Date: 14 January 2019 (Monday)

Prof. Yeguang Chen, School of Life Sciences, Tsinghua University

"Wnt and BMP signaling coordinate to maintain Lgr5+ intestinal stem cell self-renewal and epithelium homeostasis"

$Lgr5^+$ intestinal stem cells (ISCs) drive the fast renewal of intestinal epithelium. Several signaling pathways have been shown to regulate ISC fates. However, it is unclear what are the essential signals to sustain the ISC self-renewal. It is known that impairment of BMP signaling can drive hyperproliferative intestinal polyposis, resembling the phenotypes of juvenile polyposis syndrome, which frequently carries germline mutations in BMPRIA or SMAD4. BMP signaling represents a major counterforce that balances the Wnt-driven self-renewal and growth of intestinal epithelium. I will discuss how BMP negatively regulates the Lgr5+ stem cell activity to maintain intestinal epithelium homeostasis and that the coordination between Wnt and BMP signaling activity is necessary and sufficient to maintain $Lgr5^+$ ISCs self-renewal.

Prof. Tom Cheung, HKUST

"Molecular regulation of stem cell quiescence and activation"

Adult stem cells are unique in their ability to produce differentiated daughter cells while retaining their stem cell identity by self-renewal. The quiescent state of stem cells has long been viewed as a dormant state, but our understanding of the molecular regulation and physiological significance of this state remains limited. Dysregulation of quiescence results in the depletion of the stem cell pool. Deciphering the molecular mechanisms regulating the quiescent state will enable us to better devise approaches for stem cell therapies for degenerative diseases. Muscle stem cells, or "satellite cells", are a population of adult stem cells that are primarily quiescent in the absence of injury, making them an excellent model to study stem cell quiescence. We hypothesize that the state of quiescence is a poised state awaiting extrinsic signals for activation. Our data showed that the state of quiescence is actively controlled at the post-transcriptional level. Various post-transcriptional mechanisms have been identified for the regulation of stem cell quiescence and activation. Collectively, our data provide strong support for the hypothesis that the quiescent state is an actively regulated state.

Prof. Xiaohua Shen, Tsinghua University

"Novel functions of lncRNA and RNA-binding protein in transcription regulation, stem cell and development"

Much of the developmental complexity of higher eukaryotes is thought to arise from gene regulation rather than from an increase in the number of protein-coding genes. RNA represents a hidden layer of regulatory information in complex organisms. Long noncoding RNAs (lncRNAs) have been increasingly recognized as important regulators of transcription and chromatin structure. However, the functionality of vast majorities of lncRNAs is unknown. Identifying functional lncRNAs and revealing their regulatory mechanisms represent major challenges in understanding genome complexity and RNA-mediated gene regulation. The fact that RNA-binding proteins (RBPs) must be enlisted to mediate RNA functions raises the possibility that RBPs might participate in transcription and chromatin control. I will discuss recent progresses we have made in lncRNA and RBP-mediated regulation in contexts of chromatin, stem cell and development.

Prof. Zhenguo Wu, HKUST

"Regulation of quiescence exit in adult muscle stem cells by PI3 kinase"

Adult mouse muscle satellite cells (MuSCs) are quiescent in uninjured muscles. Upon injury, MuSCs exit quiescence to become activated, re-enter the cell cycle to proliferate, then differentiate to repair the damaged muscles. It remains unclear which extrinsic signal and intrinsic signaling pathway regulate quiescence exit during MuSC activation. Here, we demonstrated that inducible MuSC-specific deletion of p110α, a catalytic subunit of phosphatidylinositol 3-kinase (PI3K), rendered MuSCs unable to exit quiescence, resulting in severely impaired MuSC proliferation and muscle regeneration. Downstream of PI3K, mTORC1-Jun and FoxOs function as key components in two inter-connected signalling axes to regulate quiescence exit. Induction of a constitutively active PI3K in quiescent MuSCs resulted in spontaneous MuSC activation in uninjured muscles and subsequent depletion of the MuSC pool. Thus, PI3K is both necessary and sufficient for adult MuSCs to exit quiescence in response to activating signals.

