薬物代謝工学分野　Division of Metabolic Engineering

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◇研究目的

薬物代謝工学分野は和漢薬の薬効，毒性発現に関与する代謝系の分子生物学的研究を発展させることを設置目的とし，(1) 和漢薬の薬効発現に関与する腸内細菌の役割の解明，(2) LC/MS/MS による和漢薬成分分析と薬物動力学的研究，(3) AIDS，C 型肝炎ウイルスに有効な天然薬物の探索，(4) 霊芝，樟芝などの担子菌類の薬効評価，(5) 内分泌調節作用を有する和漢薬の研究 などを研究テーマとしている。

◇研究概要

Ⅰ．和漢薬の薬効発現に関与する腸内細菌の役割の解明

紅花種子に含まれるリグナン tracheloside のヒト腸内細菌による代謝を検討した結果，この化合物もまたエストロゲン様作用を有する enterolactone に変換されることを明らかにした。また得られた中間代謝物のエストロゲンレセプターαおよびβとの結合の強さを比較検討した。

Ⅱ．LC/MS/MS による和漢薬成分分析と薬物動力学的研究

台湾産樟芝菌糸体中に含まれる antrodin D, E の吸収，代謝，分布，排泄等の体内動態を明らかにする目的で動物に経口投与後，血漿，尿，糞中の成分の LC/MS/MS による分析を行い，代謝物の生成を認めた。

Ⅲ．AIDS，C 型肝炎ウイルスに有効な天然薬物の探索

トリテルペンの A 環の開裂した化合物や化学的に合成した種々の類似化合物の HIV-1 および HCV プロテアーゼに対する阻害作用を検討し，強い阻害活性物質を見出した。

Ⅳ．霊芝，樟芝などの担子菌類の薬効評価

ベトナム産の黄芝から単離した化合物の HIV-プロテアーゼ阻害活性を調べた結果，プロテアーゼの活性中心を競合的に阻害する ganomicin 誘導体と，酵素の二量体形成を阻害するトリテルペンに大別されることが判明した。

Ⅴ．内分泌調節作用を有する和漢薬の研究

中医学理論に基づいて創製された春至カプセルの生殖内分泌効果を調べ, そのメカニズムを検討した。

◇原著論文

1) **Phuong D. T., Ma C. M., Hattori M., and Jin J. S.: Inhibitory effects of antrodins A-E from *Antrodia cinnamomea* and their metabolites on hepatitis C virus protease. Phytother. Res., 23: 582-584, 2009.**

Abstract: *Antrodia cinnamomea* is a highly valued folk medicine used for liver cancer, a disease often caused by the long term infection of hepatitis C virus (HCV). In the present study, the maleic and succinic acid constituents (antrodins A-E) of this medicinal fungus, the *in vivo* metabolites of antrodin C and the analogue of one of the metabolites were tested for their inhibitory activity on HCV protease. Most of the compounds showed potent inhibitory activity, with antrodin A being the most potent (IC_{50}=0.9μg/mL). Antrodin A was isolated as one of the constituents of *A. cinnamomea* and was also detected as an *in vivo* metabolite of the major constituent antrodin C. The mode of inhibition for antrodin A on HCV protease was revealed by a Lineweaver-Burk plot as competitive inhibition. These results strongly support the use of this folk medicine for liver cancer and HCV infection which is a global problem.

2) **Sato N., Ma C., Komatsu K., and Hattori M.: Triterpene-farnesyl hydroquinone conjugates from *Ganoderma sinense*. J. Nat. Prod., 72: 958-961, 2009.**

Abstract: Three new lanostane-type triterpenoids having farnesyl hydroquinone moieties, named ganosinensins A-C (**1**-**3**), were isolated from the fruiting body of *Ganoderma sinense*, together with three known lanostane triterpenes, ganodermanontriol, ganoderiol A, and ganoderiol D. The structures of compounds **1**-**3** were determined by spectroscopic data interpretation.

