VGLL3 overexpression, we have found that VGLL3 binds key factors in the Hippo signaling pathway, which has recently been linked to organ fibrosis. Further, we have shown that the half-life of PKC\(\delta\) is reduced nearly 2-fold, as well as a 2-fold reduction in gene expression of Th17 promoting factors. Therefore, VGLL3 overexpression, production of IL-17 by C. acnes-stimulated PBMCs is reduced in Trim32 null mice showed compromised AD-like phenotypes in the MC903 AD mouse model. Our previous studies, we showed that Trim32 null mice developed Th2 biased skin inflammation in response to iniquimod and associated low level of TRIM32 with Th2 polarization. Thus, our findings elucidate the molecular mechanisms by which VGLL3 promotes autoimmunity and Th2 cell differentiation in vitro. Analysis of TRIM32-associated proteins from public databases identified PKC\(\zeta\) as a TRIM32-associated protein that contributes to the regulation of Th2 signaling. We demonstrated that PKC\(\zeta\) was specifically ubiquitinated by TRIM32, and further, that the half-life of PKC\(\zeta\) was increased in the Th2 cells in Trim32 null mice. Furthermore, PhcZ null mice showed compromised AD-like phenotypes in the MC903 AD model. Consistently, the high PKC\(\zeta\) and low TRIM32 ratio were associated with CD4\(^+\) cells in AD human skin and in Th2 cells differentiated from in vitro AD patients compared to healthy controls. Taken together, these findings suggest that TRIM32 functions as a regulator of PKC\(\zeta\) that controls the differentiation of Th2 cells important for AD pathogenesis. Because TRIM32 is an E3 ubiquitin ligase with innate antiviral activity, Th2 regulation by TRIM32 provides a potential connection between defective innate immunity and Th2 activation in AD pathogenesis.

**Biographical differences in gene segment usage**

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Biogeography is known to shape the human skin metagenome, which in turn, helps to shape the adaptive immune system. Human-immune-mediated diseases like hidradenitis, lichen planus, atopic dermatitis, psoriasis, palmoplantar psoriasis/pustulosis have predilections for specific anatomic sites (axilla, groin, and inguinal folds; dorsal hands, volar wrists, anterior lower legs and oral mucosa; antecubital fossa and popliteal fossa; elbows and knees; and palms and soles, respectively). A better understanding of how immune composition and function differs by anatomic location remains a major gap in our understanding of skin diseases. For instance, the skin resident-commensal microbiome is known to differ among superficial and deep skin sites. Therefore, as a first step toward identifying anatomic-specificity in human response to microbes, we have employed our in-house developed bioinformatics pipeline, TCRminer, to characterize intra-personal differential TCR gene usage by body site. This analysis revealed differentially expressed several TCR gene segments. Specifically, TRAV5-6 was overexpressed in hip skin in comparison to peripheral blood (FDR = 1.7e-13), a finding that was independent of HLA haplotype. The TCR repertoire of the blood was also found to be more diverse than that of the hip. The skin-resident repertoire of the palm was also compared to that of the hip. Results revealed that TRAV9 was overexpressed (relative fold change = 2.74, FDR = 6.39e-03) in palm skin, a finding that was independent of HLA haplotype. Palm skin also had significantly less T cell repertoire diversity. Analysis of BCR genes revealed that IgH1 was poorly expressed in the palm when compared to the hip (relative fold change = 0.023, FDR = 2.02e-05). These findings are relevant because diseases such as palmoplantar psoriasis, hand dermatitis, and palmoplantar pustulosis have a predilection for palmar skin, which according to these results has differential expression of both TCR and BCR receptors.

**Evaluating T cell activation and polarization impact in morphea**

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Autoimmune blistering diseases (ABDs), mainly bullous pemphigoid, epidermolysis bullosa acquisita (EBA), pemphigus vulgaris (PV) and bullous pemphigoid (BP), are a large class of autoimmune diseases presenting the blistering eruptions on the skin and mucosa membrane. Circulating autoantibodies play a critical role in the pathogenesis, antibody-specific B cells and CD4\(^+\) T cells involved in autoimmunity. While vitiligo, a common pigmentation disorder, is mostly considered as CD8\(^+\) T cell-mediated, with multiple melanocyte-derived autoantibodies also detectable in part of the patients, although its pathogenicity remains undetermined. ABDs concomitant with vitiligo have rarely been reported. We report 3 cases in our institution, highlighting to date the second case of EBA with vitiligo and the first case of vitiligo underlying PV, while in the literature the onset of ABDs was mostly preceded by vitiligo. It is not clear whether the concomitance of ABDs and vitiligo may have some immune mechanism in which particular patient develop just as a mere chance occurrence. Some interesting correlation has been noticed in the onset, severity, and location of the two entities, which might indicate the interaction in their pathogenesis. We hypothesis that a probable undiscovered antigen-antibody crossover reaction or activation of auto-reactor after some component exposure caused by the cell destruction in the underlying diseases may explain the situation of the comorbidity. Genetic susceptibility may contribute to the occurrence of multiple autoimmune diseases in an individual while infection, trauma, and anxiety can act as a trigger. In a word, the clinicians should be aware of the possible coexistence of vitiligo and ABDs, the inner immunopathologic interaction leaves more to explore.

**Evaluating T cell activation and polarization impact in morphea**

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Morphea is an idiopathic disorder that can result in functional impairment and long-lasting disfigurement from sclerotic plaque development. Insight into the immune phenotype of morphea patients provides guidance into the development of new disease-modifying agents. Based on preliminary studies, we hypothesize that the development and progression of morphea results from early dysregulation of the Th1 immune axis in the tissue microenvironment which triggers and/or maintains an inflammatory cytokine environment. We utilized multicolor flow cytometry to compare immune cells in peripheral blood of patients with active morphea (defined by clinical activity score, LoSii \(\geq 3\), and no treatment with immunosuppressives for \(\geq 3\) months) to matched healthy controls (\(n = 15\) to \(p < 0.023\). These findings are relevant because diseases such as palmoplantar psoriasis, hand dermatitis, and palmoplantar pustulosis have a predilection for palmar skin, which according to these results has differential expression of both TCR and BCR receptors.