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Is targeting circulating T blood cells a therapeutic option for vitiligo?

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Vitiligo is an autoimmune depigmenting skin disorder that results from the loss of melanocytes due to an altered proportion and/or function of effector and regulatory T cells.[1,2] More specifically, the T-helper/cytotoxic T-cell (Th)1/(Tc)1 immune response is affected by an increased production of interferon (IFN)-γ and tumour necrosis factor (TNF)-α.

In this issue of the *BJD*, Martins *et al.* reaffirm the role of Th1 and Tc1 cell subsets in vitiligo disease and its production of both IFN-γ and TNF-α.[3] Furthermore, their results show that the frequency of $CD4^+$ and $CD8^+$ circulating Th17/Tc17, Th1/Th17 and Tc1/Tc17 effector memory T-cell subsets is significantly lower in patients with vitiligo (both with stable and active disease) and psoriasis, in comparison with healthy donors. These findings suggest a possible migration of distinct T-cell subsets from the blood into the skin. The same authors have previously shown that vitiligo perilesional skin is imprinted with pathogenic $CD8^+$ resident memory T cells (T_{RM}).[4] Future studies should investigate which blood memory T-cell subsets ultimately differentiate into vitiligo-pathogenic T_{RM} cells.

Many studies on patients with vitiligo focus exclusively on patients with active disease. However, Martins *et al.*[3] show that the same immune response is found in the blood of patients with active and stable disease. Previous studies have shown the presence of T_{RM} cells in vitiligo skin,[4–6] which are likely involved during flares, as previously shown in psoriasis.[7]

The precise role of circulatory Th1/Th17, Tc1/Tc17 and Th17 cells and the production of interleukin (IL)-17 in patients with vitiligo remains unclear. Studies have shown increased IL-17 expression both in blood and perilesional skin of patients with vitiligo,[8] and serum level of IL-17 correlated with disease activity,[9] while other studies have observed a similar frequency of IL-17-producing CD4 and CD8 T cells in vitiligo skin and skin from unaffected individuals.[4] A single-arm pilot study using secukinumab showed that directly targeting the IL-17 pathway is not a reliable strategy in vitiligo.[10] The work of Martins *et al.*[3] raises important questions, such as whether pathogenic IFN-γ-producing cells also secrete IL-17 in patients with vitiligo or whether the IL-17 production is a consequence of the activation of Th1/Th17 or Tc1/Tc17 cells.

Together, these findings indicate that targeting blood-specific T-cell subsets that migrate into the skin of patients with vitiligo could prevent the flare of the disease. Nevertheless, further studies will have to elucidate which circulating skin-homing T-cell subsets truly cause the cutaneous changes seen in patients with vitiligo.

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