Class Room

Nanomedicine: Promising Tools in Biomedical Sciences

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Dr. Agnishwar Girigoswami, Associate Professor, Department of Medical Bionanotechnology, CHRI, has earned his Ph.D. from University of Kalyani in 2004. In the course of PhD, he explored fluorescence probing techniques to understand the biological phenomenon. In 2006, he joined the Korea Advanced Institute of Science & Technology (KAIST), South Korea as Postdoctoral Researcher with a prestigious Government (Brain Korea) fellowship. There, he developed a novel DNA/PNA-chip for genetic diagnosis coupling microarray technology and nanotechnology along with specific enzymatic reactions. Later he joined Jadavpur University, Kolkata; JIS College of Engineering, Kalyani; RKVM Girls College, Kolkata for research and teaching before joining CHRI in 2010. His 14 years research and 10 years teaching have brought many publications in peer reviewed journals.

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Lately nanotechnology is acquiring interest with rapid pace in biomedical sciences. This growing interdisciplinary field provides enormous technological platform for application in several areas like molecular diagnosis, imaging, nano-based therapeutics etc[1]. The nanotechnology is developed by the combination of science and technology for designing, synthesis and manipulation of materials with smallest functional unit confines in nanometer scale to attribute specific function at the supramolecular level. Classically, nanotechnology refers to the particle size ranging from 1 to 100 nm but it can be extended to below 1 μm to obtain ordered structure for useful application[2]. The key feature of nanomaterials is its excellent physicochemical properties that differ from their bulk due to the high surface to volume ratio (fig. 1). These unique physicochemical properties frame them to be excellent candidates for screening, imaging, diagnosis, treatment of diseases and altogether it is known as 'nanomedicine'.

Nanomedicine is defined as the "monitoring, repair, construction, and control of human biological systems at the cellular, molecular, and atomic levels using engineered nanodevices and nanostructures"[3]. National Institute of Health states another definition of nanomedicine for the medical research as "an offshoot of nanotechnology, which refers to highly specific medical interventions at the molecular scale for curing disease or repairing damaged tissues, such as bone, muscle, or nerve"[4]. The cutting edge technological field nanomedicine deals with five major disciplines in medical and biological sciences namely, analytical tools, nanoimaging, nanomaterials and nanodevices, novel therapeutics and drug delivery systems, and regulatory & toxicological issues in relation with clinical practices[4]. The ultimate goal of nanomedicine is to understand the mechanism of action of biological machinery inside the living cells at nanoscale and based on these information, it is possible to redevelop new engineering technology to treat disease conditions.

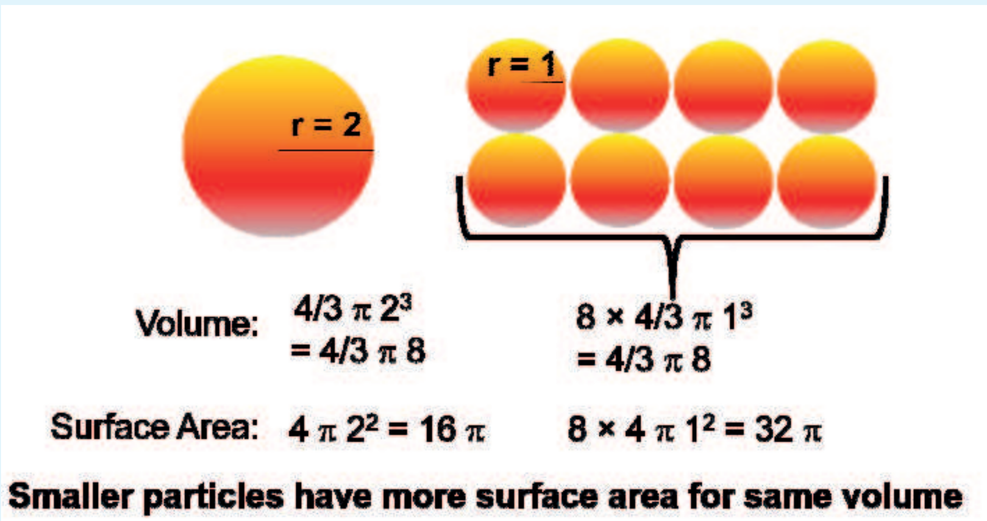

Fig 1: Schematic diagram to show the effect of particle size on the surface area to volume ratio. The surface to volume ratio increases with the reduction of particle size.

