Uses of Nanotechnology in Cancer

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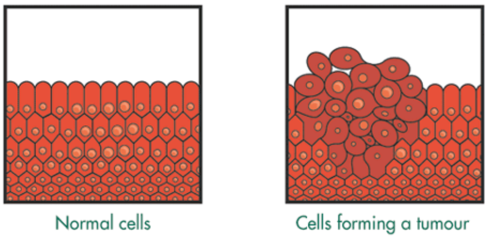
Abstract

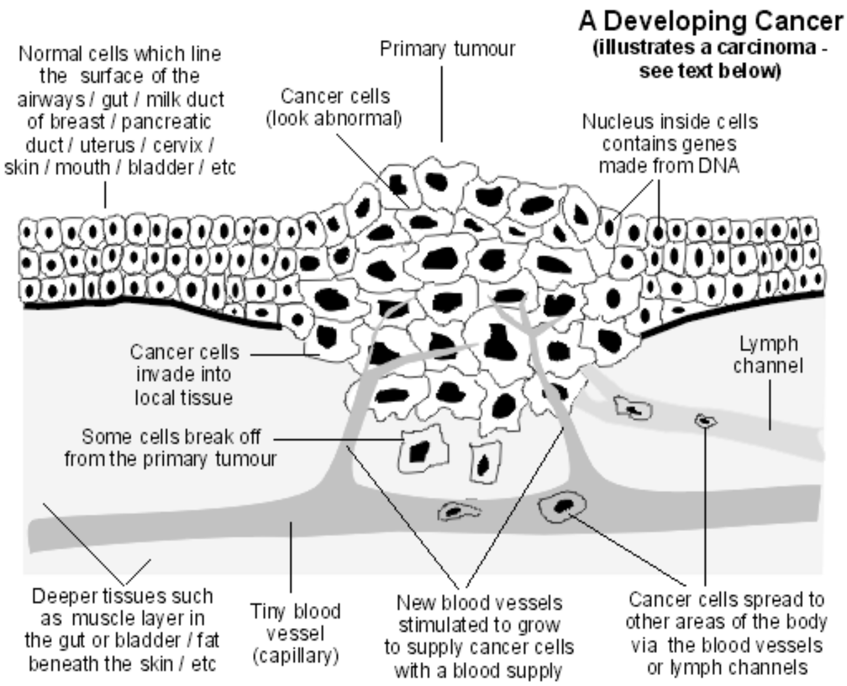
Cancer is one of the leading causes of death across the world; with 297,991 cases diagnosed in 2007 and 156,723 deaths in the UK alone (a shocking 52.6% mortality rate). It is clear that a cure for cancer would be miraculous* for the world. Due to cancerous cells dividing very quickly, it is important to target the disease as early as possible – at a molecular level. In order to this, we must use equipment** that can operate at this level. Nanotechnology is the branch of engineering that deals with things smaller than 100 nanometres (e.g. molecules/organelles concerned in cancer research). To go about combating cancer, we shall break it up into two parts: Detection and Treatment. We shall also discuss the practicality and ethics of using nanotechnology, not only in cancer, but medicine in general.**

Introduction



Cells are constantly dividing, predominantly through mitosis, throughout the body. metastasis; this can quickly lead to exponential growth which produces a lump or a tumour. Tumours can be benign or malignant.

A benign tumour does not damage the cells or surrounding tissue – it cannot metastasize and is not cancerous. They can grow fairly large without causing any harm to the body. However, should the growth become too big, the tumour may start to hinder and damage other organs simply due to its size. There are also other problems which may occur such as excess hormone production, bleeding or anaemia, or simply looking unsightly.



A malignant tumour does damage cells and surrounding tissue. These tumours can metastasize – therefore, cancerous cells can spread to other parts of the body via the bloodstream or lymphatic system. A new, secondary tumour may start to form where the cells are deposited or in the blood (leukaemia). Malignant much more dangerous than benign, and can often be life threatening.

