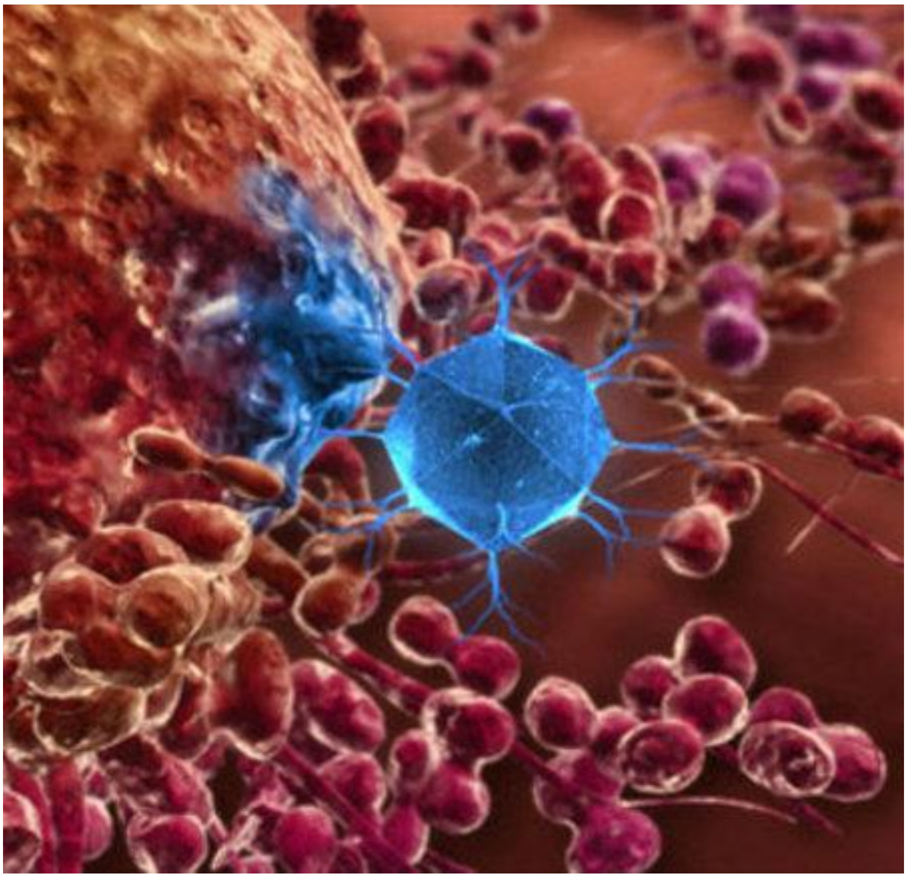
Nanotechnology
A Future in Medicine?



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ABSTRACT

Cancer is seen to be one of the most well-known groups of diseases, according to research by Cancer Research UK, 1 in 3 people will develop some sort of cancer in their lifetime. [1] It affects thousands of people each year, consequently leaving many left feeling helpless. Our project focuses on exploring current ways of diagnosing and treating cancer, as well as suggesting future methods of reducing the severity of this high profile disease with the use of the young discovery of nanoparticles. These future suggestions include replacing the gene that causes cancer to spread with a gene made up of nanoparticles, as well as using them to modify current drug delivery systems. We will also be considering the ethical and economical issues with the integration of nanotechnology in the future.

INTRODUCTION

Many scientists hope that nanotechnology will revolutionise treatment and diagnostics of all sorts of diseases. . [2] The previous Labour government provided Nanotech centres with £50 million to fund research. The latest research in Britain into the uses of nanotechnology in medicine is currently being conducted at North Bristol's NHS Trust, where they're using nanotechnology to construct a medical dressing which detects and treats infected wounds. The dress works by having the nanoparticles, which contain antibiotics, penetrate the skin which are then delivered to specific areas that need treatment. [5]. Nanotechnology is not only researched in England, in fact the biggest countries when it comes to the development of nanotechnology are Portugal and Spain. They have recently announced the construction of research centres that will initially receive an investment of $140 million. [3]. It seems as though the world is interested in nanoscience because it has many uses and possibilities which would hugely benefit different aspects of our lives, including aspects of medicine.

