

**THE DEVELOPMENT OF MODERN SCIENCE:  
NANOTECHNOLOGY IN MEDICINE**

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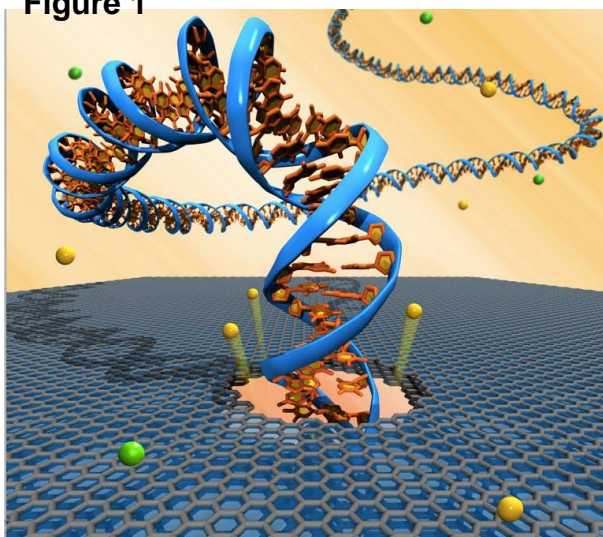
## Abstract

One of the fastest developing modern sciences in the 21<sup>st</sup> century is nanotechnology in medicine. Nanotechnologies have many major impacts in the developing treatments for diseases, drug delivery and cell reparation. The approaches to nanomedicine can be change from the use of nanomaterials to nanoelectronic biosensors, and even future development of molecular nanotechnology. On the other hand, there is great debate regarding to what extent nanotechnology will benefit or pose risks for human health. Nanoparticles can be used for CNS gene therapy. Nanomaterials can improve the safety and efficacy of such devices. Nano-engineered probes can deliver drugs at the cellular level using nanofluidic channels. There is some concern about the safety of nanoparticle entry in the brain and this need to be resolved before human use. In this paper, I am going to explore into general nanomedicine with its ethnical issues and potential risks, and also its future developments to overcome the current negative aspects.

## Introduction

Nanotechnology is an area of modern science that is on an extremely miniature scale; often described as a nanoscale level; where techniques are being developed to probe and manipulate single atoms and molecules. 'Nano' is the Greek word for midget and it means  $10^{-9}$  which is a billionth part. On scalable terms, a nanometer is about 3 atoms, and the human's hair has a diameter of 200 000 nm.

The treatment, diagnosis, monitoring, and control of biological systems using nanotechnology have been termed 'nanomedicine' by the National Institutes of Health (NIH). It is widely developed in all areas of science, especially in the recent years the development of nanotechnologies for medical applications has become a priority of the NIH. On the official website of the NIH, their research in Nanomedicine has been reported, as stated between 2004 and 2006, they established a network of eight Nanomedicine Development centers as a part of the NIH Nanomedicine Roadmap Initiative. Currently there is a second phase under development, the fundamental knowledge and developed tools will be applied to understand and treat diseases. The centers are continuing to expand knowledge on the basic science of nanostructures in living cells and they are gaining the capability to work with biological nanostructures, and then the research can focus on specific target diseases like cancer. In 2005, the National Cancer Institute (NCI) committed 144.3 million over 5 years for its 'Alliance for Nanotechnology in Cancer' program which funds seven centres of Excellence for Cancer Nanotechnology (Kim, 2007). The funding supports range of different research projects in areas of diagnostic, devices, biosensors, micro fluidics and therapeutics.

**Figure 1**

Nanotechnologies are used to design multi-functional and multi-analyte diagnostic systems which are not only to define the changing state of an early stage disease, but it allows the identification of unique biological molecules as well. The current work on nanotechnology is on nanotubes which are folded sheets of carbon atoms; they are 100 times stronger than steel and one sixth the weight of steel. As the scale is extremely tiny, there are atomic force microscope and laser tweezers which allows manipulation of the atoms. The latest research is in platinum electrode on AFM that are 1/100nm,

gearwheels that will form 'nanobots', and 'nanopore' device to analyse DNA. It is very useful to analyse DNA, "The first mapping of the human genome - where the content of the human DNA was read off ('sequenced') - was completed in 2003 and it cost an estimated 3 billion US dollars. Imagine if that cost could drop to a level of a few 100 euro, where everyone could have their own personal genome sequenced. That would allow doctors to diagnose diseases and treat them before any symptoms arise." Professor Cees Dekker of the Kavli Institute of Nanoscience at Delft explains. Figure 1 is a model of a nanopore, it shows the DNA sequence being analysed.

