V-B Bioinorganic Chemistry and Structural Biology of Heme Proteins

One of research activities of my group is directed toward developing a rigorous, quantitative understanding of the biochemical function of heme proteins such as oxygenases, peroxidases and oxidases by characterization of their structural and functional properties. We use different experimental strategies including protein engineering, spectroscopic characterization of the molecular structure of the active centers, measurements of dynamics of substrates and inhibitor binding, and X-ray crystallography.

My current heme protein projects include (1) elucidation of the catalytic mechanism of heme oxygenase, one of the essential components of the heme catabolism and biosynthesis of carbon monoxide, a versatile physiological messenger molecule, (2) elucidation of the mechanism of controlling reactivity of hemoglobin and myoglobin, and (3) determination of heme sensing mechanism of Bach1, a heme-dependent transcription factor which regulates heme oxygenase gene expression. Effective clues to delineate the detailed active site structure have been obtained by X-ray crystallography, resonance Raman and magnetic resonance studies. The synergy of site-directed mutagenesis, structural biology, and spectroscopic techniques has revealed the specific roles of amino acids located in the active centers of heme proteins. Ligands and substrates binding measurements complement the structural data for our understanding functional properties displayed by heme proteins at the molecular level.

V-B-1 Compound I of Heme Oxygenase Can Not Hydroxylate Its Heme meso-Carbon

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Heme oxygenase (HO) catalyzes heme catabolism through three successive oxygenation where the substrate heme itself activates O2. It has been thought that the reactive species responsible for the first heme oxygenation, meso-hydroxylation, is the hydroperoxy-ferric heme intermediate (Fe–OOH) rather than an oxo ferryl porphyrin cation radical, so called compound I. A recent theoretical study (Kamachi et al., J. Am. Chem. Soc. 127, 10686 (2005)), however, proposed that compound I can oxidize its meso-carbon atom with the assistance of a bridging water molecule. In this communication, we have reported the first direct observation of compound I of a heme–HO-1 complex, generated by reaction of ferric–HO-1 with m-chloroperbenzoic acid. HO compound I slowly decays to compound II without producing any meso-hydroxylated products. It does react with guaiacol and thioanisole, however. Our findings unambiguously rule out involvement of compound I in the HO catalysis.