



REVIEW ARTICLE

## Nanomedicine : Future Prospective in Disease Diagnosis and Preventions

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### ABSTRACT

Medical practice is about to enter a new era focused on the nanoscale and the practice of "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. Nanomedicine is, in a broad sense, the application of nanoscale technologies to the practice of medicine, namely, for diagnosis, prevention, and treatment of disease and to gain an increased understanding of complex underlying disease mechanisms. The potential medical applications are predominantly in detection, diagnostics (disease diagnosis and imaging), monitoring, and therapeutics. The availability of more durable and better prosthetics and new drug-delivery systems are of great scientific interest and give hope for cancer treatment and minimum invasive treatments for heart disease, diabetes and other diseases. Many novel nanoparticles and nanodevices are expected to be used, with an enormous positive impact on human health. Nanotechnology provides the field of medicine with promising hopes for assistance in diagnostic and treatment technologies as well as improving quality of life. Humans have the potential to live healthier lives in the near future due to the innovations of nanotechnology. Some of these innovations include: Disease diagnosis, Prevention and treatment of disease, Better drug delivery system with minimal side effects, Tissue Reconstruction. The vision is to improve health by enhancing the efficacy and safety of nanosystems and nanodevices. Products based on nanotechnology in medicine and medical technology are reaching the market, with an anticipated enormous positive impact on human health, in the coming years. Ethical and moral concerns also need to be addressed in parallel with the new developments. Today, nanotechnology and nanoscience approaches to particle design and formulation are beginning to expand the market for many drugs and are forming the basis for a highly profitable niche within the industry, but some predicted benefits are hyped.

**Key words:** Nanotechnology, Nanomedicine, Health risks

### INTRODUCTION

A broad array of present and future research developments are generally lumped together as "nanotechnology." A common feature is only that they are concerned with large and small things where at least some relevant measures are in the nanometer range ( $10^{-9}$  to  $10^{-7}$  metres) and thus in the size-range of DNA molecules or viruses. Nanotechnology can be defined as the manipulation, precision-placement, modeling and manufacture of material at the nanometer scale (One meter consists of 1 billion nanometers) (Donlandson, 2004). It promises to provide many useful applications in many fields. Nanomedicine is the rather more well-defined application of nanotechnology in the areas of healthcare and disease diagnosis and treatment. Artificial bones implants already benefit from nanotechnologically improve materials. Nanostructured surfaces can serve as scaffolding for controlled tissue- growth. Of course, all kinds of medical devices profit from the miniaturisation of electronic components as they move beyond micro to nano. This affects diagnostic tools, pace-makers, "cameras in a pill," etc. Nanoparticulate pharmaceutical agents can penetrate cells more effectively as well as being able to cross the blood- brain-barrier. After injecting nanoparticles into tumours, these can be stimulated electromagnetically from outside the body - by emitting heat, the stimulated particles can then destroy the tumour cells. Antibacterial surfaces incorporating photocatalytic or biocidal nanoparticles reduce the risk of infection in doctors' offices and public buildings. Portable testing kits allow for self-monitoring and speedy diagnosis. New contrast agents and visualization tools provide a closer look at cellular processes. But this, too, is nanotechnology in action: nanoparticulate steroids are introduced into the body's own red blood

cells; as the cells die their natural deaths, the steroids are released to the body in very small doses, thus minimising, if not excluding the side-effects of many steroid treatments. These examples and many more of ongoing developments can be found in various reports on the prospects and promises of nanomedicine.

The application of nanotechnology in medical diagnostics can be categorised into *in-vitro* and *in-vivo*. Within *in-vitro* application, the ability to characterise cells or cell compartments are of paramount importance to Nanomedicine. Early diagnostic of diseases such as cancer, cardiovascular, lungs, neurodegenerative, infectious, orthopaedic and diabetic are expected to benefit from the developments in nanotechnology within the next few decades. The complexity of cancer detection involves the analysis of a spectrum of molecular and cellular processes – due to genetic changes in specific cells. Highly efficient nanomarkers and quantum dot detection technologies should help with early detection leading to the reduction of mortality rates and the amelioration of a patient's quality of life. In addition, with the aid of specifically engineered nanodevices which have the ability to pass biological barriers, it should be possible to deliver highly concentrated drugs directly and locally to cancer cells in a swift and highly effective manner. Similarly, in respect to neurodegenerative diseases, due to an improved understanding of how the brain functions, nanotechnology offers better diagnosis and treatments for diseases such as Multiple Sclerosis, Alzheimer's and Parkinson's disease. Finally, nanotechnology offers opens the doors to an advancement in molecular imaging too (also called nanoimaging) leading to the detection of a single cell in a complex biological environment (Loo *et ai* 2004).

