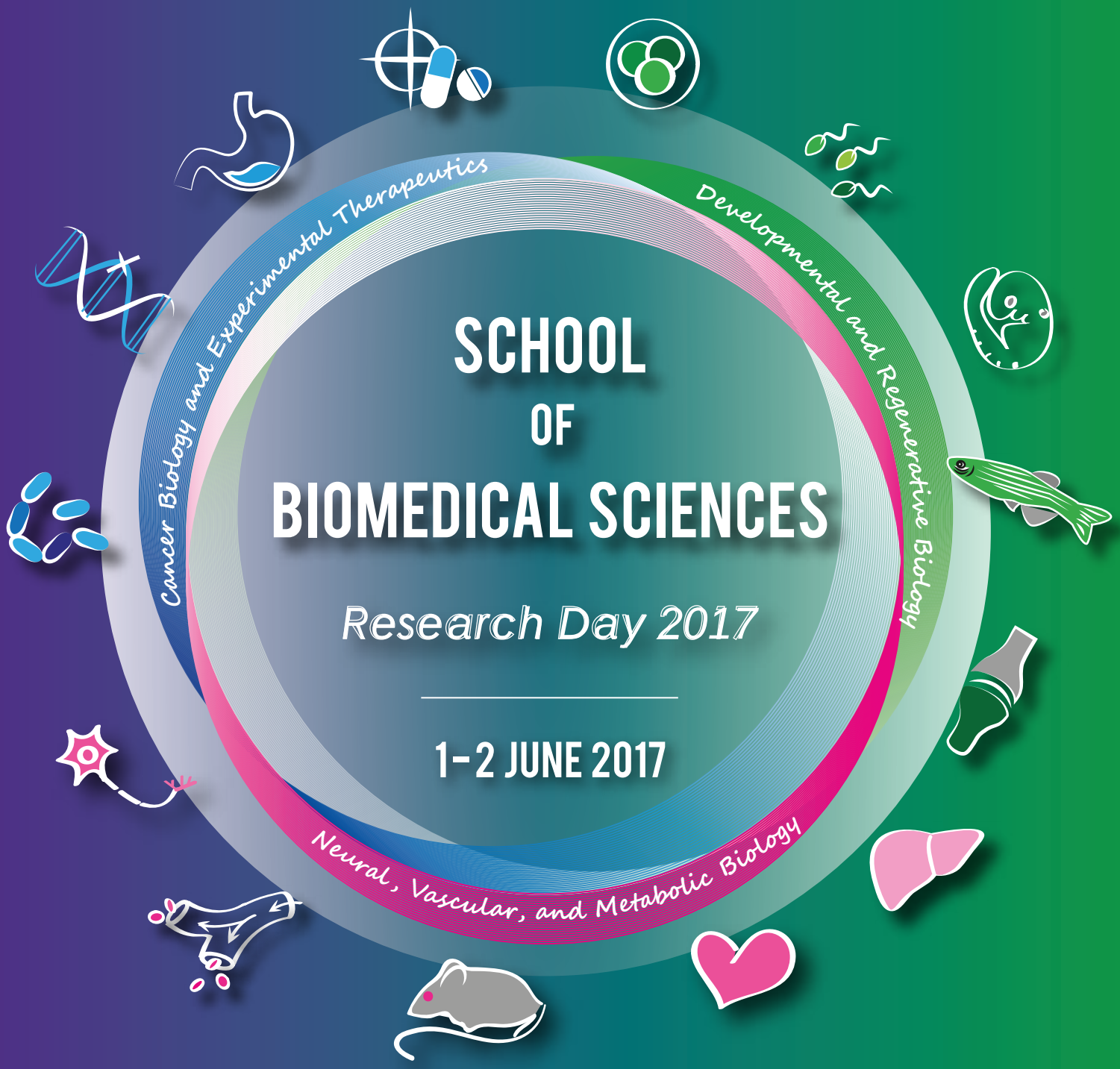

SCHOOL OF BIOMEDICAL SCIENCES

Research Day 2017

1-2 JUNE 2017

The Chinese University of Hong Kong

Lo Kwee-Seong Integrated Biomedical Sciences Building

香港中文大學
The Chinese University of Hong Kong

CU Medicine HONG KONG
香港中文大學醫學院
Faculty of Medicine
The Chinese University of Hong Kong

35th Anniversary 三十五週年

香港中文大學 生物醫學學院 CUSBS

School of Biomedical Sciences Research Day 2017

Members of the Organizing Committee

Professor Huang Yu (Chairman)
Professor Chan Wai Yee
Professor Cheung Chi Kwan Vincent
Professor Ke Ya
Professor Lau Hang Yung Alaster
Professor Lee Tin Lap
Professor Tian Xiaoyu
Professor Zhao Hui

COVER: The three Thematic Research Programs of School of Biomedical Sciences, CUHK

Designed by Ms. WAN Tai Fung, Department of Anatomical and Cellular Pathology, Faculty of Medicine, CUHK

CONTENTS

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Welcome Message from the Dean of Faculty of Medicine

I am honoured to be here to welcome all of you to the School of Biomedical Sciences Research Day 2017.

Since last year, we have invited our junior staff, whom we consider to be rising stars in the scientific community, to present the latest research findings and to share their creative thoughts with attendees. Similar to past years, by bringing together researchers and experts from various fields in biomedical sciences, the one-and-a-half-day programme provides great opportunities for speakers and attendees to engage in interesting interactions and meaningful discussions.

The School of Biomedical Sciences has put a lot of effort into organizing each year's Research Day. It signifies its commitment to pursue research excellence through fostering closer collaborations with different parties and expanding the academic network.

I sincerely hope that all participants will have enriching experiences and be inspired by the animated discussions in the coming one and a half days.

Professor Francis K.L. Chan
Dean, Faculty of Medicine
Choh-Ming Li Professor of Medicine & Therapeutics
The Chinese University of Hong Kong

Welcome Message from the Director of School of Biomedical Sciences

It is my pleasure to welcome you to the School of Biomedical Sciences Research Day 2017.

This is the eighth Research Day since the formation of our School in 2009. With your unfailing support and contribution, our annual flagship event continues to provide an interactive platform for our School members not only to exchange research findings and latest discoveries, but also to create chances for networking and outreaching.

In order to better respond to the fast-changing research landscape and to continually enhance our research competitiveness, our School has initiated a comprehensive review on its theme-based model. In the fall of 2016, our School has restructured the existing Thematic Research Programs (TRP) into three directions, namely Cancer Biology and Experimentation Therapeutics TRP, Developmental and Regenerative Biology TRP, and Neural, Vascular, and Metabolic Biology TRP. Similar to the previous years, the presentations are grouped by themes and research topics in order to facilitate interactions among School members and enhance possible collaborations. I sincerely hope that all participants will enjoy and find inspiration in the coming one and a half day.

I would like to take this opportunity to express my gratitude to members of the Organizing Committee of the Research Day. The event would not be possible and successful without their thorough planning and dedication. I am also very grateful for the generous support from all sponsoring companies.

Wai-Yee Chan, Ph.D.
Professor of Biomedical Sciences
Director, School of Biomedical Sciences
The Chinese University of Hong Kong

SBS Research Day 2017 Programme
1 June 2017 (Thursday)

Venue: Room G02, Lo Kwee-Seong Integrated Biomedical Sciences Building

09:00 – 09:20 **Opening Ceremony:**
Prof. CHAN Ka Leung Francis (Dean of Faculty of Medicine) &
Prof. CHAN Wai Yee (Director of School of Biomedical Sciences)

09:20 – 09:30 **Presentation of the prize for SBS Research Day 2017 Programme Book Cover / Banner Design Competition / Photo Taking**

Time	*Title of Presentation*	*Speaker*	*Abstract No.*
Session I ***Chairpersons: Prof. CHAN Man Lok Andrew & Prof. YU Jun***			
09:30-10:15	Epigenetic regulation of non-coding DNA in development and diseases	Prof. LEUNG Chi Yeu Danny (HKUST)	O1
10:15-10:45	The emerging roles of orphan nuclear receptors in prostate cancer and their potential as therapeutic targets	Prof. CHAN Leung Franky (CBET)	O2
10:45-11:00	***Tea Break***		
Session II ***Chairpersons: Prof. CHAN Man Lok Andrew & Prof. WONG Nathalie***			
11:00-11:30	Anti-emetic potential of ghrelin mimetics against chemotherapy-induced nausea and emesis	Prof. RUDD John A. (CBET)	O3
11:30-12:00	Whole-exome sequencing of head and neck cancers and NEXT	Prof. LUI Wai Yan Vivian (CBET)	O4
12:00-13:30	***Lunch***		
Session III ***Chairpersons: Prof. LEE Ka Ho Kenneth & Prof. LUI Oi Lan Kathy***			
13:30-14:15	New generation of biomaterials for healthcare inspired by zoology	Prof. GREEN David (Yonsei University, South Korea)	O5
14:15-14:45	Migration of sacral neural crest cells in the mouse	Prof. CHAN Wood Yee Woody (DRB)	O6
14:45-15:15	G protein-coupled estrogen receptor expressed on human bronchial epithelia inhibits the P2Y receptor-mediated pro-inflammatory effect	Prof. KO Wing Hung (DRB)	O7
15:15-15:45	Sodium/myo-inositol cotransporter 1: a new therapeutic target for type 2 diabetes mellitus?	Prof. LEUNG Po Sing (DRB)	O8
15:45-16:00	***Tea Break***		
Session IV ***Chairpersons: Prof. YAO Xiaoqiang & Prof. MA Ching Wan Ronald***			
16:00-16:45	Molecular mechanism of dense core biogenesis	Prof. XIA Jun (HKUST)	O9
16:45-17:15	Anti-inflammatory effects of green tea extract in eye diseases	Prof. CHAN Sun On (NVMB)	O10
17:15-17:45	Physical exercise, shear stress, and vaso-protection	Prof. HUANG Yu (NVMB)	O11
17:45-18:15	Dysregulation of retinoid homeostasis in embryos exposed to pregestational diabetes	Prof. SHUM Sau Wun Alisa (NVMB)	O12
18:30-20:00	***Conference Banquet (by invitation)***		

SBS Research Day 2017 Programme
2 June 2017 (Friday)

Venue: Room G02, Lo Kwee-Seong Integrated Biomedical Sciences Building

Time	*Title of Presentation*	*Speaker*	*Abstract No.*
Session V ***Chairpersons: Prof. LEE Tin Lap & Prof. CHOI Chung Hang Jonathan***			
09:15-09:45	Risk of pyrrolizidine alkaloid-induced hepatotoxicity and biomarker for the risk assessment	Prof. LIN Ge (CBET)	O13
09:45-10:15	Early diagnosis *via* a new biomarker: the activity of essential pathogen expressed DNA modifying enzymes	Prof. HO Yi Ping Megan (Electronic Engineering, CUHK)	O14
10:15-10:45	Combined drugs treatment for diabetes-associated osteoporosis	Prof. KWAN Yiu Wa (NVMB)	O15
10:45-11:00	***Tea Break***		
Session VI ***Chairpersons: Prof. CHENG Sze Lok Alfred & Prof. WONG Wing Tak Jack***			
11:00-11:25	Hepatoma-intrinsic CCRK inhibition diminishes myeloid-derived suppressor cell immunosuppression and enhances immune-checkpoint blockade efficacy	Dr. ZHOU Jingying (CBET)	O16
11:25-11:50	Decoding pluripotency shades with novel lincRNAs revealed bioinformatics discovery	Dr. WANG Yaofeng (DRB)	O17
11:50-12:15	Visualizing the neurodynamics of the zebrafish brain	Dr. WALKER Steven Lester (NVMB)	O18
12:15-12:30	***Closing Remarks***		
12:30-14:00	***Closing Lunch***		

Thematic Research Programs:

- ✧ Cancer Biology and Experimental Therapeutics (CBET)
- ✧ Developmental and Regenerative Biology (DRB)
- ✧ Neural, Vascular, and Metabolic Biology (NVMB)

Session I

Speaker Biography

Prof. LEUNG Chi Yeu Danny（梁子宇）received his BSc. in human genetics from University College London and MSc. in human molecular genetics from Imperial College London. He then conducted his PhD research under the supervision of Prof. Matthew Lorincz in the Department of Medical Genetics, University of British Columbia. His research was focused on the epigenetic regulation of repetitive elements in mouse embryonic stem cells. He then went on to carry out his postdoctoral fellowship research under the supervision of Prof. Bing Ren at the Ludwig Institute for Cancer Research. He was also a fellow of the California Institute for Regenerative Medicine. During this time, he was the project manager of the San Diego branch of the NIH Roadmap Epigenomics Project. He has since taken up the position of assistant professor at the Division of Life Sciences, Hong Kong University of Science and Technology (HKUST). Prof. Leung was the 2017 recipient of the Croucher Innovation award. His laboratory's research focuses on the interplay between epigenetic pathways in the regulation of non-coding DNA. His work has been published in various journals including Nature, Proceedings of the National Academy of Sciences of the United States of America, etc.

