

Michael Blackburn**The University of Texas Health Science Center at Houston Medical School****Adenosine Metabolism and Signaling in Patients with COPD and IPF****ABSTRACT I**

Little is known about the mechanisms that drive the progressive tissue remodeling and destruction that is seen in chronic lung diseases such as chronic obstructive pulmonary disease (COPD) and idiopathic pulmonary fibrosis (IPF). Extracellular adenosine is a signaling molecule that is produced following cellular injury that is elevated in the lungs of patients with chronic lung disease. Work from our lab using mouse models of COPD and pulmonary fibrosis have shown that adenosine contributes to disease progression in these models. Moreover, adenosine-based therapies are useful in treating features of alveolar airway destruction and pulmonary fibrosis in these models. The predictability of success of adenosine-based therapies in these models is associated with specific alterations in enzymes of adenosine metabolism and the adenosine receptors; a feature we call “purinergic remodeling”. The focus of this proposal is to utilize tissues from the Lung Tissue Research Consortium (LTRC) to determine if “purinergic remodeling” exists in patients with COPD and/or pulmonary fibrosis. Our specific hypothesis is that that purinergic signaling components will be altered in a manner that promotes adenosine production in tissue samples from patients with COPD and pulmonary fibrosis. Two Specific Aims are designed to address this hypothesis: Aim 1. Profile purinergic remodeling components at the transcript and protein level using tissue specimens from COPD and IPF patients; Aim 2. Identify the cellular localization of key components of purinergic metabolism and signaling in paraffin embedded lung tissue from COPD and IPF patients. Successful completion of these experiments will provide novel and important proof of concept information into patient populations that may be suitable for adenosine-based therapies. Please note that this project has been submitted as part of RFA # RFA-HL-08-008 entitled “Small Grants for Lung Tissue Research” and tissue availability has been confirmed.