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Integrin $\alpha_9\beta_1$ potentially plays a role in reducing airway smooth muscle contraction

Contraction of airway smooth muscle in response to innocuous stimuli is pathognomonic of asthma. However the mechanisms responsible for the loss of normal control are only partially understood. Therefore the authors sought to explore the modulatory role of integrin $\alpha_9\beta_1$ on airway smooth muscle contraction given previous results demonstrating high expression levels in mouse airway smooth muscle and the respiratory phenotype of α_9 knockout (KO) mice.

Through a number of elegant experiments the protective effect of integrin $\alpha_9\beta_1$ was found to be related to control of calcium release from the sarcoplasmic reticulum following G protein coupled receptor ligation. The authors established that ligation of $\alpha_9\beta_1$ reduces local levels of phosphatidylinositol 4,5-bisphosphate (PIP₂) through co-localisation of the enzymes phosphatidylinositol-4-phosphate 5-kinase 1 α (PIP5K1 γ (responsible for production of PIP₂)) and spermidine/spermine N¹-acetyltransferase (SSAT). As PIP5K1 γ activity requires the presence of higher order polyamines for full function the co-localisation with SSAT and hence its activity resulted in a localised reduction of higher order polyamines leading to reduced PIP₂ and hence Inositol trisphosphate (IP₃). The reduction in IP₃ resulted in a reduction in intracellular calcium oscillations from the sarcoplasmic reticulum and hence airway smooth muscle contraction. The authors also confirmed some of their findings in ex vivo human airways.

Further exploration and confirmation of the role for integrin $\alpha_9\beta_1$ in the airway hyper-responsiveness characteristic of human asthma should be considered. Pharmacological manipulation of either PIP5K1 γ or SSAT or promotion of their co-localisation may be of clinical relevance.

► Chen C, Kudo M *et al.* Integrin $\alpha_9\beta_1$ in airway smooth muscle suppresses exaggerated airway narrowing. *J Clin Invest* 2012;122: 2916–27

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