School of Biomedical Sciences
Virtual Research Day 2020

SCHOOL OF BIOMEDICAL SCIENCES CUHK 2010-2020

Cancer Biology and Experimental Therapeutics

Developmental and Regenerative Biology

Neural, Vascular, and Metabolic Biology

2 - 3 June 2020

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

香港中文大學 生物醫學學院
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School of Biomedical Sciences
Virtual Research Day 2020

Members of the Organizing Committee

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Professor CHAN Man Lok Andrew
Professor CHAN Wai Yee
Professor BLOCKI Anna
Professor CHAN Hon Fai
Professor CHEN Yangchao
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Professor KO Wing Hung
Professor SO Hon Cheong

COVER: The three Thematic Research Programs of School of Biomedical Sciences, CUHK
Designed by Ms. Law Wing Yan Rhoda, School of Biomedical Sciences, Faculty of Medicine, CUHK

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https://www2.sbs.cuhk.edu.hk/

Welcome Message from the Dean of Faculty of Medicine

I warmly welcome all of you to the School of Biomedical Sciences (SBS) Virtual Research Day 2020.

Since the establishment of the School, SBS Research Day has been an important date marked on our calendar each year when researchers and collaborators from different disciplines gather together to showcase significant progress in advancing biomedical sciences over the past year.

Amidst the COVID-19 pandemic and an advisory on social distancing, for the first time, the Research Day is to be conducted via a virtual platform. Yet, our enthusiasm for exchange of research ideas and insights has become even stronger. Speakers and participants from the School, Faculty and other institutions are very much looking forward to the excitement of meeting online. Together, we will revisit progress and open doors to innovations and new possibilities that shed light on conundrums in biomedical sciences, baffling basic scientists and clinicians alike.

In this one-and-a-half-day, I believe that all participants will benefit enormously from the stimulating interactions and sparks of novel ideas that may pave the way for new research directions and more extensive collaboration.

May I wish all of you good health and continued success in your research endeavours!

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

Welcome Message from the Director of School of Biomedical Sciences

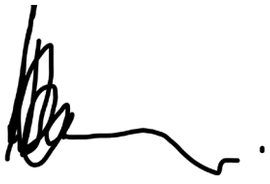
I am pleased to welcome all of you to the School of Biomedical Sciences Virtual Research Day 2020.

This year is the 10th anniversary of the School since its official inauguration in January 2010. In the past decade, Research Day had been our flagship annual event for Principal Investigators to share their research findings and to establish academic collaborations. Despite the COVID-19 pandemic, we are keen to sustain this annual tradition by holding the Research Day via a virtual platform for the first time. Online video conferencing platform is becoming an indispensable part of our research life and we need it to stay connected with our colleagues locally and internationally.

Following the restructuring of our Thematic Research Programs in 2016, the various research components of the School have achieved greater integration. With the tremendous hard work and dedication of all our staff and students, the research competitiveness of our School has been ever increasing. In this one-and-a-half-day event, investigators from our three Thematic Research Programs will showcase their latest discoveries in 15 oral presentations. Your active participation in the Q&A session will help nurture new ideas and enhance the scientific quality of our work. I hope all of you will benefit from the comprehensive nature of the scientific topics and be inspired to start new collaborations with your colleagues, which is important in this fast-changing research environment.

Last but not least, I would like to express my gratitude to members of the organizing committee for their thoughtful planning in organising the Research Day in this new format, as well as to the sponsoring companies for their supports in this event.

Wish all of you a great time with us and good health!



Andrew M. Chan
Professor and Director
School of Biomedical Sciences
Faculty of Medicine
The Chinese University of Hong Kong

SBS Virtual Research Day 2020 Programme

2 June 2020 (Tuesday)

09:00-09:30	**Opening Ceremony:** Prof. CHAN Ka Leung Francis (Dean of Faculty of Medicine) & Prof. CHAN Man Lok Andrew (Director of School of Biomedical Sciences)

Time	*Title of Presentation*	*Speaker*	*Abstract No.*
Session I (DRB) *Chairpersons: Prof. BLOCKI Anna (iTERM / DRB, CUHK) and Prof. CHOY Kwong Wai Richard (OBG, CUHK)*			
09:30-10:00	Improving the success rate of IVF with novel quality assessment and treatment	Prof. LEE Tin Lap (DRB)	O1
10:00-10:30	Mechanistic insights of complex genomic rearrangements	Prof. GU Shen Linda (DRB)	O2
10:30-11:00	***Break***		
Session II (DRB) *Chairpersons: Dr. LI Linxian (KI) and Prof. FOK Kin Lam Ellis (SBS, CUHK)*			
11:00-11:30	Modulation of macrophages by bioactive glass/ sodium alginate hydrogel is crucial in skin regeneration enhancement	Prof. CHAN Hon Fai (iTERM / DRB)	O3
11:30-12:00	Epigenetic regulation of adult stem cells and its implication in organism aging	Prof. JIANG Xiaohua Cynthia (DRB)	O4
12:00-12:30	Technologies for tissue engineering and regenerative medicine	Prof. KER Dai Fei Elmer (iTERM / DRB)	O5
12:30-14:00	***Break***		
Session III (NVMB) *Chairpersons: Prof. CHAN Chung Ngor Juliana (MEDT, CUHK) and Prof. MIU Kai Kei Kelvin (SBS, CUHK)*			
14:00-14:30	Defective brown adipose tissue development in fetal programming of obesity in offspring of diabetic pregnancy	Prof. SHUM Sau Wun Alisa (NVMB)	O6
14:30-15:00	Endothelial cell homeostasis and dysfunction during vascular repair	Prof. TIAN Xiaoyu (NVMB)	O7
15:00-15:30	***Break***		
Session IV (NVMB) *Chairperson: Prof. YUNG Wing Ho (SBS, CUHK)*			
15:30-16:00	The role of platelet-glycolipid interactions in the stimulation of neuronal electric and synaptic activity	Prof. PONOMAREV Eugene (NVMB)	O8
16:00-16:30	Achieving flexibility in a modular motor system for learning, development, and recovery from injury	Prof. CHEUNG Chi Kwan Vincent (NVMB)	O9
16:30-17:00	The roles of locally coordinated synaptic plasticity in health and disease	Prof. IP Pak Kan Jacque (NVMB)	O10

SBS Virtual Research Day 2020 Programme
3 June 2020 (Wednesday)

Time	*Title of Presentation*	*Speaker*	*Abstract No.*
Session V (CBET) *Chairperson: Prof. ZHOU Jingying (SBS, CUHK)*			
09:00-09:30	Analysis of *Pten*-null mouse astrocytes revealed overlapping transcribed genes with human glioblastoma transcriptome	Prof. CHAN Man Lok Andrew (CBET)	O11
09:30-10:00	Epigenetic regulation of non-coding RNAs in cancer	Prof. CHEN Yang-chao (CBET)	O12
10:00-10:30	***Break***		
Session VI (CBET) *Chairpersons: Prof. TO Kin Wah Kenneth (PHA, CUHK) and Prof. JIANG Yangzi (SBS, CUHK)*			
10:30-11:00	Translating genomics data to clinical applications: drug repositioning and disease subtyping	Prof. SO Hon Cheong (CBET)	O13
11:00-11:30	Neutrophils in inflammatory cancer	Prof. CHEUNG Wing Tai (CBET)	O14
11:30-12:00	Targeting the tumor microenvironment for combination immunotherapy	Prof. CHENG Sze Lok Alfred (CBET)	O15
12:00-12:15	***Closing Remarks***		

Abbreviations:
CUHK = The Chinese University of Hong Kong
iTERM = Institute for Tissue Engineering and Regenerative Medicine
KI = Karolinska Institutet
MEDT = Department of Medicine and Therapeutics
OBG = Department of Obstetrics and Gynaecology
PHA = School of Pharmacy
SBS = School of Biomedical Sciences

SBS Thematic Research Programs:
CBET = Cancer Biology and Experimental Therapeutics
DRB = Developmental and Regenerative Biology
NVMB = Neural, Vascular, and Metabolic Biology

Session I (DRB)

Speaker Biography

Prof. LEE Tin Lap（李天立）is an Associate Professor in the School of Biomedical Sciences at The Chinese University of Hong Kong. He has previously conducted research at National Institutes of Health in the United States for 11 years and was a Staff Scientist at National Institutes of Child Health and Human Development (NICHD) and Project Coordinator at National Center for Biotechnology Information (NCBI).

His research interests include germ cell biology and biomedical informatics. He developed algorithms and databases to facilitate the decoding of genomic regulations that contribute to normal and disease states in germ cell and stem cell development. The achievements in these areas are substantial, as exemplified on academic level with an H-index of 37, and secured more than 16.5 millions of competitive funding from General Research Funds (GRF), Collaborative Research Fund (CRF), Health and Medical Research Fund (HMRF) and Innovation and Technology Commission Funding Schemes (ITCFS).

To translate the research findings, he has recently teamed up with Faculty members from four other Departments (Obstetrics & Gynaecology, The Institute for Tissue Engineering and Regenerative Medicine (iTERM), Biomedical Engineering and Computer Science and Engineering) to form EggLogics, a biotech start-up which aims to deliver next-generation fertility treatment and diagnostics solutions.

