Effect of cadmium on structure and enzymatic activity of Cu, Zn-SOD and oxidative status in neural cells

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摘要.

Abstract

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disorder disease. Ten percent of the ALS patients are congenital (familial ALS), and the other 90% are sporadic ALS (SALS). It has been shown that mutations found in the Cu,Zn-SOD cause 20% of the familial ALS due to its low enzyme activity. We hypothesized that heavy metals may interfere the structure of Cu,Zn-SOD protein to suppress its activity in some of the SALS. In this study, we expressed and characterized the recombinant human Cu,Zn-SOD under various concentrations of Cu(2+), Zn(2+), and Cd(2+). By atomic absorption spectrophotometry, we demonstrated that adding of cadmium significantly increased the content of cadmium ion, but reduced its Zn(2+) content and enzyme activity of the Cu,Zn-SOD protein. The data of circular dichroism spectra demonstrated that the secondary structure of Cu,Zn-SOD/Cd is different from Cu,Zn-SOD, but close to apo-SOD. In addition to the effect of cadmium on Cu,Zn-SOD, cadmium was also shown to induce neural cell apoptosis. To further investigate the mechanism of neural cell apoptosis induced by cadmium, we used proteomics to analyze the altered protein expressions in neural cells treated with cadmium. The altered proteins include cellular structural proteins, stress-related and chaperone proteins, proteins involved in reactive oxygen species (ROS), enzyme proteins, and proteins that mediated cell death and survival signaling. Taken together, in this paper, we demonstrate that cadmium decreases the content of Zn(2+), changes the conformation of Cu,Zn-SOD protein to decrease its enzyme activity, and causes oxidative stress-induced neural cell apoptosis. (c) 2006 Wiley-Liss, Inc.