Mitogen-activated protein kinase phosphatase-1 in rat arterial smooth muscle cell proliferation.

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Abstract

Smooth muscle cell proliferation and migration is important in arteriosclerosis. In this process, cytokines and growth factors are upregulated and bind to their respective receptors, which in turn stimulate mitogen-activated protein (MAP) kinases. MAP kinases then relay signals to the nucleus that activate quiescent smooth muscle cells. Phosphatases downregulate MAP kinases. We investigated the role of a dual-specificity tyrosine phosphatase, MAP kinase phosphatase-1 (MKP-1), in smooth muscle cell proliferation. MKP-1 expression was high in arterial tissue by Northern analysis, and MKP-1 message was detected mainly in the arterial smooth muscle layer by in situ hybridization. After balloon injury of the rat carotid artery, expression of MKP-1 decreased greatly, whereas that of MAP kinases, especially p44 MAP kinase, increased. The time course of the reduction in MKP-1 message correlated with increased tyrosine phosphorylation and elevated p44 MAP kinase enzymatic activity. In rat arterial smooth muscle cells overexpressing MKP-1, growth was arrested in the G1 phase and entry into the S phase was blocked. A reduction in MKP-1 expression may contribute in part to proliferation of smooth muscle cells after vascular injury, possibly through a decrease in dephosphorylation of p44 MAP kinase.