# RESEARCH DAY 2022

## SCHOOL OF BIOMEDICAL SCIENCES (SBS)

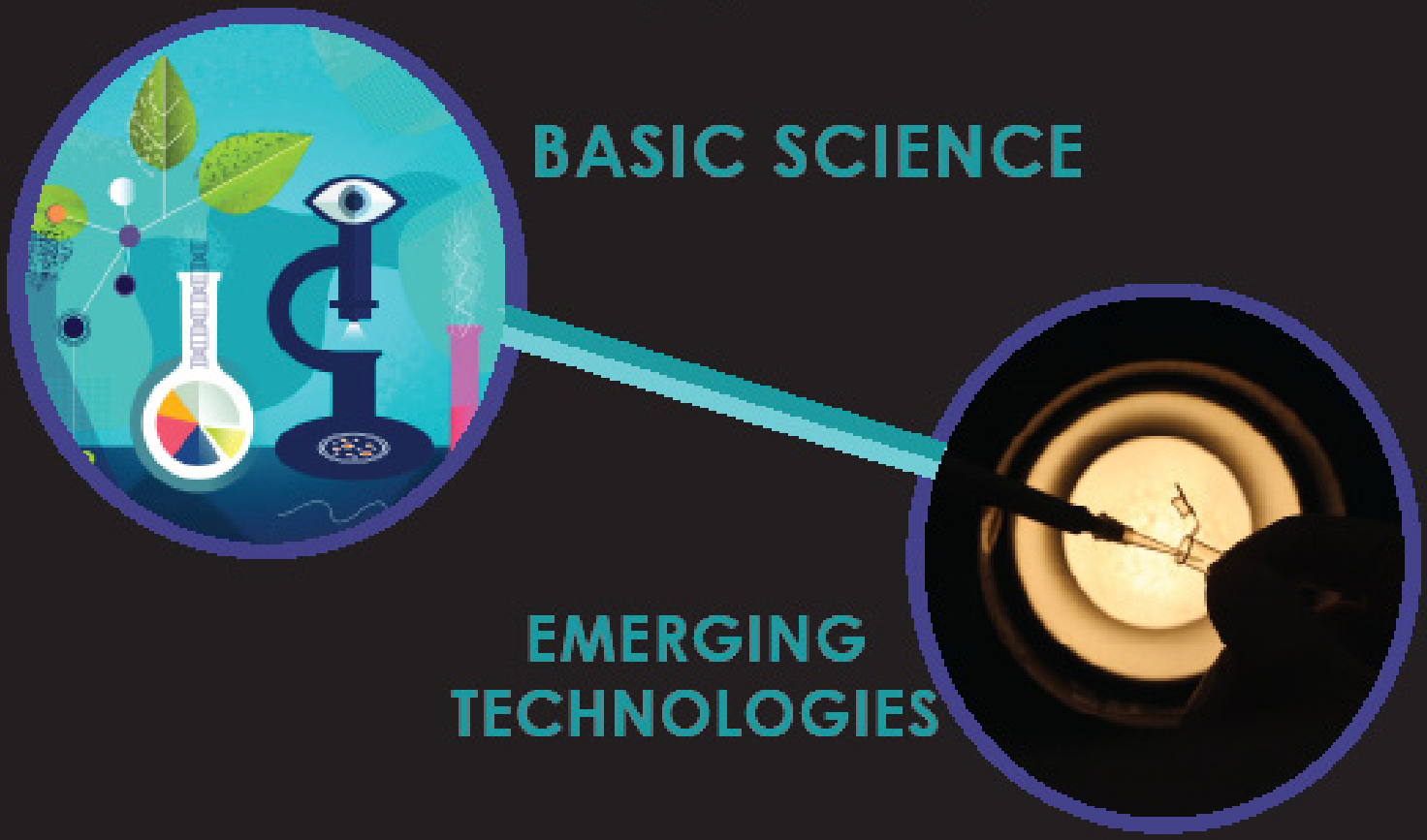
## AND

## HONG KONG SOCIETY FOR DEVELOPMENTAL BIOLOGY (HKSDB)

Joint Symposium on

**Advances in Developmental and Stem Cell Biology:**

From Basic Science to Emerging Technologies




**16-17 JUNE 2022 | HYBRID**

G/F, Lo Kwee-Seong Integrated Biomedical Sciences Building,
Area 39, The Chinese University of Hong Kong / Online

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The Chinese University of Hong Kong

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HKSDB

# Research Day 2022 & Joint Symposium on "Advances in Developmental and Stem Cell Biology: From Basic Science to Emerging Technologies"

Organized by the School of Biomedical Sciences (SBS), CUHK and the Hong Kong Society for Developmental Biology (HKSDB)

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# *Welcome Message from* the Dean of Faculty of Medicine



It is my pleasure to welcome you to the Research Day 2022 & Joint Symposium on "Advances in Developmental and Stem Cell Biology: From Basic Science to Emerging Technologies".

This year, the annual Research Day of the School of Biomedical Sciences (SBS) is jointly organized with the Hong Kong Society for Developmental Biology (HKSDB), bringing together many distinguished scientists from our School of Biomedical Sciences, the University, and other academic institutions to showcase their latest research insights with the specific theme on developmental and regenerative biology.

We are much honoured to have three keynote speakers in this meaningful event, Prof. Stephen DALTON from the School of Biomedical Sciences, The Chinese University of Hong Kong (CUHK); Prof. Naihe JING from Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences (CAS); and Prof. Ting XIE from the Division of Life Science, The Hong Kong University of Science and Technology (HKUST). The active participation from all notable speakers and participants will definitely open a door for extending interdisciplinary research collaborations, further strengthening the connections amongst all these renowned institutions.

This event is a golden opportunity for everyone to seize new opportunities in this one-and-a-half-day programme. I trust you will enjoy the animated discussions and be able to exchange thought-provoking scientific ideas. The Faculty and clinicians at the Prince of Wales Hospital will continue to support the members of SBS to foster sustainable relationship with different academic and industry partners to accelerate bench-to-bedside researches. Let us work together for the better health and hope of mankind and the world.

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 most delighted to welcome you all to Research Day 2022 & Joint Symposium on "Advances in Developmental and Stem Cell Biology: From Basic Science to Emerging Technologies", organised by our School and the Hong Kong Society for Developmental Biology (HKSDB).

The Research Day is one of the annual signature events of the School and this comes to its thirteenth year. It has been always a valuable platform to gather our School members, clinical colleagues and friends from tertiary institutions to share their latest research insights and widen their academic networks. This year we partner with HKSDB to organise this event in hybrid format to provide all participants with the opportunity to exchange and discuss scientific ideas physically and virtually.

With the main theme "Advances in Developmental and Stem Cell Biology", we are glad to have six speakers from SBS, and ten speakers from The University of Hong Kong, The Hong Kong Polytechnic University, Hong Kong Baptist University, The Hong Kong University of Science and Technology, and Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences. The programme is divided into three sessions on Developmental Biology, Emerging Technologies, and Stem Cell Biology. It is expected this diverse programme with top-notched experts in this field will be filled with all-rounded and stimulating discussions. We hope all of you will get inspired from the cross-pollination of ideas, build up new connections, and further explore collaboration opportunities for future research progress.

I would like to express my gratitude to members of the Organizing Committee for their efforts, as well as to the sponsoring companies for their supports in this event. Thank you for joining and wish all of you a great time with us!

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

# *Research Day 2022 & Joint Symposium on "Advances in Developmental and Stem Cell Biology: From Basic Science to Emerging Technologies"*

## 16 June 2022 (Thursday)

| | |
|---|---|
| 09:00-09:20 | **Opening Ceremony:**<br>Prof. CHAN Ka Leung Francis (Dean of Faculty of Medicine),<br>Prof. SHAM Mai Har (Pro-Vice-Chancellor / Vice-President, CUHK; President, Hong Kong Society for Developmental Biology) &<br>Prof. CHAN Man Lok Andrew (Director of School of Biomedical Sciences)<br><br>Presentation of the prize for Programme Book Cover / Banner Design Competition / Photo Taking |

| *Time* | *Title of Presentation* | *Speaker* | *Abstract No.* |
|---|---|---|---|
| ***Session A: Developmental Biology***<br>***Chairpersons: Prof. KWAN Kin Ming (CUHK) & Prof. CHOY K.W. Richard (CUHK)*** | | | |
| 09:20-10:20 | Metabolic reprogramming and cell fate determination in development and disease | DALTON Stephen (CUHK) | O1 (Keynote) |
| 10:20-10:50 | The roles of Sonic Hedgehog signaling factors in cochlear epithelial cell differentiation | SHAM Mai Har (CUHK) | O2 |
| 10:50-11:20 | PHF5A-SF3B1-DLC1 splicing complex determines avian trunk neural crest cell fate | CHEUNG C.H. Martin (HKU) | O3 |
| **11:20-11:30** | ***10-min Break*** | | |
| 11:30-12:00 | The role of autophagy in hematopoiesis – what we have learned with zebrafish model | MA C.H. Alvin (PolyU) | O4 |
| 12:00-12:30 | Disease models of Carpenter syndrome: novel functions of *RAB23* in ciliopathy and primary cilium-dependent hedgehog signaling pathway | HOR H.H. Catherine (HKBU) | O5 |
| **12:30-14:00** | ***Event Lunch*** | | |
| ***Session B: Emerging Technologies***<br>***Chairpersons: Prof. Prof. LAI Kwok On (CityU) & Prof. CHAN C.N. Juliana (CUHK)*** | | | |
| 14:00-15:00 | Time, space and single-cell resolved molecular trajectory of cell populations and the laterality of the body plan at gastrulation | JING Naihe (CAS) | O6 (Keynote) |
| 15:00-15:30 | Cilia-secretory hybrid cells in airway development and disease states | HE Mu (HKU) | O7 |
| 15:30-16:00 | In the hunt for the "cycling" mature neurons—how modern bioinformatics complements with the traditional methods in characterizing these cells | CHOW H.M. Kim (CUHK) | O8 |
| **16:00-16:15** | ***15-min Break*** | | |
| 16:15-16:45 | Liver-specific knock-in using low-dose AAV-CRISPR restored hemostasis in neonatal hemophilia B mice | FENG Bo (CUHK) | O9 |
| 16:45-17:15 | Mechanical folding induces development of engineered intestinal tissue | CHAN Hon Fai (CUHK) | O10 |

