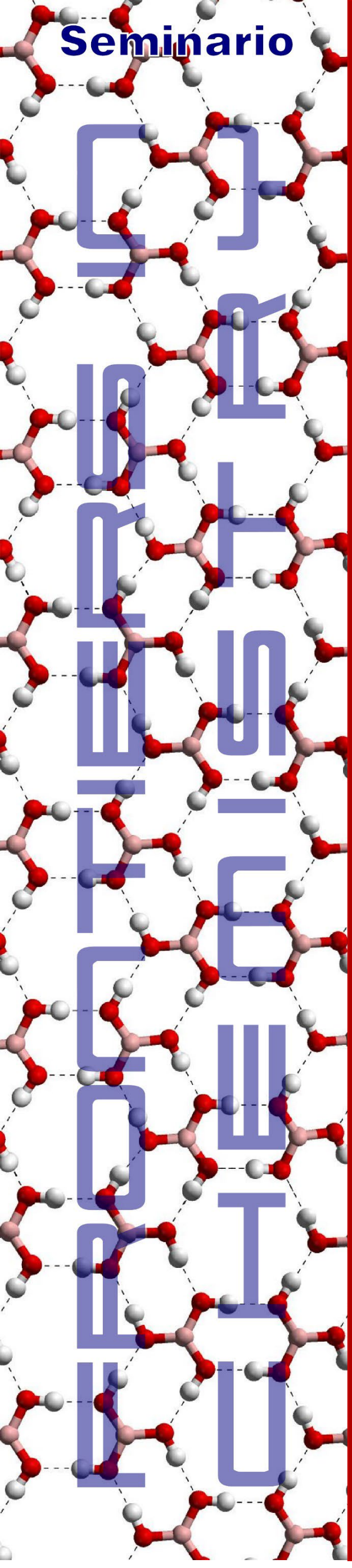

Università degli Studi di Padova
Dipartimento di Scienze Chimiche

Ciclo di Seminari 'Frontiers in Chemistry'

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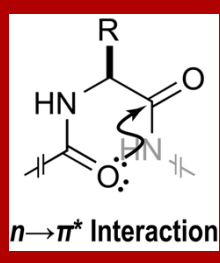
Lessons from Collagen

Monday July 7th, 2025, 10:00AM

ROOM A - NASINI

Department of Chemical Sciences, via Marzolo 1, I-35131 Padova

Collagen is the most abundant protein in animals, including humans.[1] A typical human body has 10 pounds of collagen in its extracellular matrix. Dinosaurs also deployed collagen as their bodily scaffold.[2] In animals, three collagen strands wind into a tight triple helix. Each strand contains many (2*S*,4*R*)-hydroxyproline (Hyp) residues, resulting from the most prevalent post-translational modification in animals.[3,4] Using synthetic collagen-mimetic peptides (CMPs) that contain (2*S*,4*R*)-4-fluoroproline and other subtly nonnatural residues, we have shown that previously unappreciated forces—stereoelectronic effects—are responsible for the increased stability endowed upon the collagen triple helix by its prevalent Hyp residues. This discovery led us to articulate the importance of C=O···C=O n-to-π* interactions between main-chain carbonyl groups as a significant contributor to the conformational stability of not only collagen but all proteins.[5,6] Exploiting these stereoelectronic effects with synthetic amino acids has enabled us to exert exquisite control over collagen stability. Especially promising are CMPs that anneal specifically to the damaged collagen triple helices in wound beds, fibrotic tissue, and the tumor microenvironment. This annealing can anchor pendant probes, chemotherapeutic agents, or beneficial ligands at the site of collagen damage in vivo, providing new modalities and opportunities for the clinical detection and treatment of wounds, fibrosis, cancer, and other indications.[7–9] The approach is akin to antibody–drug conjugates but with much simpler molecules and mechanisms of action.



For selected references, see:

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[7] S. Chattopadhyay, R. T. Raines, *Biopolymers* 2014, *101*, 821–833.
[8] S. Chattodadhyay, L. B. C. Teixeira, L. L. Kiessling, J. F. McAnulty, R. T. Raines, *ACS Chem. Biol.* 2022, *17*, 314–321.
[9] I. M. Borgula, S. Shuvaev, E. Abston, N. J. Rotile, J. Weigand-Whittier, I. Y. Zhou, P. Caravan, R. T. Raines *ACS Sens.* 2023, *8*, 4008–4013.

Your presence will be very much appreciated

Prof. Stefano Mammi
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