THE POTENTIAL OF USING NANOTECHNOLOGY TO DETECT, PREVENT AND TREAT CANCER

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ABSTRACT

Nanotechnology is the study of the manipulation of compounds at the scale of 1-100 nanometres. It can be used for many things from packaging to engineering and electronics. It is a very diverse subject as both traditional and new ideas can also be used at nano scale to make them more effective and precise. At the moment, research into nanotechnology to aid with the diagnosis and treatment cancer is very promising with new discoveries being made all the time. Experiments and tests on nanotechnological substances are proving to be potential cures for cancer in the future. At the moment, cancer has no cure but nanotechnology could be the way forward for the diagnosis and treatment of cancer.

INTRODUCTION

What is Cancer?

Cancer is a term to describe over a hundred different types of disease where a cell mutates due to either environmental or genetic factors which lead to the abnormal, uncontrollable growth and division of cells. As it is often very difficult to control; it can spread easily through the body, blood and lymph systems. The study of cancer is given the name oncology. Cancers are often named according to the organ at which it originated from. Cancers can be classified into five main categories. These are:

Carcinoma Cancers	Carcinoma cancers are cancers which originates in the skin or tissues which line or cover internal organs.
Sarcoma Cancers	This is a cancer which originates in the bone, cartilage, fat, muscle, blood vessels or other connective or supportive tissues.
Leukaemia Cancers	Leukaemia is a cancer which begins in tissues which produce blood, for example bone marrow, therefore causing a large quantity of abnormal blood cells to be formed. These then enter the bloodstream and are carried throughout the body.
Lymphoma and Myeloma Cancers	These are cancers that start in cells relating to the immune system.
Central Nervous System Cancers	Cancers of the central nervous system are those that begin in the brain or spinal chord tissues.

It is an ongoing and increasing problem as more and more people are being diagnosed with it each year. Every year about 10-11 million people are diagnosed with cancer and about 6-7 million of these died. The rate of diagnosed people increases every year.

Current Treatment for Cancer

In the nineteenth century, the microscope was developed and this made it easier for scientists to study diseased and abnormal tissues such as cancerous tissues. Soon after this development, oncology became a medical speciality. Microscopic pathology not only improved our understanding of cancer, its causes and the damage it does to the body, but also helped to develop the current cancer treatments and make them more effective.

However, more people are surviving the disease due to treatments such as surgery, radiotherapy and chemotherapy. Surgeons can now remove solid cancerous tissues and, most of the time, the body remains unharmed. This is the most common form of treatment and can cure a patient of the disease completely, as long as the tumour is not extremely large and has not spread outside of the organ in which it began. However, this treatment can also be used in conjunction with radiotherapy or chemotherapy, if this is the case, and can be very affective but not all cancers can be completely removed from the body due to the size, position or complex surgery needed to remove it. Pathologists can then make examinations on these cells either before or after removing the whole cancer, making an accurate diagnosis and can even tell if the cancer has been completely eliminated from the body. To diagnose the cancer, a small sample of the tissue can be removed and examined to determine if cancerous cells are present, the grade of the cancer and how far the cancer has spread. This is called a biopsy.

Radiotherapy is a form of radiation where a stream of particles is fired directly onto the affected tissue with a very high-energy and therefore can be used on either solid or non-solid tumours. This is aimed to destroy any cancer cells in or around the tumour but is not very accurate and, therefore, can kill any normal cells it hits as well. Therefore this form of treatment is complicated and the dosage and recovery period must be balanced with the need to remove the cancer. Radiotherapy is commonly used before surgery to reduce the size of the tumour, often after an operation to prevent the regrowth of cancerous cells or to destroy any cancer cells which may have been missed during surgical removal.

Chemotherapy is a drug based treatment for cancer. There are many different types of chemotherapy drugs which are used and often combined which is called Combination Chemotherapy. The drugs used depends on a number of factors including:

- The type of cancer
- The grade of the cancer
- The stage at which the cancer is at and how far it has spread
- The age and health of the patient

Chemotherapy is most commonly used after surgery to destroy any remaining cancer cells either at the origin or cells that may have spread to other parts of the body. It can be used before surgery but this is not very common. Chemotherapy has some common side effects including hair-loss, nausea, vomiting, and diarrhoea. However, most of these side effects will either clear up at the end of the treatment or can be minimised during treatment with other medication.

