LB708
ILC1-like innate lymphocytes in human autoimmunity: Lessons from Alopecia Areata
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Alopecia areata (AA) is a chronic immune-mediated disease of the scalp hair follicle (HF) epithelium, and down-regulated immunoreactivity for the HF immune privilege (IP) guardians, cultured with organ-cultured, stressed human scalp hair follicles (HFs) in/around non-lesional AA HFs, together with a dominant infiltrate of CD8+/NKG2D+ ILC1-like cells in and around the anagen hair bulb of lesional AA HFs, but also human AA. Triple immunofluorescence staining of AA sections revealed pathological infiltrates diagnostic algorithm and clinical characteristics of patients with PG.

Relevant for PG pathogenesis. Although this is a limited patient number, our data expand the membrane zone. In half of them anti-full-length BP180 autoantibodies and reactivity against periumbilically. Notably, in three cases blistering started on the extremities. All patients had fully addressed. We retrospectively characterized clinically and serologically 11 PG patients, XVII/ BP180. Due to the rarity of the disease, the detailed autoantibody profile has not been of the disease. Previous studies report that in PG IgG autoantibodies target epidermal collagen during late pregnancy. Skin blisters and erythematous, itchy plaques are the clinical hallmarks pertal, Germany and 4 Dermatology, Royal Melbourne Hospital, Faculty of Medicine, Technology, Haifa, Haifa, Israel, 2 Monasterium, Münster, Germany, 3 Department of Medicine Division of Rheumatology, University of Massachusetts Medical School, Worcester, Massachusetts, United States

Cutaneous Lupus Erythematosus (CLE) is a spectrum of autoimmune connective tissue diseases that are characterized histopathologically by interface dermatitis and lupus band reaction. Current treatment options for CLE are based on SLE treatments and include topical steroids, antimalarials, and other immunosuppressants. Many CLE patients exhibit flares which can be triggered by environmental stimuli such as UV light. Tissue-resident memory T cells (Trm) mediate flares in autoimmune skin disorders, though their specificities, functional properties, and survival factors in CLE have not yet been described. We used a mouse model of CLE to examine the development of Trm skin lesions. In this model, OVA peptide-activated DO11 1 CD4+ T cells were injected intravenously into sub-lethally irradiated TLR9KO II-TGO mice that express TGO transgene in the MHCII cells after being fed with Dox chow. We also took blister biopsies from CLE patients. Mice in this model developed IgM and IgG1 auto-antibodies and exhibited cutaneous Trm cell accumulation that positively correlated with the severity of skin lesions. We found that approximately 70% of antigen-specific skin Trm cells in these mice expressed phenotypic markers consistent with Trm, which persisted after antigen withdrawal. Trm cells were enriched in the skin as compared to the draining lymph node and spleen. Disease scores also peaked more rapidly during flare induction than during primary disease, as do ANA titers. Preliminary analysis of human blister biopsies from CLE patients exhibited phenotypic markers of Trm (CD69+CD103+CD69+ T cells) in the skin. Based on our data and previously published studies in other autoimmune skin disorders, we hypothesize that targeting Trm in CLE may be a durable treatment strategy.

LB711
Characterizing Skin Resident Memory T cell formation in Murine Cutaneous Lupus Erythematosus
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LB709
Therapeutic effect of γTregs cells in Alopecia Areata
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Regulatory γT cells (γTregs) may exert therapeutic effects under some experimental autoimmune disease (AID) conditions. This encouraged us to explore whether this this also applies to alopecia areata (AA), one of the most common human AIDs. Triple immunofluorescence (IF) staining was performed to determine the distribution of γTregs in human skin presence of γTregs on skin sections of AA patients. Autologous circulating human γTregs were expanded and either co-cultured with organ-cultured, stressed human scalp hair follicles (HFs) ex vivo or injected into experimentally induced AA lesions on human scalp skin xenografts on SCID mice. The IF staining revealed the presence of γTregs around the bulge region of scalp HF and around the hair bulb of lesional and non-lesional scalp skin of AA patients. Next, by using human HFs organ culture, we asked whether γTregs possess the ability to suppress the premature catagen induction and IP collapse induction by activated CD8+-NKG2D+ T cells. The results demonstrated that γTregs significantly reduced prem-ature catagen induction as compared to HF co-culture with CD8+-NKG2G2D+ alone (p<0.01). Moreover, γTregs significantly reduced the staining intensity of HFs immune privilege collapse markers such as HLA-ABC, CD1d, MICAB and of the AA-associated chemokine, CXCL10. In addition, γTregs increased the expression of IP guards, such as TGF-β and NKG2D in the HFs inner root sheath, indicating that γTregs can restore HF immune privilege. Finally, hair growth with normal histological and IF appearance were observed in the AA induced xenografts following transfer of autologous γTregs. Collectively, this shows that γTregs play a critical role in suppressing AA and in restoring HF immune privilege and thus deserve targeting in AA management and raises the possibility that expanded autologous γTregs may be used directly for autologous cell-based future AA therapeutics.

LB712
Transcriptomic profiling of Necrobiotic Xanthogranuloma and Necrobiosis Lipidosa provides insight into pathogenic role of T and B cells
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Necrobiotic Xanthogranuloma (NXG) is a chronic cutaneous disorder that results in development of violaceous-yellow papules and nodules that can progress to ulceration. Similarly, Necrobiosis Lipidica Diabeticaformis (NLD) is a chronic skin disease with clinical and histologic features overlapping with NXG. Also, treatment of these two conditions is similar, with anti-TNF agents and other immunomodulators showing promise. Although there is increasing evidence for NXG and NLD being immune-mediated diseases, more precise mechanistic insight is still lacking. To fill this gap, we performed whole-tissue RNA sequencing of healthy control, NXG, and NLD skin. This revealed a broad degree of agreement between the two diseases, including a similar decrease in antimicrobial peptide levels (DDC) and upregulation of T and B cell genes activation genes. Genes related to autoimmunization (SPP1, R B1 and Ile6) were also upregulated (FDR < 0.01, FC < 5). Biological pathway analysis revealed significant (FDR < 0.01) alterations in B cell receptor signaling, interferon gamma signaling, complement activation, and cell adhesion pathways both in NXG and NLD. Thus, transcriptomic profiling of NXG demonstrates immune alterations paralleling those observed with NLD, and implicate pathologic T and B cell signatures in NXG pathophysiology.