PSORIASIS

MIR-183 AFFECTS KERATINOCYTES PROLIFERATION AND PSORIASIS-LIKE INFLAMMATION BY TARGETING 15-LOX THROUGH LIPOXIN A4 SIGNALING

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Background: Current studies show that the level of miR-183 is up-regulated obviously in human psoriasis skin lesion. Our previous studies verified that lipoxin A4 (LXA4) could inhibit keratinocytes proliferation and psoriasis-like inflammation. Meanwhile, we found that there exists the binding site of miR-183 in the 3'-UTR of 15-LOX, which is the regulatory gene of LXA4. However, the specific effects and mechanisms of those are needed further research.

Objective: Our study aimed to investigate the effects of miR-183 on keratinocytes proliferation and psoriasis-like inflammation, and the possible molecular mechanisms.

Materials and Methods: Normal human epidermal keratinocytes (NHEKs) were isolated and cultured in vitro. Psoriasiform dermatitis mouse models were were established by Imiquimod (IMQ). qRT-PCR were used to identify the dysregulated miR-183. Histochemical staining was performed to evaluate skin leions of psoriasiform dermatitis and control mice. The cell proliferation was examined by WST-8, the protein levels of inflammatory cytokines and LXA4 were quantified by ELISA. TRAF6 and STAT3 were analyzed using Western blotting. Luciferase assays were performed to determine whether miR-183 targets 15-LOX.

Results: miR-183 was overexpressed in the lesions of the progressive stage psoriasis patients and IMQ induced psoriasiform dermatitis mouse. The lesions of IMQ induced psoriasiform dermatitis mouse were ameliorated by down-regulating the level of miR-183. The expression of inflammatory cytokines of psoriasiform dermatitis mouse and lipopolysaccharide (LPS)-treated NHEKs were suppressed by down-regulating miR-183. Low-expression of miR-183 suppressed LPS-treated NHEKs proliferation. The levels of TRAF6 and STAT3 of psoriasiform dermatitis mouse lesions were down-regulated through low-expression of miR-183. miR-183 negatively regulated the level of LXA4. Luciferase assays showed that 15-LOX is a direct target of miR-183.

Conclusions: Our findings indicate that down-regulation miR-183 contributes to ameliorate keratinocytes proliferation and psoriasis-like inflammation by targeting 15-LOX through LXA4, TRAF6 and STAT3 signals were involved.