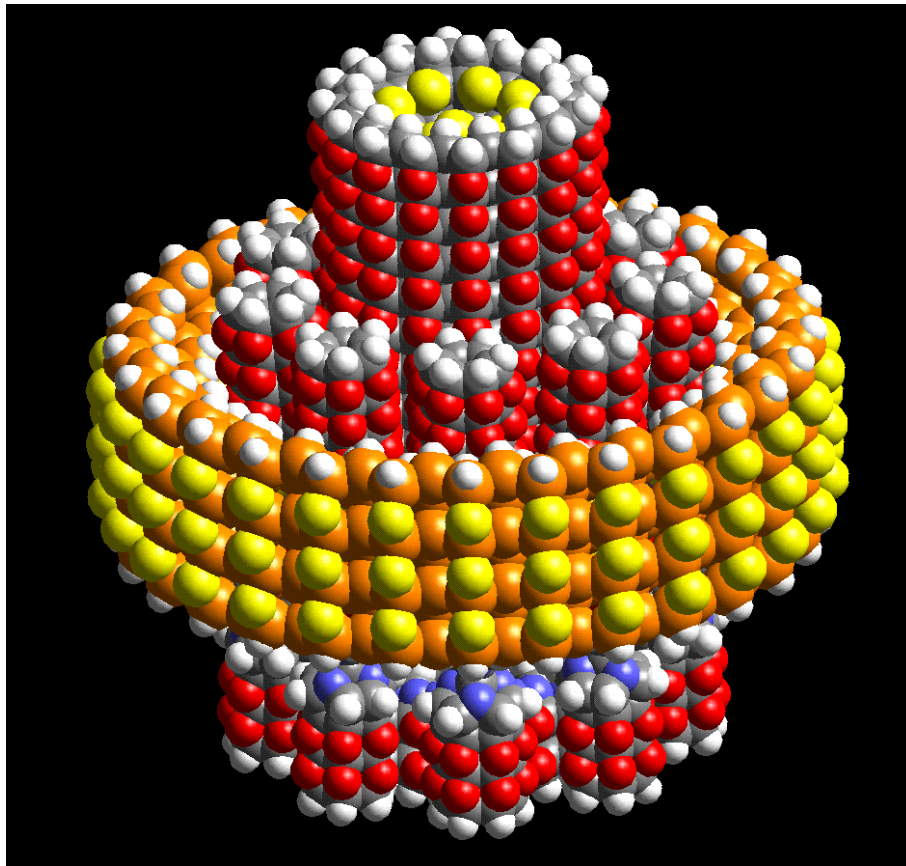


Exploring advancement in Nanotechnology research which may lead to the discovery of a cure, improved treatments and accurate methods of diagnosis of cancer.



By

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## Abstract.

This article is aimed at exploring the current advancement in nanotechnology research which could lead to the discovery of a cure, improved treatments and accurate methods of the diagnosis of cancer. From the review of previous studies I am able to conclude that nanotechnology could revolutionize the treatment of cancer; however more research is needed to really know the full uses of nanotechnology in cancer research.

## INTRODUCTION

Nanotechnology is an essentially modern scientific field of research that is constantly evolving as commercial and academic interest continues to increase and as new research is presented to the scientific community. The field's simplest roots can be traced, albeit arguably, to 1959 but its primary development occurred in both the eighties and the early nineties. This early history is most importantly reflected in the initial vision of molecular manufacturing. Overall, an understanding of development and the criticism of this vision is integral for comprehending the realities and potential of nanotechnology today (Center for Responsible Nanotechnology website; Wikipedia).

What is Nanotechnology? Nanotechnology is the ability of manipulating matter on an atomic, molecular and supra molecular scale of 1 to 100nm for the sole purpose of understanding, creating and using material structures, devices and systems with fundamentally new properties. The goal of nanotechnology can be described as the ability to assemble molecules into objects hierarchically along several length scales and to disassemble objects into molecules (Center for Responsible Nanotechnology website; Wikipedia).