3) **Wei Y., Ma C., and Hattori M.: Synthesis of dammarane-type triterpene derivatives and their ability to inhibit HIV and HCV proteases. Bioorg. Med. Chem., 17: 3003-3010, 2009.**

Abstract: We synthesized dammarane-type triterpene derivatives and evaluated their ability to inhibit HIV-1 and HCV proteases to understand their structure-activity relationships. All of the mono- and di-succinyl derivatives (**5a**−**5f**) were powerful inhibitors of HIV-1 protease (IC_{50}<10μM). However, only di-succinyl (**5e**) and 2,3-*seco*-2,3-dioic acid (**3b**) derivatives similarly inhibited HCV protease (IC_{50}<10μM). A-nor dammarane-type triterpenes (**4a** and **4b**, IC_{50} 10.0 and 29.9 μM, respectively) inhibited HIV-1 protease moderately or strongly, but were inactive against HCV protease. All compounds that powerfully inhibited HIV-1 or HCV protease did not appreciably inhibit the general human proteases, renin and trypsin (IC_{50}>1000μM). These findings indicated that the mono-succinyl dammarane type derivatives (**5a**−**5d**) selectively inhibited HIV-1 protease and that the di-succinyl (**5e**, **5f**) as well as 2,3-*seco*-2,3-dioic acid (**3b**) derivatives preferably inhibited both viral proteases.

4) **Ma C., Wei Y., Wang Z., and Hattori M.: Triterpenes from Cynomorium songaricium-analysis of HCV protease inhibitory activity, quantification, and content change under the influence of heating. J. Nat. Med., 63: 9-14, 2009.**

Abstract: Inhibitory activity of the three major triterpenes from the stems of *Cynomorium songaricum*－ursolic acid, acetyl ursolic acid, and malonyl ursolic acid hemiester－and their related compounds were tested for their inhibitory activity on HCV protease; malonyl ursolic acid hemisester was the most potent. A HPLC-PAD (photo diode array detector) －MS method was established to quantify the contents of each triterpene in *C. songaricum*. Using this method, the effect heating had on the contents was also investigated. It was found that among the three triterpenes, the content of malonyl ursolic acid hemiester decreased most quickly during the heating process.

5) **Yu J., Ma C., Long C., Wang X., Shang M., Cai S., Hattori M., and Namba T.: A new aristololactam from *Asarum maximum*. J. Chin. Pharm. Sci., 18: 183-185, 2009.**

Abstract: The whole plant or the root of *Asarum maximum* Hemsl. (Aristolochiaceae) is used for the treatment of cough, headache and rheumatism as a folk medicine in South China, especially in Hubei and Sichuan Provinces. In our previous papers, we reported the isolation of 15 compounds from the roots and rhizomes of *Asarum maximum* Hemsl., including phenylpropanoids, alkaloids, flavonoids, benzoic acids

and sterols. As a continuing study on the chemical constituents of this plant, we describe herein the isolation and structural elucidation of a new aristololactam.

6) **El-Mekkawy S., Abdel-Sattar E., Hattori M., Kawahata T., and Otake T.: Screening of Medicinal Plants in Egypt for anti-human immunodeficiency virus type-1 (HIV-1) activity. JASMR, 4: 1-8, 2009.**

Abstract: **Background/aim:** Our aim is to develop a promising anti-HIV-1 [anti-human immunodeficiency virus type-1] extract from medicinal plants available in Egypt. The inhibitory effects of 59 plants (water and methanol extracts) on HIV essential enzymes; protease (HIV-1 PR) and reverse transcriptase (HIV-1 RT Rnase H), and on MT4-cells infected with HIV were evaluated. **Methods:** HIV-1 PR inhibitory effect was quantitatively evaluated by HPLC (measuring the hydrolysate and remained substrate, His-Lys-Ala-Arg-Val- Leu-(pNO_2-Phe)-Glu-Ala-NLe-Ser-NH_2). The HIV-1 RT Rnase H inhibitory effect was evaluated by measuring the degradation of 3 H-labeled RNA in a hybrid in the presence of the tested extract. The anti-HIV-1-induced cytopathic effect (CPE) was evaluated on MT-4 cells infected with HIV-1 (IC_{100} was determined through an optical microscope and cell growth was examined to give the CC that reduces the viability of MT-4 cells). **Results:** Potent inhibitory effect on HIV-1 PR was demonstrated by the methanol extracts of the aerial parts of *Calligonium comosum* L'Herit, leaves of *Chrysophyllum cainito* L., *Carissa carandas* L., *Eugenia rosea* DC and *Raeumaria hirtella* Jaub. Et Spthe (IC_{50} 3~10 μg/ml). Significant anti-HIV-1 induced CPE was demonstrated by two samples; the methanol and water extracts of the root of *Chelidonium majus* L. (IC_{100}= 3.9 μg/ml, similar to that of azidothymidine (AZT) followed by the methanol extract of the fruits of *Berberis vulgaris* L. (IC_{100}= 7.81 μg/ml). **Conclusion:** Promising plant extracts will be subjected to further investigation to isolate pure active natural compound(s). Also, screening of other Egyptian medicinal plant extracts for anti- HIV-1 activity will be highly valuable.

