

LTRC Concept Sheet # 09-99-0001

Signaling Sphingolipids in COPD

ABSTRACT

Chronic obstructive pulmonary disease (COPD) is a prevalent fatal disease, defined by a functional defect, that of an irreversible obstruction of airflow from the lungs. We have recently identified a novel role for ceramides in the lung as a central mediator of alveolar cell apoptosis and emphysema. Signaling sphingolipids are essential for ensuring an optimal balance of cell death (ceramides) / survival (sphingosine-1-phosphate, S1P) in tissues. We hypothesize that lungs of patients with emphysema have an increased ceramide / S1P ratio compared to non-diseased lungs. Furthermore, the pattern of ceramide molecular species expression may correlate with the COPD disease phenotype. Those hypotheses will be tested in a proof-of-concept study using tissues and plasma samples from COPD and non-COPD patients provided by Lung Tissue Research Consortium, NIH (LTRC).

Specifically: the aims of this project are - Aim #1: To determine whether ceramide/S1P ratio is increased in the LTRC lung parenchyma samples obtained from patients with COPD compared to those without lung disease. Aim #2: To determine which enzymatic pathways responsible for the ceramide/S1P homeostasis are dysregulated in the LTRC lung parenchyma samples obtained from patients with emphysema. Aim #3: To establish whether a distinct ceramide species profile present in the lung parenchyma is recapitulated in the plasma obtained from individuals with a specific COPD phenotype. Together, the studies proposed are expected to improve our understanding of emphysema pathobiology and, importantly, to position sphingolipid signaling as a potential therapeutic target and/or biomarker of emphysema.