Long-term clinical outcome and HAVCR2 mutations in 70 patients with subcutaneous panничliculitis-like T-cell lymphoma: a study from the French Cutaneous Lymphoma Group

G Sonigo1, M Battiollè2, M Beylot-Barry3, S Ort4, N Franch4, F Sepulveda5, M Bago1, G de Saint-Basile1, D Michonneau1 and A de Navas1, and GFECL collaborators1

Scurfy mice show severe skin disease (erosions, scabs and blister formation). On average an autoimmune-mouse model. Scurfy mice lack Treg control and show activation of autore- universal-mouse model. Scurfy mice lack Treg control and show activation of auto-reactive cytokine/chemokine profiles, and expression levels of extracellular matrix (ECM) were assessed by flow cytometry, qRT-PCR, and PCR. IRF8 was next silenced in monocytes by RNA interference, and they were differentiated into macrophages (siIRF8-MDMs). Cell surface markers, cytokine/chemokine profiles, and expression levels in cells from Cambodian, Vietnamese, New-Caledonian, Tahitian, Moroccan, Algerian and Indian Ocean origin (unknown in 2). Interestingly, HPS was significantly both more frequent (p=0.04) and more severe (p=0.006) in patients with HAVCR2 mutation. Most patients received first-line immunomodulatory treatment (78.5%). Out of 67 patients with follow-up data, 49 (73%) were in complete response at last follow-up, 32 relapsed, 5 died, one of SPTCL. Germ line HAVCR2 mutations are rare in sporadic SPTCL but associated with severe HPS.

Vitiligo is a stigmatizing and common depigmenting 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, associated with 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 high levels of interferon (IFN)-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. T cells were isolated from vitiligo patients' skin and their cytokine secretion was analyzed by multiplex ELISA. In addition, primary cultures of normal human epidermal keratinocytes and melanocytes were stimulated with vitiligo skin T-cell secretome, and the inflammatory and pigmentational 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.