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Title: Distribution of vitamin C transporters in the lower airways of humans

Dr. G.D. 1094 Rankin greg.rankin@lung.umu.se¹, Dr. N. 1095 Larsson nirina.larsson@lung.umu.se MD¹, Dr. E. 1096 Roos-Engstrand ester.roos-engstrand@umu.se¹, Dr. J. 1098 Pourazar jamshid.pourazar@lung.umu.se¹, Prof. Dr A. 1100 Blomberg anders.blomberg@lung.umu.se MD¹, Dr. I. 1101 Mudway ian.mudway@kcl.ac.uk² and Dr. A.F. 1103 Behndig annelie.behndig@lung.umu.se MD¹.¹ Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden and ² MRC-HPA Centre for Environment and Health, King's College London, London, United Kingdom .

Body: Vitamin C (ascorbate, AsC₂H₂ + dehydroascorbate, DHA) is an important low-molecular weight antioxidant at the air-lung interface. Despite its critical role, little is known about its transport and the regulation of intra-cellular concentrations in the lung. Whilst several vitamin C transporters are identified, such as sodium-ascorbate co-transporters (SVCT1/2) and glucose transporters (GLUTs), the latter transporting the AsC₂H₂ oxidation product DHA, knowledge of their presence and distribution in the human lung is limited (GLUTs) or unknown (SVCTs). We hypothesised that these transporters are present within the bronchial airways and play a vital role in the regulation of epithelial and respiratory tract lining fluid vitamin C concentrations. We investigated the distribution of these transporters in endobronchial biopsies obtained by bronchoscopy from 16 mild asthmatics and 16 age-matched healthy controls. Positive staining was found in blood vessels for SVCT1 and 2; with SVCT 2 and GLUT2 also present in the apical epithelium. Staining with GLUT1 yielded a distinct cell membrane staining. There were no apparent differences between asthmatics and controls. SVCT2 staining was further shown to be predominately localised to goblet cells. SVCT2+goblet cells were negatively correlated with total vitamin C concentrations determined in the bronchial wash of these subjects ($\rho=-0.661$, $p<0.05$). This is the first study to demonstrate that SVCT2 is present in the human lung epithelium, localised mainly within goblet cells. The negative correlation between SVCT2+goblet cells and vitamin C suggests that these cells may play a hitherto unknown function in vitamin C re-uptake and recycling at the air-lung interface.