Abstract Group: 3.3. Mechanisms of Lung Injury and Repair

Keyword 1: Epithelial cell  Keyword 2: COPD - mechanism  Keyword 3: Smoking

Title: Antioxidant tetrapeptide UPF1 exerts an immediate effect on cigarette smoke-altered metabolic state of human bronchial epithelial cells

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Body: We evaluated the protective capacity of UPF-1 (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 1h, 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 full spectra between mass-to-charge (m/z) ratios 50-1700 Da. Principal component analysis, partial least squares regression analysis and t-test were used. Levels of many compounds (e.g. 226, 310, 408 Da) were significantly (p<0.001) elevated in response to CSC. Exposure to CSC caused a rapid and significant shift of the HBEC metabolic state visible both in positive and, to a lesser extent, in negative ionization mode, followed by a delayed return to the state close to that of untreated cells not earlier than by 12 h. Instead, addition of 10 µM UPF1 was able to return the metabolic state already by 1 h to the state, which was present in lone CSC-stimulated cells just after 6 h. By 1 h, 1 µM UPF re-established the metabolic state to that what was evident at 3 h of CSC-exposure without UPF1, showing a concentration-dependent effect of UPF1. In contrast, NAC reverted the CSC-affected metabolic state of the HBEC to near-normal not earlier than by 12 h. Compared to NAC, the novel antioxidant tetrapeptide UPF1 acts effectively towards restoring the metabolic status in HBEC by eliminating the immediate effect of CSC. The results may speed up the design of drugs that facilitate prevention of COPD. Supported by ESF grants 7856, 9043, 9103.