Five recent representative publications

1. Zhang W, Xia W, Wang Q, Towers AJ, Chen J, Gao R, Zhang Y, Yen CA, Lee AY, Li Y, Zhou C, Liu K, Zhang J, Gu TP, Chen X, Chang Z, **Leung D**, Gao S, Jiang YH, Xie W. "Isoform switch of TET1 Regulates DNA demethylation and mouse development." ***Molecular Cell***, 2016; 64(6):1062-1073.
2. **Leung D***, Jung I*, Rajagopal N*, Schmitt A, Selvaraj S, Lee AY, Yen CA, Lin S, Lin Y, Qiu Y, Xie W, Yue F, Hariharan M, Ray P, Kuan S, Edsall L, Yang H, Chi NC, Zhang MQ, Ecker JR, Ren B. "Integrative analysis of haplotype-resolved epigenomes across human tissues." ***Nature***, 2015; 518(7539):350-354. (*Co-first authorship)
3. **Leung D***, Du T*, Wagner U*, Xie W, Lee AY, Goyal P, Li Y, Szulwach KE, Jin P, Lorincz MC, Ren B. "Regulation of DNA methylation turnover at LTR retrotransposons and imprinted loci by the histone methyltransferase Setdb1." ***Proc Natl Acad Sci USA***, 2014; 111(18):6690-6695. (*Co-first authorship)
4. **Leung D**, Dong KB, Maksakova IA, Goyal P, Appanah R, Lee S, Tachibana M, Shinkai Y, Lehnertz B, Mager DL, Rossi F, Lorincz MC. "Lysine methyltransferase G9a is required for *de novo* DNA methylation and the establishment but not maintenance of proviral silencing." ***Proc Natl Acad Sci USA***, 2011; 108(14):5718-5723.
5. Matsui T*, **Leung D***, Miyashita H, Maksakova IA, Miyachi H, Kimura H, Tachibana M, Lorincz MC, Shinkai Y. "Proviral silencing in embryonic stem cells require the histone methyltransferase ESET." ***Nature***, 2010; 464(7290):927-931. (*Co-first authorship)

Technical expertise

- ✧ Epigenetics and epigenomics
- ✧ Genetics and genomics
- ✧ Genome and epigenome editing
- ✧ Bioinformatic analyses

Epigenetic regulation of non-coding DNA in development and diseases

LEUNG Chi Yeu Danny

Division of Life Science, Hong Kong University of Science and Technology, Hong Kong SAR, P.R. China.

While the genome encodes the blueprint for mammalian development, it is the epigenome that allows this code to be interpreted uniquely by each cell-type. Deciphering the epigenome will reveal insights into a plethora of biological processes. Our research focuses on epigenetic mechanisms that regulate transcription of non-coding DNA sequence. Using high-throughput genomic techniques, we generated extensive profiles of epigenetic modifications, gene expression, and chromatin conformation for various cell-types. We discovered unique characteristics and roles of non-coding elements in shaping the gene expression networks important for distinct cell-type identity and function. Specifically, we aim to delineate the contributions of endogenous retroviruses, a class of repetitive genomic sequences, in normal developmental programs as well as disease states such as cancer.

Session I

Speaker Biography

Prof. CHAN Leung Franky（陳良） obtained his Ph.D. degree from the University of Hong Kong in 1989 and received his postdoctoral training in McGill University (Montreal, Canada) thereafter. He joined The Chinese University of Hong Kong as a lecturer in 1992 and is presently a full professor at the School of Biomedical Sciences. Dr. Chan has published more than 100 original research papers, including Cancer Research, Oncogene, Journal of Pathology, Journal of Clinical Endocrinology and Metabolism, Endocrinology and PNAS. Chan's primary research focus is on the hormonal carcinogenesis of prostate cancer. His current research topics include: (1) functional roles of orphan nuclear receptors, (2) calcium channels and signaling, (3) epithelial mesenchymal transition in metastasis, (4) hypoxic growth regulation in prostate cancer, and (5) molecular pathways involved in castration-resistant or hormone-independent prostate cancer.

Five recent representative publications

1. Yu S, Xu Z, Zou C, Wu D, Wang Y, Yao X, Ng CF and **Chan FL**. "Ion channel TRPM8 promotes hypoxic growth of prostate cancer cells via an O_2-independent and RACK1-mediated mechanism of HIF-1α stabilization." ***J Pathol***, 2014; 234(4):514-525.
2. Sailland J, Tribollet V, Forcet C, Billon C, Barenton B, Carnesecchi J, Gauthier KC, Yu S, Giguère V, **Chan FL**, and Vanacker JM. "Estrogen-related receptor α decreases RHOA stability to induce oriented cell migration." ***Proc Natl Acad Sci USA***, 2014; 111(42):15108-15113.
3. Wu D, Yu S, Jia L, Zou C, Xu Z, Xiao L, Wong KB, Ng CF, **Chan FL**. "Orphan nuclear receptor TLX functions as a potent suppressor of oncogene-induced senescence in prostate cancer via its transcriptional co-regulation of *CDKN1A* ($p21^{WAF1/CIP1}$) and *SIRT1* genes." ***J Pathol***, 2015; 236(1):103-115.
4. Wu D, Cheung A, Wang Y, Yu S, **Chan FL**. "The emerging roles of orphan nuclear receptors in prostate cancer." ***Biochim Biophys Acta***, 2016; 1866(1):23-36.
5. Cai G, Wu D, Wang Z, Xu Z, Wong KB, Ng CF, **Chan FL**, Yu S. "Collapsin response mediator protein-1 (CRMP1) acts as an invasion and metastasis suppressor of prostate cancer via its suppression of epithelial-mesenchymal transition and remodeling of actin cytoskeleton organization." ***Oncogene***, 2017; 36(4):546-558.

The emerging roles of orphan nuclear receptors in prostate cancer and their potential as therapeutic targets

CHAN Leung Franky

Cancer Biology and Experimental Therapeutics Program, School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.

Orphan nuclear receptors are members of the nuclear receptor (NR) superfamily. They are named because their endogenous physiological ligands are either unknown or may not exist. Because of the important regulatory roles played by the NRs in many key physiological processes, dysregulation of signalings governed by these receptors is associated with many diseases including cancer. Over years, studies of these orphan NRs have become an area of great interest not only because of their specific roles in normal physiology and pathogenesis are still not well defined but also they are promising drug targets for diseases. In this lecture, the speaker will present an overview of the recent advances in the emerging roles of orphan NRs in prostate cancer, such as cell-cycle control, hypoxia signaling, oncogene-induced senescence and cross-talk with androgen signaling, based on the findings from his laboratory and others.

Session II

Speaker Biography

Prof. RUDD John Anthony（陸臻賢） worked with Glaxo Group Research in the late 1980s to explore the potential use of the 5-HT_3 receptor antagonist, ondansetron, to antagonize chemotherapy- and drug-induced emesis. He was also part of a team that mapped 5-HT_3 receptor distribution in the human and ferret brainstem and first to show increases in of 5-HT in the plasma of patients receiving cisplatin-based chemotherapy. Pioneered the use of the ferret to model chemotherapy-induced acute and delayed emesis (now a gold standard model) and discovered that NK_1 tachykinin antagonists could be used to prevent the acute and delayed phases of emesis induced by cisplatin: now NK_1 tachykinin antagonists are a cornerstone of treatment for delayed emesis. Recently collaborated on the development of the second generation 5-HT_3 and NK_1 receptor antagonists, palonosetron and netupitant, respectively. He has an ongoing interest in broad inhibitory anti-emetic drugs and work with several leading pharmaceutical companies to aid drug development. Also examining the role of the brain-gut axis in mechanisms of neurodegenerative diseases.

Five recent representative publications

1. Lu Z, Yeung CK, Lin G, Yew DTW, Andrews PLR, **Rudd JA.** "Centrally located GLP-1 receptors modulate gastric slow waves and cardiovascular function in ferrets consistent with the induction of nausea." ***Neuropeptides***, 2017; doi: 10.1016/j.npep.2017.04.006. [Epub ahead of print]
2. Kan KKW, Wai MK, Jones RL, **Rudd JA**. "Role of prostanoid $EP_{3/1}$ receptors in mechanisms of emesis and defaecation in ferrets." ***Eur J Pharmacol***, 2017; doi: 10.1016/j.ejphar.2017.03.035. [Epub ahead of print]
3. Ullah I, Subhan F, Lu Z, Chan SW, **Rudd JA**. "Action of *Bacopa monnieri* to antagonize cisplatin-induced emesis in *Suncus murinus* (house musk shrew)." ***J Pharmacol Sci***, 2017; doi: 10.1016/j.jphs.2017.03.001. [Epub ahead of print]
4. Lu Z, Yeung CK, Lin G, Yew DTW, Andrews PLR, **Rudd JA**. "Insights into the central pathways involved in the emetic and behavioural responses to exendin-4 in the ferret." ***Auton Neurosci***, 2017; 202:122-135.
5. **Rudd JA**, Ngan MP, Lu Z, Higgins GA, Giuliano C, Lovati E, Pietra C. "Profile of antiemetic activity of netupitant alone or in combination with palonosetron and dexamethasone in ferrets and *Suncus murinus* (house musk shrew)." ***Front Pharmacol***, 2016; 7:263.

Technical expertise

- *In vivo* experimentation in conscious animals using radiotelemetry for acquisition and analysis of blood pressure (including HRV, spectral analysis), temperature, gastric myoelectric activity, or other biopotentials.
- Pharmacological assays for drug potency estimations.
- Immunohistochemistry; c-Fos.
- *In vivo* imaging for gastric emptying.
- Microelectrode array for electrophysiological recordings from ICC and other cells.
- Stereotaxic surgery for cannula placement and drug delivery.
- Whole body plethysmography in conscious animals to examine respiratory function; safety pharmacology.
- Memory testing and general activity protocols; taste aversion protocols.

Anti-emetic potential of ghrelin mimetics against chemotherapy-induced nausea and emesis

RUDD John A.[1,2], **NGAN Man P.**[1], **LU Zengbing**[1], **TU Longlong**[1], **GIULIANO Claudio**[3], **LOVATI Emanuela**[3], **PIETRA Claudio**[3]

[1] Cancer Biology and Experimental Therapeutics Program, School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.
[2] Brain and Mind Institute, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.
[3] Helsinn Healthcare SA., Research and Preclinical Development Dept., Lugano, Switzerland.

Ghrelin is peptide that stimulates feeding and gastrointestinal motility via growth hormone secretagouge receptors (GHS-R). For these reasons, ghrelin is being actively explored for clinical indications were gastric motility is disturbed and/or appetite suppressed. Common laboratory animals do not vomit, meaning that most work on emesis control must be conducted in specialized laboratory species. We showed that ghrelin could antagonize cisplatin-induced acute emesis in ferrets via central actions in the brain. Since then, several studies implicated GHS-R in mechanisms of nausea and emesis. We discovered that HM01, a brain penetrating ghrelin mimetic, could also antagonize cisplatin-induced acute emesis in *Suncus murinus* (SM), and had useful effects when combined with a palonosetron and netupitant regimen. In the present studies, we investigate the spectrum of anti-emetic activity of HM01 compared to peripherally acting GHS-R agonist, HM02. Both HM01 and HM02 (3-30 mg/kg) were administered orally 1 h prior to the injection of nicotine (5 mg/kg, s.c.), intragastric copper sulphate.$5H_2O$ (120 mg/kg), motion (10 Hz, 5 cm horizontal displacement), or cisplatin (30 mg/kg, i.p.). HM01 and HM02 failed to modify nicotine and copper sulphate pentahydrate-induced emesis, but they increased food and water intake assessed at 24 h. HM01 antagonized motion-induced emesis by ~78 % at 10 mg/kg, and HM02 reduced emesis by ~87 % at 30 mg/kg. Approximately 84 % of the emetic response induced by cisplatin occurred in the first 4 h, and was prevented by HM01 (ID_{50} ~ 6.8mg/kg); HM02 antagonized the response by ~67 %. In conclusion, the anti-emetic activity of HM02 indicates that peripheral GHS-Rs play a role in emesis induced by cisplatin and motion. However, the greater efficacy provided by HM01 suggests that an additional activation of centrally located GHS-Rs is necessary for an optimal control. GHS-Rs do not appear to be involved in nicotine- or copper sulphate-induced emesis. GHS-R agonists may be useful in combination with other anti-emetics for the treatment of chemotherapy-induced nausea and emesis.