Nanotechnology is a multi disciplinary field undergoing explosive research developments, in areas such as, Tissue engineering using nanoscaffolds; disease-malfunctioning at cell level; post surgery pain treatment; hybrid electronic and biological systems; targeting drugs using biological computer to fight cancer. The foundation of nanotechnology has emerged over many decades of research in multi disciplinary fields. As a result of the decades of research, computer circuits have been getting smaller; chemicals have been getting more complex. Biochemists have learned more about how to study and control the molecular basis of organisms due to the ability to build molecules from bottom up. Mechanical engineering has been getting more precise. According to Roco (2003), the United States has initiated a multidisciplinary strategy for the

development of science and engineering fundamentals through the National Nanotechnology Initiative (NNI). Japan and Europe have broad programs and their current plan looks ahead four to five years. More than 35 countries have developed programs in nanotechnology since 2000, illustrating the importance of this field of research. The use of nanotechnologies in medicine has provided many medical breakthroughs such as drug delivery and tissue engineering. Some of the medical nanotechnology applications are for diagnosis. These are used to assist in identifying DNA and helping detect genetic sequences. At the moment, lots of researches are being done in the creation of what is called smart drugs. The aim of smart drugs is to effectively target the areas that they need to target to effectively eradicate the cause of the ailment that the person is suffering from. As demonstrated by the work of Dana-Farber Cancer Institute (2010).

However, nanotechnology is still at an early phase of development, its future being hard to forecast. As a result of this, the Alliance for Nanotechnology in Cancer has identified the potential of nanotechnology, and aims to accelerate the application of nanotechnologies in cancer research and clinical development. The investments that they make in this direction are done with the hopes of finding breakthroughs that can help in the early detection, diagnostics, and treatment of cancer. This program encompasses both public and private sectors. The program comprises of eight Centres of Cancer Nanotechnology Excellence (CCNE), twelve platform projects, and four interdisciplinary training programs across the nation (NCI). Thus far, research programs within the Alliance have made remarkable advancements in nanotechnology-cancer research. The objective of this article is to explore some of the advancements in nanotechnology which may lead to a better, more effective treatment and diagnosis of cancer, or even a cure.

## **Discussion**

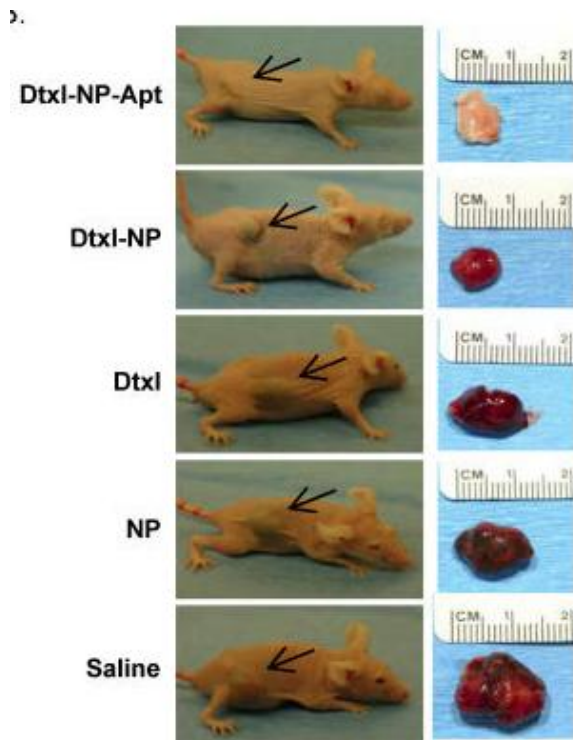
During the past decade, novel nanotechnology therapies have shown effective improvements to the therapeutic index of the cancer drugs by targeted delivery. Delivering the drugs right on target results in increased drug therapeutic effects and therefore reduced toxicity associated with the dose and the frequency of administration. Examples of nanotechnology therapies include liposomes, micelles, protein, and polymeric nanoparticles as explained by Beeta Ehdaie (2007).

