

The Physiological Significance of Metallothionein in Oxidative Stress

Kyong-Son Min (Faculty of Nutrition, Kobe Gakuin University)

Metallothionein (MT), a ubiquitous family of low molecular weight metal-binding proteins, is comprised of 30% cysteine residues. Although all of the thiol residues in MT are bound to metals, it still remains reactive to reactive oxygen species. Each cysteine residue in MT is effective more at protecting DNA from hydroxyl radical attack than the glutathione cysteine *in vitro*. Prooxidative agents, such as paraquat and carbon tetrachloride, induce MT synthesis mediated by some responsive elements. MT demonstrates strong antioxidant properties, yet the physiological relevance of its antioxidant action is not clear. An injection of ferric nitrilotriacetate (Fe-NTA), which produces reactive oxygen species, caused transcriptional induction of MT synthesis in the liver and kidney. Pretreatment of mice with Zn attenuated nephrotoxicity induced by Fe-NTA. After a Fe-NTA injection, a loss of Cd-binding properties of preinduced MT was observed only in kidneys of Zn-pretreated mice but not in liver. MT-enriched hepatocytes are resistant to Fe-NTA toxicity, cell survival and oxidative DNA damage, during conditions of glutathione depletion. In glutathione-depleted cells, but not in non-treated cells, Cd-binding properties of cellular MT decreased with increasing concentration of Fe-NTA. Moreover, Cd released from MT after an injection of Fe-NTA induced new MT protein again. Thus, MT may act as a secondary antioxidant in cellular protection system against oxidative stress.