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## LUNG ALERT .....

### Elastin fragments are pro-inflammatory in the progression of emphysema

▲ Houghton AM, Quintero PA, Perkins DL, *et al.* Elastin fragments drive disease progression in a murine model of emphysema. *J Clin Invest* 2006;**116**:753–9

**M**ice deficient in the macrophage elastase matrix metalloproteinase-12 (MMP-12) do not develop cigarette smoke induced emphysema or show high levels of macrophage accumulation in the lung on exposure to cigarette smoke. However, monocyte migration to the lung in MMP-12 deficient mice can occur in the presence of an appropriate stimulus. This study used an in vivo model to investigate that stimulus.

Bronchoalveolar lavage (BAL) fluid from wild-type smoke exposed mice (and not MMP-12 deficient controls) showed monocyte chemotactic activity. MMP-12 itself was not chemotactic. Fractionation of BAL fluid from wild-type mice found that elastin fragments were the only matrix protein fragments present in the chemotactic fraction of the fluid. The use of an elastin fragment antibody resulted in monocyte chemotaxis inhibition, even in the presence of cigarette smoke.

Porcine pancreatic elastase generates a model of emphysema that closely resembles human emphysema. Elastin fragment inhibition by elastin fragment antibody reduced lung macrophage accumulation and airspace disease in this model. The authors hypothesise that alveolar macrophage activation occurs in response to chronic cigarette smoke exposure, resulting in macrophage release of MMP-12. MMP-12 degrades lung extracellular matrix components and generates the production of elastin fragments that are chemotactic to monocytes and which drive disease progression.

**Y Aggarwal**

Senior House Officer, St George's Hospital, London, UK; dr\_y\_aggarwal@hotmail.com