Prof. Zilong Wen, HKUST

"A Novel Ectoderm-Derived Myeloid-Like Cell in Zebrafish Epidermis Functions as Antigen Transporters for Langerhans Cells"

Tissue-resident macrophages (TRMs) are highly heterogeneous and engage in a wide range of diverse functions. Yet, the heterogeneities of their origins and functions remain incompletely defined. Here we report the identification and characterization of a novel ectoderm-derived myeloid-like cell, which we refer to as metacyte. We show that metacytes are highly similar to conventional Langerhans cells (cLCs), the resident macrophages in epidermis, in transcriptome, morphology and anatomic location. However, unlike cLCs, metacytes respond neither to tissue injury nor bacterial infection, but rather sample soluble antigens from external environment through transepithelial protrusions and transfer them to cLCs via apoptosis-phagocytosis axis. This antigen transfer is critical for zebrafish to respond to soluble antigens because the depletion of metacytes significantly reduces cLC antigen uptake. Our study documents the existence of ectoderm-derived myeloid-like cells that manifest distinct function from conventional TRMs and opens a new paradigm for investigation the heterogeneities of resident immune cells.

Prof. Hong Zhang, Institute of Biophysics, Chinese Academy of Sciences

"Phase separation and transition control autophagic degradation of PGL granules"

The assembly of phase-separated structures is thought to play an important role in development and disease, but little is known about the regulation and function of phase separation under physiological conditions. We showed that during *C. elegans* embryogenesis, PGL granules assemble via liquid-liquid phase separation (LLPS), and their size and biophysical properties determine their susceptibility to autophagic degradation. The receptor SEPA-1 promotes LLPS of PGL-1/-3, while the scaffold protein EPG-2 controls the size of PGL-1/-3 compartments and converts them into less dynamic gel-like structures. Under heat stress conditions, mTORC1-mediated phosphorylation of PGL-1/-3 is elevated and PGL-1/-3 undergo accelerated phase separation, forming PGL granules that are resistant to autophagic degradation. Significantly, accumulation of PGL granules is an adaptive response to maintain embryonic viability during heat stress. We revealed that mTORC1-mediated LLPS of PGL-1/-3 acts as a switch-like stress sensor, coupling phase separation to autophagic degradation and adaptation to stress during development.

Prof. Mingjie Zhang, HKUST

"Phase separation: a fundamental molecular process in cell biology"

Synapses are semi-membraneless, protein-dense, sub-micron chemical reaction compartments responsible for signal processing in each and every neuron. Proper formation and dynamic responses to stimulations of synapses both during development and in adult are fundamental to functions of mammalian brains. There are not any identical ones among trillions of synapses in a human brain. Using a biochemical reconstitution approach, it was shown that, both in solution and on supported membrane bilayers, multivalent interaction networks formed by major excitatory postsynaptic density (PSD) scaffold proteins led to the formation of PSD-like assemblies via phase separation. A distinct feature of the phase transition-mediated assembly of PSD is that the molecular interactions are predominantly highly specific and high affinity multi-valent protein-protein interactions instead of IDP-mediated interactions. The reconstituted PSD-like assemblies can cluster receptors, selectively concentrate enzymes, promote actin bundle formation, and expel inhibitory postsynaptic protein. Additionally, the condensed phase PSD assemblies have features that are distinct from those in homogeneous solutions and fit for synaptic functions. Thus, a defined and biochemical trackable molecular platform is reconstructed for understanding how neuronal synapses are formed and dynamically regulated. I will also briefly mention our effort in reconstituting complexes for regulating presynaptic neurotransmitter releases at the end of my talk.

Prof. Li Yu, Tsinghua University

"Migrasome formation is mediated by assembly of micron-scale tetraspanin macrodomains"

Migrasomes are newly discovered vesicular organelles. During migration, retraction fibers are pulled from the rear of the migrating cells, and large vesicle-like structures named migrasomes grow on the tip or branch points of retraction fibers. Here we shown the mechanism of migrasome formation. We found that tetraspanin proteins are highly enriched on migrasomes, and a subset of tetraspanins are necessary and sufficient for migrasome formation. Using purified tetraspanins and liposomes, we established reconstitution systems which simulates migrasome formation *in vitro*. By *in vivo* and *in vitro* analysis, we demonstrated that membrane tension induces the assembly of micron-scale tetraspanin-enriched macrodomains on retraction fibers, which then swell into migrasomes. Finally, we developed a theoretical model, which demonstrated that the key factor driving the local swelling of the retraction fiber membrane into a migrasome-like configuration is membrane stiffening resulting from assembly of micron-scale tetraspanin-enriched macrodomains.

