生物試験分野　Division of Pharmacology

教　授	渡辺　裕司	Professor	Hiroshi Watanabe (Ph.D.)
助教授	松本　欣三	Associate Professor	Kinzo Matsumoto (Ph.D.)
助　手	東田　道久	Assistant Professor	Michihisa Tohda (Ph.D.)
技術専門職員	村上　孝寿	Research Associate	Yukihisa Murakami (Ph.D.)
技術補佐員	趙　琦	Research Assistant	Qi Zhao
技術補佐員	中村　政美	Research Assistant	Masami Nakamura

◇研究目的　Aims of the research projects

本研究室では，和漢薬の新しい薬効評価法を確立するための基礎研究，和漢薬の中枢作用を定量的に評価し，その作用本体を追求する研究及びその作用機序を分子レベルで明らかにすることを目的とした研究を行っている。

◇研究概要　Research projects

Ⅰ．和漢薬の新しい薬効評価法を確立するための基礎的研究

1）脳血管性痴呆病態モデル動物の確立とそれによる和漢薬および抗痴呆薬の薬効評価

2）情動ストレス反応の不安・うつ病態モデルとしての応用と和漢薬作用

3）新規リード化合物の開発をめざした各種民族薬の薬理作用の探索と作用機構の解析

Ⅱ．中枢作用薬の神経薬理学的研究

1）心理的ストレス反応に関わる神経機構，受容体機能修飾因子，分子機序の解析

2）神経伝達物質の脳内動態および代謝回転の解析と薬物作用

Ⅲ．遺伝子発現を指標とした薬物作用の解明と和漢薬作用に関する研究

1）慢性脳虚血により発現する脳内遺伝子のクローニングとその機能解析

2）うつ病態関連脳内遺伝子の発現変化と抗うつ薬・和漢薬の作用解析

◇著書　Books

1）渡辺裕司，松田治己：行動における諸指標 1.4 旋回行動，1.5 特異的薬物による誘発行動（1）アポモルヒネ，生物薬科学実験講座11，佐藤公道，野村靖幸編，神経（脳）2，pp 54-69，廣川書店，東京，2003.

2）東田道久，渡辺裕司：パーキンソン病・パーキンソン症候群，百瀬弥寿徳編，ファーマシューティカルノート，pp. 27-32，医学評論社，東京，2003.

◇原著　Original papers

1）**Tohda M. and Watanabe H.: Determination method of sense sequence based on RT/PCR.** ***Journal of Biochemical & Biophysical Methods*** **55:101-105, 2003.**

Abstract: When novel sequences are isolated by differential display and other methods, it seems useful to determine which is a sense sequence at an early stage before further experiments. A novel sequence, named MT-001, which shows enhanced expression in the permanent ischemic rat brain, was isolated by differential display. Based on this sequence, a primer set for both direction was designed. Each primer was used to make a cDNA and PCRs performed with each cDNA and both primers. One primer used in the RT step produced a PCR product at the expected position, but another primer in the reverse direction could not. This result indicated that the primer that made the expected PCR product is antisense.

2）**Puia G., Mienville J.-M., Matsumoto K., Takahata H., Watanabe H., Costa E. and Guidotti A.: On the putative physiological role of allopregnanolone on $GABA_A$ receptor function.** ***Neuropharmacology.*** **44: 49-55, 2003.**

Abstract: To obtain definitive evidence for a physiological allosteric modulatory role for endogenous brain ALLO on $GABA_A$ receptor function, we studied $GABA_A$ receptor activity under conditions in which the concentration of endogenous brain ALLO was decreased by about 80% for longer than 5 h following the administration of SKF 105111- 17β-17-[bis (1methylethyl) amino carbonyl] androstane-3,5-diene-3-carboxylic acid (SKF), a potent inhibitor of 5α-reductases Type I and II. We used the in situ patch-clamp technique to record GABA-evoked currents and spontaneous inhibitory postsynaptic currents (sIPSCs) from pyramidal neurons in neocortical slices of vehicle- or SKF-treated mice. The potency, but not the efficacy, of exogenously applied GABA was decreased in slices from mice treated with SKF. When neocortical slices were treated in vitro for 3 h with 10 μM SKF, ALLO was also reduced (25-30%) and in addition, the GABA dose-response curve was shifted to the right; however this shift was not as marked as the shift in the slices obtained from mice treated with SKF, in keeping with the smaller decrease of the ALLO content in these slices. Furthermore, direct application of ALLO to these slices shifted the dose-response curve of GABA back toward a non-SKF treated profile. We then analyzed GABAergic sIPSCs in neocortical slices obtained from vehicle or SKF-treated mice. Mean decay time and charge transfer were significantly reduced by SKF treatment. The decay of sIPSCs was best fitted by two exponentials, but only the fast component was decreased in the SKF group. Direct application of ALLO (100nM) normalizes the sIPSC kinetics in slices from ALLO depleted mice. No changes were detected in the amplitude or frequency of sIPSCs. These data demonstrate that endogenous ALLO physiologically regulates spontaneously induced Cl^- current by acting on a specific recognition site, which is probably located on $GABA_A$ receptors (a receptor on a receptor), thereby prolonging inhibitory currents by facilitating conformational transition of the GABA-gated Cl^- channel to an open state.

