October 1, 2021

Outline of the Laboratory,

Graduate School of Pharmaceutical Sciences, Kyushu University

Clinical Pharmacokinetics

Teaching staff	Professor Naoya Matsunaga, Ph.D.
Research	The following topics are currently under investigation in our laboratory: ・ Pathological analysis focusing on pharmacokinetics-related genes (Cytochrome P450, Transporter). ・ Analysis of organ linkage mechanism under pathological conditions. ・ Investigation of new therapeutic agents and pharmacodynamic and pharmacokinetic analysis.

Pharmaceutics

Teaching staff	Professor Shigehiro Ohdo, Ph.D. ※will retire on March,2024 Assistant Professor Yuya Yoshida
Research	The study on the individualization of pharmacotherapy has been carried out aiming at further improvement of pharmacotherapy. However, intraindividual variability as well as interindividual variability should be considered to aim at further improvement of rational pharmacotherapy. Because many drugs vary in potency and/or toxicity associated with the rhythmicity of biochemical, physiological and behavioral processes. One approach to increasing the efficiency of pharmacotherapy is the administration of drugs at times at which they are most effective and/or best tolerated. The application of biological rhythm to pharmacotherapy may be accomplished by the appropriate timing of conventionally formulated tabletes and capsules, and the special drug delivery system to synchronize drug concentrations to rhythms in disease activity. In all living organisms, circadian pacemaker resides in the paired suprachiasmatic nuclei (SCN). Clock genes are the genes that control the circadian rhythms in physiology and behavior. The knowledge of clock genes may be important for the clinical practice. Therefore, we aim at the development of new chronotherapy based on the following strategy: to monitor a rhythmic marker for selecting dosing time, to overcome the alteration of the clock function, a new concept of adverse effects, by devising a dosing schedule and to produce new rhythmicity by manipulating the conditions of living organs by using rhythmic administration of altered feeding schedules or several drugs.

Glocal Health Care

Teaching staff	Professor Satoru Koyanagi, Ph.D. Assistant Professor Akito Tsuruta, Ph.D.
Research	The following topics are currently under investigation in our laboratory: 1. Studies on molecular mechanism for circadian exacerbations of chronic pain and inflammation. 2. Studies on the prediction of human pharmacokinetic profile in animal scale up based molecular circadian clock 3. Optimization of dosing regimen to achieve the treatment of circadian-related diseases

Protein structure, function and design

Teaching staff	Professor Tadashi Ueda, Ph.D. ※will retire on March,2023 Assistant Professor Daishuke Takahashi, Ph.D
Research	Our group is involved in a number of areas: Structural Biology, Protein engineering and Immunology. 1.Protein preparation and analyses of protein structures and functions involved in life system (DNA replication, immune system and so on) using X-ray crystallography or NMR spectroscopy. 2. Basic study to avoid risks of protein drugs. 3. Design of next-generation beneficial proteins using protein engineering. 4. Analyses of protein aggregations or isomerizations involved in biological functions. 5. Developing methods for protein aggregations or isomerizations based on their mechanisms.

Pathophysiology

Teaching staff	Associate Professor Mami Noda, Ph.D. ※will retire on March, 2022
Research	In the Pathophysiology laboratory, we are investigating the cellular mechanism of neurodegenerative diseases and psychiatric disorders. The main topics of our research are as follows: ● Neuron-glia interaction and the role of glial cells in neurological diseases. Glial cells (astrocytes, microglial, and oligodendrocytes) play important roles in various neurological diseases. We focus on microglial and astrocytes and try to clarify the followings: 1) Receptors and ion channels in glial cells. 2) The role of glial cells in inflammation and trauma. 3) The role of glial cells in brain metastases of cancer cells. 4) The role of glial cells in neurodegenerative and psychological diseases. ● Anti-oxidative stress in model animals of neurodegeneration. We are trying to find evidences for the benefits of taking anti-oxidants using Parkinson's disease model mice. We already observed that molecular hydrogen (H_2 gas) has neuroprotective effects on animal model of Parkinson's disease and now we are trying to clarify the molecular basis.

