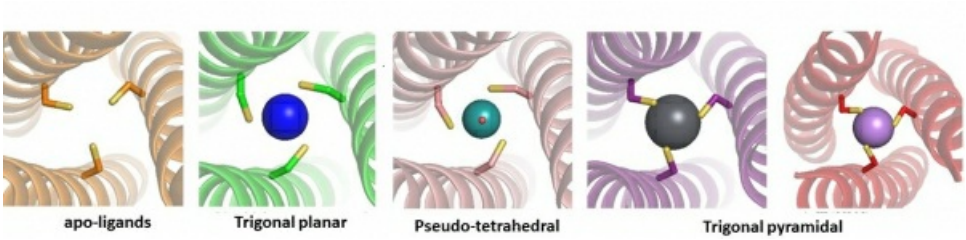
Poster Presentation

MS001.P04

Crystallographic determination of Cys ligands upon metal binding in metalloproteins

Leela Ruckthong[1], Melissa Zastrow[2], Jeanne Stuckey[3], Vincent Pecoraro[2]
[1]*Department Of Chemistry, King Mongkut's University Of Technology Thonburi, Bangkok, Thailand,* [2]*Chemistry, University of Michigan, Ann Arbor, United States,* [3]*Life Sciences Institute, University of Michigan, Ann Arbor, United States*
E-mail: leelar@umich.edu

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 (PbS3 and AsS3) 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 (HgS3) and pseudo-tetrahedral (ZnS3O) 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.
Ruckthong, L. et al. (2016). J. Am. Chem. Soc. 138, 11979–11988.



Keywords: metalloprotein structures, protein engineering, coiled coil structures