Osteopontin lung expression is a marker of disease severity in pulmonary arterial hypertension

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Rationale. Proliferation of smooth muscle cells (SMCs) and pulmonary arterial remodelling are key mechanisms in the pathogenesis of pulmonary arterial hypertension (PAH). Osteopontin (OPN) is a pleiotropic cytokine involved in the proliferation of pulmonary vascular smooth muscle cells (PASMCs). We recently discovered that OPN is upregulated in the lungs of patients with PAH associated with pulmonary fibrosis, suggesting that the lung tissue is a source of OPN. We hypothesized that OPN lung expression is elevated in PAH and is correlated with hemodynamics.

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Methods. Microarray analysis (Affymetrix®) was performed after RNA was extracted from explanted lungs in 15 patients with PAH (m/f 2:13, age 41±12 years, 6 idiopathic PAH, 4 connective tissue disease, 4 congenital heart disease and 1 chronic thromboembolic PAH) who underwent lung transplantation (LTx) and 11 normal controls (normal lung tissue surrounding lung cancer resections). Pulmonary artery pressures (PAPs) were recorded intra-operatively immediately before starting LTx: average mPAP was 39±11 mmHg, wedge pressure 7±5 mmHg, pulmonary vascular resistance 701±208 dym.sec.cm⁻⁵.

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Conclusions. In the lungs of patients with severe PAH who failed medical therapy and underwent LTx, OPN is highly expressed and the level of expression is significantly correlated with disease severity. OPN may play an important role in the pathogenesis of PAH, driving an uncontrolled proliferation of PASMCs.