Uses of Nanotechnology in Medicine

Developments in the Diagnosis and Treatment of Cancer

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Abstract

This paper will concentrate on the effect of nanotechnology on the diagnosis and treatment (delivery of drugs) of cancerous cells. This paper highlights some of the promising developments in the area that could have a significant impact in the future of treatment for cancer. We also discuss the ethical issues associated with the use of nanotechnology in medicine.

Figure 1

Introduction

Nanotechnology is the study of manipulating matter on an atomic or molecular scale. It deals with matter of sizes around 1 – 100 nanometres; one nanometre is the equivalent of three atoms. The idea of nanotechnology was first introduced in 1959 by a physicist called Richard Feynman by suggesting that eventually atoms and molecules could be manipulated. He also said that theoretically, it would be possible to build “nano-scale” machines. Eric Drexler (Figure 1), during the 1980’s, carried out further research on Feynman’s ideas and as a result, nanotechnology was formed. Manipulation of atoms was first carried out in 1989 at IBM by Don Eigler.

There are many uses of nanotechnology, such as medicine, electronics, biomaterials, and there are new areas that are constantly being discovered, researched and developed.

Nanotechnology in medicine and vetinary medicine is a fast growing area. The method by which drugs are delivered to the body can have a very large effect on its efficacy. Improvements in many areas of drug delivery are made possible by nanotechnology. Nanotechnology can help to improve issues such as pharmacokinetics and pharmacodynamics. Pharmacokinetics involves studying the distribution and absorption of a drug given inside the body. Pharmacodynamics is the study of the physiological effects that drugs have on the body. The drugs must also be protected from anything that may cause them to break down such as enzymes or chemicals within the body, however they must also be able to overcome physical barriers within the body, as well as travel to the target region. Nanotechnology can help to improve this as well as improve the drugs actual

penetration into the target cell. There have been many discoveries in the uses of nanotechnology. For example, it can be used in gene therapy. It is small enough to penetrate the body's physical barriers and redesign the genome; this can be used to prevent or treat conditions and diseases. Nanotechnology can provide molecular images which can aid the diagnosis of a variety of diseases. There are many other uses such as surgery, or nanochips which can control seizures, however, this paper will concentrate on using nanotechnology for drug delivery.

Drug delivery systems are appearing more and more frequently in medical research. Drug delivery is the delivery of pharmaceutical substances into both the human body and animals. The use of nanotechnology in drug delivery ensures that medicine is released at the right time and it eliminates human error. It targets all the routes of drug delivery into the body, from injections to implants, and can also be used in toxin removal. Nanotechnology can be used to remove lethal compounds from the blood stream for example illegal drugs and chemical and biological agents. It also targets some of the concerns of the pharmaceutical industry. Nanotechnology will improve the ability of drugs to target specific regions (the ones that require the drug). This will result in smaller doses and fewer side effects for the patients. It could also improve the speed of delivery and the solubility of drugs.

The discovery of buckyballs was, perhaps, one of the most important discoveries in reference to the topic of this paper. They are useful in drug delivery because of their small size. This means that they can move through the body efficiently. Richard Smalley is one of the scientists who discovered buckyballs in 1985. He was awarded the Nobel Prize in Chemistry in 1996 for his discovery. Buckyball is short for buckminsterfullerene; it is a molecule consisting of 60 carbon atoms. Each carbon atom is bonded to another 3 carbon atoms, similar to the structure of graphite. Infected regions have different pH levels to the healthy regions. Researchers are hoping to attach a buckyball to molecules that react to a change in the pH levels of there surroundings. Therefore the drug is only released at the infected regions. These are known as smart materials and they react to a change in their environment.

Another method of drug delivery to consider is Nanoshells. These are made of a silicon core and an outer metallic core which, in the case of cancer treatment, is gold. Gold is an inert metal and can absorb or reflect light. It is also biocompatible with the human body and animals. They could prove to be a very effective way to detect and kill cancer cells. If antibodies are attached to the surface of the nanoshells, then when injected into the body, they will bind specifically to cancer cells, leaving the healthy cells undamaged.

