# Homo- and Heterodimerization of the "Zinc Clasp" Domains in T-cell Specific Proteins CD4, CD8α and Lck

Alisa M. Davis[1,2] and Jeremy M. Berg[3]

*[1]The Johns Hopkins University School of Medicine, Baltimore, Maryland, USA*
*[2]Laboratory of Molecular Biology, National Institute of Diabetes & Digestive & Kidney Diseases and [3]National Institute of General Medical Sciences, National Institutes of Health, Bethesda, Maryland, USA*

The number of characterized protein domains utilizing zinc(II) for structural purposes has grown tremendously since the discovery of the "zinc finger" domain over two decades ago. Recently, a novel zinc motif, dubbed a "zinc clasp," was described (Kim, PW et al., *Science*, **301**(5640), 19 Sep 2003, pp. 1725-1728.). In this motif, two distinct proteins, each containing a dicysteine motif, together coordinate the metal. The C-terminal cytosolic domains of the T-cell coreceptors CD4 and CD8α have a *C-X-C* motif that interacts with the N-terminal *C-X-X-C* motif of the T-cell specific Src-family kinase, Lck. We have used cobalt(II) as a spectroscopic probe to study these interactions. Despite the lack of evidence for homodimerization of these domains from published NMR and ITC data (Kim PW et al., *ibid*), we use visible spectroscopy to show that each peptide does form 2:1, peptide:cobalt(II) complexes. Additional studies reveal heterodimeric complexes form preferentially to homodimeric complexes under appropriate conditions. We are investigating the effects of cysteine spacing and overall charge on the stability of these species. Preliminary data indicate that charge plays a considerable role in heterodimer preference.