

LTRC Concept Sheet # 08-99-0039

THE HUMAN CORRELATION: STUDIES OF DATA OBTAINED FROM A MOUSE MODEL OF IPF

ABSTRACT

Problem: Idiopathic pulmonary fibrosis (IPF) is a devastating interstitial lung disease of unknown origin. Our lab and others have focused on elucidating the mechanistic pathways that govern its development by utilizing animal models of disease, in hopes of discovering novel biomarkers of disease or potential therapeutic targets. Unfortunately, these discoveries are meager, at best. We recently published data highlighting the importance of the hematopoietic growth factor macrophage colony-stimulating factor (M-CSF), the inflammatory chemokines monocyte chemoattractant protein-1/C-C chemokine ligand 2 (MCP-1/CCL2) and mouse MCP-5/CCL12, and alveolar macrophages in the genesis of bleomycin-induced pulmonary fibrosis (1). In addition, we recently submitted a separate manuscript highlighting the importance of fibrocytes, myofibroblasts, MCP-5/CCL12, and the transcription factor ets-2 in bleomycin-induced pulmonary fibrosis in mice. To translate these findings into human data, we found that the human homolog of mouse MCP-5/CCL12 is MCP-2/CCL8, and that both of these cytokines bind the receptor for MCP-1/CCL2, termed CCR2. Our next goal is to corroborate the murine data to the human disease (IPF) to demonstrate the relevance of our discoveries and to provide supportive studies for their potential use as biomarkers of disease or therapeutic targets. Thus, the overall objective of this grant is to provide proof-of-concept studies utilizing the clinical data (CT scan, pathological diagnosis) and biological specimens (plasma, lung tissue, DNA) from humans with IPF from the Lung Tissue Research Consortium (LTRC).

Central Hypothesis: We will validate the importance of M-CSF, CCL2, CCL8, CCR2, and fibrocytes, in the pathogenesis of IPF by the use of clinical data and biological specimens from patients with IPF from the LTRC.