### **NANOTECHNOLOGY VS. NANOMEDICINES**

Nanomedicine has been an important part of nanotechnology from the very beginning. And since nanotechnology began as a visionary enterprise, nanomedicine started by applying mainly nanomechanical concepts to the body. 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. The 2004 presentation of the cancer nanotechnology initiative in the United States revolves around the goal of “eliminating death and suffering from cancer by 2015” (Robert, 2004). The 2006 European Technology Platform on Nanomedicine is more subtle than this. It speaks of a “revolution in molecular imaging in the foreseeable future, leading to the detection of a single molecule or a single cell in a complex biological environment.” This statement elegantly glosses over the fact that the problems of detecting molecules and cells are magnitudes apart: Cells are a hundred to a thousand times larger than molecules and it is certainly much easier to imagine a contrast agent or marker attached to or inside a cell. The most balanced overview of nanomedicine to date is the European Science Foundation's 2006 Forward Look on Nanomedicine. volves molecular tools for the diagnosis and treatment of disease. Nanomedicine, in other words, is diseasecentred, trying to do better and on a molecular level what physiology, pathology, and the various specialised medical sciences have been doing so far. Because it is disease-centred, nanomedicine leaves to medical nanotechnologies the more general and perhaps more profound transformations of health care. By the same token, nanomedicine inherits its focus on certain diseases from ongoing medical research. Accordingly, it is primarily concerned to reduce mortality from non-infectious disease, especially cancer. That is, it aims to incrementally reduce mortality where it is already low, namely in the highly developed world where cancer and coronary disease have become the most prominent physiological causes of death.

The objective of this review is to explain what nanotechnology is and how it can be used in the field of health care system. Applications such as drug delivery system, tissue reconstruction and disease diagnosis shall be discussed. In addition to this, the report will outline some of the problems with using this technology.

### **NANOTECHNOLOGY TOOLS**

Different methods for the synthesis of nanoengineered materials and devices can accommodate precursors from solid, liquid or gas phases and encompass a tremendously varied set of experimental techniques. There are two main approaches for the synthesis of nano-engineered materials. They can be classified on the basis of how molecules are assembled to achieve the desired product.

#### **1. Top – down technique**

The top – down technique begins with taking a macroscopic material (the finished product) and then incorporating smaller scale details into them. The molecules are rearranged to get the desired property. This approach is still not viable as many of the devices used to operate at nanolevel are still being developed.

#### **2. Bottom – up approach**

The bottom – up approach begins by designing and synthesizing custom made molecules that have the ability to self- replicate. These molecules are then organized into higher macro- scale structures. The

molecules self replicate upon the change in specific physical or chemical property that triggers the self replication. This can be a change in temperature, pressure, application of electricity or a chemical. The self replication of molecule has to be carefully controlled so it does not go out of hand (Donaldson, 2004).

## APPLICATION OF NANOMEDICINES IN HEALTH SYSTEM

### **Drug Delivery System**

During the past two decades, targeted drug delivery has been identified as of paramount importance to improve drugs efficacy. Ideally, targeted drug delivery would improve the stability and absorption within the target tissue whilst paving the way for a reduction in the frequency of drug administration and improving patient comfort. Novel targeted drug delivery systems must first work to prevent degradation of peptides and proteins *in vivo* into harmful by-products. The most preferred route by patients for drug delivery is the peroral route. However there are problems because a number of drugs are protein or peptide-based which degrade in the stomach. At present, protein drugs are usually administered by injection, but this route is less accepted by patients and also poses problems of fluctuating drug concentrations in the blood. Drugs that are developed through Nanotechnology will have advantages over other normal drugs i.e. arrival at appropriate concentrations at the target tissues without a major loss of their therapeutic efficacy whilst in circulation. Targeted systems may be passive or active to diseased tissues which show exploitable and unique pathophysiological conditions. In passive targeting, the aim is for the drugs, for example in cancer therapy, to accumulate in tumours as a result of increased blood vessel permeability combined with an impaired lymphatic drainage in tumours which allows a much better permeability and retention effect of the nanosystems within drug delivery. The tendency of nanosystems to specifically pinpoint the immune system also displays an excellent opportunity for passive targeting of drugs to the macrophages present in the liver and spleen. Thus, this natural system can be used for targeting drugs to intracellular infections. On the other hand, in active targeting the chemicals are bonded to the surface of the drug carriers that can selectively attach to diseased cells. The different drug carriers in this case include nanoparticles, nanocapsules, lipoproteins, liposomes, micelles and dendrimers, which can be engineered in such a way to react with certain stimuli, such as changes in temperature or pH, once they have reached their intended destinations. Water penetration into the drugs is prevented by the barrier membrane until the drug has reached its intended organ.