7) **Wei Y., Ma C., and Hattori M.: Synthesis and evaluation of A-*seco* type triterpenoids for anti-HIV-1 protease activity. Eur. J. Med. Chem., 44: 4112-4120, 2009.**

Abstract: 2,3-*Seco*-dioic acids derived from four different triterpene skeletons were prepared and evaluated for their anti-HIV-1 protease activity. Two A-*seco* derivatives showed potent inhibitory activity against HIV-1 protease (**3c** and **3e**, IC_{50} 5.7 and 3.9μM, respectively), while four other derivatives showed moderate to weak inhibition (**3a**, **3b**, **3d** and **3f**, IC_{50} 15.7-88.1μM). The combination of a 2,3-*seco*-2,3-dioic acid functional group in ring A and a free acid group at C-28 or C-30 significantly enhanced HIV-1 protease inhibitory activity (**3a**, **3c**-**3e**, IC_{50} 3.9-17.6μM). On the other hand, all A-*seco* derivatives were found to be very weak inhibitors of HCV, renin and trypsin proteases (IC_{50}>80μM). These findings indicate that A-*seco* triterpenes with a carboxyl group at C-28 or C-30 are novel and highly selective HIV-1 protease inhibitors.

8) **Jin J. S., and Hattori M.: Further studies on a human intestinal bacterium *Ruminococcus* sp. END-1 for Transformation of plant lignans to mammalian lignans. J. Agric. Food Chem., 57: 7537-7542, 2009.**

Abstract: A human intestinal bacterium *Ruminococcus* (R.) sp. END-1 capable of oxidizing (-)-enterodiol to (-)-enterolactone, enantioselectively, was further investigated from the perspective of transformation of plant lignans to mammalian lignans; A cell-free extract of the bacterium transformed (-)-enterodiol to (-)-enterolactone through an intermediate, enterolactol. The bacterium showed not only oxidation but also demethylation and deglucosylation activities for plant lignans. Arctiin and secoisolariciresinol diglucoside were converted to (-)-dihydroxyenterolactone and (þ)-dihydroxyenterodiol, respectively. Moreover, by coincubation with *Eggerthella* sp. SDG-2, the bacterium transformed arctiin and secoisolariciresinol diglucoside to (-)-enterolactone and (þ)-enterodiol, respectively.

9) **Ma L., Yang X. W., Cai B. C., and Hattori M.: Intestinal permeability of antitumor alkaloids from the processed seeds of *Strychinos nux-vomica* in a caco-2 cell model. Planta Med., 75:**

631-634, 2009.

Abstract: The uptake and intestinal permeability of the seven alkaloids strychnine (Str), brucine (Bru), β-colubrine (Col), strychnine *N*-oxide (S-N), brucine *N*-oxide (B-N), pseudostrychnine (Psd), and icajine (Ica), which were isolated from the processed seeds of *Strychnos nux-vomica* L., were investigated in the human intestinal Caco-2 model. Determination of compounds was carried out by HPLC. The apparent permeability coefficients (P_{app}) for Str, Bru, Col, S-N, B-N, Psd, and Ica in the apical-to-basolateral direction were (3.11± 0.17) x 10^{-5}, (1.67±0.65) x 10^{-5}, (2.67±0.30) x 10^{-5}, (0.17±0.01) x 10^{-5}, (0.35± 0.02) x 10^{-5}, (2.51±0.33) x 10^{-5}, and (2.61±0.34) x 10^{-5} cm/s, respectively. In the concentration range of 10-200 microM, Str, Bru, Col, and Psd showed substantial concentration-dependent transport across the monolayers. The transports of all seven alkaloids were linear with time and showed moderate to high permeabilities. In the presence of 2,4-dinitrophenol or sodium azide, the P_{app} of Ica was reduced significantly in both the apical-to-basolateral and basolateral-to-apical directions. The dominant mechanism of the intestinal absorption for Str, Bru, Col, S-N, B-N, and Psd was passive diffusion, while it was partially ATP dependent for Ica.

