NIHON
PHARMACEUTICAL
UNIVERSITY

Research

Faculty of Pharmaceutical Sciences


日本薬科大学

Message

from the president of Nihon Pharmaceutical University

Fourteen years have passed since Nihon Pharmaceutical University was established. Nihon Pharmaceutical University is still a young and growing university.

We provide students with not only the latest pharmaceutical sciences but also further educational fields, such as Japanese traditional medicine so called Kampo medicine.

Kampo medicine is a mainstay of integrative medicine in Japan.

We believe that the experience of learning Kampo medicine could contribute to promoting self-medication and prevent life-style related diseases.

In this leaflet, we designate to introduce present status of Nihon Pharmaceutical University and each research topic of our staffs.

We believe this leaflet will contribute to developing the relationship between universities in other countries and Nihon Pharmaceutical University in various pharmaceutical fields.

Contents

Department of Pharmaceutical Sciences

Kazuhiro HARAGUCHI, Ph.D. / Professor

Laboratory of Medicinal Chemistry, Division of Organic and Medicinal Chemistry
Department of Pharmaceutical Sciences

Research Topics

1. Development of novel method for synthesis of sugar-modified nucleoside utilizing unsaturated-sugar nucleoside and its evaluation for antiviral and antitumor activity.
2. Stereoselective synthesis of 4'-thionucleoside utilizing 4-thiofuranoid glycal as glycosyl donor and its evaluation for antiviral and antitumor activity.
3. Design and synthesis of modified nucleoside antibiotic for development of antibacterial agent

Research in our group is focused on medicinal chemistry on the basis of nucleic acid chemistry for development of novel antiviral, antitumor and antibacterial nucleoside derivatives.

Representative Publications

1. Haraguchi, K.; Delaney, M. O.; Wiederholt, C. J.; Sambandam A.; Hantosi, Z.; Greenberg, M. M., "Synthesis and characterization of oligodeoxynucleotides containing formamidopyrimidine lesions and nonhydrolyzable analogues", *J. Am. Chem. Soc.* **2002**, *124*, 3263-3269.
2. Haraguchi, K.; Itoh, Y.; Tanaka, H., "Carbon-carbon bond formation at the sugar portion of nucleosides: synthetic potential of unsaturated-sugar nucleosides", *J. Synth. Org. Chem., Jpn*., **2003**, *61*, 974-983.
3. Haraguchi K., 4-Thiofuranoid glycal-based stereoselective synthesis of 4'-thionucleosides and its inhibitory effect of angiogenesis.: Advances In Pharmaceutical Scinences, **2006**, *22*, 39-48.
4. Haraguchi, K.; Takeda, S.; Kubota, Y.; Kumamoto, H.; Tanaka, H.; Hamasaki, T.; E; Baba, M.; Paintsil, E.; Cheng, Y.-C.; Urata, Y., "Next Generation Anti-HIV Agent 4'-Ethynylstavudine: From The Bench To The Clinic", Frontiers in Clininal Drug Reseach: HIV, *Bentham Science Publishing*, **2015**, *volume 1*, 123-184.

Toshiaki SAITOH, Ph.D. / Professor

Laboratory of Organic Chemistry, Division of Organic and Medicinal Chemistry
Department of Pharmaceutical Sciences

Research Topics

1. The structure based drug design and the synthesis of heterocycles which have neuroprotective effects on the neurons of central nervous system.
2. The analysis of chemical reactions which include biochemical reactions, by computational chemistry.

Research in our group addresses an important problem which is related to neurodegenerative disease and includes investigations at the frontier of organic chemistry, medicinal chemistry and computational chemistry. The areas of research include the development of the synthetic method of heterocycles such as 1,2,3,4-tetrahydroisoquinoline derivatives, and the design and the analysis of chemical reactions and the interaction between drugs and proteins by computational chemistry. A core in our study is to clarify the reactivity of organic and biological molecules based on their chemical structures.

Representative Publications

1. Effects of 1-cyclohexcyl- and 1-cyclohexcyl-*N*-propargyl-1,2,3,4-tetrahydroisoquinoline on dopaminergic spontaneous discharge in nigral neurons of rats, Momoko Abe, Hiroko Munakata, Kenji Abe, Toshiaki Saitoh, Yoshie Horiguchi and Kyoji Taguchi, *Brain Res. Bull.*, **121**, 201-208 (2016).
2. Facil and shor-step synthesis of 5-substituted 2,3,4,5-tetrahydrobenzo[*f*][1,4]oxazepines using a modified Pictet-Spengler reaction, Toshiaki Saitoh, Michikazu Kitabatake, Takuya Sugimoto, Hiromu Kawakubo, Kunihiko Mohri, Yoshie Horiguchi, *Heterocycles*, **94**(2), 342-349 (2017).
3. Short synthesis of 5-substituted 2,3,4,5-tetrahydrobenzo[*f*][1,4]thiazepines using modified Pictet-Spengler reaction, Toshiaki Saitoh, Michikazu Kitabatake, Yuuko Sugihara, Yuuki Ono, Yoshie Horiguchi, Kunihiko Mohri, *Heterocycles*, **94**(6), 1063-1073 (2017).

Hiroki KUMAMOTO, Ph.D. / Associate Professor

Laboratory of Medicinal Chemistry, Division of Organic and Medicinal Chemistry
Department of Pharmaceutical Sciences

Research Topics

1. Design and synthesis of the novel carbocyclic nucleoside analogues and evaluation of their biological activities.
2. Synthetic endeavor for the novel fluorine containing nucleosides.
3. Application of the radical-mediated sulfur-extrusive stannylation for the modification of nucleosides.

Nucleosides play an important role not only in a human cell but for replication and multiplication of most of pathogens such as viruses, bacteria and cancer cells. Therefore, chemical modification of naturally occurring nucleosides or preparation of artificial nucleoside analogues have brought the great development for lots of excellent drugs. Based on the context, our group has been continuing to research for the synthesis and development of novel bio-active nucleoside analogues, representatively employing the radical-mediated stannylation and carbon-carbon bond formation.

Representative Publications

1. Kumamoto, H.; Fukano, M.;, Nakano, T.; Iwagami, K.; Takeyama, C.; Kohgo, S.; Imoto, S.; Amano, M.; Kuwata-Higashi, N.; Aoki, M.; Abe, H.; Mitsuya, H.; Fukuhara, K.; Haraguchi, K. “Diastereoselective synthesis of 6"-(*Z*)- and 6" (*E*)-fluoro analogues of anti-hepatitis B vireus agent entecavir and its evaluation of the activity and toxicity profile of the diastereomers” *J. Org. Chem*. **2016**, *81*, 2827-2836.
2. Kumamoto, H.; Kawahigashi, S.; Wakabayashi, H.; Nakano, T.; Miyaike, T.; Kitagawa, Y.; Abe, H.; Ito, M.; Haraguchi, K.; Balzarini, J.; Baba, M.; Tanaka, H. “Tuning efficiency of the *4-exo-trig* cyclization by the electronic effect: ring closure of 3,3-difluoro-4-pentenylcarbon radicals and synthesis of a *gem*-difluorocyclobutane nucleoside” *Chem. Commun*. **2012**, *48*, 10993-10995.
3. Kumamoto, H.; Kobayashi, M.; Kato, N.; Balzarini, J.; Tanaka, H.; “Synthesis of 5’-fluoro-2’-β-methyl analogues of Neplanocin” *Eur. J. Oeg. Chem*. **2011**,2685-2691.

Hiroyuki TAKAYAMA, Ph.D. / Associate Professor

Laboratory of Organic Chemistry, Division of Organic and Medicinal Chemistry
Department of Pharmaceutical Sciences

Research Topics

1. Development of new catalytic reactions promoted by a transition metal complex.
2. The efficient total synthesis of bioactive natural products.

3(2*H*)-Furanones and oxazoles are a common structure in a range of important pharmaceuticals. Diarylketones are also frequently found in natural products and pharmaceuticals, and they are good precursors for non-steroidal antiestrogen drugs and diarylmethyl compounds. Transition metal-catalyzed reaction of unsaturated systems has recently proven to be a powerful method for the construction of a variety of carbo- and heterocycles. The vinyl- and arylpalladium intermediates are formed by oxidative addition of a carbon-halogen bond to palladium(0).
we have presented a cyclization-carbonylation-cyclization coupling reaction of propargylic compounds catalyzed by palladium(II) complexes. Symmetrical ketones possessing two heterocyclic groups were obtained in moderate to excellent yields. We are investigating other new tandem reactions based on the cyclization-carbonylation-cyclization strategy.

Representative Publications

1. Takayama H, Kato K, Akita H., Synthesis of (4*R*,5*S*)-melithiazols F and I. *European Journal of Organic Chemistry*, **3**, 644-649 (2006).
2. Yasuhara S, Sasa M, Kusakabe T, Takayama H, Kimura M, Mochida T, Kato K., Cyclization-Carbonylation-Cyclization Coupling Reactions of Propargyl Acetates and Amides with Palladium(II)-Bisoxazoline Catalysts. *Angewandte Chemie, International Edition*, **50**, 3912-3915 (2011).
3. Yen W P, Tsai S E, Uramaru N, Takayama H, Wong F F., One-flask synthesis of pyrazolo[3,4-*d*]pyrimidines from 5-aminopyrazoles and mechanistic study. *Molecules*, **22**, 820 (2017).

Hiroki KATAOKA, Ph.D. / Assistant Professor

Laboratory of Medicinal Chemistry, Division of Organic and Medicinal Chemistry
Department of Pharmaceutical Sciences

Research Topics

1. Design and synthesis of novel nucleoside analogues for the antiviral or anti-cancer agent.
2. Discovery of novel fullerene derivatives for antioxidant and any therapeutic agents.

Research in our group is focused on medicinal chemistry on the basis of nucleic acid and fullerene for development of novel bioactive compounds.

Representative Publications

H. Kataoka, T. Ohe, K. Takahashi, S. Nakamura, T. Mashino: Novel fullerene derivatives as dual inhibitors of Hepatitis C virus NS5B polymerase and NS3/4A protease; *Bioorg. Med. Chem. Lett*., **2016**, *26*, *19*, 4565-4567.

Division of Pharmacotherapy

Tsutomu KOBAYASHI, Ph.D. / Professor

Division of Pharmacotherapy
Department of Pharmaceutical Sciences

Research Topics

1. Computer simulation of clinical phenomena by using virtual cells.
2. Analysis of the pharmaceutical industry and current medicines.

1. Virtual cell models, working in the computer, are available for cardiac myocytes and pancreas beta cells. We can reproduce various phenomena under physiological and pathological condition, such as cardiac arrhythmia, heart failure and insuline secretion. We can also “normalize” these pathological states by optimizing activities of ion channels, transporters, etc, of the cell, which is just the simulation of drug therapy. This system is a powerful tool for discovery and development of new drugs.
2. I have a career as a senior researcher in the pharmaceutical company Tanabe Mitsubishi for 32 years. Using this experience and knowledge, we study about pharmaceutical companies from their histories to current pipelines.

Representative Publications

1. Noble D, Sarai N, Noble PJ, Kobayashi T, Matsuoka S, Noma A. Resistance of Cardiac Cells to NCX Knockout: A Model Study. *Ann. N.Y. Acad. Sci*. **1099**, 306–309 (2007).
2. Kobayashi T, Sarai N, Matsuoka S, Noma A. ; A simulation study to rescue the Na(+)/Ca(2+) exchanger knockout mice. *J Physiol Sci*. **56**, 211-7 (2006).
3. Kiyonaka S, Kato K, Nishida M, Mio K, Numaga T, Sawaguchi Y, Yoshida T, Wakamori M, Mori E, Numata T, Ishii M, Takemoto H, Ojida A, Watanabe K, Uemura A, Kurose H, Morii T, Kobayashi T, Sato Y, Sato C, Hamachi I, Mori Y. Selective and direct inhibition of TRPC3 channels underlies biological activities of a pyrazole compound. *Proc. Natl. Acad. Sci*. **106**, 5400-5405 (2009).

Hiroko INOUE, Ph.D. / Professor

Division of Pharmacotherapy
Department of Pharmaceutical Sciences

Research Topics

1. Elucidation of the pathogenesis of Epstein-Barr virus related diseases.
2. Search of the food factor involved in Epstein-Barr virus reactivation.

Epstein-Barr virus (EBV) is a ubiquitous herpes virus that infects more than 90% of the world's population. Infection is usually asymptomatic and leads to lifelong persistence of the virus in resting recirculating memory B cells. The induction of lytic replication results in new viral infection and EBV-associated cellular transformation, and this induction may be a risk factor for malignant transformation, the development of autoimmune diseases and fatigue syndrome. The pathogenesis of these diseases is not fully understood. Based on these factors, we focus on the elucidation of the pathogenesis of EBV related diseases and search of the food factor involved in EBV reactivation.

Representative Publications

1. Saruta J, To M, Sugimoto M, Yamamoto Y, Shimizu T, Nakagawa Y, Inoue H, Saito I, Tsukinoki K. Salivary Gland Derived BDNF Overexpression in Mice Exerts an Anxiolytic Effect. *Int J Mol Sci*. **18**: E1902 (2017).
2. Inoue H, Kishimoto A, Ushikoshi-Nakayama R, Hasaka A, Takahashi A, Ryo K, Muramatsu T, Ide F, Mishima K, Saito I. Resveratrol improves salivary dysfunction in a non-obese diabetic (NOD) mouse model of Sjogren's syndrome. *J Clin Biochem Nutr*. **59**: 107-112 (2016).
3. Imai K, Kamio N, Cueno ME, Saito Y, Inoue H, Saito I, Ochiai K. Role of the histone H3 lysine 9 methyltransferase Suv39 h1 in maintaining Epsteinn-Barr virus latency in B95-8 cells. *The FEBS journal*. **281**: 2148-2158 (2014).

Izumi HAYASHI, Ph.D. / Professor

Division of Pharmacotherapy
Department of Pharmaceutical Sciences

Research Topics

1. Involvement of small active bioactive molecule in the body.

Research in our group is focused on bioactive small substanes, which defense or protect self difence.

Daisuke CHINO, Ph.D. / Associate Professor

Division of Pharmacotherapy
Department of Pharmaceutical Sciences

Research Topics

1. Study on the mechanisms by which omega-3 polyunsaturated fatty acids lower blood pressure.
2. Study on the effects of omega-3 polyunsaturated fatty acids on prostanoid receptors.
3. Study on agonists and antagonists of smooth muscle contraction.

