Medical University of Graz

Immune / vascular endothelial cell crosstalk drives pathogenic remodelling

Summary

Grazyna Kwapiszewska-Marsh, Otto Loewi Research Center (Physiology), Medical University of Graz/ Ludwig Boltzmann Insititute for Lung Vascular Research

Supervisor:	PD Dr. Grazyna Kwapiszewska-Marsh
Availability:	This position is available.
Offered by:	Medical University of Graz
Application deadline:	Applications are accepted between August 14, 2020 00:00 and October 10, 2020 23:59 (Europe/Zurich)

Description

Background:

Vascular abnormalities are a common feature of chronic lung diseases, such as pulmonary fibrosis (PF). These abnormalities manifest as pulmonary arterial remodelling and obliteration, as observed in pulmonary hypertension (PH), or as changes in vascularity and vessel distributions as observed in PF. Current studies indicate that endothelial cell (EC) dysfunction, with increased endothelial cell apoptosis and hyperproliferation of remaining apoptosis-resistant cells are key pathomechanisms underlying vascular remodelling. Moreover, immune cells can actively modulate EC behaviour and fostering disease progression. We have previously shown pronounced pulmonary vascular remodelling in PF, and that the immune cell signature is strongly altered and associates with vascular remodelling (Hoffmann, 2014; Marsh, 2018). Further we shown that transcription factor fos-realted antigen-2 (Fra-2) is a master regulator of pulmonary vascular and parenchymal remodelling, and controls the immune response (Birnhuber, 2019a, b).

Hypothesis and Objectives:

We hypothesize that altered cross-talk between immune and EC leads to vasculopathy and consequently to development of pulmonary fibrosis. Using a wide array of methods and models, we will investigate the influence of Fra-2 on EC function and EC crosstalk with immune cells in the development of pulmonary fibrosis.

Methodology:

Characterisation and isolation of immune cells will be conducted by flow cytometry, cell-sorting and MACS approaches. Disecting of the immune and EC cross-talk will be achieved in co-culture systems. The receptor–ligand interaction will be analysed in silico as well as in vitro. Primary endothelial cell cultures from healthy and diseased lung tissue (human and murine) will be performed for *in vitro* assays to assess endothelial cell function. Studies on human lung tissue will complement the variety of *in vivo* approaches. Additionally, in vivo approaches in the lineage tracing mouse models (El Agha, 2017; Crnkovic 2018) will prove validity of our findings.

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