APPLICATIONS OF NANOTECHNOLOGY IN LIFE SCIENCES: A BRIEF REVIEW

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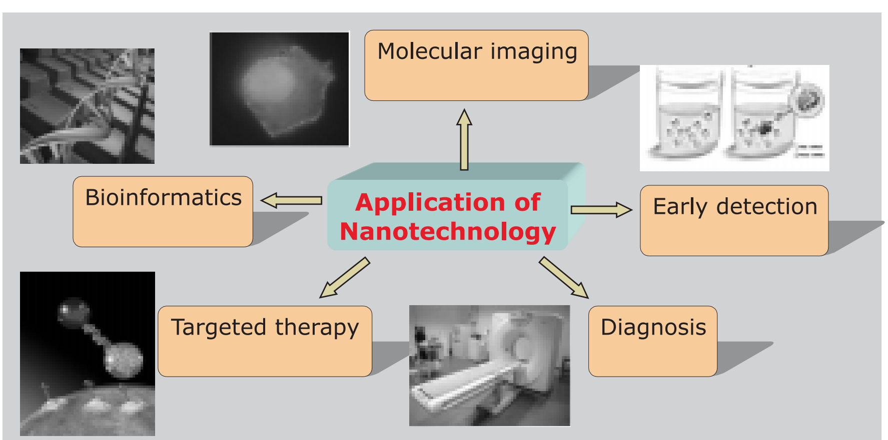
Nanotechnology, which deals with controlled synthesis and applications of nano-meter (one billionth of a meter) sized objects, has emerged as a major interdisciplinary field covering Materials Science, Applied Physics, Chemistry, Basic Biosciences and Biotechnology. These tiny functional materials have electronically, optically, magnetically, chemically and mechanically novel property features which can be exploited in various ways in diverse applications. The origin of many such properties lies in the quantum size effect behavior of electronic systems as well as the large surface to volume ratio of these nanosystems. Such materials offer interesting opportunities in Life sciences ranging from drug delivery to imaging of biomolecules due to the novel characteristics of the interactions of such spatially confined materials with biosystems and the ultra smallness of their size as compared to for example the cell size. The field is developing at several levels: materials, devices and systems. Nanomaterials are presently at the frontiers of scientific discovery and explorations of potential commercial applicability. Specific nanoparticles can now be synthesized that can carry a therapeutic molecule to the target cell. There are several approaches to synthesize nanoparticles with different property features, shapes and sizes that could revolutionize the field of biomedicine. However, various issues like target specific molecules, biocompatibility, and toxicity need to be addressed while applying this technology to the Life sciences.

In the coming few years, it is expected that nanotechnology will have great impact on health care, biomedicine and biotechnology. The National Science Foundation (USA) from their studies has anticipated that advances emerging from nanotechnology developments over the next 15 to 20 years will be worth approximately $1 trillion. In anticipation of this predicted economic impact, nanotechnology research programs in several countries have increased substantially in recent years. Indian government has recently allotted Rs. 1000 crores for the year 2007 - 2008 to promote Nanotechnology in India.

Nanotechnology has shown great promise in the areas such as disease diagnosis, drug delivery targeted at specific sites in the body, molecular imaging, fluorescent biological labels, gene delivery, detection of pathogens, and proteins, Probing of DNA structure, Tissue engineering, Tumor destruction via heating (hyperthermia), Separation and purification of biological molecules and cells, MRI contrast enhancement, Phagokinetic studies. These are being intensely investigated and some products are undergoing clinical trials



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DRUG DELIVERY

In the near future, one of the most important applications of nanotechnology is likely to be in the pharmaceutical sector. The final aim of pharmaceutical research is to deliver the drug to a specific target at the right time and in safe mode. Most of the current drugs, though effective, have drawbacks like toxicity to non-target tissues, difficulty in maintaining drug concentrations within therapeutic windows, and metabolism and excretion of drugs. Drug solubility and cell permeability issues are also common with small molecules and biologically active compounds. The oral route is one of the preferred methods of drug delivery as it most convenient and noninvasive. But adequate drug delivery via this route still remains a challenge. All these factors ultimately lead to the decreased efficacy. Nanotechnology with its multifaceted advantages could mitigate all these drug delivery problems. Nanoparticles can help deliver drug to a tissue or enable organ-specific targeting with therapeutic action.

