NANOTECHNOLOGY IN THE PREVENTION, DETECTION AND TREATMENT OF CANCER

BY

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PASS WITH DISTINCTION

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Abstract

Perhaps one of the main reasons that cancer has such a high mortality rate is that cancer cells can remain undetected for a long period of time, and by the time they are detected, the cancer is likely to have spread to other parts of the body. Nanotechnology involves dealing with substances at an atomic level. Since the only essential differences between a cancerous cell and an uncancerous cell is the oncogene and the specific chemical markers on the cell surface membrane, due to the incredible size of nanotechnology, it could be used in such a way to eliminate a cancerous cell a long time before the current methods. Therefore, nanotechnology has the potential to aid in preventing, detecting and treating cancers. In this paper, I will be outlining some of the ways in which it is currently doing so and possible future developments of how it could be used. If the techniques are successful, then the positive impacts on the population will be numerous.

Introduction

Nanotechnology is the study and application of matter at atomic and molecular levels, more specifically; nanotechnology involves substances that are nanoscale, that is, the matter has at least one dimension between 1 and 100 nanometres (one nanometre is a billionth of a metre).

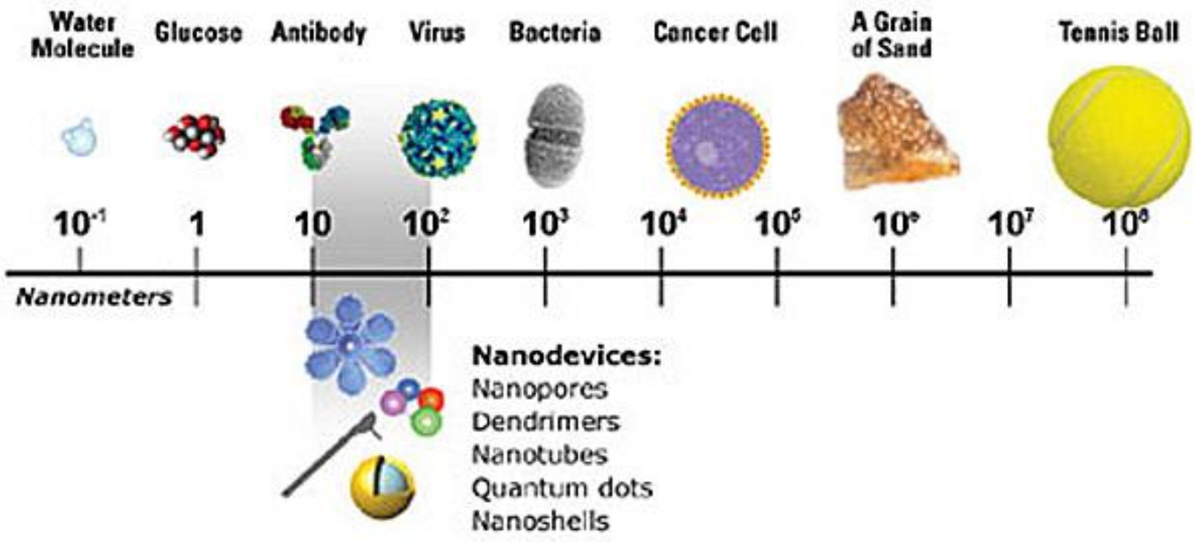

Figure 1

<u>History</u>

The physicist Richard Feynman first used the notion of nanotechnology at a talk at the Californian Institute of Technology in 1959: “There’s Plenty of Room at the Bottom”, which means that there is always a possibility to work with smaller and smaller structures. Feynman defined a procedure which individual atoms and molecules could be altered to make an identical copy in composition, but each smaller in size than the previous.

However, it was not Feynman that assigned the term "nanotechnology", but the science professor Norio Taniguchi (1974) *On the basic concept of Nano-Technology*. Taniguchi stated that "'Nano-technology' mainly consists of the processing of, separation, consolidation, and deformation of materials by one atom or by one molecule".

