Nanotechnology in Cardiovascular Disease.

BY

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PASS WITH MERIT

RESEARCH PAPER
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ABSTRACT

After spending a few days at Nottingham University on a MEDLINK course we were asked to write a paper on anything to do with nanotechnology.

After initial research and some previous back-ground knowledge I realised that this was a huge topic with masses of discoveries and decided to focus on nanotechnology in cardiovascular disease; I intend to research the topic and conclude whether nanotechnology in cardiovascular medicine is indeed revolutionary step forward or just natural progress. This paper covers a brief history of nanotechnology, a few methods that are currently undergoing research and a look at some of the ethics behind nanotechnology.

INTRODUCTION

Nanotechnology is the engineering of systems at a molecular scale. A nanometer is approximately 1/80,000 of the diameter of a single human hair;[1] a billionth of a meter.[2] It is a science purely dedicated to the study of particles and atoms. Nanotechnology has a huge impact on our future; industry is using nanotechnology to design new commercial products and change our life style such as miniaturization of electrical components to increase the portability of computers. Nanotechnology can be applied to a vast number of topics, from engineering to medicine; it has become a huge industry with many companies investing into it as they realise its full potential and marketing opportunities.

Many people are under the impression that nanotechnology is a new phenomenon and a recent discovery; this is untrue. Nanostructured materials have been around for centuries, dating back to medieval times: nanometer gold and silver particles are what gave stained glass windows their red and yellow colour. However it is a relatively recent concept to manipulate and change things using nanoparticles.

In 1959 Professor Richard P. Feynman, a physicist at California institute, gave a lecture entitled 'There's plenty of room at the bottom' at America Physical Society's Winter Meeting of the West. Although at this time his predictions were based on theoretical speculation his ideas were the start of a crucial part of modern medicine as we know it. Feynman used terminology such as small scale, small things and miniaturization; we now use nano-engineering, nanotechnology and nano-object.[3] Which is further explained in 'Nanomedicine: Webster's Timeline History' by Icon Group International.

Nanotechnology is of huge relevance to medicine, as cells and molecular machines are at nanoscale. This means that machines can enter the body and examine even the smallest parts of the body and show an image to the researcher / doctor controlling the machine. Using this method areas that we couldn't even dream of looking at before, without surgery, can be researched much easier. The advantages of this are numerous: Things can be done at nanoscale; cells can be repaired by using nanobots which can even be programmed to build more nanobots, saving money and labour. Areas of the body can be operated on without having to open up the individual as nanoparticles can be injected into the blood stream where they can correct and repair any damage from the inside, lasers can be used for nanosurgery and chance of infections minimised to name a few.

Nanotechnology in medicine, called nanomedicine, has exciting new possibilities to cure, diagnose, prevent and treat illnesses and ailments. For many people nanotechnology holds hope and the chance to have a future. Although nanotechnology is still, in cases, in early development it could hold the key to future development and much medical knowledge. For further reading 'The Handbook of Nanomedicine' by Kewal K. Jain is recommended.

Nanotechnology is an enormous topic and to focus my research I have decided to have a closer look at nanotechnology in cardiovascular disease.

Cardiovascular disease is a growing concern in the UK as more and more people are developing serious heart conditions and are therefore in desperate need of surgery. However currently there are more implications arising from surgery with regards to the physical nature of the general public. Obesity is rife and this can cause complications during procedures and consequently increase mortality rates. One of the main issues is the size of incision that must be made; in general obese people are very unfit so take much longer to recover from such a huge incision as those who have better fitness. Older patients also face similar problems; they are more susceptible to infection as their immune system is much weaker and their wounds take much longer to recover, so mortality rates increase.

DISCUSSION

Nanotechnology in cardiovascular disease is having a massively positive impact, not only is it helping to cure people in desperate need of treatment, it also increases the chances of survival and so we are able to change the way patients are treated and the face of medicine. Some examples of this follow:

Firstly nanotechnology can help to diagnose and find areas that are damaged within the heart by using a scanning ion microscopy (SICM) which give a much clearer and detailed image of the cardiac muscle than a normal microscope. This means that defects are more likely to be seen and recognised a lot quicker, catching any problems which if left could kill the patient.

In order to check for heart disease the SICM is combined with chemical probes which alerts the researcher / doctor when beta1AR or beta2AR is active.

Beta1AR is a receptor for adrenaline; beta1AR stimulates the heart to contract. Beta2AR is also a receptor for adrenaline and also causes the heart to contract but less vigorously than beta1AR; it also has protective properties whereas beta1AR can cause cellular damage.