This paper is going to discuss on the development of nanomedicine in neurological disorders treatment, it focuses on drug and gene delivery and targeting to particular sites in the nervous system. It is also going to discuss on the risks and danger of using nanotechnology. The research team of University of Michigan has developed a tool to diagnose and treat the most virulent forms of brain cancer. That is 20 to 200 nanometer diameter nanoparticles; they dubbed Probes Encapsulated by Biologically Localized Embedding (pebbles). They designed the pebbles to carry a variety of agents on their surface, each with a unique function.

"The World Health Organization has indicated that CNS disorders are the major medical challenge of the 21st Century, yet treatments for most CNS disorders are either inadequate or absent. The CNS is the most challenging frontier for drug discovery largely because of the complexity of the brain and the existence of the BBB" Alan Palmer, Chief Executive of Pharmidex, UK

## Discussion

### Central Nervous System

The delivery of drugs to central nervous system (CNS) is a massive challenge in the treatment of neurological disorders. Drugs can be either administered directly into the CNS or systematically; for example, intravenous injection; for targeted action in CNS, but carries significant risks in terms of infection as well as being invasive and unpleasant for the patient. One of the main difficulties in drug delivery is the blood-brain barrier (BBB) which limits the access of drugs to the brain substance. One of the possibilities to overcome this barrier is to use nanoparticles. The understandings of the cells of the BBB have improved drug delivery to the CNS a lot. There have been many different strategies used for manipulating the BBB for delivery to the brain, e.g. osmotic and chemical opening of the BBB as well as the use of carrier systems. This is the use of nanoparticles small enough to penetrate the BBB, ultrasonic adjunctive drug treatment, and stem-cell and gene therapy, which effectively provide cell regeneration within the central nervous system itself. Newer delivery methods such as transdermal drug delivery which can employ nanotechnology to increase absorption and bioavailability, as well as being non-invasive and simple to use are on the rise, and seems useful for a wide range of CNS disorders, including psychoses, pain and neurodegenerative disorders. In the future, the aim can be modification of existing drugs to increase BBB penetration.

The most probable mechanism is endocytosis by the epithelial cells lining the brain blood capillaries. An advantage of a nanotechnological approach is that it allows the design of the active drug to be tailored for maximal efficacy. Currently, most nanoengineered systems for crossing the BBB take advantage of drugs that are already in clinical use and therefore have greater potential for reaching the clinic relatively quickly. In addition to the delivery of drugs and other compounds across the BBB for therapeutic purposes, the ability to cross the BBB selectively and efficiently in animal models using nanoengineered technologies will have a significant impact on research that focuses on the normal physiology of the CNS, by allowing targeted studies of specific cells and processes using methods that take advantage of the intact live organism.

As previously mentioned, nanoparticles can be used as carrier systems to overcome the BBB and deliver specific medications to regions of the brain that cannot be accessed normally. The surfaces can be coated with certain materials so that they can pass the BBB and transport to the sites where they are needed. This means that the nanoparticle carrier systems can distribute medications spatially and temporally in the brain and help cure diseases that were previously untreatable. This enables a tissue-specific addition of drugs, special depot effects and overcomes the body's own barriers such as the BBB. This would allow stronger concentrations of medications to be applied with improved effects. This is a booming research and development field and shows ever greater promise in treating diseases such as Alzheimer's, Parkinson's or certain brain tumors.

