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35th Anniversary

SCHOOL OF PHARMACY
FACULTY OF MEDICINE
THE CHINESE UNIVERSITY OF HONG KONG

PHARMACY SEMINAR

30 Nov, 2017 (Thu) | 3:30p.m. – 5:30p.m.

G01, G/F, Lo Kwee-Seong Integrated Biomedical Sciences Building, Area 39, CUHK

Seminar 1 3:30p.m. – 4:30p.m.

"Regulation of Drug Transporters by Post-Translational Modifications"

Presented by
Prof. Guofeng You
Ph.D.
Distinguished Professor
Department Pharmaceutics
Ernest Mario School of Pharmacy
Rutgers University

Abstract

Drug transporters encoded by solute carrier (SLC) family are distributed in multiple organs including kidney, liver, placenta, brain, and intestine, where they mediate the absorption, distribution, and excretion of a diverse array of environmental toxins and clinically important drugs. Alterations in the expression and function of these transporters play important roles in intra- and inter-individual variability of the therapeutic efficacy and the toxicity of many drugs. Consequently, the activity of these transporters must be highly regulated to carry out their normal functions. While the regulation of these transporters tightly depends on genetic mechanisms, many studies have demonstrated that these transporters are the target of various post-translational modifications. More importantly, these post-translational modifications, although different widely with respect to their biological functions, often communicate, and jointly affect the properties of common substrate proteins. This presentation will highlight the recent advances in identifying the posttranslational modifications underlying the regulation of the drug transporters of SLC family, focusing on the organic anion transporters. Such mechanisms are pivotal not only in physiological conditions, but also in diseases.

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Biosketch

Dr. Guofeng You is a Distinguished Professor in the Department Pharmaceutics, at Rutgers University, USA. Her research interest focuses on the elucidation of the molecular, cellular and functional characteristics of drug/xenobiotic transporters, their implications in human physiology and diseases, and their applications to drug therapy. Dr. You has trained many Ph.D., M.S. students, and postdoctoral fellows, and has published numerous original research articles in the field of drug transport. Dr. You has been serving on the grant review panels of the National Institutes of Health, and is on the Editorial Boards of leading journals. She is the coeditor for the first and the second editions of the book "Drug Transporters – Molecular Characterization and Role in Drug Disposition" (Wiley, 2007 and 2014). Dr. You teaches Introduction to Pharmaceutics to the PharmD students and The Roles of Membrane Transporters in Drug Disposition to the PhD/MS students.

Seminar 2 4:30p.m. – 5:30p.m.

"Transporter Gene-Environment Interactions in Neurode-generation"

Presented by
Prof. Lauren Aleksunes
Pharm.D., Ph.D., DABT
Associate Professor
Department of Pharmacology and Toxicology
Ernest Mario School of Pharmacy
Rutgers University

Abstract

The blood-brain barrier restricts the access of xenobiotics from gaining entry into the brain parenchyma. This is an advantageous mechanism that protects against neurotoxicity but can also limit the brain penetration of neuroactive drugs. We have recently demonstrated the ability of the multidrug resistance protein 1 (MDR1, P-glycoprotein) to efflux the neurotoxic herbicide, paraquat. Pharmacological and genetic inhibition of MDR1 increases paraquat accumulation in human blood-brain barrier cells. Moreover, Mdr1a/1b-null mice exhibit significant loss of dopaminergic neurons in the substantia nigra pars compacta after a single dose of paraquat, a response not observed in wild-type mice until after the second dose. Because of the important neuroprotective properties, we have begun to delineate novel mechanisms regulating MDR1 in the blood-brain barrier. Interestingly, inhibition of histone deacetylases using commonly prescribed medications enhances the expression and function of MDR1 in human blood-brain barrier cells. This up-regulation results from enhanced histone acetylation and activation of transcription factor signaling. Taken together, our research has identified a novel neuroprotective function of MDR1 to prevent neurodegeneration that may be modulated by activation of histone signaling.

Biosketch

Dr. Lauren Aleksunes is an Associate Professor in the Ernest Mario School of Pharmacy at Rutgers University. She is also a resident scientist in the Environmental and Occupational Health Sciences Institute. She received her Pharm.D. degree in 2002 and Ph.D. degree in Pharmacology & Toxicology from the University of Connecticut in 2006. Lauren was a postdoctoral fellow at the University of Kansas Medical Center from 2007 to 2009 during which time she received a K99/R00 Pathway to Independence Grant from NIH. In 2009, Lauren joined Rutgers University where her research interests expanded into the investigation of xenobiotic and endobiotic metabolism and transport in the placenta, brain, liver and kidneys. Projects in the Aleksunes lab span basic research questions about transporter regulation to translational studies in humans. These studies include the epigenetic, genetic, transcriptional and pathologic regulation of transport pathways. For her research, Lauren received the Achievement Award from the Society of Toxicology in 2016. She has published over 100 papers and serves on the editorial boards of Drug Metabolism and Disposition and Toxicology and Applied Pharmacology. In addition, Lauren is passionate for undergraduate and graduate education. She directs the NIH T32-funded Joint Graduate Program in Toxicology and the NIH R25-funded Summer Undergraduate Research Fellowship in the School of Pharmacy.