**Rationale.** Bronchial epithelium is a primary target for reactive oxygen species. High level of oxidative stress (OS) is operative in numerous airway diseases, particularly in chronic obstructive pulmonary disease (COPD), via augmentation of chronic inflammation and remodeling of the lung and airways by oxidant-induced activation of transcription factors and other signal transduction pathways. Therefore, targeting OS with antioxidants or boosting the endogenous levels of antioxidants is most likely beneficial in COPD. Finding an antioxidant suitable for treating COPD free of problems with potency, kinetics, toxicity, and interference with metabolic and signaling pathways is of importance. Augmentation of glutathione, the most important intracellular antioxidant level using novel antioxidant peptides, could be of great perspective with this regard.

**Aim.** We aimed at studying the ability of a novel glutathione analogue, UPF1 (O-methyl-L-tyrosinyl-γ-L-glutamyl-L-cysteinylglycine) to maintain or increase the glutathione level in order to balance the glutathione level in human bronchial epithelial cells after induction of OS.

**Methods.** Cultured normal human bronchial epithelial cells (BEAS-2B) were exposed to OS by adding increasing concentrations of 0-100 µM hydrogen peroxide (H2O2) to the culture medium for 30 minutes. Thereafter, the culture medium was replaced and the cells were incubated in the presence of 0-100 µM UPF1 for 3 hours. Total glutathione levels were measured in cell lysates using a special glutathione assay kit from Cayman Chemical.

**Results.** The glutathione level was significantly decreased in response to H2O2 in a concentration-dependent manner (p<0.01). The presence of UPF1 restored the glutathione content to the level not significantly differing from that in untreated cells already at a concentration of 1 µM. At 0.1 µM, UPF1 was able to completely restore the glutathione content only when the cells were challenged with up to 25 µM H2O2, but was not able to affect the glutathione level if the OS was induced by higher H2O2 concentrations. Importantly, there was no detectable toxic effect of UPF1 to the bronchial epithelial cell viability at any of the applied concentrations.

**Conclusions.** The results demonstrate that the antioxidant tetrapeptide UPF1 is able to maintain intracellular glutathione levels in normal human bronchial epithelial cells under OS caused by oxidants with direct action. This knowledge may provide promising clinical perspectives for development of pathogenetic treatment approaches for COPD.

Funding Source: Estonian Science Foundation Grants No. 6566 and 7154

Am J Respir Crit Care Med 181;2010:A2686

OXIDATIVE STRESS, SIGNAL TRANSDUCTION AND MECHANISMS OF LUNG INJURY

Moderators: A.M. Condliffe, PhD, J.C. Horowitz, MD, E.R. Chilvers, MD, PhD

Session Info: Poster Discussion Session- Poster Presentation, [B28] OXIDATIVE STRESS, SIGNAL TRANSDUCTION AND MECHANISMS OF LUNG INJURY

Day/Date: Monday, May 17, 2010

Session Time: 8:15 AM - 10:45 AM

Poster Viewing: 8:15 AM - 9:15 AM

Discussion: 9:15 AM - 10:45 AM

Room: Room 225-227 (Second Level), Morial Convention Center