

The 38th Annual Scientific Meeting of the Japanese Society of
Clinical Pharmacology and Therapeutics

**13th JSCPT-KSCPT Joint
Symposium of Clinical Pharmacology**

Bridging
Across

Date December 8(Fri), 2017

Venue Room502, Conference center 5th floor, PACIFICO YOKOHAMA

13th Joint Symposium of JSCPT-KSCPT
Program & Abstracts



Program

13th Joint Symposium of JSCPT-KSCPT

Session Title : 13th Joint Symposium of JSCPT-KSCPT

Date : Friday, December 8th, 2017 14:40-17:30

Venue : Room502, Conference center 5th floor, PACIFICO YOKOHAMA

14:40-15:50 First Session

The roles and leadership of clinical pharmacology in multiple regional clinical trials

First session Chairman : Min Soo Park

Hidefumi Nakamura

14:40-14:57 The roles and leadership of clinical pharmacology in multiple regional clinical trials “FIMASARTAN” Case

Seong-Choon Choe

14:57-15:14 MRCT from the perspectives of academia

Choon Ok Kim

15:14-15:31 Overseas Engagement of Clinical Trials to Develop Academic Seeds: Efforts of Osaka University Hospital.

Daisaku Nakatani

15:31-15:48 A Challenge of the Asian Clinical Research Network in Emerging Infectious Diseases

Tatsuo Iiyama

15:50-16:20 Break time

16:20-17:30 Second Session

Tissue- or organ-on-a- chip potential for clinical pharmacology studies

Second session Chairman : Jae-Gook Shin

Naohiko Anzai

16:20-16:37 Kidney on a chip : a new technology for predicting drug-induced nephrotoxicity

Sejoong Kim

16:37-16:54 Anisotropically organized three-dimensional culture platform for reconstruction of a hippocampal neural network

Nakwon Choi

16:54-17:11 Multi-thoroughput multiorgans-on-a-plate: a convenient platform for multi-organ efficacy and toxicity testing

Shinji Sugiura

17:11-17:28 Pharmacokinetic modeling and application of organs-on-a-chip technology for prediction of drug disposition and interaction

Yukio Kato

First Session : The roles and leadership of clinical pharmacology in multiple regional clinical trials

Chairman : Min Soo Park

(Yonsei University Health System, Korea)

Hidefumi Nakamura

(National Center for Child Health and Medicine, Japan)

Chairman



Min Soo Park

Min Soo Park graduated from Yonsei University College of Medicine in Seoul, Korea, and was trained in Pediatrics and Neonatology at Severance Hospital, Yonsei University. He received his Master of Science in Clinical Pharmacology at University of Aberdeen, UK, and his Ph.D. in Medicine at Ajou University, Korea. He served as Vice President of Korea National Enterprise for Clinical Trials (KoNECT) between 2008-2014. And he established the Clinical Trials Center of Severance Hospital and served as Director from 2004 to 2016.

Currently he is Professor in Pediatrics and Clinical Pharmacology at Yonsei University College of Medicine. In Yonsei University Health System, composed of Colleges of Medicine, Dentistry, Nursing, Severance Hospital and branch hospitals, he is serving as Director of Medical Science Research Affairs & President of University-Industry Foundation, (YUHS) since 2016. He is a member of the Board of Trustees of KoNECT. As the Chair of Korea Clinical Trials Global Initiative (KCGI), funded by Korea Ministry of Health and Welfare, he operates the Global Centers of Excellence Program and the Convergence Technology Development Program in efforts to boost and accelerate clinical development in Korea as well as globally. He is serving as Director of External Affairs of KSCPT.



