ArsD: A novel metallochaperone for an arsenic detoxification pump

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Arsenic is a metalloid toxicant that is widely distributed throughout the earth's crust and causes a variety of health and environment problems. As an adaptation to arsenic-contaminated environments, organisms have developed resistance systems. *E. coli* plasmid R773 carries the well-studied *arsRDABC* operon. ArsA is an ATPase that is the catalytic subunit of the ArsAB As(III) extrusion pump. ArsD was shown to have weak repressor activity, but this may not be its physiological function. Most *ars* operons contain only three genes, *arsRBC*. Five gene operons have two additional genes, *arsD* and *arsA*, and these are usually adjacent to each other. Obviously *arsD* and *arsA* co-evolved suggesting a related function for the two gene products.

Recently metallochaperones have been identified for a number of metals. Metallochaperones prevent inappropriate metal interactions with other cellular components. Thus, these ubiquitous proteins have a critical biological function: to deliver metals in the cytoplasm to the site of utilization or export. In this study, we report that ArsD is an arsenic chaperone that transfers trivalent metalloids to the ArsA ATPase. Through protein-protein interactions, ArsD increases the affinity of the ATPase for As(III) and results in increased efflux and resistance. We also determined that the interaction domain on ArsD is in the N-terminus and involves the conserved cysteine residues Cys12, Cys13 and Cys18. This is the first report of an arsenic chaperone and suggests that cells can regulate the intracellular concentration of free arsenite to prevent toxicity. Supported by NIH grant AI45428.