A key to calcium signaling: Structure of the human IP3R type 3 in its ligand-free state

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IP3 receptors (IP3Rs) are calcium channels found in all animal cells. By mediating calcium ion release, IP3Rs integrate signals from different cellular pathways and metabolic states. Not surprisingly, deregulation of IP3Rs causes many diseases.

In mammals, there are three subtypes of IP3Rs, of which the type 3 receptor is found predominantly in rapidly proliferating cells including

several cancers. However, due to their large size and subunit diversity, the structure of IP3Rs has not yet been fully characterized.

Now, in a study published in the *Journal of Biological Chemistry*, Erkan Karakas, Ph.D., and colleagues present a structure of the human IP3R type 3 in its ligand-free state.

Their structure, discovered through cryo-electron microscopy, identified previously unresolved local structures, the location of lipid biding sites and the presence of a self-binding peptide (SBP) that occupies the IP3 binding site and competitively inhibits IP3 binding.

The researchers concluded that the SBP could be a key molecular determinant of subtype-specific calcium signaling in IP3Rs.

More information: Caleigh M. Azumaya et al. Cryo-EM structure of human type-3 inositol triphosphate receptor reveals the presence of a self-binding peptide that acts as an antagonist, *Journal of Biological Chemistry* (2020). DOI: 10.1074/jbc.RA119.011570

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