# Inhibition of cyclic strain-induced endothelin-1 gene expression by resveratrol

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摘要

## Abstract

Resveratrol is a phytoestrogen naturally found in grapes and is among the major constituents of wine thought to have a cardioprotective effect. Endothelin-1 (ET-1) is a potent vasopressor synthesized by endothelial cells both in culture and in vivo. The aims of this study were to test the hypothesis that resveratrol may alter strain-induced ET-1 gene expression and to identify the putative underlying signaling pathways in endothelial cells. We show that resveratrol indeed potently inhibits strain-induced ET-1 secretion, ET-1 mRNA level, and ET-1 promoter activity. Resveratrol also inhibits strain-increased NADPH oxidase activity, reactive oxygen species formation, and extracellular signal-regulated kinases1/2 (ERK1/2) phosphorylation. Furthermore, pretreating cells with resveratrol or antioxidant N-acetyl-cysteine decreases strain-increased or hydrogen peroxide-increased ET-1 secretion, ET-1 promoter activity, and ET-1 mRNA and ERK1/2 phosphorylation. Using both the electrophoretic mobility shift assay and a reporter gene assay, resveratrol and N-acetyl-cysteine also attenuated the strain-stimulated activator protein-1 binding activity and activator protein-1 reporter activity. In summary, we demonstrate for the first time that resveratrol inhibits strain-induced ET-1 gene expression, partially by interfering with the ERK1/2 pathway through attenuation of reactive oxygen species formation. Thus, this study provides important new insights in the molecular pathways that may contribute to the proposed beneficial effects of resveratrol in the cardiovascular system.