Chronic obstructive pulmonary disease and asthma-associated Proteobacteria, but not commensal Prevotella spp., promote Toll-like receptor 2-independent lung inflammation and pathology

Recent studies of healthy human airways have revealed colonization by a distinct commensal bacterial microbiota containing Gram-negative Prevotella spp. However, the immunological properties of these bacteria in the respiratory system remain unknown. Here we compare the innate respiratory immune response to three Gram-negative commensal Prevotella strains (Prevotella melaninogenica, Prevotella nanceiensis and Prevotella salivae) and three Gram-negative pathogenic Proteobacteria known to colonize lungs of patients with chronic obstructive pulmonary disease (COPD) and asthma (Haemophilus influenzae B, non-typeable Haemophilus influenzae and Moraxella catarrhalis). The commensal Prevotella spp. and pathogenic Proteobacteria were found to exhibit intrinsic differences in innate inflammatory capacities on murine lung cells in vitro. In vivo in mice, non-typeable H.influenzae induced severe Toll-like receptor 2 (TLR2)-independent COPD-like inflammation characterized by predominant airway neutrophilia, expression of a neutrophilic cytokine/chemokine profile in lung tissue, and lung immunopathology. In comparison, P.nanceiensis induced a diminished neutrophilic airway inflammation and no detectable lung pathology. Interestingly, the inflammatory airway response to the Gram-negative bacteria P.nanceiensis was completely TLR2-dependent. These findings demonstrate weak inflammatory properties of Gram-negative airway commensal Prevotella spp. that may make colonization by these bacteria tolerable by the respiratory immune system.

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