***End of Day 1***

## *Research Day 2022 & Joint Symposium on "Advances in Developmental and Stem Cell Biology: From Basic Science to Emerging Technologies"*
## 17 June 2022 (Friday)

| *Time* | *Title of Presentation* | *Speaker* | *Abstract No.* |
|---|---|---|---|
| ***Session C: Stem Cell Biology***<br>***Chairpersons: Prof. CHAN W.Y. Woody (CUHK) & Prof. LI Gang (CUHK)*** | | | |
| 09:00-10:00 | Niche and intrinsic control of adult stem cell regulation | XIE Ting (HKUST) | O11 (Keynote) |
| 10:00-10:30 | Spatiotemporal analysis of human early hematopoiesis and its engineering for cancer immunotherapy | SUGIMURA Rio (HKU) | O12 |
| 10:30-11:00 | Expanded potential stem cells: a new tool for basic and translational research | LIU Pengtao (HKU) | O13 |
| **11:00-11:15** | ***15-min Break*** | | |
| 11:15-11:45 | Engineering and modulating microenvironments to promote tissue regeneration and healing in ischemic diseases | BLOCKI M. Anna (CUHK) | O14 |
| 11:45-12:15 | Differential translational control during muscle stem cell aging | CHEUNG H.T. Tom (HKUST) | O15 |
| 12:15-12:45 | Tuning BMP signaling in nucleus by Zinc finger SWIM-type containing 4 | ZHAO Hui (CUHK) | O16 |
| 12:45-13:00 | Closing Remarks | | |
| **13:00-14:00** | ***Event Lunch*** | | |

***Abbreviations***:
CAS = Chinese Academy of Sciences
CityU = City University of Hong Kong
CUHK = The Chinese University of Hong Kong
HKBU = Hong Kong Baptist University
HKU = The University of Hong Kong
HKUST = The Hong Kong University of Science and Technology
PolyU = The Hong Kong Polytechnic University

*Session A: Developmental Biology*

# Speaker Biography



**Prof. Stephen DALTON**（杜卓勳）is a Professor in the School of Biomedical Sciences, The Chinese University of Hong Kong (CUHK) and has research interests in stem cell and developmental biology and the use of stem cells in regenerative medicine and therapeutic development. Prof. Dalton received his Ph.D. from the University of Adelaide in Australia, followed by post-doctoral research at the Imperial Cancer Research Fund in London with Sir Richard Treisman. Following this, Prof. Dalton joined Hoffman La Roche in Nutley, New Jersey and worked closely with large "pharma" on a broad range of projects while at the Roche Institute for Molecular Biology. Then, after taking an academic position in Australia, Prof. Dalton moved to the University of Georgia where he was for 19 years. During this time, he was the founding director of the Center for Molecular Medicine. At CUHK, Prof. Dalton continues his work in adult and pluripotent stem cell biology and has initiated a program focused on therapeutic development for type 2 diabetes using technology developed in his laboratory.

## Five recent representative publications

1. Zhang L, Avery J, Yin A, Singh AS, Cliff TS, Yin H, **Dalton S**. "Generation of functional brown adipocytes through a directed developmental progression of human pluripotent stem cells." ***Cell Stem Cell***, 2020; 27(5):784-797.
2. Singh AM, Zhang L, Avery J, Yin A, Du Y, Wang H, Li Z, Fu H, Yin H, **Dalton S**. "Human beige adipocytes generated from adipose-derived stem cells have utility for drug discovery and cell therapy of metabolic diseases." ***Nat. Commun.***, 2020; 11(1):2758.
3. Grubert F, Srivas R, Spacek DV, Kasowski M, Ruiz-Velasco M, Sinnott-Armstrong N, Greenside P, Narasimha A, Liu Q, Geller B, Sanghi A, Kulik M, Sa S, Rabinovitch M, Kundaje A, **Dalton S**, Zaugg JB, Snyder M. "Landscape of cohesin-mediated chromatin loops in the human genome." ***Nature***, 2020; 583(7818):737-743.
4. Colunga T, Hayworth M, Kreß S, Reynolds DM, Chen L, Nazor KL, Baur J, Singh AS, Loring JF, Metzger M, **Dalton S**. "Human pluripotent stem cell-derived multipotent vascular progenitors of the mesothelium lineage have utility in tissue engineering and vascular repair." ***Cell Reports***, 2019; 26(10):2566-2579.
5. Cliff TS, Wu T, Boward BR, Yin A, Yin H, Glushka JN, Prestegaard JH, **Dalton S**. "MYC controls human pluripotent stem cell fate decisions through regulation of metabolic flux." ***Cell Stem Cell***, 2017; 21(4):502-516.

## Research interests / Technical expertise

- ✧ Pluripotent stem cells
- ✧ Developmental biology of beige and brown adipocytes
- ✧ Therapeutic development for type 2 diabetes and obesity
- ✧ Molecular mechanisms of cell fate determination

## Metabolic reprogramming and cell fate determination in development and disease

**CLIFF Tim, WU Tianming and DALTON Stephen**

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

Switching between aerobic glycolysis and oxidative metabolism impacts cell fate decisions including those contributing to disease pathogenesis, tissue homeostasis and development. During normal development, differentiation of stem and progenitor cells is often associated with metabolic remodeling, as illustrated by a switch between aerobic glycolysis and oxidative phosphorylation (OxPhos) as the primary energy producing mechanism. Although metabolic switching has been linked to disease pathogenesis, homeostasis of normal tissue and development, an overarching mechanism for this remains to be elucidated. Most notably in cancer cells, aerobic glycolysis is frequently referred to as the "Warburg effect" where it provides the primary mode of energy generation in preference to OxPhos. The fundamental benefit endowed upon cancer cells by aerobic glycolysis, however, is unclear and is frequently explained anecdotally without supporting data. Understanding why different cell types use specific metabolic programs should provide significant insight into normal development and other disease states. Using human pluripotent stem cells as a developmental model, we have investigated how metabolic status impacts cell fate and in doing so, have uncovered basic principles that are likely to be applicable to stem and progenitor cells in disease, homeostasis and development.

*Session A: Developmental Biology*

# Speaker Biography



**Prof. SHAM Mai Har**（岑美霞）is a Choh-Ming Li Professor of Biomedical Sciences of The Chinese University of Hong Kong (CUHK). She obtained her BSc and MPhil degrees in Biology at CUHK. She obtained her PhD in Biochemistry in the University of Cambridge. She received her postdoctoral training in Developmental Genetics in the National Institute for Medical Research in London, U.K. Professor Sham's research focuses on the molecular mechanisms of mammalian development and human congenital disorders. Her research group works on transcriptional regulation and functional genomics in craniofacial and sensory neural development and diseases. Her research laboratory uses mutant mice, stem cells and organoids, and single-cell technologies as experimental platforms.

## Five recent representative publications


1. Huang T, Hou Y, Wang X, Wang L, Yi C, Wang C, Sun X, Tam PK, Ngai SM, **Sham MH**, Burns A, Chan WY. "Direct interaction of Sox10 with cadherin-19 mediates early sacral neural crest cell migration: implications for enteric nervous system development defects." ***Gastroenterology***, 2022; 162(1):179-192.e11.
2. Kwok AWC, Qiao C, Huang R, **Sham MH**, Ho JWK, Huang Y. "MQuad enables clonal substructure discovery using single cell mitochondrial variants." ***Nat. Commun.***, 2022; 13(1):1205.
3. Zhang H, Xie J, So KH, Tong KK, Sae-Pang JJ, Wang L, Tsang SL, Chan WY, Wong EYM, **Sham MH**. "*Hoxb3* regulates *Jag1* expression in pharyngeal epithelium and affects interaction with neural crest cells." ***Front. Physiol.***, 2021; 11:612230.
4. Wang L, Xie JJ, Zhang H, Tsang LH, Tsang SL, Braune E-B, Lendahl U, **Sham MH**. "Notch signalling regulates epibranchial placode patterning and segregation." ***Development***, 2020; 147(4):dev183665.
5. Zhang H, Wang L, Wong EYM, Tsang SL, Xu PX, Lendahl U, **Sham MH**. "An Eya1-Notch axis specifies bipotential epibranchial differentiation in mammalian craniofacial morphogenesis." ***eLife***, 2017;6:e30126.


## Research interests / Technical expertise

- ✧ *Irx* genes and their transcriptional regulations in craniofacial development, hearing disorders and eye diseases
- ✧ Sonic hedgehog signaling genes in sensory and non-sensory cochlear epithelium development
- ✧ Notch signaling and transcriptional regulations in cranial placode, neural crest and craniofacial development
- ✧ The role of Sox10 and Eph/ephrins in enteric nervous system development

## The roles of Sonic Hedgehog signaling factors in cochlear epithelial cell differentiation

**QIN Tianli[1], SO Kam Hei Karl[1], HUI Chi Chung[2] and SHAM Mai Har[1]**

[1] School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, China.
[2] Program in Developmental & Stem Cell Biology, The Hospital for Sick Children, Toronto, Canada.

During inner ear development, there are intricate interplay of signaling mechanisms to define the cochlear epithelial sensory and non-sensory cell fates. Sonic Hedgehog (Shh) is required for the temporal and directional control of cochlear sensory hair cell (HC) differentiation, but the underlying mechanism is not known. By genetic analysis using a series of mouse mutants, we show that *Sufu*, a negative regulator of Shh signaling, is essential for controlling the timing and progression of HC differentiation. Removal of *Sufu* leads to abnormal Atoh1 expression and a severe delay of HC differentiation due to elevated *Gli2* mRNA expression. Later in development, HC differentiation defects are restored in the *Sufu* mutant by the action of Spop which promotes Gli2 protein degradation. We demonstrate that restriction of Gli2 expression, the major transcriptional activator of Shh signaling pathway, is a prerequisite for cochlear HC differentiation. Gli2 blocks HC differentiation by maintaining the progenitor state of $Sox2^{+}$ prosensory cells. The spatiotemporal differentiation pattern of HCs along the basal-apical axis of the cochlea is thus achieved by controlling the level of Gli2 transcription in the sensory progenitor cells.

The different types of non-sensory cells in the cochlear duct have specialized functions to maintain the endocochlear potential and ion homeostasis, these non-sensory cells are essential for hearing function. However, the regulation of non-sensory cell differentiation and formation of non-sensory structures in the cochlea are not well understood. By single-cell transcriptomics and mouse mutant analyses, we discovered that the Shh receptor *Ptch1* is required for marginal cell (MC) differentiation and stria vascularis development. We show that Gli2 functions as the key mediator of Shh signaling in regulating MC development. MC precursors are maintained in the progenitor state when Gli2 level is elevated. Our results demonstrate the coordinated regulation of both sensory and non-sensory components by Shh signaling and Gli2 during cochlear development. As patient with *PTCH1* mutation suffers from hearing loss, our results highlight important pathogenic mechanisms for human deafness.

