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Morphomolecular motifs of pulmonary neoangiogenesis in interstitial lung diseases

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Pulmonary injury patterns are the common denominator in progression of fibrosing lung diseases. This study identified distinct manifestations of neoangiogenesis as drivers of pulmonary remodelling in human ILDs, modulated by bone marrow-derived monocytes. http://bit.ly/34F7KNS

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ABSTRACT The pathogenetic role of angiogenesis in interstitial lung diseases (ILDs) is controversial. This study represents the first investigation of the spatial complexity and molecular motifs of microvascular architecture in important subsets of human ILD. The aim of our study was to identify specific variants of neoangiogenesis in three common pulmonary injury patterns in human ILD.

We performed comprehensive and compartment-specific analysis of 24 human lung explants with usual intersitial pneumonia (UIP), nonspecific interstitial pneumonia (NSIP) and alveolar fibroelastosis (AFE) using histopathology, microvascular corrosion casting, micro-comupted tomography based volumetry and gene expression analysis using Nanostring as well as immunohistochemistry to assess remodelling-associated angiogenesis.

Morphometrical assessment of vessel diameters and intervascular distances showed significant differences in neoangiogenesis in characteristically remodelled areas of UIP, NSIP and AFE lungs. Likewise, gene expression analysis revealed distinct and specific angiogenic profiles in UIP, NSIP and AFE lungs.

Whereas UIP lungs showed a higher density of upstream vascularity and lower density in perifocal blood vessels, NSIP and AFE lungs revealed densely packed alveolar septal blood vessels. Vascular remodelling in NSIP and AFE is characterised by a prominent intussusceptive neoangiogenesis, in contrast to UIP, in which sprouting of new vessels into the fibrotic areas is characteristic. The molecular analyses of the gene expression provide a foundation for understanding these fundamental differences between AFE and UIP and give insight into the cellular functions involved.