



Nano Medicine- A Futuristic Approach

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The emergence and existence of nanotechnology is a reality now and the governments have begun to envision nanotechnology's enormous potential. Nanotechnology is based on the design, characterization, production and application of the structures, devices and systems by controlled manipulations of size and shape at the nanometer scale (atomic, molecular and macromolecular level) with atleast one novel/superior characteristic or property (1).

The importance of upcoming field of nanotechnology can be assessed from the fact that it is gaining the federal support day by day to explore promising areas such as nanotechnology, supercomputing and alternative energy sources (1).

It was in 1959, Nobel laureate Richard Feynman had predicted the emergence of a new science with a wide range of applications - *The Nanotechnology* (2). The application of nanotechnology to the biological system is referred to as nanomedicine, which can be defined as the "application of nanoscale technologies to the practice of medicine for monitoring, construction, repair, control of human biological systems, drug delivery and in vivo imaging by using engineered nanodevices and nanostructures" (3). Today, nanomedicine is a big industry with about 200 companies involved and 10 billion dollars are being invested in research and development every year, nanomedicine is credited with incorporation of more than 30 billion dollars worth of manufactured goods world wide. This figure is estimated to rise to 1 trillion dollar by 2015.

Medical Use of Nanomaterials

1. Drug Delivery

Drug delivery approach is aimed at developing nanoscale particles or molecules to improve the bioavailability of a drug. This can be achieved by using nanoengineered devices for target cells at molecular level. Almost 65 billion dollars are wasted every year due to poor bioavailability of drug. Nanoparticles have unusual properties that can be used to improve drug delivery. The lipid or polymer based nanoparticles have been developed which are capable to alter the pharmacokinetics and biodistribution of a drug. While larger particles are soon cleared from the body, nanoparticles through drug delivery

system are able to cross the cell membrane and enter into cell cytoplasm. This enhances the efficacy of the drug since many disease processes occur inside the cell and can be inhibited only by the drugs that make entry into the cell. Nanoparticulate drug delivery vehicles are under development which would allow faster drug absorption, controlled dosage release and shield the drug from body's immune system. For example the drug paclitaxel is approved for treatment of breast cancer after the failure of combination chemotherapy but the problem faced with use of paclitaxel is that of its insolubility. This problem has been resolved by using paclitaxel in nanoparticle form (with a size of 100-200 nm) integrated with biocompatible protein i.e. albumin. Similarly, a drug with poor solubility can be incorporated in a drug delivery system where both hydrophilic and hydrophobic characteristics exist to improve the solubility. The effective drug delivery is based on three facts: (a) efficient encapsulation of drugs (b) targeted delivery and (c) successful release. A drug may cause tissue damage but with a drug delivery system, regulated drug release can overcome this problem. If a drug is cleared too rapidly from body, it requires high doses but with drug delivery system, clearance can be reduced by altering the pharmacokinetics of the drug (4).

2. Nanotechnology for Carcinoma

The small size of nanoparticles imparts them the properties that are very useful in oncology particularly in imaging. Nanoparticles of cadmium selenide (quantum dots) glow when exposed to ultraviolet light. When injected, they seep into tumor tissue. The surgeon can see the glowing tumor and use it as a guide for more accurate tumor removal. Quantum dots when used in conjunction with MRI produce exceptional images of tumor sites as these produce much brighter image as compared to that produced by organic dyes used as contrast media. Moreover, the small size of nanoparticles allows them to preferentially accumulate at tumor sites since tumors lack an effective lymphatic drainage system (5,6). Sensor test chips containing thousands of nanowires are able to detect proteins and other biomarkers left by carcinomatous cells. These are used for detection and diagnosis of carcinoma in the early stages from a few drops of a patient's blood.

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Nanoparticles-Radiowaves

Nanoparticles of gold or carbon are attached to the carcinomatous cells. These are then exposed to radiowaves from a radiomachine which leads to heating up of nanoparticles leading to destruction of carcinomatous cells.

Nanoparticles-Infrared Shells

Nanoshells of 12 nm diameter coated with gold are used to target the carcinomatous cells by conjugating antibodies or peptides, to their surface. The tumor area is then irradiated with infrared laser, the waves pass through the tissue without heating it, while gold coated nanoparticles get heated which lead to destruction of carcinomatous cells.

