

Mitchell Olman**University of Alabama at Birmingham****Coagulation and Fibrinolytic System Expression in Idiopathic Pulmonary Fibrosis****ABSTRACT I**

Prior work by this PI and others has shown that the coagulation/fibrinolytic system is deranged in both animal models and in idiopathic pulmonary fibrosis. The normal anti-coagulant/pro-fibrinolytic alveolar environment is switched to a pro-coagulant/anti-fibrinolytic environment that, in the presence of plasma-derived factors, supports the deposition of fibrin in the alveolar compartment at sites of fibroblastic foci. Despite this, recent work in animal models suggests that the coagulation/fibrinolytic cascades induce a fibroproliferative response that is independent of fibrin (ogen). These include but are not limited to tissue factor/FVIIa/FXa complex and/or activated protein C signaling of cytokine production, adhesion molecule expression and mesenchymal cell proliferation through protease activated receptors. We have preliminary data indicating a role for the fibroblast urokinase receptor in affecting several protean processes of fibrogenesis including fibroblast migration and myofibroblast differentiation. Similarly, we published the original description of alterations in tissue factor and fibrinolytic cascade expression in animal models of pulmonary fibrosis. There remains to be carefully described, as a basis for more mechanistic research, is the cell type-specific expression of these proteins and their activity in human idiopathic pulmonary fibrosis. Through a combined approaches of laser capture microdissection, immunohistochemistry and histologic and extracted protein tissue-based enzyme assays we will measure key components of the fibrinolytic cascade and coagulation cascades and correlate their expression/activity with a) the severity of pulmonary fibrosis and b) the presence of fibrosis and c) their colocalization in fibroblastic foci. Furthermore, using cell-type-specific markers and double labeling, we will determine the cell type(s) that express the major coagulation/fibrinolytic components in idiopathic pulmonary fibrosis, in comparison with non-fibrotic lungs (mild emphysema). All proposed assays have been utilized in prior publications and/or are up and running in the PI's lab.