It is important to recognise that caner is not one single disease; it is a general term incorporating over 200 diseases. These different types mainly arise from there being growths of different cells. Due to this, cancer becomes very difficult to treat.

The cause of these cell abnormalities cannot be pinned down to one reason, there are many:

- Chemical and toxic compound exposures
- Ionising Radiation
- Pathogens
- Genetics

These are just a few major causes – new causes are frequently added as a result of new research. Although we call these factors 'causes', not everybody who experiences them will definitely have cancer. For example, sunlight is an example of ionising radiation, but we do not contract cancer when sunbathing. These factors only increase the risk/ chance of contracting cancer.

Cell division is normally controlled by four main mechanisms – cyclins, CDKs, APCs and cell cycle checkpoints.

Tim Hunt (1982) discovered that cyclins bind to CDKs (cyclin-dependent kinases) which, in turn, activates the CDK. Certain types of CDK are used for different stages of the cell cycle (see fig. 3) – this is what drives the cell cycle and cell division.

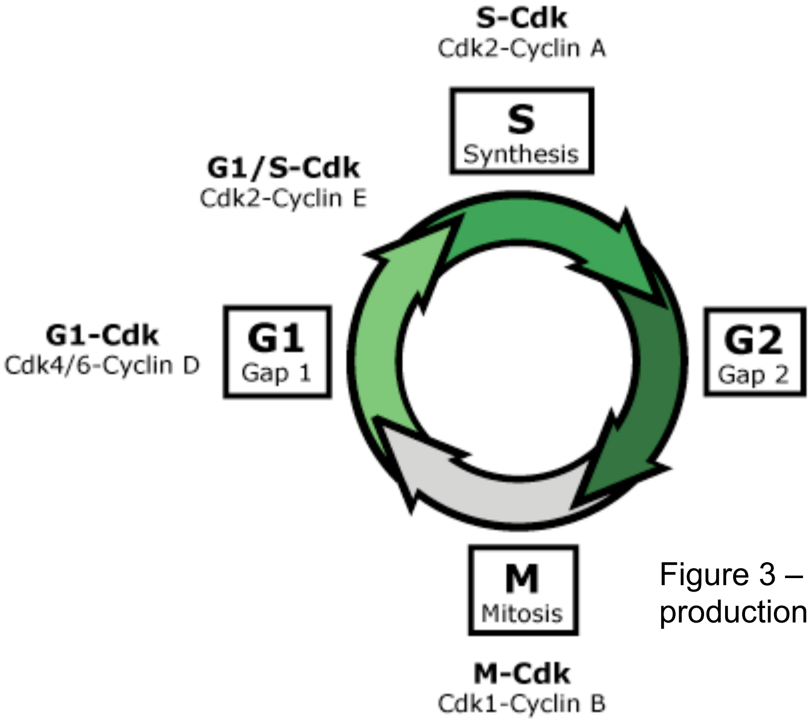


Figure 3 – CDK/Cyclin production during the cell cycle

APC (adenomatous polyposis coli) is a tumour suppressant gene (it protects the cell from cancer). Therefore, if this gene mutates, cancer can quickly occur – with this gene, colorectal cancer in particular. APC controls how often a cell divides, how it attaches to other cells within a tissue, whether a cell moves within or away from a tissue, and ensures there are the correct amount of chromosomes produced in the new cell.

Cell cycle checkpoints are a control mechanism that checks each phase of the cell cycle has been accurately completed before moving on to the next. It is effectively the body's 'double check' system to ensure everything is going as planned.

