School of Life Sciences
The Chinese University of Hong Kong

香港中文大學理學院
FACULTY OF SCIENCE
THE CHINESE UNIVERSITY OF HONG KONG

School of Life Sciences Research Day 2020

Plant Science & Biodiversity

Translational Biomedicine & Structural Biology

26 September 2020

0900 - 1705

Message from Director of School of Life Sciences

The School of Life Sciences was established in 2010 under the Faculty of Science by merging the Departments of Biochemistry and Biology, which are among the oldest departments in CUHK. Our School offers six major programmes: Biochemistry, Biology, Cell & Molecular Biology, Environmental Science, Food & Nutritional Science, and Molecular Biotechnology, which have trained over 8400 alumni over the years. Our curriculum is designed to meet the diverse interests of life science students. The students will receive training in fundamental knowledge in life sciences in their junior years, before they specialize into one of the six programmes in their senior years.

In addition to quality teaching, we also strive for excellence in research. For example, three research projects "Plant and Agricultural Biotechnology", "Centre for Organelle Biogenesis and Function", and "Centre for Genomic Studies on Plant-Environment Interaction for Sustainable Agriculture and Food Security" led by our school have been selected by the University Grants Committee (UGC) as one of the Areas-of-Excellence (AoE) in Hong Kong. Many members of our School are also members of the State Key Laboratory (SKL) of Agrobiotechnology.

We believe that the best way to train future generation of scientists is to inspire the students and give them the opportunities to take part in cutting-edge research themselves. This is the reason that we have this first SLS Research Day 2020. We hope you will be able to learn something from our invited speakers, and/or make new collaborations. Enjoy.

K.B. Wong
Director
SLS, CUHK

Message from Convenor of Research Committee

On behalf of the Research Committee, I would like to thank Professor Jerome Hui for taking up the task of organising this symposium and to thank speakers for sharing their work and experience. This is the first formal research symposium of the School and we anticipate this will be the beginning of a good tradition for the years to come. We also anticipate this activity will allow staff and students within and outside the School be more familiar with our research activities. Our School has 38 professorial staff with six research focuses: (1) Structural Biology and Protein Science, (2) Plant Molecular Cell and Agricultural Biology, (3) Omics and Bioinformatics, (4) Neurosciences, Cancer and Stem Cell Biology, (5) Food and Nutrition, (6) Environmental and Marine Sciences. It is impossible to cover all the good work in a one-day symposium. Therefore, this time we only focus on the topics that are related to the strategic research areas at the University level.

Our School always emphasises on a collaborative research environment and promotes multi-disciplinary research, for greater impacts and substantial external funding. Collaboration is also facilitated by the starry research activities in the State Key Laboratory on Agrobiotechnology and through a number of Area of Excellence grants to some members. To further enhance multi-disciplinary collaboration, School has provided seed fund for initiating new collaborative projects. With the seed fund, colleagues have been able to secure a number of Collaborative Research Fund from the Research Grants Council. Beginning from 2019/20, Research Committee has also initiated support for cultivating R & D activities with social impacts.

This one-day research symposium is yet another initiative for providing opportunity for new collaboration. We hope members and friends of the School will enjoy the talks and have a fruitful day.

P.C. Shaw
Convenor
Research Committee

PROGRAMME	
09:00 – 09:05	**Welcome Speech** *Professor SONG Chunshan* *Dean of Science*
09:05 – 09:15	**Group Photo taking**
09:15 – 09:30	**Introduction to School of Life Sciences** Professor Kam Bo WONG Professor, Director of School of Life Sciences
	Plant Science and Biodiversity
09:30 – 09:55	**Stout camphor tree genome: massive diversification and evolution of Terpene synthase genes** Professor Shu-Miaw CHAW Director of Biodiversity Research Center, Academia Sinica, Taiwan
09:55 – 10:20	**Protein chemistry: from basic science to translational research (infection, osteoarthritis and autism)** Professor Jiang XIA Associate Professor, Department of Chemistry
10:20 – 10:45	**Genomic Research of Soybean and Its Implications** Professor Hon-Ming LAM Professor, School of Life Sciences
10:45 – 10:55	**Break**
10:55 – 11:20	**Changes in the Plasmodesma Structure and Permeability at the Bundle Sheath and Mesophyll Interface During the Maize C4 Leaf Development.** Professor Byung Ho KANG Associate Professor, School of Life Sciences
11:20 – 11:45	**Genomic insights into the adaptations and diversification of Brachyuran crabs** Professor Ling Ming TSANG Assistant Professor, School of Life Sciences
11:45 – 12:10	**Autophagosome biogenesis in plants and green algae** Professor Xiaohong ZHUANG Assistant Professor, School of Life Sciences
12:10 – 12:35	**Genomes of jellyfish, millipede, and tree – new models for understanding biodiversity and environmental issues?** Professor Jerome HUI Associate Professor, School of Life Sciences
12:35 – 14:00	**Lunch Break**

