CANCER NANOTECHNOLOGY
(NANO-ONCOLOGY)

BY

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Abstract

One of the most stimulating and dynamic area of technology and science today is nanotechnology. This detailed description is targeted to emphasis how nanotechnology works in relation to medicine. In order to accomplish this, this documentary describes the early stages of development nanotech, and goes on informing future developments that can be beneficial to medicine. This documentary also provides a detailed discussion on how nanotechnology and nanoscience influence each medical field, as well as the impact that nanotechnology holds for future medicine. The main discussion will be on detection, diagnosis and treatment of cancer. This project backs up each hypothesis, predictions and conclusions with research and biological evidence. This paper focuses mainly on positive aspects of nanotechnology. However, there are also other negative effects (such as, expensive, time consuming, etc), which are discussed in detail in this paper. Finally, reference for further reading for readers are quoted towards the end of the article.

Introduction

Various technologies (such as, invention of telescopes, microscopes, satellite communication and numerous other mind blowing innovation) have roused after the dark ages. These technologies endowed humankind to come across numerous discoveries and methodological mechanism as well as methodological science, which allow us to broaden our range of knowledge and wisdom. E.g. the discovery of deoxyribonucleic acid (DNA) by James Watson and Francis Crick is considered as the "secret of life", Galileo Galilei's improvements to telescopes brought in new discoveries and evidence on the subject of astronomy. Similarly Nanotechnology is one of the most engaging and fascinating discoveries. The word 'nano' in Greek defines tiny, therefore, the name 'nanotechnology' itself emphasis manipulation of minute particles. "Manipulating and controlling things on a small scale", Richard Feynman gave a typical speech in 1959 emphasising that "there is plenty of room at the bottom".

Nanometre (nm) is the unit of length used for the sizes of atoms, molecules and ions. A billionth of metre (10^{-9} m) is one nanometre (1 nm). Therefore, nanoparticles are components of size that lie between the ranges of 1nm to 100nm. Scanning tunnelling electron microscope is one the beneficial inventions, which allows us to observe and manoeuvre atoms, molecules and ions within nanoparticles. Nanoparticles such as fullerenes and carbon nanotubes can be produced. Since they are relatively very small, they have innovative properties. Therefore, when nanoparticles are manoeuvred in nanoscale they increase the surface area, this again allows nanoparticles to have such innovative properties.

Several beneficial fullerenes can be formed by manipulating carbon atoms (such as, 'buckyball', buckministerfullerene, C_{60}, was discovered in 1985 by Harry Kroto *et al* at Sussex university. C_{28}, C_{32}, C_{50}, C_{70} are various other spherical fullerenes of carbon. There are also various cylindrical fullerenes, also known as nanotubes. These cylindrical forms of fullerene are arranged in hexagons in a similar way to graphite-like sheets of atoms rolled up into tubes. Properties of these tubes vastly vary (such as, it can be integrated into plastic, make them conduct electricity, etc). They are also relatively strong and tough fibres. This is due to the strong covalent bonds that are formed between carbon atoms.

When we zoom into nanoscale, there are infinite ways in which the nature arranges and rearranges atoms and molecules to carry out its functions efficiently. Studying particles in the smallest possible scale is essential, since, there can be various ways we can improve our technology to copy nature at least to a certain extent and go beyond nature's probabilities. This Study of particles in smallest possible scale allows us to do nanoscience. Thus, we can put science into action to provide ourself with the best solutions for environmental problems, etc e.g. sunblocks are made from particles of zinc oxide or titanium dioxide, consequently, skin damaging ultraviolet rays are blocked by these particles. However, they also reflect visible light, which made the sunblocks appear as white ointment on the skin. Nanoparticles also block UV rays but does not reflect larger visible light, thus, the ointment appears to be clear, as well as protecting the skin.

