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Nano Detection, Drug/Gene Delivery, Medical Diagnosis and Therapy

Vol. 4

Frontiers in Nanobiomedical Research

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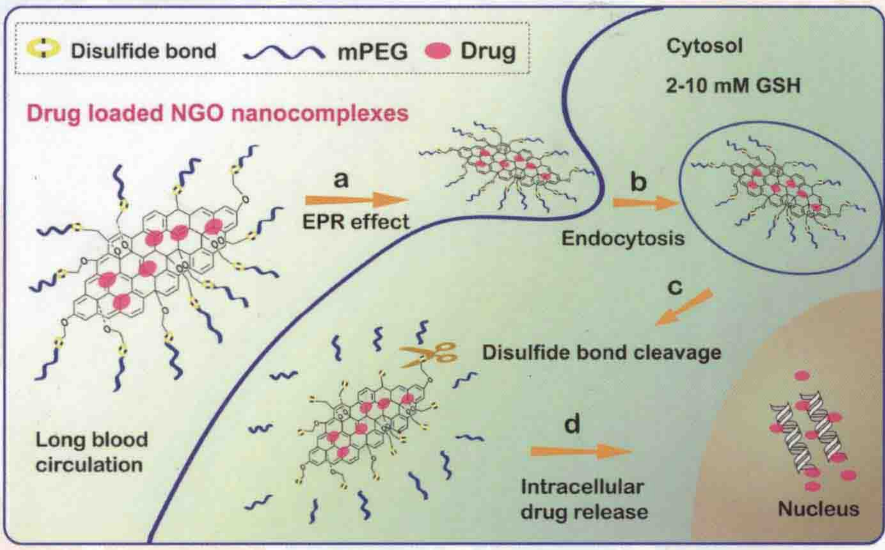

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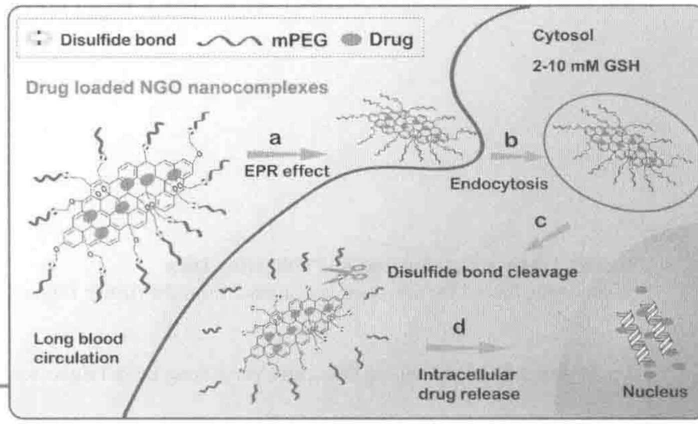

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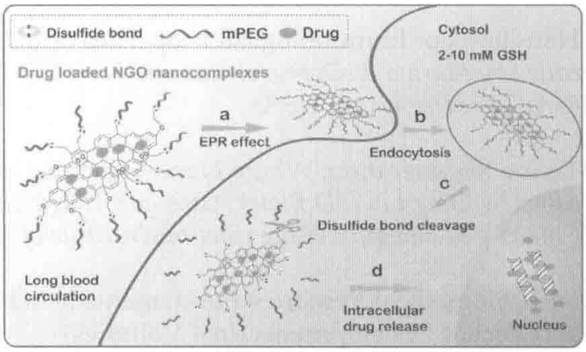

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Preface

Materials science and engineering has been a field that is primarily concerned with the studies of the structure, property, and processing of all bulk solids with considerable rigidities. These materials are often known as metals, ceramics, polymers, and composites. Based on their distinctively different properties, the materials can also be divided into structural and functional materials. The former is widely employed, with large volumes, in mechanical systems where high strengths are required, such as building constructions, automobiles, aviation, and naval vessels. The latter, for its unique electromagnetic properties, may be characterized as the electronic materials. Sensors and semiconductor thin films fall into this category that makes up the main components of today's electronic devices and electrical instruments. Another important group, for its main applications in medical implants, is called biomaterials. Typical biomaterials include hydroxyapatite bone graft and titanium alloy hip joint. These materials are designed, selected, processed, and developed according to specific applications where important materials properties are correlated to the (micro)structures and optimized for both engineering and economic considerations.

