School of Engineering Distinguished Workshop:
The Future of Health Technology in Modern Medicine

The Hong Kong University of Science and Technology

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ABSTRACT

Synthetic Biology and Biomolecular Engineering

Inorganic Phosphorus Materials in Chemical Biology

Prof. Jing ZHAO

Nanjing University

Abstract

Phosphorus is an element essential to sustaining life largely through phosphates. Phosphorus-based materials, such as Black Phosphorus and Red Phosphorus, are emerging important biomaterials.

Polyphosphate (PolyP) is one of the most compact inorganic polyanionic biopolymers that participates in various physiological processes. [1, 2]. We found that polyP interact with positively charged green fluorescent protein, +36GFP, resulting in liquid-liquid phase separation (LLPS) by intermolecular electrostatic interactions in cells. Medium chain-length polyP (60-mer) could induce the formation of +36GFP coacervates in vitro at a protein concentration as low as 200 nm, which is of the same magnitude as native proteins. In contrast, shorter polyP (14-mer) could not induce LLPS under the same conditions.

Next, polyP-manganese nanosheets were designed and synthesized via the assistance of CTAB and oleate ions by a hierarchical assembly strategy. The thickness and the lateral size of the resulting polyP-Mn nanosheets are 5nm and 120nm, respectively. Molecular dynamics simulations suggested that the larger polyP-CTAB complex serves as the template for the 2D assembly of poly-Mn. These polyP-Mn nanosheets could trigger silent macrophages cGAS-STING pathway activation, and induce macrophages to M1 polarization, recovering their innate immune response. Our work suggest polyP-based nanomaterials as a unique type of biocompatible and biodegradable nanomaterials in biology.

About the Speaker

Prof. Jing Zhao is a distinguished chemist currently affiliated with Nanjing University in China. He obtained his Ph.D. from Yale University, working under the guidance of Prof. John Hartwig. Prior to that, he earned his B.Sc. from Nanjing University. With an illustrious career, Prof. Zhao has held positions as a senior scientist at Rohm and Haas Company and as a research scientist at the University of Chicago. He also conducted postdoctoral research at the University of California, Berkeley, under the supervision of Prof. F. Dean Toste. Prof. Zhao's contributions to the field of chemistry have been recognized with prestigious awards, including the National Natural Science Award and the Thieme Chemistry Journal Award.

Engineering and Safeguarding Synthetic Genomes

Prof. Patrick Yizhi CAI

The University of Manchester

Abstract

Over the last 10 years, my lab has been building synthetic yeast chromosomes from scratch. These synthetic yeast cells are engineered to allow genome-wide directed evolution with a system call SCRaMbLE (Synthetic Chromosome Recombination and Modification by LoxP-Mediated Evolution). SCRaMbLE allows the synthetic cells to process the information (e.g. environmental stress) differently from their wildtype counterparts, and also enables them to re-configure the genomes to cope with the environments. Finally, I will also discuss the progress of developing safety mechanisms for synthetic genomes.

About the Speaker

Professor Patrick Cai (PC, Manchester) is Chair Professor in Synthetic Genomics and a world-leading expert in synthetic chromosomes, with a highly interdisciplinary research group. In 2017, Prof. Cai's team published 7 research articles in the journal of Science and featured on its cover. PC is the international coordinator for the (Sc2.0) Consortium, which is composed of over 10 top universities from 4 continents aiming to synthesize the world's first synthetic eukaryotic genome. PC founded Edinburgh Genome Foundry, which is the largest automated DNA synthesis and assembly facility in academia today. PC regularly provides advice and consultancies to the Cabinet office, the Foreign Office and the Prime Minister's Council for Science and Technologies. PC holds prestigious visiting professorships with MIT (US), MRC LMB at Cambridge (UK), Hong Kong University and Chinese Academy of Sciences (China). In 2022, PC was awarded a 5year EPSRC fellowship to work on biosecurity and biosafety mechanisms for synthetic genomes. In 2023, PC was awarded an ERC Consolidator Award to engineer non-coding RNAs using a synthetic genomics approach.

Prof. Cai received his bachelor's degree in Computer Science at Central South University. Me then obtained his master's degree in Bioinformatics at University of Edinburgh and his Ph.D. degree in Genetics, Bioinformatics and Computational Biology at Virginia Tech, USA.

Microbiome for Modulating Human Metabolists Diseases

Prof. Chenhong ZHANG

Shanghai Jiao Tong University

Abstract

As a prototypical complex adaptive system (CAS), the gut microbiota is pivotal to human health, akin to an essential organ. To pinpoint core health-relevant gut microbial members, we follow the systems biology tenet that stable relationships signify core components. We identified stable genome pairs within co-abundance networks under varied environmental conditions, analyzing metagenomic datasets from a high-fiber dietary intervention in type 2 diabetes and 26 case-control studies encompassing 15 diseases. These pairings constitute a 'Two Competing Guilds' model, delineating one guild specializing in fiber fermentation and butyrate production from another characterized by virulence and antibiotic resistance. Utilizing these genomes, our Random Forest models distinctively separated cases from controls across all diseases and predicted immunotherapy outcomes. Employing a genome-centric, reference-free methodology to dissect the gut microbiome as a CAS, our research identifies a core microbiome signature, positing it as a potential holistic health indicator and a common target for health enhancement.

