Toward Uncovering The Structural Basis of RyR's Modified Behavior in Clusters

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Ryanodine Receptors (RyRs) are calcium ion channels on the endoplasmic reticulum frequently associated with pathological calcium dysregulation. The channel is regulated by many associated proteins who's binding induces allosteric signals transmitted from the large cytoplasmic shell of the channel to its pore. Only a subset of these have been characterized structurally. RyR1&2 have been observed to form checkerboard patterned arrays in muscle and heart cells, superstructures pivotal for the amplification of calcium signaling, excitation-contraction coupling (EC-coupling), and calcium oscillation (Gao *et al*., 2022). The size and arrangement of these clusters are correlated with calcium leaks and calcium-induced-calcium-release, and are modulated by auxiliary binding proteins (Asghari *et al*., 2020). To study these interactions on a structural level, sarcoplasmic reticulum from heart tissue is isolated through differential centrifugation and concentrated by on-grid affinity capture to be observed by cryo-electron tomography with sub-tomogram averaging.

References:

Gao, Zhong-Xue, Tian-Tian Li, Han-Yu Jiang, and Jun He. *Calcium Oscillation on Homogeneous and Heterogeneous Networks of Ryanodine Receptor.* arXiv, July 24, 2022.

Asghari, Parisa, David Rl Scriven, Myles Ng, Pankaj Panwar, Keng C. Chou, Filip van Petegem, and Edwin Dw Moore. *Cardiac Ryanodine Receptor Distribution Is Dynamic and Changed by Auxiliary Proteins and Post-Translational Modification*. ELife, January 9, 2020.