<u>Nanotechnology in the use of medicine against cancer</u>

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PASS WITH MERIT

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Abstract

In today's society, nanotechnology can be applied in many ways in science, engineering and medicine. With the advance in new technology, there have been many discoveries of new applications for nanotechnology, such as drug delivery, therapy techniques, diagnostic and imaging techniques, anti-microbial techniques and cell repair. For example, gold nano-particles can be used in the drug delivery and therapeutic techniques in cancer treatment. They have the ability to carry drugs and other particles into the tumour. Nanotechnology allows direct application to the cancerous cells, reducing the chance of damaging surrounding healthy cells. Recent advancements have led to the invention of nano-particle probes for molecular and cellular imaging, targeted nano-particle drugs for cancer therapy, and integrated nano-devices for early cancer detection and screening.

Introduction:

Nanotechnology is the use of nano-particles that are extremely small in size, only 5-100 nm[1] in diameter. 'Nano' in Greek means midget or 10^9 (a billionth of something). The size of a human hair is about 200,000 nm; a nano-particle is only a fraction of this. It is truly amazing with the technological advancements, that we are able to manipulate matter at the atomic scale.

Figure 1: Morinobu Endo

In the 1970's, Morinobu Endo (Figure 1: right) came up with the idea of tubes consisting of only a single layer of rolled up graphite, purely of carbon. The properties consist of strength 100 times stronger than steel, one sixth weights of steel and others such as very high young's modulus, and hardness.

However in 1991 a Japanese Physicist from IBM named Sumio Lijima (Figure 2: Left) was the scientist who finally discovered carbon nanotube[2].

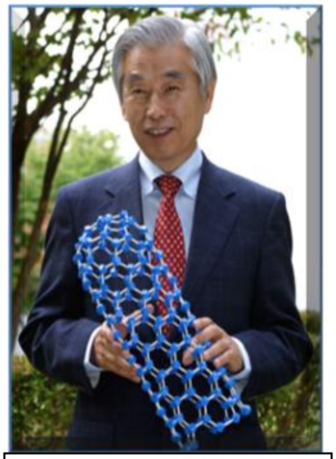

Figure 2: Sumio Lijima

During the 1990's, buckminsterfullerene[3] was discovered. It has the shape of a ball; as a result it was named 'buckyballs' or 'fullerene'. This molecule is composed completely of 60 carbons (Figure 3 below).

Nano-particles can be manipulated using an atomic force microscope and laser tweezers at the atomic level. And other molecules can be joined onto it, such as drugs and antibodies. Nanotechnology is about building bigger things from atoms. In nature, molecules in the nano-scale such as DNA molecules are joined by weak bonds, whereas scientists use strong covalent bonds.

Figure 3: Buckminsterfullerene

Nanotechnology is widely researched in the application of sports goods, cosmetics, electronic goods and medicine. For example, badminton rackets, invisible sun block, self cleaning glass in windows and many others. However medicine is the area with the least advance due to the amount of trials and test involved. is being applied in areas outside of medicine Until very recently, research in nanotechnology has been separately studied in engineering and medicine. Now that they have combined, many treatments[4] such as simple medical dressing have been improved.

Although nanotechnology is a fairly new aspect of science and is still undergoing experimental procedures, combining engineering and medicine together could lead to new treatments and improve existing procedures.

Nanotechnology is defined as the branch of technology that deals with dimensions and tolerances of less than 100 nanometres, especially the manipulation of individual atoms and molecules in the dictionary. The success of cancer treatment using nanotechnology solely depends on the type of cancer being treated and what stage it's in. There are several strategies and ideas for cancer treatment using nanotechnology, which are being improved and tested out before proceeding to human trials.

What is cancer?

Cancer[5] is a disease, of which a group of cells shows uncontrolled division. It has the ability to spread and take over other organs, which disables its functions such as digestion. When organs and body parts are affected, the body cannot carry out basic body functions to keep the sufferer alive. Cancer is largely caused by environmental factors such as smoking, improper diet management, infection, radiation and lack of physical activity. However, only about 5-10% of cancers are caused entirely hereditary. Hereditary causes regulatory genes such as oncogene and tumour suppressor genes to acquire abnormalities, resulting in malfunction of the particular gene. It is the leading cause of death worldwide[6] and have accounted for 7.6 million deaths in 2008 (around 13% of all deaths).

