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Title: Alterations of the soluble proteome of airway epithelial cells in COPD

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Body: The increasing incidence of COPD is primarily driven by the female population. Altered smoking habits cannot fully explain the increasing COPD burden among women, indicating that gender-specific mechanistic differences contribute to disease progression. Here we investigated alterations in the airway epithelial proteome due to early stage COPD, with focus on gender-related differences. The soluble proteome of airway epithelium obtained from subjects from the Karolinska COSMIC study (age- and sex matched COPD patients (GOLD I-II), smokers with normal lung function, and never-smoking healthy controls of both genders (n=20; 120 subjects total)) was analyzed by Difference Gel Electrophoresis (DIGE), followed by multivariate modeling. Comparison of non-symptomatic smokers and smoking COPD patients showed significant differences between groups for both genders (Male: R2= 0.98, Q2=0.95, p=0.0007; Female: R2= 0.82, Q2=0.73, p=0.01). Only 3 of the 22 proteins driving the separation between male healthy smokers and smoking COPD patients were the same as for the corresponding female population, indicating significant gender differences. This pilot study indicates mechanistic gender differences in the airway epithelial proteome distinct from our recent report regarding alveolar macrophages (1). New insight into gender-specific disease mechanisms and a better molecular understanding of the various sub-phenotypes of COPD are necessary to hamper the increasing morbidity of the disease. 1. Kohler M, Sandberg A, et al (2012). J Allergy Clin Immunol. In press.