THE POTENTIAL APPLICATION, DETECTION AND TREATMENTS OF CANCER USING NANOTECHNOLOGY

BY

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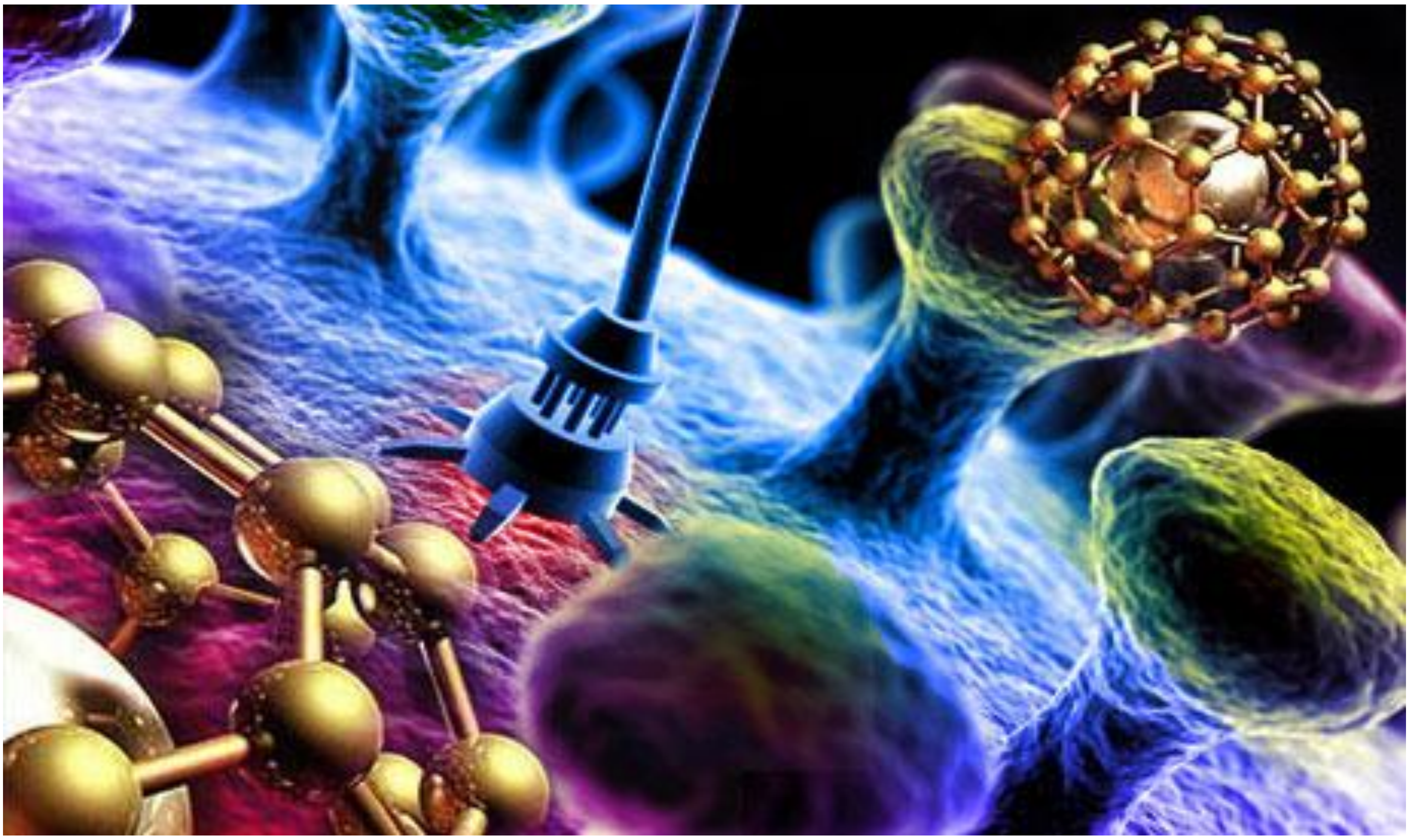