The field of medicine is vastly profited with the help of the extraordinary and exquisite properties of nanoparticles and nanotechnologies. By the use of nanotechnology, we can discover various new drug delivery systems. Cancer and tumours are one of the most life threatening causes that can be detected, diagnosed and treated in early stages by nanotechnology, which might save the lives of several individuals, as well as provide a wide accomplishment to NHS today. There are severe demands from these nanotechnologists to carry out deep studies into medicine e.g. in cardiomypathy, to cure diseases in heart muscle, fertility treatments, treat various abnormalities that are caused by minute malfunctions in central nervous system. Storage, repair and regeneration of organs (such as heart, bones, cells etc).

Discussion

Nanomedicine, the relevance of nanotechnology to medical science, is believed to change the way we diagnose, treat and prevent diseases entirely. It is vastly beneficial in various subjects amongst medicine; especially in the study of cancer, which is known as nano-oncology. This discussion covers a detailed documentary of how nanotechnology is used to diagnose cancer at its earliest stage. This document explains the vast improvements that are expected by involving the usage of nanoshells, enhanced diagnosis and treatment using targeted biological agents in the mechanism of action, and how problems related with cancer treatments might be solved using nano-oncology, which leads to a significant change in which the way the drugs are made. This involves carbon nanotubes, which can deteriorate cancerous cells and various other nanodevices, which help diagnose, detect and eradicate cancerous cells without impairing the benign cells e.g. nanoshells. Most importantly, the discussion focuses on the remarkable tools and experimental methods that will be used in nanotechnology compared with the current methods that are used to improve the detection, diagnosis and treatment of cancer.

According to the latest statistics, one of the top constituent factors that cause death among 6 million deaths every year is cancer i.e. 12% of deaths worldwide. Therefore this is a major priority is to be paid to diagnose, detect and to treat cancer. Abnormal growth of cells anywhere in the body is known as cancer or carcinoma. This occurs when cells are allowed to split by the genes in it to make cells, without control. There are numerous types of cancers. Some cancers form tumours located in specific tissues or organs, whereas other cancers are also present in the blood (leukaemia), and are transported all over the body. Cancers are known to harm cells in two ways (degenerate normal cells or replace them with cells that do not function adequately). Tumour cells are passed to other organs in the body through the bloodstream. This leads to metastatic cancer, which is life threatening since it can spread further than main tumour to numerous vital organs (such as, lungs, brain, liver, bones, etc), thus, making treatment complicated.

The distributing of cancer cells is usually rapid. A significant factor for both survival and superiority of life can be restored only when cancer particles are eradicated in any case of their location. Therefore, the cancer that is detected at its earliest stage has high chance of being cured. Surgery, chemotherapy and radiation therapy or grouping of these treatment options are the standard treatment options. These treatments and therapies have their own limitations and cause relentless side effects that frequently reduce the quality of life for the patients. With this in mind, about a million pounds invested by the National Cancer Institute (NCI) in 2007 goes towards nanotechnology, especially towards the study of detecting cancer. The NCI believe that around 2011 considerable progress in early detection, molecular imaging, assessment of therapeutic methods, and prevention and control of cancer must be developed. As a result, nanotechnology researchers are facing an enormous challenge.

Numerous new scanning techniques, which consist of highly specific targeted imaging and labelling of nanoparticles, have evolved. These techniques can be used to target anticancer drugs specifically towards cancer cells, leaving the useful cells intact. One of the primary approaches under progress to succeed this is a special device known as a nanovector. These are solid hollow structures, with diameter within 1-1000 nm range. This can be filled with anticancer and antineoplastic drugs that hinder and inhibit the growth of carcinoma e.g. PEG-docetaxel, which is produced when polyethylene glycol (also known as PEG) forms ester bondage with docetaxel. Together, these chemicals construct nano-sized particles which stimulate anticancer activity.

