PSORIASIS

IL-21 blockade—a new therapeutic approach for psoriasis?

The T-cell-derived cytokine interleukin (IL)-21 has a key role in the process of epidermal hyperplasia in psoriasis, and blocking this cytokine might be an effective therapy for patients with this disease, according to a paper published in *Nature Medicine*.

"It was shown previously that some single nucleotide polymorphisms in the region of chromosome 4q27 harboring the *IL-21* gene can associate with psoriasis," explains Dr Giovanni Monteleone, the lead researcher on this study. "This observation, together with the demonstrations that IL-21 is made by activated $CD4^+$ T cells and that IL-21 enhances the effector phase of T cell responses in tissues and exacerbates inflammation and damage *in vivo*, prompted us to explore the role of IL-21 in psoriasis."

First, the researchers analyzed the levels of IL-21 in skin biopsy specimens from patients with psoriasis, or other inflammatory diseases, and from healthy controls. Levels of IL-21 mRNA and protein were considerably higher in lesional psoriatic skin than in nonlesional psoriatic skin or skin from healthy controls or individuals with other inflammatory diseases.

Next, Monteleone *et al.* investigated whether IL-21 can induce keratinocyte proliferation and epidermal hyperplasia as seen in psoriasis. Keratinocytes from healthy volunteers were shown to proliferate in response to IL-21 *in vitro*. In addition, intradermal IL-21 injections (for 4 days) in normal mice resulted in epidermal hyperplasia and infiltration of the dermis and epidermis with inflammatory cells.

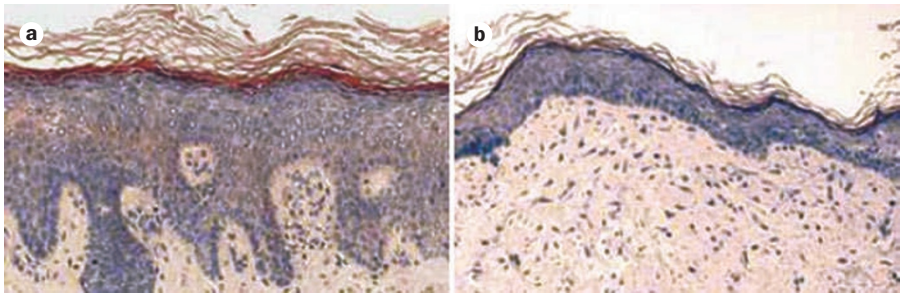

Figure 1 | Epidermal thickness in SCID mice engrafted with human psoriatic skin **a** | untreated and **b** | after 4 weeks of treatment with an anti-IL-21 antibody.

To assess the effect of blocking IL-21 in this setting, the authors used the human psoriasis SCID mouse model. Full-thickness nonlesional human skin from patients with psoriasis was transplanted onto the backs of SCID mice, and 2 weeks later the mice were injected intradermally with activated peripheral blood mononuclear cells. One week later, the normal skin developed into psoriatic plaques and the mice were then either treated for 4 weeks with an anti-IL-21 monoclonal antibody or with control IgG, or were left untreated. Xenografts from mice that received the anti-IL-21 antibody had reduced epidermal thickening and lower numbers of inflammatory cells than the grafts of untreated or control-treated mice (Figure 1), suggesting that blocking IL-21 can reduce keratinocyte proliferation and limit inflammation.

The researchers are excited about the therapeutic implications of this work, but first they want to understand more about the signaling pathways involved, which is the focus of their ongoing research.

Jenny Buckland

Original article Caruso, R. *et al.* Involvement of interleukin-21 in the epidermal hyperplasia of psoriasis. *Nat. Med.* **15**, 1013–1015 (2009).