S53-5 Human high affinity IgE receptor, FcεRI β-chain may be a good target molecule for treatment of allergic diseases

◯Yoshimichi OKAYAMA[1]

[1]Nihon Univ. Grad. Sch. Med. Sci.

The roles of FcεRIβ (β) in human mast cells (MCs) and localization of β^+ MCs in allergic diseases have not been evaluated. We compared the expression of β in giant papillae obtained from patients with chronic allergic conjunctivitis (n = 10) with that in conjunctiva from patients with non-allergic diseases (n = 10) employing a specific anti-human β antibody. The densities of MCs were significantly increased in cases of giant papillae compared with controls. The ratio of β^+ cell number to FcεRIα^+ cell number in giant papillae samples (0.69±0.08) was significantly higher than that of the control samples (0.07±0.16). The β^+ cells were preferentially localized within and around the epithelial tissue. The diminution of β by lentiviral shRNA silencing technique significantly down-regulated cell surface FcεRIα expression, IgE-dependent degranulation, and PGD_2 and cytokine production. The diminution of β inhibited the redistribution of Lyn to the cell membrane following aggregation of FcεRI. We thus developed recombinant cell-penetrating forms for intracellular delivery to disturb the redistribution of Lyn to the cell membrane after FcεRI aggregation. We found that this recombinant was localized in cytoplasm and captured cytosolic Lyn in human MCs. The recombinant significantly inhibited IgE-dependent histamine release and PGD_2 synthesis. However, the recombinant did not cause any effects on IL-8 production by U937 cells after FcγRI aggregation. Mouse forms of the recombinant had no effects on IgE-dependent degranulation in mouse MCs. Thus, the recombinant may have a good potential for treatment of human allergic diseases.