THE DEVELOPMENT OF NANOTECHNOLOGY AND THE ETHICS OF CHROMALLOCYTES AND GENE REPLACEMENT THERAPY

BY

JOANNE KITE

FELICITY POLLOCK

SARA THOMAS

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ABSTRACT

In this paper we have investigated Nanotechnology in terms of its history and applications in medicine. We have researched the idea of Chromallocytes, and how they would work, how they could perform a much more efficient method of gene delivery than any methods developed at present. We considered how Nanorobots could be created in Nanofactories and, as a result of this, we have also considered the ethical and legal issues that revolve around Nanotechnology, gene replacement therapy and Chromallocytes. We discuss how Nanotechnology may affect society.

In conclusion, we feel that Nanotechnology, in particular Chromallocytes, would be beneficial to society as a whole as long as the moral issues associated with this kind of technology are not forgotten, and the concerns of society are heeded.

INTRODUCTION

What is Nanotechnology?

The simplest definition of Nanotechnology is “the engineering of functional systems at the molecular scale”. The study of Nanotechnology is based upon the manipulation of matter on a molecular and atomic scale. The size range of structures on which Nanotechnology is focussed on is between 1 to 100 Nanometres (one Nanometer is one billionth, 10^{-9} of a meter).The size of atoms sets the lower size limit of a device based on Nanotechnology. Nanorobots are tiny robots made at a Nanometer scale. Very few Nanomachines have been manufactured, and most are in the research and development phase. Those which have been created are primitive and are only in the testing phase.

There are two main approaches used in the study of Nanotechnology. The first is the bottom up approach where materials and devices are created from molecular components, which assemble themselves chemically. In the second, top down approach, Nanodevices are created from larger entities without the use of control at an atomic level.

The topic of Nanotechnology is very varied. It ranges from the expansion and elaboration of conventional physics, to entirely original approaches based on molecular self-assembly. There is a significant amount of research concentrating on investigation into the ability to directly control matter on the atomic scale and also into the creation of innovative materials with tiny dimensions.

Objects are so small at the Nanoscale that they are impossible to see with the naked eye and even with a light microscope. In order to see a Nanoscale object Nanoscientists use tools such as the Scanning Tunnelling Microscope (STM) or the Atomic Force Microscope (AFM). The STM is a device for seeing surfaces at an atomic level, with resolutions between 0.1nm and 0.01nm. At these resolutions individual atoms can be pictured and manipulated. The AFM uses an extremely fine and small tip to scan the surfaces of the object. Both these microscopes have their data sent to a computer so that visible graphical projections can be created to display the images.

Quantum mechanics plays a large, vital role in the way that Nanoparticles are studied. The behaviour of Nanoparticles is often unexpected and goes against instinctive expectation of behaviour. They behave erratically because the rules of quantum mechanics are often dissimilar to that of classical physics. Nanoscience seems to require you to disregard all instincts and common sense in order for you to fully understand the principles of the topic.

The History of Nanotechnology

The developments in Nanotechnology were kick-started in the 1980's as a result of major advances in cluster science, which is the science that deals with finite aggregates of atoms or molecules bound by various forces, and the invention of the Scanning Tunnelling Microscope (STM) and Atomic Force Microscope (AFM). This lead to the discovery of fullerenes in 1985, including Buckminster Fullerenes (C_{60}), which are found in soot, and are the largest particles found to exhibit wave-particle duality (they are also known as Bucky balls) (Figure 1). A Fullerene is a hollow molecule entirely made up of carbon atoms. Fullerenes have since been found to occur in outer space.

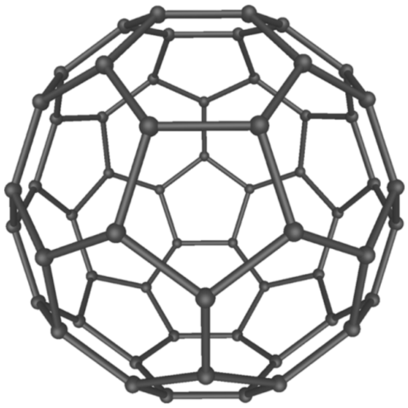

Figure 1
A Buckminster Fullerene

A few years later more research was conducted into semiconductor Nanocrystals, which are any Nanomaterials with more than one dimension and a single crystalline structure which join together to form clusters.

