Inducible skin-associated lymphoid tissue (iSALT) is detected in the scalp treated with topical immunotherapy for alopecia areata

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The lymph nodes have an optimal structure that allows the interaction between T cells, B cells and antigen-presenting dendritic cells (dDCs) on a matrix made up by stromal cells. Such organized structures can also be formed in tertiary lymphoid organs (TLOs) at sites of chronic immune responses. These structures have been named according to their anatomical site, such as inducible bronchus-associated lymphoid tissue (iBALT) and mucosa associated lymphoid tissue (MAIT). As similar structure in the skin, Streilein proposed a concept of skin-associated lymphoid tissue (SALT). Recently, through the detailed examination of the elicitation phase of contact hypersensitivity (CHS), we have revealed that iSALT in the skin is an important target organ of autoimmune disease. In this study, we have performed immunohistochemistry in the skin section obtained from AA patients treated with topical immunotherapy to detect iSALT in human skin. As a result, immunohistochemistry revealed tightly packed infiltrations of numerous T cells, B cells and dDCs in the dermal perivascular areas and around the hair follicles. These results suggest the possibility that iSALT plays an essential role in topical immunotherapy for alopecia areata.

Bach2 suppresses tumor immunity by repressing effector function-related gene in CD8+ T cells

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Bach2 is a transcription repressor which binds to Mael-recognition elements (MAREs). Bach2 plays essential roles in T cell development, immunoglobulin class-switch recombination and somatic hypermutation of immunoglobulin encoding genes. Bach2 is also required for development of effector T cells and regulatory T cells. These findings suggest that Bach2 plays important roles in development, differentiation and functions of various immune cells. We speculated that the deficiency of Bach2 would result in an altered immune response in tumor rejection. A subcutaneous transplantation model revealed that the tumor transplanted into the Bach2 KO mice grew more slowly than the wild-type (WT) mice. These observations suggested that tumor immunity in the Bach2 KO mice was upregulated. The flowcytometric analysis revealed that the absolute number of CD8+ T cells increased in the tumors in Bach2 KO mice than WT mice. A cell trace violet (CTV) assay revealed that the Bach2 KO CD8+ T cells exhibited stronger cytotoxicity against B16F10 than the WT cells in vitro. The expression levels of Granzyme B and IFNγ were higher in Bach2 KO CD8+ T cells than WT cells. An electro-phoretic mobility-shift assay revealed that Bach2 bound to the MARE-like sequence of FasL and GzmB. The binding of Bach2 to the MARE-like sequence of GzmB restricted the hetero-dimer formation with Mael. An immunofluorescent staining revealed that Bach2 was excluded into cytoplasmic regions from nuclear regions after TCR stimulation. These results suggest that Bach2 directly represses a set of effector genes and localizations changes of Bach2 is important for the acquisition of effector function in CD8+ T cells.

Estradiol plays regulatory roles in an imiquimod-induced murine psoriatic dermatitis through down-regulation of keratinocyte activation

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It has been reported that psoriasis symptoms have improved during pregnancy, while deteriorated after menopause, suggesting protective roles of estradiol in the development of psoriasis. In addition, the severity of psoriasis tends to be higher in male in female in Asian countries. However, the precise mechanisms of estradiol regulating the development of psoriasis remain largely unclear. To evaluate the potential roles of estradiol in the development of psoriasis, we firstly subjected ovariectomized-female mice to an imiquimod-induced murine psoriasis model with or without systemic estradiol administration. Mice treated with estradiol exhibited significantly attenuated dermal edema, inflammatory cell infiltration and epidermal hyperplasia when compared to vehicle-treated mice. The mRNA expressions of keratinocyte-derived cytokines such as IL-24 and CXCL1 were derived. CD11c+ dDCs in both serum and blister fluid of BP patients were correlated with BP180 antibody titers and disease activities. Sema4D-expressing cells were accumulated in BP subepidermal blister as well. The expression of membrane CD110 on granulocytes rather than lymphocytes decreased to different extents in the acute phase compared with those in normal controls, and this decline almost recovered in the stable phase. In vitro, incubation of sSema4D with BP-PBMCs resulted in significantly higher levels of anti-BP180 antibody productions. Our study demonstrated that sSema4D derived from lesional peripheral granulocytes promote the production of BP180 antibody by B cells thus contributes to the BP progression.

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