DHA and EPA, the major omega-3 polyunsaturated fatty acids (PUFAs), contained in fish oil, which show antihypertensive effects, reduction of platelet aggregation and of plasma triglycerides. Our main research is focused on the effects of these PUFAs on prostanoid receptors regulating the vascular smooth muscle tone in hypertension. We have a good command of in vivo and in vitro techniques which allow us to study how these PUFAs exert actions on the cardiovascular systems. The objectives of our research are to clarify the mechanism of hypertension and prove the effects of PUFAs contained in fish oil.

Representative Publications

1. Chino D, Yuda S, Suzuki Y, Hatsuyama F, Sato K, Obara K, Tanaka Y.; Acute effects of intravenous administration of polyunsaturated fatty acids on blood pressure and heart rate in U46619- and noradrenaline-infused rats. *Br J Pharm Res*, **15**(3), 1-12 (2017).
2. Chino D, Naramatsu M, Obara K, Tanaka Y.; Clonidine inhibits phenylephrine-induced contraction of rat thoracic aortae by competitive antagonism of α_1-adrenoceptors independent of α_2-adrenoceptor stimulation. *Pharmacol Pharm*, **8**, 172-188 (2017).
3. Sato K, Chino D, Nishioka N, Kanai K, Aoki M, Obara K, Miyauchi S, Tanaka Y.; Pharmacological evidence showing significant roles for potassium channels and CYP epoxygenase metabolites in the relaxant effects of docosahexaenoic acid on the rat aorta contracted with U46619. *Biol Pharm Bull*. **37**(3), 394-403 (2014).

Kenji ABE, Ph.D. / Associate Professor

Division of Pharmacotherapy
Department of Pharmaceutical Sciences

Research Topics

1. Pharmacological evaluation of 1,2,3,4-tetrahydroisoquinoline and its derivatives, endogenous parkinsonism inducing or preventing amines.
2. Investigation of developmental mechanisms and therapeutic agents in nerve injury-induced neuropathic pain models in mice.
3. Developmental mechanisms of itch sensation, especially relation to stress and itch.

Research in our group is focused on neuroscientific events in Parkinson's disease, neuropathic pain and itch sensation using *in vivo* experimental animal models. Recently, research of antineoplastic drugs (such as oxaliplatin, paclitaxel and so on)-induced neuropathic pain have also begun. Some of these researches have already published.

Representative Publications

1. Chiba T, Oka Y, Sashida H, Kanbe T, Abe K, Utsunomiya I, Taguchi K, Vincristine-induced peripheral neuropathic pain and expression of transient receptor potential vanilloid 1 in rat. *J. Pharmacol. Sci.* **133**: 254-260 (2016).
2. Abe M, Munakata H, Abe K, Saito T, Horiguchi Y, Nojima H, Taguchi K, Effects of 1-cyclohexyl- and 1-cyclohexyl-N-propargyl-1,2,3,4-tetrahydroisoquinoline on dopaminergic spontaneous discharge in nigral neurons of rats. *Brain Res. Bull.* **121**: 201-208 (2016).
3. Yamamoto K, Tsuboi M, Kanbe T, Abe K, Nakatani Y, Kawakami K, Utsunomiya I, Taguchi K, Oxaliplatin administration increases expression of the voltage-dependent calcium channel α2δ-1 subunit in the rat spinal cord. *J. Pharmacol. Sci.* **130**: 117-122 (2016).

Tomoji MAEDA, Ph.D. / Associate Professor

Division of Pharmacotherapy
Department of Pharmaceutical Sciences

Research Topics

1. Investigation of milk production mechanism focused on biologically active substance.
2. Investigation of phagocytosis involved in MEGF10 in neurons.

Breastfeeding benefits infants in many ways. Human breast milk not only contains normal nutrients, such as carbohydrates, fats, proteins, minerals and vitamins, but also various biologically-active constituents, including antimicrobial substances, growth factors, cytokines, immunoglobulins and specific immune cells. However, it is unknown how various substances in milk acts on infant development. Therefore, considering that various substances in milk has given many profits on infant, we research the effects of various substances on infant development.

Representative Publications

1. Chiba, T., Maeda, T., Kimura, S., Morimoto, Y., Sanbe, A., Ueda, H., Kudo, K. Inhibitory effect of fluvoxamine on β-casein expression via a serotonin-independent mechanism in human mammary epithelial cells. *Eur J Pharmacol* **766**, 56-62 (2015).
2. Chiba, T., Maeda, T., Tairabune, T., Tomita, T., Sanbe, A., Takeda, R., Kikuchi, A., Kudo, K. Analysis of serotonin concentrations in human milk by high-performance liquid chromatography with fluorescence detection. *Biochem Biophys Res Commun* **473**, 323-328 (2017).
3. Fujita, Y., Maeda, T., Kamaishi, K., Saito, R., Chiba, K., Xuefeng S., Zou, K., Komano, H. Expression of MEGF10 in cholinergic and glutamatergic neurons. Neuroscience Letters **653**, 25-30 (2017).

Naoko OKADA, Ph.D. / Assistant Professor

Division of Pharmacotherapy
Department of Pharmaceutical Sciences

Research Topics

1. Research on the epigenetic regulation mechanisms of fibroblasts in chronic inflammatory environment.
2. Investigation of molecular mechanism and regulatory pathways in chronic allergic inflammation.

Chronic allergic inflammatory diseases often cause fibrosis in local tissue and are refractory to treatment. However, the precise mechanisms increasing the severity of these diseases remain unknown. We previously focused on periostin, which was known to have an important role in allergic inflammation as a matricellular protein, and found that the concentration of periostin in the tears of allergic patients was significantly higher than that of normal donors. Furthermore, it was revealed that conjunctival fibroblasts were involved in high expression of periostin in the tear of patients. In the current studies, in order to verify the chronic inflammatory environment causes over-expression of periostin via epigenetic mechanisms, the functional relevance of DNA methylation and histone modification in the regulation of the periostin gene expression have been investigated. In addition, we aim to elucidate the signaling pathways involved in the epigenetic modifications and link it to novel therapeutics.

Representative Publications

1. Okada N, Nakayama T, Asaka D, Inoue N, Tsurumoto T, Takaishi S, Otori N, Kojima H, Matsuda A, Oboki K, Saito H, Matsumoto K, Yoshikawa M.: Distinct gene expression profiles and regulation networks of nasal polyps in eosinophilic and non-eosinophilic chronic rhinosinusitis. *Int Forum Allergy Rhinol*, **8**(5), 592-604 (2018).
2. Nakayama T, Okada N, Yoshikawa M, Asaka D, Kuboki A, Kojima H, Tanaka Y, Haruna SI.: Assessment of suitable reference genes for RT-qPCR studies in chronic rhinosinusitis. *Sci Rep*, 25, **8**(1), 1568 (2018).
3. Fujishima H*, Okada N*, Matsumoto K, Fukagawa K, Igarashi A, Matsuda A, Ono J, Ohta S, Mukai H, Yoshikawa M, Izuhara K.: The usefulness of measuring tear periostin for the diagnosis and management of ocular allergic diseases. *J Allergy Clin Immunol*, **138**(2), 459-467 (2016). (*; equal contribution)

Kensuke ARAI, Ph.D. / Professor

Laboratory of Analytical Chemistry, Division of Physical and Analytical Chemistry
Department of Pharmaceutical Sciences

Research Topics

1. Development of a Pencil-Drawn Electrode for Point-of Care-Testing in Clinical Pharmacy.

Research interest of our group has been focused on the development of a new electrochemical method for Point-of-Care-Testing in clinical pharmacy. We have examined electrochemical proprty of mechanical pencil leads, made of graphite with high quality, due to the advantages of mechanical pencil leads; at low cost, easy to handle, completely disposable, etc. We have found them to function as working electrodes of voltammetry. Pencil lead graphite electrode was successfully applied to the determination of arsenic(III) in natural water and electrochmical immnoassay of hormones such as estrogen and adiponectin.

Representative Publications

1. H. Nakajima, Y. Masuda, S. Ishino, T. Nakagama, T. Shimosaka, K. Arai, Y. Yoshimura and K. Uchida, *Bunseki Kagaku*, **54**, 817 (2005).
2. Y. Kudo, J. Tsunokawa, M. Yagi, H. Nakajima, T. Nakagama, K. Arai, Y. Yoshimura and K. Uchida, *Bunseki Kagaku*, **55**, 313 (2006).
3. K. Kubo, K. Arai and Y. Yoshimura, *Bunseki Kagaku*, **57**, 667 (2008).
4. H. Saito, K. Arai, K. Kubo, M. Mizoguchi, S. Yamada and Y. Watanabe, *Pharmacometrics (Oyo Yakuri)*, **79**, 49 (2010).
5. H. Saito, K. Arai, K. Kubo, M. Mizoguchi, S. Yamada and Y. Watanabe, *Pharmacometrics (Oyo Yakuri)*, **81**, 5 (2011).
6. K. Arai and K. Shimada, *Bunseki Kagaku*, **61**, 411 (2012).
7. T. Kajiyama, S. Sakai, J. Inoue, T. Yoshino, S. Ohmuro, K. Arai and H Kokusen, *J. Ion Exchgange*, **27**, 57 (2016).

Kazunori ANZAI, Ph.D. / Professor and Dean

Laboratory of Physical Chemistry, Division of Physical and Analytical Chemistry
Department of Pharmaceutical Sciences

Research Topics

1. Detection of reactive oxygen species/free radicals caused by irradiation of cold atmospheric plasma.
2. Measurement and prevention of lipid peroxidation and membrane damages caused by oxidative stress.
3. Finding radiation-protector and radiation-mitigator to prevent normal-cell injury by ionizing radiation.

Research in our group is focused on detection and control of reactive oxygen species (ROS)/free radicals and their effects on biological systems. To detect free radicals, we mainly use ESR spectroscopy in combination with spin-trap or spin-probe techniques. Hydroxyl radicals (•OH) are produced by various causes such as Fenton reaction, ionizing radiation, and so on. Recently, it was reported that irradiation of cold atmospheric plasma to water also produce •OH. We have found that •H are also produced in addition to •OH by the irradiation using ESR spin-trapping method. Production of H_2O_2 was also detected by colorimetric technique using peroxidase reactions. Irradiation of cold atmospheric plasma to liposome induced lipid peroxidation, which was detected by fluorescence probe and TBA reactions.

Representative Publications

1. Anzai K, Ueno M, Matsumoto K, Ikota N, Takata J; Gamma-tocopherol-*N*,*N*-dimethylglycine ester as a potent post-irradiation mitigator against whole body X-irradiation-induced bone marrow death in mice. *J. Radiat. Res*. **55**, 67-74 (2014).
2. Anzai K, Ueno M, Yoshida A, Furuse M, Aung W, Nakanishi I, Moritake T, Takeshita K, Ikota N; Comparison of stable nitroxide, 3-substituted tetramethylpyrrolidine-N-oxyls, with respect to protection from radiation, prevention of DNA damage and distribution in Mice. *Free Radic. Biol. Med*. **40**, 1170-1178 (2006).
3. Anzai K, Saito K, Takeshita K, Takahashi S, Miyazaki H, Shoji H, Lee M, Masumizu T, Ozawa T; Assessment of ESR-CT imaging by comparison with autoradiography for the distribution of a blood-brain-barrier permeable spin probe, MC-PROXYL, to rodent brain. *Magnetic Resonance Imaging* **21**, 765-772 (2003).

Kazunori TSUCHIDA, Ph.D. / Associate Professor

Laboratory of Physical Chemistry, Division of Physical and Analytical Chemistry
Department of Pharmaceutical Sciences

Research Topics

1. Analysis of the antioxidant capacities using ORAC/SOAC assay.
2. Evaluate the lipid radicals generated in lipoxygenases.
3. Biosynthesis of Chondrotin Sulfates/Heparan Sulfates.

Research in my interest is;

1. To analyse the antioxidant capacities using ORAC (Oxygen Radical Absorbance Capacity) assay and SOAC assay (a Singlet Oxygen Absorption Capacity).
2. To evaluate the physiological functions of the lipid radicals produced in a lipoxygenases at lower oxygen content.
3. To study the bioshynthesis of Chondroitin Sulfate/Dermatan Sulfate and Heparan Sulfate/Heparin.

Representative Publications

1. Takajo T, Tsuchida K, Yokota A, Koshiishi I. Trapping of fatty acid allyl radicals generated in lipoxygenase reactions in biological fluids by nitroxyl radical. *Biomed. Chromatogr*. **24**, 794-797 (2010).
2. Takajo T, Tsuchida K, Ueno K, Koshiishi I. Feedback activation of ferrous 5-lipoxygenase during leukotriene synthesis by coexisting linoleic acid. *J. Lipid Res*., **48**, 1371-1377 (2007).
3. Pedersen LC, Tsuchida K, Kitagawa H, Sugahara K, Darden TA, Negishi M. Heparan/chondroitin sulfate biosynthesis. Structure and mechanism of human glucuronyltransferase I. *J. Biol. Chem*., **275**, 34580-34585 (2000).
4. Tsuchida K, Lind T, Kitagawa H, Lindahl U, Sugahara K, Lidholt K. Purification and characterization of fetal bovine serum beta-*N*-acetyl-D-galactosaminyltransferase and beta-D-glucuronyltransferase involved in chondroitin sulfate biosynthesis. *Eur. J. Biochem*., **264**, 461-467 (1999).

Toshiyasu MIKUMA, Ph.D. / Senior Assistant Professor

Laboratory of Analytical Chemistry, Division of Physical and Analytical Chemistry
Department of Pharmaceutical Sciences

Research Topics

1. Development of analytical methods in the field of forensic science.
2. Application of temperature-responsive chromatography for various drug analysis.

Recently, scientific analysis is an essential part of criminal investigations. To obtain effective clues, more accurate and sensitive analytical techniques have been required invariably. I have developed new analytical methods in the field of forensic science. My interest is now focused on temperature-responsive chromatography, in which a thermo-responsive polymer such as poly(*N*-isopropylacrylamide) is used as the stationary phase. The polymer-grafted stationary phase exhibits temperature-regulated hydrophilic/hydrophobic characteristics as a result of the polymer's conformational changes. Using the unique features, various applications have been developed for drug analysis related to criminal scenes.

