X-ray crystallographic structural studies of the metallochaperone-like N-terminal domain (NmerA) of the mercuric ion reductase MerA

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Heavy metals such as Hg have no known biological function and are toxic to all living organisms. However, microbes have evolved naturally to deal with heavy metal toxicity resulting in elaborate heavy metal resistance mechanisms. Select bacteria possess a set of genes (the *mer* operon) that allows cells to resist poisoning in Hg-exposed ecosystems. The *mer* operon encodes specific genes that facilitate transport of Hg species, cleavage of organomercurials and reduction of ionic Hg(II) to volatile, elemental Hg(0). The mercuric ion reductase MerA is a key enzyme encoded by the *mer* operon. MerA is an NADPH-dependent flavin-disulfide oxidoreductase that catalyzes the reduction of Hg(II) to Hg(0). Many MerA proteins possess tethered metallochaperone-like N-terminal domains (NmerA) that can transfer Hg(II) to the homodimeric catalytic core domain for reduction to Hg(0). Recent studies in our lab combining SAXS and SANS with molecular dynamics simulations have characterized the conformational distribution of MerA prior to Hg(II) acquisition and defined the orientation of NmerA with respect to the catalytic core of MerA during intramolecular Hg(II) transfer. We have crystallized the reduced, metal free form of *Tn*501 NmerA and obtained X-ray diffraction data to a resolution of 3.25 Å. Molecular replacement methods are currently being used to determine the first crystal structure of NmerA. The structure of NmerA will then be used for protein-protein docking and computational simulations to further examine the molecular interactions and mechanisms of Hg(II) exchange involving the MerA core domain.