*Session A: Developmental Biology*

# Speaker Biography

**Prof. CHEUNG Chi Hang Martin**（張知恒）received his BSc in Biochemistry from The Chinese University of Hong Kong and PhD in Developmental Genetics at the University of Nottingham in the United Kingdom. He was then trained as a postdoctoral fellow in the laboratory of Dr. James Briscoe at the National Institute for Medical Research (now part of the Francis Crick Institute) where demonstrated the functional importance of SOX9 in avian neural crest development. He was recruited as a Research Assistant Professor to establish the chick model system in the former Department of Biochemistry at the University of Hong Kong and was promoted to Assistant Professor in the former Department of Anatomy in 2013. In 2019, he was further promoted to Associate Professor with tenure in the School of Biomedical Sciences. He is one of the leading scientists in the neural crest field and has made seminal contributions to unravel the molecular mechanisms in governing neural crest specification, directional migration and lineage differentiation in chick embryos. In addition, he has also expanded research interests in elucidating the molecular mechanisms underlying melanoma metastasis and spinal muscular atrophy. To date, he has published more than 30 peer-reviewed articles in leading journals and some of which he served as either first or corresponding author in *Development, Developmental Cell, PNAS x 2, Developmental Biology, Nature Communications, Stem Cell Reports, Journal of Experimental and Clinical Cancer Research, Oncogene* and *Advanced Science*. He also co-published papers with investigators locally and internationally in *Nature, Nature Neuroscience, JAMA* etc. In 2018, he was nominated for the 19th ROYAN International Research Award, and received a Faculty Outstanding Research Output Award in 2019. His work has been featured in press release at the School, Faculty and University levels as well as in the local, regional and international media.

## Five recent representative publications


1. Hu F, Fong KO, Cheung MPL, Liu JAI, Liang R, Li TW, Sharma R, IP PPC, Yang XT, **Cheung M***. “DEPDC1B promotes melanoma angiogenesis and metastasis through sequestration of ubiquitin ligase CDC16 to stabilize secreted SCUBE3.” ***Adv Sci***, 2022; 2105226. https://doi.org/10.1002/advs.202105226
2. Yang XT, Hu F, Liu JA, Yu S, Cheung MPL, Liu XL, Ng IOL, Guan XY, Wong KKW, Sharma R, Lung HL, Jiao YF, Lee LTO, **Cheung M***. “Nuclear DLC1 exerts oncogenic function through association with FOXK1 for cooperative activation of MMP9 expression in melanoma.” ***Oncogene***, 2020; 39(20):4061-4067. https://doi.org/10.1038/s41388-020-1274-8
3. Liu JA, Tai A, Hong J, Cheung MPL, Sham MH, Cheah KSE, Cheung CW, **Cheung M***. “Fbxo9 functions downstream of Sox10 to determine neuron-glial fate choice in the dorsal root ganglia through Neurog2 destabilization.” ***Proc Natl Acad Sci USA***, 2020; 117(8):4199-4210. http://doi.org/10.1073/pnas.1916164117
4. Yang XT, Liang R, Liu CX, Liu AJ, Cheung MPL, Liu XL, Man OY, Guan XY, Lung HL, **Cheung M***. “SOX9 is a dose-dependent metastatic fate determinant in melanoma.” ***Journal of Experimental and Clinical Cancer Research***, 2019; 38(1):17. https://doi.org/10.1186/s13046-018-0998-6
5. Liu JA, Rao YX, Cheung MPL, Hui MN, Wu MH, Chan LK, Ng IOL, Niu B, Cheah KSE, Sharma R, Hodgson L, **Cheung M***. “Asymmetric localization of DLC1 defines avian trunk neural crest polarity for directional delamination and migration.” ***Nature Communications***, 2017; 8(1):1185. https://doi.org/10.1038/s41467-017-01107-0


## Research interests / Technical expertise

- ✧ Transcriptional and post-transcriptional regulation of neural crest formation, migration and lineage differentiation in chick embryos
- ✧ Molecular mechanisms of melanoma metastasis and drug resistance
- ✧ Modelling of spinal muscular atrophy using organoid and lineage reprogramming approaches
- ✧ Gene therapy in a mouse model of spinal muscular atrophy

## PHF5A-SF3B1-DLC1 splicing complex determines avian trunk neural crest cell fate

**ZHENG Zhengfan[1], GUO Suisui[1,2†], RAO Yanxia[1,3‡], HUI Man Ning[1,4§], CHEUNG May Pui Lai[1], WONG Kelvin K.W[5], SHARMA Rakesh[5], LIU Jessica Aijia[6], and CHEUNG Martin C.H.[1]**

[1] School of Biomedical Sciences, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China.
[2†] Division of Life Science, The Hong Kong University of Science and Technology, Hong Kong SAR, China.
[3‡] Shanghai Key Laboratory of Psychotic Disorders, Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine, Shanghai 21108, China.
[4§] Department of Obstetrics and Gynaecology, School of Clinical Medicine, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China.
[5] Centre for PanorOmic Sciences Proteomics and Metabolomics Core Facility, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China.
[6] Department of Neuroscience, City University of Hong Kong, Hong Kong SAR, China.

[†‡§] Present address

In vertebrates, neural crest cells (NCCs) belong to a migratory population of multipotent stem cells which arise at the neural plate border located between the neural plate and non-neural ectoderm. Numerous studies in different vertebrate species have shown that NC specifier genes, *SOX9*, *SNAIL2* and *FOXD3*, determine NCC fate and their transcriptional expressions are subjected to the regulation of signaling molecules and neural plate border specifiers. Notably, intron-containing genes *SOX9* and *SNAIL2* involve an underlying additional level of post-transcriptional control of their expression and function in specifying NCC fate. However, components of the splicesome complex regulating splicing of NC specifier pre-mRNAs remain largely unclear. Here, our mass spectrometry analysis in chick embryos revealed the association between PHF5A, SF3B1 and DLC1 proteins, of which PHF5A and SF3B1 are reported components of U2 small nuclear-RNA-protein complex involved in one of the critical steps in pre-mRNA splicing. By *in ovo* electroporation to knockout ubiquitously expressed PHF5A and SF3B1 in avian trunk neural tube using CRISPR-Cas9 approach, we found their specific functional requirements in determining NCC fate via regulating the splicing of *SOX9* and *SNAIL2* pre-mRNAs. This is further supported by the treatment of splicing modulators targeting intron binding of PHF5A-SF3B1, resulting in the loss of NC specifiers expression due to aberrant splicing, without affecting their expression in somites. The specific vulnerability of trunk NCCs to the loss of PHF5A-SF3B1 expression and intron binding is due to their association with NC specific DLC1 protein which appears to weaken binding affinity of PHF5A-SF3B1 complex specifically to the introns of SOX9 and SNAIL2 pre-mRNAs compared to somites which do not express DLC1. Altogether, our findings unravel a NC specific PHF5A-SF3B1-DLC1 splicing complex in determining avian trunk NCC fate.

*Session A: Developmental Biology*

# Speaker Biography



**Prof. MA Chun Hang Alvin**（馬進恒）is currently an Assistant Professor in the Department of Health Technology and Informatics (HTI), The Hong Kong Polytechnic University (PolyU). He received his MPhil and PhD from The University of Hong Kong (HKU) in 2005 and 2009 before further trained as Research Fellow in Mayo Clinic, MN, US. He returned to Department of Medicine, HKU as Research Assistant Professor in 2013 and joined PolyU in 2016.

## Five recent representative publications

1. Xie F, Xu S, Lu Y, Wong KF, Sun L, Hasan KM, **Ma AC**, Tse G, Manno SH, Tian L, Yue J, Cheng SH. "Metformin accelerates zebrafish heart regeneration by inducing autophagy." ***NPJ Regenerative Medicine***, 2021; 6(1):62.
2. Chen XK, Yi Z, Wong GT, Hasan K, Kwan JS*, **Ma AC***, Chang RC*. "Is exercise a senolytic medicine? A systematic review." ***Aging Cell***, 2021; 20(1):e13294.
3. Chen XK, Kwan JS, Chiang RC*, **Ma AC***. "1-phenyl 2-thiourea (PTU) activates autophagy in zebrafish embryos." ***Autophagy***, 2021; 17(5):1222-1231.
4. **Ma AC**, Mak CC, Yeung KS, Pei SL, Ying D, Yu MH, Hasan KM, Chen X, Chow PC, Cheung YF, Chung BH. "Mono-allelic mutations in CC2D1A suggest a novel role in human heterotaxy and ciliary dysfunction." ***Circulation: Genomic and Precision Medicine***, 2020; 13(6):e003000.
5. He BL, Yang N, Man CH, Ng NK, Cher CY, Leung HC, Kan LL, Cheng BY, Lam SS, Wang ML, Zhang CX, Kwok H, Cheng G, Sharma R, **Ma AC**, So EC, Kwong YL, Leung AY. "Follistatin is a novel therapeutic target and biomarker in FLT3/ITD acute myeloid leukemia." ***EMBO Molecular Medicine***, 2020; 12(4):e10895.

## Research interests / Technical expertise

- ✧ Hematopoiesis - basic and translational research areas including gene regulation in normal vertebrate hematopoiesis, molecular and cellular basis of human blood diseases
- ✧ Zebrafish Disease Modelling - develop zebrafish (*Danio rerio*) into a comprehensive *in vivo* modelling platform for translational medicine, from functional evaluation of disease-related genes to large-scale chemical screening for novel therapeutic agents
- ✧ Genome Editing - develop new methods for *in vivo* genome engineering

## The role of autophagy in hematopoiesis - what we have learned with zebrafish model

**Xiang-Ke CHEN, Zhen-Ni YI, Jack Jark-Yin LAU, and Alvin Chun-Hang MA**

Department of Health Technology and Informatics, The Hong Kong Polytechnic University, Hong Kong SAR, China.

Macroautophagy, usually referred to autophagy, is an evolutionary conserved cellular process essential for maintenance of cytoplasm and clearance of damaged and expired proteins and organelles. Not only a simple recycling mechanism, autophagy is also important in cell survival under metabolic stresses, such as starvation, hypoxia and drug induction. While recent studies suggested that autophagy implicates maintenance and differentiation of different hematopoietic lineages, the role of autophagy in vertebrate hematopoiesis, particularly the underlying molecular mechanism, remains largely unknown.

With unique characteristics including high fecundity, optical transparency, amendable to genetic and chemical manipulation, as well as highly conserved autophagy and hematopoiesis comparing with human, we make use of zebrafish model to study the role of autophagy in hematopoiesis. During zebrafish embryonic development, autophagy was readily detected in multiple tissues including skin, brain and muscle. Unexpectedly, conventional tyrosinase inhibition (e.g. phenylthiourea, PTU treatment) to block pigmentation in zebrafish embryo significantly induced autophagy, which raise a novel concern in autophagy-related studies using PTU-treated zebrafish model.