Representative Publications

1. Mikuma T., Kuroki T., Yoshikawa M., Uchida R., Hiruta Y., Kanazawa H.; Analysis of psychoactive drugs by temperature-responsive chromatography. *Chromatography,* **38**, 115-121 (2017).
2. Mikuma T., Uchida R., Kajiya M., Hiruta Y., Kanazawa H.; The use of a temperature-responsive column for the direct analysis of drugs in serum by two-dimensional heart-cutting liquid chromatography. *Analytical and Bioanalytical Chemistry*, **409**, 1059-1065 (2017).
3. Mikuma T., Iwata Y.T., Miyaguchi H., Kuwayama K., Tsujikawa K., Kanamori T., Kanazawa H., Inoue H.; Approaching over 10 000-fold sensitivity increase in chiral capillary electrophoresis: cation-selective exhaustive injection and sweeping cyclodextrin-modified micellar electrokinetic chromatography. *Electrophoresis*, **37**, 2970-2976 (2016).
4. Mikuma T., Iwata Y.T., Miyaguchi H., Kuwayama K., Tsujikawa K., Kanamori T., Inoue H.; The use of a sulfonated capillary on chiral capillary electrophoresis/mass spectrometry of amphetamine-type stimulants for methamphetamine impurity profiling. *Forensic Science International*, **249**, 59-65 (2015).

Satoshi OHMURO, Ph.D. / Assistant Professor

Laboratory of Analytical Chemistry, Division of Physical and Analytical Chemistry
Department of Pharmaceutical Sciences

Research Topics

1. Analysis of mass transfer between aqueous phase and ODS phase in solid phase extraction.
2. Effect of residual silanol in ODS silica for retention of reagents in solid phase extraction.
3. Development of a new solid phase extraction system utilizing residual silanol in ODS silica.

Octadecylsilyl (ODS) silica is most popular material for reversed phased high performance liquid chromatography (RP-HPLC) in separation analytical chemistry. Residual silanol in ODS silica generally is capped by trimethylsilyl groups. This is also used in solid phase extraction (SPE). There were, however, few reports that end–capped ODS silica is suitable for SPE.
We have studied that function of residual silanol in ODS silica and retention mechanism of reagents from solution phase to ODS phase in SPE. As a result, nonpolar reagents were retained by distribution, while polar reagents were retained by both distribution and adsorption. In particular, it was clarified that adsorption to residual silanol greatly contributes to the retention of the ligand from organic phase.
In future, we would like to develop a new solid phase extraction system utilizing residual silanol groups in ODS silica and evaluate the concentration efficiency of trace elements in the environment.

Representative Publications

1. “Perchlorate Selectivity of Anion Exchange Resins as Evaluated Using Ion-Selective Electrodes” Kenji Yamamoto, Shin’ya Mitsuda, Naomi Ohtake, Natsuki Murashige, Satoshi Ohmuro, Akio Yuchi, *Anal. Sci*. **33** (2017) 159.
2. “Enhanced Retention of Chelating Reagent in Octadecylsilyl Silica Phase by Interaction with Residual Silanol Group in Solid Phase Extraction of Divalent Metal Ions” Satoshi Ohmuro, Kan Fujii, Takashi Yasui, Kazutake Takada, Akio Yuchi, Hisao Kokusen, *Anal. Sci*. **32** (2016) 343.
3. “Liquid-Liquid extraction of divalent transition metal ion with a novel bis-β-ketoester extraction reagent” Satoshi Ohmuro, Hiromasa Kishi, Nobutoshi Yoshihara, Hisao Kokusen, *Talanta* **128** (2014) 102.

Division of Kampo Pharmaceutical Sciences

Ichiro ARAI, Ph.D. / Professor

Division of Kampo Pharmaceutical Sciences
Department of Pharmaceutical Sciences

Research Topics

1. Proposal of Japanese system of integrative medicine by the survey of its utilization and provision in Japan and other countries, and analysis of its social determinant.
2. Scientific research and investigation for contributing to the development of international standard in ISO/TC249 and basic study of Kampo medicine, acupuncture and moxibustion as a part of the integrative medicine.
3. Study on the information providing website of integrative medicine for the sake of proper selections by patients, general population, and medical doctors.

Research in our group is focused on Kampo medicines, a Japanese herbal medicines derived from ancient Chinese medicine. We are now researching Kampo medicines from the aspect of regulatory science, social science and clinical evidences in comparison to other countries, especially East Asian countries with researchers of China, Taiwan and Korea.

Representative Publications

1. Motoo Y, Hakamatsuka T, Kawahara N, Arai I, Tsutani K. Standards of Reporting Kampo Products (STORK) as a reference for Kampo extracted products. *J. Integr. Med.*, **15**, 182-185 (2017).
2. Yukawa K, Ishikawa H, Arai I, Yamazaki Y, Misawa J, Tsutani K, Arai I, Motoo Y, Kiuchi T. Economic Burden, and Mental Distress in Using Complemetary and Alternative Medicine, and Formal Support by Medical Professional of Japanese Patients with Chronic Diseases. *Jpn. Pharmacol. Ther.*, **45**, 345-355 (2017).
3. Arai I. History of Japanese Kampo Medicines Manufacturers. *Jpn. J. History Pharm.*, **50**, 1-6 (2015).

Munetetsu TEI, M.D., Ph.D. / Professor and President

Division of Kampo Pharmaceutical Sciences
Department of Pharmaceutical Sciences

Research Topics

1. Clinical pharmacology of Kampo medicine.
2. Integrative medicine and Integrative health.
3. Kampo medicine and herbal medicine.

Representative Publications

1. Ichikawa H., Yagi H., Tanaka T., Cyong J. C., Masaki T.; Lagerstroemia speciosa extract inhibit TNF-induced activation of nuclear factor-kappaB in rat cardiomyocyte H9c2 cells. *J. Ethnopharmacol*., **128**(1), 254-256 (2010).
2. Kobayashi T., Iijima K., Radhakrishnan S., Mehta V., Vassallo R., Lawrence C. B., Cyong J. C., Pease L. R., Oguchi K., Kita H.; Asthma-related environmental fungus, Alternaria, activates dendritic cells and produces potent Th2 adjuvant activity. *J. Immunol*., **182**(4), 2502-2510 (2009).
3. Iwasaki K., Kobayashi S., Chimura Y., Taguchi M., Inoue K., Cho S., Akiba T., Arai H., Cyong J. C., Sasaki H.; A randomized, double-blind, placebo-controlled clinical trial of the Chinese herbal medicine "ba wei di huang wan" in the treatment of dementia. *J. Am. Geriatr. Soc*., **52**(9), 1518-1521 (2004).

Tomomi HIMENO, M.D., Ph.D. / Professor

Division of Kampo Pharmaceutical Sciences
Department of Pharmaceutical Sciences

Research Topics

1. Orthomolecular Medicine.

Representative Publications

1. Tomomi Himeno ; Mental Disorder of Women Caused by Functional Hypoglycemia. *Gender and Sex Specific Medicine*, Vol.2, No.10 (2005).
2. “GODDESSES NEVER AGE” by Christiane NORTHRUP, Translation supervisor; Tomomi HIMENO. Mikasa-Shobo Publishers Co., Ltd. (2016, Originally published in 2015 by Hay House Inc. USA)
3. “SHINRYONAIKA NI IKU MAE NI SHOKUJI WO KAENASAI” (“Change Your Meal before Having Psychosomatic Medicine”) by Tomomi HIMENO. Seishun Publishing Co., Ltd. (2010, Chinese translation published in 2015 by Keio Cultural Enterprise Co., Ltd.)

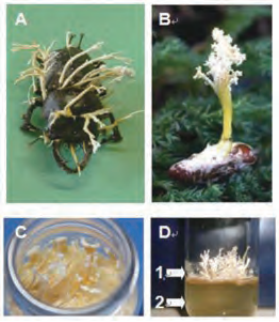
Fumihide TAKANO, Ph.D. / Professor

Division of Kampo Pharmaceutical Sciences
Department of Pharmaceutical Sciences

Research Topics

1. Isolation, identification and pharmacological evaluation of compounds from medicinal plant and microbial origin.
2. Ethnopharmacognosic studies for traditional medicines distributed in Chichibu area.

The research interests of our group include the isolation, identification, and pharmacological evaluation of compounds from medicinal plants and some entomogenous fungi, particular compounds peptides useful as immunemodulating for antiaging supplement from genera *Paecilomyves* and *Cordyceps* fungi. We newly found an unrecorded *Paecilomyces* species from mature stag beetle insect host (see Figs), and archived its artificial cultivation in the same liquid medium for *P. tenuipes* from moth chrysalis. Further, two T helper 1 cytokines, interleukin-2 and interferon-γ in cultured ileal Peyer's patch cells from mice orally administered with the filtrates are significantly elevated.



Representative Publications

1. A. Kubota, *et al.*, Effects of Kampo extract boiogito and its alkaloid sinomenine on nociceptive pain in mouse models. *Pharmacometrics*, **92**, 83-89 (2017).
2. A. E. Allam, *et al.*, Two new *p*-coumaroyl flavonoid glycosides having cytokine increasing activity from *Centaurium spicatum* L. *Phytochem. Lett.*, **17**, 144-151 (2016).
3. F. Takano, *et al.*, Placenta extracts selectively promote the proliferation of specific progenitor cells derived from murine marrow in vitro. *Pharmacometrics*, **89**, 83-90, (2015).
4. M. Suo, *et al.*, Bioactive phenylpropanoid glycosides from *Tabebuia avellanedae*. *Molecules*, **18**, 7336-7345 (2013).

Seiichi YAMAJI, Ph.D. / Associate Professor

Division of Kampo Pharmaceutical Sciences
Department of Pharmaceutical Sciences

Research Topics

1. Pharmacognosy.
2. Comparative Ethnopharmacology.
3. Herbology (Pen'tsaology (*Bencaoxue*, or *Honzogaku*)).

Research in our group is focused on Pharmacognostical studies by means of morphological and anatomical methods including LV-SEM (Low Vaccumed Scnning Electron Microscopy). And comparative ethnopharmacognosy by field investigations, especially in the present market in Japan, China, and other Asian countries. Herbology, so called "Pentsaology (*Bencaoxue* in Chinese, *Honzogaku* in Japanese)" is also one of our research field. I also have research interests in the field investigations on folk medicine in Saitama Prefecture, Japan, and present crude drug market surveys (Beijing in 2015, Bozhou,China in 2016).

Representative Publications

1. Arai I, Ikariya N, Yamaji S, Tsutani K; Usage survey of "Standard Kampo Formula Nomenclature (2015)" in formulation names in Kampo articles: Presence in title and/or abstract in PubMed indexed articles. *Ann.Rept.Nihon Pharm. Univ.*, **3**, 42-47 (2017).
2. Yamaji S, Arai I, Sakai E, Terabayashi S, Kawahara N, Iida O, Aragane M, Nakamura K, Goda Y; Comparative morphological and anatomical studies on the Japanese Pharmacopoeia Compliant, "Polygala Root(Polygalae Radix, Onji)." *Ann.Rept.Nihon Pharm. Univ.*, **2**, 64-68 (2016).
3. Harada A, Sugihara K, Watanabe Y, Yamaji S, Kitamura S, Ohta S; Aryl hydrocarbon receptor ligand activity of extracts from 62 herbal medicines and effect of cytochrome P450 activity. *Yakugaku Zasshi*, **135**, 1185-1196 (2015).

Nanae ITOKAZU, Ph.D. / Senior Assistant Professor

Division of Kampo Pharmaceutical Sciences
Department of Pharmaceutical Sciences

Research Topics

1. Curation at Takeatsu Kimura Commemoration Kampo Museum.
2. Epidemiological research in Kampo medecines for gynecological disorders.

I worked at Takeatsu Kimura Commemoration Kampo Museum as a curator. We are designing displays, marshaling materials and directing installations to introduce cultures about Traditional medicines including Kampo and crude drug materials. We introduce Japanese popular Kampo formulas as a main display for students need to study Kampo. In other hand, I'm also starting a research that focused on actual usage of Kampo medicines at hospital in Taiwan. From analysis of patients' records, especially in patients' conditions, complaints and prescribed Kampo regimen, we try to make clear the scientifically and epidemiologically effectiveness and usefulness of Kampo medicines.

Representative Publications

1. Itokazu N., Ogiwara Y., Satake M., Hanawa T., Muranushi A., Hirai T., Mikami M., Nakamura T., Okubo T., Matsumoto R., Nishikawa T., Kitayama H., Goda Y.; Actual Use Research, a new method for evaluating the effectiveness of OTC Kampo drugs and its application to Kamishoyosan formulation. *J, Trad. Med.* Vol,24, No.3 104-114 (2007).

Division of Pharmaceutical Health Biosciences

Toshiyuki HIGUCHI, Ph.D. / Professor

Division of Pharmaceutical Health Biosciences
Department of Pharmaceutical Sciences

Research Topics

1. Study on up-regulation of tissue factor expression in monocytes/macrophages, and on the inhibitor.
2. Study on regulation of expressions and functions of coagulation/fibrinolysis factors in adipocytes.
3. Study on change in expression/function of drug metabolizing enzyme in various stress and diseases.

We focus on association with a lifestyle-related disease and the vascular lesion (arteriosclerosis and/or thrombosis), and research on aberrant coagulation/fibrinolysis in various conditions such as obesity and inflammation from the viewpoint of expression and function of the blood coagulation/fibrinolysis factor. In addition, we study the expression/function of drug metabolizing enzyme in in various stress and diseases.

Representative Publications

1. Murata H., Higuchi T., Otagiri M.; Oral pharmacokinetics and *in-vitro* metabolism of metyrapone in male rats. *J. Pharm. Pharmacol*., **68**, 970-979 (2016).
2. Hirata, Y., Masuda, Y., Kakutani, H., Higuchi, T., Takada, K., Ito, A., Nakagawa, Y., and Ishii, H.; Sp1 is an essential transcription factor for LPS-induced tissue factor expression in THP-1 monocytic cells, and nobiletin represses the expression through inhibition of NF-κB, AP-1, and Sp1 activation. *Biochem. Pharmacol*., **75**, 1504 - 1514 (2008).
3. Murata, K., Higuchi, T., Takada, K., Oida, K., Horie, S. and Ishii, H.; Verotoxin-1 stimulation of macrophage-like THP-1 cells up-regulates tissue factor transcription through activation of c-Yes tyrosine kinase: Possible signal transduction in tissue factor up-regulation. *Biochim. Biophys. Acta*, **1762**, 835 - 843 (2006).

