Cross-linked Collagen Triple Helices by Oxime Ligation

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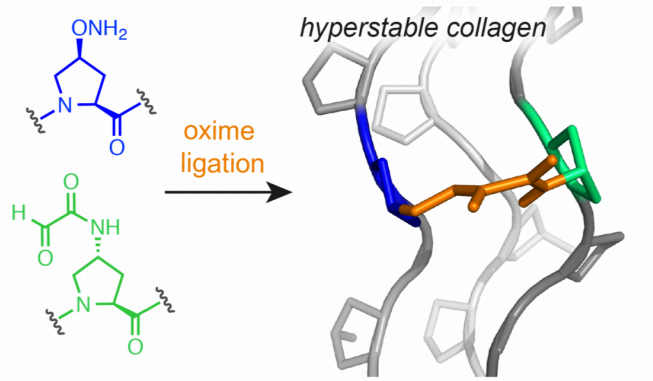
Collagen is the most abundant protein in mammals and the main component of their extracellular matrix.[1] The chemical synthesis of collagen is attractive for medical and nanotechnological applications[2] since it can provide access to structurally defined and functionalizable materials.[3] However, the bottom-up design of materials mimicking the fibrous structures of natural collagen is hampered by the entropically unfavorable assembly of short single strands into triple helices.[1] Inspired by the naturally occurring covalent cross-links that are crucial for the folding and stability of triple-helical collagen, we explored covalent cross-links between coplanar proline residues to stabilize short triple helices.[4] Specifically, we connected CMPs by oxime linkages between 4-aminooxyproline (Aop) and 4-oxoacetamidoproline (Alp) derivatives placed in neighboring strands. The covalently connected strands folded into hyperstable collagen triple helices ($T_m \approx 80$ °C). The design of the cross-links was guided by an analysis of the conformational properties of Aop, studies on the stability and derivatization of Aop-containing collagen triple helices, and molecular dynamics calculations.

Our findings put forward oxime ligation as a handle for the facile functionalization and cross-linking of collagen and open new opportunities for the design of functional collagen-based materials forming by the sticky-ended assembly of structurally well-defined triple helices.



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