Hidefumi Nakamura

Hidefumi Nakamura, MD, PhD is a Director for Clinical R & D, Department of Development Strategy, Center for Clinical Research and Development, National Center for Child Health and Development (NCCHD), Tokyo. He is a pediatrician and a pediatric pharmacologist trained at the Kurume University, Fukuoka (1987-1991), National Medical Center, Tokyo (1989-91), Hospital for Sick Children, Toronto, ON, Canada (1991-1996) and the Rainbow Babies and Childrens Hospital, Cleveland, OH, USA (1996-1999). He also has an experience as a senior reviewer at the Pharmaceutical and Medical Devices Evaluation Center, the former body of the Pharmaceutical and Medical Devices Agency (PMDA) (2000-2002). His team is currently receiving a grant for COE for pediatric clinical trials in Japan and also a member of the Global Research in Paediatrics (GRIP), a global research project funded by the EU 7th Framework Program. He is currently a member of several activities including the following: the scientific advisory board for the PMDA, the Pediatric Working Group for the Council for Off-label and Unlicensed Drugs by the Ministry of Health, Labour and Welfare (MHLW), Working Group of the Study Group on off-label and unlicensed Medical Devices of High Medical Need by the MHLW, the Committee on Drugs of Japan Pediatric Society, the Steering Committee for the Japan Society of Developmental Pharmacology and Therapeutics (vice chairman), and the Executive Committee of the Pediatric Pharmacology Section of the International Union on Pharmacology.

S1-1

The roles and leadership of clinical pharmacology in multiple regional clinical trials “FIMASARTAN” Case

Seong-Choon Choe

Deputy Head, R&D Center, Boryung Pharm. Co., Seoul, Republic of Korea

In Korea, the number of new chemical or biologic entity which was developed and registered is only 29 (as of August, 2017). The main issues which Korean pharma industry faces are lack of expertise and experience dealing with New Chemical Entity (NCE) clinical development and New Drug Application (NDA) dossier development. Foreign registration of drugs which were approved in Korea for the first time is very few. The experts for global drug development and registration is also limited in Korea and so we need cautious approach how to develop and register NCE globally.

Boryung Pharm. Co. developed fimasartan, new angiotensin receptor blocker (ARB) for management of hypertension since 1999 and registered it after review of Korean Food and Drug Administration (currently Ministry of Food and Drug Safety; MFDS) in 2010. At first, the company wanted to license out fimasartan at the early stage to multinational big pharma company to facilitate the development and registration process in developed countries such as US, EU and Japan. However, fimasartan was the 9th ARB in the world at that time, it was not easy for the company to register the product in developed markets.

Boryung made out-licensing contracts covering 51 countries (as of August, 2017) in Latin America, Russia, China, and South East Asia. Fimasartan and its combo products had already registered in 14 countries outside of Korea (as of August, 2017), more countries will be added soon. And the company will have strong willingness to register the product in developed countries, too. I will cover some details how multinational clinical trials focused on early “clinical pharmacology” trials are valuable and helpful for the registration of NCE in the world as well as show that strong leadership will be critical for these kinds of clinical development in the developed countries.



Educational background & Professional Experience

Year	Affiliation	Position
1997~1999	Seoul National University	Ph.D.
1999~2001	Chungnam National University Hospital	Assistant Professor
2002~2011	MSD, sanofi-aventis, Wyeth and Pfizer Korea	Medical Director
2014~	Boryung Pharm. Co.	Deputy R&D Head

Research Interests

Hypertension, Dyslipidemia, Atherosclerosis, New Drug Development, Clinical Pharmacology

S1-2

MRCT from the perspectives of academia

Choon Ok Kim

Yonsei University Health System, Republic of Korea

With the increasing globalization of drug development, it is more important to find out a strategy to make evidence regarding safety and efficacy more efficiently and cost effectively. Multi-regional clinical trials (MRCT) is a preferred strategy applied by sponsors for global drug evaluation. It is defined as a clinical trial conducted in more than one region under a single protocol. The use of MRCT has various advantages as follows: preventing clinical trials from conducting another countries repeatedly, enhancing enrollment from wider population and differing clinical situations, and facilitating simultaneous rather than sequential submissions for registration. Consequently, it makes the new or extended use of drug rapidly to patients worldwide, and, it could shorten the time and cost for drug development.