Molecular Biology

Teaching staff	Professor Tsutomu Katayama, Ph.D. Associate Professor Shogo Ozaki, Ph.D. Assistant Professor Kazutoshi Kasho, PhD.
Research	In the cell cycle progression, chromosomal DNA is replicated only once at a specific time by the carefully controlled molecular switch for replicational initiation. If this regulation is interfered with, various cell defects occur, such as abnormal chromosomes, inhibition of cell division, and growth of abnormal cells. Thus, a study on this regulatory mechanism is of significance as a basis for the developments of antibiotics and anticancer drugs. We have shown that a protein (DnaA) initiating E. coli chromosomal replication is inactivated by timely and direct interaction with a subunit of chromosomal replicase (DNA polymerase III holoenzyme). This interaction depends on loading the subunit onto DNA. This conformational change occurs for the nucleotide-polymerizing action of the replicase after the initiation reaction by DnaA. Thus, during the cell cycle, the initiation protein is most likely inactivated just after initiation of chromosomal replication in this manner. We have termed this regulatory system RIDA (Regulatory inactivation of DnaA). Reactivation of DnaA will occur before the next round of the replication cycle. We are investigating the molecular mechanisms in this DnaA-activity cycle including timely inactivation and activation.

Medicinal Chemistry & Chemical Biology

Teaching staff	Professor Akio Ojida, Ph.D. Assistant Professor Syouhei Uchinomiya, Ph.D.
Research	1) Development of Covalent Drug We are challenging drug discovery from chemical biology point of the view. We consider that drug discovery is a research that creates a superior molecule for treatment of disease. In particular, we are actively promoting medicinal chemistry of covalent drug, which exert its function by forming covalent bond with targeted proteins. Throughout the covalent drug research, we explore new organic chemistry that robustly operates in biological systems. 2) Development of Fluorescent Probe We are promoting chemical biology research to elucidate biological functions by utilizing the developed molecule as chemical tool. We particularly focus on cell metabolism, and are thus developing a new fluorescent probes that can detect activity of intracellular metabolism. Throughout this research, we try to open the new way of cell metabolism analysis based on chemical biology approach.

Disease Control

Teaching staff	Asssociate Professor Michio Nakaya, Ph.D.
Research	Fibrosis is a condition characterized by excess production of extracellular matrix components such as collagen. Excessive fibrosis in tissues could greatly deteriorate the function of various tissues by hardening the tissues. Fibrosis is known to contribute to approximately 45% of all deaths in developed countries and is a critical issue in a variety of diseases, including cardiac fibrosis after myocardial infarction and smoking-induced pulmonary fibrosis, chronic renal failure, NASH, and refractory cancer. However, there are no definitive methods for fibrosis control so far, and a breakthrough therapy and drug for fibrosis is necessary. Tissue fibrosis is caused by myofibroblasts that produce extracellular matrix components such as collagens. Myofibroblasts do not exist in normal tissues; however, various cells are known to differentiate into myofibroblasts upon inflammation. Myofibroblasts are not present when tissues are normal but arise mainly from the differentiation of resident fibroblasts triggered by inflammation. However, the molecular mechanisms by which myofibroblasts overproduce fibrotic factors remain largely unknown. In our laboratory, we focus on the molecular mechanisms of myofibroblast differentiation and production of fibrotic factors to establish the basis for the creation of new fibrotic therapy. On the other hand, we are also investigating various cell death, which triggers for fibrosis. and hematopoietic stem cell niche.

