

HOW CAN NANOTECHNOLOGY BE USED IN GENE THERAPY AND WHAT
ARE THE ETHICAL IMPLICATIONS?

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Abstract

In this paper I will cover the role of nanotechnology in gene therapy, using the examples of David M.Lynn's nanoscale films, cancer treatment and nanobots. I will suggest how these examples could be applied to future applications of nanotechnology. This includes the 'soap' effect films and use of hybrid nanobots. I will then discuss issues with if nanotechnology to make gene therapy successful, what would be the ethical problems. I will discuss issues with germline gene therapy with how it may cross over into eugenics but could cure disease and finally somatic gene therapy. I will then discuss my own views on gene therapy and nanotechnology and if they should be developed in the future.

Introduction

Nanotechnology is the science of manipulating matter at very small sizes. The matter has to be 1 nanometre (nm, 1 billionth of a metre) to 100nm in at least one dimension to qualify as nanotechnology. Anything made from nanotechnology is too small to be seen by conventional optical microscopes, a special microscope such as the scanning tunnelling microscope must be used.

Nanotechnology is a quickly moving field of science; it first was suggested as a concept in 1959 by physicist Richard Feynman during a talk at the American Physical Society. He suggested that matter could be manipulated at a molecular level into nanoscale machines that can manipulate chemical reactions moulding molecules into something desirable. Despite his suggestions nanotechnology first expanded in the 1980's when the invention of the scanning tunnelling microscope and major developments in scientific thinking, such as the cluster science development, allowed scientists to think about and develop nanotechnology with greater success.

Scientists are particularly interested in nanotechnology in medicine. Medicine often deals with issues with cells and problems dysfunctional groups of cells can have on the body. Cells are very small but do vary in size, simpler prokaryotic cells can be as small as 3 micrometres (μm , 3000nm) and the smallest eukaryotic cell, the red blood cell, is $8\mu\text{m}$ in diameter . Nanotechnology will always be smaller than cells, which means there is the potential for nanotechnology to get into the cells and change processes or even genetic information. Nanotechnology can produce things small enough to use the body's circulatory system to travel around the body and still stay intact.

Gene therapy is the alteration of faulty genes in the body to treat disease. Usually DNA that is does not contain the faulty gene is inserted into the body's cells but there are other methods. The most common method of insertion is the use of viral vectors. All viruses attach to body cells and insert their genetic information into the cell, so by attaching the DNA with the 'normal' gene to the virus, the faulty gene can be replaced. Gene therapy has so far proved to be unsuccessful and requires much work until it can be used safely. Some scientists have had to abandon work on particular areas of viral vectors due to the side effects. In 2005 a US patient died of respiratory problems after taking a viral vector [1]. Nanotechnology provides an alternative to viral vectors for the method of insertion.

Discussion

In gene therapy using just naked DNA is ineffective, a carrier is needed, in the past this has taken the form of a viral vector. However, DNA could be embedded into nanoparticles and moved to the desired place in the body and then inserted into cells. Normal DNA is often too large to pass through the cell membrane so special polymers can be used to compact the DNA and allow it to enter the cell. This has been shown the research of David M.Lynn at the University of Wisconsin-Madison [2]. David M.Lynn's team has created a nanoscale film of water soluble polymers and DNA. The films can be coated onto medical devices such as a stent. A stent is used to widen and then support clogged up arteries but

smooth muscle can often grow around the stent and make it useless. Coating the stent in this nanoscale film that has DNA with the gene that prevents the smooth muscle growth means the smooth muscle can't grow around the stent and the artery remains open.

A problem with gene therapy of David M.Lynn is that it hard to control the length of time the cells around the stent are exposed to the gene therapy. David M.Lynn's team therefore used many layers of DNA and the water soluble polymers. More layers would mean a longer exposure to the gene therapy and also layers of alternative polymers that take longer to degrade could be used in order to further lengthen the gene therapy. This means that rather than all the ingredients being simultaneously released in the body, there is a 'soap effect' where the outer layers are slowly degraded away. This 'soap effect' could be particularly useful when using different gene therapy treatments in one. As different DNA could be placed in inner layers so it is released later. This also means the gene therapy could become more personal, with every film tailored for the individual needs of each patient. A tailored treatment for each individual would mean the amount of gene therapy needed could be control exactly to the severity of the of the person's disease. Also if the person is identified as being at risk of certain factors, for example high blood pressure, then the gene therapy could be catered to help prevent that occurring. This would create better success rates and more people would survive.

In the future the films could be applied to any medical implant. For example, transplant organs could be coated with genes that help prevent rejection, this would decrease the number of immunosuppressant drugs required. This would mean the patient is less vulnerable to disease and has a better quality of life. Another possibility is that the films could be arranged into a sphere or torus shape and released into the blood stream. This means gene therapy could be used against blood-borne diseases and for extended time because the 'soap effect' from many layers of the film.