A common characteristic among all traditional materials is its bulk form. Even for most of the materials used in the powder form assume several micrometers in diameter. For semiconducting films, the substrates of integrated circuitry extend into the millimeter range. As such, the materials behaviors are characterized as the "bulk property." It is easy to understand the bulk strength of a structural material as its stress-strain behavior must reply upon appreciable dimension of the testing bar. The electronic properties such as electrical resistivity, thermal conductivity, energy bands, magnetic domains, and dielectricity are all established based on the lattice structures of the bulk materials. The corresponding theories are developed under the boundary conditions such that the material surfaces and interfaces are not interplayed in the calculations of the intrinsic parameters.

However, the situation is complicated when the dimension of a material is reduced to nanoscale, say a few nanometers. As is well known, the surface of a particle is classically defined, in materials science, a two-dimension defect (or surface defect) where the atomic arrangement is no long ordered compared to the bulk. Therefore, the properties of the surfaces must be altered significantly. For instance, for a particle of Palladium with a diameter of 0.77 cm, the surface area is 3.6 cm^2. If the diameter is reduced to 0.01 cm, the surface area increases to 260 cm^2. The surface area will be stunningly 2.8×10^7 cm^2 for a particle of 1 nm. Therefore, for nanoparticles, the volume fraction of a given mass will be primarily the surfaces. In other words, the bulk volume fraction is negligibly small. If this is the case, application of theories that are developed based on the bulk structures may not be appropriate.

The typical nanomaterials that are being extensively investigated include nanoscale particles of polymeric micelles, oxides (Fe_3O_4, SiO_2, ZnO...), gold, and carbon-based structures (graphene and nanotubes). There has been intense current research on their new properties that have risen from the "nano effects." New physical properties have been discovered from these nanomaterials. For instance, the quantum dots are developed based quantum confinement which gives size-dependent emissions. Superparamagnetism is a unique behavior resulting from the single magnetic domains of Fe_3O_4 nanoparticles in a size range of a few nanometers. Novel synthesis routs have been developed for a variety of nanomaterials that can be used for applications in efficient energy devices, biotechnology, medical diagnosis, and cancer therapeutics.

Ever since the beginning of nanoscience, the research communities soon found the real possibilities of using nanotechnology to solve the key biomedical problems that cannot be easily dealt with by conventional approaches. Collaborations quickly began among researchers from the biomedical and physical sciences. On the other hand, the materials scientists found medical, especially clinical problems extremely inspiring to their innovative design of the nanostructures and development of multifunctional carriers for biomedical applications. However, new materials issues arise concerning the interfaces between the nanoparticles and cells, nano surface properties that affect the biological behaviors such as endocytosis and toxicity, and nano size effect on transport kinetics in a biological system. These are the new challenges rarely faced by chemists and materials scientists in conventional materials research.

For instance, the current clinical magnetic resonance imaging (MRI) scan can readily detect lesions as small as a few millimeters. Dynamic MRI of human cancer in mice has reached a high spatial resolution. But MRI is costly and time consuming to implement. Compared to MRI, optical imaging is easier to use and cost-effective, and can be applied to cancer diagnosis with high resolution in a straightforward fashion. Recently, for diagnosing breast cancer, MRI and near-infrared optics have been combined as a potentially more accurate method. By combining these two techniques, MRI produces the basic image of the breast, while the near-infrared optical means provides the functional information of the tissue, such as the oxygen consumption rate at a particular region, which could indicate early cancer development. Thus, multimodality will enable imaging from different perspectives, giving much higher accuracy in medical diagnosis. In optical imaging, quantum dots (QD) have superior properties, including higher quantum yield and much sharper emission spectra. Quantum dots can be "tuned" based on their size, resulting from quantum confinement effects. They offer great advantages as a contrasting agent for *in vivo* imaging.