Session II

Speaker Biography

Prof. LUI Wai Yan Vivian（呂偉欣） obtained her Ph.D. (Hons) training in Molecular Pharmacology at The University of Pittsburgh School of Medicine, USA, followed by post-doctoral trainings at Duke University and University of Pittsburgh, USA. Dr. Lui specializes in precision medicine development in head and neck cancers. Using genomics, proteomics, integrative genomic-proteomic discovery approaches, and a driver mutation screening platform (US patented, Co-inventor), Dr. Lui has contributed to major mutationally-driven drug sensitivity findings in head and neck cancer. Dr. Lui has published over 80 research articles in the area of precision medicine, cancer genomics and therapeutics in renowned scientific journals including Cancer Discovery, Nature Communications., JAMA Oncology, Proceedings of the National Academy of Sciences of the United States of America and Journal of the National Cancer Institute, etc.

Five recent representative publications

1. **Lui VW**, Hedberg ML, Li H, Vangara BS, Pendleton K, Zeng Y, Lu Y, Zhang Q, Du Y, Gilbert BR, Freilino M, Sauerwein S, Peyser ND, Xiao D, Diergaarde B, Wang L, Chiosea S, Seethala R, Johnson JT, Kim S, Duvvuri U, Ferris RL, Romkes M, Nukui T, Ng PKS, Garraway LA, Hammerman PS, Mills GB, Grandis JR. "Frequent mutation of the PI3K pathway in head and neck cancer defines predictive biomarkers." ***Cancer Discovery***, 2013; 3(7):761-769.
2. **Lui VW**, Peyser ND, Ng PK, Hritz J, Zeng Y, Lu Y, Li H, Wang L, Gilbert BR, General IJ, Bahar I, Ju Z, Wang Z, Pendleton KP, Xiao X, Du Y, Vries JK, Hammerman PS, Garraway LA, Mills GB, Johnson DE, Grandis JR. "Frequent mutation of receptor protein tyrosine phosphatases provides a mechanism for STAT3 hyperactivation in head and neck cancer." ***Proc Natl Acad Sci USA***, 2014; 111(3):1114-1119.
3. Van Allen EM*, **Lui VW***, Egloff AM*, Goetz EM, Li H, Johnson JT, Duvvuri U, Bauman JE, Stransky N, Zeng Y, Gilbert BR, Pendleton KP, Wang L, Chiosea S, Sougnez C, Wagle N, Zhang F, Du Y, Close D, Johnston PA, McKenna A, Carter SL, Golub TR, Getz G, Mills GB, Garraway LA, Grandis JR. "Genomic correlate of exceptional erlotinib response in head and neck squamous cell carcinoma." ***JAMA Oncology***, 2015; 1(2):238-244. (*Equal contributions)
4. Hedberg ML, Goh G, Chiosea SI, Bauman JE, Freilino ML, Zeng Y, Wang L, Diergaarde BB, Gooding WE, **Lui VW**, Herbst RS, Lifton RP, Grandis JR. "Genetic landscape of metastatic and recurrent head and neck squamous cell carcinoma." ***J. Clin. Investigation***, 2016; 126(1):169-180.
5. Li YY*, Chung GT*, **Lui VW***, To KF, Ma BB, Chow C, Woo JK, Yip KY, Seo J, Hui EP, Mak MK, Rusan M, Chau NG, Or YY, Law MH, Law PP, Liu ZW, Ngan HL, Hau PM, Verhoeft KR, Poon PH, Yoo SK, Shin JY, Lee SD, Lun SW, Jia L, Chan AW, Chan JY, Lai PB, Fung CY, Hung ST, Wang L, Chang AM, Chiosea SI, Hedberg ML, Tsao SW, van Hasselt AC, Chan AT, Grandis JR, Hammerman PS, Lo KW. "Exome and genome sequencing of nasopharynx cancer identifies NF-kB pathway activating mutations." **Nature Communications**, 2017; 8:14121. (*Equal contributions)

Technical expertise

- ✧ Functional genomics of cancer gene mutations
- ✧ Drug sensitivity genomics
- ✧ Drug target discovery by integrative genomics and proteomics

Whole-exome sequencing of head and neck cancers and NEXT

LUI Wai Yan Vivian

Cancer Biology and Experimental Therapeutics Program, School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.

Genomic characterization of head and neck cancers reveals major challenges for drugging these aggressive cancers. Recently, whole-exome sequencing results of both squamous cell carcinoma and nasopharyngeal cancer uncover numerous unanswered questions for next steps. It is clear that resolving the druggability challenges of head and neck cancers is the key next step. We will discuss successful top-down approaches and bottom-up approaches for drug target discovery in head and neck cancer. Furthermore, the involvements of viral components in head and neck carcinogenesis strongly suggest that viral-driven head and neck cancers are separate entities both in terms of genomics and treatment. Lastly, we will also discuss our next challenge to curb metastasis of head and neck cancers.

Acknowledgements: Dr. Lui is supported by research grants from the Research Grant Council, Hong Kong (#17114814, #17121616, General Research Fund; T12-401/13-R, Theme-based Research Scheme), the Hong Kong Cancer Fund, and the Start-up Fund, School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong.

Session III

Speaker Biography

Prof. GREEN David William began his research career in zoology and botany at the Natural History Museum, London 23 years ago. In 1996, Dr. Green entered into R&D of biomedical materials and devices at Aston University, Birmingham, UK and was awarded a PhD for developing a biomimetic artifical cornea. In 2000, he joined the University of Southampton, UK under the guidance of Professor Richard Oreffo and Professor Stephen Mann FRS, at Bristol University, to develop new biomimetic materials for the musculoskeletal system. Following on from this innovative work with inspirational, world leading scientists, Dr. Green went onto invent a series of innovative biomedical materials at Victoria University of Wellington, New Zealand (biomimetic nacre coatings for orthopaedic implants), at the University of Queensland, Australia, developing innovative living biocomposites for ophthalmology and at the University of Technology Sydney, Australia to develop synthetic coral structures for bone surgery. In 2012, Dr. Green began an ambitious regenerative medicine and healthcare research programme at The University of Hong Kong built on bioinspired and biomimetic engineering principles, processes and strategies. While in Hong Kong, Dr. Green was able to thrive and co-founded NatureWorks™, with Prof Kenneth Lee at The Chinese University of Hong Kong, which is a teachnology "start-up" organisation to launch bioinspired and biomimetic solutions into the market-place.

Five recent representative publications

1. **Green DW,** Lee KK, Watson JA, Kim HY, Yoon KS, Kim EJ, Lee JM, Watson GS*, Jung HS. "High quality bioreplication of intricate nanostructures from a fragile gecko skin surface with bactericidal properties." ***Sci. Rep***, 2017; 7:41023.
2. Li X, Cheung GS, Watson GS, Watson JA, Lin S, Schwarzkopf L, **Green DW***. "The nanotipped hairs of gecko skin and biotemplated replicas impair and/or kill pathogenic bacteria with high efficiency." ***Nanoscale***, 2016; 8(45):18860-18869.
3. **Green DW***, Ben-Nissan B, Yoon KS, Milthorpe B, Jung HS. "Natural and synthetic coral biomineralization for human bone revitalization." ***Trends Biotechnol***, 2017; 35(1):43-54.
4. **Green DW**, Watson GS, Watson JA, Lee DJ, Lee JM, Jung HS. "Diversification and enrichment of clinical biomaterials inspired by Darwinian evolution." ***Acta Biomater***, 2016; 42:33-45.
5. **Green DW**, Kim EJ, Jung HS. "Spontaneous gene transfection of human bone cells using 3D mineralized alginate-chitosan macrocapsules." ***J Biomed Mater Res A***, 2015; 103(9):2855-2863.

Technical expertise

- ✧ Biomimetic Materials Chemistry, Synthetic Biology, Chiral Biomaterials, 3D Printing of Biomaterials with Complex bioinks, Cell-Orchestrated Biomaterials Fabrication, Artificial Stem Cell Niches, BioTRIZ Problem Solving in Bioengineering, Bioinspired Engineering, Natural History Collections as Inspiration for Biomimicry, Development of Supersurfaces for Medicine and Technology, Biomineralisation, Darwinian Medicine, Tissue Engineering (Bone, Fat, Cartilage, Eye, Tooth), Stem Cell Therapy, Self-organizing media, Bioliquid Crystals, Microfluidics with complex fluids, Non-viral gene delivery, drug delivery, Marine Biomimetics, Structural biomaterials, Biological Imaging at small scales, artificial stem cell niches and cellular assemblies, Natural nanotopography.

New generation of biomaterials for healthcare inspired by zoology

GREEN David William[1], **WATSON G.**[2], **WATSON J.**[2], **LEE Ka Ho Kenneth**[3]

[1] Division in Anatomy and Developmental Biology, Department of Oral Biology, Oral Science Research Center, BK21 PLUS Project, Yonsei University College of Dentistry, Seoul, Korea.
[2] University of the Sunshine Coast, School of Science & Engineering, Sippy Downs, QLD 4558, Australia.
[3] Key laboratory for Regenerative Medicine, School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.

Biomaterials science is changing in ways that learn more from early development, nano synthesis and fabrication and even zoology. Biomaterials are a critical component of tissue engineering, regenerative medicine and healthcare, which relates to general medical services. Current trends in biomaterials engineering are dominated by biomimetic self-assembly, self-organisation and stimulation of host biological repair and regenerative systems. Notwithstanding, bioinspired and biomimetic design approaches promise considerable improvements in complexity and physiological functions, which ultimately lead to vastly better clinical outcomes.

The study of biomaterials and biological structures at depth (nanoscale dimensions) and measuring their exquisite performance, in zoology (and botany) provides countless problem solving functions and strategies. These are exceptionally good at resolving multiple trade-offs between conflicting physical, chemical and biological phenomena. Once known, the conflict resolutions can be incorporated into the design and manufacture of biomaterials for analogous problems in healthcare, ranging from cell and tissue templates, drug delivery vehicles and anti-microbial surfaces.

In this talk, I will illustrate how we are acquiring vital solutions to physical, biological and chemical problems relating to materials and structures that have evolved in the zoological world and how we are able to translate them into useful technological innovations, for the most pressing healthcare problems. Examples include: the induction of tissue morphogenesis and strategies to fight against antibiotic resistance. Effective translations between zoology and technology are guided by a special combination of careful in-the-field analyses of trade-offs, adaptations and functions, natural history observations and use of problem solving methodologies derived from biological ontologies; this combined with sophisticated laboratory centred analyses of chemistry, physics, architectural design and mechanical force fields,

I will describe our most recent, ongoing bioinspired translation of nature-derived surface designs into a bactericidal platform for healthcare applications. I will show the series of steps that were taken to produce a usable biotechnology. This involved fieldwork observations, bioreplication, high-resolution X-ray imaging and microcontact printing. The technology is now demonstrating significant utility as a thin-film material with properties for annihilating antibiotic resistant bacteria and hospital-acquired infections.

The problem solving strategies expressed in the design of countless zoological materials and structures will be profoundly beneficial, to the engineers of medical biomaterials, in many healthcare applications not limited to, regenerative medicine, stem cell control, microbial control, cell and tissue engineering as well as, gene and pharmaceutical drug delivery.

Session III

Speaker Biography

Prof. CHAN Wood Yee Woody（陳活彝）obtained his Bachelor and Master degrees in Biochemistry in the Department of Biochemistry and Ph.D. in Basic Medical Sciences in the Department of Anatomy of The Chinese University of Hong Kong. He went on to have his postdoctoral training in University College London, UK after he received a fellowship from the Croucher Foundation. He then returned to The Chinese University of Hong Kong, and joined the Department of Anatomy as a lecturer. He received his sabbatical training in the Brigham and Women's Hospital, Harvard Medical School, USA for three consecutive summers. He became Professor in the Department of Anatomy in 2000, Chairman of the same Department in 2007, and currently Associate Director of School of Biomedical Sciences and also Head of Division of Biomedical Sciences. His research interests focus mainly on the early development of nervous systems of both mouse embryos and human fetuses shortly after implantation to the uterus. Recently, his research focuses more on the migration and differentiation of neural crest cells in post-implantation mouse embryos, the pre- and post-natal development of the rodent enteric nervous system, stem cell therapy for congenital intestinal motility disorders such as Hirschsprung's disease, and also teratogenic effects of bioactive compounds.