An IBM researcher became the first to manoeuvre atoms, spelling out the IBM logo with 35 xenon atoms in 1989 (Figure 2).

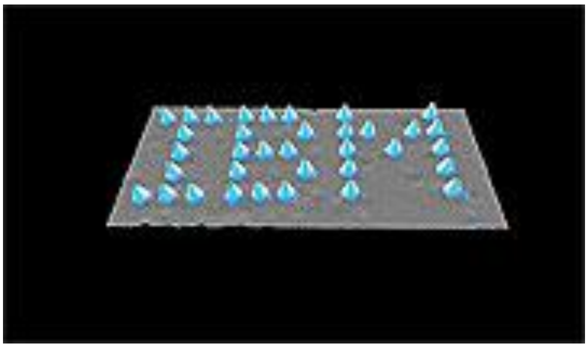

Figure 2

In the early 1990’s two American scientists, Huffman and Kraetschmer, discovered a way to synthesise and purify fullerenes, which allowed the functionality of the fullerenes to be more closely researched.

In 1991, Dr T Ebbesen, discovered and characterised Nanotubes (Figure 3), and It was soon discovered that Nanotubes have a large range of uncommon properties:

- The Nanotubes are 100 times stronger then steel.
- The denisty of the Nanotubes is one sixth that of steel.
- The Nanotubes also show superconductive qualities.

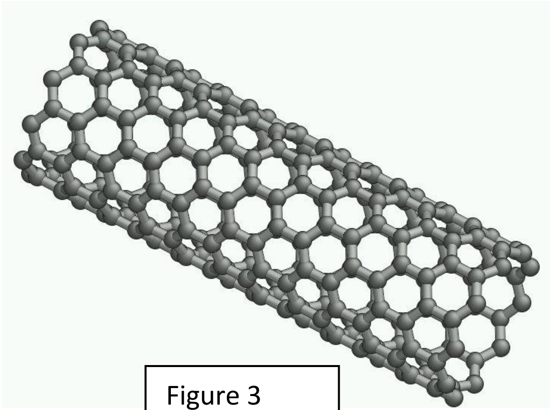

Figure 3

Applications of Nanotechnology

Currently there are several research projects being carried out to investigate the applications of Nanotechnology in medicine. The use of Nanotechnology in medicine could revolutionise the medical field. It could completely change the way that disease is detected and then treated in the human body. Some specific applications of Nanotechnology in medicine include drug delivery, therapy techniques, diagnostic and imaging techniques, anti-microbial techniques and cell repair. Particles can be engineered so that they are attracted to the diseased cells. This means that direct treatment of the cells is made easier and also reduces the damage to the healthy cells in the body.

Nowadays, there are many problems within medicine that can be diaganosed, but due to technical, and ethical, limitations they cannot be cured. One such problem is so called faulty genes. These can occur from a single changed base on the DNA structure. This can result in proteins with an incorrect amino acid code being created, and hence the secondary structure of the protein is changed. In some of these cases the faulty protein created is similiar enough to the normal structure to perform it's function successfully. However, this is often not the case.

If the faulty protein created is Haemoglobin the implications can be very serious, often resulting in sickle cell anemia. It can also be serious if enzymes are faulty as the enzyme-substrate complex cannot be created. If the enzyme that should have been created is one vital within the body, then The result can be fatal, because reactions essential to life will not occur quickly enough without the enzyme. Other diseases caused by faulty genes include; Huntingtons disease which is a degenerative disease which affects muscle co-ordination and may lead to dememtia, and Down syndrome, where the person has 47 chromosomes instead of 46, and as a result there are problems with the way the brain and body develop.

All of these conditions could perhaps be cured if we had a way of replacing and/or reparing genes. As such, a lot of time and money has gone into attempting to progress this area of Nanotechnology.

DISCUSSION

One possible new approach to treating genetic disease is the use of a type of Nanorobot called a Chromallocyte. A Chromallocyte is "lozenge shaped mobile Nanorobot" that works as a gene delivery system. This is a system of inserting and delivering foreign DNA into a body. When fully functional Chromallocytes will be a much more superior and efficient system for gene delivery than the viruses that are used for gene delivery at the present.