To examine the role of autophagy in developmental hematopoiesis, we targeted autophagy-related genes (ATGs) from the six-core autophagy machinery. Although all core ATGs mutation resulted in autophagic deficiency in both hematopoietic and non-hematopoietic cells as expected, they exhibited differential effects on various hematopoietic lineages in zebrafish larvae at different stages, which suggested the canonical autophagy-independent functions of ATGs. While the spatiotemporal expression pattern of ATGs might confer the differential effects upon various hematopoietic lineages, core ATGs mutations also resulted in unique proteomic changes. According to the proteomic dissimilarity between ATG mutants, we also examined their interactions by double mutations and synergistic effects on definitive hematopoiesis were observed between some of the core ATGs. These findings demonstrated both distinct and synergistic roles of core ATGs in zebrafish definitive hematopoiesis, highlighting that vertebrate hematopoiesis is regulated by the interplays of canonical autophagy and ATG-specific non-canonical autophagy, which warrants further investigations.

*Session A: Developmental Biology*

# Speaker Biography



**Prof. HOR Hong-Huan Catherine**（許鳳環）received her Ph.D. at the University of Hong Kong (HKU), studying mouse neural tube patterning and Hedgehog signaling pathway under the supervision of Prof. Mai Har SHAM and Prof. Chi Chung HUI at the Department of Biochemistry. She then embarked on postdoctoral training at Dr. Goh LK's lab at the Duke-NUS Medical School Singapore, pursuing research in the realm of developmental and regenerative neuroscience. During which, she was awarded her first individual national funding for young investigator, Young Individual Research Grant from the Ministry of Health, Singapore.

In 2019, Prof. Hor joined Hong Kong Baptist University (HKBU) at the Department of Chemistry as a faculty member. In 2021, she was awarded Collaborative Research Fund (CRF), in which she leads a team of international scientists from Hong Kong, Singapore, and mainland China to investigate the cellular and neurobiology of viral infection. Her research strives to understand the molecular and cellular pathology of hereditary neurological and neuropsychiatric disorders, with particular interest in deciphering the neurochemistry and neurological roles of an instrumental cell-cell signaling organelle, the primary cilium. Her current projects involve mouse disease models, and human iPSCs disease modeling of ciliopathy-like disorders.

## Five recent representative publications


1. Yang QJ, Wang ZH, **Hor CHH**, Xiao HT, Bian ZX, Wang J. "Asymmetric synthesis of flavanols via Cu-catalyzed kinetic resolution of chromenes and their anti-inflammatory activity." ***Science Advances***, 2022; 8:eabm9603. (3 June 2022, In-print)
2. **Hor CHH***, Lo JCW, Cham ALS, Leong WY, Goh ELK*. "Multifaceted functions of Rab23 on primary cilium-mediated and hedgehog signaling-mediated cerebellar granule cell proliferation." ***Journal of Neuroscience***, 2021; 41(32):6850-6863.
3. Lo JCW, Wong WL, **Hor CHH**. "Efficient and cost effective electroporation method to study primary cilium-dependent signaling pathways in the granule cell precursor." ***Journal of visualized experiments: JoVE***, 2021; 177.
4. **Hor CHH**, Goh EL. "Small GTPases in hedgehog signalling: emerging insights into the disease mechanisms of Rab23-mediated and Arl13b-mediated ciliopathies." ***Current opinion in genetics & development***, 2019; 56:61-68.
5. Tan CW, **Hor CHH**, Kwek SS, Tee HK, Sam IC, Goh ELK, ... Wang LF. "Cell surface α2, 3-linked sialic acid facilitates Zika virus internalization." ***Emerging microbes & infections***, 2019; 8(1): 426-437.


## Research interests / Technical expertise

- ✧ Primary Cilium in Neurodevelopment
- ✧ Neurological Aspects of Viral Infection
- ✧ Human iPSC & Disease Modelling of Ciliopathy and Neurological Disorders

# Abstract

## Disease models of Carpenter syndrome: novel functions of *RAB23* in ciliopathy and primary cilium-dependent hedgehog signaling pathway

**W.L. WONG[1], W.Y. LEONG[2], W.H. TSUI[1], A.O.M. WILKIE[5], E.L.K. GOH[2,3,4] and C.H.H. HOR*[1,2]**

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[2] Neuroscience Academic Clinical Programme, Duke-NUS Medical School, 169857, Singapore.
[3] Department of Research, National Neuroscience Institute, 308433, Singapore.
[4] Neuroscience and Mental Health Faculty, Lee Kong Chian School of Medicine, Nanyang Technological University, 639798, Singapore.
[5] Weatherall Institute of Molecular Medicine, University of Oxford, John Radcliffe Hospital, Headington, Oxford OX3 9DS, UK.

Primary cilium is an organelle found on the surface of nearly all cells. It serves as a signaling hub to transduce extracellular signals such as Hedgehog (Hh) and Wnt signaling ligands. Defective primary cilia lead to a spectrum of hereditary disorders collectively called ciliopathy. Resolving the intricate regulatory networks for cilia biogenesis and signaling is critical for the understanding of disease pathogenesis. *RAB23* is a small GTPases, in which its loss-of-function mutations underlie Carpenter syndrome (CS). Although not clinically known as a ciliopathy disorder, CS patients exhibit clinical features that largely resemble ciliopathies. This phenomenon suggests that *RAB23* mutation may cause dysfunctional primary cilium, and potentially contributes to the pathogenic mechanism of CS. Given this hypothesis, we aim to elucidate the disease mechanisms of CS, and its potential relationship with ciliopathy disorder.

Mouse models of CS were established by global deletion and conditionally knock-out *Rab23* in the brain using actin-cre and Nestin-cre driver lines respectively. Interestingly, *Rab23*-null and brain-specific knockout (Nes-CKO) mutants exhibited reduced ciliation rate in restricted cell types and brain regions. Additionally, these mutants also displayed neurological impairments bearing some similarities with CS and ciliopathies. Consistently, *Rab23*-KO granule neuron progenitors culture revealed compromised ciliation and desensitized against primary cilium-dependent extrinsic Hh signaling pathway stimulation. Furthermore, human disease model of CS was established from CS patient-derived induced-pluripotent stem cells (iPSC). In line with the mouse model data, patient iPSCs-differentiated neurons showed reduced ciliation, strongly suggests the clinical relationship between CS and ciliopathies. Taken together, our data uncover novel *in vivo* function of *Rab23* in ciliogenesis and neurophysiology. Our findings suggest that *RAB23* is a novel causative gene for ciliopathy, uncovering Carpenter syndrome as a ciliopathy disorder.

*Session B: Emerging Technologies*

# Speaker Biography



**Prof. JING Naihe**（景乃禾）received his Ph.D. degree in Biochemistry from Shanghai Institute of Biochemistry, Chinese Academy of Sciences (CAS), China in 1988. He has been a postdoctoral research fellow in The Institute of Physical and Chemical Research (RIKEN), Japan from 1989-1991, and a visiting scholar in Max Planck Institute for Biophysical Chemistry, Germany from 1996-1997. In 1991, Prof. Jing became the group leader and Associate Professor in Shanghai Institute of Biochemistry, CAS, and was promoted to full Professor in 1995. Since 2000, Prof. Jing became Professor and PI of Shanghai Institute of Biochemistry and Cell Biology, CAS. From April 2020, Prof. Jing moved his laboratory into Bioland Laboratory in Guangzhou, and from May 2021 he became PI of Guangzhou Laboratory, Guangzhou. Prof. Jing is now an Associate Editor for *Journal of Molecular Cell Biology*, and is in the Editorial Board of *Cell Research, Open Biology, Developmental Dynamics, Gene Expression Patterns, Mechanisms of Development.*

## Five recent representative publications

1. Peng G*, Suo S, Cui G, Yu F, Wang R, Chen J, Chen S, Liu Z, Chen G, Qian Y, Tam PPL, Han JJ*, **Jing N***. "Molecular architecture of lineage allocation and tissue organization in early mouse embryo." ***Nature***, 2019; 572, 528-532.
2. Yang X, Hu B, Liao J, Qiao Y*, Chen Y, Qian Y, Feng S, Yu F, Dong J, Hou Y, Xu H, Wang R, Peng G, Li J*, Tang F*, **Jing N***. "Distinct enhancer signatures in the mouse gastrula delineate progressive cell fate continuum during embryo development." ***Cell Research***, 2019; 29, 911-926.
3. Zhang T, Ke W, Zhou X, Qian Y, Feng S, Wang R, Cui G, Tao R, Guo W, Duan Y, Zhang X, Cao X, Shu Y, Yue C*, **Jing N***. "Human neural stem cells reinforce hippocampal synaptic network and rescue cognitive deficits in a mouse model of Alzheimer's disease." ***Stem Cell Reports***, 2019; 13, 1022-1037.
4. Chen J, Suo S, Tam PPL, Han JJ*, Peng G*, **Jing N***. "Spatial transcriptomic analysis of cryosectioned tissue samples with Geo-seq." ***Nature Protocols***, 2017; 12, 566-580.
5. Peng G, Suo S, Chen J, Chen W, Liu C, Yu F, Wang R, Chen S, Sun N, Cui G, Song L, Tam PPL, Han JJ*, **Jing N***. "Spatial transcriptome for the molecular annotation of lineage fates and cell identity in mid-gastrula mouse embryo." ***Developmental Cell***, 2016; 36, 681-697.

## Research interest

For the last 10 years, Prof. Jing has focused his research interest to understand molecular mechanisms of early embryonic development and pluripotent stem cell neural differentiation. His group established Geo-seq technology for early mouse embryos, and found lineage segregation mechanisms of three germ layers of mouse gastrula. Prof. Jing's group also established methods to differentiate mouse and human pluripotent stem cells into different subtypes of neuronal cells, and try to explore the possibility of stem cell therapy for Alzheimer's disease.

## Time, space and single-cell resolved molecular trajectory of cell populations and the laterality of the body plan at gastrulation

**Naihe JING**

Guangzhou Laboratory, Guangzhou 510005, China.
Shanghai Institute of Biochemistry and Cell Biology, Shanghai 200031, China.