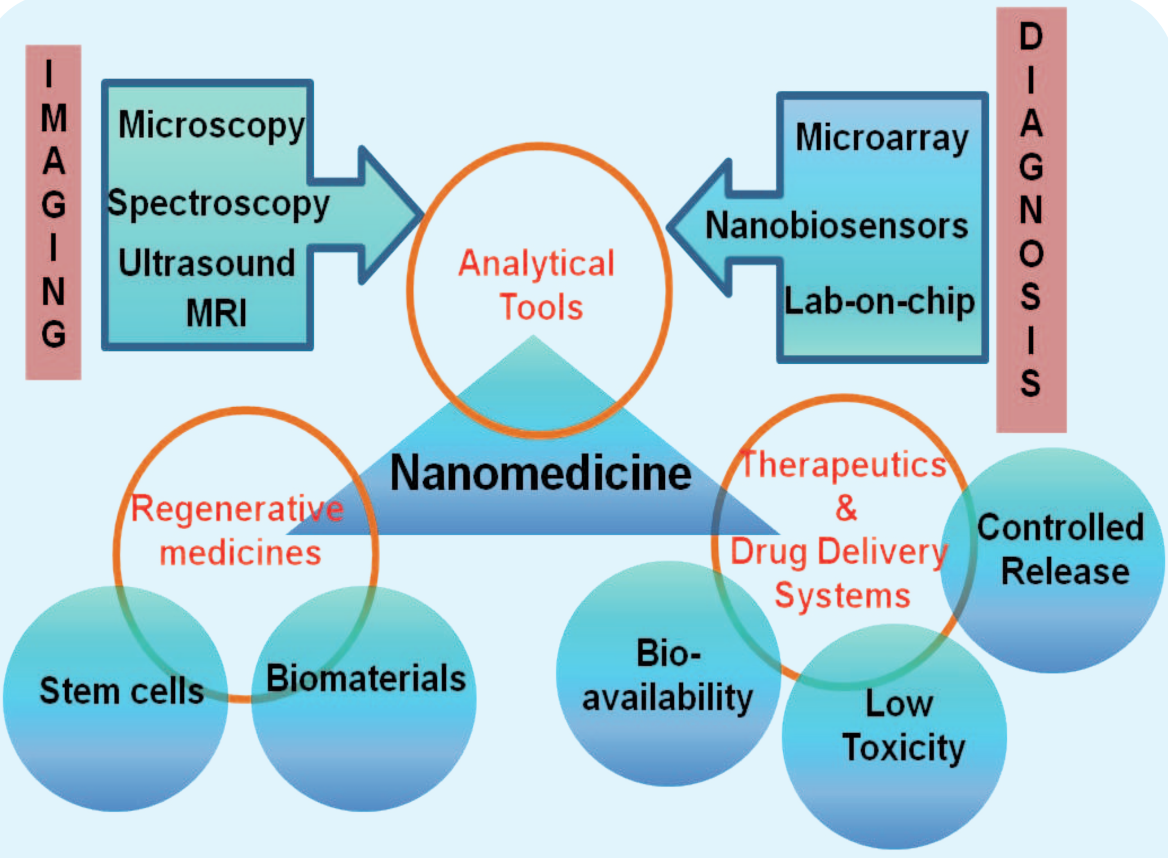

Fig 2: Schematic representation of different fields of application of nanomedicine.

The impact of nanomedicine in biology can be seen mainly in diagnostic & imaging methods, drug release kinetics and regenerative medicines which are summarized in figure 2.

Nanomedicine in Diagnostics

Recent developments in nanomedicine have made it possible to analyze biological systems at cellular and sub-cellular levels for the development of medical diagnosis and therapy. Nanomedicine based diagnostics basically concerns in vitro and in vivo models that help to quantify and visualize the expression of targeted biomolecules. To satisfy the huge demand in analyzing and scrutinizing the behavior of the human diseases and related treatment, researchers are continuously developing new nanoscale devices like micelles, liposomes, dendrimers, core-shell nanoparticles, quantum dots, polymer, inorganic nanoparticles etc. (figure 3). Currently, fluorescent labeled or radio-labeled molecules are widely used in biomedical laboratories for the diagnosis purpose, with lots of difficulties regarding sample volume, toxicity, sensitivity, specificity, detection time etc. In contrary, nanotools are most promising to overcome all these limitation of conventional methods due to their high surface to volume ratio, high reactivity, tunable size and inherent optical properties[5].