Epeius Biotechnologies Corporation, in California came up with a successful targeted biological agent known as Rexin-G. These are highly complex nanoparticles (only 100nm wide), which consist of specialised components (such as, matrix, envelope, capsid, other enzymes and genetic material). Billions of Rexin-G particles are injected in the arm of the patient. Thus, the nanoparticles travel all over the circulatory system. As a result, systematic circulation distributes them all over the circulatory system. They are designed in such as way they could withstand any enhanced interruption. These nanoparticles are designed to pierce deeply into impaired tissues. They then look for the biochemical characteristics of any tumour cells. The levels of Rexin-G rises soon after the presence of cancerous cells are encountered. Then the nanoparticles provide the cancer cells with the killer genes that block future growth of cancerous cells. "These killer cells are programmed to cause cell death in millions of tumour cells," said Frederick L. Hall. The body's own immune system takes part in eliminating the dead cells when the tumour cells die. Reximmune –C (Retroviral Expression Vectors Bearing an Immune-Stimulating Cytokine) is another anticancer agent that targets tumours. This has a unique property that stimulates the patients' immune system to

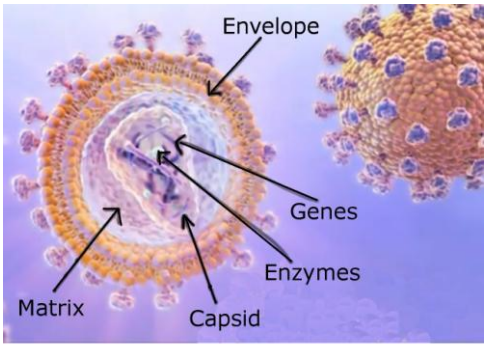

Figure 1

degenerate remaining tumour cells. The cytokine present in the Reximmune-C kindles the expansion of specific and active anticancer immunity. Thus, this is known as a personalised cancer vaccine. It is also considered that Reximmune-C enhances the build up of leukocytes, which includes B-cells, and killer T cells. This acts as a secondary immune system that may result in a secondary immune response.

These nanoparticles not only destroy the cancerous cell, but also demolish the blood vessels, associated with the tumour cells. Thus, it takes a prevention measure to avoid cancer genes spreading. This feature provides a great advantage to these nanoparticles. Further research and studies that were carried out in California back up biological evidence that this treatment "reduces tumour burden and prolong patient's life". The main advantages of these biological particles includes that they are specifically targeted to diseased tissue, which is technically known as pathotrophic. These nanoparticles of Rexin-G attack any invasive tumours in the body, which is known as histopathologic property. These properties add to the positive aspect of these nanoparticles. Side effects that are caused by chemotherapies (unable to form healthy bone marrow cells) are not found in Rexin-G treatment, therefore it is considered to be more beneficial that current cancer treatments. Rexin-G has been permitted to be used as "safe and effective treatment" in various countries (such as, Philippines, etc); therefore it is considered as reliable. Dr. Erlinda Gordon, Chairman of Epeius Biotechnologies claimed that "Rexin-G represents the first in a serious of truly effective targeted genetic medicines that seek out and destroy metastatic cancer, without eliciting deleterious side effects or organ damage". However, treatments using Rexin-G and Reximmune-C are in their infancy stage. Therefore, technologists expect there can be various side effects that can be caused. Moreover, most of the research and findings are carried out by technologists in Epeius group. Since there is a lack of research carried out by an individual company, the findings can be classified as invalid.

Similar to Rexin-G, the Rice University is Texas came up with a mechanism of tumour destruction known as nanoshells. The ingredients of nanoshells are silica covered with gold. These nanoparticles are 110nm in diameter. Then nanoshells are injected into the tumour tissue. This is followed by the nanoparticles connecting with the antibodies that distinguish tumours and/or they are specifically located using a unique scanner. When the light, near infrared wavelength is shone over that tissue, nanoparticles are heated up; this is due to the light piercing at a specific frequency into the skin to get to tumour cells. In fact, enough heat is generated to degenerate the tumour cells, which is expected to restrict the growth of the tumour. This does not affect the surrounding cells, because only cells with the nanoshells are deteriorated. This treatment was carried out on mice that contracted human brain tumour cells. In addition, scientists successfully destroyed the tumour cells in the mice using nanoshell treatment. Figure 2 shows transmission electron microscope images of nanoshells during the destruction of tumour cells.

