth and neuronal symmetry breaking (1, 2), accumulates in the neurite tips of polarizing neurons in a neurite length-dependent manner (3). Thus, neurons sense their neurites' length and translate this spatial information into a molecular signal, shootin1 concentration. Quantitative live cell imaging of shootin1 dynamics combined with mathematical modeling analyses reveals that its anterograde transport and retrograde diffusion in neurite shafts account for the neurite length-dependent accumulation of shootin1. The length-dependent shootin1 accumulation (3) constitutes a positive feedback interaction with the shootin1-induced neurite outgrowth (2). To analyze the functional role of the feedback loop, shootin1 up-regulation and shootin1-induced neurite outgrowth were quantified, and fitted to mathematical models. The parameters of both models were derived entirely from quantitative experimental data, and the models described the experimental data with good accuracy. These models were then integrated, together with the quantitative model of neurite length-dependent shootin1 accumulation, into a model neuron. The resultant model neuron spontaneously broke symmetry. The validity of the model was supported by fifteen agreements between the model predictions and experimental data. Here, the molecule, shootin, and the cellular space, neurite length, constitute a positive feedback interaction, and the present data suggest that the positive feedback loop, together with shootin1 up-regulation, constitutes a core mechanism for neuronal symmetry-breaking.(1) Toriyama et al. (2006) J. Cell Biol. 175, 147-157. (2) Shimada et al. (2008) J. Cell Biol. 181, 817-829. (3) Toriyama et al. (2010) Mol. Syst. Biol. 6, 394.

S07-1 Impact of stressful events during juvenile periods on neuropsychological development

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Stress is defined in biological systems as any conditions that seriously perturb physiological/psychological homeostasis. Experiences during a critical period of brain development may affect structural and functional development and maturation of the brain, and influence behavior including cognitive and emotional functions which could be attributable to the expression or exacerbation of developmental disorders. We have recently demonstrated that long-term social isolation or chronic restraint stress after weaning impairs hippocampal neurogenesis and hippocampus-dependent memory in mice. Furthermore, we have found that long-term social isolation reduces the expression of development-related genes including neuronal PAS domain protein 4 (Npas4) by using DNA microarray. Here, we show the possible involvement of Npas4 in stress-induced brain dysfunction. Both long-term social isolation and chronic restraint stress reduced the expression levels of Npas4 mRNA in the hippocampus. Acute corticosterone treatment also decreased the expression level of Npas4 mRNA *in vivo* and *in vitro*, while the expression level was increased by adrenalectomy. Putative glucocorticoid response elements were found at -2058 to -1060 upstream of the transcription initiation site of Npas4 promoter. Transcriptional activity of Npas4 gene was suppressed by binding of glucocorticoid receptor to the promoter regions. Furthermore, DNA methylation level of Npas4 promotor region was increased in the hippocampus of mice after restraint stress. DNA methylation of Npas4 promotor region decreased its promotor activity *in vitro*. The knockdown or overexpression of Npas4 significantly modulated the morphological and biochemical maturation of Neuro2a cells induced by LiCl. The ChIP assay indicated the interaction of Npas4 with CDK5 or NeuN genes. These results suggest that downregulation of Npas4 expression through steroidal and epigenetic pathway may play a role in stress-induced impairment of hippocampal function.

S07-2 Prostaglandin E_2-mediated desensitization of prefrontal dopaminergic activity is critical for susceptibility to repeated social defeat

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Susceptibility to stress underlies pathophysiology of various psychiatric illnesses, such as depression. Whereas dopaminergic activity is suggested to be suppressed in patients of major depression and a rodent model of depression induced by repeated stress, whether and how dopaminergic downregulation is involved in stress susceptibility remains largely unknown. Using repeated social defeat, we have examined a role of dopaminergic activity in stress-induced behavioral plasticity. Social defeat exposure evoked dopaminergic response in the medial prefrontal cortex (mPFC), but not in the nucleus accumbens, as measured by dopamine turnover, and this mPFC dopaminergic response was desensitized after repeated social defeat. This desensitization was also observed in the response of VTA dopaminergic neurons visualized by c-fos immunostaining. Notably, the level of mPFC dopaminergic response after repeated social defeat was negatively correlated with the extent of social avoidance. Dopaminergic lesions in mPFC, with noradrenaline and serotonin levels spared, promoted the development of social avoidance after repeated social defeat, suggesting the role of mPFC dopaminergic activity in protecting mice from repeated social defeat. Consistent with the reported action of prostaglandin E_2, a bioactive lipid, and its receptor EP1 in augmenting GABAergic inputs to midbrain dopamine neurons, the desensitization of mPFC dopaminergic activity and VTA dopamine neurons was abolished in mice lacking EP1. Concomitantly, EP1-deficient mice did not show social avoidance after repeated social defeat, and this behavioral abnormality was corrected by dopamine D1 receptor antagonist. Our data thus suggest that mPFC dopaminergic activity upon exposure to stress confers the resilience to stress, and that the desensitization of this pathway by PGE_2-EP1 signaling is critical for behavioral plasticity to repeated social defeat.

S07-3 Roles of metabotropic glutamate 2/3 receptors in environmental stress- or stress hormones-induced depression-like behaviors in mice

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Several lines of evidence suggest that brain glutamatergic system is involved in the pathophysiology of major depression and the mechanism of action of antidepressants. The metabotropic glutamate 2/3 receptor (mGluR2/3) is abundantly localized within forebrain regions, and recent clinical study shows that the mGluR2/3 expression is up-regulated in the prefrontal cortex of patients with major depression (*Prog. Neuropsychopharmacol. Biol. Psychiatry* 2010). We have previously found that social isolation-rearing and chronic corticosterone treatment increased immobility time of mice in the forced swim and tail suspension tests, suggesting the reliable models of depression for studying its neurobiological mechanisms (*Neuropharmacology* 2008). Thus, we examined the binding of the mGluR2/3 antagonist [^{3}H]LY341495 to mGluR2/3 in the brain by *in vitro* autoradiography and the effects of administration of the mGluR2/3 antagonist in these two models. Isolation-rearing increased [^{3}H]LY341495 binding in mouse prefrontal cortex, cortical layers I-III, and hippocampus (due to an increase in B_{max}), while chronic corticosterone did not. LY341495 decreased the immobility time in the forced swim test in both isolation-reared and corticosterone-treated mice. Moreover, isolation-rearing and chronic corticosterone markedly increased high K^+-induced dopamine release, but not glutamate and serotonin release, in mouse prefrontal cortex, and this enhanced release of dopamine was reversed by the mGluR2/3 antagonist. These findings suggest that the mGluR2/3 antagonist exhibits an antidepressant-like effect irrespective of the expression of mGluR2/3, probably via an inhibition of enhanced prefrontal dopaminergic activity, and imply that mGluR2/3 is a promising target for the treatment of depression.

S07-4 How do drugs of addiction alter the neuronal functions in the nucleus accumbens?: implications of oxidative stress

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The nucleus accumbens (NAc) works to integrate various cortical/subcortical inputs as the entrance of the basal ganglia, and drug addiction or major depression could be attributable to its dysfunction or vulnerability. By contrast, it is believed that the NAc is more resistant to oxidative stress-related neurodegenerative diseases compared to dorsal striatum that consists of the same types of neurons and neurotransmitters. However, whether the NAc is really free from oxidative stress or is suffering from other issues, instead of neuronal cell death, was not clear. Cocaine is a drug of abuse that is not so oxidative stress-inducible as amphetamine. Yet, it is reported that a widely used anti-oxidant, N-acetylcysteine, ameliorates cocaine-seeking behavior as well as impaired neuronal plasticity in animal model of cocaine addiction. In general, this compound exhibits its anti-oxidant effects by promoting glutathione synthesis. However, it is conceived that the effects of N-acetylcysteine on addicted animals are due to the activation of group I mGluRs by the elevation of extracellular glutamate, as N-acetylcysteine works as a precursor of cystine to restore the function of cystine-glutamate antiporter that is malfunctioning in cocaine-treated animals. We found that the pretreatment of N-acetyl-cysteine decreased the basal levels of many synaptic proteins in the NAc of repeatedly cocaine-treated rats, but not of control rats. N-acetylcysteine did not affect protein synthesis cascades, such as mTOR or S6K, thus, protein degradation pathways were more likely as target. Unexpectedly, the effect of N-acetylcysteine was neither mimicked by group I mGluRs agonist, nor blocked by group I mGluRs antagonist. Instead, a specific inhibitor against a rate-limiting enzyme in glutathione synthesis pathway blocked this effect. Thus, we conclude that this effect of N-acetylcysteine depends on glutathione, but not on glutamate. In addition, it is suggested that repeated cocaine administration induced oxidative stress-based alterations in synaptic protein turnover in the NAc, without promoting neurodegenerative processes. We propose that psychostimulant-induced oxidative stress (and its counteracting reactions) may be involved in the molecular mechanisms underlying drug addiction.

S08-1 Gene-environment interactions in the etiology of psychiatric disorders: pathophysiological implications of PACAP-dependent stress responses

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It is generally accepted that psychiatric disorders are complex diseases that probably result from an interaction of genetic and environmental risk factors. Stress is defined as a state of threat or perceived threat to homeostasis, inadequate adaptation of which may result in psychiatric conditions, and thus stress can be one of predisposing environmental factors in the etiology of psychiatric disorders: however, little is yet known about the underlying molecular mechanisms.
Growing evidence indicates that pituitary adenylate cyclase-activating polypeptide (PACAP) is an important regulator of the stress axes. We previously proposed a role for PACAP in modulating psychomotor activities. PACAP-deficient mice show marked behavioral and neurophysiological changes, including novelty-induced hyperlocomotion, deficits in prepulse inhibition, impaired memory retention, depression-like behavior, as well as altered responsiveness of the HPA axis to stress. In addition, the mutant mice housed alone for a two-week period were more aggressive, but their wild-type littermates were normal. Human genetic association studies provided evidence that suggests that PACAP is associated with schizophrenia and depression. Intriguingly, PACAP has recently been shown to be closely associated with PTSD. PACAP is active in brain structures that mediate anxiety- and fear-related behaviors, and the expression of PACAP and its receptors are dynamically altered under pathologic conditions. Considering all these data, PACAP may influence both hard-wired stress responses and gene-environment interactions in stress-related psychopathology.
Although it remains to be addressed how adverse environmental inputs affect the hierarchical organization of the nervous systems and eventually lead to psychiatric conditions, here we would like to focus on molecular basis and pathophysiological implications of stress responses that may facilitate the development of drug therapies for stress-related mental disorders.

S08-2 Functional involvement of DISC1 in pathogenesis of psychiatric diseases

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Disrupted-in-schizophrenia 1 (DISC1) is a promising susceptibility gene for major mental illness. By the two hybrid screening, our group found several interacters of DISC1 and we have shown an involvement of DISC1 in neurodevelopment via the interaction among them. Recent studies also have implicated DISC1 in key neurodevelopmental processes, including neurite outgrowth, neuronal migration and proliferation. On the other hand, it is well known that Neural-cadherin (N-cadherin), a calcium adhesion molecule, plays an important role in neurite outgrowth, pathfinding, and synaptic specificity of early central nervous system development. Then we examined effect of DISC1 on N-cadherin expression by overexpression or knockdown of DISC1. As a result, we found that expression level of DISC1 relates the N-cadherin expression and DISC1 regulates the expression level of beta1-integrin as well. Furthermore, we investigated the effect of DISC1 In the presence of nerve growth factor (NGF). DISC1 overexpression increased beta1-integrin expression at the cell membrane and growth cone. NGF-induced neurite extension was enhanced by DISC1, and anti-beta1-integrin antibody reduced the neurite outgrowth of DISC1-overexpressing cells to the control level. These data suggest that DISC1 regulates cell-cell adhesion and cell-matrix adhesion by regulating the expression of adhesion molecules. In conclusion, DISC1 regulates not only actin and microtubulles dynamic but also cell adhesion and plays important roles in neural development.

S08-3 Searching for functional molecules in growth cones

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The growth cone plays crucial roles in neural wiring, synapse formation, and axonal regeneration. Identification of proteins in the mammalian growth cone has the potential to advance our understanding of formation of neural circuit. We successfully used a proteomic approach to identify approximately1,000 proteins present in developing rat forebrain growth cones, including highly abundant, membrane- and actin-associated proteins. Almost one hundred of the proteins appear to be highly enriched in the growth cone, and for 17 proteins, the results of RNAi suggest a role in axon growth. Most of the proteins we identified have not previously been implicated in axon growth and thus, their identification presents a significant first step forward, providing candidate neuronal growth-associated proteins. To determine whether these 17 proteins are growth cone markers in other neuronal cell types, we examined their expression and function in PC12D cells. We found that all 17 nGAPs were highly concentrated in the growth cones of PC12D cells, and that knockdown of all of them by RNAi reduced or inhibited neurite outgrowth, indicating that all of them may be general growth cone markers. In addition, phosphoproteomic analysis revealed that some of the phosphorylation sites of growth cone proteins are specific to the growth cone. We will also discuss the mechanisms of the proteins identified by our proteomic approach, involved in axonal growth and polarity.

S08-4 New approach bridging between mind and molecules: application of Human Brain Phenotype Consortium

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One of the big issues in brain science field is to understand the molecular mechanisms of human brain function. However, there are ethical and methodological problems to analyze it directly. Thus, animal and cellular models are alternatively used, however, the results are not satisfactory in terms of human brain function, despite the strong scientific evidence of animal and cellular models. We propose a new approach to elucidate the molecular basis of human brain function, which supplements the scientific evidence of animal and cellular models. The main concept is the association study between genes and human brain phenotypes. Human brain phenotypes include neurpsychiatric disorders, neurocognitions, personality traits, neurophysiology and neuroimaging. We established research resource and database of healthy controls and mental disorders including genomic DNA, neurocognition (IQ, memory, executive function, etc), personality traits (Temperament and Character Inventory, Schizotypal Personality Questionnaire, and Autism-spectrum Quotient), brain morphology (cortical volume and thickness), frontal lobe function (Near-infrared Spectroscopy), neurophysiological function (Prepulse inhibition, EEG), etc in Human Brain Phenotype Consortium. These research resource and database were used to investigate the association with human brain phenotype and a specific gene, which a researcher in neurochemistry field is interested in. Association data between the gene and human brain phenotype facilitate the further analysis of the gene. We present our own data and several collaborative studies with researchers using animal and cellular models which are ongoing now. We are welcome for future collaborations. Detail information is available in the web site (http://www.sp-web.sakura.ne.jp).

S09-1 Roles of novel lateral hypothalamic peptides in regulation of feeding behavior

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We recently identified several novel neuropeptides by reverse pharmacology. Some of them have been implicated in the feeding behavior. I will discuss roles of these peptides in regulation of feeding behavior and energy homeostasis.

S09-2 Analyses of food-related brain neural activity by functional magnetic resonance imaging in lipodystrophy with leptin-replacement therapy

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Lipodystrophy is a disease characterized by a paucity of adipose tissue and low circulating concentrations of adipocyte-derived leptin. Leptin-replacement therapy improved hyperphagia and metabolic disorders in patients with lipodystrophy. However, there is little information about the neural networks processing leptin signals for appetite regulation. In this study, we investigated eating behavior and brain neural activities in healthy controls and lipoatrophic patients with or without leptin-replacement therapy by use of functional magnetic resonance imaging (fMRI). While there was no apparent difference of hunger feeling under fasting condition, postprandial satiety feeling in patients was significantly reduced compared to controls, which was effectively increased by leptin. In fMRI analysis, significant difference of food-related neural activity between patients and controls was detected many regions of interest (ROIs) under postprandial condition while only in a few ROIs under fasting condition. Leptin increased neural activity in orbitofrontal cortex, a region involved in satiety and suppressed in regions involved in hunger such as amygdala, hippocampus, insula, caudate and putamen in patients under postprandial condition. Leptin deficiency would account for a large part of the reduction of postprandial satiety feeling in patients. This study provides the useful notion to understand the etiology of eating disorders in leptin-deficient state and guide development of pharmaceuticals.

S09-3 Diabetes affects brain cholesterol metabolism

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Diabetes mellitus is associated with a variety of cerebral complications, including cognitive dysfunction, depression, and increased risk of Alzheimer's disease. The brain is the most cholesterol-rich organ in the body, most of which comes from in situ synthesis. Brain cholesterol turnover is increased in Alzheimer's and other neurodegenerative diseases. Here we show that in the brain in multiple mouse models of diabetes, there is a global reduction in expression of cholesterol synthetic genes and their major transcriptional regulator, sterol regulatory element binding protein 2 (SREBP-2). Indeed, Gene Set Enrichment Analysis of microarray data indicate the cholesterol biosynthesis pathway as one of the most highly down-regulated gene sets in the hypothalamus of the streptozotocin (STZ)-diabetic mouse. This was confirmed by quantitative PCR, which showed a coordinated 30-35% reduction in expression of SREBP-2 and cholesterologenic genes in the hypothalamus and cerebral cortex of STZ-, NOD- and db/db diabetic mice. This down-regulation of cholesterologenic genes resulted in a ~25% reduction in brain cholesterol synthesis as measured using ^3H_2O and a parallel decrease in synaptosomal membrane cholesterol content. SREBP-2 in the hypothalamus was also down-regulated in brain-specific insulin receptor knockout (NIRKO) mice. In vitro, insulin directly regulated the expression of SREBP-2 and cholesterol synthetic genes in cultured brain neurons and astrocytes. Reduction of SREBP-2 in cultured neurons using shRNA caused a significant decrease in post-synaptic (PSD95) and synaptic vesicle (VAMP2) markers. Furthermore, injection of the SREBP-2 shRNA lentivirus into the hypothalamus of intact mice resulted in increased feeding behavior and weight gain, and a 34% reduction of circulating norepinephrine levels. Thus, insulin and diabetes directly alter brain cholesterol metabolism. This impacts on neuronal synapse formation and may play an important role in the cerebral dysfunction observed in diabetic states.

S09-4 Molecular genetic dissecting neuronal pathway controling feeding behavior-Rapid, reversible activation of AgRP neurons potently drives feeding behavior-

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Several different neuronal populations are involved in regulating energy homeostasis. Among these, agouti-related protein (AgRP) neurons are thought to promote feeding and weight gain; however, the evidence supporting this view is incomplete. Using designer receptors exclusively activated by designer drugs (DREADD) technology to provide specific and reversible regulation of neuronal activity in mice, we have demonstrated that acute activation of AgRP neurons rapidly and dramatically induces feeding, reduces energy expenditure, and ultimately results in marked weight gain, owing to increased fat stores. All these effects returned to baseline after stimulation was withdrawn. In contrast, inhibiting AgRP neuronal activity in hungry mice reduced food intake. Together, these findings demonstrate that AgRP neuron activity is both necessary and sufficient for feeding - inhibition of AgRP neurons at a time when mice normally eat (at the beginning of the dark cycle) restrains feeding, while stimulation of AgRP neurons when mice are nutritionally replete (near the beginning of the light cycle) compels feeding. Of interest, activating AgRP neurons strikingly increased motivation for feeding and also drove intense food-seeking behavior, demonstrating that AgRP neurons engage brain sites controlling multiple levels of feeding behavior. Due to its ease of use and suitability for both acute and chronic regulation, DREADD technology is ideally suited for investigating the neural circuits hypothesized to regulate energy balance.

S10-1 The role of inositol hexakisphosphate kinases on central nerve system in the mammals

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The inositol pyrophosphates IP7 and IP8 contain highly energetic pyrophosphate bonds. Although implicated in various biologic functions, their molecular sites of action have not been clarified. Recently, IP7 phosphorylates endogenous proteins in yeast. These findings reveal that phosphorylation by IP7 is not enzyme-requiring process and may represent a novel intracellular signaling mechanism. The formation of IP7 and IP8 is mediated by three inositol hexakisphosphate kinases (IP6K1, K2, and K3). We previously reported that IP7 augmented cell death and especially, IP6K2 is a mediator of cell death in mammalian cells. Moreover, IP6K2 was translocated from the nucleus to the cytoplasm. Recently, we found that IP6Ks might play an important role of neurodegenerative diseases such as Huntington disease and amyotrophic lateral sclerosis (ALS).

S10-2 Measurement of inositol polyphosphates by ion chromatography and their physiological status in higher plants

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In higher plants, inositol hexakisphosphate (Phytic acid, InsP6), is well-known as a storage compound of phosphorus which is accumulated in seed. Recently it was reported that InsP6 was found in crystal of a plant growth hormone (auxin) receptor and InsP5 in Jasmonate receptor. InsPn might be related to plant hormone signaling. The synthetic mechanism of InsP6 is, however, still unclear in higher plants. To clarify InsPn synthesis and accumulation mechanisms in higher plant cells, we have developed a measuring system using ion chromatography. Using ion chromatography, we independently identified 25 of 64 isomers including enantiomers. The subcellular distribution of InsPn synthesis-related enzymes tagged with GFP showed that all enzymes locate in the cytosolic space. InsP6 molecules are synthesized from IP5 by IPK1 in the cytosol and accumulated in the vacuole. Recently it is reported that ABC transporter is functioning for InsP6 transport into the vacuole. In Arabidopsis, there is one gene encoding IPK1, which produces InsP6 from InsP5. We isolated IPK1 knock out plants from T-DNA tagged lines. In this plant, not only InsP6 accumulation in seeds, but plant morphology was partly affected. We have also constructed a plant having IPK1-GFP expressed under own promoter. Expression of IPK1 was detected through a whole plant. IPK1 gene was strongly expressed in a reproductive organ, such as pollen, stamen, or seeds. In the present paper, we discuss physiological roles of InsPn in higher plant life cycle.

S10-3 Calcium fluxes cause nuclear shrinkage and the translocation of phospholipase C-δ1 into the nucleus

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Phospholipase C-δ1 (PLCδ1) is the most fundamental form of the eukaryotic PLC and thought to play important roles in the regulation of inositide signaling. We previously reported that PLCδ1 shuttles between the cytoplasm and nucleus, and an influx of Ca^{2+} triggers the nuclear import of PLCδ1 via Ca^{2+}-dependent interaction with importin β1, although the physiological meaning of this is unclear. Here we have examined the distribution of PLCδ1 using primary cultures of rat hippocampal neurons. Treatment of 7DIV neurons with ionomycin or thapsigargin caused the nuclear localization of PLCδ1 as has been observed in other cell lines. Similar results were obtained with neurons treated with glutamate, suggesting that the nuclear localization of PLCδ1 plays some roles in excitotoxicity associated with ischemic stress. Generally, cells undergoing ischemic or hypoxic cell death show nuclear shrinkage. We confirmed that a massive influx of Ca^{2+} caused similar results. Furthermore, overexpression of GFP- PLCδ1 facilitated ionomycin-induced nuclear shrinkage in embryonic fibroblasts derived from PLCδ1 gene-knockout mice (PLCδ1KO-MEF). By contrast, an E341A mutant that cannot bind with importin β1 and be imported into the nucleus by ionomycin and also lacks enzymatic activity did not cause nuclear shrinkage in PLCδ1KO-MEF. Nuclear translocation and the PLC activity of PLCδ1, therefore, may regulate the nuclear shape by controlling the nuclear scaffold during stress-induced cell death caused by high levels of Ca^{2+}.

S10-4 NMDA receptor-mediated activation of PI(4,5)P_2-producing enzyme PIP5K is essential for AMPA receptor endocytosis during long-term depression

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NMDA receptor activation leads to clathrin-dependent endocytosis of the AMPA receptor at postsynaptic sites. Although this process controls long-term depression (LTD) induction in the hippocampus, how it is regulated by neuronal activities is not completely clear. Here, we show that Ca^{2+} influx through the NMDA receptor activates calcineurin and protein phosphatase 1 to dephosphorylate phosphatidylinositol 4-phosphate 5-kinase γ661 (PIP5Kγ661), the major phosphatidylinositol 4,5-bisphosphate [PI(4,5)P_2]-producing enzyme in the brain. Bimolecular fluorescence complementation analysis revealed that the dephosphorylated PIP5Kγ661 became associated with the clathrin adaptor protein complex AP-2 at postsynaptic sites *in situ*. NMDA-induced AMPA receptor endocytosis and low-frequency stimulation-induced LTD were completely blocked by inhibiting the association between dephosphorylated PIP5Kγ661 and AP-2 and by overexpression of a kinase-dead PIP5Kγ661 mutant in hippocampal neurons. Furthermore, knockdown of PIP5Kγ661 inhibited the NMDA-induced AMPA receptor endocytosis. Therefore, NMDA receptor activation controls AMPA receptor endocytosis during hippocampal LTD by regulating PIP5Kγ661 activity at postsynaptic sites.

S11-1 *Cell survival and axonal regeneration in rat retinal ganglion cells by purpurin, a novel extracellular matrix molecule after optic nerve injury*

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Nerve injury leads to retrograde neuronal degeneration and cell death in adult mammalian CNS neurons. The retinal ganglion cells (RGCs) of rat fail to regenerate their axons and become apoptotic after optic nerve injury. In contrast, fish RGCs can survive and regrow their axons and recover their visual function after injury. One of the explanations for these different regenerative properties in both animals is that some regeneration-associated molecules can be induced in the fish visual system, but not in rat. Such regeneration-associated molecules derived from fish might exert cell survival and nerve regeneration in mammals. In this view point, we sought the candidate molecules from axotomized fish retinas by differential screening. We cloned purpurin from the retinal cDNA library with differential hybridization of normal and axotomized fish retinas. The levels of purpurin mRNA peaked at 2-5 days after injury. The purpurin proteins were diffusely localized in all retinal layers, especially in the RGCs after injury. In retinal explant culture study, recombinant purpurin significantly induced neurite outgrowth. In our strategies toward optic nerve regeneration of mammals using fish derived molecule, we used purpurin overexpression systems by adeno-associated virus vector in rat retina. In rat, supply of purpurin could protect RGCs from injury-induced apoptosis through a mechanism of focal adhesion kinase(FAK) and Akt activation. Furthermore, purpurin had adhesive effect on rat RGCs from culture study with purpurin-coated dishes. We focused on the extracellular matrix-related molecules as a mechanism of purpurin adhesive and survival effects. Purpurin inhibited optic injury-induced matrix metalloprotease 9 activity and the degradation of laminin and activated FAK signaling. In the RGCs culture study, FAK overexpression induced neurite outgrowth with Akt activation and glycogen synthase kinase 3β inactivation. From these points, purpurin dramatically regenerated optic nerve after injury and FAK specific inhibitor cancelled it. Purpurin could potentially offer new avenues for developing treatments for human retinal degenerative disorders such as glaucoma.

S11-2 Long-distance axonal regeneration in mature mouse optic nerve: combined effects of intraocular inflammation, cAMP, and PTEN deletion

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The optic nerve fibers of adult animals do not normally regenerate if injured. Several strategies have been used to activate the intrinsic growth process of retinal ganglion cells (RGCs) which resulted in appreciable levels of axonal regeneration in the optic nerve. However, regeneration for the entire length of the nerve into the brain remains a major challenge. RGCs can be induced to switch into an active growth state by stimulating a controlled inflammatory reaction in the eye which enables RGCs to regenerate axons for several millimeters beyond the site of optic nerve injury (1,2). Oncomodulin (Ocm), a small, Ca^{2+}-binding protein that is secreted from activated macrophages, is associated with the inflammation-induced axonal regeneration (3,4). The ability of Ocm to bind to its cognate receptor is dependent upon [cAMP]i, and the axon-promoting effects of intraocular inflammation are enhanced by the addition of a cAMP analog (5). Another way to promote optic nerve regeneration is by deleting the gene encoding PTEN, a phosphatase and tensin homolog, which suppresses signaling through the PI3 kinase-Akt pathway (6). Our studies showed that combining intraocular inflammation, PTEN deletion, and cAMP elevation resulted in more significant regeneration than the sum of the individual treatments. The combined treatment resulted in the RGCs axons to regenerate the full length of the optic nerve, across the chiasm, and into the thalamus within 6 weeks. An induction of intraocular inflammation combined with elevated cAMP and PTEN deletion increased the activation of the PI3 kinase and MAP kinase signaling pathways, along with the activation of S6 kinase. Thus, treatments that synergistically alter the intrinsic state of RGCs produce excellent levels of axon regeneration in the mature optic nerve. (1) Leon, S., Yin, Y. et al. J Neurosci 20, 4615-26 (2000); (2) Yin, Y. et al. J Neurosci 23, 2284-93 (2003); (3) Yin, Y. et al. Nat Neurosci 9, 843-52 (2006); (4) Yin, Y. et al. Proc Natl Acad Sci USA 106, 19587-92 (2009); (5) Kurimoto T. et al J Neurosci 30, 15654-63(2010) (6) Park, K. et al., Science 322, 963-66 (2008)

S11-3 Degeneration in the visual pathway accompanying retinal and optic nerve injuries and its therapeutic strategy

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Glaucoma is a slowly progressive and irreversible ocular disease that is one of the leading causes of blindness worldwide. Glaucoma pathology has been extensively studied at the level of the retinal ganglion cells (RGC) and optic nerve, with diagnosis resulting primarily from intraocular pressure, ophthalmoscopic, and visual field measurements. On the other hand, in glaucoma the RGC death is accompanied by transsynaptic degradation of neurons in the lateral geniculate nucleus (LGN), which is the primary processing center for visual information received from the retina. However, the pathophysiological process of LGN degeneration in optic neuropathy including glaucoma is as yet unknown. Recently, we reported that neuronal degeneration in the LGN occurred in experimental retinal injury or chronic glaucoma models. Briefly, the pathological changes occurred in LGN at an early glaucoma stage and, therefore, the neuroprotection for LGN degeneration may become a new therapeutic approach for glaucoma. Here, we introduce recent findings in degeneration of the visual pathway accompanied by retinal and optic nerve injuries and in a new therapeutic strategy focusing on rescuing secondary neurons within the visual center.

S11-4 The neuroprotective treatment for glaucoma

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Glaucoma is a complex, heterogeneous disease characterized by a progressive degeneration of the optic nerve axons, and is the second highest cause of blindness worldwide affecting approximately 70 million people. Because of the loss of optic nerve axons, corresponding visual field defects was developed. The aim of glaucoma therapy is to delay the progression of visual field loss and to prevent the deterioration of quality of life (QOL). One of the significant risk factors for glaucoma progression is intraocular pressure (IOP) and therapy for lowering IOP is well established as a glaucoma treatment not only for primary open angle glaucoma (POAG) but also for normal tension glaucoma (NTG). However, in Japan, some of the patients still progress after 30% IOP reduction by treatment. Thus, the mechanism dependent-neuroprotective treatment for glaucoma is needed for the prevention of blindness. Ocular circulation is another significant risk factor for glaucoma. Recently, we used a laser speckle flowgraphy (LSFG) and accessed the ocular circulation quantitatively in the patients with glaucoma. We found that the decreased blood flow was significantly detected in glaucoma and may result in the excitotoxicity and axonal damage in the optic nerve. To clarify the causative role of the axonal damage on the RGC death, we developed the new mice model of axonal damage by crushing or administration of vinblastine onto the optic nerve. In the model, axonal damage suppressed the axoplasmic flow and induced secondary RGC death. In this lecture, I would like to review our recent works on the importance of ocular circulation in the patients with glaucoma and the ischemia-related pathogenesis including excitotoxicity, axonal damage, and oxidative stress and discuss the potential targets for the neuroprotective treatment for glaucoma.

S12-1 ER stress and neuropsychiatric disorders-Implications for therapeutic strategies

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The endoplasmic reticulum (ER) is an "assembly plant" for the manufacture of secretory and membrane proteins. However, from time to time "inferior goods", i.e. unfolded/misfolded proteins in the ER are inevitable. Under normal physiological conditions, unfolded proteins are degraded; under conditions of ER stress, however, unfolded proteins can accumulate in the ER lumen. Eukaryotes utilize the unfolded protein responses (UPR) to overcome the critical status induced by ER stress. If UPR is unsuccessful, cells go into ER stress-induced apoptosis. Recent reports show that dysregulation of the UPR is implicated in much important pathology, including some neurodegenerative diseases and cerebral ischemia. We speculate that a therapeutic strategy that induces the UPR might prevent neuronal death induced by ER stress. Among UPR, we applied the induction of ER molecular chaperone to reduce unfolded proteins. In a screen for compounds that induce the ER-mediated chaperone BiP/GRP78 (BiP), we identified BiP inducer X (BIX). 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. The sigma-1 receptor (Sig1R), much relevant to the neuropsychiatric disoredrs, is located on the ER membrane. We found that the induction of Sig1R relieve ER stress-induced apoptosis. In contrast, it is revealed that fluvoxamine induce Sig1R. Taken together, fluvoxamine can alleviate neuronal death by ER stress. Consequently, BIX and fluvoxamine are potential therapeutic agents for neuropsychiatric disorders caused by ER stress.

S12-2 The role of an ER-resident transmembrane transcription factor OASIS in astrocyte differentiation

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Endoplasmic reticulum (ER) stress response plays the roles in not only improvement of impaired environment in the ER lumen by the accumulation of unfolded proteins but also maintenance of basal cellular homeostasis. We previously identified an ER-resident transmembrane transcription factor, OASIS, which is structurally similar to one of the ER stress sensors, ATF6, and especially expressed in astrocytes in central nervous system. We have reported OASIS is activated in response to ER stress and the altered cellular homeostasis such as the cell differentiating stimuli, however, the function of OASIS in astrocytes has remained unclear. We generated *Oasis-/-* mice to examine the roles of OASIS in astrocytes. Cerebral cortex of embryonic *Oasis-/-* mice exhibited the decrease in the number of cells with GFAP, which is an astrocyte marker, and the increase in the number of cells with Nestin, which is a neural precursor cell (NPC) marker. We examined the expression levels of various markers during differentiation using NPCs prepared from E14.5 mice telencephalons. The up-regulation of *Gfap* was inhibited, in contrast, the *Nestin* expression was retained for long time in *Oasis-/-* cells during the differentiation from NPCs to astrocytes. We found glial cell missing 1 (GCM1), which has been reported to be necessary for astrocyte differentiation in *Drosophila*, was down-regulated in *Oasis-/-* NPCs. When GCM1 was introduced into *Oasis-/-* NPCs, the detention of the differentiation from NPCs to astrocytes was totally restored. Taken together, ER stress response mediated by the OASIS-GCM1 pathway plays the crucial roles in the promotion of the differentiation from NPCs to astrocytes.

Symposium

S12-3 Possible involvement of endoplasmic reticulum protein degradation in Alzheimer's disease

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Endoplasmic reticulum (ER)-associated degradation (ERAD) is a protective mechanism against ER stress in which unfolded proteins accumulated in the ER are selectively transported to the cytosol for degradation by the ubiquitin-proteasome systems. We cloned the novel ubiquitin ligase HRD1, which is involved in ERAD. We showed that HRD1 promoted amyloid precursor protein (APP) ubiquitination and degradation, resulting in decreased generation of amyloid-β (Aβ). Furthermore, suppression of HRD1 expression caused APP accumulation and promoted Aβ generation associated with ER stress and apoptosis. Interestingly, HRD1 levels were significantly decreased in the cerebral cortex of patients with Alzheimer's disease (AD), and the brains of these patients were under ER stress. Our recent study revealed that the decrease in HRD1 level was due to its insolubilization. However, controversy persists about whether the decrease in HRD1 protein promotes Aβ generation or whether Aβ neurotoxicity causes the decrease in HRD1 protein level. In the present paper we review current findings on the mechanism of HRD1 protein loss in the AD brain and the involvement of HRD1 in the pathogenesis of AD. Furthermore, we propose the possibility of HRD1 being a target for novel AD therapeutics.

S12-4 Roles of the unfolded protein response (UPR) in MPTP-induced neurotoxicity

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Injections of MPTP (acute model) or MPTP/probenecid (chronic model) into experimental animals cause neurodegeneration in the nigrostriatal dopaminergic neurons, and are widely used as Parkinson Disease (PD) models. Previous studies have demonstrated that MPTP injection activates the unfolded protein response (UPR), the stress response against endoplasmic reticulum (ER) stress, in the substantia nigra pars compacta (SNpc), while its role in the process of neurodegeneration is not clear. We demonstrate in this symposium that both of MPTP and MPTP/probenecid injection into mice activate ATF6 and PERK/eIF2α/ATF4 branches, but not Ire1/XBP1 branch, in the UPR. Deletion of ATF6α gene facilitates neuronal degeneration and protein aggregation in both models in mice. The protein aggregates observed in the ATF6α (-/-) mice after MPTP/probenecid injection are ubiquitin (Ub) and phosphorylated α-synuclein positive. An UPR-activating reagent, tangeretin, facilitates neuronal survival in both PD models. Our results suggest neuroprotective roles of the UPR against MPTP-induced neurotoxicity.

Symposium

S13-1 Astrocytic modulation of local field potential

○Hajime Hirase
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Multi-site extracellular recording is a practical and powerful approach to compare neuronal network dynamics of genetically modified animals *in vivo*. In order to address astrocytic involvement of neural activity modulation, we investigated neural dynamics in mice with genetic interventions targeted to astrocytes. More specifically, we investigated on neural dynamics in mice that lack S100B, a major Ca^{2+} binding protein predominantly expressed in astrocytes. We found that kainate-induced gamma oscillations are smaller in amplitude in S100B knockout mice *in vivo*. Local infusion of S100B in S100B knockout mice enhanced hippocampal kainate-induced gamma oscillations. In a complementary set of experiments, local application of anti-S100B antibody in wild-type mice attenuated the gamma oscillations. Both results indicate that the presence of extracellular S100B enhances the kainate-induced gamma oscillations. Moreover, in acutely isolated hippocampal slices, kainate application increased S100B secretion in a neural-activity-dependent manner. Further pharmacological experiments revealed that S100B secretion was critically dependent on presynaptic release of neurotransmitter and activation of metabotropic glutamate receptor 3 (mGluR3). Taken together, we propose a novel pathway of neuron-glia communications - astrocytic release of S100B protein modulates neural network activity. Next, we investigated the activity patterns of cerebral cortical astrocytes *in vivo*. The cerebral cortex is composed of layers with unique cytoarchitecture. Using the bolus loading technique to label neurons and glial cells with Ca^{2+} sensitive fluorescent dyes *in vivo*, we investigated Ca^{2+} dynamics of astrocytes in mature (>P28) cerebral cortex by two-photon microscopy. We found that layer 1 astrocytes are more prone to discharging spontaneous Ca^{2+} surges and that the proportion of Ca^{2+}-active astrocytes is twice that observed in layer 2/3. Interestingly, these spontaneous astrocytic Ca^{2+} surges in the somata were not influenced by surrounding neural activity in urethane anesthetized animals. Moreover, we demonstrated that Ca^{2+} fluctuations in microprocesses of astrocytes show distinct differences in layer 1 and layer 2/3. We are currently studying how these astrocytic Ca^{2+} events are relevant in information processing of a sensory circuit in the cerebral cortex involving the barrel area.

S13-2 Interaction between brain temperature and neuronal excitability; A specific subtype of astrocyte is classified by a thermo-sensor expression

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Physiological brain temperature is an important determinant for neuronal functions, and it is well established that changes in temperature have dynamic influences on hippocampal neuronal activities. Recently, we clearly revealed that a thermo-sensor TRPV4 (activated above 34°C) is activated by physiological temperature in hippocampal neurons and thereby controls their excitability (J. Neurosci. 2007, Shibasaki et al.). Therefore, if our brain temperature can dynamically change within a small range, a thermo-sensor TRPV4 can convert temperature information to electrical excitability in neurons. We found that astrocyte also express the TRPV4 in addition to neurons. Interestingly, only 20-30% astrocytes express TRPV4 in brain, indicating that we can classify astrocyte-subtypes by the expression pattern. TRPV4 is activated by heat (>34° C), hypotonic stimulus or 4α PDD (a TRPV4 specific agonist). We examined whether functional-TRPV4 was also expressed in the astrocytes. TRPV4-positive astrocyte-subtype responded to the all reported stimulus. Following the increased Ca^{2+} level in only TRPV4-positive astrocytes, significant Ca^{2+} oscillations were observed in among most of the astrocytes, indicating that communications among astrocytes were initiated through the TRPV4 activations. We hypothesized that the specific astrocyte-subtype (TRPV4-positive) might be important to regulate neural excitability, and the Ca^{2+} oscillations among the astrocytes might be a critical determinant to regulate the synaptic transmission. Therefore, we examined how astrocytes communicate each other. Upon TRPV4 activation in astrocytes, we measured neurotransmitter release by HPLC or a biosensor method, in which the HEK293 cells expressing various neurotransmitter receptors were used to detect the neurotransmitter release using a whole-cell patch-clamp method. Finally, we revealed that excitation of TRPV4-positive astrocytes modulates synaptic transmission, indicating that specific astrocyte-subtype regulates neuronal excitability through neurotransmitter release. Our results suggest that the existence of minor astrocyte-subtype produces an important advantage for modulation of neuronal transmission as a positive feedback from astrocytes to neurons.

S13-3 Specification of glial cell types in the developing central nervous system

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Astrocytes are the most abundant cell type in the central nervous system, and support neural activities by nutrients supply and blood-brain barrier formation. Recent studies further demonstrate their new roles in synapse formation, maturation, efficacy, and plasticity. Disruption of any of these functions causes serious neurological diseases. When and how astrocytes are specified to have such diverged functions is an interesting question. Thus, we and others undertook to access the basic mechanisms to induce astrocyte differentiation. Both intrinsic and extrinsic mechanisms are involved in these processes. BMP and IL-6 family cytokines play a pivotal role for activating astrocyte-related gene promoters. Epigenetic silencing and cell cycle regulator, cyclin D1, modify the activation of these signaling pathways. Receptor tyrosine kinase-feedback inhibitor Spry4 differently involves preference of neural stem cell differentiation for neurogenic versus gliogenic phases. At present, however, it is yet uncertain how functional diversity of astrocytes is developed. One possibility is that astrocytes may be classified into multiple sub-lineages with their diverse functions. As neural stem/progenitor cells generate different classes of neurons in a position-dependent manner, the different neuroepithelial domain/region may also contribute to the emergence of different classes of glial cells, including oligodendrocytes. Recent reports from the other groups regarding glial cell diversity will also be discussed.

S13-4 Astrocytes regulate neurotransmission at distant synapses through axonal modulation

○Takuya Sasaki
Department of Cerebral Structure, National INstitute of Physiological Sciences

Astrocytes are biologically active cells and locally modulate the function of adjacent neurons and synapses. Here we report that astrocytes regulate the conduction of nearby axons and thereby display long-range modulation of the transmission of downstream synapses. In hippocampal slices ex vivo, synaptically-coupled neurons were patch-clamped and visualized with fluorescent dye. A calcium fluorescent indicator and a UV-sensitive caged-calcium compound were injected into astrocytes near the presynaptic axon. UV flash increased the amplitude of unitary synaptic currents in the downstream postsynaptic neurons, an effect that was attenuated by application of glutamate receptor antagonists to the uncaging region. We carried out simultaneous axonal and somatic patch-clamp recordings from a pyramidal cell. Photo-activation of the neighboring astrocytes increased the duration of action potential in the axon. These results suggest that astrocytic calcium activity potentiates the synaptic output to postsynaptic neurons that were located far apart from these astrocytes, by enhancing the excitability of presynaptic axon conduction. This new mode of the neuro-glial interactions indicates that the effect of astrocytes reaches far more widely than previously believed.

M1-1 Marshall Warren Nirenberg, Honorary member of JSN: Nobel laureate and giant of science

○Toshiharu Nagatsu
Fujita Health Univeristy, Nagoya University

Marshall Warren Nirenberg, Honorary Member of the Japan Society for Neurochemistry (JSN), passed away on January 15, 2010 in New York City at the age of 82. Nirenberg was Chief of the Laboratory of Biochemical Genetics at the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (NIH).
In 1961, Nirenberg deciphered the genetic code universal in nearly all living entities, which is the set of rules by which information encoded in genetic materials (DNA or messenger RNA nucleotide sequences) is translated into proteins (amino acid sequences) by living cells.
For his seminal work on the genetic code, he was awarded the 1968 Nobel Prize in Physiology or Medicine at the age of 41, jointly with Robert W. Holley, then of Cornell University, Ithaca, New York, and Har Gobind Khorana, then of the University of Wisconsin, Madison, Wisconsin, "for their interpretation of the genetic code and its function in protein synthesis."
Around the time of the completion of deciphering the genetic code, Nirenberg initiated his research in neuroscience, particularly on the molecular basis of memory, and continued to work on it until his death. He always applied the most updated research information and methods to his research, such as cell culture, monoclonal antibodies, transcription factors, and RNA interference.
Over his long research career started in 1957, Nirenberg received numerous awards and honors. The very last honor bestowed upon him was on November 12, 2009, in a ceremony at NIH, when the American Chemical Society designated his work on the deciphering of the genetic code as a National Historic Chemical Landmark.
I would like to point out that the majority of branches of biochemical sciences have evolved into molecular science, around the late 1970s to 1980s. This is largely attributed to Marshall's seminal work of the elucidation of the genetic code.
I first met Marshall in 1962 at NIH, when I was working with the late Dr. Sidney Udenfriend, Chief of the Laboratory of Clinical Biochemistry, the National Heart Institute at that time, and now NHLBI, NIH on the isolation and characterization of tyrosine hydroxylase. Marshall was another Section Chief in the Udenfriend Laboratory. I formed an intimate friendship with Marshall that continued until his death. I was fortunate to have the opportunity to closely observe the progress of Marshall and his colleagues' work on the deciphering of the genetic code during that exciting period. It was my great honor to have known Marshall since that time.
Marshall was not only a giant in science himself, but also an excellent mentor. He was very modest and kind person and trained many young U.S. and foreign scientists, including nearly a dozen of Japanese scientists. Marshall's laboratory produced many scientists who made significant scientific achievements. Notable scientists trained in Marshall's laboratory include: Michael S. Brown, M.D., of the University of Texas Southwestern Medical Center at Dallas, Dallas, Texas, the recipient of the 1985 Nobel Prize in Physiology or Medicine, Alfred G. Gilman, M.D., Ph.D., of the University of Texas Southwestern Medical Center at Dallas, Dallas, Texas, the recipient of the 1994 Nobel Prize in Physiology or Medicine, Philip Leder, M.D., of the Department of Genetics, Harvard Medical School, Boston, Massachusetts, the recipient of the 1987 Albert Lasker Basic Medical Research Award and the National Medal of Science, 1989. Marshall's laboratory also produced many professors and members of academies, as well as corporate executives in biomedical industries. Many Japanese scientists trained in Marshall's laboratory also became professors in Japan.
Dr. Haruhiro Higashida, who has organized this Satellite Symposium, is a professor of the Kanazawa University Graduate School of Medicine, Kanazawa, Japan, went to Marshall's laboratory in 1976 as a visiting fellow, and since then Dr. Higashida continued to work with Marshall until his death.
Dr. Higashida has organized this Satellite Symposium in cooperation with Dr. G. David Trisler, Visiting Professor at the University of Maryland School of Medicine, Department of Neurology, Baltimore, Maryland, U.S.A., and Dr. Frank S. Walsh, Chief Executive Officer of Ossianix Inc., a biotechnology company in Philadelphia, Pennsylvania, U.S.A., who was until very recently a Visiting Professor at King's College London, London.
Marshall was invited to Japan two times for his plenary lecture at the 1980 JSN congress in Matsuyama City and the 2003 JSN congress in Niigata City. On his second visit to Japan, he left these words for young Japanese scientists to ponder: "If you are really interested in your research it is easy to work hard and you probably will discover something of great interest."
We are happy to welcome again Dr. Myrna Weissman, Marshall's wife,

who is Professor of Epidemiology in Psychiatry, Columbia University in the City of New York. In 2003, she visited Japan with Marshall. At that time, she presented her lecture at Kanazawa University.
We would like to thank all the outstanding speakers in this Symposium, especially speakers from abroad. We would expect to learn the cutting-edge information in versatile fields of neurochemistry
I am grateful to these three organizing members of this wonderful Marshall Nirenberg Memorial Symposium.
As you already know, approximately six months ago, an unprecedented magnitude 9 earthquake and resulting massive tsunami struck the Pacific coastal area of northeastern Japan on March 11, 2011, which is approximately 250 miles northeast from this symposium venue, and it left enormous damage to the coastal area over 250 miles with the death toll over 15,000 and missing persons over 11,000, and over 125, 000 housings and industrial buildings damaged or destroyed. The earthquake and tsunami have also damaged Tokyo Electric Power Company's Fukushima Nuclear Power Plant, and the residents in the area 12 miles radius from Nuclear Power Plant still remain evacuated. Japan is now in the rebuilding process of the area from the devastation of the earthquake and tsunami. It has been affected a wide range of Japanese activities. Under the difficult circumstances, Dr. Higashida has organized this wonderful Marshall Nirenberg Memorial Symposium, in cooperation with Dr. Trisler and Dr. Walsh.
I am strongly convinced that this Marshall Nirenberg Memorial Symposium will become an important milestone in neurochemistry.
Marshall Nirenberg will always be remembered for his scientific accomplishment and his mentorship.

M1-2 The potential role of ATF4 in learning and memory

○Lloyd Greene
Columbia University

Authors: Lloyd A. Greene, Jin Liu, Silvia Pasini, Carlo Corona and Michael L. ShelanskiAbstract: ATF4 (activating transcription factor 4) plays important roles in responses of cells to various stresses. It has also been implicated as a potential player in learning and memory. We have examined the effects of manipulating ATF4 expression in cortical and hippocampal neurons both *in vitro* and *in vivo*. Our *in vitro* findings indicate that endogenous ATF4 plays a role in regulating both neurite outgrowth and the morphology of dendritic spines. Moreover, *in vivo* manipulation of ATF4 expression in the hippocampus results in altered performance in memory tests and in changes in LTP. Taken together, these findings support the idea that ATF4 may be a key player in modulating learning and memory.

M1-3 Single nucleotide polymorphisms of CD38 and oxytocin treatment for 6 subjects with autism spectrum disorders

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Krasnoyarsk Medical University

Autism spectrum disorder (ASD), characterized by social and communication defects, occurs either sporadically or in a familial pattern. The etiology remains largely unknown. Therefore, the theoretical basis for pharmacological treatments is not yet established. Previously, we demonstrated that CD38 is critical in mouse social behavior by regulating release of oxytocin (OT; 1), which is essential for mutual recognition and trust. Hence, there is a strong rationale for investigating mutations in the human CD38 gene in ASD subjects. Here, we first examined the immunohistochemical expression of CD38 in the hypothalamus of post-mortem brains of non-ASD subjects and found that CD38 was colocalized with OT in secretory neurons. In studies of the association between CD38 and ASD, we analyzed 10 single nucleotide polymorphisms (SNPs) and mutations of CD38 by re-sequencing DNAs mainly from a case-control study in Japan, and Caucasian cases mainly recruited to the Autism Genetic Resource Exchange (AGRE). The SNPs of CD38, rs6449197 ($p<0.040$) and rs3796863 ($p<0.005$) showed significant associations with a subset of ASD (IQ>70; designated as high-functioning autism (HFA)) in the American 104 AGRE trios, but not with Japanese 188 HFA subjects. A mutation that caused tryptophan to replace arginine at amino acid residue 140 (R140W; (rs1800561, 4693C>T)) was found in 0.6%-4.6% of the Japanese population and was associated with ASD in the smaller case-control study. The SNP was clustered in pedigrees in which the fathers and brothers of T-allele-carrier probands had ASD or ASD traits. In this cohort OT plasma levels were lower in subjects with than in those without the T allele. One proband with the T allele and 3 others who were taking nasal OT spray showed improvements in the area of social approach, eye-contact and communication behaviors (2). The two variants of CD38 tested may be of interest with regard of the pathophysiology of ASDs.(1) Jin D et al. CD38 is critical for social behaviour by regulating oxytocin secretion. Nature 2007;446:41.(2) Munesue T et al. Two genetic variants of CD38 in subjects with autism spectrum disorder and controls. Neurosci Res 2010;67:181.

