Coordination Chemistry of a Metal Binding Domain in the *E. coli* Zinc Transport Protein, ZntA

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The NMR structure of ZntA(46-118) suggested a biologically novel asp, cys, cys coordination of the zinc ion. Here we report changes in the coordination chemistry of the Zn(II) ion that involve its function as a trafficking protein. The results for Zn(II) and other cations, such as Cd(II) and Co(II), provide insights into whether, in the physiological context of the cytoplasm, where zinc concentrations are differentially small, this coordination will be observed. In addressing these questions, the coordination of zinc in the Atx1-like domain of ZntA, ZntA(46-118), was examined by EXAFS at various levels of metal loading and found that the coordination changed from S4 at low Zn(II) levels to S_2O_2 at higher levels of Zn(II). Additionally, we investigated the ^{113}Cd-NMR and behavior of the protein by gel filtration chromatography under these conditions and found that the coordination of the cations at high metal protein ratios may be more specifically described as S_2O_2. At intracellular metal protein ratios, clear evidence is found for a zinc bridged homodimer in which Zn-S_4 environment involves cysteine side chains from two monomers. The results support a zinc transfer process in which the metal-loaded domain interacts with a metal-free domain to form a metal-bridged homodimer analogous to that seen for the homologous Cu^I bridged metallochaperone, Hah (Wernimont, 1997). We propose that this type of reversible dimer formation is part of the physiological function as a metal trafficking protein.