REVIEW ARTICLE

Nanomedicine: Current Status and Future Implications

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ABSTRACT

Adverse effects form a major part of the drawbacks of the current therapeutics. The two main reasons are: Distribution of drugs to an area, which is not the desired site of action and another is attaining higher than desired concentration at the site of action. Nanomedicine raises hopes to overcome these problems. Nanomedicine is the medical use of nanobiotechnology. It is a relatively newer technology based on the uses of engineered nanomaterials (ENMs). ENMs are medical materials available in nanometer (one-millionth of a millimeter) scale. Because of nanoscale, the molecules acquire changes in their physicochemical properties which are utilized for easier and more thorough penetration in cells. Nanomedicine has shown promising results both in diagnostics as well as therapeutics e.g. in oncology and diseases of central nervous system. Nanoparticle targeting and neuroelectronic interface raises hopes for a number of clinical disorders for which the satisfactory treatment is currently not available. The most striking use can be repairs at a molecular level. Like other modalities of treatment, nanomedicine also has disadvantages; however, currently the benefits outweigh the risks. It will be interesting to see how the rising ethical concerns will be dealt with.

Keywords: Engineered nanomaterials, nanoparticle, neuroelectronic interface, quantum dots

Adverse effects of drugs including death have remained the shadow of therapeutics right from the beginning. Two main reasons of these adverse effects were distribution of drug to whole body when given by systemic route and nonprecision about the concentration of drug at the site of action. Nanomedicine offers hope to combat both these drawbacks. Nanometer is one-millionth of a millimeter. The term nanotechnology was coined by Norio Taniguchi in 1974. Nanotechnology is defined as the "intentional design, characterization, production and applications of materials, structures, devices and systems by controlling their size and shape in the nanoscale range (1-100 nm)."[1] Nanotechnology combined with biology becomes nanobiotechnology. The use of nanobiotechnology in medicine is nanomedicine. Nanomedicine may be defined as the monitoring, repair, construction and control of human biological systems at the molecular level, using engineered nanodevices and nanostructures.[2]

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Nanomedicine ranges from the medical applications of nanomaterials, to biosensors, possible future applications of molecular nanotechnology and neuroelectronic interface. It is believed that cell repair machines will revolutionize the medical field.

Nanomedicine is a large industry, with nanomedicine sales reaching 6.8 billion dollars in 2004, and with over 200 companies and 38 products worldwide, a minimum of 3.8 billion dollars in nanotechnology research and development (R&D) is being invested every year.[3] As the nanomedicine industry continues to grow, it is expected to have a significant impact on the economy.

HISTORICAL ASPECTS

Nanomedicine has been an important part of nanotechnology from the very beginning. In his 1999 book on Nanomedicine, Robert Freitas assembled an impressive array of ingenious ideas that derive from ongoing developments and inevitably lead to extravagant speculations.[4]

To capitalize on the promise of nanotechnology in cancer, the National Cancer Institute launched the Alliance for Nanotechnology in Cancer in September 2004.[5] A group of 53 European stakeholders, composed of industrial and academic experts, has established a European Technology Platform on nanomedicine. One of its objectives is to boost innovation in nanobiotechnology for medical use. The US National Science Foundation forecasts that the global market for nanotechnology-related products and services will reach US $1 trillion by 2015 (NSF 2007).[6] The advent of nanomedicine has changed the way pharmaceutical companies are planning for new products. Drug companies are also facing other challenges that necessitate development and implementation of novel R&D strategies, including those that focus on nanotechnology and miniaturization.[7]

Nanomedicine research is receiving funding from the United States National Institute of Health. Of note is the funding in 2005 of a 5-year plan to set up four nanomedicine centers. In April 2006, the journal *Nature Materials* estimated that 130 nanotech-based drugs and delivery systems were being developed worldwide.[8]

