

# European Respiratory Society Annual Congress 2012

**Abstract Number:** 2849

**Publication Number:** P1751

**Abstract Group:** 3.1. Molecular Pathology and Functional Genomics

**Keyword 1:** COPD - mechanism **Keyword 2:** Inflammation **Keyword 3:** Biomarkers

**Title:** Gender differences in 5- and 12/15-lipoxygenases products in bronchoalveolar lavage fluid from healthy never-smokers, smoker and COPD patients

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**Body:** Background: Chronic obstructive pulmonary disease (COPD) is a leading disease that is increasing particularly among females. Smoking represents the main risk factor for developing COPD and chronic inflammation persists after smoking cessation Aims: We have investigated the effects of smoking, in relation to COPD, on lipid mediators in the inflammatory response in the lower airways Methods: Bronchoalveolar lavage fluid (BALF) was obtained from healthy never-smokers, non-symptomatic smokers, and COPD patients of GOLD stage I-II (smokers and ex-smokers) of both genders. Different lipid mediators derived from the cytochrome P450, lipoxygenase (LOX) and cyclooxygenase (COX) pathways were analyzed by mass spectrometry Results: Products of 12/15-LOX and 5-LOX clustered respectively when analyzed by multivariate analysis and were summed for further comparisons. 12/15-LOX products were selectively increased in females. 5-LOX products exhibited a distinct pattern with increases in smokers, but no gender-specificity. There was no difference in lipoxygenases products between healthy smokers and smoking COPD patients. However, in COPD ex-smokers the levels of 5-LOX products were decreased compared to COPD smokers Conclusions: LOX activity in BALF shows gender-specific regulation in relation to both smoking and COPD. The observed shifts were 5-and 12/15-LOX-specific depending on gender and smoking status. This study will be continued with the analysis of other lipid mediators derived from 5 and 12/15-LOX, that are currently pharmacological targets in other diseases, such as asthma. These facts provide potential insight into the gender imbalance in COPD.