

Histidine-rich metallothioneins - the next chapter for bacterial MTs

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Metallothioneins (MTs) are ubiquitous metalloproteins characterized by a high amount of cysteine residues, a low molecular weight and the formation of unique metal clusters. As a consequence of their metal binding abilities and abundance of Cys residues, they are important partakers in various physiological processes (e.g. metal homeostasis, metal detoxification, oxidative stress). While all MTs share these properties, across the different kingdoms of life a high diversity in amino acid sequences, 3D structures and functionalities have evolved. Although bacterial MTs (bacMTs) have resided for a long time in the shadows of their mammalian counterparts, they have several unique features that break with many MT paradigms, i.e. the contribution of histidine residues to metal ion binding, a higher percentage of secondary structure elements, as well as the presence of aromatic amino acids.¹

The presence of MTs in *Pseudomonas* species has become more apparent after sequencing of numerous bacterial strains in the last decade. These MT sequences reveal unusually high amounts of histidine residues and a high diversity in the primary structure. At the same time, they show a rather conserved Cys distribution pattern consisting of an N-terminal CxCxxCxC motif, a central YCC/SxxCA stretch, as well as a C-terminal Cxxxx(x)CxC part.

We are investigating, how differences found in the primary structure of these novel bacterial MTs influence function and 3D structure, including protein fold and the metal clusters.

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[1] Claudia A. Blindauer, Mark D. Harrison, John A. Parkinson, Andrea K. Robinson, Jennifer S. Cavet, Nigel J. Robinson, and Peter J. Sadler, Proceedings of the National Academy of Sciences of the United States of America, **2001**, 98, 9593-9598.