Why do bacterial metallothioneins contain histidine ?

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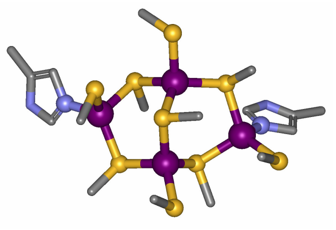
Metallothioneins are small proteins ubiquitous in eukaryotes including plants and fungi. Recent work has revealed that they are also widespread in certain bacteria.[1] Since their first discovery,[2] we have identified sequences of bacterial metallothioneins in the genomes of numerous cyanobacteria, pseudomonads, and some other bacteria including Staphylococcus. SmtA from *Synechococcus PCC7942* is the prototype for bacterial metallothioneins and exemplifies the unusual properties of these proteins. Contrary to mammalian MTs, bacterial BmtA's coordinate zinc not only via cysteines, but also histidine residues. Moreover, BmtA's adopt a well-defined zinc finger-fold, whereas no substantial secondary structure is found in any other MTs. The unusual structure of SmtA has a range of intriguing consequences. One of the four zinc ions in the cluster is inert towards metal exchange reactions. Moreover, metal depletion of SmtA does not lead to the immediate collapse of well-defined protein structure; instead, a structured intermediate is formed.



We have generated His-to-Cys mutants to investigate the contribution of the two coordinating His residues towards the unusual behaviour of SmtA, in an effort to elucidate the determinants of the metal dynamics of zinc clusters.

Our results demonstrate that the His residues are required to maintain a stable protein fold, the inertness of the "special" site, and that the thermodynamically most stable cluster is formed by the wild-type protein.

We thank the EC, the Wellcome Trust, HEC of Pakistan (fellowship to MTR), and the Royal Society for their support of this work.

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