Neutron scattering reveals conformations of the transcriptional regulator MerR in complex with its operator DNA

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Bacterial resistance to heavy metals is controlled by metal-responsive transcriptional regulators. For example, bacterial resistance to inorganic and organic mercury compounds is conferred by the *mer* operon, which is typically located on transposons or plasmids [1,2]. These proteins are involved in Hg(II) import, proteolysis of organomercurials and Hg(II) reduction to Hg(0). Expression of the *mer* operon genes is controlled by the transcriptional repressor-activator MerR.

How Hg(II) binding affects the changes in the conformation of MerR, which in turn propagate through DNA contacts to its operator DNA (MerOP) is unknown. In this study we investigate Hg(II)–induced conformational changes of MerOP in complex with its regulator MerR to reveal the transcription control mechanism conferred by MerR. Experimentally, we purified MerR and prepared a complex with a 23bp MerOP dsDNA construct. In vivo, MerR tightly binds to MerOP in a region of dyad symmetry between the -10 and -35 RNA polymerase recognition sites. In the absence of Hg(II), RNA polymerase binds to its promoter and forms a stable pre-initiation complex with dimeric MerR acting as a repressor preventing RNA polymerase from accessing the -10 recognition site. In the experiments, we examined the MerR-MerOP complex in the presence and absence of Hg(II) using small-angle neutron scattering (SANS) (Fig. 1). A contrast variation series allowed us to detect changes in the conformation of MerR and MerOP, respectively. Homology modeling and molecular dynamics simulations were used to generate atomic resolution models to interpret the data. The results provide insights on the allosteric change in MerR triggered by Hg(II), which causes a reorientation of the -10 recognition site and ultimately initiation of transcription by RNA polymerase [3].

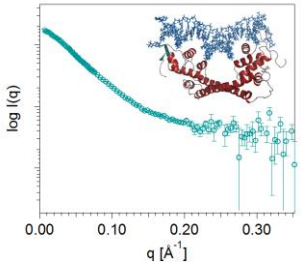

Figure 1: Small angle neutron scattering intensities I(q) vs momentum transfer (q) in 100% D_2O buffer and a model of the MerR-MerOP complex.

[1] Barkay et al. (2003) *FEMS Microbiol Rev* **27**, 385-384.
[2] Summers et al. (1986) *Annu Rev Microbiol* **40**, 607-634.
[3] Ansari et al. (1995) *Nature* **374**, 371-375.