Five recent representative publications

1. Suen HC, Qian Y, Liao J, Luk CS, Lee WT, Ng JKW, Chan TTH, Hou HW, Li I, Li K, Chan WY, Feng B, Gao L, Jiang XH, Liu YH, Rudd JA, Hobbs R, Qi H, Ng TK , Mak HK, Leung KS, **Lee TL**. "Transplantation of retinal ganglion cells derived from male germline stem cell as a potential treatment to glaucoma." ***Stem Cells and Development***, 2019; 28(20):1365-1375.
2. Liao J, Ng SH, Luk AC, Suen HC, Qian Y, Lee AWT, Tu J, Fung JCL, Tang NLS, Feng B, Chan WY, Fouchet P, Hobbs RM, **Lee TL**. "Revealing cellular and molecular transitions in neonatal germ cell differentiation using single cell RNA sequencing." ***Development***, 2019;146(6). pii: dev174953. doi: 10.1242/dev.174953.
3. Ma BB[#], **Lee TL**[#], Hu B, Li XY, Zhao XD, Li J, Zhang C, He L, Huang XX, Chen XJ, Li J, Wu J. "Molecular characteristics of early-stage female germ cells revealed by RNA sequencing of single cells and analysis of genome-wide DNA methylation." ***DNA Res***, 2019; 26(2):105-117.
4. Meng C, Liao J, Zhao D, Huang H, Qin J, **Lee TL**, Chen D, Chan WY, Xia Y. "L3MBTL2 regulates chromatin remodeling during spermatogenesis." ***Cell Death Differ***, 2019; doi: 10.1038/s41418-019-0283-z.
5. Qian Y, Liao J, Suen AHC, Lee AWT, Chung HS, Tang NLS, Chow KL, Cao Q, Yip YL, Leung TY, Chan WY, Chan DYL, Li TC, **Lee TL**. "Comparative analysis of single-cell parallel sequencing approaches in oocyte application." ***Int J Biochem Cell Biol***, 2019; 107:1-5. doi: 10.1016/j.biocel.2018.12.003.

[#] Co-first authors

Technical expertise

- ✧ Germ cell biology
- ✧ Regenerative biology
- ✧ Genomics
- ✧ Bioinformatics

Improving the success rate of IVF with novel quality assessment and treatment

LEE Tin Lap

School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.

Delayed marriage and parenthood have been increasingly common and have become a global issue, causing a significant increase of advanced maternal age (AMA) mothers. Many AMA mothers count on Assisted Reproduction Technologies (ART) for fertility restoration. However, many do not realize that the success rate of current ART is also subjected to age. Aging leads to qualitative and quantitative decline of oocytes, which translate to poor embryo development and available mature oocytes for in vitro fertilization (IVF). Currently, there is no proven solution to rescue or increase the number of usable mature oocytes in ART procedure.

To circumvent the situation, we recently developed a method to increase the number of mature (MII) oocytes through in vitro maturation of immature (GV) oocytes with the presence of mesenchymal stem cells (MSCs). This novel non-invasive method allows for producing more MII oocytes for IVF and improves the quality. We demonstrated Green Fluorescence Protein (GFP)- labelled mitochondria were transferred to mouse oocytes via tunneling nanotubes (TNT). The TNT could pass through zona pellucida and lead to a significant improvement in ATP content and maturation rate of aged oocytes. Our results revealed that mouse MSC-mediated mitochondrial transfer increased the maturation rate of aged oocytes by 59.3% and fertilization rate by 50.0%. The aneuploidy and abnormal polar body rates were decreased by 62.5% and 58.6%. Importantly, the transfer efficiency was not limited by the age of MSCs. To increase the performance and consistency of treatment, we will design a microfluidic device for maximizing TNT formation.

Session I (DRB)

Speaker Biography

Prof. GU Shen Linda（顧燊）obtained her bachelor's degree with full scholarship at The Chinese University of Hong Kong (CHUK) in 2009 and received her Ph.D. degree from the School of Biomedical Sciences (SBS) at CUHK in 2013. She then pursued postdoctoral training at Baylor College of Medicine (BCM) in the U.S. under the supervision of world-renowned geneticist Prof. James R. Lupski, focusing on molecular mechanisms for DNA rearrangements and complex chromosomal rearrangements in human diseases. Subsequently, she was selected into the highly competitive American Board of Medical Genetics and Genomic (ABMGG) fellowship program in 2016 at BCM. Graduating from the three-year fellowship training, she was certified in both clinical molecular genetics and cytogenetics. In late 2019, she returned to SBS as an independent investigator. Her research continues on copy-number variants and structural variations in human diseases, and expands to the identification and functional characterization of novel inheritable disease-causing genes. She received several national and international awards, including the 13th International Congress of Human Genetics Travel Award, finalist and semi-finalist of ASHG / Charles J. Epstein Trainee Award for Excellence in Human Genetics Research in 2014 and 2015, and three times Outstanding Research Award from the Association of Chinese Geneticists in America.

Five recent representative publications

1. **Gu S**, Chen C, Rosenfeld JA, Cope H, Launay N, Flanigan K, Waldrop M, Schrader R, Juusola J, Goker-Alpan O, Milunsky A, Schlüter A, Troncoso M, Pujol A, Tan Q, Schaff C, Meng L. "Truncating variants in *UBAP1* associated with childhood-onset nonsyndromic hereditary spastic paraplegia." ***Human Mutation***, 2020; 41(3):632-640.
2. **Gu S**, Jernegan M, Van den Veyver IB, Peacock S, Smith J, Breman A. "Chromosomal microarray analysis on uncultured CVS can be complicated by confined placental mosaicism for aneuploidy and microdeletions." ***Prenatal Diagnosis***, 2018; 38(11):858-865.
3. Song X, Beck CR, Du R, Campbell IM, Coban-Akdemir Z, **Gu S**, Breman AM, Stankiewicz P, Ira G, Shaw CA, Lupski JR. "Predicting human genes susceptible to genomic instability associated with *Alu/Alu*-mediated rearrangements." ***Genome Research***, 2018; 28(18):1228-1242.
4. **Gu S**, Szafranski P, Akdemir ZC, Yuan B, Cooper ML, Magriñá MA, Bacino CA, Lalani SR, Breman AM, Smith JL, Patel A, Song RH, Bi W, Cheung SW, Carvalho CM, Stankiewicz P, Lupski JR. "Mechanisms for Complex Chromosomal Insertions." ***PLoS Genetics***, 2016; 12(11):e1006446.
5. **Gu S**, Yuan B, Campbell IM, Beck CR, Carvalho CM, Nagamani SC, Erez A, Patel A, Bacino CA, Shaw CA, Stankiewicz P, Cheung SW, Bi W, Lupski JR. "*Alu*-mediated diverse and complex pathogenic copy-number variants within human chromosome 17 at p13.3." ***Human Molecular Genetics***, 2015; 24(14):4061-4077.

Technical expertise

- ✧ Diagnostic approaches of inheritable diseases, microarray, FISH, chromosome analysis, clinical exome sequencing, whole genome sequencing
- ✧ Medical genetics, molecular genetics, cytogenetics, clinical interpretation of genetic alterations

Mechanistic insights of complex genomic rearrangements

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[1] School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.
[2] Department of Molecular and Human Genetics, Baylor College of Medicine, Houston, Texas 77030, USA.
[3] Department of Pediatrics, Baylor College of Medicine, Houston, Texas 77030, USA.
[4] Human Genome Sequencing Center, Baylor College of Medicine, Houston, Texas 77030, USA.
[5] Texas Children's Hospital, Houston, Texas 77030, USA.

Genomic disorders are inheritable defects generated through chromosomal rearrangements and gene dosage effects, rather than the classical model of alterations at DNA coding sequences. Architectural features of the human genome can result in instability and susceptibility to DNA rearrangements that cause genomic disorders. We conducted comprehensive mechanistic studies on genomic disorders resulting from complex genomic rearrangements (CGRs), focusing on both a locus-specific region and genome-wide chromosomal insertions.

Chromosome 17 at the p13.3 genomic region lacks extensive low-copy repeat architecture; however, it is highly enriched for *Alu* repetitive elements. By performing high-density oligonucleotide array comparative genomic hybridization (aCGH) and CNV breakpoint junctions mapping to single nucleotide resolution, within the 17p13.3 region, *Alu*-*Alu*-mediated rearrangements were identified in 80% of the interstitial deletions, 46% of the tandem duplications and 50% of the CGRs, indicating that this mechanism was a predominant contributor for breakpoint junctions' formation. Further sequences analysis demonstrates that this type of mechanism is unlikely attributed to non-allelic homologous recombination, but rather may be due to a recombination-coupled DNA replicative repair process.

Chromosomal insertions are genomic rearrangements with a segment inserted into a non-homologous chromosome or a non-adjacent locus on the same chromosome, constituting ~2% of nonrecurrent copy-number gains. Little was known regarding the molecular mechanisms of their formation. We identified 16 individuals with complex insertions among 56,000 individuals tested at Baylor Genetics. Custom high-density aCGH was performed and breakpoint junctions were fine-mapped at single nucleotide resolution. We observed breakpoint junction signatures generated by replication-based mechanism(s) with iterative template switches. Herein, we propose that replicative repair can result in interchromosomal complex insertions generated through chromoanasynthesis involving two or three chromosomes, and cause a fraction of apparently balanced insertions harboring small flanking CNVs.

Session II (DRB)

Speaker Biography

Prof. CHAN Hon Fai（陳漢輝）is an Assistant Professor at the Institute for Tissue Engineering and Regenerative Medicine and School of Biomedical Sciences at The Chinese University of Hong Kong (CUHK). He received his B.Eng. from The University of Hong Kong. He then pursued his M.S. and Ph.D. degree at Duke University with the support of the Sir Edward Youde Memorial Fellowships for Overseas Studies. During his Ph.D. training, he focused on developing microfabrication technologies for tissue engineering and stem cell therapy, and investigated the effect of cell-extracellular matrix interactions in 3D culture. After graduation in 2015, Hon Fai spent one year at Columbia University as a postdoctoral researcher. He performed high-throughput screening of synthetic genes for optimization of protein expression. In 2016, Hon Fai joined Massachusetts Institute of Technology as a postdoctoral associate. There he conducted organ-on-a-chip research and studied morphogenesis of tissue folding.