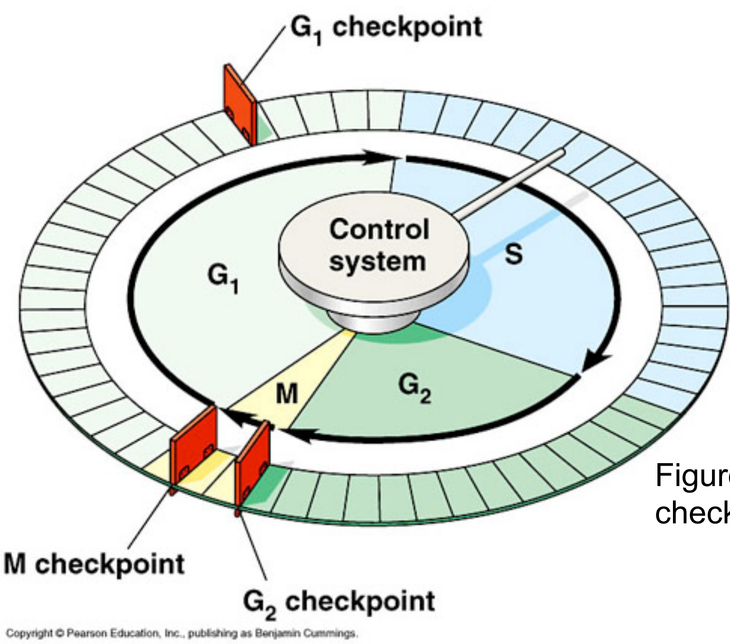


Figure 4 – Cell cycle checkpoints

History and Development of Nanotechnology

Nanotechnology is a fast moving part of medicine which is constantly progressing. It is defined as the branch of engineering which deals with things smaller than 100 nanometers. In terms of medicine this has massive potential as it means that we can deal with issues on a cellular scale.

The idea of manipulating substances on a nano scale first came from Richard Feynam who gave a talk titled "There's Plenty of Room at the Bottom." Although this never explicitly mentioned 'nanotechnology', the principles of 'nano factories' which then went on to influence many other scientists. Then in 1981 Eric Drexler wrote a paper which combined Feynam's initial thought process with modern day science with the theory of molecular manufacturing.

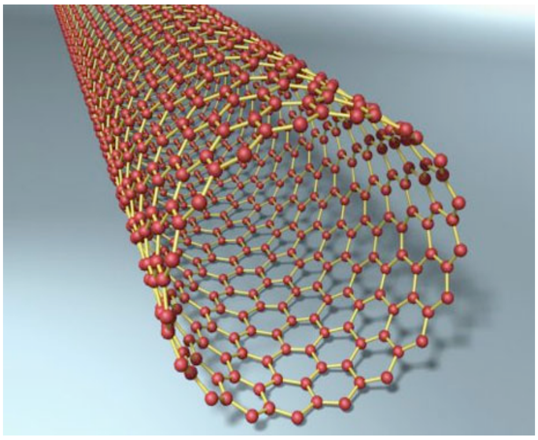


Figure 6 –A Carbon Nanotube

These basic principles were the foundations of the nanotechnology that is being researched in medicine today. Some of the most promising uses of nanotechnology at the moment are buckyballs (buckminsterfullerene.) A buckyball is a molecule made of the 60 carbon atoms. The carbon atoms bond in a way which resembles a football. Because of this shape they can be used to store and deliver medicine in the body. It releases the medicine at the site of infection due to a change in pH. Another promising piece of research with nano medicine are nanotubes. These can also be used to deliver drugs around the body.

