

“Airway remodelling in asthma; implications for disease severity”

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Airway tissue remodeling in asthma is a striking and involves the epithelium through enhanced fragility, the subepithelial compartment through fibrosis, angiogenesis, goblet cell and mucus gland proliferation and growth of airway smooth muscle[1]. The latter abnormality has been frequently postulated to account for airway hyperresponsiveness, a cardinal and somewhat refractory abnormality in asthma. The quantity of airway smooth muscle in the large airways is linked to asthma severity[2-4]. The mechanisms of airway smooth muscle growth are of intense interest and, to date, are somewhat obscure. Theories include hyperplasia of smooth muscle in situ, the addition of new muscle to existing muscle bundles through the expansion of contractile cells in the subepithelial compartment. The source of such cells may be local myofibroblasts derived from the epithelium or from mesenchymal stem cells. Evidence will be presented to demonstrate hyperplasia of airway smooth muscle in the biopsy specimens obtained from severe asthmatic patients. Furthermore the role of the epidermal growth factor receptor in the proliferative process will be explored through studies on human tissues and animal models[5;6]. Several mechanisms of such hyperplasia will be discussed. Activated CD4+ T cells, present in the smooth muscle bundles, may trigger smooth muscle proliferation. The epithelium may release ligands of the epidermal growth factor receptor to promote proliferation of the underlying muscle. Key mediators of asthmatic airway inflammation and narrowing such as leukotrienes and interleukin-13 have the potential to play a role in the growth process[5;7]. Experimental data suggest a possible ameliorating effect of some existing therapies against remodelling, but overall the process appears to be resistant. Exploring avenues for reversal of remodeling may in the long run provide the best prospects of cure of the disease.

References

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