M2-1 alpha-Synuclein in Parkinson's disease: Pathogenetic foe and therapeutic target

○M. Maral Mouradian
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alpha-Synuclein (a-Syn) is a key protein in the pathogenesis of Parkinson's disease and other alpha-synucleinopathies including Dementia with Lewy Bodies and Multiple System Atrophy. This natively unfolded protein has the tendency to aggregate into oligomeric and eventually fibrillar forms under various conditions. Accumulating evidence suggests that the process of aggregation and particularly the early soluble oligomers are toxic to neurons. Among the factors that promote a-Syn aggregation that our laboratory has focused upon is its concentration. Human genetic studies have shown that individuals with multiplication of the a-Syn gene locus develop dominantly inherited Parkinson's disease with a symptom onset age that reflects a gene dosage effect. Additionally, over-expressing a-Syn in various animal models recapitulates many of the phenotypic features of the disease including protein aggregation and neuronal dysfunction. Thus, understanding the factors that regulate a-Syn expression in the human brain is critical in our efforts to keep the amount of this protein under control. To this end, we have found that a-Syn is down-regulated by a specific microRNA. miR-7, which is expressed by neurons, binds to the 3'-untranslated region of a-Syn mRNA and degrades it resulting in less protein production. Importantly, this is associated with protection of neuronal cells against the toxicity of a-Syn. Another factor that promotes a-Syn aggregation is its phosphorylation. Postmortem human brain studies have shown that a-Syn is heavily phosphorylated at serine 129 in synucleinopathy lesions. Several kinases are known to carry out this post-translational modification making inhibition of a single kinase unlikely to be effective. In contrast, we have found that a single protein phosphatase 2A (PP2A) isoform, namely methylated-AB α C holoenzyme, is the primary a-Syn phosphatase. We have also identified from an *in vitro* screen of natural products a small molecule present in coffee extract, eicosanoyl-5-hydroxytryptamide (EHT), that promotes the activity of this phosphatase both *in vitro* and in the mouse brain by modulating the methylation state of the PP2A regulatory C subunit.

M2-2 Marshall and Medicine: impact on drug discovery

○Orest Hurko
Biologics Consulting Group, Inc.

The last fifteen years have witnessed a major shift of the pharmaceutical and biotechnology industries from an empiric approach based on incremental improvements of proven therapies, to the modern paradigm of target-based drug discovery. Target-based drug discovery arose as a consequence of three technological advances: (1) the generation and interpretation of genome sequences, which facilitated identification and characterization of novel drug targets; (2) the efficient production of candidate ligands for these putative targets through combinatorial chemistry or generation of monoclonal antibodies; and (3) the use of high-throughput screening to allow rapid evaluation of interactions between such putative ligands and targets. The basic idea underlying all three of these technologies stems from Marshall Nirenberg's dictum that science progresses best when there is a simple assay capable of rapid generation of a large amount of data. Furthermore, practical implementation of this basic concept for drug discovery was directly enabled by technologies that either originated with or were nurtured at an early stage by Marshall as well as by his post-docs and fellows. Chief among these is the deciphering of the genetic code, but also by his early adoption of clonal cell lines for pharmacological investigations, as well as the use of hybridomas to generate molecular probes that allowed physical purchase on signaling elements that were previously only hypothetical constructs. Always the pure scientist, Marshall nevertheless enabled fruitful applications in the pharmaceutical industry, several of them by his trainees. Both the successes and the shortcomings of target-based drug discovery are worthy of consideration.

M2-3 Regulatory approval of biopharmaceutical products

○James G. Kenimer
Biologics Consulting Group, Inc.

The transition of any pharmaceutical product from the research laboratory to the clinic and onward to eventual market approval is a complex process with many possible pitfalls and obstacles which can significantly delay, or even kill, a project. The approval pathway for biologic products in the US is made even more complex due to fact that biologic products are regulated under a different law (the Public Health Services Act) than other non-biologic drugs (which are regulated under provisions of the Food, Drug and Cosmetics Act). Although efforts have been made over the years to harmonize the approval requirements for biologic and non-biologic drugs, successful navigation of the biologic product approval pathway requires knowledge of, and adherence to, the unique regulations which govern these products.Historically, the law governing approval of biologic products pre-dates the law governing other drug products, and was the direct result of a series of public health disasters which stimulated public demand for legislative action. The first of these disasters occurred in 1901, prior to establishment of the FDA or of the passage of any substantive laws regulating the safety of drug products. During an outbreak of diphtheria in St. Louis Missouri, the city commissioned the production of diphtheria antitoxin produced by inoculation of a horse. Unfortunately the horse also somehow contracted an infection with Clostridium tetani and subsequently died of tetanus, however not before it was bled and an antisera prepared and administered to a number of children. Thirteen children died due to tetanus toxin contamination of the antisera, and the public outcry stimulated the US Congress to pass the Virus, Serum and Toxins Act (the precursor of the Public Heatlh Services Act) detailing various regulations concerning the testing and approval of "biologic" products. This presentation will discuss the history of the evolution of the biologic product approval process in the US, the difference in biologic and non-biologic products, and will present an overview of the product development pathway for the transition of a biologic product from the laboratory to the clinic.

M2-4 A study of generations at high-risk for major depression

○Myrna M. Weissman
Columbia University

This paper will describe how epidemiologic observations on the early age of onset of major depression were translated in a series of studies to understand clinical phenotype, risk, endophenotypes and genetics. Multiple approaches including clinical, Magnetic Resonance Imaging (MRI) and DNA studies will be presented from a 3-generation study of families at high and low risk for major depression (MDD) who have been followed in 5-waves of assessments over 25-years. The clinical assessments show the 3-6 fold increase in major depression in the high as compared to the low-risk families which is consistent across the generations and over time.A robust association of familial risk for MDD with asymmetries in cortical thickness in this region, with a 30% reduction in thickness was observed in the lateral parietal, temporal, and frontal cortices of the right hemisphere of the high risk group. The presence of the findings in individuals with and without a prior lifetime history of MDD who were at increased familial risk for MDD suggests that these abnormalities were not simply a consequence of previously having been depressed or having been treated for depression and may be an endophenotype. Preliminary findings on the differential rate of variance in transporter genes by family risk will also be presented.

M2-5 Neuroscientists of the Future: Empirical Research on the Development and Career Decisions of Young Scientists

○Richard McGee Jr
Northwestern University

Graduate student and postdoctoral neuroscientists of the 1960s, '70s and early '80s 'grew up' scientifically during an era when resources for research were relatively plentiful; faculty and other permanent positions were quite achievable; and publication expectations were such that mentors could give trainees opportunities to try novel, potentially risky new ideas. This was the setting for many of us who worked with Dr. Nirenberg. Since then, biomedical research and training have changed in many ways but few if any empirical studies have investigated how today's young scientists understand and respond to their training experiences in this transformed environment. Our previous studies, using rigorous qualitative research methods from the social sciences, have revealed novel insights into research training, including personal characteristics that predict students who will persist into research, and how altering common training practices (such as addition of purposeful co-mentoring) can speed and enhance scientific development. Our current research is following more than 350 U.S. biomedical PhD students with annual in-depth interviews to determine how their experiences with scientific training shape both their abilities to conceive and conduct highly creative research and their desire for a research career. Beyond observing and categorizing trainee experiences, the interview data are being analyzed through multiple social science theoretical 'lenses' to reveal the implicit processes that influence scientific development. This longitudinal study is already yielding much new information, and the applicability of the social science theories to the study of scientific development is very clear. In particular, new insights are emerging into why underrepresented groups, such as racial/ethnic minorities and women, have been slow to overcome their historic marginalization. Our studies also indicate new mentoring models and theory-driven interventions can advance the development of young scientists in a much more predictable way than sole reliance on classical mentoring. The debates and challenges of attempting to manage the supply/demand balance of the world-wide scientific community are not likely to be resolved any time soon. But it is essential that objective empirical research be employed as the basis for conscious construction of training environments to maximally guide scientific development for the various roles PhD scientists can play.

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M3-1 Bone morphogenetic proteins regulate ErbB3/GGF2 signaling to promote gliogenesis in the enteric nervous system

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The neural crest-derived cell (ENCDC) population that colonizes the bowel containsproliferating neural/glial progenitors. We tested the hypothesis that bone morphogenetic proteins (BMPs 2 and 4), which are known to promote enteric neuronal differentiation at the expense of proliferation, function similarly in gliogenesis. Enteric gliogenesis was analyzed in mice that overexpress the BMP antagonist, noggin, or BMP4 in the primordial ENS. Noggin-induced loss-of function decreased, while BMP4-induced gain-of-function increased the glial density and glia/neuron ratio. When added to immunoisolated ENCDC, BMPs provoked nuclear translocation of phosphorylated SMAD proteins and enhanced both glial differentiation and expression of the neuregulin receptor ErbB3. ErbB3 transcripts were detected in E12 rat gut, before glial markers areexpressed; moreover, expression of the ErbB3 ligand, glial growth factor 2 (GGF2) escalated rapidly after its first detection at E14. ErbB3-immunoreactive cells were located in the ENS of fetal and adult mice. GGF2 stimulated gliogenesis and proliferation and inhibited glial cell derived neurotrophic factor (GDNF)-promoted neurogenesis. Enhanced glial apoptosis occurred following GGF2 withdrawal; BMPsintensified this GGF2-dependence and reduced GGF2-stimulated proliferation. These observations support the hypotheses that BMPs are required for enteric gliogenesis and act by promoting responsiveness of ENCDC to ErbB3 ligands such as GGF2.

M3-2 Transmembrane agrin in filopodia regulation and synapse formation

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The processes of synapse formation and plasticity are key to learning and memory, and involve complex interactions between pre- and postsynaptic neurons. The proteoglycan agrin has a well-defined role in the formation and maintenance of the vertebrate neuromuscular junction (NMJ), in that the secretion of a motor neuron-specific isoform of agrin is required for stable postsynaptic differentiation. Several lines of evidence suggest that agrin is involved in the formation, maintenance and plasticity of synapses in regions of the central nervous system (CNS), including the cortex and hippocampus, but agrin's mechanisms of action in the CNS are not well understood. Agrin in CNS neurons is predominantly expressed as a transmembrane proteoglycan. We showed that over-expression of transmembrane agrin (TmAgrin) in skeletal muscle cells, cell lines and hippocampal neurons in culture induced the formation of stable filopodia-like processes. This induction required the transmembrane domain and the N-terminal moiety of the extracellular domain of TmAgrin, involved activation of the GTPases Rac and Cdc42, and was reduced or eliminated by deletion of the heparan sulfate GAG chains attached to the N-terminal moiety of agrin. Suppression of agrin expression in cultured hippocampal neurons by transfection with a siRNA plasmid caused a reduction in the number and stability of filopodia on neurites during the first week of culture, confirming a positive role for TmAgrin in filopodia regulation. To investigate the role of TmAgrin in the regulation of dendritic filopodia, which participate in the induction of dendritic spines and synapses, we used a siRNA lentivirus to suppress TmAgrin expression in 2-week-old hippocampal neuron cultures. This reduced the number of dendritic filopodia as well as the number of synapses detected at 3 weeks. Moreover, the number of synapses was more severely reduced in axon-dendrite contacts where TmAgrin expression was suppressed only in the postsynaptic cell (dendrites) than where it was suppressed only in the presynaptic cell (axons). Thus, TmAgrin may promote synapse formation and plasticity in the CNS largely through regulation of dendritic filopodia.

M3-3 ECT2, an ortholog of drosophila's pebble identified from RNAi screening, regulates neuronal differentiation

○Chiharu Higashida
Kanazawa University

To identify genes required for the brain development, we previously performed *in vivo* RNAi screening in Drosophila embryos. We identified pebble as a gene that disrupts development of the Drosophila nervous system. Although pebble has been shown to implicate in the neuronal development of Drosophila in the several screenings, involvement of Ect2, a mammalian orthologue of pebble, in the mammalian neur-development has not been addressed. To examine the involvement of Ect2 in the neuronal differentiation, we performed Ect2 RNA interference in the mouse neuroblastoma x rat glioma NG108-15 cell line. Depletion of Ect2 resulted in increased proportion of binucleate cells and morphological differentiation of NG108-15 cells characterized by the outgrowth of neurites. These morphological changes were correlated with an increased level of acetylcholine esterase mRNA. In addition, expression of Ect2 was decreased in differentiated NG108-15 cells induced by dibutyryl cyclic AMP. These findings indicate that Ect2 negatively regulates the morphological and functional? differentiation of NG108-15 cells and suggest that Ect2 plays a possible role in neuronal differentiation and brain development.

M3-4 Neural progenitors express topographic markers

○David Trisler
University of Maryland School of Medicine

Transplantation of neural stem cells for replacing neurons after neurodegeneration requires that the transplanted stem cells accurately reform the lost neural circuits in order to regain function. Retinal ganglion cell axons project to visual centers of the brain forming circuits in topographic order. In chick, dorsal retinal neurons project to ventral optic tectum, ventral neurons to dorsal tectum, anterior neurons to posterior tectum and posterior neurons to anterior tectum; forming a continuous point-to-point map of retinal cell position in the tectal projection. We found that when stem cells derived from ventral retina were implanted in dorsal host retina, the stem cells that became ganglion cells projected to dorsal tectum, appropriate for their site of origin in retina but not appropriate for their site of implant in retina. This led us to ask if retinal progenitors express topographic markers of cell position in retina. Indeed, we found that retinal neural progenitors express topographic markers: dorsal stem cells expressed more Ephrin B2 that ventral stem cells and ventral stem cells expressed more Pax-2 and ventroptin than dorsal stem cells. The fact that neural progenitors express topographic markers has implications in using neural stem cells in cell replacement therapy for replacing projecting neurons that express topographic order, e.g., neurons of the visual, auditory, somatosensory and motor systems.

M4-1 Regulation of neurokine receptor signaling and trafficking

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Leukemia inhibitory factor (LIF) and ciliary neurotrophic factor (CNTF) are neurally active cytokines, or neurokines. LIF and CNTF are members of the interleukin-6 family of cytokines which signal through the shared receptor subunit gp130. LIF and CNTF have a variety of actions in both the peripheral and central nervous systems. LIF signals through a receptor consisting of gp130 and the low affinity LIF receptor (LIFR), while the CNTF receptor consists of gp130, LIFR, and the low affinity CNTF receptor (CNTFR). Ser1044 of the LIFR is phosphorylated by Erk1/2 MAP kinase. Stimulation of neural cells with growth factors which strongly activate Erk1/2 decreases LIF-mediated signal transduction due to increased degradation of the LIFR as a consequence of Erk1/2-dependent phosphorylation of the receptor at Ser1044. The LIFR and gp130 are transmembrane proteins, while CNTFR is a peripheral membrane protein attached to the cell surface via a glycosylphosphatidylinositol tail. In unstimulated cells, CNTFR but not LIFR and gp130 is localized to detergent-resistant lipid rafts. Stimulation of cells with CNTFR causes translocation of LIFR and gp130 into the lipid rafts, while stimulation with LIF does not induce receptor translocation, raising the possibility that CNTF could induce different patterns of signaling and/or receptor trafficking than caused by LIF.We used a compartmentalized culture system to examine the mechanisms for retrograde signaling by LIF and CNTF from distal neurites to the cell bodies of mouse sympathetic neurons. Stimulation of distal neurites with neurokines resulted in the activation and nuclear translocation of the transcription factor Stat3. Retrograde signaling required Jak kinase activity in the cell body but not the distal neurites, and could be blocked by inhibitors of microtubule but not microfilament function. The results are consistent with a signaling endosomes model in which the ctyokine/receptor/Jak kinase complex are transported back to the cell body where Stat3 is activated. While both LIF and CNTF mediate retrograde activation of Stat3, the kinetics for retrograde signaling differ for the two neurokines.

M4-2 Removal of adult-generated neurons and hippocampal function

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Korea University

A considerable number of new neurons are generated daily in the dentate gyrus (DG) of the adult hippocampus, but only a subset of these survive, as approcimately 50-70% of adult-generated neurons undergo programmed cell death (PCD). However, the significance of such massive PCD in the adult brain for the functionality of DG circuits is not known. My research group have examined the electrophysiological and behavioral characteristics of Bax-knockout (Bax-KO) mice in which PCD of post-mitotic neurons is prevented. The continuous increase in DG cell numbers in Bax-KO mice resulted in the readjustment of afferent and efferent synaptic connections, represented by age-dependent reductions in the dendritic arborization of DG neurons and in the synaptic contact ratio of mossy fibers with CA3 dendritic spines. These neuroanatomical changes were associated with reductions in synaptic transmission and reduced performance in a contextual fear memory task in 6-month-old Bax-KO mice. These results suggest that the elimination of excess DG neurons via Bax-dependent PCD in the adult brain is required for the normal organization and function of the hippocampus.

M4-3 Botulinum neurotoxin: Lethal agent or wonder drug

○Michael Adler
USAMRICD

The botulinum neurotoxins (BoNTs) are the most potent substances in nature, and exposure to as little as 1-3 ng/kg may be sufficient to cause human lethality. The toxicity of BoNT stems from its potent and selective inhibition of acetylcholine (ACh) release at the neuromuscular junction, autonomic ganglia and structures innervated by the parasympathetic branch of the autonomic nervous system. Paradoxically, this selective inhibition of ACh release has also enabled BoNT/A to become a highly useful therapeutic agent. Since its approval in 1989 as an orphan drug for the treatment of strabismus, hemifacial spasm, and blepharospasm, BoNT/A has come to be regarded as the treatment of choice for an increasing number of neurologic, autonomic and cosmetic conditions. The ability of BoNT to serve as the treatment of choice for the above is based on its exquisite selectivity for cholinergic nerve terminals, its long duration of action and its ability to remain localized near the intended target when injected at low concentrations and volumes.

Although clinicians have learned to harness the therapeutic benefits of BoNT in ways that were not even imagined when BoNT was first approved as an orphan drug, we should not lose sight of the fact that BoNT is inherently a highly lethal toxin, that outbreaks of botulism with devastating consequences continue to occur, and that recovery from botulism can require months of intensive care and rehabilitation, often leaving patients with long lasting physical and psychological trauma. Restoration of normal muscle function, exercise tolerance and cardiovascular fitness after intoxication by BoNT has been reported to take nearly a year after BoNT/F, over 2 years after BoNT/B and greater than 5 years after BoNT/A.

In addition to natural outbreaks, the potential use of BoNT by hostile forces has become a reality that responsible governments must include in their contingency plans. The ability of BoNT to cause mass casualties led to its designation as a category A threat agent by the U.S. Centers for Disease Control and Prevention (CDC), the only non infectious agent to receive this designation. Use by terrorists, especially over the last two decades, has become an increasing concern due to the widespread availability of BoNT from both legitimate and illegitimate sources, coupled with ease of concealment and inherent vulnerabilities of our modern food and beverage distribution systems. These factors, in conjunction with a rise of religious fundamentalism and proliferation of failed states makes an attack by BoNT more likely than it has been in previous generations. BoNT is unique in its ability to both cause and alleviate human suffering. It is simultaneously a powerful weapon and a formidable therapeutic tool that can provide relief from a large number of human ailments where few other options exist. The manner in which it is deployed is entirely in the hands of the user.

M4-4 Therapeutic potentials of fetal neural stem cells treated with fluoxetine for alzheimer's disease model mice

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Recent studies have proposed that chronic treatment with antidepressants increases neurogenesis in the adult hippocampus. However, the effect of antidepressants does not define well in fetal neural stem cells.Our study shows the effects of fluoxetine in the proliferation and neural differentiation of fetal neural stem cells (FNSCs) in dose-dependent manner. Fluoxetine even in the level of nM stimulated proliferation of FNSCs and increased the number of Tuj1, NeuN positive cells, suggesting that Fluoxetine can activate the neuronal differentiation. In addition, Fluoxetine has protective effects against the toxicity of amyloid beta peptides.Next, we investigated the role of fluoxetine in fetal neural stem cell transplantation in Alzheimer's disease model mouse, Tg2576 which is designed to overexpress Swedish type of APP (sweAPP) mutated at K670N, M671L. This model demonstrates the deposition of the amyloid plaque, leading to neuronal cell death and finally memory deficit. We transplanted fetal neural stem cells into 12-month-old Tg2576 and focused their effects on pathological and behavioral deficits in early developmental stage of disease. Pathologically, injected stem cells decrease the number of deposited amyloid plaques. Transplanted Tg2576 mice also showed significant improvement in cognition compared with age-matched sham control Tg2576 mice. It was interesting that transplanted Tg2576 of FNSC treated with Fluoxetine showed less memory deficit than Tg2576 of FNSC without Fluoxetine.Taken together, this study strongly suggest that transplantation of FNSC may block the progress of AD pathology and memory loss in Tg2576 mice by inhibition of Aβ production and stimulation of Aβ clearance and Fluoxetine additionally improve the ability of learning and memory by increasing neuronal population.

M4-5 Cholinergic therapy for Schizophrenia and Alzheimer's disease: new approaches

○Dana Hilt
Envivo Pharmaceutical

Dana C Hilt, D. Bertrand, J, Prickaerts, and Gerhard Koenig Available symptomatic treatments provide some benefit for the cognitive deficits in Alzheimer patients. However, at the optimal doses used they may have significant systemic side effects. It is expected that most current disease modifying approaches will need additional augmentation by symptomatic treatments. The ligand-gated nicotinic α-7 ion channel is one candidate target based on its expression and role in synaptic modulation in neurotransmission. EVP-6124 is a potent selective partial alpha-7 nicotinic agonist. It has demonstrated procognitive effects in numerous preclinical animal models. In early human studies EVP-6124 demonstrated procognitive effects in both normal volunteers and Alzheimer's disease patients and had positive physiologic effects in patients with schizophrenia (normalization of abnormal evoked responses). These effects were observed at free drug plasma concentrations > one order of magnitude below the Ki for EVP-6124 at the receptor. In order to understand the potential mechanism of such effects a reductive model was employed: The effects of EVP-6124 on alpha-7 nicotinic channel activity expressed in oocytes in the presence and absence of ACh and AChEIs were studied. EVP-6124 significantly potentiates the response of α-7 receptors to the natural ligand Acetylcholine (ACh) at sub-nanomolar concentrations. These concentrations are in a range where the receptors do not desensitize in the presence of the drug nor are they directly stimulated by the drug. At these low concentrations, EVP-6124 sensitizes the α-7 receptor to ACh, suggesting a novel co-agonist mechanism of action. In combination studies, EVP-6124 and AChEIs showed synergy in rodent object recognition tests. Neither agent alone at very low doses had an effect on reversing the deficit, but the combination of the two agents together completely restored the cognitive deficit in these animals. The combination of EVP-6124 and AChEIs, such as Donepezil or Rivastigmine hold promise for improved pro-cognitive treatment over existing ACh inhibitor treatments because systemic exposures for both drugs can be kept below side effect-inducing levels in AD patients.

M4-6 Effects of cannabinoids on microglial and T cells: Role in an animal model of multiple sclerosis

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Cannabinoids have been shown to exert anti-inflammatory activities including in experimental models of inflammatory CNS degenerative diseases. The use of cannabinoids, which interact with the neural cannabinoid receptor CB1, is limited due to their psychotropic effects. Thus, cannabinoids which are deprived of psychoactivity, (e.g., cannabidiol - CBD), are currently being tested for reducing neuroinflammation and neurodegeneration. Using the BV-2 murine microglial cell line we found that CBD-treatment affected gene expression. The CBD gene expression profile showed changes associated with oxidative stress and glutathione depletion, involving the GCN2/eIF2 α /p8/ATF4/CHOP-TRIB3 pathway. Furthermore, CBD stimulated genes were shown to be controlled by nuclear factors involved in the regulation of stress response and inflammation, mainly via the (EpRE/ARE)-Nrf2/ATF4 system and the Nrf2/Hmox axis. Moreover, CBD was much more potent than the CB1/CB2 interacting 9-tetrahydrocannabinol (THC; the major psychotropic compound in marihuana), in inducing cellular stress response and anti-inflammatory activity (Juknat et al., Brit. J. Pharmacol 2011). At the next step, we studied the effects of CBD, on myelin oligodendrocyte glycoprotein (MOG)-induced experimental autoimmune encephalomyelitis (EAE), a mouse model of multiple sclerosis. We observed that CBD administration during disease onset reduced EAE clinical symptoms. This was accompanied by diminished axonal damage and inflammation as well as reduced T cell recruitment in the spinal cord of the diseased mice. CBD treatment also inhibited MOG-induced T cell proliferation *in vitro*. This later effect was not mediated via either the CB1 or the CB2 receptor and its target/receptor is not yet known (Kozela et al., Brit. J. Pharmacol 2011). In summary, the non-psychoactive cannabinoid CBD has anti-inflammatory effects and reduces the clinical symptoms of MOG immunized EAE mice.

M4-8 Neuromodulations mediated by dextromorphinans

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Kangwon National University

Dextromethorphan (DM; 3-methoxy-17-methylmorphinan) is a common ingredient in more than 125 cough and cold remedies. DM is a dextrorotatory optical isomer of levomethorphan, a typical morphine-like opioid that is the codeine analog of morphinan derivative levorphanol. In the past decade, investigators have documented that DM has an NMDA receptor antagonistic effect with neuroprotection. However, the DM dose for the neuroprotective effect is much higher than the cough suppressant dosage. Clinically, high doses of DM can produce psychotropic effects. That hampers the development of DM as a useful neuroprotective agent. We will discuss complex behavioural effects of DM, and then demonstrate neuroprotective effects of DM and DM analogs [i.e., dimemorfan (DF; 3-methyl-17-methylmorphinan) and 3-hydroxymorphinan (3-HM)] with improved safety profiles. We have demonstrated that DM prevents seizures, mortality and hippocampal cell loss in a dose-dependent manner. DM has been shown to attenuate epileptic seizure-induced increases in activator protein-1 (AP-1) DNA binding activity and C-Jun/Fos-related antigen (FRA) expression in the hippocampus, collectively suggesting that DM is an effective antagonist of KA and a potent protectant for convulsants. We also reported that the anticonvulsant effect of DF correlates with its σ -1 receptor-activated modulation of the AP-1 transcription factor. We also found that 3-HM provided neuroprotection in the MPTP model, in both *in vivo* and *in vitro* studies. *In vivo* studies showed that administration of 3-HM significantly reduced MPTP-induced loss of nigral DA neurons, which is similar to the effect exerted by DM. Compared to DM, the advantage of 3-HM is its neurotrophic effect, which may enhance the sprouting of DA terminal fibers in the striatum. Furthermore, the anti-inflammatory effect exerted by 3-HM resulting from the inhibition of microgliosis generated from the damaged DA neurons induced by MPTP/MPP^+. Additional neuroprotective effects and therapeutic potential of DM analogs for the treatment of neurodegenerative conditions, and their underlying mechanisms will be discussed [This study was supported by a grant (#2011K000271) from the Brain Research Center from 21st Century Frontier Research Program funded by the Ministry of Science and Technology, Republic of Korea].

M4-7 Inhibition of myostatin activity by antibodies as a therapeutic approach to Amyotrophic Lateral Sclerosis

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Amyotrophic lateral sclerosis (ALS) is an incurable and fatal neurodegenerative disease with very few treatment options. While many studies have focused on attempts to rescue motor neuron function and survival directly it is clear that non neuronal cells that are intimately in contact with neurons such as muscle cells are also potential targets of drug action. A human therapeutic drug that alters muscle growth and survival in ALS could have important benefits in patients as muscle atrophy is a hallmark of the disease and death usually occurs through weakness in respiratory muscles. Myostatin is a member of the TGF beta growth factor family and is uniquely expressed in skeletal muscle. Neutralization of myostatin activity by either genetic or pharmacological means leads to major increases in muscle mass and also muscle strength. We wished to determine whether neutralization of myostatin via a blocking monoclonal antibody approach (using antibody RK35) could alter disease outcome in the SOD1G93A model of ALS. We found major increases in muscle mass and strength in RK35 treated animals treated prior to disease onset and during early stage disease. RK35 treatment did not delay disease onset nor extend survival in the mouse model. We next tried combination studies of RK35 with the FDA approved neuroprotectant Riluzole in an attempt to protect both muscle and nerve. We showed a significant synergistic effect of both agents when given in combination. Statistically significant increases in functional and locomotor tests were present until late in the disease course. We believe that this combination therapy merits study in human ALS. In addition we are generating smaller, more potent single domain antibody reagents using the shark VNAR structure that should have increased activity and better penetration into muscle tissue.

M5-1 Molecular analysis of central feeding regulation by neuropeptide Y (NPY) neurons with NPY receptor siRNAs

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Hypothalamic neuropeptides play important roles in central feeding behavior. Among them, neuropeptide Y (NPY) has the strongest orexigenic action. It is synthesized in NPY-expressing neurons in the arcuate nucleus (ARC), which projects to other nuclei, mainly to the paraventricular nucleus (PVN). PVN, which possesses NPY Y1, Y2 and Y4, Y5 receptors, is considered a feeding center for central feeding behavior. The siRNA vectors, which lead to transcription of small RNA by U6RNA pol3 promoter to produce knockdown of the NPY and its receptor genes (Y1, Y2, Y4 and Y5), were stereotaxically injected into mouse ARC and PVN. Feeding behaviors were measured for 6 days after siRNA vector injection. NPY and its receptor mRNA levels were decreased by RT-PCR and in situ hybridization, and simultaneous decrease in their proteins was also detected in separate nuclei by immunohistochemistry. In the NPY system, decrease in NPY, Y1 and Y5 expressions in specialized nuclei diminished central feeding behavior, whereas decrease in Y2 or Y4 expression in both ARC or PVN did not affect feeding behavior. Thus, specialized change in expressions of NPY and its receptors (especially Y1 and Y5) are important for regulation of endogenous feeding behavior in central regulation.

M5-2 Retinovascular biology and pathophysiology

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Synaptic activity, memory formation and behavior are dependent upon the ability of the microvasculature to effectively deliver oxygen and nutrients to the neurons of the brain. At present, despite the vital role of the brain's circulatory system, much remains to be learned about its physiology and pathobiology. To better understand how local perfusion is regulated in the CNS, we have focused on the functional organization of the microvasculature of the retina, which is a well-studied and approachable part of the brain. In addition, the retinal microcirculation is of considerable interest due to its high vulnerability to diabetes, which is a leading cause of blindness.

Based on the premise that the transmembrane movement of ions plays a critical role in physiology and pathobiology of the microvasculature, the aim of our research is to elucidate the roles of ion channels in regulating retinal microvascular function and in mediating the response of the retinal microvasculature to diabetes. An experimental advantage of studying the retina is the ability to isolate vast retinal microvascular complexes from the normal and diabetic rodent. With this preparation, it is relatively straightforward to use the patch-clamp technique, calcium imaging and time-lapse photography to assay ionic currents, intracellular calcium levels and abluminal cell contractility in specific regions of the retinal microvasculature. Use of isolated microvascular complexes has also facilitated the testing of novel mechanistic hypotheses concerning why retinal capillaries are particularly vulnerable to pathophysiological conditions such as diabetes.

Our experiments revealed that endogenous polyamines play a key role in regulating the function of a variety of microvascular ion channels. We found that these polyamine-dependent effects are particularly potent in the capillary network and account for why most of the K_{ATP} current instigated by vasoactive signals is generated in the capillaries. Of potential pathophysiological significance, we also discovered that endogenous polyamines account, in large part, for the high vulnerability of retinal capillaries to oxidative stress and hypoxia, which are well known features of the diabetic retina.

We conclude that specialized physiological adaptations of the capillaries render this portion of the retinal microvasculature particularly vulnerable to pathological conditions such as diabetes.

M5-3 Histamine H1 receptor functions in CNS and peripheral tissues

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Histamine H1 receptor (H1R) mediates type-1 allergy in peripheral tissues and histaminergic transmission in CNS. Cell bodies of histaminergic neurons are located in tuberomammillary nucleus (TMN), and divided into five sub-groups, E1, E2, E3, E4 and E5. Sub-group specific functions remains to be elucidated. Exclusive c-Fos expression was observed in rat caudal arcuate nucleus (cARC) by food deprivation under scheduled feeding. This function was suggested to be mediated by H1R in cARC, and by E3 sub-group histaminergic neurons in TMN. Up-regulation of H1R was found by H1R stimulation, and mediated by PKC-delta-MEK-ERK-PARP-1 signaling and H1R gene expression. AP-1, Ets-1 and Ku70/Ku86 regulated the H1R promoter activity. Activation of H1R gene expression was observed in allergic model rats and human allergic disease. Co-relation between symptom and H1R mRNA level suggested that H1R gene is an allergic disease sensitive gene. Kujin, an anti-allergic natural medicine, showed improvement of both symptom and activation of H1R gene expression in allergic model rats. An active substance suppressing H1R gene expression was identified to be maackiain. Maakiain suppressed histamine-induced PKC-delta phosphorylation. It is suggested that maackiain is a therapeutic seed for allergy, and that PKC-delta is a drug target for allergy.

O1-1 Enzymes involved in pro-BDNF processing may be involved in antidepressive effects of electroconvulsive seizure in the rat hippocampus

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Electroconvulsive therapy is the most effective treatment for antidepressant-resistant depression, although the underlying mechanisms remain to be fully elucidated. It was previously shown that electroconvulsive seizure (ECS) increased mRNA levels of brain-derived neurotrophic factor (BDNF) in the rat hippocampus (Nibuya, Morinobu, Duman, 1995 J. Neuroscience). Although BDNF is known to be produced as a precursor protein (pro-BDNF) that is posttranslationally processed to mature BDNF (mBDNF) having an antidepressive effect, it remains unknown which form of BDNF is increased upon ECS. In this study, we found that single ECS increased the levels of not only pro-BDNF but also those of PC1 and t-PA, those are enzymes involved in intra- and extracellular pro-BDNF processing respectively. It was suggested that both pro-BDNF and t-PA were rapidly transported to synaptic terminals following single ECS. In rats receiving 10-day repeated ECS, pro-BDNF levels increased with a corresponding up-regulation in mBDNF levels. Interestingly, t-PA levels increased following repeated ECS as well, while PC1 did not, suggesting the dominant role of t-PA during repeated ECS. Given the negative impact of pro-BDNF on neurons, our results suggest that efficient pro-BDNF processing as well as strong induction of BDNF expression are necessary for antidepressive effects of ECS. Finally, we would like to compare these effects of ECS with those of the tricyclic antidepressant imipramine.

O1-2 Deletion of neuropeptide Y gene weakens stress resistance and shortens lifespan in calorie-restricted mice

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The effect of calorie restriction (CR) may be induced during the process of neuroendocrine adaptation to long-term reduction of dietary energy intake. Neuropepetide Y (NPY) neurons in the hypothalamic arcuate nuclei are involved in the neuroendocrine adaptation including suppression of growth and reproductive functions and activation of stress response. We investigated the role for NPY in the effect of CR. Wild type (WT) and NPY-KO mice were fed ad libitum (AL) or 30 % CR diets from 12 weeks of age. Acute stress response to oxidative stress was enhanced in the WT-CR mice as compared to the WT-AL mice; the response was diminished in the KO-CR mice. The lifespan was significantly extended in the WT-CR mice, whereas the effect was abrogated in the KO-CR mice. However, the CR-specific expression of hypothalamic neuropeptide genes was also observed in the KO-CR mice, suggesting redundancy of neuroendocrine adaptation to CR without NPY. The present results suggest importance of NPY, but not neuroendocrine adaptation at the hypothalamic level, in the effect of CR.

O1-3 Structural basis for the different stability of Cdk5-p35 and Cdk5-p39

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Cyclin-dependent kinase 5 (Cdk5) is a multifunctional protein kinase in nervous system. Cdk5 is activated by association with a neuron-specific activator, p35 or p39. p35 and p39 share 57% amino acid identity. In particular, p35 and p39 display 72% homology in the Cdk5 binding domain called globular domain (GD) in the C-terminal region. In previous study, we reported that Cdk5-p39 is a labile complex dissociating in the presence of non-ionic detergent in contrast to Cdk5-p35, which was activated, indicating that p39 has a lower binding affinity for Cdk5 than p35. Here we investigated the molecular basis of the difference. The properties of p35 and p39 were also retained in p35GD and p39GD. At first, we focused on the difference of hydrophobicity of GD. The hydrophobicities of p39GD and p35GD are different in their C-terminal region, however the exchange of amino acids related to the hydrophobicity did not change their different stabilities to detergent. Next, the 3D structure of Cdk5-p39GD complex was predicted from the crystal structure of Cdk5-p35GD. The predicted structure revealed that the decreased number of hydrogen bonds between Cdk5 and p39GD, compared to Cdk5-p35GD. The amino acids involved in hydrogen bonds to Cdk5 are different between p35GD and p39GD. Asp259, Asn266 and Ser270 of p35GD form three hydrogen bonds to His71, Lys56 and Glu57 of Cdk5, respectively. In contrast, Gln259 and Gln266 of p39GD form two hydrogen bonds to His71 and Lys56 of Cdk5, respectively. We exchanged amino acids participating in hydrogen bonds between p35GD and p39GD, and examined the effect on the stability and kinase activity of Cdk5 complexes. While their single or double mutant did not change the Cdk5 binding and activation properties, the triple mutant of p35GD did not bind to and activate Cdk5. The effect of the triple mutation was also observed in p35. In contrast, when p39GD or p39 is mutated at three amino acids corresponding to those of p35GD described above, its complex with Cdk5 was stabilized. These results indicate that the difference in the stability between Cdk5-p35 and Cdk5-p39 is caused, at least a part, by a number of hydrogen bonds in the complexes.

O1-4 1-Deoxy-nor-sominone (Denosomin) improves hindlimb dysfunction in spinal cord injury and promotes neurite outgrowth through astroglia-mediated signalling

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Background and purpose: Functional recovery after spinal cord injury (SCI) is difficult owing to the environment in injured scar being detrimental for the regeneration of axons. Since we previously obtained a novel compound, 1-deoxy-nor-sominone (Denosomin), which promotes neurite extension *in vitro*, we administered it to SCI mice to elucidate its *in vivo* activities and underlying mechanism on neuronal regeneration in injured spinal cord. Experimental approach: SCI was induced by contusion in male mice. Denosomin was administered orally for 14 days. During this period, scores for Basso Mouse Scale (BMS) and Body Support Scale (BSS) were obtained. After behavioural evaluation, axons and astrocytes were observed immunohistochemically. Primary cultured cortical or spinal cord cells and isolated astrocytes were treated with Denosomin to evaluate neurite outgrowth, synaptogenesis, and cell proliferation immunocytochemically. Key results: In the *in vivo* experiment, hindlimb dysfunction of SCI mice was recovered by Denosomin. In addition, axonal regeneration and astroglial infiltration were increased in injured scar by Denosomin. In the *in vitro* experiment, Denosomin treatment enhanced neurite outgrowth and synaptic density and increased astroglial proliferation. Neurite outgrowth in spinal cord neurons was also enhanced by co-culture with Denosomin-pretreated astrocytes or Denosomin-pretreated astroglial conditioned medium. Conclusions and implications: Denosomin improves hindlimb function, and increases axonal regrowth and astrogliosis in injured spinal cord. *In vitro* data shows that Denosomin induces beneficial effects of astrocytes on axonal growth. This is the first finding that suggests that drug-mediated astroglial regulation may enhance axonal regeneration in injured scar.

O1-5 Changes in emotional behaviors and the action of brain-derived neurotrophic factor in the prefrontal cortex after exposure to chronic restraint stress

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Stress and the resulting increase in glucocorticoid levels have been implicated in the pathophysiology of depressive disorders. In this study, we investigated the effects of chronic restraint stress (CRS: 6 hours x 28 days) on emotional behaviors in rats and on the possible changes in glucocorticoid receptor (GR) expression in the prefrontal cortex (PFC). Brain-derived neurotrophic factor (BDNF)-dependent neural function was also analyzed. We noted significant reductions in body weight and food intake from one week after the onset of CRS, while water intake remained unchanged. After the four week CRS, we conducted open-field, elevated plus-maze (EPT) and forced swim tests (FST); wherein we observed a decrease in the number of entries into open arms during the EPT (anxiety-like behavior) and increased immobility during the FST (depression-like behavior). The PFC was removed after CRS and used for western blot analysis, in which GR expression was reduced by stress exposure. The levels of BDNF and its receptors remained the same as control which was subjected to handling for 5 min. While basal glutamate concentrations measured by high performance liquid chromaography were not influenced, BDNF-induced glutamate release was attenuated in acute slices of the PFC of CRS rats. These results suggest that reduced GR expression and altered BDNF function may be involved in chronic stress-induced anxiety- and depression-like behaviors.

O1-6 Sequence and distribution decision of D-beta-amino isobutyric acid(D-BAIB): pyruvate aminotransaminase(AT) in the pig brain

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Introduction: Kakimoto et al. reported that BAIB is final product of thymine, excreted in urine is almost D type. D-BAIB:pyr AT is distributed kidney and liver abundantly. D-BAIB expressed in the brain, but the role is still unknown. We decided a cDNA sequence of pig to examine the role of this enzyme and examined distribution with the pig brain tissue.Methods: We got eight brains of pig from a farm co-op. Each brain tissue underwent RNA extraction. Each total RNA was reverse transcribed with random hexamer. With 5'- and 3' - race method, I decide a pig D-BAIB:pyr AT gene cDNA sequence. I made Taqman probe in reference to the sequence and measured quantity of D-BAIB expression with each brain tissue by quantitative RT-PCR method.Results: The D-BAIB:pyr AT gene had high homogeny of the other kind, and it was a stored gene. In comparison with kidney and liver, there is little quantity of the expression in the brain when I examine quantity of gene expression. It was confirmed that it developed ubiquitous in cerebral cortex, cerebrum white matter, basal ganglia, mid brain, cerebellum, brain stem. We examine mRNA expression in the brain with a different kind.

O2-1 Endothelin stimulates VEGF-A production and activates VEGF receptors in the rat cerebrum

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Vascular endothelial growth factors (VEGFs), a family of angiogenic factors, are up-regulated by nerve injuries. To clarify the extracellular signals involved in VEGF production in the brain, the effects of endothelins (ETs), a family of vasoconstricting peptides, were examined. Intracerebroventricular administration of 500 pmol/day $Ala^{1,3,11,15}$-ET-1, an ET_B receptor agonist, increased the level of VEGF-A mRNA in the rat cerebrum, while those of VEGF-B, placental growth factor (PLGF), angiopoietin (ANG)-1 and ANG-2 mRNAs were not largely affected by $Ala^{1,3,11,15}$-ET-1. The ET-induced increases in cerebrum VEGF-A mRNA were reduced by co-administration of 1 nmol/day BQ788, an ET_B antagonist. $Ala^{1,3,11,15}$-ET-1 also stimulated the production of VEGF-A proteins in the cerebrum. Immunohistochemical observations in the cerebrum of $Ala^{1,3,11,15}$-ET-1-infused rats showed that GFAP-positive astrocytes had VEGF-A immunoreactivity. Neurons, microglia and brain capillary endothelial cells in the $Ala^{1,3,11,15}$-ET-1-infused rats did not show VEGF-A reactivity. The intracerebroventricular administration of $Ala^{1,3,11,15}$-ET-1 stimulated tyrosine phosphorylations of VEGF-R1 and R2 receptors in the rat cerebrum, while expression levels of total VEGF-R1 and R2 proteins were not largely changed. Immunoreactivity of tyrosine-phosphorylated VEGF-R1 was selectively shown in GFAP-positive astrocytes in the cerebrum of $Ala^{1,3,11,15}$-ET-1-infused rats. Tyrosine-phosphorylated VEGF-R2 proteins were present in astrocytes and brain capillary endothelial cells. These findings indicate that activation of brain ET_B receptors increases production of VEGF-A and stimulates VEGF receptor signaling in the brain.

O2-2 Loss of glial fibrillary acidic protein marginally accelerates disease progression in a $SOD1^{H46R}$ transgenic mouse model of ALS

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Glial fibrillary acidic protein (GFAP) is an intermediate filament protein that is highly expressed in reactive astrocytes. Increased production of GFAP is a hallmark of astrogliosis in neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS). However, the physiological and pathological roles of GFAP, particularly in chronic neurodegenerative conditions, remain unclear. To address this issue, we here investigate whether absence of GFAP affects the phenotypic expression of motor neuron disease (MND) using an H46R mutant Cu/Zn superoxide dismutase-expressing mouse model of ALS ($SOD1^{H46R}$). GFAP deficient $SOD1^{H46R}$ mice showed a significant shorter lifespan than $SOD1^{H46R}$ littermates. Further, at the end stage of disease, loss of GFAP resulted in increased levels of *Vim* and *Aif1* mRNAs, encoding vimentin and allograft inflammatory factor 1 (AIF1) respectively, in the spinal cord, although no discernible differences in the levels and distribution of these proteins between $SOD1^{H46R}$ and GFAP-deficient $SOD1^{H46R}$ mice were observed. These results suggest that loss of GFAP in $SOD1^{H46R}$ mice marginally accelerates the disease progression by moderately enhancing glial cell activation. Our findings in a mouse model of ALS may have implication that GFAP is not necessary for the initiation of disease, but it rather plays some modulatory roles in the progression of ALS/MND.

O2-3 FLRT2 and FLRT3 act as repulsive guidance cues for Unc5-positive neurons

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Netrin-1 induces repulsive axon guidance by binding to the mammalian Unc5 receptor family (Unc5A-Unc5D). Mouse genetic analysis of selected members of the Unc5 family, however, revealed essential functions independent of Netrin-1, suggesting the presence of other ligands. Unc5B was recently shown to bind Fibronectin and leucine-rich transmembrane protein-3 (FLRT3), although the relevance of this interaction for nervous system development remained unclear. Here, we show that the related Unc5D receptor binds specifically to another FLRT protein, FLRT2. During development, FLRT2 and FLRT3 extra cellular domains (ECD) are shed from neurons and act as repulsive guidance molecules for axons and somata of Unc5B and Unc5D positive neurons. In the developing mammalian neocortex, Unc5D is expressed by subpopulation of neurons (UL2 cells) in the subventricular zone (SVZ), which display delayed migration to the FLRT2-expressing cortical plate (CP; future layer V/VI). When UL2 cells migrate to CP, Unc5D is downregulated to traverse FLRT2-positive layers. After reaching to layer IV, Unc5D is re-expressed. Deletion of either FLRT2 or Unc5D causes a subset of SVZ derived neurons to prematurely migrate towards the CP, whereas overexpression of Unc5D has opposite effects. Hence, the shed FLRT2 and FLRT3 ectodomains represent a novel family of chemorepellents for Unc5-positive neurons and FLRT2/Unc5D signaling modulates cortical neuron migration.

O2-4 Mice lacking in an enzyme involved in chondroitin sulfate synthesis shows better recovery from spinal cord injury

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Proteoglycans (PG) consist of a core protein with one or more attached glycosaminoglycan (GAGs) chains, formed by repeating disaccharide units. Among them, chondroitin sulfate (CS), are composed of the repeated N-acetylgalactosamine (GalNAc) and glucuronic acid. CS is known to be the most abundant inhibitory molecules to axon regrowth. To clarify the role of CS more in detail, we produced the mice lacking in the enzymes CS GalNAc transferase-1 (CSGALNACT1), which is believed to be involved in the initiation and the elongation process of the CS disaccharide chains. In the CSGALNACT1-null mice (ref. 1), we examined the recovery from spinal cord injury (SCI). The null mice showed much better and rapid recovery than the wild type from BMS scores, the footfalls scores and the motor-evoked potential. In addition, these phenotypes of the recovery from SCI in the null mice showed better and more rapid than in the chondroitinase-treated group. The mice had more 5-HT-positive axon fibers in number at the caudal side of the injury than the wild type, indicating that the rapid recovery of the null mice is due to the increased regenerating axons. Immunohistochemical approaches revealed that CS expression was reduced in the injury site, however, CS was still present. Our results show that reduction of CS synthesis provides better recovery from SCI even than the chondroitinase treatment, suggesting that controlling CS synthesis is a new strategy target for SCI treatment. Ref. 1) Biochem. J. 427, 47-55 (2010).

O2-5 The analyses of Reelin-induced neuronal aggregation in the developing neocortex

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During neocortical development in mammals, neurons are born mainly in the ventricular zone along the ventricle and migrate radially towards the pial surface to be aligned in defined patterns in the cortical plate. These precise patterns of neuronal alignment are regulated by an extracellular matrix protein, Reelin, which is secreted from Cajal-Retzius neurons in the marginal zone of the neocortex. When Reelin binds to its receptors, tyrosine phosphorylation of the intracellular adaptor protein Disabled 1 (Dab1) is induced. Although the molecular cascade of Reelin signaling is being uncovered, the biological response of cortical neurons to the Reelin signal remains uncertain. To elucidate the biological role of Reelin molecule in the developing neocortex, we used the *in utero* electroporation system. Reelin was expressed ectopically in the developing neocortex and the effect on migrating neurons was analyzed. Reelin caused the leading processes of migrating neurons to assemble in the Reelin-rich region, which in turn induced their cell bodies to form cellular aggregates around Reelin. Interestingly, the ectopic Reelin-rich region became cell-body-sparse and dendrite-rich, resembling the MZ, and the late-born neurons migrated past their predecessors toward the central Reelin-rich region within the aggregates, resulting in a birthdate-dependent "inside-out" alignment even ectopically. Reelin receptors and intracellular adaptor protein Dab1 were found to be necessary for formation of the aggregates. These findings indicate that Reelin signaling is capable of inducing the formation of a birthdate-dependent "inside-out" alignment of neurons independently of other factors/structures near the MZ.

O2-6 Protective effect of indomethacin against neuronal degeneration induced by trimethyltin in mice

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Non-steroidal anti-inflammatory drugs (NSAIDs) are drugs with analgesic and antipyretic (fever-reducing) and anti-inflammatory effects. Our previous study showed that trimethyltin chloride (TMT) causes neuronal loss in the hippocampal dentate gyrus. In this study, we investigated the protective effect of indomethacin, a common NSAID on TMT-induced neurodegeneration in dentate gyrus. TMT (2.8 mg/kg, i.p.) injected into ddY male mice and treated indomethacin (5.0 mg/kg, s.c.) at several time points after TMT injection. When TMT-treated mice were treated with indomethacin simultaneously, 2 or 4 h after TMT treatment, the mice had unalterable expression of active caspase-3 in the dentate gyrus. However, treatment with indomethacin at 12 h after TMT treatment markedly decreased the number of active caspase-3 positive cells of the dentate gyrus. Protein levels of alpha-fodrin fragments cleaved by caspases and calpain markedly induced on day 2 after TMT treatment. Expectedly, indomethacin treatment at 12 h post TMT injection decreased all products cleaved by caspases and calpain. Iba1 immunostaining revealed that Iba1-positive macrophage-like round cells were dramatically increased in the dentate granule cell layer on days 1 and 2 after TMT treatment. Indomethacin obviously decreased activated microglial cells on day 2 post-TMT treatment. Likewise, TMT-induced elevation of Iba1 level was also significantly abolished by indomethacin in the dentate gyrus. TMT neurotoxicity results from intense oxidative stress, which produces 4-hydroxynonenal (4-HNE)-adducted proteins as products of lipid peroxidation. In TMT-treated animals, a marked increase in 4-HNE-positve cells was seen predominantly in the granule cell layer on day 1 after TMT treatment. Indomethacin significantly decreased TMT-induced expression of 4-HNE-positive cells. These results suggest that indomethacin could protect neurons from TMT through blockage of activation in microglial cells as well as formation of 4-HNE.

O3-1 Coordinately gene expression changes of actin dynamics regulator 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 microM, 3min, 3 times at 24h intervals) induced a long-lasting synaptic enhancement accompanied by synaptogenesis in rat hippocampal slice cultures, a phenomenon termed RISE (for repetitive LTP-induced synaptic enhancement). To investigate the molecular mechanisms underlying this phenomenon, we performed the comprehensive screening after the 3rd stimulation using commercially available high-density microarrays and identified ywhaz/14-3-3zeta as a candidate gene which shown a large and progressive up-regulation by repetitive stimulation. Because ywhaz is known as a regulator of sshl1 (slingshot homolog 1) phosphatase that activates the actin depolymerizing factor cofilin, we investigated the effect of repetitive stimulation on the expression of ywhaz and related four genes (sshl1, pak4, limk1, and cfl1) by real-time quantitative PCR. These five genes were coordinately up-regulated by the second stimulation, resulting in a decrease in cofilin phosphorylation and an enhancement of actin filament dynamics. In contrast, after the third stimulation, they were differentially regulated to increase cofilin phosphorylation and enhance actin polymerization, which may be a key step leading to the establishment of RISE.