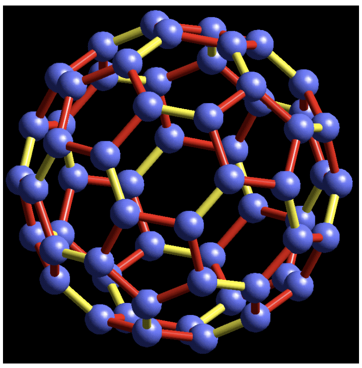


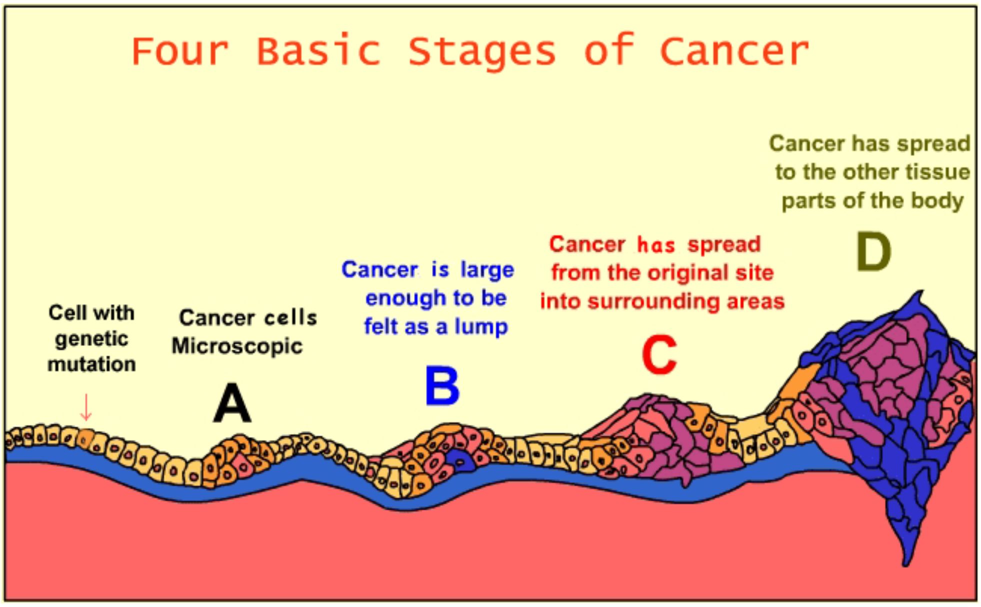
Figure 5 – A 'Buckyball'

Discussion

Detection

There are three main ways to detect most diseases: symptoms, imaging, and ELISA tests (enzyme-linked immunosorbent assay). For the detection of cancer, the ELISA test would be the best - this is due to it being quantitative rather than qualitative. With the results of these tests, we can see how much the patient's results deviate from the norm. Symptoms can often be ambiguous and we may not be able to conclude that they are appearing because of a tumour forming. Imaging techniques are qualitative and subjective - often things can easily be missed.

The methods used to detect cancer have many flaws; I will briefly explore the major detection methods in use now, and their flaws relating to fig *:



Symptoms

- Symptoms [Very late detection]
    - Often only appear around stage C/D
- Physical Exam [Very late detection]
    - Often only appear around stage C/D

Imaging

- Mammogram (x-ray of the soft breast tissue)
    - Only appears when there are hundreds or thousands to create a strong enough signal (Stage C)

- Endoscopy
    - Evidence needed for this to go ahead → late detection
    - Uncomfortable for patient

- MRI (magnetic resonance imaging)
    - Small tumours missed
    - Only appears when there are hundreds or thousands to create a strong enough signal (Stage C)
- PET scan
    - Expensive – few hospitals have them
    - Can't be used on pregnant women or babies