To gain a proper understanding of nanotechnology and its uses in medicine we must first learn about the history of this field of science. Nanotechnology is the science of all things small, down to the atomic scale. It was first thought of by famous physicist Richard Feynman. In 1959 he publicised his thoughts on the ability to manipulate individual atoms and molecules for the first time at the American physical society at the California Institute of Technology. Feynman now set two challenges. The first involved the construction of a nanomotor. [4] The second challenge was to reduce the size of letters of the Britannica encyclopaedia, so it could fit on the head of a pin. This established the basis for more research into the field of nanoscience.

The next important stage in the history of nanotechnology is the discovery of the nano scale, if this had not been found then what we know as nanotechnology today, might not exist. Therefore it can be said that biomolecular nanotechnology developed from Moore's law which was introduced in 1965 by Gordon Moore - one of the founders of Intel Corporation. This stated that the number of transistors that fit in a given area doubles every 18 months for the next 10 years. This concept exceeded these 10 years and continued to be used giving rise to much smaller scales such as the nanometre. This discovery is extremely important to the field of medicine as it allows us to delicately piece individual atoms together to form a fascinating new generation of diagnostics and treatments to ensure patients receive the best care. Therefore, nanotechnology is the manipulation of matter at an atomic scale of 10^-9. [8] To give an idea of how small this scale actually is, the diameter of a human hair is 200,000nm. [7]

The first scientist who greatly believed that nanotechnology could have uses in medicine was Eric Drexler. He wanted to use nanotechnology to diagnose and treat injuries and disease, due to the molecules negligible size; he thought that nanotechnology may be able to help in surgery. Drexler said “At present, medicine is unable to heal anything. It can help the body heal itself, but it can't, for example, take an incision and join the two sides together in such a way that the wound is healed as soon as it is closed". This quote explicitly suggests that nanotechnology has a potential use in medicine; however further developments are needed to ensure it’s completely safe and reliable for patients. Nanotechnology may also help diagnosing cancer earlier with more certainty. Drexler mentioned that "The immune system may not be able to recognize that a cancer cell is abnormal, because it's not able to look at enough different characteristics to identify the cell properly. If injected into the body, a nanomachine with an on-board computer could look at 20 different characteristics of a cell before doing anything to it". If this method of diagnosis becomes successful, nanotechnology can be the next innovation in medicine. [6]

The major medical uses of nanotechnology that scientists are currently researching into are its uses in diagnostics and treatment of cancer using drug delivery systems, which are normally made of Buckminster fullerenes.

A fullerene is any molecule that is composed of carbon atoms. The first fullerene to be discovered was Buckminster Fullerene, C60 (**see figure 1**) or informally known as “buckyballs” in 1985 by scientists at Rice University. [23] Due to their spherical structure they have the ability to carry substances inside them; making them ideal to use as a drug delivery system. Buckminster fullerene can be found in small quantities of soot. [23] In 2005, scientists from Cornell University discovered DNA buckyballs as a potential use of nanotechnology in a drug delivery system. To make DNA buckyballs, they used specially synthesised branched DNA – polystyrene hybrid which was able to construct a structure of the hollow balls of 400 nanometres (nm) in diameter and about 15 nm in length. 70% of the volume in DNA buckyballs is hollow; meaning they’re biodegradable and biocompatible, making them ideal for drug delivery systems. [24]

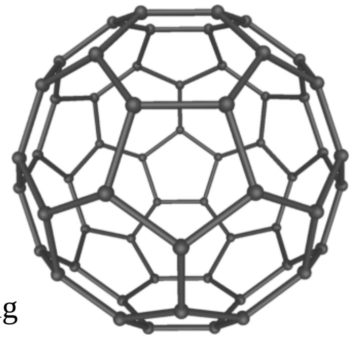

Figure 1 [25]

The definition of Cancer is the uncontrollable growth of a group of cells in the body. These cells will continue to grow, much quicker than normal body cells; their cell cycle of interphase and mitosis is much faster. [17] They then form a tumour which is a mass of cells. Death from cancer has two main causes. Either the tumour will disturb or dislodge vital organs as it gets bigger, or more commonly the tumour develops their own blood supply and diverts blood from their normal pathway. The four main treatments used to target cancerous cells are Surgery, Radiation therapy, Chemotherapy and biological therapies.

