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## *Abstract*

Homochirality is widely used by Nature in biopolymers (e.g., D-carbohydrates, L-proteins, etc.), and we explore new avenues in biomaterials by using heterochirality in minimalistic peptide sequences, composed of just a few amino acids [1]. This lecture will provide an overview of their design principles for bioactive soft matter, from the importance of the amino acidic sequence length to the effects due to the presence of non-canonical D-amino acids, which can boost and prolong bioactivity.

A milestone in our journey was the elucidation of how chirality affects spatial conformation for assembly from the molecular, nano-, micro- and all the way through to the macro-scale, to link the macroscopic properties of the final materials back to structural details of the building blocks [1]. As an example, replacement of intermolecular with intramolecular interactions was applied to direct self-organization towards cytocompatible and uniformly sized nanotubes, and to impede the uncontrolled formation of hierarchical heterogeneous structures [2]. Furthermore, heterochirality can be used to resolve the inherent tension of conflicting supramolecular instructions provided by the amino acidic components, so that assembly is directed towards different outcomes, such as macroscopic materials, or discrete nanostructures of differing morphology [3]. Other important parameters that direct self-assembly are the pKas of ionizable groups [4], and the conformational landscape visited by the building blocks in solution that drives assembly in different directions, towards crystals or gels [5].

Applications are vast, especially in the mimicry of enzymes or of the extracellular matrix, thanks not only to bioactive motifs, but also to morphological effects in guiding cell activity. Other types of bioactivities can be exploited to develop antimicrobials or new means of therapy for instance to inhibit amyloid fibrillation or stabilize protein biotherapeutics. New directions currently being explored include the use of these building blocks to attain life-programmable out-of-equilibrium soft matter.

Figure 1. Heterochiral peptide assembly as a stargate to the pillars of creation.

References:
[1] A.M. Garcia et al., Chem 2018, 4, 1862.
[2] S. Kralj et al., ACS Nano 2020, 14, 16951.
[3] A.M. Garcia et al., ACS Nano 2021, 15, 3015.
[4] S. Adorinni et al., ACS Nano 2024, 18, 3011.
[5] M. Monti et al., Chem. Commun. 2023, 59, 10948..

## *Biosketch*

PhD in Chemistry at The University of Edinburgh (2008, UK), Pharmaceutical Chemist (2007, UK) & Pharmacist (2006, Italy) qualifications, honorary researcher at UCL (London, 2005-2007), Academy of Finland Fellow at University of Helsinki (2008-2010), CRSS Fellow jointly at Monash University and Commonwealth Scientific Industrial Research Organization, CSIRO (Melbourne, 2010-2012).

In 2013 I returned to the University of Trieste where my scientific adventure had started with the M.Sc. degree, (honours). In 2018 I became Associate Professor and received the Habilitation as Full Professor. In 2021-2022 (6 mo.) I have been Visiting Academic the University of Cambridge (UK). Member the Editorial Board of ACS Nano and of the Advisory Board of Chem, ChemComm, J. Mater. Chem. B, ACS Appl. Bio Mater., Chem. Eur. J., Soft Matter, Materials Advances. Recent awards:

- Career Award by the Proteomass Scientific Society (Portugal) - 2024
- RSC Soft Matter Lectureship (UK) - 2021
- EuChemS Org. Chem. Division representative at ACS Fall meeting (US) - 2020
- Howard Lecture (Durham, UK) - 2020
- Aulin-Erdtman Lecture (KTH, Sweden) - 2019
- Nature Chemistry 10th Anniversary Special Issue "Charting a Course for Chemistry" - 2019
- Italy's representative at EuChemS Organic Chemistry Division Workshop (Austria) - 2019
- Top-11 Rising Star in the natural sciences worldwide (Nature Index) - 2018
- JSP Fellowship at Buergenstock Stereochemistry Conference (Switzerland) - 2018
- Vittorio Erspamer Award (Italian Peptide Society) - 2017.