Dr. K. Eric Drexler explored this definition in significantly greater detail in the 1980s and instigated the implications of nanoscale matter on a technology based level through numerous speeches and the publication of two books: Engines of Creation: The coming Era of Nanotechnology (1986) and Nanosystems: Molecular Machinery, Manufacturing and Computation (1992). Drexler concluded that: "Because….you have this general ability to manipulate atoms in complex patterns, you can make essentially anything that's physically possible." Drexler's interpretation of the term Nanotechnology is what we know and use today.

The arrival of nanotechnology enabled engineers to construct materials from the "bottom up" as opposed to making a current machine or a structure dramatically smaller. It was in the early 1980s, that nanotechnology had its first two developments, the arrival of cluster science and the creation of the scanning tunnelling microscope.

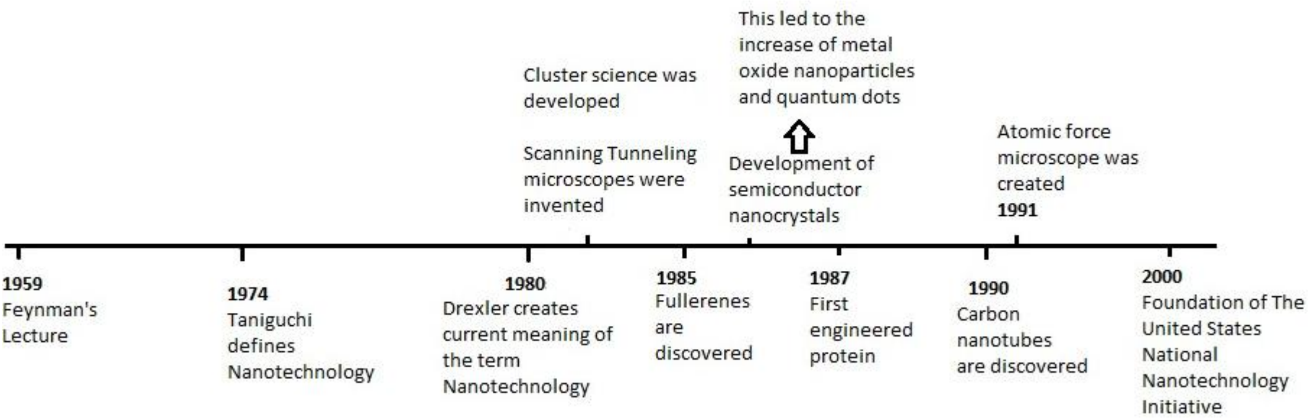

Figure 2

Cancer

Cancer occurs when there is a mutation in the genes that regulate cell division. Mutations are changes in the nucleotide arrangement of DNA and this happens reasonably often in the process of mitosis, but these cells are usually detected by the immune system as being foreign antigens. The mutation could occur naturally, or be the result of exposure to a carcinogen. The immune system then generates a response to ingest and destroy the cell containing the mutated gene, so that the mutation cannot be passed on to more cells. However, cancerous cells occur when the immune system does not recognise the mutated cell and it remains in the body undetected. The cell also has the ability to destroy itself if there are genetic errors within the cell that cannot be repaired, this process is called apoptosis. In a cancerous cell, the ability to perform apoptosis is prohibited. This cell is then able to produce identical clones of the cell during mitosis, which all contain the mutated gene. As the gene that controls cell division is faulty, the cells continually divide rapidly by mitosis, to form a tumour. The tumour absorbs nutrients from the body and is supplied with blood and lymph vessels. This continual supply of nutrients causes the tumour to thrive and gradually the tumour will push through normal body tissue, blocking off small blood vessels. The tissues then become deprived of blood and eventually die due to oxygen deprivation, which enables the tumour to invade the space. Some of the cancerous cells may break off from the tumour and be transported around the body in the lymph or blood, and so the cancer is able to infect other parts of the body to form secondary cancers, this is called metastasis. The ability of the cancer to be able to do this makes it a very dangerous disease as the secondary cancers are incredibly hard to find and remove.

