031 Inducible skin-associated lymphoid tissue (iSALT) is detected in the scalp and affects T cell trafficking in alopecia areata
Y Nakamura1, K Kassaisha1, and TM Takama1 1 Department of Dermatology, Kyushu University School of Medicine, Fukuoka, Japan

Inducible skin-associated lymphoid tissue (iSALT) is a new concept of a lymphoid tissue that is induced by topical immunotherapy for alopecia areata. This tissue is characterized by the presence of lymphoid follicles, which are composed of B cells, T cells, and dendritic cells. The presence of iSALT in the scalp of patients with alopecia areata indicates that this tissue plays a critical role in the development of the disease. Understanding the mechanisms that regulate the formation and function of iSALT may provide new insights into the pathogenesis of this disease and the development of novel therapeutic strategies.

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

Y Natsuaki1, N Ishii1, C Ohata1, K Kabashima2 and T Nakama1

Bach2 is a transcription repressor that regulates immune cell function. In this study, we found that Bach2 suppresses the function of CD8+ T cells in response to tumor antigens. This suppression is mediated by the repression of genes that are involved in the effector function of T cells, including cytokine production and cytotoxicity. These findings suggest that Bach2 may be a potential target for the development of new immunotherapies for cancer.

033 Semaphorin 4D enhances antibody production in bullous pemphigoid
S Shen1, Y Ke2, D Fang3, H Fang1 and G Wang1 1 Department of Dermatology, Xijing Hospital, The Fourth Military Medical University, Xi’an, China, 2 Department of Dermatology, Xijing Hospital, The Fourth Military Medical University, Xi’an, China

Semaphorin 4D (Sema4D) is a cytokine that plays a critical role in the immune system. In this study, we found that Sema4D enhances antibody production in bullous pemphigoid (BP) patients. We observed that patients with BP who had high levels of Sema4D in their serum had a higher percentage of antibody-producing B cells in their peripheral blood. These results suggest that Sema4D may be a potential target for the development of new treatments for BP.

034 Estradiol plays regulatory roles in an imiquimod-induced murine psoriatic dermatitis through down-regulation of keratinocyte activation
A Adachi, T Honda and K Kabashima

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 this study, we found that estradiol down-regulates the expression of pro-inflammatory cytokines in keratinocytes, which are key players in the development of psoriasis. These findings suggest that estradiol may be a potential therapeutic target for the treatment of psoriasis.

035 Temporally controlled B cell depletion with universal chimeric antigen receptor (CAR) T cells for pemphigus vulgaris (PV) therapy
CT Ellebreck1, X Mao1, JL Mellenhorst1, S Lacey1, Y Zhao1, MC Mikone and AS Payne1 1 University of Pennsylvania, Philadelphia, PA

Therapy of 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 achieve total B cell depletion. For autoimmune disease therapy, temporal control of CAR cytotoxicity is necessary to prevent lasting immunosuppression. Here, we validate 3 novel strategies to control CAR-T survival and function. We combined a B cell targeting CAR with an on-switch that permits CAR surface expression (onCAR). sCAR, revCAR and cytosine deaminase (CD) strategy to control CAR-T survival and function. We showed that onCAR-Ts showed potent and specific in vitro killing equivalent to conventional CAR-Ts that have demonstrated efficacy in human clinical trials. On the other hand, revCAR-Ts showed superior cross-presentation ability nor the simultaneous depletion of langerin+ dDCs and neonatal CD8+ T cells in vivo. These results indicate that onCAR-Ts may be a potential therapeutic option for the treatment of PV.

036 Significant contribution of CD11c+ MHC class II+ inflammatory monocytes to antigen presentation in the skin in murine contact hypersensitivity
S Ono, T Honda and K Kasaisha Department of Dermatology, Kyoto University, Kyoto, Japan

Contact hypersensitivity (CHS) response is a murine model of contact dermatis 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. Here, we show that CD11c+ MHC class II+ inflammatory monocytes (iMcs) are essential for the efficient CD8+ T cell activation in the skin. CD11c+ iMcs augment the cross-presentation of antigens by dDCs, which is necessary for the efficient CD8+ T cell activation. These findings suggest that CD11c+ iMcs play a critical role in the development of murine CHS response.

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