ABSTRACT: Adaptive Immunity and Autoimmunity

019 Long-term clinical outcome and HAVCR2 mutations in 70 patients with subcutaneous panniculitis-like T-cell lymphoma: a study from the French Cutaneous Lymphoma Group
G Sonigo1, M Battistella1, M Beylot-Barry2, S Oto3, N Frunkx4, F Sepulveda5, M Bagot6, G de Saint-Basile1, D Michonneau1 and A de Navarre1, and GFEI collaborators1 1 Saint-Louis Hospital, Paris, France; 2 Burn Hospital, Toulouse, France; 3 Centre Hospitalier Régional Universitaire, Rennes, France; 4 Human Genetics, Hospital Mondor, Creteil, France; 5 Dermatology, Hôpital Cochin, Paris, France and 5 Centre d’Étude des Déficits Immunitaires, Necker Hospital, Paris, France.

Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is a rare form of cutaneous lymphoma with a good prognosis. However, for unclear reasons, a minority of patients develop severe disease. A recent study has identified germline HAVCR2 (encoding TIM-1), a checkpoint inhibitory receptor, as a potential marker of SPTCL in Asian populations, suggesting this mutation in sporadic SPTCL is unknown. Data of 70 patients with sporadic SPTCL identified from the GFEI database between 2000 and 2019 have been reviewed regarding clinical presentation, treatment, and survival. Median follow-up was 30 years (1-90 years). We show that TIM-1 is a potential new marker to stratify patients with SPTCL.

020 Type 2 immunity mediated by CD301b+ dendritic cell subsets plays a critical role in oxazolone-induced contact hypersensitivity
S Lee1, S Kim1, T Lee1,2 and M Lee1,2 1 Department of Dermatology, Cutaneous Biology Research Institute, Yonsei University College of Medicine, Seoul, Korea (the Republic of), 2 Brain Korea 21 PLUS Project for Medical Science, Yonsei University College of Medicine, Seoul, Korea (the Republic of), 3 Yonsei University College of Medicine, Seoul, Korea (the Republic of), 4 Immunology, Yonsei University College of Medicine, Seoul, Korea (the Republic of).

Contact hypersensitivity (CHS) is a mouse model for human allergic contact dermatitis (ACD). Although human ACD lesions are frequently characterized by a mixed gene expression profile with Th1 and Th2 cytokine or antigen presentation of monocytes/macrophages have been identified on the role of Th1. Here, we found that oxazolone (Ox)-induced CHS model showed a mixed gene expression signature of IFN-γ and IL-4. A single topical sensitization with Ox strongly induced J4 gene expression starting from 72hrs in skin-draining lymph nodes (SDLNs) suggesting that IL-4-producing cells were recruited or activated during early sensitization phase. We found an increased frequency of IL-4-producing CD4+ T cells both in sensitized SDLNs and challenged ear skins and Ox-induced J4 gene expressions were significantly abrogated by depletion of CD301b+ dendritic cells. Ox-induced J4 expressions were significantly decreased by depleting Langerin+CD101b+ dendritic dermal DCs whereas local expression of IFN-γ was comparable to that of control mice. Functionally, Ox-induced CHS response was significantly attenuated both by depletion of CD301b+ dermal DCs and IL-4 neutralization. Mechanistically, Tgfp gene expression was rapidly increased in the Ox-sensitized abdominal skins and Ox-induced CHS response was effectively ameliorated by IL-7Rα blocking antibody, indicating that TSLP receptor signaling is involved in type 2 CHS response. Therefore, our findings suggest that type 2 immunity is critically involved in a mixed CHS immune response and type 2 CHS response is mediated by TSLP-CD301b+ dermal DCs-IL-4-producing CD4+ T cell cascade. Therefore, we suggest that inhibiting type 2 immunity would be a promising therapeutic approach for alleviating recurrent ACD patients with mixed Th1 and Th2 immune environment.

021 New gold compound shows immunosuppressive functions and leads to an amelioration of skin inflammation
S Haeberle1, X Cheng2, R Gambi Brambila3, Å Enk1, S Wolff1 and E Hadaschik1 1 Dermatology, University of Tübingen, Tübingen, Germany; 2 Brain Korea 21 PLUS Project for Medical Science, Yonsei University College of Medicine, Seoul, Korea (the Republic of), 3 Neurology, University of Tübingen, Tübingen, Germany.