Surgery is the primary treatment if the tumour is localised. This normally involves cutting out the cancerous cells as well as a few healthy tissue to ensure all the cancer has been removed. However the issue with surgery is that it can't be done if the cancerous cells are spread all over the body, simply because the human body cannot withstand being opened up numerous times, therefore it isn't very useful for patients in this situation. [12]

This is where other therapies such as chemotherapy and radiation therapy are used. Chemotherapy involves the use of chemicals, intravenously or orally to kill cancerous cells, while radiation therapy uses high energy electromagnetic beams externally or radioactive seeds internally to kill cancerous cells. They can be used singularly as a treatment, or assist before and after surgery. The main issue with chemotherapy and radiation therapy is that they kill all cells regardless of them being normal or cancerous. Radiation therapy is more accurate, but it still kills normal cells. Therefore they can be potentially lethal in large doses. Other side effects include pain, diarrhoea, constipation, hair loss, nausea and blood related illnesses, such as immune deficiencies. [11]

The final therapy is Biological therapy. This is different to the others because it involves training the immune system to fight the cancer compared with destroying the cancerous cells with chemicals or radiation. It sounds perfect however it's not. The treatment only works if you are in quite an early, stable stage of cancer, and there are still some side effects to deal with such as flu like symptoms and low blood pressure.[13] So could nanotechnology be used to provide safer, more effective treatment for cancer?

DISCUSSION

We already know that nanotechnology has several different potential uses in medicine. The next steps are to make sure that nanotechnology works efficiently in treating injuries and diseases. In the future, one of the main uses of nanotechnology in medicine could be to treat. We have already mentioned the traditional methods of treating cancer however these are not always successful and surgery on such delicate areas such as the brain can lead to serious permanent damage for a patient. So how can nanotechnology help?

Currently this fascinating advancement of tiny atoms is being used to locate the cancerous cells and provide imaging so that doctors and surgeons can deliver anti-cancer drugs or operate if necessary. If detection, diagnosis and treatment for cancer are carried out using nanotechnology, the patient has a higher probability of survival. This is because the faulty replicating cells are destroyed and removed before symptoms start to show thus reducing the long term effects on the body.

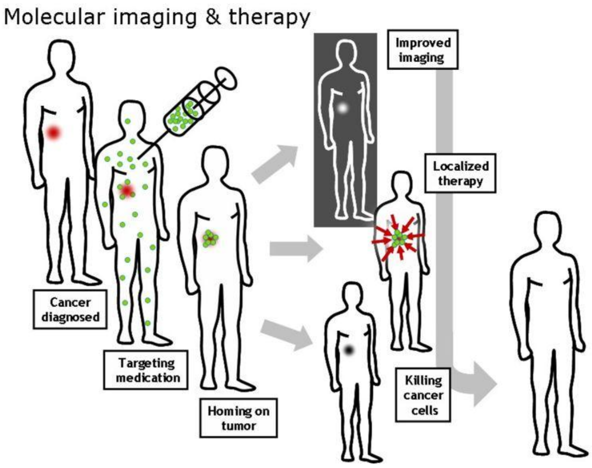

Figure2 [25]

Diagnostics of cancer using nanotechnology would involve using nanoparticles as sensors in the body. A patient is injected with fluorescent quantum dot nanoparticles which will travel around the body until they find and home in on a tumour. This mass of nanoparticles can be detected using Magnetic Resonance Imaging to provide a location of where the tumour is. Once the tumour is detected, a suitable treatment can be started. This is known as a “glowing tumour” (see **figure 2**). [21]

