

SELENOPROTEIN FUNCTIONS IN HEALTH AND DISEASE

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Selenium has long been known for its antioxidant properties, and the beneficial effects of this trace element in our diet are generally attributed to selenoenzymes. The known functions of selenoenzymes include protecting cell membranes, proteins and nucleic acids from cumulative oxidative damage. These functions are carried out by the glutathione peroxidases, enzymes that break down hydroperoxides, and by other recently identified selenoproteins. Selenoenzymes function in preserving mammalian sperm integrity and in thyroid hormone homeostasis, highlighting essential roles for the trace element in development and metabolism. Selenium has been implicated in mitigating mercury toxicity in marine mammals and in laboratory animal studies, and this role is under investigation in humans. Selenium deficiency has been linked to the pathogenesis of diabetes, cardiovascular disease, neurodegenerative diseases and other diseases in which cumulative oxidative damage is implicated. We are investigating the potential roles of selenoproteins in the pathology of Alzheimer's and Parkinson's diseases, using postmortem human tissues and CSF. Ongoing studies in the laboratory are also investigating the protective role of selenium and selenoproteins in protecting against methamphetamine-induced damage. Selenoprotein biosynthesis undergoes differential tissue-specific regulation, particularly under conditions of limiting selenium. We are investigating the pathways involved in selenium metabolism. Aspects of these varied studies will be discussed.