NANOTECHNOLOGY IN MEDICINE – Uses of nanotechnology in cancer diagnostics and treatments and the ethics surrounding nanotechnology research

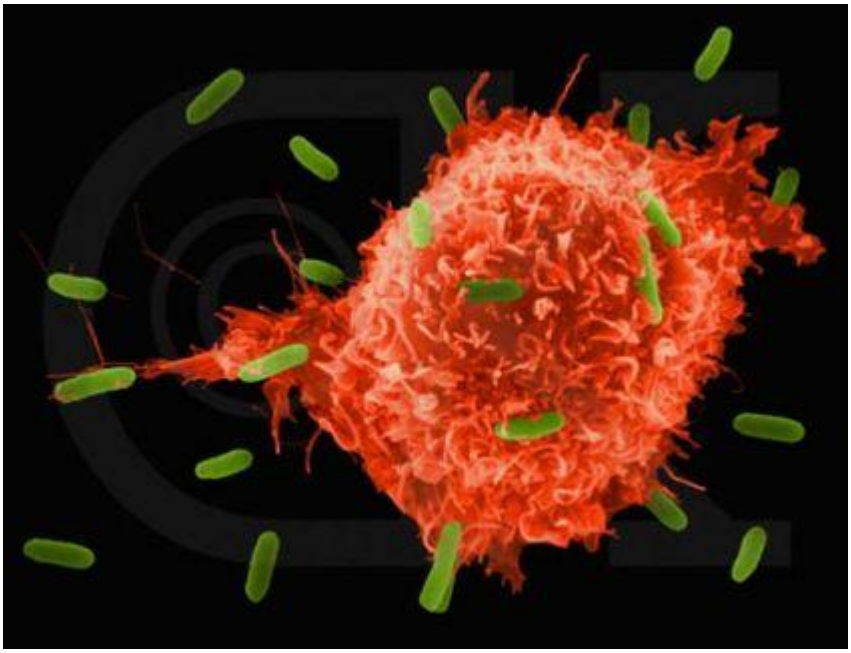

Fig 1 – Cancer being surrounded by gold nanoparticles

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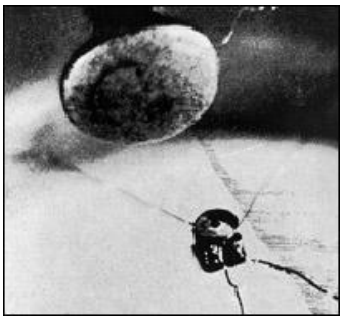
PASS WITH MERIT

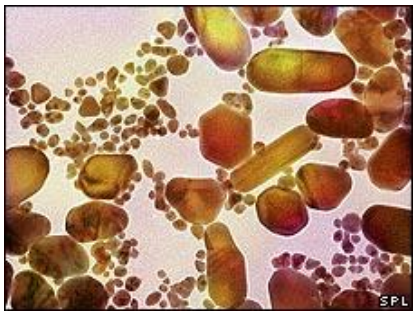
Research paper based on
Pathology lectures at Medlink 2010

Abstract

Nanotechnology is a new, exciting science that studies particles smaller than 100nm in size. This involves investigating and manipulating individual atoms to create new, innovative, useful products from motors smaller than a pinhead [fig.2] to using gold particles (colloidal gold – [fig. 3]) for both staining glass and treating arthritis! Nanotechnology is fuelling tremendous advances in engineering, technology, biology and medicine.



[Fig 2]- The large blob is a pinhead and the object near the bottom is the actual motor.



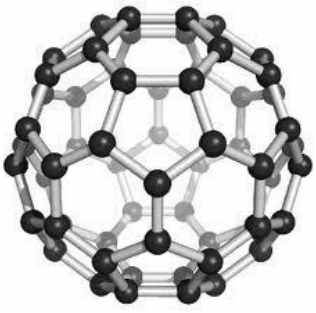
[Fig 3] – This shows the different shapes gold nanoparticles that have a multitude of uses

This paper is about nanotechnology, how it is improving the detection and treatment of cancer, and the advantages and disadvantages of it in comparison to today's options. It will also highlight ethical issues surrounding this research into the controversial topic of nanotechnology.

