

A Decade of the Liposome–Protein Corona: Lessons Learned and Future Breakthroughs in Theranostics

Prof. Anna Laura Capriotti

annalaura.capriotti@uniroma1.it

Abstract

Liposomes are among the most successful nanocarriers in biomedical applications, particularly for drug delivery. However, once introduced into biological fluids, their synthetic identity is rapidly modified by the adsorption of biomolecules, primarily proteins, leading to the formation of the so-called protein corona. This acquired biological identity strongly influences nanoparticle circulation, cellular uptake, biodistribution, targeting efficiency, toxicity and, ultimately, biological fate.

Over the last decade, extensive research has demonstrated that the composition and dynamics of the liposome–protein corona depend on multiple physicochemical and biological parameters, including lipid composition, surface charge and charge density, arrangement of surface functional groups, protein concentration, incubation time, temperature and hydrodynamic conditions. Proteomics and mass-spectrometry-based approaches have played a central role in elucidating these complex nano–bio interactions and in establishing relationships between the synthetic properties of liposomes and their biological behaviour.

More recently, the protein corona has evolved from being considered primarily an obstacle to targeted drug delivery into a potentially exploitable source of biological information. Disease-associated alterations of the plasma proteome can generate patient-specific, or “personalized”, protein coronas. This concept has opened new perspectives for nanoparticle-enabled blood tests, in which the corona acts as a nanoscale sensor capable of amplifying disease-specific molecular signatures. Such strategies have shown promise in cancer detection, including pancreatic ductal adenocarcinoma, and have stimulated the development of complementary analytical approaches based on proteomics, light scattering, fluorescence and magnetic levitation.

This presentation reviews the major lessons learned from liposome–protein corona research, highlights emerging diagnostic applications and discusses future directions toward clinically reliable nanoparticle-enabled platforms. Particular attention is given to the transition from descriptive corona profiling to integrated analytical strategies for cancer diagnosis, patient stratification and treatment monitoring, including the combined use of proteomic, lipidomic and metabolomic information.

Keywords: liposomes; protein corona; nanomedicine; proteomics; personalized protein corona; nanoparticle-enabled blood tests; cancer diagnostics.