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Abstract Group: 3.3. Mechanisms of Lung Injury and Repair
Keyword 1: Cell biology **Keyword 2:** COPD - mechanism **Keyword 3:** Smoking

Title: Acute effect of cigarette smoke on human bronchial epithelial cell metabolome is reversible by UPF1

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Body: We assessed protective capacity of glutathione analogue UPF1 (4-methoxy-L-tyrosinyl-γ-L-glutamyl-L-cysteinyl-glycine) against cigarette smoke condensate (CSC)-induced alterations in metabolic profile of human bronchial epithelial cells (HBEC). HBEC were exposed to 10 µg/mL CSC for 1 h, followed by treatment with 0-10 µM UPF1 or 2 mM N-acetylcysteine (NAC) for 1-12 h. Cell lysates were analysed on a Q-Trap 3200 mass spectrometer to obtain spectra between m/z ratios of 50-1700 Da. The data were subjected to principal component analysis, ANOVA, Pearson correlation analysis and hierarchical clustering. CSC affected the highest number of signals at 2 h (245 signals, 13.4%). Signals affected by CSC with/without UPF1 or NAC formed 3 major clusters of metabolites that followed similar changing pattern within each cluster over time. In cluster 1, CSC caused a significant decrease of signals within 4 h, which was initially inverted by UPF1, before the signals returned to baseline. In contrast to UPF1, NAC had no redeeming effect. Among metabolites in cluster 1 species of phosphatidylcholines were identified using public databases. Signals of cluster 2 were decreased by CSC before returning to baseline after 4 h, followed by prolonged up-regulation by both UPF1 and NAC. Glutamine and glutamic acid were among the metabolites identified in cluster 2. Signals in cluster 3 were elevated by CSC and inverted by UPF1 and NAC showing a negative correlation with cluster 1 (r=-0.5). UPF1 effectively inverts the immediate effect of CSC on certain metabolites and may thus provide basis for designing drugs for protecting HBEC to slow down the development of COPD. Supported by ESF grants 7856, 9043, 9103.