In the UK cancer will affect 1 in 3 people and in 2008 approximately 150,000 people were killed by cancer [3]. At the moment there is no 'wonder' treatment or drug for cancer, only chemotherapy and drugs that assist with the chemotherapy and this treatment has severe side effects. The main problem is that the treatment also affects healthy tissue surrounding the cancer. Finding a treatment that targets only the tumours could greatly decrease the side effects of the treatments.

Cancer is the uncontrolled growth of cells; therefore a possible gene therapy treatment could be to stop growth genes in the tumour. This would prevent the tumour getting larger and could keep the patient alive. Early research done by researchers at the California Institute of Technology in Pasadena show that a 'RNA interference' could slow down or possibly stop the growth of tumours [4]. As gene therapy advances, I expect it to be used to help tackle cancer through insertion of DNA into the tumour cells to stop their growth. This sort of treatment is also beneficial because it will only insert the DNA into the tumour and won't affect surrounding healthy tissue so it will reduce the side effects.

Nanobots are another form of nanotechnology that could be exploited for gene therapy. In theory, nanobots are nano-sized robots placed in humans to carry out certain tasks. Nanobots for example could insert the DNA into the cells or help identify cells suitable for gene therapy and then highlight them to other nanobots equipped for gene therapy. However I think the possibility of a completely man-made nanobot isn't likely to be achieved in the near future. More advances will be needed first and seems too science fiction for our times. However what I think is a greater possibility in the near future is the adaptation of the body's cells to create a hybrid nanobot [5]. The genes in the cell could be changed slightly to support the addition of the man-made nano-scale materials to create the hybrid cell. The hybrid could then carry out some of functions of nanobot and maybe also enhance the inhabited cells' functions. Such as a T-Lymphocyte could be made to recognise cancer cells and then stimulate the

production in hybrid B-Lymphocytes that produce the nanoparticles needed for gene therapy instead of antibodies. These hybrids would be most suitable with blood borne cells as they could exist in the blood and be able to get to any part of the body. They would have the added benefit of not being attacked by the body's immune system because the body would recognise them as their own cells.

There are issues surrounding gene therapy and if nanotechnology were to be made gene therapy treatments successful, these will have to be addressed by the world's scientists and governments. There are two main branches of gene therapy, somatic gene therapy and germline gene therapy. The difference is that somatic gene therapy changes the genetic information in the body's soma cells (everything but the reproductive cells) and germline gene therapy changes the germline cells (reproductive cells) [6].

Germline gene therapy results in a hereditary change. The descendants the individual who receives germline therapy will have changed DNA and there will be an overall man-made change to the gene pool. Scientists think the biggest benefit of germline gene therapy would be the eradication of genetic diseases, such as Huntington's and Cystic Fibrosis. The 'faulty' genes that cause these genetic diseases could be replaced by 'correct' genes. If carried out to enough of the population, in a way similar to vaccination programmes, subsequent generations could be protected from these diseases.

Clinical trials germline gene therapy are generally banned, due to the huge risk of a mistake being made and this spreading into the gene pool causing many problems for future generations.

There is also the issue of what counts as a disability or problem that should be changed by the NHS. For example, most people would agree that Huntington's would be a suitable disease for eradication from the gene pool. However would everybody agree that the genes for baldness would be suitable for eradication? The vast majority of people don't enjoy going bald, but it doesn't affect their physical health so should the NHS carry the heavy costs of changing the gene pool to stop baldness? Given the cost restraints and the cosmetic nature of the gene therapy lots of people would say no, but on the other hand many people would disagree.

Germline gene therapy focuses on the replacement of 'faulty' genes to cure diseases and the good genes pass from generation to generation. However it is only logical that once the 'bad' genes are taken out 'good' ones replace them for subsequent generations. This means germline gene therapy could very easily cross over in eugenics, the science of enhancing people and improving the human race as a whole. There would of course be no agreement on what would be an enhancement as all humans see 'perfect' or 'better' differently but of course many people would like their children or themselves to be little stronger or more intelligent. There is a risk that if nanotechnology makes gene therapy successful, many people will try to seek perfection for themselves and their children through gene therapy.

There is also the risk that germline gene therapy could be used to create a race of 'superior' human beings, capable of working longer and harder than 'normal' human beings. This 'superior' race could cause many problems with a fracture of society with the 'superior' race being seen as higher than 'normal' humans and aloof from society. The 'superior' human being could be envied and 'normal' human beings seek gene therapy to change themselves into 'superior' humans. It is also close to the ideology of Hitler who wanted to create a 'superior' race of human being; tall, blonde, blue-eyed and strong. As we know Hitler's quest for a 'superior' race led him to order the death of six million Jews.

