Role of Piccolo and Bassoon in assembling and organizing the active zone of neurotransmitter release

*Gundelfinger ED**, Dieck ST*/**, Altrock WD*, Fejtova A*, Dresbach T*, Regus H**, Qualmann B*, Kessels MM*, Brandstätter JH** Ziv NE***, Garner CC****
*Leibniz Institute for Neurobiology, Magdeburg, Germany, **Max Planck Institute for Brain Research, Dept of Neuroanatomy, Frankfurt am Main, Germany, ***Rappaport Institute, Medical School, Technion, Haifa, Israel, ****Nancy Pritzker Laboratory, Stanford University. Palo Alto, CA, USA

The active zone of neurotransmitter release in presynaptic nerve terminals appears as an electron-dense structure associated with the presynaptic membrane: the cytomatrix at the active zone (CAZ). Bassoon and Piccolo are two related proteins thought to serve as specific scaffolding components of the CAZ. During the major period of synaptogenesis both proteins are present on pre-assembled precursor vesicles that carry various major components of the active zone. To study where the pre-assembly of these precursor vesicles takes place, we have transfected primary hippocampal neurons with EGFP-tagged Bassoon and monitored its transport pathway to the active zone. Our data show that Bassoon and Piccolo may associate with membranous compartments near the Golgi region. Considering these and previously published data we propose the hypothesis that active zones are pre-assembled at the Golgi apparatus, transported into axons as discrete precursor packages and fuse with the presynaptic plasma in response to a yet unknown signal. This implies that the assembly of the active zone is a stepwise process.
To learn more about the molecular organization of the CAZ we have studied presynaptic ribbons, a specialization of the CAZ at photoreceptor synapses in the retina. In mice deficient for full-length Bassoon the assembly and anchoring to the presynaptic plasma membrane of synaptic ribbons is severely impaired. RIBEYE is a specific core component of synaptic ribbons. Interaction studies have now revealed that wild-type Bassoon can bind RIBEYE and that this binding site is absent in mutant Bassoon. Consequently, in mutant retinae the recruitment of RIBEYE to synaptic ribbons is less efficient. A homolog of RIBEYE, that also is capable of binding to Bassoon, is found at hippocampal synapses suggesting that similar assembly mechanisms apply to the CAZ brain synapses and synaptic ribbons in the retina.

Eckart D. Gundelfinger, Leibniz Institute for Neurobiology, Brenneckestr. 6, D-39118 Magdeburg, Germany, e-mail gundelfinger@ifn-magdeburg.de

Session 24