Five recent representative publications

1. Liu X, Steiger C, Lin S, Parada GA, Liu J, **Chan HF**, Yuk H, Phan NV, Collins J, Tamang S, Traverso G, Zhao X. "Ingestible hydrogel device." ***Nature Communications***, 2019; 10(1):493.
2. **Chan HF**, Zhao R, Parada GA, Meng H, Leong KW, Griffith LG, Zhao X. "Folding artificial mucosa with cell-laden hydrogels guided by mechanics models." ***Proceedings of the National Academy of Sciences of the United States of America***, 2018; 115(29):7503-7508.
3. **Chan HF**, Ma S, Tian J, Leong KW. "High-throughput screening of microchip-synthesized genes in programmable double-emulsion droplets." ***Nanoscale***, 2017; 9(10):3485-3495.
4. **Chan HF**, Zhang Y, Leong KW. "Efficient one-step production of microencapsulated hepatocyte spheroids with enhanced functions." ***Small***, 2016; 12(20):2720-2730.
5. Hong S[#], Sycks D[#], **Chan HF**[#], Lin S, Lopez GP, Guilak F, Leong KW, Zhao X. "3D printing of highly stretchable and tough hydrogels into complex, cellularized structures." ***Advanced Materials***, 2015; 27(27):4035-4040.

[#] Co-first authors

Technical expertise

- ✧ Tissue engineering
- ✧ Stem cell
- ✧ Biomaterial
- ✧ Biofabrication

Modulation of macrophages by bioactive glass/sodium alginate hydrogel is crucial in skin regeneration enhancement

ZHU Yanlun[1,2,3,4], MA Zhijie[3,4], KONG Lingzhi[5], HE Yaohua[5], LI Haiyan[3,4], CHAN Hon Fai[1,2]

[1] School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.
[2] Institute for Tissue Engineering and Regenerative Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.
[3] Shanghai Jiao Tong University Affiliated Sixth People's Hospital, School of Biomedical Engineering, Shanghai Jiao Tong University, 1954 Huashan Road, Shanghai 200030, P.R. China.
[4] School of Biomedical Engineering, Shanghai Jiao Tong University, 1954 Huashan Road, Shanghai 200030, P.R. China.
[5] Department of Orthopedics, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, 600 Yishan Road, Shanghai 200233, P.R. China.

Inflammatory response is a critical stage in typical wound healing. While some bioactive materials, such as bioactive glass (BG), have been shown to promote tissue regeneration, the roles of the inflammatory responses, especially the roles of macrophages, in tissue regeneration stimulated by these biomaterials remains unclear. In this study, the effects of BG/sodium alginate (SA) hydrogel (BG/SA hydrogel) on the behaviors of macrophages as well as on the interactions between macrophages and repairing cells were investigated using a wound healing model. In addition, macrophage-depleted mice were used to investigate the necessity of macrophages in the regeneration of full-thickness skin wounds treated with BG/SA hydrogel. Our results indicated that BG/SA hydrogel could polarize macrophages towards M2 phenotype *in vitro* and *in vivo* and upregulate the expression of anti-inflammatory genes. In addition, the M2 polarized macrophages could further recruit fibroblasts and endothelial cells as well as enhance the extracellular matrix (ECM) synthesis of fibroblasts and vascularization of endothelial cells *in vitro* and *in vivo*. Depletion of macrophages in the wound sites impeded the recruitment of repairing cells and reduced the formation of blood vessels and ECM, slowing down skin regeneration. These results provide an insight into the biomaterial-immune system interactions and demonstrate that modulation of macrophages by BG/SA hydrogel in the inflammatory response is crucial in skin regeneration enhanced by the hydrogel.

Session II (DRB)

Speaker Biography

Prof. JIANG Xiaohua Cynthia（蔣曉華）is an Associate Professor at the School of Biomedical Sciences, The Chinese University of Hong Kong (CUHK). She is an active member in the Developmental and Regenerative Biology Thematic Research Program, MOE Key Laboratory for Regenerative Medicine and Institute of Tissue Engineering and Regenerative Medicine (iTERM). Prof. JIANG graduated from School of Medicine, Shanghai JiaoTong University and completed her internship and residency at Ruijin Hospital, Shanghai. She obtained her Ph.D. degree in cell biology from The University of Hong Kong. Prof. JIANG undertook her postdoctoral training at the Department of Medicine, University of California, Los Angeles (UCLA). Her work focused on the role of protein kinase cascades in cancer development. After that, she joined the University of Southern California as a CIRM (California Institute for Regenerative Medicine) fellow and her research focused on understanding the origin and genetics of Ewing sarcoma by using human embryonic stem cells as an innovative model. In 2013, she established an independent laboratory within the School of Biomedical Sciences at The Chinese University of Hong Kong. Her major research interest is in stem cell biology and regenerative medicine, in particular, molecular regulation of stem cells, stem cell microenvironment and stem cell therapy in neurological diseases. Prof. JIANG has published more than 80 peer-reviewed papers, including *Nature Medicine, Cell Research, Cell Death and Differentiation, Stem Cells, Stem Cell Reports* and *iSciences*. She serves as editorial board member for various international journals such as *Cancer Cell International, Cell Biology International* and reviewers for numerous journals and grants. Until 2019, she has presided as PI/co-PI in ~30 local and national competitive grants including GRF, ITF, HMRF and NSFC.

Five recent representative publications

1. Huang B, Wang B, Lee WYW, U KP, Leung KT, Li X, Liu Z, Chen R, Lin JC, Tsang LL, Liu B, Ruan YC, Chan HC, Li G, **Jiang X**. "KDM3A and KDM4C regulate mesenchymal stromal cell senescence and bone aging via condensin-mediated heterochromatin reorganization." ***iScience***, 2019; 21:375-390.
2. Liu S, U KP, Tsang LL, Huang JW, **Jiang X**. "R-spodin2 enhances canonical Wnt signaling to maintain the stemness of glioblastoma cells." ***Cancer Cell Int***, 2018; 18:156.
3. Chen K, Liu Q, Tsang LL, Ye Q, Chan HC, Sun Y, **Jiang X**. "Human MSCs promotes colorectal cancer epithelial-mesenchymal transition and progression via CCL5/beta-catenin/Slug pathway." ***Cell Death Dis***, 2017; 8(5): e2819.
4. Chen R, Lee WY, Zhang XH, Zhang JT, Lin S, Xu LL, Huang B, Yang FY, Liu HL, Wang B, Tsang LL, Willaime-Morawek S, Li G, Chan HC, **Jiang X**. "Epigenetic modification of the CCL5/CCR1/ERK axis enhances glioma targeting in dedifferentiation-reprogrammed BMSCs." ***Stem Cell Reports***, 2017; 8(3): 743-757.
5. Liu Z, Guo J, Wang Y, Weng Z, Huang B, Yu MK, Zhang X, Yuan P, Zhao H, Chan WY, **Jiang X**[*], Chan HC[*]. "CFTR-beta-catenin interaction regulates mouse embryonic stem cell differentiation and embryonic development." ***Cell Death Differ***, 2017; 24(1): 98-110.

[*] Corresponding author

Technical expertise

- ✧ Animal models of neurological diseases, such as HIE, stroke, EAE
- ✧ Stem cell preclinical study

Epigenetic regulation of adult stem cells and its implication in organism aging

JIANG Xiaohua Cynthia

School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.

The life-long persistence of stem cells in the body makes them particularly susceptible to the accumulation of cellular damage. Indeed, stem cells in many tissues have been found to undergo profound changes with age, exhibiting blunted responsiveness to tissue injury, dysregulation of proliferative activities and declining functional capacities. These changes lead to reduced effectiveness of cell replacement and tissue regeneration in aged organisms. Recently, our group has identified several histone modifiers that play critical roles in controlling adult stem cell aging. Epigenetic regulation of adult stem cells and its implication in human aging and diseases is a focused research area in our team.

MSCs are extremely important adult stem cells for tissue homeostasis, regeneration and repair. However, the regenerative capacity of MSCs declines in aged people and their exhaustion is recognized as an important hallmark of aging. Thus, a better understanding of the molecular mechanisms underlying MSC aging will not only provide important guidance for how to maintain the natural physiological function of stem cells and delay the aging process, but also offer new strategies for stem cell-based therapies. We find recently that MSC aging is accompanied by heterochromatin organization. Using three different senescence models, we have identified two conserved histone H3 Lys 9 demethylases KDM3A (also known as JMJD1A) and KDM4C (also known as JMJD2C), which cooperatively mediate the heterochromatin organization in aging MSCs. Mechanistically, KDM3A and KDM4C transcriptionally activate chromosome condensation genes, in particular, components of condensins such as NCAPD2 and NCAPG2. Suppression of KDM3A or KDM4C by either genetic or biochemical approach leads to robust DNA damage response and aggravates cellular senescence. In contrast, overexpression of *KDM3A/KDM4C* or *NCAPD2* alleviates Doxorubicin-induced DNA damage response and MSC senescence. Moreover, MSCs and bone tissues derived from *Kdm3a* -/- mice exhibit defective chromosome organization and exacerbated DNA damage response. Importantly, a marked downregulation of KDM3A and KDM4C associated with a decrease in H3K9me3/2, HP1γ and chromosome condensation genes is found in MSCs derived from old human individuals. Consistently, analysis of human bone marrow MSCs transcriptome database reveals inverse correlation of KDM3A/KDM4C and NCAPD2/NCAPG2 with aging. Collectively, we have revealed a previously unrecognized role of histone demethylases in modulating condensin-mediated heterochromatin organization, which functions as a surveillance mechanism to restrain DNA damage during stem cell aging.

Session II (DRB)

Speaker Biography

Prof. KER Dai Fei Elmer（柯岱飞）joined The Chinese University of Hong Kong as an Assistant Professor in the Institute for Tissue Engineering and Regenerative Medicine and School of Biomedical Sciences in 2017. He completed his B.S. in Molecular Biology and Genetics at the University of Sydney, his Ph.D. in Biological Sciences at Carnegie Mellon University, and his postdoctoral training at the Department of Orthopaedic Surgery at Stanford University. His research interests include biomaterials, musculoskeletal biology, and computer vision-based cell tracking.

