Increase in Distal Airway Mucus-Producing Clara-Cells During Primary Pneumocystis Infection

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Background: Airway Clara cells exhibit plasticity and may differentiate into goblet cells that secrete mucus under different stimuli. Mucus originating in transformed Clara cells along distal and alveolar duct airways that normally lack goblet cells might affect narrow airway patency and increase the severity of airway disease. Pneumocystis primary infection is a highly mucogenic fungal infection prevalent in infants at 2 - 5 months of age when airways are still developing. Respiratory morbidity increases during this infancy age-window. Clara (CC10) and goblet cell (MUC5AC and MUC5B) secretion markers were investigated in lungs of immunocompetent rats during Pneumocystis primary infection at 40, 60, and 80 days of age.

Methods: Total mucus was determined using simple microscopy and Alcian-Blue-PAS stain, and frequency of Clara and goblet cells by IFI using antibodies against Cc10, Muc5ac, and Muc5b. Colocalization of Clara and goblet cell markers in distal airways <250 mic was evaluated by confocal microscopy using Fiji ImageJ software. Gene expression of Cc10, Muc5ac and Muc5b in lung tissue was determined by qRT-PCR at same age intervals.

Results: Mucus and proportion of goblet cells/distal epithelium area increased in Pneumocystis-infected rats respect to controls at 60 days of age (0.4±0.8% versus 0.01±0.02%) (P=0.0036). These cells expressed Muc5b but not Muc5ac. mRNA levels of Muc5b and Muc5ac increased 2.7 and 3.9 times at 60 days of infection (P=0.0275 & P=0.0001, respectively).

Conclusions: Clara cell frequency remained same, while mRNA levels of Cc10 increased (2.3-fold change) in Pneumocystis-infected rats at 80 days of age (P=0.0006). Cc10 and Muc5b co-localized in distal airway epithelium of Pneumocystis-infected rats at 60 days. Primary infection by Pneumocystis associates to increased frequency of goblet cells expressing Muc5b in distal airways. Colocalization of Cc10 and Muc5b suggest Clara to mucus-secreting goblet cell transdifferentiation.