Intergrin $\alpha_9\beta_1$ 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 $\alpha_9$ 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 1a (PIP5K1a) and spermidine/spermine N1-acetyltransferase (SSAT). As PIP5K1a activity requires the presence of higher order polyamines for full function, the co-localisation with SSAT and hence its activity results 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 PIP5K1a or SSAT or promotion of their co-localisation may be of clinical relevance.


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Competing interests None.

Provenance and peer review Not commissioned; externally peer reviewed.

To cite Spears M. Thorax 2013;68:793.

Published Online First 1 November 2012
Thorax 2013;68:793. doi:10.1136/thoraxjnl-2012-202843