

# **Elucidation of mechanism of suppression of collagen production by pathogen-derived and endogenous double-stranded RNA in an interferon-independent manner**

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Production of extracellular matrices, including collagen and fibronectin, is highly important for not only beauty and moisturizing, but also biological defense system, such as maintenance of barrier ability and anti-inflammatory responses, in the skin. Dermal fibroblasts mainly produce extracellular matrices in the skin. Therefore, regulation of extracellular matrix production in the dermal fibroblasts is highly important. We previously found that double-stranded RNA (dsRNA) suppressed the expression of extracellular matrices in the activated hepatic satellite cells. Dermal fibroblasts are also exposed to not only pathogen-derived dsRNA but also endogenous dsRNA. These findings made us hypothesize that pathogen-derived and endogenous dsRNA activated innate immune responses in the skin fibroblasts, leading to reduction in extracellular matrix production in the skin. In this study, treatment with a synthetic dsRNA, polyI:C, resulted in significant reduction in the expression of extracellular matrices, without significant reduction in the viabilities of normal human dermal fibroblasts. Furthermore, a short dsRNA (19 bp) also induced down-regulation of fibrotic marker gene expression in normal human dermal fibroblasts. These results indicated that dsRNA is a hazard for skin by down-regulating the production of extracellular matrices.