PNRR Missione 4, Componente 2, Investimento 1.4 “Potenziamento strutture di ricerca e creazione di "campioni nazionali di R&S" su alcune Key Enabling Technologies”
Iniziativa finanziata dall’Unione europea –- NextGenerationEU.
National Center for Gene Therapy and Drugs based on RNA Technology
Sviluppo di terapia genica e farmaci con tecnologia a RNA
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SPOKE 8: Platform for DNA-RNA delivery

Development of a Proteomic Platform to Characterize Nanoparticles Corona Proteins.

Evaluating the interaction of nanoplatforms for drug delivery (NPs) with cellular systems and/or biological fluids is of fundamental importance to acquire information on their biological identity which controls pharmacokinetics, biodistribution and cellular uptake. The contact that occurs after NPs administration, for example, generates a *biomolecular corona* due to spontaneous adsorption of proteins, lipids, carbohydrates, nucleic acids and metabolites on the surface of nanomaterials [1,2]. The composition of the biomolecular corona, which depends on the physicochemical properties of NPs and the complexity of biological matrices, can unpredictably change NPs interaction with the immune system and provide tropism for specific organs or tissues [3].

The principal aim of this PhD project is to develop an efficient proteomic platform to achieve an unambiguous identification, reliable quantification and the interaction profile of the protein *corona* for a small library of NPs, using high resolution mass spectrometry. In a first step, different methods to isolate proteins *corona* specifically adsorbed on NPs upon their interaction with cells or biological fluids will be optimized also using cross-linking strategies and, then, bottom-up proteomics and bio-informatic analysis will be performed.

The challenge to characterize protein *corona* from cells and fluids includes (i) loss of proteins with a weak interaction to nanoparticles upon lysis, (ii) the dynamic change in protein composition of *corona* along with time, (iii) the exchange of *corona* proteins in different biological environments and with different NPs. Indeed, the full characterization of the NPs interacting proteins can be exploited for the optimization of cell internalization, for improving the in vivo biodistribution and, lastly, for disease diagnosis.

[1]. Mahmoudi M. et al., Nature Reviews Materials (2023)

[2]. Wang C. et al., ACS Nano (2021)

[3]. Hajipour M. et al., Small (2023)