Synopsis of Original Research Paper

The roles of MRTF-A/B in the homeostasis of skin

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Skin fibroblasts themselves are the cells that produce extracellular matrix (ECM), but their ability to produce ECM and motility are low under the normal conditions. In contrast, when skin tissues are injured, they are changed to myofibroblasts.

Myofibroblasts exhibit an enhanced motility and accumulate at the injured area. There, they vigorously produce ECM for wound healing. Such phenotypic modulation of skin fibroblasts is caused by the inflammatory response as follows. Skin injury activates the secretion of inflammatory cytokines such as transforming growth factor-βs (TGF-βs) from inflammatory cells and the normal skin fibroblasts stimulated by these cytokines are converted into myofibroblasts. However, this mechanism has not been fully characterized. In this study, I addressed this molecular event and found that factor X (anonymity because of unpublished results) plays a critical role in the myofibroblastic phenotypic modulation of skin fibroblasts. Novel findings revealed by this study are as follows: 1) Myocardin related transcription factors A and B (MRTF-A/B) play a critical role in exhibition of myofibroblastic phenotype of skin fibroblasts, 2) In skin fibroblasts, MRTF-A/B are usually localized in the nuclear but their functions remain inactivated because of low level expression of factor X, 3) The expression levels of myofibroblasts markers such as αSM-actin and collagens are up-regulated concomitant with the increase in the expression of factor X in TGF-β-stimulated skin fibroblasts, 4) siRNA-mediated knockdown of factor X suppresses the TGF-β-induced up-regulation of these myofibroblastic markers, 5) Factor X binds to both of serum response factor (SRF) and MRTF-A and activates the SRF/CArG-box mediated transcription.