Understanding of the molecular drivers of lineage diversification and tissue patterning during primary germ layer development requires in-depth knowledge of the dynamic molecular trajectories of cell lineages across a series of developmental stages of gastrulation. Through computational modeling, we constructed at single-cell resolution a spatio-temporal compendium of the molecular trajectories of germ-layer derivatives in gastrula-stage mouse embryos. This molecular atlas infers the developmental trajectories of single-cell populations and the molecular network activity underpinning the specification and differentiation of the germ-layer lineages. Analysis of the heterogeneity of cellular composition of cell population at defined positions in the epiblast revealed progressive diversification of cell types, mirroring the process of lineage allocation during gastrulation. An unexpected observation is the difference in the contribution of cells on contralateral sides of the epiblast to mesoderm derivatives of the early organogenesis embryo, and the differences in signaling activities between the left- and right-side mesoderm at late gastrulation. Perturbation of BMP signaling activity led to disruption of left-right molecular asymmetry in the gastrula- and early-somite-stage embryo. These findings suggest that the specification of laterality of the body plan may be initiated earlier than the acquisition of functional competence of the node.

*Session B: Emerging Technologies*

# Speaker Biography



**Dr. HE Mu**（何睦）was born in China, educated in the US, and joined the School of Biomedical Sciences of the Faculty of Medicine at the University of Hong Kong (HKU) in 2021 to start her independent research group. Previously, Dr. He was a postdoctoral scholar in the laboratory of Lily Jan at the University of California, San Francisco. She received her PhD training under the guidance of Kathryn Anderson in the Developmental Biology from the joint graduate program at the Memorial Sloan Kettering Institute.

In the next 5 to 10 years, Dr. He and her team will leverage the power of mouse genetics, human organoids, and tissue engineering to understand how the respiratory system develops, repairs, and regenerates.

## Five recent representative publications


1. **He M**[#]*, Wu B[#], Le DD, Ye W, Sinclair AW, Padovano V, Chen Y, Li K, Sit R, Tan M, Caplan MJ, Neff N, Jan YN, Darmanis S*, Jan LY*. "Single cell RNAseq reveals a critical role of chloride channels in airway development." ***eLife***, 2020; 9:e53085. PMID: 32286221. [[#] co-first authors; * co-correspondent authors]
2. The Tabula Muris consortium et al. "A single cell transcriptomic atlas characterizes aging tissues in the mouse." ***Nature***, 2020; 583:590-595. PMID: 32669714.
3. Ramirez-San Juan GR, Mathijssen ATM, **He M**, Jan LY, Marshall W, Prakash M. "Multi-scale spatial heterogeneity enhances particle clearance in airway ciliary arrays." ***Nature Physics,*** 2020; 16:958-964.
   [Highlighted by preLights Developmental Biology]
4. **He M**, Ye W, Wang WJ, Sison ES, Jan YN, Jan LY. "Cytoplasmic $Cl^-$ couples membrane remodeling to epithelial morphogenesis." ***Proc Natl Acad Sci USA***, 2017; 114(52):E11161-E11169. PMCID: PMC5748203.
5. **He M**, Subramanian R, Bangs F, Omelchenko T, Liem Jr KF, Kapoor TM, Anderson KV. "The Kinesin-4 protein KIF7 kinesin regulates mammalian Hedgehog signaling by organizing the cilia tip compartment." ***Nature Cell Biology***, 2014; 16:663-672. PMID: 24952464.
   [Highlighted by Nature Cell Biology, Nature Review Molecular Cell Biology, EMBO]


## Research interests / Technical expertise

- ✧ Mouse genetics, live imaging, human airway organoids, single-cell omics
- ✧ Cellular plasticity, motile cilia, mucociliary transport, regeneration

## Cilia-secretory hybrid cells in airway development and disease states

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[2] Genentech.
[3] Department of Biochemistry and Biophysics, University of California, San Francisco, CA.
[4] Howard Hughes Medical Institute, University of California, San Francisco, CA, USA.

The conducting airway for air passage forms a protective mucosal barrier and presents the primary target of various airway disorders. Previous studies utilizing single-cell RNA sequencing (scRNAseq) have systematically characterized airway cell types in adults and lineage networks within the developed airway in normal and chronic inflammatory conditions. Whether the same programs for airway regeneration in adults are also operating during embryogenesis, however, remains an open question. To better understand how the airway developmental programs are established to support air breathing and the barrier functions in newborns, we constructed a single-cell atlas of the human and mouse developing airway. Our data reveal hitherto unrecognized heterogeneity of cell states with distinct differentiation programs and immune features associated with the airway epithelium. Ciliated cells, one of the major cell types found in the airway epithelium, form motile cilia and generate efficient ciliary flow essential for mucus clearance. From our transcriptomic analysis, we identified gene modules associated with embryonic ciliated cells and postnatal ciliated cells, as well as a ciliated precursor state conserved in mice and humans. Furthermore, we identified a cell cluster exhibiting two sets of gene modules, the *Foxj1* associated cilia module and the *Gp2* associated secretory module. This cell state has not been observed in healthy adult airway during homeostasis and regeneration, but is prevalent in human patients with asthma and airway allergies. The shared features of this newly identified cilia-secretory hybrid cells in the neonatal mouse airway and in asthma patients suggest that this hybrid cell state can occur in both physiological and pathological conditions. In parallel, we characterized a mouse mutant that shows altered epithelial cell landscape and multiple airway defects, including mucous cell hyperplasia and abnormal mucociliary clearance. Our data suggest that efficient mucociliary clearance depends on both ciliated cells and secretory cells. Together, our study illuminates unique programs for mammalian airway development and present a tractable mouse model for understanding the basis for airway regeneration and disease.

*Session B: Emerging Technologies*

# Speaker Biography



**Prof. CHOW Hei-Man Kim**（周熙文）is an assistant professor in the School of Life Sciences, The Chinese University of Hong Kong (CUHK). She received her graduate training at the University of Hong Kong (HKU), postdoctoral training at Cornell University and then a research assistant professorship training at The Hong Kong University of Science and Technology (HKUST). Prof. Chow was the recipient of multiple international fellowships, including the Alzheimer's Association Research Fellowship, the World Economic Forum Global Future Council Fellowship and the NSFC Excellent Young Scientist Fund. The Chow Lab focuses on studying mechanisms underlying pathological brain aging and related neurodegenerative disorders. Current projects aim at delineating the metabolic and molecular signatures of rare subpopulations of cell cycle re-engaged and senescent neurons in diseased brains in hope to identify new targets for drugs development.

## Five recent representative publications

1. **Chow HM**, Sun JKL, Hart RP et al. "Low-density lipoprotein receptor-related protein 6 cell surface availability regulates fuel metabolism in astrocytes." ***Advanced Science***, 2021; 8(16):e2004993. [Corresponding and 1st author]
2. Cheng A, Tse KH, **Chow HM** et al. "ATM loss disrupts the autophagy-lysosomal pathway." ***Autophagy***, 2021; 17(8):1998-2010. [3rd out of 9 authors]
3. Zhou J, **Chow HM**, Liu Y et al. "Cyclin-dependent kinase 5-dependent BAG3 degradation modulates synaptic protein turnover." ***Biological Psychiatry***, 2020; 87(8):756-769. [Co-corresponding and co-1st author]
4. **Chow HM**, Shi M, Cheng A et al. "Age-related hyperinsulinemia leads to insulin resistance in neurons and cell-cycle-induced senescence." ***Nature Neuroscience***, 2019; 2(11):1806-1819. [Co-corresponding and 1st author, Highlighted by F1000 Prime as 2 stars article]
5. **Chow HM**, Cheng A, Song X et al. "ATM is activated by ATP depletion and modulates mitochondrial function through NRF1." ***Journal of Cell Biology***, 2019; 218(3):909-928. [Co-corresponding and 1st author; Journal Spotlight with Commentary]

## Research interests / Technical expertise

- ✧ Metabolic aspects of neurological disorders
- ✧ Metabolomics and bioinformatics
- ✧ Regulation of cell cycle and senescence

## In the hunt for the "cycling" mature neurons - how modern bioinformatics complements with the traditional methods in characterizing these cells

**CHOW Hei-Man Kim**

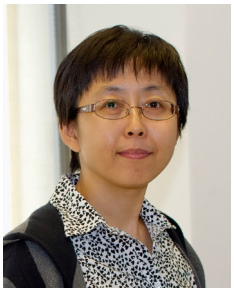
School of Life Sciences, Faculty of Science, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.

Adult, mature neurons are typically described as permanently postmitotic. However, for over two decades, mounting evidence indicated that neurons at risk of degeneration are also re-initiating a cell cycle-like process that involves the re-expression of cell cycle proteins and DNA replication. While an immediate death is being the most well-studied fate among these cells, emerging evidence also indicates that they may render "undead" for months or years, which may impose a threat to the health of the brain. Despite having this knowledge, characterization of these cells has never been an easy task. This is not only due to the fact that the brain is difficult to access, their small in population and being molecularly heterogeneous have rendered their characterization impossible with the traditional molecular methods. With recent advances in single cell-based omics technologies, unique markers and maps that describe their evolutionary details in a spatial-and-temporal framework is made possible. This talk describes our recent attempts in addressing such question, with Alzheimer's disease as a study model.

*Session B: Emerging Technologies*

# Speaker Biography





**Prof. FENG Bo（馮波）** is an Associate Professor in the School Biomedical Sciences (SBS), Faculty of Medicine, The Chinese University of Hong Kong. Prof. Feng is an active member in the Developmental and Regenerative Biology program of SBS, and she is also an associate member of the Hong Kong Hub of Paediatric Excellence (HK-HOPE) and the thematic program for Stem Cell and Cell-based Therapies in the Institute for Tissue Engineering and Regenerative Medicine (iTERM). Prof. Feng graduated from Nankai University with B.Sc. (1993) and M.Sc (1996), and received her Ph.D. (2006) from National University of Singapore. She joined Genome Institute of Singapore in 2007 as a postdoctoral fellow and her research on stem cells and reprogramming have been published in *Cell Stem Cell*, *Nature Cell Biology* etc. Prof. Feng has joined the SBS, CUHK to set up her own laboratory since 2010. Her research has focused on understanding the molecular mechanisms that control the reprogramming, self-renewal, differentiation of stem cells, as well as applying CRISPR-based genome-editing technologies to develop novel cell/gene-based therapy strategies for treating human diseases including cancer.

