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Type I collagen induces mesenchymal cell differentiation into myofibroblasts through YAP-induced TGF- β 1 activation

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Abstract

In organ fibrosis, mechanical stress and transforming growth factor beta-1 (TGF- β 1) promote differentiation into myofibroblast from mesenchymal cells, leading to extracellular matrix (ECM) remodeling or active synthesis, deposition or degradation of ECM components. A major component of ECM, type I collagen (col I) triple helical molecules assemble into fibrils or are denatured to gelatin without triple-helicity in remodeling. However, whether changes of ECM components in remodeling have influence on mesenchymal cell differentiation remains elusive. This study adopted three states of collagen I existing in ECM remodeling: molecular collagen, fibrillar collagen and gelatin to see what are characteristics in the effects on two cell lines of mesenchymal origin, murine 3T3-L1 embryonic fibroblast and murine C2C12 myoblasts. The results showed that all three forms of collagen I were capable of inducing these two cells to differentiate into myofibroblasts characterized by increased expression of alpha-smooth muscle actin (α -SMA) mRNA. The expression of α -SMA is positively regulated by TGF- β 1. Nuclear translocation of Yes-associated protein (YAP) is involved in this process. Focal adhesion kinase (FAK) is activated in the cells cultured on molecular collagen-coated plates, contributing to YAP activation. On the other hand, in the cells cultured on fibrillar collagen gel or gelatin-coated plates, oxidative stress but not FAK induce YAP activation. In conclusion, the three physicochemically distinct forms of col I induce the differentiation of mesenchymal cells into myofibroblasts through different pathways.

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