**Nanotherapeutics** can often be multifunctional, namely a single molecule can permit detection, diagnosis, transport and the controlled release of drugs. This is because many of the nanoparticles with an enlarged surface area to volume ratio can be functionalised with several different molecules simultaneously—such as DNA, RNA, targeting molecules and peptides. With advances in nanotechnology based drug delivery, many promising smart drugs can be engineered to pass the blood-brain barrier (tightly segregates the brain from the circulating blood) to treat neurological disorders too. In the future, a nanoparticle or a combination of nanoparticles may be designed to search for and destroy a single diseased cell which is a leap forward for preventative medicine. Another use for nanoparticles is in tissue engineering, e.g. for the delivery of cytokines to control cellular growth and to stimulate regeneration. Recent advancement in micro-electromechanical systems (MEMS) has enabled the production of controlled-release microchips which intrinsically links MEMS with nanoparticles in targeted drug delivery. These chips have many advantages namely: 1.They can control the storage and release many chemicals including highly potent drugs. 2.The chemical is easily released locally through the disintegration of the barrier membrane with the aid of an electric potential (Sahoo *et al* 2004).

**Nanobots** are robots that carry out a very specific function and are just several nanometers wide. They can be used very effectively for drug delivery. Normally, drugs work through the entire body before they reach the disease-affected area. Using nanotechnology, the drug can be targeted to a precise location which would make the drug much more effective and reduce the chances of possible side-effects. Medical nanorobots can be of great importance in easy and accurate correction of genetic defects, and help to ensure a greatly expanded health span. More controversially, medical nanorobots might be used to enhance natural human capabilities. A great advantage of using nanobots for drug delivery is that the amount and time of drug release can be easily controlled by controlling the electrical pulse [Robert, 2004]. Furthermore, the walls dissolve easily and are therefore harmless to the body.

**Nanoshells** are nanoparticle beads that consist of core and shell such as silica core covered with a thin gold shell. By changing the thickness of the core and the outer shell, one can make these beads absorb and scatter specific wavelengths of light. Therefore, through the use of laser light, we might be able to treat cancerous cells inside the body because the energy can pass through the healthy tissue (leaving cells intact) whilst targeting tumour cells.

**Nanotubes** are a molecular form of carbon atoms that were discovered in the late 1980s. Carbon nanotubes have been widely promoted in industrial sectors because they are 100 times stronger than

steel yet a sixth of the weight with unusual heat and conductivity properties. In cancer therapy, carbon nanotubes have primarily been used for transporting DNA into a cell and for thermal ablation therapy..

**Gene Therapy** is a method that has been recently introduced for treatment or prevention of genetic disorders by correcting defective genes responsible for diseases. At the moment, the most common approach for correcting faulty genes is inserting the normal gene with the genome to replace a malfunctioning gene (through homologous recombination) or repairing the malfunctioning gene through selective reverse mutation to return the gene to its normal function. Novel nanoparticles have already been tested to transport plasmid DNA and gold nanoparticles, tagged with small lengths of DNA, to detect a particular genetic sequence in a sample [3].

**Vaccination** Mucosal immunity is crucial in the prevention of diseases but is affected by both degradation of the vaccine and insufficient uptake by the body. However, recent advances in encapsulated drugs and the testing on animal models have demonstrated that nanoparticles are capable of improving immunisation. Recent studies show that M-cells in the Peyer's patches of the distal small intestine are capable of engulfing large nanoparticles hence highlighting the benefits of nanoencapsulation (Silva, 2005 and Weiss, 2005).

