Symposium: New concepts in dermatopharmacology

Dermatopharmacological importance of H4-receptors

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Histamine is a multifunctional biological amine with diverse activities in the immune system. During inflammation, histamine is released from preformed stores in mast cells and basophils.

Histamine exerts its effects through four defined histamine receptor subtypes, namely H1R, H2R, H3R and H4R. All HxRs belong to the superfamily of G-protein-coupled receptors (GPCRs) that possess seven transmembrane domains. Each receptor is characterized by a distinct function: the H1R is mostly involved in acute allergic reactions, the H2R is responsible for gastric acid secretion and the H3R is primarily expressed in the brain and modulates neurotransmission. The H4R is the newest of the four histamine receptors identified and is expressed in tissues and cells of the immune system such as the spleen, thymus, bone marrow and preferentially in leukocytes.

The H4R was independently identified about 10 years ago by several groups and has already attracted substantial attention by the scientific community. A major reason for the exceptional interest in the H4R is the fact that this GPCR is expressed in cells of the immune system including mast cells, eosinophils, various T cell populations and antigen-presenting dendritic cells.

Several activities of the H4R on cells involved in inflammatory responses have been investigated so far. Chemotaxis of mast cells, eosinophils, monocyte-derived dendritic cells and natural killer cells have been noted via the H4R. In former studies we could show functional effects of H4R on cells involved in inflammatory and allergic diseases such as human monocytes and dendritic cells including Langerhans cells. Furthermore we showed that the H4R is up-regulated under Th2 conditions on human T-cells. The stimulation of Th2 cells via H4R leads to the activation of AP-1 and to an increase of IL-31 mRNA.

Based on this expression pattern and functions, it is assumed that the H4R plays a pro-inflammatory role in various diseases including bronchial asthma, chronic allergic dermatitis and pruritus [4-7]. Accordingly, substantial efforts have been made towards the development of potent and selective H4R antagonists and first clinical studies have been performed or are planned with these new substances.