Five recent representative publications

1. Wang X, Chan AK, Sham MH, Burns AJ, **Chan WY**. "Analysis of the sacral neural crest cell contribution to the hindgut enteric nervous system in the mouse embryo." ***Gastroenterology***, 2011; 141(3):992-1002.
2. Zeng X, Zeng YS, Ma YH, Lu LY, Du BL, Zhang W, Li Y, **Chan WY**. "Bone marrow mesenchymal stem cells in a three-dimensional gelatin sponge scaffold attenuate inflammation, promote angiogenesis, and reduce cavity formation in experimental spinal cord injury." ***Cell Transplant***, 2011; 20(11-12):1881-1899.
3. Ni YR, Shu SY, Guo ZY, Liu SR, Bao Y, Liu SH, **Chan WY**. "Dissociated brain organization for two-digit addition and subtraction: An fMRI investigation." ***Brain Res Bull***, 2011; 86(5-6):395-402.
4. Qu ZQ, Zhou Y, Zeng YS, Lin YK, Li Y, Zhong ZQ, **Chan WY**. "Protective effects of a Rhodiola crenulata extract and salidroside on hippocampal neurogenesis against streptozotocin-induced neural injury in the rat." ***PLoS One***, 2012; 7(1):e29641.
5. Kam RK, Shi W, Chan SO, Chen Y, Xu G, Lau CB, Fung KP, **Chan WY**, Zhao H. "Dhrs3 protein attenuates retinoic acid signaling and is required for early embryonic patterning." ***J Biol Chem***, 2013; 288(44):31477-31487.

Technical expertise

- ✧ Whole mouse embryo culture
- ✧ *In situ* labelling of neural crest cells
- ✧ *Ex vivo* embryonic gut organ culture
- ✧ Live cell confocal imaging
- ✧ Cell and tissue transplantation by microinjection into mouse embryos
- ✧ *In situ* hybridization and immunofluorescence localization of gene expression

Migration of sacral neural crest cells in the mouse

HUANG Taida[1], HOU Yonghui[1], WANG Xia[1], SHAM Mai Har[2], LEE Tin Lap[1], CHAN Wood Yee[1]

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[2] School of Biomedical Sciences, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, P.R. China.

The enteric nervous system (ENS), the intrinsic innervation of the gastrointestinal tract, regulates the majority of gut activities including intestinal motility. During the early ENS development, neural crest cells (NCCs) at the vagal (cervico-thoracic) level of the neuraxis migrate long distances to and within the developing gut to form most of enteric ganglia. Defects in this long-distance migration of vagal NCCs have been ascribed as a cause of Hirschsprung's disease (HSCR), a common congenital intestinal motility disorder with absence or reduction of enteric ganglia in the colon. Recently, our studies with mouse embryos demonstrated another cellular origin of enteric ganglia: sacral NCCs. They originate from the neural tube caudal to the somite 24 and contribute significantly to the ENS of the distal colon. We mapped the migration of sacral NCCs to the gut and recorded their migratory behaviors within the developing gut. Then, we made use of the *Dominant megacolon* (*Dom*) mouse mutant, which carries a spontaneous mutation of *Sox10*, as an animal model of HSCR to find out the migration abnormality of sacral NCCs and determine the molecular events that lead to the abnormal migration of sacral NCCs in the mutant embryos. With *in situ* cell labelling and whole embryo culture, it was found that mutant sacral NCCs tended to aggregate, resulting in their delayed migration toward the hindgut. Genome-wide profiling with microarrays showed that the expression of the adhesion molecule cadherin 19 (*Cdh19*) was drastically down-regulated in mutant sacral NCCs. Results of *in situ* hybridization with E9.5 to E11.5 embryos indicated that *Cdh19* was localized to migrating sacral NCCs and their derivatives. With luciferase assay and chromatin immunoprecipitation, the expression of *Cdh19* was found to be directly regulated by Sox10, and the binding site of Sox10 on the promoter of *Cdh19* was also identified. When the expression of Cdh19 was knocked down in the wild-type sacral NCCs, their migration ability was reduced, and conversely, upon re-expressing Cdh19 in the mutant sacral NCCs, their migration ability was restored to a level close to that of wild-type sacral NCCs. Immunoprecipitation with 3T3 cells *in vitro* showed that Cdh19 interacted with catenins which are important regulators of the dynamic cytoskeleton of migrating cells. In summary, our studies showed that the Sox10 mutation in the *Dom* mutant resulted in the delayed migration of sacral NCCs with significant down-regulation of the expression of *Cdh19*, a direct downstream target of Sox10. Alterations of *Cdh19* expression subsequently affected the migration ability of sacral NCCs, probably through interactions with catenins which in turn regulated the dynamic cytoskeleton of migrating NCCs.

Session III

Speaker Biography

Prof. KO Wing Hung（高永雄）obtained his PhD from the Department of Physiology, The Chinese University of Hong Kong, in 1992. Following postdoctoral training at the Institute of Physiology, University of Glasgow, he joined his alma mater as lecturer in 1993. He is currently an Associate Professor in the School of Biomedical Sciences. Dr. Ko's recent research examines P2Y receptor–regulated Ca^{2+} signaling and ion transport in human airway epithelia, with a focus on the role of P2Y receptors in airway inflammation. Dr. Ko's laboratory is one of the few in the world that is capable of simultaneously measuring real-time (1) Ca^{2+} and I_{SC} (short circuit current; an index of electrogenic ion transport), (2) cAMP and I_{SC}, or (3) Ca^{2+} and cAMP in polarized epithelia. This approach will help unravel novel molecular mechanisms of stimulus-secretion coupling in polarized epithelia. He has over 70 articles published in reputable international journals, such as the Journal of Biological Chemistry and the American Journal of Respiratory Cell and Molecular Biology.

Five recent representative publications

1. Hao Y, Chow AW, Yip WC, Li CH, Wan TF, Tong BC, Cheung KH, Chan WY, Chen Y, Cheng CH, **Ko WH**. "G protein-coupled estrogen receptor inhibits the P2Y receptor-mediated Ca^{2+} signaling pathway in human airway epithelia." ***Pflugers Arch***, 2016; 468(8):1489-1503.
2. Liu PY, Li ST, Shen FF, **Ko WH***, Yao XQ, Yang D. "A small synthetic molecule functions as a chloride-bicarbonate dual-transporter and induces chloride secretion in cells." ***Chem Commun (Camb)***, 2016; 52(46):7380-7383. (*Co-corresponding author)
3. Hao Y, Cheung CS, Yip WC, **Ko WH**. "Nobiletin stimulates chloride secretion in human bronchial epithelia via a cAMP/PKA-dependent pathway." ***Cell Physiol Biochem***, 2015; 37(1):306-320.
4. Hao Y, Liang JF, Chow AW, Cheung WT, **Ko WH**. "$P2Y_6$ receptor-mediated proinflammatory signaling in human bronchial epithelia." ***PLoS One***, 2014; 9(9):e106235.
5. Wong AM, Chow AW, Au SC, Wong CC, **Ko WH**. "Apical vs. basolateral $P2Y_6$ receptor-mediated Cl^- secretion in immortalized bronchial epithelia." ***Am J Respir Cell Mol Biol***, 2009; 40(6):733-745.

Technical expertise

- ✧ Simultaneous measurement technique for real-time monitoring of bioelectric properties and signalling molecules by fluorescence or Fluorescence Resonance Energy Transfer (FRET) imaging microscopy in polarized epithelia, including sweat gland, reproductive, intestinal and airway epithelia.

G protein-coupled estrogen receptor expressed on human bronchial epithelia inhibits the P2Y receptor-mediated pro-inflammatory effect

HAO Yuan[1], CHOW Wai Ming[1], YIP Chung Yin[1], CHEUNG King Ho[2], CHAN Wood Yee[1], CHEN Yang Chao[1], CHENG Hon Ki[1], KO Wing Hung[1]

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[2] School of Biomedical Sciences, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, P.R. China.

P2Y receptor activation by UTP and UDP causes the release of inflammatory cytokines in the bronchial epithelium. In addition to the classical nuclear hormone receptors ERα and ERβ, a novel estrogen (E2) receptor, G protein-coupled estrogen receptor (GPER), was recently identified. Our study aimed to investigate the cellular mechanisms underlying the inhibitory effect of GPER or 17β-estradiol (E_2) receptor activation on P2Y receptor-mediated Ca^{2+} signalling pathway and cytokine production in human bronchial epithelia.

Both human bronchial epithelial cell line 16HBE14o- and primary human bronchial epithelial (HBE) cells (ScienCell Research Laboratories, San Diego, CA, USA) were used. Expression of GPER in primary HBE or 16HBE14o- cells was confirmed on both the mRNA and protein levels. Stimulation of primary HBE or 16HBE14o- cells with E_2 or with the specific agonist of GPER, G1, rapidly attenuated a UDP- or UTP-evoked increase in $[Ca^{2+}]_i$ while this effect was reversed by GPER specific antagonist, G15. G1 inhibited the secretion of two pro-inflammatory cytokines, interleukin (IL)-6 or IL-8, in cells stimulated by the P2Y receptor agonist, adenosine 5'-(γ-thio) triphosphate (ATPγS). The cytokine release was reduced in the presence of an intracellular Ca^{2+} chelator, BAPTA-AM. G1 stimulated a real-time increase in cAMP levels in 16HBE14o- cells, which could be inhibited by adenylate cyclase inhibitor, MDL 12330A or SQ 22536. The inhibitory effect of E_2 or G1 on P2Y receptor-induced Ca^{2+} increase was reversed by treating the 16HBE14o- cells with a protein kinase A (PKA) inhibitor, H89.

Our data demonstrate that the inhibitory effect of G1 or E_2 on P2Y receptor-mediated Ca^{2+} mobilization and cytokine secretion was due to GPER-mediated activation of a cAMP-dependent PKA pathway in human bronchial epithelia. This study has reported, for the first time, the expression and function of GPER as an anti-inflammatory component in human bronchial epithelia, which may mediate through its opposing effects on the pro-inflammatory pathway activated by the P2Y receptors in inflamed airway epithelia.

The work was supported by a Research Grant Council General Research Fund (Ref. No.: 466611) awarded to W.H. Ko.

Session III

Speaker Biography

Prof. LEUNG Po Sing（梁寶成） was Assistant Professor (1996-1998) and Associate Professor (1998-2003), and is currently Professor (2003-now) in the School of Biomedical Sciences, The Chinese University of Hong Kong (CUHK). He received his BSc in Biology (1986), The National Taiwan Normal University; PhD in Biochemistry (1993), The Queen's University of Belfast; UK Soulby Postdoc Fellowship (1993-1994), Japan Science and Technology Agency Postdoc Fellowship (1994-1995); CUHK Postdoc Fellowship (1995-1996).

Professor Leung has major research interest in the field of pancreatic islet cell health and diabetes, with a particular focus on islet cell function and survival, as well as islet cell regeneration and development. Since joining CUHK, he has been striving to investigate into novel factors that improve islet β-cell secretion while protecting β-cell apoptosis; these agents include FGF21, GPR120, vitamin D, GLP1 and the RAS in the past two decades. He has published over 190 original and review papers in international refereed journals as well as several books, book chapters and editorials etc, with a total citation of >4,000 and h-index=35.

Five recent representative publications

1. Li YT, Cheng TW, Zhang D, **Leung PS**. "Identification and functional implications of sodium/myo-inositol cotransporter-1 in pancreatic beta-cells and type 2 diabetes mellitus." ***Diabetes***, 2017; doi: 10.2337/db16-0880. [Epub ahead of print]
2. Liang J, Wu SY, Zhang D, Wang L, Leung KK, **Leung PS**. "NADPH oxidase-dependent reactive oxygen species stimulate beta-cell regeneration through differentiation of endocrine progenitors in murine pancreas." ***Antioxid Redox Signal***, 2016; 24(8):419-433.
3. So WY, Cheng Q, Chen L, Evans-Molina C, Xu A, Lam KS, **Leung PS**. "High glucose represses β-klotho expression and impairs fibroblast growth factor 21 action in mouse pancreatic islets: involvement of peroxisome proliferator-activated receptor gamma signaling." ***Diabetes***, 2013; 62(11):3751-3759.
4. Cheng Q, Boucher BJ, **Leung PS**. "Modulation of hypovitaminosis D-induced islet dysfunction and insulin resistance through direct suppression of the pancreatic islet renin-angiotensin system in mice." ***Diabetologia***, 2013; 56(3):553-562.
5. Leung KK, Liang J, Ma MT, **Leung PS**. "Angiotensin II type 2 receptor is critical for the development of human fetal pancreatic progenitor cells into islet-like cell clusters and their potential for transplantation." ***Stem Cells***, 2012; 30(3):525-536.