## Five recent representative publications


1. He X, Urip BA, Zhang Z, Ngan CC, **Feng B**. "Evolving AAV-delivered therapeutics towards ultimate cures." ***J Mol Med***, 2021; 99(5):593-617.
2. Wang J*, Zhang C*, **Feng B**. "The rapidly advancing Class 2 CRISPR-Cas technologies: a customizable toolbox for molecular manipulations." ***J Cell Mol Med***, 2020; 10.1111.
3. Zhang C*, He X*, Kwok YK, Wang F, Xue Y, Zhao H, Suen KW, Wang CC, Ren J, Chen GG, Lai BS, Li J, Xia Y, Chan AM, Chan WY, **Feng B**. "Homology-independent multiallelic disruption via CRISPR/Cas9-based knock-in yields distinct functional outcomes in human cells." ***BMC Biology***, 2018; 16:151.
4. 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.
5. Hu J, Lei Y, Wong WK, Liu S, Lee KC, He X, You W, Zhou R, Guo JT, Chen X, Peng X, Sun H, Huang H, Zhao H, **Feng B**. "Direct activation of human and mouse Oct4 genes using engineered TALE and Cas9 transcription factors." ***Nucleic Acids Res***, 2014; 42(7):4375-90.


## Research interests / Technical expertise

- ✧ CRISPR-based genome editing for treating liver/HSC-based inherited disorders
- ✧ Engineering immune cells for cancer immunotherapy
- ✧ Differentiation regulation of mouse and human ESC/iPSC
- ✧ Lentivirus and adeno-associated virus technologies
- ✧ Development of ACE2 decoys for SARS-CoV-2

## Liver-specific knock-in using low-dose AAV-CRISPR restored hemostasis in neonatal hemophilia B mice

**HE Xiangjun, ZHANG Zhenjie, XUE Junyi, WANG Yaofeng, ZHANG Chenzi, ZHANG Siqi, WEI Junkang, WANG Jue, URIP Brian Anugerah, NGAN Chun Christopher, ZHAO Hui, LI Chi-Kong, FENG Bo* (fengbo@cuhk.edu.hk)**

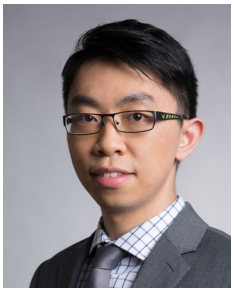
School of Biomedical Sciences, MOE Key Laboratory, Faculty of Medicine; Institute for Tissue Engineering and Regenerative Medicine (iTERM), The Chinese University of Hong Kong, Hong Kong SAR, China.

AAV-based delivery of CRISPR/Cas9 (AAV-CRISPR) has shown promising potentials in preclinical models to efficiently insert therapeutic gene sequences in somatic tissues. However, the doses of AAV input required for effective targeting were prohibitively high which posed serious risk of toxicity. In this study, we performed AAV-CRISPR mediated homology independent knock-in at the proximal *mAlb* 3'UTR and demonstrated that single dose of AAVs enabled long-term integration and expression of *hF9* transgene in both adult and neonatal hemophilia B mice (*mF9* -/-), as evidenced by high levels of circulating hFIX and restored hemostasis during the entire 48-week observation period. The germline genomes from edited mice were free of modification. No evident changes at transcriptome level were associated with AAV-CRISPR-mediated *hF9* knock-in, and no off-target editing events were detected at the top 10 *in silico*-predicted sites. Furthermore, we demonstrated that hemostasis correction can be efficiently achieved with a much lower AAV dose ($2 \times 10^9$ vg/neonate and $1.6 \times 10^{10}$ vg/adult mouse) through liver-specific gene knock-in using hyperactive $hF9^{R338L}$ variant. The serum antibodies against Cas9 and AAV in the neonatal mice receiving low-dose AAV-CRISPR were negligible, which lent support to the development of AAV-CRISPR mediated somatic knock-in for treating inherited diseases.

*Session B: Emerging Technologies*

# Speaker Biography





**Prof. CHAN Hon Fai Vivas**（陳漢輝）is an Assistant Professor at the Institute for Tissue Engineering and Regenerative Medicine and the School of Biomedical Sciences at The Chinese University of Hong Kong (CUHK). He received his Bachelor degree from the University of Hong Kong (2010), before pursuing his Ph.D. degree at Duke University with the support of the Sir Edward Youde Memorial Fellowships for Overseas Studies. During 2015-2017, he worked as a postdoctoral researcher at Columbia University and Massachusetts Institute of Technology before joining CUHK in 2018. Prof. Chan's research mainly focuses on advancing biofabrication approach and biomaterial design for stem cell tissue engineering and regenerative medicine, as well as understanding how microenvironmental cues influence stem cell proliferation and differentiation.

## Five recent representative publications

1. Deng S, Zhu Y, Zhao X, Chen J, Tuan RS, **Chan HF**. "Efficient fabrication of monodisperse hepatocyte spheroids and encapsulation in hybrid hydrogel with controllable extracellular matrix effect." ***Biofabrication***, 2021; 14(1):015002.
2. Zhu Y, Deng S, Zhao X, Xia G, Zhao R, **Chan HF**. "Deciphering and engineering tissue folding: A mechanical perspective." ***Acta Biomaterialia***, 2021; 134:32-42.
3. Zhu Y, Ma Z, Kong L, He Y, **Chan HF***, Li H*. "Modulation of macrophages by bioactive glass/sodium alginate hydrogel is crucial in skin regeneration enhancement." ***Biomaterials***, 2020; 120216.
4. 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):1-10.
5. **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***, 2018; 115(29):7503-7508.

## Research interests / Technical expertise

- ✧ Biofabrication technologies for tissue engineering
- ✧ Biomaterial for stem cell tissue engineering and regenerative medicine
- ✧ Tissue/organ-on-a-chip

## Mechanical folding induces development of engineered intestinal tissue

**ZHU Yanlun[1,2], XIA Guanggai[3], ZHANG Xuerao[1,2], MA Zhijie[4], DENG Shuai[1,2], WANG Yiwei[3], ZHAO Xiaoyu[1,2], LI Haiyan[5], GREGERSEN Hans[6], ZHAO Ruike[7], CHAN Hon Fai[1,2]**

[1] Key Laboratory for Regenerative Medicine of the Ministry of Education of China, School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Shatin, Hong Kong SAR, China.
[2] Institute for Tissue Engineering and Regenerative Medicine, The Chinese University of Hong Kong, Shatin, Hong Kong SAR, China.
[3] Department of General Surgery, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, 600 Yishan Rd, Shanghai, China.
[4] School of Biomedical Engineering, Shanghai Jiao Tong University, 1954 Huashan Road, Shanghai, China.
[5] Chemical and Environment Engineering Department, School of Engineering, RMIT University, Melbourne, Australia.
[6] California Medical Innovations Institute, San Diego, USA.
[7] Department of Mechanical Engineering, Stanford University, Stanford, USA.

It has been demonstrated that mechanical forces play a crucial role in intestinal development by contributing to gut looping, villification, and mucosal folding. In particular, mechanical strain generated from the differential growth rate of different tissue layers has been postulated to induce surface folding/buckling. While mucosal folding is a ubiquitous phenomenon observed in many hollow or tubular human tissues/organs, such as stomach and small intestine, recapitulating the process for tissue engineering has yet to be achieved. Here we developed a multilayer cell-laden hydrogel scaffold to recapitulate the folding process. We attached the cell-laden hydrogel films onto a prestretched tough-hydrogel substrate, which after relaxation induced controlled folding patterns. A combination of theory and numerical simulations predicted the folding conditions and the morphologies, thereby guiding the design of surface folding. To assess how the mechanical strain influences intestinal tissue development, we cultured intestinal organoids in the top layer of the folded scaffold and observed enhanced cell proliferation at the early stage and improved differentiation at the later stage. We also co-cultured stromal cells and epithelial cells in the multi-layer scaffold to mimic the complex structure of intestine. Following implantation in animal mice, the folded scaffold exhibited improved tissue development and emergence of folds similar to those found in human intestine. This simple strategy can facilitate the understanding and engineering of folded tissues of organs such as stomach and intestine. The work also demonstrates a new paradigm in tissue engineering via harnessing surface instabilities guided by quantitative mechanics models.

*Session C: Stem Cell Biology*

# Speaker Biography



**Prof. XIE Ting**（解亭）is the Kerry Holdings Professor of Science, Chair Professor and Head of the Division of Life Science, The Hong Kong University of Science and Technology. Before moving to Hong Kong, he was an investigator at the Stowers Institute for Medical Research and a Professor in the University of Kansas Medical Center. He obtained his PhD in Molecular Biology and Biochemistry from Rutgers University and his postdoctoral training in the Howard Hughes Medical Institute / Carnegie Institution for Science. His main research areas include stem cell biology and eye degenerative diseases. Prof. Xie is one of the leaders and pioneers in studying stem cell niches. He was the first to experimentally demonstrate the existence of the stem cell niche. In addition, his lab has also proposed and demonstrated the existence of a distinct niche for controlling stem cell progeny differentiation. Recently, his lab has also proposed that deteriorated intraocular environments lead to various kinds of degenerative eye diseases. He has published over 70 articles in high-profile journals, including *Science, Nature* and *Cell*. He received the Hudson Prize in 2003. He has been serving on the scientific advisory board of the Glaucoma Foundation and the Y-LOT Foundation and on the editorial board of *Cell Research, Development* and eight other scientific journals.

## Five recent representative publications


1. Pan L, Wang S, Lu T, Weng C, Song X, Park JK, Sun J, Yang ZH, Yu J, Tang H, McKearin DM, Chamovitz DA, Ni J, **Xie T**. "Protein competition switches the function of COP9 from self-renewal to differentiation." ***Nature***, 2014; 514(7521):233-6.
2. Wang S, Gao Y, Song X, Ma X, Zhu X, Mao Y, Yang Z, Ni J, Li H, Malanowski KE, Anoja P, Park J, Haug J, **Xie T**. "Wnt signaling-mediated redox regulation maintains the germ line stem cell differentiation niche." ***eLife***, 2015; 4:e08174.
3. Ma X, Zhu X, Han Y, Story B, Do T, Song X, Wang S, Zhang Y, Blanchette M, Gogol M, Malanowski K, Peak A, Anoja P, **Xie T**. "Aubergine controls germline stem cell self-renewal and progeny differentiation via distinct mechanisms." ***Developmental Cell***, 2017; 41(2):157-169.
4. Zuo F, Tu R, Duan B, Yang Z, Ping Z, Song X, Chen S, Price A, Li H, Scott A, Perera A, Li S, **Xie T**. "*Drosophila* YBX1 homolog YPS promotes ovarian germ line stem cell development by preferentially recognizing 5-methylcytosine RNAs." ***Proc Natl Acad Sci U S A***, 2020; 117(7):3603-3609.
5. Tu R, Duan B, Song X, **Xie T**. "Glypican Dlp-mediated Hedgehog and Wnt signaling interdependence is crucial in the niche for germline stem cell progeny differentiation." ***Science Advances***, 2020; aaz048.


