Synopsis of Original Research Paper

Analysis on the mechanism of antigen recognition by autoreactive $CD4^+$T cells in the skin

Hayato Takahashi

Department of Dermatology, Keio University School of Medicine

Interface dermatitis is a pathological term that consists of lymphocyte infiltration into dermo-epidermal junction, exocytosis, liquefaction degeneration of keratinocytes in the basal layer, Civatte body. This pathological change is commonly and frequently seen in several inflammatory skin diseases such as lichen planus, graft-versus-host disease, dermatomyositis, lupus erythematosus, severe drug adverse eruption and so on. However, the details on the pathomechanism of the disease remains still unclear. Recently we developed Dsg3-specific T cell receptor transgenic mice (Dsg3H1 mice) that T cells recognize Dsg3, epidermal targeted autoantigen by pemphigus vulgaris. Dsg3H1 $CD4^+$ T cells can recognize Dsg3 in vivo and attack epidermal keratinocyte when they are transferred into $Rag2^{-/-}$ mice. In this study, we investigated pathomechanism of interface dermatitis by using Dsg3H1 T cells. When factor X is knocked-out in Dsg3H1 $CD4^+$ T cells, recipient $Rag2^{-/-}$ mice did not develop interface dermatitis. However, Dsg3H1 $CD4^+$ T cells vigorously proliferated in skin-draining lymph nodes and prominent lymphadenopathy was observed. This result suggested that factor X is important for Dsg3H1 T cells to leave lymph nodes to target tissue but not to recognize the antigens and proliferate. On the other hand, how Dsg3H1 $CD4^+$ T cells recognize epidermal autoantigen and damage keratinocytes is another question. Antigen presentation by MHC class II on keratinocytes is believed to mediate this action. But supportive evidence is very limited. Using animal model of interface dermatitis, this fundamental question can be answered. The investigation to obtain a conclusion is still under way. In conclusion, through this study, factor X was identified as crucial molecule to achieve interface dermatitis.