A characterisation of cigarette smoke-induced lung inflammation in mice

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Chronic obstructive pulmonary disease (COPD) is an inflammatory disease of the lung usually associated with cigarette smoke exposure. It is characterised by a progressive and largely irreversible airflow obstruction for which there is currently no effective treatment other than symptomatic relievers. In contrast to other inflammatory diseases, such as asthma, the inflammation associated with COPD is not attenuated by standard glucocorticoid treatment. Given that cigarette smoke has been linked to approximately 90% of COPD cases, animal models of cigarette smoke-induced lung inflammation can provide a logical method of modelling the inflammation underlying this disease.

An acute model of cigarette smoke-induced lung inflammation was developed in C57BL/6 mice using filterless 3R4F cigarettes (Tobacco Health Research Institute, University of Kentucky, Lexington, KY). Based on dose-response data, mice were exposed to a sub-maximal dose of acute cigarette smoke (500ml/min, 50 minutes/exposure) twice daily over 3 days. This acute exposure regimen resulted in increased neutrophilia in the bronchoalveloar lavage fluid (BAL) peaking at 24 hours (Air: $0.06 \pm 0.06 \times 10^3$ vs. Smoke: $39.1 \pm 10.0 \times 10^3$) and was accompanied by an increase in pro-inflammatory cytokine release (IL-1beta, IL-18, IL-23, KC). In contrast, a more chronic model of cigarette smoke exposure where mice were exposed to cigarette smoke for 28 days, not only caused a temporal increase in BAL neutrophilia (figure 1A), but also a sustained increase in BAL macrophages from 10-14 days (figure 1B). This macrophage infiltration was also associated by an increase in the number of pro-inflammatory mediators that could be detected compared to the acute model (IFNgamma, IL-10, IL-1beta, IL-18, IL-23, KC, TNFalpha, Eotaxin, G-CSF, MIP-1alpha).

As the inflammation associated with human COPD is characterised by both neutrophil and macrophage infiltration, the use of more chronic models of cigarette smoke exposure may more closely resemble the human disease. Understanding the mechanism behind the inflammation in more chronic models of cigarette smoke-induced lung inflammation may allow us to discover new therapeutic drug targets to manage the inflammation associated with COPD.
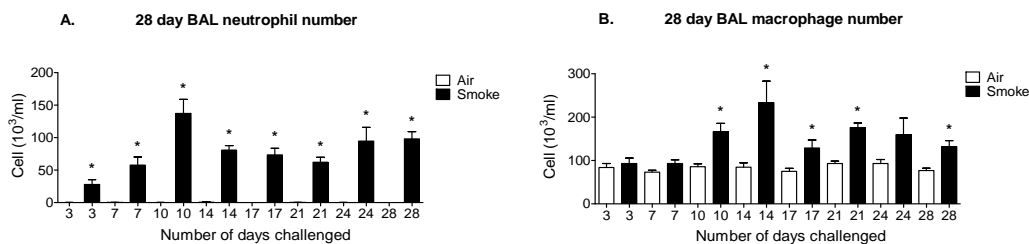

Figure 1: BAL neutrophil and macrophage number following CS exposure: (A) Neutrophil number 24 hours after *x* days CS (n=6) (B) Macrophage number 24 hours after *x* days CS (n=6). Significance (*) tested by unpaired t-test and appropriate post test (p<0.05).