Supramolecular architectures for tailored drug delivery

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Over the past years, multifunctional nanotechnology has emerged as a novel approach to overcome the biopharmaceutical pitfalls of old and new drugs and optimize their therapeutic performance or provide for proper perspective to their development and application. As a result, last generation delivery nanosystems are capable of complex functions, which enable for sequential overcoming of multiple biobarriers following a certain time/site determined "logic" of events. These nanocarriers provide longer drug circulation times, higher tolerability, and site-specific delivery, factors that result in better patient outcomes.

Novel delivery approaches offer the possibility of enhanced therapeutic performance of old molecules and clinical translation of new drugs including small synthetic molecules, biotech macromolecules and nucleic acids, which suffer from their poor stability, poor bioavailability, off-targeting, and immunoreaction. Bioconjugation chemistry combined with the advances in biophysics and material science advancement allow for combination of biomaterials to produce new supramolecules with tailored in vivo behaviour.

An emerging need of new nanocarriers is related to the delivery of nucleic acid drugs, which include a wide range of molecules with different action mechanism and physicochemical features, namely, molecular weight, structure, and chemical composition. Although these new therapeutics are not new in the clinical practice, their exploitation has been limited by delivery issues. However, according to the rapid experience gained by the rolling over experimentation of mRNA-based vaccines used in Covid-19 pandemics, their development has been recently accelerated not only for prophylactic treatments but also for genetic diseases, metabolic disorders, cancer etc.

To date lipoplexes, polyplexes, and lipid nanoparticles have been shown to be efficient delivery systems for nucleic acid delivery and recently a few of them reached the market. However, despite successful results have been obtained, there are still unmet needs for efficient nucleic acid delivery to provide for cell targeting.

Novel carriers have been obtained, by exploiting supramolecular chemistry, which combines various biomaterials with different physicochemical, biopharmaceutical and biological function that physically or chemically assemble to form systems with targeting endosomal escaping ability.

An important aspect in the development of these supramolecular systems is their characterization and regulatory compliance. Indeed, these "complex non-biological systems", are intrinsically nonhomogeneous cluster of nanoformulations where each component may have different in vivo behaviour. Therefore, a new regulatory paradigm must parallel the development of these formulations.