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Thrombospondin-1 Deficient Exacerbates the Pathogenesis of Imiquimod-Induced Psoriasis

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Introduction & Objectives:

Psoriasis is a chronic, relapsing inflammatory skin disorder, characterized by as silver scaling erythematous plaques due to epidermal hyperplasia, aberrant differentiation of keratinocytes, and increased angiogenesis. Thrombospondin-1 (TSP-1) could inhibit angiogenesis in vivo and to suppress vascular endothelial cell proliferation and migration in vitro. TSP-1 has been also described as a key immunoregulatory factor. Interaction of TSP-1 with CD47 promotes the development of regulatory T cells while inhibiting chronic inflammation associated with Th1 or Th17 cells.

Materials & Methods:

IMQ application on wild-type mouse skin induced psoriasis-like reactions, correlating with increased TSP-1 expression. We used TSP-1 to treat imiquimod (IMQ)-induced psoriasis in BALB/C mice and examined the underlying mechanisms.

Results:

Quantitative RT-PCR showed significant elevation of TSP-1 mRNA, peaking at four-fold at 24 hours and remaining elevated over three-fold at 48 and 96 hours before returning to baseline. Immunohistochemistry confirmed heightened TSP-1 expression in epidermal keratinocytes. TSP-1 deficiency exacerbated skin lesions compared to wild-type mice, accompanied by heightened inflammatory cytokines and reduced keratinocyte markers. LSKL treatment worsened lesions and inflammation.

Here we showed that TSP-1 expression is upregulated in skin lesion of IMQ mice model. However, a peptide antagonist of TSP-1, LSKL treated in wild type mice has exacerbated psoriasis-like dermatitis, correlating with increased neovascularization, leukocytes infiltration and IL-17/IL-23 cytokine expression in the skin lesion of IMQ model. In addition, the use of the TSP-mimetic peptide ABT510 drastically reduces psoriasis-like dermatitis and neovascularization in TSP-1-deficient, and wild-type mice

Conclusion:

Our findings underscore TSP-1's pivotal regulatory role in IMQ-induced psoriasiform skin inflammation, thus, wu suggested that TSP-1 may act as an important endogenous negative regulator of psoriasis pathogenesis and may be developed as a novel therapeutic strategy of psoriasis.