What is Nanotechnology?

Nanotechnology is the study of atoms or molecules between 10nm to 1000nm. Therefore it brings together very unique teams of people including physicists, mathematicians, biologists and engineers. It looks at ways in which we can make small micro-machines which increase functionality and have the exact properties needed for a particular task. As the components are so small they would be more efficient for the diagnosis and treatment of cancer. Nanotechnology is still in its early stages but during the last five years the field has developed dramatically and has been introduced into medicine. There are currently some clinical trials taking place.

DISCUSSION

One of the main causes of cancer is faulty or mutated genes. Most cancers are caused by damage to the DNA in cells mostly due to the environment such as too much sunlight, but sometimes also due to genes. The most common risks factors are age, environment and lifestyle.

DNA damage is common and happens often but, most of the time, the body repairs the DNA without us ever realising something is wrong. DNA can be damaged by UV light and other carcinogens such as tobacco smoke, asbestos and air pollution. Mutations in genes mean that the cell cannot understand its instructions and carry out its functions any more. Occasionally, the mutated cell starts to multiply uncontrollably and a tumour develops. These tumours will have faulty copies of one or more of the four main types of gene involved in cell division.

Some people are born with a fault in one of their genes. This does not mean that they will definitely develop cancer but does mean that they are more likely to due to this genetic predisposition. For instance, women born with a mutation in one of their BRCA genes (responsible for cell growth in the body) are more likely to develop breast and ovarian cancer than women who do not. Faults in a BRCA gene can also increase a man's risk of prostate cancer.

Some viruses are linked to certain types of cancer although cancer is not infectious and so it does not pass from person to person. Not everyone infected with these viruses will develop cancer.

Some examples of virus causing cancers include:

Hepatitis B and C	which are viruses which have been known to be linked to the development of primary liver cancer.
Human T-Cell Leukaemia Viruswhich	is known to be a cause of leukaemia.
Kaposi Sarcoma Virus (KSV)	which, especially in people with HIV/AIDS, can cause a certain type of soft tissue cancer.
Human Papilloma Virus (HPV)	which is one of the major causes of cervical cancer.

Epstein-Barr Virus (EBV) has been linked to a few types of childhood cancers, such as carcinomas and lymphomas.

Human Immunodeficiency Virus (HIV) suffers are often extremely at risk of developing several different cancers due the their weakened immune system.

In cancer, the cell cycle runs out of control. Cancerous cells tend to overact to growth signals and therefore multiply and grow uncontrollably, forming a tumour. Tumours have a large blood supply as they need oxygen and nutrients to grow. New tumour cells stimulate the growth of blood vessels which help it to grow bigger more quickly. Tumours can spread fairly easily throughout the body by metastasis. This is when part of the tumour breaks away from the main tumour and travels to another part of the body (for example, via the blood stream) to form secondary tumours in the part of the body it ends up in.

Cancer can occur in most organs of the body. The most common cancers in the UK are:

Lung cancer

Cancer that begins in the lungs is known as primary lung cancer. Cancer that begins in another part of the body before spreading to the lungs is known as secondary lung cancer. There are two main types of primary lung cancer, which are classified by the type of cells in which the cancer starts. These are:

- Non-small cell lung cancer
- Small cell lung cancer

Radiotherapy, chemotherapy and surgery can be used to treat lung cancer; certain factors depend on the type of treatment used such as the type of lung cancer and the stage of the lung cancer.

Small cell lung cancer is less common and more aggressive. The most common treatment for this is chemotherapy. Surgery is not usually suitable because this type of cancer has usually spread at the time of diagnosis. Radiotherapy can also be used but chemotherapy tends to be more effective.

Non-small cell lung cancer is the most common form of lung cancer and can be treated with surgery, chemotherapy, radiotherapy or a combination of these, depending on the stage when the cancer was diagnosed.

