Egr-1 identifies neointimal remodeling and relates to disease progression in human pulmonary arterial hypertension

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Introduction: Pulmonary arterial hypertension (PAH) is hallmarked by the development of neointimal lesions. The transcription factor Egr-1 plays a critical role in neointimal formation in experimental PAH. This study investigated whether Egr-1 is also associated with neointimal-type vascular remodeling in different forms of human PAH.

Methods: Using immunohistochemistry, we studied pulmonary vascular Egr-1 expression in lung tissue of 58 PAH patients with either advanced (PAH-CHD, 12 explants, 9 biopsies; iPAH, 18 explants), or early stage disease (PAH-CHD, n=19 biopsies), and compared with non-neointimal PH (hypoxic PH; n=4) and controls (n=10).

Results: Pulmonary vascular expression of Egr-1 was increased in PAH compared to non-neointimal (hypoxic) PH and controls, and expression was more abundant in PAH-CHD than in iPAH. Egr-1 expression was more pronounced in advanced PAH-CHD compared to early disease stages.

Conclusions: Pulmonary vascular Egr-1 expression is increased in patients with PAH and is specifically associated with neointimal-type vascular remodeling. These data add to the accumulating evidence that Egr-1 plays a critical role in the development of neointimal lesions in PAH and identifies it as a putative target for PAH therapy. In addition, the level of pulmonary vascular Egr-1 expression may be supportive in assessing disease stage in patients with PAH-CHD.