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p38 mitogen-activated protein kinase-dependent activation of contractility in rat thoracic aorta

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The present study was undertaken to determine whether p38 mitogen-activated protein kinase participates in the regulation of vascular smooth muscle contraction by endothelin-1 (ET-1) in rat thoracic aorta. ET-1 induced a sustained contraction. In contrast, both the intracellular Ca^{2+} and myosin light chain (MLC) phosphorylations were not sustained. Calphostin C , an inhibitor of protein kinase C (PKC), attenuated ET-1-induced contraction and phosphorylations of myosin light chain. However, an intracellular Ca^{2+} was not affected by calphostin C. Genistein, a putative tyrosine kinase inhibitor, attenuated ET-1-induced both contraction and intracellular Ca^{2+}, respectively. ET-1 increased tyrosine phosphorylations of p38 mitogen-activated protein kinase (MAPK). SB203580, an inhibitor of p38 MAPK, attenuated the ET-1-induced contraction more potently than PD98059, an inhibitor of p44/42 MAPK kinase. Moerover, SB203580 decreased tyrosine phosphorylations of p38 MAPK stimulated by ET-1. The data indicate that ET-1-induced sustained contraction may be dependent mainly on the activity of p38 MAPK than p44/42 MAPK following PKC activation in rat thoracic aorta.