Protein-based hybrid magnetic nanoplatforms for theranostic applications

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The design of polymer-based hybrid nanoparticles has become central in the field of theranostic nanoparticles. A key issue is to develop simplified approaches to design polymer nanossemblies with improved properties compared with existing methods in terms of biodegradability, toxicity and processing. Currently, there are very few methods allowing the efficient synthesis of particles made of biomacromolecules especially proteins. In coll. with the Univ. of Melbourne (Prof. F. Caruso), we pioneered an original approach using isobutyramide (IBAM) grafts to assemble non-covalently, protein-based hollow capsules and particles without the need of an additional cross-linking or other adjuvant. The process consists in a single adsorption of proteins onto silica templates prealably grafted with IBAM groups or derivatives (e.g., bromoisobutyramide, BrIBAM) followed by template removal[1]. The driving force is attributed to strong H-bonds between the IBAM interface and the polypeptide chains of the proteins. We applied this method to design bioresponsive hollow capsules and particles made of a range of proteins, including enzymes, insulin and human serum albumin.[2] Furthermore, such carriers were shown to release chemotherapeutic drugs upon biological stimuli e.g. through protease degradation or reductive mimetic cytosolic conditions[3]. This approach was also demonstrated for the design of *ca*.100 nm size multifunctional protein-based NPs displaying simultaneously delivery of silencing RNA (siRNA) to cancer cells and magnetic resonance imaging (MRI) by grafting gadolinium complexes.[4]

In a recent work, we translated this innovative protein nanocoating approach for the design of novel hybrid magnetic core-mesoporous silica nanoparticles loaded with antitumoral agents (doxorubicin, DOX), covered by a tight HSA shell to ensure biocompatibility, stealthiness, biodegradability and efficient encapsulation of DOX. The efficient drug release of such HSA-coated core-shell NPs theranostic NPs in protease media mimicking intracellular lysosomes was shown via enzymatic HSA shell biodegradation. These new theranostic magnetic hybrid NPs are currently assessed in various biological studies (ca. cell viability/toxicity, cell uptake, intracellular behavior).

References

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