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Abstract

Cancer remains a great problem worldwide and leads to millions of death every year and at the same time nanotechnology is rapidly progressing and is hoping to achieve its ultimate goal in different areas as well as cancer treatment. Several strategies that are implemented and have been tested will be discussed on detection, diagnosing and treatment. Depending on the pathophysiology of the tumour the nanoparticles can be used for efficient and effective drug delivery to detecting the tumour itself for removal to actual detecting the tumour before it becomes cancerous or too late to treat. Nanoparticles are able to work in the specific way, they are designed without being recognised and may solve the main problem of treatment of killing only cancerous cells.

Introduction

This new technology that could have the potential to make a real difference in the world, especially the medical world and could be used greatly in cancer in the near future. This paper will discuss on what is going on so far by using nanotechnology for cancer detection or diagnosis, treatment and application. What makes nanotechnology so attractive is obviously the size and how it has the potential to work and make changes within a cell at a molecular level. Nanotechnology is using (1-1000nm range in at least 1 dimension) manipulative engineering on a particle and is used at molecular and even atomic level (Asif I Haq et al; 2009). The way nanotechnology can be used in different ways for cancer is for mainly biomarkers and profiling the certain cancer type in vivo condition. In using this procedure allows it to be more specific and directed therapies. And hopefully in the near future this field can continue expanding and be applied in every area of medicine (De-Hong Hu et al; 2009).

Cancer occurs when there is alteration and mutation in the normal cell growth called neoplasia causing the growth (hypertrophy and hyperplasia) and serves no purpose at all. They continue growing not following normal tissue growth and don’t respond to stimuli and ignore it. The most common site in men is the prostate and in women the breast. Mortality is extremely high and works by proliferation being uncontrolled (Nicki R. Colledge et al; 2010). In cancer the apoptosis process is deterred because of the inhibition of p53 which allows continuous cell growth (Nicki R. Colledge et al; 2010).

Discussion

When using therapy and diagnostic tools to attack cancerous cells it’s hard as these cells are similar makeup and have properties to that of normal adjacent cells of the host. This is different for example when using anti bacterial or antivirus methods for infections etc, these have a different makeup to normal human cells and that is the main challenge in medical science, is to selectively target the cancerous cells without affecting the patient own healthy cells using chemotherapeutics. As it’s known that the quality of life of a person undergone nowadays anti-cancer therapy have a very poor quality of life and that is where nanotechnology could have a potential role in revolutionising cancer therapy.

Scientist have continued for a long time in cancer research to find effective ways to cure cancer and if not fully cure, but to reduce the effect of cancer on a patient and reduce the effects of this terrible disease. Cancer creates a huge threat on a human’s life and health and treating somebody in the later stages when it is easily traceable makes it very difficult or impossible to treat the individual. Nanotechnology is a new field that and with understanding of cancer and what they do to the body helps, but the problem remains as yet on actually detecting cancer at a very critical and early stage.

In pancreatic cancer the therapy for this cancer is very poor compared to other cancer types out there and nanomedicine is looking promising by using nanoparticles to hold and encapsulated RNA and specific antibodies to allow targeting on the tumour cells. Research from showalter and colleagues have found that using DTA which is cationic poly(beta-amino ester) biodegradable polymer(C32-117,PBAE) which is encapsulates a DNA encoding for a suicide gene known as diphtheria toxic A (DTA) (Judith Keen 2008). These DTA nanoparticles have been previously used on prostrate and ovarian cancer and now to specifically target pancreatic cancer cells they used mesothelin which up regulates in this cancer but not to the adjacent normal cells tissue. This is a critical point as it allows early detection and prevents the cells that are targeted to become cancerous. On encapsulating the DNA that encodes only DTA subunits can be toxic to mesothelin expressing cells like pancreatic “potentially’’ cancerous cells and prevent metastasis (Judith Keen 2008).

