Title: Targeted biomimetic approaches to control the transport across the brain endothelium

Abstract:
The effective delivery of non-invasive therapeutic interventions to the brain represents a formidable challenge because of the presence of the blood-brain barrier (BBB), a protective physiological layer that selectively limits the passage of molecules and pathogens into the delicate neuronal environment. Given the presence of tight junction proteins sealing the paracellular spaces and strictly regulating the transport, the BBB significantly hinders the effective delivery of about 98% of molecular therapeutic formulations administered via the bloodstream.
In our work, we selected M13 bacteriophages, harmless bacteria-specific viruses largely present in our gut virome and oral cavity, as a safe and effective vehicle to deliver molecular or nanometric cargo. Phages offer facile genetic manipulation, enabling the expression of targeting moieties on their capsids, and are produced through an easily scalable process. Here, we show how these flexible nanocarriers can transport molecules and nanomaterials across BBB in vitro models of increasing complexity, eluding the protein corona and keeping their integrity and engineered tropism.
In a complementary strategy, we studied the role of Claudin-5, the major tight-junction protein found in the brain endothelium, in paracellular sealing. Using competitive binding peptides designed with an in-silico approach, we were able to interfere in the binding of adjacent claudins, transiently modulating the paracellular space to increase the passage of small molecules in a size-selective manner.
Altogether, our approaches offer exciting prospects for advancing therapeutic interventions in neurological disorders.

Short bio:
Dr. Valentina Castagnola holds a Master's degree in Chemistry with a specialization in Photochemistry and Molecular Materials from the University of Bologna. She completed her thesis work at the Laboratory for Analysis and Architecture of Systems (LAAS) at the CNRS in Toulouse, France. In 2014, she earned a PhD in Micro- and Nano-Systems, receiving the “Best Thesis Prize” for her work.
Following her PhD, Dr. Castagnola undertook a postdoctoral fellowship at the Center for BioNano Interactions, University College Dublin (Ireland), a leading center of excellence in the study of the biomolecular corona paradigm. She subsequently joined the Center for Synaptic Neuroscience and Technology at the Italian Institute of Technology (IIT) in Genoa, Italy, where she conducted research on functional nanomaterials for the treatment of brain-related diseases.
Since 2025, she has been serving as Head of the Nanomedicine Unit at the Fondazione Pisana per la Scienza ONLUS in Pisa, Italy.