O5 SULFORAPHANE-INDUCED HEME OXYGENASE-1 EXPRESSION IN PC12 CELLS IS INDEPENDENT OF NUCLEAR FACTOR E2-RELATED FACTOR 2-MEDIATED ANTIOXIDANT RESPONSE ELEMENT ACTIVATION

Prawan A[1], Jung-Hee Jang, Mei-Hua Li, Young-Joon Surh

National Research Laboratory of Molecular Carcinogenesis and Chemoprevention, College of Pharmacy, Seoul National University, Seoul 151-742, Korea.
[1]On leave from Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand.

Sulforaphane, an isothiocyanate ingredient of cruciferous vegetables including broccoli, has been shown to possess strong phase I enzyme-inhibitory and phase II enzyme-inducing properties. The purpose of this investigation was to examine the ability of sulforaphane to up-regulate heme oxygenase-1 (HO-1) gene expression and the involvement of transcription factor nuclear factor E2-related factor 2 (Nrf2) in induction of HO-1 in PC12 cells. Exposure of PC12 cells to sulforaphane led to the induction of HO-1 in a concentration- and time-dependent manner with maximum increase at 7.5 mM and 8 hours. To better understand the signaling events involved in the up-regulation of HO-1 by sulforaphane, ARE activity was assessed by the electrophoretic mobility shift assay (EMSA), and Nrf2 and HO-1 protein levels were detected after transient transfection of PC12 cells with a mutant form of Nrf2. Sulforaphane failed to increase ARE activity but could still induce HO-1 expression in both dominant-negative Nrf2- and control pEF vector-transfected cells. Taken together, our results indicate that up-regulation of HO-1 expression by sulforaphane treatment in PC12 cells is mediated by Nrf2/ARE independent mechanism and suggest the involvement of other transcription factors.