THE CHANGES OF EXTRACELLULAR MATRIX PRODUCTION BY HUMAN DERMAL FIBROBLASTS WITH OR WITHOUT SILENCING OF CTGF

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Although the pathogenesis of systemic sclerosis (SSc) is still unknown, a fascinating hypothesis called a 2-step process of fibrosis has been proposed. The key cytokines are transforming growth factor β (TGFβ), which stimulates fibroblasts first, and connective tissue growth factor (CTGF), which acts to maintain tissue fibrosis. Following this hypothesis, a new therapeutic strategy focusing CTGF may be a promising choice for the treatment of SSc. In the present study, we aimed at silencing of CTGF production by human dermal fibroblasts (HDF) using RNAi method. We transfected siRNA, then cultured for 144 hrs. Immunoblotting study confirmed that cells transfected with one siRNA with CTGF-specific oligonucleotides markedly reduced the production of CTGF in HDF after 144 hrs. Then, further experiments are carried out to test the effects of CTGF silencing in HDF originated from normal or SSc. HDF from normal and SSc were cultured for 144 hours. Then CTGF-specific siRNA were transfected. After stimulating TGFβ, we measured the production of type I collagen and matrix metalloproteinase (MMP)1 by western blot. Then, the production of type I collagen were decreased in both fibroblasts from normal and SSc. Although the production of MMP1 was decreased in normal fibroblasts, those from SSc was increased.

This preliminary study suggests the possibility that the therapeutic use of RNAi is promising for the treatment of SSc in the future. It is of note that the opposite effects were seen in the production of MMP1 in normal and SSc fibroblasts whose CTGF was silenced.