## DIAGNOSIS OF DISEASES AND

### PREVENTION *a. Diagnosis*

Nanobiotech scientists have successfully produced microchips that are coated with human molecules. The chip is designed to emit an electrical impulse signal when the molecules detect signs of a disease. Special sensor nanobots can be inserted into the blood under the skin where they check blood contents and warn of any possible diseases. They can also be used to monitor the sugar level in the blood. Advantages of using such nanobots are that they are very cheap to produce and easily portable (Robert, 2004).

### *b. Quantum dots*

Quantum dots are nanomaterials that glow very brightly when illuminated by ultraviolet light. They can be coated with a material that makes the dots attach specifically to the molecule they want to track. Quantum dots bind themselves to proteins unique to cancer cells, literally bringing tumors to light (Kelly and Kim, 2006).

### *c. Preventing diseases*

#### **A. Heart-attack prevention**

Nanobots can also be used to prevent heart-attacks. Heart-attacks are caused by fat deposits blocking the blood vessels. Nanobots can be made for removing these fat deposits (Robert, 2004). The following figure shows nanobots removing the yellow fat deposits on the inner side of blood vessels.

Nowadays, cardiac diseases are the major cause of death and disability in developed countries. Even more people are dying of various cardiac problems including atherosclerosis, myocardial infarction, arrhythmias, ischemic heart disease and restenosis (the obstruction of an artery after procedures such as balloon angioplasty). Although we have already succeeded in developing microscale instruments to open blocked arteries and treat other cardiovascular diseases, these tools are cumbersome and prone to infection. Applications of nanotechnology to cardiovascular diseases including the non-invasive diagnosis and targeted therapy of atherosclerotic plaque are now under investigations. Devices to monitor blood clots can have a high impact in the diagnosis and treatment of stroke and embolisms. In this case, implantable devices could detect changes in conditions (e.g. nanoscale sensors like quantum dots, nanocrystals, and nanobarcodes) and transmit biological data or receive anticoagulants (or even clotting factors). Nanotechnology may also help in revealing the mechanisms involved in cardiac diseases, at a molecular level, so that machines can be devised limitation biological systems to overcome the root cause of the diseases. In regards to the lungs, research into viable targeted drug delivery needs to overcome the barrier between capillary blood and alveolar air and the digestion of protein drugs by proteases.

#### **B. Cancer treatment**

Nanomaterials have also been investigated into treating cancer. The therapy is based on "cooking tumors" principle. Iron nanoparticles are taken as oral pills and they attach to the tumor. Then a magnetic field is applied and this causes the nanoparticles to heat up and literally cook the tumors from inside out (Donaldson *et al*, 2004, Adhikari, 2005 ).

**Tumour diagnostics** and prevention is the best cure for cancer, but failing that, early detection will greatly increase survival rates with the reasonable assumption that an in situ tumour will be easier to eradicate than one that has metastasized. Nanodevices and especially nanowires can detect cancer-related molecules, contributing to the early diagnosis of tumour. Nanowires having the unique properties of selectivity and specificity, can be designed to sense molecular markers of malignant cells. They are laid down across a microfluidic channel and they allow cells or particles to flow through it. Nanowires can be coated with a probe such as an antibody or oligonucleotide, a short stretch of DNA that can be used to



recognize specific RNA sequences. Proteins that bind to the antibody will change the nanowire's electrical conductance and this can be measured by a detector. As a result, proteins produced by cancer cells can be detected and earlier diagnosis of tumour can be achieved.

Nanoparticle contrast agents are being developed for tumor detection purposes. Labeled and non-labeled nanoparticles are already being tested as imaging agents in diagnostic procedures such as nuclear magnetic resonance imaging. Such nanoparticles are paramagnetic ones, consisting of an inorganic core of iron oxide coated or not with polymers like dextran. There are two main groups of nanoparticles: 1) superparamagnetic iron oxides whose diameter size is greater than 50 nm, 2) ultrasmall superparamagnetic iron oxides whose nanoparticles are smaller than 50nm<sup>25</sup>. Moreover, quantum dots being the nanoscale crystals of a semiconductor material such as cadmium selenide, can be used to measure levels of cancer markers such as breast cancer marker Her-2, actin, microfibril proteins and nuclear antigens

**Tumour treatment** can be succeeded with nanoscale devices (such as dendrimers, silica-coated micelles, ceramic nanoparticles, liposomes). These devices can serve as targeted drug-delivery vehicles capable of carrying chemotherapeutic agents or therapeutic genes into malignant cells. As an example, a nanoparticle-based drug called "Abraxane", consisting of paclitaxel conjunctive to protein albumin particles, was approved by the Food and Drug Administration for breast cancer treatment a year ago (Donaldson *et al*, 2004, Adhikari, 2005).