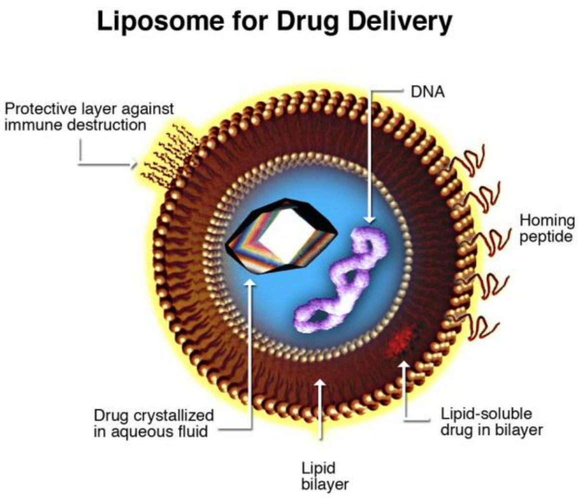

Figure 3 [27]

Nanoparticles can be used in the treatment of cancerous cells through using them as drug delivery systems. Drug delivery systems are systems that have the ability to target areas with abnormalities and treat them accordingly. For example, when it comes to cancer you can use a drug delivery system to specifically target the cancerous cells with an anti-cancer drug such as Vinblastine. Currently drug delivery systems will encapsulate the lipid soluble drug in a liposome. This consists of a lipid bilayer, with a protective layer to prevent an immune response, which would potentially destroy the system and release the drug into the body as shown in **figure 3.** The main issue with using liposomes is that they’re still large when it comes to treating cells in the body. Their size is in micrometres (x10-6). However nanoparticles are much smaller, they’re in nanometres (x10-9) therefore they can be used more precisely and effectively when targeting cancerous cells.

Moreover there have been recent discoveries of more effective and safer drug delivery systems which involve the use of gold nanoshells in a treatment known as photothermic treatment. Photothermic treatment is the use of electromagnetic radiation to target and destroy cancerous cells by heating via infrared radiation. The research into this treatment was carried out by Dr Zhifei Dai at the Harbin Institute of Technology, China. Dr Zhifei reported his findings in the *Angewandte Chemie* journal. The scientists introduced gold nanoshells (spherical nanoparticles with a gold coating) into tumours where they irradiated the nearby cancerous cells with infrared radiation. As a result the gold nanoshells conduct and overheat which leads to the destruction of the diseased tissue. Infrared is the most preferred radiation because the long wavelength will allow damage to nearby cancerous cells, but not the healthy cells as the radiation is not very penetrative. This increases the chance of successful treatment and makes treatment safer. Nanotechnology is therefore very useful in targeting cancer cells and treating them. [20]

The very latest research into drug delivery systems comes from Dean Ho, who is an associate professor of biomedical engineering at Northwestern University. It is called a Nanodiamond and could potentially beat hard to treat cancers. Nanodiamonds are carbon based and are 2-8 nanometres big. They allow a large number of materials to become attached to their surface, including chemotherapy drugs. Dean Ho and scientists tested lethal amounts of the chemotherapy drug, Doxorubicin on mice with liver and breast cancer; however they were delivered with the Nanodiamond. The Nanodiamond significantly reduced the size of tumours, without causing toxicity or death to the mice. This demonstrates a huge step forward in finding a permanent cure to cancer as 90% of failure in treatment is due to cancerous cells being resistant to therapy. The reason Nanodiamonds are so effective is because they allow the drug to circulate in the tumour for up to 10 times longer than other drug delivery systems making the drug more effective against tumours. They also don't affect white blood cell count, which is vital for a patient with cancer. However the only issue with treating humans is that the tests were done on mice so the full effects on humans are still unknown; however it is still early days for Nanodiamonds. Dean Ho and team have published their findings very recently on the 9th March 2011 in the journal "Science Translation Medicine", in which they hope Nanodiamonds, can be used in the future to treat cancer.