As my research on nanotechnology is about cancer it is important to fully understand cancer and its causes. Cancer is a group of disease (around 200 in

total) caused by a growth disorder of cells. It is the result of damage to the genes that regulate mitosis and the cell cycle. This leads to uncontrolled growth of cells. As a consequence, a group of abnormal cells called a tumor, develops and constantly expands in size as illustrated by Toole.G and Toole.S (2008)

Beeta Ehdaie (2007, p.108), asserted that "Cancer has become the leading cause of death among Americans today". According to him statistics shows that in 2006, over 500,000 Americans died due to cancer. Furthermore, Beeta Ehdaie argued that the complexity of multiple cellular physiological systems such as cell signalling and apoptosis made it very difficult to understand cancer and its treatments therefore leaving only chemotherapy, radiation, and surgery as the common treatment. He argued further that some of the current challenges seen in cancer therapies today, including lack of early disease detection, non-specific systemic distribution, inadequate drug concentrations reaching the tumour, and inability to monitor therapeutic responses are a result of limitations in cancer treatment today. He identified poor drug delivery and residence at the target site as main reasons for complications, such as multi-drug resistance (Beeta Ehdaie, 2007, p.108).

Investments in Nanotechnology research have the potential to offer solutions to these current obstacles in cancer therapies, due to its unique size (1-100nm) and large surface area-to-volume ratios. Some of the properties of nanotechnology are the ability of self-assembly, stability, specificity, drug encapsulation and biocompatibility as a result of their material composition. Some of these properties of nanotechnology were tested by Farokhzad and Langer (2006). They tested the effect of aptamer-targeted nanoparticles for treatment of prostate cancer. This study illustrates that the novel approach of using aptamers as targeted ligands, on drug-encapsulated nanoparticles, is highly effective at targeting and decreasing the sizes of cancer cells. As aptamers are often nucleic acid which is able to bind to specific target molecules, this enables them to be effectively used in successfully targeting cancer cells. Aptarmers are important requirement in drug targeting due to their non-immunogenic and fairly stable nature with long circulation times in the body in conjunction with high affinity and specificity. This research demonstrated a decrease in approximately  $300\text{mm}^3$  to  $120\text{mm}^3$ , as seen in Figure 1.



**Figure 1**  
 Prostate Cancer cells were induced in mice using LNCaP (Lymph Node Carcinoma of the Prostate) prostate epithelial cells. Tumor development was allowed for 21 days in all conditions. Tumor masses were studied over a 109 day period. Saline was used as the control in this case. Results demonstrated that the docetaxel-nanoparticle-aptamers reduced tumor volume to 120 mm<sup>3</sup> from 300 mm<sup>3</sup>. The none-targeted docetaxel nanoparticles also reduced tumor mass, however not as significantly as the aptamer-targeted Nanoparticles.

Difference in tumor mass is visibly seen with images of the mice and corresponding tumors at the end point. Black arrows point to the position of the implanted tumor. (Source: Farokhzad et al. Figure copyrighted National Academy of Sciences, U.S.A. Permission obtained.)

Source: Langer and Farhrokzad (2006) in Beeta Ehdai (2007), Application of Nanotechnology in Cancer Research: Review of Progress in the National Cancer Institute's Alliance for Nanotechnology (p.109).

Tumour sizes from Figure 1 prove that the docetaxel-encapsulated nanoparticle-aptamer bioconjugates (Dtxl-NP-Apt) are more effective in reducing cancer growth when combined together. The Dtxl-NP-Apt was more effective due to their ability to bind to the PSMA (prostrate-specific membrane antigen) protein expressed on the surface of LNCaP prostate epithelial cells.

