Mechanism of concentration-dependent induction of heme oxygenase-1 by resveratrol in human aortic smooth muscle cells

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Abstract

Resveratrol-mediated heme oxygenase-1 (HO-1) induction has been shown to occur in primary neuronal cultures and is thought to have potential neuroprotective action. Further, antioxidant properties of resveratrol have been reported to protect against coronary heart disease. We attempted to examine resveratrol's HO-1 inducing potency and its induction regulation in human aortic smooth muscle cells (HASMC). We showed that resveratrol-mediated HO-1 induction occurred in concentration- and time-dependent manners, but only at low concentrations (1-10 microM), and that it was modulated at both the transcription and translation levels. Additionally, the results of our study showed that nuclear factor-kappa B (NF-kappaB) inhibitors eliminated resveratrol-mediated HO-1 induction and promoter activity, and that deletion of NF-kappaB binding sites in the HO-1 promoter region strongly reduced promoter activity, suggesting involvement of the NF-kappaB pathway in HO-1 induction by resveratrol. Suppression of NF-kappaB activity by resveratrol at high concentrations (> or =20 microM) has been reported to be attributed to its anti-inflammatory and anti-oxidative properties. Likewise, we showed that resveratrol at concentrations of > or =20 microM blocked the activity of NF-kappaB through suppression of I kappa-B alpha (IkappaBalpha) phosphorylation, which caused inhibition of HO-1 induction. Conversely, resveratrol in a range of 1-10 microM enhanced the phosphorylation and degradation of IkappaBalpha, a key step in NF-kappaB activation, resulting in HO-1 induction. Collectively, we suggest that resveratrol-mediated HO-1 expression occurs, at least in part, through the NF-kappaB pathway, which might contribute to resveratrol's vascular-protective effect at physiological concentrations after moderate red wine consumption.