Medical University of Graz

The role of KCNMA1/BKCa channel for maintenance of vascular tone in pulmonary arteries

Summary

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Supervisor:	Prof. Dr. Andrea Olschewski
Availability:	This position is available.
Offered by:	Medical University of Graz
Application deadline:	Applications are accepted between February 10, 2020 00:00 and March 30, 2020 23:59 (Europe/Zurich)

Description

Background:

The pulmonary circulation is often abnormal in patients with inflammatory lung diseases and it is associated with a higher frequency of severe exacerbations and hospitalizations as well as poor survival (1). Better understanding of the pathobiology of the lung vascular remodelling is needed to identify new molecular targets for specific therapeutic interventions in the future. We have previously shown, that modification of ion channels in pulmonary vascular cells play a central role for controlling pulmonary vascular tone and thus for remodelling of vessels, contributing to morbidity and mortality in paediatric and adult patients (2,3,4). Using laser capture microdissected pulmonary arteries of freshly explanted healthy donors and lung from inflammatory lung diseases patients with pulmonary hypertension, we detected aberrant expression of calcium-activated potassium channels (KCNMA1/BKCa). Thus, the current project will evaluate the relevance of BKCa channel for endothelial dysfunction in pulmonary arteries. The project will focus on peroxisome proliferator–activated receptor (PPAR) agonists as activator of BKCa channel for its non-genomic and genomic influence on the pulmonarycirculation (5).

Hypothesis and Objectives:

We hypothesis, aberrant BKCa channel function leads to endothelial dysfunction and remodelling in lung disesases.

This project aims to: (1) identify the role of BKCa channel for pulmonary vascular tone and (2) prove the BKCa channels as direct targets of PPAR agonists and its potential implications for endothelial function.

Methodology:

The student will apply a broad range of in-vitro, ex-vivo and in-vivo investigations. Cellular implications will be detected with standard molecular biological methods. Ex-vivo wire-myograph on human and mouse pulmonary arteries will be carried out to investigate the role of BKCa channel in endothelium and the modification of the channels by PPAR agonists. In-vivo studies on global and cell-specific knock-out mice will be employed to investigate the functional relevance of BKCa channel for pulmonary arteries and lung function in disease models.

References:

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