031 Inducible skin-associated lymphoid tissue (iSALT) is detected in the scalp treated with topical immunotherapy for alopecia areata
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The lymphoid tissue structure that allows the interaction between T cells, B cells and antigen-presenting dendritic cells (DCs) 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 (MALT). As similar structure in the skin, Strelis estimated the prevalence of skin-associated lymphoid tissue (SALT) in diseased scalps. Recently, through the detailed examination of the elicitation phase of contact hypersensitivity (CHS) as a murine model of contact dermatitis, we have confirmed sequential dendritic cells and T cells clustering in the dermal post-capillary venule, and termed this structure inducible SALT (iSALT). However, it remains unknown whether iSALT exist in human skin. Furthermore, the contributions of B cells to iSALT have not been acknowledged. To elucidate these issues, we focused on the topical immunotherapy for alopecia areata, which is one of the most efficient therapies of AA and induces chronic delayed-type hypersensitivity responses. 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 DCs 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.

032 Bach2 suppresses tumor immunity by repressing effector function-related gene in CD8+ T cells
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It has been reported that psoriasis symptoms have improved during pregnancy, while deterio rated after menopause, suggesting protective roles of estradiol in the development of psoriasis. In addition, the severity of psoriasis tends to be higher in male than 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 on the development of psoriasis, we firstly subjected ovarietomized-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 keratin-16, a keratin-dermatan skin protein, such as IL-23p19 and IL-12p35, and the expression of CD8+ T cells were decreased to different extents in the acute phase compared with those in normal controls, and this decline almost restored in the stable phase. In vitro, incubation of strata4D with BP-PBMNCs resulted in significantly higher levels of anti-IL-18 antibody productions. Our study demonstrated that strata4D derived from lesional peripheral granulocytes promote the production of IL18R antibody by T cells and thus contribute to the progression of psoriasis.

033 Semaphorin 4D enhances antibody production in bullous pemphigoid
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Autoantibodies produced by plasmacytoid activated B cells against skin basement membrane zone is a vital but well-established mechanism in the development of bullous pemphigoid. Semaphorin 4D (Sem4D/CD100) can promote B cell activation and enhance its capacity of antibody production. We sought to illustrate the implication of Sem4D in BP that facilitates B cell activation and antibody production. In our study, soluble Sem4A/CD43(D) levels in serum and blister fluid were analyzed by enzyme-linked immunosorbent assay. Immunohistochemical staining of Sem4D was performed on BP lesional tissues. CD100 expressions on membrane of immune cells in BP lesions and peripheral blood were detected by flow cytometry. Anti-BP180 antibody titers were evaluated in the supernatant of Sem4D-treated human peripheral blood mononuclear cells. We treated freshly isolated peripheral blood mononuclear cells (PBMCs) with Sem4D or a negative control at different levels for 48 h in both serum and blister fluid of BP patients were correlated with BP180 antibody titers and disease activities. Sem4D-expressing cells were accumulated in BP subepidermal blister as well. The expression of membrane CD100 on granulocytes rather than lymphocytes decreased to different extents in the acute phase compared with those in normal controls, and this decline almost restored in the stable phase. In vitro, incubation of strata4D with BP-PBMNCs resulted in significantly higher levels of anti-IL-18 antibody productions. Our study demonstrated that strata4D derived from lesional peripheral granulocytes promote the production of IL18R antibody by T cells and thus contribute to the progression of psoriasis.

034 Estradiol plays regulatory roles in an imiquimod-induced murine psoriatic dermatitis through down-regulation of keratinocyte activation
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Psoriasis is one of the most common chronic inflammatory dermatological disorders, affecting 1–2% of the world population. It is characterized by erythema, plaques and itchy scaling. Psoriasis is more common in white Europeans and North Americans, with a sex ratio of 2:1, favoring women. The precise origin of psoriasis remains elusive, and treatment options are generally limited and associated with adverse effects. Psoriasis is a multifactorial disease that is influenced by environmental factors and genetics. One of the environmental factors is female hormones, especially estradiol. Estradiol is a major sex hormone produced by the ovaries that plays a vital role in maintaining skin homeostasis. Estradiol has been reported to regulate the development and progression of psoriasis. In this study, we aimed to investigate the role of estradiol in the development of psoriasis and explore potential therapeutic targets for psoriasis treatment. We used an imiquimod-induced mouse model of psoriasis to study the effect of estradiol on the development of psoriasis. We found that estradiol significantly decreased the levels of pro-inflammatory cytokines in the skin of imiquimod-treated mice. We also observed that estradiol suppressed the expression of key pro-inflammatory cytokines such as IL-17A and IL-23p19. These results suggest that estradiol may be a potential therapeutic target for psoriasis treatment. Further studies are needed to investigate the potential therapeutic targets of estradiol in the treatment of psoriasis.

035 Temporally controlled B cell depletion with universal chimeric antigen receptor (CAR) Therapy for PV and most autoimmune diseases relies on chronic immunosuppression, which results in significant morbidity and mortality. Complete but transient B cell depletion should cure PV, since autoreactive clones do not recur upon regeneration of the B cell repertoire. In this context, genetically engineered CAR T cells (CAR-Ts) have emerged as the most potent means to treat PV. However, there are concerns about their use in PV, since autoreactive clones do not recur upon regeneration of the B cell repertoire. In this study, we aim to evaluate the potential of CAR-Ts in the treatment of PV using a humanized allogeneic BLT mouse model. We engineered CAR-T cells for pemphigus vulgaris (PV) therapy using a CAR that recognizes a PV-specific epitope. We demonstrated that CAR-Ts showed potent and specific in vitro killing equivalent to conventional CAR-Ts that have been used in PV therapy. We also demonstrated that CAR-Ts had a lower cytokine response profile, indicating a lower potential for immunosuppression. Moreover, we showed that CAR-Ts had a lower risk of infusion-related toxicity, making them a safer and more effective treatment option for PV.

036 Significant contribution of CD11c+ MHC class II+ inflammatory monocytes to antigen presentation in the skin in murine contact hypersensitivity
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Contact hypersensitivity (CHS) response is a murine model of contact dermatitis induced by topical hapten application. In its elicitation phase, we have previously shown that dermal dendritic cells (dDCs) form clusters to serve as the niche for the efficient CD8+ T cell activation in the skin. However, the detailed mechanisms regulating CD8+ T cell activation in the skin remain largely unclear. We hypothesized that inflammatory monocytes play a role in antigen presentation in the skin. To test this hypothesis, we used a humanized allogeneic BLT mouse model and engineered CAR-T cells for pemphigus vulgaris (PV) therapy using a CAR that recognizes a PV-specific epitope. We demonstrated that CAR-Ts showed potent and specific in vitro killing equivalent to conventional CAR-Ts that have been used in PV therapy. We also demonstrated that CAR-Ts had a lower cytokine response profile, indicating a lower potential for immunosuppression. Moreover, we showed that CAR-Ts had a lower risk of infusion-related toxicity, making them a safer and more effective treatment option for PV.