There is an increasing need for the early diagnosis of cancer, prior to the detection of anatomic anomalies. A great challenge in cancer diagnosis is to locally biomark cancer cells for maximum therapeutic benefit. Tumor cell targeting has been a complex issue in medical diagnosis using nanotechnologies. Although there have been extensive efforts in this area, a few have reported successful attempts that enabled effective targeting with high specificity. Several reasons may have contributed to this difficulty, and the major one is due to the lack of biomarkers and non-specific binding. The success of targeted treatments will depend on the expression of specific proteins or genes present in cancer cells. Targeting strategies may be divided into those utilizing specific binding to ligands or receptors and those based on nonspecific adsorptive mechanism. If the cancer cells exhibit cell-specific carbohydrates, they may serve as binding sites to colloidal drug carriers containing appropriate ligands. However, none of these strategies will guarantee absolute cell targeting with high specificity as they primarily reply on common antibodies of the tumor cells.

There have been many effective approaches developed in tumor therapy by nanotechnology. But selective delivery of drugs into tumor lesions has been a key challenge for successful management of cancers. In current drug delivery, the release of the drug has mainly relied on the natural diffusion process and bio degradation of the carrier systems. However, the tumor treatment needs well-developed procedures whereby, anti-cancer drug can be delivered in a selective, localized, and timely controlled fashion. There has been a critical need to develop novel approaches that could provide precision spatial and temporal drug delivery at the tumor site. New delivery mechanisms must be identified and developed from the perspectives of materials science and biomedicine. Novel nanostructures need to be designed and developed with multi functionalities which can enable drug delivery in a selective, predictable, and controlled manner. Drugs are well protected by special coatings during transport, but released via different but intelligent mechanisms. The nanocarriers are also rendered strongly fluorescent and surface functionalized with tumor specific antibodies. Therefore they are targeted on the tumor cells and observable by *in vivo* fluorescent imaging. In medical therapy, delivery of siRNAs to target cells has been a novel approach. Using small interfering RNA for studying gene function and drug target validation has received great attention in the medical communities. The key challenge is on the design of the nanocarriers for siRNAs delivery. In the delivery systems, the chemical modification of siRNA duplex is critical for increased stability and sensitive detection of siRNA.

Recently, a new trend is becoming prevalent in the development of the nanosystems for simultaneous tumor diagnosis and therapy. This requires high versatility of the nanocarrier system with multiple functionalities of cell targeting, drug storage, optical imaging, and effective means of treatment such as magnetic and photothermal hyperthermia, photodynamic therapy, and drug release via various intelligent mechanisms (pH, temperature, and biochemical variations in the tumor environment). A new terminology "theranosics" has been frequently used and applied in medical communities, which implies simultaneous therapy and diagnosis. For instance, a nanosystem can simultaneously achieve both cell targeted *in vivo* imaging and photothermal treatment of cancer by nanotechnology. While achieving concurrent high spatial and temporal resolution of the lesions via cell targeting; special non-evasive treatments are implemented at the same time by various means, such as localized drug release, hyperthermia, and photo-thermal therapy.

Inspired by these challenging problems in biomedical fields, the development of the nanotechnologies will be the key in addressing some of the critical issues in medicine, especially in early cancer diagnosis and treatment. This book, *Bio-inspired Nanomaterials and Devices,* summarizes the most recent developments in nanomaterials, biotechnology, and medical diagnosis and therapy in a comprehensive fashion for researchers from diverse fields of chemistry, materials science, physics, engineering, biology, and medicine. Not only does the book touch up on the most fundamental topics of nanoscience, but also deal with critical clinical issues of translational medicine.

The book is written in a straightforward and tutorial fashion, typically suitable for technical non-specialists. All chapters are written by active researchers in frontier research of nanobiomedicine. We hope this book will provide timely and useful information for the progress of nanomaterials and biomedical applications. We are grateful to all invited authors for their excellent contributions to this book. We would like to thank Drs. Haiqing Dong and Yong Yong Li for their great talent and efforts in developing the schematic diagram for the book cover.

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