	Translational Biomedicine and Structural Biology
14:00 – 14:25	**Cell-nano interactions of non-cationic bionanomaterials** Professor Jonathan CHOI Associate Professor, Department of Biomedical Engineering
14:25 – 14:50	**How structural biology provides insight into how life works and opportunities for drug development** Professor Kam Bo WONG Professor, Director of School of Life Sciences
14:50 – 15:15	**Low-density lipoprotein receptor-related protein-6 (LRP6) cell surface availability regulates fuel metabolism in astrocytes.** Professor Kim CHOW Assistant Professor, School of Life Sciences
15:15 – 15:25	**Break**
15:25 – 15:50	**Critical role of Sox9 in blood-CSF barrier development and function** Professor Kin Ming KWAN Associate Professor, School of Life Sciences
15:50 – 16:15	**Structural basis of substrate recognition and thermal protection by a small heat shock protein** Professor Wilson LAU Research Assistant Professor, School of Life Sciences
16:15 – 16:40	**CAG RNAs Induce DNA Damage and Apoptosis in Polyglutamine Degeneration** Professor Edwin CHAN Professor, School of Life Sciences
16:40 – 17:05	**Concluding Remarks** Professor Pang-Chui SHAW Professor, School of Life Sciences

Stout camphor tree genome: massive diversification and evolution of Terpene synthase genes

Dr. Shu-Miaw CHAW
Director of Biodiversity Research Center, Academia Sinica, Taiwan

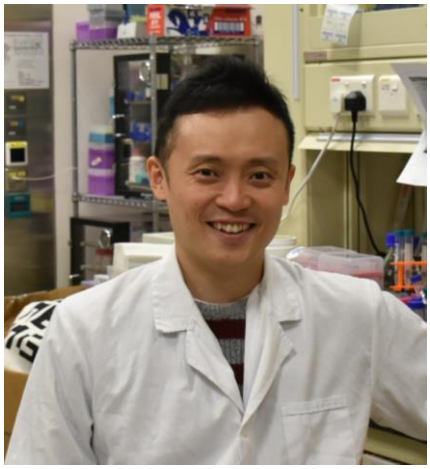
Stout camphor tree (*Cinnamomum kanehirae,* Lauraceae; SCT) is endemic to Taiwan. Conservation of SCT has become especially urgent as poachers have been illegally taking it for rot-resistant timber and cultivation of *Antrodia* fungus that has cancer-fighting agents. SCT along with magnolia, tulip tree, custard apple and nutmeg are “magnoliids”, comprising about 6% (over 9,000 species) of flowering plants. The relationship of magnoliids to moncots and eudicots has been uncertain despite years of investigation by botanists. We report the first reference-quality genome assembly and annotation of SCT. Our analysis of 13 representative seed plant genomes indicates that magnoliids and eudicots share more recent common ancestry than monocots. Two whole-genome duplications were inferred within the magnoliids: one before divergence of Laurales and Magnoliales and the other within Lauraceae. Expansion of the terpenoid synthase gene subfamilies within Laurales spawned the diversity of *Cinnamomum* monoterpenes and sesquiterpenes—the two largest aromatic oils produced by SCT. Our genomic work has defined the important roles of *CkTPSs* in SCT—especially combined large gene size with tandem duplicates and predicted diverse functions, which produce a plentiful and various mix of aromas at all stages of plant development. *CkTPSs* should also have significantly contributed to the success of SCT in its distribution at wide elevations, stout and tall woods, and long life (currently estimated to be over 1,000 years old) via competing for pollinators and protection of the plants against abiotic stress and various biotic interactions above and below ground (e.g., pathogens, insects and soil microbes).

Representative relevant publication:

Shu-Miaw Chaw* & Isheng J. Tsai -- Biodiversity Research Center, Academia Sinica. *Nature Plants* **5** (2019): 63-73.

Cell-nano interactions of non-cationic bionanomaterials

Professor Jonathan Chung Hang CHOI
Associate Professor, Department of Biomedical Engineering



Advances in nanotechnology have empowered the design of bionanomaterials by assembling different types of natural biomolecules (e.g., nucleic acids, proteins, and lipids) as building blocks into nanoparticles (NPs). To achieve optimal performance in nanomedicine applications, it is imperative that the NPs be delivered effectively to target cells. A rational approach to facilitating the delivery of NPs is to develop a detailed and comprehensive understanding in their fundamental interactions with the biological system.

Cationic liposomes and lipid NPs are conventional carriers of therapeutic cargoes into cells due to their ability to penetrate the cell membrane, a barrier comprised by an anionic phospholipid bilayer. Yet, cationic NPs tend to cause cytotoxicity and immune responses that may hamper their clinical translation. Contrary to cationic NPs, non-cationic NPs (near-neutral or anionic) generally exhibit higher biocompatibility but enter cells in much less pronounced amounts. Intriguingly, some types of non-cationic NPs exhibit high biocompatibility and cellular uptake properties, all attractive features for intracellular delivery.