The major application of nanomedicine is improved fluorescent marker for the purpose of diagnosis and screening. In this connection, quantum dots are well known nanometer-sized inorganic semiconductor[6]. Due to the unique size dependent quantum confinement effect, these inorganic chromophores show broad absorption band along with a specific and sharp fluorescence emission. The high quantum yield, excellent chemical and photo stability and tuneable size dependent optical properties make them good candidate in single molecule tracking, in vivo imaging, fluorescent cell sorting, etc over conventional organic fluorophores.

Advances in nanotechnology have led to engineer super paramagnetic nanoscale material which is an excellent promising tool for in vitro as well as in vivo MR imaging. The effectiveness of traditional contrast agents is limited due to the lack of specificity and sensitivity. These contrast agents are not effective in determining early stage of metastatic tumour where as nanomedicine based contrast material like super paramagnetic iron oxide (SPIO) nanoparticles can overcome these issues related to solubility, specific targeting, toxicity, immunological responses etc[7]. Magnetic resonance imaging signal is basically the precession of hydrogen nuclei of water molecule in an applied magnetic field. The contrast agents are used to shorten the spin-lattice relaxation time (T_1) and spin-spin relaxation time (T_2). Paramagnetic nanoscale materials such as gadolinium (Gd) and manganese (Mn) with higher relaxivities give stronger contrast enhancement for T_1-weighted MRI and super paramagnetic contrast agents like SPIO give T_2-weighted MRI[8, 9].

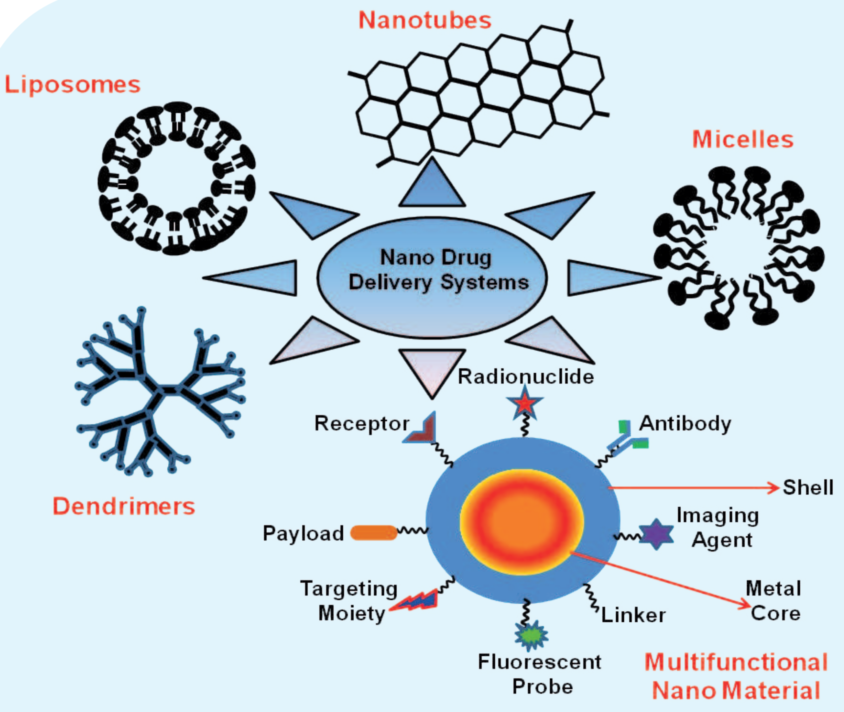

Fig 3: Engineered nano-drug delivery systems.