Cancer is the principal cause of death in the developed world, accounting roughly for 25% of deaths and the second principal cause of death in the developing world. There are over 200 different types of cancer, but the most common cause of death by cancer is lung cancer.

Worldwide cancer rates are on the increase due to the increased life span and lifestyle factors in the developing world. For example, in 2005 the UK mortality rate for all malignant neoplasm was 153 491 and in 2008 the UK mortality was 156 723. Furthermore, research carried out shows that 76% of all cancer deaths were aged 65 or older. Robert A. Weinberg, a cancer researcher, said that: “If we lived long enough, sooner or later we would all get cancer.”.

Therefore, there is a need to prevent the mortality rate from cancer increasing. In order to do this, prevention methods must be established if possible, detection of cancerous cells must happen in the early stages to prevent metastasis, diagnosis must be faster and treatment needs to be more effective.

Nanotechnology and Medicine

The individualistic properties of nanomaterials have been explored and have led to nanotechnology becoming increasingly more apparent in the world around us. Nanoparticles are used in fire protection and detection, construction, foods, textiles, household materials, feature in “self-cleaning glass”, agriculture and more specific to this paper, medicine.

This is because the size of nanoparticles is comparable to the size of the majority of biological molecules and this enables nanomaterials to be used in medical fields, such as drug delivery.

Company	Product
BioDelivery Sciences	Oral drug delivery of drugs encapsulated in a nanocrystalline structure called a cochleate
Nanosphere	Diagnostic testing using gold nanoparticles to detect low levels of proteins indicating particular diseases
Nanotherapeutics	Nanoparticles for improving the performance of drug delivery by oral or nasal methods
Oxonica	Diagnostic testing using gold nanoparticles (biomarkers)
T2 Biosystems	Diagnostic testing using magnetic nanoparticles
Z-Medica	Medical gauze containing aluminosilicate nanoparticles which help blood clot faster in open wounds.
Sirnaomics	Nanoparticle enhanced techniques for delivery of siRNA
Makefield Therapeutics	Nanoparticle cream for delivery of nitric oxide gas to treat infection
DNA Medicine Institute	Diagnostic testing system
NanoViricides	Drugs called nanoviricides™ designed to attack virus particles
NanoMedia	Targeted drug delivery
Taiwan Liposome	Drug delivery using lipsomes
Traversa Therapeutics	Delivery of siRNA molecules
Nano Science Diagnostics	Diagnostic testing system

Figure 3

Nanotechnology has also been used successfully in sunscreens; this involves nanoparticles of titanium dioxide in the sunscreen. The nanoparticles have the same protection against UV rays as the naturally occurring particles; however, as the size of the particles is reduced dramatically, the white appearance of the sunscreen is lost. This means that more people are using sunscreen when in the sun, as before it was considered "unattractive" to wear sunscreen due to the whiteness. This technique may be one way in which the skin cancer, Melanoma, is reduced.

However, the emulsion can become rubbed off and people may be under the impression that the nanoparticle sunscreen enables them to stay in the sun for longer, when actually the sunscreen has been lost, mainly due to perspiration. Furthermore, when applying sunscreen, people may not cover their entire skin surface due to tiny imperfections in the skin's surface. This allows the UV radiation to penetrate through the dead layer of skin cells, possibly diffracting, and causing damage to the fragile structure of DNA, causing mutations to occur in the genetic sequence.

Chemotherapy, a current method of cancer treatment has well known side effects, such as hair loss and nausea. This is because the current methods of chemotherapy involve the drugs being introduced into the body by the bloodstream and are not targeted to the malignant cancer cells, which means they affect both cancerous cells and healthy cells. Nanotechnology enables the drug to be deposited only in the cancerous region of the body, reducing drug consumption and side effects for the patient.