Prof. Xueliang Zhu, Shanghai Institutes for Biochemistry and Cell Biology

"Organization of cytoskeletal networks through protein phase separation"

Microtubules and actin filaments (F-actin) are dynamic cytoskeletons critical for a wide variety of cellular activities including mitosis, migration, and morphogenesis. In accordance with their functions, these cytoskeletons are organized into networks of different shape and subcellular distribution through interplays with various regulators. We have previously shown that the phase separation of BuGZ plays an important role in mitotic spindle assembly. In this talk, I'll focus on our recent progress in protein phase separation-induced actin network formation.

Prof. Pilong Li, Tsinghua University

"Phase transition in gene expression activation and repression"

Gene expression is tightly controlled in cell. A plethora of *in cis* and *in trans* factors participate in gene expression regulation, in many cases, by assembling high-order chromatin structures to ensure sustained activation or repression. Emerging evidence indicates that phase transition derived from weak interactions of multivalent binding partners is a major driving force for many cellular high-order structures. In this talk, I will show how multivalent H3K9me3 nucleosome arrays phase transition upon interacting with protein complexes containing multivalent H3K9me3 reader, chromo domain, which likely underlies constitutive heterochromatin formation for gene repression. I will also show how the low-complexity, intrinsically-disordered region of a RNA binding protein, fused in sarcoma, dictated phase transition on DNA serves as a viable mechanism explaining its transactivation activity in blood cancer development.

Prof. Wenyu Wen, Institutes of Biomedical Science, Fudan University

"Phase transition-mediated polarity complex condensation during Drosophila neuroblast asymmetric division"

Uneven distribution and local concentration of protein complexes on distinct membrane cortices is a fundamental property in numerous biological processes including *Drosophila* neuroblast (NB) asymmetric cell division (ACD) and cell polarity in general. During the ACD of NBs, the Par-3/Par-6/aPKC complex and its related proteins are unevenly distributed on the apical cortex; the cell fate determinant Numb forms a basal crescent together with Pon (Partner of Numb) and is segregated into the basal daughter cell to initiate its differentiation. We discover that Numb PTB domain, using two distinct binding surfaces, recognizes repeating motifs within Pon in a previously unrecognized mode. The multivalent Numb-Pon interaction leads to high binding specificity and liquid-liquid phase separation of the complex. Perturbations of the Numb/Pon complex phase transition impair the basal localization of Numb and its subsequent suppression of Notch signaling during NB asymmetric divisions. We further demonstrate that the conserved Par-3/Par-6 complex undergoes phase separation together with aPKC both in vitro and in vivo, which regulates the apical localization of the Par-3/Par-6/aPKC complex during the ACD of NBs. Such phase-transition-mediated protein condensations on distinct membrane cortices may be a general mechanism for various cell polarity regulatory complexes.

Prof. Xuebiao Yao, University of Science and Technology of China

"The microtubule plus-end tracking machinery is a selective condensate responsive for context-dependent dynamics"

In eukaryotes, microtubules are essential for cellular plasticity and dynamics. We show that PCAF, a kinetochore-associated acetyltransferase, acts as a dynamic modulator of microtubule plus-end through acetylation of EB1, a protein that controls the plus-ends of microtubules (Xia et al., 2012). The microtubule plus-end, a micron-scale, dynamic assembly of protein machinery, was built on the EB1 via a large collection of plus-end tracking proteins such as TIP150, MCAK and SKAP. PCAF acetylates EB1 on K220 and disrupts the stability of a hydrophobic cavity on the dimerized EB1 C terminus, which is essential for SxIP motif containing plus-end tracking proteins. Using photoactivatable complementary fluorescent protein-based super-resolution imaging analyses (Xia et al., 2014), we have delineated the structure-activity relationship of uncharacterized EB1 intrinsically disordered regions. To study how microtubule plus-end, a comet shape machinery that facilitates microtubule polymerization, we reconstituted EB1-dependent microtubule polymerization *in vitro* using purified recombinant proteins. We found that macromolecular

crowding drives assembly of the key plus-end tracking protein TIP150 into spherical condensates that morphologically and dynamically resemble *in vivo* microtubule plus-end. These TIP150 condensates recruited the microtubule depolymerase MCAK that control microtubule length in addition to plus-end stabilizer SKAP. These results establish a previously uncharacterized regulatory mechanism governing microtubule plus-end tracking machinery and thereby the plasticity and dynamics of cells.