O3-2 Anticancer agent 6-MITC derived from wasabi control seizures in epileptic mutant EL mice at extremely low dosage

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Recently, attention has focused on the anticancer properties of an aromatic component 6-(methylsulfinyl)hexyl isothiocyanate (6-MITC) in a typical Japanese spice, wasabi. 6-MITC shows selective sensitivity to human breast cancer and melanoma in 39 human cancer cell lines. And further it works against pulmonary metastasis of mouse melanoma cells. In the field of central nervous system (CNS), it is shown that antiepileptic mechanisms are related to abnormal plasticity supported by the cell cycle reentry (CCR) activation and that endogenous cytokine acts as the powerful antiepileptics. In the present study, we investigated mechanisms of antiepileptic effects of 6-MITC by analyzing the CCR, cytokine systems and $GABA_A$ receptor subunits during epileptogenesis of EL mice. EL mice show secondary generalized seizures, which initiate primarily at parietal cortex and generalize through hippocampus. ED_{50} was determined by *po* administration from 70mg/kg to 0.001mg/kg. CCR was determined by analyzing cyclin and cyclin dependent kinase (CDK) which are essential from G_0 to G_1 phase. Cytokine systems were assayed by interleukin 1 α, 1 β, interleukin receptor and receptor antagonist. And further GABAergic system were assayed by $GABA_A$ receptor subunits, α 1, 2, β 2, 3, γ 2 and δ. All protein markers were semi-quantified determined by western blotting and NIH image with macros. The ED_{50} for antiepileptic seizures was 0.001mg/kg *po*, 10^{-5} lower dose compared with ordinary antiepileptic drugs and anticancer agents. Toxicity and side effects were not found. In the hippocamous, cyclin D, essential for the CCR was down regulated. And powerful endogenous antiepileptic interleukin receptor antagonist was remarkably induced. And further inhibitory GABAergic synaptic subunits α 1, 2, β 2, 3 and γ 2 were upregulated. 6-MITC, a soluble low molecule (205D) substance inhibits not only human tumor cell growth but also tumor metastasis. And further in CNS, it was suggested that 6-MITC plays a role as an antiepileptcs through the excitatory membrane stabilizer by inhibiting abnormal CCR and activation of inhibitory signal transductions.

O3-3 Mesenchymal stem cells transmigrate across brain microvascular endothelial cell monolayers through transiently formed interendothelial gaps

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Mesenchymal stem cells (MSCs) hold much promise for cell therapy for neurological diseases such as cerebral ischemia and Parkinson's disease. Intravenously administered MSCs accumulate in lesions within the brain parenchyma, but little is known of the details of MSC transmigration across the blood-brain barrier (BBB). To study MSC transmigration across the BBB, we developed an *in vitro* culture system consisting of rat brain microvascular endothelial cells (BMECs) and MSCs. BMECs were prepared from SD-Tg(CAG-EGFP) rats, which express EGFP gene under the control of the cytomegalovirus enhancer and the chicken β-actin promoter, and seeded on Transwell or Millicell culture inserts (pore size of 8.0 μm). MSCs were isolated from rat bone marrow cells, fluorescently labeled with PKH-26, and added to the upper chamber of the culture inserts. Using this *in vitro* culture system, we first investigated the influence of the different numbers of MSCs on BMEC barrier integrity. The addition of MSCs at a density of 1.5×10^5 cells/cm^2 led to the disruption of the BMEC monolayer structure and decreased barrier function as measured by transendothelial electrical resistance (TEER). When applied at a density of 1.5×10^4 cells/cm^2, neither remarkable disruption of the BMEC monolayers nor a significant decrease in TEER was observed until at least 12 h. After the cultivation for 24 h under this condition, MSCs were found in the subendothelial space or beneath the insert membrane, suggesting that MSCs transmigrate across the BMEC monolayers. Time-lapse imaging revealed that MSCs transmigrated across the BMEC monolayers through transiently formed intercellular gaps between the BMECs. The *in vitro* culture system consisting of BMECs and MSCs is useful to investigate the molecular and cellular mechanisms underlying MSC transmigration across the BBB.

O3-4 Two different ways of vesicle transport are mediated by actin cytoskeleton and microtubules in the growth cone

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The growth cone plays important roles in neural wiring, synapse formation, and axonal regeneration. Continuous rearrangement of cytoskeletons and targeting of transported vesicles to the plasma membrane are essential to growth cone motility, but the relationship between cytoskeletons and transported vesicles is still unknown. To understand regulating machinery of vesicle traffic in the growth cone, we analyzed dynamics of vesicular trafficking in the growth cone using GFP-tagged SCAMP1 and synaptophysin expressed in NG108 cells. We found that there were two different types of vesicle movements in its peripheral region. First type of vesicles showed slowly retrograde movement. Their average speed was similar to that of actin retrograde flow. Dual color imaging of GFP-synaptophysin and mCherry-Actin showed that such vesicles transported on the F-actin bundles. Immunostaining data indicated that a part of vesicles were localized on the filopodia. In contrast, we found the second type of vesicles, namely, they moved both anterogradely and retrogradely in alternative ways, and the movements appeared on microtubules invading the peripheral region. The anterograde speed was corresponding to that of the GFP-EB3/GFP-dynactin. These data indicated that the retrograde trafficking of vesicles is caused by the result of actin retrograde flow in the peripheral region. These vesicles may be associated with F-actin bundle. Discontinuous fast anterograde movements might be associated with the dynein motor on the growing microtubule. These two different types of vesicle transport may be important to control of neuronal growth.

O3-5 Nicotine induces dendritic spine remodeling in cultured hippocampal neurons

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Cholinergic system in the central nervous system plays significant roles in cognition, plasticity, and addiction. The nicotinic acetylcholine receptors (nAChR) are involved in them, but the underlying cellular mechanism has remained elusive. In this study, we analyzed the morphological consequences of dendritic spines upon the activation of nicotinic acetylcholine receptors in cultured hippocampal neurons. Exposure of neurons to nicotine resulted in the expansion of the width of spine head. This spine remodeling was abolished by dihydro- β -erythroidine, an antagonist of α 4 β 2* nAChR, but not by α -bungarotoxin, an antagonist of α 7 nAChR. The expansion of dendritic spine head is likely to represent a sign of enhanced synaptic efficacy in a certain neural circuit that is responsible for addiction and cognitive function.

O3-6 Diversity of Neuropsin-dependent Synaptic Associativity in the Hippocampal Pyramidal Neuron

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Activity-dependent synaptic plasticity is widely accepted to provide a cellular basis for learning and memory. Synaptic tagging and capture could be involved in activity-dependent synaptic plasticity, because it distinguishes between local mechanisms of synaptic tags and cell-wide mechanisms that are responsible for the synthesis of plasticity-related proteins. We report that a plasticity related serine protease, neuropsin, is involved in the tag-setting process during LTP at basal and apical dendritic inputs. Neuropsin is involved in synaptic tagging and cross-tagging during LTP at apical dendritic inputs via integrin beta-1 and CaMKII signaling. Thus, neuropsin is a candidate molecule for LTP-specific tag-setting and could regulate the transformation of E- to L-LTP during both synaptic tagging and cross-tagging.

O4-1 Growth hormone-related molecular system that regulates both epilepsy progression and emotional symptoms

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About one-half of patients with refractory epilepsy are characterized as having mesial temporal lobe epilepsy with foci in the amygdaloid complex, hippocampus, and surrounding cortex. To screen candidate molecules that be involved in refractory epilepsy, we used amygdala-kindled mice, a model of temporal lobe epilepsy, in which unrestrained conscious mice received a biphasic square wave pulse [480 micro-A; 60 Hz, 200 micro-sec duration, for 2 sec] once a day. In this model, kindling stimulation with electrodes driven into different regions provides the stepwise neurobiological and molecular alterations along neural connections during the epileptogenic process. We demonstrated that the expression of growth hormone (GH) was up-regulated tremendously along neural circuits during and following development of epilepsy, and administrations of exogenous GH and the receptor antagonist into the hippocampus enhanced the progression of kindling and elicited a delay in the progression, respectively. Furthermore, administrations of GH and antagonist into the hippocampus without kindling-stimulation induced differential expressions of several seizure-responsive genes, and these dose-dependent expressions were related with differential emotional behaviors. Thus, the present study indicated that a GH-dependent molecular system including seizure-responsive genes regulates both epilepsy and emotional behavior in the mouse brain.

O4-2 Sigma-1 receptor stimulation with dehydroepiandrosterone ameliorates cognitive deficits in olfactory bulbectomized mice

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Dehydroepiandrosterone (DHEA) is the most abundant neurosteroid synthesized de novo in the central nervous system. We here demonstrated that sigma-1 receptor stimulation by DHEA improves cognitive function through activation of synaptic plasticity-related protein kinases in olfactory bulbectomized (OBX) mice. Repeat treatments with DHEA at 30 or 60 mg/kg p.o. for 7 days significantly improved spatial reference and fear-conditioned memory behaviors as assessed by Y-maze, novel object recognition and passive avoidance task in OBX mice. DHEA restored hippocampal LTP impaired in OBX mice. DHEA treatment restored PKC α (Ser-657) and NR1 (Ser-896) phosphorylation in OBX mice to the control levels in the hippocampal CA1 region. Likewise, DHEA treatment improved CaMKII α (Thr-286) autophosphorylation and GluR1 (Ser-831) phosphorylation as comparable to that in sham mice. Furthermore, DHEA treatment stimulated and restored ERK and CREB (Ser-133) phosphorylation to the sham levels. Finally, pretreatment with NE-100, sigma-1 receptor antagonist, significantly inhibited DHEA-improved memory-related behaviors and CaMKII, PKC and ERK activities in CA1. Taken together, sigma-1 receptor stimulation by DHEA ameliorates OBX-induced deficits in memory-related behaviors and impaired LTP through activation of CaMKII, PKC and ERK in the hippocampal CA1 region.

O4-3 Signaling pathway of SUN13837, a novel compound mimicking the pharmacological actions of bFGF

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Basic fibroblast growth factor (bFGF) is a multifunctional secretory protein that acts on various cells. bFGF has potent neurotrophic effects and has been found to improve the survival of injured neurons *in vitro* and *in vivo*. Recent studies show bFGF expression levels alter in various diseases including spinal cord injury, stroke and Alzheimer's disease.
We have been developing SUN13837, a novel small molecular compound, which mimics beneficial effects of bFGF for the treatment of neurodegenerative and traumatic diseases. It is, in particular, worth noting that SUN13837 did not promote cell proliferation but showed similar phenomena to the neuroprotection induced by bFGF.
In primary neurons, 24h-pretreatment of SUN13837 and bFGF prevented neuronal death induced by glutamate. These neuroprotective effects were antagonized by pretreatment with PD166866 (a specific inhibitor of FGF receptor-1 (FGFR1) tyrosine kinase) and U0126 (an inhibitor of MEK) but not by PLC γ and P38 MAPK inhibitors.
SUN13837 and bFGF enhanced FGFR1 Tyr phosphorylation (pY653/654) in the neuron. Unlike bFGF, SUN13837 did not phosphorylated Y766, which is an essential residue of cell proliferation. While bFGF increased the BrdU-uptake, but SUN13837 showed no increment by BrdU-uptake assay in SKN, SW1353 and NHDF cells. Basic FGF promoted the cyclin D1 expression and decreased the p27/kip1 expression, however SUN13837 did not affect their expression in 3T3 cell.
A 2D-PAGE global phosphorylation analysis showed SUN13837 phosphorylated calcineurin B, 14-3-3 zeta, creatin kinase B, TCP-1, vimentin, actin and tubulin. Ingenuity Pathway Analysis revealed that SUN13837 modulate several signaling pathways including FGF, CREB, PI3K, MAPK, mTOR and 14-3-3 signalings. Taken together, these results indicate that SUN13837 preferentially activates the intracellular signaling pathways necessary for the neuroprotective activity among the signaling cascades can be activated by bFGF.
SUN13837 might be a more advantageous agent than bFGF for the treatment of neurodegenerative and traumatic diseases.

O4-4 γ-Tubulins are decreased in the MSA patient brains and γ-tubulin 2-deficient mouse displays MSA-like neurodegeneration and ataxia

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Alteration of microtubules is associated with a variety of diseases, however its mechanism is not well understood. A member of tubulin superfamily GTPase, γ-tubulin 2 (TUBG2), is preferentially expressed in neurons. Here we found that TUBG2 is severely decreased in the striatum of patients with multiple system atrophy (MSA-P). TUBG2 KO mice exhibited L-DOPA-unresponsive MSA-P-like rigidity and propulsion, followed by degeneration of GABAergic striatal medium spiny neurons. Electrophysiological studies of TUBG2 KO mice revealed defects in striatonigral GABAergic transmission caused by decreased cellular ATP levels. Mitochondrial membrane potential of TUBG2-deficient neurons was significantly depolarized when compared with that of wild type. Mitochondrial calcium ion was reduced due to the less association between mitochondria and endoplasmic reticulum in TUBG2-deficient neurons. Importantly the numbers of microtubules and endoplasmic reticulum were decreased in dendrite of TUBG2-deficient neurons, indicating that TUBG2 functions through the controlling the molecular nature of microtubules. We showed TUBG2 has a microtubule nucleation activity like TUBG1, a conventional γ-tubulin. These findings demonstrate that TUBG2 modulates mitochondrial function via regulation of the microtubule number in striatonigral GABAergic transmission and MSA-P pathogenesis.

O4-5 Matrix metalloproteinase-9 contributes to kindled seizure development in pentylenetetrazole-treated mice by converting pro-BDNF to mature BDNF in the hippocampus

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Matrix metalloproteinases (MMPs) function to remodel the pericellular environment and promote neuronal plasticity, primarily through cleavage of extracellular matrix proteins. Here, we investigated the role of MMP-9 in the development of pentylenetetrazole (PTZ)-induced kindled seizure in mice. Repeated treatment with PTZ (40 mg/kg) produced kindled seizure, which was accompanied by enhanced MMP-9 activity and expression in the hippocampus. No change in MMP-9 activity was observed in the hippocampi of mice with generalized tonic seizure following single administration of PTZ (60 mg/kg). Coadministration of diazepam or MK-801 with PTZ inhibited the development of kindling and the increased MMP-9 levels in the hippocampus. Marked suppression of kindled seizure progression in response to repeated PTZ treatment was observed in MMP-9 homozygous knockout (MMP-9-KO) mice compared with wild-type mice, an observation that was accompanied by decreased hippocampal levels of mature brain-derived neurotrophic factor (BDNF) despite similar BDNF mRNA levels. Microinjections of the BDNF scavenger TrkB-Fc into the right ventricle before every PTZ treatment resulted in a significant suppression of the development of kindling in wild-type mice, while it had no effect in MMP-9-KO mice. Inversely, bilateral injections of pro-BDNF into the DG of hippocampus caused a significant aggravation of kindling in wild-type mice but not MMP-9-KO mice. These findings suggest that MMP-9 is involved in progression of behavioral phenotypes in kindled mice owing to conversion of pro-BDNF to mature BDNF in the hippocampus.

O4-6 The secreted ectodomain of calsyntenin-3 (sCst-3) attenuates neuronal death of cortical neurons overexpressing full-length and CTF of Cst-3

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A β may play an important role in pathogenesis of Alzheimer's disease (AD), but molecular mechanisms of A β actions, which are responsible for neurotoxicity, are not fully understood. We have previously identified a synaptic membrane protein calsyntenin-3 (Cst-3) as a A β -induced molecule. Cst-3 is accumulated in dystrophic neuritis around A β plaques in cerebral cortex of an AD mouse model Tg2576. The accumulation of Cst-3 in cultured cortical neurons results in the acceleration of neuronal death. Calsyntenin-3 undergoes two-step proteolytical processing like APP. By the first cleavage with α -secretase, the N-terminal fragment (sCst-3) is released in the cerebrospinal fluid. The C-terminal fragment (CTF) containing the transmembrane region is subsequently cleaved by γ -secretase into another two peptides: a short peptide like p3 from APP and an intracellular domain (ICD). In this study, we investigated which fragments are responsible for the acceleration of neuronal death by the overexpression of Cst-3 fragments in cultured cortical neurons. Overexpression of CTF accelerated neuronal death. However, neither synthetic p3 peptide nor overexpression of ICD accelerated neuronal death. To investigate whether sCst-3 accelerates or attenuates neuronal death, sCst-3 was purified from conditioned medium of COS7 cells expressing his-tagged sCst-3. Purified sCst-3 increased MTT reduction and decreased in neuronal death assessed by the Hoechst 33342 staining of cortical neurons. Moreover, purified sCst-3 completely diminished the death of Cst-3 CTF-expressing neurons. Neuronal death of full-length Cst-3-expressing neurons was partially attenuated by the addition of sCst-3. These results indicate that proteolytical processing of Cst-3 with & alpha;- and γ -secretase may be important to rescue neurodegeneration caused by A β -induced Cst-3 accumulation.

O5-1 Involvement of IFITM3 in brain dysfunction caused by immune activation during neurodevelopment

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Some potential environmental insults, such as viral infection during pregnancy, may include immune inflammation, which could affect fetal brain development by triggering cytokine responses. We have reported that neonatal injection of polyI:C, a synthetic analogue of double-stranded RNA that mimics innate immune responses, in mice results in behavioral alterations in adulthood. Furthermore, overexpression of interferon-induced transmembrane protein 3 (IFITM3) is demonstrated in the brains of polyI:C-treated mice, as observed in patients with schizophrenia and autism, but the pathophysiological significance remains to be determined. Here, we show the involvement of IFITM3 in polyI:C-induced neurodevelopmental abnormalities *in vitro* and *in vivo*. Cultured astrocytes were activated by polyI:C treatment *in vitro*, leading to an increase in mRNA levels of Ifitm3 as well as cytokines. Immunocytochemical analysis revealed that IFITM3 proteins are localized in early endosomes in astrocytes following polyI:C treatment. Overexpression of IFITM3 in COS7 cells resulted in a significant reduction of the activity of endocytosis. When primary cultured neurons were treated with the conditioned-medium of polyI:C-treated astrocytes (polyI:C-ACM), neurite outgrowth and spine formation were diminished, as evidenced by a significant decrease in MAP2-positive dendrite length and complexity and the number of PSD95-immunoreactive puncta on dendrites, respectively. The neurodevelopmental abnormalities of cultured neurons induced by polyI:C-ACM were alleviated when astrocytes were prepared from Ifitm3-/- mice. Furthermore, decreases in MAP2 expression in the frontal cortex *in vivo* as well as memory impairment were evident in polyI:C-treated wild-type mice, but such neurodevelopmental and behavioral abnormalities were not induced in polyI:C-treated Ifitm3-/- mice. These results suggest that reduction of endocytic activity caused by overexpression of IFITM3 may change the composition of the extracellular humoral factors released from astrocytes, which results in neurodevelopmental abnormalities in polyI:C-treated mice.

O5-2 Functional expression of carnitine/organic cation transporter OCTN1 (SLC22A4) in murine neurons

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Carnitine/organic cation transporter OCTN1 (SLC22A4) is a multispecific transporter expressed in ubiquitous organs. We have recently reported that a naturally occurring antioxidant ergothioneine (ERGO) is a good *in vivo* substrate for OCTN1. OCTN1 is functionally expressed in small intestine, liver and kidney. However, its function in the brain has not yet been examined. Therefore, the aim of the present study was to clarify the functional expression of OCTN1 in mouse brain using ERGO as a typical substrate and *octn1* gene knockout ($octn1^{-/-}$) mice. Concentration of [^{3}H]ERGO in the cerebrospinal fluid after intracerebroventricular (*i.c.v.*) administration more rapidly decreased compared with that of [^{14}C]mannitol, a bulk flow marker, in wild-type mice, whereas disappearance of [^{3}H]ERGO was delayed and almost similar to that of [^{14}C]mannitol in $octn1^{-/-}$ mice. The distribution of [^{3}H]ERGO in choroid plexus and several brain regions after *i.c.v.* administration was higher in wild-type mice compared with $octn1^{-/-}$ mice, while the distribution of [^{14}C]mannitol showed no difference between the two strains. Immunoreactivity to OCTN1 antibody was at least partially observed with neuronal marker microtubule-associated protein 2 positive cells in both cerebral cortex and hippocampus. In mouse neuroblastoma Neuro2a cells, real-time PCR analysis revealed mRNA expression for OCTN1, and immunocytochemical analysis showed colocalization of OCTN1 protein with β III-tublin, a neuronal marker protein. In these cells, uptake of [^{3}H]ERGO linearly increased up to 4 hours, while this uptake was inhibited by unlabeled ERGO. The addition of ERGO clearly prevented a marked decrease in MTT reductive activity and an obvious increase in the number of propidium iodide positive cells induced by the exposure to hydrogen peroxide. The data cited above suggest that OCTN1 may be functionally expressed in murine neurons and would be involved in protective effects against oxidative stress by uptake of the antioxidant.

O5-3 Suppression of BDNF secretion contributes to the phencyclidine-induced synaptic dysfunction

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Phencyclidine (PCP) has been reported to cause schizophrenia-like behaviors both in human and rodents, and suggested to induce synaptic dysfunction. However detail mechanisms underlying the effect of PCP on neuronal function have not been clarified. In this study, we investigated the PCP's effect on the synaptic function in cultured cortical neurons. We found that excitatory (glutamatergic) synaptic transmission and the expression of synaptic proteins were decreased by PCP exposure for 48 hours. It was also revealed that PCP caused an impairment of brain-derived neurotrophic factor (BDNF) secretion and resultant attenuation in the activation of intracellular signaling pathways through TrkB (receptor for BDNF) prior to the synaptic loss. Furthermore, PCP blocked intracellular Ca^{2+} elevation stimulated by glutamate, suggesting that PCP inhibited neuronal activity. Exogenous application of BDNF reversed the reduction in both BDNF-TrkB signaling and synaptic proteins caused by PCP. Given that BDNF is responsible for regulation and maintenance of synapses and its secretion is Ca^{2+}-dependent, the PCP-induced synaptic loss would be attribute to the impairment of BDNF secretion and its downstream signaling pathways.

O5-4 Genetic association study of synapse-associated protein 97 (SAP97) and schizophrenia

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The synapse-associated protein 97 (*SAP97*)/discs large (*DLG1*) gene encodes the synaptic scaffolding PDZ proteins that interact with NMDA type and AMPA type ionotropic glutamate receptors. Based on the recent evidence supporting disturbed glutamate neurotransmission in the pathophysiology of schizophrenia, we have investigated association between the *SAP97* gene and schizophrenia. We genotyped 23 SNPs (single nucleotide polymorphisms) capturing the known common haplotype variations of the gene in a sample comprising 229 schizophrenic patients and 214 matched controls. In a single marker analysis, ten SNPs displayed nominally significant association with schizophrenia. We also compared haplotype estimates based on case-control genotypes and observed significant association of eight two- and three- SNP haplotypes with schizophrenia following permutation-based correction. Further examination of the above series of SNPs or haplotypes in each gender revealed significant associations between some of these SNPs or haplotypes and the disorder only in males. We have further obtained confirmed evidence with a second set of case-control samples. We also found a novel splicing variant of SAP97 in human. Presently, we are investigating the expression level of this variant in schizophrenic brain, possible association with some of the SNPs, and relationship to functional domain structures of the SAP97 protein. The present findings suggest that the SAP97 gene may be a susceptibility factor in male schizophrenics and that the modification of the glutamate receptors-SAP97 protein signaling pathway could be involved in the disease pathophysiology. This genetic study was approved by the ethics committees of all institutes, and all participants gave informed and written consent.

O5-5 A conventional and quick gene silencing method in adult rat brain: a single intracerebroventricular injection of Accell siRNA

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Since the gene silencing by RNA interference in mammal had been discovered, many reports employed by small interfering RNA (siRNA) have been drastically accumulated due to both investigations of physiological or pathophysiological role of an interesting protein and developments of clinical applications for various intractable diseases. One of the limiting factors in these studies is the *in vivo* delivery of siRNA, particularly in central nervous system. Commercial available Accell siRNA is modified chemically and allows the conventional delivery of siRNA without transfection reagent, resulting in robust gene-silencing and knockdown of a targeted protein. In the present study, we challenged to apply the single intracerebroventricular injection of Accell siRNA to a gene silencing in adult rat brain. To assess whether Accell siRNA was incorporated to brain, we performed the intracerebroventricular injection of Accell FAM-labeled control siRNA (5 g/rat) in Wistar rats weighting 250-350 g. The siRNA was easily incorporated into various types of mature neurons in broad regions (cortex, striatum, hippocampus, midbrain, and cerebellum) for 1 week, not into glia such as astrocyte and microglia. The delivery efficacy in neuron was about 97%. Subsequently, to investigate whether Accell siRNA inhibited the expression levels of a targeted protein, we performed the intracerebroventricular injection of Accell Cyclophilin-B siRNA. Both immunohistochemical and Western blotting analyses demonstrated that *in vivo* delivery of Accell Cyclophilin-B siRNA remarkably reduced the expression levels of Cyclophilin-B (38~68% knockdown). Thus, the conventional procedure enables us to study quickly physiological and pathophysiological role of a targeted protein in a neuron-specific manner.

O5-6 Re-evaluation of DISC1 using its new antibodies and mice with targeted disruption of exons 2 and 3 of the DISC1 gene

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Disrupted-In-Schizophrenia 1 (DISC1) is a promising candidate gene for susceptibility to psychiatric disorders, including schizophrenia. DISC1 appears to be involved in neurogenesis, neuronal migration, axon/dendrite formation, and synapse formation by acting as a scaffold protein through interacting with the various partners. Both anatomical and behavioral analyses of mice with dysfunctional DISC1 revealed phenotypes as schizophrenia and/or depression model mice. However, the lack of DISC1 knockout mice and a well-characterized antibody to DISC1 makes it difficult to dissect the exact role of DISC1 *in vivo*. Here, we generated mice lacking exons 2 and 3 of DISC1 gene and made specific antibodies to the N- and C-termini of DISC1. DISC1 homozygous mutant mice are viable and fertile, and no gross phenotype, such as disorganization of brain cytoarchitecture, is observed. Western blot analysis revealed that the DISC1-specific antibodies recognized a protein band with a molecular mass of approximately 100 kDa, which corresponds to the size of the full-length mouse DISC1, in brain extracts from wildtype mice but not from DISC1 homozygous mutant mice. A deficiency of full-length DISC1 induced a threshold shift in the induction of long-term potentiation (LTP) in the dentate gyrus. DISC1 homozygous mutant mice displayed abnormal emotional behavior, as assessed by the elevated-plus maze test and cliff avoidance test, suggesting that a deficiency of full-length DISC1 may result in lower anxiety and/or higher impulsivity. Based on these results, we propose that both full-length DISC1 deficient mice and DISC1-specific antibodies are powerful tools to dissect the pathophysiological functions of DISC1.

O6-1 Analysis of the intercellular signaling cascade induced by chronic stress exposure in oligodendrocytes in corpus callosum

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Major depression is thought to be a multifactorial disease susceptible to both environmental and genetic factors, though the responsible genes and pathogenesis of major depression at the molecular level remain unclear. Among many environmental factors, repeated stressful events are known to be associated with the onset of depression, and stress activates the hypothalamic-pituitary-adrenocortical (HPA) system. Although dysregulation of the HPA axis by chronic stress is indicative of major depression, the molecular mechanisms and functional changes in the brain underlying depression are largely unknown. Thus, we first developed chronically stressed mice by water immersion and resistance method and identified serum- and glucocorticoid-inducible kinase 1 (SGK1) by a comprehensive analysis of the variation in the gene expression levels in the brains of stressed mice compared to that in the brains of unstressed mice. Furthermore, it was confirmed that in the chronically stressed mice, SGK1 mRNA and protein were upregulated, and that SGK1 phosphorylation level was also higher in the oligodendrocytes at bundles of nerve fibers such as corpus callosum. It is well known that SGK1 receives upstream signal from phosphatidylinositol 3-kinase, but the downstream targets of SGK1 in the brain are yet unknown. Next, we investigated the factors that interact with SGK1 in the oligodendrocytes. Our study showed that N-myc downstream-regulated gene 1 (NDRG1) interacted with SGK1 and was phosphorylated by SGK1 in the oligodendrocytes. These results indicate that phosphorylation of NDRG1 possibly plays a key role in the upregulation of adhesion molecules and causing changes in the morphology of oligodendrocytes. Moreover, the chronic stress-induced dysregulation the oligodendrocytes is suggested to be closely associated with the development of major depression.

O6-2 N-terminus cleaved PAP-III (Reg-III γ) forms fibrillar structure and provides axons with a platform for adhesion and elongation

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Pancreatitis-associated protein (PAP)-III (also known as Reg-III γ and Reg-2) is a secretory lectin, whose expression is substantially induced in Schwann cells after peripheral nerve injury. We initially identified the proteolytic cleavage of the N-terminus of PAP-III in injured sciatic nerve. Subsequent *in vitro* studies demonstrated that the cleavage was performed by trypsin-like protease and the cleaved PAP-III protein became insoluble. Immunostaining and scanning electron microscopy demonstrated that the N-terminal-truncated PAP-III (ΔN-PAP-III) polymerized into filaments with a diameter of 10-20 nm. The fibrillar ΔN-PAP-III tightly attached to neurites and cell bodies of primary cortical neurons, when ΔN-PAP-III was added to the culture media. In contrast, little association of the fibrillar ΔN-PAP-III with cultured glial cells was observed. When a dense networks of ΔN-PAP-III fibers were prepared on poly-D-lysine coated glass coverslips before neuronal culture, neurites preferentially adhere to the ΔN-PAP-III fibers and neurite extension was enhanced. This neurite outgrowth activity was significantly suppressed by simultaneous incubation with antibodies against PAP-III. These results suggest a possibility that PAP-III secreted from Schwann cells is cleaved to form the insoluble fibrillar structure around injury site and would provide regenerating axons with a platform for elongation.

O6-3 Microglial activation by zinc released from hypoosmotic stress-loaded astrocytes

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[Objective] Microglia are resident immune cells of the CNS, while under oxidative stress-loaded conditions such as ischemia and trauma, their activation deteriorates neuronal damage. Previously, we have demonstrated that zinc can activate microglia via the sequential process of microglial zinc uptake, ATP release, P2X(7) receptor activation and ROS generation by NADPH oxidase and a DNA repairing enzyme PARP-1 acivation. In general, such zinc is considered to be released from synaptic vesicles of glutamatergic neurons and dead cells. Astrocytes are major cell population in the brain, and contribute to maintain the homeostasis via release of glio-transmitters such as ATP and glutamate. In this study, we examined whether zinc was released from astrocytes and could activate microglia under hypoosmotic stress-loaded condition.[Materials & Methods] Mouse cultured astrocytes and microglia were prepared from 1-day-old ddY mice as reported previously. Hypoosmotic stress was loaded to astrocytes using balanced salt solution prepared to 214-314 mOsmol/L, followed by incubation for designated times, and then intracellular and extracellular zinc levels were assessed using Newport Green (NG) and ICP-MS, respectively. Microglial activation by the astrocytic supernatant was assessed by their morphological change and PAR accumulation as a marker of PARP-1 activity.[Results & Discussion] Hypoosmotic treatment of astrocytes increased the extracellular ATP levels in osmolarity- and time-dependent manners, indicating load of hypoosmotic stress. Administration of the osmotic stress-loaded astrocytic supernatant to microglia activated them, and their activation was suppressed by CaEDTA, an extracellular zinc chelator. By hypoosmotic stress loading to astrocytes, there was increase in the cellular NG signals and extracellular zinc levels, and these changes were significantly blocked by an intracellular zinc chelator TPEN. These findings indicated that under hypoosmotic conditions, zinc is released from astrocytes, in which intracellular free zinc levels are increased, and can activate microglia.[Conclusion] It is suggested that microglial activity is regulated by zinc released from astrocytes.

O6-4 The protective effect of endogenous erythropoietin released from astrocyte to the oligodendrocyte precursor cell against hypoxic and reoxygenation injury

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The hypoxia responsive cytokine erythropoietin (EPO) provides neuroprotective effects in the damaged brain during ischemic events and neurodegenerative diseases. The purpose of the present study is to evaluate the EPO/EPO-receptor (EPOR) endogenous system between astrocyte and oligodendrocyte precursor cell (OPC) under hypoxia. We now report elevated EPO mRNA levels and protein release in cultured astrocytes following hypoxic stimulation by quantitative RT-PCR and ELISA. Furthermore, the EPOR gene expressions were detected in cultured OPCs as in astrocytes by quantitative RT-PCR. Cell staining revealed the EPOR expression in OPC. To evaluate the protective effect of endogenous EPO from astrocyte to OPCs, EPO/EPOR signaling was blocked by EPO siRNA or EPOR siRNA gene silencing in *in vitro* study. The suppression of endogenous EPO production in astrocytes by EPO siRNA decreased the protection to OPCs against hypoxic stress. Furthermore, OPC with EPOR siRNA had less cell survival after hypoxic/reoxygenation injury. It suggested that EPO/EPOR signaling from astrocyte to OPC could prevent OPC damage under hypoxic/reoxygenation condition. Our present finding of the interaction between astrocytes and OPCs may propose the new therapeutic approach to OPCs against cellular stress and injury.

O6-5 Interferon regulatory factor-8 in spinal microglia is a transcription factor crucial for switching to a reactive phenotype after nerve injury

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The interferon regulatory factor (IRF) family of transcription factors consists of nine members, which are expressed in peripheral immune cells and play important roles in gene expression and cellular development. Recent studies have shown that some members of the IRF family are also observed in the central nervous system (CNS). However, the functional relevance of IRFs in the CNS remains unknown. Microglia cells, the resident immune-related cells of the CNS, are crucial for sensing pathological alterations in the nervous system. As a consequence of injury to the nervous system, they transform to reactive states through a series of molecular changes including expression of various genes such as cell-surface receptors and proinflammatory cytokines, which are implicated in the pathogenesis of the CNS diseases such as neuropathic pain. However, the molecular mechanisms by which microglia switch to reactive phenotypes are poorly understood. Here we report that the IRF member IRF8 plays a crucial role in converting normal microglia into a reactive phenotype. Within the spinal cord, expression of IRF8 is normally low; however, expression was specifically upregulated in microglia after peripheral nerve injury (PNI). Forced IRF8 expression in cultured microglia promoted expression of genes associated with reactive phenotypes, depending on its ability to bind to DNA. IRF8 deficiency prevented the expression of these microglial genes in the spinal cord after PNI. We also found that mice lacking IRF8 exhibited resistance to PNI-induced pain hypersensitivity. Moreover, spinal transfer of IRF8-overexpressing microglia to normal mice produced pain hypersensitivity. Together, our present findings suggest IRF8 acts as a critical transcription factor involved in converting microglia to a reactive state that drives neuropathic pain.

O6-6 Morphological changes of myelin and axons in experimental autoimmune encephalomyelitis

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Multiple Sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system (CNS). However, the mechanism of demyelination has not been fully understood. We here report morphological changes of axons and myelin in an animal model which is myelin oligodendrocytes glycoprotein (MOG)-induced experimental autoimmune encephalomyelitis (EAE). Female B6 mice were immunized with MOG35-55 peptide to develop EAE. Mice were perfused with 0.5% paraform aldehyde/ 0.5% glutaraldehyde. Then osmium-macerated tissues were prepared for scanning electron microscopy (SEM).In the white matter of control spinal cord, SEM showed typical ultrastructures of myelin and axons. In contrast, dramatic morphological abnormalities were observed in the white matter of spinal cord with EAE. The number of abnormal myelin was increased by the onset of EAE. The main histological features were focal demyelination and irregularly folded myelin complex along myelinated fibers. Interestingly, development of smooth endoplasmic reticulum-like structure was also found in these axons. These observations indicate that excess myelin folding is caused by a defect in myelinogenesis, probably initiated by disruption of oligodendrocytes-axon interaction. This technique will be powerful tool for underlying the mechanism of demyelination in demyelinating diseases in the CNS.

O7-1 Functional phospho-proteomics analysis of cellular substrates for calcium/calmodulin-dependent protein kinase I

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Intracellular calcium is a crucial mediator of signal transduction as a second messenger in most cell types, especially in neuron. The CaMK family (CaMKI, CaMKII, CaMKIV, and CaMKK) is calmodulin-dependent serine/threonine kinases that play important roles in neuronal development as well as learning and memory. Identification of specific target molecules (e.g., substrate) is critical to understand molecular mechanisms by which the CaMK family regulates neuronal functions. However, there is not comprehensive approach to identify direct substrate for CaMKs. Here we report a method to identify substrate for CaMKI. We design a mutant of CaMKI having constitutive association with substrate, which allows us to identify substrate as a protein complex with CaMKI by affinity-capture-LC-MS/MS method. In a separate experiment, phosphorylation statuses of cellular proteins from control or active CaMKI (caCaMKI) expressing cells were quantified using Immobilized-metal-affinity-chromatography (IMAC) and iTRAQ technology. Combined data from the affinity-capture-LC-MS/MS method and the IMAC-iTRAQ method, we have identified eighty-three candidates for direct cellular substrate for CaMKI including a known substrate such as beta-PIX. One of candidates, ARAF, which is MEK kinase, is great interest for us, because CaMKI has been implicated in neurite outgrowth in neuroblastoma cells as well as dendritic arborization of primary hippocampal neuron through MEK-ERK pathway. CaMKI binds and phosphorylates ARAF on Ser-582, and promotes ARAF association with protein 14-3-3. Activation of ARAF by CaMKI is dependent on phospho-Ser-582. Dominant negative ARAF and MEK inhibitor U0126 inhibits caCaMKI-induced neurite outgrowth in PC12 cells. These data suggest that CaMKI regulates neurite outgrowth via ARAF-MEK-ERK pathway in PC12 cells. Taken together, we propose that our approach to identify cellular substrate for protein kinase would be a strong method to map out signaling pathways mediated by phosphorylation.

O7-2 Antagonism of an endogenous Nogo receptor antagonist LOTUS to B-lymphocyte stimulator-induced axon growth inhibition

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Axonal regeneration after injury in the adult central nervous system (CNS) is limited by myelin-derived axon growth inhibitors (MDAGIs), such as Nogo. Recently, B lymphocyte stimulator (BLyS), a tumor necrosis factor family protein essential for B cell development, was indentified as a functional ligand for Nogo66 receptor (NgR1) which is a common receptor of MDAGIs. We have found that lateral olfactory tract usher substance (LOTUS) functions as an endogenous NgR1 antagonist. In this study, we examined whether LOTUS exerts antagonistic action on BlyS-induced axon growth inhibition. Cultured olfactory bulb neurons exposed to exogenously added BLyS did not show growth cone collapse, whereas BLyS induces growth cone collapse in lotus-deficient out mice. Exogenously applied BLyS induced growth cone collapse in cultured E13 embryonic chick dorsal root ganglion (DRG) neurons where LOTUS was not expressed, whereas the DRG neurons exposed to pre-incubation of purified LOTUS did not show the growth cone collapse. Furthermore, the neurite outgrowth was inhibited in DRG neurons cultured on BLyS coated dishes, whereas exogenously applied LOTUS rescued the inhibitory effect of BLyS on neurite outgrowth. These findings suggest that LOTUS shows antagonism in BLyS-induced axon growth inhibition.

O7-3 Signal transduction underlying chondroitin sulfate proteoglycan-mediated inhibition of axon regeneration

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[Backgrounds & Purpose] In the damaged mammalian CNS, axons form bulbous endings called dystrophic endballs and stop elongation upon contact with chondroitin sulfate proteoglycan (CSPG) gradients secreted from glial scars. Using an adult rat DRG neuron culture system that reproduces dystrophic endballs on CSPG gradients *in vitro*, we previously found that dystrophic endballs resumed forward migration after protein kinase A (PKA) inhibition or paxillin phosphorylation. The present study aims to identify the signal pathway underlying axon regeneration on inhibitory CSPG gradients, focusing on p21-activated kinase (PAK) that regulates cell-matrix adhesions (point contacts) and cell migration via paxillin phosphorylation because PAK can be negatively regulated by PKA. [Results & Discussions] Axons expressing a kinase active form of PAK (T422E PAK) crossed inhibitory CSPG gradients. In contrast, axons expressing wild type PAK hardly crossed the CSPG gradient. Treatment with KT5720, a PKA inhibitor, enhanced the crossing of axons expressing wild type PAK. However, axons expressing a kinase dead form of PAK (K298A PAK) failed to cross the CSPG gradient even after treatment with KT5720. These results suggest that PAK phosphorylation-induced axon elongation is regulated by upstream PKA inhibition. Immunostaining for an active form of PKA revealed that PKA tended to be active in dystrophic endballs on CSPG gradients. In conclusion, CSPG gradients may induce PKA activation and ensuing PAK inactivation, and inhibition of this signaling pathway can enhance axon regeneration on inhibitory CSPG gradients.

O7-5 Intra-cellular translocation of Pgc1 α is involved in PACAP induced neurite outgrowth in neuronal cells

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[Purpose] There is regional and cellular heterogeneity of the mitochondrial activity in neurons, which contributes to dendritic branching[1)]. Thus, mitochondrial function might be modulated during the neurite outgrowth. PPAR γ coactivator 1 α (Pgc1 α) is important to moderate mitochondrial activity. Pgc1 α is distributed in brain, and its KO mice exhibits defect of neurite outgrowth[2)]. There are functional similarities between Pgc1 α and pituitary adenylate cyclase-activating peptide (PACAP). PACAP can also promote neurite outgrowth[3)]. However, the exact mechanism of functional change of mitochondria during neurite outgrowth remains unclear. Here we focused on the mitochondria and characterized the mechanism of Pgc1 α to modify the mitochondrial function in neurite outgrowth by PACAP. [Methods and Results] Hippocampal neurons and Neuro2a cells were exposed with PACAP and the length of neurites was measured after 12 h. PACAP significantly promoted neurite outgrowth. Moreover, the mitochondrial membrane potential after PACAP exposure was higher compared to untreated cells, as reveled by increased ratio between red and green fluorescence of JC1. Further, we have homogenated brains and Neuro2a cells, followed by stepwise centrifugation at 600 or 11500 g to precipitate nucleus or mitochondria respectively. As a result of western blotting analysis, Pgc-1 α was detected both in brain and Neuro2a cell mitochondria. To investigate the contribution of Pgc-1 α for neurite outgrowth underlying PACAP stimulus, Neuro2a cells were exposed with PACAP for 0, 10, 30 or 60 min, followed by mitochondria isolation to determine whether Pgc-1 α is enriched in mitochondria or nucleus. Pgc-1 α subcellular localization was shifted from mitochondria to nucleus in a time dependent manner. [Discussion] Our data suggest that neurite outgrowth might be enhanced by higher mitochondrial membrane potential through translocation of Pgc-1 α from mitochondria to nucleus after PACAP stimulus. To the best of our knowledge this is the first report of direct signal transmission from mitochondria to nucleus during neurite outgrowth.
[1)] Mol Biol Cell. 2008 Jan;19(1):150-8. [2)] Cell. 2004 Oct 1;119(1):121-35. [3)] J Neurosci. 2003 Mar 15;23(6):2274-83.

O7-4 Expression analysis of *Shank3* variants possibly associated with autism spectrum disorders in the developing mouse neocoetex

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Terminal 22q13 deletion is a recognizable malformation syndrome associated with significant language delay, mental retardation, hypotonia and autistic feature. Cumulative evidence has demonstrated that haploinsufficiency of the *SHANK3* gene located at 22q13.3 is a major cause in the neurological symptoms of 22q13.3 deletion syndrome. *Shank3*, a multidomain protein containing SH3 and PDZ domains, is localized in postsynapses and interacts with various synaptic molecules, including PSD-95 and glutamate receptors. Although it has been thought that *Shank3* plays important roles in the formation and function of synapse in the developing brain and is involved in higher brain function, the molecular diversity of *Shank3* and its expression mechanism have not been fully understood. In this study, we identified novel *Shank3* variants and examined its expression mechanism. The *Shank3* gene consists of 22 exons and has five CpG islands (CpG island-P, -2, -3, -4, -5) whose methylation is involved in tissue specific expression of *Shank3* gene. We examined the rate of DNA methylation of each CpG island in the developing mouse neocortex. Interestingly, the methylation rate of CpG island-2 (vicinity of exon11) increased from birth until postnatal day (P) 14, thereafter decreased gradually, and we found that methyl CpG binding protein 2 (MeCP2), which was identified as a responsible gene for Rett syndrome and has been thought to regulate gene transcription, bound the CpG island-2 region in P14 neocortex. We further found a novel *Shank3* transcript, whose transcription start site located in an intron 10 of *Shank3* gene. We then identified full length of novel *Shank3* transcript using RT-PCR method and found many types of *Shank3* variants. Sequencing analysis indicated that one type of variant had entire exons (from exon 11 to exon 22) and the others were the truncated variants without exon 21, which encodes functional regions including homer binding region, cortactin binding region and sterile alpha motif. To clarify the role of novel *Shank3* variants in the developing brain and the involvement in development disorders including autism and mental retardation, further study is now on going.

Oral Sessions

O8-1 The coordination of the cell cycle exit and the differentiation of cerebral cortical progenitors is regulated by Rb family

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One of the fundamental principles in developmental biology is that cell cycle exit must precede differentiation, because the regulatory networks that drive cell proliferation are incompatible with those that direct differentiation. During cerebral cortical development, early-born neurons are located at deep-layer with extending their axons into subcortical areas, whereas late-born neurons are located at upper-layer with extending their axons into intracortical areas. Therefore, the timing of the cell cycle exit of progenitor cells could be essential for undergoing the proper cell differentiation program of different types of neurons. However, the mechanisms by which cortical progenitor cells exit the cell cycle are still unknown. Rb family (Rb, p107, p130) lie at the heart of the cell cycle machinery that executes cell cycle exit in coordination with differentiation during development. To elucidate the role of Rb family for the cell cycle exit of cerebral cortical progenitor cells, we used in utero electroporation method to inactivate all Rb family members in cortical progenitor cells and found that Rb family is essential for the cell cycle exit of progenitor cells. We are currently examining the fate of Rb family-deficient cortical cells that do not exit cell cycle. This study will help to understand how cell cycle exit and differentiation are coordinated during cerebral cortical development.

O8-2 Effects of neurotransmitter receptors on proliferation and differentiation into neural progenitor cells in mouse induced pluripotent stem cells

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Previous studies reported that the proliferation of neural progenitor cells may be regulated by classical neurotransmitters such as adrenaline, nicotine, and acetylcholine. Mouse induced pluripotent stem (iPS) cells display properties of self-renewal and differentiation into various cells including neural progenitor cells. However, the effects of the neurotransmitters on proliferation and differentiation of mouse iPS cells remain unknown. The present study examined whether stimulation with the neurotransmitter receptors regulates proliferation or differentiation into neural progenitor cells using mouse iPS cells. Mouse iPS cells were cultured under feeder-free conditions. The cells were treated by l-phenylephrine (an α_1-adrenergic receptor agonist) or nicotine for 8-24 h in the presence of leukemia inhibitory factor. MTT assay and BrdU incorporation assay revealed that l-phenylephrine (300 nM) or nicotine (300 nM) significantly enhanced the DNA synthesis and proliferation of the cells. Pretreatment with prazosin (an α_1-adrenergic receptor antagonist) significantly reduced the proliferation enhanced by l-phenylephrine. Pretreatment with either mecamylamine (an α_4-nicotinic acetylcholine receptor (nAchR) antagonist) or α-bungarotoxin (an α_7-nAchR antagonist) significantly reduced the proliferation enhanced by nicotine. Immunofluorescence staining revealed that mouse iPS cells express α_1-adrenergic receptor, α_4-nAchR, and α_7-nAchR. The differentiation of mouse iPS cells was initiated by forming embryoid bodies. The embryoid bodies were transferred to gelatin-coated dishes and then cultured with l-phenylephrine or nicotine for 7 days. Although the differentiation from mouse iPS cells into neural progenitor cells was evaluated by Nestin expression using immunofluorescence staining or western blot analysis, neither l-phenylephrine nor nicotine affected the change of Nestin expression. These results suggested that the stimulation of neurotransmitter receptor such as α_1-adrenergic receptor or nAchR may enhance the proliferation of mouse iPS cells, whereas the stimulation did not affect the differentiation into neural progenitor cells.

O8-3 Mammalian glial cells missing genes induce Hes5 expression by active DNA demethylation and induce neural stem cells

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Notch receptor-mediated signaling plays critical roles in the development of many organs and the maintenance of various stem cell populations. Activation of Notch signaling is first detectable by the expression of an effector gene, Hes5, in the neuroepithelium of mouse embryos at embryonic day (E) 8.0-8.5, and this activation is indispensable for the generation of neural stem cells. However, the molecular mechanism describing how Hes5 expression is initiated in stem-producing cells remain unknown. Here we show that mammalian Glial cells missing (Gcm) 1 and 2 are involved in the epigenetic regulation of Hes5 gene transcription by DNA demethylation in a DNA replication-independent manner. Loss of both Gcm genes and subsequent lack of Hes5 upregulation in the neuroepithelium of E7.5-8.5 $Gcm1^{-/-}$;$Gcm2^{-/-}$ mutants results in the impaired induction of neural stem cells. Our data suggest that Hes5 expression is serially activated first by Gcms and later by the canonical Notch pathway.

O8-4 Behavioral hyperactivity in the rat by bisphenol A, but not by its derivatives, 3-hydroxybisphenol A or bisphenol A 3,4-quinone

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Recently, we demonstrated that bisphenol A, a toxic environmental chemical, caused a deficit in the development of dopaminergic neurons in the rat. These animals showed behavioral hyperactivities, similarly to animal models for attention-deficit hyperactivity disorder. However, the mechanism of neurotoxicity of bisphenol A remains obscure, and detoxication in the central nervous system is largely unknown. In the present study, we examined the effects of bisphenol A, and its derivatives, 3-hydroxybisphenol A and bisphenol A 3,4-quinone as possible metabolites of bisphenol A, on the spontaneous motor activity in the rat. A single intracisternal administration of bisphenol A (20 μg equivalent to 87 nmol) into 5-day-old male Wistar rats caused significant hyperactivity at 4-5 weeks of age. It was about 1.3 fold more active than control rats in the nocturnal phase. However, neither 3-hydroxybisphenol A nor bisphenol A 3,4-quinone at the same amount (87 nmol) increased the spontaneous motor activity. Gas chromatographic-mass spectrometric (GC-MS) analyses of the treated brain revealed that 7% of the parent chemical resided in the brain at 8 weeks of age, but its derivatives were not detected. These results suggested a deference in metabolic turnover of these compounds or a difference in their stabilities. We conclude that bisphenol A *per se* caused hyperactivity in the rat, eliminating the possibility that possible metabolic forms of bisphenol A, 3-hydroxybisphenol A and bisphenol A 3,4-quinone have the ability to elicit rat hyperactivity, probably because of longer-lasting residence of the parent compound in the brain.

O8-5 Up-regulation of neuropeptide Y receptors in hypotensive mouse vasomotor center

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Neuropeptide Y (NPY) affects blood pressure as a risk factor for essential hypertension. Injection of NPY into the rostral ventrolateral medulla (RVLM), which is a vasomotor center sending axons to the lateral column of the spinal cord, resulted in temporal hypertension following hypotensional state. The expression level of NPY in the medulla oblongata also increased with age. At least four different NPY receptors: Y1, Y2, Y4 and Y5 are expressed in mammalian brains. Among them we have found expression of Y1, Y2 and Y5 in the mouse RVLM. To address functional roles of these receptors for central regulation of blood pressure, mice were treated with reserpine, a hypotensive agent, and thereafter expression level of these NPY receptors were evaluated by immunofluorescent staining using a confocal laser scanning microscope. NPY- immunoreactivity (ir) was decreased 24 hrs after reserpine treatment, however, immunoreactivitis for NPY receptors were not altered. Sequentially daily reserpine treatment for five days resulted in decrease of NPY-ir and up-regulation of Y1-ir and Y2-ir in the RVLM, but not that of Y5-ir. These findings indicated that the central regulation of blood pressure would involve both Y1 and Y2 receptors, of which up-regulation might compensate for paucity of NPY in the RVLM and conserve the blood pressure.

O8-6 Serum levels of anterior pituitary hormones in children with autism

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The neurobiological basis of autism remains poorly understood. The diagnosis of autism is based solely on behavioural characteristics, since there is currently no biologic marker that has been proven to be characteristic of autism. To test whether the anterior pituitary hormones and cortisol were useful as biologic markers for autism, we assessed basal serum levels of them in subjects with autism.We determined the serum levels of six anterior pituitary hormones, including adrenocorticotropic hormone and growth hormone in 32 male subjects with autism (age: 6-18 years) and 34 healthy age- and sex-matched control subjects by a Bio-Plex suspension array system. Additionally, we also determined cortisol in these subjects by enzyme-linked immunosorbent assay. Serum levels of adrenocorticotropic hormone, growth hormone and cortisol were significantly higher in subjects with autism than in controls. Additionally, there was a significantly positive correlation between cortisol and adrenocorticotropic hormone levels in autism.Our results suggest that increased basal serum levels of adrenocorticotropic hormone accompanied by increased cortisol and growth hormone may be useful biologic markers for autism.