CytImmune is a company that has manufactured drugs (Aurimune) containing gold nanoparticles that detect cancerous cells in the body and target treatment to that specific area. This is possible because gold nanoparticles are able to absorb and scatter light, which enables detection of cancerous cells using white light and a basic microscope. The majority of cancer cells have a large number of epidermal growth factor receptors (EGFRs) on the cell surface membrane, and these can be used to detect cancerous cells. The gold nanoparticles can be bound to antibodies that have complementary shapes to the EGFRs. When present in the body, these antibodies will flow in the bloodstream until they collide with the EGFRs and bind to them. Once the antibodies are attached, the gold nanoparticles will reflect white light, allowing the cancerous cells to be clearly recognised against the surrounding healthy cells. If the body is then exposed to radiation, the gold nanoparticles will then superheat and destroy the body cells surrounding them.

However, this development of nanotechnology poses problems. Firstly, people may object to the idea of introducing gold into their body, no matter how small the particle, and may refuse this method of treatment. Secondly, the body still has to be exposed to radiation, which is a carcinogen and is known to disrupt the genetic sequence of DNA. Furthermore, when the gold nanoparticles become superheated, they will destroy any surrounding cells, which may also cause the death of healthy cells. Therefore, it could be considered debateable where this new revelation of cancer treatment is effectively better than current radiotherapy techniques. However, it is clear that the detection side of this notion appears to be much more effective than current methods.

Additionally, Chemotherapy provides a problem in the treatment of brain tumours. The blood brain barrier is a device that defends the brain from toxic chemicals that could potentially cause harm to the brain. Currently, there are only a few chemotherapeutic drugs that are able to pass through this barrier. Research in early November 2010, shows the introduction of nanotechnology to create the drug: “nanobioconjugate” that is between 20 and 30nm long. The drug is able to be intravenously introduced into the body, carried in the blood and across the blood brain barrier into the brain and is protected from being dismantled in the blood during delivery because of the strong chemical bonds within it. Also, the drug has been effectively engineered so that the constituents of the drug are activated only when they are present in the tumour cells. Unlike traditional chemotherapy, this spares the healthy cells from being affected by the toxic drugs. Julia Y. Ljubimova, M.D. Ph.D. states: "This nanobioconjugate is different from earlier nanomedicine drugs because it delivers and releases antitumor drugs within tumor cells, not just at the site of a tumor,". It has been noted that once the drug has served its purpose as a drug, it is broken down by the body into carbon dioxide and water, which is not toxic to the body. Furthermore, research has been conducted and has shown that the drug does not cause allergic reactions stimulated by the immune system. However, the drug has yet to complete the human clinical trials, so is not yet available for usage.

Currently, the population is concerned about the toxicity of nanodrugs, which is why I believe that this particular development will be very important in the treatment of cancer, and the starting point for peoples' trust in nanodrugs. The only obvious issue here is that the drug is on the nanoscale, which means it is able to penetrate the blood brain barrier because of its incredible size. Even though the drug itself is non-toxic, perhaps if excess amounts of the drug penetrated through the blood brain barrier and were degraded into carbon dioxide, the carbon dioxide itself could be toxic. If too much carbon dioxide was produced in the brain by the decomposition of the drug, it may not be diffused out of the brain at a fast enough rate. Carbon dioxide combines with the haemoglobin in the blood, causing the oxygen to be disassociated, which means that insufficient oxygen will be transported to all the cells in the brain, eventually causing death by oxygen starvation. Furthermore, too much carbon dioxide in the bloodstream will alter the pH levels, causing acidosis. Therefore, the trials need to establish an effective dosage of the cancer drug that will not lead to such a dangerous situation.

