Chirality as a stargate for peptide self-assembly into functional nanostructures

Silvia Marchesan *

University of Trieste, Italy

**E-mail: smarchesan@units.it*

Homochirality is Nature's choice for biomolecules (*e.g.*, D-carbohydrates, L-proteins) and functional structures, and we explore new avenues in green nanomaterials based on heterochirality of minimalistic peptides [1]. Non-canonical D-amino acids are strategic to direct molecular conformation towards self-assembly, to increase resistance against enzyme-mediated hydrolysis and fine-tune the lifetime of the nanostructures, whilst boosting bioactivity. Furthermore, short peptides can be produced at low-cost on a large scale whilst having a low molecular weight to avoid immunogenicity.

A milestone in our scientific endeavor was the elucidation of design rules for heterochiral di- and tri-peptides able to form discrete nanotubes of varying diameter and good cytocompatibility, whilst avoiding uncontrolled formation of hierarchical heterogeneous structures [2-3]. Anisotropic nanomaterials bear great potential in terms of applications, including the possibility to directionally guide cell growth for tissue regeneration [4]. Heterochirality can be used also 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 [5]. Other important parameters that direct self-assembly are the pKas of ionizable groups [6], and the conformational landscape visited by the building blocks in solution that drives assembly in different directions, towards crystals or gels [7].

Applications are vast, spanning from the mimicry of enzymes or of the extracellular matrix, to the development of smart 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.

References

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