Naoto URAMARU, Ph.D. / Senior Assistant Professor

Division of Pharmaceutical Health Biosciences
Department of Pharmaceutical Sciences

Research Topics

1. Design and synthesis based on metabolic activation of low-molecular-weight compounds.
2. Toxicology based on metabolic activation of environmental chemicals.
3. Research for traditional herbal medicines with anti-allergic activity.

Drug allergy is rare, but seriously and potentially lifethreatening. There are many reports that T-lymphocytes react specifically to low-molecular-weight compounds, even though peptide structures are required for antigen presentation. The reason for such hypersensitivity is that some low-molecular-weight drugs are metabolically activated and form complexes with proteins in vivo. We reported confirm the validity of our strategy of blocking metabolic activation of pyrazolones by means of structural modification to obtain compounds that can not be metabolically activated to bind to biomacromolecules and so do not show allergenicity but tetain potent antipyretic and analgesic activites. Research in our group is focused on medicinal chemistry on the design and synthesis based on metabolic activation of low-molecular-weight compounds.

Representative Publications

1. Jiang W. P., Huang S. S., Matsuda Y., Saito H., Uramaru N., Ho H. Y., Wu J. B., Huang G. J.; Protective Effects of Tormentic Acid, a Major Component of Suspension Cultures of Eriobotrya japonica Cells, on Acetaminophen-Induced Hepatotoxicity in Mice. *Molecules*, **22**(5), 830 (2017).
2. Uramaru N., Inoue T., Watanabe Y., Shigematsu H., Ohta S., Kitamura S; Structure-activity relationship of a series of 17 parabens and related compounds for histamine release in rat peritoneal mast cells and skin allergic reaction in guinea pigs. *Journal of Toxicological Sciences*, **39**, 83-90 (2014).
3. Uramaru N., Shigematsu H., Toda A., Eyanagi R., Kitamura S., Ohta S.; Design, synthesis, and pharmacological activity of nonallergenic pyrazolone-type antipyretic analgesics. *Journal of Medicinal Chemistry*, **53**, 8727-8733 (2010).

Makoto OSABE, Ph.D. / Senior Assistant Professor

Division of Pharmaceutical Health Biosciences
Department of Pharmaceutical Sciences

Research Topics

1. Molecular and cellular mechanisms of peroxisome proliferator-activated receptors (PPARs) activation.
2. Determining the regulatory mechanism of PPARs-mediated function.
3. Biomarkers for prediction of idiosyncratic adverse drug reactions and its molecular mechanisms.

Peroxisome proliferator-activated receptors (PPARs) are ligand-activated transcription factors belonging to the nuclear receptor family. PPARs function as regulators of lipid and lipoprotein metabolism and glucose homeostasis and influence cellular proliferation, differentiation and apoptosis. We investigate the molecular and cellular mechanisms of PPARs activation, focusing on those xenobiotics that activate the receptor without the direct binding.
Idiosyncratic adverse drug reactions (IADRs), as seen in Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), are unpredictable and potentially life threatening. These reactions involve immune mechanisms, and genetic association studies have identified strong links between hypersensitivity to specific drugs and certain human leukocyte antigen (HLA) alleles. We investigate the biomarkers for prediction of SJS/TEN associated with mogamulizumab, a humanized anti-CC chemokine receptor 4 (CCR4) monoclonal antibody.

Representative Publications

1. Osabe M, Tajika T, Tohkin M: Allopurinol suppresses expression of the regulatory T cell migration factors TARC/CCL17 and MDC/CCL22 in HaCaT keratinocytes via restriction of NF-κB activation. *J. Appl. Toxicol*. 2017 **38**(2), 274-283.
2. Shizu R, Osabe M, Perera L, Moore R, Sueyoshi T, Negishi M: Phosphorylated nuclear receptor CAR forms a homodimer to repress its constitutive activity for ligand activation. *Mol Cell Biol* 2017, **37**(10): e00649-16
3. Osabe M, Negishi M: Active ERK1/2 protein interacts with the phosphorylated nuclear constitutive active/androstane receptor (CAR; NR1I3), repressing dephosphorylation and sequestering CAR in the cytoplasm. *J. Biol. Chem*. 2011, **286**(41): 35763-35769.

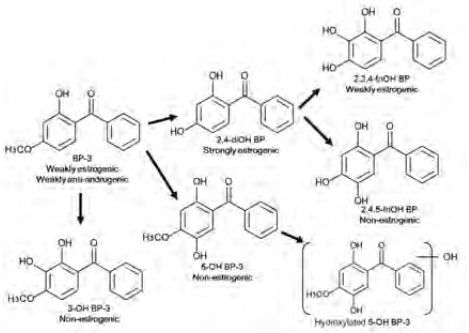
Yoko WATANABE, Ph.D. / Assistant Professor

Division of Pharmaceutical Health Biosciences
Department of Pharmaceutical Sciences

Research Topics

1. Metabolic modification of nuclear receptors caused by environmental chemicals.
2. Effect of environmental chemicals on transcriptional activities of nuclear receptors.

Nuclear receptor transcriptional activities of various environmental chemicals are metabolically activated. For example, the estrogen receptor (ER) and antiandrogen receptor transcriptional activities of Benzophenone-3, a representative UV absorbant, are activated by oxidative metabolism. In contrast, the ERα and ERβ agonistic activities of butylparaben (used as antimicrobial agents) may be diminished by carboxylesterase. Indeed, 4-hydroxybenzoic acid itself showed little estrogenic activity.
PPARs are involved in variety of disease conditions, such as obesity and metabolic syndrome.



Representative Publications

1. Fujino C, Tamura Y, Tange S, Nakajima H, Sanoh S, Watanabe Y, Uramaru N, Kojima H, Yoshinari K, Ohta S, Kitamura S. Metabolism of methiocarb and carbaryl by rat and human livers and plasma, and effect on their PXR, CAR and PPARα activities. *J Toxicol Sci.*, **41**, 677-691, (2016).
2. Watanabe Y., Kojima H., Takeuchi S., Uramaru N., Sanoh S., Sugihara K., Kitamura S., Ohta S., Metabolism of UV-filter benzophenone-3 by rat and human liver microsomes and its effect on endocrine-disrupting activity. *Toxicol. Appl. Pharmacol.*, **282**, 119-128 (2015).
3. Watanabe Y., Kojima H., Takeuchi S., Uramaru N., Ohta S., Kitamura S., Comparative study ontranscriptional activity of 17 parabens mediated by estrogen receptor α and β and androgen receptor. *Food Chem.Toxicol.*, **57**, 227-234 (2013).

Division of Microbiology and Molecular Cell Biology

Toshiyuki YAMADA, Ph.D. / Professor

Division of Microbiology and Molecular Cell Biology
Department of Pharmaceutical Sciences

Research Topics

1. Analysis of regulatory mechanisms of T cell development.
2. Analysis of regulatory mechanisms of ocular development and function.

1. Research in our group is focused on developmental regulation of T cells by using a hairless mutant rat (Hirosaki hairless rat; HHR) showing differentiation failure of $CD4^+$ regulatory T cells in the thymus and helper T cells in the spleen, and deletion of the *Ly49s3* gene (ref. 1). As the *Ly49s3* gene, regulating interaction of immune cells, is expressed in thymic stromal cells in normal rat, we are now trying to demonstrate that thymic microenvironment of HHR affects differentiation of $CD4^+$ T cells.
2. We also focus on another mutant rat (Hirosaki small eye rat, HiSER) showing abnormalities in its eyes including lens involution and retinal detachment. We have demonstrated that deletion of the βA3/A1-cystallin (*Cryba1*) gene is the reason for the HiSER phenotype (ref. 2). By using HiSER, we are investigating mechanisms of ocular development and function. We are also exploring the possibility that HiSER to be a model animal of human ocular diseases, such as age-related macular degeneration.

Representative Publications

1. Yamada T, Nanashima N, Akita M, Shimizu T, Miura T, Yamana D, Sawano T, Sakurai T, Tsuchida S.; Lectin-like receptor Ly49s3 on dendritic cells contributes to the differentiation of regulatory T cells in the rat thymus. *J. Immunol.*, **191**, 3799-3809 (2013).
2. Yamada T, Nanashima N, Shimizu T, Nakazawa Y, Nakazawa M, Tsuchida S.; Establishment of a recessive mutant small-eye rat with lens involution and retinal detachment associated with partial deletion and rearrangement of the *Cryba1* gene. *Biochem. J.*, **471**, 293-305 (2015).

Jun-ichi YAMAGISHI, Ph.D. / Professor

Division of Microbiology and Molecular Cell Biology
Department of Pharmaceutical Sciences

Research Topics

1. Mechanistic understanding of fluoroquinolone resistance in gram-negative bacteria.
2. Screening of natural compounds for antibacterial agents using anucleate cell blue assay.
3. Development of new *in vitro* screening methods to identify antibacterial inhibitors.

Recently, antibacterial-resistant (AMR) bacteria have been emerging increasingly in clinical practice. AMR bacteria become a serious social problem. We strive to discover new methods for controlling infectious diseases caused by AMR bacteria. Research in our group is focused on molecular mechanisms of fluoroquinolone resistance in the important human pathogen, multidrug-resistant *Acinetobacter baumannii* (MDRA) and multidrug-resistant *Pseudomonas aeruginosa* (MDRP). It is known that principal mechanisms of bacterial resistance to fluoroquinolones are mutations of two target enzymes, DNA gyrase and DNA topoisomerase IV, or reduction of intracellular concentration due to mutations in the regulatory genes for efflux system. However, we demonstrated novel fluoroquinolone-resistance mechanism which lacks mutations of both types. We are also trying to discover effective antibacterial agents against MDRA and MDRP.

Representative Publications

1. Kawai M, Yamada S, Ishidoshiro A, Oyamada Y, Ito H, Yamagishi J. Cell wall thickness: Possible mechanism of acriflavine resistance in methicillin-resistant *Staphylococcus aureus*. *J Med Microbiol*. **58**, 331-336 (2009).
2. Ito H, Ura A, Oyamada Y, Yoshida H, Yamagishi J, Matsuyama S, Tokuda H. A New screening method to identify inhibitors of the Lol (Localization of lipoproteins) system, a Novel antibacterial target. *Microbiol Immunol*. **51**, 263-270, (2007).
3. Oyamada Y, Ito H, Fujimoto K, Niga T, Okamoto R, Inoue M, Yamagishi J. Combination of known and unknown mechanisms confers high-level resistance to fluoroquinolones in *Enterococcus faecium*. *J Med Microbiol*. **55**, 729-736 (2006).

Mamoru KYOGASHIMA, M.D., Ph.D. / Professor

Division of Microbiology and Molecular Cell Biology
Department of Pharmaceutical Sciences

Research Topics

1. Development of analytical techniques for sphingolipids and glycosphingolipids.
2. The roles of sphingolipids and glycosphingolipids in cardiovascular diseases, inflammations and cancer progression.

Sphingolipids (SLs) and glycosphingolipids (GSLs) are not only fundamental components of the cell membranes but also play crucial roles for cell signaling to maintain cell homeostasis. Compared to glycerophospholipids, SLs and GSLs are minor components of the cell membrane lipids but show considerable diversity in lipid portions of ceramides and/or sugar sequences. Therefore, sophisticated techniques to analyze them are still required even though current mass spectrometry has been developed. We investigate the roles of SLs and GSLs in cardiovascular diseases, inflammations and cancer progress by use of techniques we have established. We demonstrated critical roles of a specific ceramide for cancer metastasis and importance of an acidic GSL, sulfatide for atherothrombosis.

Representative Publications

1. Suzuki M, Cao K, Kato S, Komizu Y, Mizutani N, Tanaka K, Arima C, Tai MC, Yanagisawa K, Togawa N, Shiraishi T, Usami N, Taniguchi T, Fukui T, Yokoi K, Wakahara K, Hasegawa Y, Mizutani Y, Igarashi Y, Inokuchi JI, Iwaki S, Fujii S, Satou A, Matsumoto Y, Ueoka R, Tamiya-Koizumi K, Murate T, Nakamura M, Kyogashima M, Takahashi T.; Targeting ceramide synthase 6-dependent metastasis-prone phenotype in lung cancer cells. *J. Clin. Invest*., **126**, 254-265 (2016).
2. Tanaka K, Yamada M, Tamiya-Koizumi K, Kannagi R, Aoyama T, Hara A, Kyogashima M.; Systematic analyses of free ceramide species and ceramide species comprising neutral glycosphingolipids by MALDI-TOF MS with high-energy CID. *Glycoconj. J*., **28**, 67-87 (2011).
3. Kyogashima M.; The role of sulfatide in thrombogenesis and haemostasis. *Arch. Biochem. Biophys*., **426**, 157-162 (2004).

Hiroyuki YAMAMOTO, Ph.D. / Senior Assistant Professor

Division of Microbiology and Molecular Cell Biology
Department of Pharmaceutical Sciences

Research Topics

1. Activation mechanisms of neuropeptides in non-endocrine tissue.
2. Identification of novel bioactive peptides cleaved from precursor proteins.
3. Isolation of novel prohormone convertases involving in the extracellular processing.

Our research questions center on the post-translational modification of neuropeptides produced in the peripheral tissue. Neuropeptides are usually matured by specific proteolytic cleavages of their precursor proteins in the intracellular. We have found that some non-endocrine cells release bioactive peptides as precursors, and would like to determine how these precursors are converted to active forms in the extracellular milieu. We are interested in the mechanism of bioactive peptide processing in peripheral tissues and in carcinoma. We are now attempting to find the novel bioactive peptides in the secretion of the neuropeptides after UV-irradiation and during inflammation.