G1-1 The Cdk5-LMTK1/AATYK1-Rab11 pathway, a novel cascade regulating axon outgrowth

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Membranes are supplied to extending neurites of neurons through recycling endosomes. Membrane trafficking to and from recycling endosomes is regulated by Rab11 small GTPase, but the regulatory mechanism remains elusive. We have recently shown that LMTK1 (previously called AATYK1) Ser/Thr kinase plays a role in the formation of Rab11A-positive pericentrosomal endocytic recycling compartment in CHO-K1 cells and that activity is regulated by Ser34 phosphorylation of LMTK1 with cyclin-dependent kinase 5 (Cdk5). Considering that both LMTK1 and Cdk5 are expressed highly in brains, it is important to identify the neuronal function of the Cdk5-LMTK1 pathway. Here, we investigated a role of LMTK1 and its phosphorylation by Cdk5 in axon outgrowth using primary cortical neuron cultures. Exogenously expressed LMTK1 co-localized with Rab11A-positive recycling endosomes at perinuclear region and axon. LMTK1 expression and Ser34 phosphorylation of LMTK1 were increased in cultured neurons at DIV2 at the time of axonal outgrowth. Neither LMTK1-WT nor LMTK1-S34D affected outgrowth of axon, but the expression of LMTK1-S34A resulted in longer axon. LMTK1-S34A showed co-localization with Rab11A more than LMTK1-S34D in axon. LMTK1-WT showed co-localization with constitutively active Rab11A-Q70L more than dominant negative Rab11A-S25N in axon. Enhancement of axon outgrowth by LMTK1-S34A was abolished by downregulation of Rab11A and overexpression of dominant negative Rab11A-S25N, indicating the Cdk5-LMTK1-Rab11 cascade in axonal outgrowth. Surprisingly LMTK1-deficient neurons induced by RNAi or derived from LMTK1-/- mice showed enhanced axon outgrowth. These effects were reversed by expression of LMTK1-WT or S34D, phosphorylation mimic mutant. Taken together, the Cdk5-LMTK1-Rab11A pathway is a novel regulating system of axon formation in mammalian neurons.

G1-2 Functional domain of LOTUS serving as endogenous Nogo66 receptor antagonist

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Neurons in the adult central nervous system have been known to fail to regenerate after injury. Nogo66 receptor (NgR1) is a common receptor of myelin-derived axon growth inhibitors, such as Nogo. Recently, we have found that lateral olfactory tract usher substance (LOTUS) binds to NgR1 and functions as endogenous antagonist to NgR1. However, which region of LOTUS exerts the antagonistic action to NgR1 has not been determined. Analysis using the deletion mutant of LOTUS revealed that two carboxyl-terminal regions of LOTUS were important in the binding to NgR1. The C-terminal domains, named UCa, co-expressed with NgR1 on COS7 cells completely abolished the binding of Nogo66 to NgR1 as well as the full length of LOTUS. Furthermore, overexpression of UCa domain in cultured dorsal root ganglion neurons suppressed Nogo66-induced growth cone collapse. These data suggest that UCa region of LOTUS acts as a functional domain in antagonism to NgR1. In future therapeutic approaches, the blockade to NgR1 with UCa domain may help to promote neural regeneration.

G1-3 Physiological roles of molecular interaction between LOTUS and Nogo receptor in lateral olfactory tract formation

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We discovered a novel axon guidance molecule LOTUS that serves for lateral olfactory tract (LOT) development of mouse telencephalon, and identified Nogo-66 receptor (NgR1) as its binding partner. We have found that binding of NgR1 ligands such as Nogo-66 (Ng66) to NgR1 was inhibited by LOTUS coexpressed with NgR1 *in vitro*. We examined formation of LOT visualized with DiI staining and found defasciculated LOT in lotus deficient mice, whereas these abnormal phenotypes were not observed in ngr1 deficient mice. Furthermore, the both of abnormal phenotypes seen in single mutant of lotus deficient mice was rescued in double mutant of lotus and ngr1 deficient mice. These findings suggest that NgR1 induces defasciculation of LOT and the antagonism to NgR1 by LOTUS may contribute to LOT formation.

G1-4 Promoting action of an endogenous Nogo66 receptor antagonist LOTUS on neurite outgrowth

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Lateral olfactory tract usher substance (LOTUS) was identified as a novel key molecule for LOT formation. As a LOTUS binding protein, we further identified Nogo66 receptor (NgR1), which was a common receptor of myelin-derived axon growth inhibitors, such as Nogo proteins. We have shown that LOTUS functions as an endogenous NgR1 antagonist. In this study, we found that LOTUS promoted neurite outgrowth in retinal ganglion cell (RGC) and dorsal root ganglion (DRG) neurons. Furthermore, RGC neurons in ngr1-deficient mice also showed the similar promoting effect of LOTUS on neurite outgrowth. These findings suggest that LOTUS promotes neurite outgrowth in RGC and DRG neurons and its promoting action may be mediated by unidentified LOTUS binding molecule.

G1-5 The function and expression of sigma-1 short receptor, a novel splice variant in the brain

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Sigma-1 receptor (sigma-1R) is characterized as an endoplasmic reticulum (ER)-associated chaperone protein, regulating ER-mitochondrial interorganellar Ca^{2+} mobilization through inositol 1,4,5-trisphosphate receptors (IP3Rs) and promoting cell survival. We cloned a novel splice variant of sigma-1R, termed sigma-1 short R (sigma-1SR) from mouse brain cDNA libraries. Sigma-1SR lacks 47 nucleotides that encode the second transmembrane domain encoded in exon 2. The deletion of 47 nucleotides resulted in a frame shift and gave rise to a novel 4 amino acid sequence in the C-terminus that was not seen in sigma-1R sequence reported. The sigma-1SR protein expression levels were 30-40% of those in mouse cortex, hippocampus and striatum, but it was not detected in brainstem. When sigma-1SR was expressed in neuroblastoma Neuro-2a cells, it localized on ER and Golgi apparatus, and interacted with sigma-1R, but not with IP3Rs. The stable expression of sigma-1SR reduced the efficiency of mitochondrial Ca^{2+} influx in response to IP3R-driven stimuli. In addition, coexpression of sigma-1R with sigma-1SR interfered the sigma-1R action on mitochondrial Ca^{2+} mobilization. Taken together, sigma-1SR dimerizes with sigma-1R and disrupts its action on the mitochondrial Ca^{2+} homeostasis.

G1-6 Dynactin-1 knock-down C.elegans is a novel sporadic amyotrophic lateral sclerosis (SALS) model simulating axonal transport defect and motor neuron degeneration

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Axonal degeneration and transport defects are observed in several motor neuron diseases from its early stage. Sporadic ALS(SALS) is one of those diseases which exhibit severe axonal degeneration. However the mechanisms by which axonal degeneration might occur in SALS are still unclear. Recent explorations of human mutations causing motor neuron disease identified several genes important for axonal biology. Dynactinl(DCTN1) is one of such genes and, interestingly, we previously reported that its expression level is markedly reduced in spinal motor neurons of SALS patient from early stage of disease. In this work, in order to determine the relationship between reduced level of DCTN1 and the pathogenesis of SALS, we generated a C.elegans model harboring motor neuron-specifically knocked-down dnc-1, homologue of DCTN1. This model exhibited severe locomotory defect, significant axonal degeneration and abundant whorl-like inclusions in axons. Time-laps imaging of co-expressed synaptobrevin-1 (SNB-1) revealed axonal transport defect. In addition, we found impaired movement and accumulation of autophagosomes in degenerated axons. Interentingly, many autophagosome-like structures were also observed in spinal motor neurons of SALS patient. Furthermore we also found that activation of autophagy by starvation attenuated locomotory defect in this model. Taken together, these results suggest that down regulation of DCTN1 causes axonal transport defect and degenerations associated with abnormal accumulation of autophagosomes, which may simulate the SALS pathogenesis. This new model of SALS will be instrumental for not only clarifying disease mechanisms in ALS, but also for testing therapeutic strategies to ameliorate this devastating disease.

G2-1 Neural circuits in controlling paternal parental behavior in male ICR mice

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Appropriate parental care by the father can greatly facilitate healthy family life. Fathers play a substantial role in infant care in a small but significant number of mammalians including humans. However, the neural circuitry controlling paternal behavior is much less understood than its female counter part. To support the wellbeing of the parent –infant relationship, the neuromolecular mechanism of paternal behavior should be clarified. Laboratory (ICR strain) mice are very active in reproduction (Jin et al., Nature, 2007), but are not monogamous. ICR males are not spontaneously parental and can induce maternal-like parental care (retrieval of pups), when separated from their pups by signals (olfactory and auditory) from the mother (in preparation). Here we studied neuronal circuits that are important in paternal parental care. In order to characterize brain areas activated by paternal parental care, ICR wild-type male or female mice in male-female pairs were given an electrolytic brain lesion, a useful tool to disrupt maternal parental care, in the medial preoptic area (MPOA) or ventral pallidum (VP) region of both sides. We found that the lessoned males and females showed sever deficits in all components of parental behavior, including retrieval behavior compared to the control group with no electrical brain lesion. Our result suggests that these areas play a role in paternal parental behavior in male ICR mice. The result well accords with previous observations, in that MPOA and VP are critical in rat mothers for the expression of maternal behavior and protective voluntary maternal response.

G2-2 Involvement of transient inhibition of histone deacetylase in valproic acid-induced autisitic-like behaviors and cortical pathology in mice

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Valproic acid (VPA) is widely used to treat epilepcy and bipolar disorder. On the other hand, the dose of VPA during pregnancy is related to the pathogenesis of autism spectrum disorders and mental retardation in children. Accordingly, rodents prenatally exposed to VPA display autistic-like behaviors. However, the exact mechanisms underlying the VPA-induced behavioral abnormalities are still unclear. In the present study, we demonstrated that mice exposed to VPA at the embryonic day 12.5 (E12.5), but at E14.5, displayed autistic-like behaviors, such as impaired social behaviors, increased anxiety-like behavior and learning deficit after 4 and 8 weeks of age. In addition, the exposure to VPA at E12.5 caused significant decreases in the Nissl-positive cell numbers in the layers IV–V of the somatosensory cortex and the BrdU-positive cell numbers in the lower layers (a BrdU pulse at E12.5) and the middle layers (a BrdU pulse at E13.5) of the somatosensory cortex, compared with saline-treated controls. Futhermore, the VPA exposure immediately caused an increase in acetylation levels of histone H3 and H4 in the whole embryonic brain, followed by an increase in apoptotic-cell death in the neocortex, and a reduction in cell proliferation in the ganglionic eminence. In contrast, mice exposed to valpromide, a VPA analog lacking histone deacetylase (HDAC) inhibition activity, at E12.5 did not display behaivioral, biochemical and histological abnormalities. These findings suggest that transient inhibition of HDAC at the embryonic stage is involved in abnormal behaviors in mice exposed to VPA at E12.5 and the somatosensory cortical pathology.

G2-3 Denosomin enhances axonal regrowth associated with motor function recovery in spinal cord injury

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We previously found that a novel compound, 1-deoxy-nor-sominone (Denosomin) has neurite regrowth activity in cultured cortical neurons (Org.Lett.(2009), 11;3970-3973). In addition, Denosomin treatment improves hindlimb dysfunction in spinal cord injury (SCI) mice (Our meeting report in Neuro2010). However, the detail of axonal regrowth by Denosomin in SCI had not been elucidated. Therefore, we aimed to investigate that Denosomin may be a pharmacotherapeutic candidate for axonal regeneration beyond the lesion site in SCI mice.
After laminectomy at T10 level, contusion injury was performed by dropping a 6.5 g weight from a height of 3 cm onto L1 lumber spinal cord two times. Denosomin (10 or 20 μmol/kg/day) or vehicle solution was administrated orally for 14 days from 1h after SCI on day 0 to day 14. Motor functions were scored on the basis of BMS and Body Support Score(BSS). Hindlimb dysfunction of SCI mice was significantly recovered by Denosomin. Immunohistochemistry for NF-H showed that axonal density increased significantly in the surrounding and center of lesions in the spinal cord of Denosomin-treated SCI mice. Density of 5-HT-positive raphespinal fibers significantly increased by Denosomin in the caudal side of the lesion treatment. In addition, density of the corticospinal tract which was traced by BDA injection tended to be increased by Denosomin in the rostral and caudal sides of the lesion.
Although the mechanism of Denosomin-induced axonal growth in under the investigation, effects of Denosomin show a possibility of pharmacotherapy of SCI and may be a clue of the mechanism of axonal growth.

G2-4 Exploring the role of cystatin F in demyelination disease

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Myelin is a membrane structure enabling saltatory conduction of action potential and is formed by oligodendrocytes in the CNS. Multiple sclerosis (MS) is one of the demyelinating diseases. In chronic demyelinating lesions in the MS patient brain, oligodendrocyte precursor cells are found abundantly, and moreover pre-myelinating oligodendrocytes are also found, but they fail to achieve terminal differentiation into myelin-forming oligodendrocytes.It has been reported that the TNF-alpha pathway is implicated in MS susceptibility through the observations in human clinical studies. Thus, we focused on the behavior of microglia, the major TNF-alpha producing cells in the CNS, in the demyelinating brain.We found that cystatin F (CysF), which is a cysteine protease inhibitor, is expressed in microglia during remyelinating stage and the expression level decreased when chronic demyelinated lesions appeared. CysF mRNA expression was induced when microglia phagocytosed myelin debris. Interestingly, CysF mRNA expression was not induced during normal developmental stages or hypoglossal nerve injury, which results in the Wallerian degeneration. CysF is expressed in some immune cells but not in infiltrating T cells in the demyelinating lesions of MOG induced EAE model. In addition, the expression pattern of cathepsin C (CatC), which is the target of CysF, was similar to that of CysF in remyelinating regions but we found CatC+/CysF- regions in chronic demyelinated lesions. Additionally, we found that CatC is expressed in microglia and CatC co-localized with that of CysF in primary cultured microglia. It is reported that CatC is involved in the production of pro-inflammatory cytokines. Together, we propose that CysF which is expressed in microglia dominates the production of pro-inflammatory cytokines in the re-myelinating phase of demyelinating lesions.

G2-5 Hypothalamic necdin regulates thyroid hormone-mediated energy expenditure

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Necdin, a multifunctional protein expressed in virtually all neurons, is abundantly expressed in the hypothalamus. In humans, the necdin gene (NDN) is mapped to chromosome 15q11-q12, a region deleted in Prader-Willi syndrome (PWS). PWS is a classic genomic imprinting-associated neurodevelopmental disorder characterized by hyperphagia, obesity and hypogonadism, which are all highly suggestive of hypothalamic dysfunction. These findings suggest that necdin plays a key role in the maintenance of hypothalamic functions such as neuroendocrine control of energy homeostasis. We have previously found that acetylation of FoxO1 increases and thyrotropin-releasing hormone (TRH) expression decreases in the hypothalamus of paternal Ndn mutant mice. In the present study, we examined whether necdin regulates expression of genes associated with energy metabolism in the hypothalamus and peripheral tissues. We found that Ndn-deficient mice exhibited hypothermia and reduced serum levels of thyroid hormones (T4, T3) at 4 weeks of age, suggesting that necdin deficiency causes hypothyroidism. Because thyroid hormones control thermogenesis, we examined the expression levels of thermogenic marker genes for peroxisome proliferator-activated receptor gamma coactivator-1 alpha (PGC-1alpha) and uncoupled proteins (UCPs). We found that PGC-1alpha and UCP-3 mRNA levels decreased in both hypothalamus and brown adipose tissues of Ndn-deficient mice, but not in muscle and liver. This suggests that necdin promotes expression of PGC-1alpha and UCP-3 genes in these tissues through activation of thyroid function. On the other hand, it has been reported that PGC-1alpha is activated through deacetylation by NAD-dependent deacetylase Sirt1. We have previously found that necdin binds to Sirt1 to enhance its deacetylation activity. Coimmunoprecipitation assay revealed that necdin interacted with PGC-1alpha. Thus, necdin may enhance Sirt1-dependent deacetylation of PGC-1alpha to activate downstream genes involved in energy expenditure. These data suggest that necdin promotes energy expenditure not only by activating the hypothalamic-pituitary-thyroid axis but also by complexing with PGC-1alpha and Sirt1.

G2-6 Necdin forms multiprotein complexes with Smc5/6 components in mammalian brain

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Necdin, a member of MAGE (melanoma antigen) family expressed predominantly in neurons, is required for neuronal development and survival in mammalian brain. Over 30 MAGE genes have been identified in mammals, whereas only a single MAGE gene is found in the genome of non-mammalian species. Yeast MAGE is known as Nse3, a component of Smc (Structural maintenance of chromosomes) 5/6 complex which is related to the Smc family proteins cohesin and condensin. The yeast Smc5/6 complex, which is composed of Smc5, Smc6 and four major non-Smc elements (Nse1, Nse2, Nse3 and Nse4), functions in DNA repair, maintenance of telomere length and homologous recombination. However, little is known about the structure and function of mammalian Smc5/6 complex. We hypothesized that necdin serves as an Nse3-like component of the mammalian Smc5/6 complex and is functionally similar to its yeast counterpart. In the present study, we analyzed whether necdin is a component of the Smc5/6 complex in mouse brain. Coimmunoprecipitation analysis revealed that necdin formed stable complexes with Nse4, Smc5 or Smc6 in transfected HEK293A cells. In addition, necdin formed a ternary complex with Nse1 and Nse4. We then examined the expression levels of necdin, Nse4, Smc5, and Smc6 during mouse brain development by Western blot analysis. The necdin and Nse4 levels were high during embryonic period but low in adulthood. In contrast, modified Smc5 (146 kDa) and unmodified Smc6 (130 kDa) forms were increased in adulthood. We next examined whether necdin forms multiprotein complexes containing Smc5, Smc6 and Nse4 in E18.5 mouse brain by blue-native PAGE followed by two-dimensional SDS-PAGE. Necdin was detected at 100-1000 kDa, but its monomeric form (43 kDa) was undetected. On the other hand, Nse4 was detected mainly at 120 kDa, but its monomeric form (48 kDa) was undetected. Thus, we speculate that the 120 kDa complex contains necdin, Nse4, and Nse1 (30 kDa), but not Smc5 (130 kDa) or Smc6 (130 kDa). These results suggest that necdin forms multiprotein complexes with only non-Smc components different from the Smc5/6 holocomplex during mammalian brain development.

G3-1 Microglia release ATP by a mechanism of exocytosis

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Microglia are brain immune cells that monitor environmental changes in the CNS. In cases of abnormal conditions such as trauma, ischemia and inflammation, microglia change their characteristic features into activated state, and then, start to migrate, proliferate, produce/release several cytokines or even phagocytose damaged cells or debris to maintain brain homeostasis. For these events, extracellular nucleotides released/leaked from damaged cells and activation of P2 receptors have critical roles. However, so far, whether microglia themselves release ATP or its mechanisms remain largely unknown. Here we show that microglia have a potential to release ATP by a mechanism of exocytosis. Microglial showed many quinacrine-positive vesicular-like structures that were de-stained in response to ionomycin. They also expressed vesicular nucleotide transporter (VNUT), a transporter that uptakes cytosolic ATP into vesicles, whose colocalization was not associated with a lysosome marker LAMP-1. When stimulated with ionomycin, microglia released ATP, which was measured by a lucifelin-luciferase chemiluminescent assay. The ionomycin-evoked ATP release was inhibited by a vesicular H^+-ATPase inhibitor bafilomycin A, an intracellular calcium chelator BAPTA-AM, and a SNARE protein protease Botulinum toxin A, but not by a connexin hemichannel inhibitor carbenoxolone. All these data suggest that microglia release ATP by a mechanism of exocytosis.

G3-2 Expression of Transglutaminase 2 and Factor XIII-A in Microglia

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Transglutaminase 2 (TG2), a cross-linking enzyme, has been activated in various neurodegenerative diseases such as Alzheimer's disease (AD), Parkinson's disease and Huntington's diseases. Coagulation factor XIII-A (FXIII-A), which is another TG, is reported to be expressed mainly in microglia in AD patient's postmortem brain. In the monocyte/macrophage, deficiency of FXIII-A is known to cause the reduction of phagocytosis. It is also reported that overexpression of FXIII-A might induce cell migration. However, mechanism contributing to the increased TG activity and FXIII-A expression in neurodegenerative diseases remain to be clarified. We previously demonstrated that the expression of TG2 in cultured rat hippocampal astrocytes was remarkably induced by lipopolysaccharide (LPS)-stimulation and might associated with nitric oxide (NO) production. In the present study, we examined the mRNA expressions of inducible NO synthase (iNOS), TG2, and FXIII-A in mouse microglial cell line BV-2 with RT-PCR techniques. TG2 mRNA in BV-2 was induced by LPS in a dose-dependent manner, as well as iNOS mRNA. We found that amphotericin B (AmB), an antifungal drug, significantly increased TG2 and iNOS mRNA expression in a dose-dependent manner similarly to LPS. On the other hand, both LPS and AmB remarkably decreased FXIII-A mRNA. LPS reduced FXIII-A mRNA dose-dependently to about 1% of control. Similarly, AmB caused a dose-dependent reduction of FXIII-A mRNA to 25% of control. We then observed the uptake of fluorescent microbeads in BV-2 to assess the ability of phagocytosis. After stimulation by LPS or AmB for 24 h, phagocytotic activity in BV-2 significantly increased in similar concentration ranges to the TG2 induction and the FXIII-A reduction described above. These results suggest that changes in the expression of TG2 and FXIII-A might be involved in microglial cell activation, which is a key event in various neurodegenerative diseases.

G3-3 Role of glial and fibrotic scars in inhibition of axonal regeneration and tissue healing after traumatic injury of the brain

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The scar tissue has been considered as an impediment to axonal regeneration in the damaged central nervous system (CNS), while the beneficial role in the tissue healing has been recently proposed. The scar tissue is divided into two types according to the cellular components. Fibrotic scar is formed in the lesion center by meningeal fibroblasts, and glial scar surrounding the fibrotic scar is formed by reactive astrocytes. To explore the role of these scar tissues, we have examined the mouse brain with a unilateral transection of nigrostriatal dopaminergic pathway. Transected axons did not regenerate beyond the lesion site in which the fibrotic scar was deposited. Continuous administration of LY-364947, a small molecule inhibitor of transforming growth factor-β (TGF-β) receptor kinase, into the lesion site suppressed formation of the fibrotic scar and promoted axonal regeneration beyond the lesion site, indicating that the fibrotic scar is a crucial impediment to axonal regeneration. In second, we have investigated process of the glial scar formation by using the new astrocytic lineage marker calmodulin-regulated spectrin-associated protein 1 (Camsapl). At 3 days after injury, disruption of the BBB was observed around the lesion site where GFAP-positive astrocytes were absent and Camsapl+/GFAP- cells proliferated. These Camsapl-positive cells were considered as astrocyte precursors, because these cells expressed the astrocytic transcription factors Sox2 and Sox9, the neural stem cell marker nestin, and, the glial precursor marker NG2. By 10 days after injury, Camsapl-positive astrocytes which acquired GFAP formed the glial scar around the lesion site where the BBB was reconstructed, indicating that astrocyte precursors are involved in the BBB repair through elaboration of the glial scar. Taken together, two types of the scar tissue play the distinct roles in the injured CNS; the fibrotic scar is crucial for the inhibition of axonal regeneration and glial scar is involved in the tissue healing, respectively.

G3-4 Regulation of PLD4 expression under microglial activation

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Phospholipase D1 (PLD1) and PLD2 hydrolyzes phosphatidylcholine to produce phosphatidic acid and choline, and are involved in various cellular functions including membrane trafficking, secretion and mitogenesis. Previously, we reported that the expression of a novel member of PLD family, PLD4, was specifically upregulated in amoeboid microglia in the white matter of mouse cerebellum, both in the developmental stage and the pathological conditions. In primary microglia and microglial cell line (MG6), PLD4 was markedly accumulated in nucleoplasm by LPS treatment. Experiment using siRNA suggested that increase of this protein in the nucleus was related to cell proliferation. Thus, regulation of PLD4 is one of the key event when microglia is activated by LPS. In the present study, we focused on how PLD4 expression was controlled in primary cultured microglia and in MG6 cells. Various kinase inhibitors, including those for MAPK (ERK and p-38), PI3K inhibitor and nuclear factor-kappa B (NFB) activation were added to the culture medium to modify main signaling pathways under LPS stimulation. PLD4 expression was examined at different time points. The results showed that PLD4 expression was downregulated at 15min after p-38 inhibitor was added. Increase of PLD4 mRNA and protein levels were well correlated with phosphorylated p-38 levels. Inhibition of NFB significantly suppressed PLD4 upregulation under LPS treatment. In contrast, suppression of other pathway did not influence PLD4 expression. Thus, nuclear increase of PLD4 was regulated by p-38 and NFB signaling pathways under microglial activation.

G3-5 Sema4D Promotes Oligodendrocyte Differentiation and Myelin Formation

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The specific functions of intrinsic regulators of OL differentiation are poorly understood. Sema4D, originally found as a negative regulator of axon guidance, is mainly expressed by oligodendrocytes in the postnatal brain, and our previous study revealed that the lack of Sema4D induced an increase in the number of oligodendrocytes in the cerebral cortex, suggesting that Sema4D may function as a intrinsic regulator of oligodendrocyte development and myelination. Sema4D deficiency induced an increase in the number of oligodendrocytes in the cerebral cortex at postnatal day 14 and later. Then we investigated whether Sema4D deficiency can increase the proliferation of the progenitor cells or influence the apoptosis. Apoptotic oligodendrocytes were markedly reduced in number in the developing cerebral cortex of Sema4D-deficient mice, although no significant change was found in proliferation of oligodendrocyte progenitor cells. Thus, Sema4D may act as an intrinsic inhibitory regulator of oligodendrocyte differentiation by promoting apoptosis. Furthermore, to examine whether the promoted differentiation of OLs by Sema4D deficiency affects the formation of myelin and promotes myelination during developing, we observed the myelination of optic nerve at P7 and at P28 using Electron microscope.

G3-6 Important role of plasma membrane monoamine transporters in histamine uptake by human astrocytes

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Histamine plays a pivotal role as a neurotransmitter in various physiological processes including sleep-wake cycle and appetite regulation. In addition, recent studies showed that neuronal histamine was also involved in several pathological conditions like Alzheimer,s disease and depression. Most neurotransmitters in the synaptic cleft are immediately transported through Na^+/Cl^- dependent transporters into presynaptic neurons and/or adjacent glial cells to avoid excessive neuronal activities. However, the molecular mechanism of histamine transport is far from being elucidated except that rodent astrocytes are important for extraneuronal histamine clearance. In the present study, we first examined histamine uptake in normal human astrocytes using [^{3}H]-histamine. Histamine was taken up into the cells in a time- and dose-dependent manner (Km = 3.477 mM, Vmax = 54.13 nmol/mg protein/min). Next, we examined whether histamine was transported through Na^+/Cl^- dependent transporters. The uptake of histamine was not dependent on the concentration of Na^+ or Cl^-. Histamine has been reported to be a substrate for three Na^+/Cl^- independent transporters, organic cation transporter 2 (OCT2), OCT3 and plasma membrane monoamine transporter (PMAT). Thus we investigated the inhibitory effects of tetraethylammonium (TEA) as an OCT inhibitor and decynium-22 (D22) as a PMAT inhibitor on histamine uptake. Low concentration of D22 significantly reduced histamine uptake, whereas high concentration of TEA did not have any inhibitory effect. RT-PCR analysis revealed that PMAT was most highly expressed in normal human astrocytes among three transporters. Furthermore, PMAT knockdown using siRNA resulted in a remarkable reduction of histamine uptake with a corresponding decrease in the PMAT mRNA expression. Here, we clearly demonstrated that human astrocytes had enough ability of histamine transport and PMAT played a predominant role in histamine transport of human astrocytes. These lines of evidence could indicate that histamine transport through PMAT in human astrocytes is involved in the regulation of extraneuronal histamine concentration and the activities of histeminergic neurons.

G4-1 7-Nitroindazole, a neuronal nitric oxide synthase inhibitor, attenuates the development of L-DOPA-induced dyskinesia in 6-hydroxydopamine-lesioned rats

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The dopamine precursor levodopa (L-DOPA) is an effective medicine for Parkinson's disease patients. However, the long-term L-DOPA therapy frequently induces tardive dyskinesia, which is characterized by motor fluctuations and disabling involuntary movements. Previous studies using animal models demonstrated that chronic treatment of L-DOPA caused increases in several post-synaptic signaling molecules such as ΔFosB, DARPP32 and GluR1 AMPA receptor. In addition, evidence is accumulating suggesting the role of NO in the dyskinesia: L-DOPA stimulates nitric oxide (NO) generation in the striatum, and inhibitors of neuronal nitric oxide synthase (nNOS) attenuate the expression of L-DOPA-induced dyskinesia. However, it is unknown whether NO is involved in the development of dyskinesia. The present study aimed to examine the role of NO in the development of dyskinesia in unilateral 6-hydroxydopamine (6-OHDA)-lesioned rats, a well-known hemi-Parkinsonian model. 6-OHDA was injected into the right medial forebrain bundle of rats to achieve unilateral lesions of the nigrostriatal dopaminergic system. The well-lesioned rats were screened by an apomorphine-induced rotational test, and then administrated with L-DOPA for 3-4 weeks to induce dyskinesia symptoms. Daily repeated treatments of a broad-spectrum NOS inhibitor N^G-nitro-L-arginine methyl ester and a specific nNOS inhibitor 7-nitroindazole, but not a specific inducible NOS inhibitor aminoguanidine, prior to L-DOPA administration significantly attenuated the development of dyskinesia. Chronic treatment of 7-nitroindazole also inhibited the L-DOPA-induced increases in ΔFosB, phospho-DARPP32 and phospho-GluR1 AMPA receptor levels in 6-OHDA-lesioned rats, without affecting dopamine and its metabolite levels in the midbrain. These findings suggest that NO derived from nNOS may play a key role in the development of chronic L-DOPA administration-induced dyskinesia through the post-synaptic mechanisms.

G4-2 GAPDH aggregate accelerates fibrillation of amyloid-β

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Glyceraldehyde-3-phosphate dehydrogenase (GAPDH), a classic glycolytic enzyme, is implicated in etiology of Alzheimer's disease, which is characterized by deposition of amyloid-β (Aβ) fibril formation in pathological lesions such as the diffuse and senile plaques. It has been reported that GAPDH aggregate presents around these lesions, as well as co-localizing with plaque-like structures in these lesions. We have previously discovered that formation of GAPDH aggregate participates in neuronal cell death (Nakajima *et al.*, *J. Biol. Chem.* at 2007 and 2009). Additionally, GAPDH is shown to be secreted extracellulary. These findings lead us to hypothesize that GAPDH aggregate acts as a seed of amyloid-β fibril formation. In the present study, we investigated whether GAPDH aggregate accelerates amyloid-β fibril formation. The intensity of Thioflavin-T, the amyloid-binding dye, fluorescence was increased fast when Aβ (1-40) was incubated with GAPDH aggregate. We calculated the $T_{1/2}$, the half point of the day that all Aβ (1-40) formed amyloid fibril. The $T_{1/2}$ of Aβ (1-40) amyloid fibril formation shows 3.9 days, whereas the $T_{1/2}$ with GAPDH aggregate shows 1.6 days. To analyze the amyloidal structure morphologically, the samples at 2-day incubation were stained with Congo red. The Congo red birefringence was emerged when Aβ (1-40) was incubated with GAPDH aggregate, whereas the Congo red birefringence in Aβ (1-40) alone had been unchanged. To assess the effects of GAPDH aggregate on Aβ (1-40) amyloid fibril formation in details, atomic force microscopy was employed. The images showed that GAPDH aggregate accelerated fibrillation of Aβ (1-40) in a concentration-dependent manner. Taken together, these data suggest that GAPDH aggregate acts as a seed of amyloid-β fibril formation. We are going to investigate the effect of GAPDH aggregate on Aβ-induced cell death in PC12 cells.

G4-3 The I2020T LRRK2 transgenic mouse exhibits impaired locomotive ability accompanied by characteristic features of dopaminergic neurons

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Aim: *Leucine-rich repeat kinase 2 (LRRK2)* is the gene responsible for autosomal-dominant Parkinson's disease (PD). We have found an I2020T mutation in the kinase domain of LRRK2 in a Japanese PD family (the Sagamihara family). To elucidate the etiology of PD caused by I2020T LRRK2, we created a transgenic (TG) mouse model.Methods: Locomotive ability was examined using the beam test, rotarod test, and cylinder test. Behavioral characteristics were assessed by the open field test. Olfactory function was examined by the hidden prey test. Immunostaining of the TG brain was performed for tyrosine hydroxylase (TH), phosphorylated tau, phosphorylated α-synuclein, and Golgi apparatus. An *in vitro* microtubule-polymerization assay was carried out using the assembly/disassembly method. Striatal dopamine content was measured by HPLC. Apoptotic cells in primary neuron culture were detected using the TUNEL method.Results: The TG mouse expressed I2020T LRRK2 in TH-positive dopaminergic (DA) neurons of the substantia nigra, ventral tegmental area, and olfactory bulb. In both the beam test and rotarod test, the TG mice exhibited impaired locomotive ability in comparison with their non-transgenic littermates. In the cylinder test, on the other hand, TG mice showed a rather high rearing frequency, although they behaved normally in the open field test and exhibited a normal sense of smell in the hidden prey test. Although there was no detectable loss of DA neurons in either the substantia nigra or striatum, the TG brain showed several characteristic features such as a reduced striatal dopamine content, fragmentation of the Golgi apparatus in DA neurons, and increased degree of microtubule polymerization. Furthermore, the primary neurons of the TG mouse showed an elevated frequency of apoptosis. On the other hand, immunostaining and Western analysis of the TG brain showed no particular pattern of phosphorylated tau or α-synuclein. Conclusion: We have established a TG mouse line expressing I2020T LRRK2, which exhibits impaired locomotive ability and several characteristic features of DA neurons. The TG mouse should provide valuable clues to the etiology of PD caused by the LRRK2 mutation.

G4-4 Alterations in local thyroid hormone metabolism in the young senescence-accelerated SAMP8 mice: association with delayed myelination and behavioral abnormalities

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The senescence-accelerated mouse (SAM) strains which consist of senescence-prone (SAMP) and senescence-resistant (SAMR) strains have been established through selective inbreeding of the AKR/J strain based on phenotypic variations of accelerated aging. Among them, SAMP8 strain shows age-related deficits in learning and memory with AD-like characteristics. Since thyroid disorders have been linked to various psychiatric and neuropsychological disorders including learning deficits, impaired attention, anxiety and depression, we examined whether brain thyroid hormone (TH) metabolism is involved in the pathological aging of SAMP8 mice. Compared with the senescence-resistant SAMR1 mice at different ages (1, 3, 5, 8 & 10M), SAMP8 mice showed progressive deficits in learning and memory in the passive avoidance test starting at 5M of age as well as hyperactivity at 1, 3, 5 & 8M and lower anxiety at 3 & 5M in the open-field test. Plasma levels of thyroxine as well as thyroid stimulating hormone were comparable in both strains at all time points, indicating that the overall thyroid status was not altered in SAMP8. However, the expression of TH metabolizing enzymes in the hippocampus showed significant differences between the two strains. In SAMP8, deiodinase 2 which converts T4 into active T3 was down-regulated at 1, 3, 5 & 8M, while T3-degrading enzyme deiodinase 3 tended to be up-regulated. Expression of the two known TH-dependent genes was significantly down-regulated in SAMP8; *hairless* at 1, 3 & 5M, and *myelin basic protein (mbp)* at all time points. MBP protein was further confirmed immunohistochemically to be decreased at 1, 3 & 10M in the SAMP8 hippocampus. The results thus suggest a decrease in active T3 leading to delayed myelination in the young SAMP8 and earlier onset of myelin loss in the aged SAMP8 hippocampus. Alterations in local TH metabolism may thus underlie behavioral abnormalities as well as the pathological aging of SAMP8.

G4-5 Possible involvement of ubiquitin ligase RNF19B and Dorfin in amyloid-β production

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Amyloid-β (Aβ) oligomers are toxic to neuronal cells. The amyloid precursor protein (APP) is cleaved by β-secretase to generate C-terminal fragment β (CTFβ), which in turn is cleaved by γ-secretase to generate Aβ. Alternative cleavage of APP by α-secretase generates CTFα, which is cleaved by γ-secretase to generate P3. Misfolded proteins in the endoplasmic reticulum (ER) lumen are exported to the cytosol, where they are degraded by the ubiquitin-proteasome system. This process is called ER-associated degradation (ERAD). Several ubiquitin ligases (E3) are involved in ERAD. Our previous studies have shown that HRD1, an E3 involved in ERAD, suppresses Aβ production by promoting APP ubiquitination and degradation. In this study, we investigated the possible involvement of RNF19B and Dorfin/RNF19A, which are similar in sequence and may be involved in ERAD, in Aβ production. In WtAPP-stable SH-SY5Y cells, which show stable overexpression of wild-type APP, inhibition of HRD1 expression caused an increase in Aβ levels, while that of RNF19B and Dorfin expression caused a decrease in Aβ levels. In normal Neuro2a cells, inhibition of HRD1 expression did not affect Aβ levels, whereas that of RNF19B and Dorfin expression induced a decrease in Aβ levels. These results suggest that RNF19B and Dorfin are involved in Aβ production through a mechanism different from that of HRD1. To investigate the involvement of RNF19B and Dorfin in the production of Aβ, we determined CTFα and CTFβ levels in SweAPP-stable SH-SY5Y cells, which show stable overexpression of the Swedish mutant form of APP. When RNF19B and Dorfin expression were inhibited, CTFα and CTFβ levels increased, indicating that cleavage of CTFα and CTFβ by γ-secretase is inhibited because of decreased RNF19B and Dorfin expression. Taken together, we suggest that the decrease in Aβ levels caused by decreased RNF19B and Dorfin expression is due to the inhibited cleavage of CTFβ by γ-secretase.

G4-6 Donepezil reduces phosphorylation levels of tau protein in cellular model of tauopathy

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Neurofibrillary tangle (NFT) is the pathological hallmark of Alzheimer's disease (AD). Hyperphosphorylated tau is major constitute of NFT. Donepezil hydrochloride is a potent acetylcholinesterase inhibitor, which is widely used for the improvement of cognitive function in AD. Recently, it was disclosed that the AD patients who underwent donepezil for a long period showed slowing of the disease progression. But the mechanisms are not yet clear. M1C cells that express wild type human brain tau (4R0N) via Tetracycline Off induction (Ko et al., J Alzheimers Dis 2004; Hamano et al., Eur J Neursci 2008) were treated with 0.1 to 10 μM of donepezil for 24 h. The levels of total and phosphorylated tau were examined before and after donepezil treatment by Western blotting and immunocytochemistry. We have found that 0.1 to 10 μM of donepezil reduces tau phosphorylation levels by Western blot analysis, as well as immunocytochemical study. Although the mechanisms responsible for the reduction of phosphorylation levels of tau protein by donepezil require further examination, this report sheds light on the possible therapeutic approaches to tauopathy.

G5-1 Transplantation of mouse neural stem cells derived from ES cells to dorsal hippocampus of epileptic mutant EL mice

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Recently we have established a simple technique, the Neural Stem Sphere (NSS) method, which can induce unidirectional differentiation of ES cells into neurons via neural stem cells (NSCs) *(Neurosci. Res., 46, 241-249, 2003)*. EL mice show secondary generalized seizures, which initiate primarily at parietal cortex and generalize through hippocampus. At the age of 20 weeks, when EL mice show seizures automatically, the narrow pocket-like region of low glutamate decarboxylase (GAD) levels was formed in the parieto-temporal area. The purpose of the present study is to examine whether transplanted NSCs differentiate inhibitory neurons and play the role of antiepileptic effects in EL mice. NSCs were prepared from mouse ES cells by the NSS method and the cells were proliferated with bFGF or induced to differentiate into neurons with astrocyte conditioned medium (ACM) *(Neuroreport, 15, 487-491, 2004)*. The proliferating NSCs (NSCs) or NSCs induced to neuronal differentiation for 1 day (nNSCs) were harvested from dishes and suspended in phosphate buffered saline. The head of the EL mouse exhibiting seizures was placed in a stereotaxic device, and one micro liter of suspension of the NSCs or nNSCs ($2x10^5$ cells each) were injected into dorsal hippocampus bilaterally. Control mice were sham operated and transfused with the vehicle only. Four weeks after, it was checked that seizures were controlled or not by seizure induction. Transplanted groups, EL mice transplanted with NSCs or nNSCs, showed no seizure at all, in contrast vehicle control group showed grandmal tonic clonic seizures. These results suggest that in the field of focus complex area, hippocampus, in EL mice may have the capacity to induce differentiation of NSCs into inhibitory neurons. This work was partly supported by Selective Research Fund of Tokyo Metropolitan University.

G5-2 PACAP regulates dendritic spine morphology

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Pituitary adenylate cyclase-activating polypeptide (PACAP) is a multifunctional neuropeptide with activities including neurotransmission, neural plasticity, and neurotrophy. We have reported that PACAP-deficient (PACAP-/-) mice display remarkable behavioral and neurological abnormalities including hyperactivity, depression-like behavior, deficits in prepulse inhibition (PPI), and memory impairment, most of which were reversed by the atypical antipsychotic drug risperidone, and that SNPs in the PACAP gene was associated with schizophrenia. These results suggest a convergent role of PACAP in the regulation of neuropsychological functions. However, the underlying molecular mechanism remains to be elucidated.In order to address this issue, we have recently examined PACAP-induced neuritogenesis in primary cultured neurons, and observed that PACAP stimulates early neuritogenesis, with a concomitant increase in mRNA expression levels of Egr-1, a transcription factor implicated in neuronal differentiation. In the present study, we therefore examined the role of exogenous and endogenous PACAP in the dendrite formation and the maturation of dendritic spines. PACAP increased the size and density of PSD-95-labeled synaptic puncta in primary cultured hippocampal neurons. Interestingly, the volume of PSD-95 puncta was decreased in PACAP-/- mice compared with wild-type mice. Golgi staining of hippocampal CA1 neurons in PACAP-/- mice at 8 weeks of age revealed that spine density was reduced and their morphology was atypical in PACAP-/- mice. These results indicate that PACAP is critically implicated in spine formation and that dysfunction of PACAP signaling may contribute to the pathogenesis of psychiatric disorders.

G5-3 Histological profile of synaptic matrix metalloproteinase activity in the mouse hippocampus

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Structural plasticity of synapses is thought to be an important process for learning and memory. Recent analyses have demonstrated that the efficiency of synaptic functions depends on the shape and size of synaptic structures. In such studies, rapid remodeling of synaptic connections is postulated to be dependent on the activity of extracellular matrix proteins and/or cell adhesion molecules. We hypothesized that molecules which are cleaved by proteinases at the synapse of the hippocampus during an animal's learning behavior might induce dynamic changes in synaptic morphology, and hence affect long-term potentiation in the Schaffer-collateral pathway. To test this hypothesis, we examined the local activity of matrix metalloproteinases (MMPs) at the hippocampal synapse, using high-resolution fluorescent *in situ* zymography in thin sections of polyester wax-embedded mouse brain tissue. Successful staining patterns were obtained, with excellent preservation of fine structural detail. Gelatinolytic activity of MMPs, determined using dye-quenched gelatin as a substrate, was observed as a fine fluorescent punctate profile indicative of active synaptic MMPs. In addition, intraperitoneal injection of kainic acid, which induces neural hyperexcitation, caused an increased number and intensity of fluorescent punctate structures in the CA1 area of the hippocampus. Double staining of spine markers by immunostaining and MMPs by *in situ* zymography showed that MMPs was localized in the synaptic spines. These observations of neural activity-dependent changes in MMP activity in the synapse, particularly that of MMP9, suggest an involvement of metalloproteinases in structural synaptic plasticity.

G5-4 The molecular mechanism of SNAP-25 dephosphorylation in mouse brain

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Synaptosomal-associated protein-25(SNAP-25) plays essential role in neurotransmitter release by exocytosis as a t-SNARE protein at presynaptic membrane. SNAP-25 forms complex (SNARE complex) with syntaxin and VAMP-2, the complex causes fusion of synaptic vesicle membraine and presynaptic membrane. It is revealed that the exocytosis of neurotransmitter is facilitated in endocrine cell through a protein kinase C–dependent phosphorylation of SNAP-25 at Ser187, however, the mechanisms of dephosphorylation are not yet clarified. In the present study, we examined the dephosphorylation mechanism by using crude synaptosomal preparation (P2 membrane) of mouse brain and living mice under a stress. The phosphorylation level of of SNAP-25 in synaptosomes increased remarkably after a treatment of PDB. Ionomycin treatment caused a reduction of the phosphorylation level in a time-dependent manner. In living mice, restraint stress induced a facilitation of SNAP-25 phosphorylation in cereberal cortex and hippocampus, and dephosphorylation was induced after the mouse came back to their home cage. Intraperitoneal administration of FK506, a potent inhibitor of calcineurin, 30 minutes prior to the restraint stress markedly induce a dephosphorylation of SNAP-25. All of these results indicate that calineurin was involved in dephosphorylation of SNAP-25 in mouse brain.

G5-5 The effect of antipsychotics on interneurogenesis of adult neural stem cells

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Currently hypothesis focused on the progressive morphological brain changes in schizophrenia, especially on the relation to the altered GABA neurotransmitter system and density of GABA interneurons.In the previous study, we investigated the effects of recently developed atypical antipsychotics on the neural stem cell (NSC) function change especially focusing on the neuronal differentiation prepared from rat embryos. The atypical antipsychotics have shown the suppressive effects on the non competitive NMDA receptor antagonist MK-801-induced inhibition of NSC differentiation to neurons, indicating that atypical antipsychotics-induced alteration of neurogenesis could contribute to the neural network repair impaired in the schizophrenic brain. In the present work, we examined the effect of atypical antipsychotics against MK-801/GABAA antagonist-induced impairment of NSC differentiation to neurons those considered parallel observations in the pathophysiology of schizophrenia, using cultured adult hippocampal and subventricular zone (SVZ)-derived NSCs, and analyzed its characteristic change of neuronal phenotype differentiation. Several antipsychotics suppressed the MK-801/GABAA antagonist-induced inhibition of neuronal differentiation of adult NSCs. Their promotions of each neuronal phenotype differentiations were different among tested antipsychotics. The results suggested that the increase of adult interneurogenesis by antipsychotics might be involved in the mechanism of recovering of the neural network change in schizophrenia and the different proportion of each antipsychotic-induced cell phenotype differentiation of NSCs might relate to its characteristic of clinical efficacy in the treatment of schizophrenia.

G5-6 *Radiosensitivity of X-irradiated neural stem cells* in logarithmic growth phase: Proliferation, cell cycle regulation, apoptosis, and DNA repair

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Radiation exposure in a developing fetal period is known to cause neuronal disorders, such as microcephaly and mental retardation, which are considered mainly due to the radiation damage produced in neural stem cells (NSCs). NSCs, which are the dominant number in the fetal brain, have an ability to proliferate themselves, and to differentiate into other cell types that construct the central nervous system (CNS), such as neurons, astrocytes, and oligodendrocytes. Our aim is to clarify the cellular and molecular responses of NSCs against ionizing radiation. In this presentation, we will focus on the radiation sensitivity related to cell inactivation of NSCs in growth phase. Following biological endpoints were measured to demonstrate the radio-sensitivity of NSCs: maintenance of their ability to proliferate as NSCs, growth curve, cell cycle regulation, apoptosis, and DNA double strand break repair. The NSCs, derived from embryonic stem cells (HK) of C57BL/6 mice using Neural Stem Sphere method, were irradiated up to 10 Gy by 200 kVp X-ray. Growth curve were measured up to 4 days after irradiation. Cell cycle analysis was performed flow cytometry to detect G1 and G2/M arrest. Poly ADP ribose polymerase (PARP) were used as a marker for apoptosis induction and detected with western blot analysis. Growth delay, cell cycle arrest and cleaved PARP were detected with 1 Gy irradiation. DNA double strand break and its repair were observed by immunostaining against phospholyrated H2AX, and fluorescence of the γ-H2AX decreased after irradiation, indicating its repair. As a conclusion, 1 Gy irradiation induced growth delay, cell cycle arrest, and apoptosis induction. These results may indicate that NSCs in growth phase are highly sensitive compared to other well-known somatic cells.

Graduate Oral Sessions

G6-1 A novel method to quantify brain cells using flow cytometer and a study of the postmortem brains from patients with major depressive disorder

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Recent postmortem brain studies of major depressive disorders revealed neuronal and oligodendroglial abnormalities. Stereological methods were usually used to estimate the number of cells in discrete brain regions. However, stereological methods are laborious and intrinsically low throughput, taking typically long periods to complete a large study. We therefore developed a novel quantitative cell-counting method for unfixed, frozen postmortem brains using a flow cytometer. Anisotropic brain tissue was transformed into an isotropic suspention of nuclei and immunostained with nuclear (7-AAD), neuronal (NeuN), and oligodendroglial (olig2) markers. This method was able to count stained nuclei and measure quantitatively their sizes and fluorescence intensities. In our flow cytometry measurement, the number of total (7-AAD(+)) and NeuN(+) nuclei were comparable in the number of total and neuronal cells from the whole rat cerebral cortex reported by others (Herculano-Houzel and Lent. J Neurosci 2005; 25:2518-2521). We then applied this method to frozen unfixed postmortem human brains. The entire gray matter of the frontopolar and inferior temporal cortex from patients with major depressive disorder (frontopolar cortex, n=10; inferior temporal cortex, n=11) and normal controls (frontopolar cortex, n=12; inferior temporal cortex, n=12) were analyzed. Most of the available confounding factors were matched between the groups. We found significant reductions of the number of oligodendrocyte lineage cells in the frontopolar cortex of major depressive disorders, but no significant differences were found in the inferior temporal cortex. These findings suggest that the pathogenesis of major depressive disorders may involve some abnormalities in cortical myelination in the frontopolar cortex.

G6-2 Activation of both σ_1 and 5-HT_{1A} receptors enhances prefrontal dopamine release in adrenalectomized/castrated mice

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Fluvoxamine acts as not only a selective serotonin (5-HT) reuptake inhibitor (SSRI), but also a σ_1 receptor agonist. We have previously found that fluvoxamine increases extracellular levels of dopamine (DA), noradrenaline (NA) and 5-HT in the prefrontal cortex (*Neuropsychopharmacology*, 2005), but it is not known whether σ_1 receptors are involved in the neurochemical effect of fluvoxamine. In view of the fact that circulating steroids exert a tonic modulatory effect on σ_1 receptor-mediated effects, we have recently examined the effects of fluvoxamine on prefrontal extracellular monoamine levels in adrenalectomized/castrated (AdX/CX) mice lacking the peripheral sources of steroids. Fluvoxamine increased prefrontal DA, NA and 5-HT levels in sham-operated mice, but these effects were not affected by pretreatment with a selective σ_1 receptor antagonist. The increasing effect of fluvoxamine on extracellular levels of DA, but not of 5-HT and NA, was enhanced by AdX/CX, and this was completely blocked by a selective σ_1 receptor antagonist. These studies suggest that SSRI with σ_1 receptor activation increases prefrontal DA release under circulating steroids-deficient conditions (*Psychopharmacology*, 2011). However, the receptor mechanism for fluvoxamine-induced increase in prefrontal DA release is not known. The present study addressed on this point using 5-HT receptor antagonists such as WAY100635 (5-HT_{1A}), ritanserin (5-HT_2) and azasetron (5-HT_3). We found that the increasing effect of fluvoxamine on DA release in AdX/CX mice was blocked by pretreatment with WAY100635. The finding suggests that activation of both σ_1 and 5-HT_{1A} receptors enhances prefrontal dopaminergic neurotransmission preferentially under circulating steroids-deficient conditions.

G6-3 Mechanisms underlying fluoxetine-evoked increase in BDNF in hippocampal astrocytes

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Many lines of evidence show that astrocytes regulate various neuronal functions, and thus, their dysfunctions could be involved in various brain diseases. Although psychotropic drugs should act on glia cells, affect glial functions and may reveal their therapeutic actions, little is known about their effect on glial cells. Brain derived neurotrophic factor (BDNF) has emerged to be involved in depression. In addition to inhibition of serotonin-uptake, antidepressants SSRIs increase BDNF levels in neurons, which is thought to be one of the molecular mechanisms underlying therapeutic effect of SSRI. Here we showed that fluoxetine, a typical SSRI, upregulates BDNF in astrocytes *in vitro* and *in vivo*. When stimulated with fluoxetine, cultured astrocytes upregulated both mRNAs and protein of BDNF in a concentration-dependent fashion. The fluoxetine-evoked BDNF production was independent of serotonin, but was dependent on extracellular ATP, a typical gliotransmitter, and adenosine, a metabolite of ATP. Fluoxetine increased extracellular ATP concentration in astrocytes. The fluoxetine-evoked increase in BDNF was mimicked by exogenously applied ATP and adenosine, and was inhibited by antagonists of both P2 and P1 receptors. Using more elaborate pharmacological approach, we revealed that the responsible receptors for the BDNF production were P2Y11 and adenosine A2b receptors. As for intracellular signaling cascades, we found that PKA-mediated phosphorylation of CREB was important for the BDNF upregulation. We also found that when administered chronically, fluoxetine upregulated BDNF in hippocampal astrocytes. Given that a number of astrocytes is considered to be 10 times higher than that of neurons, astrocytes serve as an important source of BDNF. Taken together, we demonstrate that fluoxetine acting on astrocytes enhances the main gliotransmitter ATP-mediated pathways to increase BDNF. This could be a new pharmacological profile of fluoxetine, which might be involved in its therapeutic effects.