Pharmaceutical Cell Biology

Teaching staff	Professor Yoshitaka Tanaka, Ph.D. Associate Professor Yuji Ishii, Ph.D. Assistant Professor Yuko Hirota, Ph.D. Assistant Professor Keiko Fujimoto, Ph.D.
Research	This laboratory focuses on lysosomes because they exhibit a number of important basic functions (digesting proteins, lipids, carbohydrates and organelles and supplying acid hydrolases for programmed cell death) as well as having a highly specialized organization and functions in specialized cells (melanosomes in melanocytes, lytic granules in lymphocytes)(Project 1). We want to understand the molecular basis of lysosomal membrane proteins and how they contribute to cell physiology. Our initial approach was to study the function of specific lysosomal membrane proteins. We have prepared and used knockout mice to understand their physiological significance and found that LAMP2 function plays a role in a number of human diseases. We subsequently showed that LGP85 responds to membrane traffic to lysosomes via the cell expression system. An important goal is to identify the protein machinery that regulates membrane traffic to lysosomes. Using specific probes and materials (antibodies, ligands and cDNAs), we have been studying the molecular mechanism of membrane traffic to lysosomes and successfully identified several molecules which regulate membrane traffic to lysosomes. Our research has implications for some neurodegenerative diseases, since lysosome dysfunction is directly linked to many human diseases. Lysosomal biogenesis has relevance to virus budding, and thus our research also has many potential implications for viral pathogenesis. This laboratory is also involved in the following toxicological areas: the molecular mechanism of dioxin toxicity (Project 2); and functional cooperation of phase I and II drug metabolizing enzymes (Project 3). In the Project 2, our main interest is focused on the molecular mechanism whereby dioxins produce their reproductive and developmental toxicity. Accumulating evidence we provided suggests that dioxin-mediated damage to fetal gonadotropins imprints defects which are continued until adult ages. The methodology how we can combat with TCDD-produced damage to next generations is also being investigated. We are trying to establish a new concept in the Project 3. It is well known that drug-metabolizing enzymes play an important role in the detoxification and activation of foreign chemicals. Although different sorts of drug-metabolizing enzymes have long been considered to work separately, our recent studies have demonstrated that cytochrome P450 (representative phase I enzyme) binds to phase II enzymes such as UDP-glucuronosyltransferase. This association is functional interaction resulting in a change in the function of both enzymes. It is one possibility that such interaction explains the inter-individual difference in drug sensitivity.

Green Pharmaceutical Chemistry

Teaching staff	Professor Takashi Ohshima, Ph.D. Lecturer Hiroyuki Morimoto, Ph.D. Assistant Professor Ryo Yazaki, Ph.D.
Research	The following topics are currently under investigation in our laboratories: 1. Development of New Environmentally Benign Catalytic Processes 2. Development of New Chemoselective Catalyses 3. Synthesis of Biologically Active Natural Products Using One-Pot Multistep Catalysis 4. Development of New Molecularly-Targeted Anticancer Drugs 5. Promotion of “Green Pharma”

Physical Chemistry for Life Science (Bio-functional Science)

Teaching staff	Professor Ken-ichi Yamada, Ph.D. Assistant Professor Yuta Matsuoka, Ph.D. Assistant Professor Kazushi Morimoto, Ph.D.
Research	The following topics are currently under investigation in Laboratory of Physical Chemistry for Life Science: 1. Development of Detection Probes and Structural Analysis Methods for Oxidized Lipids 2. Molecular Mechanism of Oxidized Lipids Related Diseases such as AMD, Dementia, and NASH 3. Drug Discovery Research Targeting for Oxidized Lipids 4. Promotion of Radical-omics Study 5. Development of Molecular Imaging and Theranostics Study

International Chemical and Physical Pharmacy(Bioorganic and Synthetic Chemistry)

Teaching staff	Associate Professor Mariko Aso, Ph.D
Research	The research activities of our laboratory have focused on the following topics: 1. Design of artificial nucleic acids with useful functions 2. Site specific protein modification for development of biodrugs 3. Development of bone targeting therapeutic proteins

Frontier in Biofunction of Nucleic Acid and Organic Chemistry

Teaching staff	Associate Professor Yosuke Taniguchi, Ph.D.
Research	1. Synthesis of artificial nucleoside analogues for the formation of the triplex DNA and development of oligonucleotide therapeutics. 2. Development of artificial nucleoside analogues for the recognition of oxidative nucleoside damage in DNA 3. Creation of nucleoside or nucleotide mimic.