Discussion

Taking the previous problem of the use of nanotechnology in sunscreens into consideration, further developments to the nanotechnology used could equate to a better form of UV light protection. If nanoparticles are attached to substances that scatter UV light such as titanium oxide and then targeted to the cell surface proteins of skin cells, then each individual cell is coated with sunscreen. Doing so will eliminate the problem of missing a potentially minute area of skin cells due to tiny imperfections in the skin, which means that UV rays cannot be deflected and cause damage to the delicate double helix of DNA. However, there is an issue with this form of prevention, which is the toxicity of the substance and therefore extensive clinical trials must take place for this application to be used in society. Furthermore, the advantage of the cosmetic properties discussed earlier will still exist. If this notion is used, there will hopefully be a huge reduction in the cases of cancer of the skin due to UV rays, such as Melanoma.

Another known carcinogen, like UV rays, is asbestos which can cause Mesothelioma and lung cancer. Although there are laws against the use of asbestos as a building material, it is still present. An environment containing asbestos causes a person to inhale the fibres, which cause irritation and inflammation of the lung tissue, which then causes the fibres to become lodged. It is not known exactly how asbestos fibres cause cancer, whether it is the direct interaction with the cells of the lungs, or whether toxic chemicals are released by the fibres. Currently, dust masks are worn in order to stop inhalation of the fibres; however the threads may not be woven tightly enough, allowing some asbestos fibres to filter through the pores. Future developments of nanotechnology could reduce this problem. If the pores between the woven threads of the dust mask are on the nanoscale, it is very unlikely that any asbestos fibres will filter through the gaps. However, the atomic radii of an oxygen atom is 0.048nm, so careful research will be needed to ensure that sufficient oxygen is able to enter through the nanopores, without allowing the admission of asbestos fibres.

Gold nanoparticles are currently being used for the detection of cancer, but using this concept and the concept of the current research of Quantum dots, the detection using nanotechnology may be able to be taken even further. Since cancer cells have specific cell chemical markers on their surface which aren't present in normal, healthy body cells (EGFRs), a nanodrug containing a receptor that specifically binds to these receptors and a colour indicator could be developed, which could be used in the detection of cancer. When the nanodrug binds to the chemical markers on the cancerous cells, the indicator could cause a colour to be emitted at the site of binding, that was visible on the skin directly above, to the human eye in normal light. If such a development was possible, people could check themselves regularly for such a colour change, which would increase the rate at which the cancerous cells could be dealt with. If the colour change was spotted early enough in the tumour development, when it only consisted of a few cells, treatment would be a lot quicker and would save thousands of lives each year.

However, there are problems with such an idea. Firstly, the extent to which the concentration of the colour indicator had to be in order to be seen through the skin may be too high that it wouldn't be possible to contain such a high number of particles in a nanodrug. Also, the toxicity of the indicator used may be too high for usage in the human body. However, if such a nanodrug passed the standard laboratory testing and was approved by the FDA, there may be problems with its application in society. It may be difficult for some people to "check" themselves for the colour change on their skin, for example, to get close enough in order to see the colour change. Furthermore, the colour may be too subtle for detection. Additionally, if the tumour was imbedded deep in the body, for example in the stomach, the colour indication may be too far away from the skin to be able to be detected. Therefore, perhaps it is only cancers close to the eye proximity that will be detected by the colour change, such as skin cancer. However, this application of nanotechnology, in theory, will be incredibly useful, as the method involving gold nanoparticles involves white light and a microscope, this method just involves the human eye for detection. Currently, there is a lot of advertisement urging people to check themselves for "lumps", especially for women in the detection of breast cancer. The development of using nanotechnology here is very similar to this idea and if it has a similar success rate, thousands of lives will be spared.

Moreover, the future could see the introduction of nanovalves used in the treatment of cancer. This new method is developed by Jeffrey Zink and Jinwoo Cheon and it involves mesoporous silica nanoparticles and magnetic zinc-doped iron oxide nanocrystals with nanovalves attached. The nanovalves contain the drug held in the pores such that when a magnetic field-stimulus is applied, the valves discharge the drugs from such pores into the targeted cells. This research would become effective if used in cancer treatment, as the drugs can be specifically targeted to cancerous cells using EFGRs, sparing the healthy tissues. Furthermore, the introduction of magnetic particles into the nanodrug will be useful in MRI scans, to enable the tumour to be more obviously seen, which will ultimately aid in the detection process. Furthermore, the magnetic particles will also reveal secondary cancers in the body in the process of MRI scanning, which may have been missed without such technology.

