Runx2-mediated bcl-2 gene expression contributes to nitric oxide protection against hydrogen peroxide-induced osteoblast apoptosis

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Abstract

Nitric oxide (NO) can regulate osteoblast activities. This study was aimed to evaluate the protective effects of pretreatment with sodium nitroprusside (SNP) as a source of NO on hydrogen peroxide-induced osteoblast insults and its possible mechanisms. Exposure of human osteosarcoma MG63 cells to hydrogen peroxide significantly increased cellular oxidative stress, but decreased ALP activity and cell viability, inducing cell apoptosis. Pretreatment with 0.3 mM SNP significantly lowered hydrogen peroxide-induced cell insults. Treatment of human MG63 cells with hydrogen peroxide inhibited Bcl-2 mRNA and protein production, but pretreatment with 0.3 mM SNP significantly ameliorated such inhibition. Sequentially, hydrogen peroxide decreased the mitochondrial membrane potential, but increased the levels of cytochrome c and caspase-3 activity. Pretreatment with 0.3 mM SNP significantly lowered such alterations. Exposure to hydrogen peroxide decreased Runx2 mRNA and protein syntheses. However, pretreatment with 0.3 mM SNP significantly lowered the suppressive effects. Runx2 knockdown using RNA interference inhibited Bcl-2 mRNA production in human MG63 cells. Protection of pretreatment with 0.3 mM SNP against hydrogen peroxide-induced alterations in ALP activity, caspase-3 activity, apoptotic cells, and cell viability were also alleviated after administration of Runx2 small interference RNA. Thus, this study shows that pretreatment with 0.3 mM SNP can protect human MG63 cells from hydrogen peroxide-induced apoptotic insults possibly via Runx2-involved regulation of bcl-2 gene expression. J. Cell. Biochem. 108: 1084-1093, 2009. (c) 2009 Wiley-Liss, Inc.