

[P-32]**NQ304, A NOVEL ANTITHROMBOTIC AGENT, INHIBITS THE PROLIFERATION OF VASCULAR SMOOTH MUSCLE CELLS**Jin-Ho Kim, Tack-Joong Kim, Chung-Kyu Ryu^{*}, Jin-Tae Hong, Yeo-Pyo Yun

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Several 1,4-naphthoquinone derivatives have been reported to possess many pharmacological effects such as anti-viral, anti-fungal, anti-cancer and anti-platelet activities. However, little has been known about functional role in vascular smooth muscle cells (VSMCs). Among the synthetic 1,4-naphthoquinone derivatives, we found that 2-chloro-3-(4-hexylphenyl)-amino-1,4-naphthoquinone (NQ304) is a potent growth inhibitor on VSMCs.

In this study, a possible anti-proliferative mechanism of NQ304 on rat aortic VSMCs was investigated. NQ304 (1-10M) significantly inhibited 5% fetal bovine serum (FBS)-induced proliferation of rat aortic VSMCs evaluated by direct counting of cell number and [3H]-thymidine incorporation assay. There was no evidence of cellular toxicity or apoptosis of NQ304 (10uM) as determined by trypan blue exclusion assay, flow cytometric analysis and DNA fragmentation assay. The intracellular signaling effect of NQ304 on the FBS-induced activation of extracellular signal-regulated kinase 1/2 (ERK 1/2) and Akt cascade by western blot and electrophoretic mobility shift assay (EMSA) in cultured VSMCs were also examined. Pre-treatment of VSMCs with NQ304 resulted in a significant inhibition of the FBS-induced phosphorylation of ERK1/2 and Akt kinase.

These results indicate that NQ304 may inhibits vascular smooth muscle cell proliferation through blocking of ERK 1/2 and Akt cascade.

keyword : antiproliferation. ERK 1/2. Akt. NQ304. 1,4-naphthoquinone