One way of detecting cancer early before it develops is based on a computer chip, which is a diagnostic tool that is very accurate and sensitive because of its nanoarrays. These chips contain nanoshells that are able to attach to specific tumour antibodies as indicators. The nanoshells are taken up by the tumour cells and enable it to flag which allows infa-red light to be applied to that flagged region so tumour cells can only be killed. Any adjacent normal cells live which is a great advantage compared to routine normal cancer treatments. As well as nanoshells have been used there are nanotubules that have been used on animals and works in the same principle just discussed. When nanotubules are in solution exposed to infa-red rays they are excited and heat up to 70°C in under 2 minutes[4] and these nanotubules surface is coated with folate molecules (Kwangjae Cho et al; 2008). So this distinguishes it to bind with cancerous cells that have receptors for the vitamin folate on their surface unlike normal healthy cells that don’t have folate receptors on the surface[4] (Kwangjae Cho et al; 2008). So only exposure of the infared rays kills selectively cancerous cells and not normal cells, but this promising technique has only been performed in vivo conditions and has worked on mouse with lymphoma but using it in the human body involves lots of complications and the very problematic environment[4]. Both nanoshells and nanotubules work in the same principle and consist of a silicon core and surrounded by a thin layer of gold shell and work to cause localised tissue ablation. Thermo-ablation has been used with nanoshells in mice for breast cancer using anti HER-2 conjugated antibodies nanoshells (Asif I Haq et al; 2009). Dendrimers is a new tool that has been specially engineered and they look for cancer cells and also attach to inject and used as a target for drug delivery using the folate principle (Kwangjae Cho et al; 2008). Dendrimers have many hooks to attach and their surface is attached with folate for the folate receptor cancer cells but in this case they are vessel containing anticancer drugs to be absorbed by the cancer cells[9].

Diagnosing and detection is a very key step and especially in cancer, making very early diagnosis then allows clinicians to make quick and easy treatments and cure the patient before allowing the cancer to develop and become malignant. This is where nanoscale cantilevers look promising, they are constructed as tiny microscopic flat comb shaped beams with many rows of elongation edges similar to a comb but flat[1](refer to fig 1). Each row is heavily coated with antibodies that are different from the other rows and can detect specific proteins or DNA[1]. When they are near cancerous cells that secrete lots of molecular products like proteins etc, the antibodies attached to the nanometer sized cantilever binds to the specific antibody[7]. When the specific antibody has bound causes a physical change (refer to fig 1) to the cantilever and this can be measured by presence or absence of cancer and the concentration because of the correlation and the molecular expression[7, 1]. These nanoscale cantilevers have been constructed as a diagnostic tool and make quick detection and so further action can be taken. The same principle of nano-sized cantilever is used for detecting super bugs like MRSA[6].

