This study investigates kinetic processes that regulate the rate of insertion of heavy metals such as Hg(II) and Cd(II) into the TRI series of peptides. The studies for Hg(II) binding show a well-separated biphasic behavior for metal encapsulation. The two phases of the reaction are most easily rationalized by the Dissociation mechanism corresponding to the correct formation of a metal inserted three-stranded coiled coil (fast phase) and the rearrangement of the improperly folded coiled coil to the properly folded structure (slow phase). At the same time, the “d” substituted peptide, TRI L12C shows a faster reaction profile for Hg(II) insertion compared to the “a” substituted peptide, TRI L9C. The encapsulation of another heavy metal, Cd(II) has also been investigated and shows a different mechanistic pathway. These two metals allow us to probe whether the preferred coordination geometry of a metal has a significant impact on the rate and mechanism of metal incorporation into a helical bundle (important in heavy metal detoxification and regulation) and the transfer of heavy metals from protein based systems (a process important in metallochaperone and metalloregulatory proteins).

We acknowledge the National Institute of Health (# 5 R01 ES012236-02) for funding this research work.