Combination of cigarette smoke, environmental pollutions and lipopolysaccharide to reproduce an experimental murine model of Chronic Obstructive Pulmonary Disease (COPD)

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BACKGROUND COPD is characterized by chronic and abnormal lung inflammation that determines a progressive and irreversible airflow obstruction. According to the latest WHO estimates, currently 64 million people have COPD and WHO predicts that COPD will become the 3rd leading cause of death worldwide by 2030.
Since COPD is a multifactorial disease, it is difficult to reproduce a valid animal model that is able to express all the phenotypic features clinically observed in patients. The main experimental protocols used so far require genetic approaches or the exposure of animals to noxious stimuli such as tobacco smoke (Eltom et al. 2013) and irritant agents (Wagner et al., 2006; Kodavanti et al, 2000). To date in the literature no protocol considers the chronic treatment with multiple risk factors.
Our aim was to develop a model of COPD, exposing animals to environmental conditions similar to those of patients with COPD, in order to reproduce a chronic inflammatory state, emphysema and bronchial remodelling. The validation of this model may be useful for future therapy studies.
METHODS Mice were exposed for 1, 3 or 6 weeks to the main COPD risk factors:

- cigarette smoke
- lipopolysaccharide, to mimic bacterial exacerbations of the disease
- particulate matter (PM10) from urban pollution

We evaluated inflammatory cytokines and tissue-degrading enzymes levels, activation of remodelling pathway and bronchial tissue modifications.
RESULTS The 1st week of exposure is able to induce an increase of inflammatory cytokines that remain significantly elevated in the following weeks. From the 3rd week we observed an increase in gene expression of FGF2, TGF*beta* and *alpha*SMA (key factors in remodelling pathway) and proteolytic enzymes, with a peak in the 6th week of exposure. Histological analysis has shown a progressive thickening of bronchial wall, destruction of lung tissue and enlargement of air spaces (emphysema), in particular in the 6th week of treatment. These data were confirmed with immunochemistry and Western Blot.
CONCLUSIONS This new experimental protocol seems to reproduce a chronic inflammatory response that causes lung tissue injury and consequently activation of tissue repair processes; this condition leads to lung structural alterations with a progressive and irreversible reduction of luminal spaces in the airways. The structural changes observed are very similar to those found in patients with COPD.

Eltom et al. (2013).Curr Protoc Pharmacol. Chapter 5, Unit 5.64
Wagner (2006).J Occup Med Toxicol. 1:12
Kodavanti (2000).Chest. 117:299S-302S