3）**Pinna G., Dong E., Matsumoto K., Costa E. and Guidotti A.: In socially isolated mice, the reversal of brain allopregnanolone down-regulation mediates the anti-aggressive action of fluoxetine.** ***Proceedings of the National Academy of Sciences of the United States of America*** **100:2035-2040, 2003.**

Abstract: Social isolation (SI) of male mice lasting >4 weeks is associated with aggression toward intruders and a down-regulation of brain allopregnanolone (Allo) content. SI of female mice fails to down-regulate brain Allo content or to induce aggressiveness. Fluoxetine (Prozac in clinical use) is an S- and R-fluoxetine (FLX) mixture, which in mammals is metabolized into S- and R-norfluoxetine (NFLX). The S isomers of FLX and NFLX are more active than their respective R isomers in normalizing brain Allo down-regulation and in reducing the aggressiveness induced by SI. Thus, FLX stereospecifically reduces brain Allo down-regulation and the aggressiveness induced by SI, whereas serotonin (5-HT) uptake inhibition lacks stereospecificity. The doses of S-FLX and S-NFLX that reduce aggressiveness and Allo brain content down-regulation induced by SI are at least one order of magnitude lower than the doses that block 5-HT reuptake. Doses of imipramine that inhibit 5-HT uptake neither reduce aggressiveness nor normalize brain Allo down-regulation. We conclude that Allo brain content normalization is a better candidate than 5-HT reuptake inhibition to explain the reduction of aggressiveness elicited by S-FLX and S-NFLX.

4) **Vajragupta O., Boonchoong P., Sumanont Y., Watanabe H., Wongkrajang Y. and Kammasud N.: Manganese-Based complexes of radical scavengers as neuroprotective agents.** ***Bioorganic & Medicinal Chemistry*** **11:2329-2337, 2003.**

Abstract: Manganese was incorporated in the structure of the selected antioxidants to mimic the superoxide dismutase (SOD) and to increase radical scavenging ability. Five manganese complexes (1-5) showed potent SOD activity in vitro with IC_{50} of 1.18-1.84 μM and action against lipid peroxidation in vitro with IC_{50} of 1.97-8.00 μM greater than their ligands and trolox. The manganese complexes were initially tested in vivo at 50 mg/kg for antagonistic activity on methamphetamine (MAP)-induced hypermotility resulting from dopamine release in the mice brain. Only manganese complexes of kojic acid (1) and 7-hydroxyflavone (3) exhibited the significant suppressions on MAP-induced hypermotility and did not significantly decrease the locomotor activity in normal condition. Manganese complex 3 also showed protective effects against learning and memory impairment in transient cerebral ischemic mice. These results supported the brain delivery and the role of manganese in SOD activity as well as in the modulation of brain neurotransmitters in the aberrant condition. Manganese complex 3 from 7-hydroxyflavone was the promising candidate for radical implicated neurodegenerative diseases.

5) **Mahakunakorn P., Tohda M., Murakami Y., Matsumoto K., Watanabe H. and Vajaragupta O.: Cytoprotective and cytotoxic effects of curcumin: Dual action on H_2O_2-induced oxidative cell damage in NG 108-15 cells.** ***Biological & Pharmaceutical Bulletin*** **26:725-728, 2003.**

Abstract: The ability of curcumin, a natural antioxidant isolated from *Curcuma longa,* to inhibit hydrogen peroxide (H_2O_2)-induced cell damage in NG108-15 cells was examined. When added simultaneously with 500 μM H_2O_2, curcumin (25-100 μM) effectively protected cells from oxidative damage. However, when the cells were pretreated with curcumin (25-100 μM) for 1.5 h before H_2O_2 exposure, curcumin was unable to inhibit H_2O_2-induced cell damage. Instead, it caused a significant concentration-dependent decrease in cell viability after H_2O_2 exposure. This dual action of curcumin suggests that pretreatment with curcumin by itself did not have any significant effect on the viability of the NG108-15 cells, but it sensitized them to oxidative damage induced by H_2O_2 under our experimental conditions. It appears that these events may not relate to the antioxidant and free radical scavenging activities of curcumin.

