Pulmonary artery stiffening is an early driver of pulmonary hypertension

2 June 2016

Pulmonary hypertension is an abnormal elevation of pressure in the pulmonary circulation that results in stress on the heart and remodeling of blood vessels in the lung. Pulmonary hypertension is caused by a variety of factors, and patient prognosis often depends on the underlying cause. Increased stiffness of pulmonary arteries has been linked to increased mortality in patients with pulmonary hypertension, but it is not clear how stiffness develops or drives worsening of disease.

In this issue of *JCI Insight*, a team led by Laura Fredenburgh of Brigham and Women's Hospital shows that alterations in pulmonary arterial stiffness occur early during disease and promote vascular remodeling by altering signaling mediated by prostaglandins, a class of hormones that regulate inflammation, smooth muscle contraction, and vasoconstrictoin.

Using very high-resolution microscopy, Frendenburgh and colleagues detected vascular matrix stiffening in early stages of pulmonary hypertension in both humans and experimental animal models. Pulmonary artery smooth muscle cells grown on matrices with enhanced stiffness exhibited increased proliferation, contraction, and production of matrix proteins. Additionally, the stiff matrix reduced production of a class of prostaglandins that are known to protect against vascular remodeling. Importantly, in a rat model, treatment with a prostaglandin analog reduced pulmonary arterial stiffening and attenuated pulmonary hypertension.

The results of this study reveal pulmonary arterial stiffening as an early driver of pulmonary hypertension.

More information: Fei Liu et al, Distal vessel stiffening is an early and pivotal mechanobiological regulator of vascular remodeling and pulmonary hypertension, *JCI Insight* (2016). DOI: 10.1172/jci.insight.86987

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