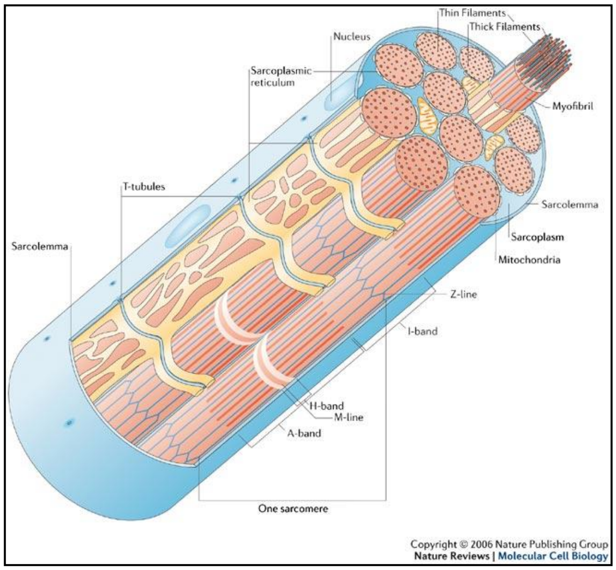

Figure 1

Beta2AR receptors are most commonly found in the t-tubules (figure 1) but when these cells are damaged through heart failure they move, often to areas where beta1AR is commonly found; this change of location prohibits beta2AR's ability to protect the heart, leaving the cardiac muscle susceptible to even more damage. This research means that a doctor could give the individual with these results beta blockers which would enable the beta cells from being targeted by the adrenaline, thus slowing down or stopping any more heart failure and damage. This method of diagnosis is currently undergoing research at Imperial College London, where researchers are looking single cells from healthy and failing hearts from rats.

Dr Julia Gorelik, at Imperial College London, said: "Our new technique means we can get a real insight into how individual cells are disrupted by heart failure. Using our new nanoscale live-cell microscopy we can scan the surface of heart muscle cells to much greater accuracy than has been possible before and to see tiny structures that affect how the cells function. Through understanding what's happening on this tiny scale, we can ultimately build up a really detailed picture of what's happening to the heart during heart failure and long term, this should help us to tackle the disease. The main question for our future research will be to understand whether drugs can prevent the beta2-AR from moving in the cell and how this might help us to fight heart failure,"[4]

Medication is the primary step to help control and prevent coronary heart disease. The medication can not only help to prevent the chance of a heart attack by keeping arteries open, but it can also make the heart beat faster and harder and stop capillaries from narrowing. Nanotechnology is able to deliver drugs to the exact location that they are needed and intended for, meaning they will be more effective and heal and treat patients a lot quicker. Nanotechnology can also be used to regulate medication, ensuring that it is taken at the correct time with the correct dosage avoiding human error such as taking too much or none at all.

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Many conventional methods of drug delivery are on nanoscale, but this is just coincidence; they were not designed because of their nanoscale properties. Examples of these are liposomes and nanoparticles. As we are now aware of how we can manipulate things in a nanoscale we are able to improve these systems greatly.

Liposomes were first used in the 1960's and nanoparticles in the 1970's. Gold particles at a nanoscale were first used more than 150 years ago by Michael Faraday, although the concept of nanotechnology had not yet been introduced. These gold particles were used with an antibody for immunogold staining. Nowadays Nanotechnology is used to target the drug to a specific location; conventional liposomes are now called 'nanovehicles'.

The main issues that drug delivery faces include solubility, intestinal absorption and side effects to name a few. Nanotechnology is designed to overcome these issues. Nanostructures which encapsule the drugs stop the drugs from being absorbed into the intestine, meaning more of the drug will reach the targeted area. They can deliver drugs that are highly soluble in water and are able to remain in the blood circulation for longer than the drug would be by itself. Nanostructures also control how much of the drug can pass into the blood so there is a constant, steady release of the drug into the blood stream and not a sudden hit, decreasing chance of side effects. Nanoparticle's size also allows them to penetrate through tissue allowing them to deliver the drug to the exact point that needs it without damaging any other cells. This ability to pass through tissue and to the exact location which the medication is needed means that the individual undergoing treatment feels better during the process as not only are they less likely to have any side effects the drug will reach and treat the ailment or defect a lot quicker; thus the individual will be in good health again quicker, leaving hospital sooner. "Nanotechnology is the key to optimizing drug delivery, by presenting drugs at the nanoscale, the immediate impact is making otherwise poorly soluble drugs much more bioavailable, soluble, and safer." Dr. Roger Aston, Director of Strategy at pSivida Limited in Australia.[5] This method of drug delivery will prevent heart attacks as drugs will be able to reach the exact location in which it is needed.

