Synopsis of Original Research Paper

Identification of the histamine-producing cells in chronic allergic contact dermatitis model using HDC-gene reporter mice.

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Reducing the rate for contact dermatitis caused by cosmetic materials is crucial in cosmetology. Histamine is one of the physiological substances which produce itching sensation in contact dermatitis. We generated histamine-deficient mice by knocking out the gene for histamine producing enzyme, histidine decarboxylase (HDC), to be used for the analysis of histamine activity in vivo. The mechanisms of histamine activity in contact dermatitis were analyzed in mouse model which was produced by the repeated ointment of trinitro-chlorobenzene (TNCB) on their back skin. The inflammation of histidine decarboxylasae knock out (HDC-KO) mice were milder compared to their wild type counterpart. The number of regulatory T cells (Tregs) in the dermis was found to be reduced by the existence of histamine. This control mechanism appeared to be transmitted by TGF-β1 for its positive effect on the number of Tregs. The action of histamine is known to be transmitted through 4 types of histamine receptors (H1 to H4). H1 and H4 receptors among these receptors were pharmacologically found to transmit the signal of inflammation in this contact dermatitis model. Including these information histamine is a key substance for producing noxious symptom in dermatological diseases e.g. chronic inflammation, would healing and contact dermatitis. The regulatory mechanisms of histamine synthesis, however, in their pathological contexts have not been completely clarified because of lack of experimental materials. We lately produced the reporter mice which produce fluorescent signal according to their expression of histidine decarboxylase gene. Since these gene-manipulated mice emit fluorescent signal when they are active in transcription of histamine-synthesizing gene, we could analyze the timing and source of cells for histamine production in disease model through observation of fluorescence using this reporter mice. Previously we generated plasmid-based reporter mice to this purpose, however, the mice were prove to be useless, since the emission of fluorescence was not limited to histamine producing cells. We produced lately a BAC (bacterial artificial chromosome)-based transgenic mice to dodge this problem. We will produce a model of contact dermatitis in the new transgenic mice and discuss the role of histamine producing cells in contact dermatitis.