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Title: Sputum biomarkers of inflammation in smokers and subjects with COPD

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Body: Background: The study aimed to compare compounds postulated to represent potential COPD biomarkers from hypothesis and/or recent non-biased proteomics derived investigations using carefully characterized groups. Methods: Sputum samples were processed from 211 subjects, never smokers (NS), non-symptomatic smokers (NSS), symptomatic smokers (SS), and from smokers with recently diagnosed mild-moderate COPD. Subjects with COPD produced sputum, they had no asthma/COPD overlap, no other diseases, no previous COPD exacerbations and no anti-inflammatory medications. The compounds selected included myeloperoxidase (MPO), human neutrophil lipocalin 2 (HNL), matrix metalloproteinase-9 (MMP-9), surfactant proteins A and D (SP-A, SP-D) and alpha-1-antitrypsin (AAT). The analyses were conducted by EIA/ELISA methods. Predictions of the biomarkers were tested using receiver operating characteristic (ROC) curves. Results: HNL was elevated significantly in COPD and could differentiate COPD from smokers, NSS and SS from each other. Levels of MPO, MMP-9, and SP-A were elevated in smokers and COPD compared to NS, while those of SP-D and AAT were not changed significantly. The predictive capabilities of MPO, HNL, MMP-9, and SP-A to distinguish smokers (COPD, NSS, SS altogether) from controls (NS) and patients with COPD from the smokers (NSS, SS) were good and poor, respectively. Conclusion: In this cohort, HNL appeared to be the most promising COPD marker in sputum. These results combined with our recent plasma studies indicate that some of these compounds hold potential for identifying COPD from sputum while for some others (SP-A, AAT) appear to be more useful in plasma specimens.