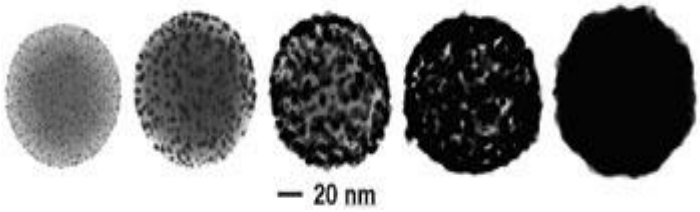

Figure 2

Evaluating the usage on nanoshells, provide us with many positive and negative analyses. The main advantages of these nanoshells are they can accumulate themselves using the components (silica and gold). When they are introduced into the bloodstream, they make their own means towards the tumour cells. If this fails, they are easily directed using magnets to tumour cells. Professor Thomas Rademacher, from University College London said that there "are so many potential applications for this technology, because, with the self-assembling nanoparticles, they could be constructed with gold, or iron, allowing us to heat them up, and to guide them around the body". There are many researchers who claimed that this treatment has negative aspects that may overweigh the positive feature. Professor Rademacher again claimed that "the particles that Rice University in Texas used are very large – they could never be injected in the blood stream". Other researchers prove that this treatment causes the physical burning of tissues, and worse, toxic fumes are released accordingly during the treatment. If the nanoparticles form a link to healthy normal tissues, there is a great risk of healthy cells being degenerated. Therefore, there is high risk which could lead to severe side effects. Another main disadvantage of the study is that most of the treatment was carried out in laboratory in tissue culture. Therefore, the study lacks in ecological validity, since the study was not carried out in mundane realistic ways to the natural human lifestyle. Even though the usage of animals in study of nanotechnology is permitted, mice cannot be generalised to humans. Hence, the results may be biased. However, few positive characteristics of the usage of nanoshells overweigh most of the criticisms. Glioma is one of the most hostile and complex ways to treat tumour cells that rise in the brain and spinal cord. According to the statistics, less that 5 percent of patients those who contracted glioma were able to survive beyond 5 years. However, researchers carried out research in Texas among glioma patients and found that seven patients had completely recovered. However, the cancer returned among three of those seven patients. Therefore, the use of nanoshells is not wholly reliable. Nevertheless, researchers have claimed that nanoshells might work more efficiently if the size of the nanoparticles is further reduced to up to as small as 1nm.

Nanotubes are other minute devices that are used similarly to nanoshells. A group of researchers from Stanford University attached Folate to the nanotubes. This enables them to attach the nanotube into the receptor of the cancer cell. Since these nanotubes have similar properties to nanoshells i.e. near infrared wavelength is absorbed well by the nanoparticles. This allows the cells to heat up as the light is shone over the particles and thus, the cells are degenerated and this restrict the growth of the tumour, similarly to nanoshells, which we discussed earlier this discussion. Therefore, this method prevents the growth of the tumour without damaging the healthy cells. Like nanoshells, this treatment was carried out in mice that contracted human cancer cells. Findings prove evidence that this method works efficiently by deteriorating only the cancer cells. This treatment also has an advantage that it does not bring forth any other unnecessary symptoms (such as, nausea, hair loss, loss of hearing, etc. These symptoms are commonly caused by chemotherapy agents).

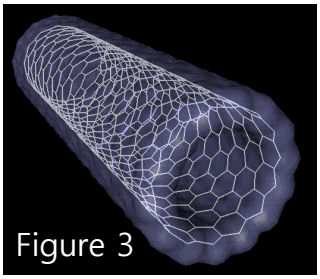
Figure 3

Stanford University nanotechnology researchers' also showed evidence that nanotubes can be used as a drug delivery device. Hongjie Dai, Professor of Chemistry said, "That means you will also have fewer drugs reaching the normal tissue". Therefore, reduced amount of drugs are needed to be injected in the individual who suffers cancer. Thus, this method acts more efficiently than other chemotherapy agents that required to be injected in vast amounts and may degenerate the growth of normal cell along with cancerous cells. In this case, carbon nanotubes are targeted specifically to deliver the drugs to only the cancerous cells. Nanotubes are designed in such a way that they can attach to the receptors in cancerous cells. Nanotubes that recognise cancer cells are injected into the blood vessels, thus, the nanotubes can be circulated in the bloodstream all over the body. Then the drugs are released in the blood stream allowing those drugs to get to the nanotubes. In this way, only tumour cells are delivered by drugs (not the healthy cells).

