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Hosted by Assoc Prof Liou Yih-Cherng

By YAN Nieng

Director of Shenzhen Bay Laboratory (SZBL), Shenzhen Medical Academy of Research & Translation (SMART)

Prof. Yan Nieng earned her Bachelor's Degree in Biological Science and Technology from Tsinghua University in 2000 and completed her Ph.D. in Molecular Biology at Princeton University in 2004, where she also conducted postdoctoral research. She became a professor at Tsinghua University's School of Medicine in 2007 and returned to Princeton in 2017 as the inaugural Shirley M. Tilghman Professor. In 2022, she was the Founding President of the Shenzhen Medical Academy of Research & Translation (SMART) and in 2023, she became the Director of Shenzhen Bay Laboratory (SZBL).Dr. Yan specializes in the structural and mechanistic investigation of membrane transport proteins, significantly contributing to our understanding of human glucose transporters, voltage-gated sodium and calcium channels, and proteins involved in sterol metabolism. Her current research focuses on structure-guided drug discovery for pain relief, earning her numerous accolades.

CryoSeek: A Structure-First strategy for discovery

Carbohydrates are the most abundant biomolecules on Earth. Despite their physiological importance, the structural biology of glycans has significantly lagged behind that of proteins and nucleic acids. The crystal structure of the human glucose transporter GLUT3 bound to D-glucose at 1.5 Å resolution clearly demonstrates that the transporter can recognize both α- and β-anomers. This finding underscores the power of high-resolution structures in elucidating the stereochemistry of sugars. While cryo-EM has enabled the structural resolution of glycan chains that modify the extracellular surface of membrane proteins, it has largely been limited to a small number of sugar residues near the modification site and at moderate resolutions. We have been striving to solve high-resolution structures of full glycan chains with little success until recently. By employing a strategy called CryoSeek, we have successfully resolved the high-resolution structures of numerous glycans with higher-order structural assemblies. In this presentation, I will focus on the serendipitous discovery of an 8,000-residue glycoprotein, which we named Mstax. This protein serves as the central shaft for the lateral hairs, known as mastigonemes, that line the cilia of Chlamydomonas. Mstax alone extends over 600 nm from the cilia surface. Notably, it contains a PDK2-like transmembrane domain, which provides an immediate explanation for the previously reported association between mastigonemes and PKD2 subunits. Whether Mstax and PKD2 proteins, along with a third component SIP, form a functional channel remains to be investigated.