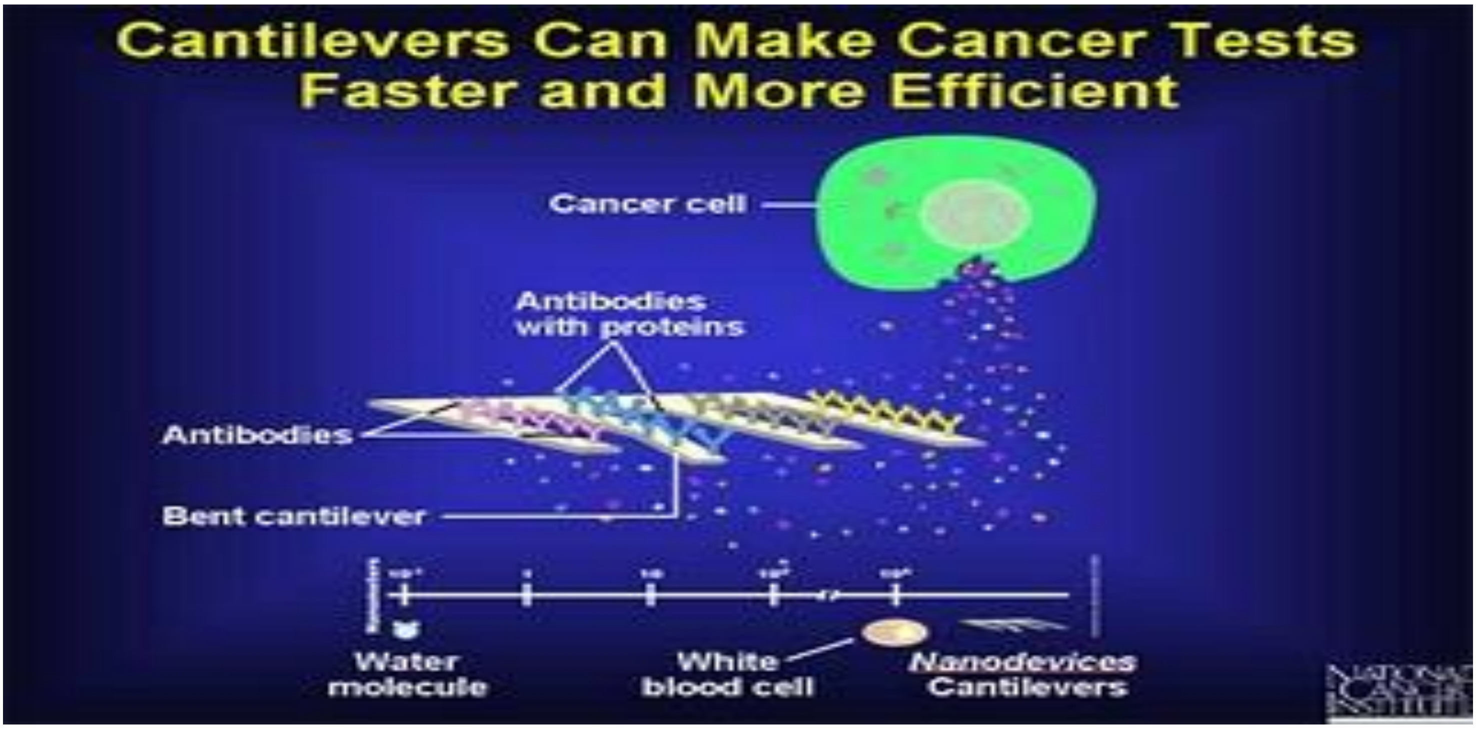

Fig1- An image of nano-sized cantilevers with different bound antibodies on each beam[7].

Another detection tool is using a sensory test chip that contains nanowires that have continuous flow of specific proteins and biomarkers secreted from the cancer cell and help to make a detection of cancer very early[9]. These nano wires are laid on a micro fluidic channel and with great specificity and sensitivity are able to detect the biomarkers of cancer and then relay a signal to an electrode to the outside environment to the clinician testing it. It acts like a device with a similar idea to glucose meter and point of care testing but at a nano scale and genes that are altered gives a great understanding that cancer maybe developing so earlier action can be taken[1, 9] (De-Hong Hu et al; 2009).

