

LTRC Concept Sheet # 07-99-0009

The Role of FAK-related Non-kinase and FAK in Idiopathic Pulmonary Fibrosis

ABSTRACT

The proposed study will investigate the potential aberrant cell migration and differentiation signaling in IPF lung tissues. Focal adhesion kinase (FAK) is known for its role in promoting cell migration and myofibroblast differentiation. FAK-related-non-kinase (FRNK), an endogenous FAK inhibitor, is known for its function in blocking cell migration. We found that lung fibroblasts isolated from IPF patients have enhanced FAK signaling and decreased FRNK expression when compared to normal human lung fibroblasts. Based on our current data, we hypothesize that the increased FAK signaling and the decreased FRNK expression lead to the persistent fibroblast migration and myofibroblast differentiation in IPF lung tissues. To correlate our in vitro data to the in vivo events, we would like to know 1) the FAK/FRNK expression and activation, 2) the location and cell types of FAK/FRNK expression and activation, 3) the cytokines known (and potentially) regulating the expression and activation of FAK/FRNK, and 4) FAK/FRNK downstream signaling in IPF lung tissues and in control human lung tissues. A combination of molecular and cellular approaches will be used in the studies, such as immunohistochemistry staining, laser-capture microdissection followed by real-time RT-PCR, in situ hybridization, gene expression and array, and proteomic assays.