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Title: Role of Interleukin-17 in Fibrotic Lung Disease and COPD

ABSTRACT I

Cystic fibrosis and chronic obstructive pulmonary disease (COPD) have been increasing for the past years. Today COPD is the most common cause of death in the US and is classified amongst the top five killers. Other lung diseases such as atopic asthma have been steadily increasing in the population of industrialized countries. The prevalence of asthma over the past 20 years has increased by 100% and today it affects 10% of the U.S. population. Both patients affected by atopic asthma and patients with COPD develop airway obstruction. Unlike asthma airway obstruction in patient affected by COPD is progressive and mostly irreversible. Although, many similarities are shared between clinical features of allergic asthma and COPD, there are significant differences in the immunological mechanisms that underlie these two diseases. Atopic asthma is characterized by an overproduction of Th2 cytokines (IL-4, IL-5 and IL-13), peripheral blood eosinophilia and elevated IgE level to a specific allergen. COPD is usually caused by tobacco smoke that disrupts the epithelial barrier and induces a migration of different cell type such as neutrophils, macrophages, T lymphocytes and natural killer cells through the airway epithelium. In contrast to asthma, CD4+ T cells that infiltrate the inflamed lung are mainly Th1 cells. Recent studies showed that bronchoalveolar fluid lavage (BALF) from patients with COPD have an increased number of Th2 cells making the distinction between these two diseases more complex. Furthermore, it has been recently shown that a new CD4+ T cells subset distinct from Th1 and Th2 that produces interleukin-17 (IL-17) is found increased in patients with atopic asthma. Based on the fact that atopic asthma, fibrotic lung and COPD share several similarities, our study will focus on the role of IL-17 cystic fibrosis and COPD. We hypothesize that IL-17 is increased in lungs of patients with cystic fibrosis and chronic obstructive pulmonary disease. In specific Aim 1, we will test the hypothesis that IL-17 production is increased in fibrotic lungs and lungs affected by COPD. We will determine IL-17 levels and localize in situ IL-17 producing cells. In specific Aim 2, we will determine the signaling pathway involved in fibrotic lung and COPD by using microarrays methods. Understanding the role of IL-17 in fibrotic lung and COPD will provide new therapeutic approaches.

Groups:

10 Subjects per group. Four groups.

COPD: FEV1>80%, and FEV1<50%,

IPF: FVC>80%, and FVC<50%

Types:

RNA Later (1 aliquot/subject)

Plasma (1 aliquot per subject)

Serum (1 aliquot per subject)