## Research interests / Technical expertise

- ✧ Stem cell biology
- ✧ Degenerative eye diseases
- ✧ Stem cell therapy

## Niche and intrinsic control of adult stem cell regulation

**Ting XIE**

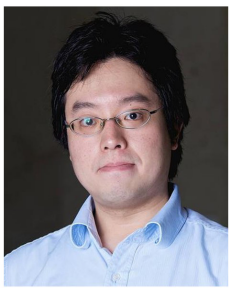
Division of Life Science, The Hong Kong University of Science and Technology, Hong Kong SAR, China.

Stem cells in adult tissues undergo self-renewal and generate differentiated cells that replenish the lost cells caused by natural turnover, injury or disease. The molecular mechanisms underlying stem cell regulation are also critical for regenerative medicine and fighting against cancer and aging. Prof. Xie has been using germline stem cells in the *Drosophila* ovary as a model system to elucidate niche structures, functions and the mechanisms underlying self-renewal, differentiation and aging. Prof. Xie was the first to experimentally demonstrate the existence of the stem cell niche. Recently, his lab has also proposed a separate differentiation niche for stem cell lineage specification. In addition, his lab has elucidated how the two niches work together to control stem cell development and thus tissue regeneration. Furthermore, his lab has demonstrated the roles of various signaling pathways (BMP, Hh, Wnt, Netrin and Notch), cadherin-mediated cell adhesion, epigenetic factors, non-coding RNAs, RNA modifications and various protein complexes (COP9, CCR4-NOT and eIF4) in the regulation of self-renewal, differentiation and aging. The most recent work suggests that the differentiation niche consists of multiple compartments orchestrating stepwise GSC progeny differentiation steps. In addition to stem cell biology, his lab has begun using mice to study molecular mechanisms and stem cell therapy for degenerating eye diseases. His lab has recently proposed that the ciliary body creates the intraocular “niche” for maintaining the survival and functions of various eye tissues, providing a new paradigm for studying eye degenerative diseases. Prof. Xie will share the recent research progress on stem cell regulation from his lab.

*Session C: Stem Cell Biology*

# Speaker Biography





**Prof. Rio SUGIMURA** received his M.D. from Osaka University, Japan, in 2008, and his Ph.D. in Stem Cells and Regeneration from the Stowers Institute for Medical Research, USA, in 2012. He has been trained at world-leading institutes, including Harvard Medical School and Kyoto University. He is an Assistant Professor in the School of Biomedical Sciences, The University of Hong Kong. Dr. Sugimura is a full faculty member of the Stem Cells & Regeneration Section in F1000Prime, a member of American Association of Immunologists (AAI), American Society of Hematology (ASH), Biomedical Engineering Society (BMES), Association for Cancer Immunotherapy (CIMT), Federation of American Societies for Experimental Biology (FASEB), International Society of Experimental Hematology (ISEH), International Union of Immunological Societies (IUIS), the North American Vascular Biology Organization (NAVBO), Society for Immunotherapy of Cancer (SITC), and a co-founder of the medical branch of Kagakusha-Net. Prof. Sugimura is a recipient of the ASH Scholar Award, March of Dimes, Early Career Grant from Japanese Ministry, Genius Award from Young Hematologist Meeting in Japan, Takeda Science Foundation, iPS Academia Japan Foundation, SMRF Fellowship, Kanehara Memorial Foundation, and Uehara Memorial Foundation. Prof. Sugimura mastered grantsmanship at the Cold Spring Harbor Laboratory Scientific Writing Retreat 2019.

## Five recent representative publications


1. Chao Y, **Sugimura R**. "Deciphering innate immune cell-tumor microenvironment crosstalk at a single-cell level." ***Frontiers in Cell and Developmental Biology***, 2022; 10:803947. doi: 10.3389/fcell.2022.803947.
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## Research interests / Technical expertise

- ✧ Cancer Immunology
- ✧ Organoids
- ✧ CAR-T Cells
- ✧ Single-cell Analysis
- ✧ Spatial Transcriptomics

## Spatiotemporal analysis of human early hematopoiesis and its engineering for cancer immunotherapy

**SUGIMURA Rio**

School of Biomedical Sciences, Li Ka Shing Faculty of Medicine, The University of Hong Kong; Centre for Translational Stem Cell Biology, Hong Kong SAR, China.

Hematopoietic tissues develop through interactions with various cell types and signals in the embryos. We have identified crucial role of WNT signal in hematopoietic stem cell maintenance (Sugimura, 2012. *Cell*) and discovered transcriptional programs to specify hematopoietic stem cells from human pluripotent stem cells (Sugimura, 2017. *Nature*). However, the lack of experimental systems to intervene human hematopoietic tissue development hampers its application for disease modeling and cell therapy. Here we generated multi-lineage organoids (MLOs) from human expanded potential stem cells which possess both embryonic and extraembryonic capacity. Our single-cell RNA-sequencing analysis revealed MLOs encompassed yolk sac, placenta, cardiac, and hematopoietic tissues. Time-course sampling identified that MLOs followed the course of human embryonic development. To define the interactions of hematopoietic tissues with other cell types, our spatial transcriptomics analysis identified that yolk sac tissues physically interacting with the emergence of erythro-megakaryocyte cells, consistent with early hematopoiesis in the yolk sac in the embryos. These spatiotemporal analysis of MLOs revealed the early hematopoiesis in human embryos .We further applied MLOs as a platform to engineer immune cells for cancer immunotherapy. In this talk, we will share the preliminary data of chimeric antigen receptor-macrophages (CAR-Ms) generated from MLOs.

*Session C: Stem Cell Biology*

# Speaker Biography



**Prof. LIU Pengtao**（劉澎濤）is a biologist and a geneticist with a long-standing interest in stem cells, development and immunity. He is most recognized for his work on developing genetic tools for engineering mouse stem cells, discovery of functions of Bcl11a and Bcl11b genes in lymphocyte development, and establishment of expanded potential stem cell. Prof. Liu was born in China. He graduated from Henan Normal University with a BS degree in Biology and from Institute of Genetics, Chinese Academy of Sciences, with MPhil. Prof. Liu received a Ph.D. from Baylor College of Medicine. He did postdoctoral training at National Cancer Institute USA. Prof. Liu joined the faculty of the Wellcome Trust Sanger Institute in Cambridge, U.K. He was recruited to the Faculty of Medicine of the University of Hong Kong as a professor. Prof. Liu heads Centre for Translational Stem Cell Biology aiming to develop new stem cell technologies, produce clinically relevant cell products and screen drug candidates.

## Five recent representative publications

1. Zhao L, Gao X, ….(19 authors)…, Liu P*, **Li X**.* "Establishment of bovine expanded potential stem cells." ***PNAS***, 2021; 118:e2018505118. [Co-senior authors]
2. Gao X, Nowak-Imialek M, ...(23 authors)..., Teichmann S, Niemann H*, **Liu P**.* "Establishment of porcine and human expanded potential stem cells." ***Nature Cell Biology***, 2019; 21(6):687-699. [Co-senior authors]
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4. Yang J, Ryan DJ, …(27 authors)…,Lu L, **Liu P**.* "Establishment in culture of mouse expanded potential stem cells." ***Nature***, 2017; 550:393-397.
5. Yu Y, Tsang JC, …(11 authors)…, Dougan G, **Liu P**.* "Single-cell RNA-seq identifies a PD-1hi ILC progenitor and defines its development pathway." ***Nature***, 2016; 539:102-106.

## Research interests

Prof. Liu's laboratory has developed a widely used approach to rapidly generate conditional knockout alleles in mouse embryonic stem cells for mice, and an efficient six-factor approach to rapidly reprogramme somatic cells to iPSCs. The laboratory investigates transcription factors Bcl11a and Bcl11b in development and in disease and discovered a new type of cancer cell killers. Prof. Liu's laboratory used single cell genomics and analysed immune cells and stem cells, including the stem cells with totipotency that the laboratory established. Standard stem cell technologies have failed to derive embryonic stem cell lines from most mammals. Prof. Liu's EPSC technology on the other hand has successfully derived stem cell lines from preimplantation embryos of all the mammalian species attempted so far: mouse, human, pig and bovine. These cells are being explored for applications in reproductive biology, cell-based therapy, transgenics, animal cloning, biotechnology and agriculture.

## Expanded potential stem cells: a new tool for basic and translational research

**Pentao LIU**

School of Biomedical Sciences, Li Ka Shing Faculty of Medicine, The University of Hong Kong; Centre for Translational Stem Cell Biology, Hong Kong SAR, China.

Embryonic stem cells (ESCs) derived from the epiblast contribute to the somatic lineages and the germline upon reintroduction to the blastocyst but are excluded from the extraembryonic tissues that are derived from the trophectoderm (TE) and the primitive endoderm (PrE). By inhibiting signal pathways implicated in the earliest embryo development, we recently established cultures of mouse expanded potential stem cells (EPSCs) from individual 4-cell and 8-cell blastomeres, by direct conversion of mouse embryonic stem cells (ESCs) or induced pluripotent stem cells (iPSCs). A single EPSC can contribute to both the embryo proper and the TE lineages in chimera assay. *Bona fide* trophoblast stem cell (TSC) lines, extra-embryonic endoderm stem (XEN) cells, and ESCs could be directly derived from EPSCs *in vitro*. Molecular analyses of the epigenome and single-cell transcriptome revealed that EPSCs had enriched features of cleavage stage embryos. The knowledge of mouse EPSCs has enabled the establishment of EPSCs of human, pig, bovine and additional mammalian species. EPSCs of these species share similar molecular features and have the potential to differentiate to extra-embryonic as well as embryonic cell lineages *in vitro* and in chimeras (animal EPSCs). EPSCs provide new tools for studying embryonic development and open up a wealth of avenues for translational research in biotechnology, agriculture, and regenerative medicine. I will share our published and unpublished data of EPSC projects.

**Keywords: EPSCs, totipotency, pluripotency, development, pre-implantation embryo, epigenome**

*Session C: Stem Cell Biology*

# Speaker Biography



**Prof. Anna Maria BLOCKI** has joined The Chinese University of Hong Kong (CUHK) since February 2018 as an Assistant Professor at the Institute for Tissue Engineering and Regenerative Medicine (iTERM) and the School of Biomedical Sciences (SBS). Her current work focuses on developing innovative approaches to modulate diseased microenvironments and guide healing and regenerative processes. Prof. Blocki has received her PhD from the National University of Singapore (NUS) in 2013. Following that, she carried out her first postdoctoral appointment at the Agency for Science Technology and Research (A*STAR), Singapore. In 2015, Prof. Blocki was able to secure a competitive postdoctoral fellowship from the Charité Universitätsklinikum Berlin, where she worked before joining CUHK.

