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Binding of the Substrate Analog Azide to the Active Site of Human Manganese Superoxide Dismutase. J.F. Domsic[§], P.S. Quint[¶], L. Govindasamy[§], C.K. Tu[¶], D.N. Silverman[¶], R. McKenna[§], [§]Dept. of Biochemistry and Molecular Biology, [¶]Dept. of Pharmacology and Therapeutics, College of Medicine, Univ. of Florida, Gainesville, FL, 32610.

Human Manganese superoxide dismutase (MnSOD) is a mitochondrial enzyme that scavenges superoxide radicals from its environment. MnSOD catalyzes the disproportionation of superoxide, leading to the formation of oxygen and hydrogen peroxide. However, during the oxidation of the manganese ligand, a product inhibited form occurs, consisting of a side-on or end-on peroxy complex. In order to better understand how this inhibition occurs, we used crystallographic and spectrophotometric analyses to observe the binding of the substrate analog azide in the active site pocket. The crystal structure of MnSOD bound with azide was solved to 2.3 Å resolution with an R_{cryst} of 0.201. Azide is positioned such that one end interacts with the hydroxyl group on the side chain of Tyr34 while the other coordinates with the Mn ligand. This orientation corroborates well with the previously solved structure of azide bound to MnSOD from *Thermus thermophilus*. It is also further supported by UV/Vis spectrophotometry, which revealed that azide binding was greatly inhibited by the presence of 3-fluorotyrosine substituted at position 34.