There are an estimated 2.6 million people in the UK that have coronary heart disease alone; ignoring all other cardiac related diseases, many of these people eventually need to have surgery. Traditional procedures involve opening up the chest, through the sternum, then putting the patient onto a cardiopulmonary bypass machine where the heart can be arrested. Techniques then vary once operating on the actual heart. However as the patient must be opened up large areas of the body will be susceptible to infection and therefore mortality rates are higher. Nanotechnology offers the chance for surgery to be less invasive, minimising infection and lowering rates of mortality. Robot systems are now being developed so that smaller incisions can be made by having robot arms with small instruments to operate at much a more accurate degree. This method can be used to look at tissue whilst operating. These robot arms would be controlled by surgeons. This method has the potential to speed up recovery time as there would be smaller wounds to heal and decrease length of time of operation.

Another exciting piece of research currently being done is the investigation into how nanobots are able to be programmed to build themselves, and are able to build structures such as a stent once inside the body. Some people however are concerned that if a nanobot can build another independently they ay ultimately become out of control. This is not actually possible, as nanobots need to have an energy input in order to work, they cannot just start building.

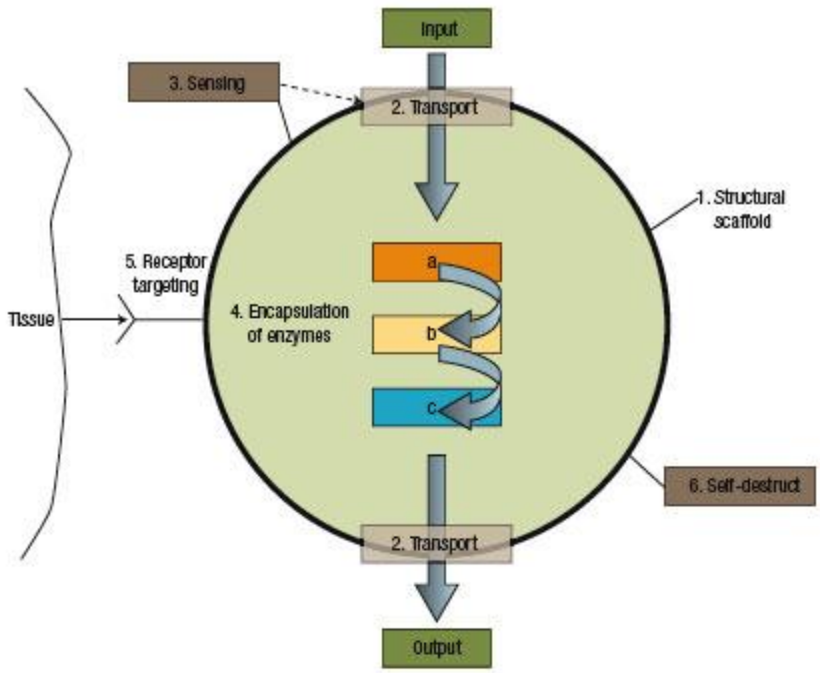

Figure 2

Lastly, Cell nanofactories are a key development for future nanomedicine. This will consist of 6 major components: "We would need six essential components for realizing a biochemical/biomaterials-based pseudo-cell factory" says Michael S. Wong, assistant professor in chemical and biomolecular engineering at Rice University: "(1) a structural shell or scaffold; (2) transport to convey biomolecules to and from the environment; (3) sensing functionality; (4) encapsulation of biochemical machinery; (5) targeting of the factory within the body; and (6) externally triggered "kill switch" to terminate a treatment in a controlled fashion."[6] (Figure 2)

This nanofactory will take in cells and repair them and change them into what they are programmed to be, enabling large quantities of cells to be screened and changed. The sensing mechanism on the outside of the factory (3) will be able to sense the biomolecules that it needs. The actual structure of the cell will be built to withstand the body's natural immune system for as long as possible. Finally, there is a self destruct sequence which can be put into motion externally. This doesn't just stop the factory from working; it breaks it down, stopping any side effects which could be caused from having particles in the body. This will have a positive effect on those suffering from cardiovascular disease as damaged cells can then be treated without changing those surrounding affected areas, they can clean out arteries, potentially avoid heart attacks or any further strokes this is a method of non invasive surgery.

Nanotechnology has the potential to change medicine, change how patients are treated, prevent disease and many other aspects of cardiovascular disease. However as nanomedicine is a relatively new concept there are knowledge gaps which could in the long run do more damage than good. One fear is that the toxicity of the materials used in invasive techniques could harm or damage cells. Animal and tissue studies show that Nanoparticles can cross cell membranes and the blood barrier, meaning that nanoparticles can cross over into unwanted areas. Once in the circulatory system these particles could diffuse into the liver, spleen and bone marrow to name a few. This could cause an accumulation of materials in unwanted areas and potentially have a large detrimental effect. Another issue to do with the toxicity of the nanoparticles is that as they all have such a range of properties you cannot predict what might happen by comparing it to another material. Size also plays a part in how toxic the material is; just because a material is non-toxic at 50nm doesn't mean it will be safe at 1nm; therefore every material must be tested before use at the concentrations it will need to be used at.