Technical expertise

- ✧ Murine islet/ β cell isolation and cultures, human pancreatic progenitor cells/islet cell clusters/ mesenchymal stem cell models, obese/diabetic/islet regeneration animal models.

Sodium/myo-inositol cotransporter 1: a new therapeutic target for type 2 diabetes mellitus?

LI Stephen, CHENG Sam, ZHANG Dan, LEUNG Po Sing

Developmental and Regenerative Biology Program, School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.

Type 2 diabetes mellitus (T2DM) accounts for >90% of all cases of diabetes, with high rates of morbidity and mortality because of its chronic complications. T2DM develops when insulin secretion from pancreatic β cells no longer compensates for long-standing increases in insulin resistance. Therefore, preservation of islet β-cell function and cell mass is a key strategy for the management of obesity and obesity-related T2DM.

Inositol is a cyclitol naturally present in animal/plant cells, and myo-inositol (MI) is a predominant form of the nine inositol stereoisomers. Apart from being an organic osmolyte for the regulation of cell volume, MI is well-known to be the precursor of the second messenger phosphoinositide (PI) system that mediates an array of biological cell events. Meanwhile, rat islets were reported to actively transport MI over three decades ago. Despite this finding, the transport and function of MI in islets/ β cells remain largely ambiguous. In this study, it was the first time to report the expression of sodium/myo-inositol cotransporter 1 (SMIT1) in rat islets and, specifically, in β cells as well as rat INS-1E cell line. Additionally, our genetic and pharmacological inhibition of SMIT1 studies showed that glucose-stimulated insulin secretion by INS-1E cells was impaired, probably via the down-regulation of PI signaling. Furthermore, we found that SMIT1 expression in INS-1E cells and isolated islets was upregulated by acute high-glucose exposure but reduced in chronic hyperglycemic conditions. Consistently, our *in vivo* functionality assessment with MI supplementation in Zucker diabetic fatty rats improved the disease phenotypes of diabetic rats and islets. These data prompt us to speculate that SMIT1 is required to maintain a stable PI pool in pancreatic β cells in order that PI remains available despite its rapid turnover. Given the relatively ubiquitous expression of SMIT1, our study findings provide not only a new perspective on the pathophysiology of T2DM, but also a broad physiological significance with respect to the molecular aspects of other diseases, which are characterized by altered inositol metabolism.

Session IV

Speaker Biography

Prof. XIA Jun（夏軍） received his medical degree in 1993 from the Xiangya Medical School of Central South University in China. After obtaining his initial scientific training from the Shanghai Brain Research Institute at Chinese Academy of Sciences, he went to study in the Johns Hopkins University School of Medicine in the United States and received his PhD in Neuroscience in 2001. He joined the Division of Life Science, Hong Kong University of Science and Technology as a faculty member in 2002. Prof. Xia is interested in synapse organization and function with implications in learning, memory and brain disorders. He also works on molecular mechanism of protein trafficking and its implication in diseases.

Five recent representative publications

1. He J, Xia M, Tsang WH, Chow KL, **Xia J***. "ICA1L forms BAR-domain complexes with PICK1 and is critical for acrosome formation in spermiogenesis." ***J Cell Sci***, 2015; 128(20):3822-3836.
2. Xu J, Kam C, Luo J, **Xia J***. "PICK1 mediates synaptic recruitment of AMPA receptors at neurexin-induced postsynaptic sites." ***J Neurosci***, 2014; 34(46):15415-15424.
3. Cao M, Mao Z, Kam C, Xiao N, Cao X, Shen C, Cheng KK, Xu A, Lee KM, Jiang L, **Xia J***. "PICK1 and ICA69 control insulin granule trafficking and their deficiencies lead to impaired glucose tolerance." ***PLoS Biol***, 2013; 11(4):e1001541.
4. Xu J, Xiao N, **Xia J***. "Thrombospondin 1 accelerates synaptogenesis in hippocampal neurons through neuroligin 1." ***Nat Neurosci***, 2010; 13(1):22-24.
5. Xiao N, Kam C, Shen C, Jin W, Wang J, Lee KM, Jiang L, **Xia J***. "PICK1 deficiency causes male infertility in mice by disrupting acrosome formation." ***J Clin Invest***, 2009; 119(4):802-812.

Technical expertise

✧ Neuronal culture, fluorescence imaging, mouse genetics, cell biology.

Molecular mechanism of dense core biogenesis

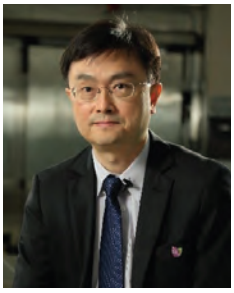
XIA Jun

Division of Life Science and Division of Biomedical Engineering, The Hong Kong University of Science and Technology, Hong Kong SAR, P.R. China.

Mammalian cells are divided by elaborate membrane compartments. Proteins are transported between different compartments via trafficking vesicles. There are two distinct types of vesicles observed under electron microscopes, the clear core vesicles (CCVs) and the dense-core vesicles (DCVs). DCVs are responsible for the secretion of various hormones and neuropeptides that are vital to multiple biological processes. Deficiencies in their secretions can lead to many human diseases; for example, defective insulin secretion causes diabetes. Our knowledge about the molecular machinery controlling the biogenesis, transportation and secretion of DCVs is limited. We identified PICK1 and ICA69, a pair of BAR domain containing proteins, as important regulators for DCV biogenesis. PICK1-ICA69 heterodimers were recruited to trans-Golgi network by small G protein and facilitate the biogenesis of DCVs. The switch from heteromeric PICK1-ICA69 to homomeric PICK1-PICK1 BAR domain complex provides an important mechanism for vesicle sorting and refinement. Deficiencies in PICK1 and ICA69 caused impaired insulin secretion and acrosome formation defects, which eventual led to glucose intolerance and infertility.

Session IV

Speaker Biography



Prof. CHAN Sun On（陳新安）graduated from The Chinese University of Hong Kong with a BSc degree in Biology. He then studied a MPhil degree in the Department of Anatomy. He was awarded the Croucher Foundation Scholarship to study a DPhil programme in Neuroscience in University of Oxford, under the supervision of Prof. Ray Guillery.

After graduation, he moved back to Hong Kong and started to teach in the Department of Anatomy (now School of Biomedical Sciences) as a lecturer, Associate Professor and Professor. His major research interests are on development of visual pathway and recently mechanisms of ocular inflammation and its protection.

Five recent representative publications

1. Chu WK, Law KS, **Chan SO**, Yam JC, Chen LJ, Zhang H, Cheung HS, Block NL, Schally AV, Pang CP. "Antagonists of growth hormone-releasing hormone receptor induce apoptosis specifically in retinoblastoma cells." ***Proc Natl Acad Sci USA***, 2016; 113(50):14396-14401.
2. Zhang XY, Ng TK, Brelen ME, Wu D, Wang JX, Chan KP, Yung JS, Cao D, Wang Y, Zhang S, **Chan SO**, Pang CP. "Continuous exposure to non-lethal doses of sodium iodate induces retinal pigment epithelial cell dysfunction." ***Sci Rep***, 2016; 6:37279.
3. Yang Y, Qin YJ, Yip YW, Chan KP, Chu KO, Chu WK, Ng TK, Pang CP, **Chan SO**. "Green tea catechins are potent anti-oxidants that ameliorate sodium iodate-induced retinal degeneration in rats." ***Sci Rep***, 2016; 6:29546.
4. Qin YJ, **Chan SO**, Chong KK, Li BF, Ng TK, Yip YW, Chen H, Zhang M, Block NL, Cheung HS, Schally AV, Pang CP. "Antagonist of GH-releasing hormone receptors alleviates experimental ocular inflammation." ***Proc Natl Acad of Sci USA***, 2014; 111(51):18303-18308.
5. Qin YJ, Chu KO, Yip YW, Li WY, Yang YP, Chan KP, Ren JL, **Chan SO**, Pang CP. "Green tea extract treatment alleviates ocular inflammation in a rat model of endotoxin-induced uveitis." ***PLoS One***, 2014; 9(8):e103995.

Technical expertise

- ✧ Confocal microscopy, immunohistochemistry, cell and tissue culture, axon tracing, brain slice imaging.

Anti-inflammatory effects of green tea extract in eye diseases

CHAN Sun On[1], REN Jialin[1], PANG Chi Pui[2]

[1] Neural, Vascular, and Metabolic Biology Program, School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.
[2] Department of Ophthalmology and Visual Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.

Aim: To evaluate the anti-inflammatory effect of Green Tea Extract (GTE) on Lipopolysaccharides (LPS)-induced retinal inflammation in Sprague Dawley (SD) rat and its underlying mechanism.

Methods: Forty-eight SD rats were randomly divided into four groups. i). Control Group, injected with saline into one footpad and fed with water 2/8/26/32 hours after injection. ii) LPS group, injected with 1mg/kg LPS and fed with water for four times as above. iii) 550mg/kg GTE Group, footpad injected with LPS and fed with 550mg/ml GTE for four times. iv) 275mg/kg GTE Group, footpad injected LPS and fed with 275mg/ml GTE for four times (n=12 in each group). Rats were sacrificed at 48 hrs after footpad injection and 6 rats in each group was used for retinal whole-mount staining and H&E staining. Meanwhile, the remaining 6 rats in each group were prepared for vitreous humor collection and retinal RNA and protein detection.

Results: Whole mount staining of the rat retina showed that the number of activated OX-42 positive microglial cells were significantly decreased after GTE treatment from 570.3±30 cells/field (LPS) to 287.2±28.7 cells/field (275 GTE group) and 186.5±28.2 cells/field (550 GTE group), respectively. Moreover, H&E staining demonstrated that fewer inflammatory cells accumulated around the optic nerve after GTE treatments. By counting the cell number in the vitreous humor, we found GTE decreased the infiltrated cell density from 36.7±9.7×105/ml (LPS) to 9.8±3.2×105/ml (275 GTE group) and 8.8±4.5×105/ml (550 GTE group). The protein concentrations in the vitreous humor of GTE-treated group were lowered significantly as well. Meanwhile, the RNA expression of inflammatory cytokines such as interleukin-1 beta (IL-1β) and tumor necrosis factor-α (TNF-α) was also down-regulated in GTE groups comparing that in LPS group. However, interleukin-6 (IL-6) and inducible-nitric oxide synthases (iNOS) genes in retina were not changed substantially after LPS treatment.

Conclusions: Our results demonstrate that GTE is an effective agent in suppressing retinal inflammation in rats, and support strongly a potential use of GTE on treatment of retinal inflammation.

Session IV

Speaker Biography

Prof. HUANG Yu（黄聿） received his PhD degree from University of Cambridge. He is the Professor of Biomedical Sciences and the Associate Director (Research) of School of Biomedical Sciences, The Chinese University of Hong Kong (CUHK). He is the founding Director (Basic Sciences) of Institute of Vascular Medicine, CUHK. Prof. Huang Yu is currently the President of Asian Society for Vascular Biology and the Vice-President for both Chinese Society for Vascular Medicine and the Chinese Section, the International Society for Heart Research (http://www.cuhk.edu.hk/proj/HuangLab/). Huang's team has been actively exploring clinically relevant research aiming to elucidate cellular and molecular events involved in the initiation and progression of endothelial cell dysfunction in hypertension, obesity, diabetes, estrogen deficiency and aging, to uncover novel relevant biomarkers for vascular pathogenesis, and to develop venues to reverse vascular dysfunction in animal models of cardio-metabolic disorder. He has co-authored 383 publications in SCI-indexed journals including Antioxidants & Redox Signaling, Arteriosclerosis, Thrombosis and Vascular Biology, Cell Metabolism, Circulation Research, Diabetes, European Heart Journal, Hypertension, Kidney International, Nature, Science, and Stroke with 17400 Google scholar citations and h-index 67. He has so far served (past and present) as the editor, guest editor, associate editor, and editorial board member for 38 journals. He received the Croucher Senior Research Fellow Award from Hong Kong Croucher Foundation in 2014 and the second-class Award, the State Natural Science Award, China in 2015.