I present the nano–cell interactions of three types of non-cationic bionanomaterials that effectively enter cells, including akyl-terminated NPs, DNA-coated NPs and polydopamine (PDA)-coated NPs. We dissect the route of intracellular trafficking, pathway proteins that dictate cellular uptake, and trafficking of NPs. Our data offer design rules of NPs for achieving effective intracellular delivery and even guide us to explore nanomedicine applications that we did not conceive before, such as using DNA-coated NPs for targeting atherosclerotic plaques and PDA-coated plasmonic nanoworms for photothermal killing of cancer cells.

Representative relevant publication:

1) Ho LWC, Liu Y, Han R, Bai Q, Choi CHJ*. Nano-cell interactions of non-cationic bionanomaterials. *Acc. Chem. Res.*, 52, 6, 1519-1530 (2019).

2) Choi CKK, Zhang L, Choi CHJ*. Efficient siRNA delivery with non-cationic carriers. *Nat. Biomed. Eng.*, 2, 275-276 (2018).

3) Yin B, Li KHK, Ho LWC, Chan CKW, Choi CHJ*. Toward understanding in vivo sequestration of nanoparticles at the molecular level. *ACS Nano*, 12, 3, 2088-2093 (2018).

Protein chemistry: from basic science to translational research (infection, osteoarthritis and autism)

Professor Jiang XIA
Associate Professor, Department of Chemistry

Protein chemistry is an ancient but ever-renewing topic. Our lab focuses on protein reaction, protein assembly and protein-based therapies.

A critical challenge in protein chemistry is how one can precisely control the reaction site during a protein reaction. By a principle called “proximity-induced reactivity”, site-selective cysteine, tyrosine and lysine reactions have been developed. Initially site-selective cysteine reactions were developed in the test tube [Bioconjugate Chem 2014a, 2014b, 2017], the reaction was then successfully achieved inside cells [Mol. Pharmaceutics 2017, ACS Chem. Biol. 2016], and more recently in animals to control signal transduction as a means to prevent bacterial infection [PNAS 2020].

Protein chemistry also enables new therapies for disease treatment. By engineering the surface protein of exosomes, chondrocyte specific delivery vehicles were developed for targeted delivery of osteoarthritis drugs [ACS Appl Mater Interfaces 2020]. The MSC-derived exosomes were also effective against autism [ACS Appl Bio Mater 2020]. These projects showcase a universally applicable drug delivery platform, and cell-free, organelle-based therapies for various diseases.

Representative relevant publications:

1) Qiu, J.; Nie, Y.; Zhao, Y.; Zhang, Y.; Li, L.; Wang, R.; Wang, M.; Chen, S.; Wang, J.*; Li, Y.Q.*; Xia, J.* “Safeguarding Intestine Cells Against Enteropathogenic Escherichia Coli by Intracellular Protein Reaction, a Preventive Antibacterial Mechanism” *Proc. Natl. Acad. Sci. U. S. A*. 2020, *117*, 5260-5268.

2) Liang, Y.; Xu, X.; Li, X.; Xiong, J.; Li, B.; Duan, L.*; Wang, D.*; Xia, J.* “Chondrocyte-Targeted MicroRNA Delivery by Engineered Exosomes toward a Cell-Free Osteoarthritis Therapy” *ACS Appl. Mater. Interfaces* 2020, 12, 33, 36938–36947.

3) Liang, Y.; Duan, L.; Xu, X.; Li, X.; Liu, M.; Chen, H.; Lu, J.*; Xia, J.* “Mesenchymal Stem Cell − Derived Exosomes for Treatment of Autism Spectrum Disorder” *ACS Appl. Bio. Mater.* 2020 DOI: 10.1021/acsabm.0c00831.

Genomes of jellyfish, millipede, and tree – new models for understanding biodiversity and environmental issues?

Professor Jerome Ho Lam HUI
Associate Professor, School of Life Sciences

Biodiversity is a measure of variation of life on earth. The feasibility to carry out genome sequencing allows us to reveal the hidden variations in both the marine and terrestrial habitats at unprecedented levels. One research area in our laboratory is to utilise next-generation sequencing data to better understand the hidden variations of life. In this talk, I will present the analyses of new genomes carried out by our laboratory, including jellyfishes, millipedes, and a tree, to demonstrate their potential usefulness in understanding biodiversity as well as solving environmental issues.

Representative relavant publications:

1) Qu Z, Nong WY, So WL, Barton-Owen T, Li YQ, Leung TC, Li C, Baril T, Wong AY, Swale T, Chan TF, Hayward A, Ngai SM, Hui JHL*. (2020). Millipede genomes reveal unique adaptation of genes and microRNAs during myriapod evolution. *PLOS Biology*.

2) Nong WY, Law ST, Wong AY, Baril T, Swale T, Chu LM, Hayward A, Lau DT, Hui JHL*. (2020). Chromosomal-level reference genome of the incense tree Aquilaria sinensis. *Molecular Ecology Resources*.

