

PSORIASIS

## PPAR-β/δ PLAYS AN IMPORTANT ROLE IN THE PATHOGENESIS OF PSORIASIS AND DYSLIPIDEMIA COMORBIDITY

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Background: Psoriasis patients are at increased risk of developing lipid metabolism disorders. The interactive mechanism is complicated and still unclear. Therefore, we established a composite animal model by imiquimod (IMQ) application on the dorsal skin of ApoE-/- mice for the study of psoriasis and dyslipideamia comorbidity.

Objective: To explore the pathological mechanism of psoriasis combined with dyslipidemia by IMQ-induced ApoE-/- mice model.

Materials and Methods: We used sequencing technology to perform transcriptomic analysis on mice skin lesions and LC-MS to perform lipid metabolomics analysis on mice serum. The differentially expressed genes (DEGs) and differential metabolites were conducted by KEGG and IPA databases respectively. The predictive targets and pathways validated by animal experiments.

Results: We identified 544 up-regulated DEGs and 422 down-regulated DEGs in IMQinduced ApoE-/- mice compared to WT mice. KEGG analysis suggested PPAR signaling pathway may play a main role. We also studied serum differential metabolites by IPA, which revealed that PPAR- $\beta/\delta$  agonist GW501516 was the major upstream regulatory factor. Animal experiments confirmed that the gene and protein expressions of PPAR- $\beta/\delta$  in skin of IMQ-induced ApoE-/- mice upregulated. PPAR- $\beta/\delta$  agonists could significantly aggravate skin lesions, increase PASI, promote the secretion of inflammatory cytokines IL-17A and IL-23 in serum and increase the protein expression of PPAR- $\beta/\delta$  in the skin. Whereas, PPAR- $\beta/\delta$  antagonist could significantly improve psoriasiform lesions, inhibit the expressions of IL-17A, IL-6, IL-22 and TNF- $\alpha$  in the skin, and reduce PPAR- $\beta/\delta$  gene and protein expressions.

Conclusions: PPAR- $\beta/\delta$  plays an important role in the pathogenesis of psoriasis and dyslipidemia comorbidity. PPAR- $\beta/\delta$  antagonist might be a new drug for psoriasis therapy.





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