## Five recent representative publications

1. Später T, Assunção M, Lit KK, Gong G, Wang X, Chen Y-Y, Rao Y, Li Y, Yiu CHK, Laschke MW, Menger MD, Wang D, Tuan RS, Khoo K-H, Raghunath M, Guo J, **Blocki A**. "Engineering microparticles based on solidified stem cell secretome with an augmented pro-angiogenic factor portfolio for therapeutic angiogenesis." ***Bioactive Materials***, 2022; https://doi.org/10.1016/j.bioactmat.2022.03.015. (In press)
2. Wan H-Y, SHIN RLY, Chen JCH, Assunção M, Wang D, Nilsson SK, Tuan RS, **Blocki A**. "Dextran sulfate-amplified extracellular matrix deposition promotes osteogenic differentiation of mesenchymal stem cells." ***Acta Biomaterialia***, 2021; 140:163-177. https://doi.org/10.1016/j.actbio.2021.11.049.
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## Research interests / Technical expertise

- ✧ Tissue engineering
- ✧ Angiogenesis
- ✧ Biomaterials
- ✧ Hydrogels
- ✧ Extracellular matrix
- ✧ Cell-based therapy
- ✧ Micro-physiological systems
- ✧ Microvasculature

## Engineering and modulating microenvironments to promote tissue regeneration and healing in ischemic diseases

**BLOCKI Anna Maria**

1. Institute for Tissue Engineering and Regenerative Medicine,
2. School of Biomedical Sciences, Faculty of Medicine,
3. Department of Orthopaedics & Traumatology, Faculty of Medicine,

The Chinese University of Hong Kong, Shatin, Hong Kong SAR, China.

Chronic ischemic conditions, such as coronary artery, cerebrovascular, and peripheral vascular diseases are leading causes of death and disability worldwide. As revascularization is dysregulated and insufficient, the resultant malperfusion leads to cell death and growth of necrotic tissue areas, further impairing healing and regeneration. Current established therapies focus on re-establishing re-perfusion by pharmaceutical or surgical approaches, they fail however, to modulate the dysregulated tissue environment and to promote regeneration and repair of damaged micro- and macro-vasculature, as well as affected tissue. Experimental strategies face unmet challenges, as therapeutic cells, such as mesenchymal stem cells (MSCs) do not survive long enough *in situ*, while the administration of soluble bioactive factors is hampered by fast clearance and insufficient ability to emulate complex spatiotemporal signaling. It is thus noteworthy, that in physiological conditions bioactive factors are stabilized by being properly integrated into the extracellular matrix (ECM). Indeed, the accurate organization of the ECM is a prerequisite to harness their full complex bioactivity.

We have thus established a platform technology to promote ECM assembly *in vitro* and to generate cell-derived ECM-based biomaterials with tailored bioactivities. In particular, we have recently developed MIcroParticles of Solidified Secretome (MIPSOS) that are concentrating the pro-angiogenic activities of MSCs. The insoluble format of MIPSOS protects protein components from degradation, while facilitating their sustained release. Intravital microscopy of full-thickness skin wounds treated with MIPSOS demonstrates accelerated revascularization and healing, far superior to the therapeutic potential of unmodified MSC-derived ECM (cECM). Hence, the microparticle-based solidified stem cell secretome provides a promising platform to address major limitations of current therapeutic angiogenesis approaches.

*Session C: Stem Cell Biology*

# Speaker Biography



**Prof. CHEUNG Hiu Tung Tom**（張曉東）is currently the S H Ho Associate Professor of Life Science in the Division of Life Science at The Hong Kong University of Science and Technology (HKUST). He received his PhD in Biochemistry from the University of Colorado at Boulder and did his postdoctoral training at Stanford University. He specializes in the field of stem cells and the biology of aging using murine muscle stem cells to identify the key molecular pathways that underlie stem cell quiescence and tissue regeneration. Furthermore, Prof. Cheung is Director of multiple institutes and centers, including the Biotechnology Research Institute, the HKUST-Nan Fung Life Sciences Joint Laboratory, and the HKUST-BGI Joint Research Center. He is also the Associate Director of the Biosciences Central Research Facility and the HKUST-Shanghai Sixth People's Hospital Joint Research Center for Brain Science, as well as being a key member of the Hong Kong Center for Neurodegenerative Diseases (HKCeND) at the Hong Kong Science Park.

## Five recent representative publications

1. Yue L, Wan R, Luan S, Zeng W, **Cheung TH**. "Dek modulates global intron retention during muscle stem cells quiescence exit." ***Developmental Cell***, 2020; 53(6):661-676.e6.
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3. Dong A, Preusch CB, So WK, Lin K, Luan S, Yi R, Wong JW, Wu Z, **Cheung TH**. "A long noncoding RNA, *LncMyoD*, modulates chromatin accessibility to regulate muscle stem cell myogenic lineage progression." ***Proceedings of the National Academy of Sciences***, 2020; 117(51):32464-32475.
4. Zeng L, Li X, Preusch CB, He GJ, Xu N, **Cheung TH**, Qu J, Mak HY*. "Nuclear receptors NHR-49 and NHR-79 promote peroxisome proliferation to compensate for aldehyde dehydrogenase deficiency in *C. elegans*." ***PLoS Genetics***, 2021; 17(7), e1009635.
5. Zeng W, Yue L, Lam KSW, Zhang W, So WK, Tse EHY, **Cheung TH**. "CPEB1 directs muscle stem cell activation by reprogramming the translational landscape." ***Nature Communications***, 2022; 13(1):947.

## Research interests / Technical expertise

- ✧ Exploration of the signaling pathways involved in regulating stem cell activity
- ✧ Understanding how aging affects quiescence and senescence in muscle stem cells

## Differential translational control during muscle stem cell aging

**Tom CHEUNG**

Division of Life Science, The Hong Kong University of Science and Technology, Clear Water Bay, Hong Kong SAR, China.

Age-related impairments in stem cell (SC) function correlate with a decline in somatic tissue regeneration following injury or disease development. Skeletal muscle contains adult muscle stem cells (MuSCs) which are prone to aging. Examination of the chromatin accessibilities of aged MuSCs revealed they display a chronically activated chromatin signature, suggesting that the heterochromatin environment is disturbed. Importantly, we observed that these regions of open chromatin were located near genes associated with cellular senescence and the cell cycle, suggesting some precocious activation in aged MuSCs.

Previously, our laboratory studied the proteomes of aged and adult MuSCs. In MuSCs, mitochondrial activity is essential to maintain SC homeostasis and function, and thus it is crucial to understand how alterations in energy metabolism affects SC function during the aging process. Using our low-input mass spectrometry technique, we detected changes in the proteomics landscape of MuSCs during aging. Specifically, senescence-associated proteins were significantly upregulated in aged MuSCs compared to adult MuSCs. However, transcription and translation-related proteins were downregulated, indicating alterations in the maintenance of cellular activity in MuSCs during aging.

*Session C: Stem Cell Biology*

# Speaker Biography



**Prof. ZHAO Hui**（趙暉）is now working at the School of Biomedical Sciences, The Chinese University of Hong Kong (CUHK). He also serves as the Associate Director of KIZ/CUHK Joint Laboratory of Bioresources and Molecular Research in Common Diseases. He is the Visiting Professor at Jinan University and Ningxia Medical University. He joined CUHK in 2008. His research interests cover early embryonic development, genome editing, and heart development and regeneration. His laboratory studies the mechanism of neural crest differentiation, germ layer formation, and cell migration, and how these multiple events affect embryonic patterning. He has published over 90 papers in high-impact journals, including *Nat Comm, PNAS, Development, EMBO Journal, Nucleic Acids Res,* and *FASEB J*. His research is supported by funding from the Ministry of Science and Technology, the National Natural Science Foundation of China, and the Research Grants Council (RGC) of Hong Kong.

## Five recent representative publications


1. Teekakirikul P, Zhu W, Xu X, Young CB, Tan T, Smith AM, Wang CD, Peterson KA, Gabriel GC, Ho S, Sheng Y, de Bellaing AM, Sonnenberg DA, Lin JH, Fotiou E, Tenin G, Wang MX, Wu YL, Feinstein T, Devine W, Gou H, Bais AS, Glennon BJ, Zahid M, Wong TC, Ahmad F, Rynkiewicz MJ, Lehman WJ, Keavney B, Alastalo TP, Freckmann ML, Orwig K, Murray S, Ware SM, **Zhao H**, Feingold B, Lo CW. "Genetic resiliency associated with dominant lethal TPM1 mutation causing atrial septal defect with high heritability." ***Cell Rep Med***, 2022; 3:100501.
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## Research interests / Technical expertise

- ✧ Neural crest and its derived neuroblastoma
- ✧ Molecular mechanisms of germ layer formation during early embryonic development
- ✧ Comparable studies of heart development and regeneration

## Tuning BMP signaling in nucleus by Zinc finger SWIM-type containing 4

**WANG Chengdong, LIU Ziran, ZENG Yelin, LONG Qi, HASSAN Imtiaz UI, and ZHAO Hui**

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

The BMP signaling is complex and involved in the specification of the primary body axes, further differentiation of ectoderm, mesoderm and endoderm, and the maintenance of adult tissue homeostasis. During the embryonic development, the dorsoventral gradient of BMP signaling plays an essential role in embryonic patterning, with high BMP signal activating ventral-lateral mesoderm markers directly. The Zinc finger SWIM domain-containing protein 4 (*zswim4*) is expressed in the dorsal blastopore lip at the onset of *Xenopus* gastrula and then enriched in the anterior neural plate and neural crest at neurula stages. Zswim4 contains a nuclear location signal and indeed is specifically localized in the nucleus. Overexpression of *zswim4* in embryos causes inhibition of the anterior axis and shortened body. Knockdown or knockout of *zswim4* disturbed embryonic body axis formation and head development. The expression of ventral-lateral mesoderm marker genes was reduced after *zswim4* overexpression and increased in embryos with *zswim4* knockdown. Neural marker genes were repressed in zswim4 morphant. Mechanistically Zswim4 attenuates BMP signal through reducing protein stability of Smad1 in both *Xenopus* embryos and HEK293T cells. Co-immunoprecipitation and immunostaining showed that Zswim4 physically interacts with Smad1 in the nucleus. Zswim4 forms a complex with the Cul2-RING ubiquitin ligase, promoting ubiquitination and degradation of Smad1 in the nucleus. Collectively, the Zswim4 is a novel inhibitor of BMP signaling and plays an essential role in early embryonic patterning.

# Acknowledgements



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