3) Nong WY, Cao JQ, Li YQ, Qu Z, Sun J, Swale T, Yip HY, Qian PY, Qiu JW, Kwan HS, Bendena WG, Tobe SS, Chan TF, Yip KY, Chu KH, Ngai SM, Tsim KY, Holland PW, Hui JHL*. (2020). Jellyfish genomes reveal distinct homeobox gene clusters and conservation of small RNA processing. *Nature Communications*, 11, 3051.

Changes in the Plasmodesma Structure and Permeability at the Bundle Sheath and Mesophyll Interface During the Maize C4 Leaf Development.

Professor Byung Ho KANG
Associate Professor, School of Life Sciences

Plasmodesmata (PD) are intercellular channels that mediate molecular diffusion between neighboring plant cells. Development and permeability of PD are regulated by multiple intra- and intercellular signaling pathways. PD are critical for the dual cell C4 photosynthesis in maize because the shuttling of organic acids occurs via specialized PD that connect bundle sheath (BS) and mesophyll (M) cells. We examined PD at the BS-M interface along the maize leaf development gradient and the establishment of dimorphic chloroplasts using combined microscopy approaches. Young BS and M cells in the leaf base had indistinguishable proplastids, and their PD were simple, devoid of cytoplasmic sleeves. In maturing BS and M cells, chloroplasts had different thylakoid structures with varying protein compositions, and the diversification was accompanied by PD modifications. They became equipped with an electron-dense ring in the M side, and their cytoplasmic sleeves widened in the BS side. Furthermore, suberin accumulated in the BS cell wall where the PD are embedded. Symplastic transport between BS and M cells dropped after these changes in a callose-dependent manner. We compared PD elaboration and suberin deposition kinetics in wild-type (WT) B73 with those in ppdk mutant and dct2 mutants in which C4 cycle is affected. PD development, symplastic transport inhibition, and suberin accumulation were observed in younger BS-M cell pairs of mutant leaves. Transcriptomic analysis indicated that genes involved in cell-wall suberization were upregulated earlier in the mutant lines than WT. These data suggest that the maize C4 photosynthetic system controls PD development and gating to ensure that C4 metabolites are correctly distributed over the two cell types.

Representative relevant publications:

1) Mai KKK, Gao P, Kang B-H*. Electron Microscopy Views of Dimorphic Chloroplasts in C4 Plants. *Front Plant Sci* 2020;11:1020. doi:10.3389/fpls.2020.01020.

2) Mai KKK, Yeung W-T, Han S-Y, Cai X, Hwang I, Kang B-H*. Electron Tomography Analysis of Thylakoid Assembly and Fission in Chloroplasts of a Single-Cell C4 plant, Bienertia sinuspersici. *Sci Rep* 2019;9:19640. doi:10.1038/s41598-019-56083-w.

3) Wang P, Liang Z, Kang B-H*. Electron tomography of plant organelles and the outlook for correlative microscopic approaches. *New Phyto* 2019;223:1756–61. doi:10.1111/nph.15882.

Genomic Research of Soybean and Its Implications

Professor Hon-Ming LAM
Professor, School of Life Sciences

Soybean is an environment-friendly economic crop that is a major source of dietary protein, edible oil, and nutraceutical compounds. Germplasm collections, containing natural variations, are important resources for the identification of important genes and alleles. We performed genomic studies to show the high diversity of wild soybeans and completed the first wild soybean reference genome. We also participated in international efforts on upgrading the quality of cultivated soybean. A combination of genomic and genetic technologies enabled us to identify important QTLs controlling various traits of soybean. Genomic and proteomic researches, as well as metabolic modeling, were conducted to provide a better understanding of the symbiotic relationship between soybean and its microbial partner Rhizobium. Using a marker-assisted selection approach, in combination with field observations via collaboration with breeders, we are able to generate new soybean cultivars that exhibit good performance in a stressful environment in NW China. These cultivars have already been distributed to local farmers with an aim to increase income, maintain soil fertility, and reduce environmental pollutions.

Representative relevant publications:

