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Resveratrol Upregulates Heme Oxygenase-1 Expression via Activation of NF-E2-related Factor 2

Chu Yue Chen, Jung Hee Jang and Young Joon Surh
College of Pharmacy, Seoul National University, Seoul 151-742, South Korea

Resveratrol (3,4',5-trihydroxy-stilbene), a phytoalexin found in the skin and seeds of grapes, has been reported to possess antiinflammatory, anticarcinogenic and antioxidant activities. In this work, we assessed the ability of resveratrol to upregulate heme oxygenase-1 gene expression via activation of NF-E2-related Factor 2 (Nrf2). Nrf2 is a transcription factor involved in the protection against oxidative stress through antioxidant reponse element (ARE)-mediated transcriptional activation of several phase 2 detoxifying and antioxidant enzymes, such as heme oxygenase-1 (HO-1). Here, we report that resveratrol induces heme oxygenase-1 expression via the Nrf2 signaling. PC12 cells treated with resveratrol exhibited transient activation of AKT/protein kinase B and extracellular signal-regulated kinase1/2. Treated with pharmacological inhibitors of phosphoinositol-3 kinase (LY294002) and MEK1/2 (U0126) reduced reveratrol-induced HO-1 expression and antioxidant effects. In addition, resveratrol increased nuclear translocation and ARE-mediated transcriptional activity of Nrf2. The above findings, taken together, suggest that resveratrol augments cellular antioxidant defense capacity through induction of HO-1 via Nrf2, thereby protecting PC12 cells from oxidative stress.

Keyword : Resveratrol, Heme oxygenase-1, Nrf2, PC12 cells