Future analyses of my study cohort can hopefully provide more data on the association between local and systemic inflammation and cardiac comorbidities in COPD.

## Intracellular antioxidant enzyme differency in COPD reflects age-related declines in function, rather than disease state

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*Background:* Numerous studies have demonstrated evidence of oxidative stress in COPD, in both respiratory tract lining fluids and biopsies. Antioxidant response in airway inflammatory cells to a pro-oxidative environment is however poorly understood. We have previously demonstrated an enhanced antioxidant enzyme activity in macrophages from asthmatics. This study was performed to assess whether a similar adaptation in intra-cellular antioxidants occurred in subjects with COPD. The activities of enzymatic antioxidants were examined in alveolar mixed cell populations and compared to healthy age-matched controls (ACs) and young adults, to permit the relative contributions of disease state and natural ageing to be disentangled.

*Methods:* Airway leukocytes were obtained by bronchoscopy-based lavage and cellular activities of Cu,Zn superoxide dismutase (SOD1), glutathione peroxidase (GPx), catalase (CAT) and glutathione reductase (GSSG-red) were determined. In addition, cellular glutathione and glutathione disulphide concentrations were quantified to determine cellular redox status.

*Results:* No differences in the activity of the major enzymatic antioxidants or intra-cellular GSH concentration were observed between COPD patients and ACs. In contrast, significantly reduced SOD1 ($p<0.001$), GPx ($p=0.04$) and GSSG-red ($p=0.01$) activities were observed in the ACs relative to the young adult group. In contrast, catalase activity was elevated in the ACs ($p=0.001$), but again with no further enhancement in the COPD group.

*Conclusion:* These data demonstrate a loss of adaptive plasticity associated with ageing, rather than a COPD-specific down regulation of antioxidant defences. These data do however highlight that in COPD, unlike asthma, the imposition of oxidative stress does not induce protective adaptations, implying a greater sensitivity to oxidant injury *in vivo*.

## Neurotrophins in COPD

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Nerve growth factor (NGF) and neurotrophin-3 (NT-3) belong to the neurotrophin family and are important growth- and survival factors for neurons. Lately, they have also been shown to be potent inflammatory mediators as well as factors promoting tissue repair processes. Increased levels of neurotrophins have previously been shown in the airways of patients with asthma and sarcoidosis.

In this study we investigated the levels of neurotrophins in the airways of patients with moderate to severe COPD (n=25), healthy non-smokers (n=12) and asymptomatic smokers (n=16). We found decreased levels of NGF and NT-3 in bronchoalveolar lavage fluid (BALF) in COPD patients and asymptomatic smokers as compared to healthy non-smokers. These findings suggest that smoking per se decreases the release of neurotrophins in the airways. Structural cells, such as epithelial cells and fibroblasts, are known sources of neurotrophins. We found that NGF secretion was decreased from cultured human lung fibroblasts exposed to cigarette smoke extract.

These results indicate that smoking have inhibitory effects on neurotrophin secretion in the airways. The functional consequence of lower levels of neurotrophins in the airways of smokers and COPD patients is still unknown and further studies are required to elucidate the role of neurotrophins in inflammatory pulmonary diseases.

## Non-invasive markers of airway inflammation in COPD

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Chronic airway inflammation is a key feature in the pathogenesis of COPD, and inhaled corticosteroids (ICS) are widely used to alleviate airway inflammation in COPD. We tested if non-invasive markers of airway inflammation are related to lung function in COPD, or if these markers can predict responsiveness to ICS.