GABAergic system as a target for treatment in asthma


Overproduction of mucus is an important cause of death in asthma. This study investigated the role of γ-aminobutyric acid (GABA) synthetic enzyme, glutamic acid decarboxylase (GAD) and the subtype A GABA receptor (GABA_A_R) in airway epithelial cells and mouse models and their roles in asthma.

The authors performed immunoblot assays and immunohistochemistry to look at expression of GABA_A_R subunits in pulmonary epithelial cell lines, and investigated GABA evoked currents. They also sensitised and challenged mice with ovalbumin (OVA) to induce asthma-like reactions, and studied interleukin (IL-13) expression.

GABA_A_R and GABA production mechanisms were expressed in pulmonary epithelial cells and mouse lung tissue. GABA evoked rapid inward flow of current which was inhibited by GABA antagonists. GABA also induced an increased level of mucin-like glycoprotein production. The expression of GAD and GABA_A_R in airway epithelial cells was significantly increased after allergen exposure in both human asthmatic subjects and mice sensitised to OVA. Mice demonstrated an increased expression and production of IL-13 after allergen exposure. In vivo, GAD and GABA_A_R expression was significantly increased in mice given IL-13. When sensitised mice were challenged with OVA in the presence of GABA antagonists, goblet cell hyperplasia and mucus production were reduced but the increased expression of IL-13 was unaffected.

Inhibition of this GABAergic system resulted in reduced goblet cell activation and less mucus production. The airway epithelial GABA_A_R may be a useful target for therapeutic interventions in asthma. IL-13 may have an important role in initiating the airway epithelial GABA signalling pathway in asthma.

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