### **C. Tissue Reconstruction**

Nanoparticles can be designed with a structure very similar to the bone structure. An ultrasound is performed on existing bone structures and then bone-like nanoparticles are created using the results of the ultrasound (Silva, 2005). The bone-like nanoparticles are inserted into the body in a paste form (Adhikari, 2005). When they arrive at the fractured bone, they assemble themselves to form an ordered structure which later becomes part of the bone.

Another key application for nanoparticles is the treatment of injured nerves. Samuel Stupp and John Kessler at Northwestern University in Chicago have made tiny rod like nano-fibers called *amphiphiles*. They are capped with amino acids and are known to spur the growth of neurons and prevent scar tissue formation. Experiments have shown that rat and mice with spinal injuries recovered when treated with these nano-fibers.

### **NANOPARTICLES AFFECTED HEALTH SYSTEM**

The risk of nanoparticles to the health of human beings is of far greater concern, but Nanoparticles are likely to make contact with the body via the lungs, intestines and skin (Hoet, 2004, NewMednet, 2004).

#### **1. Risk to Lungs**

Nanoparticles are very light and can easily become airborne. They can easily be inhaled during the manufacturing process where dust clouds are a common occurrence. Particles passing into the walls of air passage can worsen existing air disease such as asthma and bronchitis and can be fatal.

#### **2. Effects on Brain**

Some nanoparticles that are inhaled through the nose can move upward into the base of the brain. This may damage the brain and the nervous system and could be fatal.

#### **3. Problems in Blood**

Nanoparticles flowing thorough the bloodstream may affect the clotting system which may result in a heart-attack. If these nanoparticles travel to organs like the heart or the liver, they may affect the functionality of these organs.

### **THE FUTURE SCENARIO OF NANOMEDICINE**

Nanotechnology is beginning to change the scale and methods of vascular imaging and drug delivery. Indeed, the NIH Roadmap's 'Nanomedicine Initiatives' envisage that nanoscale technologies will begin yielding more medical benefits within the next 10 years. This includes the development of nanoscale laboratory- based diagnostic and drug discovery platform devices such as nanoscale cantilevers for chemical force microscopes, microchip devices, nanopore sequencing, etc . . The National Cancer Institute has related programs too, with the goal of producing nanometer scale multifunctional entities that can diagnose, deliver therapeutic agents, and monitor cancer treatment progress. These include design and engineering of targeted contrast agents that improve the resolution of cancer cells to the single cell level, and nanodevices capable of addressing the biological and evolutionary diversity of the multiple cancer cells that make up a tumor within an individual. Thus, for the full in vivo potential of nanotechnology in targeted imaging and drug delivery to be realized, nanocarriers have to get smarter. Therefore, it is essential that fundamental research be carried out to address these issues if successful efficient application of these technologies is going to be achieved. The future of nanomedicine will depend on rational design of nanotechnology materials and tools based around a detailed and thorough understanding of biological processes rather than forcing applications for some materials currently in

vogue. The approaches to nanomedicine range from the medical use of nanomaterials to nanoelectronic biosensors, and even possible future applications of molecular nanotechnology. The basic aim of molecular nanotechnology would be to conduct balanced chemical reactions in positional controlled locations and orientations and then to build systems by assembling the byproducts of these reactions (ECV, 2005).

## CONCLUSION

Nanotechnology can offer diagnostic tools of better sensitivity (through nanoelectronics and implantable nanodevices), specificity and reliability. It also offers the possibility of integrating many devices into one single miniaturised device that can transmit data externally to a practitioner or be used autonomously by a patient. Early diagnosis will also be possible with 'smart' materials which allow early stimulation of the body's own self-healing processes as being the key in regaining health. Nanomedicine is a new age phenomenon which the international medical community is eagerly looking forward to come into full swing. The ever increasing demands and challenges that the present medicine field is posing can be met by nanomedicine. The stakes are high and the need is ours, so all we need is to embrace innovations. Overall, to say that nanomedicine and molecular nanotechnology, in their best light, could lead humankind and the planet to a new era of health and longevity is not an exaggeration. If everything runs smoothly, nanotechnology will one day become part of our everyday life and will help save many lives.

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