Pharmaceutical Synthetic Chemistry

Teaching staff	Professor Go Hirai, Ph.D. Assistant Professor Makoto Yoritate, Ph.D.
Research	In our group, several research projects based on synthetic organic chemistry are in progress: 1. Development of novel bioactive-molecules designed based on natural products or biomolecules 2. Design of carbohydrates/glycolipids probes to clarify their mode-of-actions in cells 3. Development of synthetic strategy and methodology for novel structural motifs

Cellular Biochemistry

Teaching staff	Professor Masatoshi Fujita, M.D.,Ph.D. Assistant Professor Nozomi Sugimoto, Ph.D. Assistant Professor Torahiko Higashi, Ph.D.
Research	We have been clarifying molecular mechanisms of chromosomal DNA regulations, deregulation of which would lead to chromosomal instability and eventually cancer. Now, we have been especially focusing on: 1. Function and cell cycle regulation of DNA replication initiation proteins, ORC, CDC6, Cdt1, MCM and related factors. 2. Involvement of the replication initiation proteins in telomere homeostasis. 3. Molecular mechanisms for ATM- and ATR-mediated cellular responses to chromosomal stress and involvement of the replication initiation proteins in such process. 4. Relationship between chromatin regulations (by chromatin remodeler and histone chaperone) and replication/telomere/checkpoint regulations. 5. Novel anti-microtubule agents with carbazole and benzohydrazide structures we identified. 6. Search for Cdt1-geminin binding inhibitors that could selectively damage cancer cells by inducing re-replication.

Natural Products Chemistry

Teaching staff	Associate Professor Tomofumi Miyamoto, Ph.D.
Research	We have been developing the novel medicinal seed compounds from various natural resources (medicinal plants, marine invertebrates, micro-organisms, unused natural resources). Several research projects are in progress. 1. Search for new medicinal seeds derived from natural products. 2. Chemical biology and chemical ecology based on the natural products. 3. Isolation and structure determination of natural products with novel skeleton.

Pharmacognosy

Teaching staff	Professor Satoshi Morimoto, Ph.D. ※will retire on March,2023 Associate Professor Seiichi Sakamoto, Ph.D. Assistant Professor Naoya Shindo, Ph.D
Research	Research on *Cannabis sativa* ・Plant tissue culture for medicinal plant breeding ・Production of transgenic medicinal plant yielding high amount of bioactive secondary metabolite ・Quality control and standardization of crude drugs and Kampo products

Laboratory of Global Healthcare

Teaching staff	Associate Professor Jose Caaveiro, Ph.D. Assistant Professor Tomohiro Yamashita, Ph.D
Research	・Biomolecular recognition between proteins and drugs. ・Structural biology and thermodynamics of membrane proteins ・Novel therapeutic approaches against cancer, infection, and Parkinson's disease ・Drug discovery for pain and itch. ・Greenpharma research.

Clinical pharmacy and Pharmaceutical care

Teaching staff	Associate Professor　Takao Shimazoe, Ph.D. ※will retire on March,2024 Lecturer　Daisuke Kobayashi, Ph.D. Assistant Professor　Takehiro Kawashiri, Ph.D
Research	・Establishment of pharmaceutical education system ・Study on leftover drugs for reduction of medical expenses and improvement of adherence (Setsuyaku-bag campaign) ・Study of prevention and treatment for various diseases with drugs, herbs, foods, and so on ・Establishment of objective indexes in Kampo medicines ・Study on development of simultaneous determination of clinically used drugs for therapeutic drug monitoring ・Study on circadian rhythms ・Establishment of evaluation method for patient education on various diseases ・Studies on mechanisms and prevention of chemotherapy-induced peripheral neuropathy

Drug Discovery and Evolution

Teaching staff	Professor　Kenji Hamase, Ph.D. Assistant Professor　Manabu Nakazono, Ph.D. Assistant Professor　Takeyuki Akita, Ph.D Assistant Professor　Chiharu Ishii, Ph.D
Research	Drug discovery and diagnosis using chiral amino acid metabolomics. Anti-aging research focusing on isomerization of proteins. Industrial-academic-government cooperation research on heart and renal disorders. Development of analytical reagents, materials and instruments. Development of novel functional foods, beverages and cosmetics including D-amino acids.

International Biological and Clinical Pharmacy

Teaching staff	
Research	

Molecular and System Pharmacology

Teaching staff	Professor　Makoto Tsuda, Ph.D. Associate Professor　Takahiro Masuda, Ph.D. Assistant Professor　Miho Shiratori-Hayashi, Ph.D.
Research	Work in my laboratory is primarily directed to elucidating glia-neuron interactions in the spinal cord and brain and to understanding the cellular and molecular mechanisms of pain and itch signaling (in particular pathological chronic pain and itch) with the goal of counteracting these mechanisms in order to devise strategies for new types of pain and itch relieving medications.

