

## **What the Experts say....**

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*One major criticism of mouse models of airway remodelling has been that the murine airways are relatively simple compared with those of humans. Other models have emerged that use larger animals that are arguably more anatomically similar to humans. A recent sheep model takes advantage of the fact that ovine lung innervation and blood supply is nearer to that of humans than mice [Snibson et al].*

**Lloyd CM and DS Robinson. "Airway remodelling: from basic science to clinical practice." Eur Respir J 2007; 29:1020-1032**

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*Persistence of remodelling in parallel with increased AHR has been an inconsistent finding in mouse models.....A chronic inhalation model using HDM has also recently been developed in sheep [Snibson et al], with changes...observed...which have close resemblance to human disease. Since sheep lungs are anatomically more similar tot those of humans than are mouse lungs and are large enough for repeat airway sampling using bronchoscopy, such a model has major potential for the investigation of mechanisms of disease, as well as of modifying interventions.*

**Walters EH et al "Airway remodelling:from basic science to clinical practice" Eur Respir J 2007; 30:547-588**

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*So where does the experimental model presented by Bischof et al. lie in relation to...existing ovine models of human allergic asthma?*

*In the first instance, these authors have sought to define the immunological features of the lung allergic response. In this regard the use of house dust mite represents a welcome and shrewd initiative in that, in addition to the well-recognized relevance of this allergen to human asthma, sensitization and challenge with an allergen to which sheep would be unlikely to be naturally exposed facilitates interpretation of immunological and cellular responses in relation to a defined exposure history. This contrasts with the situation relating to A.suum where allergic skin reactivity can develop in sheep unlikely to have had prior contact with this antigen [62]....*

*In the second instance these authors adopt a local lung challenge protocol to evaluate pulmonary responses to allergen. Segmental approaches have hitherto proved valuable in the context of defining, at functional, cellular and immune levels, the local lung response to antigen challenge in both experimental animals and in humans [63-71].*

**Collie DDS "Comparative, complementary and relevant: the immunological basis of ovine lung allergic responses" Clin Exp Allergy 2003; 33:282-286**

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*As there is no need for anesthetizing the animals, the allergic sheep is an interesting model for prolonged and repeated investigations of the respiratory function and there is evidence for a progressive decline of lung function in chronically challenged sheep [Koumoundourous et al].*

*..a variety of equipments of human pneumology has been applied successfully to calves, sheep and pigs...Such techniques allow the assessment of airway obstructions using the same parameters as known and evaluated for humans...In so far, direct comparisons between data obtained in large animal models and data obtained in patients becomes possible. The same is true for techniques obtaining samples from the respiratory tract or imaging techniques. In a lot of cases, the technical equipment to perform bronchoscopy, BAL, biopsy or EBC collection in animals with body weights comparable to humans are applicable directly or with less modifications.....*

*Large animal species present unique physiological and natural preconditions as well as experimental advantages that are of great value to develop alternative models of allergic an non-allergic chronic airway diseases....alternative models in larger animals may supplement well established asthma models in laboratory species, and may contribute to a better understanding of complex respiratory diseases as asthma or COPD.*

**Kirschvink N and P Reinhold "Use of alternative animals as asthma models"  
Current Drug Targets, 2008, 9:470-484**