Defining the Mechanism of Fibroblast Death in Pulmonary Emphysema To Target Novel Therapies for COPD

Crawford, Jonathan (School: University School of Milwaukee)

There is currently no cure for chronic obstructive pulmonary disease (COPD), the third leading cause of death worldwide with over 70 million cases and 3.5 million deaths per year. Treatment options remain palliative and are directed towards risk-factor modification and symptom-control to optimize quality of life due to the inability of current technology to define the pathogenesis and map the multifaceted and multicellular interaction of the disease. I show that the previously unknown pathogenic mechanism of cigarette-smoke induced COPD is the apoptosis of lung fibroblasts. In order to prove the pathogenic mechanism, I show that the following conditions exist: the pathology between fibroblasts and the epithelium, the apoptosis of fibroblast when exposed to cigarette smoke, and the pathway of apoptosis in fibroblasts. I demonstrate the pathogenic mechanism between fibroblast and the epithelium by utilizing self-organizing alveolar lung organoids developed from basal cells, a new technology used to mimic, in-vitro, the in-vivo pathologies of multicellular processes. The impairment of cigarette smoke on lung fibroblast function and apoptosis is shown using fluorescence activated cell sorting (FACS), optical density test (LDH), and live/dead antibody staining. A pathway of apoptosis in fibroblasts is identified using the lentiviral transduced antioxidant genes Nrf2, thioredoxin, and catalase on human and mouse fibroblasts, and assessing the development of oxidative stress and cell death following exposure to cigarette smoke. I posit that by developing an understanding of the mechanism of COPD development through fibroblast death, a cure for COPD may result.

Awards Won:
First Award of $5,000