NUS National University of Singapore | Department of Pharmacy, Faculty of Science

AY1819 Semester 2 Postgraduate Seminar
25 February 2019
S4 Level 2, PPS Hub
9 am - 12.30 pm

Program

9 - 9.15 am	Opening Address (Assoc Prof Eric Chan)
9.15 - 9.45 am	Mr Lee Sze Han
9.45 - 10.15 am	Ms Chen Shiyan
10.15 - 10.45 am	Ms Wong Xin Yi
10.45 - 11 am	Break
11 - 11.30 am	Ms Cai Yiying
11.30 am - 12 pm	Mr Ouyang Hongyi
12 - 12.30 pm	Mr Tay Yong Soon Justin

ALL ARE WELCOME

*** mandatory for all PG students**

Understanding pathology and discovering biomarkers in bladder cancer via an integrated systems biology approach

Mr Lee Sze Han
Supervisor: Assoc Prof Eric Chan

ABSTRACT An understanding of disease pathology is essential for its screening and intervention. Using an integrated systems biology approach, we investigated the pathology of bladder cancer (BC), a recurrent malignancy with the highest lifetime management cost across all cancers. Global urinary metabolomics yielded differentiating metabolic signatures between diseased and controls, one of which was the tryptophan-kynurenine pathway. A follow-up case-control study replicated the enhanced catabolism of tryptophan to kynurenine in BC, and showed increased expression of the mediating enzyme, indoleamine 2,3-dioxygenase 1 (IDO1). Our findings corroborate with other clinical studies and human bladder cancer cell lines, highlighting IDO1 as a potential therapeutic target. We are currently evaluating (1) the longitudinal variation of tryptophan and kynurenine in patients undergoing clinically routine treatment, and (2) a novel combination therapy containing an IDO1 inhibitor (BMS-986205) in orthotopically-implanted BC mice. We envision these studies to yield results to improve surveillance and therapy of BC significantly.

BIOGRAPHY Lee Sze Han graduated from the National University of Singapore in 2014 with a BSc (Pharmacy) (Hons) and was recipient of the Lijen Industrial Development Medal for excellence in his Honours Project. He underwent pre-registration preceptorship at Khoo Teck Puat hospital and is a registered pharmacist under the Singapore Pharmacy Council. Funded by the President's Graduate Fellowship, he is currently pursuing his PhD degree under the supervision of A/Prof Eric Chan in the Department of Pharmacy, National University of Singapore. Sze Han’s academic research focuses on untargeted and targeted mass spectrometry-based metagenomics for the study of urological and gastrointestinal diseases.

The Regulation of Human Aldehyde Oxidase Expression by Modulators of Pregnane X Receptor in LS180 Colon Adenocarcinoma

Ms Chen Shiyan
Supervisor: Asst Prof Lau A.J.

ABSTRACT Aldehyde oxidase (AOX-1) is a phase I drug-metabolizing enzyme that catalyzes the biotransformation of a broad variety of xenobiotics, including aromatic N-heterocycles commonly present in drugs and drug candidates. Despite the increasing role of AOX-1 in drug metabolism and toxicity, very little is known about the factors regulating AOX-1 gene expression in human. Pregnane X receptor (PXR) is a nuclear receptor that is activated by many structurally-diverse drugs and chemicals. It functions as an important regulator of drug disposition. Activation of PXR leads to induction of many genes, including major drug-metabolizing enzymes (e.g. CYP3A4, UGT1A1) and drug transporters (e.g. ABCB1). To date, it is not known whether PXR regulates AOX-1. In this project, we found that human AOX-1 expression is regulated by modulators of PXR, suggesting the possibility of an interaction between a PXR modulator and an AOX-1 drug substrate when they are administered concurrently.

BIOGRAPHY Chen Shiyan graduated with a Specialist Degree in Biochemistry and a Major Degree in Human Biology (Hons) from The University of Toronto in Canada in 2013. She is currently pursuing her PhD in Department of Pharmacy, National University of Singapore, under the supervision of Dr Lau Aik Jiang. Her research interests focus on the regulation of the expression and function of the drug-metabolizing enzyme aldehyde oxidase and the pharmacological and toxicological consequences upon its modulation.

Performance of Single Nucleotide Polymorphisms in Breast Cancer Risk Prediction Models: A Systematic Review and Meta-analysis

Ms Wong Xin Yi
Supervisor: Asst Prof Wee H.L.

ABSTRACT Breast cancer is the most common cancer among women and is rising in incidence worldwide. Early detection and mortality reduction are possible with mammography screening. Researchers have shown that Single Nucleotide Polymorphisms (SNP) risk information can potentially improve the accuracy of breast cancer risk prediction. This can translate into a more efficient risk-based screening programme. We aim to review and assess the performance of SNP-enhanced risk prediction models.

Studies that reported Area Under the receiver operating characteristic Curve (AUC) and/or Net Reclassification Improvement for both traditional and SNP-enhanced risk models were identified. Meta-analyses were conducted to compare across all models and within similar baseline risk models.

