Investigation of the Structure/Function Relationships in Nickel-Containing Superoxide Dismutase

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Nickel superoxide dismutase (NiSOD) is the newest member of a group of enzymes (superoxide dismutases, SODs) that are responsible for the protection of cells from superoxide.[1,2] SODs catalyze a reaction where two equivalents of superoxide are converted to oxygen and hydrogen peroxide. The metal acts as an electron acceptor/donor in the redox reaction, which has an optimum potential of +270eV.[3] Unlike other metals used in SODs (Fe, Mn and Cu), Ni(II) ion does not catalyze this reaction because it does not have appropriate redox potential. As with other redox-active nickel enzymes, sulfur ligation provides a means for producing activity in a biologically relevant potential range. Since NiSOD shows no sequence homology to other SODs, site-directed mutagenesis was used to determine the specific residues in the protein responsible for the catalytic properties of the enzyme. These include the three enzyme residues directly coordinated to the metal (His1, Cys2, and Cys6) and two conserved tyrosine residues (Tyr9 and Tyr62). Although these tyrosine residues are not directly coordinated to the metal, they may act as a proton source, structural stabilizer, or as an outer sphere redox site. The metal specificity of the enzyme has also been studied by substituting the Ni with other metals, including Co and Cu. Neither of these metal-substituted SODs is active, indicating that the protein site is specific for tuning the redox properties of nickel.

The mutant and metal-substituted NiSODs were characterized by a number of techniques aimed at addressing structure/function relationships. The structure and kinetic capabilities of the enzymes were investigated using XAS, EPR, and pulse radiolysis. The results of these studies will be discussed.

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