Representative Publications

1. Yamamoto, H., Okada, R., Tanaka, R., Unno, K., Iguchi, K.; Expression of a urokinase-type plasminogen activator during tumor growth leads to angiogenesis via galanin activation in tumor-bearing mice. *FEBS Open Bio*, **7**, 1784-1792 (2017).
2. Yamamoto, H., Ramos-Molina, B., Lick, A.N., Prideaux, M., Albornoz, V., Bonewald, L., and Lindberg, I.; Posttranslational processing of FGF23 in osteocytes during the osteoblast to osteocyte transition. *Bone*, **84**, 120-130 (2016).
3. Yamamoto, H., Yamane, T., Iguchi, K., Tanaka, K., Iddamalgoda, A., Unno, K., Hoshino, M., Takeda, A. Melanin production through novel processing of proopiomelanocortin in the extracellular compartment of the auricular skin of C57BL/6 mice after UV-irradiation. *Sci. Rep*. **5**, 14579 (2015).

Division of Clinical Pharmaceutics

Takanori NAKAJIMA, Ph.D. / Professor

Division of Clinical Pharmaceutics
Department of Pharmaceutical Sciences

Research Topics

1. Supply the evidence for drug management and the clinical evaluation of hospital preparations.
2. Study on controlled-release formulation and clinical evaluation of Ulinastatin vaginal suppository.
3. Development of the new preparation to use for stomatitis treatment after the chemotherapy.

Hospital preparations (HPs) prepared by hospital pharmacists have contributed to advanced medical care depending on various and individual medical needs. Advanced pharmaceutical knowledge and skills are needed to prepare HPs. Hospital pharmacists have inherited formulations and skills to prepare them. However, there has been a decrease in the number of HPs prepared in hospitals due to an increase in commercial formulations. It is not acceptable for hospital pharmacists to have a lack of experience when a doctor requests an original HP. Therefore, we consider that it is the role of the university to support the supply and usage of HPs in cooperation with the hospital pharmacy.

Representative Publications

1. Nawata S, Kohyama N, Uchida N, Numazawa S, Ohbayashi M, Kobayashi Y, Iwata M, Nakajima T, Saito H, Izuka A, Yamamoto T. *J Pharm Health Care Sci*. , **2**:12. doi: 10.1186/s40780-016-0046-7. eCollection (2016).
2. Nakajima T, Iwata M, Nawata S, Saito H, Nakamura Y, Kobayashi Y, Yamamoto T, Matsuda Y, Kimura M. *Jpn. J. Pharm. Health Care Sci*. **38**, 702-707 (2012).
3. Satake K, Nakajima T, Iwata M, Fujikake Y, Kimura M. *Yakugaku Zasshi*. **131**, 1639-44 (2011).

Yasuhiro YAMADA, Ph.D. / Professor

Division of Clinical Pharmaceutics
Department of Pharmaceutical Sciences

Research Topics

1. The investigation of metabolism-mediated drug-drug interactions (DDIs).
2. The creation of human alternatives hepatocytes and enterocytes from stem cells or hepatoma cell lines.
3. The construction of an *in vitro* test system to evaluate chronic and idiosyncratic hepatotoxicity.

In order to effectively overcome the "valley of death" in the process to drug development from discovery research and increase the probability of success, it is important to accurately predict pharmacokinetics and side effects (toxicity) for humans in new drug seeds (new chemical entities and/or drug candidates) at the pre-clinical stage. For that purpose, it becomes the key to stably supply high-quality human hepatocytes and enterocytes as research support tools. Hence, we are constructing a system to create human alternative hepatocytes and enterocytes using induced pluripotent stem (iPS) cells or cell fate transformation without the mediation of iPS cells (direct or epigenetic reprogramming), and constructing an evaluation system for predictions of clinical pharmacokinetics and DDIs using those cells. We are also studying three-dimensional co-cultures of human hepatocytes and heterologous cells to evaluate the chronic and idiosyncratic toxicity of drugs *in vitro*.

Representative Publications

1. Ogasawara A., Torimoto N., Tsuda N., Aohara F., Ohashi R., Yamada Y., Taniguchi H.; New screening criteria setting on evaluation of cytochrome P450 induction using HepaRG cells with multiplex branched DNA technologies in early drug discovery. *Drug Metab Lett*., **10**, 152-160 (2016).
2. Kozakai K, Yamada Y., Oshikata M, Kawase T, Suzuki E, Haramaki Y, Taniguchi H.; Cocktail-Substrate Approach-Based High-Throughput Assay for Evaluation of Direct and Time-Dependent Inhibition of Multiple Cytochrome P450 Isoforms. *Drug Metab Pharmacokinet*., **29**, 198-207 (2014).
3. Yamada Y., Kaji H, Shion H., Oshikata M., Haramaki Y.; Distribution of chloroquine in ocular tissue of pigmented rat using matrix-assisted laser desorption/ionization imaging quadrupole time-of-flight tandem mass spectrometry. *Rapid Commun Mass Spectrom*., **25**, 1600-1608 (2011).

Takuro KURITA, Ph.D. / Associate Professor

Division of Clinical Pharmaceutics
Department of Pharmaceutical Sciences

Research Topics

1. Development of bioavailability of orally dosed poorly water-soluble drugs.
2. Design of novel drug delivery systems composed of newly ionic liquids.
3. Development of new enhancement methods for transdermal absorption.

To develop novel drug delivery products, co-operations with other companies or universities are actively being done. Major activities include some topics listed above.

1. To enhance oral bioavailability of poorly water-soluble drugs such as paclitaxel, curcumin, tacrolimus etc., we tried to prepare powders or water-based suspensions contain novel nano-sized particles by build-up or break-down methods, and estimated its particle characteristics.
2. We prepare Ionic liquids by several pharmaceutical additives and estimated its characteristics, especially ability as solvent of poorly water-soluble drugs.
3. To develop novel transdermal therapeutic systems, we try to enhance transdermal absorption of several drugs such as opioids, antigens in vaccine and NSAIDs etc.

Representative Publications

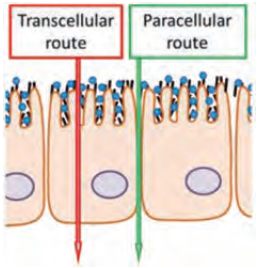
1. Kurita T and Makino Y; Novel Curcumin Oral Delivery Systems. *Anticancer Research*, **33** (7) 2807-2821 (2013).
2. Matsuyama S, Tokumura T and Kurita T; Degradation Rate of Ebastine in an Aqueous Solution at pH 1.2 and the Effects of Cyclo dextrins. *Sch. Acad. J. Pharm*., **5** (4), 87-91 (2016).
3. Tokumura T, Yoshida N, Mori-Yasumoto K, Shirota O and Kurita T;Degradation rates and products of fluticasone propionate in alkaline solutions. *Journal of Pharmaceutical Analysis*, **7** (5) 297-302 (2017).
4. Medication liquid supporting jig and method of applying medication to micro-needle using same. US Patent 9,067,048 (2015).

Yusuke TAKIZAWA, Ph.D. / Senior Assistant Professor

Division of Clinical Pharmaceutics
Department of Pharmaceutical Sciences

Research Topics

1. Influence of dairy products on intestinal membrane permeability of drugs and nutrients ~Study on interaction between lactose and galectin-3~.
2. Influence of decrease/increase of cellular GTP amount on membrane transport of drugs.
3. Changes in membrane transport via paracellular and transcellular permeability during intestinal inflammatory condition.



Our main research field is "intestinal absorption", and the current research theme is development of novel absorption regulation system using changes in amount of GTP which is second intracellular energy currency and mucin which is a main constituent factor of unstirred water layer.
In addition we are also studying about changes in the membrane transport of nutrients and drugs under special conditions such as foods intake condition, ingestion of multiple medicines, and gastrointestinal inflammation condition.

Representative Publications

1. Kishimoto H, Miyazaki K, Takizawa Y, Shirasaka Y, Inoue K, Absorption-Enhancing Effect of Nitric Oxide on the Absorption of Hydrophobic Drugs in Rat Duodenum, *J Pharm. Sci*., **105**, 729-733 (2016).
2. Takizawa Y, Kishimoto H, Tomita M, Hayashi M, Changes in the Expression Levels of Tight Junction Components during Reconstruction of Tight Junction from Mucosal Lesion by Intestinal Ischemia/Reperfusion. *Eur. J. Drug Metab. Pharmacokinet*., **39**, 211-220 (2014).
3. Takizawa Y, Kishimoto H, Nakagawa M, Sakamoto N, Tobe Y, Furuya T, Tomita M, Hayashi M, Effects of Pharmaceutical Excipients on Membrane Permeability in Rat Small Intestine. *Int. J. Pharm*., **453**, 363-370 (2013).

The Center for Promotion of Pharmaceutical Education

Hiroshi NOGUCHI, Ph.D. / Professor

The Center for Promotion of Pharmaceutical Education
Department of Pharmaceutical Sciences

Research Topics

1. Translational research based on the Bechet disease or SSC Specific HLA analyzed by calculation chemistry.
2. Biosyntheses by Type III Polyketide Synthase.

Research in our group is focused on the selective binding of HLA-B*51:01 with different Bechet-genic peptides such as MICA-TM, HSP65, HLA-B*51:01, PSD-Ag and h-TMP. To reveal the selective binding of topo-I peptide by human leukocyte antigens (HLA) associated and non- associated with systemic sclerosis (SSc) Stable and active amino acid of bechetogenic peptides bound to HLA-B*51:01 Stabilization in the binding groove of HLA-DR alleles with SSc complexed Topo-I peptide (RIANFKIEPPGLFRGRGNHP) using MD simulation Reveal the selective binding of antigenic peptide by human leukocyte antigens (HLA) associated in both genetic diseases; BD and SSc.

Representative Publications

1. Yamamoto T., Tsunematsu Y., Hara K., Suzuki T., Kishimoto S., Kawagishi H., Noguchi H., Hashimoto H., Tang Yi, Hotta K., Watanabe K.; Oxidative *trans* to *cis* Isomerization of olefins in polyketide biosynthesis, *Angew. Chem. Int. Ed. Engl*. **55**(21): 6207-6210 (2016).
2. Yang X., Matsui T., Kodama T., Mori T., Zhou X., Taura F., Noguchi H., Abe I., Morita H.; Structural basis for olivetolic acid formation by a polyketide cyclase from *Cannabis sativa*, *FEBS J*. **283**(6): 1088-1106 (2016).
3. S. Kongkaew, P. Yotmanee, T. Rungrotmongkol, N. Kaiyawet, A. Meeprasert, T. Kaburaki, H. Noguchi, F. Takeuchi, N. Kungwan, S. Hannongbua; Molecular Dynamics Simulation Reveals the Selective Binding of Human Leukocyte Antigen Alleles Associated with Behçet's Disease, *PLOS ONE* **vol. 10**(9): e-published e013117 (2015).

Takayoshi DOI, Ph.D. / Professor

The Center for Promotion of Pharmaceutical Education
Department of Pharmaceutical Sciences

Research Topics

1. Relatoinships of aromatase, carcinogenesis and teratogenesis on AhR(-/-) mouse.
2. Application of hiPS cell-derived hepatocytes for toxicological evaluation.
3. Investigative research on side effects of antidiabetic drugs using JADER.
4. Consciousness survey on smoking and its culture.

Representative Publications

1. T. Doi, N. Nagai, R. Tsukuda and T. Suzuki; Dose-relationships cytotoxicity, PFC response and histology in the spleen in rats treated with alkylating agents, *Toxicology*, **107**, 47 (1996).
2. T. Doi, H. Yoshimura and K. Tatsumi; Properties of nitorofuran reductase from E. coli B/r, *Chem. Pharm. Bull.*, **31**, 1105 (1983).

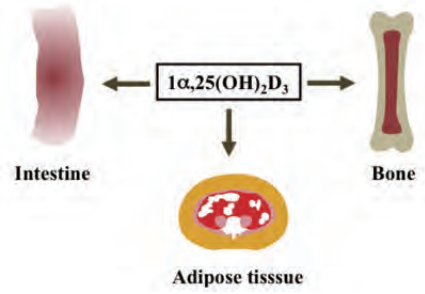
Toshimasa SHINKI, Ph.D. / Professor

The Center for Promotion of Pharmaceutical Education
Department of Pharmaceutical Sciences

Research Topics

1. Molecular function of vitamin D in the bone and intestine.
2. Vitamin D, vitamin D receptor, and adipogenesis.

The purpose of my research program is the investigation of vitamin D endocrine system. The kidney plays an important endocrine role by producing $1\alpha,25(OH)_2D_3$. $1\alpha,25(OH)_2D_3$ is delivered to target tissues where it acts as an endocrine hormone to regulate the various functions.



Representative Publications

1. Shinki T, Ohyama Y.; Handbook of Hormones: comparative endocrinology for basic and clinical research. Academic Press (2016).
2. Shinki T, Shimada H, Wakino S, Anazawa H, Hayashi M, Saruta T, DeLuca HF, Suda T.; Cloning and expression of rat 25-hydroxyvitamin D_3-1α-hydroxylase cDNA. *Proc. Natl. Acad. Sci. USA*. **94**, 12920-12925 (1997).
3. Woo JT, Kawatani M, Kato M, Shinki T, Yonezawa T, Kanoh N, Nakagawa H, Takami M, Lee KH, Stern PH, Nagai K, Osada H.; Reveromycin A, an agent for osteoporosis, inhibits bone resorption by inducing apoptosis specifically in osteoclasts. *Proc. Natl. Acad. Sci. USA*. **103**, 4729-4734, (2006).

Shinji FUNAYAMA, Ph.D. / Professor

The Center for Promotion of Pharmaceutical Education
Department of Pharmaceutical Sciences

Research Topics

1. Chemical reactions of acridone alkaloids.
2. Isolation and structure determination of naturally occurring new compounds.
3. History of poisons and medicines.

Research in our group is focused on the isolation and structure determination of naturally occurring alkaloids and other compounds. We are also interested in the chemical reactions of acridone alkaloids. In addition, we are interested in the history and the use of various kinds of poisons and medicines.

Representative Publications

1. Tanaka N, Takizawa T, Miyamoto N, Funayama S, Tanaka R, Okano S, Iwasaki T; Real world data of a veterinary teaching hospital in Japan: a pilot survey of prescribed medicines. *British Veterinary Association J*., in press.
2. Yang J-L, Lien J-C, Chen Y-Y, Hsu S-C, Hsu S-C, Chang S-J, Huang A-C, Amagaya S, Funayama S, Wood WG, Kuo C-L, Chung J-G; Crude extract of *Euphorbia formosana* induces apoptosis of DU145 human prostate cancer cells acts through the caspase-dependent and independent signaling pathway. *Environ. Toxicol*., **34**, 1600-1611 (2017).
3. Funayama S; About the relationship between Shosoin O-oh and Chin-doku – Does the shape of Shosoin O-oh suggest that this is the egg of Chin, a phantom poisonous bird ? *Nihon Yakka Daigaku Kyoiku Kiyo*, 1-6 (2017).

