第8回日中薬理学・臨床薬理学
ジョイントミーティング

The 8th Japan-China Joint Meeting of Basic and Clinical Pharmacology

Wed., March 10, 2021 Room A 13:30−17:00

札幌コンベンションセンター

SAPPORO CONVENTION CENTER

Welcome Message

On behalf of the Japanese Pharmacological Society and the Organizing Committee of the 94th Annual Meeting of the Japanese Pharmacological Society, we cordially invite you to attend the 8th Japan-China Joint Meeting of Basic and Clinical Pharmacology. This joint meeting will be held as the Japan-China Joint Session of the 94th Annual Meeting of the Japanese Pharmacological Society held in Sapporo on March 10, 2021.
The last Japan-China Joint Meeting of Basic and Clinical Pharmacology was organized by the Chinese Pharmacological Society, and it was held in Kunming, Yunnan Province, China, at August 4-5, 2019. The Japan-China Joint Meeting has picked up the most advanced topics on pharmacology and contributes great progress of pharmacological sciences in both countries. It should be noted that young pharmacologists and students in both countries could get to know each other through the Joint Meeting, and had grown up to leading the pharmacological sciences in both countries.
This Joint Meeting is the important basis of continued collaboration and partnership on basic and clinical pharmacology between Japan and China. This Joint Meeting is planned to provide excellent opportunities to discuss among the scientists for pharmacological research, and to foster active pharmacologists responsible for international collaboration in the future. This meeting is sponsored by several Japanese foundations. The organizing committee appreciates their great contributions for giving us this opportunity for organizing the wonderful lectures on basic and clinical pharmacology. It is worth noting that this will be the first Joint Meeting to be held online due to the epidemic of COVID-19 infections in the world.

Mitsuhiro Yoshioka, M.D., Ph.D
President, The 94th Annual Meeting of the Japanese Pharmacological Society
Dean, Faculty of Medicine, Hokkaido University
Professor, Department of Neuropharmacology, Faculty of Medicine, Hokkaido University

Kazuhiko Yanai, MD., Ph.D.
President, the Japanese Pharmacological Society
Professor, Department of Pharmacology, Tohoku University Graduate School of Medicine

Dear Colleagues,

As the 8th Japan-China Joint Meeting of Basic and Clinical Pharmacology is coming, on behalf of Chinese Pharmacological Society, I wish to extend our warm greetings and sincere invitations to all our colleagues on pharmacological research in both Japan and China.

With great endeavors and struggles, we bid farewell to the extraordinary 2020, and embraced the beautiful spring of 2021. Looking back at 2020, The sudden pandemic of COVID-19 hit the world with a great threat to the people's life and health. People around the world went all out to fight the pandemic, and have achieved great progress. During this process, we deeply realized the important role of science and technology, and also the essential significance of innovation and rapid new drug R&D in prevention and control of the pandemic.

The Japan-China Joint Meeting of Basic and Clinical Pharmacology co-organized by the Chinese Pharmacological Society (CNPHARS), the Japanese Pharmacological Society (JPS) and the Japanese Society of Clinical Pharmacology and Therapeutics (JSCPT) has been successfully held for 7 times, playing an important role in promoting the academic exchanges and cooperation, improving the mutual understanding and friendship, and boosting the development of pharmacology in our two countries.

The topics of this joint meeting are Molecular Pharmacology Study and Early Clinical Trials related pharmacological research which are all the current hot research areas in basic pharmacology and clinical pharmacology. Due to COVID-19, this meeting will be a virtual one. JPS and JSCPT are making thoughtful and meticulous preparations for this event. We believe that the meeting will be a complete success as always.

Dear colleagues, welcome to attend this meeting, take part in the scientific communications, and make new contributions to the development of pharmacology.

Yongxiang Zhang

The President of Chinese Pharmacological Society

Chair

Jianguo Chen
Tongji Med. Coll., Huazhong Univ. Sci. Technol.

Yoshikatsu Kanai
Grad. Sch. Med., Osaka Univ.

Wei Wei
Inst. Clin. Pharmacol., Anhui Med. Univ.

Ichiro Ieiri
Grad. Sch. Pharmaceut. Sci. Kyushu Univ.

Speaker

3-S32-1 Networks of organelle function in cardiovascular diseases
Yong Zhang
Dept. Pharmacol., Coll. Pharm., Harbin Med. Univ.

3-S32-2 Redox regulation of mitochondrial quality as a therapeutic target of cardiac senescence
Motohiro Nishida
Grad. Sch. Pharm. Sci., Kyushu Univ. / NIPS

3-S32-3 Accelerating development of proton pump inhibitors: a mechanism-based PK/PD model to optimize dose design with ilaprazole as a case drug
Hongyun Wang
Clin. Pharm. Res. Cent., Peking Union Med. Coll. Hosp.

3-S32-4 Development of endogenous biomarkers to assess drug-transporter-mediated drug-drug interactions in drug development
Hiroyuki Kusuhara
Grad. Sch. Pharm. Sci., Univ. Tokyo

* The presentation order will be changed as follows: 1. Hongyun Wang(3-S32-3), 2. Hiroyuki Kusuhara(3-S32-4), 3. Yong Zhang(3-S32-1), 4. Motohiro Nishida(3-S32-2)

3-S32-1

Networks of organelle function in cardiovascular diseases

Yong Zhang

Dept. Pharmacol., Coll. Pharm., Harbin Med. Univ.

