Unlocking the power of nanomedicine through the surface's functionalization

Prof. Massimo Fresta
Department of Health Science, University "Magna Græcia" of Catanzaro Campus Universitario-Germaneto, Viale Europa, 88100 Catanzaro, Italy.
and
Research Center "ProHealth Translational Hub", Department of Experimental and Clinical Medicine, "Magna Graecia" University of Catanzaro, Campus Universitario "S. Venuta"—Building of BioSciences, Viale S. Venuta, 88100 Catanzaro, Italy
fresta@unicz.it

Nanomedicine is a multidisciplinary field which combines medicine and nanotechnology to develop advanced therapeutic approaches and overcome the limits of conventional therapies. In particular, lipid-based nanosystems reached the market more than 30 years ago and gained the final anointing during the covid pandemia.

The strength of these nanosystems is their versatility and their capability to be used in the treatment of several diseases through the optimization of their physicochemical properties according to medical needs. In this context, a pivotal role in the fate of a nanomedicine after systemic injection is played by its surface features which affect several parameters, ranging from the circulation time to the selective accumulation in specific tissues. Different engineering strategies can be used to reach the clinical goals and improve the efficacy of payloads. PEGylation technique for example currently represents the gold standard approach to realize stealth nanosystems. However, due to the presence of several stress conditions in the bloodstream, such as serum proteins, conventional PEGylated lipids on the market can be detached from the surface of nanomedicine, thus increasing their clearance rate. A potential strategy to reduce this phenomenon was proposed by my team by using a PEGylated dendron which improves the lipid anchoring effect on liposomes' bilayer and enhances the in vivo effectiveness of resulting nanomedicine. This aspect highlights another pivotal point to be studied during the early stages of the realization of a potential nanomedicine, i.e. its bio-features after injection. Indeed, right after the injection, several proteins can adsorb on the surface of nanosystem, thus creating an extra layer called "protein corona" which completely changes its fate. Although this effect may represent a crucial challenge into the development of an effective nanomedicine, the surface properties can be previously tailored to exploit the acquired new entity as a natural targeting strategy. In these attempts, ganglioside, a molecule physiologically exposed to the surface of long-circulating cells may provide an alternative approach to the PEG to realize stealth nanomedicine and improve the targeting properties of liposomes towards the brain tissue. The natural tropism of monosialic ganglioside (GM1) towards the blood brain barrier can be further enhanced using other ligands which target the transferrin receptor, such as the OX26 antibody, thus providing an effective treatment for brain disorders.

Taken together, all these aspects may in light the crucial role of nanomedicine surface properties and the importance of a systematic approach to realize an effective precision medicine.