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THE HONG KONG UNIVERSITY OF SCIENCE & TECHNOLOGY

Division of Life Science

Seminar Notice

"Molecular Choreography of KATP visualized by cryo-EM"

by

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(Faculty Candidate)

Abstract

Electrical signaling in neurons, muscle and endocrine cells is coupled to metabolic activity by KATP channels. These molecular devices are large ~0.9 MDa membrane protein complexes composed of a tetrameric K^+-channel (Kir6) and four ATP-binding cassette (ABC) transporters (SUR). Using the abundance of ADP and ATP as a proxy for cellular energy level, they suppress electrical activity when a shortfall in energy supply is detected. In pancreatic beta cells, KATP's ADP/ATP sensing capability is harnessed to couple insulin secretion to blood glucose levels. Exactly how KATP channels sense changes in the intracellular adenine nucleotide pool is not well understood but is fundamental to an understanding of how improper regulation of KATP can cause disease and how deficits in KATP function may be corrected. I will discuss my efforts to understand the energy sensing mechanism by leveraging single-particle cryo-electron microscopy to visualize two dramatically different poses of human pancreatic KATP complexed with both ATP and ADP. These structures reveal how ATP binding to Kir6 inhibits KATP channels and identifies the SUR "consensus" ATPase site as the molecular sensor of ADP. They also suggest a plausible mechanism by which ADP binding induces large conformational changes in SUR to allosterically override basal inhibition of Kir6 by ATP. My work illustrates how nature re-purposed an ABC transporter to regulate an ion channel and provides a paradigm to understand the operation of related KATP channels in neurons and muscle.

Date : 28 February 2018 (Wednesday)

Time : 4:30 p.m.

Venue : Room 4582 (Lifts 27/28)
The Hong Kong University of Science & Technology

(Host faculty: Prof. Mingjie Zhang)

ALL ARE WELCOME!!