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〈Regular Article〉

SPARC Up-Regulates Production and Pericellular Organization of Collagen I and Hyaluronan *via* TGF-*β* Signaling in Skin Fibroblasts

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Abstract

Background: Secreted protein acidic and rich in cysteine (SPARC) regulates extracellular matrix (ECM) production, interaction of cells with ECM and growth factor-dependent cell signaling. Here we examined SPARC's effects on production and pericellular organization of type I collagen and hyaluronan (HA) in normal human dermal fibroblasts.

Methods: Production of procollagen I and HA, and gene expression were analyzed by ELISA and quantitative real-time PCR, respectively. The pericellular deposition of mature collagen I and HA was examined by immunocytochemistry.

Results: SPARC enhanced production of procollagen I and HA in fibroblasts by up-regulating mRNA expression of *COL1A1* (*collagen α-1(I)*) and *HAS* (*HA synthase*) *2*/*3*, respectively. SPARC also increased the deposition of mature collagen fibrils on the cell surface of fibroblasts, accompanying the increased mRNA expression of procollagen C-proteinase (*BMP1*) and N-proteinase (*ADAMTS2*). The pericellular deposition of newly produced HA was also enhanced on the cell surface of SPARC-treated fibroblasts. Furthermore, SPARC up-regulated TGF-*β*1 production in fibroblasts, and SPARC-induced procollagen I and HA production was abolished by blockade of TGF-*β*/Smad2/3 signaling.

Conclusion: SPARC simultaneously up-regulates production of procollagen I and HA in fibroblasts by up-regulating Smad2/3-dependent TGF-*β* signaling, and also promotes the pericellular organization of mature collagen I fibrils and HA.

Key words: SPARC (BM40/Osteonectin), Skin fibroblast, Collagen I, Hyaluronan, TGF-*β* signaling.