Five recent representative publications

1. Shanjani Y, Siebert SM, **Ker DFE**, Mercado-Pagán AE, Yang YP. "Acoustic Patterning of Growth Factor for 3D Tissue Engineering." ***Tissue Engineering Part A***, 2020; doi: 10.1089/ten.TEA.2019.0271. [Epub ahead of print]
2. **Ker DFE**, Yang YP. "Ruminants: Evolutionary past and future impact." ***Science (Perspective)***, 2019; 364(6446):1130-1131. doi: 10.1126/science.aax5182.
3. **Ker DFE**, Wang D, Sharma S, Zhang B, Passarelli B, Neff N, Li C, Maloney W, Quake S, Yang YP. "Identifying deer antler *uhrf1* proliferation and *s100a10* mineralization genes using comparative RNA-seq." ***Stem Cell Research & Therapy***, 2018; 9(1):292. doi: 10.1186/s13287-018-1027-6.
4. **Ker DFE**[*#], Wang D[#], Behn AW, Wang ETH, Zhang X, Zhou BY, Mercado-Pagan AE, Kim S, Kleimeyer J, Gharaibeh B, Shanjani Y, Nelson D, Safran M, Cheung E, Campbell P, Yang YP[*]. "Functionally-Graded, Bone- and Tendon-Like Polyurethane for Rotator Cuff Repair." ***Advanced Functional Materials***, 2018; 28(20):1707107. doi: 10.1002/adfm.201707107.
5. **Ker DFE**, Eom S, Sanami S, Bise R, Pascale C, Yin Z, Huh S, Osuna-Highley E, Junkers SN, Helfrich CJ, Liang PW, Pan J, Jeong S, Kang SS, Liu J, Nicholson R, Sandbothe MF, Van PT, Liu A, Chen M, Kanade T, Weiss LE, Campbell PG. "Phase contrast time-lapse microscopy datasets with automated and manual cell tracking annotations." ***Scientific Data***, 2018; 5:180237. doi: 10.1038/sdata.2018.237.

[*] Co-corresponding authors
[#] Co-first authors

Technical expertise

- ✧ Biomaterials
- ✧ Musculoskeletal biology
- ✧ Artificial intelligence (Computer vision)

Technologies for tissue engineering and regenerative medicine

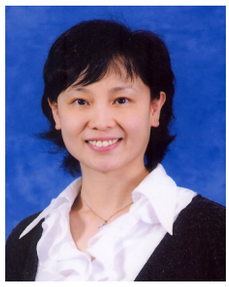
LI Ke[1,2], ZHANG Xu[1,2], WANG Chenyang[1,2], HUANG Na[1], FU Bruma Sai-chuen[3], BISE Ryoma[4], LEE Kenneth Ka-ho[1], WANG Dan[1,2], YUNG Patrick Shu-hang[3], TUAN Rocky Sung-chi[1,2], KER Dai Fei Elmer[1,2]

[1] School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.
[2] Institute for Tissue Engineering and Regenerative Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.
[3] Department of Orthopaedics and Traumatology, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.
[4] Department of Advanced Information Technology, Kyushu University, Japan.

Diseases and trauma have significant impact on society and national healthcare systems. In this study, we report on our progress in developing growth factor-based therapies and biomaterials as well as novel computer vision-based cell tracking approaches for muscle-tendon, bone-tendon, and auricular tissue engineering. To treat muscle-tendon injuries, we have identified Fibroblast Growth Factor-2 (FGF-2), Transforming Growth Factor-Beta3 (TGF-β3), and Insulin-like Growth Factor-1 (IGF-1) as candidate cues for muscle-tendon regeneration. Together, these growth factors promoted proliferation and expression of tendon-associated growth factors including Collagen Type I, Tenascin C, and Scleraxis in human bone-marrow-derived mesenchymal stem cells and inhibited adipogenesis in an *in vitro* model of muscle fatty degeneration. To treat bone-tendon injuries, we have been developing and optimizing the design of biomaterials. Our novel 3D-printed biomaterial exhibits tendon-like tensile properties and cytocompatibility. *In silico* simulations demonstrate that by optimizing biomaterial geometry to mimic attributes of native bone-tendon tissues, material failure can be minimized. To treat microtia defects, we have initiated efforts in developing a 3D-printed auricular scaffold. To support our efforts in studying cell:biomaterial interactions, we have also developed a novel, multi-modal, high dynamic range imaging method to aid in label-free detection of cells. In summary, our efforts in developing growth factor-, biomaterial-, and computer vision-based technologies hold promise to engineer complex tissues and study cell-biomaterial interactions.

Session III (NVMB)

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
- ✧ Streptozotocin-induced diabetic and diet-induced obesity mouse models

Defective brown adipose tissue development in fetal programming of obesity in offspring of diabetic pregnancy

LIN Nansheng Kenneth, 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.

Maternal diabetes has become one of the most frequent medical complications during pregnancy. A growing body of evidence shows that babies born to diabetic mothers are prone to develop metabolic disorders, such as obesity and type 2 diabetes mellitus (T2DM), in later life. However, how an intrauterine diabetic milieu predisposes the offspring to these metabolic disorders remains far from clear.

Brown adipose tissue (BAT) dissipates stored chemical energy as heat, and contributes to triglyceride clearance, and improving whole-body glucose homeostasis and insulin sensitivity. BAT is now regarded as an important organ to combat against obesity and diabetes. Animal studies show that a deficit in BAT mass or a decline in BAT function in early life may perpetuate throughout life, perturbing energy homeostasis, and lead to the development of metabolic disorders. Using a pregestational type 1-like diabetic mouse model, we found that maternal diabetes perturbed retinoic acid homeostasis and impaired fetal BAT development. After birth, the offspring showed increased propensity to develop obesity and T2DM in adulthood. Importantly, maternal supplementation of retinoic acid corrected fetal BAT development, with a concomitant reduction in the risk of developing obesity and T2DM. Taken together, our findings underscore the importance of defective BAT development in prenatal programming of disease in offspring exposed to maternal diabetes, and pave the way to derive in utero therapeutic intervention to prevent metabolic disorders later in life.

Session III (NVMB)

Speaker Biography

Prof. TIAN Xiaoyu（田小雨）is currently an Assistant Professor of the School of Biomedical Sciences, The Chinese University of Hong Kong (CUHK). She received Ph.D. from CUHK Department of Physiology. During her PhD, she studied the therapeutic effect of PPARs on vascular dysfunction in hypertension and type 2 diabetes, and mitochondrial oxidative stress in endothelial cell function. After graduation, she continued as a postdoctoral fellow in the lab of Prof. Ajay Chawla, Cardiovascular Research Institute, The University of California San Francisco, studying macrophage dynamics in obesity-induced adipose tissue inflammation, and also in the atherosclerosis. Her current research interests include the vascular cell homeostasis and dysregulation in the microenvironment of various metabolic organs in the context of cardiovascular diseases. She also works on immune regulation of adipose tissue inflammation.

Five recent representative publications

1. Tian D[#], Hong H, Shang W, Ho CC, Dong J, **Tian XY**[*]. "Deletion of Ppard in CD11c^{+} cells attenuates atherosclerosis in ApoE knockout mice." ***The FASEB Journal***, 2020; 34(2):3367-3378.
2. Cheang WS[#], Wong WT, Wang L, Cheng CK, Lau CW, Ma RCW, Xu A, Wang N, Huang Y[*], **Tian XY**[*]. "Resveratrol ameliorates endothelial dysfunction in diabetic and obese mice through sirtuin 1 and peroxisome proliferator-activated receptor δ." ***Pharmacological Research***, 2019; 139:384-394.
3. Chan CKW, Zhang L, Cheng CK, Yang H, Huang Y, **Tian XY**[*], Choi CHJ[*]. "Recent Advances in Managing Atherosclerosis via Nanomedicine." ***Small***, 2018; 14(4). doi: 10.1002/smll.201702793.
4. Huo M[#], Huang Y[#], Qu D, Zhang H, Wong WT, Chawla A, Huang Y, **Tian XY**[*]. "Myeloid *Bmal1* deletion increases monocyte recruitment and worsens atherosclerosis." ***The FASEB Journal***, 2017; 31(3):1097-1106.
5. **Tian XY**[#], Ganeshan K[#], Hong C[#], Nguyen KD, Qiu Y, Kim J, Tangirala RK, Tontonoz P, Chawla A[*]. "Thermoneutral housing accelerates metabolic inflammation to potentiate atherosclerosis but not insulin resistance." ***Cell Metabolism***, 2016; 23(1):165–178.

[#] Co-first authors

[*] Co-corresponding authors

Technical expertise

✧ Vascular biology

Endothelial cell homeostasis and dysfunction during vascular repair

TIAN Xiaoyu

School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.

The stress-sensing mechanisms in endothelial cells, especially those involved in the cell-cell interactions between endothelial cells and other cells within the vascular microenvironment are still poorly understood. In the past, we and others have showed that nuclear receptor PPARδ plays an essential role in regulating vascular endothelial function against diabetic endothelial dysfunction. PPARδ activation is also anti-inflammatory against atherosclerosis. Our current focus is to further explore how PPARδ as a transcription factor senses stress, and to identify its downstream signaling pathways and co-factors in protecting endothelial homeostasis and improving vascular repair in post-ischemic angiogenesis. We used hindlimb ischemia in mice as the animal model. By using the endothelium selective Ppard knockout mice, we found that deletion of Ppard in endothelial cells delayed vascular repair, enhanced vascular inflammation and hyperpermeability, and impaired angiogenesis in the injured hindlimb muscles. We also found activation of PPARδ by hypoxia which is responsible for expression of genes involved in angiogenesis, arteriogenesis, and vascular integrity. Single cell RNA-seq of endothelial cells collected from ischemic muscles showed that PPARδ might be involved maintaining in endothelial integrity and enhancing angiogenesis. Our current data suggested an important role of PPARδ in maintaining endothelial integrity to promote vascular repair. These findings might be useful in understanding the complex regulatory network of vascular homeostasis duing tissue injury and repair.