The focus of nanotechnology is on formulating biocompatible nanosystems such as nanoparticles, nanocapsules, micellar systems, and conjugates that will accommodate bioactive agents. Nanoparticle formulations can be used to (i) provide targeted (cellular/tissue) delivery of drugs, (ii) improve oral bioavailability, (iii) sustain drug/gene effect in target tissue, (iv) solubilize drugs for intravascular delivery, (v) improve the stability of therapeutic agents (e.g., against pH and enzymatic degradation), and (vi) control drug release rate in target tissue for required duration of the treatment for optimal therapeutic efficacy. The unique properties of nanoparticles have a direct influence on their behavior as drug delivery devices and their production, hence accurate assessment of these characteristics is important. Evading phagocytosis is also an important element of the attendant strategies and shapes of nanoparticles have been recently shown to have considerable influence on this phenomenon. How to make biocompatible nanoparticle drug carriers into complex shapes which are non-phagocytable remains an evolving challenge.

Nanoparticle formulations protect drugs or therapeutic agents from degradation or denaturation in a variety of physiological conditions and also prolong the duration of exposure of a drug by increasing retention of the formulation in circulation. Nanomaterial mediated intracellular delivery of various drugs including DNA, RNA, enzymes, antibodies has become a reality, which needs intense investigations.

Many pharmaceutical agents, including various large molecules (proteins, enzymes, antibodies) and even drug-loaded pharmaceutical nanocarriers need to be delivered intracellularly to exert their therapeutic action inside cytoplasm or onto nucleus or other specific organelles, such as lysosomes, mitochondria, or endoplasmic reticulum. Intracellular transport of different biologically active molecules is one of the key problems in drug delivery in general.

HYPERTHERMIA

Generation of local heat adds to the effectiveness of radiotherapy and/or chemotherapy in the treatment of cancer lesions and promises to reduce side effects when combined with targeted drug delivery. Many heating techniques have thus been developed to increase the temperatures in a pre-defined body region. These are commonly termed as hyperthermia treatment and can be further categorized as whole-body hyperthermia, regional or local hyperthermia, and interstitial hyperthermia. Nanomaterials which can be heated by radiofrequency (typically 100-500 kHz) or by lasers can serve as vehicles for drugs and when anchored suitably on the desired tumor or lesion location by different available routes can be used to implement hyperthermia treatment. Magnetic nanoparticles are found to be particularly interesting in such therapy because they can be magnetically guided to the desired location and they can also be heated by RF source to the desired temperature range in a controlled manner. The temperature has to be in a small window between 45-48^{0}C at which normal cells are not destroyed but the cancerous cells are destroyed. The notion of magnetic fluid hyperthermia (MFH) was introduced in 1993 and has since been a subject of many studies. Generally for MFH super-paramagnetic Fe_3O_4 (magnetite) nanoparticles coated with biofriendly and fluidizable polymers or organic molecules such as dextran or amino-silan are used. The RF power absorption is caused by a solid state oriental excitation of the magnetization within the core crystal, called Neel relaxation or by the Brownian rotation due to a friction between the rotating subdomain nanoparticles (due to magnetically generated torque) with the surrounding liquid. Currently research is ongoing on various aspects of this interesting field including search for more effective and biocompatible magnetic nanoparticles fluids.

BIOIMAGING

Fluorescence is a widely used tool in biology. As the field is growing there is increasing demand to measure more biological indicators simultaneously and efficiently. Organic dyes are conventionally used for fluorescence. Multimodal imaging has been tried with these dyes like measuring the number of parameters on cellular antigens with flow cytometry, combinational labeling in cytogenetics for spectral karyotyping. However, conventional dyes impose stringent requirements on the optical systems used to make these measurements. Apart from these, their narrow excitation spectrum, broad emission profiles, and low photo bleaching thresholds have limited their effectiveness in long-term imaging and multiplexing.