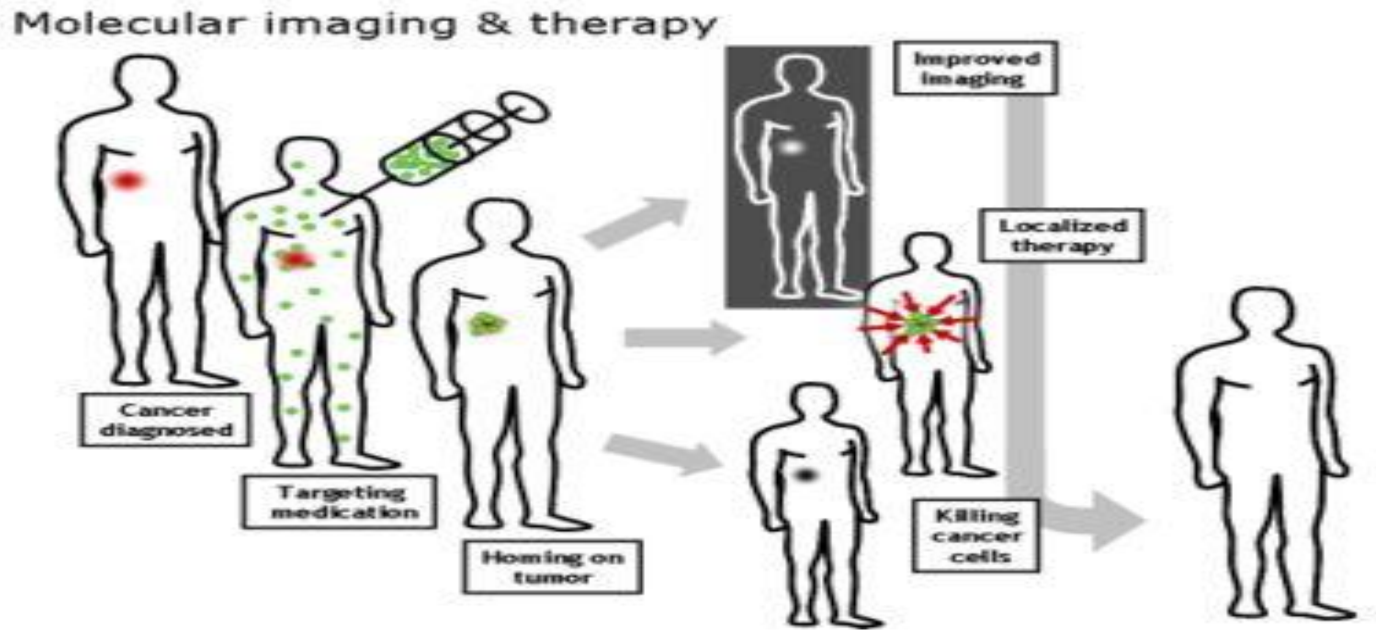

Fig 2- A schematic illustration showing how nanoparticles might be used to treat cancer[2].

Fig 2 is illustrating the use of nano-xray nanoparticles that are injected into the cancer suffering patient and these tiny particles have been engineered with a soft protected layer to prevent it from having any unwanted interaction with the body. Nanoparticles can be composed with small molecular drugs, proteins, nucleic acids (Xu Wang et al; 2009). Once these particles are injected using a syringe near the proximity of the tumour they accumulate in that region. Now in normal standard radiotherapy treatment the body is exposed of x-rays that causes the production of free radicals from the breakdown of water. These free radicals would damage the DNA structure of the tumour cells but also the normal healthy cells and so there is no differentiation or selection, so this approach is very limited. But a person who has been injected with nano-xray nano-particles and then is exposed to standard x-ray radio, the nano particles absorb the x-ray waves and are optimised and this allows them to be activated. This in turn allows the nano particles to produce more free radicals than water and so disrupts the DNA of the tumour more than the neighbouring healthy cells. This treatment is local because of the nanoparticles amplified effect and location and so the tumour's DNA and cellular structure are disrupted causing the tumour cells to die[3]. And yes the result is toxic but only to the tumour cells and this whole therapy provides fewer side effects than the traditional chemotherapy which causes weakness, hair loss and other problems[4]. The gold nanoparticles is the most popular type and using a dye called phthalocyanine that reacts with light energy and transfers the dye to the cancerous cells as these only uptake it causing the DNA alterations and then killing of the cells. Again selectively is being observed here and that different approaches are been biomedically engineered to allow to fight and kill many types of cancer[8] (Xu Wang et al; 2009).

In vitro experiment has been carried by works from (Safaa Sebak et al; 2010) who used a cough suppressant drug called noscapine for killing the tumour in the breast. Using nanoparticles that derives from human serum albumin (HSA) to increase the load in a very tightly packed product and provides greater efficacy. It was found that the drug delivery was greatly increased and used on HER-2 positive SK-BR-3 breast cancer cells and worked at the right concentration and certain therapeutic conditions were met (Safaa Sebak et al; 2010).