Session IV (NVMB)

Speaker Biography

Prof. PONOMAREV Eugene D. （龐佑信）has main research interests related to neuroinflammation associated with neurodegenerative diseases multiple sclerosis, traumatic brain injury, Alzheimer's disease, and epilepsy. Particularly he is interested in 1) epigenetic and transcriptional control of macrophage and microglia activation during CNS inflammation, and 2) the role of platelets and brain-specific gangliosides in the regulation of neuroinflammation and neurodegeneration. Both directions of his research program are supported by prestigious NIH, RGC, and HMRF grants. Prof. Ponomarev is a well-known scientist in the field of neuroinflammation and neurodegeneration and has more than 40 publications in top international academic journals such as the *Journal of Immunology, Frontiers in Immunology, Journal of Neuroscience, Brain Behavior and Immunity, Progress in Neurobiology, Circulation Research, Nature Medicine*. Prof. Ponomarev's publications have been cited about 4000 times, his publication h-index is 23, and he is serving as an editorial board member for *Immunology & Cell Biology* journal of an Australian Immunological Society.

Five recent representative publications

1. Kopeikina E, Dukhinova M, Yung AWY, Veremeyko T, Kuznetsova IS, Lau TYB, Levchuk K, **Ponomarev ED**. "Platelets promote epileptic seizures by modulating brain serotonin level, enhancing neuronal electric activity, and contributing to neuroinflammation and oxidative stress." ***Prog Neurobiol***, 2020; 188:101783. doi: 10.1016/j.pneurobio.2020.101783.
2. Dukhinova M, Veremeyko T, Yung AWY, Kuznetsova IS, Lau TYB, Kopeikina E, Chan AML, **Ponomarev ED**. "Fresh evidence for major brain gangliosides as a target for the treatment of Alzheimer's disease." ***Neurobiol Aging***, 2019; 77:128-143. doi: 10.1016/j.neurobiolaging.2019.01.020.
3. Veremeyko T, Yung AWY, Anthony DC, Strekalova T, **Ponomarev ED**. "Early growth response gene-2 is essential for M1 and M2 macrophage activation and plasticity by modulation of the transcription factor CEBPβ." ***Frontiers in Immunology***, 2018; 9:2515. doi: 10.3389/fimmu.2018.02515.
4. Dukhinova M, Kuznetsova I, Kopeikina E, Veniaminova E, Yung AWY, Veremeyko T, Levchuk K, Barteneva NS, Kam KWH, Yung WH, Liu JYH, Rudd J, Yau SSY, Anthony DC, Strekalova T, **Ponomarev ED**. "Platelets mediate protective neuroinflammation and promote neuronal plasticity at the site of neuronal injury." ***Brain Behav Immun***, 2018; 74:7-27. doi: 10.1016/j.bbi.2018.09.009.
5. Veremeyko T, Yung AWY, Dukhinova M, Kuznetsova IS, Pomytkin I, Lyundup A, Strekalova T, Barteneva N, **Ponomarev ED**. "Cyclic AMP pathway suppress autoimmune neuroinflammation by inhibiting functions of encephalitogenic CD4 T cells and enhancing M2 macrophage polarization at the site of inflammation." ***Frontiers in Immunology***, 2018; 9:50. doi: 10.3389/fimmu.2018.00050.

Technical expertise

- ✧ Immune cell isolation from different organs and their identification
- ✧ Cell cultures: neuronal and immune cells
- ✧ Mouse model of multiple sclerosis (experimental autoimmune encephalitis)
- ✧ Mouse models of Alzheimer's disease
- ✧ Mouse model of epilepsy
- ✧ FACS analysis (cell subsets, intracellular staining)
- ✧ Brain histology
- ✧ Transcriptional factors
- ✧ microRNA
- ✧ Platelets
- ✧ Glycolipids

The role of platelet-glycolipid interactions in the stimulation of neuronal electric and synaptic activity

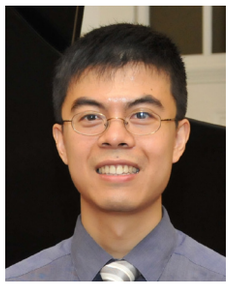
KOPEIKINA Ekaterina, DUKHINOVA Marina, VEREMEYKO Tatyana, YUNG Amanda W.Y., PONOMAREV Eugene D.

School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.

Many types of neurodegenerative diseases such as traumatic brain injury (TBI) and Alzheimer's disease (AD) are associated with decreased levels of synaptic and neuronal electric activity, while neuronal stimulation has a beneficial effect for these conditions. However, exact factors that could enhance neuronal electric activity and synaptic plasticity after brain injury or neurodegeneration are not well known. Previously, we found that platelets interact with neuronal glycolipids and actively secrete pro-inflammatory mediators during central nervous system (CNS) pathological conditions such as multiple sclerosis and TBI. These platelet-derived factors could further increase the permeability of the blood-brain barrier (BBB), which may create a predisposition for direct interaction of platelets with neurons. In this study, we demonstrated that platelets substantially enhanced brain electric activity recorded by an electroencephalogram (EEG) in a mouse model of pentylenetetrazole (PTZ) -induced seizures. We found that platelets actively secreted serotonin, contributed to increased BBB permeability, and were present in the CNS parenchyma during epileptic seizures. Furthermore, platelets directly stimulated neuronal electric activity both *in vivo* and *in vitro* and induced the expression of specific genes related to early neuronal response, neuroinflammation, and oxidative phosphorylation, leading to oxidative stress in neurons. Platelet also stimulated the formation of dendritic spines and expression of post-synaptic marker PSD95 near the trauma site. The intracranial injection of physiological numbers of platelets that mimicked TBI-associated bleeding was sufficient to induce severe seizures, which resembled conventional PTZ-induced epileptic activity. These findings highlight a conceptually new role of platelets in the development of epileptic seizures and indicate a potential new therapeutic approach, targeting platelets to prevent and treat epilepsy. The results of these studies can be also applied for the development of new approaches to treat TBI and AD by stimulating neuronal activity and plasticity.

Session IV (NVMB)

Speaker Biography



Prof. CHEUNG Chi Kwan Vincent（張智鈞）is a motor neuroscientist and biomedical engineer. He is at present an assistant professor at the School of Biomedical Sciences of The Chinese University of Hong Kong (CUHK). He obtained his bachelor degree in Mathematics and Pharmacology & Therapeutics from the University of British Columbia, Vancouver, and subsequently, Ph.D. in Neuroscience and Biomedical Engineering from Massachusetts Institute of Technology (MIT) and the Harvard Medical School, and postdoctoral at the McGovern Institute for Brain Research of MIT. Prof. Cheung's research has focused on understanding how the central nervous system (CNS) controls voluntary movement and enables learning of motor skills. He is also interested in exploring how knowledge of movement modules may be translated into a new rehabilitation strategy for stroke survivors. Prof. Cheung's papers have appeared in many journals including *PNAS, Journal of Neuroscience,* and *Neural Computation*. He has been invited to speak at both meetings of professional societies (e.g., Neural Control of Movement Society) and seminars for the general public. Vincent was the 2016 recipient of The CUHK Faculty of Medicine Faculty Innovation Award. His research is supported by Hong Kong Research Grants Council and other sponsors.

Five recent representative publications

1. Severini G, Koenig A, Adans-Dester C, Cajigas I, **Cheung VCK**[*], Bonato P[*]. "Robot-driven locomotor perturbations reveal synergy-mediated, context-dependent feedforward and feedback mechanisms of adaptation." ***Scientific Reports***, 2020; 10(1):5104.
2. **Cheung VCK**[#], Zheng X-C[#], Cheung RTH, Chan RHM. "Modulating the structure of motor variability for skill learning through specific muscle synergies in elderlies and young adults." ***IEEE Open Journal of Engineering in Medicine and Biology***, 2020; 1:33-40.
3. **Cheung VCK**[#], Niu CM[#], Li S, Xie Q, Lan N[#]. "A novel FES strategy for post-stroke rehabilitation based on the natural organization of neuromotor control." ***IEEE Reviews in Biomedical Engineering***, 2019; 12:154-167.
4. Caggiano V[#], **Cheung VCK**[#], Bizzi E. "An optogenetic demonstration of motor modularity in the mammalian spinal cord." ***Scientific Reports***, 2016; 6:35185.
5. Devarajan K[#], **Cheung VCK**[#]. "On non-negative matrix factorization algorithms for signal-dependent noise, with application to electromyography data." ***Neural Computation***, 2014; 26(6):1128-1168.

[#] Co-first authors

[*] Co-senior authors

Technical expertise

- ✧ Electromyography
- ✧ Motion analysis
- ✧ Electrophysiology
- ✧ Optogenetics
- ✧ Data analysis
- ✧ Matlab programming

Achieving flexibility in a modular motor system for learning, development, and recovery from injury

CHEUNG Chi Kwan Vincent

School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.

For any motor act, the CNS must assemble a coordinated pattern of muscle activities to achieve the intended motion. The computations behind this assembly are extraordinarily complicated, in that the hundreds of muscles constitute a large search space of motor commands even for an apparently simple movement. The CNS likely circumvents this complexity by generating muscle commands through the combination of a manageable number of pre-specified units, each of which would simultaneously recruit a specific group of muscles. These units, variously called motor primitives, neuromotor modules, or muscle synergies, are in essence neural mechanisms for synchronizing motoneuronal activities for purposeful behaviors. Muscle synergies have been viewed as hard-wired neural constraints that limit possibilities of motor commands. Here, I argue that the coordinative structures of muscle synergies are not insusceptible to change over time. Such alterations, underscored by neuroplasticity, are necessary to accommodate gradual changes in motor behaviors and the musculoskeletal system. I will illustrate the limit of the invariance of muscle synergies with both cross-sectional and longitudinal data collected in scenarios that demand behavioral changes in different time scales. These include achieving within-session adaptation to perturbations, acquiring bipedal locomotion in developing babies, and optimizing sports performance in athletes with years of training. In addition, neural pathologies, including stroke and neuronal degeneration, may compromise the muscle synergies. The specific patterns of synergies that could be related to reduction of motor impairment in stroke survivors undergoing rehabilitation will also be described.