The Center of Clinical Pharmacology and Pharmaceutics

Yoshikazu MATSUDA, Ph.D. / Professor

The Center of Clinical Pharmacology and Pharmaceutics
Department of Pharmaceutical Sciences

Research Topics

1. Cognitive function improvement by Porcine Liver Decomposition product (PLDP).
2. The Effect of Aromatherapy on autonomic nervous system function.

1. Porcine Liver Decomposition product (PLDP) enhanced cognitive function in preclinical and clinical study. We thought phospholipid included in PLDP may act important role on cognitive function improvement.
2. Autonomic nervous system influences to the onset several diseases. We thought aromatherapy may improvement to imbalance of autonomic nervous system. We expect the aromatherapy available for prevent lifestyle-related disease.

Representative Publications

1. Tsukahara T, Matsuda Y, Haniu H; Lysophospholipid-Related Diseases and PPARγ Signaling Pathway. *Int J Mol Sci*. 2017 Dec 16;**18**(12). pii: E2730. doi: 10.3390/ijms18122730.
2. Tsukahara T, Yamagishi S, Matsuda Y, Haniu H. Lysophosphatidic acid signaling regulates the KLF9-PPARγ axis in human induced pluripotent stem cell-derived neurons. *Biochem Biophys Res Commun*. 2017 Sep 9;**491**(1):223-227. doi: 10.1016/j.bbrc.2017.07.082. Epub 2017 Jul 14.
3. Tsukahara T, Haniu H, Matsuda Y, Murakami-Murofushi K, Short-term treatment with a 2-carba analog of cyclic phosphatidic acid induces lowering of plasma cholesterol levels in ApoE-deficient mice.*Biochem Biophys Res Commun*. 2016, 22;**473**(1):107-13. doi: 10.1016/j.
4. Matsuda Y, Haniu H, Tsukahara T et al,: Effects of Porcine Liver Decomposition product on the cognitive function in non-dementia patients. *Jpn.J.Med.Phram.Sci*., 2016, **73**(8):1057-1066.

Katsuhiro SUZUKI, Ph.D. / Professor

The Center of Clinical Pharmacology and Pharmaceutics
Department of Pharmaceutical Sciences

Research Topics

1. Role of community pharmacies and pharmacists in Japan's aging society.

In Japan's aging society, the environment surrounding pharmacies and pharmacists is drastically changing due to advances in medical care, and separation of dispensatory function from medical practice. These changes have led to various discussions regarding functional assignments of pharmacists and pharmacies. Research in our group is focused on role of pharmacies and pharmacists in providing pharmaceutical care and health support to community residents.

Kunihiko FUJIWARA, Ph.D. / Professor

The Center of Clinical Pharmacology and Pharmaceutics
Department of Pharmaceutical Sciences

Research Topics

1. Study on mental stress caused by long-term clinical pharmacy practice in medicine students.

In six-year pharmacy education in Japan, long-term clinical training is conducted with the aim of acquiring practical attitudes and abilities for pharmacists. On the other hand, practical training in an environment different from the university is assumed to give various stress to students, and there are reports of student health or mental disorder caused by this. In this study, we measure salivary amylase activity in students and instructors in long-term clinical training , and evaluate the degree of stress. And then, we investigate the linkage between learning outcomes (effects) and stress in detail.

2. Study on the computer system using an algorithm that allows for selection and proper use of OTC.

As a pharmacist's role for developing self-medication, it is expected to triage to recommendation for consultation, correspondence of OTC medicine and daily guidance from customer's symptom complaint etc. Especially, the role of advising medicine appropriate for the constitution, condition, and symptoms of patients is expected in the selection of OTC drugs. Our research objective is to create a database for system development with an algorithm that enables safe and optimal OTC drug selection.

Representative Publications

1. Kunihiko Fujiwara, Makoto Matsuura, Takeshi Chiba, Kenichi Sako, Miho Fujisawa, Tomoji Maeda.; Questionary survey about the stress caused by pharmacy rotation in Nihon Pharmaceutical University. *jjphe.**1**,1-12(2017).*

Yoko KUBOTA, Ph.D. / Professor

The Center of Clinical Pharmacology and Pharmaceutics
Department of Pharmaceutical Sciences

Research Topics

1. Proper use of medicines (Antimicrobial Resistance,External preparations, Palliative care etc).
2. Board of pharmaceutical Practice.
3. Pharmaceutical education.

Research in our group is focused on Pharmacists are required to contribute to improving the quality of life (QOL) of patients and consumers by using the medicines more effectively and safely. Future pharmacists are involved in life in various. Therefore, from student days, to mutually compete and learn while understanding, it is important to form our team.
In addition to their own research themes, seminars are held once a month on "New topics", "Papers read" and "Clinical questions". Our group would like to collaborate with overseas pharmacists so please contact us anytime.

Representative Publications

1. Sakaguchi M, Kubota Y, Ohtsuka M, Sekine Y, Qualitative Study of Success Factors for Deploying Health Support System at a Community Pharmacy, *J. Community Pharmacy and Pharmaceutical Sciences*, **10**(1), (2018). in press.
2. Ohmoto M, Takahashi T, Kubota Y, Kobayashi S, Mitsumoto Y, Genetic influence of Dopamine Receptor, Dopamine Transporter and Nicotine Metmetabolism on smoking cessation and nikotine dependence in a Japanese population, *BMC Genetics*, **15**(1), 151 (2014).
3. Kubota Y, Tuchiya M, Yamakami J, Terajima T, Hori S, Kizu J, Pharmaceutical and Pharmacological Evaluation of “Indometacin M Ointment” as a PharmacoPreparation, *Lpn. J. Pharm. HealthCare Sci.* **43**(2), 174-180 (2008).

Yoshio FUJIKAKE / Professor

The Center of Clinical Pharmacology and Pharmaceutics
Department of Pharmaceutical Sciences

Research Topics

1. Survey on the use of thalidomide in the treatment of multiple myeloma.
2. Relationship between the number of blood culture submission and AUD.
3. Evaluation of SGLT2 inhibitors in patients with impaired renal function.

Research in our group is focused on investigation of the usefulness of thalidomide for multiple myeloma resistant to recurrence / treatment based on thalidomide proper use guidelines in 12 subjects surveyed, it was administered 100 to 200 mg / day. Regarding the effectiveness, although the presence of serum M protein was observed at 100 mg / day, there were 6 stable cases, 4 cases requiring more than 2 years from the start of administration until 200 mg / day PR was reached, increasing from 100 to 200 mg reduction of serum M protein was observed in one case.

Nobuaki YUI / Professor

Division of Clinical Pharmacy
Department of Pharmaceutical Sciences

Research Topics

1. Research on Drug Information.

It is important to refer Drug Information such as Risk Management Plan (RMP) provided by pharmaceutical companies and information on adverse drug reactions, safety which are provided by Pharmaceutical and Medical Devices Agency (PMDA) to use drug medicines effectively and safely. We research these data to use Drug Information effectively at clinical site.

2. Research on the benefit of generic drugs to medical economy.

Generic drugs have been widely used in Japan in recent years. We research the influence of the kind and quantity of generic drugs on medical care cost.

3. Research on how to treat diseases with drug medicines depending on the kind of diseases to formulate a guideline for drug usage.

There are a lot of drugs for the treatment of lifestyle diseases. It is important to formulate a guideline which gives thought to effectiveness and safety, economic performance to decide how to use these drugs at healthcare facilities.

Hisao MATSUMURA, Ph.D. / Associate Professor

The Center of Clinical Pharmacology and Pharmaceutics
Department of Pharmaceutical Sciences

Research Topics

1. Suspension method using Supersonic wave.
2. Suspension method using rotation-revolution.

Research in our group is focused on A common method to prepare suspension grinding tablets and/or capsules is one of the medication methods for the administration of tablets or capsules by tube. As for this method, there was a problem of the loss of drug due to adhesion to instruments, feeding tube obstruction, the health damage which various medicines exposure to pharmacists. The simple suspension method is a convenient method in clinical site; however, it has the several problems associated with controlling water temperature and a slow disintegration. In this study, we attempted the establishment of the improved simple suspension method using supersonic wave vibration. In the conventional simple suspension method, VOLTAREN® Tablets 25 mg and LOXONIN TABLETS® 60 mg needed to crush before disintegration for its hard surface. In this study, these tablets were completely disintegrated within 10 min by the improved simple suspension method using supersonic wave vibration (42 kHz; 26 W). Moreover, these disintegrated preparations were passed through 8Fr. feeding tube. These data suggest that this new method enables the avoidance of tube obstruction and slow disintegration of tablet, leading to a more convenient medication. In conclusion, we consider the improved simple suspension method using supersonic wave vibration is applicable to clinical site.

Representative Publications

1. Matsumura H, Morimoto K, Uesaka M, Tanabe R, Iida M, Saitou H, Nakajima T, Matsuda Y.; Development of New Method using Supersonic Wave into the Administration of Tablets or Capsules by Tube. *J. Jpn. Soc. Hosp. Pharm*., **51**, 1249-1253 (2015).
2. Matsumura H, Hara A, Hashizume H, Maruyama K, Abiko Y.;Protective effects of ranolazine, a novel anti-ischemic drug, on the hydrogen peroxide-induced derangements in isolated, perfused rat: comparison with dichloroacetate. *Jpn. J. Pharmacol*., **77**, 31-39 (1998).

Takeshi KAWAMURA, Ph.D. / Associate Professor

The Center of Clinical Pharmacology and Pharmaceutics
Department of Pharmaceutical Sciences

Research Topics

1. Control mechanism of carboxypeptidase R in vivo.
2. Relation between procarboxypeptidase R in the patient serum and the disease.
3. Design of peptide to react to the target point of target molecules.

Research in our group is focused on Control of excessive inflammation and blood clotting abnormality. At the site of bacterial infection, complement is one of the first systems to react with invading microorganisms. At the sites of inflammation, inflammatory peptides including C5a are generated. Carboxypepticlase R (CPR) suppress the function of those peptides by removing their carboxyl terrninal basic amino acids. We discovered that elastase released from activated neutrophils has the ability to activate procarboxypeptidase R converting to CPR. We are interested in the in vivo role of the enzyme carboxypeptidase R which is thought to control both of inflammation and fibrinolysis. The study about its control is being done.

Representative Publications

1. Yaoita N, Satoh K Satoh T, Sugimura K, Tatebe S, Yamamoto S, Aoki T, Miura M, Miyata S, Kawamura T, Horiuchi H, Fukumoto Y, Shimokawa H,: Thrombin-Activatable Fibrinolysis Inhibitor in Chronic Thromboembolic Pulmonary Hypertension. *Arterioscler Thromb Vasc Biol.* , **36(6)** ,1293-301 (2016).
2. Ishijima Y, Kawamura T, Kimura A, Kohno A, Okada T, Tsuji T, Watanabe Y,: Toll-like receptor 4-dependent adjuvant activity of Kakkon-to extract exists in the high molecular weight polysaccharide fraction. *Int J Immunopathol Pharmacol.*, **24** (1):43-54 (2011).
3. Kawamura T, Okada N, Okada H,: Elastase from activated human neutrophils activates procarboxypeptidase R. *Microbiol Immunol*., **46(3)**: 225-30 (2002).

Tsuyoshi MURAHASHI, Ph.D. / Associate Professor

The Center of Clinical Pharmacology and Pharmaceutics
Department of Pharmaceutical Sciences

Research Topics

1. Monitoring of fine particulate matter ($PM_{2.5}$) and polycyclic aromatic compounds in the air.

Fine particulate matter, $PM_{2.5}$, was collected by a high-volume air sampler in Saitama prefecture and Tokyo metropolitan, and $PM_{2.5}$ and polycyclic aromatic hydrocarbons in $PM_{2.5}$ were measured.

Left: High volume air sampler

Right: $PM_{2.5}$ (left filer) and coarse particulate matters (right filter)

2. Monitoring of pharmaceutical compounds in river water.

Pharmaceutical drugs were determined in river water from Ayase River and Arakawa River flowing through Saitama Prefecture and Tokyo metropolitan.

3. Monitoring of suspended pharmaceutical drugs in the air of prescription pharmacy.

Medicinal drugs in the room air in dispensing pharmacy were determined, and inhalation to pharmacist was estimated.

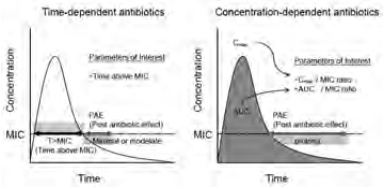
Ken-ichi SAKO M.S. / Senior Assistant Professor

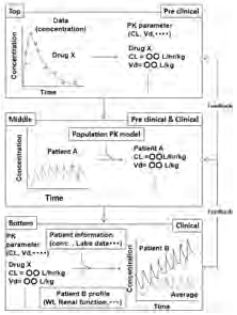
The Center of Clinical Pharmacology and Pharmaceutics
Department of Pharmaceutical Sciences

Research Topics

1. External evaluation of Population Pharmacokinetic-Pharmacodynamic (PK-PD) models.
2. Population Pharmacokinetic-Pharmacodynamic (PK-PD) modeling and simulation.
3. Application of Pharmacometrics (PMx) to Clinical Pharmacology and Pharmacokinetic consultation.

Research in our group is focused on Vancomycin dosage optimaization in cancer patients by PK-PD analysis. There is no sufficient evidence for routinely Therapeutic Drug Monitoring (TDM) with increased initial VCM dosages in cancer patients. Cancer-induced changes in Pharmacokinetics should be taken into account in addition to the large inter-individual variability in VCM clearance.





