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Suppression of the Protein Phosphatase 2A 2C B Subunit (PPP2R2C) Enhances Immune Responses in Human Bronchiole Small Airway Epithelial Cells

Introduction: Protein phosphatase 2A (PP2A), a major serine-threonine phosphatase, plays a critical role in the regulation of inflammation, proliferation, apoptosis, and protease expression, which are critical processes in the pathogenesis of chronic obstructive pulmonary disease (COPD).
PP2A consists of a dimeric core enzyme composed of a structural A and catalytic C subunit, and a variable regulatory B subunit. While C and A subunit sequences are conservative, the regulatory B subunits are more heterogeneous (16 identified in humans) and their expression in the airways is not characterized. In the present study, we investigated the PP2R2C subunit in airway epithelial cells to determine if the subunit is critical for the activity of PP2A and its influence on immune and proteolytic responses.
Methods: PPP2R2C expression levels were quantified in human small airway epithelial (SAE) cells isolated from healthy subjects and COPD subjects, and mice exposed to cigarette smoke. SAE cells were transfected with PPP2R2C siRNA and were treated with 5% cigarette smoke extract (CSE). Protein and RNA levels of genes of interest were quantified to investigate effect of PPP2R2C expression on cytokine secretion, caspase-3 activity and MAPK activity.
Results: Expression of PPP2R2C is decreased in CSE treated cells, and SAE cells isolated from COPD compared to cells from healthy subjects. MMP1, IL-6 and IL-1β expressions increased in CSE exposed cells Silencing 2C increased basal IL-1β protein levels and caused trend increases in other cytokines. Loss of PPP2R2C increased MAPK, NF-κB, and JNK activities.
Conclusions of the study: These data demonstrate that reduced expression of PPP2R2C is observed in SAE cells from COPD subjects and smoke exposed mice, and loss of PPP2R2C expression enhances MMP1, IL-6 and IL-1 responses. Therefore, PPP2R2C may play a major role in pathogenic responses in COPD.