1) C.A. Contador, S.-K. Lo, S.H.J. Chan*, H-M. Lam*. 2020. Metabolic analyses of nitrogen fixation in the soybean micro-symbiont Sinorhizobium fredii using constraint-based modeling. *mSystems* 5:e00516-19.
2) X. Lin, W. Lin, Y.-S. Ku, F.-L. Wong, M.-W. Li, H.-M. Lam*, S.-M. Ngai*, T.-F. Chan*. 2020. Analysis of soybean long non-coding RNAs reveals a subset of novel small peptide-coding transcripts. *Plant Physiol.* 182:1359-1374.
3) H.M. Rehman, W.-L. Cheung, K.-S. Wong, M. Xie, C.-Y. Luk, F.-L. Wong, M.-W. Li, S.-N. Tsai, W.-T. To, L.-Y. Chan, H.-M. Lam*. 2019. High-throughput mass spectrometric analysis of whole proteome and secretome of Sinorhizobium fredii strains CCBAU25509 and CCBAU45436. *Front. Microbiol.* 10:2569.
4) M. Xie, C.Y.-L. Chung, M.-W. Li, F.-L. Wong, X. Wang, A. Liu, Z. Wang, A.K.-Y. Leung, T.-H. Wong, S.-W. Tong, Z. Xiao, K. Fan, M.-S. Ng, X. Qi, L. Yang, T. Deng, L. He, L. Chen, A. Fu, Q. Dong, J. He, G. Chung, S. Isobe, T. Tanabata, B. Valliyodan, H.T. Nguyen, S.B. Cannon, C.H. Foyer, T.-F. Chan*, H.-M. Lam*. 2019. A reference-grade wild soybean genome. *Nat. Commun.* 10:1216.
5) K.-M. Fung, A.P.K. Tai*, T. Yong, X. Liu, H.-M. Lam. 2019. Co-benefits of intercropping as a sustainable farming method for safeguarding both food security and air quality. *Environ. Res. Lett.* 14:044011.
6) C.H. Foyer*, K.H.M. Siddique, A.P.K. Tai, S. Anders, N. Fodor, F.-L. Wong, N. Ludidi, M.A. Chapman, B.J. Fergusson, M.J. Considine, F. Zabel, P.V.V. Prasad, R.K. Varshney, H.T. Nguyen, H.-M. Lam. 2019. Modelling predicts that soybean is poised to dominate crop production across Africa. *Plant Cell Environ.* 42:373-385.
7) J. Jiao, M. Ni, B. Zhang, Z. Zhang, J.P.W. Young, T.-F. Chan, W.X. Chen, H.-M. Lam*, C.F. Tian*. 2018. Coordinated regulation of core and accessory genes in the multipartite genome of Sinorhizobium fredii. *PLOS Genet.* 14:e1007428.
8) C. Foyer*, H.M. Lam, H. Nguyen, K. Siddique, R. Varshney, T. Colmer, W. Cowling, H. Bramley, T. Mori, J. Hodgson, J. Cooper, T. Miller, K. Kunert, B. Vorster, C. Cullis, J. Ozga, M. Wahlqvist, Y. Liang, H. Shou, K. Shi, J. Yu, N. Fodor, B. Kaiser, F.-L. Wong, B. Valliyodan, M. Considine. 2016. Neglecting legumes has compromised human health and sustainable food production. *Nat. Plants* 2:16112.
9) X. Qi, M.-W. Li, M. Xie, X. Liu, M. Ni, G. Shao, C. Song, A.K.-Y. Yim, Y. Tao, F.-L. Wong, S. Isobe, C.-F. Wong, K.-S. Wong, C. Xu, C. Li, Y. Wang, R. Guan, F. Sun, G. Fan, Z. Xiao, F. Zhou, T.-H. Phang, X. Liu, S.-W. Tong, T.-F. Chan, S.-M. Yiu, S. Tabata. J. Wang, X. Xu*, H.-M. Lam*. 2014. Identification of a novel salt tolerance gene in wild soybean by whole-genome sequencing. *Nat. Commun.* 5:4340.
10) H.-M. Lam*, X. Xu, X. Liu, W. Chen, G. Yang, F.-L. Wong, M.-W. Li, W. He, N. Qin, B. Wang, J. Li, M. Jian, J. Wang, G. Shao, J. Wang*, S.S.-M. Sun*, G. Zhang*. 2010. Resequencing of 31 wild and cultivated soybean genomes identifies patterns of genetic diversity and selection. *Nat. Genet.* 42:1053-1059 (cover).

Genomic insights into the adaptations and diversification of Brachyuran crabs

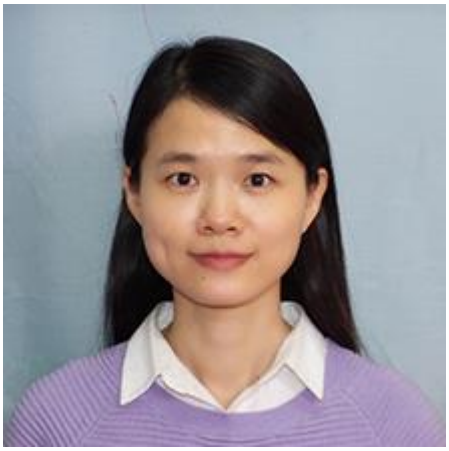
Professor Ling Ming TSANG
Assistant Professor, School of Life Sciences

