targets include the pro-fibrotic factor CTGF and members of the TGF-β/Smad pathway, which have been implicated in SSc pathogenesis. Consistent with this, transgenic mice with epidermal VGLL3 overexpression show gross and microscopic features of skin fibrosis. These findings elucidate the molecular mechanisms by which VGLL3 promotes autoimmunity and the molecular mechanisms by which VGLL3 promotes autoimmunity and the potential for future miRNA-based therapeutics.

Enhancement of Th2 cell differentiation by TRIM12 deficiency is negatively associated with PKCα

We have shown that morphea patients present increased systemic and local inflammation related to Th17 cell activation. In vitro, we demonstrated that TRIM12 deficiency increased Th2 cell differentiation in vitro. Analysis of TRIM12-associated proteins from public databases identified PKCα as a TRIM12-associated protein that contributes to the regulation of Th2 cell differentiation. We demonstrated that PKCα was specifically ubiquitinated by TRIM12, and further that the half-life of PKCα was increased in the Th2 cells from TRIM12 null mice. Furthermore, PH ez5 null mice showed compromised AD-like phenotypes in the MC903 AD model. Consistently, the high PKCζ and low TRIM12 ratio were associated with CD4+ cells in AD human skin and in Th2 cells differentiated in vitro from AD patients compared to healthy controls. Taken together, these findings suggest that TRIM12 functions as a regulator of PKCα that controls the differentiation of Th2 cells important for AD pathogenesis. Because TRIM12 is an E3 ubiquitin ligase with innate antiviral activity, Th2 regulation by TRIM12 provides a potential connection between defective innate immunity and Th2 activation in AD pathogenesis.

Biogeographical differences in gene segment usage

Previous studies have shown that C. acnes, as a potent inducer of T helper 17 (Th17) cells, a unique class of CD4+ T cells characterized by their ability to secrete large quantities of IL-17, plays a significant role in the pathogenesis of acne vulgaris. Previous studies have shown that miRNAs (miRNAs) play an important role in modulating the body's inflammatory response. Understanding the role of miRNAs in acne pathogenesis has not been extensively looked at in prior studies. Here we investigated the role of miRNAs in the response of human peripheral blood mononuclear cells (PBMCs) to Cutibacterium acnes (formerly Propionibacterium acnes). Using a high-throughput miRNA expression analysis approach, we identified several miRNAs that were differentially expressed in response to C. acnes stimulation. Among these, miR-146a was shown to negatively regulate differentiation of Th17 cells in various autoimmune diseases, dampening production of IL-17. Increased expression of miR-146a was detected in C. acnes-stimulated PBMCs, with a corresponding decrease in IL-17 production. These findings are relevant because diseases such as palmoplantar pustulosis, 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.