Five recent representative publications

1. Cheang WS, Wong WT, Zhao L, Xu J, Wang L, Lau CW, Chen ZY, Ma RC, Xu A, Wang N, Tian XY, **Huang Y**. "PPARδ is required for exercise to attenuate endoplasmic reticulum stress and endothelial dysfunction in diabetic mice." ***Diabetes***, 2017; 66(2):519-528.
2. Wang L, Luo JY, Li B, Tian XY, Chen LJ, Huang Y, Liu J, Deng D, Lau CW, Wan S, Ai D, Mak KK, Tong KK, Kwan KM, Wang N, Chiu JJ, Zhu Y, **Huang Y**. "Integrin-YAP/TAZ-JNK cascade mediates atheroprotective effect of unidirectional shear flow." ***Nature***, 2016; 540:579-582 with Comment in Nature News and Views, ***Nature***, 2016; 540:531-532.
3. Zhang H, Liu J, Qu D, Wang L, Luo JY, Lau CW, Liu P, Gao Z, Tipoe GL, Lee HK, Ng CF, Ma RC, Yao X, **Huang Y**. "Inhibition of miR-200c restores endothelial function in diabetic mice through suppression of COX-2." ***Diabetes***, 2016; 65(5):1196-1207 with Commentary, ***Diabetes***, 2016; 65(5):1152-1154.
4. Hu W, Zhang Y, Wang L, Lau CW, Xu J, Luo JY, Gou L, Yao X, Chen ZY, Ma RC, Tian XY, **Huang Y**. "Bone morphogenic protein 4-Smad induced upregulation of platelet-derived growth factor AA impairs endothelial function." ***Arterioscler Thromb Vasc Biol***, 2016; 36(3):553-560.
5. Liu J, Wang L, Tian XY, Liu L, Wong WT, Zhang Y, Han QB, Ho HM, Wang N, Wong SL, Chen ZY, Yu J, Ng CF, Yao X, **Huang Y**. "Unconjugated bilirubin mediates heme oxygenase-1-induced vascular benefits in diabetic mice." ***Diabetes***, 2015; 64(5):1564-1575 with Commentary, ***Diabetes***, 2015; 64(5):1506-1508.

Technical expertise

✧ Animal models of cardiovascular and metabolic diseases; assay for examining vascular function/dysfunction, platform for identifying relevant new biomarkers and therapeutic targets.

Physical exercise, shear stress, and vaso-protection

HUANG Yu

Neural, Vascular, and Metabolic Biology Program, School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.

The haemodynamic patterns (laminar or unidirectional versus oscillatory blood flow) profoundly impact vascular function through exerting different mechanical forces (or shear stress) on the luminal endothelial cell layer of blood vessels. Laminar flow mainly occurring along the straight part of the vascular tree is considered to be vaso-beneficial while oscillatory (or disturbed) flow primarily experienced by vascular curvature or branches is believed to be vaso-harmful. The latter is closely associated with the initiation of atherosclerosis, a condition that may lead to fatal events in the heart and brain. Physical exercise reduces the impact of oscillatory flow, thus producing benefits on health, particularly on vascular and metabolic function although the underlying molecular mechanisms are largely unclear. Our recent study demonstrates that PPARδ-mediated inhibition of endoplasmic reticulum stress contributes to the vascular benefits of exercise in diabetic and obese mice and provides potentially effective targets for treating diabetic vasculopathy (Cheang et al., Diabetes, 2017). We have also recently explored the role of YAP and TAZ, the effectors of the Hippo pathway known as mediators for mechanical stimuli, in haemodynamics-induced mechanotransduction and pathogenesis of atherosclerosis. Atheroprone-disturbed flow increases whereas atheroprotective unidirectional shear stress inhibits YAP/TAZ activity. Unidirectional shear stress activates integrin and promotes integrin-$G\alpha_{13}$ interaction, leading to RhoA inhibition and YAP phosphorylation and suppression. YAP/TAZ inhibition suppresses JNK signalling and downregulates pro-inflammatory genes expression, thereby reducing monocyte attachment and infiltration. *In vivo* endothelial-specific YAP overexpression exacerbates, while CRISPR/Cas9-mediated Yap knockdown in endothelium retards, plaque formation in $ApoE^{-/-}$ mice (Wang et al., Nature, 2016). The present results indicate that integrin-$G\alpha_{13}$-RhoA-YAP pathway holds promise as a novel drug target against atherosclerosis.

Session IV

Speaker Biography

Prof. SHUM Sau Wun Alisa（沈秀媛） is an Associate Professor at the School of Biomedical Sciences of The Chinese University of Hong Kong (CUHK). She received her BSc degree in cell biology from University of Glasgow. She then obtained a DPhil degree in developmental biology from University of Oxford, studying the pathogenic mechanism of neural tube defects. After graduation, she was awarded a Croucher Fellowship to conduct postdoctoral research on genomic imprinting at University of Cambridge prior to joining CUHK.

Prof. Shum has used animal models to study different types of congenital malformations, including neural tube, heart and kidney defects, cleft palate and caudal regression. She has focused on the effect of retinoic acid and maternal diabetes on embryo development. Her group has unraveled a paradoxical teratogenic mechanism for retinoic acid, a key regulator of growth and development, which has important implications for retinoid-based therapies. Her group is the first to demonstrate a mechanistic link between perturbation of retinoid homeostasis and increased susceptibility to malformations in embryos exposed to diabetes. Recent findings from her group also support an association of subnormal retinoid levels with fetal programming of chronic diseases in adulthood. She aims to develop in utero therapeutic interventions to reduce the risk of birth defects and prevent the development of diabetes, obesity and related complications later in life in offspring of mothers with pregestational diabetes. Her current research also includes preclinical studies on novel drugs that have anti-obesity and insulin-sensitizing effects.

Five recent representative publications

1. Lee LM, Leung MB, Kwok RC, Leung YC, Wang CC, McCaffery PJ, Copp AJ, **Shum AS**. "Perturbation of retinoid homeostasis increases malformation risk in embryos exposed to pregestational diabetes." ***Diabetes***, 2017; 66(4):1041-1051.
2. Lee LM, Leung CY, Tang WW, Choi HL, Leung YC, McCaffery PJ, Wang CC, Woolf AS, **Shum AS**. "A paradoxical teratogenic mechanism for retinoic acid." ***Proc Natl Acad Sci USA***, 2012; 109(34):13668-13673.
3. Tse HK, Leung MB, Woolf AS, Menke AL, Hastie ND, Gosling JA, Pang CP, **Shum AS**. "Implication of *Wt1* in the pathogenesis of nephrogenic failure in a mouse model of retinoic acid-induced caudal regression syndrome." ***Am J Pathol***, 2005; 166(5):1295-1307.
4. Leung MB, Choy KW, Copp AJ, Pang CP, **Shum AS**. "Hyperglycaemia potentiates the teratogenicity of retinoic acid in diabetic pregnancy in mice." ***Diabetologia***, 2004; 47(3):515-522.
5. Chan BW, Chan KS, Koide T, Yeung SM, Leung MB, Copp AJ, Loeken MR, Shiroishi T, **Shum AS**. "Maternal diabetes increases the risk of caudal regression caused by retinoic acid." ***Diabetes***, 2002; 51(9):2811-2816.

Technical expertise

- ✧ Rodent embryo culture and organ culture for drug testing
- ✧ Manipulation of preimplantation and postimplantation rodent embryos
- ✧ Whole mount in situ hybridization
- ✧ Streptozotocin-induced diabetic and diet-induced obesity mouse models

Dysregulation of retinoid homeostasis in embryos exposed to pregestational diabetes

LEE Man Yuen Leo, SHUM Sau Wun Alisa

Neural, Vascular, and Metabolic Biology Program, School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.

Pregestational diabetes is highly associated with an increased risk of birth defects. However, factors that can increase or reduce the expressivity and penetrance of malformations in pregnancies in women with diabetes remain poorly identified. All-*trans* retinoic acid (RA) plays crucial roles in embryogenesis. We find that *Cyp26a1*, which encodes a key enzyme for catabolic inactivation of RA required for tight control of local RA concentrations, is significantly downregulated in embryos of diabetic mice. Embryonic tissues expressing *Cyp26a1* show reduced efficiency of RA clearance. Embryos exposed to diabetes are thus sensitized to RA and more vulnerable to the deleterious effects of increased RA signalling. Susceptibility to RA teratogenesis is further potentiated in embryos with a preexisting genetic defect of RA metabolism. Increasing RA clearance efficiency using a preconditioning approach can counteract the increased susceptibility to RA teratogenesis in embryos of diabetic mice. Our findings provide new insight into gene-environment interactions that influence individual risk in the manifestation of diabetes-related birth defects and shed light on the environmental risk factors and genetic variants for a stratified medicine approach to screening women with diabetes who are of childbearing age and assessing the risk of birth defects during pregnancy.

Session V

Speaker Biography

Prof. LIN Ge（林鴿）is currently working as a full professor at School of Biomedical Sciences, The Chinese University of Hong Kong (CUHK). She also serves as Director of Joint Research Laboratory for Promoting Globalization of Traditional Chinese Medicines between Shanghai Institute of Materia Medica, Chinese Academy of Sciences and CUHK. Prof. Lin has a long-standing interest in pharmaceutical research including: 1) drug metabolism (DM) and pharmacokinetics (PK); 2) pharmacology and mechanisms of drug actions; 3) idiosyncratic adverse effect/toxicity; 4) herb-drug interactions; and 5) globalization of TCM herbs. She is an expert in applying multidisciplinary studies for investigating TCM herbs. Her research in TCM herbs integrates chemical analysis, PK, PD, and toxicology studies for the identification of bioactive ingredients with confirmed bioavailability and verified PK fates, safety assessment, and development of quality control of TCM herbs and their beneficial interactions with orthodox drugs. Prof. Lin is also working on translational research. One of her on-going research projects is to develop biomarkers for the diagnosis and assessment of hepatotoxicity induced by pyrrolizidine alkaloids (PA)-containing herbs and PA-contaminated foods. Her team is one of the world leading groups in this field and has been well recognized internationally.

Five recent representative publications

1. Zhu L, Xue J, Xia Q, Fu PP, **Lin G***. "The long persistence of pyrrolizidine alkaloid-derived DNA adducts *in vivo*: kinetic study following single and multiple exposures in male ICR mice." ***Arch of Toxicol***, 2017; 91(2):949-965.
2. Ma BL, Yin C, Zhang BK, Dai Y, Jia YQ, Yang Y, Li Q, Shi R, Wang TM, Wu JS, Li YY, **Lin G***, Ma YM*. "Naturally occurring proteinaceous nanoparticles in Coptidis Rhizoma extract act as concentration-dependent carriers that facilitate berberine absorption." ***Sci Rep***, 2016; 6:20110.
3. Ruan J, Gao H, Li N, Xue J, Chen J, Ke C, Ye Y, Fu PP, Zheng J, Wang J, **Lin G***. "Blood pyrrole-protein adducts – A biomarker of pyrrolizidine alkaloid-induced liver injury in humans." ***J Environ Sci Health C Environ Carcinog Ecotoxicol Rev***, 2015; 33(4):404-421.
4. Zhang S, Chu Z, Yin C, Zhang C, **Lin G***, Li Q*. "Controllable drug release and simultaneously carrier decomposition of SiO2-drug composite nanoparticles." ***J Am Chem Soc***, 2013; 135(15):5709-5716.
5. **Lin G***, Wang JY, Li N, Li M, Gao H, Ji Y, Zhang F, Wang H, Zhou Y, Ye Y, Xu HX, Zheng J. "Hepatic sinusoidal obstruction syndrome associated with consumption of *Gynura segetum*." ***J Hepatol***, 2011; 54(4):666-673.

Risk of pyrrolizidine alkaloid-induced hepatotoxicity and biomarker for the risk assessment

MA Jiang, ZHU Lin, YANG Meng Bi, WANG Zhang Ting, HE Yi Seng, LIN Ge

Cancer Biology and Experimental Therapeutics Program, School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.

The increasing usage of alternative medicines for the health care and disease treatment worldwide results in more public concerns on their safety problems. However, comparing with the orthodox drugs, there are less awareness and investigation on the adverse effects/toxicity induced by herbal preparations and natural products. Herbal medicines and natural products consist of multi-ingredients acting on multi-targets, which makes the investigation of their adverse effects/toxicity much more difficult and challenging. Among drug-induced adverse effects/toxicities, drug-induced liver injury (DILI) is one of the leading causes of acute liver failure. Unlike well-recognized DILI caused by orthodox drugs, the hepatic impairments caused by natural products, including herbal remedies and dietary supplements, often have less public awareness and are also lack of the confirmative diagnosis in clinic. In the recent decades, herbs and natural products induced hepatotoxicity have been reported as one of the major causes of DILI worldwide. The diagnosis of herbal hepatotoxicity is challenging due to the lack of characteristic clinical features and specific biomarkers for the diagnosis. This has subsequently hindered the development of specific and efficacious clinical treatment. Among differential natural products that can cause DILI, pyrrolizidine alkaloids (PAs) are one of the most significant naturally occurring toxins. To date, over 660 PAs and PA *N*-oxides have been identified in approximately 3% of flowering plants, and about half of PAs have been reported to be hepatotoxic. Yearly numerous incidences of PA-induced liver injury (PA-ILI) associated with the intake of PA-containing herbal products and/or PA-contaminated foodstuffs have been reported worldwide. On the other hand, although PA *N*-oxides coexist with PAs in plants with varied quantities sometimes even higher than that of PAs, hepatotoxicity of PA *N*-oxides remains largely unclear. In this presentation, using PA-ILI and PA *N*-oxide-ILI as examples, our methodical translational studies, from the identification of clinical problems, to the laboratory basic science for delineating toxic mechanism and developing the mechanism-based specific biomarker, and then the transformation of such biomarker to the clinical diagnosis of PA-ILI and risk assessment of exposure to PAs and PA *N*-oxides will be illustrated.