Figure 4: Cut surface of a liver showing multiple metastatic nodules originating from the pancreas.

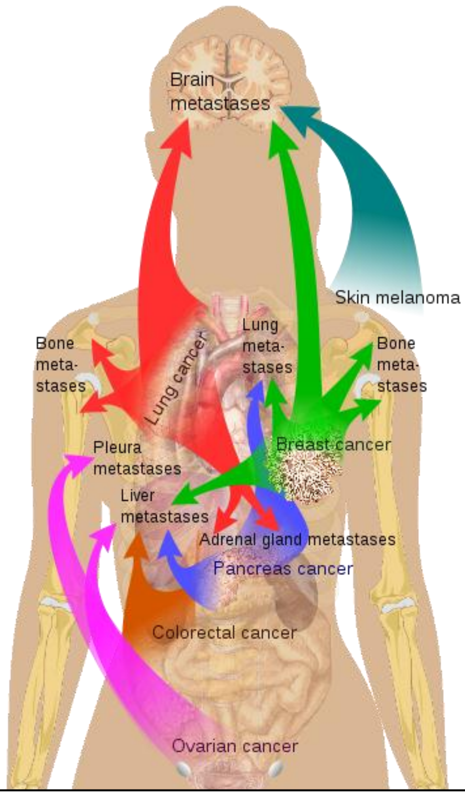

Figure 5: Likely routes of metastasis.

Cancer occurs when group of cells are displaying uncontrollable growth, invasion and destruction of other cells near the cell group. This situation starts when a single cell in a tissue is progressively genetically damaged to produce a cancer stem cell. These stem cells are able to undergo uncontrolled mitosis, which in turn increases the overall number of cancer cells at that particular site. When the area of which the cancer cells originated from is clinically detectable, it is called a 'primary tumour'. However in other cases, some of these cells have the ability to penetrate and infiltrate surrounding healthy tissues to form a new tumour.

The term ‘metastatic’[7], means the ability of a particular disease to spread from one organ to another. When tumour cells spread to another location, the cells are still the same. For example: when pancreatic cancer metastasizes to the liver. It is not true that the tumour cells in the liver are of pancreatic cancer. The tumour in the liver would then be classed as metastatic pancreatic cancer (Look at Figure 4 above).

Metastasis is different for all types of cancer. Each type of cancer has a particular route of spreading; these are the most common routes taken by the metastasis of different tumours (See Figure 5):

- Lung
- Breast
- Skin: melanoma
- Colon
- Kidney
- Prostate
- Pancreas
- Cervix

<u>Current Treatments:</u>

Conventionally, we have always used a treatment to try to kill cancer cells before you kill the body. Therefore as long as the tumour disappears at the end of the treatment, it does not matter how much the other cells are damaged in the process. Traditionally, a chemotherapy drug does not only destroy the cancer cells but healthy cells alike. Examples of the sort of drugs we use in chemotherapy are Paclitaxel, Docetaxel and Cisplatin. Now the goal is to cure cancer and induce as little damage to the surrounding body cell as possible, or more optimistically none at all.

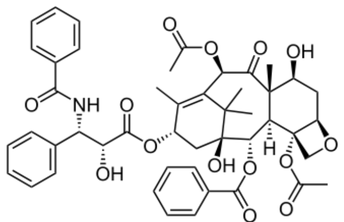

Figure 6: Paclitaxel

Paclitaxel[8] (figure 6: right) is a mitotic inhibitor first isolated from the bark of Pacific yew tree in 1967, widely given to sufferers of lung, ovarian or breast cancer. It is not water soluble and so it is mixed with eremophor, which can cause many side effects such as hair loss.

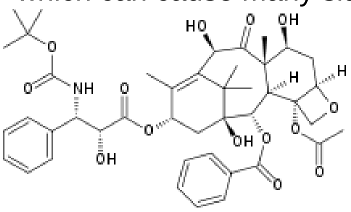

Figure 7: Docetaxel

Docetaxel[9] (figure 7: left) is an anti-mitotic chemotherapy medication that inhibits the cell division of the cancer cells. It is mainly used in the treatment of breast, ovarian, prostate or lung cancer.

