SKIN CANCER (OTHER THAN MELANOMA)

TWEAK/FN14 INTERACTION CONFERS AGGRESSIVE PROPERTIES TO CUTANEOUS SQUAMOUS CELL CARCINOMA

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Background: Recent studies showed that tumor necrosis factor (TNF)-like weak inducer of apoptosis (TWEAK)/fibroblast growth factor-inducible 14 (Fn14) signaling participates in the progression of internal malignancies. However, its role in the biological properties of cutaneous squamous cell carcinoma (SCC) remains unclear.

Objective: This study was designed to explore the effect of TWEAK/Fn14 activation on cutaneous SCC as well as the relevant mechanism.

Materials and Methods: The expression of TWEAK and Fn14 was determined in tissue samples of patients with cutaneous SCC. Human primary keratinocytes and SCC cell lines were cultured in vitro, receiving stimulation of TWEAK. The xenografts of SCC were generated subcutaneously in BALB/c nude mice.

Results: The results showed that both TWEAK and Fn14 were highly expressed in human cutaneous SCC. Moreover, TWEAK/Fn14 activation promoted the proliferation, migration, and invasion of cultured SCC cells. Interestingly, TNF receptor type 2 (TNFR2) was upregulated in cultured SCC cells, and the transfection of TNFR2 siRNA abrogated the effect of TWEAK on these cells. Finally, the favorable effect of TWEAK/Fn14 signals was confirmed in BALB/c nude mice with SCC xenografts.

Conclusions: TWEAK/Fn14 signals contribute to the progression of cutaneous SCC, possibly involving the TNF-α-independent TNFR2 signal transduction.