NANYANG TECHNOLOGICAL UNIVERSITY SINGAPORE

School of Biological Sciences
College of Science

Seminar Announcement

Structure of a voltage-gated K+ ion channel form human T lymphocytes

Date: **26 March 2021, Friday**

Time: **4pm**

Venue: **Classroom 1, SBS**

Ion channels are a vast super-family of membrane proteins that play critical physiological roles in excitable and non-excitable cells. Mutations in ion channels are responsible for more than 130 diseases in humans called “channelopathies”, which include epilepsy, cardiac arrhythmias, kidney disorders and muscle diseases. Due to their presence on the cell membrane, ion channels can be directly targeted by pharmacological compounds. Ion channels have been modulated for local anaesthetics, and for the treatment of cardiovascular, metabolic (type-2 diabetes) and neurological disorders (pain, stroke, epilepsy). Ion channel-modulators account for 2.8% of FDA-approved drugs, and many are included as essential medicines by the World Health Organization. The functional channel in human T lymphocytes is a tetramer of KV1.3 subunits complexed to a tetramer of Kv□2 accessory subunits. KV1.3/KVbeta2 regulates the membrane potential of T cells and provides the counterbalancing K+ efflux to sustain calcium signalling during activation. Peptides from venomous creatures (scorpions, snakes, spiders, centipedes, sea anemone) and diverse small molecules are known to block KV1.3 channel. Despite successes defining binding sites for pharmacological ligands using mutational and electrophysiological approaches, structure-guided design of channel-modulators remains a challenge due to a lack of the structure of human KV1.3/KVbeta2. I will present our recent progress towards structural determination of KV1.3/Kv□2 complex.

Speaker:

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