Collagen model peptides: from structural insight to controlled self-assembly

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Collagen model peptides (CMPs), composed of proline–(2*S*,4*R*)-hydroxyproline–glycine (POG) repeat units, have been extensively used to study the structure and stability of triple-helical collagen – the dominant structural protein in mammals. Despite the more than 50-year history of CMPs and numerous studies on the relationship between the composition of single-stranded CMPs and the thermal stability of the assembled triple helices, little attention has been paid to the effects arising from their terminal residues. We discovered that the terminal amino acids, capping groups, and charges profoundly affect the thermal stability of collagen triple helices. The observed effects are additive and can be used to predict the stability of new triple helices. Our findings provide important guidelines for the rational design of collagen-based materials and probes. We have used these insights in our endeavors to create highly stable heterotrimeric collagen, i.e., a single triple helix formed out of 27 possible combinations of three strands. Demonstrating that we can now precisely control the stability of CMP triple helices, we have synthesized the most stable, selectively assembled collagen heterotrimer to date as well as the shortest stable collagen heterotrimer ever made. These results provide the foundation for the development of collagen-mimicking materials as scaffolds for cell growth and wound healing.