WOUND HEALING

FIBROBLAST GROWTH FACTOR 2 ENHANCES EPITHELIAL MESENCHYMAL TRANSITION ON KERATINOCYTES DURING WOUND HEALING PROCESS

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Introduction: In a wound healing process, keratinocytes at a wound edge temporarily change their form into spindle, which is thought to enable rapid migration on wound bed. The morphological alternation of keratinocytes belongs in a concept of epithelial-mesenchymal transition (EMT). Fibroblast growth factor 2 (FGF2) has a potential to accelerates wound closure mainly due to activation of vascular endothelial cells and fibroblasts.

Objective: The aim of the present study was to examine FGF2 effects on wound healing from a view point of keratinocytes' EMT.

Materials and Methods: Six millimeter-circular wounds were created on the dorsal skin of C57BL/6 mice and treated daily with or without recombinant FGF2. The isolated wounds were immunohistopathologically and immnofluorescently examined about EMT associated cell structure and transcriptional factors. Tissue PCR array about EMT associated 84 molecules were performed using RNA extracted from full thickness wounds. In in vitro experiments, EMT associated factors in keratinocyte cell lines were evaluated by real-time RT-PCR under stimulation of FGF2 and TGFβ1.

Results: Wounds treated with FGF2 day 4 after wounding histopathologically revealed that wound edge keratinocytes formed multilayered epithelia with morphological transition to spindle shape in comparison with control wound. In addition, we found some wound edge keratinocytes migrated individually toward the wound center with a reduction of E-cadherin and an acquisition of vimentin. In FGF2 treated wounds, PCR array demonstrated upregulated tendencies of EMT, TGF/BMP and WNT signaling. Indeed, keratinocytes in wound edge showed expression of EMT associated transcriptional factors such as Snail, Slug and Twist. In vitro examination about keratinocytes demonstrated that FGF2 cooperated with TGFβ1 to express EMT associated morphological components and transcriptional factors.

Conclusions: FGF2 had a potential to enhance keratinocytes' EMT in wound healing process by supporting function of TGFβ1, which might accelerate reepithelialization process in wound healing.