Metal ion binding to three-stranded coiled coils controls the formation of parallel homotrimers vs antiparallel heterotrimers

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Work in our group has focused on the generation of heavy metal ion binding sites in the designed parallel α-helical peptide family TRI (Ac-G(LKALEEK)$_4$G-CONH$_2$). Replacement of leucine in either the "a" or the "d" position of the heptad repeat motif by cysteine generates binding sites for Hg(II), Cd(II), Pb(II), and As(III), with high affinities and unique properties. In order to expand the scope of our knowledge, we are now interested in designing binding sites into antiparallel coiled-coils to address the binding of these metals to asymmetric sites. For this objective, Coil-Ser (CS = Ac-E WEALEKK LAALESK LQALEKK LEALEHG-CONH$_2$), an antiparallel three-stranded coiled-coil which has been structurally characterized,[1] was used as a starting point and leucine was substituted by cysteine at either position 9 or 19. Binding of Hg(II) to different mixtures of these peptides ((CS-L9C)$_{3-x}$(CS-L19C)$_x$ where x = 1-3) shows a statistical population of parallel homotrimer and antiparallel heterotrimer coiled coils reflecting the initial relative stoichiometries of the individual peptides. Surprisingly, binding of Cd(II) to the same mixtures of peptides shows only the formation of parallel homotrimer coiled coils. This different behavior will be discussed based on the different characteristics/properties of these metal ions and peptides. We acknowledge the National Institute of Health (# 5 R01 ES012236-02) for funding the research work conducted.

1. Lovejoy, B.; Choe, S.; Cascio, D.; McRorie, D. K.; DeGrado, W. F.; Eisenberg, D. *Science* **1993**, 259, 1288-1295