Researches of my lab focus on studying the evolution and ecology of marine invertebrates using integrated molecular, morphological and ecological approaches. Model organisms include, but not limited to, scleractinian corals, horseshoe crab and in particular decapod crustaceans. In the current sharing, I would introduce my ongoing research work on the brachyuran crabs, which is my most favorite organism. With over 7,000 described species in 100+ families, true crab from the infraorder Brachyura represents one of the most species rich marine invertebrates and exhibit high diversity in body form and lifestyle. Over the years, my lab attempt to reconstruct the most comprehensive brachyuran molecular phylogeny to infer their evolutionary and determine the factors promoting speciation in the group. Co-diversification with mangrove species revealed to one mechanism leading to rapid radiation in Brachyura, with divergent time of mangrove associated crabs highly congruent with the origin of mangrove species. The mangrove crabs, on the other hand, play an important role in trophic linkage and promote nutrient recycling in the mangrove ecosystem by feeding on the mangrove leaves that are unusable for most of the other organisms. However, how can they digest the lignocellulose in the plant materials and acquire enough nutrient remain unknown. To evaluate the role of endogenous enzyme and gut microbial lignocellulase in mangrove crab digestion, we are sequencing the genome and transcriptome of mangrove crab species as well as their gut metagenomic of their gut microbiome. Preliminary data indicate the cellulase genes are present in almost all of the crabs and other crustacean transcriptomes and genomes, regardless of the diet of species analyzed. On the other hand, the mangrove crab gut microbes are enriched with cellulolytic bacterial species and metagenomic analyses reveal genes necessary for synthesis of essential amino acids. These results indicate that both endogenous and microbial enzyme are participating in hydrolysis of lignocellulose while the microbes may contribute additional nitrogen source to the mangrove.

Representative relevant publications:

1) Tsang TT, Schubart CDS, Chu KH, Ng PKL, Tsang LM* (in press) Origin of Terrestrialization in the periods of global warming in Thoracotremata (Crustacea: Decapoda: Brachyura) Crabs. *Molecular Phylogenetic and Evolution*.
2) Ma KY, Qin J, Lin C-W, Chan T-Y, Ng PKL, Chu KH, Tsang LM* (2019) Phylotranscriptomic analyses of brachyuran crabs support early divergence of primary freshwater crabs. *Molecular Phylogenetic and Evolution* 135: 62-66.
3) Tsang LM, Schubart CD, Ahyong ST, Lai JCY, Au EYC, Chan TY, Ng PKL, Chu KH (2014) Evolutionary history of true crabs (Crustacea: Decapoda: Brachyura) and the origin of freshwater crabs. *Molecular Biology and Evolution* 31:1173-1187.
4) Tsang LM, Chan T-Y, Ahyong ST, Chu KH (2011) Hermit to king, or hermit to all: Multiple transitions to crab-like forms from hermit crab ancestors. *Systematic Biology* 60:616-629.

Autophagosome biogenesis in plants and green algae



Professor Xiaohong ZHUANG
Assistant Professor, School of Life Sciences

Under nutrient/energy limit conditions, plants involve efficient pathways to reutilize the nutrient/energy from source to sink via multiple metabolism reprogramming pathways. Among them, autophagy plays a pivotal role to sequester the resource (e.g. proteins, starch and lipids) into *de novo* formed double-membrane vesicles known as autophagosomes, subsequently they dispatch the source materials into the lytic vacuole to be catalysed into basic units for reuse (e.g., amino acid, sugar or ATP). In addition, some cargoes (e.g. immunity receptors or small RNAs) employ autophagosome as a functional maturation/delivery strategy via compartmentalization, which finally contribute to cellular reprogramming. By doing so, autophagy assists in manifesting the metabolic process that arise from these alterations by modifying cellular expression profiles or cargo conformation. Thus, identification of the regulatory modules and their biological function in plant autophagy is one long-standing challenge for future application in metabolic engineering in plant-based systems. Here we will present our recent progress on the autophagy-related machinery in multiple plant-unique cell layers (single cell/cell lineage/organ system).

Representative relevant publications:

1) Wun C-L, Quan Y and Zhuang, X*. (2020) Recent Advances in Membrane Shaping for Plant Autophagosome Biogenesis. *Frontiers in plant science.* 11, 565.

2) Zhuang, X.*, Chung, K.P., Luo, M., and Jiang, L. (2018). Autophagosome Biogenesis and the Endoplasmic Reticulum: A Plant Perspective. *Trends in Plant Science.* 23, P677-692.

3) Soto-Burgos, J., Zhuang, X.*, Jiang, L., and Bassham, D.C. (2018). Dynamics of Autophagosome Formation. *Plant Physiology* 176, 219-229.

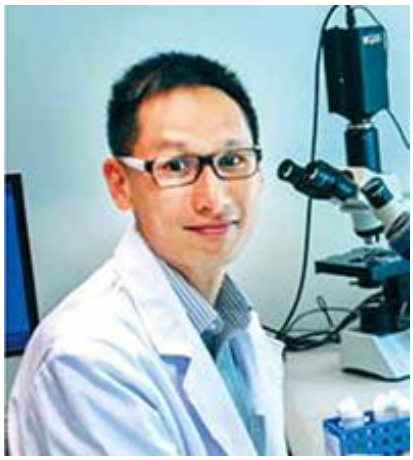
4) Zhuang, X.*, Chung, K.P., Cui, Y., Lin, W., Gao, C., Kang, B.H., and Jiang, L. (2017). ATG9 regulates autophagosome progression from the endoplasmic reticulum in Arabidopsis. *Proc Natl Acad Sci U S A*. 114, E426-E435.