In 2008, the conventional medicine did not work for the 1.38 million people who died from lung cancer. Conventional diagnostic methods for lung cancer are unsuitable for widespread screening because they are costly and can miss tumours. Gas chromatography/mass spectrometry studies show that some volatile organic compounds which normally appear at levels of 1–20 ppb in healthy human breath, are much higher at levels between 10 and 100 ppb in lung cancer patients. New methods of diagnosis using nanotechnology based on gold nanoparticle sensors can quickly and efficiently distinguish between these different levels of organic compounds in human breath. This method of diagnosing would be much less invasive, easily portable and probably less expensive. It would be more effective and quicker than scanning or biopsies. It works by the metallic particles providing electric conductivity and the organic film component provides sites for the absorption of analyte molecules. The film is selective and swells in response to certain chemicals. This causes the nanoparticles to be pushed apart and, therefore, increases the resistance across the device. Each of the films were designed to be broadly responsive to a variety of the volatile organic carbons that are characteristic of lung cancer sufferers. Although the sensor has not been fully tested, it could potentially save thousands of lives in the future.


The nanoparticle device. © http://www.technologyreview.com/

Breast cancer

There are several different types of breast cancer, which can develop in different parts of the breast. Breast cancer is divided into non-invasive and invasive types:

- Non-invasive breast cancer is a cancer found in the ducts of the breast and does not spread outside the breast. This type of cancer seldom shows as a lump in the breast but is usually detected on a mammogram. The most common type of non-invasive cancer is ductal carcinoma.

- Invasive cancer is able to spread outside the breast, although this does not mean it necessarily will. The most common form of breast cancer is invasive ductal breast cancer, which develops in the cells that line the breast ducts. Invasive ductal breast cancer accounts for about 80% of all cases of breast cancer.

At the moment mammograms, ultrasound and biopsies are used to diagnose breast cancer. Currently, the main treatments are surgery, such as:

- **Mastectomy** which is the removal of the whole breast
- **Lumpectomy** which is when only the cancerous lump is removed
- **Quadrantectomy** which is the removal of part of the breast

Radiotherapy, chemotherapy and hormone therapy are used to treat breast cancer. Unfortunately, only 16% of patients will respond to surgery or radiotherapy. In 2008, 458,000 women died from breast cancer.

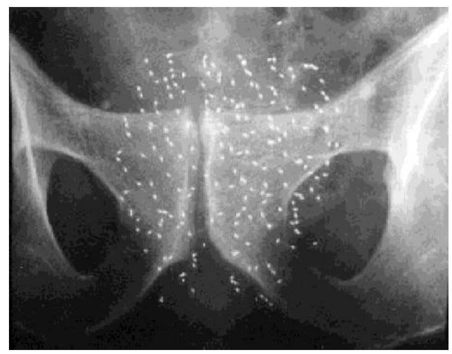
Recently, tests on mice which have been infected with human breast cancer have shown that nanoparticles made from a biodegradable polymer combination could drastically increase the mortality rates of breast cancer sufferers. The nanoparticles firstly releases a powerful anti-cancer drug before delivering a compound which tricks the cancerous cell into committing suicide. These nanoparticles are effective in maintaining high levels of these chemicals in the cancer cells. The experiment used bioprobes of iron-oxide nanospheres and radiolabeled monoclonal antibodies. The bioprobes were 'hidden' in polymers and sugars which made them 'invisible' to the body's immune system so they were not attacked by antibodies. The bioprobes were injected into the mice and, once in the bloodstream, began to seek out and attach to the cancerous cells and destroy HER2 protein (an abundant protein associated with aggressive tumours). Three days later, the team applied an alternating magnetic field to the tumour region, causing the magnetic nanospheres which had latched onto the tumour cells to change polarity thousands of times per second, instantaneously generating heat. As soon as the alternating magnetic field stopped, the bioprobes cooled down. This caused the tumour growth to slow down significantly. This showed a correlation between the cancerous cells and the high heat dose which suggests that the bioprobes could be used to target aggressive forms of breast cancer.

