

Histamine Production by Non-mast Cells and the Roles of Histamine in Allergic Inflammation

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Histamine plays roles in inflammation, allergic responses, immune responses, gastric acid release and neurotransmission in the central nervous system via H1 – H4 receptors. Mast cells and basophils release histamine within a few minutes after stimulation. On the other hand, the inflammatory cells, such as macrophages and neutrophils, become to express HDC at the inflammatory site and release histamine without storing it in the cells. We have reported that histamine induces the vascular permeability increase in the anaphylactic phase, inhibits the production of inflammatory cytokines in acute phase of allergic inflammation and induces angiogenesis in chronic inflammation.

A mouse macrophage-like cell line RAW 264 cells produced histamine by the stimulation with tumor promoters such as 12-*O*-tetradecanoylphorbol 13-acetate (TPA), which induce the increase in HDC activity in mouse skin. In this paper, we found that the application of TPA on the mouse ear 5 and 10 days after the sensitization with picryl chloride changed picryl chloride-induced contact hypersensitivity to biphasic response. The numbers of eosinophils and mast cells in the inflammatory lesion were also increased by the application of TPA. In this TPA-modified contact dermatitis model, the picryl chloride-induced ear swelling was potently inhibited by the combined treatment of the histamine H3/H4 receptor antagonist thioperamide and the H1 receptor antagonist pyrilamine. Thus, histamine might be involved in the development of allergic dermatitis.