Notable alleviation of allergic symptoms through suppression of both histamine H₁ receptor and IL-9 gene expressions

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Allergic rhinitis is a representative incurable disease. Symptoms are not sufficiently improved by current therapeutics. Then the novel therapy having notable alleviation is highly expected. We succeeded in finding the correlation between symptoms and level of histamine H₁ receptor (H1R) mRNA in the nasal mucosa of pollinosis patients. Treatment of antihistamines alleviated allergic symptoms, and suppressed H1R mRNA up-regulation. H1R gene expression was suggested to participate in allergic symptoms.

H1R gene expression was induced by H1R stimulation and protein kinase C-delta (PKC-delta) activation, and H1R up-regulation was not only with antihistamines but also with *Kujin*, an anti-allergic *Kampo* medicine. PKC-delta and heat shock protein 90 (HSP90) are known to form complex. (-)-Maackiain was successfully identified as an active substance of *Kujin*, and HSP90 was observed to be a target molecule. Allergic symptoms were alleviated by the treatment of (-)-maackiain as well as antihistamines to nasal hypersensitivity model rats.

Combination treatment of antihistamines and suplatast tosilate to the model rats induced notable alleviation of allergic symptoms. Combination treatment of antihistamines and Awa-tea, a local fermented tea in Tokushima, or extract of lotus root showed similar notable alleviation. We discovered that suplatast, Awa-tea and extract of lotus root all suppressed IL-9 gene expression.

In conclusion, H1R and IL-9 gene expressions participate in allergic symptoms, and combination therapy using suppressors of the two gene expressions is expected for notable alleviation of allergic rhinitis. Gene expression of H1R is suggested to be a pathological mechanism of allergic rhinitis, and IL-9 is suggested to be the second one. The intracellular target molecules of (-)-maackiain and pyrogallol are expected to be novel drug targets for allergic rhinitis.