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Nkx2.5 regulates Nsd1 in response to oxidative stress in cardiac muscle cells

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Nuclear receptor-binding SET domain-containing protein 1 (Nsd1) is a histone lysine methyltransferase, and the effect of NSD1 in response to oxidative stress in cardiac muscle cells remains poorly understood. Current study demonstrated that the protein and mRNA levels of NSD1 was reduced by H₂O₂ in H₉C₂ cells. We analyzed the promoter of NSD1 gene, predicted an NK2 transcription factor related locus 5 (Nkx2.5) binding element (NKE) at position -412/-406 in the NSD1 promoter, and confirmed it by an electrophoresis mobility shift assay and a chromatin immunoprecipitation assay. Luciferase activity analysis indicated H₂O₂ decreased the p646-luc promoter activity, and Nkx2.5-specific siRNA weakened H₂O₂ inhibition on the p646-luc promoter. However, H₂O₂ did not affected mutant NKE promoter p646-luc-mut compared with wild p646-luc promoter. Furthermore, overexpression and depletion of Nkx2.5 led to the increase and decrease of NSD1 protein and mRNA levels in H₉C₂ cells. In addition, Nkx2.5 was downregulated by H₂O₂. Therefore we hypothesized that oxidative stress reduced NSD1 expression through suppression of Nkx2.5, and we going to focus on the alteration of histone methylation of NSD in response oxidative stress in future study.

Biography

Yanyan Zhao is director of Department of Clinical Genetics in Shengjing Hospital of China Medical University. She was completed MD in 1984 and PhD in 1996 at China Medical University. She did postdoctoral studies in Department of Cell Biology of State University of New York. Over the past decades she has focused on molecular genetics of cardiovascular disease and prenatal diagnosis of Genetic diseased, and published more than 50 papers.

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