Allergic airway disease
Studies on diesel exhaust exposures, oxylipins and antioxidants

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Allergic airway disease, i.e. allergic rhinitis (AR) and asthma, is a common health problem. The prevalence is increasing in most countries of the world. Traffic-related air pollution has been found to induce and enhance allergic airway disease, but the underlying mechanisms are not known.

Oxylipins are fatty acid metabolites, of which several have been linked to asthmatic airway inflammation. Oxylipin profiles have previously been investigated in bronchoalveolar lavage (BAL), mainly reflecting the peripheral lung, but not in bronchial wash (BW), which better reflect the proximal airways.

The airway epithelium is covered by a respiratory tract lining fluid (RTLF) The RTLF contains antioxidants to protect from oxidative stress, which may be caused by exposure to air pollution. Previous studies have reported diminished levels of the antioxidant ascorbate (vitamin C) in the RTLF of patients with asthma. Little is known about the regulation of vitamin C in the lung.

The aim of this thesis was to investigate airway inflammatory responses to diesel exhaust exposure in patients with AR and allergic asthma; to evaluate oxylipin profiles in different regions of the lung in patients with allergic asthma; and to study the distribution of vitamin C transporters in the airways of patients with allergic asthma.

Diesel exhaust (PM$_{10}$ 100 µg/m$^3$ for 2 h) induced a neutrophilic airway inflammation in healthy individuals evaluated 18 h after exposure. Patients with AR and asthma did not respond with an enhanced airway inflammation. However, a small increase in myeloperoxidase was found in BAL from patients with AR, as well as decreases in epithelial tryptase and BW stem cell factor. This indicates that other mechanisms than classical inflammation are responsible for the increased sensitivity to traffic-related air pollution in patients with allergic airway disease.

Oxylipin baseline profiles differed between peripheral and proximal airways in both allergic asthmatics and healthy individuals. Total oxylipin concentrations, and five individual oxylipins, primarily from the lipoxygenase (LOX) pathway, were elevated in BW from asthmatics compared to healthy controls, supported by immunohistochemical staining of 15-LOX-1 in the bronchial epithelium. This suggests that lung compartment-specific sampling should be considered in future studies.

Sodium dependent vitamin C transporter 2 (SVCT2) was, for the first time, found present in the human lung epithelium, localised mainly within goblet cells. A negative correlation between SVCT2+ goblet cells and vitamin C suggests that these cells may play a hitherto unknown function in ascorbate re-uptake and recycling at the air-lung interface.

Keywords
Asthma, allergic rhinitis, diesel exhaust, airway inflammation, oxylipins, metabolomics, antioxidants, SVCT2, bronchoscopy