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A possible mechanism for metal-ion induced DNA–protein dissociation in a family of prokaryotic transcriptional regulators

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The Synechococcus PCC 7942 protein smtB (1) is a transcriptional repressor of the smtA gene which codes for a metallothionein. It has been shown that smtB binds to a region immediately upstream of the smtA gene and that the complex between smtB and DNA is dissociated in presence of zinc ions. SmtB is a protein of 122 residues which is highly similar to the arsR and cadC proteins. ArsR from plasmids R773 (2), pSX267 (3) and p1258 (4) acts as a transcriptional repressor of an arsenic-resistance operon (ars) which, in R773, includes the gene arsA coding for an ATPase which catalyses the extrusion of the metal-oxyanions arsenite, antimonite and arsenate. The action of arsR is alleviated by exposure to these metal oxyanions (5). CadC from plasmid p1258 (6) and from Bacillus firmus OF4 (7) is a protein required for full cadmium resistance in addition to the cadA gene which encodes for an ATPase responsible for cadmium extrusion.

It has been shown that a region in the middle part of these proteins (Figure 1) fulfils the requirements (8) for a DNA-binding helix–turn–helix (H–T–H) region. An interesting feature of this putative H–T–H region is that it contains at its N-terminal extremity one perfectly conserved cysteine residue and another one which is found in arsR and cadC but not in smtA and at its C-terminal extremity at least one and generally two histidine residues. Cysteine and histidine are not generally conserved in the H–T–H region of other characterized families of bacterial regulatory proteins (9) but are ubiquitous as metal-binding ligands.

We therefore believe that the above-mentioned residues could be involved in metal-binding (zinc in smtB, metal-oxyanions for arsR, and cadmium for cadC). Binding of a metal ion could induce a conformational change which would prohibit the protein from binding to DNA. Such a mechanism is highly suitable for regulatory systems that act to regulate the transcription of proteins involved in metal-ions efflux and/or detoxification.

REFERENCES

Figure 1. Alignment of the six proteins in the region of the putative H–T–H DNA-binding motif. The cysteines and histidines that could participate in metal-binding and disrupt DNA-binding are shown in upper case.