Others are concerned that people will be left disappointed. Nanotechnology is believed to be able to cure people, however like every other drug nothing is ever 100% guaranteed; so some argue that by nanotechnology being highly regarded and so many people excited by it, it will only leave disappointment and upset to those that cannot be cured / healed or families left when a loved one dies.

The cost of these drugs can also raise an issue among patients especially in countries that do not have guaranteed health care. As when these drugs, machines, implants etc are first on the market they will be very expensive to buy, creating a social divide between the rich and the poor. People will argue that the poorer have just much a right to these methods as the more wealthy people and health care should not be judged purely on wealth; if someone is in need of these methods then surely they should be given access to them.

Research is already looking at methods of removing certain chromosomes from living cells without damaging other chromosomes around it; this enables defective chromosomes to be removed improving the quality of life for some people. However, this evokes the question of 'how far it too far?'. At which point do we say that removing a chromosome is essential? If a parent would prefer to have a child with blue eyes then should they be able to have treatment to remove any other chromosome that codes for a different colour? Or remove and replace a chromosome that codes for which sex the child is? This nanotechnology could give us more 'god like' responsibilities and options.

What we use it for will need to be monitored to make sure that it is used in a responsible and ethical way.

CONCLUSION

To conclude, I believe that nanotechnology in cardiovascular disease will revolutionise medicine and will improve the national health care service greatly. Not only will it decrease mortality rates, it will, in the long run, reduce costs drastically as a smaller volume of the drug will be needed due to the accuracy of the treatment.

I disagree with the individuals that say that the hype around nanomedicine is a bad thing and that it should not be marketed as such a good thing to avoid disappointment to others; I believe that it give hope and a sense of the future to those that most need it. Often with treatment, if the individual believes it will work, it works better as they are not fighting the system. I think that the excitement surrounding new research is fantastic as it shows what amazing discoveries and ideas are still be found and formulated today. It builds a key interest in the younger generation in science and encourages them to think "outside the box" and amazes the general public.

These key developments will help cure and treat millions of people, once more research has been done and clinical trials finalised. So many more people will be able to afford surgery or medication which will be a huge benefit for those in countries that do not have free national health care.

Nanomedicine will take time and patience before many of the methods currently in research are used as common practice, but with the benefits that it can give us, it's surely worth the wait.

I personally cannot wait to see what researchers come up with next; this is truly a fascinating subject and is very inspiring as to what can be achieved in the future.

REFERENCES

[1]

http://www.touchcardiology.com/articles/benefits-nanotechnology-cardiovascular-surgery-a-review-potential-applications

[2]

http://www.cdc.gov/niosh/topics/nanotech/faq.html#a

[3]

http://www.ajol.info/index.php/tjpr/article/viewFile/44546/28048

[4]

http://www.understandingnano.com/nanopipette-scanning-ion-conductance-microscopy.html

[5]

http://www.drugdeliverytech.com/ME2/dirmod.asp?sid=1422453332174B129DB8EFFF82BF81E7&nm=Back+Issues&type=Publishing&mod=Publications%3A%3AArticle&mid=8F3A7027421841978F18BE895F87F791&tier=4&id=C9F3C47A1C3F450C8010E8793CA4D051

[6]

http://www.nanowerk.com/spotlight/spotid=1418.php

http://www.nanotech-now.com/news.cgi?story_id=07839

http://www.frost.com/prod/servlet/market-insight-top.pag?docid=130393722

http://www.ethicsweb.ca/nanotechnology/

http://www.azonano.com/Details.asp?ArticleID=1705

http://www.ncbi.nlm.nih.gov/pubmed/20544800

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2695932/

http://downloads.hindawi.com/journals/jbb/2006/051516.pdf

http://www.medgadget.com/archives/2010/10/multiple_drug_delivery_via_one_targeted_nanoparticle.html

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http://discoverysedge.mayo.edu/de08-3-biotech-mukho/index.cfm

http://www.cdc.gov/niosh/topics/nanotech/faq.html#a

http://www.touchcardiology.com/articles/benefits-nanotechnology-cardiovascular-surgery-a-review-potential-applications

http://www.capurro.de/nanoethics.html

http://www.answers.com/topic/nanotechnology#ixzz1GVHmS4Px