However, a MRCT is much more complicated than a trial conducted in a single region, and there is no clear global guidance on MRCT. It may be challenging in designing, conducting, analyzing, and evaluating data of MRCT. There are several papers to deal with these challenges more specifically. Among them, I would like to discuss about the region that is mentioned in the definition of MRCT. In the ICH E17, region may refer to a geographical region, country or regulatory region. Region is related to ethnic factors, and they are a major point of considering when planning MRCTs.



1. Qualification

- 2000 Bachelor of Biochemistry, Yonsei University, Republic of Korea
- 2004 Bachelor of Medicine, Inha University, Republic of Korea
- 2011 Master of Public Health, Yonsei University, Republic of Korea
- 2017 PhD Candidate, Clinical Pharmacology, Catholic University, Republic of Korea

2. Positions held

- 2005~2008 Resident, Department of Family Medicine, Severance Hospital, Republic of Korea
- 2008~2010 Clinical Fellow, Department of Family Medicine, Severance Hospital, Republic of Korea
- 2010~2012 Clinical Fellow, Department of Clinical Pharmacology, Severance Hospital, Republic of Korea
- 2012~Present Clinical Assistant Professor, Department of Clinical Pharmacology, Severance Hospital, Republic of Korea
- 2011~Present IRB Reviewer, Severance Hospital, Republic of Korea

Overseas Engagement of Clinical Trials to Develop Academic Seeds: Efforts of Osaka University Hospital.

Daisaku Nakatani, Junzo Seki, Xiang Yao, Yukio Tanaka, Hideaki Harada, Tomomi Yamada, Yoichi Yamamoto, Akira Myoi and Kouji Nishida

Department of Medical Innovation, Osaka University Hospital, Japan

As of October 2016, Osaka University Hospital was adopted as one of members of the Global Clinical Trial Development Project by Japan Agency for Medical Research and Development (AMED). We started to develop the infrastructure of this project. First of all, the Global Clinical Research Support Office (GCRSO) was established under the director of Department of medical innovation. The GCRSO has the secretariat function related to the Global Clinical Trial Development Project, and carry out the various administrative works.

The Osaka University Hospital collaborated with other hospitals which are the Clinical Research Core Hospital in Law and made an agreement in order to proceed this project. Besides, we developed a meeting with them aiming to resolve current issues when the academia would try to perform multiregional clinical trials with new drugs, devices and regenerative medicine and so on, which are derived from academia. The kick off meeting was held on end of August 2017. The main topics were planned to be as follows.

- 1) Cooperation on designing and implementation of global clinical trials /research.
- 2) Discover the seeds related to global clinical trials /research
- 3) Share the information on implementation of the global clinical trials / research.
- 4) Others.

The GCRSO conducts a Global Clinical Trials / Research Support Meeting on a regular basis in order to support and promote individual projects in Osaka University Hospital. As of today, we started to support three global clinical projects. In order to support and proceed these projects effectively, Global Project Managers (GPM) were allocated to the each project. The GPM may try to support the project to collect information on regulation and grant in other countries. Furthermore, we have tried to visit academic research organization in each country to make collaboration and develop infrastructure for conducting multiregional clinical trials. We would like to introduce our activity and discuss about efforts on global clinical research at Osaka University Hospital.



Dr. Nakatani graduated Kawasaki Medical School in 1995 and became a member of Osaka University Graduate School of Medicine, department of cardiovascular medicine. He started to work as a clinical fellow at Kawachi General Hospital and Sakurabashi Watanabe Hospital, one of the best affiliated hospitals of Osaka University Graduate School of Medicine, Osaka, Japan. After a 5-year experience as a cardiologist, he entered Osaka University Graduate School of Medicine and started his postgraduate course in 2000 to study the epidemiology and preventive medicine for cardiovascular disease in Japan. After getting his PhD, he worked as a postdoctoral clinical and research fellow at Osaka University Hospital and further specializing in risk stratification after acute myocardial infarction. Between 2007 and 2010, he worked at Stanford University, Center for Cardiovascular Technology as a postdoctoral fellow. His research focus was to investigate relationship between plaque characterization assessed by intravascular ultrasound (IVUS) and future cardiovascular events after newly developed coronary artery stent implantation. After leaving Stanford University, he returned to the Osaka University as an assistant professor at department of cardiovascular medicine. Between 2012 and 2014, he worked for the Ministry of Health, Labor and Welfare, Tokyo as an officer of the advanced medical service. He contributed to get approval for huge number of clinical trials with specified medical care coverage under the advanced medical service system. In 2014, He returned to the Osaka University Hospital again. Until now, he is belonging to both department of cardiovascular medicine and medical innovation as specialized associate professor. In 2016, He became a director of the Global Clinical Trial Support Office that is a branch of the medical innovation. He supports global projects not only internal but also external projects. His contribution may resolve the drug and device lag between other and our countries.