Date: 15 January 2019 (Tuesday)

Prof. Nancy Ip, HKUST

"Understanding synaptic dysfunctions in Alzheimer's disease: Insights for therapeutic development"

Alzheimer's disease (AD), a leading cause of mortality in the elderly, is characterized by memory loss and impaired cognitive functions. Its pathological hallmarks are the accumulation of amyloid plaques comprising amyloid-beta (Aβ) peptides and neurofibrillary tangles in the brain. The soluble oligomeric forms of Aβ are thought to be detrimental to synaptic functions and plasticity, which lead to cognitive impairment in AD. Thus, investigating the molecular mechanisms that mediate Aβ accumulation and synaptic dysfunctions is critical for understanding of the pathological basis of AD and enables the identification of molecular targets.

In this seminar, I will talk about our recent work, which led to the identification of two cell surface receptors as potential drug targets for AD. My team and I first determined the role of EphA4, a receptor tyrosine kinase and negative regulator of synaptic plasticity in the brain, in mediating the synaptic dysfunctions in AD. EphA4 in the postsynaptic hippocampus is activated by ephrin-A on astrocytes, resulting in dendritic spine loss and a decrease of excitatory synapses. We found that in AD transgenic mouse models, postsynaptic EphA4 is overactivated in the hippocampus, leading to synaptic plasticity impairment. We subsequently identified small molecule EphA4 inhibitors and demonstrated their ability to alleviate impaired synaptic plasticity and pathology in AD. Thus, we discovered a potential therapeutic strategy for AD. Meanwhile, microglia, the major myeloid cell type in the brain, have emerged as important mediators of AD pathogenesis. We first determined that impaired signaling of interleukin-33 (IL-33) and ST2 (its receptor, which is expressed on microglia) is associated with disease progression, and subsequently demonstrated that injection of IL-33 into an AD transgenic mouse model rescued synaptic dysfunctions and contextual memory deficits. The beneficial actions of IL-33 were mediated by regulating the activation state and functions of microglia. Specifically, IL-33 enhanced microglial motility towards amyloid plaques as well as phagocytosis and degradation of Aβ. Our work reveals new signaling pathways for the development of therapeutic interventions for AD.

Prof. Peng Li, Tsinghua University

"Organelle contact and lipid homeostasis"

Organelle-organelle cross-talk via a direct contact plays a crucial role in metabolic regulation and aging development. Lipid droplets (LDs) are responsible for lipid storage and intracellular lipid homeostasis. We have shown that CIDE family proteins, a class of LD- and ER-associated proteins, are important regulatory factors for LD growth and lipid storage by highly enriching at LD-LD contact sites (LDCS) and promoting atypical form of LD fusion. We have also identified several other factors that control LD fusion and growth and elucidated their detail biochemical and biophysical mechanism. Recently, we have identified Rab18 as an important RabGTPase in controlling LD growth and maturation. Rab18 interacts with the ER-associated NAG-RINT1-ZW10 (NRZ) tethering complex and their associated SNAREs (Syntaxin18, Use1, BNIP1), resulting in the recruitment of ER to LD and the formation of direct ER-LD contact. Overall, we have identified various protein machineries that mediate LD-LD or ER-LD contact and elucidated their role in regulating lipid homeostasis and the development of metabolic diseases.

Prof. Yi Zhong, Tsinghua University

"Molecular mechanisms underlying reversible forgetting-based dynamic memory maintenance"

Memory consolidation theory suggests that upon completing formation, memory cannot be further enhanced, but can be maintained at a stable strength with sufficient proteins synthesized to compensate their turnovers. The current study, however, reveals that hippocampus-dependent memory could be enhanced, even long after formation. We found that contextual fear memory is maintained at a middle level determined via learning-induced interplay between Rac1 activity that causes forgetting and expression of a suppressor of Rac1 activity, □2-chimaerin. A stronger inhibition of activated Rac1 through overexpression of □2-chimaerin orpharmacological Rac1 inhibition not only enhance memory at any time during maintenance period, but also bring back optogenetically-induced forgotten memory or naturally decayed memory. Our findings demonstrate a fundamental role of reversible forgetting in dynamic memory maintenance.

