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Endocan as contributor in pathogenic remodelling of pulmonary vasculature

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Systemic Sclerosis (SSc) is a severe chronic disease with a 50% chance of direct lung involvement; this can manifest as either pulmonary fibrosis, pulmonary arterial hypertension, or both. The Fos-related antigen 2 transgenic (Fra2 TG) mouse line has been established as functional model for SSc associated pulmonary fibrosis, recapitulating important features of SSc. Furthermore, this model suggests direct involvement of the pulmonary endothelium.

We have investigated changes in lungs of Fra2 TG mice at two different time-points (8 and 16 weeks) representing early-onset and severe disease progression, using: lung function and hemodynamic measurements, immunofluorescence and electron microscopy and RNA bulk sequencing of sorted endothelial cells. Further, in vitro silencing experiments utilizing human microvascular endothelial cells and GSE datasets from human patients suffering from lung fibrosis are being investigated.

Lung function measurements showed hampered respiratory capabilities and increased pulmonary arterial pressure in Fra2 TG mice. Gene expression analyses of lung homogenates suggested an imbalance of endothelial cell homeostasis. Electron microscopy visualized swelling of the endothelium in pulmonary arteries and capillaries increasing with age in TG subjects. Using RNAseq, we found Endocan as one of the most downregulated genes in the pulmonary endothelium of young Fra2 TG mice. Endocan is involved in extracellular matrix organization, cellular migration and proliferation, processes all linked to fibrosis. Similarly, endocan expression is decreased in human pulmonary fibrosis.

We conclude that endothelial cells have prominent contribution in early onset and development of the disease. Further studies are needed to elucidate pathomechanisms and investigate the role of Endocan.