Crystallographic determination of Cys ligands upon metal binding in metalloproteins

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Understanding levels of ligand organization upon metal complexation is essential for evaluating molecular recognition in biology. While native protein structures containing a Cys-rich core are usually unavailable in both non- and metallated forms, a series of three-stranded coiled coil peptides are designed to chelate metals in geometries that were proposed in bacterial metalloregulatory sites. Protein X-ray crystallographic evidence has confirmed that the preferred coordination determines the degree of Cys reorientation toward metal binding. The apo-environment where the Cys rotamers direct toward the helical core is found to be preorganized for trigonal pyramidal species (PbS\textsubscript{3} and AsS\textsubscript{3}) in an endo form in which the metal is oriented toward the C-termini of the structure; however, significant thiol rotation is required for trigonal planar (HgS\textsubscript{3}) and pseudo-tetrahedral (ZnS\textsubscript{3}O) complexations. This study helps unravel the unappreciated features on defining metal behaviors, metal selectivity and metal-protein relationships in biological system. The knowledge could allow for broader applications of future metallprotein designs to generate novel bio-architectures for biophysical and industrial advantages; i.e. developing de novo peptide biosensors, that can selectively bind a specific ion, applicable for detoxifying heavy metals from industrial waste.


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