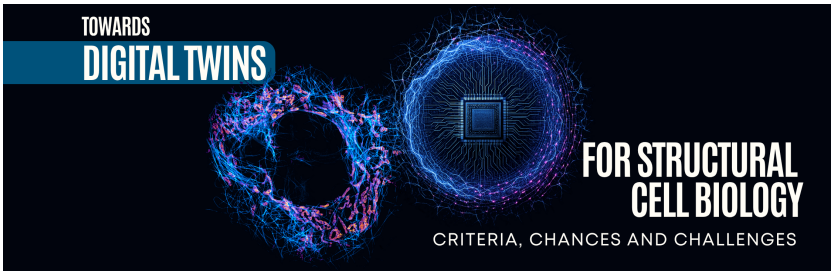

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Insights into the plasma membrane association of Extended Synaptotagmin 3

Wednesday, 4 March 2026 12:05 (20 minutes)

Membrane contact sites between the ER and the PM are site of non-vesicular lipid transport as they harbor various lipid transfer proteins. They are established by protein tethers among which Extended Synaptotagmins (E-Syts) are the most abundant family in mammals. E-Syts are ER-resident and regulate ER-PM connectivity via reversible association of their C2 domains with lipids at the PM. Here, we study exact lipid binding properties of the individual C2 domains of E-Syt3 as well as of a large unstructured linker between the C2B and C2C domains. We use coarse-grained molecular dynamics simulations as well as live-cell confocal and TIRF imaging. We identify novel protein-lipid interactions like PI binding of the C2AB domains and PI4P binding of the C2C domain. Moreover, we show that the unstructured C2B-C2C linker associates with the PM via its aromatic residues. For the C2C domain, we identified two different PM association configurations with different lipid binding profiles.

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Session Classification: Short Talk