Prostate cancer

Prostate cancer grows within the prostate, often for many years before it is apparent. Eventually, prostate cancer can spread outside of the prostate. Prostate cancer can spread beyond the prostate by invasion, spreading through the lymph system and by metastasis.

At the moment, the only ways of testing for prostate cancer are to have the prostate examined by a specialist or to take a blood test and look for prostate specific antigens in the sample. If the blood test shows that there are higher than normal levels of prostate specific-antigens, this could be due to prostate cancer. However, further tests must be done to check that it is prostate cancer as other factors can cause this rise. Researchers have developed a sensitive screening tool based on nanotechnology which detects minute amounts of prostate specific-antigens in patients who have had a prostatectomy and it is thought that all cancer cells have been removed as blood tests have shown no raised levels of prostate specific-antigens. The tool is 300 times more sensitive than the current prostate specific-antigens blood test tool. The device will be used to find out if cancer has returned in a patient and can detect the prostate cancer much earlier than conventional medical tools for prostate screening. The device is based on gold nanoparticle probes covered in DNA and antibodies which recognise and bind with the prostate specific-antigens, even at extremely low levels. Another nanoparticle also attaches to the prostate specific-antigens and DNA records the amount of prostate specific-antigens. The particles containing prostate specific-antigens are removed and the DNA shows the new amount of prostate specific-antigens present.

Another study in the treatment of prostate cancer is the radioactive gold isotope 198 which could be used at nanoscale. The nanoparticles of gold are coated with Arabic glycoprotein to make sure the nanoparticles can escape the blood stream and accumulate in tumours. These biocompatible nanoparticles only accumulate in prostate tumours and emit electromagnetic radiation to destroy the tumour. When this was tested on animals, it showed an 82% decrease in the size of the tumours in the prostate and showed that these radioactive nanoparticles are only dangerous to tumours and not healthy cells. Although tests have not started on human volunteers, it could potentially be an effective way to destroy tumours as, so far, tests have shown the treatment to be non toxic to humans.



Abdominal radiograph of the procedure
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Bowel cancer

About 80% of bowel cancer cases develop in people who are aged 60 years or over. Two-thirds of bowel cancers develop in the colon, the other third develops in the rectum. Screening for bowel cancer includes:

- Proctoscopy which is looking inside the rectum
- Biopsies
- Rectal examination
- X-ray of the large bowel (Barium enema)
- CT and Ultrasound scans

Treatment for bowel cancer includes chemotherapy, radiotherapy, surgery and biological therapy. Over the years, the number of patients surviving bowel cancer has doubled. Although, in 2008 there were still 600,000 people who died from bowel cancer. This is a considerably high number which scientists hope to drastically reduce with the aid of nanotechnology.

In recent investigations into nanotechnology, a team of investigators have designed a nanoscale, polymer based drug delivery vehicle that, when loaded with a widely used anti-cancer agent, should be a very effective treatment as it cures colon cancer in mice with just one single dose. This invention represents a huge leap in a global effort to create a nanoscale drug delivery vehicle in order to maximize the anticancer activity of the drug in the nano sized vehicle.

Taking drugs orally is one of the most common ways of taking medication. This could still be used by making nanoparticle sized oral drugs to treat bowel cancer. This can only be done providing that the drug is able to survive in the acidic conditions of the stomach, the mucus layers lining the gut and the fast clearance of the gut so as not to be excreted. Being able to deliver a drug by mouth has several benefits over injection or suppository:

- It is easy to take a dose.
- Patients tend to prefer oral medicine.
- It goes straight to the bowel through the alimentary canal.

Various methods have been tried, including coating drug molecules with a polymer shell. However, researchers at The University of Texas at Austin, have reviewed the various techniques being investigated and suggest that encapsulating a drug molecule in nanoparticles is the best option for targeting the bowel and controlling drug delivery.

