Journal club

Histamine-releasing factor: a possible future therapeutic target for asthma and allergy

Mast cells and basophils are key players in the IgE-dependent allergic response. These cells trigger an inflammatory cascade by secreting numerous preformed pro-inflammatory chemical mediators such as histamine, proteases and cytokines into the blood. Histamine-releasing factor (HRF), found in nasal, skin blister and bronchoalveolar lavage fluids, is a protein secreted by macrophages that can stimulate histamine, interleukin 4 and IL-3 production from IgE-sensitised basophils and mast cells. Despite considerable efforts, research has failed to identify a HRF receptor. However, HRF is known to have intracellular and extracellular functions, with the latter implicated in late-phase allergic reactions and chronic inflammation.

This study identified a subset of IgE and IgG antibodies as HRF-interacting molecules in vitro. Through complex molecular research techniques it was confirmed that HRF together with HRF-reactive IgE triggered mast cell activation in vitro, confirming its pro-inflammatory role. Specific HRF inhibitor peptides were also characterised. Through several different intricate experiments these peptides were found to suppress passive cutaneous anaphylaxis and mast cell-dependent airway inflammation and substantially reduce allergic airway inflammation. These findings provide further clarification that HRF promotes allergic inflammation in the skin and lung via an immediate hypersensitivity reaction.

The authors conclude that HRF could be a future novel therapeutic target for asthma and allergy. However, this development may be reliant on the discovery of a specific HRF receptor. Furthermore, the additional intracellular activities of HRF are extensive and more specific research related to these functions may also be essential.

► **Kashiwakura JC**, Ando T, Matsumoto K, *et al*. Histamine-releasing factor has a proinflammatory role in mouse models of asthma and allergy. *J Clin Invest* 2012;**122**:218–28.

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