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Inhibition of Growth Factor-induced MAP kinase and Akt Activation by NQ304, a 1,4-Naphthoquinone Derivative in Rat Aortic Vascular Smooth Muscle Cells

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We recently reported that 2-chloro-3-(4-hexylphenyl)-amino-1,4-naphthoquinone(NQ304), a naphthoquinone derivative, had potent inhibitory effects on the platelet aggregation in vitro and thrombosis in vivo. Furthermore, we reported the antiplatelet mechanism of NQ304 by the reduction of the thromboxane A2 formation, inhibition of adenosine triphosphate release and intracellular calcium mobilization. In this study, we examined the possible antiproliferative effect of NQ304 on rat aortic vascular smooth muscle cells (VSMCs). NQ304(1-10mM) significantly inhibited the serum(10% fetal bovine serum)- and PDGF-BB(50ng/ml)- induced proliferation in a dose-dependent manner on rat aortic VSMCs. Furthermore, flow-cytometric analysis showed that NQ304 arrested the G0/G1 and S phase of cell cycle progression. We also examined the intracellular signaling effect of NQ304 on the serum- and PDGF-BB- induced activation of mitogen-activated protein kinase(ERK1/2) and Akt by western blotting in cultured rat VSMCs. Pretreatment of rat VSMCs with NQ304 resulted in a significant inhibition of the serum- and PDGF-BB- induced activation of ERK1/2 and Akt. These results suggest that the antiproliferative effects of NQ304 may be exerted by the inhibition of the serum- and PDGF-BB induced ERK 1/2 and Akt, which can contribute to prevent atherosclerosis by inhibiting VSMCs proliferation.