Advances in particle engineering techniques have recently made it possible to make drug products on a nano scale. Techniques such as spray drying, anti-solvent methods, dialysis methods, emulsion methods and cryogenic methods are now all available for drug formulation. Converting a drug powder into nanoparticles can often make a compound poorly soluble in water due to an increase in the surface area to volume ratio. However, smaller particles mean that there is a bigger surface area to interact with absorbing surfaces in the alimentary canal, such as the small intestine which needs a big surface area for nutrients absorption. Therefore, a fatty, solid compound called quercetin is used as it is absorbed nearly 6 times more effectively by the gut in nanoparticle form than in the common form of the drug compound. Hence showing that nanoparticles will be very valuable in treatment of bowel cancer in the future.

General Diagnosis and Treatment of Cancer Using Nanoparticles

For the diagnosis of cancer, sensors based on nanoparticles or nanowires can detect proteins related to specific types of cancer cells in blood samples. This could allow early diagnosis of cancer. Superparamagnetic nanoparticles that bind to cancer indicating proteins mean that 'clusters' of these can be detected as they provide a magnetic resonance signal, thus indicating the presence of the cancer related protein.

A chemotherapy related treatment which delivers a tumour-killing agent called tumour necrosis factor alpha (TNF) to cancer tumours, could be used in the future. TNF can be attached to a gold nanoparticle along with Thiol-derivatized polyethylene glycol (PEG-THIOL) which hides the TNF bearing nanoparticle from the immune system. This allows the nanoparticle to travel through the blood stream without being attacked.

Another treatment for cancer uses heat therapy to destroy cancer tumours using nanoparticles is called AuroShell. The AuroShell nanoparticles travel through a patient's bloodstream and exit where the blood vessels are leaking at the site of cancer tumours. Once the nanoparticles build up at the tumour, the AuroShell nanoparticles are used to concentrate the heat from infra-red light and destroy cancer cells.

CONCLUSION

Altogether nanotechnology will play an important role in the future of curing cancer. Nanotechnology provides a way to cure diseases without having to use surgery on a patient to find the tumour and then remove or reduce it in size.

Nevertheless, there are still many ethical questions that need to be assessed such as whether nanotechnology should just be used for medical reasons, if it should be used to create an abundance of food and water for the whole population and also if it should also be used for luxuries such as cleaning houses, or making cars. Nanotechnological uses seem unlimited and, therefore, the problem is where to stop.

Many people argue that nanotechnology should just be used for high priority problems such as a flu epidemic or for military use, but medicine is about making the lives of people better and so if nanotechnology allows medical research and eventually diagnosis and treatment to improve, should it not be used? Nanotechnological medical devices pose many problems such as the cost of testing and manufacturing them and also the waste products of these need to be taken into account. However, the benefits of nanotechnology could make up for these. Also, many people argue that conventional medicines also create waste when they are made and disposed of and that nanotechnology is worth will reduce this dramatically.

The potential of nanotechnology in medicine is limitless and, over time, findings in nanotechnology will improve the lives of the human population. The diversity of nanotechnology is huge, ranging from nano scale versions of traditional devices to brand new pioneering devices. Unfortunately, the effects of nanotechnology in the future are unknown and, therefore, many tests on nano material must be carried out to prevent or minimise the risks nanotechnology could create.

Using nanotechnology to diagnose and treat cancer does not necessarily mean that existing treatments would be discarded and replaced by ones using nanotechnology, as the current treatments are very affective at destroying cancer cells. Nanotechnology could improve the accuracy at which these treatments are implemented as the treatment could be delivered specifically to the cancer cells. Consequently normal cells would not be affected by the treatment and any side effects would be dramatically minimised.

Currently, new particles and constructs are being developed that could help to diagnose the cancer early. A combination of early diagnosis and therapeutics could save the lives of thousands of people.

REFERENCES

What is Cancer? www.cancer.gov/cancertopics/cancerlibrary/what-is-cancer
Learn About Cancer www.cancer.org/Cancer/CancerBasics/TheHistoryofCancer/index
Cancer Nanotechnology Podcasts www.nano.cancer.gov/learn/impact/podcasts.asp
Nanotechnology and Cancer www.nano.cancer.gov
Cancer Help www.cancerhelp.org.uk
Nanotechnology www.nanowerk.com
Nanotech Now www.nanotech-now.com