Science we found that the gut microbiota from distal symmetric polyneuropathy (DSPN) patients induced more severe peripheral neuropathy in db/db mice, we would like to figure out that whether we can modulate the gut microbiota guilds to attenuate this most common neuropathy in patients with diabetes mellitus. Gut microbiota from healthy donors significantly alleviated DSPN independent from glycemic control in patients in a randomized, double-blind and placebo-controlled trial. The gut bacterial genomes correlated with Toronto Clinical Scoring System score were organized in two competing guilds. Increased Guild 1 that had higher capacity in butyrate production and decreased Guild 2 that harbored more genes in synthetic pathway of endotoxin were associated with improved gut barrier integrity and decreased proinflammatory cytokine levels. Moreover, matched enterotype between transplants and recipients showed better therapeutic efficacy with more enriched Guild 1 and suppressed Guild 2. Thus, the two competing guilds may mediate the causative role of the gut microbiota in DSPN and have the potential to be an effective target for treatment.

About the Speaker

Professor Chenhong Zhang is a Professor in School of Life Sciences and Biotechnology at Shanghai Jiao Tong University. She received her bachelor’s degree in Biotechnology, master’s and Ph.D. degree in State Key Laboratory of Microbial Metabolism at Shanghai Jiao Tong University. She then joined her postdoctoral fellow in Functionality of the Intestinal Ecosystem (FInE) at French Institute of Agronomic Research (INRA), France.

Prof. Zhang is an expertise in microbiology. Her main research interests are Intestinal Microbiota in Health, Obesity-related Chronic Diseases, Ageing, Foods, Molecular Cross-talk of Intestinal Bacteria and Host Cells and Intestinal Ecosystem.

A Synthetic Protein-level Neral Network in Mammalian Cells

Prof. Zibo CHEN

Westlake University

Abstract

Artificial neural networks provide a powerful paradigm for information processing that has transformed diverse fields. Within living cells, genetically encoded synthetic molecular networks could harness principles of neural computation to classify molecular signals. Here, we combine de novo designed protein heterodimers and engineered viral proteases to implement a synthetic protein circuit that performs winner-take-all neural network computation. This “perceptein” circuit includes modules that compute weighted sums of input protein concentrations through reversible binding interactions, and allow for self-activation and mutual inhibition of protein components using irreversible proteolytic cleavage reactions. Altogether, these interactions comprise a large network of chemical species and reactions involving diverse cleavage products of up to 10 co-expressed starting protein species. The complete system achieves multi-output signal classification with tunable decision boundaries in mammalian cells, and can be used to control cell death. These results demonstrate how engineered protein-based networks can enable programmable signal classification in living cells.

About the Speaker

Zibo Chen is an Assistant Professor in the School of Life Sciences at Westlake University. He received his Ph.D. degree in biochemistry in the labs of David Baker and Frank DiMaio at the University of Washington and worked on mammalian synthetic biology with Michael Elowitz at Caltech as a Damon Runyon Fellow. His work focuses on programming biology using proteins as the coding language.

Shedding Light on Mitochondria and ER Mechanobiology by Optogenetic Mechanostimulators

Prof. Liting DUAN

Chinese University of Hong Kong

Abstract

The ability of cells to perceive and respond to mechanical cues is essential for numerous biological activities. Tremendous efforts have investigated the roles of the plasma membrane, the cytoskeleton, and many intracellular signaling pathways in cellular mechanosensing and mechanotransduction. Recently, the nucleus has also been identified as a crucial cellular mechanosensor. However, whether and how mitochondria and endoplasmic reticulum (ER) perceive and react to mechanical cues remains largely unexplored, due to the lack of experimental means to precisely apply forces on intracellular organelles. To address this challenge, we developed optogenetics-based light-gated mechanostimulators that are able to exert mechanical pulling forces remotely and exclusively on ER or mitochondria inside living cells with controllability in time, space, and force strength. We revealed that force could drive DRP1/Mff-dependent asymmetrical mitochondrial fission, which involves the wrapping of ER tubules and generates mitochondrial fragments without mtDNA to recruit Parkin proteins. With the ER-specific optogenetic mechanostimulator, we found that mechanostimulation of ER could elicit a transient and rapid efflux of Ca^{2+} from ER, inhibit ER-to-Golgi trafficking, and induce ER stress. Our results provide direct evidence for ER and mitochondria mechanosensitivity and the tight mechanoregulation of their functions, placing ER and mitochondria as important players on the intricate map of cellular mechanotransduction.

About the Speaker

Liting Duan received a Bachelor's degree in Chemistry from Renmin University of China (People's University of China) and a Ph.D. in Chemistry from Stanford University. Her thesis focused on the development of optogenetic strategies to control intracellular activities. During postdoctoral research at Stanford, she further studied and engineered the photosensory proteins interactions for optimized optogenetic toolkits. In July 2018, she joined the Department of Biomedical Engineering at the Chinese University of Hong Kong as an Assistant Professor. Now her group is focused on developing novel optical methods to control intracellular signaling pathways and organelle activities