G6-4 Lithium inhibits methamphetamine-induced hyperactivity and behavioral sensitization via modulation of prefrontal dopamine and serotonin release in mice

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Lithium is currently used for the treatment of manic symptoms and long-term stabilization of mood in bipolar disorder. Lithium attenuates psychostimulant-induced hyperactivity and behavioral sensitization, but the exact mechanisms are not known. This study examined whether prefrontal monoaminergic neurotransmission is involved in the effects of lithium on methamphetamine-induced behavioral alterations in mice. Lithium at doses of 30 and 100 mg/kg inhibited methamphetamine (1 mg/kg)-induced hyperactivity in a dose-dependent manner. Lithium (100 mg/kg) also attenuated methamphetamine-induced increase in extracellular dopamine, but not serotonin (5-HT), levels in the prefrontal cortex. Repeated administration of methamphetamine (1 mg/kg) caused the enhancement of methamphetamine-induced hyperactivity (behavioral sensitization) and increase in prefrontal 5-HT release (neurochemical sensitization). Co-administration of lithium (100 mg/kg) with methamphetamine attenuated behavioral sensitization and neurochemical sensitization. The repeated methamphetamine also reduced the 5-HT_{1A} receptor agonist osemozotan-induced decrease in prefrontal 5-HT release, suggesting the desensitization of presynaptic 5-HT_{1A} autoreceptors. This desensitization was reversed by co-treatment with lithium (100 mg/kg). These results suggest that lithium attenuates methamphetamine-induced hyperactivity via an inhibition of the prefrontal dopamine release and also attenuated behavioral sensitization via an increase in the 5-HT release in a 5-HT_{1A} receptor-mediated mechanism.

G6-5 Localization of neural cell adhesion molecule Caspr3 at the basal ganglia in mice

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It has been well documented that neural cell adhesion molecules play important roles in cell-cell recognition, adhesion or dissociation, and reciprocal induction during development of the nervous system. Among these molecules, Caspr (Contactin associated protein) family which belongs to neurexin superfamily is composed of five members: Caspr, Caspr2, Caspr3, Caspr4 and Caspr5. Caspr and Caspr2 play essential roles in formation and maintenance of myelinated nerves via interaction with Contactin and TAG-1, respectively. By contrast, the localization and function of Caspr3, Caspr4, and Caspr5 remain unclear.
To elucidate the localization of Caspr3, we produced the monoclonal antibody against the extracellular domain of Caspr3 by the rat lymph node method. The antibody yielded strong signals in the brain section of wild-type mice, whereas no signal was detected in Caspr3-deficient mice. This indicates that the antibody specifically reacted with Caspr3. Then, we analyzed the developmental change of Caspr3 expression by Western blotting of mouse brain lysate using this antibody. The expression of Caspr3 was detected at the embryonic stage, reached its peak between first and second week after birth, and decreased thereafter. Then we examined the Caspr3 immunoreactivity in the mouse brain at postnatal days 7 and 14. Caspr3 was expressed in the cerebral cortex, olfactory bulb, hippocampus, cerebellum, and especially highly in the basal ganglia. The basal ganglia with complicated structure have various functions such as adjusting movement, emotion, motivation, and learning. However, the molecular mechanism underlying the development of the basal ganglia is largely unknown. Then, we stained the basal ganglia with double immunofluorescence using antibodies against Caspr3 and marker proteins. The results indicate that Caspr3 was localized in both direct and indirect pathways of the basal ganglia. From these results, Caspr3 may play important roles in development of the basal ganglia during the early postnatal days.

G6-6 Analysis of the interaction between neural recognition molecule NB-3 and receptor protein tyrosine phosphatase γ

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Contactins are a subgroup of molecules belonging to the immunoglobulin superfamily that are exclusively expressed in the nervous system, consisting of six members (Contactin, TAG-1, BIG-1, BIG-2, NB-2 and NB-3). We have reported that NB-3 plays important roles in the synapse formation of the cerebellum and hippocampus. It was recently reported that four members of Contactins including NB-3 interact with the receptor protein tyrosine phosphatase γ (RPTPγ) *in vitro*. It is well known that the receptor protein tyrosine phosphatases (RPTPs) have an important role in cell survival, differentiation, migration and other cellular processes in conjunction with protein tyrosine kinases. The type R5 RPTP consists of RPTPζ and RPTPγ and contains a carbonic anhydrase-like domain and a fibronectin type III-like domain in the extracellular domain, and two tandem tyrosine phosphatase domains in the intracellular domain. While RPTPζ has been reported to be involved in various functions, the localization and function of RPTPγ remain largely unknown. In this study, we examined the interaction between RPTPγ and NB-3 and the possible co-localization of these two molecules in the mouse brain. First, we confirmed the interaction of RPTPγ with NB-3 by cell surface binding assay. Next, to reveal the distribution of RPTPγ in the mouse brain, we performed in situ hybridization. RPTPγ mRNA was expressed in the olfactory bulb, cerebral cortex, hippocampus, amygdala, piriform cortex and entorhinal cortex, where NB-3 mRNA was also expressed, indicating that RPTPγ and NB-3 may be co-localized at these area. In order to examine the localization of RPTPγ, we generated anti-RPTPγ monoclonal antibodies. Immunohistochemical staining showed that RPTPγ and NB-3 proteins were both localized in the cerebral cortex, hippocampus, thalamus, inferior colliculus and cerebellum. Furthermore, double immunofluorescence using antibodies against RPTPγ and NB-3 revealed that RPTPγ-positive signals were overlapped with NB-3 immunoreactivity in the molecular layer of the cerebellum. These data suggested that NB-3 might interact and function with RPTPγ in the mouse brain.

G7-1 Encounter with an unfamiliar mouse increases prefrontal neuronal activity with dopamine and serotonin release in isolation-reared mice

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Mice reared in post-weaning social isolation exhibit several abnormal behaviors including aggressive behaviors. The aggressive behavior is induced by an intruder, but the neurochemical basis for the interaction with an intruder is not known. The present study examined the effect of encounter with an unfamiliar mouse on neuronal activity in the brain of group- and isolation-reared mice. Three-week-old male ddY mice were housed either in groups of 5-6/cage or isolated in the same-sized cage for 6 weeks before the experiments. A group- or isolation-reared mouse was placed in a novel clear Plexiglas cage which was divided in two compartments by a mesh partition allowing the mouse to visual, auditory and olfactory stimulation, without physical contact. After a 3-h habituation, an unfamiliar mouse (nine-week-old male ddY mice) was placed into the unoccupied compartment for 20 min. The encounter-induced increase in the expression of c-Fos, a neuronal activity marker, was observed only in the nucleus accumbens shell in group-reared mice, while it was observed in nucleus accumbens shell and prefrontal cortex in isolation-reared mice. The encounter also increased prefrontal dopamine and serotonin release in the prefrontal cortex in isolation-reared mice, but it did not affect the amine release in group-reared mice. When the unfamiliar mouse was pretreated with pentobarbital, the encounter did not affect prefrontal dopamine and serotonin release in isolation-reared mice. The prefrontal excitability in response to the encounter was inhibited by the anxiolytic diazepam in isolation-reared mice. These findings suggest that encounter with an unfamiliar partner affects presynaptic monoaminergic function in the prefrontal cortex of isolation-reared mice, and imply that these changes reflect the neurochemical aspects of abnormal behaviors of isolation-reared mice.

G7-2 Social crowding during the nocturnal period produces anxiolytic- and antidepressant-like effects in mice

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Environment in early life affects psychological behaviors in adulthood. Environmental stress, such as maternal separation or social isolation during development, can induce a variety of behavioral abnormalities including increased aggressiveness, anxiety-related behaviors and hyperlocomotion. On the other hand, the effect of the condition reared in social environment on the behaviors is not known. The present study examined the effect of rearing in social crowding during the nocturnal period (active in rodents) on emotional behaviors, motor performance and learning and memory in mice. Four-week-old male ICR mice were housed in clear plastic cages (24 × 17 × 12 cm^3) in groups of 4 animals under controlled environmental conditions (22 ± 1 °C; 12:12-h light-dark cycle, lights on at 08:00 h; food and water) *ad libitum*). During 20:00 h-10:00 h, the mice for the social crowding group were housed in groups of 20 animals in opaque polypropylene cages (24 × 17 × 12 cm^3), while the control group were housed in groups of 4 animals in same-sized clear plastic cages. Two weeks after the social crowding, the behavioral experiments were performed. Mice reared under the social crowded condition during the nocturnal period showed the decrease in body weight gain and the increase in adrenal weight. The spontaneous locomotor activity in the open-field test and the learning and memory performance in the fear conditioning test did not differ between social crowding-reared and control mice. On the other hand, the social crowding increased the open-arm entries and time spent in open arms in the elevated plus-maze test and decreased immobility time in the forced swim test. These findings suggest that the social crowding during the nocturnal period produces anxiolytic- and antidepressant-like effects in mice.

G7-3 Measurement of biomarkers for physical and mental fatigue in animal model

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Fatigue is considered to be associated with oxidative stress. Therefore, biomarkers for oxidative stress may be available for those of fatigues. There are many biomarkers for oxidative stresses have been found in several tissues; 8-hydroxy-deoxyguanosine (8-OHdG), L-carnitine, isoprostanes, TBARS, protein carbonyls, catalase, glutathione peroxidase, and oxidized and reduced glutathiones etc., including reactive oxygen species. However, it is less known whether biomarkers for oxidative stress are useful for physical and/or mental fatigues using body fluids from humans or experimental animals. In the present study, we examined whether those biomarkers are available for both fatigues after loading of physical or mental stress, compared with 8-OHdG or c-fos expression as authentic markers. We also tried to investigate that it is possible to distinguish between physical and mental fatigue using oxidative stress biomarkers. This study (No.22500614) is supported by Grant-in-Aid for Scientific Research (KAKENHI); Grant-in-Aid for Scientific Research(C) in 2010 and 2011.

G7-4 Identification of the determinant sites of Gi/o coupling by rat melanin-concentrating hormone receptor 1

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Melanin-concentrating hormone (MCH) receptor 1 (MCHR1) is a G-protein coupled receptor that is highly expressed in central nervous system. MCH-MCHR1 system plays important roles of regulation in food intake and emotional processing. Although knowledge concerning the structure-activity relationship of mammalian MCHR1 can provide a comprehensive list including ligand binding, there is no insight into selectivity mechanisms between mammalian promiscuous MCHR1 and different subtypes of G&alpha proteins. Our previous studies have shown that the signaling properties of goldfish MCHRs are quite different from mammalian MCHRs. That is, mammalian MCHR1 couples to both Gi/o and Gq, whereas goldfish MCHR1 exclusively couples to Gq. Therefore, we take advantage of our experience and try to identify amino acid residues of rat MCHR1 that is specifically responsible for Gi/o coupling. We first performed sequence alignment between mammalian and goldfish MCHR1, and systematically designed a series of substituted mutants. Next, using transiently transfection into HEK293T cells, the amounts of receptor expression and glycosylation pattern of mutations were examined by Western blotting. We further analyzed the effect of mutations on Gi/o activity in calcium mobilization with Gi/o-sensitive pertussis toxin, and then judged by Gi/o-dependent GTP&gammaS-binding assay. The mutant at a membrane-proximal site of the third intracellular loop and helix 5, exhibited significantly reduced GTP&gammaS-binding. Proximal region of helix 8 is also found to be required for Gi/o activation. These mutant receptors are not only useful tools for determining specific signal transduction pathway, but they also have the potential to be developed into a biased agonist/antagonist.

G7-5 Phosphorylation at Ser847 of nNOS regulates NO-ROS signaling in neurons

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[Background] Nitric oxide synthases (NOS) generate NO from arginine and produce reactive oxygen species (ROS). It has been proved that NO generation by neuronal NOS (nNOS) are reduced through the phosphorylation at Ser847. We have already reported that phosphorylation increases the uncoupling efficiency. However, the physiological effects of the phosphorylation remain unclear. In the present study, in order to reveal the effects of the phosphorylation on the NO-ROS signaling in neurons, we prepared a phosphorylation-mimic mutant (Ser847 to Asp) of nNOS and examined the enzyme activities *in vitro* and the NO-ROS signaling in PC12 cells and rat cerebellar granule neurons (CGNs), including the formation of 8-nitro-cGMP which is downstream molecule of NO-ROS signaling.
[Method] We produced the mutant nNOS gene (847D); the gene was overexpressed in *E. coli* and purified on ADP-Sepharose. We determined the nNOS activities, including NO and ROS production, NADPH oxidation, and uncoupling efficiency. Further, we generated the 847D-expressing PC12 cells, detected the intracellular activities, and examined the generation of 8-nitro-cGMP in the cells treated with nicotine. Then, we determined nicotine-induced ROS and 8-nitro-cGMP generation in CGNs.
[Result] *In vitro*, the NO and ROS production rates of 847D reduced by 24% and increased by 110% as compared to the wildtype (WT), respectively. The NADPH oxidation activity of 847D increased by 32%. The uncoupling efficiency of WT and 847D was 49% and 62%, respectively. We confirmed that the intracellular nNOS activity of 847D exhibited a tendency similar to the above-mentioned results when compared with the WT in PC12 cells. By immunostaining using an 8-nitro-cGMP-specific antibody, we observed strong immunoreactivity only in nNOS-expressing cells; the fluorescent intensity in 847D-expressing cells was greater than that in WT-expressing cells. We detected nicotine-induced ROS and 8-nitro-cGMP production in CGNs. These activities were diminished by the pretreatment of CGNs with a CaMK inhibitor. These results suggested that nNOS regulates NO-ROS signaling, including 8-nitro-cGMP, in neurons via phosphorylation at Ser847.

G7-6 Development of a feasible method to assess serotonergic differentiation from mouse embryonic stem (ES) cells: implication of inhibition of bone morphogenetic protein (BMP) type I receptor kinases

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Serotonergic systems are critically involved not only in many aspects of brain function, but also in neuropsychiatric disorders; however, the underlying mechanisms are largely unknown. This is partly because very few serotonergic neurons exist in the brain (~ 20,000 neurons in the rat) that hampers the study *in vivo* and *in vitro*. We have recently found that mouse ES cells differentiate into serotonergic neurons when cultured on Matrigel with noggin, an antagonist of BMP and a neural-inducing factor in the Spemann organizer. This protocol is composed of a simple, single step, without need of formation of embryoid bodies, coculturing on stromal cells, or additional factors: however, the underlying mechanism remains unknown. Here, we first developed a feasible and convenient detection method of serotonergic differentiation, and then, using this method, we tried to determine the signaling pathways that might be involved.E14tg2a ES cells were transduced with a knock-in vector targeted to the ROSA26 locus consisting of naturally secreted *Gaussia* luciferase and AcGFP, separated by an IRES element, under control of the enhancer sequence of *Pet-1*, a precise marker of central serotonin neurons. After the resultant ES cells were differentiated as above, the luciferase activity increased in a similar time course to that of mRNA expression levels for *Pet-1*, which preceded those for tryptophan hydroxylase 2 and the serotonin transporter. Using this system, it was revealed that a selective inhibitor of BMP type I receptor kinases, LDN-193189, induces the differentiation.Here, we succeeded in developing a feasible method to assess serotonergic differentiation from ES cells and demonstrated, for the first time, that the inhibitor of BMP type I receptor kinases induces the serotonergic differentiation. The present study is expected to facilitate future studies to address complex issues of serotonergic differentiation and its psychiatric implications.

P1-01 Ca^{2+}-activated K^+ (K_{Ca}) channels as potential novel molecular targets for pain control

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Neuropathic pain that occurs after nerve injury depends on neuronal hyperexcitability in the spinal dorsal horn. Previous our study, newly synthesized enantio-purified S-ketamine preferentially inhibited nerve transection induced neuropathic pain through suppression of neuronal hyperexcitability such as activation of NMDA receptors. Furthermore, S-ketamine showed potent inhibition of microglial activation in the spinal cord compared with racemate or R-ketamine. The aim of this study is to elucidate the mechanism how S-ketamine suppress microglial activation. S-ketamine strongly inhibited the elevation of microglial number in the spinal cord after nerve injury. We next focused our attention on Ca^{2+}-activated K^+ (K_{Ca}) currents in spinal microglia, which are associated with activation and migration of microglia after nerve injury. Ipsilateral spinal microglia exhibited significant outward K^+ currents in slices prepared at 3 days after nerve injury. Voltage-activated outward rectifier K^+ currents of microglia after nerve injury were highly sensitive to charybdotoxin (ChTX), but not to apamine. Furthermore, these K_{Ca} currents were significantly suppressed by S-ketamine. S-ketamine preferentially inhibited voltage-activated outward rectifier K^+ currents induced by NS1619, a specific BK channel opener, in cultured microglia. Intrathecal administration of NS1619 in the normal mice induced allodynia-like behavior and accumulation of microglia in the spinal dorsal horn. Furthermore, intrathecal administration of ChTX significantly inhibited nerve injury-induced allodynia and microglial accumulation in spinal dorsal horn. These results strongly suggest the preferential inhibition of K_{Ca} currents in microglia in addition to neuronal NMDA receptors may account for the preferential and potent analgesic effects of S-ketamine on neuropathic pain. Microglial K_{Ca} channels are thus considered to be potential new molecular targets for pain control.

P1-02 Interferon regulatory factor-5 in spinal microglia is a crucial transcription factor for the development of neuropathic pain

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Neuropathic pain occurs after several diseases accompanied by nerve damage, which is characterized by abnormal sensory perception such as tactile allodynia (pain responses evoked by innocuous mechanical stimuli). Recent studies indicate that reactive spinal microglia induce or enhance expression of various genes including proinflammatory cytokines and are implicated in producing neuropathic pain. However, the mechanisms underlying gene expression in microglia associated with neuropathic pain is not fully understood. In the present study, we examined the role of interferon regulatory factor-5 (IRF5), a member of IRF family transcription factor, in generating tactile allodynia after peripheral nerve injury (PNI). We found that PNI increased the expression of IRF5 in the ipsilateral spinal cord. By performing in situ hybridization analysis, we found that signals of IRF5 mRNA were specifically observed in cells immunostained by Iba1, a marker of microglia, in the spinal dorsal horn of PNI mice. Interestingly, knockdown of IRF5 protein by spinal administration of siRNA targeting IRF5 attenuated tactile allodynia after PNI without affecting normal pain sensitivity. Together, our present findings suggest that IRF5 critically contributes to the pathogenesis of neuropathic pain.

P1-03 Subtypes of macrophages in the peripheral nerve and dorsal root ganglia after the peripheral nerve injury

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After the peripheral nerve injury, macrophages infiltrate the injured nerve and dorsal root ganglia (DRGs). Now, it is well-known that macrophages are mainly divided into M1 (classically activated) and M2 (alternatively activated) subtypes. However, it is unclear which subtypes of macrophages infiltrate these regions after the nerve injury. In the present study, we investigated the subtypes of macrophages in the sciatic nerve and DRGs of mice after partial ligation of the sciatic nerve. In the ipsilateral side of the sciatic nerve, many inflammatory cells infiltrated, including macrophages, around the injured region on day 1 after the nerve injury, and continued to increase until day 3. All of infiltrating macrophages in the injured nerve were inducible nitric oxide synthetase $(iNOS)^+$/arginase-1 $(Arg-1)^-$ M1 type on day 1. On day 3 after the nerve injury, many $iNOS^+/Arg-1^-$ M1 macrophages infiltrated the injured nerve with some $iNOS^-/Arg-1^+$ M2 macrophages. In addition, we observed the $iNOS^+/F4/80^-$ neutrophils in the ipsilateral side of the sciatic nerve from day 1. Significant increase in macrophages was observed in the ipsilateral side of DRGs on day 2 after the nerve injury, while microglia was not increased in the ipsilateral side of spinal cord until day 2. Almost all macrophages were $iNOS^-/Arg-1^+$ M2 type in the ipsilateral side of DRGs. Double-immunofluorescence staining revealed that the increased macrophages were positive for CD163 and CD206. However, $CD86^+$ macrophages were not increased in the ipsilateral DRGs. These findings suggest that functional phenotypes of infiltrating macrophages in the DRGs are distinct from those in the injured peripheral nerves. Thus, infiltrating macrophages after the peripheral nerve injury may have unique roles dependent of the location. This work was supported by a Grant-in-Aid for Scientific Research (C) from The Ministry of Education, Culture, Sports, Science and Technology (21600011) and a Research Grant on Priority Areas from Wakayama Medical University.

P1-04 P2Y12 receptors mediate chemokines expression in primary rat microglia

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Microglia are immune cells in the central nervous system and have many important roles on several CNS disorders including Alzheimer's disease, Parkinson's disease and neuropathic pain. Chemokine release is one of the important microglial functions in such pathological conditions. Furthermore accumulating evidences indicate that chemokines play an important role in the pathology of neuropathic pain. We have previously reported that P2Y12R, one of metabotropic purinergic receptors, is also crucially involved in the pathogenesis of neuropathic pain. However its detail mechanism remains to be elucidated. P2Y12R mediates microglial chemotaxis and membrane ruffling but its function in chemokine release has not been reported. Here we demonstrate that P2Y12R regulate chemokine production. The levels of CCL2 and CCL3 mRNA expression were significantly increased by P2Y12R agonists, ADP and 2MeSADP, in primary microglia. ADP induced CCL2 gene expression was maximal level at 15 min and CCL3 gene expression was at 30 min. These gene expressions were settled within 1hr. ADP induced not only gene expression but also chemokine release for extracellular media. ADP induced these gene increases were suppressed by pretreatment of P2Y12R antagonists, ARC69931MX and ARC66096. ADP also exerts other purinergic receptor P2Y1R. But its antagonist MRS2179 was not effect for ADP induced gene expression. Additionally, pertussis toxin, inactivator of G α i subunit, also inhibited increase of CCL2 and CCL3 gene expression. Inhibition of intracellular calcium increase by BAPTA-AM, an intracellular calcium chelator, completely reduced ADP induced chemokine gene expression. Furthermore an NFAT inhibitor, INCA-6, and a calcineurin inhibitor, cyclosporine A, partially blocked ADP elicited these genes expression. Actinomycin D, an inhibitor of RNA polymerase, completely suppressed ADP induced gene expression. These results indicate that P2Y12R regulates chemokine production via G α i coupled protein and NFAT-involved gene transcription in primary microglia.

P1-05 Dopamine attenuates LPS-induced cytokine expression by inhibiting the nuclear translocation of NF- κ B p65 in microglial cells

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It has been reported that inflammatory cytokines and nitric oxide (NO) produced by microglial cells mediate neuronal cell death in brain ischemia/reperfusion injury and traumatic brain injury. Release of dopamine has been known to be accelerated in cerebral ischemia and trauma. We recently reported that dopamine attenuated lipopolysaccharide (LPS)-induced NO production in mouse microglial cell line BV-2. In this study, we investigated the effect of dopamine on LPS-induced mRNA expression of cytokines in BV-2 cells. The mRNA levels of cytokines were determined by RT-PCR and real-time RT-PCR, and the levels of NF- κ B p65 and I κ B α were determined by Western blotting. LPS (10 μ g/mL) increased mRNA levels of IL-1 β , IL-6 and TNF- α . Pretreatment with dopamine (1-30 μ M) for 24 h concentration-dependently attenuated the LPS-induced mRNA expression of these cytokines. Neither SCH23390 nor sulpiride, D1-like and D2-like dopamine receptor antagonists, respectively, affected the attenuation of LPS-induced mRNA expression of cytokines by dopamine. N-acetylcysteine (NAC), a free radical scavenger, inhibited the attenuation of LPS-induced mRNA expression of cytokines by dopamine. On the other hand, hypoxanthine/xanthine oxidase, a super oxide generating system, did not affect the LPS-induced mRNA expression of cytokines. Dopamine concentration-dependently increased the level of quinoproteins, and the increase was inhibited by NAC. LPS increased the levels of NF- κ B p65 in nuclei of BV-2 cells, and decreased the levels of I κ B α in the cytosol. Although dopamine did not affect the LPS-induced decrease of I κ B α , dopamine attenuated the increase in the levels of NF- κ B p65 in the nuclei. NAC inhibited the effect of dopamine on the levels of NF- κ B p65. These results suggest that dopamine attenuates LPS-induced expression of cytokines by inhibiting the nuclear translocation of NF- κ B p65 through the formation of quinoprotein in microglial cells.

P1-06 Zinc enhances LPS-induced nitric oxide production in cultured astrocytes

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Zinc plays a crucial role in the CNS; chelatable zinc accumulated in synaptic vesicles is released by stimuli serving as an endogenous modulator in synaptic neurotransmission. Synaptically released zinc is taken up in neurons and astrocytes. Under pathological conditions such as brain ischemia and trauma, extracellular zinc concentration may reach as high as 400 μ M. In the present study, we examined the effect of zinc elevation on nitric oxide (NO) production in cultured astrocytes prepared from rat embryo cortex, which is experimentally stimulated by lipopolysaccharide (LPS). Increasing zinc concentration to about 125 μ M did not directly evoke NO production, but doubled the level of NO production stimulated with 1 μ g/ml LPS for 24 hr. Zinc showed no effects on the cell viability up to 125 μ M; however, at the higher concentrations of zinc than 250 μ M, the cell viability decreased remarkably. The LPS-induced expressions of both mRNA and protein of inducible NO synthase were augmented by 125 μ M zinc. Zinc also enhanced the LPS-induced phosphorylation of mitogen-activated protein kinases (MAPKs) at 0.5-3 hr. *N,N,N',N'*-Tetrakis(2-pyridylmethyl) ethylenedamine (TPEN), a membrane permeable zinc chelator, inhibited the enhancement of NO production by zinc. These results suggest that the elevation of zinc concentration modify astrocytic cell functions and that such potentiation of NO production from astrocytes may aggravate neuronal damage during neuroinflammation.

P1-07 Role of extracellular RNA in neuronal injury-induced astrocyte activation

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In the brain under pathological conditions such as cerebral ischemia and traumatic injury, glial cells are remarkably activated, and then the expression of a variety of chemokines/cytokines is dramatically increased. We previously demonstrated that NMDA-evoked neuronal injury induced astrocytic monocyte chemoattractant protein-1 (MCP-1) production in rat organotypic corticostriatal slice cultures. However, the signaling molecule(s) from injured neurons to astrocytes remains unclear. Emerging evidence suggests that RNA is leaked from damaged cells and plays a role as an intercellular signaling molecule. Thus, we investigated whether extracellular RNA is involved in intercellular communication between injured neurons and astrocytes, which leads to MCP-1 production. Corticostriatal slice cultures were prepared from postnatal day 2-3 rats and cultivated for 10-12 days. NMDA treatment (50 μM, 3 h) caused the remarkable accumulation of RNA in the culture medium. NMDA-induced MCP-1 upregulation at both the mRNA and protein levels was partially but significantly suppressed in the presence of RNase A (10 μg/mL). In addition, TLR3 agonist poly I:C (0.1-10 μg/mL), a synthetic double-stranded RNA analogue, induced MCP-1 production in astrocytes. On the other hand, IL-1β (10 μg/ml)-induced astrocytic MCP-1 production was not suppressed by the addition of RNase A. These results suggest the possibility that the inhibitory effect of RNase A on NMDA-induced MCP-1 production was due to the degradation of RNA extracellularly, but not to the direct inhibitory action on astrocytes, and that RNA leaked from injured neurons is, at least in part, involved in astrocytic MCP-1 production after neuronal injury.

P1-08 Inhibitory effect of tributyltin on neurite formation and synatpogenesis in cultured cortical cells

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Tributyltin (TBT) compounds have been widely used as agricultural fungicides and antifouling agents for fishing nets and ships. Though their use has been restricted recently, TBT and its degradation products remain in marine sediment and accumulate in marine animals, resulting in human exposure through ingestion of marine products. In addition to endocrine-disrupting effects on marine organisms, TBT is reported to have toxic effects on the central nervous system and immune system of mammals. In cultured neurons, TBT was originally reported to exhibit cytotoxicity through inhibiting mitochondrial ATP synthesis. Recently, however, several other mechanisms of TBT action have been proposed, such as through its chloride ionophore activity or nuclear receptor-binding activity. In the present study, we investigated the effect of TBT on neurite formation and synaptogenesis in cultured cortical neurons at low concentrations at which cell death was not induced (100 nM and lower). Primary cultures were obtained from cerebral cortices of fetal rats at 18 days of gestation. After 2 days in serum-containing medium, the cultures were transferred to serum-free medium containing TBT-Cl. Cell viability was assessed by LDH release and mitochondrial activity assay at 2 days after medium change. Under the present conditions, neuronal cell death was observed at 200 nM TBT and higher, so that further experiments were carried out at 100 nM and lower concentrations of TBT. In the control, non-exposed cultures, expression of microtubule associated protein 2 (MAP2) and Synapsin 1 (Syn1) evaluated by western blotting at 1, 2, 3 and 4 days after transfer to serum-free medium increased progressively with time. On the other hand, MAP2 and Syn1 in cultures exposed to 100 nM TBT were dramatically decreased at 1 and 2 days of exposure, demonstrating the acute inhibition of neurite formation and synaptogenesis by low concentration of TBT. Since TBT has been shown recently to bind to and activate members of the nuclear receptor family such as the retinoid X receptor (RXR) which heterodimerizes with thyroid hormone receptors, the effect of TBT on thyroid hormone-dependent gene expression is also being examined.

P1-09 Neuroprotective effect of thalidomide and its enantiomers against oxidative stress

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It is known that thalidomide has teratogenicity that induces birth defects. However, thalidomide is focused again because it is useful to treat several diseases such as leprosy, multiple myeloma, and various cancers. Several groups reported the neuroprotective effect of thalidomide against neuronal damage resulting from focal cerebral ischemia (Hyakkoku et al. *Neuroscience* 159, 760-769 (2009)) and amyloid beta-induced impairment of recognition memory (Alkam et al. *Behav Brain Res* 189, 100-106 (2008)). But the molecular mechanism of these observations is unknown. Thalidomide contains a asymmetric carbon in its chemical structure, so (*R*)-enantiomer and (*S*)-enantiomer are existed. Here we examined the neuroprotective effect of thalidomide enantiomers against neuronal cell death. Thalidomide inhibited neuronal cell death induced by oxidative stress in dose dependent and enantiospecific manner. Thalidomide also inhibited the production of H_2O_2 radicals in an enantiospecific manner. We performed Western blotting analysis of several molecules associated with neuroprotection and found that several signaling pathways were associated with the neuroprotective effect of thalidomide in SH-SY5Y cells. These results indicate that thalidomide protect neuronal cell death through several specific cell signaling pathways and it may have a possibility to retard neuronal cell death of Alzhimer's disease and Parkinson's disease.

P1-10 Protective effect of *kampo* medicine yokukansan on glutamate-induced neuronal death in primary cultured rat cortical neurons

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Effects of a traditional Japanese medicine, yokukansan, which is composed of seven medicinal herbs, on glutamate-induced cell death were examined using primary cultured rat cortical neurons. Yokukansan (10-300 μg/mL) inhibited the 100 μM glutamate-induced neuronal death in a concentration-dependent manner. Among seven constituent herbs, higher potency of protection was found in Uncaria thorn (UT) and Glycyrrhiza root (GR). A similar neuroprotective effect was found in four components (geissoschizine methyl ether, hirsuteine, hirsutine, and rhynchophylline) in UT and four components (glycycoumarin, isoliquiritigenin, liquiritin, and 18β-glycyrrhetinic acid) in GR. In the NMDA receptor binding and receptor-linked Ca^{2+} influx assays, only isoliquiritigenin bound to NMDA receptors and inhibited the glutamate-induced increase in Ca^{2+} influx. These results suggest that various neuroprotective components (isoliquiritigenin, glycycoumarin, liquiritin and 18β-glycyrrhetinic acid in GR, and geissoschizine methyl ether, hirsuteine, hirsutine and rhynchophylline in UT) are contained in yokukansan, and isoliquiritigenin which is one of them is a novel NMDA receptor antagonist.

P1-11 GluN2D subunit of the N-methyl-D-aspartate receptor is required for phencyclidine-induced behavior, gene expressions and FOS-positive cell increases

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Noncompetitive *N*-methyl-D-aspartate (NMDA) receptor antagonists evoke behavioral and neurobiological syndrome in experimental animals. We have previously reported that the NMDA receptor antagonist phencyclidine (PCP) significantly increased the extracellular levels of dopamine in the striatum and prefrontal cortex of wild-type (WT) mice but not of GluN2D knockout (KO) mice. Furthermore, acute and repeated administration of PCP does not increase locomotor activity in GluN2D KO mice. Our aim of this study is to elucidate the role of the GluN2D subunit of the NMDA receptor in the PCP-induced behavioral and neurobiological syndrome. We performed a rotarod test, gene expression analyses, and FOS-immunohistochemical analyses involving WT and GluN2D KO mice. Motor impairment was measured by placing WT or GluN2D KO mice on a fixed-speed rotarod, at 30 min after PCP (3 or 5 mg/kg, s.c.) administration. For gene expression and FOS-immunohistochemical analyses, we used samples obtained from WT and GluN2D KO mice at 2 h after injecting saline or PCP (10 mg/kg, s.c.). In the rotarod test, the WT mice-but not the GluN2D KO mice;showed potent motor impairment when injected with 3 or 5 mg/kg PCP. Comparing the gene expression levels in WT and GluN2D KO mice, we identified several PCP-dependent differentially expressed genes (DEGs). *c-fos* was one of the DEGs that showed the greatest increase in expression. FOS-immunohistochemical analysis showed that the number of FOS-positive cells increased after PCP administration in almost all the brain areas in the WT mice, but not in those of the GluN2D KO mice. Considering that the expression of the GluN2D subunit is region-specific, our results suggest that the neural inputs from the region containing the GluN2D subunit are necessary to cause PCP-dependent DEGs. Thus, the GluN2D subunit of the NMDA receptor plays an important role in PCP-induced motor impairment, abnormal gene expressions and increased FOS-immunoreactivity.

P1-12 A multi-pass membrane protein, TMEM168, is induced in the nucleus accumbens by repeated treatment of methamphetamine in mice

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Methamphetamine is one of the most commonly abused drugs in Japan. We thus focus on illustrative examples of candidate genes/molecules involved in the development of methamphetamine dependence. In this study, we investigated the expression pattern of TMEM168 which was induced by the repeated treatment with methamphetamine (METH) in the nucleus accumbens of mice.
We repeatedly administered mice with METH (2 mg/kg/day, s.c.) or saline for 6 days. The nucleus accumbens were removed 2 hours after the last administration of METH. Using PCR-select cDNA subtraction method, we found TMEM168 as one of inducible molecule in the nucleus accumbens of METH-treated mice. TMEM168 contains several estimated transmembrane regions. However any function of TMEM168 is unknown at the present.
We carried out real-time RT PCR to examine the expression of TMEM168 mRNA in various organs, including the brain, heart, lung, small intestine, muscle and testis, of mice. We also measured the expression of TMEM168 mRNA in the various brain regions of mice treated with METH. TMEM168 is ubiquitously expressed in the various organs tested in the present study, and especially, high level was found in the brain. High levels of TMEM168 mRNA was detected in the striatum and nucleus accumbens among the various brain regions. Furthermore, the repeated administration of METH for 6 days was significantly increased TMEM168 mRNA expression in the nucleus accumbens and hippocampus in mice.
These results suggest that TMEM168 might play important roles in the striatum and nucleus accumbens, which are projected area of the dopaminergic neuronal system, where is related to the establishment of drug dependence. Further study should be done to investigate the effect of TMEM168 on the METH responses in *in vitro* and *in vivo*.

P1-13 Lower sensitivity to methamphetamine in accumbal dopamine D2 receptor knockdown mice

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Addictive drugs lead to their rewarding effects by targeting the mesolimbic dopaminergic neuronal system, which originates in the ventral tegmental area and projects mainly to the nucleus accumbens (NAc). Almost all neurons in the NAc (>95%) are medium spiny neurons divided into two major subtypes expressing dopamine D1 receptor (D1r) versus D2r. In the present study, we investigated the role of accumbal D2r-mediated neurotransmission in behavioral responses induced by methamphetamine (METH), using specific knockdown mice generated by the infection of the adenoassociated virus vector containing the iRNA sequence for D2r (AAV-iD2r vector).
We bilaterally injected AAV-iD2r or AAV-Mock vector into the NAc of male C57BL/6J mice. The mRNA expression levels of D2r in AAV-iD2r vector-injected mice were assessed at about 50% reduction in the NAc, but at no change in the dorsal striatum, compared with that in AAV-Mock vector-injected mice. On the other hand, there were no differences in the mRNA expression levels of D1r in the NAc between both groups. Acute treatment with METH (1 mg/kg)-induced hyperlocomotion in the D2r knockdown mice was significantly decreased compared with that in the control mice. Furthermore, the development of locomotor sensitization induced by repeated treatment with METH (1 mg/kg/day for 7 days) exhibited a significantly less extension in the D2r knockdown mice. In the place conditioning paradigm, METH (1 mg/kg in every other day, 3 times) induced place preference in both groups. However, the preferred effects of METH were significantly weaker in the D2r knockdown mice than the control mice.
These findings suggest that accumbal D2r knockdown suppresses behavioral sensitivity to METH. Thus, the D2r-mediated neurotransmission in medium spiny neurons of the NAc plays an important role in the development of drug dependence.

P1-14 Effect of psychotropic drugs on cerebral proteins of mice deficient neuroglycan C , a brain-specific chondroitin sulfate proteoglycan

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Neuroglycan C (NGC), a typical part-time chondroitin sulfate proteoglycan, is predominantly expressed in the brain. To clarify the roles of NGC in the brain development, we planned to generate NGC-gene mutant mice that show abnormal expressions of NGC by conditionally targeted gene disruption, and now have four strains including NGC-knockout (NGC-KO) mice that are completely deficient in all splice variants. In the 53rd Annual Meeting, we partly reported on the effect of several psychostimulants such as methamphetamine on the behavior of NGC-KO mice using the open field test. It has been reported that the behavioral sensitization to some psychotropic drugs is associated with up- and down- regulation of NGC gene expression. As expected, NGC-KO mice showed different behavior compared with wild mice, suggesting that NGC-KO mice may be evaluated as an animal model of attention-deficit / hyperactivity disorder (ADHD). After the open field test, the changes of protein patterns in the cerebral cortex were examined using two- dimensional gel electrophoresis. The sizes of several protein spots were different between NGC-KO and wild mice, and between NGC-KO mice injected with methamphetamine and non-treated NGC-KO mice, respectively. The spots were identified using MALDI-TOF MS, and further investigations are going on to know the meaning of the differences in protein expression.

P1-15 Analysis of the interaction of neural recognition molecule NB-2 with amyloid precursor-like protein 1

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NB-2, also referred to as contactin-5, is a neural recognition molecule in the contactin subgroup of the immunoglobulin superfamily. NB-2 is expressed transiently during the first postnatal week in the central auditory system and is localized at the glutamatergic synapses. NB-2 deficiency caused a deficient in synapse formation and induces apoptosis in the auditory neurons. NB-2-deficient mice exhibited abnormal responses to auditory stimuli and increased interpeak latencies for auditory brainstem response. However, the NB-2 signaling mechanism leading to the change in synapse formation remains unknown. Recently, it was reported that NB-2 bound to amyloid precursor-like protein 1 (APLP1), an amyloid precursor protein (APP) homologue, *in vitro*. APP has been reported to play a key role in the neurite outgrowth and synaptic maturation. Therefore, there is the possibility that APLP1 may participate in the synaptic formation through interacting with NB-2. In this study, we studied the mode of the interaction between APLP1 and NB-2, and the possible co-localization of these two molecules at the synaptic site. We carried out immunoprecipitation from HEK293 cells co-transfected with APLP1 and NB-2. APLP1 was co-immunoprecipitated with NB-2, confirming that APLP1 interacts with NB-2. In addition, we performed cell surface binding assay using HEK293 cells transfected with APLP1 and NB-2-Fc fusion protein to identify the domains that mediate the interaction between APLP1 and NB-2. Furthermore, immunoprecipitation from the synaptosomal fraction from the mouse cerebral cortex suggested the interaction of NB-2 with APLP1 *in vivo*. To examine their localization at the synapses, we prepared the pre- and postsynaptic membrane fractions from the synaptosomal fraction and subsequently performed western blotting. Both NB-2 and APLP1 were enriched in the synaptosomal fraction, and were detected in the presynaptic fraction rather than the postsynaptic fraction. From these results, NB-2 may interact with APLP1 on the presynaptic membrane.

P1-16 Involvement of autism-related factor MARCKSL1 in Neural network formation

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Autism is a neurodevelopmental disorder characterized by lack of social interaction and communication, obsessiveness, and repetitive behavior. Although it is reported that the prevalence of autism is about 1–2 per 1000 people in Japan, the number has been increased, recently. However, no treatment and prevention, even diagnosis for autism has been established, because little is known about the pathogenesis of autism. Recently, it is reported that the risk of autism is associated with a lot of genes for neural network formation, including genes expressed in cortex during embryonic stage, or involved in neurotransmission. So far, we have identified MARCKSL1 as an interactor with SGK1 induced by stress condition in mice. To clarify the mechanism of onset of autism from the point of view of brain developmental disorder by means of neural network malformation, we investigate about role of the MARCKSL1 in neural network formation, because MARCKSL1 is known as an autism-related factor. Here, we report about the expression pattern of MARCKSL1 with the localization in developmental mice brain. Furthermore, we show the result about down-regulation of MARCKSL1 by short interfering RNA(siRNA) to neurite outgrowth in PC12 cell.

P1-17 Possible involvement of MeCP2-dependent regulation of gene expression in the autism-like developmental disorder induced by fetal thalidomide exposure in rats

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Autism is a developmental disorder of the brain characterized by three major symptoms; impaired social interactions, impaired communication ability, and restricted and repetitive behaviors and interest. Previous studies suggest that a combination of genetic and environmental factors contribute to the etiology of autism. One of the known environmental factors is fetal exposure to thalidomide between gestational days 20~24 which results in external ear malformation together with high incidence of autism. A rat model of autism was developed by administering thalidomide (500 mg/kg body-weight) to pregnant rats at 9th day of gestation which corresponds to the above period in humans, which exhibits symptoms in common with human autism such as increases in non-exploratory behavior and in the concentration of blood serotonin (Narita et al, 2002). In addition, we found an increase in the concentration of cerebral and hippocampal serotonin in fetal thalidomide-exposed (THA) rats at postnatal day 20 (P20) and P40. In the present study, gene expression profiles in the cerebral cortices of THA rats and control (CTL) rats were first compared at P14 using DNA microarrays in order to elucidate how thalidomide exposure affected brain development. The results revealed that several genes suppressed by MeCP2 (methyl CpG binding protein 2) were up-regulated in THA rats; these include *mobp, fkbp5, igfbp3, ucp2*. Among these, up-regulation of *mobp* and *ucp2* was further validated by real-time PCR, although expression of *MeCP2* gene itself was not altered. In addition to *mobp*, other myelin component genes such as *mbp, plp1, cnp*, and *mag* were co-ordinately up-regulated at P14 and P20, suggesting an earlier onset of myelination in THA rats. This was confirmed by an increase in the protein level of MBP. Further investigations are carried out on the expression of other MeCP2-regulated genes such as one of the exons of *bdnf* gene. Since loss-of-function mutations of the *MeCP2* gene has been shown to cause a severe developmental disorder, Rett syndrome, similar epigenetic mechanisms may also be involved in the development of THA-induced autism.

P1-18 TSC2 mutation upregulates dendritic mitochondria and shaft synapse formation in an mTOR-dependent manner

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Disruption of regulatory machinery for synapse formation has been thought to contribute to abnormal brain functions in various pediatric, neurological, and psychiatric disorders. Mutations in TSC2 (tuberous sclerosis complex-2) gene cause tuberous sclerosis complex (TSC), which is a hereditary autistic disorder. Its characteristic symptoms are severe epilepsy, mental retardation and autism. TSC2 is a GTPase-activating protein towards the Ras family small GTPase Rheb (Ras-homologue enriched in brain), thereby Rheb is changed to a GDP-bound form, which suppresses the mTOR signaling pathway. In TSC patients, TSC2 mutation converts Rheb to a GTP-bound form, which thereby activates the mTOR, leading to various neurological symptoms. However, the detailed mechanistic relationship between these symptoms and the mTOR signaling pathway remains unclear. Here, we examined neuronal morphology from Eker rats that are heterozygous for a mutation in the TSC2. Cultured neurons from Eker rats exhibited an increase in dendritic shaft synapse (but not spine synapse), as compared with that in WT rats. Rapamycin, a specific mTOR inhibitor, reversed shaft synapse density in Eker neurons. On the other hand, we found that dendritic mitochondrial area was significantly increased in Eker neuron. This finding was also supported by proteomic study showing that certain mitochondrial proteins were upregulated in Eker synaptoneurosomes. Thus, perturbations of the TSC-Rheb-mTOR pathway may regulate dendritic mitochondria that may be accompanied with mitochondrial abnormality, leading to shaft synapse formation in TSC patients. We are now investigating how the increased mitochondria accelerates shaft synapse formation in dendrites of Eker neurons.

P1-19 Kamikihi-to improves memory impairment and axon degeneration in a mouse model of Alzheimer's disease, 5XFAD

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Neuritic atrophy and loss of synapses underlie the pathogenesis of Alzheimer's Disease (AD). We previously found that Kamikihi-to (KKT ; traditional Japanese medicine) improved Aβ (25-35)-induced neuritic atrophy in cultured rat cortical neurons. We aimed to examine effects of KKT using 5XFAD mice, transgenic AD model overexpressing mutated human APP gene and human PS1 gene. 5XFAD mice (male, 7-8 months old) were given KKT (20 mg/kg/day, 200 mg/kg/day, p.o.) or physiological saline for 15 days. We carried out novel object recognition test on vehicle-treated wild-type and 5XFAD mice, and KKT-treated 5XFAD mice. Vehicle-treated 5XFAD mice showed marked impairment of object recognition memory compared with wild-type mice. However, KKT treatment significantly improved object recognition memory compared with vehicle-treated 5XFAD mice. Next day of novel object recognition test, the brains of mice were cut in 20-μm successive coronal slices for immunohistochemistry. In the brain of wild-type mice, amyloid plaques were hardly observed. However, in the cerebral cortex and hippocampus of 5XFAD mice, a lot of amyloid plaques were detected. KKT treatment significantly reduced the number of amyloid plaques in the cerebral cortex and hippocampus. Additionally, bulb-like axons and swollen presynaptic boutons were markedly observed only inside amyloid plaques in 5XFAD mice. KKT treatment reduced the number of bulb-like axons in the frontal cortex, but not in the hippocampus. In conclusion, KKT improved object recognition memory deficit in 5XFAD and restored axonal degeneration. Abnormal structures of axons which were limited to the amyloid plaque were reported also in the case of AD patients and other AD model mice. It is supposed that the neuronal network may be disconnected at the plaque site, which may induce memory deficit. We are now investigating the mechanism of KKT action to obtain a clue of signaling for amyloid plaque-regulating axonal degeneration.

P1-20 Aβ43-converting activity requires two active domains of ACE

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Amyloid β-protein (Aβ) varies in length at its carboxyl terminus. The longer Aβ species, Aβ42 or Aβ43, is highly amyloidogenic and responsible for the neurotoxicity and the early amyloid plaque formation that lead to memory and cognitive defects in Alzheimer's disease (AD). In contrast, a shorter Aβ species, Aβ40, is easier to be maintained as a monomer, which has a neuroprotective effect. We have demonstrated that angiotensin-converting enzyme (ACE) converts Aβ42 to Aβ40 and this activity is specifically located in its N-terminal active domain. Here we found that ACE with two active domains converts Aβ43 to Aβ41, whereas ACE with either N- or C-terminal active domain did not convert Aβ43 to Aβ41. A mixture of N- and C-terminal active domain of ACE also failed to convert Aβ43 to Aβ41. This study suggests that a certain carboxyl dipeptidase activity may require ACE with two active domains. We also demonstrated that Aβ43 and Aβ42, but not Aβ40, deposit in diffuse amyloid plaques in APP transgenic (Tg2576) mouse brain. This Aβ43-to-Aβ41-converting activity of ACE may also be involved in the regulation of brain Aβ deposition.

P1-21 Proteomic analysis of cultured cells expressing APP intracellular domain

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Accumulation and deposition of fibrillar amyloid β (Aβ) is considered the primary cause of Alzheimer's disease. Aβ is derived from Alzheimer amyloid precursor protein (APP) by sequential proteolytic cleavage involving β- and γ-secretase. γ-Secretase was shown to cleave near the cytoplasmic membrane boundary of APP (termed ε-site), as well as in the middle of the membrane domain (termed γ-site). Recently, it has been reported that the γ-secretase processing mechanisms of Aβ generation from APP C-terminal fragments (CTFs) by γ-site cleavage ere distinct from the mechanisms of epsilon-site cleavage. This processing involves γ-secretase activating protein (gSAP) binding to the cytoplasmic domain of APP CTFs. gSAP/γ-secretase/APP CTF ternary complex alters the structural relationship between γ-secretase and APP CTFs. γ-secretase cleaves at ε-site near the cytoplasmic domain of APP CTFs in the absence of gSAP, while γ-secretase may directly cleave at γ-site in the middle of the membrane domain of APP CTFs in the presence of gSAP. Therefore, γ-secretase produces two AICDs, C50 from epsilon-site cleavage and C57/59 from γ-site cleavage. Recently, transgenic mice overexpressing AICD show age-dependent tau phosphorylation and aggregation, memory deficits, and neurodegeneration, suggesting that AICD might contribute to AD pathology. To understand the pathogenic mechanism and to develop the potential therapy of AD, it is important to clarify the relationship between these processing products of the γ-secretase. In this study, we carried out proteomic analysis of cultured cells expressing APP C50 and APP C59. We found increased expression of stress response proteins (HSP60, HSP86, BiP, and so on) in CHO cells expressing C50. These changes were not observed in CHO cells expressing C59. This suggests that C50 and C57/59 are metabolized in different pathway, respectively.

P1-22 CHRNA7 as scaffold molecule for Aβ aggregation

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The nicotinic acetylcholine receptors, key players in neuronal communication, convert neurotransmitter binding into membrane electrical depolarization. CHRNA7 is a type of the neuronal nicotinic receptor, thought to have association with Alzheimer's disease, because Aβ42 is reported binding to CHRNA7 protein with high affinity. To investigate the interaction between two proteins furthermore, we utilized RNAi technique to knock down CHRNA7 in SH-SY5Y cells and detected the reduction of intracellular Aβ42. Smaller aggregates of Aβ, called soluble oligomers, are increasingly believed to be the primary cause of Alzheimer's disease. We made one aggregated form of Aβ and examined its binding to CHRNA7 *in vitro*. As a consequence, CHRNA7 bind to both Aβ monomers and oligomers. Based on these results, we hypothesized that Aβ aggregation requires CHRNA7 as scaffold molecule. We are going to prove this hypothesis.

P1-23 Peptidyl-prolyl isomerase Pin1 stimulates dephosphorylation of Tau phosphorylated by Cdk5-p25

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Tau is a microtubule-associated protein predominantly expressed in neurons. Hyper-phosphorylated Tau is a major component of neurofibrillary tangles in Alzheimer's brains. Tau is phosphorylated by Cyclin-dependent kinase 5 (Cdk5). Cdk5 is a Ser/Thr kinase that is hyper-activated by p25. Cdk5-p25 is suggested to induce the hyper-phosphorylation of Tau. However, it is not known yet why the hyper-phosphorylation of Tau occurs in disease brains. We reported previously that dephosphorylation of Tau phosphorylated by Cdk5 was enhanced by Pin1. Pin1 is a peptidyl-prolyl isomerase catalyzing the cis/trans isomerization of phospho-Ser/Thr-Pro sequences, stimulating dephosphorylation by protein phosphatase 2A (PP2A). We analyzed interaction between Pin1 and Tau phosphorylated by Cdk5-p25 using the GST-pulldown assay and Biacore. We firstly confirmed Ser202, Thr205, Ser235, and Ser404 as all major Cdk5 phosphorylation sites using two-dimentional phosphopeptide map analysis. Pin1 bound to Cdk5-phosphorylated Tau but not Tau Ala mutants at four Cdk5 phosphorylation sites, indicating that Pin1 binds one of above Cdk5 phosphorylation sites. We searched for Pin1 binding site using Ala mutant of Tau at phosphorylation sites, and found that Pin1 bound to any of Cdk5 phosphorylation sites. Interestingly, however, dephosphorylation was enhanced in Tau with phospho-Ser202 and phospho-Ser404. FTDP-17 mutant Tau, P301L or R406W, showed slightly weaker binding to Pin1 than WT Tau. Based on these results, we discuss how FTDP-17 mutant Tau is highly phosphorylated in patient's brains.