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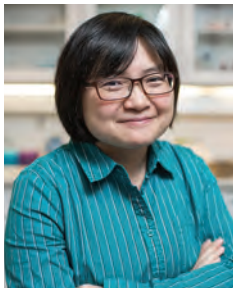
Session V

Speaker Biography



Prof. HO Yi Ping Megan（何亦平） is currently an Assistant Professor in the Department of Electronic Engineering (Division of Biomedical Engineering) at The Chinese University of Hong Kong. She received her B.S. and M.S. in Power Mechanical Engineering from National Tsing-Hua University, Taiwan. She then spent a year as a R&D engineer in Walsin-Lihwa MEMS Business Unit, Taiwan. In 2008, she received her Ph.D. in Mechanical Engineering from the Johns Hopkins University. After her postdoctoral training with Duke University, she joined the Interdisciplinary Nanoscience Center (iNANO) and the Department of Molecular Biology and Genetics in Aarhus University, Denmark, as an Assistant Professor in 2012. She is also a co-founder of a start-up company, Zymonostics, situated in Demark. She has received 15 academic honors and awards, published 42 peer-reviewed journal articles, 61 conference abstracts, 2 granted patents and 4 invention disclosures. The results that she presented have been recognized internationally by the American Society of Gene Therapy and Controlled Release Society. Her research focuses on integrating nanophotonics, novel molecular constructs and microfluidics for disease diagnostics.

Five recent representative publications

1. Jepsen ML, Harmsen C, Godbole AA, Nagaraja V, Knudsen BR, **Ho YP***. "Specific detection of the cleavage activity of mycobacterial enzymes using a quantum dot based DNA nanosensor." ***Nanoscale***, 2016; 8(1):358-364.
2. Gaglianone N, Hvam ML, Aslan H, Dong M, Howard KA, **Ho YP***, "Chip-free microscale incubator-based synthesis of chitosan-based gene silencing nanoparticles." ***Particle and Particle Systems Characterization***, 2016; 33(5):279-285.
3. Chiu YL, Chan HF, Phua KK, Zhang Y, Juul S, Knudsen BR, Leong KW*, **Ho YP***, "Synthesis of fluorosurfactants for emulsion-based biological applications." ***ACS Nano***, 2014; 8(4):3913-3920.
4. Juul S, Iacovelli F, Falconi M, Kragh SL, Christensen B, Frøhlich R, Franch O, Kristoffersen EL, Stougaard M, Leong KW, **Ho YP**, Sørensen ES, Birkedal V, Desideri A, Knudsen BR. "Temperature-controlled encapsulation and release of an active enzyme in the cavity of a self-assembled DNA nanocage." ***ACS Nano***, 2013; 7(11):9724-9734.
5. Juul S, Nielsen CJ, Labouriau R, Roy A, Tesauro C, Jensen PW, Harmsen C, Kristoffersen EL, Chiu YL, Frøhlich R, Fiorani P, Cox-Singh J, Tordrup D, Koch J, Bienvenu AL, Desideri A, Picot S, Petersen E, Leong KW, **Ho YP**, Stougaard M, Knudsen BR. "Droplet microfluidics platform for highly sensitive and quantitative detection of malaria-causing Plasmodium parasites based on enzyme activity measurement." ***ACS Nano***, 2012; 6(12):10676-10683.

Technical expertise

- ✧ DNA nanosensors
- ✧ Diseases diagnostics via enzymatic activities
- ✧ Microfabrication
- ✧ Droplet microfluidics

Early diagnosis *via* a new biomarker: the activity of essential pathogen expressed DNA modifying enzymes

JEPSEN Morten Leth[1,2], HARMSEN Charlotte[2], HEDE Marianne Smedegaard[3], GODBOLE Adwait Anand[4], NAGARAJA Valakunja[4], KNUDSEN Birgitta R.[1,2], HO Yi Ping[1,2,5]

[1] Aarhus University, Interdisciplinary Nanoscience Center (iNANO), Aarhus, Denmark.
[2] Aarhus University, Department of Molecular Biology and Genetics, Aarhus, Denmark.
[3] Zymonostics, Aarhus, Denmark.
[4] Indian Institute of Science, Department of Microbiology and Cell Biology, Bangalore, India.
[5] Division of Biomedical Engineering, Department of Electronic Engineering, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.

Infectious disease represents a major threat to global health causing millions of human lives often due to late diagnosis and inefficient treatment. Many of the currently prevalent diagnostics methods are not preferred in the clinics because they rely heavily on pre-amplification or post-separation steps. Motivated by the appeal of a sensitive, yet easy-to-assay, diagnostic approach, this talk will highlight the potential of adopting a new biomarker, the activity of pathogen expressed DNA-modifying enzymes, for the diagnostics of infectious diseases. Of particular emphasis, this talk will discuss our recent development on the rolling-circle amplification based detection and a quantum dot based DNA nanosensor designed for ultrasensitive and rapid detection, respectively. The sensor in its current form is designed to specifically target the cleavage–religation activity of an essential DNA-modifying enzyme, topoisomerase I. The developed assay can be easily extended to dissect other relevant enzymatic activities. More importantly, we have further advanced the field by introducing miniaturized droplets produced by microfluidics for effective sample processing and enzyme extraction, which has enabled the potential of using noninvasive samples, such as saliva, as new test materials. The initial development has paved the way to the diagnosis of many major infectious diseases, such as malaria, tuberculosis and HIV. The development of an effective and sensitive diagnostic platform is envisioned not only to help interrupt disease transmission, but also help evaluate therapeutic efficacy of new drugs.

Session V

Speaker Biography

Prof. KWAN Yiu Wa（關耀華） received his Bachelor degree (Hons) from Liverpool University (UK), and his PhD degree from Strathclyde University (Scotland). He is a pharmacologist by training, and his main research interests are related to the pharmacology of different drugs in treating metabolic and vascular diseases e.g. type 2 diabetes mellitus, osteoporosis and pulmonary hypertension. He also has research interests in the utilization of alternative / un-conventional approaches in treating metabolic diseases.

Five recent representative publications

1. Vong CT, Tseng HH, **Kwan YW**, Lee SM, Hoi MP. "Antrodia camphorata increases insulin secretion and protects from apoptosis in MIN6 cells." ***Front Pharmacol***, 2016; 7:67.
2. Poon CC, Li RW, Seto SW, Kong SK, Ho HP, Hoi MP, Lee SM, Ngai SM, Chan SW, Leung GP, **Kwan YW**. "In vitro vitamin K_2 and 1α,25-dihydroxyvitamin D_3 combination enhances osteoblasts anabolism of diabetic mice." ***Eur J Pharmacol***, 2015; 767:30-40.
3. Li S, Dang Y, Zhou X, Huang B, Huang X, Zhang Z, **Kwan YW**, Chan SW, Leung GP, Lee SM, Hoi MP. "Formononetin promotes angiogenesis through the estrogen receptor alpha-enhanced ROCK pathway." ***Sci Rep***, 2015; 5:16815.
4. Hoi PM, Li S, Vong CT, Tseng HH, **Kwan YW**, Lee SM. "Recent advances in structure-based drug design and virtual screening of VEGFR tyrosine kinase inhibitors." ***Methods***, 71:85-91.
5. Li S, Dang YY, Oi Lam Che G, **Kwan YW**, Chan SW, Leung GP, Lee SM, Hoi MP. "VEGFR tyrosine kinase inhibitor II (VRI) induced vascular insufficiency in zebrafish as a model for studying vascular toxicity and vascular preservation." ***Toxicol Appl Pharmacol***, 2014; 280(3):408-420.

Technical expertise

- ✧ Ion channels (whole-cell) measurements
- ✧ Isolation of vascular smooth muscle cells, osteoblasts and pancreatic β-cells
- ✧ Bio-active peptides isolation and synthesis
- ✧ New drug designs and drug-receptors docking
- ✧ Cranial window construction and cerebral artery recording

Combined drugs treatment for diabetes-associated osteoporosis

POON Chiu Wa Christina[1], LI Wai Sum Rachel[1,2], SETO Sai Wang[3], KONG Siu Kai[4], HO Pui Ho[5], HOI Pui Man[6], LEE Ming Yuen Simon[6], NGAI Sai Ming[4], CHAN Shun Wan[7], LEUNG Pak Heng George[2], KWAN Yiu Wa[1]

[1] Neural, Vascular, and Metabolic Biology Program, School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.
[2] Department of Pharmacology and Pharmacy, Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, P.R. China.
[3] National Institute of Complementary Medicine, School of Science and Health, University of Western Sydney, Australia.
[4] School of Life Sciences, Faculty of Science, The Chinese University of Hong Kong, Hong Kong.
[5] Department of Electronic Engineering, Faculty of Engineering, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.
[6] Institute of Chinese Medical Sciences, The University of Macau, Macau, P.R.China.
[7] State Key Laboratory of Chinese Medicine and Molecular Pharmacology, Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hong Kong SAR, P.R. China.

Diabetes mellitus (DM) is a growing global epidemic crisis. DM patients suffer increased morbidity and mortality not only because of increased complication in cardiovascular diseases, but also an increased fracture related to osteoporosis - a skeletal disorder of bone loss and fractures. Diabetic patients have a higher risk of developing spontaneous hip fractures by falls. In this study, we evaluated the anabolic effects and the underlying cellular mechanisms involved of vitamin K_2 (10 nM) and 1α,25-dihydroxyvitamin D_3 ($1,25(OH)_2D_3$) (10 nM), alone and in combination, on primary osteoblasts harvested from the iliac crests (anatomically equivalent to the hips of humans) of C57BL/KsJ lean (+/+) and obese/diabetic (*db/db*) (leptin receptor-deficient) mice (female; 4-6 months old). A lower alkaline phosphatase (ALP) activity plus a reduced expression of bone anabolic markers and bone formation transcription factors (osteocalcin, Runx2, Dlx5, ATF4 and OSX) were consistently detected in osteoblasts of *db/db* mice compared to lean mice. A significantly higher calcium deposits formation in osteoblasts was detected in lean mice when compared to *db/db* mice. Co-administration of vitamin K_2 (10 nM) and $1,25(OH)_2D_3$ (10 nM) caused an enhancement of calcium deposits in osteoblasts in both strains of mice. Vitamins K_2 and $1,25(OH)_2D_3$ co-administration time-dependently (7, 14 and 21 days) increased the levels of bone anabolic markers and bone formation transcription factors, with a greater magnitude of increase was consistently observed in osteoblasts of *db/db* mice. Combined vitamins K_2 plus $1,25(OH)_2D_3$ treatment significantly enhanced migration and the re-appearance of surface microvilli and ruffles of osteoblasts of *db/db* mice. Thus, our results illustrate that vitamins K_2 plus D_3 combination could be a novel therapeutic strategy in treating diabetes-associated osteoporosis.

Acknowledgements:
The work described in this paper was fully supported by a grant from the Research Grants Council of the Hong Kong Special Administrative Region (HKSAR), P. R. China (Project no. CUHK467613) and the Health and Medical Research Funds (Food and Health Bureau, Department of Health, HKSAR) (Project reference number: HMRF: 10110371). Dr. S.W. Seto is a recipient of fellowship from the National Heart Foundation, Australia (PF12B6825).

Session VI

Speaker Biography

Dr. ZHOU Jingying（周京穎） received her Ph.D. degree from the AIDS Institute and Department of Microbiology in The University of Hong Kong in 2013, and then joined Prof. Alfred Cheng's lab as a postdoctoral fellow in the School of Biomedical Sciences, The Chinese University of Hong Kong.