Session IV (NVMB)

Speaker Biography

Prof. IP Pak Kan Jacque（葉栢勤）obtained his B.Sc. in Biochemistry from the University of Sydney with first class honours and university medal, and then received his Ph.D. in Biochemistry at The Hong Kong University of Science and Technology. Prof. Ip received further post-doctoral training at the Picower Institute for Learning and Memory, Massachusetts Institute of Technology (MIT). During his postgraduate study and postdoctoral training, he received a number of awards including the Croucher Studentship, the Sir Edward Youde Memorial fellowship, the International Brain Research Organization (IBRO) Rita Levi-Montalcini Research fellowship, and Human Frontier Science Program (HFSP) Long-Term fellowship. Prof. Ip has devoted his research to investigate the mechanisms of synaptic plasticity, and will continue to expand his research focus on how such mechanistic defects result in autism-related disorders through the use of multidisciplinary approaches. His long-term goal is to apply multidisciplinary cutting-edge neurotechnology to probe brain function in health and disease.

Five recent representative publications

1. El-Boustani S[#], **Ip JP**[#], Breton-Provencher V, Okuno H, Bito H, Sur M. "Locally coordinated synaptic plasticity shapes cell-wide plasticity of visual cortex neurons *in vivo*." ***Science***, 2018; Vol. 360, Issue 6395, pp. 1349-1354.
2. **Ip JP**[#], Nagakura I[#], Petravicz J, Wiemer EAC, Sur M. "Major vault protein, a candidate gene in 16p11.2 microdeletion syndrome, is required for the homeostatic regulation of visual cortical plasticity." ***Journal of Neuroscience***, 2018; 18;38(16):3890-3900.
3. Mellios N[#], Feldman D[#], Sheridan SD[#], **Ip JP**[#], Kwok S, Rosen B, Li Y, Crawford B, Jaenisch R, Haggarty S, Sur M. "MeCP2-regulated miRNAs control early human neurogenesis through differential effects on ERK and AKT signaling." ***Molecular Psychiatry***, 2018; 23(4):1051-1065.
4. **Ip JP**[#], Shi L[#], Chen Y, Itoh Y, Fu AW, Betz A, Yung WH, Gotoh Y, Fu AK, Ip NY. "α2-chimaerin controls neuronal migration and functioning of cerebral cortex through CRMP-2." ***Nature Neuroscience***, 2012; 15(1):39-47.
5. **Ip JP**, Mellios N, Sur M. "Rett Syndrome: genetic, molecular and functional insights into multi-stage dysfunction." ***Nature Review Neuroscience***, 2018; 19(6):368-382.

[#] Co-first authors

Technical expertise

- ✧ Molecular neuroscience
- ✧ Dendritic spine imaging *in vivo*
- ✧ Synaptic proteins tracking

The roles of locally coordinated synaptic plasticity in health and disease

IP Pak Kan Jacque

School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.

Neuronal circuits in our brain are known to be plastic and are subject to experience-driven changes causing neurons to modify their structure, and functional connectivity and responses. Each individual neuron receives and integrates inputs from numerous sources and produces relevant outputs. Plasticity refers to the ability of the neuron to reorganize its synaptic connections and functions in response to alterations in sensory experience or learning. Neuronal plasticity is a leading theory for how the brain learns and forms memories. However, the synaptic mechanisms underlying such plasticity remain to be resolved *in vivo*. With the recent advancements in cutting-edge techniques in molecular genetics, optogenetics, synaptic tagging, tissue clearing technology and high-resolution two-photon *in vivo* imaging, it is now possible to examine functional properties and structural changes at the level of dendritic spines *in vivo*. This talk will highlight a novel synaptic mechanism, termed locally coordinated plasticity (LCP). The mechanism relies on local synaptic potentiation and depression based critically on a heterogeneous distribution of synapses along dendrites. My ongoing research addresses how disruption of LCP impacts the functioning of cortical circuits and its relationship with X-linked neurodevelopmental disorders such as Fragile X syndrome, an autism-related disorder that causes a range of developmental problems including learning disabilities and cognitive impairment.

Session V (CBET)

Speaker Biography

Prof. CHAN Man Lok Andrew（陳文樂）is a cancer biologist. He obtained his Ph.D. degree in Molecular Biology from the Institute of Cancer Research at the Royal Marsden Hospital, University of London. He was a Fogarty International Fellow at the National Cancer Institute of the United States National Institutes of Health, and Faculty Members at the Mount Sinai School of Medicine and the Medical College of Wisconsin. Prof. Chan joined the School of Biomedical Sciences in 2012 and he is currently a member of the Cancer Biology & Experimental Therapeutics Thematic Research Program. Prof. Chan serves on multiple governmental granting agencies and has published 72 peer-reviewed papers with some in high impact journals such as *Science*, *Nature Genetics*, *Cancer Cell*, *PNAS, Blood*, and *Nature Neuroscience*. The laboratory of Prof. Chan focuses on cancer cell signaling pathways in the initiation and progression of human cancer. His research aims to understand the regulatory mechanisms of the PTEN tumor suppressor in brain cancer, as well as in neurodevelopmental and neurodegenerative disorders.

Five recent representative publications

1. Wong CW, Wang Y, Liu T, Li L, Cheung SKK, Or PM, Cheng AS, Choy KW, Burbach JPH, Feng B, Chang RCC, **Chan AM***. "Autism-associated PTEN missense mutation leads to enhanced nuclear localization and neurite outgrowth in an induced pluripotent stem cell line." ***FEBS J***, 2020; doi: 10.1111/febs.15287.
2. Yan M, Wang Y, Wong CW, Or PMY, Wong KL, Li L, Many AM, Guan H, Khoo US, **Chan AM***. "PTEN PDZ-binding domain suppresses mammary carcinogenesis in the MMTV-PyMT breast cancer model." ***Cancer Letters***, 2018; 430:67-78. doi: 10.1016/j.canlet.2018.05.012.
3. Wong CW, Or MY, Wang Y, Li L, Li J, Yan M, Cao Y, Luk HM, Tong TMF, Leslie NR, Lo IFM, Choy RKW, **Chan AM***. "Identification of three germline *PTEN* mutations in Hong Kong patients with autistic features, neurodevelopmental delay and macrocephaly." ***Autism Research***, 2017; 11(8):1098-1109. doi:10.1002/aur.1950.
4. Knafo S, Sanchez-Puelles C, Palomer E, Delgado I, Draffin JE, Wahle T, Kaleka K, Pereda-Perez I, Klosi E, Faber EB, Lozano-Montes L, Ortega-Molina A, Ordonez-Gutierrez L, Wandosell F, Vina J, Dotti CG, Hall RA, Pulido R, Gerges NZ, **Chan AM**, Spaller MR, Serrano M, Venero C, Esteban JA. "PTEN recruitment controls synaptic and cognitive function in Alzheimer's models." ***Nature Neuroscience***, 2016; 19(3):443-453. doi: 10.1038/nn.4225.
5. Odriozola L, Singh G, Hoang T, **Chan AM***. "Regulation of PTEN activity by its carboxyl-terminal autoinhibitory domain." ***Journal of Biological Chemistry***, 2007; 282(32): 23306-23315.

* Corresponding author

Technical expertise

- ✧ Mouse model of human cancer
- ✧ Cell signalling
- ✧ Primary neural cultures

Analysis of *Pten*-null mouse astrocytes revealed overlapping transcribed genes with human glioblastoma transcriptome

LIU Tian, OR Mei-Yu Penelope, WONG Chi-Wai, CHEUNG Kwok-Kuen Stanley, WANG Yubing, WANG Yiwei, CHAN M. Andrew

School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.

Glioblastoma is an aggressive form of brain cancer with universally poor prognosis. Even with optimal therapy, the cancer recurs frequently. Phosphatase and tensin homolog (*PTEN*) is a tumor suppressor gene whose mutations are often found in multiple human cancers. *PTEN* encodes a lipid phosphatase and serves as a negative regulator of the phosphoinositide 3-kinase (PI3K) pathway. Cumulative evidence suggests that PTEN mutations play significant roles in tumorigenesis of glioblastoma as 60% of glioblastoma patients acquired mutations in this gene. Based on our preliminary data, transcriptomic profiling of primary astrocytes derived from *Pten* knockout mice revealed an overlapping enrichment of mitotic regulators and cell cycle related pathways with human GBM. 4 genes (RCC1, RCC2, NEK2, and CHK2) were validated to be significantly upregulated in *Pten*-null astrocytes by qRT-PCR. Regulator of chromatin condensation 2 (RCC2) has been reported to be guanine-nucleotide exchange factor (GEF) for Rac1 and RalA GTPases and acts as a regulator of cell cycle progression. Accumulating evidence revealed a pro-tumorigenic role of RCC2 in multiple cancers such as tumor growth and tumor metastasis. Using RNA-seq, we identified 993 differentially expressed genes between control siRNA- and RCC2 siRNA-treated A1172 cells. GSEA analysis revealed glycolysis and G2-M progression as the most notably altered pathway by knockdown of RCC2. Indeed, RCC2 knock down inhibits hexokinase 2 (HK2) expression, which is a key driver of metabolic regulation. We also demonstrated that the loss of RCC2 in glioblastoma cell lines suppresses cell growth and RCC2 is essential for G2-M progression. Additionally, we utilized connectivity map (C-map) analysis and identified cephaeline as a promising inhibitor of RCC2-associated gene signatures. Indeed, RCC2 knock down and cephaeline inhibit glioblastoma cell viability in a synergistic manner. In summary, PTEN deficiency leads to the upregulation of RCC2, which may promote tumorigenesis of glioblastoma by dysregulating glucose metabolism and cell cycle progression.

