S18-4 Molecular architecture of Ca^{2+} release

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Ca^{2+} release from the endo/sarcoplasmic reticulum (ER/SR) regulates important cellular functions including muscle contraction, hormone secretion and transcription, and its derangements are direct causes of cardiovascular and neurologic disorders. A major aim in our research group is to understand the mechanism of Ca^{2+} release mediated by ryanodine receptor channels, and two proteins related to Ca^{2+} release will be focused in this session. Junctional membrane complexes shared by excitable cells are subcellular ultrastructures characterized by close association between the plasma membrane and ER/SR. Junctophilin subtypes, originally identified in our screening muscle SR components, contribute to the physiological formation of junctional membrane complexes by spanning the ER/SR membrane and interacting with the plasma membrane. In excitable cells from junctophilin-konockout mice, functional coupling between cell-surface channels and ryanodine receptor channels is obviously disturbed to induce lethal phenotypes. On the other hand, it has been proposed that counter ion movement across the ER/SR membrane compensates for charge imbalance generated by release of Ca^{2+} as a cation. We have recently identified TRIC channels acting as a monovalent cation channel. Because TRIC channel-deficient muscle shows severe dysfunction in ryanodine receptor-mediated Ca^{2+} release, TRIC channel subtypes likely correspond to the counter ion channel on the ER/SR.