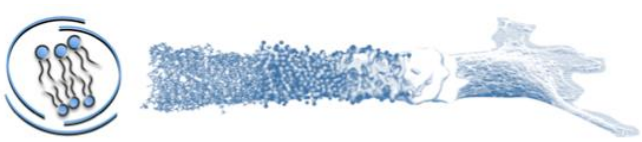
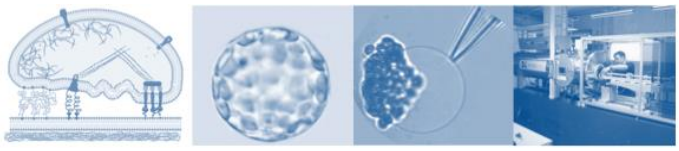

Research Training Group 1962

Dynamic Interactions at Biological Membranes from Single Molecules to Tissue

Speaker: Prof. Dr. Rainer Böckmann, Computational Biology

Invitation to
RTG 1962 – Guest Talk

Tuesday, 13th of November 2018 at 05.00 p.m. (s.t.)

Prof. Dr. Anna Fejtova

(University Hospital Erlangen)

"Role of CtBP1-driven membrane remodelling in the compensatory endocytosis of synaptic vesicles"

Neurotransmitter release from presynapse relies on complex yet precisely regulated sequence of membrane trafficking events. Exocytosis is the rate-limiting factor of evoked neurotransmitter release, but during repetitive stimulation neurotransmission also depends on the time needed for the replenishment of releasable pool of synaptic vesicles. This process is determined by efficiency, by which proteins and membranes of released vesicles are retrieved by compensatory endocytosis and aligned to their release sites to become available for the next cycle of release. In the presynaptic compartment, endocytosis is spatially segregated but temporarily tightly coupled with exocytosis. Moreover, it occurs in different modes that are engaged dependently of synaptic release frequency and presumably accomplished by distinct cellular machineries. The molecular mechanisms behind are far from being completely understood.

We identified C-terminal binding protein 1 (CtBP1) as a new molecular player contributing to the effective retrieval of synaptic vesicles in the presynapses. CtBP1 acts as a scaffold for macromolecular complexes involved in the nuclear regulation of gene expression and in the membrane trafficking at Golgi and plasma membranes in non-neuronal cells. In neurons CtBP1 shows a distinct localization to presynapses in addition to its somatic expression. To assess its synaptic functions we depleted CtBP1 either by RNAi interference or gene knock-out and studied the consequences of these manipulations on neuronal structure and function. The synapses without CtBP1 had normal structure and basal transmission, but showed strongly increased short-term depression of neurotransmission upon repetitive stimulations. Electrophysiological and imaging experiments revealed normal exocytosis but strongly impaired compensatory endocytosis in the absence of CtBP1. These phenotypes could be rescued by expression of CtBP1 but not by its mutant deficient in driving fission of invaginated membranes. Further molecular characterization revealed that CtBP1 regulates endocytosis via activating of PLD1, that catalyses production of the fusogenic phosphatidic acid. Thus, CtBP1 regulates synaptic vesicle retrieval by remodelling of membrane lipids by enabing formation of membrane nanodomains with environment that promotes compensatory endocytosis. Finally, we showed that CtBP1 phosphorylation by the signaling kinase Pak1 regulates a switch in its association from the active zone protein Bsn to the endocytic effector PLD1, thus fine-tuning the membrane trafficking activity of CtBP1 and potentially linking presynaptic endo- and exocytotic processes.

Guests are welcome!

gez. Prof. Dr. R. Böckmann

→ *Venue: Department Biology, Seminar Room Cell Biology (00.581), Building B1, Floor 00, Staudtstraße 5, 91058 Erlangen*