Dendrimer-Carcinomatous Cells

Dendrimers are a class of synthetically prepared polymer molecules. A dendrimer molecule has atoms arranged in many branches and sub-branches radiating out from a central core. A dendrimer may have over one hundred hooks on it that allow it to attach to the cells in the body for a variety of purposes. In one study, folic acid molecules were attached to a few of its hooks and simultaneously the anticancer drug was attached to the other hooks. Carcinomatous cells having more affinity for folic acid as they have more receptors for this vitamin so when dendrimer carrying folic acid attaches itself with its receptor on the cell and gets absorbed easily due to high requirement. The anticancer drug also gets simultaneously delivered to carcinomatous cells for a biological response (7).

Metallic Nanoparticles-Photodynamic Energy

Area of carcinomatous cells containing metallic particles is illuminated by light from outside. The light energy absorbed by metallic particles gets heated up, produce high energy oxygen molecules which destroy the carcinomatous cells. Such a therapy is more appealing as it does not have a "toxic trail" of reactive molecules as left by chemotherapy in the body. This non-invasive procedure of photodynamic therapy has promising results as a targeted therapy for tumors. Nanomedicine appears to dominate the entire scene of cancer diagnosis and therapy. Already, a half dozen nanoparticles based imaging and therapeutic agents that are in various stages of development have yielded promising results (8).

3. Nanosurgery

A liquid containing gold-coated nanoshells have been developed. Fusion of two pieces of tissue into one has been achieved by use of this liquid. The two pieces of tissue are put together touching each other, then the liquid is dribbled and infrared laser is traced along the seam, the two pieces "weld" together and the process is termed

as "Tissue Welding" which is going to replace the suturing of wounds. This will also solve the problem of restitching the artery when it gets cut during surgery or a heart/kidney transplant. The "tissue welder" would cause perfect seal of the cut artery (9).

4. Nanoparticles-Tissue Targeting

Gold nanoparticles selectively target certain organ based on their size and charge. The composites of these particles are encapsulated by a dendrimer and assigned a specific charge and size. Positively charged gold nanoparticles have been found to enter the kidneys while negatively charged remain in liver and spleen. Thus, the targeting and distribution of a drug complexed with gold nanoparticles can be augmented for an organ or tissue (10).

5. Molecular Nanomedicine-Nanorobots

Molecular nanomedicine envisages the development of machines (molecular assemblers, nanorobots) which could function at a molecular or atomic scale e.g computational gene introduced into the system can carry out the job of a missing or defective gene. A nanorobot will be between 0.5-3 micrometer in size, the size of a particle which can pass through the capillary. Carbon is the primary element used to build these nanorobots due to inherent strength and other characteristics of some forms of carbon (diamond/fullerene composites). These devices injected into a human body would work in a specific organ or a tissue mass (11,12). The nanodevices can be scanned for their location having congregated around their target (tumor mass) inside the body.

6. Cell Repair-Nanomachines

Cell biology has revealed that basic operations of cell repair are carried out at molecular level. Nanomachines that are able to enter the cells, sense differences from healthy one and make modifications of faulty structure (13).

7. Nanotechnology-Drug Discovery

Nanoparticles and nanodevices such as nanobiosensors and nanobiochips are under development for their use for drug discovery and development. Nanoscale assays are going to reduce the cost of screening. Some nanosubstances such as fullerenes could be potential drugs of future. Fullerene molecules have numerous points of attachment that allow precise grafting of active chemical group in three dimensional orientation. This is the hallmark of rational drug design as it allows positional control in matching fullerene compounds to biologic targets. It is also possible to tailor fullerene based compounds to the requisite pharmacokinetic characteristics and to optimize their therapeutic use (14). Fullerenes have potential applications in the treatment of diseases in which oxidative stress plays a role in the pathogenesis e.g. neurodegenerative disorders. Fullerenes



also act as an alternative to chelating compounds that prevent the binding of toxic metal ions to serum components (15)

Nanotechnology in Diagnostics

What is being seen as a major breakthrough in detection of carcinomas and other deadly diseases, the researchers at University of Toronto, Canada, have developed an inexpensive and small ultra sensitive microchip for detection of various malignant and benign tumors as well as severe infectious diseases like HIV and H1N1. This is going to revolutionize the field of diagnostics. The innovation is indicative of beginning of renaissance. The microchip developed is of the size of a black berry. (Information retrieved from Internet).

