

Lung alert

A role for cigarette fumes in the development of emphysema through reduced alveolar cell proliferation and upregulation of apoptosis

This paper describes a molecular mechanism for the loss of alveolar tissue in cigarette smoke-induced lung injury. Under the influence of adverse environmental conditions including hypoxia, the intracellular stress protein Rtp801 is transcribed. This study sought to demonstrate that Rtp801 downregulates the kinase mammalian target of rapamycin (mTOR) which is responsible for alveolar cell proliferation and upregulates the apoptotic and inflammatory pathways through the activation of the transcription factor nuclear factor kappa B (NF- κ B).

Increased levels of Rtp801 were measured in alveolar cells of patients with chronic obstructive pulmonary disease compared with healthy individuals through histological staining and electrophoresis. Western blotting studies in mice showed significantly increased Rtp801 levels following exposure to cigarette smoke for 7 days. Mice treated with the antioxidant N-acetyl-L-cysteine followed by exposure to smoke showed no overall increase in Rtp801 levels. Overexpression of Rtp801 in mice without exposure to smoke led to significant alveolar apoptosis. Rtp801 knock-out mice were protected from alveolar inflammatory and apoptotic changes in the presence of smoke. Inhibition of NF- κ B activity resulted in decreased levels of inflammation and apoptosis.

These results confirm the role of this cellular stress response in alveolar damage and provide further evidence for a genetic component to emphysema.

► **Yoshida T**, Mett I, Bhunia AK, *et al.* Rtp801, a suppressor of mTOR signalling, is an essential mediator of cigarette smoke-induced pulmonary injury and emphysema. *Nat Med* 2010;**16**:767–73.

M East

Correspondence to M East, AcFY2, Department of Microbiology, Leeds Teaching Hospitals NHS Trust, Old Medical School, Leeds General Infirmary, Great George Street, West Yorkshire, UK; m.east@doctors.net.uk

Thorax 2010; **■**:1. doi:10.1136/thx.2010.149898