10) Wei Y., Ma C. M., and Hattori M.: Anti-HIV protease triterpenoids from the acid hydrolysate f *Panax ginseng*. Phytochem. Lett., 2: 63-66, 2009.

Abstract: Three artificial triterpenoids, (20R)-20,25-epoxy-dammaran-2-en-6α,12β-diol (**1**), (20R)-20,25- epoxy-3-methyl-28-nordammaran-2-en-6α,12β-diol (**2**) and isodehydroprotopanaxatriol (**3**), were isolated from an acidic hydrolysate of *Panax ginseng* C.A. Meyer, along with three known triterpenes, (20R)- panaxadiol (**4**), (20R)-panaxatriol (**5**) and oleanolic acid (**6**). Compounds **1-3** and **6** showed inhibitory activity against HIV-1 protease with IC_{50} of 10.5, 10.3, 12.3 and 6.3μM, respectively. The results indicated that acid treatment of Ginseng extract could produce diverse structures with interesting bioactivity.

11) Zhang Q., Zuo F., Nakamura N., Ma C. M., and Hattori M.: Metabolism and pharmacokinetics in rats of ganoderiol F, a highly cytotoxic and antitumor triterpene from *Ganoderma lucidum*. J. Nat. Med., 63: 304-310, 2009.

Abstract: The metabolism of ganoderiol F (GF), a cytotoxic and antitumor triterpene from *Ganoderma lucidum*, by intestinal bacteria and its pharmacokinetics in rats were investigated by using liquid chromatography/mass spectrometry/mass spectrometry (LC/MS/MS). GF was converted to ganodermatriol by anaerobic incubation with bacterial mixtures from rats and humans. This metabolite was detected in rat feces, but not in plasma and urine, after oral administration of GF. The fate of GF after oral (p.o.) and intravenous (i.v.) administration to rats was examined in pharmacokinetics studies. Plasma samples pretreated by solid-phase extraction were quantified by HPLC/MS/MS over a GF concentration range of 1.25-100 ng/ml (S/N = 5). The intra- and interday precision (CV%) was below 8% and accuracy was within the range of 95.9-103.6% for all samples. The range of recovery ratios was 89.2-98.2%. After the administration of GF at 0.5 mg/kg i.v., the plasma concentrations of GF quickly declined and the elimination half-life values ($t_{1/2\alpha}$ and $t_{1/2\beta}$) were about 2.4 and 34.8 min. On the other hand, the elimination half-life values ($t_{1/2a}$) after p.o. administration of GF at doses of 20 and 50 mg/kg were 14.4 and 143.3 min for the former, and 18.6 and 114.6 min for the latter. The AUC_{0-t} value was 11.17 (ng/ml) h at a GF dose of 0.5 mg/kg i.v., but 49.4 and 111.6 (ng/ml) h at GF doses of 20 and 50 mg/kg p.o., respectively, indicating that the AUC_{0-t} value is proportional to the administered oral doses. The estimated absolute bioavailability of GF in rats was F = 0.105.

12) Sato N., Zhang Q., Ma C., and Hattori M.: Anti-human immunodeficiency virus-1 protease activity of new lanostane-type triterpenoids from *Ganoderma sinense*. Chem. Pharm. Bull., 57: 1076-1080, 2009.

Abstract: Five new highly oxygenated lanostane-type triterpenoids [ganoderic acid GS-1 (1), ganoderic acid GS-2 (2), ganoderic acid GS-3 (3), 20(21)-dehydrolucidenic acid N (4) and 20-hydroxylucidenic acid

A (5)] were isolated from the fruiting body of *Ganoderma sinense*, together with known compounds including 6 triterpenoids and 3 sterols. The structures of the new triterpenoids determined by spectroscopic means including 2D NMR were 7*β*-hydroxy-3,11,15-trioxo-lanosta-8,24(*E*)-dien-26-oic acid (1), 7*β*,15α-dihydroxy- 3,11-dioxo-lanosta-8,24(*E*)-dien26-oic acid (2), 12*β*-acetoxy-3*β*,7*β*-dihydroxy-11,15-dioxo- lanosta-8,24(*E*)- dien-26-oic acid (3), 3*β*,7*β*-dihydroxy11,15-dioxo-25,26,27-trinorlanosta-8,20-dien-24-oic acid (4), and 7*β*,20*ξ*-dihydroxy-3,11,15-trioxo-25,26,27-trinorlanost-8-en-24-oic acid (5), respectively. Among these, ganoderic acid GS-2, 20-hydroxylucidenic acid N, 20(21)-dehydrolucidenic acid N and ganoderiol F inhibited human immunodeficiency virus-1 protease with IC_{50} values of 20-40μM.