Physiology

Teaching staff	Professor　Motohiro Nishida, Ph.D. Lecturer　Kazuhiro Nishiyama, Ph.D. Assistant Professor　Yuri Kato, Ph.D. Assistant Professor　Akiomi Nagasaka, Ph.D.
Research	1.　Comprehensive understanding of the maintenance of cardiovascular robustness via multi-level interactions 2.　Elucidation of the physiological role of reactive sulfur species and its therapeutic application 3.　Establishment of therapeutic strategies for curing intractable diseases targeting mitochondrial quality control 4.　Promotion of Green-Pharma research by collaborating with National Institutes

Clinical Pharmacology and Biopharmaceutics

Teaching staff	Professor Ichiro Ieiri, Ph.D. ※will retire on March,2024 Associate Professor　Nobuaki Egashira, Ph.D.
Research	The landmark of our research is to establish the rational and efficient personalized pharmacotherapy with sufficient safeness. The efficacy and safety of drug therapy is closely related to each pharmacokinetics, pharmacodynamics and toxicology. Therefore, we developed the various research techniques and intelligences as follows: 1. Clinical application of biomarkers reflecting pharmacological and toxicological responses in pharmacotherapy. 2. Establishment of countermeasures against drug-induced neurotoxicity and nephrotoxicity based on clarification of their molecular mechanisms. 3. Pharmacogenomics in personalized immunosuppressive therapy in organ transplant patients. 4. Clarification of pathophysiological role of renal drug transporters in patients with acute kidney injury and/or chronic kidney disease. 5. Establishment of personalized anticancer chemotherapy by pharmacokinetic, pharmacodynamics and pharmacogenomic analyses. 6. Pharmaceutical informatics to improve pharmaceutical practice by epidemiological approach

Translational Pharmaceutical Sciences

Teaching staff	Professor　Yoshito Kumagai, Ph.D. Professor　Takashi Uehara, Ph.D. Professor Hirosato Kondo, Ph.D
Research	Activation and disruption of cellular redox signaling pathways during combined exposure to environmental electrophiles Regulation of reactive sulfur species in covalent modification of cellular proteins caused by environmental electrophiles Research for the new generation of drug discovery Physiological/Pathophysiological roles of nitric oxide

Molecular Recognition of Chemotherapy

Teaching staff	Professor　Soichi Takiguchi, Ph.D.
Research	We are studying the physiological function of a cancer metastasis-associated protein and the mechanism of bone metastasis, and more using latest established technique.

R&D Laboratory for Innovative Biotherapeutics Science

Teaching staff	Professor Yoshikazu Yonemitsu , M.D.Ph.D. Associate Professor Yui Harada , Ph.D.
Research	・Development of novel and highly efficient RNA viral drug for treatment of peripheral arterial disease (SeV vector) ・Development of the new adoptive immunity−based medicine for cancer ～ NK cells ・Research of the rational targets for the development of therapeutics to manage malignancies ・High-throughput 3D tumor spheroid screening model for drug discovery ・Development of iPS-derived cell based extracorporeal-circulating artificial liver support ・Collaborations with industries (university-launched venture, pharmaceutical companies)

Drug Delivery System

Teaching staff	Professor Yasunari Michinaka , Ph. D. Associate Professor Hiroyuki Kojima, Ph. D. Associate Professor Kenji Hyodo, Ph. D.
Research	The role of drug delivery system (DDS) is to provide optimized drug therapy for patients, enhancing the efficacy and safety by controlling drug release rate and the amount to be absorbed in body. Together with this, recent research effort is targeted at making drugs easier to administer to patients. Further role of employing DDS for companies is product value maximization, including life cycle management.

Global Pharmacy

Teaching staff	Lecturer Eiji Kawanishi, Ph. D.
Research	The research is focused on follows (1) Identification of disease-specific molecular using clinical samples (2) Functional analysis of disease specific molecules (3) Molecular design for drug discovery (4) Development of conversion platform from macromolecule to small molecule (5) Research support for practical use

Kampo-Medicinal Chemistry

Teaching staff	
Research	

For further information, please visit the following website.
http://www.phar.kyushu-u.ac.jp/eng/index.php