A Challenge of the Asian Clinical Research Network in Emerging Infectious Diseases

Tatsuo Iiyama

Department of International Trial Center for Clinical Sciences (CCS), National Center for Global Health and Medicine (NCGM), Japan

Progress in pharmaceutical industry regarding the research and development of new drugs and devices lead to a more careful concern about the usage of such products. Diversity of populations in terms of genetic and physiological factors [intrinsic factors], environmental and cultural factors, medical practice, regulatory issues [extrinsic factors] makes difficult the extrapolation of data from trials conducted elsewhere. To be approved in a new country, the pharmacokinetics, pharmacodynamics, dose-response, efficacy and safety of the new medicine should be well characterized in the foreign country. Furthermore, the conduct of clinical trial involves the commitment of huge financial means and especially if all phases of the trial should be repeated in each country.

To overcome these situations, Multi-Regional Clinical Trials (MRCTs) were implemented to expedite enrolment of participants and to facilitate a global approval of new investigational products concomitantly in different regions. This also helps for the expansion of new medical practices, advanced technologies and technical expertise into developing countries. The tripartite harmonized ICH developed the ICH E5 (R1) to deal with the effect of ethnic factors on the drug bioavailability, safety and efficacy. To complete the ICH E5 (R1) and to facilitate the acceptance of MRCT data by multiple regulatory agencies, the ICH E17 will be soon launched.

Clinical pharmacology, a science that studies drugs properties and theirs therapeutic effects in human, including safety, pharmacodynamics and pharmacokinetics is one of the key factors for the conduction of MRCT. Clinical pharmacologists can work in various sectors including academia, industry and government. One of their roles in office setting is to design and evaluate clinical trials. They are key persons during the conduction of MRCT because they have to evaluate the safety and the efficacy of new medicines, taking into account drug properties in relation with regional disparities.

Neglected diseases including emerging and re-emerging infectious diseases constitute a public health and global economy burden. Whatever their nature, they are easily transferred from one country to another and become a global threat. On the other side, with the emergence of antimicrobial resistance and given the regional diversities of populations, the implementation of MRCT becomes mandatory.

We develop a new academic CRO aiming to standardize medical practice, with capacity building programs for facilitating MRCT in concerned regions. For this purpose, we are going to start the online training program on MRCT planning and implementation. Clinical pharmacology expertise is one of essential key on our activities.



Management with communication skills and a 10 year's experience on facilitating clinical trials related to cancer researches and other fields.

I am passionate for finding new ways to diagnose and to treat neglected tropical diseases.

I focus on Multi-Regional Clinical Trials (MRCTs), to connect people beyond borders of languages, customs, and procedures, etc, this for a global advancement of clinical practice and safety of patients.

Second Session : Tissue- or organ-on-a- chip potential for clinical pharmacology studies

Chairman : Jae-Gook Shin

(Department of Pharmacology and Department of Clinical
Pharmacology, Inje University College of Medicine, Korea)

Naohiko Anzai

(Department of Pharmacology, Chiba University Graduate
School of Medicine, Japan)

Chairman



Jae-Gook Shin

Dr. Jae-Gook Shin is currently a Professor and Chair of the department of Pharmacology and Clinical Pharmacology and founding Director of the Pharmacogenomics Research Center at Inje University College of Medicine, Busan, Korea. He is also Director of the Global Center of Excellence in Clinical Trials at Inje University Busan Paik Hospital. Dr. Shin is currently serving as the Chair of the Board of Directors for the Korean Society for Clinical Pharmacology and Therapeutics (KSCPT). He has published over 280 papers in clinical pharmacology including Pharmacogenomics and personalized medicine, clinical PK/PD, DM/PK and drug interaction, PK/PD modeling, and other clinical pharmacology areas.