13) El Dine R. S., El Halawany A. M., Ma C., and Hattori M.: Inhibition of the dimerization and active site of HIV-1 protease by secondary metabolites from the Vietnamese mushroom *Ganoderma colossum*. J. Nat. Prod., 72: 2019-2023, 2009.

Abstract: A new farnesyl hydroquinone, ganomycin I(**1**), was isolated along with ganomycin B(**2**) from the chloroform extract of the fruiting bodies of the Vietnamese mushroom *Ganoderma colossum*. These compounds inhibited HIV-1 protease with IC_{50} values of 7.5 and 1.0μg/mL, respectively. Kinetic studies using Zhag─Poorman and Lineweaver plots revealed that compound **2** competitively inhibited the active site of the enzyme, whereas the tetracyclic triterpene schisanlactone A, previously isolated from the same fungus, was a dimerization inhibitor, with an IC_{50} value of 5.0μg/mL. The previous findings were also confirmed by the virtual docking of both compounds with HIV-1 protease crystal structure.

14) Sasivimolphan P., Lipipun V., Likhitwitayawuid K., Takemoto M., Pramyothin P., Hattori M., and Shiraki K.: Inhibitory activity of oxyresveratrol on wild-type and drug-resistant varicella-zoster virus replication in vitro. Antiviral Res., 84: 95-97, 2009.

Abstract: The anti-herpes simplex virus (HSV) compound, oxyresveratrol, purified from a Thai traditional medicinal plant of *Artocarpus lakoocha*, was evaluated for its anti-varicella-zoster virus (VZV) activity. This compound exhibited IC_{50} values (50%-inhibitory concentrations for virus plaque formation) of 12.82, 12.80, 12.99 and 12.82μg/ml against wild type, thymidine kinase-deficient and two types of DNA polymerase mutants with acyclovir-resistance, respectively. Thus oxyresveratrol showed a broad spectrum of anti-VZV activity with a mechanism of action different from that of acyclovir.

学会報告　（∗：特別講演，シンポジウム，ワークショップ等）

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2) Chung M. H.: Estrogenic effects of Tokishakuyakusan (Japanese traditional medicine) and differences between Tokishakuyakusan and 17b-estradiol. NRCT-JSPS Core University Program on Natural Medicine in Pharmaceutical Sciences, The 8th Joint Seminar, Innovative Research in Natural Products for Sustainable Development. 2009, 2, 3-4, Bangkok, Thailand.
3) Sato N.: Isolation of lanostane type triterpenes from *Ganoderma sinense* and their anti-protease activity from HIV. NRCT-JSPS Core University Program on Natural Medicine in Pharmaceutical Sciences, The 8th Joint Seminar, Innovative Research in Natural Products for Sustainable Development. 2009, 2, 3-4, Bangkok, Thailand.
4) 鄭 美和, 伊藤絵理, 服部征雄 : 当帰芍薬散の dendritic spine 回復に対する効果について. 日本薬学会第 129 年会, 2009, 3, 26-28, 京都.
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6) 水野めぐみ, 鄭 美和, 陳 琮湜, 馬 超美, 服部征雄 : 樟芝菌糸体成分 Antrodin D のラットにおける体内動態. 日本薬学会第 129 年会, 2009, 3, 26-28, 京都.
7) 馬 超美, 阿倍 剛, 小宮山忠純, 服部征雄, Mohsen Daneshtalab : カフェー酸及びキナ酸誘導体の合成と真菌 1,3-グルカン合成酵素に対する阻害活性の比較. 日本薬学会第 129 年会,

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8) 高田弘弥, 萩原由季子, 岸 香苗, 松本正巳, 五十嵐久幸, 服部征雄 : 霊芝エキス抽出法の改良とその機能性評価. 日本薬学会第 129 年会, 2009, 3, 26-28, 京都.

