Tata Institute of Fundamental Research
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Seminar

Dynamics Transitions of the KvAP Voltage Sensor during Lipid-Dependent Gating

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Voltage-dependent potassium (Kv) channels play a fundamental role in neuronal and cardiac excitability and are potential therapeutic targets. They assemble as tetramers with a centrally located pore domain surrounded by a voltage-sensing domain (VSD), which is crucial for sensing transmembrane potential and subsequent gating. Although the sensor is supposed to be in "Up"/activated conformation in both micelles and phospholipid membranes in the absence of membrane potential, toxins that bind VSD and modulate the gating behaviour of Kv channels exhibit dramatic affinity differences in these membrane-mimetic systems. In response to changes in membrane potential, the S4 helix of VSD undergoes a structural transition from resting/'Down' to activated/'Up' conformation, which is an extremely important step for the functioning of a voltage-gated ion channel. Interestingly, apart from voltage-dependent gating, the gating of KvAP channel can also be influenced by the change in membrane lipid composition in a voltage-independent manner (*i.e.*, lipid-dependent gating). My talk will highlight the impact of altered lipid-protein interface that has a strong influence on the structural dynamics of the functionally-important conformations of the KvAP sensor.

Wednesday, Jul 12th 2023

4:00 PM (Tea / Coffee 03.45 PM)

Auditorium, TIFR-H