Heme oxygenase: function, multiplicity, regulatory mechanisms, and clinical applications

Maines MD

Author information

1Department of Biophysics, University of Rochester School of Medicine, New York 14642

Abstract

In biological systems oxidation of heme is carried out by two isozymes of the microsomal heme oxygenase, HO-1 and HO-2. HO-1 is the commonly known heme oxygenase, the activity of which can be induced by up to 100-fold in response to a wide variety of stimuli (metals, heme, hormones, etc.). HO-2 was only recently discovered, and the isozyme appears to be uninducible. The two forms are products of two different genes and differ in their tissue expression. The primary structure of HO-1 and an HO-2 fragment of 91 amino acid residues show only 58% homology, but share a region with 100% secondary structure homology. This region is believed to be the catalytic site. Most likely, HO-1 gene is regulated in the same manner as metallothione in the gene. HO-1 has a heat shock regulatory element, and possibly many promoter elements, which bind to respective inducers and cause transcription of the gene. In vivo induction of HO-1 activity in the liver is accompanied by decreases in the total P-450 levels and, in a reconstituted system, cytochrome P-450b heme can be quantitatively converted to biliverdin by HO-1 and HO-2. The enzyme activity is inhibited in vivo for extended periods subsequent to binding of Zn- and Sn-protoporphyrins. This property appears useful for the suppression of bilirubin production. The metalloporphyrins, however, are not innocuous and cause major disruptions in cellular metabolism. In this review recent findings on heme oxygenase are highlighted.