PSORIASIS

INFLAMMATION INDUCED BY INTRADERMAL IL-23 IN THE EAR OF MICE: A MODEL OF PSORIASIS?

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Introduction: The intradermal (i.d.) injection of IL-23 in mice ear induces a psoriasis-like phenotype mediated by IL-22 and IL-17A and characterized by keratinocyte proliferation, thickening of epidermis and dermal inflammation. Recent publications suggest that IL-23 also induces a Th2 profile, considered a molecular signature of atopic dermatitis.

Objective: Our aim has been to characterize the IL23 model and challenge its suitability as a psoriasis or atopic dermatitis experimental model.

Material and methods: The disease was induced by repeated i.d. injections of recombinant mouse IL-23 from day 0 to 6, every other day into the dorsal skin of the ear. Skin thickness and cumulative clinical score comprising erythema, swelling and scaling were determined at different time points. Ear punch biopsies were taken cytokines were measured by Luminex, IL-17A, IL-17F and IL-22 mRNA levels were determined by qRT-PCR TaqMan, and histological analysis performed. Finally, the effect of neutralizing antibodies against IL-17, IL-22 and IL-23, and of 3 oral and 3 topical drugs on skin thickness was studied.

Results: Ear thickness and cumulative clinical score peaked at day 7 after id injection of IL23. A marked local induction of Th22 and to a lesser extent of Th17 cytokines, was observed in the biopsies. There was no induction of Th2 cytokines. Histological evaluation showed a mixed-cell inflammatory infiltrate composed of macrophages, CD3+ lymphocytes and neutrophils and a secondary epidermal hyperplasia. Relevance of IL-22 was confirmed in the model as anti-IL-22 antibody treatment achieved highest ear thickness inhibition (85%). The model was sensitive to oral and topical drugs with different mechanism of action, including corticosteroids, cyclosporine, tacrolimus and JAK inhibitors.

Conclusions: The inflammation evoked by IL-23 in our experimental protocol induces a Th17/Th22 signature with no effect on Th2. The model is suitable for evaluating novel drugs for psoriasis.