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P11 The Role of Smooth Muscle Integrin Alpha V and TGF-Beta Pathways in Vascular Fibrosis

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ABSTRACT

It has been demonstrated that arterial stiffness is linked to arterial fibrosis manifested by increased collagen and other extracellular matrix synthesis in smooth muscle cells (SMC). Transmembrane receptors integrins mediating cell-cell and cell-matrix signalling pathways are involved in tissue fibrosis. We study the role of one integrin subunit av in angiotensin II (AngII)-induced SMC proliferation and arterial fibrosis and stiffness using SMC specific knock-out av mouse model (avSMKO) induced in adult mice by injection of tamoxifen. There is no difference in vascular fibrosis in basal conditions between control and mutant mice. However, decreased arterial fibrosis is observed in avSMKO mutant mice after 28-day perfusion of AngII. Analysis of RNA from aorta of control and mutant mice by Affymetrix microarrays indicated an alteration of the TGF-β pathway in AngII-treated mutant mice. In order to examine the mechanism associated to the decreased fibrosis in vascular SMC from avSMKO mice, isolated VSMC from the aorta of control and avSMKO mice were treated with TGF-β1 or AngII. The results indicated that these two treatments increased the expression of collagen, fibronectin and integrin αv at the protein and RNA levels as well as the phosphorylation of ERK and smad2/3 in the control cells. Inactivation of integrin αv partly inhibited all above effects induced by TGF-β1 and AngII. Our study indicates a role of av and TGF-β1 in the arterial fibrogenesis. Therefore, av signaling could be a therapeutic target against arterial fibrosis and stiffness in pathological conditions.

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