Dr. Zhou's current research interests are innate and adaptive immune regulation in cancer, with particular focus on the mechanisms of tumor immune escape in hepatocellular carcinoma. She has published over 10 first author/co-author peer-review articles in decent journals including *Journal of Clinical Investigation* and *Cancer Research*. In addition, she has a U.S. patent on the soluble programmed death 1 (sPD-1)-based dendritic cell (DC) targeting vaccine.

Five recent representative publications

1. Liu M*, **Zhou J***, Chen Z, Cheng AS. "Understanding the epigenetic regulation of tumours and their microenvironments: opportunities and problems for epigenetic therapy." ***J Pathol***, 2017; 241(1):10-24. (*Equal First Author)
2. Tan Z*, **Zhou J***, Cheung AK, Yu Z, Cheung KW, Liang J, Wang H, Lee BK, Man K, Liu L, Yuen KY, Chen Z. "Vaccine-elicited CD8+ T cells cure mesothelioma by overcoming tumor-induced immunosuppressive environment." ***Cancer Res***, 2014; 74(21):6010-6021. (*Equal First Author)
3. **Zhou J**, Cheung AK, Tan Z, Wang H, Yu W, Du Y, Kang Y, Lu X, Liu L, Yuen K, Chen Z. "PD1-based DNA vaccine amplifies HIV-1 GAG-specific CD8+ T cells in mice." ***J Clin Invest***, 2013; 123(6):2629-2642.
4. **Zhou J***, Cheung AK*, Liu H*, Tan Z, Tang X, Kang Y, Du Y, Wang H, Liu L, Chen Z. "Potentiating functional antigen-specific CD8+ T cell immunity by a novel PD1 isoform-based fusion DNA vaccine." ***Mol Ther***, 2013; 21(7):1445-1455.
5. Liu L, Wei Q, Alvarez X, Wang H, Du Y, Zhu H, Jiang H, **Zhou J**, Lam P, Zhang L, Lackner A, Qin C, Chen Z. "Epithelial cells lining salivary gland ducts are early target cells of severe acute respiratory syndrome coronavirus infection in the upper respiratory tracts of rhesus macaques." ***J Virol***, 2011; 85(8):4025-4030.

Technical expertise

- ✧ Immune cell isolation, culture and identification
- ✧ FACS analysis (cell subtypes, intracellular cytokine/chemokine/transcription factor staining)
- ✧ Hepatocellular carcinoma and mesothelioma mouse models
- ✧ DNA and viral vector vaccination

Hepatoma-intrinsic CCRK inhibition diminishes myeloid-derived suppressor cell immunosuppression and enhances immune-checkpoint blockade efficacy

ZHOU Jingying, CHENG Sze Lok Alfred

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Myeloid-derived suppressor cells (MDSCs) comprise a heterogeneous population of immature myeloid cells that induce the exhaustion of anti-tumor immune responses. The accumulation of MDSC correlates with tumor stage, metastatic burden and immune-checkpoint blockade resistance in various cancers. Cancer cells can secrete a variety of cytokines and chemokines to facilitate the generation, tumor infiltration and function of MDSC. However, the cancer cell-specific signaling cascades that promote MDSC expansion and suppressive function remain poorly understood. Emerging evidence highlights the pivotal functions of cyclin-dependent kinases (CDKs) in tumor immunity. Here we elucidated the role of tumor-intrinsic CDK20, or cell cycle-related kinase (CCRK) on immunosuppression in hepatocellular carcinoma (HCC). Tumor-infiltrating $CD11b^{+}CD33^{+}HLA\text{-}DR^{-}$MDSCs from HCC patients potently inhibited autologous $CD8^{+}$T cell proliferation. Concordant over-expression of CCRK and MDSC markers (CD11b/CD33) positively correlated with tumor recurrence and poor survival rates. Hepatocellular CCRK stimulated immunosuppressive $CD11b^{+}CD33^{+}HLA\text{-}DR^{-}$MDSC expansion from human peripheral blood mononuclear cells (PBMCs) through up-regulating IL-6. Mechanistically, CCRK activated nuclear factor-kappa B (NF-κB) via enhancer of zeste homolog 2 (EZH2) and facilitated NF-κB-EZH2 co-binding to IL-6 promoter. Hepatic CCRK induction in transgenic mice activated the EZH2/NF-κB/IL-6 cascade, leading to accumulation of polymorphonuclear-MDSCs with potent T cell-suppressive activity. In contrast, inhibiting tumoral Ccrk or hepatic IL-6 increased $IFN\text{-}\gamma^{+}TNF\text{-}\alpha^{+}CD8^{+}$T cell infiltration and impaired tumorigenicity, which was rescued by restoring polymorphonuclear-MDSCs. Notably, tumoral Ccrk depletion up-regulated programmed death ligand 1 (PD-L1) expression and increased intratumoral $CD8^{+}$T cells, thus enhancing PD-L1 blockade efficacy to eradicate HCC. Our results delineate an immunosuppressive mechanism of the hepatoma-intrinsic CCRK signaling and highlight an over-expressed kinase target whose inhibition might empower HCC immunotherapy.

Session VI

Speaker Biography

Dr. WANG Yaofeng（王曜峰） obtained his Bachelor in Biological Sciences from Zhejiang University (2005), Master in Bioinformatics from Uppsala University, Sweden (2008), and PhD in Computational Biology from Nanyang Technological University, Singapore (2015). Then he joined Prof. Feng Bo's lab since 2015.

His current research interests include the bioinformatics study in pluripotent stem cells, including transcriptional and epigenetic regulation network in pluripotency. He is also interested in the mammalian early embryonic development.

Five recent representative publications

1. He X, Tan C, Wang F, **Wang Y**, Zhou R, Cui D, You W, Zhao H, Ren J, Feng B. "Knock-in of large reporter genes in human cells via CRISPR/Cas9-induced homology-dependent and independent DNA repair." ***Nucleic Acids Res***, 2016; 44(9):e85.
2. Hinks J, **Wang Y**, Matysik A, Kraut R, Kjelleberg S, Mu Y, Bazan GC, Wuertz S, Seviour T. "Increased Microbial Butanol Tolerance by Exogenous Membrane Insertion Molecules." ***ChemSusChem***, 2015; 8(21):3718-3726.
3. Hinks J*, **Wang Y***, Poh WH, Donose BC, Thomas AW, Wuertz S, Loo SC, Bazan GC, Kjelleberg S, Mu Y, Seviour T. "Modeling cell membrane perturbation by molecules designed for transmembrane electron transfer." ***Langmuir***, 2014; 30(9):2429-2440. (*Co-first author)
4. Friemann R, Larsson DS, **Wang Y**, van der Spoel D. "Molecular dynamics simulations of a membrane protein-micelle complex in vacuo." ***J Am Chem Soc***, 2009; 131(46):16606-16607.
5. **Wang Y***, Larsson DS*, van der Spoel D. "Encapsulation of myoglobin in a cetyl trimethylammonium bromide micelle in vacuo: a simulation study." ***Biochemistry***, 2009; 48(5):1006-1015. (*Co-first author)

Technical expertise

- ✧ Bioinformatics
- ✧ Molecular Modeling (Molecular Dynamics Simulations)
- ✧ In silico drug discovery

Decoding pluripotency shades with novel lincRNAs revealed bioinformatics discovery

WANG Yaofeng, FENG Bo

Developmental and Regenerative Biology Program, School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.

The enormous value of stem cell-based therapy has attracted broad attention and prompted its applications in clinical regenerative medicine. Topipotent cell, which is capable of developing into a complete organism from a single cell, is expected as an important tool in regenerative medicine and disease modeling. However, to date, *in vitro* totipotent cell model has not been well established in mammal. Thus, it is foreseeable that an *in vitro* cultured cell model of mammalian totipotent stem cells is of paramount interests to both biomedical and clinical research. Long intergenic non-coding RNA (lincRNA) has been identified to play the critical roles in circuitry controlling and maintaining the pluripotency of embryonic stem (ES) cells. Recent studies suggest lincRNAs bind to chromatin regulatory proteins and primarily regulate pluripotent gene expressions. Thus, lincRNA is expected as a novel important tool to induce cell reprogramming by altering the cell epigenetic landscape. However, lincRNAs active in totipotent stage are so far rarely studied. Here, we initially discovered ~3000 novel lincRNAs from mouse pluripotent stem cells by bioinformatics data mining of public RNA-seq data. Subsequently we performed a bioinformatics pipeline to identify the functional annotations of these novel lincRNAs. To our surprising, a gene module which is specifically active in mouse totipotent stage was obtained from single cell RNA-seq (scRNA-seq) of ~1000 mouse ES cells. The gene module contains ~300 novel lincRNAs and ~700 protein coding genes including totipotent markers. Besides, the gene module has distinct epigenetic features compared to pluripotent genes.

In summary, our results discovered a gene module active in totipotency including ~300 novel lincRNAs. They are potential candidates to alter the epigenetic landscape of mouse pluripotent stem cells, and eventually promote the establishment of mouse totipotent stem cell lines *in vitro*.

Session VI

Speaker Biography

Dr. WALKER Steven Lester has experience in performing high-throughput drug screens, having collaborated and published in eLife Sciences, and Nature Protocols on developing tools and methods for *in vivo* neural imaging in zebrafish and on a prior work in regards to establishing measures to perform a drug screen using transgenic zebrafish in a fluorescent plate reader. Recently, Dr. Walker co-wrote an application to ITF to build a high-throughput behavioral system, which has received funding to Summer 2018. Current projects focus on behavior, cognition and memory in larval zebrafish. Dr. Walker has more than 8 years of experience using the zebrafish model and is an active member within the zebrafish community.

Five recent representative publications

1. White DT, Eroglu AU, Wang G, Zhang L, Sengupta S, Ding D, Rajpurohit SK, **Walker SL**, Ji H, Qian J, Mumm JS. "ARQiv-HTS, a versatile whole-organism screening platform enabling in vivo drug discovery at high-throughput rates." ***Nat Protoc***, 2016; 11(12):2432-2453.
2. Wang G, Rajpurohit SK, Delaspre F, **Walker SL**, White DT, Ceasrine A, Kuruvilla R, Li RJ, Shim JS, Liu JO, Parsons MJ, Mumm JS. "First quantitative high-throughput screen in zebrafish identifies novel pathways for increasing pancreatic β-cell mass." ***Elife***, 2015; doi: 10.7554/eLife.08261.
3. Jiang J, Zhang D, **Walker SL**, Gu C, Ke Y, Yung WH, Chen SC. "Fast 3-D temporal focusing microscopy using an electrically tunable lens." ***Opt Express***, 2015; 23(19):24362-24368.
4. **Walker SL**, Ariga, J, Mathias JR, Coothankandaswamy V, Xie X, Distel M, Köster RW, Parsons MJ, Bhalla KN, Saxena MT, Mumm JS. "Automated reporter quantification *in vivo*: high-throughput screening method for reporter-based assays in zebrafish." ***PLoS One***, 2012; 7(1):e29916.
5. Teng Y, Xie X, **Walker SL**, White DT, Mumm JS, Cowell JK. "Evaluating human cancer cell metastasis in zebrafish." ***BMC Cancer***, 2013; 13:453.

Technical expertise

- ✧ Proficient in Matlab, R, Python, & SQL
- ✧ Knowledgeable in Windows operating system and Linux
- ✧ Proficient in Immunohistochemistry & *in vivo* Time lapse imaging in Zebrafish
- ✧ Knowledgeable in statistical analytics: Kruskal-Wallis, Permutations, Bayesian Analysis
- ✧ Experience with plasmid cloning, qPCR, and Reverse Transcription PCR
- ✧ Trained to use Confocal Microscopes and Two-Photon Microscopes
- ✧ Trained to use Zebrabox behavioral apparatus: OKR, OMR, Predator capture Response

Visualizing the neurodynamics of the zebrafish brain

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Brain diseases including neurodegenerative disorders pose one of the major challenges to the health care system worldwide particularly in regions, such as Hong Kong, that are facing a rapidly aging population. Development of new, more effective drug treatments to cope with neural diseases is a burning issue. However, current drug screening systems and procedures, especially for those targeting brain diseases, have severe limitations. To identify novel therapeutics, we have designed an *in vivo* imaging system which integrates behavioral dynamics of zebrafish, microfluidic devices, OLEDs, and multi-photon imaging into a robust imaging platform. Utilizing a preliminary design of this system, we were able to capture larvae zebrafish in a transferable microfluidic device, position under a multi-photon microscope for *in vivo* calcium imaging in the presence of a red light stimulus. This method was able to statistically and reproducibly differentiate between epileptic and healthy, Parkinson's and healthy, and their respective treatments in zebrafish larvae. *In vivo* neural imaging provided an avenue for distinguishing differences between currently available therapeutic drugs with the potential of identifying newer drugs in the future.

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