How application of nanotechnology can transform the medical procedures, to sum up this: "Diagnostic nanomedicine could be employed to monitor the internal chemistry of the body. The nanorobots equipped with wireless sensors and transmitters could freely move in lymph and blood to detect imbalances and send warning signals." "Nanomachines can be planted in brain to monitor the pulse and brain-wave activity. "Implanted nanodevice could release drugs and hormones in chronic imbalance and deficiency states". Artificial antibodies, artificial WBC's & RBC's or anti-viral nanorobots can be devised to correct the related disorders.

Recent Advances

Landscape phage fusion protein-mediated targeting of nanomedicines enhancing the prostate tumor cell association and cytotoxic efficiency of anticancer drugs, Self assembled lipid nanomedicines for siRNA tumor targeting anticancer drugs have been introduced recently (16,17). Effective uptake and distribution of fullerenes (a potent inhibitors of mast cell mediated allergies/ inflammation) in human mast cells is now possible by nanomedicine (18).

Ethics & Nanomedicine

As the science and technology of nanomedicine speed ahead, ethics, policy and law struggle to catch up. It is important to proactively address the ethical issues as current GCP may not be sufficient to address important concerns/risk related to engineered nanomaterials (19).

Conclusion

Nanomedicine is going to have a potential impact on the society. It will drastically improve patient's quality of life, reduce societal and economic costs associated with healthcare, will offer early detection of pathologic conditions, reduce the severity of disease and result in improved clinical outcome for the patient.

References

1. Bawa R, Bawa SR, Meibius SB *et al.* Protecting new ideas and invention in nanomedicine via patent. *Nanomedicine* 2005; 1 (2) :150-58.
2. Feynman RP. "There is plenty of room at bottom". *Eng Sci (Caltech)* 1960; 23: 22-36.
3. Webster P. World nanotechnology market Frost and Sullivan *Nanomedicine* 2005; 1(2): 140-42.
4. Lockman PR. Nanoparticle technology for drug delivery across the blood brain barrier. *Drug Dev Ind Pharm* 2002; 28 (1):1-13.
5. Gourley PL, Hendricks JK, Mac Donald AE *et al.* Mitochondrial correlation microscopy and non laser spectroscopy - new tools for biophotonic detection of cancer in single cells. *Technol Cancer Res Treat* 2005; 4 (6): 585-92.
6. Jain KK. Nanotechnology in clinical laboratory diagnostics *Clin Chim Acta* 2005; 358: 37-54.
7. Svenson S, Tomalia DA. Dendrimers in biomedical applications-reflections on the field. *Adv Drug Deliv Rev* 2005; 57 (15): 2106-29.
8. Ferrari M. Cancer nanotechnologies: Opportunities and Challenges. *Nat Rev Cancer* 2005; 5: 161-71.
9. Bergman RM. Innovations in biomaterials: Achievements and Opportunities. *MRS Bull* 2005; 30 : 540.
10. Langer R, Vacanti JP. Tissue engineering. *Science* 1993; 260: 920-26.
11. Gelain F, Lomander A, Vescovi AI *et al.* Systemic studies of a self assembling peptide nanofiber scaffold with other scaffolds. *J Nanosci Nanotechnol* 2007; 7: 424-34.
12. Jain KK. Nanodiagnostics: Application of nanotechnology in molecular diagnostics. *Expert Rev Mol Diagn* 2003; 3: 153-61.
13. Alivisatos AP. The use of nanocrystals in biological detection. *Nat biotechnol* 2004; 22: 47-52.
14. Gareth Huges A. Nanostructure-mediated drug delivery. *Nanomedicine* 2005; 1: 22-30.
15. Wilson SR. Nanomedicine: Fullerene and Carbon nanotube biology. In: Osawa E, (ed). *Perspectives influence nanotechnology*. Norwell MA: Kluwer Academic Publishers, 2002.pp.225-35
16. Jayanna PK, Bedi D, Gillespie JW *etal.* Landscape Phage Fusion Protein-mediated targeting of nanomedicines enhances their prostate tumor cell association and cytotoxic efficiency. *Nanomedicine* 2010 Feb,4 [Epub Ahead of Print]
17. Tseng YC, Huang L. Self Assembled Lipid nanomedicines for siRNA Tumor targeting. *J Biomed Nanotechnol* 2009; 5(4):351-63.
18. Dellinger A, Zhou Z, Nurton SK *et al.* Uptake and distribution of fullerenes in human mast cells. *Nanomedicine* 2010 Feb, 4 [Epub Ahead of Print]
19. Dand BR, Sally ST. Ethics in nanomedicine. *Nanomedicine* 2007; 2(3): 345-350.