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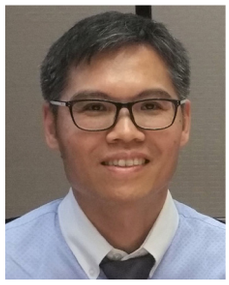
Session V (CBET)

Speaker Biography



Prof. CHEN Yangchao（陳揚超）is currently an Associate Professor at the School of Biomedical Sciences, The Chinese University of Hong Kong (CUHK). He was trained as a postdoctoral fellow at University of Washington, Seattle and obtained his Ph.D. from Sun Yat-sen University. He has been faculty member as Research Assistant Professor, Assistant Professor at Faculty of Medicine, CUHK since 2007. His research interests include epigenetics in cancer, histone modification particularly methylation, long and short non-coding RNAs, development of novel therapeutics for cancer. The ultimate goal of his lab is aimed at the identification of novel diagnostic markers and therapeutic targets for cancer.

Five recent representative publications

1. Wong CH, Li CH, He Q, Tong JHM, To KF, **Chen Y***. "The Establishment of CDK9/ RNA PolII/H3K4me3/DNA Methylation Feedback Promotes HOTAIR Expression by RNA Elongation Enhancement in Cancer." ***Nucleic Acids Res***. In revision, 2020; bioRxiv 812776; DOI: 10.1101/812776.
2. Zhu YX, Li CH, Li G, Feng H, Xia T, Wong CH, Fung FKC, Tong JHM, To KF, Chen R, **Chen Y***. "LLGL1 is a potential biomarker predicting gemcitabine response in PDAC and represses OSMR through modulation of the ERK-SP1 pathway." ***Cell Mol Gastroenterol Hepatol***, 2020; Accept with revision.
3. Wong CH, Lou UK, Li Y, Chan SL, Tong JHM, To KF, **Chen Y***. "CircFOXK2 Promotes Tumor Growth and Metastasis of Pancreatic Ductal Adenocarcinoma via Complexing with RNA Binding Proteins and Sponging MiR-942." ***Cancer Res***, 2020; DOI: 10.1158/0008-5472.
4. Wong CH, Li CH, He Q, Chan SL, Tong JHM, To KF, Lin LZ, **Chen Y***. "Ectopic HOTTIP expression induces noncanonical transactivation pathways to promote growth and invasiveness in pancreatic ductal adenocarcinoma." ***Cancer Lett***, 2020; 477:1-9.
5. Xu F, Li CH, Wong CH, Chen GG, Lai PBS, Shao S, Chan SL, **Chen Y***. "Genome-wide screening and functional analysis identifies tumor suppressor long non-coding RNAs epigenetically silenced in hepatocellular carcinoma." ***Cancer Res***, 2019; 79:1305-1317.

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Technical expertise

- ✧ Long and short non-coding RNAs in cancer
- ✧ *In vitro* and *in vivo* genome-wide RNAi and CRISPR/CAS9 screening
- ✧ Lentiviral vector mediated gene transduction
- ✧ Functional Genomics and Proteomics

Epigenetic regulation of long non-coding RNAs in cancer

CHEN Yangchao

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Long noncoding RNAs (lncRNA) play critical roles in the development of cancer. However, the mechanisms underlying their deregulation remain largely unexplored. Epigenetics including histone and DNA methylation has been shown to play important roles in regulating gene expression. In this presentation, I will report: (1) Genome-wide identification of lncRNAs epigenetically silenced in cancer; (2) Non-canonical trans-acting lncRNA HOTTIP regulatory pathway in promoting oncogene expression; (3) Role of DNA methylation in promoting lncRNA HOTAIR expression.

We identified two lncRNAs TCAM1P-004 and RP11-598D14.1 frequently downregulated in hepatocellular carcinoma (HCC) which are epigenetically silenced by histone methyltransferase EZH2. Both lncRNAs inhibited cell growth, cell survival, and transformation in HCC cells *in vitro* as well as tumor formation *in vivo*. Using RNA pull-down and mass spectrometry, we demonstrated that TCAM1P-004 bound IGF2BP1 and HIST1H1C, whereas RP11-598D14.1 bound IGF2BP1 and STAU1. These lncRNA-protein interactions were critical in regulating p53, MAPK, and HIF1α pathways that promoted cell proliferation in HCC.

HOTTIP is upregulated in various cancer, but the HOTTIP-mediated oncogenic pathway is not fully understood. We identified canonical HOTTIP-HOXA13 targets responsible for cell growth and cell invasion. Genome-wide analysis revealed that 38% of HOTTIP-regulated genes contain H3K4me3 and HOTTIP enrichment at their promoters, without HOXA13 binding. HOTTIP complexes with WDR5-MLL1 to trans-activate oncogenic proteins by directly inducing H3K4me3 at their promoters. These results indicate the importance of the noncanonical trans-acting HOTTIP-WDR5-MLL1 pathway in the HOTTIP regulatory mechanism by promoting oncogenic protein expression. Furthermore, HOTTIP is regulated by miR-497 in PDAC cells.

HOTAIR is overexpressed in multiple cancers with diverse genetic profiles, which heavily contributed to cancer progression. However, the underlying mechanism leading to HOTAIR deregulation is largely unexplored. We revealed that gene body methylation promoted HOTAIR expression through enhancing the transcription elongation process in cancer. We linked up the aberrant gene body histone and DNA methylation in promoting transcription elongation via phosphorylation of Polymerase II Ser 2 by CDK7-CDK9, and elucidated the mechanism of a positive feedback loop involving CDK7, MLL1 and DNMT3A in promoting gene body methylation and overexpressing HOTAIR.

Session VI (CBET)

Speaker Biography

Prof. SO Hon-Cheong（蘇漢昌）received his Bachelor of Medicine and Bachelor of Surgery (MBBS) degree together with a PhD degree in 2012 from University of Hong Kong (HKU). His PhD research focused on statistical and psychiatric genomics. He has received numerous awards for his academic achievement, including the Croucher Foundation Scholarship, the Dr Stephen KP Chang Gold Medal for the best PhD thesis in the Faculty of Medicine, Young Researcher Award CUHK 2018 and CINP Rafaelsen Young Investigators Award. Prior to taking up the current academic post, he worked as a resident psychiatrist in Queen Mary Hospital and Castle Peak Hospital. He joined the School of Biomedical Sciences of The Chinese University of Hong Kong as an Assistant Professor in January 2016.

His main research interests include the development and application of novel statistical and computational methodologies to "omics" and clinical data in general. In particular, he is interested in uncovering the genetic architecture of complex diseases and predicting disease risk and phenotypes based on bioinformatics and clinical data. He has developed methodologies for evaluating the heritability explained by individual genetic variants and the entire set of markers on a genome-wide association study (GWAS) panel. He has also developed novel methods to combine genetic information with family history in improving risk prediction, as well as new ways to construct polygenic risk scores. He is one of the lead-authors in a schizophrenia GWAS in Chinese population, leading to discovery of a novel susceptibility loci on the X chromosome. His recent interest also includes bioinformatics approaches to repurposing drugs for new indications, and has developed several repurposing methodologies using GWAS and other "omics" data.

Five recent representative publications

1. Yin LY, Chau CKL, Sham PC, **So HC**[*]. "Integrating clinical data and imputed transcriptome from GWAS to uncover complex disease subtypes: Applications in psychiatry and cardiology." ***The American Journal of Human Genetics***, 2019; 105(6):1193-1212.
2. **So HC**[*], Chau CK, Chiu WT, Ho KS, Lo CP, Yim SH, Sham PC. "Analysis of genome-wide association data highlights candidates for drug repositioning in psychiatry." ***Nature Neuroscience***, 2017; 20(10):1342-1349
3. **So HC**[*], Sham PC[*]. "Exploring the predictive power of polygenic scores derived from genome-wide association studies: a study of 10 complex traits." ***Bioinformatics***, 2017; 33(6):886-892.
4. Wong EH[#], **So HC**[#], …Sham PC. "Common variants on Xq28 conferring risk of schizophrenia in Han Chinese." ***Schizophr Bull***, 2014; 40(4):777-786.
5. **So HC**, Kwan JS, Cherny SS, Sham PC. "Risk prediction of complex diseases from family history and known susceptibility loci, with applications for cancer screening." ***Am J Hum Genet***, 2011; 88(5):548-565.

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Technical expertise

- ✧ Bioinformatics and statistical genomics
- ✧ Neuropsychiatric genomics
- ✧ Machine learning

Translating genomics data to clinical applications: drug repositioning and disease subtyping

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The time and cost for novel drug discovery is ever-increasing. Drug repositioning, i.e. using existing drugs for new therapeutic indications, represents a cost-effective approach to speed up drug development. With increased availability of large-scale "omics" data, computational methods will play an important role for prioritizing candidates suitable for repositioning. Here we will present several approaches to computational drug repositioning. For example, we developed an approach by comparing imputed expression profiles from genome-wide association data and drug transcriptomes. We also propose another method based on the principles of gene-set analysis. We focus our applications on psychiatric disorders since few repositioning studies were targeted towards these disorders. We found that the above methods successfully "re-discovered" known drugs for the studied diseases and revealed novel repositioning candidates that are supported by the literature.

Besides guiding drug discovery, genomic data may also be used for other translational purposes, including the subtyping of diseases. Classifying patients into clinically and biologically homogenous subgroups will facilitate the understanding of disease pathophysiology and development of targeted prevention and interventions. Traditionally, disease subtyping is based on clinical characteristics alone, however disease subtypes identified by such an approach may not conform exactly to the underlying biological mechanisms. We have derived a new framework for disease subtyping by integrating genomic profiles (such as those from genome-wide association studies) with clinical symptoms. Applications of the framework to schizophrenia and cardiometabolic disorders showed that addition of genomic data may result in more accurate subtyping.