Representative Publications

1. Nakamura Y, Nakajima T, Iwata M, Hayashi Y, Takayama K, Saito H, Sako K, Matsuda Y, Kimura M.; Influence of temperature and humidity on physico-pharmaceutical characteristics of Rasilez(®) tablets. *Yakugaku Zasshi.* ;**134**(4):555-61(2014).
2. Sako K, H Haniu, Hasegawa M, Doi H, Yano S, Ohsawa Y, Kishino T, Matsuki Y, Arisue Y, Kawamura T, Kimura M, Matsuda Y.; The Application of Proteomics to PK-PD Modeling and Simulation. *J Bioequiv Availab S2.* doi: 10.4172/jbb.S2-002 (2011).
3. Tatsunami S, Sako K, Kuwabara R, Yamada K.; Using Gaussian-like input rate function in the two-compartment model. Formulation and application to analysis of didanosine plasma concentration in two Japanese hemophiliacs. *Int J Clin Pharmacol Res.*:**18**(3):129-35(1998).

Teppei KAKU, Ph.D. / Senior Assistant Professor

The Center of Clinical Pharmacology and Pharmaceutics
Department of Pharmaceutical Sciences

Research Topics

1. Structural and functional studies of xenobiotics by UDP-glucuronosyltransferases.

The UDP-glucuronosyltransferases (UGTs) have been a subject of intense research during the last several decades. This multiple-enzyme system shares many similarities with cytochromes P-450. Both systems display extremely broad substrate specificity, catalyzing the biotransformation of a variety of endogenous and exogenous substrates with diverse chemical structures and physicochemical properties. UGTs also play a critical role in the bioactive or even toxic compounds.
In this study, UGTs can be responsible simultaneously for metabolism of endogenous compounds and structurally unrelated xenobiotics.

Representative Publications

1. Okada M, Murase K, Makino A, Nakajima M, Kaku T, Furukawa S, Furukawa Y. Effects of estrogens on proliferation and differentiation of neural stem/progenitor cells. *Biomed Res*., **29**(3), 163-70 (2008).
2. Ogura K, Ishikawa Y, Kaku T, Nishiyama T, Ohnuma T, Muro K, Hiratsuka A. Quaternary ammonium-linked glucuronidation of *trans*-4-hydroxytamoxifen, an active metabolite of tamoxifen by human liver microsomes and UDP-glucuronosyltransferase 1A4. *Biochem Pharmacol*., **71** (9), 1358-1369 (2006).
3. Kaku T, Ogura K, Nishiyama T, Ohnuma T, Muro K, Hiratsuka A. Quaternary ammonium-linked glucuronidation of tamoxifen by human liver microsomes and UDP-glucuronosyltransferase 1A4. *Biochem Pharmacol*., **67**, 2093-2102 (2004).

Takumi SATO, Ph.D. / Professor

The Center for Liberal Arts Education
Department of Pharmaceutical Sciences

Research Topics

1. Practical study of antidiabetic drugs to obtain the highest effect with the lowest dosage.
2. Practical study of active learning for the lower grade students using new approaches.

Representative Publications

1. Inoue T., Matsuda Y., Sato T., Sakurada C., Haniu H., Tsukahara T., Sigita K., Mabuchi T., Emizu T., Sato K., The impact of repeated administration of choline on spinal cognitive memory in rats. *Jap. J. Med. Pharm. Sci*. **73**(8), 1009-1016(2016).
2. Mizoguchi H., Takagi H., Watanabe C., Yonezawa A., Sato T., Sakurada T., Sakurada S., Involvement of multiple μ-opioid receptor subtypes on the presynaptic or postsynaptic inhibition of spinal pain transmission., *Peptides*. **51**, 15-25 (2014)
3. Mizoguchi H., Watanabe C., Higashiya T., Takeda S., Moriyama K., Aoki Y., Kon-no T., Takagi H., Yonezawa A., Sato T., Sakurada T., Sakurada S., Distinct physiological role of amidino-TAPA-sensitive and DAMGO-insensitive μ-opioid receptor splice variants in the mouse spinal cord., *Eur. J. Pharmacol*. **711**, 80-86 (2013).
4. Tan-No K., Sato T., Shimoda M., Nakagawasai O., Niijima F., Kawamura S., Furuta S., Sato T., Satoh S., Siberring J., Terenius L., Tadano T., Suppressive effects by cysteine inhibitors on naloxone-precipitated withdrawal jumping on morphine-dependent mice. *Neuropeptides*. **44**(3), 279-83(2010).

Shigeo WADA, Ph.D. / Professor

Department of Basic Parmacy

Research Topics

1. First year experience for scholastic aptitude increase.
2. Study on educational method leading to deep learning using educational robots and tablets.
3. Development of environmental education materials.

Student's scholastic aptitude decline is regarded as a problem recently. The reason is because the learning for which I depend on memorization is being performed. I am conducting research on educational methods to raise comprehensive problem-solving skills and thinking skills suitable for each stage from elementary to university students. For university students, I am studying educational method to establish active learning method accurately as first year experience. And I am creating teaching materials to acquire basic academic skills. For elementary and junior high school students, I am developing teaching materials using tablets and educational robots.
In order to be interested in familiar environmental issues and to be able to carry out sustainable environmental protection activities, I am developing environmental education teaching materials that can be used in school classes.

Representative Publications

1. WADA S., NIWANO, J., KUMAMOTO, T., HORIE, H.: Development and practice of the environmental education teaching materials for observing the influence of chemicals to the germination of a seed. *JSSE Research Report,* **32**(3),51-56(2017)
2. WADA S., KITOH S.: Basic knowledge for pharmacy learning 2 ; -Organic Chemistry-, *Kodansha co.*(2017)
3. WADA S., KITOH S.: Basic knowledge for pharmacy learning 1 ; -Chemical Calculation-, *Kodansha co.*(2017)

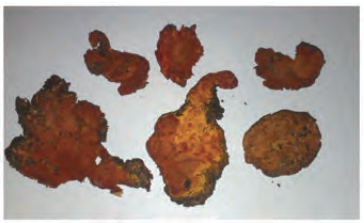
Hiroshi SAITO, Ph.D. / Associate Professor

The Center for Liberal Arts Education
Department of Pharmaceutical Sciences

Research Topics

1. Practice of active learning for lower grades in the college of pharmacy.
2. Study of a Taiwanese origin crude drug ingredients as a leukaemia curative candidates.
3. Study of the validity of the apparatus which prevents scatter of medicine.

Research in our group is focused on the scholastic aptitude of the lower grades. The basic academic skill is indispensable to become a pharmacist. However, the scholastic aptitude decline of pharmaceutical student in our university is remarkable. In particular, they can't do computation. There are more problems with the reading comprehension. So we're considering education necessary to settlement of a basic academic skill. For example making of a drill and implementation of supplementary lessons. Furthermore, our group is considering whether a Taiwanese crude drug ingredient indicates toxicity to a leukaemia cell. Several Taiwanese crude drug extractives indicate toxicity to a specific leukaemia cell.



Representative Publications

1. Nawata S, Kohyama N, Uchida N, Numazawa S, Ohbayashi M, Kobayashi Y, Iwata M, Nakajima T, Saito H, Izuka A, Yamamoto T, The pharmacokinetics of mianserin suppositories for rectal administration in dogs and healthy volunteers: a pilot study, *J Pharm Health Care Sci*. May 17;2:12. doi: 10.1186/s40780-016-0046-7., 2016.
2. Hiratsuka A, Saito H, Hirose K, Watabe T., Marked expression of glutathione S-transferase A4-4 detoxifying 4-hydroxy-2(E)-nonenal in the skin of rats irradiated by ultraviolet B-band light (UVB)., *Biochem Biophys Res Commun*., 260(3):740-6., 1999.

Michio KIMURA, Ph.D. / Associate Professor

The Center for Liberal Arts Education
Department of Pharmaceutical Sciences

Research Topics

1. Search of a protein in the brain which relates depressingly.
2. Characterization of respiration mutant of *Candida albicans*.
3. The antifungal activity of Phellodendron extract to *Candida albicans* in the presence of azole antifungal drug.

Estrogen is involved in numerous activities in the brain, such as learning, memory, fear, anxiety and mood. we examined the effects of ovariectomy (OVX)-a model of estrogen deficiency and menopause-on psychiatric functions, including voluntary activity. Voluntary momentum and circadian activity were monitored at 2 and 6 weeks, respectively. Rats also underwent microdialysis of the amygdala to determine serotonin (5-HT) and dopamine levels. Although the circadian rhythm was unchanged at 2 weeks, voluntary activity at 6 weeks was significantly lower in OVX rats than that in sham rats. This was due to significantly reduced voluntary activity in the 12-h dark phase, while no significant difference was detected in the 12-h light phase. Both 5-HT and dopamine levels in the amygdala were significantly lower in OVX rats than those in sham rats at 6 weeks after the procedure. In conclusion, these results indicate that estrogen is an important mediator of voluntary activity in rats, particularly during the dark phase. Moreover we examined the change of protein expression in the brain after OVX operation and found several proteins. They were cytochrome c, Elongation factor 1-alpha and High mobility group protein B1.

Representative Publications

1. Yamamoto H., Saito S., Sawaguchi Y., Kimura M., Identification of protease specificity using biotin-labeled substrates., *Open Biochem. J.*,**11**, 27-35, (2017).
2. Sustained Neutrophilic Effects of a Novel G-CSF Preparation: Protein-Zinc Carbonate/Complexes. M. Kimura, T. Eto, N. Izumo, and Y. Mizushima, *The Annual Report of Nihon Pharmaceutical University*, **2** 53-63 (2016).

Terumasa CHIBA, Ph.D. / Assistant Professor

The Center for Liberal Arts Education
Department of Pharmaceutical Sciences

Research Topics

1. Study of anticancer drugs-induced peripheral neuropathy.

Peripheral neuropathy is a common adverse effect of paclitaxel, vincristine and oxaliplatin treatment. The symptoms of anticancer drug-induced neuropathy are mostly sensory and peripheral in nature, consisting of mechanical allodynia or hyperalgesia. Research in our group is focused on analysis of transient receptor potential vanilloid 1 channel expression in the rat dorsal root ganglion and release of substance P in the rat spinal cord dorsal horn after anticancer drugs treatment.

Representative Publications

Chiba T, Oka Y, Kambe T, Koizumi N, Abe K, Kawakami K, Utsunomiya I, Taguchi K; Paclitaxel-induced peripheral neuropathy increases substance P release in rat spinal cord. *European Jounal of Pharmacology* **770**: 46-51 (2016).

Department of Pharmaceutical and Medical Business Sciences

Sakae AMAGAYA, Ph.D. / Professor

Department of Pharmaceutical and Medical Business Sciences

Research Topics

1. Pharmacological effects of Kamo Medicines.
2. Qualitative Research of Kampo Medicine and Composed Crude Drugs.
3. Design of New Pharmacological Testing Methods using Serum obtained from Kampo Treated Animals.

Research in our group is focused on the pharmacological actions of kampo medicines (Traditional Japanese medicines). To know the detailed action mechanisms, the usual in vitro methods are not available for the mixture (kampo medicines) and the proper methods for the estimation of kampo medicines are necessary. By the proper methods, the scientific action mechanism should be clarified.

Representative Publications

1. Tanabe H., Yasui T., Kotani H., Nagatsu A., Makishima M., Amagaya S., Inoue M: Retinoic acid receptor agonist activity of naturally occurring diterpenes, *Bioorganic & medicinal Chemistry*, **22**(12), 3204-3212 (2014).
2. Inoue M., Tanabe H., Matsumoto A., Takagi M., Umegaki K., Amagaya S.:Astraxanthin functions differently as a selective peroxisome proliferator-activated receptor Y modulator in adipocytes and macrophages. *Biochemical Pharmacol.*, **84**, 692-700 (2012).
3. Kotani Hitoshi, Tanabe Hiroki, Mizukami Hajime, Amagaya Sakae, Inoue Makoto. : A naturally occurring rexinoid, honokiol, can serve as a regulator of various retinoid X receptor heterodimers. *Biol. Pharm. Bull.*, **35**(1), 1-9 (2012).

Chikai SAKURADA, Ph.D. / Professor

Department of Pharmaceutical and Medical Business Sciences

Research Topics

1. Neuropeptides degradation related to expression of the physiological action of neuropeptides.

The physiological action of neuropeptides as a neurotransmitter or neuromodulator in the central nervous system may be related to degradation of neuropeptides by peptidase(s). For instance, Met-enkephalin is metabolized by neprilysin and aminopeptidase. In addition, inhibitors of neprilysin are analgesic and substitute in opiate abstinence. Definition of inactivation pathway allows the design of enzyme inhibitor that may be of pharmacological interest. Research in our group is focused on degradation of endomorphin, an endogenous opioid peptide, and substance P as a pain transmitter or modulator.

Representative Publications

1. Sakurada C, Mizoguchi K, Komatsu T, Sakurada S, Sakurada T.; Neuropeptides degradation related to expression of the physiological action of neuropeptides. p.27-44 (edited by F. J. Nyberg) CRC Press (Taylor & Francis Group)(2012).
2. Sakurada C, Sakurada S, Hayashi T, Tan-No K, Sakurada T.; Degradation of endomorphin-2 at the supraspinal level in mice is initiated by dipeptidyl peptidase IV: an in vitro and in vivo study. *Biochem Pharmacol.* **66**, 653-661(2003).
3. Sakurada C, Watanabe C, Sakurada T.; Occurrence of substance P(1-7) in the metabolism of substance P and its antinociceptive activity at the mouse spinal cord level. *Methods Find Exp Clin Pharmacol.* **26**, 171-176(2004).

Hiroko HASHIMOTO, M.D., Ph.D. / Professor

Department of Pharmaceutical and Medical Business Sciences

Research Topics

1. Practice of integrative medicines.
2. Exploring the importance of kampo medicines in modern society.

Research in our group is focused on integrative medical care at pharmacy. In Japan, we can receive treatment both in western medicines and kampo medicines (Traditional Japanese medicines). We receive integrative medical treatment naturally. The risk and benefit of the treatment should be studied. And characteristics of integrative medical care in pharmacies should also be studied.

Representative Publications

1. Iijima K, Hashimoto H, Hashimoto M, Son BK, Ota H, Ogawa S, Eto M, Akishita M, Ouchi Y.:Aortic arch calcification detectable on chest X-ray is a strong independent predictor of cardiovascular events beyond traditional risk factors. Atherosclerosis. May;**210**(1):137-44 (2010).
2. Hashimoto H, Iijima K, Hashimoto M, Son BK, Ota H, Ogawa S, Eto M, Akishita M, Ouchi Y.: Validity and usefulness of aortic arch calcification in chest X-ray. J Atheroscler Thromb. Jun;**16**(3):256-64 (2009).
3. Hashimoto H: The existence significance of Kampo treatment in modern society Saitama Prefecture Pharmaceutical Association newsletter (2016).

