

LTRC Concept Sheet # 08-02-0002

INCREASED DENSITY OF LYMPHATICS IN FIBROSING LUNG DISEASE

ABSTRACT

The underlying etiology and pathogenesis of idiopathic pulmonary fibrosis (IPF) is unknown, thus, there do not exist any current treatments that have been shown to successfully alter disease progression or improve survival. Current investigations have focused on both inflammatory cascades and repeated episodes of micro acute lung injury as the inciting event with a pathologic-fibrotic repair mechanism causing persistent disease. Proposing a novel concept in the pathogenesis of this disease may allow the development of novel therapies. The Fibroblast foci which is thought to be the leading edge of fibrosis in IPF, is composed of parallel-arranged fibroblasts and myofibroblasts and newly formed collagen within the interstitium of the lung. Recently, the fibroblast foci were found to be a continuous matrix called the fibroblast reticulum rather than discrete sites of lung injury. The reticulum was found to extend from the pleura into the parenchymal and is surrounded by a network of vessels originally thought to be blood vessels. However, preliminary work suggests that rather than blood vessels, these vessels are lymphatics. In IPF these lymphatics are found to be in higher density, particularly surrounding the fibroblast reticulum. Lymphatics play an important role in facilitating interstitial protein transport, and serve important immunologic functions. It is known that lymphangiogenesis is stimulated as a consequence of injury and inflammation. Thus, lymphangiogenesis serves an important role in re-establishing and maintaining homeostasis after insult. Lymphatics are attached to the extracellular matrix thus may play a critical role in the aberrant wound healing in the lung leading to fibrosis. It is unclear if other fibrosing lung diseases, such as non-specific interstitial pneumonitis (NSIP) also exhibit this feature or it is unique to the pathogenesis of IPF.