Histamine signaling-related gene expression in allergy model rats

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Abnormal expression of various genes has been reported in allergy. There is considerable interest in developing novel therapeutics that target allergy-sensitive gene expression. Histamine plays a major role in allergy. Expression of both histamine H_1 receptor (H1R) and histidinde decarboxylase (HDC) genes is thought to play essential role in histamine signaling, and these genes could be allergic disease-sensitive genes. Allergy model rat was developed by sensitization with toluene 2, 4-diisocyanate (TDI). Severe sneezing, rhinorrhea and nasal swelling were induced immediately after the provocation. Levels of both H1R mRNA and HDC mRNA were elevated for several hours resulting in up-regulation of H1R and increased HDC activity in nasal mucosa. Glucocorticoid, suplatast tosilate and some *Kampo* medicines suppressed symptoms moderately, but strongly suppressed elevations of both H1R mRNA and HDC mRNA. Single treatment of antihistamines partially suppressed elevation of H1R mRNA whereas prolonged pretreatment suppressed it strongly. Elevation of H1R gene expression was observed in vitro after the stimulation of H1Rs in HeLa cells. H1R stimulation induced the activation of H1R promoter through PKC-delta isoform-mediated signaling. Glucocorticoid strongly suppressed H1R gene promoter activity. However, suplatast, *Sho-seiryu-to* and *Kujin* (Sophorae radix) did not. IL-4 induced H1R mRNA elevation, and suplatast and prolonged pretreatment of antihistamines almost completely suppressed IL-4 mRNA elevation. These results show that gene expression mechanisms of H1R and HDC are targeted by therapeutics for allergy. Mechanisms of action each drug remains to be elucidated.