

Biological Implications of Heme Metabolism

Shigeru Sassa (The Rockefeller University, New York, N.Y., USA)

Protein-unbound free heme is toxic to cells as it is a potent pro-oxidant. To cope with this problem, the body is equipped with various defense mechanisms. One of which is heme oxygenase (HO) that oxidatively cleaves heme. There are two isozymes of HO, i.e., HO-1 and HO-2. HO-1 is the key molecule in the degradation of free heme and shows marked induction in response to oxidative stress such as acute inflammation. In contrast, HO-2 is not inducible, but functions as an oxygen sensor. Biliverdin IX α and CO, the two reaction products of heme by HO, have also been shown to be important in the protective response in oxidative tissue injury, indicating that these heme metabolites have their own biological functions. Thus HO-1 induction, i.e., increased heme metabolism, is a signature of oxidative tissue injury and plays a critical role in the defense against oxidative stress. Recent evidence also suggests that there may be an oscillatory control of gene expression in oxidative stress as well as in heme biosynthesis. Thus, in addition to its toxic property, free heme may also function as a regulatory molecule for gene expression in pro- and anti-oxidative responses. Controlling free heme levels in the cell may be a useful strategy in new drug discovery for the protection of tissue injury from oxidative stress.