

LTRC CONCEPT SHEET #08-99-0017

Chronic Inflammation Increases Susceptibility to Pneumococcal Pneumonia

Abstract

Advanced age and chronic obstructive pulmonary disease (COPD) are associated with increased lung inflammation and increased risk for community-acquired pneumonia (CAP). *Streptococcus pneumoniae* (the pneumococcus) is the leading cause of CAP and is a leading cause of infectious death among the elderly. Considerable laboratory studies have found that inflammation is requisite for *S. pneumoniae* infection; in vitro and laboratory animal studies have determined that the pneumococcus co-opts the NFkB regulated (i.e. inflammation regulated) proteins polymeric immunoglobulin receptor (plgR) and platelet activating factor receptor (PAFr) to attach to and invade cells. To date, no studies have examined human tissues and confirmed that elevated levels of plgR & PAFr are a mechanism by which aging and lung inflammation contributes towards human disease. **The goal of this proposal is to determine if aging and COPD modulate plgR and PAFr expression in human lung tissue.**

We will use LTRC tissues to:

Aim 1: Determine if advanced age is associated with increased plgR and PAFr expression.

Using Western blot, Real Time (RT)-PCR, and immunohistochemistry we will determine if age-related changes occur in the amount of activated NFkB, plgR and PAFr in normal lung samples isolated from subjects 30-50, 51-64, and 65-89 years of age.

Aim 2: Determine if chronic lung inflammation is associated with changes in plgR and PAFr levels. We will determine if lung samples isolated from individuals with COPD have elevated levels of activated NFkB, plgR and PAFr versus age-matched controls.

Obtaining a better understanding of the molecular mechanisms responsible for age- and COPD-associated susceptibility to CAP is an important step towards improving lifespan and productivity of the elderly. In 2020, 1/5 of the United States population will be >65 years of age, for this reason it is critical that we begin working towards an improved knowledge of these mechanisms today.