Biomolecular mechanisms of microbial mercury resistance in the environment

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Microbes have naturally evolved to deal with heavy metal toxicity resulting in elaborate heavy metal resistance mechanisms. Bacterial mercury resistance is mediated by the \textit{mer} operon. It encodes specific genes that facilitate removal of toxic mercury species from the cell. Here, we apply experimental biophysics and high performance computer simulation to investigate molecular mechanisms of bacterial resistance to mercury.

Expression of \textit{mer} genes is mediated by MerR, a metal-responsive transcriptional regulator. \textit{In vitro} studies have shown that MerR forms a non-transcribing pre-initiation complex with RNA polymerase and the promoter DNA. We have used small-angle X-ray scattering (SAXS) and molecular dynamics (MD) simulations to describe changes in the conformation of MerR in response to Hg(II). Our results show that Hg(II) triggers a reconfiguration of the MerR dimer, from a compact state to a conformation revealing two distinct domains. Such a dramatic change in the MerR structure may be the driving force behind a reorientation of DNA recognition sites and ultimately result in initiation of transcription. MD also revealed large amplitude motions in the two DNA-binding domains on a nanosecond timescale.

Reduction of Hg(II) to Hg(0) is catalyzed by mercuric reductase, MerA. All MerA proteins have a homodimERIC catalytic core and many have an N-terminal metallochaperone-like domain, NmerA, which acquires Hg(II) and transfers it to an active site in the core homodimer for reduction. We have applied SAXS and MD simulations to explore the structure and dynamics of full length MerA and the docking site of NmerA with core. Our data show that the two N-terminal domains in dimeric MerA sample a large number of conformations and that the transfer of Hg(II) between NmerA and the catalytic core is mediated by transient docking of NmerA to the catalytic core near the protomer interface.