A Special Section

Journal of
Nanoscience and Nanotechnology
Vol. 15, 1–3, 2015
www.aspbs.com/jnn



# *A Special Section on* Cutting-Edge Nanosystems for Biomedical Applications

To date, nanotechnology is one of the most fascinating branches of science as it is at the interface of physics, chemistry and engineering. Among the different nanotech applications, those in the biomedical field are ever growing. This requires additional knowledge of biochemistry, pharmacology and medicine. In this context, nanostructures are worldwide studied as intriguing alternatives to molecular systems due to their final unconventional properties, which may pave the way to new horizons in diagnostic and therapeutic strategies.

Among the most important biomedical-focused nanosystems, films exhibit a great potential. These nanostructured platforms may be exploited for their biocompatibility, for instance within tissue engineering strategies or against infections upon implants and in biomedical devices. On the other hand, nanoparticles endowed with an organic or inorganic scaffold represent new opportunities within the therapeutic challenges of the 21st century. In fact, they are interesting candidates for the development of innovative vaccines, and new strategies in photodynamic therapy and in gene delivery. These nanoarchitectures could be exploited also as actual medicines with improved efficacy against a number of diseases. In this field, drugs (e.g., small molecules, enzymes and/or antibodies) are either loaded into the nanoparticles or conjugated to/adsorbed by the functionalized surface, to be used as antifungal, antibacterial, thrombolytic or antitumor agents.

As early as 1960s various polymers have been studied for controlled release of drugs in order to increase both their water solubility and their half-life, thus refining on the final chemotherapeutic index. Since then, great strides have been made. In the past three decades indeed, several therapeutics dressed up as nanoparticles have been clinically established for the treatment of infectious diseases, pain and tumors. For instance, in 1995 FDA (US Food and Drug Administration) approved the first liposome-based therapeutic (Doxil®, OrthoBiotech-Alza Janssen), namely Doxorubicin encapsulated in liposomes for the treatment of different malignancies, including ovarian cancer and multiple myeloma. In the same year, Abelcet® (Enzon) was FDA-approved as well, being a liposomal formulation of the antifungal antibiotic Amphotericin B.

The inherent nature of the nanoparticle core (organic or inorganic), along with particle size and shape, strongly affect the loading efficiency (alternatively the conjugation grade) and the final surface properties, which play a key role under physiological conditions. All these features in turn deeply influence the release of the therapeutic cargo.

The aim of this Special Section is to gain a deeper insight into many of the aspects mentioned so far. We first present four reviews. Two are focused on functional coatings while the remaining ones deal with noble metal nanoparticles (e.g., gold and silver) and the magnetic counterparts (based on cobalt, nickel and iron).

The first review by Naik et al. is related to nanomaterial-based approaches for preventing the so-called biofilm, associated with infections on implants and medical devices. Bactericidal and anti-adhesion coatings of several metal nanoparticles and their composites with supporting matrices, such as hydroxyapatite, titanium dioxide, collagen, metal oxide and fluorides, are discussed.

With regard to future sustainable biotechnologies, the second review by Levchenko et al. presents the peculiar properties of the carbon-based nanostructured platforms, with a focus on dense arrays of vertically-aligned architectures, such as carbon nanotubes and vertical graphene flakes. Advantages and disadvantages of these systems are taken into account.

The third one by Reznickova et al. is mainly focused on activated polymers grafted on metal nanoparticles. Organic polymers can be designed and chemically functionalized for single and multimodal applications, including biosensing, drug delivery in anticancer and antibacterial strategies, and photothermal therapy. In this context, tailored surface properties, such as hydrophilicity, cross-linking density, crystallinity, morphology, roughness and conductivity, are necessary for the success of these applications. However, since most polymers do not possess the required features, there has been a growing interest in the development of advanced functionalization techniques. It should be underlined that in this review toxicity aspects of various

unmodified or modified nanoparticles were also taken into account.

The fourth contribution by Long et al. discusses metal- and oxide-based magnetic nanoparticles aimed at hyperthermia therapy, magnetic resonance imaging (MRI) and drug delivery. Alloy and core–shell nanoparticles have been also included.

In the second part of this Special Section research papers involving different organic molecules or polymers as nanoparticle scaffold are presented.

The first one by Xiao et al. deals with a non-viral vector based on hydrophobically modified PAMAM (poly(amidoamine)) dendrimers encapsulating two different plasmid DNAs (pDNAs) encoding luciferase (Luc) or enhanced green fluorescent protein (EGFP) for gene transfection studies.