Naohiko Anzai

Dr. Naohiko Anzai is a Full Professor and the chairman of the Department of Pharmacology, Chiba University Graduate School of Medicine, and Head of Chiba University Library Inohana Library, Chiba, Japan. He is a Councilor and the member of Academic Committee as well as International Exchange Committee of JSCPT, a Councilor and the member of International Exchange Committee of Japanese Pharmacological Society, and a Councilor of the Physiological Society of Japan, etc. He published more than 100 papers in pharmacology and physiology, particularly regarding membrane transporters that are related to drug and nutrient (uric acid) transport and pharmacogenomics.

Kidney on a chip: a new technology for predicting drug-induced nephrotoxicity

Sejoong Kim

Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, Korea

The kidneys play a pivotal role in most drug removal processes and are important when evaluating drug safety. Kidney dysfunction resulting from various drugs is an important issue in clinical practice and during the process of drug development. Traditional in vivo animal experiments are limited with respect to the evaluation of drug efficacy and nephrotoxicity due to the discrepancies of drug pharmacokinetics and pharmacodynamics between humans and animals, and static cell culture experiments cannot fully reflect the real microphysiological environment in humans. A kidney on a chip is a microfluidic device that allows the culture of living renal cells in 3D channels and mimics the human microphysiological environment, enabling the simulation of actual drug filtering, absorption, and the secretion process. Recent microfluidic culturing technique developments may lead to advances in research on pharmacological interactions and drug-induced nephrotoxicity.



EXPERIENCE

Seoul National University Bundang Hospital, Seongnam, Republic of Korea — Associate Professor
September 2011 - PRESENT
Division of Nephrology, Department of Internal Medicine

Gachon University Gil Hospital, Incheon, Republic of Korea
Company — Assistant Professor
March 2008 - August 2011
Division of Nephrology, Department of Internal Medicine

University of Michigan, Ann Arbor, MI, USA — Postdoctoral Research Fellow
March 2014 - August 2015
Department of Biomedical Engineering

EDUCATION

Seoul National University College of Medicine, Seoul, Korea — Doctor of Medicine
March 1992 - February 1998
Seoul National University Hospital, 1998 (internship), 1998-2003 (Residency), 2006-2008 (Fellowship)

Seoul National University College of Medicine, Seoul, Korea — Ph. D. Degree
March 2006 - February 2008
Adaptive Mechanism of Sodium and Potassium Transporters in Chronic Renal Failure Rat Kidneys.

Anisotropically organized three-dimensional culture platform for reconstruction of a hippocampal neural network

Nakwon Choi

Center for BioMicrosystems, Brain Science Institute

Korea Institute of Science and Technology (KIST), Korea

In native tissues, cellular and acellular components are anisotropically organized and often aligned in specific directions, providing structural and mechanical properties for actuating biological functions. Thus, engineering alignment not only allows for emulation of native tissue structures but might also enable implementation of specific functionalities. However, achieving desired alignment is challenging, especially in three-dimensional constructs. By exploiting the elastomeric property of polydimethylsiloxane and fibrillogenesis kinetics of collagen, here we introduce a simple yet effective method to assemble and align fibrous structures in a multimodular three-dimensional conglomerate. Applying this method, we have reconstructed the CA3–CA1 hippocampal neural circuit three-dimensionally in a monolithic gel, in which CA3 neurons extend parallel axons to and synapse with CA1 neurons. Furthermore, we show that alignment of the fibrous scaffold facilitates the establishment of functional connectivity. This method can be applied for reconstructing other neural circuits or tissue units where anisotropic organization in a multi-modular structure is desired.



