Identification of Nucleophosmin as an NF-κB Co-activator for the Induction of the Human SOD2 Gene

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Abstract

Manganese superoxide dismutase (MnSOD) is an antioxidant enzyme essential for the survival of life. We have reported that NF-κB is essential but not sufficient for the synergistic induction of MnSOD by phorbol 12-myristate 13-acetate and cytokines. To further identify transcription factors and co-activators that participate in the induction of MnSOD, we used NF-κB affinity chromatography to isolate potential NF-κB interacting proteins. Proteins eluted from the NF-κB affinity column were subjected to proteomic analysis and verified by Western analysis. Nucleophosmin (NPM), a nucleolar phosphoprotein, is the most abundant single protein identified. Co-immunoprecipitation studies suggest a physical interaction between NPM and NF-κB proteins. To verify the role of NPM on MnSOD gene transcription, cells were transfected with constructs expressing NPM in sense or antisense orientation as well as interference RNA. The results indicate that an increase in NPM expression leads to increased MnSOD gene transcription in a dose-dependent manner. Consistent with this, expression of small interfering RNA for NPM leads to inhibition of MnSOD gene transcription but does not have any effect on the expression of interleukin-8, suggesting that the effect of NPM is selective. These results identify NPM as a partner of the NF-κB transcription complex in the induction of MnSOD by phorbol 12-myristate 13-acetate and cytokines.

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