ELISA

- Blood/Urine Tests

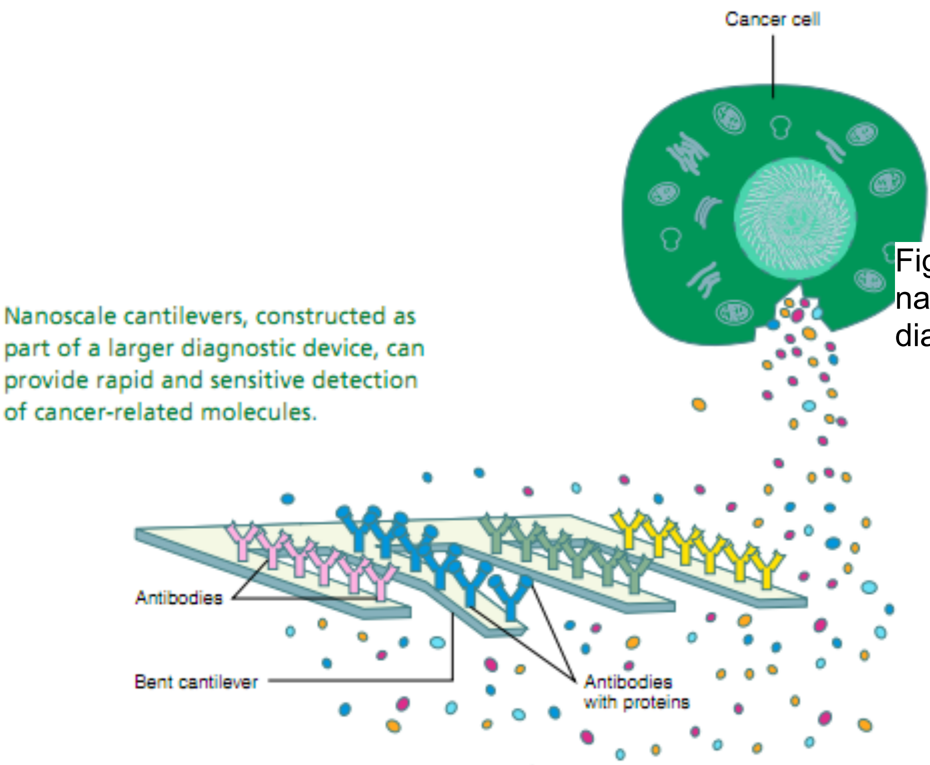


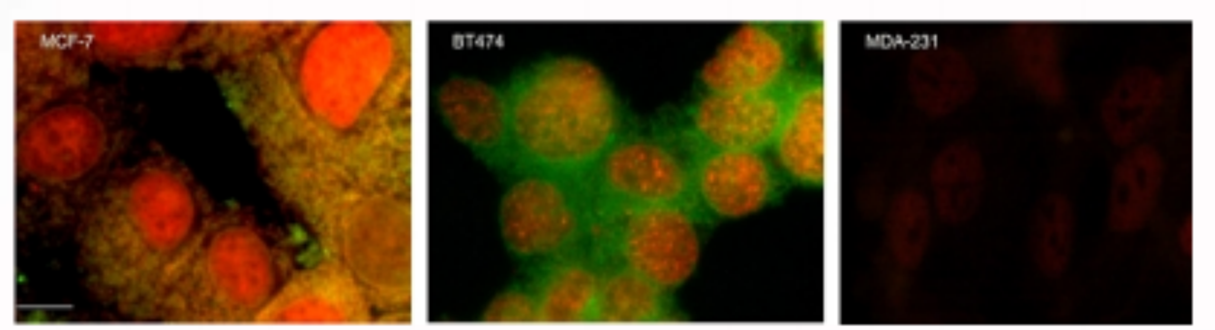
Figure 8 – The use of nanoscale cantilevers in diagnosing cancer

- Ambiguous – may not be cancer

Using nanotechnology, we can create a detection method that is qualitative, (2004), we can combine the ELISA technique with nanotechnology. "1-2 nanometre-wide built on a micron-scale silicon grid can be coated with monoclonal antibodies directed against various tumour markers. With minimal cancer cell sample preparation, substrate binding to even a small number of antibodies produce a measurable changed in the device's conductivity leading to a 100-fold increase in sensitivity over current diagnostic techniques.

This method could be used in a lab with cancerous samples; but if it is done In Vivo, then it may get caught or rip an artery/vein wall, and may not diffuse out of the blood. To solve this problem, we can coat the device in hydrophilic molecules, allowing it to dissolve into the blood. This avoids the previous problems and allows it to diffuse out of the blood.

