PSORIASIS

IL-38 HAS AN ANTI-INFLAMMATORY ACTION IN PSORIASIS AND ITS EXPRESSION CORRELATES WITH DISEASE SEVERITY AND THERAPEUTIC RESPONSE TO ANTI-IL-17 TREATMENT

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Background: IL-36 cytokines, a subgroup of IL-1 family, play a pathogenic role in psoriasis. IL-36s comprise three agonists, IL-36, IL-36 and IL-36, abnormally expressed in psoriatic skin, and two receptor antagonists, IL-36Ra and IL-38, this last being yet poorly investigated in psoriatic context.

Objectives: to analyze skin and serum levels of IL-38, together with other IL-36 members, in affected patients before and after the biological inhibition of IL-17A with secukinumab; to investigate the effects of IL-38 in preclinical models of psoriasis.

Materials and methods: IL-38, IL-36Ra and IL-36 levels were analyzed in vivo in skin biopsies and serum of psoriatic patients before and 8-week after secukinumab treatment, as well as of healthy donors. Recombinant IL-38 was administrated in vitro in human keratinocyte and endothelial cell cultures activated by psoriasis-related cytokines, as well as in vivo in a murine model induced by topical 5% Imiquimod. The expression of pro-inflammatory molecules and epidermal markers, as well as the characterization of inflammatory immune infiltrate, were performed by Real-time PCR and IHC.

Results: The balance of IL-36/IL-38 serum levels in psoriatic patients is sharply in favor of agonist and is associated with disease severity. Treatment of psoriatic patients with secukinumab leads to the upregulation of skin and serum IL-38 levels, which positively correlate with the therapeutic efficacy. IL-38 administration reduces the inflammatory

responses and restores the keratinocyte proliferation and differentiation programs in experimental in vitro and in vivo models of psoriasis. Further studies are ongoing to investigate IL-38 expression in different clinical forms of psoriasis, and to identify the molecular interactors of IL-38.

Conclusions: IL-38, a cytokine with a protective role on skin homeostasis, represents a valid responsive biomarker of psoriasis and has strong anti-inflammatory effects in the psoriatic context. Its manipulation could represents an efficacious therapeutic strategy for psoriasis.