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Title: Discovery of candidate proteins, PIGR and SELENBP1, as novel markers of airway diseases in COPD

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Body: Introduction: COPD is characterized by chronic airway inflammation, although useful biomarkers and treatment targets of COPD have not been identified. Aims: To discover novel proteins in airways to distinguish COPD patients from healthy smokers using proteomic approaches. Methods: Two-dimensional gel electrophoresis coupled with mass spectrometry was performed for epithelial lining fluid (ELF) obtained from bronchus of COPD patients (n=4) and control smokers (n=4). Expression at mRNA levels was quantified by RT-PCR and microarray for some of the candidate proteins using airway epithelial cells and peripheral lung tissues from COPD patients and smoking controls. C57BL/6 male mice were subjected to cigarette smoke for 3 months and airway epithelial cells were harvested by laser capture microdissection (n=6). Non-smoking mice were served as controls (n=6). Results: We first identified 29 proteins in ELF which were different between COPD and control smokers. For 14 out of 29 proteins, the difference was consistent at mRNA levels in human epithelial cells. Same trend was clearly observed for 2 proteins out of 14 at mRNA levels in peripheral lung tissues (i.e., increase of polymeric immunoglobulin receptor (PIGR) and decrease of selenium-binding protein 1 (SELENBP1)). Mouse Airway epithelial cells also exhibited increase of PIGR and decrease of SELENBP1 expressions along with the development of emphysema following 3 months-smoke exposure. Conclusions: Proteomic approaches for ELF followed by gene expression analyses identified 2 COPD-related proteins, PIGR and SELENBP1, which might be functional in mucosal immunity and antioxidant properties, respectively, in the airways of COPD.