A05-3 Inhibitory regulation of fibrosis in systemic sclerosis by apelin

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The secreted protein apelin is mainly produced from endothelial cells, and regulates several functions, including angiogenesis. Recently, it has been reported that apelin expression was inhibited in pulmonary artery endothelial cells in the patients of pulmonary arterial hypertension, and impaired apelin signaling led to increased fibroblast growth factor 2 (FGF2) and FGF receptor expression, resulting in hyperproliferative endothelial and vascular smooth muscle cells. These findings suggest that apelin regulates fibrosis as well as angiogenesis. The aim of this study was to elucidate the role of apelin in fibrosis in systemic sclerosis (SSc). The expression of apelin in SSc fibroblasts was significantly lower than that in normal fibroblasts. There is no change in apelin receptor (APJ) expression in normal and SSc fibroblasts. siRNA depletion of apelin from fibroblasts enhanced collagen type 1 expression. These results suggest that apelin inhibits fibrosis, and might involve in the pathogenesis of SSc. Next, we examined the effect of hypoxia on the inhibitory regulation of fibrosis by apelin. The expression of apelin in normal and SSc fibroblasts was induced by hypoxia, and the inhibition of HIF-1α using siRNA attenuated hypoxia-induced apelin production. Furthermore, the expression of hypoxia-induced apelin in SSc fibroblasts was significantly lower than that in normal fibroblasts. The expression of collagen type I was increased in hypoxia treated normal fibroblasts, and this hypoxia-induced collagen type I was enhanced by siRNA depletion of apelin. These results suggest that apelin might regulate fibrosis in the hypoxia condition associated with the pathogenesis of SSc.