9) Kitalong C., El-Halawany A. M., Ma C., and Hattori M.: A new benzophenone rhamnoside from *Phaleria nisidai* with estrogenic activity. The 50th Annual Meeting of the American Society of Pharmacognosy, 2009, 6, 27- 7, 1, Honolulu, Hawaii.

10) Mizuno M., Chung M., Ma C. and Hattori M.: Metabolism and disposition of antrodin D in rats. The 50th Annual Meeting of the American Society of Pharmacognosy, 2009, 6, 27- 7, 1, Honolulu, Hawaii.

11) Hattori M., El Dine R. S., Ma C., and Sato N.: Inhibitory substances from medicinal mushrooms: Ganoderma species against HIV-1 protease. The 50th Annual Meeting of the American Society of Pharmacognosy, 2009, 6, 27- 7, 1, Honolulu, Hawaii.

12) Furuhashi K., Chung M., and Hattori M.: Effect of Tokishakuyakusan on ovary and hypothalamus Kiss-1 mRNA expression in hypophsectomized rats. The 50th Annual Meeting of the American Society of Pharmacognosy, 2009, 6, 27- 7, 1, Honolulu, Hawaii.

13) 宅江孝修, 馬 超美, 服部征雄 : 甘草の新たな腸管収縮抑制成分の探索. 第26回和漢医薬学会学術大会, 2009, 8, 29-30, 千葉.

14) 王 偉, 馬 超美, 服部征雄 : Hydroxylation of rhynchophylline followed by glucuronidation with rat liver microsomes. 第 26 回和漢医薬学会学術大会, 2009, 8, 29-30, 千葉.

15) 古橋慶子, 鄭 美和, 服部征雄 : 多嚢胞性卵巣症候群（PCOS）モデルラットに対する当帰芍薬散の効果. 第 26 回和漢医薬学会学術大会, 2009, 8, 29-30, 千葉.

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17) 馬 紅, 鄭 美和, 呂 華, 服部征雄 : 春至カプセルの生殖内分泌学的効果と作用メカニズム - 第 2 報 - . 日本生薬学会第 56 回年会, 2009, 10, 3-4, 京都.

18) 光田聖庸, 水野めぐみ, 馬 超美, 岩佐衣子, 服部征雄 : 黄連エキスの LC/NMR とラットにおける体内動態. 日本薬学会北陸支部平成21年度第2回総会及び第121回例会, 2009, 12, 6, 富山.

◇その他

1) 馬 超美 : ハワイ大学薬学部のセミナーに参加, 研究発表. 2009, 1, 27-28, ヒロ, ハワイ島.
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5) 服部征雄 : 上海交通大学訪問, 講演. 2009, 9, 27-10, 1, 上海, 中国.
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7) 服部征雄 : 東洋人の知恵, 富山大学医学薬学祭 09 特別講演会. 2009, 10, 31, 富山.
8) 服部征雄 : 大邱カトリック大学において講演. 2009, 11, 18-21, 大邱, 韓国..
9) 服部征雄 : アシュート大学, ミネア大学, カイロ大学, ジャーマン大学において講演. 2009, 12, 16-28, エジプト.

◇ 共同研究

学内

1) 腸内嫌気性菌による生薬成分の代謝　　富山大学薬学部　赤尾光昭

2)　抗 HSV 薬の開発研究　　富山大学医学部　白木公康

3)　体内女性ホルモンに与える和漢薬の影響に関する研究　富山大学和漢医薬学総合研究所　松本欣三

国内

1)　抗 HCV 薬の開発研究　　慶応大学医学部　下遠野邦忠
慶応大学薬学部　下遠野久美子
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1)　抗 HSV 薬開発研究　　チュラロンコン大学　Pornpen Pramyothin

◇研究費取得状況

1)　「ほくりく健康創造クラスター」（財）北陸産業活性化センター（服部征雄）365 万円.
2)　「杜仲葉を用いた高機能食品の研究開発」独立行政法人科学技術振興機構（服部征雄）30 万円.
3)　「春至の粒子の生殖内分泌学的効果と作用メカニズム」独立行政法人日本学術振興会（服部征雄）60 万円.
4)　「樟芝菌糸体成分のラットにおける体内動態研究と，新規化合物の発見」平成 21 年度笹川科学研究助成金（水野めぐみ）55 万円.

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修士論文：

佐藤直人：*Ganoderma sinense* の新規成分とその生物活性 (3 月)
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