Targeted Ablation of *AIMP1* in Lipopolysaccharide-induced Acute Lung Injury

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Background and Hypothesis:

Infants with Bronchopulmonary dysplasia (BPD), a chronic lung disease of premature infants, are more susceptible to acute lung injury (ALI). Endothelial-Monocyte Activating Polypeptide II (EMAP II, encoded by *Aimp1*) is a proinflammatory cytokine that originates from bronchiolar club cells and plays a role in the inflammatory response during BPD development. Prolonged EMAP II exposure has been shown to worsen BPD pathogenesis by activating alveolar macrophages. The targeted ablation of EMAP II in the bronchial club cells of a mouse model (*Scgb1a1-ERTCre*;*Aimp1/fl/fl*) is hypothesized to decrease the inflammatory effects of ALI.

Experimental Design:

Aged-matched littermate mice (ages ranging from 20-25 weeks) with Tamoxifen inducible, Cre-mediated, bronchial club cell specific ablation of *Aimp1* (*Scgb1a1-ERTCre*;*Aimp1/fl/fl*, denoted cKO) or with only partial ablation (Scgb1a1-ERT2Cre;Aimp1/fl/wt denoted Ctrl) were given three doses of 120 micro-liters of 20mg/ml tamoxifen over a seven day period. 24 hours after the final dose they were administered a single intratracheal delivery of lipopolysaccharide (LPS) (5mg/kg) 24 hours later immunohistochemistry (IHC) for EMAP II and inflammation was assessed by immunoblotting (IB) for IL-6 in bronchoalveolar lavage (BAL) and cytospin of BAL.

Results:

IHC showed a decrease of EMAP II expression in the bronchioles of the cKO as compared to ctrl. IL-6 was increased 1.95 fold in the BAL fluid of cKO by IB. Cytospin analysis showed: (Cell Type: Ctrl%, cKo%), Macrophages: 4.66%, 4.70%, Mature neutrophils: 44.44%, 60.25%, Banded Neutrophils: 41.93%, 26.20%, Lymphocytes: 4.30%, 5.10%, Eosinophils: 2.51%, 2.10%, Monocytes: 2.15%, 1.64%.

Conclusions:

Ablation of bronchial club cell EMAP II, in LPS-induced ALI increased the amount of IL-6 and percentage of mature neutrophils in bronchoalveolar lavage fluid. No significant difference in macrophage were noted in either group. These findings suggest that EMAP II influences immune response time; however, more experiments would be required to establish a link.