However the opposite could happen, as an 'inferior' human being race could be created, that could possibly be made mentally weaker so more easily manipulated. Possibly used by their creators as a slave race for cheap labour. The issues with both these scenarios are huge, mainly to do with the

discrimination against weaker minorities in society and the abuse of our knowledge and abilities to create human beings that aren't made out of love and care amongst a family, but for the harshness of slave labour. This scenario of an entire race genetically altered to be different is extreme, but some people think germline therapy could be abused like this and are therefore against the development of it.

People who favour germline gene therapy often counter arguments against germline gene therapy with the ideas of Utilitarianism and Relativism, which suggests that the end justifies the means. This means that even if we make mistakes and cause suffering, we will eventually get it right and long-term benefits could be experienced by humanity, so the greatest number has the greatest good. Many say the risks of the germline gene therapy are unknown and the pioneering scientist, James Watson, says; "Never put off something useful for fear of evil that may never arrive. We can react rationally only to real, not hypothetical, risks." [7]. James Watson is a strong supporter of germline gene therapy and in April 2001 called for a campaign to rid society of genetic defects by gene therapy. When asked of the 'risk against reward' argument against germline gene therapy he, with utilitarianism stance, says; "Never postpone experiments that have clearly defined future benefits for fear of dangers that cannot be quantified. Working intelligently and wisely to see that good genes dominate as many lives as possible is truly moral way to proceed." James Watson is clear to make out predisposition to disease is often due to a single gene, which could be simply altered. However changing things like intelligence and height in the area of eugenics are linked to many genes. The more genes one changes, the greater chance of side effects, therefore it will be a long time until some human characteristics can be changed. Watson is of the opinion that eliminating disease and enhancing characteristics are different and the two should be separated.

Despite the campaigns from popular scientists, it has been generally decided germline gene therapy shouldn't be developed for humans until the effects known better and this ban includes using nanotechnology for germline gene therapy.

Somatic gene therapy is the correction of genetic defects in the body's cells. This form the gene therapy is considered more popular than germline therapy because of the principle of the Weismann Barrier. The Weismann Barrier states that genetic information cannot pass from soma cells (everything but reproductive cells) to the germline cells (reproductive cells). This principle, although under recent scrutiny over its permeability, this means that somatic gene therapy isn't hereditary [8].

The risks in somatic gene therapy are less than germline gene therapy, although there are risks to the patient being treated. There is a proportionalist response to the risks and benefits of somatic gene therapy. At the moment the benefits are considered to outweigh the risks, so it is being developed (in the future with nanotechnology). However in the future the risks may be greater due to new knowledge and be considered to outweigh the benefits. It is also popular because of its similarity to traditional medicine with restoring an individual suffering a defect being resorted normality.

There are two main views of gene therapy amongst religious groups. The first view is that because of the sanctity of life (the idea that because God created humans life is holy) humans shouldn't mess with God's creation as we cannot be the designers only God can. They believe that we may cause more problems than we could solve by playing the role of the designer messing with the genetics of humans. The second view is that gene therapy could become useful for removing suffering the in the world. As Pope Pius XII says, when justifying the use of painkillers: "Man preserves, even after the Fall, the right of dominating the forces of Nature, of using them in this service, and of employing the resources so offered to him to avoid or suppress physical suffering." Pope Pius XII is saying that God has given us the

ability to use nature, so we could use our abilities to remove suffering. Although these religious groups with this view accept that there are risks attached that could cause suffering [9].

Conclusion

Gene Therapy is a very contentious issue because of the risks and because it is the changing of the way people are. I think if nanotechnology were to be used in gene therapy it would be successful. It is a safer way of delivering DNA into the body's cells than using viral vectors and as nanotechnology advances more efficient ways of applying nanotechnology to gene therapy will occur.

However, I think any form of gene therapy should be avoided, although I can understand the benefits of using gene therapy to cure diseases. Using gene therapy to change DNA loses sight of what it is to be human. Striving to be perfect using DNA will never work, as we can never be the 'perfect human'. I also think gene therapy is also anti-inclusive. Today's society is getting closer to be inclusive of all people, regardless of race or disability. Suddenly treating disabilities is very anti-inclusive towards those who still have the disability as I think it is saying that those who don't have a disability are better and have a more fulfilling life. So therefore using gene therapy to cure disability is saying that having a disability is like having a disease. I think this is too discriminating and we should treat each other well and with the greatest respect possible.

Although I think gene therapy is an application of nanotechnology that shouldn't be explored, I think that nanotechnology could be applied to many other sectors of medicine and be put to great use. Therefore I fully support the development of nanotechnology in the future.

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