Metalloproteins Responsible for Signal Transduction in Biological System

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A variety of gas molecules serve as substrates and/or reaction products in many enzymatic reactions including oxygen respiration, denitrification, nitrogen fixation and methanogenesis. Recently, a novel physiological function of gas molecules as signaling molecules has been elucidated and studied extensively. In these systems, the corresponding receptor (sensor) proteins are required for these gas molecules to act in this way. All of the gas sensor proteins so far reported have a metal-containing prosthetic group at the sensor active site. Specific interactions between protein and a gas molecule, for which the metal-containing prosthetic group is used, are required for the gas sensor protein to detect its physiological effector gas. Heme groups have been widely found at the active sites of the O_2, NO, and CO gas sensor proteins. This is not surprising as heme can bind O_2, NO, and CO reversibly.

In this lecture, I will discuss the structure and function relationships of an oxygen sensor protein (HemAT-Bs) and a CO-sensor protein (CooA). HemAT-Bs is a signal transducer protein responsible for aerotaxis of *B. subtilis*. The recombinant HemAT-Bs shows similar spectroscopic properties to myoglobin. However, HemAT-Bs shows a unique resonance Raman spectrum in the O_2-bound form suggesting a unique hydrogen bonding network between the heme-bound oxygen and distal amino acid residues in the distal heme pocket. Thr95 is involved in the hydrogen bonding to the heme-bound oxygen. I will discuss the mechanisms of the selective sensing of O_2 and signal transduction by HemAT-Bs.

CooA is a CO sensing transcriptional activator, which contains a b-type heme as the active site for sensing its physiological effector, CO. We are studying about the structure-function relationships of CooA from *Rhodospirillum rubrum* (Rr-CooA) and CooA from *Carboxydothermus hydrogenoformans* (Ch-CooA) by spectroscopic and mutagenesis studies. Comparing the properties of Ch-CooA and Rr-CooA provides that the essential elements for CooA function will be that (i) the heme is six-coordinate in the Fe(III), Fe(II), and Fe(II)-CO forms; (ii) the N-terminus is coordinated to the heme as an axial ligand; and (iii) CO replaces the N-terminus bound to the heme upon CO binding.

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[2]. S. Aono, Acc. Chem. Res. **36**, 825 (2003).