CXCL10 is central to autoimmunity in vitiligo and is a viable therapeutic target

Vitiligo is a disfiguring autoimmune disease of the skin caused by T cell-mediated destruction of melanocytes. We recently discovered that the IFN-γ-CXCL10-CXCR3 chemokine axis is active in both human vitiligo and in a vitiligo mouse model that we developed, and that CXCL10 is critical for both the progression and maintenance of vitiligo, implicating this pathway as a potential treatment target. In order to focus our treatment strategy, we sought to identify which cell types produce CXCL10 during vitiligo. We found that there are multiple sources, and each source varied in their magnitude and timing of CXCL10 expression. These included Langerhans cells, dermal dendritic cells, γδ T cells, endothelial cells, fibroblasts, and keratinocytes. To determine which cellular source was functionally required to drive depigmentation in vitiligo, we used genetically modified strains that were deficient in each cell type, or lacked the ability to respond to IFN-γ signaling (STAT1-deficient). While mice that lacked Langerin+ dermal dendritic cells and γδ T cells developed normal depigmentation, Langerhans cell-deficient mice developed worse disease. Vitiligo in mice with STAT1-deficient keratinocytes was largely abrogated, revealing that keratinocytes promote vitiligo, while Langerhans cells suppress disease. Therefore, suppressing IFN-γ signaling in KCs through topical treatments may be an effective targeted treatment strategy for vitiligo.