Additionally, nanotechnology is making a breakthrough in tissue engineering. It is possible to create biological structures that are incredibly similar to living organisms. This revelation may mean that the prosthetic limbs and organ transplants of today may be replaced by using nanotechnology to create or repair tissue structures. For example, using carbon nanotube as framework, bones can be regrown. In future decades, it may be possible for this technique to be used in the treatment of cancer, as the entire cancerous area could be removed and replaced by the nanotechnology "grown" structure. However, this may not be preferable to patients, as their newly formed structure would not be biologically be a part of them. Furthermore, such treatment may not succeed in removing the cancerous cells entirely from the patient, as the cancer may have spread to form secondary cancers in other areas of the body. Also, the cost of such technology would be high and it is possible that the created structures are not able to carry out the processes identical to that of the natural structure. This then requires the judgement of society of whether the advantages outweigh the disadvantages.

In the future, perhaps an injection or drug will be introduced containing nanoparticles with structures on the surface that are complementary to the specific chemical markers on the cell surface membrane of cancerous cells. These nanoparticles could contain destructive enzymes, similar to lysosomal enzymes used to digest pathogens, which will break down the cancerous cell into non-toxic nutrients that can be absorbed and used by the body and waste products that will be removed by the body.

However, this may cause problems of who to make the injection or drug available to, as it is impossible to administer it to the world population. Additionally, there is a problem with clinical trials. If the treatment passes all of the laboratory tests such as toxicity, the treatment will need to be tested on humans to assess possible side effects and its effectiveness as a treatment, which may involve assessing a large sample of people throughout their lifetimes, which will take a long time. This will cause problems of whether this is ethically possible and also, people may refuse to take part. Furthermore, in an economic aspect, the health system in both the developed and developing countries may not be able to afford to offer the treatment free of charge to their populations, meaning people will have to pay for it themselves. This means that it is highly unlikely that people in the developing world will benefit from such treatment, which further increases the gap between developed and developing countries.

Conclusion

As cancer is a change in the nucleotide arrangement of DNA in one gene and nanotechnology operates at a molecular level, in the future, it may be possible to use nanotechnology to discover why an oncogene occurs in a particular cell. In finding the reason for this, it is possible that nanotechnology will open doors to finding the reason as to why cancer occurs in some cells and not in others. This will then enable the medical industry will be able to find ways of prevention, detection, diagnosis and treatment involving new innovations that are much more efficient compared to the methods that currently exist, perhaps using nanotechnology.

However, although some of the methods in the discussion section seem far-fetched currently, with the rapid development of nanotechnology in industry, including the health industry, future techniques may make it possible.

The National Cancer Institute aims to "eliminate death and suffering from cancer by 2015" and believes that nanotechnology is the way to achieve this. It is hoped that one drug will be formed that prevents, detects and treats cancer, is safe to use, is not toxic, does no damage to healthy cells, works for everyone and checks that cancer has successfully been removed. The chance of this happening in the next four years seems incredibly small. However with the huge amount of people working in nanotechnology and cancer the current developments of nanotechnology is only the tip of the iceberg and nanotechnology is on the brink of dramatically exceeding itself, taking the term medicine to a whole new dimension.

As it is a relatively new technology, the obvious downside is that it will need a lot of investment, research and trials before it can be used to its full potential. Furthermore, the population may be wary of introducing such technology into their bodies, so the safety of the nanotechnology needs to be fully assessed. Additionally, patients and their relatives need to be fully educated about the procedure, benefits and risks associated with such technology. However, if nanotechnology continues to thrive at the rate that is currently doing so, the possibilities of nanotechnology seems infinite.

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