P1-24 Proteomics analysis of hippocampus and cortex under the influence of amyloid β oligomers using mutant APPE693Δ-transgenic mice

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[Objective] Amyloid precursor protein (APP) mutations cause famillial Alzheimer's disease. Recently, it was reported that APP E693Δ transgenic mice show synaptic alternation, abnormal tau phosphorylation, glial activation and neuronal loss in the absence of amyloid plaques. However, it remains unsolved whether APP E693Δ mutation causes the changes of protein expression and/or modification. Thus, we analyzed the comparative proteomics for the levels of protein expression and phosphorylation in the brain of the APP E693Δ transgenic mice and non-transgenic littermate.[Methods] Samples prepared from mouse hippocampus and cortex were applied to two-dimensional gel electrophoresis (2DE), and the gels were stained with SyproRuby and ProQ Diamond. [Results] The 2DE profiles showed more than 200 spots in the hippocampus and cortex. Of these, proteins showing different expression level were identified. The significantly decreased proteins were α-synuclein, coactosin like-protein, actin related protein, SH3 domain-bind glutamic acid-rich-like protin3, tumor metastatic process-associated protein NM23, astrocytic phosphoprotein PEA-15 isoform 2, α-crystallin B chain, dual specifity protein phosphatase 3, eukaryotic translation initiation factor 5A-1, phosphatidylethanolamine-binding protein, phosphoglycerate mutase 1, and adenylate kinase isoenzyme 1 in the hippocampus, andprofilin-2, stathmin, ferritin heavy chain, lmw phosphotyrosine protein phosphatase, coactosin-like protein, histidine triad nucleotide-binding protein, ß-synuclein, fatty acid-binding protein, glia mutation factor, tumor metastatic process-associated protein NM23 and splicing factor in the cortex. The significantly increased proteins were dynamin, profilin-2, vacuolar adenosine triphosphatase, transketolae, dihydropyrimidinase-related protein 2, Atp5b protein, fascin and neurofilament-L in the hippocampus, and creatine kinase B, isocytrate dehydrogenase and guanine nucleotide binding protein in the cortex. The significantly changed phosphoproteins were also detected and identified.

P1-25 Dopaminergic neuroprotective effects of L-DOPA and inhibition by 3-OMD target astrocytes

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We have previously reported low availability of L-DOPA/dopamine administered in the striatal astrocytes in damaged dopaminergic neural system that L-DOPA uptaken into the reactive astrocytes is hard to be converted to dopamine, while dopamine uptaken rapidly metabolized in astrocytes in parkinsonian models. To evaluate effects of 3-o-methyldopa (3-OMD), a metabolite of L-DOPA, on striatal astrocytes, we examined changes in number of primary cultured dopaminergic neurons after L-DOPA treatment and effects of 3-OMD using primary cultured mesencephalic neurons and striatal astrocytes in the present study. Although the number of tyrosine hydroxylase-positive dopamine neurons showed no changes with L-DOPA treatment on mesencephalic neurons alone, it was significantly higher than that in the control group after the L-DOPA treatment on mixed cultured mesencephalic neurons and striatal astrocytes. This neuroprotective (proliferating) effect of L-DOPA was almost completely inhibited by simultaneous treatment with 3-OMD. These results suggest that L-DOPA exerts the dopaminergic protective effect and 3-OMD competes with L-DOPA through both acting on some target molecules in astrocytes.

P1-26 Availability of L-DOPA uptaken into striatal astrocytes

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Our previous studies showed that the repeated L-DOPA treatment increased expression of dopamine transporter (DAT) and apparent dopamine (DA)-immunoreactivity in the reactive astrocytes in the striatum of animal models of Parkinson's disease. Astrocytes can uptake both L-DOPA and DA via neutral amino acid transporter LAT and DAT, respectively. Futhermore, we revealed the expression of neutral amino acid transporter LAT and aromatic amino acid decarboxylase (AADC) in striatal astrocytes. Therefore, uptake and metabolism of L-DOPA/DA in the striatal astrocytes may influence their availability in dopaminergic system of parkinsonian patients. In the present study, we measured the contents of L-DOPA, DA and their metabolites after the L-DOPA/DA treatment using primary cultured striatal astrocytes to clarify uptake and metabolism of L-DOPA/DA in astrocytes. The level of L-DOPA in the striatal astrocytes was markedly increased after the L-DOPA treatment for 4 hr, but DA was not detected in the astrocytes 4 or 8 hr after the treatment. On the other hand, the DA treatment for 4 or 8 hr increased levels of DA and its metabolites, especially DOPAC in the striatal astrocytes. These results indicate that DA uptaken into astrocytes is rapidly metabolized and that uptaken L-DOPA never be converted to DA in astrocytes, suggesting low availability of L-DOPA administered in the damaged dopaminergic neural system such as Parkinson's disease.

P1-27 Neuroprotective effect of magnolol *in vitro* and *in vivo* models of Parkinson's disease

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Magnolol and honokiol are the main constituents of the stem bark of *Magnolia obovata* Thunb and *Magnolia officinalis* Rhed. They have been used as traditional medicines in China and Japan and have a wide spectrum of pharmacological activity. These compounds exhibit neuroprotective effects on the central nervous system using both *in vitro* and *in vivo* studies. However, it has not been determined whether magnolol and honokiol exert neuroprotective effects in Parkinson's disease (PD) model. We investigated the role of magnolol in preventing 1-methyl-4-phenylpyridinium ion (MPP^+)- and rotenone- induced cytotoxicity to human neuroblastoma SH-SY5Y cells and 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced neurodegeneration in the mouse model of PD. The neuroblastoma cells were treated with MPP^+ or rotenone and magnolol in DMEM containing N2 supplement. Mitochondrial oxidation-reduction (REDOX) activity and production of reactive oxygen species (ROS) were measured by Alamar blue fluorescence and dichlorofluorescein, respectively. In *in vivo* study, magnolol was orally administered to C57BL/6N mice, either before or after MPTP injection. Striatal tissues were processed for Western blot analysis of dopamine transporter (DAT), tyrosine hydroxylase (TH) and glial fibrillary acidic protein (GFAP) to evaluate the degree of dopaminergic neurodegeneration. In *in vitro* experiment, MPP^+ or rotenone caused a decrease of mitochondrial REDOX activity and an increase of ROS production. Magnolol effectively attenuated the cytotoxicity and suppressed the ROS generation. In the PD mouse model, MPTP injections substantially decreased DAT and TH protein levels and increased GFAP levels in the striatum. These changes were partly prevented by both treatments with Magnolol. These results indicate that magnolol has neuroprotective effect in *in vitro* and *in vivo* PD models, and its neuroprotective effect against these toxins may be associated with the attenuating ROS production. Thus, magnolol may have beneficial effects in slowing or preventing the progression of PD.

P1-28 Involvement of TRAP1 in regulation of mitochondrial morphology

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Mitochondria are highly dynamic organelles that can change in response to extracellular stimuli. The morphological changes are essential for normal mitochondrial and cellular functions including proliferation, differentiation and apoptotic events. The changes are controlled by a tight balance between two antagonistic pathways that promote fusion and fission. Although some molecules have been identified to mediate mitochondrial fission and fusion process, underlying mechanisms of the fission/fusion balance are not well understood. TRAP1 (Tumor necrosis factor receptor associated protein 1) is a mitochondrial molecule which regulates a variety of mitochondrial function. However, it is still not clear whether TRAP1 regulates mitochondrial morphology or not. In this study, we examined role of TRAP1 in regulation of the morphology. Knockdown of TRAP1 expression showed abnormal morphology of mitochondria. We also found that TRAP1 regulated some mitochondrial fission proteins, such as Drp1. These results suggest that TRAP1 regulates the mitochondrial dynamics, which affects mitochondrial/cellular functions.

P1-29 Regulation of tachykinin receptor 1 signaling by regulator of G protein signaling-8 (RSG8)

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Tachykinin receptor 1 (TACR1) is a G protein-coupled receptor (GPCR) that is activated by the substance P. TACR1 shows a widespread distribution in the central nervous system and the substance P-TACR1 system regulates many biological functions such as depression. Recently, evidence has been accumulated that fine-tuning of GPCR activity can be regulated by receptor-interacting proteins. However, TACR1-associated partner has not been determined until now. Regulators of G-protein signaling (RGS) proteins act as GTPase activating proteins which bind to G α subunits via G α -interacting domain (RGS domain). Many studies have shown that RGS proteins are not only G protein regulators but also equally inhibit the signaling from various GPCRs. Here, using biochemical and functional approaches we demonstrated that RGS8, a brain-specific RGS protein, functions as an effective negative modulator of the Gq mediated TACR1 signaling. In transiently transfected HEK293T cells, TACR1 and RGS8 co-localized to the plasma membrane. Moreover, TACR1-mediated calcium mobilization was markedly attenuated by RGS8 in a dose-dependent manner. This effect was not observed for RGS4, which is expressed in nucleus accumbens as well as TACR1/RGS8. Truncation experiments revealed that the N-terminal region of RGS8 (amino acids 1-9) was involved in the RGS8 modulation of TACR1 activity. Further, RGS8(L153F), a point mutant of RGS8 with reduced affinity to G α in RGS domain, showed a lesser suppressive effect of TACR1 signaling as compared to authentic RGS8. These data indicate that both of the N-terminal 9 amino acids and RGS domain in RGS8 contribute to the optimal capacity to downregulate the TACR1 signaling. Because RGS8 does not modulate the signal from other GPCRs such as GH secretagogue receptor, RGS8/TACR1 interaction could be a strategy worthy of further study for the treatment of depression.

P1-30 Identification of cilialy targeting sequence of MCHR1 to primary cilia

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Primary cilia are microtubule-based organelles present on nearly every cell in the mammalian body. It is generally accepted that primary cilia serve important specialized signaling function. Ciliary dysfunction underlies a multitude of human disorders such as the Bardet-Biedl syndrome (BBS). The functions of cilia are defined by the signaling proteins localized to the ciliary membranes. Subsets of neuronal cilia contain certain G protein-coupled receptor (GPCR), including melanin-concentrating hormone receptor 1 (MCHR1) and serotonin receptor 6 (Htr6). However, very little is known about the underlying mechanism of trafficking of GPCRs to the cilium. Recently, the cilialy targeting sequences of certain GPCRs are predicted to contain the loose motif Ax[S/A]xQ in the third intracellular (i3) loop, and VxP/LxP in the C-terminal tail. Yet, the precise identification of ciliary targeting sequences in GPCRs is still unknown. To address the question, we pinpoint the structure of Flag-tagged rat MCHR1. More than 30 mutants were constructed and transiently transfected into ciliated hRPE1 cells, which derived from human retinal pigment epithelial cells. Then we evaluated the resulting changes in receptor function and ciliary localization. This approach showed that two amino acid residues in i3 loop were responsible for ciliary localization of MCHR1. Authentic MCHR1 localized cilia in 67% of transfected cells, while ciliary localization of the mutated version in i3 loop was reduced to 37% of cells. In contrast, any serial C-terminal truncation mutants did not prevent ciliary localization. MCHR1 is involved in the regulation of feeding and energy homeostasis, and obesity is a hallmark of some human ciliary disorders including BBS. Therefore, the further characterization of MCHR1 as a ciliary GPCR provides a potential molecular mechanism to link defects in cilia with obesity.

P1-31 Reduced activation of Na^+, K^+-ATPase through enhancement of oxidative stress in noise-induced hearing loss

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It is well known that noise-induced hearing loss results mainly from enhancement of oxidative stress and mitochondrial damage. In particular, oxidative stress is thought to produce hair cell death in organ of Corti and dysfunction of lateral wall structure. Accumulating evidence indicates that Na^+, K^+-ATPase in cochlear spiral ligament fibrocytes (SLFs) plays a critical role in hearing system. Activity degradation of Na^+, K^+-ATPase is known to be related to deafness through lack of pathway for the recycling of K^+ in the cochlear endolymph. In this study, we evaluated the activity of Na^+, K^+-ATPase during hearing loss induced by intense noise exposure. Adult male Std-ddY mice were exposed to 8 kHz octave band noise of 110 dB SPL for 1 h. The noise exposure produced a dramatic threshold shift at frequencies of 4, 12, and 20 kHz. 4-Hydoroxy tempo (tempol, ROS scavenger) was significantly reduced the threshold shift on day 2 to 7 post-exposure. Additionaly, noise exposure was induced expression of 4-hydroxynonenal (4-HNE)-adducted protein at immediately in the SLFs. Immunohistochemical studies revealed that Na^+, K^+-ATPase was located in the type II and type IV SLFs of the cochlear lateral wall in naïve mice. Noise exposure was reduced the activity of Na^+, K^+-ATPase in the SLFs at least 2 h to 7 days post-exposure. At 2 h later post-exposure, in addition, a significant decrease in the expression of ATPase1a1 and ATPase1a2 mRNA which is genes of Na^+, K^+-ATPase alpha subunit, was seen in the SLFs. Noise-induced reduction in Na^+, K^+-ATPase activity was completely abolished by pre-treatment with tempol. Taken together, our data suggest that intense noise exposure was induced the reduction of Na^+, K^+-ATPase activity in the SLFs of the cochlea. Furthermore, the reduction of Na^+, K^+-ATPase activity is involved in noise-induced hearing loss probably through enhancement of oxidative stress in the SLFs.

P1-32 Neurite outgrowth regulated by carnitine/organic cation transporter OCTN1 (SLC22A4)

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Carnitine/organic cation transporter OCTN1 (SLC22A4) is expressed in various organs and transports various organic cations *in vitro*, although the information of its physiological role *in vivo* is limited. Recently, we have reported that OCTN1 is functionally expressed in small intestine, liver, kidney and brain using ergothioneine (ERGO), a naturally occurring antioxidant, as a typical substrate. Moreover, we have indicated that OCTN1 may be expressed in murine neurons, although its physiological role in neurons has not been clarified. Therefore, the aim of the present study was to clarify the physiological role of OCTN1 expressed in neurons using mouse primary cultured neurons and neuroblastoma Neuro2a cells. For this purpose, neurons were prepared from the cerebral cortex of embryonic 15-day-old mice. Neuro2a cells were cultured in Dulbecco's modified Eagle medium (DMEM) supplemented with 10% fetal calf serum (FCS) for 1 day, followed by the further cultivation in DMEM supplemented with 2% FCS and all-*trans* retinoic acid (ATRA). Neuro2a cultured in the absence of ATRA were almost cells with neurites shorter than the cell size (undifferentiated cells), but the addition of ATRA induced marked outgrowth of neurites (differentiated cells). Real-time PCR analysis revealed the expression of mRNA for OCTN1 in both primary neurons cultured for 3 days and Neuro2a cells. Expression of OCTN1 mRNA was significantly higher in differentiated Neuro2a cells than in undifferentiated cells. In these cells, uptake of [^{3}H]ERGO linearly increased, whereas this uptake was inhibited by unlabeled ERGO. The expression of OCTN1 mRNA was largely decreased in Neuro2a cells transfected with small interfering RNA for OCTN1. Knockdown of OCTN1 did not affect the MTT reduction activity, slightly increased the release of lactate dehydrogenase into culture medium, and markedly decreased the number of cells with neurites longer than the cell size in differentiated Neuro2a cells. The data cited above suggest that OCTN1 expressed in murine neurons may play a pivotal role in mechanisms underlying the neurite outgrowth and could be involved in neuronal differentiation required for the brain development.

P1-33 Intracellular calcium channels regulate proliferative activity in neural stem/progenitor cells derived from subventricular zone of adult mice

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Subventricular zone (SVZ) of adult brain has neural stem/progenitor cells (NPCs) that generate new neurons throughout life. In the NPCs, intracellular Ca^{2+} is known to play a critical role in regulating different stages of early brain development and neurogenesis. To elucidate participation of Ca^{2+} signaling pathway in proliferation of the NPCs, we evaluated the effect of blockers for intracellular Ca^{2+} channel including ryanodine receptor and inositol trisphosphate (IP_3) receptor on proliferative activity in the NPCs of adult mouse SVZ. Cells were prepared from the SVZ of 5-week-old male mice and then primarily cultured in DMEM/F12 medium with EGF and bFGF for 8-11 days *in vitro* (DIV). After replating, the cells were secondarily cultured for 5 DIV under the same conditions in the absence or presence of KCl, dantrolene (ryanodine receptor blocker) or 2-aminoethoxydiphenyl borate (2-APB; IP_3 receptor blocker). KCl markedly enhanced proliferation of the NPCs, whereas dantrolene and 2-APB markedly attenuated the proliferation. In addition, dantrolene and 2-APB completely abolished high K^+-induced enhancement of the proliferation. In the cells cultured on 1 DIV after replating, level of proteins related to proliferation signaling was determined by immunoblot analysis. Both Ca^{2+} channel blockers decreased the level of EGF receptors in cell membranes of the NPCs. RT-PCR analysis revealed that of 3 subunits of ryanodine receptor, ryanodine receptor 3 was the highest level in the NPCs. These results suggest that ryanodine receptors and IP_3 receptors positively regulate cell proliferation through maintaining EGF receptors in cell membrane of the NPCs derived from adult mouse SVZ.

P1-34 Metformin suppresses proliferation coincident with reduction in intracellular potassium level in P19 cells

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Neural stem/progenitor cells (NPCs), which are defined by their ability to self-renew and differentiate into 3 major cell types including neurons, astrocytes, and oligodendrocytes, play a key role in the development and maturation of the central nervous system. P19 embryonic carcinoma cells resemble NPCs. 5'-AMP-activated protein kinase (AMPK) acts as an efficient sensor for cellular energy state. To elucidate the roles of AMPK in proliferation of NPCs, we examined the level of phosphorylated AMPK alpha subunit (active form) during proliferative state as well as the effect of metformin (AMPK activator) on the proliferation in P19 cells. P19 cells were cultured in alpha minimum essential medium, supplemented with 10% fetal bovine serum and penicillin/streptomycin in a 5% CO2 humidified chamber at 37 ˚C. Cell viability was measured by abilities of MTT reduction. The levels of protein expression and its phosphorylation were investigated by immunoblot analysis. Valinomycin (2 M)-induced hyperpolarization was determined by DiSC3(5), which is accumulated by hyperpolarized membrane potential into the cells. Metformin suppressed the proliferation of P19 cells in a concentration-dependent manner. Immunoblot analysis revealed that metformin (2.0 and 20 mM) treatment elevated the level of phosphorylated AMPK alpha subunit up to twice and 5 times, respectively. However, no significant change in the level of AMPK alpha subunit was seen by metformin treatment at the same concentrations. Under the same conditions, metformin treatment significantly attenuated hyperpolarized membrane potential-induced by valinomycin. Taken together, metformin produced AMPK activation, suppression of the proliferation, and decrease in intracellular potassium level in P19 cells.

P1-35 Anticancer drug irinotecan inhibits the response of 5-HT3A receptor

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Anti cancer drugs are commonly used for many types of cancers, although the side-effect is serious problem for quality of life and compliance with treatment. It has been shown that nausea and vomiting during chemotherapy are caused by released of serotonin (5-HT) from the small intestine. 5-HT3 receptor antagonists are widely used as anti emetics. It has been also reported that 5-HT has mitogenic effects on colon cancer cells and 5-HT3 antagonists can inhibit the cancer cell growth. Interestingly, we found that an anti cancer drug irinotecan itself inhibited 5-HT-gated currents of 5-HT3A receptor in a concentration-dependent manner. On the other hand, SN-38, the metabolite of irinotecan, did not change the response of 5-HT3A receptor. Our finding that the blockade of 5-HT3A receptor by irinotecan, not by SN-38, might be helpful for considering the structure and usage which has anti-mitogenic activity concomitant with lower side effect by the blockage of 5-HT3A receptor.

P1-36 Effects of synthetic N1-ribose-modified analogues of cyclic ADP-carbocyclic ribose on depolarization-induced cytosolic Ca^{2+} elevation in NG108-15 neuronal cells

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Cyclic ADP-ribose (cADPR) is the second messenger or endogenous modulator of CICR, acting on ryanodine receptors or TRPM2 channels in a variety of cells including neurons. Using CD38 knockout mice, we recently showed that cADPR is the critical molecule for social behavior by regulating oxytocin secretion. Due to its important physiological roles, synthesis of cADPR analogs has been widely studied, as they are expected for the development of potential drug candidates. We recently developed cyclic ADP-carbocyclic-ribose (cADPcR) as a stable mimic of cADPR and found that its degree was equivalent to or significantly greater than that induced by cADPR for Ca^{2+} mobilization in NG108-15 neuroblastoma x glioma hybrid cells. This time we synthesized a series of N1-ribose modified cADPcR analogues, including 3"-deoxy cADPcR and 2",3"-dideoxydidehydro-cADPcR, and their biological activities were determined using NG108-15 neuronal cells that were pre-loaded with fura-2 AM and subjected to whole-cell patch-clamp. Application of these two analogs through patch pipettes potentiated elevation of cytoplasmic free Ca^{2+} concentration ($[Ca^{2+}]_i$) at the depolarized membrane potential. Though, increase in $[Ca^{2+}]_i$ evoked upon sustained membrane depolarization was less potent than that induced by cADPcR. The different effects between two analogues seem to be resulted from different binding affinity for the target protein, as both compounds would be similarly stable in the evaluation system. We further developed the unsaturated carbocyclic-ribose analogs of cADPR, 4",6"-didehydro-cADPcR (8a) and its inosine congener 4",6"-didehydro-cIDPcR (8b) and the Ca^{2+}-mobilizing potency of these compounds were examined in NG108-15 neuronal cells. Our results indicate that compound 8a does not possess apparent Ca^{2+}-mobilizing activity in NG108-15 cells, in contrast to cADPcR as the potent ligand. It is suggested that the difference between cADPcR and 4",6"-didehydro-cADPcR for the biological activity might be related to the protonation-dependent conformational behavior of the molecule.

P1-37 Neuropsin-dependent synaptic plasticity in the hippocampal CA1 field of freely moving mice

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Long-term potentiation (LTP) is supposed to be a cellular mechanism involved in memory formation. Similar to distinct types of memory formation, LTP can be separated into a protein synthesis-independent early phase (early-LTP) and a protein synthesis-dependent late phase (late-LTP). An important question is whether the transformation from early- into late-LTP can be elicited by behavioral conditions such as the attention to novel events. In our previous study, we found that synaptic plasticity in the hippocampal Schaffer collateral pathway depended on neuropsin (kallikrein-related peptidase 8 or KLK8), a plasticity-related extracellular protease in acute hippocampal slices and in anaesthetized mice. However, neuropsin dependent synaptic plasticity in freely moving mice remains poorly understood. Therefore, we investigated the neuropsin-dependent effect of early-LTP and novelty-exploration with early-LTP in the hippocampal CA1 of freely moving mice. In the present study, we investigated how neuropsin participates in synaptic plasticity in the hippocampal CA1 of freely moving mice. We found that neuropsin-knockout mice were significantly impaired in early-LTP induced by a single tetanus.

P1-38 Involvement of BDNF release in the long-lasting synaptic enhancement in cultured slices

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Long-lasting plasticity of synaptic transmission is assumed to underlie the formation of long-term memory. LTP (long-term potentiation) in the rodent hippocampus, the potentiation of transmission in existing synapses after an intense activity of input pathway, has been analyzed in detail regarding that the phenomenon is an example of long-lasting plasticity. However, since LTP has often been analyzed using acute slices of the hippocampus that remain viable for several hours, a day-to-week order pursuit has not been done. Using stable cultures of hippocampal slices, we found previously that repetitive inductions, but not a single induction, of LTP led to a slowly developing (taking 1-2 weeks to reach maximum) enhancement in synaptic strength accompanied by formation of new synapses. This enhanced transmission state lasted more than 3 weeks. Naming this novel plasticity phenomenon RISE (repetitive LTP-induced synaptic enhancement), we are analyzing the cellular processes underlying the conversion of short-lasting plasticity to long-lasting one. It is known from previous studies including ours that exogenously applied BDNF (brain-derived neurotrophic factor) shows a potent neurotrophic activity including neuronal survival promotion, axonal growth and synapse formation. So we tested the hypothesis that RISE is mediated by endogenously secreted BDNF (increased BDNF expression has been shown in a separate study –Kawaai et al.). Here we applied a BDNF-scavenger (a chimeric protein of BDNF-specific receptor and immunoglobulin-Fc), concomitantly with LTP induction and showed the abolishment of RISE. To confirm this hypothesis further, an analysis is under way whether masking of BDNF receptor with a function-blocking antibody produces the same effect. We recently showed that another long-lasting plasticity LOSS (LTD-repetition-operated synaptic suppression; a long-lasting decrease in synaptic strength after repetitive inductions, not a single induction, of long-term depression in the cultured hippocampal slice) is mediated by precursory form of BDNF and its putative receptor p75NTR (--Egashira et al.). RISE and LOSS, having apparently mirror-image phenotypes, might have mirror-image cellular mechanisms involving BDNF and proBDNF.

P1-39 Filip play a role in cortical development and spine morphology

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The actin cytoskeleton plays a major role for morphological control of neurons during the development and morphological changes in the spines of adult neurons. FILIP (Filamin A-Interacting Protein) controls an amount of Filamin A in the migrating neurons and controls actin dynamics through this mechanism. We made FILIP knockout mice (FILIP-KO mice) and studied on abnormalities of central nervous system to investigate the function of FILIP *in vivo*. We performed *in utero* electroporation and found that FILIP-KO mice showed displacement of the neurons in the cortex, indicating that FILIP-KO mice have a disturbance in the radial migration. We further examined the significance of FILIP in the adult, as the expression of FILIP was also observed in the adult cortical neurons. We investigated the influence of FILIP deletion on the cortex physiologically. The voltage-sensitive dye imaging revealed the suppressed propagation of excitation in the cortex of FILIP-KO mice. We then thoroughly examined on the morphology of neurons using Golgi-Cox staining method. The morphology of spines on the apical dendrite of pyramidal neurons of FILIP-KO mice was different from that of wild-type and heterozygous littermates in the piriform cortex where FILIP expression was observed. In order to investigate FILIP function on the spine morphology further, FILIP was overexpressed in primary cultured hippocampal neurons. Spines with exogenous FILIP were morphologically different from those without FILIP. To elucidate the underlying mechanisms, we searched for another binding partner of FILIP because the expression of Filamin A decreased in the adult brain. Finally, one of myosin family protein was identified. We also found that the overexpression of FILIP resulted in the disarrangement of actomyosin in cultured cell lines. These results suggested that FILIP is involved in proper spine formation through the actomyosin dynamics.

P1-40 Possible in-vitro reproduction of hippocampus-mediated memory consolidation in the cerebral cortex

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Behavioral studies suggest that episode memory is stored transiently in the hippocampus and then transferred to and consolidated in the cerebral cortex. But the cell biological substrates underlying these transfer and consolidation processes remain unclear.

We previously reported that three repeated inductions, but not a single induction, of LTP led to a slowly-developing long-lasting enhancement in synaptic strength coupled with new synapse formation in the CA3-CA1 pathway in the stable cultures of the rodent hippocampal slice. Naming this novel plasticity phenomenon RISE (Repetitive-LTP-Induced Synaptic enhancement), we are analyzing the cellular mechanisms of RISE regarding it as an in-vitro reproduction of the "consolidation" process. However, the preparation is not sufficient for the analysis of "transfer" process, since it lacks the output target from the CA1. So we expanded the culture to include the entorhinal cortex (EC), the principal target of the CA1 neurons, and found that the repeated LTP induction led to the production of RISE in the EC, not in the CA1 (Iijima et al., 2010). Here we continued the analyses and confirmed that RISE was not established in the subiculum (Sb; the region of relay neurons linking CA1 and EC), either. Interestingly, forskolin, the chemical we used to induce LTP in the CA3-CA1 pathway, did not induce LTP in the CA1-Sb-EC pathway. These results suggest either (1) that RISE transiently formed in the CA1 is transferred to the EC, or (2) that LTP induced in the CA1 produced RISE in the EC. So we made a knife-cut in the Sb either 1h before or 24h after the third induction of LTP in the CA1 and found that RISE was not produced in the CA1 or Sb. These support the notion (2), although the establishment of RISE in the EC has not been confirmed (due to cutting of the input pathway for test). We propose that the cellular mechanisms underlying hippocampus-mediated long-term memory is analyzable *in vitro* in the present system.

P1-41 Possible involvement of BDNF in expression of anxiety-likebehavior

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Anxiety is a normal reaction to stress, however, when anxiety becomes excessive, they often cause mental diseases called anxiety disorders. For the understanding of neurobiological mechanisms of anxiety and anxiety disorders, animal models will be useful. A pilocarpine model has become the most popular and widely used animal model of temporal epilepsy. When mice are given pilocarpone, muscarinic acetylcholine receptor agonist, they present status epilepticus (SE), and after an average latent period of 2-3 weeks, they show spontaneous recurrent epileptic seizures. Since the mice also exhibit anxiety-like behavior and cognitive alterations, the pilocarpine model seems to be useful for the study of anxiety. Previously, we reported that mice exhibited anxiety-like behavior within three days after SE. We also showed that the anxiety-like behavior appeared either reversibly or irreversibly depending on duration of SE. In this study, we examined the expression of various proteins in hippocampus obtained from the mice exhibiting either reversible or irreversible anxiety-like behavior. The amounts of AMPA receptor (GluR2), NMDA receptors (NR1, NR2A, and NR2B), and their scaffold proteins (PSD-95, γ-2 and γ-8) decreased remarkably after having SE. The reduction occurred much faster in 4.5 h SE mice than 1.5 h SE mice. In contrast, the expression of glial fibrillary acidic protein (GFAP) was upregulated in both 1.5 and 4.5 h SE mice. Among proteins tested, only the expression of brain-derived neurotrophic factor (BDNF) was changed in parallel with expression of the anxiety-like behavior. These findings suggest that the BDNF signaling participate in the induction of anxiety like-behavior.

P1-42 Lack of BRINP1 in mice causes increase of hippocampal adult neurogenesis and abnormal behavior

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We have previously reported that BRINP (BMP/RA-inducible neural-specific protein-1, 2, 3) family genes are induced during the course of neuronal differentiation and continued to be expressed into adulthood. Among the three family members, BRINP1 is most highly expressed in various brain regions including hippocampus in adult mice. Intraperitoneal administration of kainic acid (KA) induced a transient up-regulation of BRINP1 expression in mouse hippocampal neurons especially in dentate gyrus (DG).

To clarify the physiological functions of BRINP1 in brain, we generated BRINP1-deficient (KO) mice. BRINP1-KO mice showed a significant neurodegeneration in hippocampal CA3 regions after KA administration. These results suggest that activity-induced BRINP1 in DG protects CA3 neurons from KA-evoked excitotoxicity via mossy fiber. In addition, we found an increase of neurogenesis and an expansion of immature neuronal population in SGZ of DG in adult BRINP1-KO mice. These results suggest that lack of BRINP1 causes increase of neurogenesis from stem cells and subsequent inhibition of neuronal differentiation resulted in the abnormal network formation and its maintenance between DG granule neurons and CA3 pyramidal neurons, leading to failure of protection of CA3 neurons from excitotoxicity. On the other hand, behavioral analysis of BRINP1-KO mice showed a remarkable increase in motility and a poor social interaction as compared to wild-type mice. These results suggest that the immature neural circuitry in hippocampus of BRINP1-KO mice may constitute the endophenotype of human mental disorders such as schizophrenia and ADHD.

P1-43 Systemic treatment of SUN13837, a novel small molecular compound mimicking the pharmacological actions of bFGF, enhances functional recovery after spinal cord injury in rats

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Spinal cord injury (SCI) often causes serious and permanent functional disability. Despite being more vigorous research, there are few therapeutic interventions for SCI.
A bioactive substance bFGF, when delivered into CNS ventricles, has been reported to enhance recovery of spinal motor functions in a rat SCI model. We have been developing SUN13837, a novel small molecular compound, which mimics some biologically active properties and mode of action for neuroprotection by bFGF. We therefore investigated the effect of SUN13837 on neuronal dysfunction in a contusion model of SCI in rats.
Rat SCI model were prepared by contusion of a 200-kdyn force at Th9-vertebra. SUN13837 (1mg/kg) was administered intravenously once daily for 10 days, starting at 90 minutes after injury. In behavioral study, the motor function of the hindlimbs was evaluated according to the BBB score once a week for 8 weeks. Remarkable functional recovery was observed with significant increase in BBB score by treatment with SUN13837 compared to vehicle-treated SCI rats. Furthermore, SUN13837 showed a therapeutic time window of at least 12 hr after injury in the SCI model. After the final behavioral evaluation, rats were utilized to examine the recovery of motor function electrophysiologically and the neuronal/axonal regeneration histologically. The latency of the motor evoked potentials (MEP) following electrical stimulation of the hindlimb area of motor cortex was prolonged in SCI rats, and SUN13837-treated rats exhibited significantly shorter MEP latency than vehicle-treated rats. Histological study with fluorescent dye DiI demonstrated that SUN13837 extremely enhanced axon regeneration of the damaged corticospinal tract, and the regenerating axons proceeded caudally beyond the caudal end of SCI to the lumbar spinal cord.
These results indicate that SUN13837 might be a promising candidate of therapeutic agent for SCI.

P1-44 Manipulation of cathepsin c gene expression in mouse

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Cathepsin C (CatC) or dipeptidyl peptidase 1 is a lysosomal cysteine protease. Its function is to cleave dipeptide from the amino terminal of various peptides and protein substrates, and activates many granule-associated serine proteases. Few previous studies revealed CatC function in the central nervous system (CNS). CatC plays a functional role on death signaling pathway and inflammatory process and might also exhibit similar function in the CNS inflammatory diseases. So it is very interesting to study the CatC function in the CNS that has not been elucidated before. We generated CatC a mouse line to manipulate CatC expression by the use of Flexible Accelerated STOP Tetracycline Oprerator-Knockin (FAST) system (Tanaka K.F. et al., 2010). LoxP FRT Neo STOP-FRT-tetO-lopx cassette was inserted into a locus before translation initiation site of the CatC gene (CatCSTOPtetO knock in mouse). The CatCSTOPtetO knock in mouse homozygotes showed no expression of CatC, which was similar to CatC knock out. The CatCSTOPtetO mouse were also crossed with tTA mice, such as CamKII-tTA mouse and Iba1-tTA mouse to induce CatC tTA-mediated ectopic expression in neuron and microglia, respectively. All of these mouse models will be useful for further CatC function study.

P1-45 Decreased microvessel density and altered astrocyte morphology in the hippocampus of diabetic Goto-Kakizaki rats

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Type 2 diabetes mellitus (T2DM) is a systemic metabolic abnormality characterized by insulin deficiency and insulin resistance, affecting also cognitive function. The Goto-Kakizaki (GK) rat, obtained by selective inbreeding of Wistar rats based on impaired glucose tolerance, is considered as a polygenic model of T2DM with mild hyperglycemia starting around postnatal day 8. We have investigated the effect of hyperglycemia and insulin-signaling impairment on the brain by comparing gene expression profiles in the hippocampus of GK and Wistar rats, and found that characteristic changes in gene expression in GK rats were already apparent at 5w of age (5w). Since impairments in the blood-brain-barrier caused by hyperglycemia may be the cause for the expression changes observed in the brain of GK rats, we focused on microvessels and astrocytes in the present study. At 3, 5, 10, and 20 weeks postnatally, immunohistochemcal analyses were carried out on methanol-fixed cryosections of GK and Wistar rat brains using antibodies against von Willebrand factor (vWF) and glial fibrillary acidic protein (GFAP) as markers for microvessels and astrocytes, respectively. Between 5 and 20w, GK rats exhibited fasting blood glucose levels which were consistently higher by 20-60% compared with that of Wistar rats, and 10% increase in body weights. In the dentate gyrus and the CA1 region of the hippocampus, there was a 20% reduction in the total length of vWF-positive vessels per unit area in GK rats compared with that in Wistar rats at 3w. In the CA2, 3 regions, reduction in the total vessel length of GK rats at 3w was 10%. In all the regions examined, differences in total vessel length between the two strains became larger with development, and were 30% at 20w. On the other hand, GFAP-positive astrocytes in the hippocampus exhibited stellate morphology at 3w and 5w in both strains. At 10w and 20w, hippocampal astrocytes in Wistar rats were no longer stellate, whereas those in GK rats showed further elaboration of their processes. The results indicate that early impairments in microvessels lead to activation of astrocytes and gene expression changes in the GK rat brain.

P1-46 P301S mutant human Tau transgenic mice show early symptoms of human tauopathies with dementia and altered sensorimotor gating

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Tauopathies are neurodegenerative disorders characterized by the accumulation of abnormal tau protein leading to cognitive and/or motor dysfunction. To understand the relationship between tau pathology and behavioral impairments, we assessed behavioral abnormalities in a mouse tauopathy model expressing the human P301S mutant tau protein in the early stage of disease to detect its initial neurological manifestations. Behavioral abnormalities of this mouse model recapitulated the neurological deficits of human tauopathies with dementia. Furthermore, we discovered that prepulse inhibition (PPI), a marker of sensorimotor gating, was enhanced in these animals concurrent with initial neuropathological changes associated brain regions in 4 months of age. This finding provides evidence that our tauopathy mouse model displays neurofunctional abnormalities in prodromal stages of disease, since PPI enhancement is characteristic of amnestic mild cognitive impairment, a transitional stage between normal aging and dementia such as Alzheimer's disease (AD), in contrast with attenuated PPI in AD patients. Therefore, assessment of sensorimotor gating could be used to detect the earliest manifestations of tauopathies exemplified by prodromal AD, in which abnormal tau protein plays critical roles in the onset of neuronal dysfunctions.

P2-01 Inhibition of PKA or neuronal activity alters BDNF level with a change in the level of MeCP2 reversely, but not p-CREB, in the rat visual cortex

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Brain-derived neurotrophic factor (BDNF) is an important regulator of ocular dominance plasticity in the visual cortex because cortical application of BDNF disturbs the effect of monocular deprivation. On the other hand, inhibitors of extracellular signal-regulated kinase (Erk) and protein kinase A (PKA) are reported to block the ocular dominance plasticity. Because *in vitro* studies reported that expression of BDNF is regulated by protein kinases including Erk and PKA in activity-dependent manner, there is a possibility that the kinases suppress the ocular dominance plasticity through the effect on the BDNF level. However, little is known about the regulatory mechanisms of BDNF level *in vivo* and it is not clear whether the inhibitors of PKA or Erk affect on BDNF level in the brain. So we measured BDNF level in the visual cortex of young rats treated with the various kinase inhibitors for 2 days to examine the contribution of individual kinases to the BDNF contents *in vivo*. We found that inhibition of PKA increased BDNF protein and mRNA levels contrary to our expectation. Inhibition of Erk induced no detectable change in the BDNF protein level. Furthermore, whereas γ-aminobutyric acid A ($GABA_A$) receptor agonist decreased BDNF protein and mRNA levels, inhibition of Ca^{2+}/calmodulin-dependent protein kinases or p38 mitogen-activated protein kinase induced no detectable change in the BDNF protein level. Interestingly, inhibition of PKA or activity blocked by $GABA_A$ receptor agonist induced no detectable change in the levels of phospho-cAMP response element binding protein (p-CREB) and acetyl-CREB-binding protein. Instead, PKA inhibition and activity blockade induced a decrease and increase of methyl-CpG binding protein 2 (MeCP2) level respectively. *In vivo* BDNF expression might be negatively regulated by a PKA pathway including MeCP2, but not p-CREB, as a transcriptional repressor.

P2-02 Distinct receptor affinities of neuregulin-1 splicing variants to ErbB3 and ErbB4

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Neuregulin1 (NRG1) is one of NRG family of ligands and it plays important roles in the central nervous system by regulating on neuronal development via ErbB4 receptors and glial proliferation via ErbB3 receptors. Alternative splicing of NRG1 gene produces more than 30 structural variants although biological activities of the individual variants remain to be characterized or compared. To assess biochemical difference of major NRG1 variants, we purified soluble type 1-3 NRG1b3 proteins (NDF, GGF2, SMDF) from cell lysates or culture supernatants of the free-style HEK cells transfected with their cDNAs. We carried out *in vitro* translation/transcription of cDNA for type 1 NRG1b3 in the presence of S35 methionine and obtained a radiolabeled ligand of NRG1 for a receptor-binding assay. We replaced the radiolabeled ligand with purified type 1-3 NRG1 proteins in L929 cells expressing ErbB3 or ErbB4 and determined receptor binding affinities of these NRG1 variants to ErbB receptors. Type 1 NRG1b3 exhibited the highest affinity to ErbB4 followed by that to ErbB3. The affinity of type 2 and 3 NRG1b3s was more than ten times lower. These results reveal significant difference among type-1-3 NRG1 variants in receptor-binding affinity to ErbB3 and ErbB4. As these ErbB receptor subtypes are differentially expressed in neurons and glia, each NRG1 variants may target different cell populations and exert distinct biological activities with the given receptor preference.

P2-03 Expression and cellular localization of Gpnmb, a glioma-associated glycoprotein, in the rat central nervous system

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The glycoprotein non-metastatic melanoma B (Gpnmb), also known as dendritic cell heparan sulfate proteoglycan integrin-dependent ligand, osteoactivin, or hematopoietic growth factor-inducible neurokinin-1 type, is a type-I transmembrane protein that is localized to cell-surface and lysozomal membranes. Several studies have shown that Gpnmb is frequently expressed in highly metastatic glioblastoma, malignant melanoma, and breast cancer, implying its involvement in tumor invasion and metastasis. However, little is known about its presence and pathophysiological roles in non-tumorous neural tissues. We previously reported that both mRNA and immunoreactivity for Gpnmb was widely expressed in the cerebrum, cerebellum, brain stem, and spinal cord of normal adult rats. In this study, to define more in detail the nature of cells that express Gpnmb in the rat central nervous system (CNS), we performed double-immunofluorescent staining using specific cellular markers. In the cerebrum, Gpnmb-immunoreactivity (IR) was prominent in a population of cells in cortical layers II, IV and VI. These cells were frequently co-stained with microglia/macrophage-specific antibodies including OX-6, OX-42 and ED1, and with isolectin B4; additionally, some Gpnmb-positive cells were labeled with radial glial cell marker-2 (RC2). In the cerebellum, in addition to Gpnmb-positive macrophages-like cells, cells adjacent to Purkinje cells and their processes in the molecular cell layer were stained with both glial fibrillary acidic protein and RC2, indicating that Gpnmb is expressed in Bergmann glial cells. In the brain stem and spinal cord, as well as in the cerebrum, Gpnmb-IR was detected in cells positive for the microglia/macrophage markers. Our data indicate that the Gpnmb protein is preferentially expressed in subpopulations of cells that belong to microglia/macrophage and radial glial cell lineages. These results suggest that Gpnmb may play important roles in the regulation of immune/inflammatory and developmental processes in the rat CNS.

P2-04 Localization of VEGF in the neurovascular unit of adult mouse brain

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It has been suggested that neurons, glia, and capillaries are organized into neurovascular units, which are involved in the regulation of cerebral blood flow. Within the neurovascular unit, the abluminal surface of the cerebral capillaries is almost completely covered by the foot processes of astrocytes, and this peculiar anatomical feature has been supposed to be the structural basis for the induction and maintenance of the blood-brain barrier by astrocytes. On the other hand, it has been suggested that blood vessels in the brain are not silent bystanders as originally considered but active regulators that play crucial roles in neural development and functions. In this respect, molecules that have crucial functions in both nervous and vascular systems have attracted keen attention recently, and the term "angioneurins" has been proposed. The most striking example of angioneurins is vascular endothelial growth factor A (VEGF), which was originally identified as a key regulator of angiogenesis and has only recently been found to have important functions in the nervous system. In this study, we compared VEGF expression in the vasculature in the brain with that in the aorta and the vasculature in the kidney in mice. In larger vessels containing smooth muscle cells, VEGF was expressed by smooth muscle cells covering the lining of endothelial cells, both in and outside the brain. In cerebral capillaries lacking smooth muscle cells, endothelial cells were closely covered by VEGF-expressing foot processes of astrocytes, whereas capillaries were surrounded by VEGF-expressing processes of podocytes in the renal glomeruli. We also found that cultured cerebral microvessel endothelial cells do not express VEGF, whereas cultured cortical astrocytes do express VEGF. Specific expression of VEGF in the astrocytic foot processes covering capillaries in the neurovascular unit suggests that VEGF plays important roles in the unit. Elucidation of these roles may contribute not only to understanding of physiology of the neurovascular unit but also to developing the therapeutic strategy for neurodegenerative diseases.

P2-05 Isolation of S-nitrosylated proteins from the epileptic brains in rats

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Nitric oxide (NO) exerts diverse cellular responses on apoptosis, neurotransmission, and neurotoxicity by means of protein S-nitrosylation. This modification occurs via oxidative reaction between NO and cysteine (Cys) thiol in the presence of an electron acceptor. On the other hand, there has been reported that NO might participate in kindled seizures. In this study, to elucidate the involvement of NO in pentylenetetrazol (PTZ) –induced seizure or amygdale kindled model, we attempted to isolate and identify the S-nitrosylated proteins.
Under pentobarbital anesthesia (35 mg/kg, i.p.), the rats were fixed to a stereotaxic apparatus and bipolar electrodes were implanted into the right amygdala and monopolar electrodes were implanted into the frontal cortex, hippocampus and left amygdala. Bipolar stimulation of the amygdala was applied everyday with a constant electric stimulator and continued until a generalized convulsion was obtained. Stimulation parameters were monophasic square pulses with a pulse duration of 1.0 ms, a frequency of 60 Hz, and a train duration of 1.0 s. After the animals developed the final stage of generalized seizures (kangaroo posture and falling back), stimulation was repeated for 5 more days to establish completely kindled rats.Alternatively, the rats were administrated subcutaneously at a dose of 60mg/kg.
S-nitrosylated Cys residues in brain homogenates were converted to their biotinylated form by using the biotin-switch technique. Then, samples derived from epileptic brains purified on streptavidin-agarose and eluted by using 2-mercaptoethanol. The samples were then subjected to SDS/PAGE and the gels were stained with silver. A significant increase in the number of S-nitrosylated proteins was evident in epileptic brains. Each protein was identified by mass spectrometry. We will discuss the possible roles of protein S-nitrosylation in kindled seizures.

P2-06 Expression of ecto-nucleo6tidases and equilibrative nucleoside transporter in the rat circumvallate papillae

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Taste bud cells have been classified into four cell types on the basis of their cytological and ultrastructural characteristics, and their communication plays crucial roles in gustatory function. ATP is one of the intra- and intercellular signaling molecules in taste buds, and extracellular ATP fate is considered to be regulated by both metabolism and cellular clearance of ATP. As for ATP metabolism, ectonucleoside triphosphate diphosphohydrolase 2 (ENTPD2), is expressed by type I glial-like cells, but little is known about expression of other ecto-nucleotidases, such as ecto-5'-nucleotidase (NT5E), ecto-nucleotide pyrophosphatase/phosphodiesterase (ENPP) 1, 2 and 3. Equilibrative nucleoside transporters (ENTs), are major molecules that regulate extracellular adenosine level in brain neuronal cells. However, there is no information on their expression in taste bud cells. Therefore, we examined expression profiles of ecto-nucleotidases and ENTs in rat circumvallate by real-time PCR and immunohistochemistry. Expression of mRNAs for *Nt5e* and *Enpp1*, *2* and *3* in the rat circumvallate papillae was detected, NT5E immunoreactivity was detected in a region of non-taste bud cells of the circumvallate papillae, while neither PLC-β2-positive type II, chromogranine-A-positive type III nor SNAP25-positive type III cells were immunoreactive for NT5E. On the other hand, ENT1 immunoreactivity was detected in the PLC-β2-positive type II, chromogranine-A-positive type III and SNAP25-positive type III cells, but not in the non-taste bud cells. These results indicate that there is ATP metabolism and clearance system mediated by ecto-nucleotidases and equilibrative nucleoside transporters. The system may be important in modulation of taste cell signaling.

P2-07 Role of mitochondrial c-Src in respiratory functions

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Non receptor tyrosine kinase, c-Src, is located on the cytoplasmic surface of the plasma membrane, and is implicated as being involved in intracellular signaling pathways from cell surface receptors to various cytoplasmic targets. Recent reports have revealed that c-Src is also present in mitochondria where it phosphorylates mitochondrial proteins such as subunit II of respiratory complex IV, suggesting a pivotal role of c-Src in mitochondrial functions. In the present study, we identify novel substrates of c-Src in mitochondria, and investigate their function in the regulation of oxidative phosphorylation. Treatment of T98G cells with PP2, a Src family kinase inhibitor, resulted in a significant reduction of the mitochondrial oxygen consumption rate at state 3 with dose-dependent decreases in tyrosine phosphorylation levels of total mitochondrial proteins. Similar results were obtained using cells expressing negative regulators of c-Src, MTS-KD-c-Src or MTS-CSK, which harbor a mitochondrial targeting sequence (MTS). These results suggest that mitochondrial c-Src regulates the oxidative phosphorylation system, and that c-Src activity is essential for respiratory functions in mitochondria. Novel molecular targets of oxidative phosphorylation system for c-Src and regulatory mechanism through protein phosphorylation will be discussed.

P2-08 Cdk5-dependent phosphorylation of Drebrin

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Cyclin-dependent kinase 5 (Cdk5) is a proline-directed serine/threonine kinase that is activated by neuron-specific regulatory subunits, p35 and p39. It is shown that Cdk5 is highly expressed in postsynaptic densities and regulates dendritic spine morphology, but it is not known how Cdk5 regulates spine morphology. Developmentally-regulated brain protein (Drebrin) is also a protein involved in dendritic spine morphology, both patterning and maintenance of the spines. Although Drebrin is highly phosphorylated *in vivo*, the relation to Cdk5 has not been addressed yet. Here, we investigated the phosphorylation of Drebrin by Cdk5 and its function. We coexpressed Drebrin with Cdk5/p35 in Neuro2A cells and examined the phosphorylation using Phos-tag SDS-PAGE. The band pattern of Drebrin was up-shifted by co-expression with Cdk5/p35, suggested that Drebrin is phosphorylated by Cdk5. Further, p35 and Drebrin are coloclized on actin filaments in COS-7 cells. Drebrin has thirteen (S/T)P Cdk5 consensus sequences. We divided Drebrin with two regions, N-terminal 430 amino acids (NT) and C-terminal 277 amino acids (CT). The N-terminal fragment of Drebrin showed phosphorylation as was observed with full length Drebrin. Then, we also constructed alanine mutants at (S/T)P sites in Drebrin-NT and looked at their phosphorylation in Neuro2A after cotransfection with Cdk5-p35. The most highly phosphorylated band was lost with Drebrin-NT-S142A, Ala mutant at Ser142. These results suggest that Cdk5 phosphorylates Drebrin at Ser142. We are now going to investigate a role of Cdk5 phosphorylation of Drebrin at Ser142 in the dendritic spine morphology.

P2-09 Sigma-1 receptor agonists enhance K^+-evoked dopamine release from PC12 cells

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Sigma-1receptor is a novel target for the development of therapeutic drugs for many mental disorders; however, the molecular mechanism of sigma-1 receptor signaling is still unclear. Due to a lack of precise evidence of agonist-mediated cellular responses, sigma-1 ligands are incompletely categorized as agonist or antagonist based on their biochemical and pharmacological classifications. In this study, we tested several sigma-1 receptor ligands, SA4503, fluvoxamine, haloperidol, and NE100 for their effects on dopamine release in PC12 cells. The putative sigma-1 agonists SA4503 and fluvoxamine, but not antagonists haloperidol and NE100, enhanced high-K^+-evoked dopamine release in a concentration-dependent manner. None of the tested sigma-1 receptor ligands affected basal dopamine release. We also found that agonist-selective enhancement of dopamine release was inhibited by concurrent addition of the antagonist, NE100, and was abolished in the absence of extra-cellular Ca^{2+}. These results indicate that SA4503 and fluvoxamine can enhance K^+-evoked dopamine release via activation of the sigma-1 receptor. We demonstrate that the sigma-1 receptor agonists specifically modulate dopamine release; thus the reaction can be useful to the biochemical and pharmacological classification of sigma-1 ligands.

