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Title: Profiling the proteome of the lower airway respiratory tract lining fluid in chronic obstructive pulmonary disease

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Body: Chronic Obstructive Pulmonary Disease (COPD) is a chronic inflammatory condition of the airways associated with protease, anti-protease imbalance and oxidative stress. Relatively little is known about how underlying airway immunopathology impacts upon the protective function of the respiratory tract lining fluid (RTLF). Aim: To investigate compositional differences in the RTLF proteome in COPD patients compared against aged and smoking history matched controls. Broncholaveolar lavage samples were obtained from COPD smokers (n=5, 63.8±6.0 years), COPD ex-smokers (n=10, 66.0±6.8 years), healthy smokers (n=5, 61.4±6.2 years) and healthy non smokers (n=5, 66.8±5.9 years). Samples were analysed by one-dimensional gel electrophoresis and nanoliquid chromatography-tandem mass spectrometry, data processed using MASCOT and SCAFFOLD. We identified 342 unique proteins, the greatest number, 153, observed in healthy non smokers, with only 49 proteins identified in COPD ex-smokers. Proteins were classified according to their gene ontology annotation, with COPD smokers found to possess the greatest number with roles in inflammation, immune response and protease, anti-protease balance. Employing the sum of major ion intensities permitted a semi-quantitative assessment of protein concentrations with Calgranulin A, Surfactant protein A and Alpha-1 antitrypsin decreased in COPD smokers versus non smokers. Secretoglobulin concentrations were elevated in COPD patients versus smoking and non-smoking controls. Data suggests a simplified RTLF proteome in COPD, with a shift in protein expression in COPD smokers consistent with ongoing inflammation and protease, anti-protease imbalance.