6) **Jeenapongsa R., Tohda M. and Watanabe H.: Effects of Choto-san and Chotoko on thiopental-induced sleeping time.** ***Journal of Traditional Medicines*** **29:165-167, 2003.**

Abstract: Choto-san has been used for treatment of centrally regulated disorders such as dementia, hypertension, headache and vertigo. Our laboratory showed that Choto-san improved learning memory in ischemic mice. It is noticeable that Choto-san treated animals and underwent conducting occlusion of common carotid arteries (2VO)

operation slept longer than the normal animals. Therefore, this study aimed to clarify the effects of Choto-san and its related component; Chotoko and Choto-san without Chotoko on thiopental-induced sleeping time. The results show that Choto-san (0.3, 1 and 3 g/kg, p.o.) dose dependently prolonged the sleeping time induced by thiopental (50 mg/kg, i.p.). Chotoko (71.4 mg/kg, p.o.) and diazepam (1 mg/kg, i.p.) also increased the sleeping time while Choto-san without Chotoko (1 g/kg, p.o.) had no effect. This indicates that the effects of Choto-san and Chotoko, main active constituent of Choto-san, may be mediated in part via their suppressive effect on the central nervous system of which the precise mechanisms remain unknown.

7) **Sukma M., Tohda M., Watanabe H.: Chronic Treatment With Imipramine Inhibits Cell Growth and Enhances Serotonin 2C Receptor mRNA Expression in NG 108-15 Cells. Journal *of Pharmacological Sciences* 92:433-436, 2003.**

Abstract: We previously reported that NG108-15 cells contain intrinsic serotonin 2C receptor (5-HT2CR). The effects of imipramine, a 5-HT2CR antagonist, on cell growth, cell viability, and the 5-HT2CR mRNA level were investigated in this study. Repeated treatment with imipramine at concentrations of 1 - 10 μM for 5 days inhibited cell growth in a concentration-dependent manner without affecting cell viability. In addition, the level of 5-HT2CR mRNA was elevated. At 30 μM, imipramine significantly reduced cell viability. Our findings suggest that the effect of imipramine on neuronal growth may be related to its effects on 5-HT2CR.

8) **Watanabe H., Zhao Q., Matsumoto K., Tohda M., Murakami Y., Zhang S.-H., Kang T.-H., Mahakunakorn P., Maruyama Y., Sakakibara I., Aimi N., Takayama H.: Pharmacological evidence for antidementia effect of Choto-san (Gouteng-san), a traditional Kampo medicine. *Pharmacology Biochemistry & Behavior* 75:635-643, 2003.**

Abstract: To clarify the clinical efficacy of one of the traditional medicines in the treatment of patients with vascular dementia, we investigated the pharmacological activities of Choto-san in animal models. Pretreatment with Choto-san (0.75-6.0 g/kg po), a component herb, Chotoko (75-600 mg/kg po), and indole alkaloids and phenolic fractions of Chotoko prevented ischemia-induced impairment of spatial learning behaviour in water maze performance of mice. A single administration of Choto-san (0.5 to 6.0 g/kg po) or Chotoko (*Uncaria genus*) produced a dose-dependent antihypertensive effect in spontaneously hypertensive rats (SHR) and partly inhibited the induction of the apoplexy in stroke-prone SHR (SHR-SP). Choto-san, Chotoko, and its phenolic constituents, (-)epicatechin and caffeic acid, significantly protected NG108-15 cells from injury induced by H_2O_2 exposure in vitro and also inhibited lipid peroxidation in the brain homogenate. Indole alkaloids, rhynchophylline and isorhynchophylline (1-100 μM), reversibly reduced *N*-methyl-D-aspartate (NMDA)-induced current concentration dependently in NMDA receptor-expressed *Xenopus oocytes.*

These results suggest that antidementia effects of Choto-san are due to antihypertensive, free radical scavenging and antiexcitotoxic effects, which are attributed at least partly to phenolic compounds and indole alkaloids contained in Chotoko.

