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Article

Obesity and Dyslipidemia Synergistically Exacerbate Psoriatic Skin Inflammation

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Abstract: Patients with psoriasis are frequently complicated with metabolic syndrome; however, it is not fully understood how obesity and dyslipidemia contribute to the pathogenesis of psoriasis. To investigate the mechanisms by which obesity and dyslipidemia exacerbate psoriasis using murine models and neonatal human epidermal keratinocytes (NHEKs), we used wild-type and *Apoe*-deficient dyslipidemic mice, and administered a high-fat diet for 10 weeks to induce obesity. Imiquimod was applied to the ear for 5 days to induce psoriatic dermatitis. To examine the innate immune responses of NHEKs, we cultured and stimulated NHEKs using IL-17A, TNF-α, palmitic acid, and leptin. We found that obesity and dyslipidemia synergistically aggravated psoriatic dermatitis associated with increased gene expression of pro-inflammatory cytokines and chemokines. Treatment of NHEKs with palmitic acid and leptin amplified pro-inflammatory responses in combination with TNF-α and IL-17A. Additionally, pretreatment with palmitic acid and leptin enhanced IL-17A-mediated c-Jun N-terminal kinase phosphorylation. These results revealed that obesity and dyslipidemia synergistically exacerbate psoriatic skin inflammation, and that metabolic-disorder-associated inflammatory factors, palmitic acid, and leptin augment the activation of epidermal keratinocytes. Our results emphasize that management of concomitant metabolic disorders is essential for preventing disease exacerbation in patients with psoriasis.

Keywords: psoriasis; obesity; dyslipidemia; leptin; palmitic acid; chemokine

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