Regulation of discoidin domain receptor 2 by cyclic mechanical stretch in cultured rat vascular smooth muscle cells

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摘要

Abstract

Discoidin domain receptor 2 (DDR2) plays potential roles in the regulation of collagen turnover mediated by smooth muscle cells in atherosclerosis. How mechanical stretch affects the regulation of DDR2 in smooth muscle cells is not fully understood. We sought to investigate the cellular and molecular mechanisms of regulation of DDR2 by cyclic stretch in smooth muscle cells. Rat vascular smooth muscle cells grown on a flexible membrane base were stretched by vacuum to 20% of maximum elongation, at 60 cycles/min. Cyclic stretch significantly increased DDR2 protein and mRNA expression after stretch. Cyclic stretch also significantly increased DNA-protein binding activity of Myc-Max. Addition of SB203580, transforming growth factor-beta1 (TGF-beta1) monoclonal antibody, p38 small interfering RNA (siRNA), and c-myc siRNA 30 minutes before stretch inhibited the induction of DDR2 protein and abolished the DNA-protein binding activity induced by cyclic stretch. Cyclic stretch increased, whereas SB203580 abolished the phosphorylated p38 protein. Conditioned medium from stretched smooth muscle cells and exogenous administration of angiotensin II and TGF-beta1 recombinant proteins to the nonstretched cells increased DDR2 protein expression similar to that seen after stretch. In conclusion, cyclic mechanical stretch enhances DDR2 expression in cultured rat smooth muscle cells. The stretch-induced DDR2 is mediated by angiotensin II and TGF-beta1, at least in part, through p38 mitogen-activated protein kinase and Myc pathway.