Using these small and manmade objects that are minute in size but provide a large surface area and creates opportunities to hold and attach drugs providing a longer efficacy (De-Hong Hu et al; 2009). The longer bioavailability or half life of the drug because they have a larger and complex internal volume allowing no changes to the anticancer drug itself but the way it is administered to the body[8]. Drug delivery is thought to be easier as the nanoparticles size allows them a great advantage and be able to be up taken by cells increasing the strength of the drug, its pharmacokinetics and biodistribution. Pharmacokinetics is duration the drug is present within the body and if cleared out too quickly then the patient requires higher doses and nanoparticles using drug delivery system removes this problem. Moreover, poor distribution of the drug spreading on normal healthy tissue and creating lots of side effects but with nanotechnology particles using the drug delivery system allows localised and reduces non target tissue action[9].

2 main features that have made nanotechnology so attractive and may make medical science change is that the size of the nanoparticles they can be controlled in certain way that they're big enough to prevent rapid leakage from the blood capillaries but small enough that they are not captured by innate immunity cells i.e. macrophages. They should ideally be around 200nm in size to bypass and refrain from these 2 vascular structures. The other characteristic is that their surface characteristics to able to have a greater bioavailability but also to distinguish a cancer cell to a normal healthy cell (Kwangjae Cho et al; 2008).

Surgery

Nanotechnology can be used in the surgical area in the use of nanoparticles of cadmium selenide known as quantum dots that glow when they are exposed to U.V light. If injected to the patient the quantum dots go near to the cancerous region and as they glow the clinician can see effectively where exactly the cancer is situated for efficient removal[9]. The quantum dots are also used with MRI machines to produce amazing images because they produces brighter images and better contrast compared to traditional dyes used as the contrast media. And so the cancers location can be found effectively and at a lower cost for removal[2].

Ethics of nanotechnology

On the issue of ethics new forms of bio weapons could be created and in that the very small engineered particle used for health causes can be used for crime and terrorism or create mass poisoning as nobody knows that they are in close proximity to these products. Also could have an effect on the brain and they can easily cross the blood brain barrier and cause poisoning[10] as the nano sized particles have many different makeup of coating around them causing risks. The main ethical complication is that nanotechnology used for helping or treating illnesses is at a very early stage and yes they can be created but we don't fully understand the long term what these creation can do to the body[10]. They create mutations if used commercially and even use nanotechnology for higher intelligence but there would be money involved. Cancer treatment may used for the rich and take too long or too expensive to reach lower class of people[10]. Nanotechnology is too early to talk about in ethics but some ideas and perennial ethical issues have been thought e.g. there is thought to be great sensitivity and changes of blood biochemistry could be traced by nanotechnology but could create misunderstanding and being meticulous on any changes. Nanotechnology can be used to detect any changes in DNA so how then could we define if a person is cancerous or is healthy person or an ill person. How can we determine at what stage of detection that this patient needs treatment or not and this gives a similarity or correlation to abortion. In abortion at what stage do we believe that a child is a living person from when they are conceived, their first heartbeat, their first movement or their brain starts functioning. So the same question would be played at what stage is a person cancerous and then money would be involved in who has priority to be treated[11]. Using the nanoarrays and nanowires etc give large amount of information to the outside world for collection but too much information could create confusion of if cancer or not and the information collected could break confidentiality[11].

Conclusion

Nanotechnology for the treatment of cancer which is the second most killer of health disease after heart attack and diabetes would help to reduce mortality, less invasive, early detection and may become cheaper in the long term. Nanotechnology would revolutionise all aspects of sciences and non science areas but in terms of cancer the early detection and the specific killing of cancerous cells plays a huge advantage. But yet nobody knows how long it would take to eliminate cancer or even if it is possible and if nanotechnology is the answer to this horrible disease. Most research are laboratory based and have not been used clinically as they are not ready (De-Hong Hu et al; 2009) but hopefully it will replace the conventional chemotherapy that affects both healthy and cancerous cells (Xu Wang et al; 2009).

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