**ABSTRACTS** | Adaptive Immunity and Autoimmunity

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**043** Persistent deficiency of mucosal associated invariant T cells in dermatomyositis

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Mucosal associated invariant T (MAIT) cells are innate like lymphocytes found in peripheral blood and mucosa; they are decreased during systemic lupus erythematosus and other autoimmune diseases. However, MAIT cell levels and functions have not previously been investigated in dermatomyositis (DM). Herein, we studied MAIT cell levels and activation status before and after treatment during DM (n=21) and compared them to healthy controls (n=19), psoriasis (n=7) and atopic dermatitis (n=5). We showed that DM was associated with a dramatic reduced number of circulating MAIT cells (median: 0.12% [0.07-0.25%] versus 2.13% [1.05-3.94%]; p < 0.0001). This disappearance was specific to DM. Residual MAIT cells displayed an activated/exhausted phenotype with higher expression of CD25, CD19, CTLA4 and increase of the TREGRA. We found an inverse correlation between CD25 and CTLA4 expression on MAIT cells and the level of circulating MAIT cells. After a median follow up of 0.9 year, we observed a slight increase of MAIT cells (median: 0.25% [0.24-0.66%]) versus 0.73% [0.47-1.16%]; p = 0.002). Nevertheless, it did not return to normal healthy controls level. We next compared skin from DM with healthy controls for PZL, the master transcription of MAIT cells thanks to microarray analysis. PZL was not elevated in lesional skin. Finally, preliminary in vitro assays showed that strong stimulation by both TCR and IL-12 induced PZL expression was elevated during DM. Our results led to decreased expression of CD161 and higher mortality. Taken together, our data indicate that in DM peripheral blood MAIT cells, which are thought to have regulatory role, are dramatically reduced in relationship with an activated abnormal phenotype potentially leading to activation induced cell death rather than their migration in affected tissue.

**044** A unique mechanism of epithelial detachment in mucous membrane pemphigoid caused by autoantibodies against the C-terminus of COL17

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MMP patients show reduced inflammatory findings in histological analyses. One blustering mechanism in MMP may be associated with the inhibition of protein binding by autoantibodies against the C-terminus of COL17. We investigated the interaction of COL17 with the extracellular matrix component collagen IV (COL4). We performed immunoprecipitation using mAb TS3-19 against COL17, NC16A, and mAb TS3-17 against the C-terminus of collagen XIV (COL17). COL17 was detected in both cell lysates from normal human oral keratinocytes and from normal human epidermal keratinocytes (NHKs). In contrast, when COL17 was precipitated with mAb TS3-19, COL4 was not detected in NHKs. We also examined the isoform differences of COL4 between NHKs and OMKS. COL4 genes (COL4A1, A2, A3, A4, A5, A6) encode the distinct chains of COL4x1 (IV) through IV (V), which forms the hetero- and isoforms. The mRNA expressions of COL4A1 and A2 were mainly observed in both keratinocytes, but the ratio (A1/A2) was different. We reasoned that the different binding in COL17 and COL4 between NHKs and OMKS may be attributed to the different expression of COL4 genes. Finally, with in vitro binding inhibition assay, the precipitation of COL17 with MAP-IGs, but not BP-IGs significantly reduced the amounts of COL17 binding to COL4, confirming the disturbance effects of MAP-IGs. In summary, we demonstrate a unique mechanism behind the oral lesions in MMP, in which pemphigoid IgG targeting the C-terminus of COL17 may play a pathogenic role by disturbing the COL17-COL4 interaction.

**045** Role of effector and regulatory B cells in patients with systemic sclerosis: IL-6 producing effector B cells associated with skin fibrosis

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Systemic sclerosis (SSc) is an autoimmune disease characterized by skin and lung fibrosis. Over 90% of the patients with SSc are positive for autoantibodies. In addition, the serum levels of BAFF, a potent B cell stimulator, are correlated with SSc severity and activity. Thus, B cells play an important role in SSc pathogenesis. However, two opposing B cell subsets exist: effector and regulatory B cells. IL-6 producing effector B cells promote scleroderma mouse model, whereas, IL-10 producing regulatory B cells inhibit it. In the present study, we have investigated the clinical association of effector and regulatory B cells in patients with SSc. The levels of IL-6 producing effector B cells associated with skin fibrosis with the extent of skin fibrosis in SSc patients. The result suggested that the dysregulation of effector and regulatory B cell balance contributes to SSc pathogenesis.

**046** Effect on CD3, Treg and TH17 cell numbers in skin biopsies after 16-week mirikuzumab treatment, evaluated by an epitogenic assay

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Pemphigus is a group of autoimmune diseases characterized by presence of autoantibodies against the desmocollin and dermobulin in the circulation and skin. The major autoantigen of pemphigus is desmoglein (Dsg), and we previously reported desmocollin (Dsc) also as pemphigus is desmoglein (Dsg), and we previously reported desmocollin (Dsc) also as.

**047** Pemphigus autoantibodies to desmocollin 3 exclusively recognize calcium-dependent epitope in extracellular domain 2

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**048** Antibodies to calcium-dependent epitope in desmoglein 2 target the C-terminus of COL17

T. Matsushita1, T. Kobayashi1, M. Kano1, Y. Hamaguchi1, M. Hasegawa1, M. Fujimoto1 and K. Tachibana1 1 Kanazawa University, Japan

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