Prof. Kai Liu, HKUST

"Neuronal Intrinsic Mechanisms Regulating Axon Regeneration"

The failure of axon regeneration in the adult mammalian central nervous system (CNS) attributed to two properties of the adult CNS, the inhibitory extrinsic environment and a diminished intrinsic regenerative capacity of mature CNS neurons. Deleting Pten (phosphatase and tensin homolog) in retinal ganglion cells (RGCs) and corticospinal motor neurons (CSMNs) promotes robust axon regeneration. Importantly, the loss of the regrowth potential of axons is accompanied by a corresponding down-regulation of mTOR activity in neurons upon completion of development. An injury further diminishes neuronal mTOR activity. Our recent findings suggest that Pten deletion promotes regeneration in a chronic spinal cord injury model, and enhancing neuronal activity by melanopsin/GPCR signaling promotes axon regeneration in adult CNS. We also demonstrated that rapamycin-resistant mTOR function is required for sensory axon regeneration induced by a conditioning lesion. By doing single cell analysis on isolated regenerated neurons, we further revealed the downstream effectors of mTOR signaling in the axon regeneration.

Prof. Yiguo Wang, Tsinghua University

"Hormonal Regulation of Glucose Homeostasis"

Hepatic glucose is tightly regulated by hormonal and nutritional signals. Dysfunction of regulatory signals and glucose metabolism is linked to metabolic diseases such as type 2 diabetes. Therefore, it is extremely important to find novel modulators of glucose metabolism and investigate their regulatory roles. Here we show that hormonal signaling orchestrate glucose metabolism in the liver during fasting.

Prof. Guangshuo Ou, Tsinghua University

"Cooperation of Microtubule-based Motility Determines Organelle Fidelity in C. elegans Neurons"

The kinesin-2 family motor proteins powers anterograde intraflagellar transport (IFT). In Caenorhabditis elegans sensory cilia, the anterograde IFT is driven by cooperation of heterotrimeric kinesin-II and homodimeric OSM-3-kinesin. Our combination of genome-editing method and super-resolution time-lapse microscopy offers nanometer and millisecond resolutions to understand motor behaviors in live animals. We show that IFT-motor proteins move differently along doublet microtubules in cilia. We reveal how the slow kinesin-II motor and the fast OSM-3 motor move the same cargo. While the loss of either kinesin-II or OSM-3 does not perturb the formation of the middle ciliary segments, transmission electron microscopy uncovers that the organization of nine doublet axonemal microtubules are defective in mutant cilia. Our results indicate that axonemal doublet microtubules are heterogeneous to support kinesin motility and highlight that the coordinated motility of different motors is essential for organelle fidelity.

Prof. Hongwei Wang, Tsinghua University

"Methodology development in pushing the boundary of Cryo-EM"

As Cryo-EM is becoming a powerful tool in structural biology, there are still many challenges on the way for the technique to span its full wing. We are devoted to develop new methods in Cryo-EM from specimen preparation to electron optics. We found that the combination of Cs-corrector and phase plate allows novel cryo-EM imaging strategies. We also developed new supporting materials for more successful and robust Cryo-EM specimen preparation. In combination, we have pushed the lower boundary of single particle Cryo-EM in solving macromolecules as small as 50 kDa.

Prof. Shangyu Dang, HKUST

"Structural insight into TRPV5 channel function and modulation"

TRPV5 (transient receptor potential vanilloid) is a unique calcium-selective TRP channel that is essential for calcium homeostasis. Unlike other TRPV channels, TRPV5 and its close homologue, TRPV6, do not exhibit thermosensitivity or ligand-dependent activation, but are constitutively open at physiological membrane potentials and modulated by calmodulin in a calcium-dependent manner. Here, we report high resolution electron cryo-microscopy (cryo-EM) structures of truncated and full-length TRPV5 in lipid nanodiscs, as well as that of a TRPV5 W583A mutant and TRPV5 in complex with calmodulin (CaM). These structures highlight the mechanism of calcium regulation and reveal a flexible stoichiometry of calmodulin binding to TRPV5.

Prof. Bailong Xiao, Tsinghua University

"Feeling force with the mechanosensitive Piezo channels"

The evolutionarily conserved Piezo family of proteins forms the long-sought bona fide mammalian mechanosensitive cation channel, and plays critical roles in various mechanotransduction processes such as touch, proprioception, vascular development and blood pressure regulation. Mammalian Piezo proteins contain over 2500 amino acids with 30-40 predicted transmembrane segments (TM), and do not bear sequence homology with any known class of ion channels. These features make their structure-function studies and drug discovery challenging. Taking a multidisciplinary approach combining protein engineering and purification, cryo-EM, electrophysiology, drug screening and mouse genetics, we aim to understand how the mechanosensitive Piezo channels serve as effective mechanotransducers for converting mechanical force into electrochemical signals, and how their mechanosensitivity and ion permeation properties precisely control various biological processes involving mechanotransduction. In this talk, I will present our recent progress in revealing the structure, ion-permeation, mechanogating, molecular and pharmacological regulation mechanisms of the Piezo channels.