HOW IT WORKS

Many devices such as biosensor, nanoelectronic instruments, pacemakers, monitoring apparatuses and advanced ECG machines are all the inventions of nanomedicine. Changes in physical properties of elements and materials can be produced as their surface to area ratio is dramatically increased, i.e. when nanoscale sizes are achieved. These changes such as colloidal properties, solubility and catalytic capacity are the foundations of use of engineered nano-materials (ENMs) in nanomedicine. The nanoparticles are physically attracted to infected cells like a magnet, breaking their membrane walls without destroying healthy cells around them. In this way they are superior to conventional chemotherapeutic agents that they can differentiate between pathogenic microorganisms or malignant cell from the healthy host cell. These agents prevent the bacteria from developing drug resistance by breaking through the cell wall and membrane, a fundamentally different mode of attack compared to antibiotics.[9]

APPLICATIONS AND POTENTIAL

Nanomedicine has significant applications in medical sciences. Many different types of nanoparticles are currently being studied for applications in nano-medicine. They can be carbon-based skeletal-type structures, such as the fullerenes or micelle-like, lipid-based liposomes, which are already in use for numerous applications in drug delivery and the cosmetic industry. Many devices, instruments and machines based on nanotechnology have been introduced.

A recent study looked into the antimicrobial properties of carbon nanotubes and showed that they are strong antibacterial agents.[10] Two forms of nanomedicine that have already been tested in mice and are awaiting human trials are use of gold nanoshells to help diagnose and treat cancer, and liposomes as vaccine adjutants and as vehicles for drug transport. Similarly, drug detoxification is also another application for nanomedicine, which has shown promising results in rats. Nanodevices are faster and more sensitive than typical drug delivery.[11]

Diagnostics

It is expected that soon nanorobots will be used, which will circulate in the vascular system and send out signals when imbalances appear within the circulatory and lymphatic system. Fixed nanomachines could be inserted in the nervous system of the human body to monitor brain activity.

Advanced and fully equipped nanomedical heart trackers are present in the major hospitals to accurately track the heart beat and its downfalls and also for treating it as needed in the body.[12] In human heart defibrillators and pacemakers, nanodevices could influence the behavior of individual cells. The list of current and potential diagnostic uses is large viz. endoscopic robots and microscopes, Fullerene-based sensors, imaging (cellular etc.), monitoring, lab on a chip, nanosensors, protein microarrays, scanning probe microscopy, intracellular devices, intracellular biocomputers and intracellular sensors/reporters.

Drugs Dispersion and Delivery

Implantation of nanomedicine devices could disperse drugs or hormones as required in people with chronic imbalance or deficiency states. Drug delivery in the form of nanomedicine is based on developing nanoscale molecules to improve drug bioavailability. Nanomedicine based tools and devices are being developed for uses in imaging. Using nanoparticle contrast agents, images such as ultrasound and magnetic resonance imaging (MRI) have a favorable distribution and improved contrast.[13] The strength of drug delivery systems is their ability to alter the pharmacokinetics and biodistribution of the drug. When designed to avoid the body's defense mechanisms, nanoparticles have beneficial properties that can be used to improve drug delivery. Triggered response is one way for drug molecules to be used more efficiently. Drugs are placed in the body and only activate on encountering a particular signal. For example, a drug with poor solubility will be replaced by a drug delivery system where both hydrophilic and hydrophobic environments exist, improving the solubility.

Protein and Peptide Delivery

Protein and peptide molecules are one of the most common functional units of cells. Their molecular derangements are the causes for many illnesses. Targeted and/or controlled delivery of these molecules using nanomaterials such as nanoparticles and dendrimers is an emerging field called nanobiopharmaceutics, and these products are called nanobiopharmaceuticals.

