



PSORIASIS

MECHANICAL STRETCH EXACERBATES PSORIASIS BY STIMULATING KERATINOCYTE PROLIFERATION AND CYTOKINE PRODUCTION

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Introduction: Psoriasis is a chronic autoimmune inflammatory skin disease that often occurs in rubbed areas undergoing stronger mechanical stretch, such as the elbows and knees. However, the pathologic role of mechanical tension in the pathogenesis of psoriasis remains unclear.

Objective: To investigate the effect of mechanical stretch on keratinocytes that contributes to the clinical features of psoriasis.

Materials and Methods: Primary human keratinocytes were cultured on flexible silicone dishes to simulate stretching-induced mechanical force and the effect of mechanical stretch on cell proliferation and differentiation was assessed in vitro. Further, a novel murine model of skin expansion were established by subcutaneously implanting a dilator into the dorsum of BALB/c mice, followed by imiquimod (IMQ) treatment to induce psoriatic lesions. The effect of mechanical stretch on skin barrier function and corresponding cutaneous phenotypes under the physiological and pathological conditions were assessed in vivo.

Result: We found that cellular proliferation and skin barrier-associated gene expression of primary human keratinocytes increased significantly after 24 h of continuous stretching. Additionally, continuous stretching induced production of psoriasis-associated pro-inflammatory cytokines, antibacterial peptides, and chemokines in primary human keratinocytes. Furthermore, we established a novel murine model of skin expansion by implanting dilator into the dorsum of BALB/c mice to assess the effect of mechanical stretch on the epidermis in vivo. The dilator-implanted mice displayed prominent epidermal hyperproliferation, impaired skin-barrier function, and upregulation of psoriasis-associated cytokines in epidermal keratinocytes. Most importantly, the dilator-implanted psoriatic mice treated with IMQ or IL-23 displayed an aggravated psoriatic phenotype compared to mice without dilator implantation.

Conclusions: our results suggest that mechanical stretch can exacerbate psoriatic lesions by promoting cell proliferation and amplifying pro-inflammatory effects of keratinocytes,





thereby providing novel insights into the pathogenesis of psoriasis.