P2-10 The effect of 8-nitro-cGMP on proteins in synaptosomes

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[Background] Exocytosis is triggered by the formation of a SNARE complex. The formation of this complex is a crucial step in exocytosis, and the process is regulated by several factors. We found that 8-nitro-cGMP functions as a cGMP analog and possesses unique characters such as membrane permeability and protein *S*-guanylation. The physiological significance of 8-nitro-cGMP, however, is not yet fully elucidated. We found that 8-nitro-cGMP regulated exocytosis, possibly by *S*-guanylation of the SNARE proteins. In the process of analyzing the *S*-guanylation of proteins in synaptosomes by treatment with 8-nitro-cGMP, we found that certain proteins in the detergent-soluble fraction, including the SNARE proteins, translocate to the detergent-insoluble fraction. The study aimed at examining the details of this translocation.
[Method] Rat synaptosome was treated with 8-nitro-cGMP and solubilized in detergent. The solubilized sample was ultracentrifuged to separate the detergent-soluble and detergent-insoluble fractions. Proteins were analyzed by SDS-PAGE and western blotting for which anti-*S*-guanylated and anti-SNARE protein antibodies were used.
[Result] SDS-PAGE analysis showed that the amount of proteins in the detergent-soluble fraction decreased; in contrast, those in the detergent-insoluble fraction increased depending on the concentration of 8-nitro-cGMP. Western blotting with anti-*S*-guanylated protein antibody indicated that on treatment with 8-nitro-cGMP, *S*-guanylated proteins localized in the detergent-insoluble fraction. Western blotting using anti-SNARE protein antibodies showed that SNARE proteins (synaptobrebin, SNAP25, and syntaxin) translocated to the detergent-insoluble fraction after treatment with 8-nitro-cGMP. The translocation of SNARE proteins triggered by 8-nitro-cGMP may be involved in regulating exocytosis. In this paper, we also illustrate the localization of the SNARE proteins in the detergent-insoluble fraction.

P2-11 Brain response to environmental change: Odor-evoked induction of activity-dependent gene expression in mouse brain

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Survival of an organism largely depends on its ability to interact appropriately with the environment. Sensory input has been shown to modulate development of neural circuit by inducing plasticity. Mammalian olfactory system provides several fascinating advantages to delineate stimulus-activity relationship in the nervous system. Olfactory epithelium recognizes odorants from the environment and directly connects the central processing area generating a topographical map in the olfactory bulb (OB). Odorous information, refined by both sensory and central inputs, is conveyed to a number of cortical and subcortical areas. One of the early events initiated by neuronal activity is the induction of activity-dependent gene expression. Expressions of several immediate-early genes (IEGs) such as c-fos, Fosb, Egrl and Arc have been well characterized for tracing odor-evoked neuronal activity in the brain. Using in situ hybridization, here we describe the expression patterns of a set of activity-dependent genes in the olfactory circuitry of mouse brain after olfactory manipulation. We also investigated mRNA expression of activity-dependent genes in cyclic nucleotide gated channel alpha 2 (Cnga2) knockout mice which are anosmic. Our results indicate that expressions of several activity-dependent genes, in addition to the routinely used IEGs, are dynamically regulated by olfaction in an activity-dependent manner in mammalian brain. The in situ hybridization probe set used in our study can be utilized to demarcate the temporal and spatial patterns of brain activities in response to environmental changes.

P2-12 Formation of 8-nitro-cGMP and S-guanylation of SNARE proteins in neural cells

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[Background] 8-nitro-cGMP, which is formed in an NO-dependent manner, has been identified as a novel second messenger in cells. In addition to functioning as a cGMP analog, 8-nitro-cGMP possesses unique characteristics such as membrane permeability and protein S-guanylation. We have found that 8-nitro-cGMP regulates exocytosis. The exocytosis of a neurotransmitter is triggered by the formation of a stable trimer complex of v-SNARE (synaptobrevin on a synaptic vesicle) and t-SNAREs (SNAP25 and syntaxin on a presynaptic membrane). In this study, we examined the formation of 8-nitro-cGMP in neural cells and the effects of 8-nitro-cGMP.
[Method] Coronal sections of a mouse brain were cut on a cryostat for an immunohistochemical analysis. The sections were labeled with anti-8-nitro-cGMP and anti-S-guanylated protein antibodies. In order to analyze an S-guanylated protein, a rat synaptosome was incubated with 8-nitro-cGMP. The S-guanylation of SNARE proteins was detected by immunoprecipitation using an anti-S-guanylated protein antibody, and western blotting was performed using the anti-SNARE protein antibodies. The SNARE complex was detected using a low-temperature SDS-PAGE. Recombinant SNAP25 cysteine mutants was incubated with 8-nitro-cGMP; then, the target cysteine of 8-nitro-cGMP in SNAP25 was examined.
[Result] Immunohistochemistry revealed that 8-nitro-cGMP and protein S-guanylation were detected at the cerebral cortex, hippocampus, and the cerebellum. SNAP25 was detected in the immunoprecipitated proteins with an anti-S-guanylated protein antibody. Low-temperature SDS-PAGE revealed that the amount of the SNARE complex in the synaptosome increased after the 8-nitro-cGMP treatment. An *in vitro* S-guanylation analysis of mutant SNAP25 revealed that C90A mutant exhibited reduced reactivity to 8-nitro-cGMP as compared to the wildtype. This result suggests that 8-nitro-cGMP targeted cysteine 90 of SNAP25.

P2-13 Analysis of the nucleocytoplasmic shuttling of Dab1 required for cortical structure formation

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Formation of highly sophisticated cortical structures of mammalian brain depends on correct migration 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 *reelin* 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* (*reelin* mutant mice). Although Dab1 has been considered a cytoplasmic protein, we previously showed that Dab1 is a nucleocytoplasmic shuttling protein. In its steady state, Dab1 is mainly located in the cytoplasm. However, treatment with leptomycine B, a specific inhibitor of CRM1, resulted in nuclear accumulation of Dab1. By using deletion or substitutional mutants of Dab1, we have mapped a classic bipartite nuclear localization signal (cNLS) and two CRM1-dependent nuclear export signals. To reveal the functional significance of Dab1 shuttling, we examined whether mutation to the cNLS of Dab1 inhibits nuclear translocation of Dab1. Although the cNLS amino acid sequence (RKKGQDRSEATLIKRFK) solely can give an ability to proteins to translocate to the nucleus and mutation into the cNLS inhibits its ability, unexpectedly, Dab1 mutant which has mutation in the cNLS could translocate and accumulate in the nucleus, suggesting that Dab1 is transported into the nucleus by an unidentified nuclear localization signal or mutation into the cNLS within "full-length" Dab1 is insufficient to inhibit its binding to its import receptor. Therefore, we tried to determine the unidentified nuclear translocation mechanism of Dab1 and found that mutations to both cNLS and some amino acids inhibit nuclear translocation of Dab1. We are trying to determine whether Dab1 translocate to nucleus by two independent nuclear translocation pathways.

P2-14 Neural network formation with RNA binding protein Musashi2

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The Musashi (Msi) proteins comprise a family of highly conserved RNA-binding proteins that regulate the expression of target proteins at the translational level. *Drosophila*-Msi regulates asymmetric cell division in neural development. In mammalian CNS, Msi1 and Msi2, are co-expressed in neural stem cells, suggesting Msi family proteins maintain the CNS stem cells. To reveal the roles of Msi *in vivo*, we generated Msi1$^{-/-}$ mice which frequently died of obstructive hydrocephalus. Msi1$^{-/-}$ results also indicate Msi2 have cooperative roles, thus we generated Msi2$^{-/-}$ mice. Msi2$^{-/-}$ survived to adult showing the phenotype of hypersensitivity to touch (allodynia) and fewer-than-normal synapses in the deep layer of the dorsal horn of the spinal cord with fewer innervation of sensory axons from the dorsal root ganglion (DRG) to the appropriate targets. Target mRNA screening of Msi2 revealed that one of the target mRNAs control the neurite out growth. Detailed behavioral and histological analyses confirmed that the Msi2 regulate the projection of specific timing and specific subtypes of sensory neurons by controlling the expression of target mRNA. The phenotypes of Msi2$^{-/-}$ indicate that Msi2 regulates the formation of the sensory neural network by controlling protein expression of its target.

P2-15 Role of the transglutaminase family on optic nerve regeneration in fish

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Unlike the mammalian CNS neurons, lower vertebrates neurons such as fish and amphibians can successfully regenerate their axons following nerve lesion. We have investigated the molecular mechanisms for regeneration using fish visual system. To search involving factors in this process, we constructed cDNA library from goldfish retina 5days after optic nerve transection. Out of 200,000 cDNA clones, we identified two types of cDNA clones belonging to transglutaminase (TG) family as upregulated genes after nerve injury. Using molecular cloning techniques, we concluded these TGs as tissue type-like TG and Factor XIII-A. Since the former showed that the increase of expression was localized only in the ganglion cells in the regenerating retina, we named retinal TG (TGR). The enzyme activity and mRNA level of TGR were peaked at 20 days after optic nerve lesion. Factor XIII-A, well known as A-subunit of plasma transglutaminase that catalyzes the formation of covalent cross-linking reactions in polymerized fibrin to yield mature clots. The cellular localization of FXIIIA was also detected only in retinal ganglion cells in the regenerating retina. However, the peak expression of FXIIIA was clearly different. The level of FXIIIA mRNA started to increase in the retina 1-2 days, peaked at 5–7 days and returned to the control level by 20 days after optic nerve injury. Furthermore, *in situ* hybridization study in the optic nerve revealed that a lot of Factor XIII-A positive cells could be seen in non-neuronal cells around the injured site. To elucidate molecular involvement of these TGs, we studied the effect of recombinant TGR protein or overexpression of Factor XIII-A using retinal explant culture system. TGR protein significantly enhanced neurite outgrowth from primed retina. In contrast, Factor XIII-A effectively induced neurite outgrowth only from naïve retina. These data suggest that stage specific activation of TGs is important for optic nerve regeneration.

P2-16 Genetic and cellular interaction analyses of a repulsive axonal guidance cue, draxin

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We found that all three forebrain commissures are missing in draxin KO mice and that netrin receptor DCC is a draxin receptor. Double hetero mouse of Dra(+/-)DCC(+/-) showed that corpus callosum formation was severely affected but hippocampus and anterior commissures were not affected, indicating that DCC is a really functional *in vivo* receptor for draxin and that anterior and hippocampus commissures formation might use other draxin receptors. We also found that anterior commissure was not formed in Tsukushi (TSK), which has an inhibitory activity against BMP and Wnt, KO mice. Double hetero mouse of Dra(+/-)TSK(+/-) showed that anterior commissure was not connected well, suggesting draxin effect on the anterior commissure formation might be mediated by Wnt inhibitory activity.

P2-17 Expression pattern of kirrel3 in the central nervous system of adult mice

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Kirrel3 is a member of the immunoglobulin superfamily, which is expressed in the central nervous system (CNS), including the olfactory bulb, hippocampus, brainstem, and cerebellum. Recent reports have suggested that kirrel3 plays important roles in axonal fasciculation in the olfactory bulb, nuclei formation in the developing pons, and synapse formation in the hippocampus. However, the detailed characterization of kirrel3-expressing cells and its functions in the CNS are largely unknown. To get insights into the roles of kirrel3 in the CNS, we characterized kirrel3-expressing cells in the adult CNS using kirrel3-*lacZ* knockin mice. β-galactosidase (β-gal) staining revealed that kirrel3 was highly expressed in the olfactory, limbic (hippocampus, proisocortex, ventral striatum, prefrontal cortex), and auditory pathways, in addition to the cerebellum. Double-immunofluorescence staining of β-gal with parvalbumin (PV), NeuN, or neurogranin revealed that β-gal was expressed in PV-positive basket/stellate cells and NeuN-positive granule cells in the cerebellum. In addition, calbindin-positive Purkinje cells expressed β-gal in a stripe pattern in nodular, central, and posterior zones and flocculus, which are related to vestibular nuclei. In the dentate gyrus of the hippocampus, almost all the β-gal-positive cells expressed calbindin without the colocalization with nestin and doublecortin, indicating that β-gal-positive cells were differentiated granule cells. These results suggest that kirrel3 was localized to functionally related brain nuclei or compartments in the CNS and may be involved in the formation and maintenance of functional circuits, such as the olfactory-limbic, auditory, and vestibular systems. This work was supported by a Grant-in-Aid for Scientific Research (B) from Japan Society for the Promotion of Science (22390036).

P2-18 Expression of kirrel3 in the dorsal root ganglia during development

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Kin of irregular chiasm-like 3 (kirrel3) belongs to the immunoglobulin superfamily and is expressed in the sensory systems, such as the olfactory, auditory, visual, and somatic sensory systems. In the previous study, we have reported that kirrel3 is mainly expressed in the tyrosine kinase receptor (Trk) C-positive proprioceptive neurons of the dorsal root ganglia (DRGs) and may play a role in targeting of these nerve fibers on muscle spindles through the interaction with nephrin during development (Komori et al., J Comp Neurol 511: 92-108, 2008). Although kirrel3 is also expressed in some of TrkA- or TrkB-positive DRG neurons in adulthood, the roles of kirrel3 in these DRG neurons remains to be elusidated. To get further insights into the function of kirrel3 in DRG neurons, we investigated the detailed expression pattern of kirrel3 in the developing and adult DRGs using kirrel3-lacZ knockin mice. X-gal staining of kirrel3 heterozygote mice revealed that expression of kirrel3 was first observed in a few DRG neurons at embryonic day (E) 11.5. From E12.5 to E17.5, the number of kirrel3-expressing DRG neurons gradually increased and reached the adult level at E17.5. In the adult DRGs, kirrel3 was expressed in some of small-sized neurons as well as in many medium- to large-sized neurons of DRGs. These results suggest that expression pattern of LacZ in the DRGs was consistent with our previous data of in situ hybridization histochemistry and immunohistochemistry. In addition, X-gal staining combined with immunohistochemistry for TrkA, TrkB, TrkC, and Ret revealed that kirrel3 was expressed in some of TrkA-, TrkB-, TrkC-, or Ret-positive DRG neurons from embryonic stages to adulthood. Therefore, kirrel3 was expressed in nociceptive, thermoceptive, and mechanoceptive DRG neurons as well as in proprioceptive DRG neurons, suggesting that the involvement of kirrel3 in axonal targeting, synapse formation, and transmission of sensory information of these neurons. This work was supported by a Grant-in-Aid for Scientific Research (B) from Japan Society for the Promotion of Science (22390036).

P2-19 Effects of heat shock on proliferation of primate ES cell-derived neural stem cells

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It has been known that heat shock causes various responses such as cell death, changes in the gene expression and induction of heat shock proteins and also that high temperature during pregnancy has large effects on brain growth in embryos. Neural stem cells (NSCs) that symmetrically proliferate and differentiate into neurons and glia play an important role in brain development. We have reported the effects of heat shock on proliferation of mouse NSCs derived from ES cells *in vitro*. In this study, effects of heat shock on proliferation of the monkey NSCs were investigated to evaluate effects on human NSCs. NSCs were prepared from cynomolgus monkey ES cells by the Neural Stem Sphere (NSS) method. The NSCs were exposed to heat shock for 20 minutes and cultured with fibroblast growth factor-2 for 4 days. After exposure to heat shock at 37(Control), 40, 42° C, the NSCs could stably proliferate for 4 days. Meanwhile, the proliferation of the cells exposed to heat shock at 43° C and above was temperature-dependently inhibited by causing cell death. The results indicate that heat shock have effects on proliferation of the monkey NSCs over 43° C as well as mouse NSCs. The heat-exposed cells were demonstrated to be nestin-positive by immnofluorescent staining. Real-time RT-PCR analysis also demonstrated that nestin and musashi-1, makers of neural stem cells, were highly expressed in the heat-exposed NSCs. The NSCs showed no change in the gene expression patterns of makers of NSCs after the heat-shock exposure. These results indicate that the heat-exposed NSCs maintained cellular properties as NSCs. As a result, the effects of heat shock on proliferation of primate NSCs were very similar to those of rodent NSCs. This work was partly supported by Selective Research Fund of Tokyo Metropolitan University.

P2-20 Influence on neuronal differentiation; enhancement by tunicamycin-induced ER stress: role of ubiquitin ligase HRD1

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Objectives: Neural stem cells (NSCs) play an essential role in the development and maturation of the central nervous system. It is known that strong endoplasmic reticulum (ER) stress induces neuronal cell death. After neuronal cell death, neurogenesis is generally enhanced for repairing the damaged region. However, it is not cleared whether ER stress directly activates neurogenesis. In this study, we evaluated whether neuronal differentiation is activated under mild condition of tunicamycin-induced ER stress that does not induce neuronal cell death.Methods: Neurons were prepared from the mouse embryonal carcinoma P19 cells by inducing to differentiate using retinoic acid. The differentiated cells were cultured for 8 days in the absence or presence of 2 ng/mL tunicamycin with or without HRD1 knockdown. Results: Tunicamycin for 4 days markedly led to increase of the levels of GRP94 and GRP78 (ER stress marker). At the time, the number of surviving cells was unaffected in the presence of tunicamycin. Additionally, tunicamycin had no influence on the level of nestin (NSC marker protein) 4 days after the exposure. At 8 days after the exposure, tunicamycin resulted in a marked reduction of levels of nestin, MAP-2 (mature neuronal marker protein) and glial fibrillary acidic protein (GFAP, glial marker protein). However, tunicamycin led to increase of level of Tuj-1 (neural marker protein). In contrast, knockdown of ubiquitin ligase HRD1 abolished the changes in the expression of these proteins by tunicamycin. Moreover, Treatment with tunicamycin significantly led to decrease of Hes1 mRNA, Hes5 mRNA, Pax6 mRNA and STAT3 mRNA levels, which are transcription factors and negatively regulate the neuronal differentiation.Conclusion: These results suggest the possibility that tunicamycin-induced ER stress enhances the neuronal differentiation from NSCs via HRD1 protein, but inhibits maturation of neuron. Moreover, the neuronal differentiation might be regulated by expression of Hes1, Hes5, Pax6 and STAT3.

P2-21 Effects of ultrasound on mouse neural stem cells derived from embryonic stem cells

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Ultrasound is widely used for diagnosis and treatment, and data on the therapeutic effects of ultrasound have been recently accumulating. In this study, we examined effects of ultrasound on neural stem cells (NSCs). NSCs were prepared from mouse embryonic stem cells by the Neural Stem Sphere (NSS) method, and the NSCs were attached to dishes and cultured with mitogen, basic fibroblast growth factor. Ultrasound treatment were applied to the NSCs, after 1 day in culture, at 1.0 MHz, from 0.5 to 3.0 W/cm^2, for 5 min through the bottom of the dish via coupling gel between the ultrasonic transducer and the dish. The cells were cultured for 3 days after the treatment, and the effects of the treatment were analysed. In some experiments, to investigate effects on the NSCs which were unattached to dishes, suspended cells in non-adhesive dishes were treated as above, and the treated cells were attached onto dishes and cultured for 4 days afterward. NSCs, treated at medium intensity range from 1.5 to 2.5 W/cm^2 both under attached and unattached conditions, proliferated exponentially as untreated cells. The cells were demonstrated to be nestin-positive NSCs by immunofluorescent staining. In contrast, by treatment at 3.0 W/cm^2 the cell number decreased remarkably the next day and a growth rate of the cells became decreased afterward. As the temperature of the medium was observed to become 45.8° C after the treatment in parallel experiments, it is speculated that the high temperature may have induced apoptosis of the treated NSCs. Treated at low intensity range from 0.5 to 1.0 W/cm^2, the NSCs under unattached conditions proliferated exponentially as control, in contrast, the cells under attached conditions were significantly lost by the next day, and the growth rates of cells decreased afterward.

P2-22 Olig2 expression pattern in the retina of adult mouse

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Recent studies have revealed that Olig2 expressing cells exist ubiquitously throughout the normal adult brain as they do in embryonic stages. These cells, except Olig2 expressing premature oligodendrocyte, are characterized as progenitor cells, based on their potential to proliferate and differentiate. Because they dramatically increase especially in the pathological niche, Olig2 expressing progenitors can be an attractive target of therapeutic approach. Therefore, the distribution pattern of Olig2 expressing cells in the normal adult CNS should be clarified in detail.

We focused the adult retina that is originated from developing brain. Thus far, there has been reported different opinions concerning the presence or absence of Olig2 expression in the adult retina, but this subject is as yet inconclusive. In agree with a previous report (Shibasaki et al., 2007), we detected Olig2 immunoreactivity in inner nuclear layer (INL) in the retina of adult mouse. And we observed that, in addition to INL, a part of outer nuclear layer (ONL) cells also have Olig2 immunoreactivities.

In this report we demonstrate the Olig2 expression pattern in the retina of adult mouse using immunohistochemical methods.

P2-23 Yamanaka factors expressions in the zebrafish retina during optic nerve regeneration

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CNS neurons in fish can regenerate their axons after nerve injury, while CNS neurons in mammals can not regenerate their axons after injury. The regenerating mechanism of fish CNS neurons has not been so far studied. Recently, Yamanaka group established the iPS cells by exogenously transfecting four key transcription factors (Klf4, Oct3/4, Sox2, C-myc) into somatic cells. From their stimulatory results, we hypothesize that adult fish CNS neurons might be initialized (reprogrammed) to become stem cell-like after nerve injury. Therefore, we tested this possibility in the zebrafish retina and spinal cord after nerve injury. We measured temporal changes of Yamanaka factors in the CNS neurons after nerve injury. We performed time-course analysis of these factors mRNAs using RT-PCR for 40 days after nerve injury. The levels of Yamanaka factor mRNAs increased at 3-10 days after optic nerve injury (ONI) and returned to control levels by 40 days post injury (dpi). To investigate mRNA localization, we performed in situ hybridization. In control retina, the signals of these mRNAs detected weakly while in 5dpi retina, mRNA increased in retinal ganglion cells (RGCs). Next, we studied the changing expression of nestin which is known as neural stem cells marker. Nestin mRNA increased at 3-5 dpi and the increasing signal was also detected in the RGCs after ONI. Optic nerve lesion induced 2-3 folds increase of Yamanaka factors mRNA in the ZF retinal ganglion cells (RGCs). The temporal changes of Yamanaka factors levels in the ZF RGCs at 3-10 days after axotomy corresponded to the early preparative stage of optic nerve regeneration in ZF. Therefore,The Yamanaka factors involve in reprogramming of injured RGCs leading to regrow their axons after ONI fish retina regeneration.

P2-24 Disruption of axo-glial interaction causes focal axonal damage in cerebellar Purkinje neurons

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Paranodal axo-glial junctions play a crucial role in the organization and maintenance of molecular domains in myelinated axons. Cerebroside sulfotransferase (CST) deficient mice show disruption of the paranodal axo-glial junction both in the CNS and the PNS. Previously we reported that axonal mitochondria at the nodes of Ranvier were large and swollen, and that axonal transport related protein levels decreased in the PNS of CST-deficient mice. We also presented the finding of frequent focal axonal swellings in the cerebellar Purkinje neurons. For the present study, we investigated the state of the axonal swellings in Purkinje neurons in order to improve understanding of the role of paranodal axo-glial junctions in the cerebellum. These axonal swellings did not occur in development prior to the onset of myelination (P5). Some calbindin D-28K-positive axonal swellings were found in 15-day-old mutant mice, although they were small. The number of swellings and their size did increase with age. In the analysis of various stages of the swellings in 12-week-old mutant mice, we found accumulation of phosphorylated neurofilament as an early stage, and later deposition of amyloid precursor protein became prominent. Ultrastructural analysis showed accumulations of tubular structures closely resembling smooth endoplasmic reticulum (ER), of numerous membranous organelles, of dense bodies, and of mitochondria in the myelinated swollen axon, suggesting that degeneration is probably secondary to impaired axonal transport. The internal mesaxon was undulating and vacuoles were sometimes present, but most of the compact myelin was intact. Staining of cerebellar sections of the mutant mice for type I IP3 receptor (IP3RI) revealed high immunoreactivity within the swellings, and this IP3R1 deposition was the initial change we observed at the swellings. This suggests that local calcium regulation through ER was involved in these axonal swellings. Therefore, continuous signals via the paranodal axo-glial junctions may be necessary for maintenance of axonal homeostasis in Purkinje cells.

P2-25 Protein arginine N-methyltransferase 8 (PRMT8) is expressed in activated microglial cells after spinal cord injury

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Protein arginine N-methyltransferase 8 (PRMT8) was originally reported as a neuron-specific type II PRMT whose subcellular distribution is dominantly nuclear. However, when we examined the expression level of PRMT8 in the soma of spinal neurons that were injured by hemiectomy, nuclear immunoreactivity that was overlapped with NeuN was extinguished. Instead, the observed signal exhibited cytoplasmic distribution, most of which delineated a population of densely-packed cells around the injured region. This group of cells were well-overlapped with CD11b-positive microglial cells, demonstrating that PRMT8 is expressed in the activated microglial cells. In keeping with *in vivo* data, immortalized microglial cell line MG5 also expressed PRMT8. The knockdown of PRMT8 caused enhancement of inflammatory response, including induction of iNOS and alpha TNF.

P2-26 Alteration of the expression balance of hnRNP C1 and C2 changes the expression of myelination-related genes in the human neuroblastoma cell line

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The heterogeneous nuclear ribonucleoprotein C (hnRNP C) protein is involved in pre-mRNA splicing, stabilization of mRNA, and internal ribosome entry site-dependent translation of proteins. The hnRNP C protein exists in two variants, hnRNP C1 and hnRNP C2, but the functional differences between the two variants, if any, remain unclear. Recently, it was reported that the expression level of hnRNP C1/C2 protein was significantly decreased in the post-mortem brains of schizophrenic patients. Various risk factors are associated with the onset of schizophrenia; one of the most notable is the differential expression of myelination-related genes, suggesting a disruption in oligodendrocyte function in schizophrenia. We constructed expression vectors for the two hnRNP C variants, hnRNP C1 and C2, and investigated using quantitative real-time RT-PCR whether the overexpression of these proteins changed the expression of myelination-related genes: the quaking (*QKI*) isoforms (*QKI-5, -6, -7*, and *-7b*) and myelin basic protein (*MBP*), in the human neuroblastoma cell line SK-N-SH. In both hnRNP C1- and C2-overexpressing cells, the expression of *QKI-6* and *QKI-7* was significantly increased or decreased compared with the control, respectively. Intriguingly, *QKI-5* and *MBP* were markedly up- or down-regulated by overexpressing hnRNP C2, respectively. Moreover, we demonstrated that the *MBP* up-regulation by hnRNP C2 was not mediated by the QKI proteins, suggesting that the phenomenon might be direct or via a novel pathway. These findings suggest that altered expression levels of hnRNP C in the brain of patients with schizophrenia might be involved in the pathophysiology of this disease through alteration of QKI isoform and MBP expression. Also, our findings demonstrate distinct functions of hnRNP C1 and C2, and might be helpful in understanding the functions of these molecules.

P2-27 Ability of microglia to eliminate glutamate toxicity in the axotomized rat facial nucleus

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Activated microglia around injured motoneurons were observed to highly express a glial-type glutamate transporter GLT-1 in the axotomized facial nucleus, suggesting that the microglia uptake glutamic acid (Glu) in the vicinity of synapse. On the other hand, microglia (primary microglia) isolated from newborn rat brain-derived primary culture were found to uptake ^{14}C-Glu through GLT-1 acitivity. These results allowed us to examine the fate of Glu incorporated into microglia. Therefore, in this study we investigated a possibility that microglia change Glu into glutamine (Gln) by glutamine synthetase. At first, whether or not glutamine synthetase activity is detected in microglia was examined in the newborn primary microglia. The enzyme activity was detected in the cell homogenate, although the specific activity was lower than that of astrocytes. Subsequently, to confirm the presence of glutamine synthetase in microglia, immunoblotting analysis was carried out. The analysis revealed that the newborn primary microglia express glutamine synthetase proteins. The proteins were immunocytochemically observed in cytoplasm out of nucleus in the microglia. These results suggested that microglia in axotomized facial nucleus incorporate Glu by GLT-1 and change it to Gln by glutamine synthetase in cytoplasm. In fact, axotomized facial nucleus-derived microglia *in vitro* were found to express GLT-1 and glutamine synthetase proteins. Therefore, microglia in axotomized facial nucleus were strongly suggested to serve as a glutamate scavenger that converts excitotoxic Glu to safe Gln around excitatory synapse.

P2-28 A neuropathy-associated 36K isoform of myelin P0, L-MPZ, is produced by the stop codon readthrough mechanism

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Myelin protein zero (P0 or MPZ) is a N-glycosylated type I transmembrane adhesion molecule (~30K), which is a major PNS myelin protein in vertebrates. Extracellular and intracellular domains are involved in membrane adhesion of compact myelin. Previously, we identified P0-related 36K protein recognized by the neuropathy patients' sera as an novel P0 isoform containing full P0 sequence and a unique peptide translated from 3'UTR of P0 in its C-terminus. This predicted extra amino acid sequences between regular stop codon and the next stop codon are evolutionarily highly conserved in higher animals. We named this protein as a large myelin protein zero, L-MPZ. However, the production mechanism and function of L-MPZ are still unknown. According to the reported P0 gene structure, there was no possibility to be a splicing variant. In this study, we investigated whether stop codon readthrough mechanism was involved. The specific anti-L-MPZ antibody produced against the peptide of L-MPZ unique region was able to detect 36K band in the lysate from NIH/3T3 cells transfected with human P0 cDNA, indicating that both P0 and L-MPZ were produced from identical mRNA. The L-MPZ molecule of predicted size was also produced from the identical P0 cDNA in conjunction with P0 in the *in vitro* transcription/translation system using stop codon readthrough enhancer, G418. Using this system, the several types of point mutations in the sequence around regular P0 stop codon revealed that the original sequence was more effective for the stop codon readthrough. The immunostaining of sciatic nerve indicated that the L-MPZ was localized in the compact myelin. In the transfected cells, the L-MPZ was colocalized with P0 at the site of cell-cell adhesion. These results suggest that L-MPZ is produced by stop codon readthrough mechanism, involved in compact myelin formation/maintenance and in the pathological conditions of various neuropathies. Since this is the first finding of a stop codon readthrough in a common mammalian protein not in genetic disease but in normal situation, detailed analysis of L-MPZ expression may yield greater understanding of the mechanism of expanding the functions of normal proteins.

P2-29 Molecular mechanism by which microgla proliferate in the transected rat facial nucleus

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Transection of rat facial nerve leads to an increase of microglial cell number in the ipsilateral facial nucleus. We demonstrated previously that up-regulated macrophage-colony stimulating factor (M-CSF) in the transected facial nucleus triggers the induction of cFms (receptor for M-CSF) and proliferating cell nuclear antigen (PCNA) in microglia, and causes the microglia to divide. However, it remains to analyze in detail the molecular mechanism for microglial proliferation. In the present study, we analyzed cell cycle-associated proteins including cyclins, cyclin-dependent protein kinases (Cdk) and Cdk inhibitors in the axotomized rat facial nucleus, and also examined a role of MAP kinases in the process of microglial proliferation *in vitro*. Immunoblotting revealed that cyclin A is induced in injured facial nucleus 3 days after transection, and immunohistochemically recognized in activated microglia. Cyclin D was observed to increase during 3-7 days after transection. Cdk2 and Cdk4 were suggested to serve as mitotic promoting factor by forming complex with suitable cyclin. A Cdk inhibitor p21 turned out to increase 5 days after axotomy. Furthermore, using a culture system in which microglia from newborn-rat brain-derived primary culture proliferate in response to M-CSF, we analyzed the cell cycle-associated proteins (cyclins and Cdks) and examined a role of MAP kinases on the microglial proliferation. By stimulation with M-CSF, three MAP kinases, ERK, JNK and p38, were transiently activated, and then the amounts of cyclin A and D, PCNA and cFms elevated in microglia. A series of inhibitor experiments indicated that JNK is associated with induction of cyclins and PCNA, while p38 is linked to cFms induction in M-CSF-stimulated microglia. Taken together, we demonstrated that the microglial proliferation triggered by M-CSF in transected facial nucleus is regulated by the addtitive actions of cyclins (A and D), PCNA, Cdk inhibitor (p21) and cFms expression, and the M-CSF-dependent elevation of cyclins/PCNA and cFms levels is differentially regulated by JNK and p38, respectively.

P2-30 The role of Bergmann glia in cerebellar development

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Bergmann glia are in astrocyte-lineage and their cell bodies locate in the cerebellar Purkinje cell layer. They are characterized by the Bergmann fiber that extends from the cell body to pial surface through the molecular layer. In the early postnatal cerebellum, granule cell progenitors proliferate in the outer granular cell layer and migrate through Purkinje cell layer to reach inner granular cell layer. It is well accepted that Bergmann glia guide the granule cell migration. In the course of study aiming at altering the expression of Mlc1 in astrocyte-specific manner, we found a unique phenotype in their cerebellar development. Mlc1 is predominantly expressed in astrocyte-lineage cells and its mutation causes "Megalencephalic leukoencephalopathy with subcortical cyst" in human. we found disturbance of Purkinje cell and granule cell alignments in the cerebellum, which should have been caused by Mlc1 over-expression in Bergmann glia. Moreover, many Bergmann glia mislocalized in the cerebellar molecular layer and showed reactive astrocyte-like shape. In this mouse, Mlc1 is over-expressed since embryonic day 14 in radial/ Bergmann glia. When the Mlc1 over-exoression level was returned to the normal level after postnatal day 0, there was no abnormality in the cerebellar architecture. Therefore, Mlc1 overexpression postnatally should have caused this abnormality.

Poster Sessions

P2-31 Involvement of adenosine A3 receptor in microglial process extension

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Microglia have motile cell processes and monitor the brain parenchyma under physiological conditions. Within minutes of brain damage, microglial processes extend toward the injured site. The chemoattractive response is triggered by the release of ATP from injured tissue and the consequent activation of the purinergic receptor P2Y12 on microglia. Adenosine, a phosphohydrolytic derivative of ATP, is known as a neuromodulator and its effects are mediated by G protein-coupled adenosine receptors (ARs) of four distinct subtypes A1, A2A, A2B, and A3. A recent study showed that A2A stimulation causes the process retraction of microglia activated by LPS (Orr et al., 2009). In this study, we showed that A3 signaling modulates P2Y12-mediated microglial process extension.
We have previously established an *in vitro* assay system using rat primary-cultured microglia and collagen gels-coated transwell chambers. We first examined effects of antagonists of AR subtypes on ADP-induced process extension in the assay. An A3 antagonist MRS1523 significantly inhibited the process extension and antagonists of the other AR subtypes had no effect. Microglia stimulated with ADP showed chemotactic process extension along the ADP concentration gradient, whereas microglia stimulated with a potent P2Y12 agonist 2-methylthio-ADP (2MeSADP) protruded their processes in random directions. The chemotactic activity of 2MeSADP-stimulated microglia was recovered by the addition of adenosine and an A3 agonist 2CL-IB-MECA, but not by agonists of the other AR subtypes. Recent studies have demonstrated that Jun-N-terminal kinase (JNK) is implicated in regulation of cell motility. Western blot analysis with a phospho-specific JNK antibody showed that 2CL-IB-MECA stimulation induced JNK phosphorylation in microglia, and a JNK inhibitor SP600125 inhibited ADP-induced microglial process extension. RT-PCR analysis showed that A1 and A3 were expressed by microglia sorted from normal adult rat brains and that the level of A2A expression was very low. These results suggest that A3 stimulation by adenosine may be involved in microglial process extension toward injured sites.

P2-32 Identification of CSPG constituting DACS, a novel brain extracellular matrix

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An anti-chondroitin sulfate antibody CS56 delineated a structure with a unique morphology like a dandelion clock. Accordingly, we named it DAndelion Clock-like Structure (DACS) (BBRC; 364: 410-5, 2008). In the adult brain, CSPGs exhibit a distribution pattern, named PNNs, distinct from that of DACS. PNNs surround cell bodies and proximal dendrites of GABAergic interneurons, and consist of several kinds of CSPGs, hyaluronan, and cell adhesion molecules. The functions of PNNs have not been fully elucidated, but some studies indicate that the PNNs are formed in response to neuronal activity. On the other hand, DACSs surrounded a group of NeuN-positive/GABA-negative neurons. At an ultrastructural level, CS56-immunoreactivities were localized in the cytoplasm and on the membrane of astrocytes. As the postnatal cerebral cortex matured, DACSs became visible from the end of the critical period. Furthermore, DACSs is conserved among species. In this study, we have identified the core protein of DACS-constituting CSPG. DACS-constituting CSPG has been purified from the mouse cerebral cortex by anion charge, charge transfer and size exclusion chromatographies, and has been identified as Tenascin-R (TNR). TNR is an extracellular matrix protein expressed primarily in the central nervous system, and is localized around some GABAergic interneurons. However, in situ hybridization analysis showed that TNR mRNA was selectively localized at CS56-positive astrocytes, but not WFA-positive GABAergic interneurons in the adult mouse brain. These results suggest that TNR may be expressed in a subpopulation of astrocytes and may constitute DACSs.

P2-33 Voluntary exercise promotes astrogliogenesis from Olig2 cells in some nuclei of the basal ganglia of adult mouse

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In the last annual meeting, we reported that astrocytes derived from Olig2 cells dramatically increased in the subthalamic nucleus (STN) after voluntary exercise in adult mice. Immunohistochemical study identfied that these astrocytes were positive for glutamine synthetase and/or S100 β and/or 3-phosphoglycerate dehydrogenase, but never expressed GFAP. We also observed c-fos expression in STN neurons increased significantly by exercise. Recently we comfirmed that astrogliogenesis is promoted in not only STN but also another nuclei of basal ganglia, e.g., the globus pallidus (GP), substantial nigra (SN), by voluntary excercise. It is well known that tha basal ganglia regurate motor activity by processing descending information from cortical regions. These our recent findings implied the neuron-astrocyte relationship based on glutamate metabolism in response to exercise-stimuli.To confirm this relationship, we used fluorocitrate (FC) to metabolically inhibit astrocyte functions. As would be expected, mice regionally deficient of astrocytes in the STN exhibited reduction of spontaneous activities. On the other hand, FC-microinjection into other but neighboring regions had little influence on motor activities. These findings suggest that astrocytic activities of the STN are closely related to neuronal outputs of the STN, possibly through the glutamate metabolism.

P2-34 Astrocyte-derived factor leads to upregulation of tumor necrosis factor alpha (TNF α) induced in microglia

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A proinflammatory cytokine, tumor necrosis factor alpha (TNF α) is generally recognized to be induced in pathological state of brain, and to play a role on the inflammation and the neuronal degeneration. A major cell-type for the source is activated microglia in the brain parenchyma. However, it is not known precisely how the production of TNF α in activated microglia is regulated. In the present study, we examined *in vitro* a mechanism for the modulation of TNF α production in microglia from the standpoint of cellular interaction with astocytes. Microglia and astrocytes were prepared from neonatal rat brain-derived primary cultures. Both cell-type did not produce any TNF α in non-stimulated condition. However, microglia were shown to respond to lipopolysaccharide(LPS) and to produce actively TNF α. The amounts of TNF α induced in LPS-stimulated microglia were enhanced in the presence of astrocytes, suggesting that astrocytes stimulate microglia. Next, to separate the contact effects and the soluble factor-mediated effects of astrocytes, trans-well plate having double bottoms was used. Microglia and astrcytes were seeded on the outer bottom and inner bottom, respectively, and stimulate with LPS. Although microglia alone induced some amounts of TNF α, and astrocytes alone hardly induced it, considerable amounts of TNF α were induced in the combined wells, suggesting that astrocytes-derived soluble factor stimulates microglia. The conditioned medium recovered from astocytes had an ability to enhance the production of TNF α in LPS-stimulated microglia. Collectively, the effects of astrocytes to promote the amounts of TNF α in activated microglia can be explained by the presence of astrocytes-derived soluble factor(s).

P2-35 Microglia as a member of lactate supplier in the CNS

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A major energy substrate used in the CNS is glucose, and the glucose is taken through blood brain barrier into brain parenchyma. The concentration of glucose is considered to be strictly regulated for active neuronal functions. So far, astrocytes have been described to be the main regulatory cells in the CNS. However, the association of microglia with the glucose metabolism is poorly known. Thus, in this study we examined the involvement of microglia in energy metabolism in the CNS. At the beginning of the study, we tried to determine the presence of glycogen in primary cells including microglia. Alkali extraction and ethanol precipitation method revealed that microglia as well as astrocytes have some amounts of glycogen, suggesting that microglia synthesize glycogen in the cells. The substantial enzyme, glycogen synthase (GS) was detected in microglial cell homogenate, indicating that microglia have the ability to store glucose. We next examined a possibility that microglia are able to produce and release lactate, preferable energy source for neurons. Immunoblotting analysis indicated that lactate dehydrogenase (LDH), an essential enzyme for producing lactate from pyruvate, and monocarboxylate transporters (MCTs) for transporting lactate from cytosol to extracellular space are present in highly purified microglia. These results indicate that microglia are able to actively release lactate. Conclusively, microglia are strongly suggested to serve as an energy material-supplying cells for neurons in the CNS.

P2-36 Attenuation of microglial activation/proliferation in axotomized facial nucleus by administration of GDNF

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Transection of adult rat facial nerve leads to an increased number of activated microglia in the ipsilateral facial nucleus. We tested whether or not glial cell line-derived neurotrophic factor (GDNF) is able to modulate microglial activation and proliferation in the injured facial nucleus. The influence of GDNF on microglia was assessed by determining the amount of ionized Ca^{2+}-binding adapter molecule 1 (Iba1) as a microglial marker, cFms as a receptor of macrophage-colony stimulating factor (M-CSF) and proliferating cell nuclear antigen (PCNA) as a proliferation marker. Transacting one side of facial nerve, the amounts of Iba1, cFms and PCNA in the ipsilateral nucleus increase during 5 days after operation. If both facial nerves are cut, the amounts of Iba1, cFms and PCNA in both nuclei elevate at similar levels. In such both facial nerves-cut models, GDNF was applied to one side and the effects were investigated. The administration of GDNF in an injured facial nerve decreased the amounts of Iba1, cFms and PCNA compared to those of PBS-administered nucleus (control side). In support of this result, immunohistochemical studies revealed that the number of Iba1-, cFms- and PCNA-positive cells in GDNF-administered nucleus was lower than that in PBS-administered nucleus, suggesting that GDNF prevents microglial activation and proliferation. In addition, we observed that GDNF tends to restore the levels of vesicular acetylcholine transporter (VAChT) and gamma-aminobutyric acid (GABA) receptor that depresses in injured facial nucleus. In conclusion, the administration of GDNF into transacted facial nerve was found to prevent microglial activation/proliferation, and to possibly restore the depressed state of motoneurons.

P2-37 Involvement of protein kinase D in UDP-stimulated microglial macropinocytosis

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The clearance of tissue debris by microglia is one of the crucial components in the maintenance of the brain homeostasis. Recently, it was reported that extracellular UDP facilitates the microglial uptake of microsphere in a P2Y6 receptor dependent manner (Koizumi S et al., Nature, 2007). However, the intracellular mechanism underlying these phenomena has not been identified. In this study, we demonstrated that UDP stimulation induced immediate and long-lasting dynamic movements of the cellular membrane up to 60 min. After 60 min of UDP stimulation, we observed an upregulation in the number of vacuoles formed in each cell and the enhanced incorporation of extracellular FITC-dextran. This data indicated that UDP stimulated active movement of cellular membrane resulting an the internalization of extracellular fruid as well as microspheres. To investigate the mechanism of UDP-stimulated macropinocytosis, we focused on PKC, a downstream signaling molecule involved in P2Y6 receptor activation. The vacuole formation was significantly suppressed by Gö6976, a PKC and PKD (PKC μ) inhibitor and CID755673, a selective PKD inhibitor, but not by Gö6983 which has low sensitivity to PKD. The inhibition of PKD also inhibited the incorporation of fluorescent dextran which was visible after UDP stimulation. In addition, Immunoblot and immunocytochemical analysis revealed that upon UDP-stimulation, PKD first translocated to the plasma membrane, and underwent phosphorylation. Then PKD was translocated to juxtamembrane of intracellular vacuoles. Unexpectedly, these phosphorylation and translocation of PKD were little affected by Gö6976 and CID755673. However, UDP-stimulated phagocytosis of microspheres was almost completely inhibited by Gö6976 and CID755673, but not by Gö6983. These data suggest that PKC-independent function of PKD regulates UDP-induced membrane movement and increased both type of endocytosis, macropinocytosis and phagocytosis.

P2-38 Functional analysis of HOXD9 in human gliomas and glioma cancer-initiating cells

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HOX genes encode a family of homeodomain-containing transcription factors involved in the determination of cell fate and identity during embryonic development. They also behave as oncogenes in some malignancies. In this study, we found high expression of the HOXD9 gene transcript in glioma cell lines and human glioma tissues by quantitative real-time PCR. Using immunohistochemistry, we observed HOXD9 protein expression in human brain tumor tissues, including astrocytomas and glioblastomas. To investigate the role of HOXD9 in gliomas, we silenced its expression in the glioma cell line U87 using HOXD9-specific siRNA, and observed decreased cell proliferation, cell cycle arrest, and induction of apoptosis. The HOXD9 gene was highly expressed in glioma cancer-initiating cells (GCICs) from patient specimens compared to normal astrocyte cells and neural stem/progenitor cells (NSPCs). HOXD9 siRNA treatment of GCICs resulted in reduced cell proliferation and induced apoptosis as seen in U87 cells. Our results suggest that HOXD9 may be a novel marker of GCICs and cell proliferation and/or survival factor in gliomas and GCICs, and a potential therapeutic target.

P2-39 Analysis of the novel sialylated N-glycan expressed in the mouse brain

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Sialic acid is an acidic monosaccharide binding to sugar residues of sugar chain through α 2,3-, α 2,6- or α 2,8-linkage. Siglec can recognize the difference of these linkage types. For example, MAG (myelin-associated glycoprotein) recognizes sialic acids which bind to the terminal galactose (Gal) residue through α 2,3-linkage and does not recognize sialic acids binding to sugar residue through other linkage types. The linkage type of sialic acid is an important factor for the signaling by siglec-sialic acid interaction. We established a technique for determining sialylated sugar chain structure from a trace amount of sample and analyzed sialylated N-glycans from the mouse brain. In this study, [Gal β 1,3(NeuAc α 2,6)GlcNAc-] was detected. This is a novel structure found in the mouse brain. Sialic acid residue in [Gal β 1,3(NeuAc α 2,6)GlcNAc-] binds directly to GlcNAc residue which locates next to the terminal Gal reidue. There are no sialic acids reported that bind to GlcNAc residue which are linked to Gal residue by β 1,4-linkage. [Gal β 1,3(NeuAc α 2,6)GlcNAc-] is a partial structure of the sugar chain called " sialylated A2G"2F ". Relative abundance of α 2,6-linked residues against total sialic acid residues changed during developmental (Embroynic day 16 = 74%, 12week old = 86%). Although sialic acids of sialylated A2G"2F in the rat brain bind not only to the Gal residue but also to the GlcNAc residue ([NeuAc α 2,3Gal β 1,3(NeuAc α 2,6)GlcNAc-]). [Gal β 1,3(NeuAc α 2,6)GlcNAc-] is suggested to be synthesized from [NeuAc α 2,3Gal β 1,3(NeuAc α 2,6)GlcNAc-] by enzyme reaction. Although sialidases which specifically remove the sialic acid from NeuAc α 2,3Gal structure contained in tetra sialyl A2G"2F is not known and the pathway how [Gal β 1,3(NeuAc α 2,6)GlcNAc-] is synthesized is very interesting. In addition, siglec which recognizes [Gal β 1,3(NeuAc α 2,6)GlcNAc-] is not found and the existence of this is expected.

P2-40 Long-term treatment of RN46A cells with cAMP analog upregulates the function of serotonin transporter (SERT)

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Serotonin transporter (SERT) is a membrane protein that regulates serotonergic neurotransmission by reuptaking serotonin (5-HT) from the synapse cleft. In order to examine the SERT behavior in serotoninergic neuron, we have observed its function in RN46A cells, derived from embryonic rat raphe neurons, As a result, we elucidated that RN46A cells had the nature that could express the SERT with high performance. Stimuli that elevate intracellular cAMP modulates the SERT function. However, the mechanism underlying cAMP-dependent SERT regulation is unclear. In this study, we examined whether SERT uptake activity was affected by Dibutyl cAMP (dbcAMP), a cAMP analog, in RN46A cells. We expressed FLAG-SERT into RN46A cells by adenoviral transfection and the [^{3}H]5-HT uptake via SERT per protein was measured as SERT activity. We found that the long-term treatment (>4 hour) of SERT-expressed RN46A cells with dbcAMP significantly upregulated the SERT activity, compared with non-treated cells. The same result was observed when forskolin, another cAMP elevator, was applied. The treatment with dbcAMP or forskolin caused time-dependent upregulation of SERT activity, which is accompanied with the arrest of cell growth and neurite outgrowth. In addition, retinoic acid (RA), which can differentiate RN46A cell to neural cells, also upregulated SERT. These results suggests that the upregulation of SERT function is linked to the differentiation of RN46A cells. To elucidate the mechanism by which dbcAMP upregulates the SERT activity, we examined the level and subcellular localization of SERT after the dbcAMP treatment. DbcAMP elevated the SERT protein level, probably inhibiting its degradation. Immunohistochemical analysis revealed that membrane localized SERT was abundant in dbcAMP-treated cells, compared with non-treated cells. Next we examined whether PKA or EPAC, a major intracellular target of cAMP, contributed to this phenomenon. For this purpose, We examined the effects of selective EPAC activator 8CPT-cAMP (800 μ M) and the specific PKA activator 6-BNZ-cAMP (800 μ M) on the SERT activity. A PKA activator, but not an Epac activator, increased 5-HT uptake activity, suggesting the importance of PKA in the dbcAMP-induced SERT upregulation.

P2-41 Effects of chemical chaperons on the serotonin transporter functions

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Serotonin transporter (SERT) is a membrane protein that terminates serotonergic neural transmission by reuptaking serotonin from synaptic cleft into presynaptic terminal. SERT is known as a target of antidepressant and abusive drugs, and is involved in mood disorders and drug addiction. Proper folding and trafficking of membrane proteins, including SERT, are crucial for functional expression of these proteins. Chemical chaperons are agents, which assist the folding of protein as well as molecular chaperons. In this study, we examined whether chemical chaperons, including 4-Phenyl Butylate (4-PBA), trehalose, Trimethylamine N-oxide (TMAO) and Tauroursodeoxycholic acid (TUDCA), affected the SERT uptake activity and its membrane expression, using COS-7 cells expressing SERT. Twenty four-hr or 48-hr treatment of 4-PBA (3 mM) increased the serotonin uptake activity of SERT-transfected COS-7 cells. In accordance with increasing serotonin uptake activity, the expression of maturely-glycosylated SERT was elevated, while immaturely-glycosylated one was reduced. The SERT activity was increased even when the de novo synthesis of SERT was stopped by using Tet-off system, suggesting that 4-PBA increased the functional SERT via acceleration of its folding and trafficking, not via transcriptional upregulation.We attempted to chase the change in the SERT intracellular localization using COS-7 cells expressing SERT-HaloTag. Time-lapse imaging of SERT-HaloTag stained with HaloTag ligand revealed that 4-PBA increased the plasma membrane–localized SERT. Next, we asked if 4-PBA relieved the ER stress induced by unfolded SERT. To address this issue, we expressed the C-terminus-deleted SERT (SERT Δ CT), which is not maturely glycosylated and accumulated at ER. 4-PBA increased the uptake activity of SERT Δ CT. Furthermore, immunoblotting for ER stress marker proteins demonstrated that 4-PBA relieved SERT Δ CT-induced ER stress by decreasing its expression. In addition to 4-PBA, 48-hr treatment of trehalose (>100mM), not TMAO or TUDCA, increased the SERT activity. These findings demonstrated that chemical chaperons could modulate the SERT function, suggesting that these agents are possible therapeutic candidates as emotion modulating drugs.

