Abstract ID: 93528

Student: Wojcik Gabriela

Area of Research: Immunology, microbiome research and respiratory diseases

PhD Programme: PhD Immune Modulation in Respiratory Diseases (RESPImmun)

Semester: 3

Loss of ANGPTL4 attenuates lung fibrosis

Valentina Biasin; Gabriela Wojcik; Anita Sahu-Osen; Malgorzata Wygrecka; Julia Hoffmann; Sander Kersten; Lena Mischkulnig; Ehsan Bonyadirad; Paul Vesely; Slaven Crnkovic; Konrad Hoetzenecker; Panja Böhm; Saverio Bellusci; Leigh M. Marsh; Elie El Agha; Grazyna Kwapiszewska

Idiopathic pulmonary fibrosis (IPF) is a morbid disease of unknown origins. New findings suggest the influence of lipid metabolism in IPF progression. In a healthy lung, lipoprotein lipase (LPL) hydrolyses triglycerides (TG) to free fatty acids (FFA), which are necessary for processes such as surfactant production. Surfactant is produced by type II alveolar epithelial cells, which are supported by the adjacent lipofibroblasts in terms of lipid metabolism. As an inhibitor of LPL angiopoietin Like 4 (ANGPTL4) can, hence influence lipid metabolism and FFA availability. Therefore, we hypothesize that high levels of ANGPTL4 can alter FFA availability and hence lung fibrosis progression. ANGPTL4 KO mice exhibit higher levels of FFA at baseline condition, and lower collagen deposition upon bleomycin instillation. ANGPTL4 KO mice showed a decreased number of PDGFR? positive cells, suggesting that the decrease of collagen could be a consequence of the decreased number of collagen producing cells. In vitro experiments, confirmed that FFA stimulation of human parenchymal fibroblasts (hPF) reduced the collagen production, further suggesting an influence of FFA on collagen producing cells. Similar results were obtained with stimulation of hPF with Rosiglitazone and Metformin, two drugs whose efficacy in lung fibrosis mouse model has been already shown. These data suggest that ANGPTL4 via FFA availability can influence lung fibrosis development and progression. ANGPTL4 could serve as a potential target for lung fibrosis treatment, however further investigations are necessary to elucidate the underlying mechanism.