Nanomedicine in Therapeutics

Nanoparticles are popular for their biomedical applications due to their ability to overcome different biological barriers and to target specific tissues with sustained release of drugs. The non-specific action of chemotherapeutic anti-cancer drugs causes significant side effect in cancer patients. Engineered nanoparticles drug carriers can deliver drugs to the specific tumour tissues and enhanced permeability and retention (EPR) effect allows accumulation of anticancer drugs in cancerous tissues with reduced drug toxicity. These nanoscale drug delivery systems include polymer-based nanoparticles, polymeric micelles, dendrimers, liposomes etc. These engineered nanocarriers can be made slowly degradable, pH sensitive, temperature sensitive, and targeted by conjugating them with specific monoclonal antibodies or macromolecules like folic acid, sugar, etc. The surface functionalization of nano carriers with ligands that are selectively recognized by the receptors on the cancer cell surface facilitate active tumour cells targeting strategy. For passive targeting mechanism, the nanomedicine reach tumour cells through the leaky vasculature of the blood capillaries and the enhanced vascular permeability of tumour tissues causing accumulation of chemotherapeutic agents in tumours (figure 4).

Another advantage of nanocarriers is continuous release of drug with controlled rate to the specific targeted site. Various biodegradable polymer nanoparticles, liposomes, dendrimers have been used in drug delivery research as they can efficiently deliver the drug to the specific site with therapeutic benefit minimizing the side effect. Such nanodevices are formulated by dissolving, attaching, encapsulating or entrapping the pharmacologically active agent to nanoparticles matrix. The major goal in designing these devices are sustained release of therapeutic agents to the specific site of action with the therapeutically optimal rate and reduced toxicity[10].

Challenges in Nanomedicine

It was expected that the nano-invention would improve the quality of life, upgrade the diagnostics and therapeutics with reduced cost and it is. But, there are lots of issues regarding the potential health effects associated with exposure to man-made nanomaterials. Due to the lack of information for the prediction of impact of engineered nanomaterials on the environment and human health, there is a need for additional research. Presently, numerous regulatory agencies concerned with nanomedicine, insurance companies, and public health groups are raising questions for the implementation of nanomedicine in routine clinical practice[11].

Sanhai et al recently addressed possible seven challenges for nanomedicine in Nature Nanotechnology[12]. Most important challenge is the determination of the distribution of nanomaterials in the human body after systemic administration through possible routes and understanding the transport of these materials across compartmental boundaries in the body. Other challenges are the development of new mathematical and computer models for predicting risk and benefit parameters through a 'periodic table of nanoparticles'. Success on these issues urgently needs collaborative effort from all government and non-government agencies.

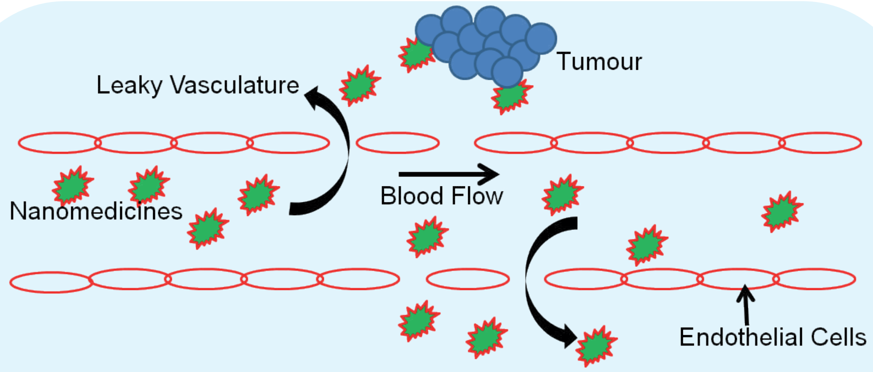

Fig 4: Diagram shows the delivery of drugs to the tumour through leaky vasculature of the blood capillaries

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Smoke, if you are eager to age quickly!

Reputations of marijuana, red wine and chocolates have been redeemed recently by the discovery of hidden benefits associated with their use. But no such luck for cigarettes; each new study damns it further. In a new study carried out on 79 pairs of identical twins, in whom one sibling is a smoker, the researchers compared the faces for the effects of aging. A panel of three plastic surgeons analysed the twin's facial features and graded the aging using standard assessment tools. The smoking twin, when compared to his non-smoking sibling, had worse scores for baggy eyes, baggy cheeks, smile lines and wrinkles along upper and lower lips. The cigarette induced damage affected mainly the lower two thirds of the face. Smoking for even five years appeared to make a significant difference. Smoking induces damage by depriving the cells of oxygen and by disrupting the collagen and elastin. Apart from its other effects, smoking is really bad for one's appearance. The study is published in the November 2013 issue of Plastic and Reconstructive Surgery

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