Nanotechnology could help to control cancer and its severity by removing faulty genes, however in order to explain this we need to understand DNA and genetics in greater detail. The discovery of Deoxyribonucleic Acid informally known as DNA has revolutionised modern science, especially within the field of medicine. In 1952 Frank Hershey and Martha Chase coordinated an experiment which proved that DNA was the part of the nucleus that coded for the production of proteins. This now meant that further investigation could take place to uncover how DNA worked and what parts of the DNA formed particular features within an organism. The Human Genome Project was set up and set out with an aim to do just this. They intended to unravel the structure of each gene and identify the protein for which it codes. If this was successful it meant that we would be able to understand how people are affected by certain diseases and target early treatments. The recent discovery of the Rogue gene shows that the basic ideas that are made evident in the Human Genome Project were successful. [18]

The Rogue gene scientifically known as WWP2 is seen to be the specific part of DNA which attacks and breaks down a natural inhibitor within the body which would normally prevent cancer cells from spreading. It's suggested that if the correct drugs could be developed to prevent WWP2 from functioning, then cancer would not spread because the natural inhibitor would increase in amounts and stop the mutated cells from spreading. See **figure 4** for simplified version of cancer's route.

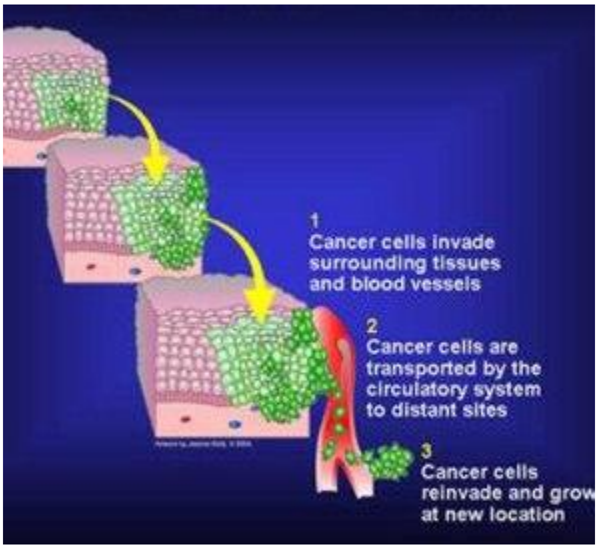

Figure 4 [28]

Once the difficult task of developing this potent drug is overcome, it can be suggested that using nanotechnology could mean that the drug could get into the cancer cells and destroy the activity of the Rogue gene. We know that this could be successful because medicine, at the moment, is using nanotechnology for delivering other drugs via the drug delivery systems as mentioned before. 'Lead author Andrew Chantry said the discovery could lead to a new generation of drugs within the next decade that could stop the aggressive spread of most forms of the disease, including breast, brain, colon and skin cancer'.[22]

We can suggest that a possible future use of nanotechnology, that would be a very farfetched jump within medicine, would be replacing the Rogue gene all together. WWP2 is produced in all humans but can become faulty and help cancer cells not only grow, but spread too. If this gene was to be replaced by its corresponding triplet code formed from nanoparticles then there would be a part of the DNA that was dormant completely - known as an interon. This would diminish the possibility altogether of cancer spreading, however, this comes with several complications as well as many different ethical issues that would immediately need to be addressed before further investigation was undertaken with regards to this theory.

A possible way of replacing this section of DNA would be by combining the usage of nanoparticles and recombinant DNA technology. The nanoparticles that are to form the nucleotides would need to be created and modified so that they were able to act like normal parts of DNA. This means that they would need to be able to perform as though they have been acted upon by enzymes to cut themselves from another region of DNA. The performance of these nanoparticles would be mirroring those of the actual process that takes place where enzymes called restriction endonucleases would have acted like scissors to cut DNA; this leaves a sticky end free to bind with that of a sticky end of another DNA sequence. The triplet code for replacing the Rogue gene made of nanoparticles would then combine its manufactured end with that of the sticky end of the rest of the DNA sequence. [19]

It is evident that this process would have to be carried out on both males and females to ensure their gametes do not exist with this gene. However, this would be extremely expensive as well as complicating factors such as family planning. This is because the gametes would need to be treated to remove the Rogue gene to prevent cancer from growing extensively and also from it spreading. If this could be addressed successfully in addition to easier methods being discovered over time, this theory of replacing the Rogue gene would be very successful in reducing the deaths of patients with cancer. This is because it is said that the spreading of cancer is what kills the majority of patients in the end. This would also allow diagnosis to be improved as the cancer could be found with ease by using nanotechnology as it would be expected to be found in one place only – known as the glowing tumour.

