PSORIASIS

FN14 DEFICIENCY AMELIORATES PSORIASIS-LIKE SKIN DISEASE IN A MURINE MODEL

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Background: Tumor necrosis factor (TNF)-like weak inducer of apoptosis (TWEAK) is a multifunctional cytokine that acts through its receptor fibroblast growth factor inducible 14 (Fn14). Recent studies demonstrated that the TWEAK/Fn14 signals participate in the development of psoriasis.

Objective: The purpose of this study was to further explore the effect of Fn14 inhibition on experimental psoriasis.

Materials and Methods: Psoriasis-like skin disease was induced in the wild-type and Fn14-knockout BALB/c mice. Psoriasis-like lesion was monitored on these mice by immunohistochemistry and histological evaluation. Human primary keratinocytes were cultured in vitro, followed by stimulation with M5 cocktail or recombinant TWEAK.

Results: Fn14 deficiency ameliorates psoriasis-like lesion in this model, accompanied by less inflammatory cell infiltration and proinflammatory cytokine production in lesional skin. The cutaneous expression of TNF receptor type 2 also decreased in the Fn14-deficient mice. Moreover, the topical application of TWEAK exacerbated psoriatic lesion in the wild-type but not in the Fn14-deficient mice. Furthermore, TWEAK promoted the expression of interleukin 8, keratin 17 and epidermal growth factor receptor (EGFR) but inhibited the expression of involucrin in psoriatic keratinocytes in vitro. Interestingly, such effect of TWEAK was abrogated by an EGFR inhibitor (erlotinib). TWEAK also enhances the proliferation and interleukin 6 production of dermal microvascular endothelial cells under psoriatic condition.

Conclusions: TWEAK/Fn14 signals contribute to the development of psoriasis, and involves the modulation of resident cells and the transduction of the EGFR pathway. Fn14 inhibition might be a novel therapeutic strategy for patients with psoriasis.