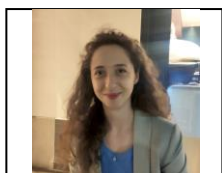




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OTHER GROUP COMPONENTS

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Research topics (EN)

The research activity of the group "Biologia Strutturale" (Structural Biology) focuses on the structure, folding and self-assembly mechanism of proteins and bioactive peptides to investigate the structural bases of their biological properties and to design new polypeptide sequences and smart biomaterials with improved properties. The experimental approach includes rational design, synthesis and structural analysis by optical spectroscopies, high-resolution microscopy techniques, biomolecular NMR and molecular dynamics simulations. The main topics currently under investigation in the group are:

1) Protein nanocages with new biotechnological applications, with particular emphasis on drug delivery systems and biomaterials design.

The study aims to unveil the mechanisms behind the ordered aggregation of proteins to form soluble nanobodies or nanocages that can be exploited in medical and biotechnical applications. Currently, the group is focused on the production and structural characterization of a human-derived ferritin composed of heavy (H) chains, which spontaneously self-assembles into a highly stable 24-subunit nanocage, exhibiting exceptional chemical and thermal stability. Such properties make it an ideal platform for diverse applications, including the targeted delivery of small to medium-sized therapeutics, the presentation of antigens, and the development of biocompatible, biosimilar nanomaterials.

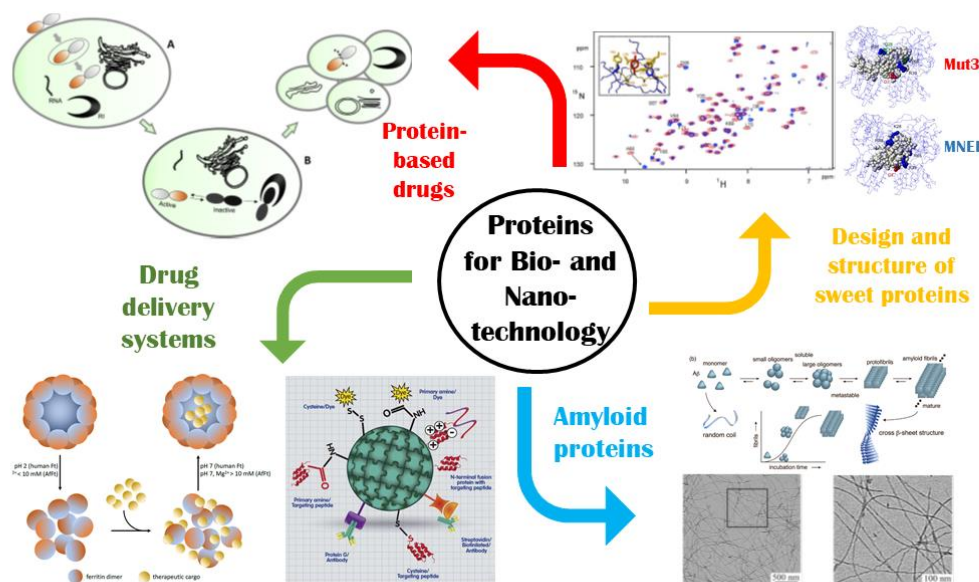
2) Protein fibrillary aggregates and functional amyloids

Several naturally occurring proteins and peptides can be converted in vivo, under physiological or pathological conditions, into linear fibrillary aggregates called amyloid structures. These structures are often associated with human neurological pathologies, such as Alzheimer's and Parkinson's diseases. On the other hand, amyloid-forming proteins are also considered versatile building blocks of functional biomaterials.

The structural characterization of amyloidogenic proteins and peptides focuses on how various factors, such as pH, temperature, solvent composition, ionic strength, and post-translational modifications like glycation, affect their stability and modulate the aggregation process. Understanding these interactions is essential to elucidate the molecular basis of aggregation and to identify potential control strategies.

Rational design, production and characterization of Sweet Proteins, in light of the prospective applications as high-intensity sweeteners.

monellin is a naturally occurring sweet protein that is significantly sweeter than sucrose (hundreds of thousands times), but its instability under different pH levels and temperatures restricts its industrial applications. To overcome these challenges, single-chain versions of monellin with improved thermal and chemical stability have been developed. In addition, the rational design based on high-resolution structural studies produced several mutants with even higher sweetness. There is ongoing research focused on optimizing these mutants as sustainable sweeteners for the food and beverage industries, with a specific emphasis on applications related to diabetes management and calorie reduction.



Number of publications:

- Rosanna Lucignano, Andrea Bologna, Simona Gramazio, Po-Hsung Wang, Christof Taxis, Lars-Oliver Essen, Delia Picone & Spadaccini, R. Unravelling the amyloid aggregation mechanism of the sweet protein Monellin: Insights from circular permuted mutants. *International Journal of Biological Macromolecules*, **(2025)** 308, 142239.
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- Rosanna Lucignano, Roberta Spadaccini, Antonello Merlino, Diletta Ami, Antonino Natalello, Giarita Ferraro, Delia Picone. Structural insights and aggregation propensity of a super-stable monellin mutant: A new potential building block for protein-based nanostructured materials. *International Journal of Biological Macromolecules*, (2024) 254, 127775.
- Rosanna Lucignano, Ilaria Stanzione, Giarita Ferraro, Rocco Di Girolamo, Carolina Cané, Angela Di Somma, Angela Duilio, Antonello Merlino, Delia Picone. A new and efficient procedure to load bioactive molecules within the human heavy-chain ferritin nanocage. *Frontiers in Molecular Biosciences*, (2023) 10, 1008985.
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- Luciana Esposito, Federica Donnarumma, Alessia Ruggiero, Serena Leone, Luigi Vitagliano, Delia Picone, Structure, stability and aggregation propensity of a Ribonuclease A-Onconase chimera, *International Journal of Biological Macromolecules* (2019), 133, 1125-1133.
- Alessandro Emendato, Giulia Milordini, Elsa Zacco, Alessandro Sicorello, Fabrizio Dal Piaz, Richard Thorogate, Remo Guerrini, Delia Picone, Annalisa Pastore; Glycation affects fibril formation of A β peptides, *Journal of Biological Chemistry* (2018), 293 (34), 13100-13111.
- Federica Donnarumma, Alessandro Emendato, Serena Leone, Carmine Ercole, Gerardino D'Errico, Delia Picone, Salt Modulated Fibrillar Aggregation of the Sweet Protein MNEI in Aqueous Solution, *Journal of Solution Chemistry* (2018), 47 (5), 939-949.
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single chain monellin MNEI through molecular design'. Scientific Reports (2016), 6, 34045.

- Jan Stanek, Loren B Andreas, Kristaps Jaudzems, Diane Cala, Daniela Lalli, Andrea Bertarello, Tobias Schubeis, Inara Akopjana, Svetlana Kotelovica, Kaspars Tars, Andrea Pica, Serena Leone, Delia Picone, Zhi-Qiang Xu, Nicholas E Dixon, Denis Martinez, Mélanie Berbon, Nadia El Mammeri, Abdelmajid Noubhani, Sven Saupe, Birgit Habenstein, Antoine Loquet, Guido Pintacuda. 'NMR Spectroscopic Assignment of Backbone and Side-Chain Protons in Fully Protonated Proteins: Microcrystals, Sedimented Assemblies, and Amyloid Fibrils' Angewandte Chemie International Edition (2016) 55, 15504.
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Ongoing projects:

Progetto PRIN-2022 SISTERS - Sea Inspired STructured hybrid biomatERials based on Self-assembling protein scaffolds