This is very useful when it comes to cancer treatment. Current methods do not target specific cancer cells, harming healthy cells and causing severe side effects to the

patient. Nanotechnology will help to improve methods of drug delivery currently in use, as well as being useful in the development of more effective methods. Nanotechnology can also help to improve the diagnosis of cancer. It could help to diagnose cancerous tissue a significant period of time before there are any visual growths or signs.

Discussion

Cancer is a disease caused by cells that divide uncontrollably to form an abnormal growth known as a tumour. They develop faster than healthy cells. This causes them to be 'leaky' as blood vessels to the tumours are not fully developed. This allows small particles to pass through. These can develop almost anywhere in the body however are more common in certain areas, for example breast cancer in females. Cancer is one of the most highly researched areas in medicine therefore all new avenues of drug delivery are being researched thoroughly, for example nanoshells. Although chemotherapy is effective in treating cancer, it is distributed throughout the entire body so results in some damage to healthy cells. By using nanotechnology, scientists and researchers hope to improve the efficiency of the anti – cancer drugs as well as minimise any side effects and therefore improve the patients experience while undergoing treatment.

Nanotechnology has provided a means to generate new and more effective ways to deliver drugs into both animals and humans. It affects nearly every route of delivering drugs. Drugs work by altering chemical reactions that occur in the body.

One method of delivering drugs is via injection. Incorporating nanotechnology into injectable drugs means the dosage can be more accurate, so the doses are smaller which means that it is easier to administer and less unsettling for the patient. Nanotechnology has had a huge effect on this method for example the nanofountain probe. Researchers from McCormick School of Engineering and Applied science have used nanodiamonds to construct a tool that can accurately deliver tiny doses of the drug required to individual cells**.**

We would like to explore the current methods of treating cancer, and methods that are being researched that could have a significant impact in the future.

Surgery

This method of treating cancer involves physically cutting out the tumour. However, this is not always effective as cancerous cells may travel round the body, or not all cells will be removed so another tumour will grow. Therefore surgery is normally used alongside other treatments.

Radiotherapy

Radiotherapy involves the use of radiation to treat cancer. Unlike healthy cells, cancerous cells cannot repair themselves so are destroyed. This method also has several side effects including hair loss, nausea and vomiting.

Chemotherapy

Chemotherapy is a method which uses drugs. They can be given in many forms, such as injections or tablets. These drugs will destroy the cancerous cells or stop them dividing; however, they also affect areas of the body where the cells divide quickly such as the mouth, digestive system, skin and hair. Many patients exposed to chemotherapy, will undergo extreme tiredness.

Nanodiamonds

Many drugs are water insoluble which limits the ways that these drugs can be administered to the body. This is one of the major barriers affecting the efficiency of drug delivery as most drugs are delivered orally or intravenously. It therefore becomes a problem in clinical situations and in severe situations, harmful solvents are needed to dissolve the drugs. Nanodiamonds could be used to deliver these water insoluble drugs. They are soluble in water and are chemically inert. Drugs can bind to these nanodiamonds and therefore be delivered to cells.

Nanodiamonds have useful physical and chemical properties which make them an area of interest in research for the treatment of diseases. They are part of the carbon nanomaterial group (others include carbon nanotubes and nanofibres) and the average size of the particles is 4 to 5 nanometres.

Nanoshells

As mentioned before, gold is most commonly used in nanoshells as it is biocompatible and can absorb (or reflect) different wavelengths of light depending on the thickness. The electrons in the metallic surface of these nanoshells are ‘exited’ by the light and will vibrate. They will even oscillate at the same frequency as the light. A wavelength close to infrared is used because it transmits well through biological tissues.