Keywords: drug repositioning, psychiatry, genome-wide association studies, disease subtyping

Session VI (CBET)

Speaker Biography

Prof. CHEUNG Wing-Tai（張榮泰）trained initially in The Chinese University of Hong Kong (CUHK) as a biochemist and pharmacologist working on G protein-coupled receptor (GPCR)-regulated smooth muscle contraction and lipid metabolism. As a Croucher scholar, Prof. Cheung received his Ph.D. degree in Cambridge University on molecular neurobiology studying orphan GPCRs. Postdoctoral training with Dr. John Rogers worked on calcium binding proteins. Prof. Cheung's laboratory is built on his life-long pursuit of GPCR being a valuable drug target, research themes are focused on pathophysiology of cancers and metabolic syndromes, and exploring protein engineering for therapeutic anti-GPCR antibody development.

Five recent representative publications

1. Jin L[#], Li ZF[#], Wang DK, Sun M, Qi W, Ma Q, Zhang L, Chu C, Chan EYM, Lee SST, Wise H, To KF, Shi Y, Zhou N[*], **Cheung WT**[*]. "Molecular and functional characterization of tumour-induced factor (TIF): Hamster homolog of CXCL3 (GROγ) displays tumour suppressive activity." ***Cytokine***, 2018; 102:62-75.
2. Feng L, Yuen YL, Xu J, Liu X, Chan MYC, Wang K, Fong WP, **Cheung WT**[*], Lee SST[*]. "Identification and characterization of a novel PPARα-regulated and 7α-hydroxyl bile acid-preferring cytosolic sulfotransferase mL-STL (Sult2a8)." ***J Lipid Res***, 2017; 58:1114-1131. (Paper is accompanied with an editorial Commentary by Paul Dawson and Kenneth Setchell)
3. Leung SO, Gao K, Wang GY, Cheung BKW, Lee KY, Zhao Q, **Cheung WT**, Wang JZ. "Surrogate target cells expressing surface anti-idiotype antibody for the clinical evaluation of an internalizing CD22-specific antibody." ***mAbs***, 2015; 7(1):66-76.
4. Zhao Q, Wong PF, Lee SST, Leung SO, **Cheung WT**[*], Wang JZ[*]. "Generation of anti-idiotype scFv for pharmacokinetic measurement in lymphoma patients treated with chimera anti-CD22 antibody SM03." ***PLoS One***, 2014; 9(5):e96697.
5. Jiang LL, Teng GMK, Chan EYM, Au SWN, Wise H, Lee SST, **Cheung WT**. "Impact of cell type and epitope tagging on heterologous expression of G protein-coupled receptor: A systematic study on angiotensin type II receptor." ***PLoS One***, 2012; 7(10):e47016.

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Technical expertise

- ✧ Organ bath tissue pharmacology
- ✧ Phage-displayed Library
- ✧ Protein chemistry
- ✧ Protein engineering
- ✧ Proteomics analysis

Neutrophils in inflammatory cancer

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High expressions of inflammation cytokines and factors, such as IL8 and CXCL1/3, are commonly found in cancers. However, the underlying mechanism of how these inflammatory factors lead to cancer formation is largely unknown. Ovarian cancer is one of the devastating diseases as most of the patient (~ 60 %) are diagnosed at the advanced stage that cancer cells have already spread within the abdomen. Previously, our lab has established a mouse xenograft model of copy number variation (CNV)-mediated; GPCR MAS-driven epithelial ovarian cancer which expressed the inflammatory chemokines CXCL1 and CXCL3 abundantly [*Int J Cancer 125: 1316-1327 (2009)*]. Proteomic study indicated a specific expression of coactosin-like protein 1 (COTL1) in xenograft stroma. Consistent with previous reports that COTL1 enhanced leukotriene production, a significant amount of leukotrienes B4 (LTB4) was detected in xenografts. Subsequent study indicated that the tumor was highly infiltrated with $Ly6G^+$, $CXCR1^+$, $CXCR2^+$, $LTB4R1^+$ neutrophils which also expressed all the key enzymes for leukotrienes synthesis. Selective blocking of LT synthesis with 5-lipoxygenase inhibitor zileuton and specific depletion of neutrophils with an anti-Ly6G antibody suppressed significantly tumor growth *in vivo*, suggesting neutrophils were recruited to tumor via a LTB4-mediated positive feedback loop and played a critical role in tumor formation. Leukotrienes did not exert any growth-promoting effects on the tumorigenic *Mas*-transformed ovarian cells (Mc0M80) nor cancer-associated fibroblasts (CAF). By contrast, growth of the Mc0M80 cells was significantly enhanced when co-cultured with neutrophils. The growth-stimulatory effect of neutrophils was as potent as that of CAF. Consistent with neutrophils promoted stemness of the ovarian tumor cells, cells isolated from xenografts induced secondary xenograft formation. These results suggested inflammatory cytokine promotes cancer formation via LT-mediated neutrophils recruitment, which in turn enhances stemness and growth of tumor cells. Importantly, present study reveals that neutrophil is a therapeutic target for treating inflammatory cancers.

Session VI (CBET)

Speaker Biography

Prof. CHENG Sze Lok Alfred（鄭詩樂）is a Professor in the School of Biomedical Sciences and Assistant Dean (Research) of the Faculty of Medicine at The Chinese University of Hong Kong (CUHK). He completed his Ph.D. under the supervision of Prof. Joseph Sung in the Department of Medicine and Therapeutics at CUHK in 2002 and went on his postdoctoral training in Ohio State University until 2007. Prof. Cheng has published in international journals including *Molecular Cell, Nature Genetics, Journal of Clinical Investigation, Cancer Research, Gastroenterology, Gut, Journal of Hepatology, Nature Communications* and *Nucleic Acids Research*. He has received >20 academic honors and awards, including recognitions from the American Association of Cancer Research (AACR) and United European Gastroenterology (UEG). He was a recipient of the Most Promising Young Investigator Award by Hong Kong SAR Government (2014) and CUHK (2015). He has been recently awarded the Asa Briggs Visiting Fellowship in 2017 by the University of Sussex and the Visiting Professorship in 2018 by the Southwestern Medical University. Until 2020, he has presided as Principal Investigator (PI)/co-PI in ~30 local and national competitive grants with a sum of over 90 million HK dollars. His current research focuses on the epigenetic mechanisms in tumors and their microenvironment, aiming at the enhancement of cancer immunotherapy.

Five recent representative publications

1. Liu M, Zhou J, Liu X, Feng Y, Yang W, Wu F, Cheung OK, Sun H, Zeng X, Tang W, Mok, MT, Wong J, Yeung PC, Lai PB, Jin H, Chen J, Chan SL, Chan AW, To KF, Chen Z, Sung JJ, Chen M, **Cheng ASL***. "Targeting monocyte-intrinsic enhancer reprogramming improves immunotherapy efficacy in hepatocellular carcinoma." ***Gut***, 2020; 69(2):365-379.
2. Tian Y, Yang B, Qiu W, Hao Y, Zhang Z, Yang B, Li N, Cheng S, Lin Z, Rui YC, Cheung OK, Wu WK, Yang W, Cheung Y, Lai PB, Luo J, Sung JJ, Chen R, Wang H, **Cheng ASL***, Yang P*. "ER-residential Nogo-B accelerates NAFLD-associated HCC mediated by metabolic reprogramming of oxLDL lipophagy." ***Nature Communications***, 2019; 10(1), 3391.
3. Xiong L, Wu F, Wu Q, Xu L, Cheung OK, Kang W, Mok MT, Szeto LLM, Lun CY, Lung RW, Zhang J, Yu KH, Lee SD, Huang G, Wang CM, Liu J, Yu Z, Yu DY, Chou JL, Huang WH, Feng B, Cheung YS, Lai PB, Tan P, Wong N, Chan MW, Huang TH, Yip KY*, **Cheng ASL***, To KF*. "Aberrant enhancer hypomethylation contributes to hepatic carcinogenesis through global transcriptional reprogramming." ***Nature Communications***, 2019; 10(1), 335.
4. Sun H, Yang W, Tian Y, Zeng X, Zhou J, Mok MTS, Tang W, Feng Y, Xu L, Chan AWH, Tong JH, Cheung YS, Lai PBS, Wang HKS, Tsang SW, Chow KL, Hu M, Liu R, Huang L, Yang B, Yang P, To KF, Sung JJY, Wong GLH*, Wong VWS*, **Cheng ASL***. "An inflammatory-CCRK circuitry drives mTORC1-dependent metabolic and immunosuppressive reprogramming in obesity-associated hepatocellular carcinoma." ***Nature Communications***, 2018; 9(1), 5214.
5. Zhou J, Liu M, Sun H, Feng Y, Xu L, Chan AWH, Tong JH, Wong J, Chong CCN, Lai PBS, Wang HK, Tsang SW, Goodwin T, Liu R, Huang L, Chen Z, Sung JJ, Chow KL, To KF, **Cheng ASL***. "Hepatoma-intrinsic CCRK inhibition diminishes myeloid-derived suppressor cell immunosuppression and enhances immune-checkpoint blockade efficacy." ***Gut***, 2018; 67, 931-944.

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Technical expertise

- ✧ Epigenomics analysis
- ✧ Liver and tumor microenvironment

Targeting the tumor microenvironment for combination immunotherapy

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Understanding of cancer epigenome provides new opportunities to rewire transcriptional programs that drive hallmark tumor traits. Transcriptional enhancers are distal regulatory elements that drive lineage-specific gene expressions. Genetic and epigenetic alterations of these non-coding sequences have emerged as common molecular traits of various human cancers. Recent high-dimensional omics studies in various cancers including hepatocellular carcinoma (HCC) have emphasized on much importance for the strong immunosuppressive tumor microenvironment that counteracts the activation and infiltration of cytotoxic T lymphocytes into the tumor. In this talk, I hence intend to describe our investigative scope from HCC cell epigenetics to enhancer regulation of tumor immune evasion. Based on our discoveries, we have developed mechanism-based combination immunotherapies that are supported by pharmacological proof-of-concept using preclinical models.

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