Chromallocytes are the first reasoned model of a cell repair machine, a type of medical Nanorobot. The Chromallocytes enter specific cells in the person, fix what is in need of repair there and then harmlessly withdraw from the person's body.

The Chromallocyte (Figure 4) was designed by Robert Freitas who has written several papers and books on the subject, including: ‘The Ideal Gene Delivery Vector: Chromallocytes, Cell Repair Nanorobots for Chromosome Replacement Therapy Chromallocytes’ and ‘Nanotechnology and Radically Extended Life Span’, as well as his book Nanomedicine. The Chromallocyte is in a very advanced class of Nanorobots with ~4000 billion atoms per device. This is huge compared to the relatively simple Respirocytes (artificial red blood cell) (Figure 5), which will probably be the first medical Nanorobots to be built they are only ~18 billion atoms per device, it is estimated that Respirocytes and the Nanofactories needed to build them will take ~20 years to build. After the Respirocytes have been built it will take ~5-10 years of expensive additional research before Chromallocytes will be manufactured.

Figure 4
A Chromallocyte

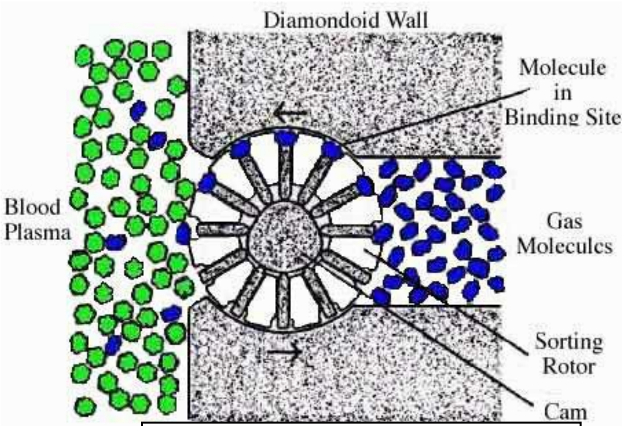

Figure 5
Respirocytes delivering oxygen molecules to tissue.

If the name of the Chromallocytes is analysed, we can get a clear idea of what they would involve:

- Chrom: this means ‘to colour’ and is so called because in biological experiments, the chromatin or chromosomes being observed were stained easily. The prefix indicates that these Nanorobots are going to be centred around the genetic material inside human cells.
- -allo- : this has several roots. Amongst which are the derivatives: ‘another’; ‘other’; ‘to change’. From this we can assume that our Chromallocytes will be involved in the exchange of certain components.

- -cyte: From the Greek 'cyto', this suffix means 'of a cell' or 'cells'. From this, we can determine that Chromallocytes will be working in cells.

Hence, by simply breaking down the name it can be seen that Chromallocytes are Nanorobots whose role is to exchange chromosomes within human cells; hence carrying out the principles of gene replacement therapy.

How Chromallocytes Will Work

Although purely hypothetical, Chromallocytes have been rigorously planned and designed to the extent that if ever put into practice they should be successful. Using them we could theoretically wipe out all genetic diseases as the damaged chromatin is replaced with 100% new correctly manufactured chromatin. This means that any risk of aneuploidy-having the wrong number of chromosomes is avoided.

To fully understand Chromallocytes, the mechanics of how they work must be looked at:

- The Chromallocytes would enter the body via the blood stream (Figure 6). To do this they will be injected by a flexible telescoping Nanocanular. The structure of the Nanorobots has had to be specifically designed for its travel in the blood stream. It will have a maximum diameter across its lozenge shape of 7.33 microns so as not to be trapped in the small diameters of the capillaries (Figure 7).

