BLOCK COPOLYMER SELF-ASSEMBLY: A POWERFUL TOOL FOR THE DESIGN OF NEW SMART BIOMIMETIC NANO-CARRIERS

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In which manner can polymers be useful for biological applications? The main physical characteristic of a polymer chain is its length, which can largely exceed the micrometer range. This unique feature is responsible of the establishment of short and long range interactions tunable by the choice of the chemical nature of the monomer i.e. the repetitive unit. Such interactions can lead to the formation of small objects with well-defined shapes such as particles, vesicles or micelle-like structures. Medical interest of these objects is infinite if we consider them at a nanoscopic scale. Indeed, these polymeric systems can be synthesized at this scale in such a manner that they are able to carry a drug or a biomolecule having a therapeutic interest, to reach a biological target (organs, cells or tissues), to overcome the chemical and/or biological degradation and to release the encapsulated molecules in a triggered or controlled fashion.
Our strategy concerns the design of self-assembled nanostructures from weak interactions. Playing with the so-called weak interactions (electrostatic, Van der Waals, hydrogen bonds, hydrophobic effect) allows to mimic the interactions found in biological media and to create objects having a high plasticity, a reversible mechanism of assembly and a high affinity with biomolecules. Naturally occurring polymers, biodegradable polymers and polypeptide-based copolymers are mainly used in regards to their known biocompatibility and biodegradability. The formation of nanoparticles in the range 10-200 nm, such as micelles and vesicles from these copolymers was undertaken and the encapsulation/delivery of various molecules (drug, peptides, and magnetic particles) was investigated as well.

The self-assembly of well-defined polypeptide-based diblock copolymers into micelles and vesicles is presented. The stimuli-responsive behavior of polypeptides to pH and ionic strength is used to produce stimuli-responsive nanoparticles with a control size and shape.[1] Results focusing on polymersomes[1,2] will be detailed by means of static and dynamic light scattering analysis, UV circular dichroism, NMR and small angle neutron scattering experiments. Systems that are able to form vesicles with a narrow size distribution at basic and acid pH going through and intermediate state of single molecule will also be detailed.[2] In addition, the encapsulation of iron oxide nanoparticles into these vesicles, forming hybrid supramolecular hollow objects with a magnetic membrane, which deformation under an applied magnetic field will be evidenced.[3] These multi-responsive nanoparticles, with a structure and physical characteristics similar to viral capsids, are particularly interesting for encapsulation and delivery purpose at a controlled pH or under a specific magnetization (Figure 1).[4,5] Finally, recent results on the preparation of such polymersomes, fully biocompatible and biodegradable poly(trimethylene carbonate)-*b*-poly(glutamic acid)[6] and multi-responsive (pH, temperature)[7] polymersomes poly(dimethylaminoethylmethacrylate)-*b*-poly(glutamic acid)[8] will be described. Different projects are currently under development in collaboration with biologists and medicists using this strategy for the delivery of drug and genes in the central nervous system or for the treatment of motor neuron diseases.

References:

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Figure 1: block copolymer vesicles, a versatile and multi-functional platform for drug-delivery and diagnosis.