

LTRC Concept Sheet # 08-99-0001

The Role of Fibroblast Activation Protein- α in the Pathobiology of Idiopathic Pulmonary Fibrosis

ABSTRACT

Idiopathic Pulmonary Fibrosis (IPF) has failed to respond to immunosuppressants or α -interferon; there remains a critical need for a disease-modifying therapy. The pathology of IPF, usual interstitial pneumonitis (UIP), is characterized by the patchy distribution of fibrosis and fibroblastic foci, areas of active fibroblast proliferation and extracellular matrix deposition. The fibroblastic foci stain more intensely for fibroblast activation protein- α (FAP- α), a membrane-bound serine protease with collagen type I-specific gelatinase activity, compared to control or emphysematous lung tissue. Since a higher number of fibroblastic foci on pathology predicts a worse prognosis, FAP- α expression, which is restricted to fibroblastic foci, may play a role in disease severity. Studies of epithelial-derived tumors point to the role of FAP- α in tissue invasion and fibroblast migration, mechanisms that may be necessary for net extracellular matrix deposition. The role of FAP- α in the pathogenesis of UIP in IPF is unknown. We hypothesize that the level of expression of FAP- α correlate with clinical markers of disease severity in IPF. This exploratory study will help better define levels of FAP- α expression in control and IPF subjects and serve as preliminary data to power future studies.