PhD 'Cell and non-cell autonomous requirements of L-type calcium channels in pancreatic hormone secretion'

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Deadline: 04.09.2023
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About the Project

**Background:** Endocrine cells of the pancreas express a broad spectrum of voltage gated calcium channel genes. Currently, the contribution to hormone secretion of individual genes is not well understood. The Meyer group previously showed that in zebrafish, all endocrine cells co-express the L-type channel genes CaV1.2 and CaV1.3a and that loss of CaV1.2 results in embryonic hyperglycemia combined glucose-independent activation of embryonic β–cells (Lorincz et al., 2018). Further work now revealed that the ectopic β-cell activation is indirectly caused by a loss of inhibition through δ-cells. The data hint for multiple direct and indirect roles of CaV1.2 in hormone secretion. The Meyer group now generated transgenes for conditional and cell-type specific cacna1c-mutagenesis (using 3C-CRISPR/CAS9 methodology (Hans et al., 2021)) and for whole islet in vivo Calcium imaging (neuroD:H2B-GCaMP6). We will expand our 3C-CRISPR/CAS9 toolbox by two additional transgenes for mutating cacna1da and cacna2d2a, which is the only a2δ-subunit encoding gene expressed in the zebrafish islet.

The successful candidate will characterize these lines regarding the cell and non-cell autonomous functions of these genes on islet-specific calcium dynamics. The candidate will examine their electrophysiological properties via ex vivo patch-clamp experiments in order to identify the underlying mechanisms of the observed phenotypes from our in vivo experiments.

**Methods:** Zebrafish, gene editing using 3C-CRISPR/CAS9, in-vivo calcium imaging, Immunohistochemistry, electrophysiology.


**Salary:** According to the rates of the Austrian Science Fund (FWF) plus travel funds for international scientific meetings and stay abroad.

*The PhD candidate will be part of the International PhD program CavX*

**Contact:** Please send your application including a short letter of motivation, your CV and, if available, a reference letter to dirk.meyer@uibk.ac.at.

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