

# Loss of the metal binding properties of metallothionein induced by hydrogen peroxide and free radicals

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The relationship between the metal-binding properties of metallothionein (MT) and its ability to interact with peroxides and free radicals was explored in vitro. The binding of  $^{109}\text{Cd}$  to MT and the thiol density of the protein were determined after incubation of a purified Zn/Cd-metallothionein preparation with either hydrogen peroxide alone, or with a number of free radical generating systems. Exposure of MT to  $\text{H}_2\text{O}_2$ , whether in the presence or absence of  $\text{Fe}^{2+}$ , resulted in the progressive loss of the thiol residues of the protein and led to a parallel decrease of its  $^{109}\text{Cd}$ -binding capacity. These changes correlated with  $r$  values of 0.999 ( $P = 0.001$ ) and 0.998 ( $P = 0.001$ ), in the absence and presence of iron, respectively. The effects of  $\text{H}_2\text{O}_2$ , alone or plus  $\text{Fe}^{2+}$ , on MT were completely prevented by catalase, but totally unaffected by superoxide dismutase or desferrioxamine. Exposure of MT to xanthine/xanthine oxidase also led to thiol oxidation and to a concomitant loss of the Cd-binding