Adhesion-GPCR signaling in synapse formation

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The brain processes information in millions of parallel and intersecting neural circuits. In neural circuits, neurons are connected by synapses that compute a circuit's information by transmitting and processing neuronal signals. Neural circuit computations critically depend on the number, location and properties of their constituent synapses. We hypothesize that the construction of neural circuits by formation of defined synapses is based on a molecular logic that is produced by the interactions between pre- and postsynaptic recognition and signaling molecules. Understanding how synaptic adhesion molecules build synapses and control their properties requires insight into the identity, function, and mechanism of action of these adhesion molecules. Our recent studies uncovered a central role of two families of adhesion-GPCRs, Latrophilins and BAI's – both erroneously named since latrophilins are not presynaptic α-latrotoxin receptors and BAIs are not brain-angiogenesis inhibitors – in synapse formation. Strikingly, both families of adhesion-GPCRs operate via multiple ligand interaction as GPCRs whose spatially restricted postsynaptic signaling organizes synaptic junctions. Unlike other adhesion-GPCRs, neither family seems to operate via a tethered agonist exposed by GAIN-domain cleavage, but both families mediate G-protein signaling that is essential for the initial formation of specific subsets of synapses. In my presentation, I will discuss our recent results on these fascinating molecules that serve as key drivers of the molecular logic of neural circuits.