Calcium signaling and gene regulation

Summary

Rainer Schindl, Institute for Biophysics, Medical University of Graz

Supervisors: Prof. Dr. Roland Malli
PD Dr. Rainer Schindl

Availability: This position is available.

Offered by: Medical University of Graz

Application deadline: Applications are accepted between August 02, 2017 00:00 and September 17, 2017 23:59 (CEST)

Description

Background:
An increase in cellular calcium concentration in an important mechanism to stimulate various cell processes. These calcium signals can be fast, in microsecond range to stimulate release of vesicles in a neuronal cell or can last over hours to stimulate gene regulation (Berridge, Biochemical Society Transactions). In addition, calcium signals form repetitive spikes and waves or can be localized to micro-domains in a single living cell. The store-operated Ca\(^{2+}\) channel complex is a ubiquitously expressed system to generate long lasting Ca\(^{2+}\) signals at junctions of the plasma-membrane and the endoplasmic reticulum. The slow Ca\(^{2+}\) influx activates transcription factors like the nuclear factor of activated T-cells (Frischauf et al., Science Signaling). How enhanced cellular calcium levels can generate such diverse signaling modes is still not well understood. Moreover dysfunctional Ca\(^{2+}\) signaling is suggested as a cofactor for cancer cell development.

Hypothesis and Objective:
Calcium signaling complexes to stimulate gene regulation
The PhD will study the role of calcium ion channels and Ca\(^{2+}\) dependent gene regulation for physiological and patho-physiological processes (Frischauf et al., Science Signaling). The investigated Ca\(^{2+}\) channels will include the store-operated Ca\(^{2+}\) channel complex, STIM1 and Orai1 but also the recently discovered endoplasmic reticulum Ca\(^{2+}\) load activated channel TMCO1 (Wang et al.). Specifically, this PhD project will investigate how physiological calcium signaling in single immune and muscle cells are regulated. These live cell recordings will aim to understand micro-domain signaling and ion-channel protein network to activate transcriptional programs. Experiments will be conducted in close collaboration with international laboratories. This will include structural biologists to collaborate on atomic structure of transcription factors. Oncologists to investigate the impact of Ca\(^{2+}\) for cancer cell development. As well as computer simulation experts to model the Ca\(^{2+}\) signaling processes. Pathological calcium signaling will focus on immune deficiency, myopathy and cancer.

Methodology:
The PhD student requires the spirit to learn different techniques and likes to be involved in intense collaboration with leading laboratories in this multifaceted research field. At the institute of biophysics the PhD student will perform live cell techniques including electrophysiological patch-clamp recordings and fluorescence imaging. Calcium proteins will be genetically engineered by using molecular biology techniques and biochemical techniques such as cysteine scanning methods.

References:
Calcium signalling remodelling and disease. Michael J. Berridge. Biochemical Society Transactions Apr 01, 2012, 40(2)297-309; DOI: 10.1042/BST20110766


To get more information or to apply online, visit https://mug.glowbase.com/positions/79 or scan the code on the left with your smartphone.