THE EFFECT OF N-ACETYLCYSTEINE ON CHLORIDE EFFLUX IN AIRWAY EPITHELIAL CELLS

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**Background:** Cystic fibrosis (CF) is characterized by defective chloride transport in airway epithelial cells. This defect leads to dehydration of sputum, chronic inflammation and subsequent oxidative stress in the CF lung. N-acetylcysteine (NAC) is a well known antioxidant glutathione prodrug which can improve the redox instability in CF cells. We tested whether NAC has not only anti-inflammatory effects, but also stimulates Cl\textsuperscript{⁻} efflux.

**Methods:** CF bronchial epithelial cells (CFBE) were treated with 1mM, 5mM, 10mM or 15mM NAC and normal bronchial epithelial cells (16HBE) with 10mM NAC, for 4h at 37°C. The cells were cultured to adherence flasks in medium 199 supplemented with 10% fetal calf serum, 100 U/ml penicillin, and 100 µg/ml streptomycin; at 37°C in a humidified atmosphere of 5% CO\textsubscript{2}/95% O\textsubscript{2}.

Cells were loaded with the fluorescent probe MQAE for 2h prior to analysis. Cover slips were placed as bottom in a perfusion chamber on the stage of an inverted microscope. The effect of NAC on Cl\textsuperscript{⁻} transport was measured by exposure of cells to a chloride buffer of 150mM Cl\textsuperscript{⁻}, following by exposure to a Cl\textsuperscript{⁻} free buffer with NO\textsubscript{3}⁻ as the substituting anion. For intracellular calibration a K\textsuperscript{⁺} rich buffer and various concentrations of Cl\textsuperscript{⁻} and NO\textsubscript{3}⁻, in the presence of nigericin and tributylin was used. The experiments were ended by a quenching solution.

**Results:** Chloride efflux from CFBE cells was stimulated by NAC in a dose dependent manner, with 10mM NAC causing a significant increase in Cl\textsuperscript{⁻} efflux with nearly 100%. This corresponded to about 40% of the efflux in 16HBE cells. At concentrations higher than 10mM NAC the efflux apparently decreased, possibly due (in part) to an inhibition of MQAE loading by NAC. 10mM NAC did not increase chloride efflux from 16HBE cells.

**Conclusion:** The stimulation of Cl\textsuperscript{⁻} efflux in CF airway epithelial cells could lead to increased hydration of the sputum. In addition to the anti inflammatory properties, this effect might be beneficial when NAC is used for CF patients treatment.