STUDYING NORMAL AND DISEASED FUNCTIONS OF ALPHA-2-DELTA PROTEINS IN CULTURED NERVE CELLS

Lead partner:
Karl Landsteiner Privatuniversität für Gesundheitswissenschaften

Field(s) of action
Health and nutrition

Scientific discipline(s)
3014 - Neurowissenschaften (30 %)
3011 - Anatomie, Pathologie, Physiologie (30 %)
3030 - Gesundheitswissenschaften (20 %)
1060 - Biologie (20 %)

Funding tool: Dissertations

Project-ID: FTI22-D-032

Project start: 01. Jänner 2024

Project end: 31. Dezember 2026

Runtime: 36 Monate / ongoing

Funding amount: ca. € 71.000,00

Brief summary:
In the brain, calcium regulates important functions e.g., neurotransmitter release, neuronal plasticity. Calcium channels are composed of a pore-forming alpha1 subunit and the auxiliary beta and alpha2delta subunits. Particularly alpha2delta subunits have emerged as major drug targets for gabapentinoid drugs which are currently among the top sold anti-epileptic drugs. Four different alpha2delta proteins exist out of which three are expressed in the brain. A growing number of mutations of alpha2delta proteins have been identified and linked to neurological disorders and the genes encoding for alpha2delta proteins are considered as risk genes for e.g., epilepsy etc. In stark contrast to these important disease associations only little is known about the specific functions of the three alpha2delta proteins found in brain. The fact that many neurons express all three alpha2delta proteins at the same time makes it experimentally challenging to study their individual functions in health and disease. In previous studies the laboratory of Prof. Obermair has identified critical synaptic functions of alpha2delta proteins. In the proposal for my PhD thesis project, I can now build on novel experimental tools developed in an ongoing research project funded by the NFB (LSC19-017) to establish in vitro differentiated nerve cells, which allow investigating the individual neuronal functions of the three alpha2delta proteins. More specifically, I will study the functions of each neuronal alpha2delta proteins in synapse formation, synaptic transmission, and neuronal excitability and I plan to develop an experimental setup for analysing the specific underlying pathophysiological mechanism of alpha2delta mutations associated with autism, schizophrenia, and epilepsy. Taken together, my PhD thesis project will provide novel insights into the formation and function of synapses and may ultimately contribute to understanding the causes for neurological and neuropsychiatric disorders.

Keywords:
calcium channels, neurophysiology, brain research, pathophysiology of brain disorders, in vitro nerve cell culture, imaging