Oncology

The small size of nanoparticles endows them with properties that can be very useful in oncology. Quantum dots (nanoparticles with quantum confinement properties, such as size-tunable light emission), when used in conjunction with MRI, produces exceptional images of tumor sites. A very exciting research question is how to make these imaging nanoparticles do more things for cancer. For instance, is it possible to manufacture multifunctional nanoparticles that would detect, image and then proceed to treat a tumor? This question is under vigorous investigation; the answer to which could shape the future of cancer treatment.[14]

Sensor test chips containing thousands of nanowires, able to detect proteins and other biomarkers left behind by cancer cells, could enable the detection and diagnosis of cancer in the early stages from a few drops of a patient's blood.[15] Prof. Jennifer West has demonstrated the use of 120 nm diameter nanoshells coated with gold to kill cancer tumors in mice. By irradiating the area of the tumor with an infrared laser, which passes through flesh without heating it, the gold is heated sufficiently to cause death of the cancer cells.[16]

Surgery

There are examples that with the help of gold-coated nanoshells, infrared laser and flesh welder bloodless surgery can be done.[17]

NEURO-ELECTRONIC INTERFACES

It is expected that neuro-electronic interface with the construction of nanodevices will permit computers to be joined and linked to the nervous system. This will help not only in degenerative diseases of central nervous system, but also in many injuries and accidents which results in dysfunctional systems and paraplegia. About 130 nanotech-based drugs and delivery systems and 125 devices or diagnostic tests have entered pre-clinical, clinical or commercial development since 2005, according to NanoBiotech News.[18]

CELL REPAIR MACHINES

Using drugs and surgery, doctors can only encourage tissues to repair themselves. With molecular machines, there will be more direct repairs. Access to cells is possible because biologists can insert needles into cells without killing them. Thus, molecular machines are capable of entering the cell. The healthcare possibilities of these cell repair machines are impressive.

ETHICS AND NANOMEDICINE

At present, the most significant concerns involve risk assessment, risk management of ENMs and risk communication in clinical trials.[19] As expected, the possibility of implanting a computing chip in humans raises many ethical concerns. While this chip can diagnose diseases from which the person is suffering currently, it can also analyze our DNA to determine the diseases to which one may be susceptible to in future. Ethical issues concerning a patient's right-to-know, right-not-to-know and the duty-to-know arise.[20] While advancement of research proves that we can increase the current level of accuracy and efficiency of diagnostic and therapeutic procedures by augmenting the targeting and distribution by nanoparticles, the dangers of nanotoxicity become an important next step in further understanding of their medical uses.[21]

ADVERSE EFFECTS

There are some reports on the adverse effects of individual ENM; for example multiwalled carbon nanotubes (MWCNT) were found to cause asbestos-like effects on the mesothelium following intracavitary injection of high doses in rodents. The important question of whether inhaled MWCNT will translocate to sensitive mesothelial sites has not been answered yet.[22] However, currently the benefits of nanomedicine definitely outweigh the risks. We should not forget that till date ENMs have not been exposed to a huge population in uncontrolled conditions. It will also be important to know their adverse effects, if any, in pediatric, geriatric and differing pathophysiological conditions like pregnancy, lactation, congestive heart failure, uremia, etc. Currently, there are no regulatory guidelines developed specifically for ENMs.

CONCLUSION

With the conventional methods of treatment it is not possible to repair the defect at a molecular level. Nanomedicine will have an impact on many medical applications. The usefulness is not only therapeutic but also diagnostic. Development of nanomedical applications is complex and needs an integrated approach of all stakeholders. Future applications of nanomedicine will include activity monitors, biochips, insulin pumps, needle less injectors, medical flow sensors and blood pressure, glucose monitoring devices and drug injecting systems. At its best it is hoped that nanomedical machines will cover up the deficiencies by replacing or improving the DNA molecules of body. What nanomedicine will be able to achieve in the future is beyond current imagination. However, it will be a tough task to handle the ethical issues which will be arising with the same pace.

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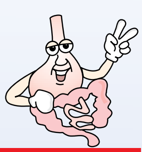

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