Education

- | | | |
|-----------------|--|--------------|
| 08/2004-12/2009 | Cornell University , School of Chemical and Biomolecular Engineering
Ph.D. in Chemical Engineering
Ph.D. Advisor: Prof. Abraham D. Stroock
Ph.D. Dissertation: "Microfluidic Biomaterials for in vitro 3D Culture"
M.S. in Chemical Engineering | Ithaca, NY |
| 03/1997-02/2004 | Seoul National University , School of Chemical and Biological Engineering
B.S. in Chemical Engineering | Seoul, Korea |

Research and Work Experience

- | | | |
|-----------------|--|---------------|
| 03/2017-present | Korea Institute of Science and Technology (KIST)
Center for BioMicrosystems, Brain Science Institute
Principal Research Scientist | Seoul, Korea |
| | Korea University of Science and Technology (UST)
Division of Bio-Medical Science & Technology (Biomedical Engineering)
KIST School
Associate Professor | Seoul, Korea |
| 07/2015-08/2017 | Hanyang University
Department of Medicine
Adjunct Professor | Seoul, Korea |
| 01/2012-02/2017 | Korea Institute of Science and Technology (KIST)
Center for BioMicrosystems, Brain Science Institute
Senior Research Scientist | Seoul, Korea |
| 06/2010-12/2011 | Novartis Institutes for Biomedical Research (NIBR)
Center for Proteomic Chemistry (CPC), Lead Finding Platform (LFP),
Hits Discovery Group (HDG)
Presidential Postdoctoral Fellow
Massachusetts Institute of Technology (MIT) , Department of Chemical Engineering
Research Affiliate (Postdoctoral Fellow) | Cambridge, MA |
| 01/2010-05/2010 | Cornell University , School of Chemical and Biomolecular Engineering
Postdoctoral Associate | Ithaca, NY |
| 08/2004-12/2009 | Cornell University , School of Chemical and Biomolecular Engineering
Research Assistant | Ithaca, NY |
| 12/2003-08/2004 | Korea Institute of Science and Technology (KIST)
Complex Fluids Research Laboratory
Research Scientist | Seoul, Korea |
| 06/2000-08/2002 | 8th United States Army (EUSA) , Headquarters, 20th Area Support Group
Korean Augmentation to the United States Army (KATUSA) | Busan, Korea |

S2-3

Multi-thoroughput multiorgans-on-a-plate: a convenient platform for multi-organ efficacy and toxicity testing

Shinji Sugiura

Drug Assay Device Research Group, Biotechnology Research Institute for DrugDiscovery, National Institute of Advanced Industrial Science and Technology (AIST), Japan

Organ-on-a-chip (OOC) is attracting attention as a new culture device, which reproduces the three-dimensional tissue structure, blood flow, and organ-specific movement on a microfluidic device to reproduce the organ specific function in vitro. Furthermore, multiorgans-on-a-chip (MOC), which connects multiple organ models, is an evaluation method that can detect “response from whole animal body”, which is usually obtained from animal experiments and clinical trials. Therefore, expectations from industry for OOCs and MOCs are rapidly growing. However, it is necessary to clear some hurdles in order to broaden the use of OOCs and MOCs as an alternatives to animal experiment. For example, cell cultivation using microfluidic devices, including OOCs and MOCs, generally require a troublesome tube connections and liquid delivery by a syringe pump, which are too complicated for biological researchers. This complicated system has been one of the obstacles to broaden the use of OOCs and MOCs. In order to address above mentioned issues, we have developed a multi-thoroughput multiorgans-on-a-plate as a convenient platform for multi-organ efficacy and toxicity testing. Our platform device possesses the following advantages for use in drug discovery: (i) simultaneous operation of multiple multi-organ culture units, (ii) design flexibility of the microfluidic network, (iii) pipette-friendly liquid handling, and (iv) applicability to experimental protocols and analytical methods widely used in microplates. We have demonstrated the usefulness of our system by detecting the effect of metabolism-dependent anticancer drugs in two-organ and four-organ systems. In addition, the advantages of our system for convenience and high-throughput work are very important for the industrial application in drug discovery. Together with our academic and industrial partners, we are working on a couple of application studies based on this multi-throughput multi-organ culture platform.