Introduction

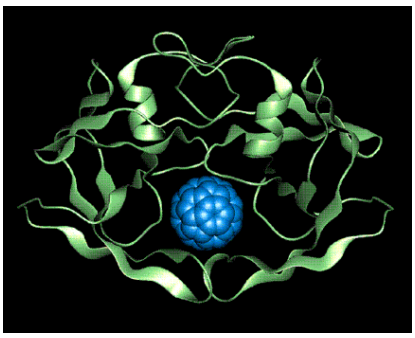
Nanotechnology was a concept first conceived by a physicist called Richard Feynman in 1959, when he set two challenges on a nano-scale. His first challenge was to take all the words on the first page of a book and shrink them to 25000 times smaller and his second was to create a rotating motor which was smaller than a cube with sides of 0.4mm. The second task was completed by William McLellan the following year (shown in [fig.2] above). However, the first task was a lot harder and wasn't completed until 1986 by Tom Newman when he successfully used an electron beam machine to shrink the first page of 'A Tale of Two Cities' to Feynman's requested size.

Another major discovery was done by Richard Smalley in 1985 when he found an allotrope of carbon that looked like a hollow, football-shaped molecule. Smalley named the pattern of hexagon and pentagons a Buckminster fullerene or 'Bucky Ball' [fig. 4] after an architect Richard Buckminster Fuller who created large dome buildings of a similar structure. The 60 carbon atoms bonded together in this molecule gave it its remarkable and unique properties; they are extremely hard to break, even at high temperatures and also difficult to compress. Not only this, but also they are very aromatic, hence very stable and inert and they are the only known carbon allotropes to be soluble. It was originally found in candle soot but is now made commercially in other ways.



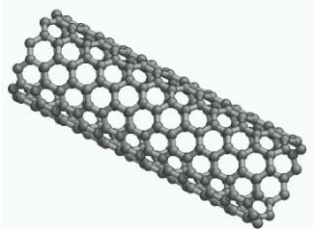
[Fig 4] - A model of the Buckminster Fullerene

These buckyballs are now being researched into in greater depth to find other applications of these extraordinary molecules. One application they have found is in fighting the deterioration of motor functioning due to multiple sclerosis because of the fullerenes antioxidant properties. Also, there is present research to suggest Buckminster fullerenes could reduce growth of bacteria in pipes used in water systems which in turn could reduce any illnesses caused by drinking contaminated tap water. A further function of these molecules could be to block the inflammation caused by an allergic reaction by trapping free radicals generated in the response to the allergen. Some researchers are also attempting to modify buckyballs to possibly inhibit the spread of the HIV virus. They are looking at modifying the fullerenes to fit the section of the HIV molecule that binds to proteins. This in particular could be a phenomenal development as '33.4 million people are living with AIDS' [1] (according to UNAID statistics from 2008) and it is consequently 'the most deadly virus'. [2]



[Fig 5] – A Buckminster fullerene docked in the binding site of HIV-1 protease.

Smalley's discovery sparked the interest of many more scientists and led to the unearthing of another unusual molecule which is one of the most useful products to come out of nanotechnology research – the carbon nanotube [fig. 6]. Its structure is like that of a tube of chicken wire and is the reason why this nano-sized molecule is stronger than steel - by about 100 times yet still extremely light-weight! It has the ability to be conducting or semi-conducting and a possible material to use for creating cheap solar panels or touch screens. Not only this but there is already research into the use of these nanotubules in tissue replacement therapy by using nanotubes scaffolds for bone to grow on, in the healing of broken bones. It is also suggested that they could be used in simple sensors to detect the presence of bacteria in drinking water, but their biggest suggested use by far is in the treatment of cancer which is the main discussion topic of this paper.

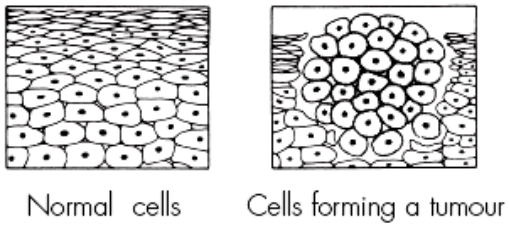


[Fig 6] – The structure of a carbon nanotube.

Discussion

Within medicine one of the most substantial developments at present is that of the trials into cancer detection and treatment. Current treatment such as chemotherapy is a non-specific treatment (in the sense that it does not just target cancer cells but damages healthy ones too) and also there are quite severe side effects of the treatment. Now, researchers from around the world in various laboratories and universities alike are looking into how nanotechnology can help reduce the suffering caused by cancer.