Cardiovascular diseases (CVDs) are the leader global cause of death. Cell organelles determines cells fate in CVDs. Here we studied the regulatory effects of non-coding RNAs on function and crosstalk among cell organelles especially in endoplasmic reticulum (ER) and mitochondria in different CVDs. In mitochondria, we found mitomiR-4485-3p and lncRNA MIAT impaired myocardial infarction (MI) by inducing cardiomyocytes apoptosis. MitomiR-4485-3p released to cytosol in response to injury in MI, which targeted PPARα and induced dysregulation of mitochondrial energy metabolism and apoptosis in cardiomyocytes. In addition, lncRNA MIAT induces cardiomyocytes apoptosis and impairs cardiac contractile function by acting on mitochondrial translocator protein TSPO in MI. In ER, we identified lncRNA ZFAS1 as a regulator of calcium homeostasis in a mouse model of pressure-overload HF. We found that circulating level of lncRNA ZFAS1 was significantly lower in MI than in non-MI patients. Then we revealed lncRNA-ZFAS1 as a natural inhibitor of SERCA2a by binding to SERCA2a protein. Abnormally increased ZFAS1 in MI significantly impaired cardiac function. Most prominently, we identified a region of high degree conservation across man and mouse species named functional sequence domain of ZFAS1, which is much shorter and responsible for its deleterious effects. Our study identified functional non-coding RNAs as network hub of organelles in CVDs, which provides potential therapeutic agents for ameliorating cardiac dysfunction.

3-S32-2

Redox regulation of mitochondrial quality as a therapeutic target of cardiac senescence

Motohiro Nishida

Grad. Sch. Pharm. Sci., Kyushu Univ. / NIPS

Mitochondria are dynamic organelles that continuously undergo fission and fusion, which are necessary for maintaining bioenergetic homeostasis and robustness in heart. Mitochondrial fission and fusion cycle is precisely regulated by three GTP-binding proteins, dynamin-related protein 1 (Drp1), mitofusins (Mfn1 and mfn2) and optic atrophy 1 (Opa1), and these three G proteins have redox-sensitive cysteine (Cys) residues. Especially, mitochondria predominantly show tubular form in adult cardiomyocytes and are reported to be fragmented by the exposure to electrophilic chemical substances produced by hypoxic and hyperglycemic stress. We found that depolysulfidation of Cys624 on Drp1, caused by endogenous or exogenous electrophiles, increased basal Drp1 GTPase activity as well as cardiac vulnerability to hemodynamic load in mouse hearts. Reactive sulfide species such as Cys persulfide produced through mitochondria-localized Cys tRNA synthetase (CARS2) preferentially eliminate and metabolize electrophiles. Protein persulfide detection assay revealed that endogenous Drp1 protein possesses several Cys persulfides in a CARS2) dependent manner, and exposure to environmental electrophiles such as methylmercury (MeHg) reduced Drp1 persulfide levels. Supplementation of sulfur to Cys-624 by exogenous treatment with NaHS completely abolished MeHg-induced sulfur deprivation of Drp1 protein as well as exacerbation of myocardial injury induced by mechanical stress. These results strongly suggest that formation of Drp1 Cys624 polysulfidation negatively regulates electrophile-mediated mitochondrial hyperfission and cardiac stress resistance against environmental stresses.

3-S32-3

Application of Clinical Pharmacology in Early Clinical Drug Development: PK/PD studies of a new proton pump inhibitor

Hongyun Wang

Clin. Pharm. Res. Cent., Peking Union Med. Coll. Hosp.

Clinical pharmacology is critical in drug development. This presentation introduces the current status of its application in China, and then presents a PK/PD model for proton-pump inhibitor (PPI) drugs. This mechanism-based model is established using ilaprazole as a case drug in which food effect and circadian rhythm are taken into account, and it provides a potential strategy to accelerate the development of novel PPIs.

3-S32-4

Development of endogenous biomarkers to assess drug-transporter-mediated drug-drug interactions in drug development

Hiroyuki Kusuhara

Grad. Sch. Pharm. Sci., Univ. Tokyo

Drug transporters act as determinant for the clearance of drugs from the blood circulation in the liver and kidney. Inhibition of such transporters by drugs causes accumulation of their substrate drugs, and thereby increasing the risk of adverse reactions in combination use. In drug development, it is prerequisite to assess the inhibition potency of the investigation drugs against major drug transporters. Recently, endogenous biomarkers have emerged to advance this risk assessment in the clinical stage. We identified some endogenous substrates in healthy volunteers using well characterized inhibitors and metabolomic approach for the drug transporters such as OATP1B1/1B3, OAT1, OAT3 and OCT2, MATE1/2-K whose pharmacokinetic parameters, such as AUC and renal clearance (CLR), changed according to the degree of inhibition of drug transporters. Physiologically based pharmacokinetic (PBPK) models for the endogenous substrates have been also constructed to explain the effect of inhibitors. PBPK-model based approach are highly expected to extrapolate the biomarker data to the DDI. The endogenous biomarkers are highly expected to improve predictability of the DDI in early phase of clinical stage of drug development, and aids design of the strategy to de-risk of the DDI in the clinical settings.