NUS National University of Singapore | Department of Biological Sciences, Faculty of Science

SEMINAR

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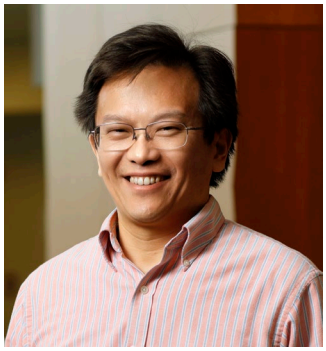
Hosted by Assoc. Prof Liou Yih-Cherng

Cryo-EM applied to define long-sought anion shunter in regulated secretion and advance molecular therapeutics

By **Qiu-Xing Jiang**

Taishan Professor & Director, Cryo-EM Center for Marine Biology, Laoshan National Laboratory; Affiliate professor at State University of New York at Buffalo



Cryo-EM single particle analysis has produced thousands of near-atomic resolution structures in 10 years. Although most of (>90%) these structures do not reach 2.5 Å in resolution and are not suitable for conventional methods in structure-based drug design (SBDD), they revealed significant mechanistic insights on key cellular processes. The first part of the talk will focus on characterization of the anion shunt channel in regulated secretion. All our evidence supports that chromogranin B (CHGB), recombinant and native, suffices to reconstitute a highly selective anion channel, and makes an essential component of the anion shunter. Further, a near-atomic resolution cryo-EM structure of bovine CHGB dimer reveals the ultrastructural features suitable for forming a multi-ion pore. The second part will discuss a recent success in utilizing computational analysis of a large number of ligand poses to rank their binding potency, and select the best ones based on a 3.1 Å cryo-EM structure, which allowed us to design and improve significantly the potency of a MTA-synergic inhibitor against human protein arginine methyl transferase 5 (PRMT5). This new strategy, even though still needing more tests, suggests that computational analysis of ligand poses can support cryo-EM SBDD at current achievable resolutions.

About the Speaker

Prof. Qiu-Xing Jiang obtained his B.S., M.S. and PhD from the University of Science and Technology of China (USTC), Chinese Academy of Sciences Institute of Biophysics, and Yale University School of Medicine, respectively. After postdoctoral training in Yale and the Rockefeller Universities, he taught at the University of Texas Southwestern Medical Center, the University of Florida, Hauptman-Woodward Medical Research Institute / University of Buffalo in New York, and directed and/or built cryo-EM centers in the three institutions. He recently joined Laoshan National Laboratory as a Taishan Professor and director of the cryo-EM Center for Marine Biology. Prof. Jiang was granted the National Institute of Health EUREKA award, American Heart Association National Innovative Award, Cystic Fibrosis Foundation Pilot Research Award, etc. His group has published ~45 papers, including those in high-impact journals, such as Nature, Cell, PNAS, Nature Communications, eLife, etc. His research area is Molecular Physiology and Biophysics, and he has made original contributions in the lipid-dependent gating of voltage-gated ion channels, roles of ion channels in regulated secretory pathways, ON-OFF control of intracellular RNA-binding proteins and structural basis, and chemical functionalization of nanometer-thick carbon or graphene films for cryo-EM and membrane biology.