

## **Regulated SNARE assembly in membrane fusion**

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In the neuron, SNARE (soluble *N*-ethylmaleimide-sensitive factor attachment protein receptors) assembly plays a central role in driving membrane fusion, a required process for neurotransmitter release. In the cytoplasm, vesicular SNARE VAMP2 (vesicle-associated membrane protein 2) engages with two plasma membrane SNAREs syntaxin 1A and SNAP-25 (synaptosome-associated protein of 25 kDa) to form the core complex that bridges two membranes. While various factors regulate SNARE assembly, the membrane also plays the regulatory role by trapping VAMP2 in the membrane. The fluorescence and EPR analyses revealed that the insertion of seven C-terminal core-forming residues into the membrane controls complex formation of the entire core region, even though preceding 54 core-forming residues are fully exposed and freely moving. When two interfacial Trp residues in this region were replaced with hydrophilic serine residues, the mutation supported rapid complex formation. The results suggest that the membrane-proximal region of synaptobrevin is a regulatory module for SNARE assembly, which provides new insights into the calcium-triggered membrane fusion.