

The pore opening mechanism of store-operated CRAC channels

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Store-operated CRAC channels formed by the Orai proteins are a major pathway for calcium signaling in virtually all animal cells and serve a wide variety of functions ranging from gene expression, motility, and vesicle exocytosis which impact a diverse set of physiological processes from neurogenesis to the immune response. CRAC channels are activated by the depletion of Ca^{2+} from the endoplasmic reticulum (ER), triggered physiologically through stimulation of diverse metabotropic surface receptors. In this talk, I will discuss our recent work on the activation mechanism of CRAC channels, focusing on the mechanism of pore opening following interaction of the CRAC channel pore protein Orai1, with its physiological activator, STIM1, and the mechanistic effects of human gain- and loss-of-function mutations on the gating of CRAC channels.