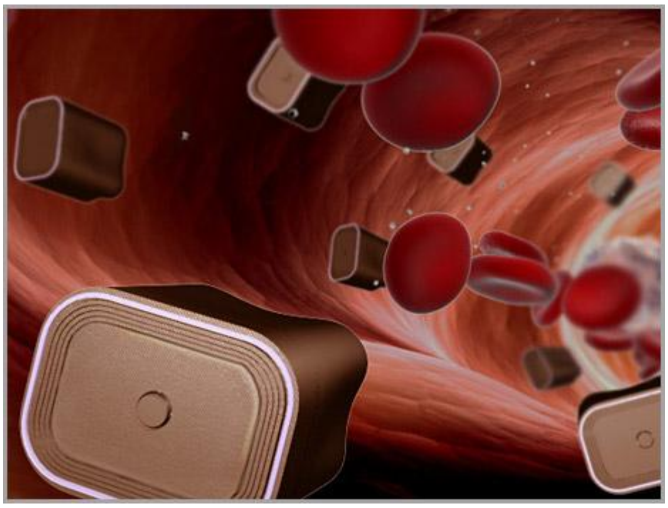

Figure 6
Chromallocytes making their way through the blood stream.

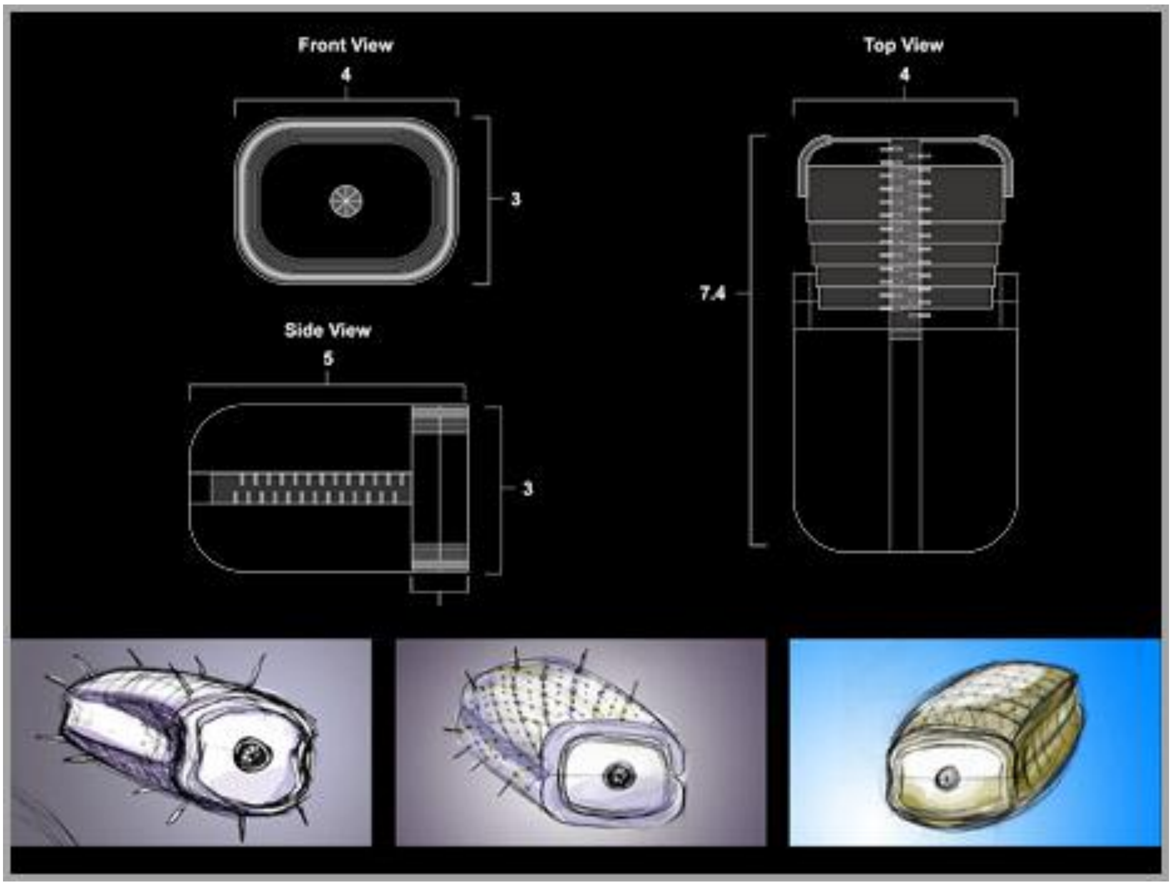

Figure 7
Diagram's and Illustrations of the shape of Chromallocytes and what they might look like.

