Investigating the potassium homeostasis of the nucleus

Summary

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Supervisor: Prof. Dr. Roland Malli
Availability: This position has been occupied.
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:
We recently developed a series of novel genetically-encoded potassium ion (K⁺) indicators, which enable real-time monitoring of K⁺ in single cells and subcellular compartments (patent pending, manuscript submitted). Our data point to high K⁺ levels and spatial subcellular K⁺ dynamics (e.g. within the nucleus) of intact living cells. However, the regulatory mechanisms and the role of K⁺ signals within the nucleus in physiology and pathology remains largely elusive. Just few reports from the 1970ties [1] and 1980ties [2] speculate about increased nuclear K⁺ levels and their putative impact on DNA stability and gene expression. Within this thesis project the mechanisms responsible for controlling the nuclear K⁺ homeostasis should be investigated. Moreover, K⁺ fluctuations within the nucleus in response to defined stresses and stimuli should be explored using high resolution fluorescence microscopy. Finally, DNA stability, DNA-protein interactions, and changes in gene expression should be correlated with defined nuclear K⁺ alterations.

Hypothesis and Objectives:
We hypothesise that K⁺ fluctuations within the nucleus are fundamental to dynamically control DNA metabolism and gene expression in health and diseases. With the usage of the novel K⁺ probes in combination with genetic manipulations of the expression levels of K⁺ channels, exchangers and transporters of the nuclear envelope the nuclear K⁺ homeostasis will be characterized. Consequences of K⁺ variaitons within the nucleus on DNA integrity and gene expression will be analyzed.

Methodology:
In addition to classical cell culture, biochemistry- (WB) and molecular biology techniques (PCR, siRNA library screens) the Ph.D. candidate will work with genetically encoded tools and probes as demonstrated in references [3,4] and use state-of-the-art fluorescence imaging techniques [3,4] to visualize subcellular K⁺ signals in real-time on the level of individual cells.

References:


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