-2002 Ph. D. in Engineering., Department of Chemistry and Biotechnology, Graduate School of Engineering, The University of Tokyo

-2002-2004 Postdoctoral research associate, Radiology Division, National Cancer Center Hospital East

-2004-Current: Senior Scientist, Biotechnology Research Institute for Drug Discovery, National Institute of Advanced Industrial Science and Technology (AIST)

-2010-2011: Research Fellow at Brigham Wimen’s Hospital, Harvard University

-2015- Current: Associate Professor, School of Integrative and Global Majors, University of Tsukuba

Current interest: Organs-on-a-chip, Microfluidics, Tissue engineering, Biomaterials

Pharmacokinetic modeling and application of organs-on-a-chip technology for prediction of drug disposition and interaction

Yukio Kato, Takumi Kawanishi, and Hiroshi Arakawa

Department of Molecular Pharmacotherapeutics, Faculty of Pharmacy, Kanazawa University

Quantitative prediction of drug disposition profiles in humans is critical for appropriate drug development and pharmacotherapeutics. Nevertheless, *in vitro* experimental systems currently available have limitation in their application to such prediction of *in vivo* profiles. Especially, there would be limited *in vitro* systems available for analyzing long-term effects of drugs, indicating necessity of establishment of additional strategies for overcoming their defect in quantitative prediction. Physiologically-based pharmacokinetic (PBPK) modeling would be one of the promising tools to bridge a gap between *in vitro* and *in vivo*. The PBPK model incorporates multi-organ compartments, inter-organ blood flow, metabolism, and membrane permeability. We have recently constructed PBPK model for several anti-cancer agents to precisely describe change in their hepatic uptake, plasma protein binding, and their relevance to toxicity in renal-diseased patients. PBPK model may thus be useful tool to understand overall *in vivo* profiles, but sometimes include redundant number of parameters which cannot be definitively determined by the data and/or literature information available. Therefore, more physiologically relevant *in vitro* experimental systems would be needed for precise prediction. Organs/body-on-a-chip technology has recently been proposed as microphysiological systems incorporating multi-organs/cells and inter-organ microfluid, and are expected to be useful technologies for quantitatively predicting drug disposition and organ-organ interactions. Since this technology much more mimics physiological condition and allows to perform multiple sampling at various location, compared with traditional single organ/cells culture systems, it might be promising approach to obtain appropriate parameters in PBPK model. Based on microphysiological systems incorporating both liver and intestinal compartments, we have recently attempted to construct mathematical model to extrapolate drug-drug interaction via CYP3A metabolism. Interestingly, such PBPK modeling approach would also be helpful to optimize the microphysiological systems themselves to estimate appropriate values of parameters. Thus, mathematical modeling and multi-organs-on-a-chip technology are complementary, and their combination may help understanding complicated organ-organ interactions involved in drug disposition and efficacy.

[References] 1) Fujita K et al. *Pharm Res* 33: 269-282, 2016. 2) Taguchi T et al. *J Pharm Sci* 105: 2231-2239, 2016. 3) Masuo Y et al. *Pharm Res* 34: 1233-1243, 2017.



Biography

Dr. Yukio Kato graduated University of Tokyo in 1990 and received Ph.D. degree in 1998. He was appointed Research Associate in University of Tokyo in 1993, Visiting Fellow in National Institutes of Health, USA in 2001, Associate Professor in Kanazawa University in 2002, and Full Professor in Kanazawa University in 2008. He was also assigned in 2012 to a Visiting Research Staff in Sugiyama Laboratory, RIKEN.

His major research interests are transporter-mediated drug disposition, efficacy and toxicity, transporter-related inflammation and diseases, and protein-protein interaction and functional regulation of xenobiotic transporters. He published 159 original research articles including 5 Nature journal series papers, and 13 review articles.