Resveratrol inhibits angiotensin II-inducd endothelin-1 gene expression and subsequent proliferation in rat aortic smooth muscle cells

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摘要

Abstract

Resveratrol is a phytoestrogen naturally found in grapes and is the major constituent of wine thought to have a cardioprotective effect. The aims of this study were to examine whether resveratrol alters angiotenisn II-induced cell proliferation and endothelin-1 gene expression and to identify the putative underlying signaling pathways in rat aortic smooth muscle cells. Cultured rat aortic smooth muscle cells were preincubated with resveratrol then stimulated with angiotensin II, after which [3H]thymidine incorporation and endothelin-1 gene expression were examined. The intracellular mechanism of resveratrol in cellular proliferation and endothelin-1 gene expression was elucidated by examining the phosphorylation level of angiotensin II-induced extracellular signal-regulated kinase (ERK). The inhibitory effects of resveratrol (1-100 microM) on angiotensin II-induced DNA synthesis and endothelin-1 gene expression were demonstrated with Northern blot and promoter activity assays. Measurements of 2'7'-dichlorofluorescin diacetate, a redox-senstive fluorescent dye, showed a resveratrol-mediated inhibition of intracellular reactive oxygen species generated by the effects of angiotensin II. The inductive properties of angiotensin II and H2O2 on ERK phosphorylation and activator protein-1-mediated reporter activity were found reversed with resveratrol and antioxidants such as N-acetyl-cysteine. In summary, we speculate that resveratrol inhibits angiotensin II-induced cell proliferation and endothelin-1 gene expression, and does so in a manner which involves the disruption of the ERK pathway via attenuation of reactive oxygen species generation. Thus, this study provides important insight into the molecular pathways that may contribute to the proposed beneficial effects of resveratrol on the cardiovascular system