Katsuhiko KITAMOTO, Ph.D. / Specially Appointed Professor

Department of Pharmaceutical and Medical Business Sciences

Research Topics

1. Microbiology of sake yeast and *koji* mold for sake making.
2. Molecular and cellular biology of *koji* mold, *Aspergillus oryzae.*
3. Analysis of functional ingredients in *Amazake.*

My science field is microbiology of sake yeast and *koji* mold used for sake making. I have studied molecular breeding of sake yeast, *Saccharomyces cerevisiae*, some of which are being used for sake making in Japan. My research objective is the elucidation of the "life phenomenon" of a microbe, and search for solutions of "life, food, and environmental problems" which form the main subjects of the 21st century.

Representative Publications

1. Ohnuki S, Okada H, Friedrich A, Kanno Y, Goshima T, Hasuda H, Inahashi M, Okazaki N, Tamura H, Nakamura R, Hirata D, Fukuda H, Shimoi H, Kitamoto K, Watanabe D, Schacherer J, Akao T, Ohya Y. Phenotypic Diagnosis of Lineage and Differentiation During Sake Yeast Breeding. G3 (Bethesda). **7**, 2807-2820 (2017).
2. Kawaguchi K, Kikuma T, Higuchi Y, Takegawa K, Kitamoto K ; Subcellular localization of acyl-CoA binding protein in *Aspergillus oryzae* is regulated by autophagy machinery. Biochem Biophys Res Commun. **480**, 8-12 (2016).
3. Kitamoto K.; Cell biology of the Koji mold *Aspergillus oryzae.* Biosci. Biotechnol. Biochem., **17**, 1-7 (2015).

Noriko WAKITA / Professor

Department of Pharmaceutical and Medical Business Sciences

Research Topics

1. Health information management.
2. Health informatics.
3. Measuring of Quality Indicators for assessing healthcare quality.
4. Hospital information system.

Quality Indicators (QIs) are a tool for assessing healthcare quality, and QIs monitoring works to improve the quality of healthcare.
The healthcare quality improvement will decrease medical cost in Japan.

Representative Publications

1. Wakita N.; The expansion role of health information manager -Measurement of Quality Indicators-. *Health Information Management,* **22**(2), 68 (2010).
2. Wakita N.; Audit of electronic medical records -Audit and review of discharge summaries-. *J. society for POS health care,* **17**(1), 42-45 (2013).

Yoshiharu OHYAMA, Ph.D. / Professor

Department of Pharmaceutical and Medical Business Sciences

Research Topics

1. Hospital information system and quality of medical care.
2. Calcium channel blockers and myocardial infarction: a case-control study in a Japanese hospital.

We conducted a case-control study nested within a small cohort identified by using a hospital information system in Japan to examine the relationship often use of calcium channel blockers (CCBs) to myocardial infarction. Although the crude odds ratio of myocardial infarction associated with CCBs was high, the ratio was reduced when adjusted by known confounding factors, suggesting a mechanism of confounding by indication. In addition, the results obtained in this study using records from a single hospital should not be generalized. Quality Indicators (QIs) are a tool for assessing healthcare quality, and QIs monitoring works to improve the quality of medical care. When QIs would be analyzed by using a hospital information, confounding factors should be removed if we measure QIs using the same method in the same hospital in chronological order. QIs analyzed by using a hospital information system are valuable and applicable to patients. It would be a driving force of the medical quality improvement that the number of the pharmaco-epidemiology experts would increase more and more. Because they can make the drug information conformed to Evidence-based Medicine using a medical database. Then, the medical quality improvement will decrease medical cost in Japan.

Representative Publications

1. Ohyama Y.; Hospital Information System and Quality of Medical Care. *Jpn J Pharmacoepidemiol.*, **21**(1),45-50 (2016).
2. Ohyama Y, Funao K, Kawabe E, Hayashi D, Yamazaki T, Iga T, Koide D, Ohe K, Kubota K.; Calcium channel blockers and myocardial infarction: a case-control study in a Japanese hospital. *Pharmacoepidemiol. Drug Safety*, **11**(6), 487-492(2002).

Toshio INOUE, Ph.D. / Professor

Department of Pharmaceutical and Medical Business Sciences

Research Topics

1. Evaluation of drug efficacy based on behavioral pharmacology.
2. Evaluation of novel disease model animal.
3. Development of functional food materials using disease model animals.

My research field is functional analysis of drugs and functional foods based on behavioral pharmacology. In a recent study, we have found that phospholipids derived from pig liver have an effect of preventing dementia using an 8-arm radial maze.

Representative Publications

1. Inoue T., Matsuda Y., Sato T., Sakurada1 C., Haniu H., Tsukahara T., Sugita K., Mabuchi T., Emizu T., Sato K.; The impact of repeated administration of choline chloride on spatial cognitive memory in rats. *Japanese Journal of Medicine and Pharmaceutical Science*. **73**(8), 1009-1016(2016).
2. Wu T., Matsumoto K., Tachibana S., Inoue T., Nomura M.: Novel Physiological Roles of Mango Seed Oil using Proteomic Analysis of Differentially Expressed Proteins. *OyoYakuri Pharmacometrics*. **88**, 57-65 (2015).
3. Nakasone T., Sato T., Matsushima Y., Inoue T., Kamei C.; Characteristics of scratching behavior in ADJM mice (atopic dermatitis from Japanese mice). *Immunopharmacol Immunotoxicol*. **37**, 202-206 (2015).

Takaaki YASUDA, Ph.D. / Associate Professor

Department of Pharmaceutical and Medical Business Sciences

Research Topics

1. Research for bioactive naturally occurring compounds.

Research in our group is focused on bioactive naturally occurring compounds, such as flavonoids, coumarins, phenolic compoumds, and so on.

Representative Publications

1. Kubota A., Shindo H., Fukushima Y., Komatsu T., Sakurada T., Yasuda T., Fushiya S., Kondo Y., Sakurada C., Takano F.; Effect of Kampo extaract Boiogito and its alkaloid sinomenine on nociceptive pain in mouse models. *Pharmacometrics,* **92**, 83-89 (2017).
2. Yasuda T., Yamaki M., Iimura A., Shimotai Y., Shimizu K., Noshita T., Funayama S.; Anti-influenza virus principles from Muehlenbeckia hastulata. *J. Nat. Med.,* **64**, 206-211 (2010).
3. Yasuda T., Yoshimura Y., Yabuki H., Nakazawa T., Ohsawa K., Mimaki Y., Sashida Y.; Urinary metabolites of nobiletin orally administered to rats. *Chem. Pharm. Bull.,* **51**,1426-1428 (2003).

Yasuyuki MURAI, Ph.D. / Associate Professor

Department of Pharmaceutical and Medical Business Sciences

Research Topics

1. Analysis of the graphic image generation process of the visually impaired.

Visually impaired people try to understand figures and shapes with fingers. However, the understanding process of figures and shapes by fingers is not clear, and it is not easy to guarantee information for visually impaired people. In this research, we try to elucidate the understanding process of figures and shapes with fingers of visually impaired persons. Specifically, it detects and tracks the position of the finger position and quantitatively analyzes and evaluates the touch process from its tactile information (similarity, feature value, etc.).

Representative Publications

1. Murai Y., Hisayuki T., Masahiro M.; Analysis of the graphic image by tracking fingertip locations of the visually impaired. *Proceedings of the Human Interface Symposium 2017,* 757-760(2017).

Sachiko OIZUMI, Ph.D. / Senior Assistant Professor

Laboratory of Pharmaceutical Business Sciences
Department of Pharmaceutical Medical Business Sciences

Research Topics

1. Pharmaceutical medical business education.
2. Accounting for healthcare organization.
3. Assessment of the rubrics on the authentic assessment in learning.

Research in laboratory is focused on pharmaceutical medical business education and accounting for healthcare organization, assessment of the rubrics of performance in learning on the authentic assessment.

Representative Publications

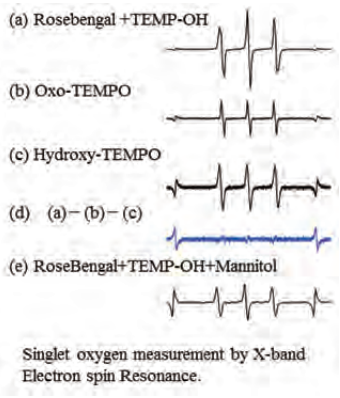
1. Sachiko Oizumi: Development to the Flipped Learning in the Business Course Lectures of the Department of Pharmaceutical Medical Business Sciences The annual report of Nihon Pharmaceutical University.3, 48-55, (2016).
2. Sachiko Oizumi: Literacy Education of Accounting for Healthcare Organization ~Mainly on Inspection for the Deep Active Learning Introduction~The annual report of Nihon Pharmaceutical University.2, 16-21, (2015).
3. Sachiko Oizumi: A Study on Rubric Assessment in the Performance of the learner~Development of Assessment of the Communication Lecture of the Department of Pharmaceutical Medical Business Sciences~The annual report of Nihon Pharmaceutical University.1, 105-112, (2014).

Tokuko TAKAJO, Ph.D. / Senior Assistant Professor

Department of Pharmaceutical and Medical Business Sciences

Research Topics

1. Measurement of antioxidant activity.
2. Mechanism of lipid peroxidation.
3. Redox reaction of biological components.



Singlet oxygen measurement by X-band Electron spin Resonance.

The reactive oxygen species (ROS) and reactive nitrogen species (RNS) create oxidative stress in various pathophysiological conditions. ROS and RNS are highly reactive molecules and can damage cell structures such as lipids, nucleic acids and proteins and alter their functions. Antioxidants are molecules that inhibit or quench free radical reactions and delay or inhibit cellular damage. Research in our group is focused on establishment of a specific measurement system for ROS and RNS, and evaluate an antioxidant activity.

Representative Publications

1. Koshiishi I, Yokota A, Takajo T.; Nitric oxide converts fatty acid alkoxyl radicals into fatty acid allyl radicals. *Arch Biochem Biophys*., **516**, 154-159 (2011).
2. Takajo T, Tsuchida K, Ueno K, Koshiishi I.; Feedback activation of ferrous 5-lipoxygenase during leukotriene synthesis by coexisting linoleic acid. *J Lipid Res.* **48**, 1371-1377 (2007).
3. Takeshita K, Takajo T, Hirata H, Ono M, Utsumi H.; In vivo oxygen radical generation in the skin of the protoporphyria model mouse with visible light exposure: an L-band ESR study. *J Invest Dermatol*.,**122**, 1463-1470 (2004).

Harunobu IWASE, M.S. / Assistant Professor

Department of Pharmaceutical and Medical Business Sciences

Research Topics

1. Biological Effects of the Plasticizer Tris (2-Ethylhexyl) Trimellitate.

An alternative plasticizer, tris (2-ethylhexyl) trimellitate (TOTM), was developed from di-(2-ethylhexyl) phthalate (DEHP) for use in medical tubing. However, little is known about the biological effects of TOTM and thus its safety is not yet well-established.
Our group studies about the biological effects of TOTM and thus its safety.

Representative Publications

1. Iwase H, Oiso S, Kariyazono H, Nakamura K; Nutritional Effect of Oral Supplement Enriched in ω-3 Fatty Acids, Arginine, RNA on Immune Response and Leukocyte–platelet Aggregate Formation in Patients Undergoing Cardiac Surgery. *Nutr Metab Insights.*, **7**, 39-46 (2014).
2. Iwase H, Oiso S, Kariyazono H, Nakamura K.; Biological Effects of the Plasticizer Tris (2-Ethylhexyl) Trimellitate. *Clin Pharmacol Biopharm.,* S2:004. doi: 10.4172/2167-065X.S2-004 (2014).
3. Iwase H, Kariyazono H, Arima J, Yamamoto H, Nakamura K.; Relationship between Platelet Aggregatory and Heparin-Induced Thrombocytopenia Type II. *Science Research,* **2**(4), 78-86 (2014).

Umon AGATA, Ph.D. / Senior Assistant Professor

Laboratory of Pharmaceutical Sport Sciences
Department of Pharmaceutical and Medical Business Sciences

Research Topics

1. Research focus is mainly on building a strong skeleton through the life-long exercise. Current projects investigate factors during growth and how they affect the aging process in bone.
2. Also my current (academically funded) projects investigate the relationships between nutritious food and oxidative stress which refers to elevated intracellular levels of reactive oxygen species (ROS) that cause damage to lipids, proteins and DNA.

Research in our group is focused on the discipline related to the scholarly study of sport, exercise and related activities from anatomical, biomechanical, developmental, physiological, psychological, sociological, philosophical and historical perspectives.
Our course is also designed to prepare students for a variety of career opportunities in sport, recreation, and leisure services. After completing this program, students will have the foundation of the skills they need to perform their future job and to solve individual or organizational problems.

Representative Publications

1. Agata U, Park JH, Hattori S, Iimura Y, Ezawa I, Akimoto T, Omi N. The effect of different amounts of calcium intake on bone metabolism and arterial calcification in ovariectomized rats. *J Nutr Sci Vitaminol*. **59**(1): 29-36 (2012).
2. Agata U, Park JH, Hattori S, Aikawa Y, Kakutani Y, Ezawa I, Akimoto T, Omi N. The impact of different amounts of calcium intake on bone mass and arterial calcification in ovariectomized rats. *J Nutr Sci Vitaminol*. **61**(5): 391-9 (2015).
3. Iimura Y, Agata U, Takeda S, Kobayashi Y, Yoshida S, Ezawa I, Omi N. The protective effect of lycopene intake on bone loss in ovariectomized rats. *J Bone Miner Metab*. **33**(3): 270-8 (2015).

Shuhei KIJI, M.S. / Senior Assistant Professor

Laboratory of Pharmaceutical Sport Sciences
Department of Pharmaceutical and Medical Business Sciences

Research Topics

1. A study on the improvement of the competitiveness in men’s long-distance athletes.
2. A research about career development concerning athletes in Track & Field.
3. A study on the improvement of consciousness for the anti-doping of the Japanese athletes.

The aim of our study is to analyze on the international competitiveness of Japanese men's long-distance running discipline to suggest the direction of the reinforced in international competitiveness from the relationship between sports and companies and university.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