



SCHOOL OF PHARMACY

FACULTY OF MEDICINE

THE CHINESE UNIVERSITY OF HONG KONG

PHARMACY SEMINAR

9 FEBRUARY, 2018 (FRIDAY) 4:00P.M. – 5:30P.M.

G02, G/F, LO KWEE-SEONG INTEGRATED BIOMEDICAL SCIENCES BUILDING, AREA 39, THE CHINESE UNIVERSITY OF HONG KONG

SEMINAR 1 (4:00p.m. – 4:45p.m.)

“Service Learning in Pharmacy: CARE for Haiti”

Presented by

Prof. Cheryl L. ZIMMERMAN, Ph.D.

Professor of Pharmaceutics, Emeritus
College of Pharmacy
University of Minnesota
U.S.A.



Abstract

Clinics and Relief Efforts (CARE) for Haiti was established in 2011 by University of Minnesota College of Pharmacy students to provide primary care in a rural area of Haiti. Beginning in 2012, an interprofessional team has traveled to Chabin, Haiti on an annual basis and set up a 3.5-day clinic to provide acute care in this small mountainous community. The interprofessional team includes 8-10 Pharmacy students (PD1-PD3), 2 pharmacist/preceptors, a nurse, physicians and translators. The funds for the initiative are raised by the Pharmacy students. During the most recent trip in March 2017, the CARE clinic served 523 patients and dispensed 2170 prescriptions.

Biosketch

Cheryl L. Zimmerman is Professor Emeritus of Pharmaceutics at the University of Minnesota College of Pharmacy, Minneapolis MN. She received her B.S. in Pharmacy at the University of Wisconsin in 1976 and her Ph.D. in Pharmaceutics at the University of Washington in 1983. She then joined the faculty of the University of Minnesota, where she taught and did research until 2016. Her research interests included pharmacokinetics and drug metabolism, in particular the influence of intestinal metabolism on the activation of retinoids and nucleotide prodrugs. She was active in the leadership of the AAPS, including serving as a Member-at-Large and Chair of the PPDM section. She is an AAPS Fellow, and a University of Minnesota Distinguished Teacher.

SEMINAR 2 (4:45p.m. – 5:30p.m.)

“Translation of Data from Mouse to Man: How to Go from Point A to Point B”

Presented by

Prof. K. Sandy PANG, Ph.D.

Professor of Pharmacy and Pharmacology
Leslie Dan Faculty of Pharmacy
University of Toronto
Canada



Abstract

We highlight our works on the mouse to provide information on $1\alpha,25\text{-dihydroxylvitamin D}_3$ [$1,25(\text{OH})_2\text{D}_3$] active metabolite and natural ligand of the vitamin D receptor (VDR), to predict data in man. Temporal data of $1,25(\text{OH})_2\text{D}_3$ and fold-changes in mRNA of VDR target-genes in response to intraperitoneal doses of $1,25(\text{OH})_2\text{D}_3$ provided the backbone data on the E_{max} or I_{max} and EC_{50} or IC_{50} values, showing that $1,25(\text{OH})_2\text{D}_3$ inhibited its synthetic enzyme, mCYP27B1, and induced its degradation enzyme, mCYP24A1, providing shorter half-lives and higher clearances at higher doses. We proceeded to build physiologically-based pharmacokinetic (PBPK) models, which showed that $1,25(\text{OH})_2\text{D}_3$ reduced plasma and liver cholesterol via inhibition of liver small heterodimer partner (mSHP), the repressive nuclear receptor of mCYP7A1 (rate-limiting enzyme for cholesterol metabolism) and brain b-amyloid peptides, precursors of plaques, via induction of MDR1 (multidrug resistance protein and its gene product P-glycoprotein), and increased plasma calcium levels via induction of the calcium channel, mTRPV6. These events were explained well by pharmacodynamic (PD) modeling. The parameters describing $1,25(\text{OH})_2\text{D}_3$ disposition and the tight, feedback-regulation of $1,25(\text{OH})_2\text{D}_3$ on mCYP27B1 and mCYP24A1 were scaled up to predict the published, human data of $1,25(\text{OH})_2\text{D}_3$ for cancer patients, who were given $1,25(\text{OH})_2\text{D}_3$ intravenously or orally. The intrinsic clearances of CYP24A1 in kidney, liver, intestine and brain for man were adjusted according to tissue weights. First order rate constants (such as absorption rate constant or k_a) were scaled allometrically based on a power function = $a \cdot W^b$, with simulations using ADAPT5®. **Conclusion:** The PBPK-PD model was successful to translate $1,25(\text{OH})_2\text{D}_3$ data from mouse to man.

Biosketch

K. Sandy Pang received her BSc (Pharmacy) from the University of Toronto then Ph.D. from the University of California at San Francisco with Dr. Malcolm Rowland. After a postdoctoral fellowship at NIH with Dr. James R. Gillette, Sandy started her career in academia. She is now Professor of Pharmacy and Pharmacology at the University of Toronto. Sandy's work covers fields in pharmacokinetics and drug metabolism/transport and regulation/influence of nuclear receptors. Her research aims towards a mechanistic understanding of drug and metabolite handling, by embracing experimentation on organ or whole body, physiologically-based pharmacokinetic and pharmacodynamic modeling, and pharmacological pursuits. Her works on the vitamin D receptor reveals VDR regulation of CYP7A1, rate-limiting enzyme in cholesterol metabolism on lowering cholesterol via repression of the small heterodimer partner, and up-regulation of the multidrug resistance associated protein for reducing brain beta amyloid peptides. Sandy has served on various leadership positions in AAPS, AAAS, AASPET, and ISSX and has published over 250 original articles/chapters/reviews. She was the recipient of the NIH Research Career Development Award, Faculty Development award from MRC Canada, McNeil Award from Faculties of Pharmacies in Canada, Research Achievement Award in PPDM from AAPS and Award from the Nagai Foundation.