9) **Matsumoto K., Nomura H., Murakami Y., Taki K., Takahata H., Watanabe H.: Long-term social isolation enhances picrotoxin seizure susceptibility in mice: up-regulatory role of endogenous brain allopregnanolone in GABAergic systems. *Pharmacology Biochemistry & Behavior* 75:831-835, 2003.**

Abstract: Allopregnanolone (ALLO, 3α,5α-tetrahydroprogesterone), a positive allosteric modulator of actions of γ-aminobutyric acid (GABA) at $GABA_A$ receptors, is synthesized in the brain from progesterone by the sequential action of two enzymes: a type I 5 α-reductase and a 3 α-hydroxysteroid oxidoreductase. We previously demonstrated that long-term social isolation of mice caused a significant decrease in brain ALLO content via suppression

of type I 5 α-reductase and its mRNA expression. In this study, to clarify a physiological role of endogenous brain ALLO, we investigated changes in seizure susceptibility of mice following protracted social isolation and compared with those of mice treated with SKF105111 (SKF), an inhibitor of types I and II 5 α-reductase. Social isolation of mice for 7 weeks prior to the experiments caused a significant increase of seizure susceptibility to the $GABA_A$ receptor antagonist picrotoxin but not to the glycine receptor antagonist strychnine or the glutamate receptor agonist kainic acid. The change in the seizure susceptibility was completely reversed by 2.5 mg/kg ip ALLO, a dose that per se had no effect on picrotoxin-induced seizure. Treatment of mice with SKF (20 mg/kg ip) also reduced a threshold dose of picrotoxin, but not that of strychnine or kainic acid, which was required to elicit seizure in group-housed mice. The effect of SKF was attenuated by ALLO (2.5 mg/kg ip). In contrast, SKF treatment had no effect on picrotoxin-induced seizure in socially isolated mice. These findings suggest that endogenous brain ALLO plays a suppressive role in seizure susceptibility via a positive modulation of $GABA_A$ receptor function and that social isolation enhances seizure susceptibility in mice via reduction of $GABA_A$ receptor function caused by a decrease of endogenous ALLO.

10) **Vajragupta O., Boonchoong P., Watanabe H., Tohda M., Kummasud N., Sumanont Y.: Manganese complexes of curcumin and its derivatives: evaluation for the radical scavenging ability and neuroprotective activity.** ***Free Radical Biology & Medicine*** **35:1632-1644, 2003.**

Abstract: In this study, three manganese complexes of curcumin (Cp) and related compounds, diacetylcurcumin (AcylCp) and ethylenediamine derivative (CpED), were synthesized and evaluated in vitro for antilipid peroxidation and superoxide dismutase activity. The manganese complexes exhibited a great capacity to protect brain lipids against peroxidation with IC_{50} of 6.3-26.3 μM. All manganese complexes showed much greater SOD activity than their corresponding antioxidant ligands as well as trolox with IC_{50} values of 8.9-29.9 μM. AcylCp and curcumin manganese complexes (AcylCpCpx and CpCpx) also gave the highest inhibitory activity to H_2O_2-induced cell damage (oxidative stress) at 0.1 mg/ml (< 0.2 μM) in NG108-15 cells, which were more potent than curcumin and related compounds. The neuropharmacological tests in mice supported the idea that the SOD mimicking complexes were able to penetrate to the brain as well as their role in the modulation of brain neurotransmitters under the aberrant conditions. The complexes significantly improved the learning and memory impairment induced by transient ischemic/reperfusion. AcylCpCpx, CpCpx, and CpEDCpx showed significant protection at 6.25, 25, and 50 mg/kg (i.p.), respectively, whereas manganese acetate and curcumin had no effect at doses of 50 mg/kg. In addition, treatment of AcylCpCpx and curcumin significantly attenuated MPTP-induced striatal dopamine depletion in mice, which was in accordance with the increase in the density of dopaminergic neurons when compared with MPTP-treated mice. These results support the important role of manganese in importing SOD activity and consequently, the enhancement of radical scavenging activity. AcylCpCpx and CpCpx seem to be the most promising neuroprotective agents for vascular dementia.

◇学会報告　Scientific presentation

1）松本欣三, Puia G., Mienville J.-M., 渡辺裕司, Costa E., Guidotti A.: 隔離飼育マウスの攻撃行動に対するフルオキセチン及びノルフルオキセチンの抑制効果：アロプレグナノロンの関与. 第76回日本薬理学会年会, 2003, 3/24-26, 福岡.