All these discussions above (nanovector, Rexin-G, Reximmune-C, nanoshells, nanotubes) are in the experimental stage. Therefore, currently the nano-oncology researchers are more interested in positive aspects and the way nanoparticles and nanodevices work in preventing cancer growth than in side effects and disadvantages. The disadvantages are vastly ignored because the nanotechnology is constructed from tiny fragments, which can be taken as an advantage to avoid major side effects and disadvantages. Various studies were carried out to prove evidence that these methods using nanodevices work efficiently without damaging the healthy cells. There can be another risk in this data; since most of the study on oncology was carried out by the same technicians who came up with the hypothesis, so there is a high chance that the results are biased to prove their hypothesis. The data will be more reliable and consistent if the study and research was conducted by more companies that are individual and came up with similar outcomes. Moreover, even though the nanodevices and nanoparticles that are discussed above are not available to the public to use nowadays. There is a high belief that they will come to markets in coming years or a more powerful mechanism will be designed to tackle metastatic cancers further effectively. Other researchers argue that most of the cells that are tested are grown and cultured in laboratory. This makes the study lack in ecological validity, since the results have a high chance to vary if they were conducted in natural settings due to other factors getting into action. Following on from that most of the studies were conducted in animals, even though US researchers say that experiments in mouse tumours have proved successful, the results can be disapproved as biased, since animals such as mice can't be generalised to humans.

Conclusion

Nanotechnology itself is a whole ocean of material and information that we humans need to discover and explore. Going into special topics, such as nanotechnology in study of cancer has its numerous benefits. Nanotechnology was introduced in the 1980s and it astonished our ideas and studies since then. Currently there are various areas where nanotechnology had a breakthrough. Nanovector, Rexin-G, Reximmune-C, nanoshells, nanotubes are only very few of that millions devices, nanoparticles, etc. However, it is believe that there will be other powerful and further astonishing devices and drugs will be designed through nanotechnology to help and improve medicine.

I personally recommend that study into nanotechnology must be backed up with more research evidence i.e. more tests needs to be carried out with large samples. This will make the study more reliable and accurate. From the time when nanotechnology was studied, there is lack of findings and studies that were carried out. Among most of those studies the sample size is very low. Therefore, more studies must be carried out by various companies with more participants. I do bear in mind that the new medicine takes a minimum of around 12-14 years to get into local markets and local pharmacies. Hence, it is expected that some of the drugs that have developed using nanotechnology will be more popular around 2020.

There are plenty of possible ethical issues that could rise in study of nanotechnology. One of the most vital issues that need to be considered is its cost and efficiency. Most debaters claim that the research and findings are very expensive

and may lead to failure, so the money that is spent in this can be invested in other factors (such as, fair trade, help provide food to individuals in starving communities in developing countries, etc). However, on the other hand, studies and findings into nanotechnology have a potential to come up with possible ways to reduce poverty and other world problems. Therefore, a serious discussion needs to be carried out with budgets that need to allocated into nanotechnology. Even though studies into nanotechnology are allowed to use animals in the research, it is still cruel and brutal to torture animals in such ways. Therefore, many groups may protest against the usage of animal cruelty in tests. These issues need to be dealt wisely.

I would totally agree that nanotechnology would make such an impact in reduction in death rates due to cancer in coming years. As we have seen in the above discussion, the use of nanotechnology is valuable in diagnosing, detaching, treating, eradicating and preventing metastatic cancer. Few methods that we discussed (such as, Rexin-G, nanoshells) are more astonishing and positive in treating cancer than current chemotherapy and radiation therapy agents that may lead to many side effects such as hair loss, nausea, loss of hearing, etc. The use of nanotechnology is also more beneficial in treating cancer in regions where it is very dangerous to treat using current methods, such as areas in brain, etc. Logically, nanotechnology is considered to be having more impact in medicine, most probably the lifestyle. This is because the devices and particles that nanotechnology comes up with are small enough to penetrate into anywhere. Therefore, I conclude this paper with a personal opinion that nanotechnology will lead our humankind, who was astray so far, into a remarkable future in the coming years.

