SynCAMs Organize Synaptic Membranes Through Heterophilic Adhesion

Thomas Biederer1, Adam Fogel1, Massimiliano Stagi1, Alexander Krupp2, Valentijn Stein2

1Yale University, Department of Molecular Biophysics and Biochemistry, New Haven, Connecticut, USA
2Max-Planck-Institute of Neurobiology, Martinsried, Germany

Overview
SynCAMs are a family of four adhesion molecules expressed strongly during the major period of brain circuit development. Previous work has shown that SynCAMs can play an active role in synapse development, similar to activities described for neurotrophins, Eph receptors, and NGL. We have now developed tools to study each of the SynCAM isoforms. Our studies focus on SynCAM 1 and 2, which we hypothesize to form a synaptic adhesion complex with roles in synapse development and stabilization. We also identified interactions between SynCAMs 3 and 4 (not shown here) in the central nervous system, which play important roles in the regulation of neurotransmitter release (Spiegel et al., 2007; Ménard et al., 2007).

Background
 Tight adhesion between the presynaptic and postsynaptic neuron is a critical biochemical and morphological feature of synapses in the central nervous system. The adhesion complexes have been visualized using cryo-electron tomography.

Model of synapse-organizing adhesive interactions. SynCAMs are neuronal surface molecules mediating adhesion at synaptic sites. Their activity is critical for synapse formation and stabilization during development.

Results
SynCAMs fractionate in synaptic plasma membranes. Equal total protein fractions of a subcellular fractionation of rat brain were loaded and analyzed by immunoblotting. Both SynCAM 1 and 2 are enriched in synaptic membranes compared to control proteins. SynCAMs 1 and 2 are highly enriched in synaptic membranes with the control protein Rab3a. SynCAMs 1 and 2 are highly enriched in synaptic membranes compared to control proteins. SynCAMs 1 and 2 co-localize at sites of cell-cell contact, a critical biochemical and morphological feature of synapses in the central nervous system. The adhesion complexes have been visualized using cryo-electron tomography.

Discussion
SynCAMs are a family of four adhesion molecules expressed strongly during the major period of brain circuit development. Previous work has shown that SynCAMs can play an active role in synapse development, similar to activities described for neurotrophins, Eph receptors, and NGL. We have now developed tools to study each of the SynCAM isoforms. Our studies focus on SynCAM 1 and 2, which we hypothesize to form a synaptic adhesion complex with roles in synapse development and stabilization. We also identified interactions between SynCAMs 3 and 4 (not shown here) in the central nervous system, which play important roles in the regulation of neurotransmitter release (Spiegel et al., 2007; Ménard et al., 2007).

References