## Risks in nanotechnology

In general, there are many risks and dangers in the development of nanotechnology. 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. 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 which can also be fatal. Nanoparticles flowing through 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 most recent controversial topic is on the toxicity of the nanoparticles. Because of their ultra-small size, nanoparticles can penetrate cell membranes and integrate themselves into larger molecules. They can resist cellular defense systems but are large enough to interfere with cell processes. Nanoparticles are useful but can also be considered as toxic, thorough testing on the safety of nanoparticles, there are risks of them being absorbed through the skin. When used for remediation, their release in the environment is also risky due to possible exposure to humans and other animal species. In a press release on April 17, 2007, the American Association for Cancer Research reported research presented at the 2007 annual meeting that suggests nanoparticles could cause cancer and should be thoroughly investigated and used with caution. Researchers at the University of Massachusetts studied two types of nanoparticles, and found an increase in DNA damage, single and double-stranded breakages. Although DNA breakages do not necessarily mean a substance is cancer-causing, it is widely accepted that chemicals causing DNA damage are highly likely to promote mutations which can lead to cancer. There can be potential solutions in order to solve these risks. Modifications to the carbon surface of nanotubes for carrying drugs, making them more soluble can reduce their toxicity. Bucky balls can be modified to reduce free radical formation and make them less toxic.

Apart from the risks, there have been ethical issues globally about unequal access to technology; many developing countries cannot get the access to the nanomedicine and treatments. The major problem is the uneven balance of economy around the world, theoretically if all countries have the same amount of wealth, nanotechnology can be developed in every country, and however in reality this is not possible. The only solution to the problem is to try and balance the world's economy and development; the developing countries should have to opportunity to gain assistance from advanced countries in order to improve the health standards equally.

The moral issues arise from the practical use of the nanotechnology. Nanoscale science involves synthetic biology like the construction of artificial organisms and genetic modification. Many suggest that it is a promotion for biological weapons development. Atomic weapons can now be more accessible and made to be more powerful and more

destructive. These can also become more accessible with nanotechnology. Since these particles are very small, problems can actually arise from the inhalation of these minute particles, much like the problems a person gets from inhaling minute asbestos particles.

## Conclusion

The blood-brain barrier is the most important factor limiting the development of new drugs for the central nervous system. The BBB is characterised by relatively impermeable endothelial cells with tight junctions, enzymatic activity and active efflux transport systems. It effectively prevents the passage of water-soluble molecules from the blood circulation into the CNS, and can also reduce the brain concentration of lipid-soluble molecules by the function of enzymes or efflux pumps. The BBB only permits selective transport of molecules that are essential for brain function. Strategies for nanoparticle targeting to the brain rely on the presence of and nanoparticle interaction with specific receptor-mediated transport systems in the BBB. There are possible promising strategies that can be used in drug delivery to the central nervous system in the future, it is important to investigate in nanoparticles for drug delivery specifically across BBB.

There can be many developments in the future as nanotechnology is still in its early stages. As further research continues in this field, more treatments will be discovered. Many diseases that do not have cures today may be cured by nanotechnology in the future. Some of the concerns were also discussed but with proper care these problems can be avoided. The advancement in nanotechnology should continue because this field promises great benefits, but testing should be carried out to ensure the safety of the people.

## References

1. Silva GA (2007) Nanotechnology approaches for drug and small molecule delivery across the blood brain barrier.
2. Silva, GA (2004) Introduction to Nanotechnology and Its Applications to Medicine.
3. Nanotechnology news, articles and information  
<http://www.naturalnews.com/nanotechnology.html>
4. NIMH Research in Mental Health <http://www.nimh.nih.gov/index.shtml>
5. Nanotechnology applications and approaches for neuro-regeneration and drug delivery to the central nervous system. <http://www.ncbi.nlm.nih.gov/pubmed/20633128>
6. Nanotechnology and Medicine <http://www.nanotechproject.org/inventories/medicine/>
7. Nanowerk Spotlight [http://www.nanowerk.com/phpscripts/n\\_spotlight.php?cat=risk](http://www.nanowerk.com/phpscripts/n_spotlight.php?cat=risk)
8. Department of Health and Human Services  
<http://grants.nih.gov/grants/guide/pa-files/PA-08-052.html>
9. Nanotechnology Project <http://www.nanotechproject.org/>
10. Nanomedicine and Disease  
<http://biotech.about.com/od/nanotechnology/a/nanomedicine.htm>
11. Benefits of Nanotechnology in Cardiovascular Surgery  
<http://www.touchcardiology.com/articles/benefits-nanotechnology-cardiovascular-surgery-a-review-potential-applications>
12. New Nanopore Device to Analyze Single DNA Molecules  
<http://www.azonano.com/news.asp?newsID=20732>
13. Editorial Future Medicine – Nanomedicine (2006), KK Jain, Role of nanotechnology in developing new therapies for disease of the nervous system 1(1), 9-12