Prof. Xuhui Huang, HKUST

"From Molecular Dynamics to Genomic Biology: Constructing Kinetic Network Models to Elucidate Transcriptional Fidelity of RNA Polymerases"

Transcription, the synthesis of RNA from a complementary DNA template, plays a crucial role in cellular regulation, including differentiation, development, and other fundamental processes. In this talk, I will discuss our results on modeling the RNA polymerase II (Pol II, a system with ~400K atoms) Translocation and other functional conformational changes of this enzyme at sub-millisecond timescales. We have developed a novel algorithm, Hierarchical Nystrom Extension Graph method, to construct kinetic network models to extract long timescale dynamics from short simulations. For example, we reveal that RNA polymerase II translocation is driven purely by thermal energy and does not require the input of any additional chemical energy. Our model shows an important role for the bridge helix: Large thermal oscillations of this structural element facilitate the translocation by specific interactions that lower the free-energy barriers between four metastable states. The dynamic view of translocation presented in our study represents a substantial advance over the current understanding based on the static snapshots provided by X-ray structures of transcribing complexes. I will also present our recent progress on extending our kinetic network model to include sequence-dependent molecular dynamics of Pol II elongation to predict transcriptional accuracy in the genome-wide transcriptomic datasets. This model creates a critical link between the structural-mechanics understanding of Pol II fidelity and the genome-wide transcriptional accuracy. At the end of my talk, I will also briefly discuss our recent work on developing small-molecular compound inhibitors of polymerase inhibitors.

Prof. Jiguang Wang, HKUST

"Mutational Landscape of Secondary Glioblastoma Guides MET-Targeted Trial in Brain Tumor"

Low-grade gliomas almost invariably progress into secondary glioblastoma (sGBM) with limited therapeutic option and poorly understood mechanism. By studying the mutational landscape of 188 sGBMs, we find significant enrichment of *TP53* mutations, somatic hypermutation, *MET*-exon-14-skipping (*MET*ex14), *PTPRZ1-MET* (ZM) fusions, and *MET*amplification. Strikingly, *MET*ex14 frequently co-occurs with ZM fusion and is present in ~14% of cases with significantly worse prognosis. Subsequent studies show that *MET*ex14 promotes glioma progression by prolonging MET activity. Furthermore, we describe a MET kinase inhibitor, PLB-1001, that demonstrates remarkable potency in selectively inhibiting *MET*-altered tumor cells in preclinical models. Importantly, this compound also shows blood-brain barrier permeability and is subsequently applied in a phase I clinical trial that enrolls *MET*-altered

chemo-resistant glioma patients. Encouragingly, PLB-1001 achieves partial response in at least two advanced sGBM patients with rarely significant side effects, underscoring the clinical potential for precisely treating gliomas using this therapy.

Prof. Ting Zhu, Tsinghua University

"Building mirror-image biology systems"

The overwhelmingly homochiral nature of life has left a puzzle as to whether mirror-image biology systems based on a chirally inverted version of molecular machinery could also have existed. So far, we have shown that two processes in the central dogma of molecular biology, the template-directed polymerization of DNA and transcription into RNA, can be catalyzed by a chemically synthesized D-amino acid polymerase on an L-DNA template. The establishment of molecular systems with an opposite handedness is a small step towards chemically synthesizing an alternative, mirror-image form of life in the laboratory. It also highlights the potential to exploit enzymatically produced mirror-image biomolecules as research and therapeutic tools.

Prof. Fei Sun, HKUST

"Unleashing Chemical Power from Protein Sequence Space for Bio Material Design"

A central question facing the bottom-up approach toward material design is how to faithfully transfer the function at the molecular level to the material properties at the macroscopic level. In the past years, there has been a growing trend of designing functional materials with dynamically tunable properties. These 'smart' materials necessitate a new level of control over the structural and functional properties of macromolecules as well as their interactions with external stimuli. Although natural evolution has led to the creation of a vast number of protein molecules with extraordinary structural and functional diversity, such an ecological diversity has yet to be fully utilized to design and create macroscopic 'smart' materials. Taking advantage of a new category of protein chemistries—genetically encoded click chemistry, we focus on the development of protein materials through the combined use of cellular synthesis and directed assembly of recombinant protein molecules, which has led to a variety of applications ranging from tissue engineering to environmental remediation.