CD36-SREBP1 axis mediates thymic stromal lymphopoietin production in obesity-exacerbated atopic dermatitis

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Abstract

Background: Obesity is associated with an increased risk of atopic dermatitis (AD) and may accelerate its development. Keratinocyte dysfunction has been observed in obesity-related skin diseases, including psoriasis and acanthosis nigricans, but is not fully understood in AD. Here, we aim to emphasize the important role of keratinocytes in obesity-aggravated AD.

Methods: C57BL/6 mice were fed a high-fat diet (HFD) for 12 weeks before calcipotriol (MC903) administration to induce AD-like dermatitis. Fatty acid intake was quantified using BODIPY 500/510 staining. Palmitic acid (PA) treatment of keratinocytes mimicked the obese state at the cellular level. CD36 or sterol-regulatory element binding protein1 (SREBP1) inhibitors were topically applied to mouse ears to explore the roles of CD36 or SREBP1 in obesity-aggravated AD. A chromatin immunoprecipitation assay (ChIP) was conducted to assess the transcriptional control of SREBP1 on thymic stromal lymphopoietin (TSLP) expression.

Results: HFD-induced obesity exacerbated AD-like dermatitis in mice, with elevated inflammatory molecules and fatty acid accumulation in the lesional skin. Blocking CD36, a fatty acid transporter, with a chemical antagonist effectively alleviated AD-like inflammation and decreased TSLP levels in obese MC903-treated mice. Moreover, PA treatment induced TSLP overexpression via CD36 and activated the downstream SREBP1 signaling pathway in keratinocytes. The ChIP assay further revealed increased binding of SREBP1 to the TSLP promoter region.

Conclusion: Obesity activates the CD36-SREBP1-TSLP axis in keratinocytes, inducing epidermal lipid disorders and aggravating AD-like inflammation. Targeting CD36 or SREBP1 will facilitate the development of future combination therapies or modified therapies for treating patients with obesity and AD.

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Figure 1, Yu et al.

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