5) Zhuang, X.*, Chung, K.P. and Jiang, L. (2017) Targeting tail-anchored proteins into plant organelles. *Proc Natl Acad Sci U S A*. 114:1762-1764.

6) Zhuang, X.*, and Jiang, L. (2014). Autophagosome biogenesis in plants: roles of SH3P2. *Autophagy.* 10, 704-705.

7) Zhuang, X.*, Wang, H., Lam, S.K., Gao, C., Wang, X., Cai, Y., and Jiang, L. (2013). A BAR-domain protein SH3P2, which binds to phosphatidylinositol 3-phosphate and ATG8, regulates autophagosome formation in Arabidopsis. *The Plant Cell.* 25, 4596-4615.

CAG RNAs Induce DNA Damage and Apoptosis in Polyglutamine Degeneration.



Professor Edwin Ho Yin CHAN
Professor, School of Life Sciences

Polyglutamine (PolyQ) diseases are caused by genomic CAG triplet repeat expansion in the coding region of disease loci. DNA damage plays a central role in polyQ pathogenesis. We found mRNA X was reduced in levels in neurons expressing mutant polyQ disease transcripts. Interestingly, depletion of X causes DNA damage in normal cells, while its overexpression restored DNA damage response pathway and rescued apoptosis in polyQ disease models. We discovered small CAG (sCAG) RNAs, species generated from mutant CAG transcripts, hybridized with CUG-containing mRNA of X and formed CAG/CUG RNA heteroduplex. We further identified a compound that can specifically interact with major groove of CAG RNA homoduplex, and disfavored CAG/CUG heteroduplex formation. This action subsequently mitigated RISC-dependent gene silencing of X. Upon compound treatment, DNA damage, apoptosis and locomotor defects were rescued in mouse disease model. Our study unveiled a novel pathogenic pathway in polyQ diseases and highlights the therapeutic potential of a small molecule for treating polyQ diseases.

Representative relevant publications:

1) Lee, L.K., Leong, L.I., Liu, Y., Luo, M., Chan, H.Y.E.* and Choi, C.H.J.* (2020) Preclinical nanomedicines for polyglutamine-based neurodegenerative diseases (Invited Review). *Mol. Pharm.* (in press) doi: 10.1021/acs.molpharmaceut.0c00506

2) Zhang, Q., An, Y., Chen, Z.S., Koon, A.C., Lau, K.F., Ngo, J.C.* and Chan, H.Y.E.* (2019) A peptidylic inhibitor for neutralizing r(GGGGCC)exp-associated neurodegeneration in C9ORF72-associated amyotrophic lateral sclerosis and frontotemporal dementia. *Mol. Ther. Nucleic Acids* 16, 172-185.

3) Chen, Z.S., Li, L., Peng, S., Chen, F.M., Zhang, Q., An, Y., Lin, X., Li, W., Chan, T.F., Lau, K.F., Ngo, J.C., Wong, W.T., Kwan, K.M. and Chan, H.Y.E.* (2018) Planar cell polarity gene Fuz triggers apoptosis in neurodegenerative diseases. *EMBO Rep*. 19, e4541.

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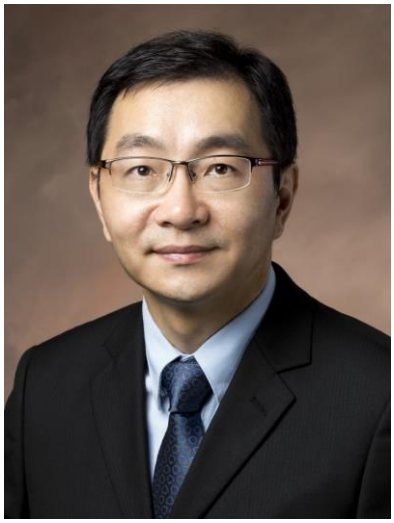
Low-density lipoprotein receptor-related protein-6 (LRP6) cell surface availability regulates fuel metabolism in astrocytes.

Professor Kim Hei Man CHOW
Assistant Professor, School of Life Sciences

Early changes in astrocyte energy metabolism is associated with late-onset Alzheimer's disease (LOAD), but the mechanistic side remains elusive. We show that LRP6 is the unique Wnt coreceptor on astrocytes which serves as a bimodal switch that modulates their metabolic landscape. The LRP6-Wnt mediated mTOR-AKT axis is essential for sustaining glucose metabolism. In its absence Wnt instead activates the LRP6-independent Ca2+-PKC-NFAT axis, switching to a transcription network that reprograms the TCA cycle depending alternatively on glutamine and BCAAs catabolism. Exhaustion of these raw materials essential for neurotransmitter biosynthesis and recycling results in synaptic dysfunction; cognitive and memory decline. Diminished surface availability of LRP6 triggered by interacting with APOE4, the greatest LOAD-related risk factor, rendered astrocytes behave as if they have lost LRP6 expression. We highlight that intranasal supplementation of glutamine and BCAAs is effective in preserving neuronal integrity and functions, offering a tangible perspective for delaying disease onset and progression.