Nanoshells can also be used for imaging. They can absorb light but they can also reflect light and a camera can then pick up the scattered light. Due to the fact that the nanoshells are small, they cover the cells so you get a high quality image. As the gold nanoshells are seen as foreign substances, they are coated with poly (ethylene glycol), (PEG) which allows them to circulate around the body (via the bloodstream) without being removed. Protein-based antibodies are attached to the nanoshells in a

laboratory. These are then injected into the body where they attach specifically to cancer cells. About 20 nanoshells will bind to each cancer cell. When the nanoshells are exposed to low-intensity infra red radiation they illuminate allowing the tumour to be located via 'optical coherence tomography'. A high powered laser is then applied to the tumour to heat the tissue resulting in the death of the cancer cells. When the tumour is subjected to the laser, the electrons in the metallic layer oscillate more. This increase converts the light energy into heat energy**.** Although this could be an effective way to treat cancer, there is a major problem. The infrared light only allows one to see the nanoshells 2 mm below the skin. Therefore this treatment is only useful for cancers such as skin, mouth and cervical rather than to treat, for example, pancreatic cancer.

Experiments have been carried out by Nanospectra Biosciences Inc.; live mice were injected with tumour cells. They were then split into 3 groups. One was given no treatment; one was injected with saline and exposed to 180 seconds of infrared laser. The final group was given injections containing nanoshells and laser treatments. After injecting the nanoshells the scientists waited six hours to give them time to accumulate and then they exposed the tumour to a laser. The temperature of the skin above the tumours during this treatment for the mice given nanoshells drastically increased however there was no increase in temperature in areas other than the tumour sites. There was no significant increase in temperature for the group of mice given saline injections. The mice given the nanoshells survived for the full 60 days and remained cancer free after the treatment. However, the mice from the other 2 groups had to be euthanized by day 19 of the experiment as the tumour had grown and was more than 5% of their body weight. Overall the experiment was a success. The results show that there is actually a way to treat cancer without harming healthy cells.

Another method involves the use of silica-based nanoshells that contain light-sensitive drugs. These are referred to as photosensitizers. These nanoshells are taken up by cancer cells, and when these cells are exposed to light, the nanoshells are activated. They then produce reactive oxygen molecules that kill the cancer cells.

Micelles

Micelles may also be used to effectively treat cancer. Micelles are spherical groups of amphiphiles; each of these is made up of a hydrophilic head and a hydrophobic tail. A critical micelle concentration is reached when sufficient amphiphiles are present so they are attracted to one another, rather than the surface of the liquid, to form micelles. This is more efficient than putting them together individually. They are also very useful in industry as they can be various sizes. When the amphiphiles form a bilayer it is known as a vesicle. This tiny structure can be used as a 'vehicle' for delivering drugs to specific areas of the body.

Vesicles can imitate liposomes; these are used to deliver drugs directly into cells. You can prepare them outside the body and can enclose the drugs. They are injected into the bloodstream where they are carried to the targeted cells and the drug is released. This can be done by attaching to the surface of the cell, therefore allowing the drugs to diffuse through the cell membrane. The drug can also be delivered if the vesicle breaks down or if it fuses with the cell membrane.

Polymers can also be used to make vesicles and this provides more stability and flexibility within the structure. Recently, scientists at the University of Florida have developed a nanoparticle that has the potential to improve the diagnosis and treatment of cancer. The particle being developed is known as an aptamer - micelle. The micelle itself is constructed of aptamers. “An aptamer is a single stranded oligonucleotide (a short polymer made up of nucleic acid) that is able to recognize the target molecules due to non covalent interactions for example hydrogen bonding or hydrophobic interactions**”**. They have more advantages than antibodies; they are easier to produce as the micelles are self-assembling, and have a quicker response time as well as being smaller in size. They have a larger surface area to volume ratio than larger micro particles, as well as an improved solubility. This can improve the diffusion of the drugs into the target cells. A hydrophobic tail is attached to the end of the aptamer (to form a single amphiphile) and many of these will then form the micelle.

