Fachbereich Biologie (10)

JOHANNES GUTENBERG UNIVERSITÄT MAINZ

AG Functional Neurobiology (AG Heine)
Institute for Developmental and Neurobiology (IDN)

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Bachelor and Master projects

Genomic modification of presynaptic targets via CRISPR/Cas9 for imaging

Neuronal communication via chemical synapses is associated with fast electrochemical conversion of signals. At the presynaptic site, arriving action potentials open voltage-gated calcium channels (VGCCs), allowing Ca^{2+} ions to enter the cell. Further, Ca^{2+} ions trigger the rapid release of synaptic vesicles (SV), packed with neurotransmitters, which are subsequently recognized by receptors on the postsynaptic membrane. The strength of the synaptic output can be modified by subcellular localization and composition of VGCCs, calcium sensors, buffers or pumps. Long-lasting changes in synaptic transmission are thought to serve as molecular base of learning and memory formation (Dolphin and Lee 2020; Devendahl and Müller, 2019).

At the presynapse, Ca^{2+} regulates not only SV release but also SV endocytosis, with both processes operating side by side and overlapping in time and space. Thus, precise spatial and time control of Ca^{2+}-dependent processes is essential for synaptic transmission. Using *Drosophila* as a model, we found spatial and functional separation of Cav2-mediated SV release and Cav1-dependent SV recycling at the neuromuscular junction (NMJ, Krick et al., 2021). We demonstrated that the plasma membrane-bound calcium ATPase, PMCA, is a potential key player in spatiotemporal separation of these processes in the *Drosophila* NMJ.

In this project, we aim to investigate the subsynaptic localization and the function of PMCA at presynaptic terminals of mammalian neurons. For this purpose, we apply the CRISPR/Cas9 approach for labeling the target gene on genomic level using murine hippocampal cultures. In your Bachelor/Master thesis you will analyze the success of the knock-in and subsynaptic localization of the target using confocal microscopy. Functional analysis of the labeled target could include single particle tracking or presynaptic calcium imaging in cultured hippocampal neurons.

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