Phenotypic fibroblast switch leads to lung fibrosis

Summary

Grazyna Kwapiszewska, Otto Loewi Research Center, Physiology & Ludwig Boltzmann Institute for Lung Vascular Research, Medical University of Graz

Supervisor:	PD Dr. Grazyna Kwapiszewska
Availability:	This position is available.
Offered by:	Medical University of Graz
Application deadline:	Applications are accepted between February 04, 2019 00:00 and March 31, 2019 23:59 (Europe/Zurich)

Description

Background:

Vascular and parenchymal abnormalities are a common feature of chronic lung diseases such as pulmonary fibrosis (PF). Vascular abnormalities manifest as remodelling and obliteration of pulmonary arteries, whereas changes in lung parenchyma are caused by epithelial cell apoptosis and exaggerated proliferation of fibroblasts. Recently we revealed that in addition to the exacerbated fibro-proliferation, a phenotypic switch from lipofibroblasts to myofibroblasts occurs (1). However, which molecular mechanisms are involved in these processes is still not known.

Hypothesis and Objectives:

We hypothesize that distinct fibroblasts subpopulations expand and undergo phenotypic changes in chronic lung diseases. Using a wide array of methods and models, we aim to identify fibroblast cell subpopulations and their contribution to parenchymal remodelling in chronic lung disease.

Methodology:

Fibroblasts subpopulations from PF or healthy donor lung tissue will be isolated by fluorescence activated cell sorting and analysed by single cell RNA sequencing (scRNAseq). A detailed assessment of parenchymal remodelling will be acquired using standard histology techniques (immunohistochemistry/immunofluorescence stainings) and semi-automated image analysis. Studies on human lung tissue will be complemented by a variety of *in vivo* and *in vitro* approaches: Primary fibroblasts cultures from healthy and diseased lung tissue will be established for in vitro assays to assess fibroblasts cell function. Additionally, lineage tracing of fibroblast cells will be performed (2) in a mouse model of bleomycin-induced fibrosis and lineage-labelled cells will be sorted for scRNAseq and further analysis.

References:

1. El Agha E, Kramann R, Schneider RK, Li X, Seeger W, Humphreys BD, Bellusci S. Mesenchymal Stem Cells in Fibrotic Disease. Cell Stem Cell. 2017; 21(2):166-177
2. Crnkovic S, Marsh LM, El Agha E, Voswinckel R, Ghanim B, Klepetko W, Stacher-Priehse E, Olschewski H, Bloch W, Bellusci S, Olschewski A, Kwapiszewska G. Resident cell lineages are preserved in pulmonary vascular remodeling.J Pathol. 2018; 244(4):485-498

To get more information or to apply online, visit https://mug.glowbase.com/positions/144 or scan the the code on the left with your smartphone.