The research implies that a drug could be attached to the aptamer, which can locate the tumour and bind to it, so that the drug can easily diffuse into the cell. This allows the treatment to be more specific to a particular area, rather than distributing the drug around the body. The micelle would therefore reduce the amount of damage caused to healthy cells. The centre of the micelle is hydrophobic, thus can be filled with drugs which in this particular case are required to treat cancer.

Perhaps it would also be a good idea to provide a method of drug delivery that is biodegradable. Smart materials release drugs when triggered by changes in there environment. Once the drug is released is there a way for the casing (method by which the drug has been delivered) to disintegrate so that it may be expelled from the body? Both micelles and nanoshells currently incorporate PEG into there structure, so that they are not targeted by the body for removal. Theoretically, they could be injected into a patient who doesn’t suffer from cancer but whose family has a history of it. Therefore if the cancer cells develop, they will be treated by the micelles. However, extensive research must be done to ensure that the drug delivery system does not break down and release the drugs around healthy cells. This would only be useful if the drugs used to treat cancer had a very long life, and they don’t expire while inside the body.

Ethical Issues

Not all the outcomes of the use of nanotechnology are positive. So much so that the U.K Royal Society has been and continues to research potential risks of nanotechnology's. The U.S Environmental Protection Agency also has researched into possible damages and advantages to human health and the environment. Areas where nanotechnology is used to enhance human health are specifically being thoroughly inspected. There is increasing concern on the subject of nanotechnology, as it is a new area that humans have never experimented with although it has been steadily developed toxicity.

An experiment by Southern Methodist University in Dallas was performed to investigate the possible effects of buckyballs to living cells. The results showed that buckyballs can disturb the membranes of fish brain cells. This alarming result caused further experiments' to be performed to assess whether there could be similar effects on human cells. Researchers from Rice University subjected laboratory grown human liver and skin cells to buckyballs solutions. The results were that half the living cells were killed when the solution was at around 20 parts per billion. These results help create a picture of limits and possible negative effects of using nanotechnologies in living human cells but they are not conclusive so further testing and research needs to be carried out.

A possible solution to the toxicity is under development. The toxicity is found to be reduced when adding simple chemical to the buckyballs. This is particularly useful in drug delivery systems. This effect is unfortunately reversed when the modified buckyballs are subjected to the sun's ultraviolet light.

However the companies carrying out the research have to be considered as some may have an interest in the outcome so the results may have a bias outcome to benefit them.

There is also fear that products of nanotechnology research will not be shared between LEDC's and MEDC's. MEDC's have the money to research all the opportunities of nanotechnology and the chance to patent and reap all the rewards. Perhaps the countries which have the highest demand for the products' (possibly specifically in the medicine area) can't afford to purchase them or carry out research themselves, so as to have a chance at developing their own products so they don't have to depend on MEDC's or accept their price for the products.

There is concern about the management of production of the treatment after the patent expires. There is no governing body at present that has developed and enforced any safety regulations or any quality control measures, specifically for nanotechnology. Without these there is a real risk to the health of any human or animal using nanotechnology.

With regard to the ethical issues concerning medicine, there are strong objections to the use of nanotechnology as a means of diagnosing and treating both animals and humans. Some people believe that by altering our future by any means not just medically we are interfering with God's plan for our individual futures, and our world's future. By doing so we are demonstrating a lack in trust and faith in God.

Conclusion

Overall, we think there is a real possibility that nanotechnology will be able to be used effectively in the future to treat and diagnose cancer and a variety of other illnesses. Although some ethical issues are opinion based, some of them are important issues and will need to be considered if nanotechnology is to be used in medicine. The aptamer – micelles is probably the most promising development for the future of cancer treatment. Although, all the prospective treatment we have studied offer a hopeful and attainable way of treating and diagnosing cancer. With all theses different ways being developed the patient will have a dynamic and diverse range of treatments to choose from which will suit them best allowing the profession to perhaps tailor treatments to the individuals needs.

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