**Tata Institute of Fundamental Research**
Survey No. 36/P, Gopanpally Village, Serilingampally Mandal, Ranga Reddy Dist., Hyderabad – 500 046

# Seminar

## Investigating the Role of STX11 in Store-Operated Calcium Entry

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### TIFR, Hyderabad

Store-Operated Calcium Entry (SOCE) is necessary for sustained calcium signaling in numerous cell types. Orai1, which forms the pore of the plasma membrane resident CRAC (Calcium Release Activated Calcium) channel, has been studied for nearly two decades, but the sequence of molecular steps that regulate the gating of the channel is not completely characterised. Stim1 (Stromal Interaction Molecule 1), the endoplasmic reticulum (ER)-membrane resident calcium sensor, clusters Orai1 in the ER-PM junctions and was thought to be sufficient for the activation of the CRAC channels. Previous work from our lab has established a crucial role of α-SNAP, a molecule involved in SNARE complex disassembly, in the regulation of SOCE. With the hypothesis that SNARE proteins are also involved in the regulation of SOCE, a previous targeted RNAi screen identified STX11 as one of the potential positive regulators of SOCE. I have studied the molecular basis of STX11 mediated regulation of CRAC channel activity and have found that STX11 co-localises with resting Orai1 in the plasma membrane and directly binds to the C-terminus of Orai1 via the $H_{abc}$ domain. Mutation of key residues in the $H_{abc}$ domain of STX11 and Orai1 C-terminus showed reduced binding with each other leading to diminished SOCE. Although STX11 did not co-localise with Stim1:Orai1 clusters at the ER–PM junctions, its depletion disrupted functional clustering of Orai1, suggesting that STX11 is essential for a relatively early molecular step in the process. Further analysis with constitutively active mutants of Orai1 suggested that STX11 “prepares” resting Orai1 and acts as a molecular switch inducing a conformational change which is crucial for subsequent Stim1 dependent gating of Orai1.

***Tuesday, Feb 17th 2026***

***16:00 Hrs (Tea / Coffee 15:45 Hrs)***

***Auditorium, TIFRH***