Synopsis of Original Research Paper

Therapeutic approach for allergic skin diseases via blocking prostaglandin D2 receptors

Takahiro Satoh

Department of Dermatology Graduate School, Tokyo Medical and Dental University

Biological activities of prostaglandin D2 (PGD2) are thought to be mediated by the classical DP receptor and CRTH2 (chemoattractant receptor-homologous molecule expressed on Th2 cells). In the present study, to examine the role of PGD2-CRTH2 interaction in development of allergic inflammation, we generated mice that contain a targeted disruption of the CRTH2 gene. We used these mice to characterize chronic cutaneous inflammatory processes, including IgE-mediated very-late-phase responses and chronic contact hypersensitivity induced by repeated hapten application. The present findings indicate that IgE-mediated cutaneous responses are dependent on PGD2. Ear swelling responses were suppressed by administration of HQL-79, which is a PGD synthase inhibitor. CRTH2-deficient mice failed to develop IgE-induced very-late-phase cutaneous responses, which are histologically characterized by a decrease in infiltrative lymphocytes, eosinophils and basophils, associated with inhibited production of MDC and RANTES. However, local production of IL-4 and IFNγ was not affected by lack of CRTH2. In chronic contact hypersensitivity models, CRTH2 deficiency also resulted in diminished skin responses and serum IgE production. These findings indicate that PGD2 signaling via the CRTH2 receptor plays important roles in IgE-mediated cutaneous responses and chronic contact hypersensitivity reactions. CRTH2 may represent a novel therapeutic target for the treatment of chronic allergic skin inflammation, such as atopic dermatitis.