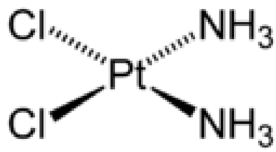

Figure 8: Cisplatin or Cisplatinium

Cisplatin[10] (figure 8: right) or Cisplatinium is a chemotherapy drug which inhibits apoptosis and increase DNA repair. Apoptosis is the process of programmed cell death (PCD). When a cell changes its morphology and dies, apoptosis produces apoptotic bodies in which phagocytes are able to engulf before the content of the cell spills out and damage healthy cells.

Radiation therapy is used for its ability to control cell growth. The ionizing radiation works by damaging the DNA of exposed tissue. It is believed that cancerous cells are more likely to die from this procedure. A prescription is needed from your doctor for the radiation dosage; this depends on the stage of your cancer and what type it is.

Reasons for using nano-particles:

There is specific interest nowadays in nanotechnology in the application of medicine. As the different types of cancer treatments are limited with a big chance of recurrence. The development of new treatments is very important. The ultimate goal of cancer treatment is the complete removal of the cancer without damaging the rest of the body; however this is an extremely difficult process to carry out with our current treatments such as chemotherapy, radiation therapy, surgery, immunotherapy and monoclonal antibody therapy. All current treatments have the same trend, with an earlier diagnosis comes a higher success rate. Earlier diagnosis means less time for the tumor to metastasis to the adjacent organs or surrounding tissues via the bloodstream. With the use of gold nano-particles and its functions, the success rate of this new cancer treatment should be greatly improved.

Discussion: What can nano-particles such as gold do?

In the process of using gold silica nano-shell, cancerous cells are identified, and doctors should then be able to remove the tumour cells using lasers.

There have been many new discoveries over the past 2 century, with gold nano-particle being one of many; it has extraordinary properties, allowing it to be used in drug delivery, therapeutic techniques, earlier detection of cancerous cells and a more precise method of screening. They are extremely small and can be as small as a few nano-metres; this allows the nano-particles to pass in and out of the cells easily. The gold nano-particle is a foreign material to the body and so a problem is posed as it might face rejection by the white blood cells (WBCs), many researchers have looked into this problem and have come up with a solution. By using thiol –derivatized polyethylene glycol (PEG- Thiol), it hydrates the gold nano-particle, surrounding it with water preventing recognition by the body's immune system without being detected (Figure 9 above)[11].

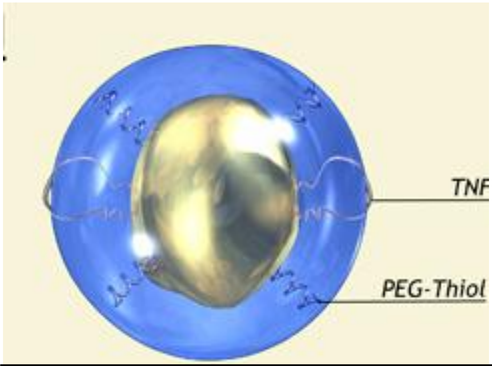

Figure 9: Gold nano-particle coved by PEG-thiol

This technology can also provide doctors with visual aid. It is necessary to bind gold nano-particles onto antibodies, which therefore allows doctors to identify the tumour. The antibodies are one of the few naturally occurring molecules that can detect tumour cells and so it can find the tumour. Others for example, lectins, super-antigens, glycans (polysaccharides), nucleic acids, 'Gold nano-particles are also contrast agent, using a beam of UV light will create a contrast. Allowing surgeons to visualise where the tumours are, and where the tumour margins are', says Dr. Shuming Nie, Wallace H. Coulter[12].

Identification of cancerous cells is very important, as without identification, an unaffected area could be destroyed or surgically removed along with the cancerous tumour. This can cause additional side effects to the sufferer's body, in worst cases death.

Early diagnoses[13] can be possible with the help of gold nano-particles that have been covered with a layer of peptides or larger proteins; this allows the nano-particles to have the ability to attach itself onto the tumour. When performing the screening process, bright reflections of nano-particles that have attached to the cancer will appear.

