

Editorial

Nanotechnological Applications of Block Copolymers in Biomedicine

Block copolymers (BCP) are comprised of at least two different, immiscible polymers that are covalently linked. These materials evolve spontaneously in organized structures with domains of nanometer size. With dependence on the ratio of each polymer, BCPs are able to form lamellae, cylinders, spheres, or more complicated structures. They have been demonstrated to be of broad importance in nanotechnological applications in several different fields, including nanostructured membranes, BCP templates for nanoparticle synthesis, photonic crystals, high-density information storage media and nanomedicine. Their applicability to nanotechnology stems from the scale of the microdomains and the convenient tunability of size, shape, periodicity and properties afforded by changing their molecular parameters [1].

In this Editorial, we wish to focus on the use of BCPs in nanomedicine. One of the most promising research fields is the use of amphiphilic BCPs made up of at least two biocompatible and biodegradable polymers having different water solubility and linked by covalent bonds to prepare nano-objects for targeted drugs and gene delivery. In aqueous media, these amphiphilic BCPs form well-defined micelles with a core consisting of the less soluble block(s) and a highly swollen corona of the more soluble block(s). Depending on the degree of swelling of the corona and the relative composition of the copolymer, spherical and worm- or rod-like micelles are formed as well as more complex vesicles and compound micelles [1]. It has been shown that encapsulation of a pharmaceutical agent within the hydrophobic core associated with the high

water solubility of nano-sized micelle, may result in greatly improved drug safety and efficacy with the possibility of new therapies. In particular, the incorporation of molecules that target specific cellular signals on the outer surfaces of such smart nano-objects, or the construction of nano-assemblies with copolymers that have specific interaction with cells, is essential for designing carrier systems with specific cellular recognition. These systems have been explored as smart nano-carriers for drugs, which should recognize a biological target, e.g., inflamed tissue, and only release the drug at this site to ensure local treatment [1-3]. With this approach, bioactive compounds like DNA/RNA molecules could even be transported into cells and delivered at specific cell organelles [1-3].

BCP based nano-structures that somehow approach natural assemblies in terms of their complexity, functionality, and performance, have also been designed to respond in a controlled manner to external stimuli. Such stimulus-responsive nanostructures, which are also referred to as "smart", "intelligent", or "environmentally sensitive" nanostructures, are systems that exhibit sharp changes in response to physical stimuli such as heat, ultrasound, and light, or to chemical stimuli such as pH, ions in solution, and chemical substances [4]. In this way, a specific drug delivery to a target tissue and specific activation of the delivered drug within the targeted cell, may enhance efficacy and minimize any adverse drug effects during drug targeting [4]. A direct extension of BCP approach for building micellar nano-object consists in the preparation of external stimuli - responsive nanoassemblies to be used *in vivo*,

loaded with magnetic resonance imaging (MRI) [5] contrast agents or fluorescent dyes for near infrared (NIR) imaging [6]. These systems have the potential of facilitating the use of an external trigger and enhancing the therapeutic effects of smart drug carriers.

Besides drug delivery and therapeutic nanomedicine applications, another large area of nanomedicine research in which BCPs have demonstrated profound impact consists in their use for fabrication via the bottom-up approach of the basic elements for LAB-on Chip devices that allow for the electrophoretic routing, preconcentration, and separation of ions and biomolecules and/or of electronic nanodevices for molecular recognition of DNA and plasmide [1,7]. For such applications, the ability of BCPs is exploited to evolve spontaneously in organized periodic nanostructures. As explained above, with dependence on the ratio of each polymer, lamellae, cylinders, spheres, or more complicated structures can be formed. Typically, considering a cylindrical or lamellar structure, nanochannels are simply formed by selectively etching one of the components. This is the case in which one of the components of the copolymer is used as a structural material, another one as a sacrificial material, while the last one determined the surface chemistry of the channel. An alternative approach is to use BCPs after selective etching, as a mask to pattern a film or a substrate (block copolymer lithography) [7].

A typical application of long channels with sections of nanoscopic size obtained using the BCP approach, is building innovative nanofluidic devices for proteomics and/or genomics. The section of these channels, indeed, are close to the typical size of biomolecules such as DNA and proteins. Though well established, high-throughput genotyping techniques are now routinely used; implementation of such nanofluidic chips have the potential advantages of reducing the costs of applied and basic research in this field, drastically improving the diagnostic and the early detection of eventual predisposition to diseases, providing better and faster separation

tools to analyze the tiny changes of proteome and track their evolution [8,9].

In the field of molecular recognition, effective immobilization of enzymes require a high specific functionalized area. Use of self-assembly of amphiphilic BCPs for nanopatterning conductive surface with functionalized nanodomains is a viable tool in this research area [1,2,7].

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