The ethics with this would be similar to that of, artificial selection and any other process that revolves around human involvement. Religious parties would say that it was playing God with preventing a way someone may pass away, and that no human has the right to do that. A further problem could be that gametes could have been scanned inaccurately; therefore you could remove something which in reality was safe and was required for a particular protein in the body.

Investigating whether or not replacing the gene was successful would be very difficult. The reason being, the person would have to be monitored throughout their lifetime to see if they suffered from cancer and whether it spread.

This idea for the future uses of nanotechnology is farfetched however, over the coming decades with increasing development in equipment and knowledge within this fairly new field, there is no particular limit to its potential.

CONCLUSION

Benefits of nanotechnology in medicine:

By using nanotechnology, the tools and equipment to execute surgery would be much cheaper and more efficient. Currently, the Government are trying to reduce costs within the medical system; therefore the use of nanotechnology would reduce these costs. Henceforth, using nanotechnology will not only be beneficial for doctors and surgeons in the likelihood of carrying out successful operations and successfully diagnosis of illness, but also for the government that funds the NHS.
Secondly, due to the minute size of the nanoparticles, it will be more efficient and more precise in detecting illnesses early which is obviously beneficial for patients. For example if a tumour or cancerous cells were detected in the early stages, then treatment could start as soon as possible to try and control the division of the cancerous cells, making it easier to treat. Sub-sequentially it could increase life expectancy of a patient. [15]

Disadvantages of nanotechnology in medicine:

Despite being more accurate and creating higher success rates in operations, nanotechnology does have its disadvantages. A serious problem with nanoparticles is cytotoxicity. This is when nanoparticles are toxic to the body. Cytotoxicity can be caused by the particles being contaminated by harmful or poisonous products. The chances of such contamination can be increased especially if nanoparticles are being manufactured on a large scale. Therefore, instead of nanoparticles being useful to the body, it has the opposite effects. Secondly in contrary to the benefits of costs when using nanotechnology the nanoparticles do cost thousands of pounds to produce. In the current economic climate, it will be very difficult to produce such extravagant items, even if they could potentially save money due to increased chances of long lasting treatment for patients [14].

Ethical considerations

There are many guidelines set by organisations that aid research into nanotechnology. An ethical issue raised involves the military researching into applications of nanotechnology; which should be limited due to privacy and security issues. Information from these parties can be shared to other parties, and if private information is leaked on nanotechnology, it can have serious consequences for the country. Secondly, scientists who develop and experiment with nanotechnology must have a firm knowledge of ecology and public safety to ensure the community don’t suffer with any carelessness that takes place in the research. [16i] Furthermore as the development of nanoparticles is expensive, some fear that it can cause a rich-poor social divide where the rich will have the advantage of using these devices over the poorer population. This would not be a problem if the treatment was put on the NHS [16ii]. All these ethical issues have to be addressed and scientists have to do their best to tackle these issues.

Conclusively it seems as though nanotechnology will become increasingly important in medicine. We think that using nanotechnology as drug delivery systems will be the most effective use of nanoparticles in medicine, as they will become more effective as technology improves. A good example of this is the recent discovery of the Nanodiamond which massively increases the effectiveness of chemotherapy. However in order to make these important discoveries there needs to be extensive research, which requires funding. Therefore this current economic climate could hinder the development of important discoveries. Overall we deduce it will best to focus on modifying old types of nanoparticles, or discovering new types in order to create the most effective drug delivery system, because so far they’re the most effective long term treatment to cancer.

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