Gold nano-particles can have other abilities other than to identify tumour cells. It can be used in a minimal invasive technique known as heat ablation[14]. The nano-particle will pass into the tumor (Figure 10[15], right.) After which, a low powered laser can be used to fire at the nano-particle filled tumour but not the surrounding tissue. The tumour should then die and disappear (Figure 11[16] left).

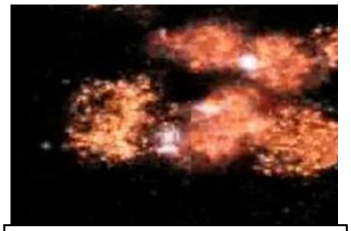

Figure 10: A still image from a video showing gold nano-particles inside the tumor.

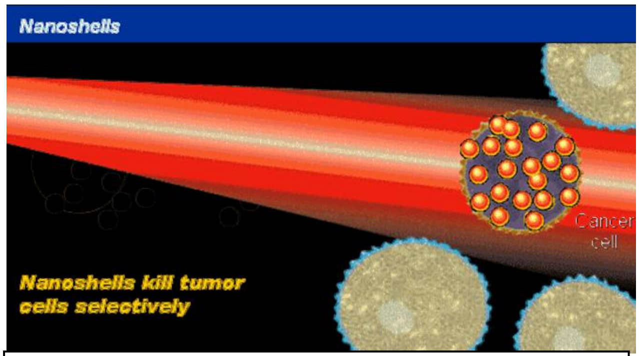

Figure 11: Heat ablation killing tumour cells selectively

<u>Alternative application using nanotechnology:</u>

Kanzius RF Therapy[17] (KRFT) was invented by a man named John S. Kanzius. This technique uses a combination of either gold or carbon nano-particles or radio waves to heat and destroy cancerous cells without damaging surrounding cells.

The specific absorption rate of radio waves determines the rate of radio waves absorbed by a material. Living tissue has a very low specific adsorption rate in the presence of some radio waves; however metals can absorb this energy much more efficiently. Metal atoms are able to vibrate rapidly, thus creating heat, whereas living tissues does not. Richard Smalley, who discovered a new form of carbon 'buckminsterfullerene' or 'buckyballs', a professor of chemistry, physics and astronomy at Rice University. He suggested that carbon nanotubes could be used for a similar purpose. If nano-particles are able to bind the cancer sites, cancer cells could be destroyed leaving healthy tissues unharmed.

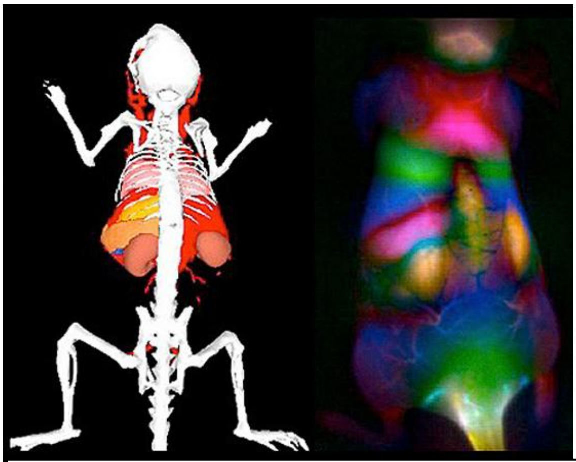

Figure 12: A scan of laboratory mice. (Left shows a better image with less or little haziness)

Fluorescent nano-particle[18] Dye composed of carbon nanotubes designed to fluoresce can be used to give a better image of the internal organs. Traditionally, CT or MRI scans are needed to give an image of the internal organs when conducting drugs test on laboratory mice. However, traditional dye can give a foggy image if it is deeper than a few centimetres from the surface. This is because of the light scatter properties of the dye at the frequency of the scanning technique. A team of scientists in Stanford University announced that they had created a dye composed of carbon nanotubes designed to have fluorescence that is different than the natural fluorescent properties of biological tissue (Figure 12, right).

This greatly minimizes light scatter. They have been able to image the tissue of mice at a depth of several millimetres without the haziness and distortion that occurs with regular dyes.