2）姜太炫, 村上孝寿, 松本欣三, 高山廣光, 北島満里子, 相見則郎, 渡辺裕司：リンコフィリン及びイソリンコフィリンの NMDA 受容体に対する抑制効果：アフリカツメガエル卵母細胞受容体発現系での検討. 第76回日本薬理学会年会, 2003, 3/24-26, 福岡.

3）Sukma M., 東田道久, 渡辺裕司：NG108-15 細胞の神経分化に伴うセロトニン 2C 受容体 RNA editing. 第76回日本薬理学会年会, 2003, 3/24-26, 福岡.

4）Jeenapongsa R., 東田道久, 渡辺裕司：釣藤散の中枢薬理作用：慢性虚血脳中で発現増大する新規

因子 vof-21 の発現抑制と薬物誘発睡眠増強効果. 第76回日本薬理学会年会, 2003, 3/24-26, 福岡.

5）趙琦, 村上孝寿, 東田道久, 渡辺裕司：脳卒中易発症高血圧ラットにおける釣藤散構成生薬エキスの抗高血圧効果. 第20回和漢医薬学会大会, 2003, 8/30-31, 熊本.

6）松本欣三, 姜太炫, 村上孝寿, 東田道久, 渡辺裕司, 高山廣光, 北島満里子, 相見則郎：釣藤鉤アルカロイド成分リンコフィリン及びイソリンコフィリンの in vitro 海馬虚血モデルにおける神経保護作用とその機序. 第20回和漢医薬学会大会, 2003, 8/30-31, 熊本.

7）東田道久, 渡辺裕司：神経分化・増殖へのセロトニン 2C 受容体の関与と和漢薬作用. 第14回天然薬物の開発と応用シンポジウム, 2003, 11/6-7, 仙台.

8）渡邉裕司, 趙琦, 張紹輝, 姜太炫, 村上孝寿, 東田道久, 松本欣三, 高山廣光, 相見則郎, 榊原巌：釣藤散の脳血管性痴呆改善効果の薬理学的裏付け. 第14回天然薬物の開発と応用シンポジウム, 2003, 11/6-7, 仙台.

9）Mahakunakorn P., Tohda M., Murakami Y., Matsumoto K., Watanabe H.: Antioxidant and free radical scavenging activity of Choto-san and its related constituents. 日本薬学会北陸支部第109例会, 2003, 11/30, 富山.

10) Jaruchotikamol A., Watanabe H., Mahakunakorn P., Priprem A.: Poterntial cytotoxicity of astaxanthin. The sixth joint seminar: Recent advances in natural medicine research, 2003, 12/2-4, Bangkok.

11) Hussein G., Zhao Q., Nakamura M., Iguchi T., Goto H., Sankawa U., Watanabe H: Antihypertensive and neuroprotective effects of astaxanthin in experimental animals. The sixth joint seminar: Recent advances in natural medicine research, 2003, 12/2-4, Bangkok.

◇その他　Others

1）Watanabe, H.: CNS effects of water extract of Uncaria spp. Teleconference with UC Dasvis and Mars Foods, 2003, 5/2, Saitama.

2）Watanabe, H.: Traditional medicine for oral health. Joint Seminar with TMPU, UC Davis and Master Foods, 2003, 8/23. Honolulu.

3）Matsumoto K. Pinna G., Watanabe H., Guidotti A., Costa.: Psychopathological roles of endogenous brain allopregnanolone: elucidation in a mouse model of protracted social isolation. 1st International symposium of neurobehavioral pharmacology, 2003, 9/13-15, Okayama.

4) 松本欣三, Guidotti A., Costa E., 渡邉裕司: 中枢γ-アミノ酪酸神経系制御における神経ステロイドallopregnanoloneの生理的・精神病理的役割. 第2回北陸ポストゲノム研究フォーラム（金沢大学がん研究所・富山医科薬科大学和漢薬研究所合同シンポジウム）, 2003, 10/24, 金沢.