Cancer is a term used to describe a disease where DNA randomly mutates which causes a malignant growth due to an uncontrolled cell division (as there is no longer a hayflick limit to the cell.) It can spread to other parts of the body (metastasis) through the lymphatic system or blood stream. It affects millions of people - 'The National Cancer Institute estimates that approximately 11.4 million Americans with a history of cancer were alive in January 2006.'[3]



[Fig 7] – The structure of a tumour formation.

Current treatment and its disadvantages

At present there are three different types of cancer treatment: surgery, chemotherapy or radiation therapy.

Surgery is used for a multitude of reasons; to prevent, treat, stage (find how advanced it is) and diagnose cancer. Surgically removing tumours (or as much of it as possible) is often combined with chemotherapy or radiation therapy in order to try and treat the cancerous growth. However, as always it does have a few risks or problems – in surgery there is the issue that it may cause damage to organs in the body, as well as blood loss and adverse reactions to medication. There are a few problems after surgery too that vary in severity; from pain and discomfort, to infections, blood clots or loss and other illnesses such as pneumonia.

Chemotherapy is administered to patients by drugs in the form of pills or intravenously. It is not specific – it affects the whole of the body- but then targets the rapidly dividing cells. One of the main problems with this treatment is that cancer cells are not the only cells without hayflick limits – hair follicles, and also cells in the stomach lining have similar properties and are therefore attacked by the chemotherapy treatment. This causes some of the side effects such as hair loss, flu-like symptoms and stomach upsets. As with all these treatments, it is generally used in conjunction with other methods of treatment to try and achieve the best result.

Radiation therapy eliminates cancer cells or destroys tumour through the use of certain types of energy as the cancer cells are very sensitive to radiation and are killed. The multiplication of cancerous cells is disabled by damaging

their DNA. However, a disadvantage of this type of treatment is that the radiation damages nearby healthy cells too– although this isn't a large disadvantage as the normal cells are resilient and generally have the ability to fully recover.

Why we need nanotechnology to improve cancer treatment

As explained above, current treatments are somewhat limited and have a multitude of side effects such as hair loss, fatigue, flu-like symptoms and stomach upsets. Also, treatment isn't accurate enough; many of them destroy healthy cells as well or affect the whole body. This is undoubtedly going to put yet more strain on the individual's body. Imagine if there were specific cancer targeted treatments, easier methods of diagnosis, less painful treatments with reduced side effects – imagine nanotechnology. From the current research and future ideas surrounding nanotechnology's possible advances and applications it's suggested that all of these dreams may become a reality – and maybe in a few decades it will become affordable and accessible for all.

Research into improved diagnosis and detection of cancer

The earlier any illness is recognised and diagnosed, the quicker it can be treated and earlier treatment hopefully means lower mortality rates. Below are just a few examples of current ideas being developed and tested at the moment:

One way nanoparticles are being developed to help fight cancer through improving the diagnostic methods is by making improvements to the quality of MRI scans. Iron oxide can help do this due to its magnetic property, but only on a nano-scale. The iron oxide nanoparticles are coated with a peptide which bonds to the tumour. The magnetic property of the iron oxide therefore means that the MRI scan image produced in much clearer and enhanced.

[Fig 8] – Current example of an MRI scan of the knee.

Nanoparticle and nanowire sensors that detect proteins specific to cancer in blood samples allowing the possibility for early detection - superparamagnetic nanoparticles in the T2 Biosystems bind to cancer specific proteins and cluster together. A magnetic resonance signal is given off by the cluster indicating the presence of the cancer which can be seen in a digital image. This makes it easier as there is a pinpointed location to concentrate treatment onto.

Quantum dots are another diagnostic tool being investigated by researchers at John Hopkins University that work by emitting a fluorescent glow when DNA strands that are early cancer indicators, are detected.

Research into improved treatment of cancer

Some researchers are currently looking into targeted heat therapy. The breast cancer cell produces a protein which strongly attracts a particular kind of antibody. In this treatment, that particular antibody is attached to carbon nanotubes which cause the nanotubules to accumulate around the tumour. The tumour is then incinerated by the infrared light the nanotubes absorb.

Another improvement of chemotherapy treatment is where two separate nanoparticles are used; one to guide the drug carrier to the tumour and another one to deliver the chemotherapy drug. Gold nanoparticles exit through the leaking blood vessels (site of the cancer). Heat from infrared light is concentrated onto the accumulated nanoparticles – this heats them up. The heat causes increased stress levels (due to increased amount of stress related proteins on the tumour surface). Amino acids that are bound to the multiple liposomes (drug carrying nanoparticles) can bind to these increasing numbers of proteins causing an accumulation of the chemotherapy drugs at the tumour.

