Medical University of Graz

# Immune cell crosstalk as drivers of vascular remodelling

## Summary

*Leigh Marsh, Ludwig Boltzmann Insititute for Lung Vascular Research*

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| Supervisor: | PD Dr. Leigh 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:

Cardiovascular diseases are one of the leading causes of adult mortality worldwide and associated with poor quality of life. A common theme underlying these diseases is inflammation and an altered immune response. In pulmonary hypertension (PH) the degree of immune cell infiltration is associated with degree of vascular remodelling. Previously, we have used advanced flow cytometry to shown that the idiopathic form of PH presents with a distinct inflammatory cell landscape. Within this landscape, two previously uncharacterized populations were identified, potentially involved in disease pathogenesis namely, γδT-cells and plasmacytoid dendritic cells (pDC). Both cell types exist at the cross-roads between innate and adaptive immunity and therefore may control the transistion to a chronic inflammatory environment found with in PH.

Hypothesis and Objectives:

We hypothesise that γδT-cells and pDC potentiate vascular remodeling by altering the local inflammatory environment. We will investigate how the cellular crosstalk between these cells, other immune cells (e.g. macrophages and T cells), and structural cells alters vascular homeostasis and ultimately controls disease pathogenesis.

Methodology:

Flow cytometry will be used to identify pDC and γδT-cells and their activation states in both healthy and diseased lung tissue. Immune cell cross-talk will be investigated in vitro using isolated (FACSsorting/MACS) pDC/ γδT-cells and effector cells to determine cell activation or polarisation (proliferation/ cytokine production). To determine how the immune cells control structural cell behaviour, direct and indirect co-culture systems, using primary human cells isolated from both healthy and diseased lung tissue, will be used. Secreted factors will be identified determined by multiplex ELISA and expression profiling, and functional blocking experiments (antibodies/small molecule inhibitors) will test their role in modulating structural cell behaviour.

References:

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