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JOHANNES GUTENBERG UNIVERSITÄT MAINZ

Fachbereich Biologie (10)

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

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Master and Bachelor projects

How do STIM proteins impact Ca^{2+} signals in the endoplasmic reticulum of organotypic hippocampal cultures?

Signalling by calcium ions (Ca^{2+}) governs the most fundamental processes in all types of tissues. Its importance is especially evident in neurons, which rely on Ca^{2+} signals to trigger the release of neurotransmitter. While neuronal plasma membrane Ca^{2+} channels have been studied for decades and are now well characterised, much less is known about the Ca^{2+} machinery that is located in the endoplasmic reticulum (ER). Stromal interaction molecules 1 and 2 (STIM1 and STIM2) serve as sensors of Ca^{2+} concentration in the ER and can activate the so-called store-operated calcium entry (SOCE). Since neurons are equipped with a variety of different Ca^{2+} influx mechanisms (e.g., voltage-gated calcium channels), SOCE was long thought to be a dispensable process for this type of cells. However, recent data provided strong evidence for the importance of SOCE proteins in central neurons.

Previously, in dissociated hippocampal culture we found that stimulation of neurons with glutamate causes massive clustering of STIM molecules, whereas knockdown of STIM2 is associated with drastic reduction of ER Ca^{2+} concentration. The goal of this project is to determine how STIM proteins shape ER Ca^{2+} signals in a more natural neuronal preparation, namely in organotypic hippocampal slices. This will bring new knowledge on the ER-PM communication in a 3D model with physiologically relevant inter-cellular architecture.

Organotypic hippocampal slice cultures will be established from two mouse lines that had been genetically engineered to enable knockdown (KD) of STIM1 or STIM2. To validate the efficiency of the knockdown, immunohistochemical labelling and confocal fluorescence microscopy will be performed. ER Ca^{2+} signals will be monitored by live-cell fluorescence microscopy. Pharmacological treatment and electrical stimulation will be used to investigate the mechanism by which STIM proteins contribute to ER Ca^{2+} signals.

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