P2-42 Down-regulation of cyclin-dependent kinase 5 activity by mood stabiliozer valproic acid

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Cyclin-dependent kinase 5 (Cdk5) is a neuron-specific Ser/Thr kinase, which is activated by regulatory subunit p35. Over-activation of Cdk5 induced by cleavage of p35 with calpain is implicated in neuron death of various neurodegenerative diseases. In contrast, depletion of the Cdk5 activity makes neurons vulnerable to stresses. Thus, appropriate regulation of the Cdk5 activity is essential for neurons to survive. Cdk5 also regulates synaptic activity. Long term potentiation (LTP) is easily induced in mouse brains lacking Cdk5. Cdk5 may determine the threshold of neuronal excitation. Recent reports suggest the involvement of Cdk5 in mental disorders. We thought perturbation of the Cdk5 activity is related to mental conditions. To approach this question, we investigated the effect of valproic acid (VPA) on the Cdk5 activity in cultured neurons. VPA is a drug of choice for the psychiatric treatment. VPA decreased protein and mRNA expression levels of p35 in cultured neurons in a dose-dependent manner. VPA is a well known inhibitor for histone deacetylase (HDAC). To see whether the effect of VPA is mediated via HDAC inhibition, we used valpromide (VPM), a VPA analogue without HDAC inhibition activity, and trichostatin A (TSA), another HDAC inhibitor. TSA, but not VPM, reduced p35 expression at both levels of protein and mRNA, indicating that VPA decreases p35 mRNA via HDAC inhibition. In addition, proteasomal inhibitors MG132 and epoxomicin also suppressed the VPA-induced p35 reduction, indicating that VPA induces p35 protein degradation by proteasome.VPA administration decreased the behavior activity of mice in open field. We compared the effect of VPA on the protein amount of p35 and behavior. Acute administration of VPA induced behavior abnormality at 5 min earlier than 3~6 h when p35 protein was decreased. We would like to discuss a possibility of Cdk5-p35 modulation as a possible VPA target in therapeutic treatment of mental disorder.

P2-43 Neonatal maternal separation increases leaning-against-wall behavior in open field test

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Quality of early family environment can serve as a major source of vulnerability in later life. Individuals who are the victims of physically or sexually abusive families are at considerably greater risk for mental illness in adulthood. Persistent emotional neglect increase the risk of depression and anxiety disorders. Thus postnatal stressful environment induce long-lasting psychological influences in later life. Maternal-separation (MS) in rodents is an important model to study the effects of maternal care on infant neurological development. It has been shown that MS increases depression- and anxiety-like behaviors and hypothalamic-pituitary- adrenal responses to stress in adulthood. However, it has not been well established which type of behavior can be reliable indicators of MS effects. In the aim of treating the mental illness in adulthood, we first compared various depression- and anxiety-like behaviors to explore the reliable indicators of MS effects. Sprague-Dawley pups were separated from their dam daily for 180 min during postnatal day 2-14, and subjected to behavioral experiments including open-field test and forced-swim test at postnatal day 40-50. Moreover, in some experimental groups, rats were exposed to enriched environment for 2 weeks at postnatal day 22-36 or 100-114. We found that the number and duration of leaning-against-wall behavior in open field test increased in MS rats compared with control rats. On the other hand, other measures including time spent in center area were not so different as leaning-against-wall behavior between MS and control rats. Therefore, the number and duration of leaning-against-wall behavior could be a reliable indicator to assess the influence of MS stress. Moreover, to determine whether the leaning-against-wall behavior reflects anxiety, we investigated the effect of diazepam treatment on the behavior.

P2-44 Identification of orexin regulatory element 1-binding proteins

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Orexin (also called hypocretin), a neuropeptide, regulates various physiological processes, such as arousal, sleep, food intake, energy expenditure, and the reward circuit. Prepro-orexin expression is localised exclusively on the perifornical area of the lateral hypothalamus. Two well-conserved promoter regions - orexin regulatory element (OE) 1 and OE2 - were identified within upstream of the human prepro-orexin gene, and OE1 (58bp) were found to target specific expression within the lateral hypothalamus. Our previous study showed that some orexin neurons might be generated from progenitors of 3rd ventricular zone before E12 and prepro-orexin expression starts from E10, suggesting that transcription factors, which bind to OE1 and regulate prepro-orexin expression, could appear in murine hypothalamus before E10 at least. First, we conducted yeast-one hybrid (Y1H) screening using OE1 and E8~10 murine brain cDNA library, however the background activities, which might depend on the recognition of OE1 by endogenous yeast proteins, could not be completely disturbed by antibiotics. According, we identified that three regions included in OE1 were completely conserved residues between human and murine. One out of these three conserved regions was conserved from fish to human and showed no activity under presence of antibiotics. Using this region and E8~10 murine brain cDNA library, some nuclear proteins were identified as having of OE1-binding activities on Y1H screening. One zinc finger protein (Zfp) has been already identified as down-regulated gene in the hypothalamic orexin neuron-ablated transgenic mice. The expression patterns of this Zfp and prepro-orexin are considerably similar at E14.5 in Euexpress database. Reporter assay showed that overexpression of this Zfp in NIH3T3 cells activated murine and human orexin promoter activity (8-fold and 50-fold, respectively). Protein-DNA binding assay showed that this Zfp binds to the consensus motif for these family proteins and OE1.To clarify whether this Zfp induces orexin development, further *in vivo* studies will need to be completed.

P2-45 Double in situ hybridization analyses of serotonin 3A and 3B receptor in the rat geniculate ganglion

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Serotonin was previously regarded as a candidate for neurotransmitters between gustatory receptor cells and primary taste nerve fiber endings, because serotonin is present in taste papillae. However, ionotropic serotonin 3 receptor gene knockout mice did not show attenuation of gustatory sensing. Following that, ATP was focused as the neurotransmitter in the synapses, and the subtype 2 and 3 ionotropic purinergic receptors, P2X2- and P2X3-knockout mice expectedly revealed taste disorder. Thus, ATP is the most plausible for the neurotransmitter between taste cells and primary afferent nerve fibers at present. Gene-knockout studies have indicated that ATP plays a crucial role in taste transduction, but these findings do not necessarily mean that ATP is the only neurotransmitter used for gustatory signal transduction. That is, serotonin could not generate electrical potentials large enough to reach the activation threshold of neurons in the absence of ATP. Furthermore, the fact serotonin exists in taste buds may indicate that serotonin also participates in gustatory sensing. In this study, we investigate that the expression of serotonin 3A and 3B receptor genes in the rat geniculate ganglion, which is deeply relating in taste signal transmission, using double in situ hybridization analyses. In this conference, we show the results and discuss the significance of serotonin 3A and 3B receptors in gustatory signal transduction.

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学会掲示板

【助成・褒章案内】

財団法人 井上科学振興財団
第28回（2011年度）井上学術賞受賞候補者推薦要項

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2011年９月20日現在で50歳未満の研究者に限る。

学術賞：【本賞】賞状及び金メダル　【副賞】200万円
授賞件数は５件以内とする。
（注）受賞者は、原則として１件につき１人とする。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すこと。但し、この場合においても１件として取り扱う。

推薦依頼先：次の団体及び個人に推薦を依頼する。
(1) 下記の36学会
(2) 井上科学振興財団の選考委員経験者（現任者を除く）
(3) 受賞後５年を経過した井上学術賞受賞者

推薦件数：各推薦学会からは２件以内、各推薦者からは１件とする。

提出方法：所定の推薦書用紙（井上科学振興財団HP⇒http://www.inoue-zaidan.or.jp/からダウンロード可能）に必要事項を記載し、井上科学振興財団宛てに提出すること。なお、書類の返却はしない。
日本神経化学会の推薦をご希望の方は、当会研究助成金等候補者選考委員会宛てにご送付下さい。同委員会で選考の上、推薦候補者を決定致します。

締切期日：2011年９月20日（火）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2011年９月７日（水）必着。
※学会締切を延長致しました。

選考：井上科学振興財団選考委員会において選考し、同財団理事会において決定する。
選考の結果は、2011年12月中旬に推薦者に通知される。

学術賞の贈呈：2012年２月３日（金）午後４時から　東京で開催の予定。

推薦書提出先及び連絡先：

財団法人 井上科学振興財団
〒150-0036　東京都渋谷区南平台町15-15 南平台今井ビル601
TEL 03-3477-2738　　FAX 03-3477-2747
E-mail inoue01@inoue-zaidan.or.jp

応用物理学会	日本気象学会	日本セラミックス協会
高分子学会	日本金属学会	日本天文学会
触媒学会	日本顕微鏡学会	日本動物学会
地球電磁気・地球惑星圏学会	日本細胞生物学会	日本農芸化学会
電気化学会	日本地震学会	日本発生生物学会
電子情報通信学会	日本植物学会	日本物理学会
日本遺伝学会	日本植物生理学会	日本分子生物学会
日本応用数理学会	日本神経化学会	日本分析化学会
日本解剖学会	日本神経科学学会	日本免疫学会
日本海洋学会	日本数学会	日本薬学会
日本化学会	日本生化学会	プラズマ・核融合学会
日本癌学会	日本生物物理学会	有機合成化学協会

財団法人 井上科学振興財団
第28回（2011年度）井上研究奨励賞受賞候補者募集要項

候補者の対象：2008年4月1日～2011年3月31日（2008年度～2010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（2011年9月20日現在／ただし医学、歯学、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。

研究奨励賞：【本賞】賞状及び銅メダル　【副賞】50万円
授賞予定件数は30件。

推薦者：原則として、博士論文の作成を指導した研究者とする。

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する。
(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、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する。

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、井上科学振興財団のホームページhttp://www.inoue-zaidan.or.jp/からダウンロードできる。
(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・氏名を記入すること。(上記「(1) 推薦書」(4ページ) とは異なるので、注意す

ること)
(4) 博士論文(写しでも可)…2部

なお、提出書類の返却はしない。

締切期日:2011年9月20日(火)井上科学振興財団必着

選考:井上科学振興財団選考委員会において選考し、同財団理事会において決定する。
選考の結果は、2011年12月中旬に推薦大学の学長に通知される。

研究奨励賞の贈呈:2012年2月3日(金)午後4時から　東京で開催の予定。

推薦書提出先及び連絡先:

財団法人 井上科学振興財団
〒150-0036　東京都渋谷区南平台町15-15 南平台今井ビル601
TEL 03-3477-2738　　FAX 03-3477-2747
E-mail inoue01@inoue-zaidan.or.jp

公益財団法人 東レ科学振興会

第52回(平成23年度)東レ科学技術賞候補者推薦要領

候補者の対象:日本神経化学会が関与する分野で、下記のいずれかに該当する方
(1) 学術上の業績が顕著な方
(2) 学術上重要な発見をした方
(3) 効果が大きい重要な発明をした方
(4) 技術上重要な問題を解決して、技術の進歩に大きく貢献した方
年齢は問いません。

科学技術賞:1件につき、賞状、金メダルおよび賞金500万円(2件前後の予定)

推薦者:東レ科学振興会指定の学協会の代表者および東レ科学振興会指定の推薦委員(非公開)

候補者推薦件数:1学協会から2件以内および1推薦委員から1件以内

推薦手続:所定の推薦書用紙に選考に必要な事項を正確に記載し、東レ科学振興会宛て1部ご送付願います。
日本神経化学会の推薦をご希望の方は、日本神経化学会研究助成金等候補者選考委員会宛てにご送付下さい。同委員会で選考の上、推薦候補者を決定致します。
推薦用紙等詳細はこちら>>http://www.toray.co.jp/tsf/info/inf_003.html

推薦締切期日:平成23年10月7日(金)必着
日本神経化学会の推薦をご希望の方は　平成23年9月16日(金)必着。

選　考　方　法：下記委員からなる選考委員会において選考し、東レ科学振興会理事会で受賞者を決定します。

選考委員	湯浅　　誠（委員長）	榊　　裕之	田村剛三郎
	末松　　誠	玉尾　皓平	永宮　正治
	前川　禎通	山本　　雅	岡崎　　健

選考結果は平成24年２月下旬に推薦者に通知します。

科学技術賞の贈呈：平成24年３月の予定

（注）　a．推薦を受けた候補者は、その年度および次の年度にわたって選考の対象としております。したがって平成22年度に推薦された候補者については、平成23年度候補者として再度推薦の必要はありません。ただし平成22年度の推薦以降において、追加すべき顕著な業績または発表や受賞があり加筆が必要な場合は、再提出いただいても結構です。

b．受賞者は、原則として１件１人とします。特に複数人であることを必要とするときは理由を明確にして下さい。

c．この科学技術賞は、所得税法（第９条第１項第13号ニ）の規定により非課税となっております。

d．推薦書の用紙は、下記東レ科学振興会ホームページからダウンロードできます。
東レ科学振興会＞＞http://www.toray.co.jp/tsf/index.html

賞に関するお問合せ先：

公益財団法人東レ科学振興会
〒279-8555　千葉県浦安市美浜一丁目８番１号（東レビル）
TEL（047）350-6103　　FAX（047）350-6082

公益財団法人 東レ科学振興会
第52回（平成23年度）東レ科学技術研究助成候補者推薦要領

候補者の対象：日本神経化学会が関与する分野で国内の研究機関において、自らのアイディアで萌芽研究に従事しており、かつ今後の研究の成果が科学技術の進歩、発展に貢献するところが大きいと考えられる若手研究者（原則として推薦時45才以下）。本助成が重要な研究費と位置づけられ、これにより申請研究が格段に進展すると期待されることが要件。
従来の研究の多くが海外で行われていても差し支えありません。

研　究　助　成　金：総額１億３千万円。１件３千万円程度まで10件程度とします。

推　　薦　　者：東レ科学振興会指定の学協会の代表者および東レ科学振興会の推薦委員（非公開）

候補者推薦件数：１学協会から２件以内および１推薦委員から１件以内

推　薦　手　続：所定の推薦書用紙に選考に必要な事項を正確に記載し、東レ科学振興会あて１部ご送付願います。
日本神経化学会の推薦をご希望の方は、日本神経化学会研究助成金等候補者選考委員会宛てにご送付下さい。同委員会で選考の上、推薦候補者を決定致します。
推薦用紙等詳細はこちら＞＞http://www.toray.co.jp/tsf/info/inf_004.html

推薦締切期日：平成23年10月７日（金）必着
日本神経化学会の推薦をご希望の方は　平成23年９月16日（金）必着。

選　考　方　法：下記委員からなる選考委員会において、提出された書類により一次選考を行ったのち面接による二次選考を経て、東レ科学振興会理事会で決定します。
なお、二次選考は平成23年12月下旬に行います。

選考委員	湯浅　　誠（委員長）	榊　　裕之	田村剛三郎
	末松　　誠	玉尾　皓平	永宮　正治
	前川　禎通	山本　　雅	岡崎　　健

選考結果は平成24年２月下旬に推薦者（学協会の代表者および東レ科学振興会の推薦委員）に通知します。

研究助成金の贈呈式：
平成24年３月の予定
（注）
a．東レ科学振興会の選考では、専門分野の異なる選考委員全員が関与します。推薦書の内容は、他分野の研究者にもわかりやすい表現をご使用下さい。
b．この研究助成金は、研究目的を達成するために有効に使用されるものであれば、どのような使途で申請されても結構です。ただし、原則として間接経費、管理経費、共通経費は助成の対象になりません。また、助成金受領決定後、その使途を変更される場合は、事前に東レ科学振興会の承諾を得て下さい。
助成研究の期間は、特別の事情がない限り助成金受領決定の次年度から３年以内とします。
c．助成金の受領者は、研究終了時まで毎年「助成研究年次報告書」を、また研究終了時に、「助成研究終了報告書」を提出していただきます。
d．この助成金は、所得税法（第９条第１項第13号ニ）の規定により非課税となっています。
e．推薦書の用紙は、下記東レ科学振興会ホームページからダウンロードできます。
東レ科学振興会＞＞http://www.toray.co.jp/tsf/index.html

賞に関するお問合せ先：
公益財団法人東レ科学振興会
〒279-8555　千葉県浦安市美浜一丁目８番１号（東レビル）
TEL（047）350-6103　　FAX（047）350-6082

公益財団法人 内藤記念科学振興財団

第43回（2011年度）内藤記念科学振興賞候補者推薦要領

趣　　　旨：人類の健康の増進に寄与する自然科学の基礎的領域において、進歩発展に顕著な功績のあった研究者に対してほう賞を授与するものである。

候 補 資 格：１）人類の健康の増進に寄与する自然科学の基礎的研究において、独創的テーマに取り組み、進歩発展に顕著な功績を挙げた研究者。
２）候補者は単独とするが、異なる研究グループによる共同研究の場合には、連名であっても良い。
３）候補者の再度の推薦は差支えない。

推　薦　者：１）下記27学会の代表者

高分子学会	日本獣医学会	日本農芸化学会
日本遺伝学会	日本植物生理学会	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。
日本神経化学会の推薦をご希望の方は、当会研究助成金等候補者選考委員会宛てにご送付下さい。同委員会で選考の上、推薦候補者を決定致します。

締　切　日：2011年10月３日（月）（内藤記念科学振興財団必着）
日本神経化学会の推薦をご希望の方は、2011年９月16日（金）当会必着。
※学会締切を延長致しました。

選 考 方 法：内藤記念科学振興財団選考委員会で審査し、理事会で決定する。
採否の結果は、2012年２月に候補者および推薦者に通知する。

授賞式・顕彰：受賞者夫妻は2012年３月19日（月）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、監事又は評議員推薦の場合は、私印を捺印する。

お問合せ先：公益財団法人 内藤記念科学振興財団
〒113-0033 東京都文京区本郷３丁目42番６号 NKDビル８階
TEL 03-3813-3005 FAX 03-3811-2917
URL http://www.naito-f.or.jp/ E-mail joseikin@naito-f.or.jp

公益財団法人 内藤記念科学振興財団
第43回（2011年度）内藤記念海外学者招へい助成金 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・先駆的に取り組み、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
2012年１月１日～2012年６月30日	前期
2012年７月１日～2012年12月31日	後期

4）内藤記念科学振興財団の選考委員（HP参照 http://www.naito-f.or.jp/）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：※内藤記念科学振興財団HPのQ&A「推薦者の欄」を必ずご覧下さい。
1）大学関係…①大学院：研究科長 ②学部：学部長 ③研究所：研究所長、①②③以外の大学組織（研究センター、研究施設等）：学長
ただし、同一専攻の研究科（大学院）と学部（大学）の両方からは申請できない。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・監事及び評議員
（参照⇒http://www.naito-f.or.jp/）
4）内藤記念科学振興財団の指定した学会の代表者

※推薦件数は１推薦者につき１件（前期・後期 各１件）

申請方法：〈推薦者が上記１）２）４）の場合〉
申請者⇒大学・研究機関事務⇒内藤記念科学振興財団
〈推薦者が上記３）の場合〉
申請者⇒内藤記念科学振興財団理事・監事・評議員⇒内藤記念科学振興財団

※3）の場合のみ、内藤記念科学振興財団への申請書類の送付は、申請者、推薦者のどちらからでもよい。
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。
日本神経化学会の推薦をご希望の方は、当会研究助成金等候補者選考委員会宛てにご送付下さい。同委員会で選考の上、推薦候補者を決定致します。

締　切　日：〈前期〉2011年6月1日（水）　〈後期〉2011年10月3日（月）
※いずれも内藤記念科学振興財団必着
日本神経化学会の推薦をご希望の方は、〈前期〉2011年4月28日（木）〈後期〉2011年9月16日（金）当会必着。
※〈後期〉の学会締切を延長致しました。

選考方法・採択件数：
〈選考方法〉内藤記念科学振興財団選考委員会で審査し、理事会で決定する。
〈採択件数〉前期・後期各10件以内（予算範囲内）
採択の結果は、前期：2011年10月、後期：2012年2月に申請者及び推薦者に通知する。

助成額・送金時期：

エリア	助成額（万円）
中東・アジア	80
米国・カナダ（西海岸除く）、ヨーロッパ	60
米国・カナダ西海岸、オーストラリア、ニュージーランド	50
東南アジア、インド	30
中国、台湾、韓国	20

前　　　期：2011年12月、後期：2012年3月

注　意　事　項：1）組織委員長及び招へい学者が明記されている書面（当該学術集会プログラム・サーキュラー等）を申請書と共に必ず提出する。
2）来日の中止について：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ので、内藤記念科学振興財団事務局へ必ず連絡下さい。

報　告　の　義　務：1）スポンサーについて：当該学術集会で海外学者による招待講演が行われる場合は、プログラム等に内藤記念科学振興財団（英文：The Naito Foundation）の助成によるものであることを明記する。なお、プログラム等を一部送付する。
2）学会成果報告書及び使途報告書について：組織委員長は招へい終了1ヶ月以内に所定用紙にて必ず報告する。

◎申請書記載内容に変更が生じた場合は、すみやかに内藤記念科学振興財団事務局にご連絡下さい。
◎申請書等詳細は、内藤記念科学振興財団ホームページ（http://www.naito-f.

or.jp/）内「助成金事業」に掲載しております。

お問合せ先：公益財団法人 内藤記念科学振興財団
〒113-0033　東京都文京区本郷３丁目42番６号　NKDビル８階
TEL 03-3813-3005　　FAX 03-3811-2917
URL http://www.naito-f.or.jp/　　E-mail joseikin@naito-f.or.jp

公益財団法人 内藤記念科学振興財団
第39回（2011年度）内藤記念講演助成金　申請要領

趣　　　旨：国際会議の開催において、四半期毎に申請を受理し、所定の選考を経て採否を決定する助成事業である。

候補者資格：大学、研究機関に所属する者が主催する自然科学の基礎的研究に関する国内で開催される国際会議（シンポジウム、講演会）の開催責任者。
国際会議とは参加者総数が50名以上で、かつ参加国が日本を含む２カ国以上を占める会議をいう。
なお、下記の申請者は対象外とする。
①国内で開催される学術集会の定例的な年会や季会
②当該年度に既に内藤記念科学振興財団が採択した助成金と同一のシンポジウム、講演会
内藤記念科学振興財団の理事・監事・評議員及び選考委員に対する推薦は基本的に行わない。ただし、助成金を個人のために使用しないことが明白な場合はこの限りではない。

推　薦　者：１）内藤記念科学振興財団の理事・監事及び評議員
（参照⇒http://www.naito-f.or.jp/）
２）内藤記念科学振興財団の指定した学会の代表者
※推薦件数は１推薦者につき年間１件

申請方法：〈推薦者が上記１）の場合〉
申請者⇒内藤記念科学振興財団理事・監事・評議員⇒内藤記念科学振興財団
※内藤記念科学振興財団への申請書類の送付は、申請者、推薦者のどちらからでもよい。
〈推薦者が上記２）の場合〉
申請者⇒学会事務⇒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。
日本神経化学会の推薦をご希望の方は、当会研究助成金等候補者選考委員会宛てにご送付下さい。同委員会で選考の上、推薦候補者を決定致します。

締　　切　　日：

申請区分	国際会議開催月	申請書受付期間（必着）	採否通知
夏季	7月～9月	4月1日～5月20日	6月中旬
秋季	10月～12月	5月21日～8月22日	9月中旬
冬季	1月～3月	8月23日～11月21日	12月中旬
春季	4月～6月	11月22日～2月20日	3月上旬

日本神経化学会の推薦をご希望の方は、〈夏季〉2011年4月28日（木）、〈秋季〉2011年7月15日（金）、〈冬季〉2011年11月11日（金）、〈春季〉2012年2月10日（金）当会必着。

※〈冬季〉と〈春季〉の学会締切を延長致しました。

選考方法・採択件数：

内藤記念科学振興財団常務理事、選考担当理事、選考委員長全ての承諾により採択する。同一年度の同一学術集会への複数助成はしない。

採択件数は、予算枠の範囲内。

採否の結果は、上記の時期に申請者および推薦者に通知する。

助成額・送金時期：上限は1件50万円。当該国際会議の開催日を勘案し、送金する。

注　意　事　項：プログラム・アブストラクト等会議の概要がわかるものを6部添付すること。
※日本神経化学会の推薦をご希望の方は、学会保管分1部も添付すること。

報 告 の 義 務：1）結果報告について：
助成対象の行事終了後1ヵ月以内に概要を所定用紙にて必ず報告する。
2）外部発表について：
当該学術集会のプログラム等に当財団（英文：The Naito Foundation）の助成によるものであることを明記する。

◎申請書記載内容に変更が生じた場合は、すみやかに内藤記念科学振興財団事務局にご連絡下さい。

◎申請書等詳細は、内藤記念科学振興財団ホームページ（http://www.naito-f.or.jp/）内「助成金事業」に掲載しております。

お 問 合 せ 先：公益財団法人 内藤記念科学振興財団
〒113-0033　東京都文京区本郷3丁目42番6号　NKDビル8階
TEL 03-3813-3005　　FAX 03-3811-2917
URL http://www.naito-f.or.jp/　　E-mail joseikin@naito-f.or.jp

公益財団法人 ブレインサイエンス振興財団
第26回塚原仲晃記念賞受賞候補者推薦要領

趣旨：生命科学の分野において優れた独創的研究を行っている、当該年度（平成24年3月31日まで）において50歳以下の研究者（国内外を問わない）に対して塚原仲晃記念賞を贈呈します。

褒賞金：贈呈件数は原則として1件とし、賞牌ならびに副賞（100万円）を贈呈します。

推薦締切日：平成23年10月14日（金）とします。

推薦者：候補者の業績についてよく知る人。（1推薦者から1件に限ります。）

推薦方法：所定の推薦書に必要事項を記入し、ブレインサイエンス振興財団に提出して下さい。推薦書は下記のURLから表示、印刷できます。
※必ず片面印刷でご提出下さい（両面印刷はご遠慮下さい）。
塚原仲晃記念賞受賞候補者推薦書＞＞http://www.bs-f.jp/tsukahara.html#yoryo

審査方法：ブレインサイエンス振興財団の選考委員会において審査選考し、理事会において決定します。

審査結果の通知：平成24年3月末日までに推薦者および受賞者あて通知します。

賞牌ならびに副賞の贈呈：贈呈決定者に対して別途通知します。

推薦書提出先および連絡先：
公益財団法人ブレインサイエンス振興財団
〒104-0028　東京都中央区八重洲2-6-20
電話（03）3273-2565（直通）

公益財団法人 ブレインサイエンス振興財団
第26回研究助成候補者応募要領

趣旨：ブレインサイエンスの広い分野における研究に対して助成を行いますが、特に、下記の各項について、脳のメカニズムを解明する独創的な研究計画の助成に重点をおきます。研究分野は実験研究のみならず、理論、モデリング研究をも含みます。
(1) 神経科学の基礎研究
(2) 工学から脳へのアプローチ
(3) 物理学から脳へのアプローチ

研究助成額：助成額は1件100万円、助成件数は8～12件とします。

応募締切日：平成23年10月14日（金）とします。

応募方法：所定の応募用紙に必要事項を記入し、ブレインサイエンス振興財団に提出して下さい。
（研究についての問い合わせ可能な所属長名を明記して下さい。）

応募用紙：応募用紙は下記のURLから表示、印刷できます。
※必ず片面印刷でご提出下さい（両面印刷はご遠慮下さい）。
研究助成候補者応募用紙＞＞http://www.bs-f.jp/kenjo.html#yoryo

審査方法：ブレインサイエンス振興財団の選考委員会において審査選考し、理事会において決定します。

採否の通知：平成24年３月末日までに応募者宛て採否を通知します。

助成金の交付：平成24年６月末日までに助成決定者の指定口座に振り込みます。

助成金の使途：助成金は応募用紙記載の通り使用することを原則とします。なお、経理報告書を平成25年５月末日までに提出して下さい。

成果の報告：平成25年５月末日までに、研究成果報告書を提出して下さい。また、助成金による研究を専門誌に載せる場合には、「公益財団法人ブレインサイエンス振興財団（英文＝Brain Science Foundation）の助成による」旨を書き添えて下さい。

推薦書提出先および連絡先：

公益財団法人ブレインサイエンス振興財団
〒104-0028　東京都中央区八重洲2-6-20
電話（03）3273-2565（直通）

公益財団法人 ブレインサイエンス振興財団
海外派遣研究助成候補者応募要領

趣旨：我が国におけるブレインサイエンスの研究の促進を図るため、国際学会、シンポジウム等への参加、あるいは短期間（６ケ月以内）の共同研究のための研究者の海外派遣を助成します。
但し、平成24年４月から平成25年３月の間に出発できるものに限ります。

助成予定額：１件あたりの助成額は往復の航空運賃を主とし、30万円までを限度として必要額を若干件数助成します。

応募締切日：平成24年１月13日（金）とします。

応募方法：所定の応募用紙に必要事項を記入し、ブレインサイエンス振興財団に提出して下さい。

○学会、シンポジウム等の問い合わせ可能な所属長の名前を明記して下さい。
○受入先の承諾書を添付して下さい。
(学会、シンポジウム等参加の場合は参加証明書または招待状の写し。短期の共同研究の場合は受入機関または共同研究者の手紙の写し。)

応　募　用　紙：応募用紙は下記のURLから表示、印刷できます。
※必ず片面印刷でご提出下さい（両面印刷はご遠慮下さい)。
海外派遣研究助成候補者応募用紙
＞＞http://www.bs-f.jp/kokusai_haken.html#yoryo

審　査　方　法：ブレインサイエンス振興財団の選考委員会において審査選考し、理事会において決定します。

採　否　の　通　知：平成24年３月末日までに応募者宛て採否を通知します。

助成金の交付：平成24年４月以降出発時期に応じて助成決定者の指定口座に振り込みます。

助成金の使途：助成金は応募用紙記載のとおり使用することを原則とします。

成　果　の　報　告：帰国後２ヶ月以内に、派遣の成果についての報告書及び派遣助成金の使途内訳を提出して下さい。

応募用紙提出先および連絡先：

公益財団法人 ブレインサイエンス振興財団
〒104-0028　東京都中央区八重洲2-6-20
電話（03）3273-2565（直通)

公益財団法人 ブレインサイエンス振興財団
第25回海外研究者招聘助成候補者申込要領

趣　　　　旨：ブレインサイエンス研究分野において、独創的テーマに意欲的に取り組んでいる外国人研究者の短期間（３ヶ月以内）の招聘を助成します。
ただし、平成24年４月１日から平成25年３月31日の間に招聘するものとします。
また、助成金は招聘する受入責任者に交付します。

招聘助成予定額：１件あたりの助成額は往復の航空運賃を主とし、30万円までを限度として必要額を若干件数助成します。

申　込　締　切　日：平成24年１月13日（金）とします。

申　込　方　法：所定の申込書に必要事項を記入し、ブレインサイエンス振興財団に提出して下さい。
申込書は下記のURLから表示、印刷できます。
海外研究者招聘助成候補者申込書
＞＞http://www.bs-f.jp/kokusai_syouhei.html#yoryo

審　査　方　法：当財団の選考委員会において審査選考し、理事会において決定します。

採　否　の　通　知：平成24年３月末日までに申込者あて採否を通知します。

助　成　金　の　交　付：平成24年４月から必要に応じて受入責任者あて指定口座に振り込みます。

助　成　金　の　使　途：助成金は申込書記載のとおり使用することを原則とします。

成　果　の　報　告：招聘後２ヶ月以内に、招聘の成果報告書及び招聘助成金の使途内訳を提出して下さい。

申込書提出先および連絡先：

公益財団法人 ブレインサイエンス振興財団
〒104-0028　東京都中央区八重洲2-6-20
電話（03）3273-2565（直通）

女性科学者に明るい未来をの会
第32回猿橋賞

対　　　　　象：推薦締切日に50才未満で、自然科学の分野で、「創立の主旨に沿った」優れた研究業績を収めている女性科学者

表　彰　内　容：賞状、副賞として賞金30万円、１件（１名）

応　募　方　法：女性科学者に明るい未来をの会ホームページ　http://www.saruhashi.net/から推薦書類をダウンロードし、A4用紙に印刷して①推薦者（個人・団体、自薦も可）・受賞候補者の略歴・推薦対象となる研究題目②推薦理由（800字程度）、及び③研究題目に関連する主な業績リスト（指定は１頁です。やむを得ない場合でも追加は１頁までです）を記入して、主な論文別刷５編程度（各２部、コピーも可）を添え、下記推薦書類送付先までお送り下さい。

締　　切　　日：2011年11月30日（必着）

推薦書類送付先：〒247-0022　横浜市栄区庄戸5-14-3　女性科学者に明るい未来をの会
※封筒には、「猿橋賞推薦書類」と明記して下さい。書類は、猿橋賞選考のためにのみ選考委員会などで用いられます。書類は返却致しませんのでご了承下さい。

今後、募集要項に変更がある場合は、女性科学者に明るい未来をの会ホームページに掲載致しますので、応募の際は同ホームページをご確認下さい。

お　問　合　せ　先：女性科学者に明るい未来をの会事務局
E-mail saruhashi2011@saruhashi.net

【セミナー・講習会】

千里ライフサイエンス技術講習会（第54回）
「クロマチン免疫沈降法」

日時・場所：【講義】平成23年９月26日（月）13：00～16：50
千里ライフサイエンスセンタービル（北大阪急行千里中央駅徒歩５分）
【実習】平成23年９月27日（火）９：30～16：00
大阪大学理学部（大阪モノレール柴原駅徒歩10分）

コーディネーター：大阪大学大学院理学研究科 教授　升方 久夫

プログラム：【講義】
１）クロマチン免疫沈降法の原理と分裂酵母のクロマチン免疫沈降解析
升方　久夫（阪大院・理学 教授）
２）動物培養細胞のクロマチン免疫沈降：native法とclosslink法
木村　　宏（阪大院・生命機能 准教授）
３）酵母でのChIP法実験操作解説
中川　拓郎（阪大院・理学 准教授）
【実習】
１）酵母からの免疫沈降操作実習（午前）
中川　拓郎（阪大院・理学 准教授）
２）リアルタイムPCR解析実習（午後）
中川　拓郎（阪大院・理学 准教授）

参加費（定員）：【講義のみ】3,000円（34名）　【講義と実習】5,000円（16名）

申込方法：①氏名、勤務先、所属、役職名、所在地、電話、FAX　②希望コース（「講義のみ」または「講義と実習」）を明記の上、以下申込先へE-mailでお申し込み下さい。折り返し参加費の振込み先等をご連絡致します。

申込先：公益財団法人千里ライフサイエンス振興財団　技術講習会G54係
E-mail：tkd@senri-life.or.jp（TEL：06-6873-2001）

＊講習会の詳細につきましては下記Web siteをご覧下さい。
http://www.senri-life.or.jp/gijyutsukosyukai.html

千里ライフサイエンス技術講習会　第55回
「細胞動態の生体内観察技術の新展開」

日時：平成23年11月９日（水）10：00～17：15

場所：大阪大学免疫学フロンティア研究センター（IFReC研究棟２階会議室１）

（千里中央よりバス「小野原東・富士火災」方面行　阪大口バス停下車徒歩５分）
（大阪モノレール彩都線阪大病院前駅下車　西へ徒歩25分）
（阪急電車千里線北千里駅下車　東へ徒歩15分）

趣　　　　旨：免疫学フロンティア研究センターIFReCでは、免疫系を構成するいろいろな細胞や細胞内の免疫シグナル経路に関与する分子などの動的ふるまい及び相互作用を非侵襲的に、高い時間および空間分解能でin vivo観察することを目指して、様々なイメージング（画像化）方法（装置、プローブ）の最先端開発が進められている。IFReCにおけるその開発の特徴は、単なる技術開発ではなく、多様な免疫現象を追及している多くの免疫学研究者と連携しながら進められていることである。したがって、そこで蓄積されている“know-how”は、免疫系に限らず、細胞生物学の実験的研究全般に応用展開できる可能性がある。
今回の講習では、細胞内の分子や細胞内小器官の非標識イメージングが可能なラマン顕微鏡法および生体分子の情報を読み取り可能な化学情報へと変換できるプローブ分子の開発について講義するとともに、研究現場の見学を実施する。

コーディネーター：児玉　孝雄　　大阪大学免疫学フロンティア研究センター　教授

プ ロ グ ラ ム：【技術解説Ⅰ】10：00～12：20
1．蛍光プローブが招いた分子イメージング技術の出現
　　菊地　和也 教授
2．Advances in optical microscopy: Nonlinearity and high resolution imaging（光学電子顕微鏡の進化：非線形性と高解像度イメージング）
　　ニック・スミス 准教授

【昼食】12：20～14：00（必要な方には、実費にてお弁当をご用意します）

【技術解説Ⅱ】14：00～15：30
1．蛍光蛋白質からin vivoイメージングへ
　　菊地　和也 教授
2．Laser irradiation as a tool to highlight details in cell imaging（レーザー光照射による生細胞内構造のイメージング）
　　ニック・スミス 准教授

【技術実習】15：30～17：15（機器等の操作が出来ないことを予めご了承下さい）
生体フォトニックス研究室・生命機能研究科MRI・化学分子イメージング施設見学

【講師】
菊地　和也　　大阪大学免疫学フロンティア研究センター化学分子イメージング　教授
ニック・スミス　　大阪大学免疫学フロンティア研究センター生体フォトニックス　准教授
（スミス准教授の講演の使用言語は、英語になります）

定　　　　員：40名（但し、実習参加者は20名）

参　加　費：技術解説のみ：3,000円、技術解説と技術実習：5,000円

申 込 方 法：以下の要領にてお申込み下さい。
①氏名、勤務先、所属、役職名、〒、所在地、電話、FAX番号、お弁当の有無を明記の上、E-mailで（dsp@senri-life.or.jp宛）お申込み下さい。
②財団事務局より受付の通知をお送り致しますので、そこに記載した振込先口座に参加費および必要な方はお弁当代（500円）を同時にお振込み下さい。
③入金を確認後、通常２週間以内に領収書兼参加証をお届け致します。

申 込 締 切：（定員になり次第締め切ります）

主　　　催：公益財団法人 千里ライフサイエンス振興財団

共　　　催：大阪大学免疫学フロンティア研究センター

お問合せ先：公益財団法人 千里ライフサイエンス振興財団
〒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：dsp@senri-life.or.jp　　URL http://www.senri-life.or.jp

日本神経化学会　賛助会員（50音順）

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レノバサイエンス株式会社

謝　辞

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。

●寄附

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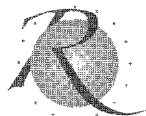
新発売



アルツハイマー型認知症治療剤

薬価基準収載

リバスタッチ®パッチ 4.5mg・9mg 13.5mg・18mg

リバスチグミン経皮吸収型製剤　Rivastigmine transdermal patch

劇薬、処方せん医薬品注)　注)注意ー医師等の処方せんにより使用すること

〔禁忌(次の患者には投与しないこと)〕
本剤の成分又はカルバメート系誘導体に対し過敏症の既往歴のある患者

■効能・効果
軽度及び中等度のアルツハイマー型認知症における認知症症状の進行抑制

〈効能・効果に関連する使用上の注意〉
(1)アルツハイマー型認知症と診断された患者にのみ使用すること。
(2)本剤がアルツハイマー型認知症の病態そのものの進行を抑制するという成績は得られていない。
(3)アルツハイマー型認知症以外の認知症性疾患において本剤の有効性は確認されていない。
(4)本剤の使用が適切であるか、以下に示す本剤の特性を十分に理解した上で慎重に判断すること。
1)国内臨床試験において、本剤の貼付により高頻度に適用部位の皮膚症状が認められている。(「副作用」の項参照)
2)本剤は維持量に到達するまで12週間以上を要する。

■用法・用量
通常、成人にはリバスチグミンとして1日1回4.5mgから開始し、原則として4週毎に4.5mgずつ増量し、維持量として1日1回18mgを貼付する。
本剤は背部、上腕部、胸部のいずれかの正常で健康な皮膚に貼付し、24時間毎に貼り替える。

〈用法・用量に関連する使用上の注意〉
(1)1日18mg未満は有効用量ではなく、漸増又は一時的な減量を目的とした用量であるので、維持量である18mgまで増量すること。
(2)本剤は、維持量に到達するまでは、1日量として18mgを超えない範囲で症状により適宜増減が可能である。消化器系障害(悪心、嘔吐等)がみられた場合は、減量するかこれらの症状が消失するまで休薬する。休薬期間が4日程度の場合は、休薬前と同じ用量又は休薬前より1段階低い用量で投与を再開する。それ以外の場合は本剤4.5mgを用いて投与を再開する。投与再開後は、再開時の用量を2週間以上投与し、忍容性が良好であることを確認した上で、減量前の用量までは2週間以上の間隔で増量する。
(3)本剤の貼付による皮膚刺激を避けるため、貼付箇所を毎回変更すること。(「重要な基本的注意」、「適用上の注意」の項参照)
＊(4)原則として、1日1回につき1枚のみ貼付すること。
(5)他のコリンエステラーゼ阻害作用を有する同効薬(ドネペジル等)と併用しないこと。
(6)医療従事者又は介護者等の管理のもとで投与すること。

■使用上の注意(抜粋)
1.慎重投与(次の患者には慎重に投与すること)
(1)本剤のコリン作動性作用により以下に示す患者では、症状を誘発又は悪化させるおそれがあるため慎重に投与すること。
1)洞不全症候群又は伝導障害(洞房ブロック、房室ブロック)等の心疾患のある患者〔迷走神経刺激作用により徐脈又は不整脈が起こるおそれがある。〕
2)胃潰瘍又は十二指腸潰瘍のある患者、あるいはこれらの既往歴のある患者、非ステロイド性消炎鎮痛剤投与中の患者〔胃酸分泌量が増加し、胃潰瘍又は十二指腸潰瘍を誘発又は悪化させるおそれがある。〕
3)尿路閉塞のある患者又はこれを起こしやすい患者〔排尿筋を収縮させ症状を誘発又は悪化させるおそれがある。〕
4)てんかん等の痙攣性疾患又はこれらの既往歴のある患者〔痙攣閾値を低下させ痙攣発作を誘発させるおそれがある。〕
5)気管支喘息又は閉塞性肺疾患、あるいはこれらの既往歴のある患者〔気管支平滑筋の収縮及び気管支粘液分泌の亢進により症状を悪化させるおそれがある。〕
6)錐体外路障害(パーキンソン病、パーキンソン症候群等)のある患者〔線条体のコリン系神経を亢進することにより、症状を悪化させるおそれがある。〕
(2)重度の肝機能障害のある患者〔血中濃度が上昇するおそれがある。(「重要な基本的注意」、「薬物動態」の項参照)〕
2.重要な基本的注意
(1)本剤の投与により、徐脈、心ブロック等があらわれることがあるので、特に心疾患(心筋梗塞、弁膜症、心筋症等)を有する患者や電解質異常(低カリウム血症等)のある患者等では、重篤な不整脈に移行しないよう観察を十分に行うこと。(「重大な副作用」の項参照)
(2)他の認知症性疾患との鑑別診断に留意すること。
(3)本剤投与で効果が認められない場合には、漫然と投与しないこと。
(4)アルツハイマー型認知症では、自動車の運転等の機械操作能力を低下させる可能性がある。また、本剤は主に投与開始時又は増量時にめまい及び傾眠を誘発することがある。このため、自動車の運転等の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。
(5)本剤の貼付により皮膚症状があらわれることがあるため、貼付箇所を毎回変更すること。皮膚症状があらわれた場合には、ステロイド軟膏又は抗ヒスタミン外用剤等を使用するか、本剤の減量又は一時休薬、あるいは使用を中止するなど適切な処置を行うこと。
(6)本剤を同一箇所に連日貼付・除去を繰り返した場合、皮膚角質層の剥離等が生じ、血中濃度が増加するおそれがあるため、貼付箇所を毎回変更すること。
(7)本剤の貼り替えの際、貼付している製剤を除去せずに新たな製剤を貼付したために過量投与となり、重篤な副作用が発現した例が報告されている。貼り替えの際は先に貼付している製剤を除去したことを十分確認するよう患者及び介護者等に指導すること。(「過量投与」の項参照)
(8)嘔吐あるいは下痢の持続により脱水があらわれることがある。脱水により、重篤な転帰をたどるおそれがあるので、嘔吐あるいは下痢がみられた場合には、観察を十分に行い適切な処置を行うこと。(「重大な副作用」の項参照)
(9)アルツハイマー型認知症患者では、体重減少が認められることがある。また、本剤を含むコリンエステラーゼ阻害剤の投与により、体重減少が報告されているので、治療中は体重の変化に注意すること。
(10)重度の肝機能障害のある患者では、投与経験がなく、安全性が確立していないため、治療上やむを得ないと判断される場合にのみ投与すること。
3.相互作用(抜粋)
本剤は、主にエステラーゼにより加水分解され、その後硫酸抱合を受ける。本剤のチトクロームP450(CYP)による代謝はわずかである。(「薬物動態」の項参照)
併用注意(併用に注意すること)
薬剤名等　コリン作動薬(アセチルコリン、カルプロニウム、ベタネコール、アクラトニウム)、コリンエステラーゼ阻害剤(アンベノニウム、ジスチグミン、ピリドスチグミン、ネオスチグミン等)、抗コリン作用を有する薬剤(トリヘキシフェニジル、ピロヘプチン、マザチコール、メチキセン、ビペリデン等)、アトロピン系抗コリン剤(ブチルスコポラミン、アトロピン等)、サクシニルコリン系筋弛緩剤(スキサメトニウム等)
4.副作用(抜粋)
国内臨床試験において安全性解析の対象となった858例中720例(83.9%)に副作用(臨床検査値の異常を含む)が認められた。主な副作用は、適用部位紅斑370例(43.1%)、適用部位瘙痒感345例(40.2%)、接触性皮膚炎249例(29.0%)、適用部位浮腫119例(13.9%)、嘔吐77例(9.0%)、悪心75例(8.7%)、適用部位皮膚剥脱52例(6.1%)及び食欲不振48例(5.6%)であった。(承認時)
(1)重大な副作用
1)狭心症、心筋梗塞、徐脈、心ブロック、洞不全症候群　狭心症(0.2%)、心筋梗塞(0.3%)、徐脈(0.8%)、心ブロック(0.1%)、洞不全症候群(頻度不明※)があらわれることがあるので、このような場合には直ちに投与を中止し、適切な処置を行うこと。
2)脳血管発作、痙攣発作　脳血管発作(頻度不明※)、痙攣発作(0.2%)があらわれることがあるので、このような場合には直ちに投与を中止し、適切な処置を行うこと。
3)食道破裂を伴う重度の嘔吐、胃潰瘍、十二指腸潰瘍、胃腸出血　食道破裂を伴う重度の嘔吐、胃潰瘍(いずれも頻度不明※)、十二指腸潰瘍(0.1%)、胃腸出血(0.1%)があらわれることがあるので、このような場合には直ちに投与を中止し、適切な処置を行うこと。
4)肝炎　肝炎(頻度不明※)があらわれることがあるので、このような場合には直ちに投与を中止し、適切な処置を行うこと。
5)失神　失神(0.1%)があらわれることがあるので、このような場合には直ちに投与を中止し、適切な処置を行うこと。
6)幻覚、激越、せん妄、錯乱　幻覚(0.2%)、激越、せん妄、錯乱(いずれも頻度不明※)があらわれることがあるので、このような場合には減量又は休薬等の適切な処置を行うこと。
7)脱水　嘔吐あるいは下痢の持続により脱水(0.2%)があらわれることがあるので、このような場合には、補液の実施及び本剤の減量又は投与を中止するなど適切な処置を行うこと。
※：頻度不明は承認時までの海外での報告による。
5.妊婦、産婦、授乳婦等への投与
(1)妊婦又は妊娠している可能性のある婦人には、治療上の有益性が危険性を上回ると判断される場合にのみ投与すること。〔妊娠中の投与に関する安全性は確立されていない。〕
(2)授乳中の婦人に投与する場合には授乳を避けさせること。〔動物実験(ラット)において、乳汁中への移行が報告されている。〕
6.小児等への投与　低出生体重児、新生児、乳児、幼児又は小児に対する安全性は確立していない(使用経験がない)。
7.過量投与
徴候、症状：外国において本剤の過量投与(1回108mg、2日間)の2週間後に死亡したとの報告がある。また、外国における経口投与及び経皮投与による過量投与例では、嘔吐、悪心、下痢、腹痛、めまい、振戦、頭痛、失神、傾眠、錯乱状態、幻覚、多汗症、徐脈、高血圧及び倦怠感等が認められている。
処置：過量投与時には、速やかに本剤をすべて除去し、その後24時間はそれ以上の貼付を行わない。重度の悪心、嘔吐には制吐剤の使用を考慮すること。その他の有害事象に対しては、必要に応じて対症療法を行う。また、大量の過量投与時には、アトロピン硫酸塩水和物を解毒剤として使用できる。最初にアトロピン硫酸塩水和物として1～2mgを静脈内投与し、臨床反応に応じて投与を追加する。解毒剤としてスコポラミンの使用は避けること。
8.適用上の注意
(1)貼付時
1)本剤は、背部、上腕部又は胸部の正常で健康な皮膚で、清潔で乾燥した体毛が少ない、密着した衣服を着用してもこすれない箇所に貼付すること。
2)貼付箇所の皮膚を拭い、清潔にしてから本剤を貼付すること。
3)皮膚の損傷又は湿疹・皮膚炎等がみられる箇所には貼付しないこと。
4)貼付する箇所にクリーム、ローション又はパウダーを塗布しないこと。
5)皮膚刺激を避けるため、貼付箇所を毎回変更し、繰り返し同一箇所には貼付しないこと。
6)原則、1回につき1枚のみ貼付し、貼付24時間後に新しい製剤に貼り替えること。
(2)保管・廃棄
1)使用するまでは小袋内で保管すること。
2)小児の手及び目の届かない、高温にならない所に保管すること。
3)貼付24時間後も本剤の成分が残っているので、使用済みの製剤は接着面を内側にして折りたたみ、小児の手及び目の届かない所に安全に廃棄すること。
4)本剤を扱った後は、手を眼に触れず、手を洗うこと。

●その他の使用上の注意等、詳細は製品添付文書をご参照ください。

＊ 本剤は新医薬品であるため、厚生労働省告示第97号(平成20年3月19日付)に基づき、2012年7月末日までは、投薬期間は1回14日分を限度とされています。

(＊2011年7月改訂)

資料請求先
ono 小野薬品工業株式会社
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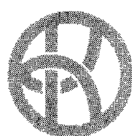
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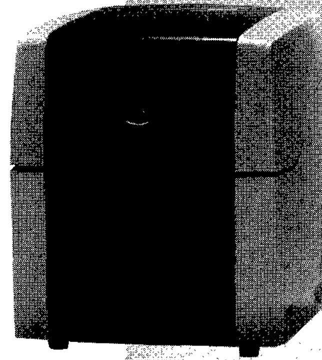

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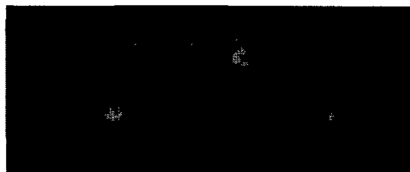

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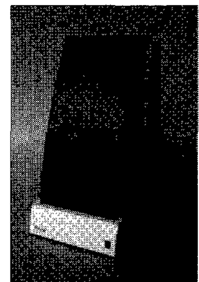

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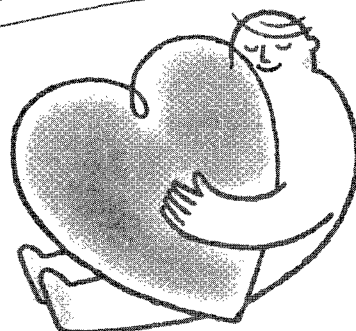

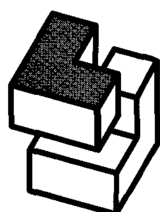

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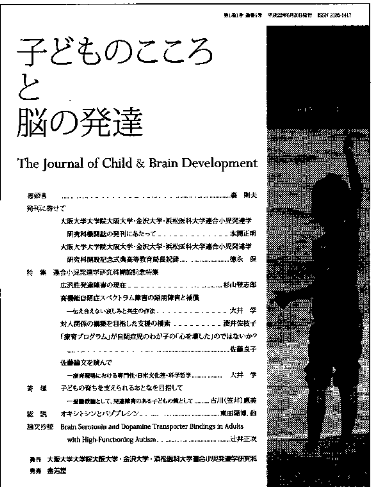
子どものこころと脳の発達

The Journal of Child & Brain Development



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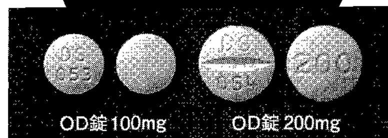

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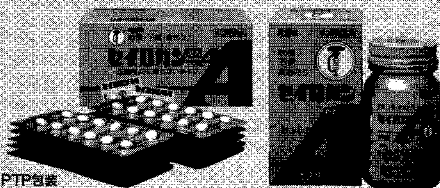

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