From Langer and Farhrokzad's experiments I am able to deduce that nanotechnology could possibly increase the effectiveness of current cancer treatments such as chemotherapy. This could be possibly done by encapsulating chemotherapy drugs in nanoparticles and using aptamers as targeted ligands. The encapsulated nanoparticle may also need to be coated with lipids or antibodies that are specific to the targeted cancer cells to help protect them from antibodies inside the cells recognising them as foreign. This approach could help minimise the side effects of chemotherapy drugs by specifically targeting only the cancer cells.

In addition to reducing tumour size, the targeting methods used by Langer and Farhrokzad had fewer side effects on healthy cells within the body due to the ability of the nano particles to deliver the drug to the exact location where it is needed in comparison to current methods of chemotherapy which are well known

for side effects such as hair loss because they affect other cells like hair cell which undergo rapid cell division. However the tests have been performed on rats and further research would be needed to attain the effects of the nanoparticles in the more complex environment of the human body.

Another possible way which cancer cells could be treated more effectively is by inserting microscopic synthetic rods called carbon nanotubes into cancer cells. When the rods are exposed to near-infra red light from a laser they heat up, killing the cell, while cells without rods are left unscathed. This aspect of nanotechnology is currently being researched by Researchers at Stanford University BBC (2005). In 2005 A BBC news headline stated that **"Nanotechnology has been harnessed to kill cancer cells without harming healthy tissue."**

According to this BBC (2005) article, the relatively small size of nanoparticles were useful in this research as the carbon nanotube used were only half the width of a DNA, allowing thousands of carbon nanotubes to fit inside the cell. Under normal circumstances, near-infra red light passes through the body harmlessly. Furthermore, the researchers found that if they placed a solution of carbon nanotubes under a near-infra red laser beam, the solution heated up to about 70°C in two minutes. With this knowledge the researchers decided to place the nanotubes inside normal cells. As expected they found out that the cells were quickly destroyed by the heat generated by the laser beam.

Consequently the researchers had to find a way to introduce the nanotubes into cancer cells, but not healthy cells. They did this by taking advantage of the fact that, unlike normal cells, the surface of cancer cells is covered with receptors for a vitamin known as folate. Coating nanotubes with folate molecules, makes it easy for them to pass into cancer cells, but unable to bind with their healthy cousins. This approach was duly effective as the exposure of the cancer cells to the laser successfully killed off the diseased cells, but left the healthy ones untouched. This treatment as proved more effective than existing treatments of cancer such as chemotherapy which destroys cancer cells and normal cells alike. However the use of near-infra red light could cause other problems such as denaturing of enzymes. The intense heat could denature enzymes of healthy cells around the cancer tumour as enzymes in the cells get denatured after 40°C. It could be possible to further refine the techniques by attaching an antibody to a nanotube to target a particular kind of cancer cell. The researchers have shown that near-infra red light can cause nanotubes to produce heat that can kill cancer cells. But their work so far has focused on cells that have been grown in culture in the laboratory. Further research will be crucial to see whether these effects can be reproduced in the more complex

environment of a tumour and, ultimately, the human body without introducing other problems such as denaturing enzymes that catalyse important reactions and processes around the health cells. The denaturing of enzymes could lead to a low immune system as the enzymes in the lymphocytes could be denatured. If the cancer cells are in the pancreas or bowel, the enzymes which catalyse reactions in the digestive system could get denatured and a bowel obstruction could occur as a result of the food being unable to be digested.

A number of the researches in nanotechnology currently being studied are investigating methods to overcome the challenges in maintaining drug circulation and avoiding multi-drug resistance. Due to chemical compositions and lack of targeting, many current therapeutic agents are removed from the body's circulation by the reticulo-endothelial system (RES) or immune system.

