

## LTRC Concept Sheet # 05-01-0002

### Dendritic Cell Maturation and T-Cell Activity in Chronic Obstructive Pulmonary Disease

**Abstract:** We will study the distribution and function of dendritic cells and T cells, and correlate these findings to airflow limitation to provide insight into how these immune cells are of relevance to the pathogenesis and progression of COPD. We propose two central hypotheses: 1) dendritic cells are increased in the lungs of smokers and correlate with the development of airflow limitation, are functionally immature and hypo-responsive, and interact with CD8+ T cells in sub-epithelial regions forming follicles; and 2) the increase in CD8+ T cells in the lungs of COPD patients is principally due to activated cytolytic effector cells. To test the hypothesis that smoking-impaired dendritic cell function predisposes to chronic infection in COPD, we will perform *ex vivo* experiments on dendritic cells from lungs of smokers with COPD and controls to compare dendritic cell cytokine secretion and regulation of co-stimulatory molecules following challenge by bacterial lipopolysaccharide.

Our three main aims are as follows: 1) We will determine the quantity, distribution, state of activation, and functional correlates of dendritic cells in COPD lungs. These data lead us to hypothesize that COPD is associated with an increase in lung dendritic cells that have impaired T cell stimulatory capacity, predisposing the host to chronic infections. 2) We will characterize the state of activation of CD8+ T cells and correlate the presence of activated cytolytic CD8+ T cells with the degree of functional impairment in COPD. We hypothesize that the majority of CD8+ T cells in COPD lungs and control lungs are activated, cytolytic type-1 CD8+ T cells, and the extent of infiltration with these activated CD8+ T cells correlates with severity of COPD; and 3) We will determine differences in the expression of genes that regulate immune cell function in COPD. We propose that there are inherent differences in inflammatory gene expression profiles between smokers who develop COPD when compared to control smokers without airflow limitation. Findings will be confirmed by using quantitative methods and localization of specific genes will be performed *in situ* hybridization methods.