

Histamine H₁ Receptor Gene Expression Mechanism as a Target of Therapeutics for Allergy

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Histamine H₁ receptors (H₁Rs) mediate type-1 allergy and H₁ anti-histamines are major therapeutics for allergic diseases. The expression level of H₁Rs is regulated by two mechanisms and seems to play important roles in allergic symptoms. The two mechanisms include receptor down-regulation through desensitization and receptor up-regulation through gene expression. Phosphorylation of H₁Rs seemed crucial in H₁R-mediated down-regulation. Several protein kinases could phosphorylate H₁Rs. On the other hand, H₁R up-regulation was also induced by H₁R stimulation through H₁R gene expression. Protein kinase C was suggested to mediate the gene expression. Up-regulation of H₁R and H₁R mRNA was induced in nasal mucosa of nasal hypersensitivity allergy model rats upon allergy provocation suggesting the dominance of H₁R gene expression, compared with H₁R desensitization. Therapeutics for allergic diseases strongly suppressed the elevation of H₁R mRNA in the nasal mucosa. Dexamethasone targeted H₁R gene promoter, while targets of other therapeutics including suplastat, Sho-seiryu-to and Kujin seemed at up-stream mediators. Suplastat strongly suppressed the elevation of interleukin-4 mRNA, whereas Sho-seiryu-to and Kujin strongly suppressed interleukin-5 mRNA in the nasal mucosa of allergic rats.