Another piece of current research into cancer treatment that is being trialled is targeted chemotherapy that provides a tumour killing agent (tumour necrosis factor alpha or TNF) to the affected area. A gold nanoparticle is attached to the TNFR with Thiol-derivatized polyethylene glycol. This 'PEG-THIOL' has the ability to hide the TNF and nanoparticles from the immune system so it can flow through the blood uninterrupted. Aurmine is the combined name for the gold nanoparticles, PEG-THIOL and TNF.

Heat therapy using nanoparticles to destroy cancer tumours (AuroShell™) is another current piece of cancer based nanotechnology research. The AuroShell™ nanoparticles, after circulating through the bloodstream, exit where the blood vessels are leaking (as this is the site of a tumour). Heat from infrared light is concentrated on the accumulated nanoparticles destroying the cancerous cells in the area whilst doing minimal damage to the healthy ones.

A further idea being developed is destroying the cancer tumour through the use of x-ray therapy using a nanoparticle called 'nbtxr3'. These nanoparticles can be activated by x-rays which consequently produce electrons that annihilate the tumour they are attached to. This could be less damaging than current radiation therapy and it is thought that in a matter of years, this x-ray therapy could possibly replace radiation therapy permanently.

An alternative way is by increasing the number of cancer fighting immune cells. It is a concept in which some of the bodies T-cells would be altered by attaching nanoparticles containing interleukins to them. Nanoparticles only release the drug when T-cells reach a tumour which causes the T-cells to reproduce. Cancer tumours can be fought and destroyed if enough T-cells are produced. This particular research has been tested on mice with good results.

Gold nanoparticles have been used in a further improvement in the treatment of cancer – by reducing the side effects of platinum cancer therapy. This works by using the nanoparticles to deliver platinum to tumours but it can be too toxic. To reduce the toxicity, researchers have found a less toxic isotope to attach to the gold nanoparticle. As the platinum reaches the tumour it mixes with an acid and changes to its toxic state, meaning it then kills the surrounding cells - cancer cells.

Ethical and moral issues of research into nanotechnology

One ethical issue people have with nanotechnology research is that it is unnatural, relatively unproven and new. It is manipulating atoms to get what humans want and creating chemical mixtures to give to people, without us knowing the long term side effects – who knows how this may affect them in 50 years time, or how it may affect their following generations? At the moment – nobody knows!

Some people believe nanotechnology could be dangerous in the fact that it could be used as a weapon of war– mechanical/biological weapons that are invisible to the naked eye but that could have the potential to be destructive.

Also, there is the idea that if cells in a human body can mutate to form harmful tumours like cancer, then what's to say that a form of nanotechnology might not do the same – but the likelihood of this occurring when used in a medical context is very unlikely.

It is a belief of many religions that life is a gift given by their god and that it is a sacred and precious gift that is not to be given or taken away by anyone but that god. Using nanotechnology to extend a person's life may not be wanted or accepted in many religions as some hold the opinion that it is like 'playing god' and altering humans for our own selfish reasons. The possibility of using nanotechnology to create life without 'divine intervention' brings up many moral issues as well as ethical.

One of the main issues is the problem of knowing when to stop – which things shouldn't be replaced with nanotechnology and which things should? It is suggested that the advances in nanotechnology could be a slippery slope. If scientists could extend everyone's lives so we all live for many more years, where would we all live? Also, how would this impact on our planet – we would use more resources, there would be much more overcrowding, less rainforests and fields as they would be needed for building new houses. Not only this, but it would affect the financial system hugely as the increased number of elderly would mean less people working and more people needing a pension!

A further dilemma is the way these new medical technologies are tested. Most treatments have trials done on various animals before they reach human trials, which brings up the ethical issues of consent especially with anti-vivisectionists.

But then there are the ethics of if we DON'T do anything – think how nanotechnology could change the world, save millions of lives, improve quality of life. There would be an outrage by many if scientists discovered this huge development but then decided it was too unethical to continue and to be used.

It could allow a huge reduction in the amount of pain and suffering in the world and possibly even wipe out some of the biggest illnesses we struggle with at the moment.

