Synopsis of Original Research Paper

Regulation of the pathogenesis of allergic dermatitis by the interference of amplification loop between skin and immune cells

Miyuki Omori-Miyake

Dept. of Infections and Host Defenses, Ehime University Graduate School of Medicine

Repeated exposures to a certain antigen onto the skin develop the pathogenesis of allergic contact dermatitis (ACD) with the itchy skin rash. For the treatment of ACD, topical steroids have commonly been used. However, the use of steroids induces a variety of adverse effects including skin thinning and atrophy, ecchymosis and impaired wound healing. Therefore, the development of any non-steroid drugs such as immunomodulatory drugs with minimized unfavorable effects have been expected to treat ACD. In this study, we have asked if any immunomodulatory drugs could have the potential to be used for the treatment of ACD.

The inflammatory responses to an allergen in ACD result in cascading events: the activation, differentiation and memory generation of antigen-specific T cells, the infiltration of inflammatory cells in the lesional skin by inflammatory cytokines and chemokines, and the disruption of epidermal structure and barrier functions. The impaired barrier of the epidermis could amplify the penetration of antigen. Since T cells play an essential role in the development of ACD, we evaluated several drugs whether each drug could have a potential to regulate functions of T cells. Consequently, we decided to focus on a Jak inhibitor in this study. The mice that received a Jak inhibitor on ACD showed milder skin symptoms, a lower number of T cells in the lesional skin and the skin-draining lymph nodes, a lower capability of inflammatory cytokine-productions in T cells, a lower number of neutrophils accumulated in the lesional skin than the control mice. In addition, differentiating T cells *in vitro* that were treated with a Jak inhibitor had lower levels of the extracellular acidification rate, the mTORC1 activity and the expression of genes that were related to glycolysis under the stimulation with recombinant IL-2. All the results suggested that a Jak inhibitor could be used for the treatment of ACD with a potential to down-regulate T cell-functions via interference of glycolysis.