For the treatment of autoimmune diseases, drugs from the gold group are still in use. We evaluated the potential of a newly synthesized gold compound (MC3) in an oxazolone (Ox)-induced CHS model, an established model for atopic dermatitis and TH2 type diseases. Furthermore, we investigated the effects of MC3 in a bleomycin-induced skin fibrosis model and on gene expression levels of pro-fibrotic cytokines and extracellular matrix (ECM) in skin fibrosis. MC3 showed an upregulation of CYP1A1 and TGFβ1 in vitro. The effect of MC3 was additionally investigated using real time PCR. In addition, flow cytometry analysis showed a 2-3 fold higher melanocyte loss. Importantly, these effects depended on the activation of the JAK/STAT signaling pathway. Taken together, immunity-induced senescence surveillance protects skin from pathologies thereby enabling the diseased mice to recover.

022 Crosstalk between vitiligo skin T-cell secretome and epidermal cell response
C Martinelli1, C Drulion1, L Migayron2, C Jaquemin1, F Lucchese1, A Taieb1,2,4 and J Seneschal1,2 1 University of Bordeaux, Bordeaux, France and 2 Bordeaux Hospital, Bordeaux, France.

Vitiligo is a skin disfigurement disorder affecting 1% of the global population. This disease is characterized by white patches on skin resulting from the loss of epidermal melanocytes. Vitiligo is a complex disease, associating environmental factors, genetic predispositions and altered immune and inflammatory responses. Consistent with the prominent role of the immune system, vitiligo skin harbors an important infiltrate of resident memory T-cells expressing the chemokine receptor CXCR3 that produce high levels of interferon (INF)-γ and tumor necrosis factor (TNF)-α, involved in melanocyte loss. However, the precise cytokine-secretion profile of T cells infiltrating vitiligo skin, and importantly, the impact of the global T cell-secretome on the epidermal barrier remains to be deciphered. This study aimed to identify vitiligo skin T cells and their secretome and to compare them with the prominent role of the immune system, vitiligo skin harbors an important infiltrate of resident memory T-cells expressing the chemokine receptor CXCR3 that produce high levels of interferon (INF)-γ and tumor necrosis factor (TNF)-α, involved in melanocyte loss. However, the precise cytokine-secretion profile of T cells infiltrating vitiligo skin, and importantly, the impact of the global T cell-secretome on the epidermal barrier remains to be deciphered. This study aimed to identify vitiligo skin T cells and their secretome and to compare them with the global T cell-secretome, the inflammatory and pigmentary transcriptional profiles were studied. We found that in addition to a type 1 skewed immune profile, vitiligo skin T cells have the propensity to mount high levels of type 2 cytokines. Furthermore, vitiligo skin T cell secretome not only downregulated the expression of pigment associated genes in melanocytes, but also upregulated signaling pathways, cytokines, and chemokines that will further be involved in the inflammatory response and recruitment of additional immune cells in the skin, further contributing to melanocyte loss. Importantly, these effects depended on the activation of the JAK/STAT signaling pathway. Our findings add novel insights regarding the role of T cells and the involvement of JAK/STAT signaling in vitiligo pathogenesis.

023 Downregulated expression of Interferon regulatory factor 8 in monocyes/macrophages exhibits pro-fibrotic phenotype and may contribute to the pathogenic process of systemic sclerosis
Y Otabe1, Y Yamaguchi1, M Asami1, N Komitsu1, T Watanabe1, D Kuratoki1, T Tamura1 and M Akahira1 1 Environmental Immuno-Dermatology, Yokohama City University Graduate School of Medicine, Yokohama, Japan; 2 Immunology, Yokohama City University Graduate School of Medicine, Yokohama, Japan.

Recent observations suggest that monocyes/macrophages play important roles in the pathogenesis of systemic sclerosis (SSc). Interferon regulatory factor (IRF) 8 is a transcriptional regulator that plays essential roles in the differentiation and function of monocytes and macrophages. We hypothesized that IRF8 may be involved in the fibrotic process of SSc by regulating phenotypes of monocyes/macrophages. In this study, we first determined IRF8 expression in cells from 13 of SSc patients (11 limited cutaneous SSc (lcSSc); n=11), 18 healthy controls by quantitative RT-PCR (qRT-PCR). IRF8 was next silenced in monocyes by RNA interference, and they were differentiated into macrophages, cyto- and chemokine expression, and extracellular matrix expression levels of extracellular matrix (ECM) were assessed by flow cytometry, qRT-PCR, and bead-based immunoassay. Finally, bleomycin-induced skin fibrosis was assessed in monocyes/macrophages infected with lentivirus expressing IRF8 knockdown (IRF8) or control (mock) virus. As a result, IRF8 levels in circulating monocyes from SSc patients were significantly lower than that from healthy controls and lcSSc patients. IRF8 levels were negatively correlated with modified Rodnan total skin thickness score. siIRF8-MDMs exhibited M2 phenotype, and mRNA expression levels of pro-fibrotic factors were increased in monocyes/macrophages than that from controls. These results suggest that IRF8 may be involved in the fibrotic process of SSc by regulating phenotypes of monocyes/macrophages.