**ABSTRACTS | Adaptive Immunity and Autoimmunity**

**043** Persistently deficient of mucosal associated invariant T cells in dermatomyositis

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=18). 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 TEMRA state. 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 PLZF, the master transcript of MAIT cells thanks to microarray analysis. PLZF was not elevated in lesional skin. Finally, preliminary in vitro assays showed that strong stimulation by both TCR and IL-2 led to increased PLZF expression in elevated DM samples, led to decreased expression of CD46 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

Mucous membrane pemphigoid (MMMP) is a rare autoimmune bullous disease that affects the mucous membranes, especially the oral cavity and conjunctiva. Autoantibodies against collagen XVII (COL17) are found in the sera of most patients with MMPP. We previously reported that autoantibodies against desmocollin 3 (Dsc3) are positive in MMPP. Although the precise mechanism of epithelial detachment in MMPP is not well understood, we have shown that autoantibodies against the C-terminus of COL17 (mAb TS39-1) block the adhesion of oral epithelial cells (OMKs) and from normal human epidermal keratinocytes (NHEKs). In contrast, when mAb TS39-3, which targets COL4, is added, OMKs were not detached. This study revealed that autoantibodies against the C-terminus of COL17 (mAb TS39-3) led to cell death by apoptosis and cell lysis. We concluded that autoantibodies against COL17 (mAb TS39-3) participate in the pathogenesis of MMPP by causing epithelial basement membrane detachment. In addition, we also showed that autoantibodies against Dsc3 were associated with decreased expression of CD161 and higher mortality. Taken together, our data indicate that autoantibodies against COL17 and Dsc3 play a role in the pathogenesis of MMPP.

**045** Role of effector and regulatory B cells in patients with systemic sclerosis: IL-6 producing effector B cells associated with skin fibrosis
S. Nishiya, Y. Nishimura, K. Kajiyama, and S. Nakamura

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 a major 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 blood levels of IL-6-producing effector B cells and IL-10-producing regulatory B cells were measured in SSc patients with skin and 16 healthy subjects. The frequency of IL-6-producing effector B cells in blood was significantly elevated in patients with SSc (55 ± 12.1%) than that in healthy controls (41.9 ± 10.6%, P<0.001). In contrast, the frequency of IL-10-producing regulatory B cells in blood was significantly decreased in patients with SSc (4 ± 0.7%) than in healthy controls (20.0 ± 8.3%, P<0.001). With respect to SSC subtypes, the frequency of IL-6-producing effector B cells was significantly higher in patients with diffuse cutaneous SSc (severe form of SSC) than that in patients with limited cutaneous SSc (mild form of SSC). Furthermore, the frequency of IL-6-producing effector B cells positively correlated 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** Vitamin D3 promotes human Th2 responses by TSLP-dependent and -independent regulation of dendritic cells
A. Sušin, J. Schmidt, D. Patzel, R. Higgi, H. Sonnenger, K. Liü and K. Reich

Vitamin D3 promotes human Th2 responses by TSLP-dependent and -independent regulation of dendritic cells. Atopic dermatitis is an inflammatory skin disease characterized by chronic pruritus, erythema, and lichenification. The development of atopic dermatitis is also associated with an impaired microbial flora and a reduced number of MAIT cells. In the present study, we investigated the effects of vitamin D3 on MAIT cell activation in vitro. The results showed that vitamin D3 treatment led to an increase in MAIT cell activation and IL-17 production. These findings suggest that vitamin D3 treatment may be a potential therapeutic option for the treatment of atopic dermatitis.

**047** Pemphigus autoantibodies to desmocollin 3 exclusively recognize calcium-dependent epitope in extracellular domain 2
H. Koga, K. Teyev, N. Ishii, and T. Nakama

Pemphigus is a group of autoimmune diseases characterized by presence of autoantibodies against the desmosomal cadherin in the skin and mucosae. One of the main autoantigens in pemphigus is desmoglein 3 (Dsg3) and we previously reported desmocollin 3 (Dsc3) also as autoantigen. In the present study, we sequenced the mRNA expressions of COL4A1-10, which forms the heterotrimeric isoforms. The mRNA expressions of COL4A1-10 were significantly increased in pemphigus patients than healthy controls. COL4A1-10 was the most upregulated gene in pemphigus patients. We also examined the isoform differences of COL4A1-10 in skin samples from healthy controls and pemphigus patients. COL4A1-10 expression was significantly higher in pemphigus patients than healthy controls. These results suggest that COL4A1-10 may be a potential target for the diagnosis and treatment of pemphigus.

**048** Effects on CD3, Treg and TH17 cell numbers in skin biopsies after 16-week mirikizumab treatment, evaluated by an epitogenic assay
R. Bissinette, J. Schmitz, D. Patzel, R. Higgi, H. Sonnenger, K. Liü, and K. Reich

Mirkizumab (Mini) is a humanized monoclonal antibody against the p19 subunit of inter leukin-21 (IL-21), in patients (pts) with moderate-to-severe plaque psoriasis. Past studies showed increased number of CD3+ T cells remaining in skin after treatment, potentially contributing to flares, whereas psoriasis is clinically resolved at the biopsied sites. To determine the cellular skin milieu of pts in the current study, we evaluated the relationships between mini exposure, efficacy and skin biomarkers. Psoriasis Area and Severity Index (PASI)/C21, PASI/C21 and Lymphocytosis (Lymphocytes/C21) were collected from primary care. Lesional skin biopsies from each group were assessed at baseline and Week 16 for infiltrating T cells. Microparticles (MPs) were collected. In conclusion, 16-week mirikizumab treatment resulted in a significant decrease in the number of CD3+ T cells in skin, while the number of psoriasis area and severity index (PASI)/C21 was also reduced. These results suggest that the use of mirikizumab may provide a beneficial effect in the treatment of plaque psoriasis.