Another method, using imaging, is using 'Quantum Dots'- single crystals, a few nanometres wide, with unique optical and electronic properties related to the size of the molecule.



A Qdot can be covalently bonded to an antibody or enzyme, at a site away from the active/antigen binding sites, which targets a tumour marker. When the antibody/enzyme binds to the tumour marker, the covalent bond between Qdot and antibody/enzyme is broken. The Qdot therefore loses an electron and, due to the very small size of the molecule, changes its shape. This change in shape alters its optical and electronic properties meaning that it emits a lower wavelength photon or less electricity. This can be measured (e.g. using a fluorescence microscope) and compared to the norm to diagnose cancer.

Figure 9 - Fluoroscopy of three cancer patients using Qdots

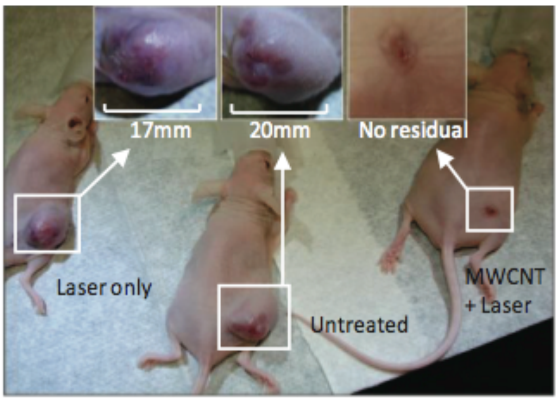
Treatment of Tumors

We can treat tumors by using Multi-Walled Carbon Nanotubes which can be used to give laser induced thermal therapy. This method can potentially be a massive improvement on the current methods used to treat cancer because primarily it gives us the ability to destroy tumors leaving all other cells unharmed.

These MWCN are cylindrical structures which have been made to be one millionth the size of a hair follicle. MWCN have been tested to have the strength of 63 gigapascals (this is the equivalent of a cable of 1mm cross section being able to endure tensions from a weight of 6422 kg.) They are made of multiple layers of carbon and heavier metals making them perfect for conducting heat. MWCN have been proven to reach high temperatures in much less time than single walled nanotubes.

Laser induced thermal therapy (LITT) works because the multi-walled carbon nanotube can absorb energy from a laser which it will then respond by vibrating, creating heat energy. As the MWCN heats up it triggers a process called Coagulative Necrosis. This is a form of cell death which happens due to proteins denaturing.

In theory this idea sounds great but there can be issues with the detection of the tumor. I believe that this can be solved by using the nano particles. I am proposing that we attach antigens onto the nano particles which will be complimentary to the tumor cells. We then fill these nano particles with a magnetic metal. If the nano particles attach to the tumor cells then we will be able to detect the area which the tumor is in on an MRI scanner. This is because MRI scanners will pick up the magnetic field from the metal and then represent it as a shaded area on the scan. Therefore we will be able to tell where the tumor is on the scanner



Treatment Using Chemotherapy Drugs

One of the most common current treatments of cancer is chemotherapy. This is where a patient is given chemicals which will effectively inhibit mitotic division of their cells. This is aimed to target rapidly dividing cancerous cells but it could also lead to the inhibition of normal cells dividing. Therefore there is the issue that the dividing cells will die leaving the patient feeling generally weak. But I believe with nano technology we can prevent the loss of cell division in healthy cells. We can do this by targeting individual cancer cells with nano particles.

Cancer cells have specific antigens on them, these antigens will fit a complimentary antibody. Artificial antibody can be produced which could in theory be complementary to the antigens on the cancer cells. These artificial antibodies could change shape when they are attached the cancer cell antigen. The antibodies could be attached to a nano particle which has the ability to store substances inside of it. A nano particle which could potentially be used for this are carbon nanotubes. Inside of this nano particle we could store the chemotherapy drugs which will then prevent each individual cell from dividing.

