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Keynote 2, Prof. Yifan Cheng: Single particle cryo-EM of membrane proteins

Wednesday 9 October 2019 14:35 (40 minutes)

With the technological breakthroughs in the past few years, single particle cryo-electron microscopy (cryo-EM) has enabled rapid progresses in structure determination of integral membrane proteins, particularly ion channels. The pace of structure determination of integral membrane proteins by single particle cryo-EM is unprecedented in structural biology. With such a rapid progress, it is also very critical to interpretation of cryo-EM density maps carefully to ensure that interpretation is data-driven. I will discuss some practical examples to demonstrate the significance of careful interpretations of single particle cryo-EM density maps.

Furthermore, as a prominent example in structural biology of membrane proteins, structural studies of transient receptor potential (TRP) channel superfamily demonstrated nicely how technological breakthroughs impacts scientific discoveries. As an example of our recent studies of TRP channels by single particle cryo-EM, TRPV5 (transient receptor potential vanilloid 5) represents a unique calcium-selective TRP channel essential for calcium homeostasis. Unlike other TRPV channels, TRPV5 and its close homolog, TRPV6, do not exhibit thermosensitivity or ligand-dependent activation but are constitutively open at physiological membrane potentials and modulated by calmodulin (CaM) in a calcium-dependent manner. Structural studies of truncated and full-length TRPV5 in lipid nanodiscs, as well as of a TRPV5 W583A mutant and TRPV5 in complex with CaM provide novel insights to the mechanism of calcium regulation and reveal a flexible stoichiometry of CaM binding to TRPV5.

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