X-ray activated nano-particles that are activated exposed to X-ray radiation have proved to be promising in the new treatment for cancer. When the nano-particles are exposed to X-ray, electrons are generated causing the destruction of cancer cells to which they have attached themselves onto. This technique is to replace radiation therapy as it causes less damage to healthy cells. Nanobiotix a nanomedicine company dedicated to develop new treatments for cancer, with the combination of nanotechnology and biotechnology. Nanobiotix have released preclinical results indicating successful application in most of the animals in the animal testing stage.

'Nbtxr3 leads to a total regression of tumor on all animals compared to 5% glucose-treated mice subjected to radiotherapy alone. After 60 days, 90% of animals are still tumor free when treated with nbtxr3 plus radiotherapy.' Reported Nanobiotix[19].

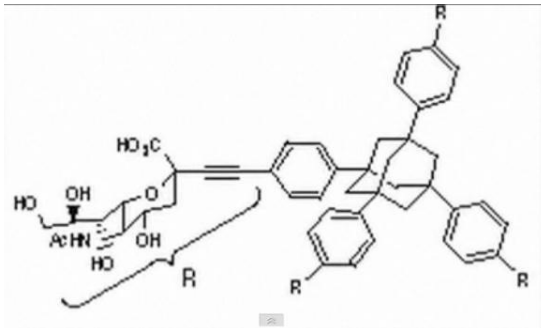

Figure 13: trojan horse theory

'Trojan horse theory[20]**'**, first discovered in the 1980's. This theory consists of nano-bots (Dindromia) (Figure 13, Right), which are made up of several arms, one of which has a food source on it whilst the others have cancer killing agents on them. It is believed that the cancer cells will recognise the food source, and when it engulfs the nano-bot it also takes in the cancer killing agent, thus exterminating the cancer. The reason behind the how this can work is that the tumour will need a food source to grow and metastasize. When it sees a food source, the tumour will be excited and engulfs the food without realising the danger behind it. The food source would be major nutrients of which the cancer needs to grow.

Ethical Implications: Animal testing

Animal testing is required for the development of any new treatment. In the UK, the Scientific Procedures Act passed in 1986 restricts any harmful treatments to the animals and governs the number and type of animal to be used in research. On the other hand, breeding healthy mice for the sole purpose of dying in a laboratory would seem very cruel. In some instances, an ailment is deliberately induced to test the effectiveness of a treatment that may or may not work, causing pain and suffering.

However, others would say that considering mice as "humane" would be foolish, for mice do not necessarily follow human behaviour or thinking patterns. With trillions of mice worldwide, the loss of a few could help millions of people with cancer and could help unearth other life-saving discoveries as the effect different drugs and treatments. Animal testing is one of many crucial stages of scientific development; to stop doing so could effectively kill thousands or even millions of people suffering from cancer or other serious illnesses.

Environmental Implications:

Nano-pollution is the name given to all waste produced by a nano-device or during the production process. The kind of waste is definitely an issue due to its size, visibility and maybe some unknown properties as it is a fairly new discovery in our modern society. As it is very small and light, there is a possibility of the waste floating in the air. This can therefore lead to penetration of animal and plant cells causing unknown effects. Most nano-particles have been man-made and developed; it is not something that is naturally occurring in the environment. Therefore animals and other living organisms may not have the means to survive or handle the nano-technology waste.

These nano-particles' life cycle needs to be assess and evaluated, to reassure the researchers and the general public. The following will have to be assessed, for example:

- Storage
- Distribution
- Application
- Potential abuse (terrorism)

The idea of nanofiltration using nanotubes with pores smaller than those used in the manufacturers would be suitable to remove most of the nano-particles.

Conclusion:

The use of gold nano-particles is possibly the key to victory in the war against cancer. The theory makes sense and animal testing stages have all proven successful. Treatment using gold nano-particles also comes with the perk of not only the treatment for cancer, but many others against major diseases. Volunteers who are sufferers of cancer will be the next stage of the development process once the technique has been refined. However saying this, I personally think that the 'Kanzius RF Therapy' and 'X-ray activated nano-particles' also looks very promising and have shown successful results. The gap of defining which technique is better in all aspects is hard to tell at such an early stage, especially if they have all been successful in the past. It would be hard to judge whether there will be any difference at all, if any, as they all have the same goal. The only problem I have, would be the cost of the nanotechnology development, it cost millions and millions year on year. This could potentially mean that when the final treatment is complete, it could cost a fortune to have this treatment carried out.

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