◇共同研究　Co-operative researches

1）相見則郎, 高山廣光, 北島満里子：千葉大学大学院薬学研究院,「タイ薬用植物中のインドールアルカロイド類に関する創薬基礎科学研究」1994, 4 -

2）山崎和男, 笠井良次：広島大学大学院医歯薬学総合研究科, グエン・チー・スー・フォン：ベトナム薬物研究所,「ベトナム人参の薬理作用の研究」1994, 4 -

3）Erminio Costa, Alessandro Guidotti : イリノイ州立大学シカゴ校精神医学研究所,「ストレス病態における神経活性ステロイドの役割」1997, 4-

4）Boonyong Tantisira : タイ国チュラロンコン大学薬学部,「新規バルプロ酸類縁化合物の抗てんかん作用の作用機構の解明研究」2000, 4/1-

5）Opa Vajragupta : タイ国マヒドン大学薬学部,「SOD mimics の脳血管性障害に対する抑制作用の研究」2001, 4/1 -

◇研究費取得状況　Acquisition of research funds

1）文部科学省科学研究費，萌芽的研究（代表：渡辺裕司）「和漢処方処置による脳内遺伝子発現変化に関する基礎的研究」 180万（1/2年目）

2）文部科学省科学研究費，基盤研究C（代表：松本欣三）「GABA神経系機能調節およびストレス病態発現における内因性神経ステロイドの役割」 270万（1/2年目）

3）文部科学省科学研究費，21世紀中核的研究拠点形成プログラム（分担：松本欣三）「東洋の知に立脚した個の医療の創生」 200万

4）受託研究費，（財）北陸産業活性化センター（代表：渡辺裕司）地域新生コンソーシアム研究開発事業「藻類培養によるアスタキサンチンの製造及び健康補助食品の開発」 1,000万

5）富山県，和漢薬・バイオテクノロジー研究費，（代表：渡辺裕司）「免疫系。血液血管系に作用する家庭薬や薬食同源食品の開発：脳血管性痴呆，高血圧などの生活習慣病を予防治療する和漢薬の研究」 50万

◇研究室在籍者　Research members

学部3年生：　林寿枝，原田恒介

学部4年生：江村真実，中西絵里香

大学院前期1年：井口知美，平尾顕三

大学院前期2年：天野佑三子，森繁亮

大学院後期1年：Yaowared Sumanont

大学院後期3年：Monrudee Sukma

Pramote Mahakunakorn

外国人客員研究員：

日本学術振興会・拠点大学交流事業

Ms. Tran My Tien（ベトナム薬物研究所，2003, 2/3-3/31）

Dr. Duong Kim Toa（ベトナム薬物研究所，2003, 3/3-3/31）

Dr. Somsak Ruchizawat（チュラポン研究所副所長，2003, 3/20-3/27）

Dr. Boonsri Ongipipattanakul（チュラロンコン大学薬学部助教授，2003, 3/22-3/29）

Dr. Boonyong Tantisira（チュラロンコン大学薬学部長，2003, 3/28-30）

Dr. Mayuree Tantisira（チュラロンコン大学薬学部，2003, 3/28-30）

Ms. Orathai Tangvarasittichai（ナレスアン大学講師，2003, 2/20-3/31）

Ms. Jaruchotikamol Atika（マハサラカム大学講師，2003, 7/2-9/26）

Dr. Neti Warachu（ナレスアン大学，2003, 7/14-26）

Mr. Boontium Kongsaktrakoon（マヒドン大学，2003, 8/18-9/30）

Dr. Nguyen Thi Thu Huong（ベトナム薬物研究所，2003, 8/25-12/26）

東京生化学研究会外国人研究者招聘奨学金

Dr. Rattima Jeenapongsa（ナレスアン大学講師，2002, 4/1-2003, 4/10）

富山伝統医学センター

相婷博士（2001, 4/1-）

Dr. Ghazi Hussein（2001, 4/1-）

富山医科薬科大学国際交流基金

Dr. Suree Jianmongkol（チュラロンコン大学薬学部助教授，2003, 3/15-5/15）

その他

Dr. Justin Dann（Master Foods Japan, 2003, 10/1- ）

外国人特別研究学生

Ms. Chantana Boonyarat（日本国際教育協会及びタイ王立教育協会，マヒドン大学大学院，2002,

4/26-2003, 4/19)

Ms. Onrawee Khongsombat（日本国際教育協会，チュラロンコン大学大学院，2002, 5/26-2003, 4/25)

Ms. Yaowared Sumanont（文部科学省奨学金，コンケン大学講師，2002, 10/1-2003, 3/31）

◇学位取得者　Academic degrees and theses

博士：2003年3月

Kang Tai-Hyun　Study on oxindole alkaloids isolated from Uncaria species: neurotransmitter receptor-based approaches for treating and preventing neurodegenerative disorders with memory impairment

博士：2003年9月

Monrudee Sukma　The expression and physiological functions of 5-HT2C receptor mRNA in NG108-15 cells: involving RNA editing in neuronal differentiation and proliferation.