We would inject a patient with the nano particles in an area near the cancer cells, then once they have reached the cancer cells the antigens on the their surface will recognize the antibodes on the nano particle which can then change shape therefore releasing the chemotherapy drug into the cancer cell. This chemotherapy drug will then have the same effect as before although it is not effecting any cells other than the individual cancer cell. This will therefore reduce side effects of the chemotherapy significantly as well as being a more effective and efficient way of using the drug. There would be much greater chance of the cancer being completely wiped out if we can attack specific cells.

Ethics of Nanotechnology

As nanotechnology is such a cutting edge part of medicine that is moving very fast the ethics of it are often forgotten. It is fundamentally important to consider the social implications of the future of nanotechnology.

156,723 people died of cancer in the UK in 2007 this only makes research into Nano medicine even more important. But Nano medicine is a highly advanced field which costs billions of pounds to research and develop. Because of this there is the possibility that it could cause segregation in our society. This could happen because of the high prices of nanotechnology. Do we really want to live in a society where such an important cure such as ‘the cure for cancer’ is only available to those who can afford it? Especially in countries such as America where health care already must be paid for now we are now only making those who can afford health care an even smaller minority with such expensive treatment as nanotechnology. What is the point in providing this treatment if it is only available to the very privileged?

Although nanotechnology might cause segregation between societies within nations, it is a different story when we are talking about cross-nation segregation. Twenty years ago scientific research was a very confidential thing with a small group of nations moving forward with the research as they did not share research papers with other nations. But now with the use of the internet most research papers are fully available for anyone in the world. This is a massive advantage to nanotechnology because it means that improving it is a global effort. Surely this is only right that information on how to save millions of lives is available to everyone?

Environmental Problems

The nano-particles we are suggesting using in our treatment for cancer are potentially very harmful to humans as well as being useful. They are harmful simply because of the size of them. Phagocytes can usually protect the body from foreign substances in the blood stream but if a nano particle were to get in the bloodstream then there is nothing a phagocyte could do because quite simply the nano particle is too small. This creates a big issue as the nano particle can then access anywhere in the body it possibly wants to access including the brain.

The size of nano particles means that they have a large surface area: volume ratio. This means that they are highly reactive but this is depending on their coating. The chemical qualities of nano particles are not yet fully understood though they are suspected to be different due to their size.

Once the nano particles have been used in the body where do they go? This depends on the coating of the particles. If the coating is bio-degradable then they can be excreted via the kidneys but if it is non-biodegradable then there can be a build up of particles in places which are potentially harmful. For example if there was a build up of nano particles in the brain what might happen?

As nano particles are so small they are usually airborne, because of this they can easily be breathed in by humans. Breathing in nano particles will eventually lead to the risks mentioned earlier. We know such little about the chemistry of nano particles that we simply don't know what they can do to our environment but what we do know is that they are chemically different to larger molecules and so they may have different effects.

Conclusion

In conclusion, nanotechnology has great potential to improve the quality of cancer treatment. We are not saying that it is a perfect cure for cancer, but it can certainly help and also make patients feel more comfortable. But, we also believe that this treatment can significantly reduce the number of patients dying.

However, there is an issue with the detection. If we are to use this technology to detect cancer at an early stage we must screen people for it at an early stage, but it is highly unlikely that a patient would have any symptoms at such an early stage. So to combat this problem we should automatically scan people who are in high risk categories, e.g. people with a family history. This way we will be able to catch cancer at an early stage and get rid of it quickly.

Although there are ethical issues with our research which should be addressed, ultimately you can't put a price on life. This is why we believe that we have to carry on with this research. Nanotechnology has such incredible potential to sort out such a massive issue like cancer. These future developments in nano technology could really revolutionise way we think about cancer. To quote Marie Curie 'Nothing in life is to be feared. It is only to be understood.'

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