Reference

1. 'A-Z handbook 4th edition – Chemistry' – Andrew Hunt, 2009.
2. Brookhaven National Laboratory, Scanning Transmission Electron Microscopy Facility; STEM Operation and Methods - http://www.bnl.gov/biology/stem/Operations.asp
3. Cancer Therapy Enters Human Trials, Center for Biological and Environmental Nanotechnology - http://cben.rice.edu/highlights.aspx
4. Nanovector for anticancer agents based on super paramagnetic iron oxide nanoparticles, Dove Press - http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2676819/
5. Drexler, K.E. Nanosystems: Molecular Machinery, Manufacturing, and Computation, Wiley 1992.
6. Nanotube cancer killer, eLab- http://www.scientistlive.com/European-Science-News/Nanotechnology/Nanotube_cancer_killer/20896/
7. International journal of oncology, Epeius Biotechnologies Corporation 24: 177-185, 2004 www.epeiusbiotech.com/pdfs/Rexin-G_Product-Sheet.pdf
8. Rexin-G® - Tumour-Targeted Injectable Genetic Medicine, Epeius Biotechnologies Corporation - http://www.epeiusbiotech.com/oncology-RexinG-factsheet.asp
9. Giving cancer the 'nano-bullet' - http://news.bbc.co.uk/go/pr/fr/-/1/hi/health/3238373.stm
10. Hybrid Medical Animation, Cancer killer in action - http://www.nanowerk.com/nanotechnology/videos/Cancer_killer_in_action.php
11. Hongjie Dai's research lab at Stanford University, Dai laboratory - http://www.stanford.edu/dept/chemistry/faculty/dai/group/
12. Institute of Science in Society, Nanotechnology, a Hard Pill to Swallow - http://www.i-sis.org.uk/nanotechnology.php
13. Galileo Galilei, J J O'Connor and E F Robertson - http://www-history.mcs.st-andrews.ac.uk/Biographies/Galileo.html
14. Nanotechnology 101 by John Mongillo, ABC-CLIO/Greenwood.
15. Michael Berger, Nanotechnology trap captures cancer cells in blood - http://www.nanowerk.com/spotlight/spotid=13743.php
16. What's the big deal?, The Nanoethics Group, http://www.nanoethics.org/bigdeal.html
17. Nanotechnology kills cancer cells - http://news.bbc.co.uk/go/pr/fr/-/1/hi/health/4734507.stm
18. World Health Organisation, Leading causes of death, http://www.who.int/mediacentre/factsheets/fs310/en/index.html
19. NUS Nanoscience and Nanotechnology Initiative, National University of Singapore (NUS), Cancer Diagnosis and Treatment – Nanobiotechnology - http://www.azonano.com/Details.asp?ArticleID=1286
20. National Cancer Institute, NCI Alliance for nanotechnology in cancer - http://nano.cancer.gov/
21. National Cancer Institute, Video journey into nanotechnology - http://nano.cancer.gov/learn/understanding/video_journey.asp
22. National Cancer Institute, Nanoshells - http://nano.cancer.gov/learn/understanding/nanotech_nanoshells.asp
23. Nanoshell particles: synthesis, properties and application, Suchita Kalele, S. W. Gosavi, J. Urban and S. K. Kulkarni - http://www.ias.ac.in/currsci/oct252006/1038.pdf
24. Nanoshell-Enabled Photonics-Based Imaging and Therapy of Cancer (p. 33-40) - http://www.tcrt.org/Nanoshell-Enabled-Photonics-Based-Imaging-and-Therapy-of-Cancer-p-33-40-p12032.html
25. National Cancer Institute, Cancer Nanotechnology - http://nano.cancer.gov/objects/pdfs/Cancer_brochure_091609-508.pdf