Critical role of Sox9 in blood-CSF barrier development and function

Professor Kin Ming KWAN
Associate Professor, School of Life Sciences



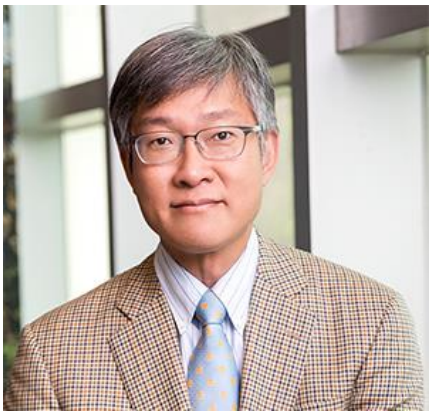
The highly vascularized choroid plexus (CP) located within each brain ventricle is an integral part of the blood-cerebrospinal fluid (CSF) barrier. The CP epithelium acts as a discriminatory barrier so that desired molecules are secreted into CSF while unwanted substances are constrained at peripheral circulation. However, the genetic mechanisms responsible for CP development and function are poorly understood. Here we identified the transcription factor Sox9 was robustly expressed in mouse hindbrain CP epithelium. Using genetic loss-of-function approach, we show that Sox9 is essential for CP development and function. In this seminar, we will discuss how Sox9 involve in multifaceted and pivotal role in the regulation of CP development and blood-CSF barrier establishment.

Structural basis of substrate recognition and thermal protection by a small heat shock protein

Professor Wilson Chun Yu LAU
Research Assistant Professor, School of Life Sciences

Small heat shock proteins (sHsps) function as a first line of defense against protein aggregation through binding to unfolding proteins, thereby playing a pivotal role in the maintenance of proteostasis in virtually all living organisms. Structural elucidation of sHsp-substrate complexes has been hampered by the transient and heterogeneous nature of their interactions, and the precise mechanisms underlying substrate recognition, promiscuity, and chaperone activity of sHsps remain obscure. Here we report on the formation of a stable complex between a plastid sHsp, Hsp21, and its natural substrate 1-deoxy-D-xylulose 5-phosphate synthase (DXPS) under heat stress, as well as its cryo-electron microscopy structure at near-atomic resolution. Monomeric Hsp21 binds across the dimer interface of DXPS and engages in multivalent interactions by recognizing highly dynamic structural elements in DXPS. Hsp21 partly unfolds its central α-crystallin domain to facilitate binding of DXPS, which preserves a native-like structure. This unanticipated mode of interaction unveils a mechanism of the anti-aggregation activity of sHsps towards a broad range of substrates.

How structural biology provides insight into how life works and opportunities for drug development



Professor Kam Bo WONG
Professor, Director of School of Life Sciences

My group has been using NMR spectroscopy, X-ray crystallography and cryo-EM to understand how proteins function at the atomic resolutions. First, I am going to use the urease maturation pathway as an example to illustrate how structural biology provides insights into how life works at the molecular level. Urease is a metalloenzyme that require nickel ions to become active. Its hydrolysis of urea into ammonia is essential to the survival of *Helicobacter pylori* in acidic human stomach. Correct metallation of urease is ensured through specific protein-protein interactions among metallochaperones along the nickel delivery pathway, which is assisted by four accessory proteins, UreE, UreF, UreG and UreD(H). We have been combining structure determination, mutagenesis and biochemical analysis to understand the urease maturation pathway [1-3]. Our work demonstrated a paradigm on how a metallochaperone UreG couples GTP hydrolysis to allosterically regulate the binding/release of nickel ions and the switching of protein-binding partners, thus providing a mechanism where nickel ions are delivered to the urease without releasing the "free" toxic metal to the cytoplasm. In the end of my talk, I will briefly introduce my work on coronaviral main proteases and their broad-spectrum inhibitors [4] and hopefully will attract collaboration on drug development for COVID-19.

Representative relevant publications:

1) Fong YH, Wong HC, Chuck CP, Chen YW, Sun H, Wong KB*: Assembly of preactivation complex for urease maturation in Helicobacter pylori: crystal structure of UreF-UreH protein complex. *J Biol Chem* 2011, 286(50):43241-43249.

2) Fong YH, Wong HC, Yuen MH, Lau PH, Chen YW, Wong KB*: Structure of UreG/UreF/UreH complex reveals how urease accessory proteins facilitate maturation of Helicobacter pylori urease. *PLoS Biol* 2013, 11(10):e1001678.

3) Yuen MH, Fong YH, Nim YS, Lau PH, Wong KB*: Structural insights into how GTP-dependent conformational changes in a metallochaperone UreG facilitate urease maturation. *Proc Natl Acad Sci U S A* 2017, 114(51):E10890-E10898.

4) Chuck CP, Chen C, Ke Z, Wan DC, Chow HF, Wong KB*: Design, synthesis and crystallographic analysis of nitrile-based broad-spectrum peptidomimetic inhibitors for coronavirus 3C-like proteases. *Eur J Med Chem* 2013, 59:1-6.