Another interesting field involving nanotech is the photodynamic therapy. In particular, a work by Zhou et al. is focused on hydrophobic photosensitizers able to ready aggregate in aqueous media. These nanostructured colloidal particles were obtained by an one-pot preparation exploiting different types of biopolyelectrolyte as stabilizing agents.

In the subsequent study by Casa et al., nanoparticles based on bovine serum albumin (BSA) and containing amphotericin B (AmB) were obtained by the desolvation method. This formulation was aimed at treating systemic fungal infections and at improving various PK aspects of AmB (e.g., prolongation of drug release and reduction of its molecular aggregation).

In a similar approach by Erdoğar et al., cationic chitosan-based nanoparticles, encapsulating the live attenuated mycobacterium BCG (Bacillus Calmette-Guerin), were evaluated for intravesical immunotherapy of bladder neoplasia (induced in rat model). In fact, these nanoformulations were shown to induce a local inflammatory response, leading to a non-specific immune stimulation–with the release of natural killer cells, macrophages, T and B lymphocytes, and various cytokines– and, ultimately, to antiproliferative effects.

We present also a work by Baharifar et al. involving again chitosan nanocarriers but prepared via self-assembly with the enzyme streptokinase (SK), a thrombolysis agent. On the basis of computational models–highly capable to predict and optimize the preparation conditions–the chitosan concentration, the stirring time and the solution pH value were studied as independent variables to evaluate their effects on size, polydispersity index (PDI) and loading efficiency of nanoparticles. This SK nanoformulation holds a significant potential for use as a thrombolytic agent *in vivo*.

Likewise, a paper by Lindner et al. investigates the influence of the formulation parameters on the mean particle size and encapsulation efficiency (set as the dependent variables) of PLA(polylactide) and PLA-PEG(polylactide-polyethylene glycol) nanoparticles containing resveratrol, a polyphenol with anti-inflammatory, antioxidant and anti-tumor activities. This $2^3$ factorial design proved to be a key tool to optimize various formulation parameters for a prolonged controlled release.

The third part of this Special Section is related to papers involving nanoparticles with an inorganic core.

A contribution by Kolarova et al. is focused on silver nanoparticles stabilized using chitosan films for antibacterial applications, such as wound dressing or antimicrobial packaging materials. The nanosystems exhibited strong antiseptic activity against the strains *Gram-positive Staphylococcus epidermidis* and *Gram-negative Escherichia coli*.

The next work by Yazdi et al. is based on multiple injections to mice of selenium nanoparticles in combination with breast tumor cell lysate (4T1 cell antigens) as a vaccine, followed by tumor induction. In this breast cancer murine model, these nanoparticles showed an immunomodulatory effect (45 total animals including controls), boosting both the immune response and the mice survival.

The last part of this thematic section on *Cutting-edge Nanosystems for Biomedical Applications* reports composite coatings based on hematite ($\alpha$-$Fe_2O_3$) mesocrystals and chitosan molecules, obtained by electrophoretic deposition (Cabanas-Polo et al.). Optimization of deposition conditions in terms of film homogeneity was achieved.

In conclusion of this foreword, we would like to thank the authors and all the referees that contributed to this Special Section. Our thanks are addressed also to the journal staff, the Editor in Chief Dr. Hari Singh Nalwa and the European Editor Dr. Davide Barreca for their support as well as Dr. Tebera for the typesetting service.

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**Chiara Nardon** got in 2009 the Chemistry Master Degree at the University of Padova (Italy). In 2010 she started her Ph.D. at the University of Padova and in 2011 she was visiting researcher at the Karmanos Cancer Institute in Detroit (USA). After receiving her Ph.D. in Molecular Sciences in 2013, she was awarded with a Post-doc Fellowship at the same University (Department of Chemical Sciences-DiSC) on the synthesis and biological investigation of anticancer gold(III) complexes. She has been demonstrator for the courses "General and Inorganic Chemistry" at Disc and "Organic and Biological Chemistry" at the Department of Agronomy Food Natural resources Animals Environment. To her credit, 13 peer-reviewed papers (in international journals), 1 chapter in an ebook series, participation in 20 national/international schools/courses and 22 total conference proceedings (11 oral presentations with two best oral awards including an IUPAC prize). She has been awarded with several Italian and International Prizes and Fellowships including being worldwide selected among thousands to be one of the 600 final participants in the 63rd *Meeting of Nobel Laureates* (Lindau, Germany).

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