Semiconductor quantum dots (QDs) are nanocrystals in the range of 1 to 10 nm with unique photochemical and photophysical properties not available with common organic dyes and fluorescent proteins. The size tunable optical features allow their use as direct probes or as sensitizers replacing traditional probes. QDs have been successfully used in molecular imaging of live cells and whole organisms. One of the most exciting properties of QDs is that depending on their size, the QDs, excited at appropriate wavelengths, will emit light in different color zones. Quantum nanobeads with different colors and different intensities are used with high uniformity, accuracy and reproducibility for multimodal imaging that can encode over 1 million combinations. The development of Quantum dot technology opens up new possibilities for diagnostics, direct immunolabeling, *in situ* hybridization etc. In addition, nanocrystal probes may prove useful for other contrast mechanisms such as x-ray fluorescence, x-ray absorption, electron microscopy, and scintillation proximity imaging. Use of far red or infrared-emitting nanocrystals as tunable, robust infrared dyes is another possibility.

QDs can also prove useful in developing non-invasive molecular imaging technologies. It has great potential in tracing techniques: viral particles to be followed *in vivo*, analyzing of drug molecules in biological systems, and tracking of tumor cells. These techniques involving metal and semiconductor nanoparticles for molecular profiling studies and multiplexed biological assays are under intense development. The techniques like Surface Enhanced Raman Scattering Spectroscopy with nanoparticles like gold and silver has tremendously increased the potential of protein, DNA detection techniques. This technique is based on the significant enhancement of the detection Raman signal when the molecule to be detected in anchored on the surface of a nanoparticle due to intense electric field at the high curvature of the nanosurface.

THERAPY

Nanotechnology has its substantial advantageous implications for the field of tissue engineering as well. Various materials used in hip or knee prosthesis have the disadvantages of loosening of the implant and inflammation due to their smooth surfaces. By creating nano-sized features on the surfaces of these materials they can be made biocompatible as it can stimulate the production of osteoblasts. Many polymeric, ceramic and, more recently, metallic materials are used successfully for more durable and longer lasting hip or knee replacements. Titanium is widely used bone repairing material in orthopedics and dentistry because of its high fracture resistance, ductility and weight to strength ratio. But it does not support the growth of cells on its surfaces. Coating of nanostructured apatite film over titanium by biomimetic approach can make it bioactive. Other materials and coatings also need to be examined. This field envisages many new developments in the field of surface nano-engineering involving nanoparticles, polymers, organic and biomaterials: nanohybrids.

Recent advances in nanotechnology have also shown great potential in targeted cancer therapy. The genetic and molecular differences in normal and cancer cells are used to predict disease development, progression, and clinical outcomes. The tremendous development of proteomics and genomics in the last few years has helped to exploit these differences and find out unique cancer markers. The synergy between Nanotechnology, genomics and proteomics has great potential to develop an effective cancer therapy. Techniques like killing of cancer cells by hyperthermia, cancer drug delivery with nano-carriers may eventually become a 'main-stream' practice in the future, although it awaits considerable scientific efforts. In particular, many issues related to potential nanohazards need to be sorted out.

Most of the major and established pharmaceutical and biotech companies have started internal research and development programs in Nanotechnology. Some companies are exclusively involved in the development and commercialization of nanomaterials in biological and medical applications. Nanomedicine now seems within the realm of reality starting with nanodiagnostics and drug delivery facilitated by nanobiotechnology. Miniature devices such as nanorobots (nanobots) may be able to carry out integrated diagnosis and therapy by refined and minimally invasive procedures, nanosurgery, as an alternative to any conventional crude surgery approaches. Nanotechnology will markedly improve the implants and tissue engineering approaches as well.

The data on safety and toxicological aspects associated with the fate of nanoparticles introduced in the body are insufficient at this stage. More detailed fundamental research on interaction of nanomaterials and biomolecules, biofluids should be conducted. Future perspectives should address these aspects and should also concern the tailoring of the shape and physicochemical properties of these 'smart nanoparticles' to make them 'active' in Life sciences. Although commercial applications are currently few, this interdisciplinary work has a great potential for generating advanced materials, which might lead to novel devices for fundamental biological research, imaging, diagnostics, and therapy.

Nanotechnology holds promise of the next industrial revolution. The joint venture between different disciplines of Science, Engineering and Nanotechnology can revolutionize the field of biomedicine and health care. In anticipation to this the expertise, tools and logic from different disciplines need to be brought together.

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