



Inhaled Cationic Salts Modulate Macrophage Function to Reduce Inflammation During LPS Induced Lung Injury

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Pulmatrix is developing PUR118 as a host-targeted, dry powder therapy based on the inhalation of calcium salts for acute exacerbation (AE) control in chronic obstructive pulmonary disease and other inflammatory lung disease. Preclinical data suggest that this approach is effective against an array of pathogens and also reduces inflammation resulting from environmental stimuli such as tobacco smoke. We hypothesized that this treatment could be efficacious in reducing lipopolysaccharide (LPS) induced lung inflammation by modulating the function of pulmonary macrophages. Mice were exposed to nebulized LPS (*Pseudomonas aeruginosa*) and PUR118, was delivered via whole body exposure 1h post-LPS challenge. Four hours after LPS exposure inflammatory cell counts and chemokine and cytokine concentrations were determined in BAL. PUR118 treatment decreased total inflammatory cell counts and neutrophil counts in the BAL fluid of LPS challenged mice and correlated with reduced KC, IL-6 and TNF- α in BAL fluid. Separately, peritoneal macrophages were isolated from naïve mice and challenged with LPS in media supplemented with calcium to simulate conditions thought to be found in lung fluid lining after PUR118 treatment. Inflammatory mediator secretion and gene expression were determined 2h post LPS exposure. Macrophages stimulated with LPS in the presence of calcium exhibited a dose dependent decrease in KC, IL-6 and TNF- α secretion as well as reduced gene expression for these inflammatory mediators. These data suggest that PUR118 can act through macrophages to reduce lung inflammation and may reduce the risk of AE caused by infections during chronic lung disease.