Manganese Superoxide Dismutases and Substrate Mimic Derivatives

Simon H. Oakley[a], James R. Salvador[a], Bryan F. Anderson[a], Dianne Cabelli[b], Mei M. Whittaker[c], James W. Whittaker[c], Geoffrey B. Jameson[a], [a]*Centre for Structural Biology, Massey University, Palmerston North, New Zealand.* [b]*Brookhaven National Laboratory.* [c]*OGI School of Science & Engineering, Oregon Health & Science University.* E-mail: S.H.Oakley@massey.ac.nz

Superoxide dismutases (SODs) are enzymes that catalyse the elimination of the oxygen-derived free radical superoxide, making an aerobic existence more viable. Our research interest is in manganese SODs from *Escherichia coli* [1,2] and *Deinococcus radiodurans,* an extremophile, which can tolerate very high radiation exposure and dessication. Presented here are four new structures: the *E. coli* iron-substituted MnSOD with bound azide (a substrate mimic/inhibitor) to 2.2-Å resolution, the *E. coli* Y174F-MnSOD complexed with azide to 1.5 Å (the first ordered Mn^{II}/Mn^{III} structure), the wild-type form of MnSOD from *D. radiodurans* to 2.0 Å, and *D. radiodurans* MnSOD with bound azide to 2.0 Å.

The binding of azide to wild-type, mutant and wrong-metal MnSODs is associated with a change in coordination of the metal centre. Azide binding also leads to major changes of the water structure of the solvent-access funnel, especially near the conserved Tyr34 (*E. coli* numbering). Azide is observed to bind quite differently to that previously reported for an MnSOD [3], and adopts an orientation very similar to that reported for wild-type FeSODs [3].

[1] Edwards R. A., et al., *J. Biol. Inorg. Chem.*, 1998, **3(2)**, 161-171. [2] Edwards et al., *J. Am. Chem. Soc.*, 1998, **120(37)**, 9684-9685. [3] Lah et al., *Biochemistry*, 1995, **34(5)**, 1646-60.

Keywords: metalloenzymes, superoxide dismutases, azide