METAL ASSISTED ASSEMBLY OF COLLAGEN PEPTIDES

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Abstract

The modification of natural collagens has proved challenging, and these difficulties are compounded by immunological problems when modified collagens are expressed in higher animals. Consequently there is a demand for collagen-like peptides (CLPs) to serve as models in which these problems are minimized. The tertiary structure of collagen consists of a triple helix of polyproline type (II) sequences $(Xaa\text{-}Yaa\text{-}Gly)_n$ with the consensus triplet Pro-Hyp-Gly (Hyp is (4R)-hydroxyproline). We have developed short CLPs whose assembly into collagen triple helices is directed by interchain metal-ligand interactions. The covalent attachment of 2,2'-bipyridyl ligands to the N-termini of $(Pro\text{-}Hyp\text{-}Gly)_5$ CLPs directs the formation of the collagen triple helix in the presence of hexacoordinate nickel(II). We describe the remarkable stability of these metal-assembled CLPs, and the enrichment of a preferred heterotrimeric CLP from a mixture of PPII sequences. Crystal structures of the apo-homotrimers are guiding the redesign of sequences that adopt the staggered collagen triple helix.