TARGETING TMEM16A ION CHANNELS SUPPRESSES AIRWAY HYPERREACTIVITY, INFLAMMATION, AND REMODELING IN AN EXPERIMENTAL GUINEA PIG ASTHMA MODEL.

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TMEM16A belongs to the protein family of calcium-activated chloride channels. They are involved in the functions of several airway-resident cell types, especially epithelial secretory cells, immune cells and also can modify the membrane potential of excitatable airway cells. In addition to their physiological function, there is evidence of their participation in inflammation, increasing contractility, mucus production, and airway remodeling. The present study investigates the effect of an inhaled selective antagonist of TMEM16A (CaCCinh-A01 (10 μM)) in experimental model of ovalbumin-induced allergic asthma. Ovalbumin sensitization increases the expression of TMEM16A in the airways, indicating their involvement in pathological processes. *In vivo* experiments show the ability of the CaCCinh-A01 to reduce hallmarks of increased airway defense reflexes such as cough and airway resistance without significant influence on mucociliary clearance. Immunological analyses of inflammation and remodeling markers indicate that administration of CaCCinh-A01 led to a reduction in Th_2 cytokine and MUCA5 levels. Results of this study indicate that inhibition of TMEM16A by CaCCinh-A01 appears to be beneficial in allergic asthma, but further studies are needed to confirm the antiasthmatic effect.

Keywords: asthma, inflammation, TMEM16A, CaCCinh-A01

The study was financially supported by grant APVV-19-033, VEGA 1/0314/21, VEGA 1/0253/19, and Comenius University Grant UK/188/2023.