Studies of the Conformational Changes of Metal Coordination Environments in Three-Stranded Coiled Coils

Kyung-Hoon Lee[1], Lars Olsen[2], Lars Hemmingsen[3], and Vincent L. Pecoraro[1]

[1]Department of Chemistry, University of Michigan, [2]Department of Medicinal Chemistry, The Danish University of Pharmaceutical Sciences and [3]Department of Mathematics and Physics, Royal Veterinary and Agricultural University

Modification of the packing of hydrophobic layers in a designed TRI peptide system allows for the control of metal coordination number and geometry. Substitution of a leucine for a cysteine at position 16 (TRI L16C) generates a thiolate for metal binding. The sequence of the peptide, TRI L16C, is Ac-G $(LKALEEK)_2$ **C**KALEEK LKALEEK G-NH_2. Further substitution of the smaller alanine for leucine allows for an alteration of the packing of the leucine residues in layers above (TRI L12A/L16C) or below (TRI L16C/L19A) the metal binding site. (TRI L9A/L16C) and (TRI L16C/L23A) were also prepared to study longer range effects of substitution at a hydrophobic layer. The corresponding Cd(II) resonances of the mono-alanine substitutions of TRI L16C were 583 ppm in (TRI L9A/L16C), 574 ppm in (TRI L12A/L16C), 605 ppm in (TRI L16C/L19A), and 643 ppm in (TRI L16C/L23A), indicating changes of coordination environment of the metal by the alanine substitution at different hydrophobic positions of the (TRI L16C). Due to the absence of crystallographic information of (TRI L16C) derivatives, PAC (Perturbed Angular Correlation) spectroscopy and DFT (Density Functional Theory) calculations were employed to figure out the coordination number and geometry of the metal site. According to the PAC measurements, (TRI L9A/L16C) and (TRI L12A/L16C) Cd complexes exhibited one distorted tetrahedral structure and (TRI L16C/L19A) Cd complex showed one distorted trigonal planar structure with an apical water molecule. (TRI L16C/L23A) Cd complex showed two geometries, 60% of distorted trigonal planar and 40% of distorted tetrahedral structure. The Cd(II) chemical shifts of the complexes found in ^{113}Cd NMR spectroscopy were consistent with the ones estimated by DFT method using simplified models of the metal coordinated environment. We have presented a simple designed system that allows control of metal coordination geometry through remote modification to helical packing. The metal coordination numbers and geometries of the designed helical peptide system could be estimated by ^{113}Cd NMR spectroscopy, PAC spectroscopy and DFT calculations.