Addition of SNP information improved model performance, despite the lack of trend between AUC improvement and number of SNPs. It could be most beneficial for women at intermediate risk. Screening could be a two-step process where a questionnaire is first used to identify intermediate-risk individuals, followed by SNP testing for these women only.

BIOGRAPHY Wong Xin Yi graduated with BSc Pharmacy (Hons) from the National University of Singapore in 2012, and practised at Khoo Teck Puat Hospital as a pharmacist until 2015. She is currently pursuing her Ph.D. under the supervision of Dr Wee Hwee-Lin. Her research investigates the acceptability and cost-effectiveness of risk-based breast cancer screening.

The economic burden of healthcare associated infections caused by carbapenem-resistant Enterobacteriaceae in Singapore

Ms Cai Yiying
Supervisor: Assoc Prof Christine Teng
Co-Supervisor: Assoc Prof Andrea Kwa

ABSTRACT Healthcare-associated infections (HAIs) caused by carbapenem-resistant Enterobacteriaceae (CRE) is a mounting public health crisis. Quantifying the economic burden of CRE HAIs to hospitals can assist decision makers in determining the investment in CRE prevention and control. Hence, we determined the economic burden of CRE HAIs from the hospital's perspective, and compared it to the cost of a carbapenem-susceptible Enterobacteriaceae (CSE) infection. In addition, we extrapolated the cost data to the CRE incidence in Singapore, and further conducted four scenario analyses. We found that the median cost of a single CRE HAI from the hospital perspective was markedly higher than a CSE HAI, with more than half of the costs attributable to loss in opportunity costs due to lost bed-days and productivity losses of healthcare workers. Within a single year, CRE HAIs will cost Singapore hospitals more than SGD$10 million, highlighting the substantial costs to the hospital associated to CRE in Singapore.

BIOGRAPHY Cai Yiying graduated from NUS pharmacy in Year 2008. She obtained a Master in Infectious Diseases from the London School of Hygiene and Tropical Medicine in 2013, and currently works as a Specialist pharmacist in Singapore General Hospital. She joined NUS Pharmacy in 2015 as a part-time student to pursue her PhD, and her research interest is on the epidemiology on healthcare infections caused by carbapenem-resistant Gram negative bacteria.

Effect of drug particle size and lipid additives on the taste-masking and sustained release properties of paraffin wax in spray congealing

Mr Ouyang Hongyi
Supervisor: Assoc Prof Chan L.W.
Co-Supervisor: Assoc Prof Paul Heng

ABSTRACT Paraffin wax has not been well investigated for developing specialized drug delivery systems. Being hydrophobic and readily meltable, it is potentially useful for producing spray-congealed drug-loaded microparticles with taste-masking and sustained release properties. However, these desired properties will be hampered if the surface drug particles are not properly coated by the paraffin wax matrix. Moreover, highly viscous melts are unsuitable for spray congealing. It is therefore of interest to understand the effects of various formulation parameters to achieve the desired outcome. In this study, drug-loaded paraffin wax microparticles were produced by spray congealing. The effects of drug particle size and lipid additives, such as stearic acid, cetyl alcohol and cetyl esters, on the melt viscosity and degree of surface drug coating by paraffin wax were investigated. A judicious choice of matrix materials and drug is important for successful spray congealing and production of microparticles with desired characteristics.

BIOGRAPHY Ouyang Hongyi graduated with a Bachelor of Science (Pharmacy) (Hons.) degree from the National University of Singapore (NUS) in 2013. He completed his pre-registration training and went on to work as a pharmacist in Khoo Teck Puat Hospital, before returning to pursue his Ph.D. in 2015. He is currently working in GEA-NUS Pharmaceutical Processing Research Laboratory, under the supervision of A/P Chan Lai Wah and A/P Paul Heng. His present research interest is on the use of paraffin wax in spray congealing for taste-masking and sustained release of drugs.

Understanding in die flow with particle surface roughness

Mr Tay Yong Soon Justin
Supervisor: Assoc Prof Paul Heng
Co-Supervisor: Dr Celine Liew

ABSTRACT Particle rearrangement takes place during the initial phase of tablet compaction. In this study, rough lactose particles were prepared by roller compaction and their surface roughness modified by partial surface dissolution using a fluidized bed processor. Flow characteristics of the particles were determined using various flow methods and their compaction characteristics studied using a compaction simulator with punches of differing geometry and compaction pressure. Rougher particles demonstrated poorer compressibility and powder flow due to the higher inter-particulate frictional forces required for particle movement. Rearrangement energy during tablet compaction was found to be correlated with compressibility ($R2 = 0.92$) and increased with surface roughness of the particles. Particle rearrangement was found to be dependent on inter-particulate frictional forces which could be measured using FT4 powder rheometer. Plastic energy decreased as a result of the increased rearrangement energy requirements. Roller compacted lactose particles produced tablets of higher tensile strength compared to crystalline lactose, due to pre-fragmentation of the crystalline structure during roller compaction.

BIOGRAPHY Justin graduated with BSc (Pharmacy) Hons from National University of Singapore in 2013. He is currently pursuing his PhD under the supervision of A/P Paul Heng and Dr Celine Liew. His research is focused on the particle surface modification and their impact on tableting and dry powder inhaler technology.