Advantages and disadvantages of the use of nanotechnology in cancer

There are many obvious advantages of the work on nanotechnology and medicine. One of which is that the treatment does little or no damage to healthy cells unlike current treatments which can have harmful side effects. Also, as far as we know, there are no or very little side effects from the use of nanotechnology as a treatment for cancer.

Another advantage of using nanotechnology to treat cancer is that it would be much less invasive than surgery meaning a lesser chance of infections, no risk of blood loss or damage to internal organs. It will also assist in the treating of tumours in areas that would not be able to be operated on, for example the areas near vital organs.

However, not enough tests have been done to support this; the affect it would have on humans is still unknown as human trials have not been done yet - currently most of the trials are done on mice. Also there is no way of predicting the long term effects as this kind of treatment has only recently been established.

One of the main disadvantages is that when, and if, these treatments complete there trials and human testing they may not be available to all. The amount of money spent on this research will be astronomical as it is so revolutionary and needs to use very expensive, complex equipment to develop. Therefore, once a company has developed the technology they will more than likely copyright it so they can set their own price guide in order to get a profit for their discovery. This may be a problem as not everyone will be able to afford it and there will consequently be many ethical issues. It will be a treatment only available to those who can provide the money as the NHS possibly won't be able to take the economic strain, meaning that even though a better treatment or even possibly a cure exists – many won't benefit from it.

Nevertheless, with charities raising money to fund cancer research, it may not be long before it does become more affordable and possibly an NHS treatment.

Another benefit of this research is that the treatments would mean less, and shorter, visits to hospital for cancer sufferers which would help take the strain off of our healthcare system somewhat.

On the other hand, all of these drugs will need to have human trials which means those people will have to do *more* hospital visits, have *more* tests and scans (which in turn can make them more anxious) and no-one really knows how this treatment will affect them. This could possibly just make them feel worse in the long run! Although it wouldn't be all negative; you may be receiving a brilliant treatment to make you better and instead of paying for it, they are paying you to trial it! Also it may give patients the satisfaction that they are helping millions of others who are suffering like them.

The Future

Researchers are constantly coming up with new concepts and ideas on how we could further utilise the information we already know about nanotechnology to create a new application for them.

Another ground breaking concept in relation to cancer care is the use of magnetic nanoparticles which is being investigated by a team from the University of Edinburgh. They have discovered a type of bacteria that can takes up iron from its surroundings to produce tiny magnetic particles. It is thought that they could be guided magnetically to the tumour site where they could either release drugs they were carrying or be exposed to an opposite magnetic field which would cause it to heat up killing the cancer cells it is surrounding. This is currently just a theory but again has the potential to grow into an innovative cancer treatment method.

[Fig 9] – Bacteria-produced magnets that are better than manmade ones due to their uniform size and shape.

Some of the mentioned treatments are currently being tested on animals such as mice, with very promising results.

But it's not just improvements in cancer treatments that are accelerating rapidly – new, promising uses of nanotechnology consist of reducing the transmission of AIDs, helping stop CHD (coronary heart disease) and even re-growing tissue for repairing human bodies. Numerous companies and organisations are doing individual research, but so are places such as the US National Cancer Institute and the 'Alliance for Nanotechnology in Cancer'. With nanotechnology the possibilities are infinite.

Conclusion

The average life expectancy over the last 100 years has doubled by vaccinating against some of the most harmful illnesses, finding new ways to treat others and by furthering our knowledge of the world of medicine and its possibilities. Now nanotechnology has been discovered and explored, who knows what the life expectancy could be in another century. In the next decade or so, due to the speed of current developments, it is thought that the number of deaths from cancer and CHD will be significantly reduced and maybe even a reduction in the number of people suffering with AIDs.

Although there are the odd moral and ethical issues with nanotechnology due to the belief it is unnatural and like 'playing god', the benefits in my opinion outweigh the downfalls by far. Many people are wary as it is so new and misunderstood but in the future it is sure to become part of our everyday lives. With its timesaving, moneysaving and lifesaving potential, it looks like nanotechnology is the way forward.

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Images:-
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Fig 2 – The world's smallest rotating motor
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Fig 3 – Colloidal gold (gold nanoparticles)
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Fig 4 – A model of a Buckminster fullerene
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Fig 5 – A 'Bucky-ball' docked in the binding site of HIV-1 protease
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Fig 6 – The structure of carbon nanotubes
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Fig 7 – The structure of a tumour formation
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Fig 8 – A current MRI scan of the knee
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Fig 9 – Magnets produce by bacteria
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