Examples of current researches which has made it possible not only to monitor and detect nanomaterials moving through the circulation, but also to detect single cancer cells tagged with carbon nanotubes, is the introduction of Raman spectroscopy. Dr. Alex Biris (2009) states that, "Until now, nobody has been able to fully understand and study in vivo and in real time how these nanoparticles travel through a living system," By using Raman spectroscopy in this way, clearance rate and their biodistribution kinetics of nanoparticles through the lymph and blood systems can be measured. However, it is very important to determine the danger of nano particles in the body as illustrated by a study on seven Chinese<sup>1</sup> factory workers developing severe lung damage from inhaling nanoparticles, this proves that there could be consequential damages induced by nanotechnology. This study raises the bar for doing appropriate research as fast as possible to find out where the dangers might lie when working with nanomaterials.

The use of Raman spectrometer was illustrated by the research of Biris and Zharov (2009). In their experiment a carbon nanotube material was inserted in a single human cancer cell and injected into the tail of a rat. They were able to use Raman spectrometer to track the circulation of the carbon nanotubes in the blood vessels to the rat's ear. This illustrates how nanotechnology can be used to enhance diagnosis. Raman's spectroscopy can be used to diagnose cancer because of its ability to provide specific molecular information about tissues. There is still extensive time needed for research into the ultimate utility for

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<sup>1</sup> Sited from <http://www.medindia.net/news/Inhaling-Nanoparticles-Could-Cause-Lung-Damage-56763-1.htm>.  
retrieved 7/3/11

these approaches and for human subject experiments. But this early work is exciting and provides long-term hope for more effective cancer treatments.

Nanotechnology is also overcoming challenges of early detection and imaging in current cancer therapies. Sathe *et al* (2006) in their study demonstrated the use of nanotechnology in cancer detection. Current detection methods are restricted in spectrum range, penetration depth, cell targeting, and signal/noise clarity. Through nanotechnology, highly sensitive and specific imaging agents are being developed with biocompatible and multi-functional properties. Emory university and Georgia institution of Technology has been focusing on the development of quantum dots to improve detection methods. In the study mentioned above, they developed dual-functioning beads comprised of quantum dots and iron oxide nano-crystals embedded in silica beads. These particles were able to target specific cells, due to the iron oxide crystals; they also have high imaging qualities, due to the quantum dot component. Bioconjugated quantum dots can be finely tuned to a myriad of different colors depending on the size of dots. This quantum dots can tag a multitude of different proteins or genetic sequences in a process called "multiplexing." This is possible by processing Bioconjugated quantum dots to consist of different sized dots embedded in tiny beads made of polymer material (Sathe et al 2006). Current research is being developed into the ideal combinations of iron oxides and quantum dots that would give the best imaging qualities. However, in early 2002, researchers at the University of California in San Diego revealed that cadmium selenide nanoparticles, also known as quantum dots, may cause cadmium poisoning in humans. Exposures to cadmium have been related to a significant increase in kidney stones, urinary tract cancer, and prostate cancer (Sathe et al 2006).

## **Conclusion**

Nanotechnology in medicine could be seen as the future of better health and as a result it is being actively used in creating a better drug delivery system that makes the absorption of the components of medication more effective. As thoroughly referenced above, Nanotechnology provides numerous opportunities for the discovery of a cure, improved treatments and accurate methods of diagnosing cancer. Variety of approaches, such as drug encapsulation, carbon nanotubes and Raman spectroscopy have been reviewed above with the sole aim of discovering a better more effective way of treating cancer.

In the process of trying to solve cancer using Nanotechnology, it is important not to neglect possible problems that could occur when Nanotechnology is used

in the body. During the course of my research I have uncovered different researches that could further increase the effectiveness of diagnosis, treatments and possible cure of cancer. However none of these experiments have been tested in the human body making it difficult to establish whether or not the results from these researches could provide a better treatment for cancer. Nanoparticles will require further development and clinical trials before they are ready for patient care. Companies such as nanobiotix are currently designing drugs that could specifically target cancer.

Some of the factors limiting the advancement in nanotechnology research are the lack of scientific recognition of the scientists involved in the research and the lack of public awareness to nanotechnology. The full potential of nanotechnology in the effective treatment of cancer could be discovered if more funding is awarded towards research in the treatment of cancer using nanotechnology.

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