Capsaicin-induced bronchoconstriction in passive sensitized human precision-cut lung slices is mast cell dependent

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Introduction

Mast cells play an pivotal role in the pathogenesis of allergic asthma. Their activation and degranulation is the primary event of the early airway response (EAR). The most extensively studied stimulus for mast cell activation and degranulation is the aggregation of their high-affinity IgE-receptor (FcεRI) by IgE and antigen. However, there is an increasing evidence of a mast cell degranulation induced by neuropeptides. Capsaicin is an active component of chili pepper and is able to stimulate neural C-fibers via activation of the transient receptor potential cation channel subfamily V member 1 (TrPV1) leading to neuropeptide secretion. The aim of the project is to develop a suitable model to mimic an acute airway response and bronchoconstriction including immunologic features in human passive sensitized precision cut lung slices (PCLS).

Methods

Human lungs were filled with agarose and cut into ~400µm thick slices with cross-sectioned airways using Krumdieck tissue slicer. Generated precision cut lung slices (PCLS) were incubated overnight with 1% plasma derived from allergic (+/-H1 receptor antagonist (Ceterizine®)) or non-allergic human donors, as well as IgE inactivated allergic plasma. After overnight sensitization, lung tissue was stimulated with capsaicin (50 µM) or HDM (10 µg/ml) and bronchoconstriction was visualized using video microscopy. Bronchoconstriction were determined as reduction of the airway area in % of the initial area (Fig.1). Cyrosection preparations from human bronchus were immunostained using the pan neuronal marker PGP9.5, antibodies against the human IgE, and the mast cell tryptase (yellow). Human bronchus were treated with (D-F) or without (A-C) capsaicin.

Results

Spatial interactions of mast cells with C-fiber nerves in human bronchus

Immunostaining of C nerve fibers and mast cells showed the anatomical proximity between neural and mast cells in human bronchus (Fig.2). This close contact may enable nerves-mast cells communication.

Caspase induced mast cell degranulation in human bronchus

Mast cell degranulation was observed in human bronchus after capsaicin stimulation. Immunostaining of mast cells revealed degranulation as evidenced by loss of cell-stored and appearance of freely located mast cell tryptase (Fig.3).

Passive sensitization of human PCLS leads to increased bronchoconstriction after C-fiber stimulation by capsaicin

Caspase induced bronchoconstriction (Fig.4 hypothesis) leads to a significant reduction of the airway area of 43% in sensitized PCLS. PCLS treated with non allergic plasma or medium showed a reduction of the airway area of 2% and 13% after two days incubation, respectively (Fig. 5 A). Additionally, capsaicin-induced bronchoconstriction was totally inhibited by 10 µM of the histamidine 1 receptor antagonist (Fig. 5 B).

Discussion & Conclusion

- The presence of allergic plasma influences neurally induced bronchoconstriction in human PCLS.
- Anatomic colocalization of mast cells and nerve fibers in human bronchus.
- Capsaicin induced mast cell degranulation in human bronchus.
- Passive sensitized human PCLS can mimic an early airway response (EAR) by HDM stimulation.
- Passive sensitized human PCLS show increased bronchoconstriction in response to the C-fiber agonist capsaicin which is histamine 1 receptor dependent.

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This work was funded by Fraunhofer ITEM / DFG / DZL.