- The Nanorobots will be engineered to target specific cells, so they will penetrate the capillary bed nearest to their target tissues. Once they have reached their target cells they will move into it through the plasma membrane. Once they have navigated their way through the cell, the front end of the chromallocytes will bind to the nuclear envelope.
- It is now that the proboscis the Chromallocyte will be fitted with comes into action. (A in Figure 8) The proboscis is a long probe that penetrates the cell nucleus. It will be ejected from the Nanorobots into the nucleoplasm. The proboscis is a hollow tube with a smooth exterior. It has a valve to allow fluids out, but prevent unwanted substances entering the Nanorobots. It is also

possibly the most vital construction of the Nanorobots as it is this that allows extraction of the damaged genetic material.

- The front end of the Nanorobots will sink into the nuclear envelope so that the proboscis is fully exposed to the nucleoplasm and can rotate into its chromosome binding position. The surface of the proboscis is engineered to be the one to which the chromatin will strongly adhere. To increase the probability of chromatin-proboscis collisions it will be fitted with probe-like structures to increase the surface area. (B in Figure 8)

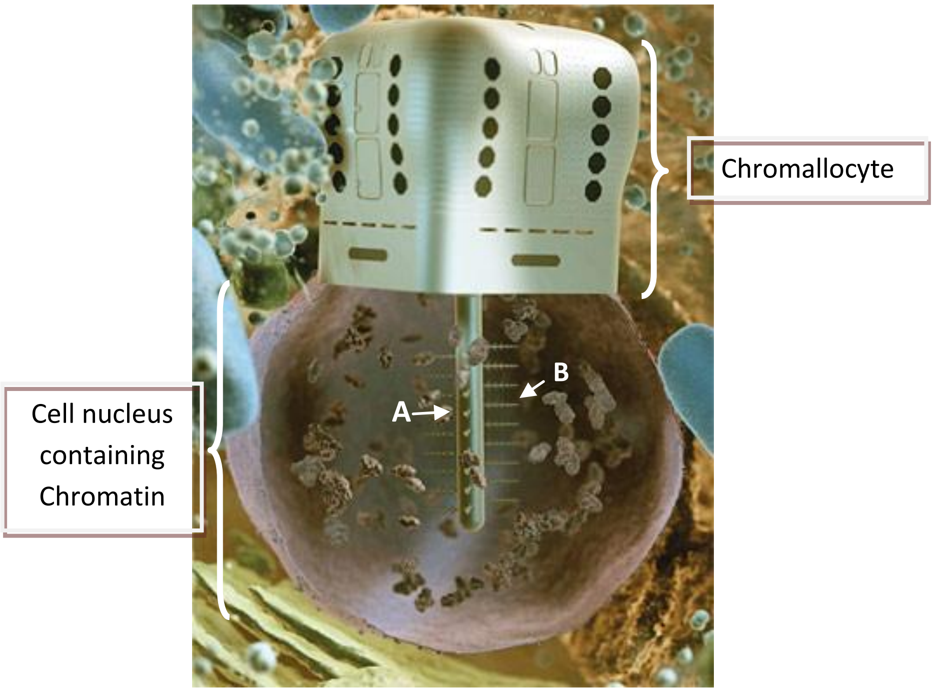

Figure 8
The Chromallocyte attached to a cell.

- The Proboscis will then rotate. This would cause any loose chromatin to form in a mass around the probe which can then be extracted easily from the cell. As the old, damaged chromatin is drawn up, the new healthy chromatin will be forced out to replace it. This is the principles of gene replacement therapy.
- The last stage to undergo is the removal of the Chromallocytes from the body. The Chromallocytes will exit the body, the same way they arrived, by

travelling through the blood stream until they reach the kidneys where they will be filtered out.

We can theoretically give many people lives that they would not otherwise had. Down syndrome is one example where applying the theory of Chromallocytes for chromosome replacement therapy lives can be changes. Many children are aborted because of the syndrome which could in the future be unnecessary (Figure 9)

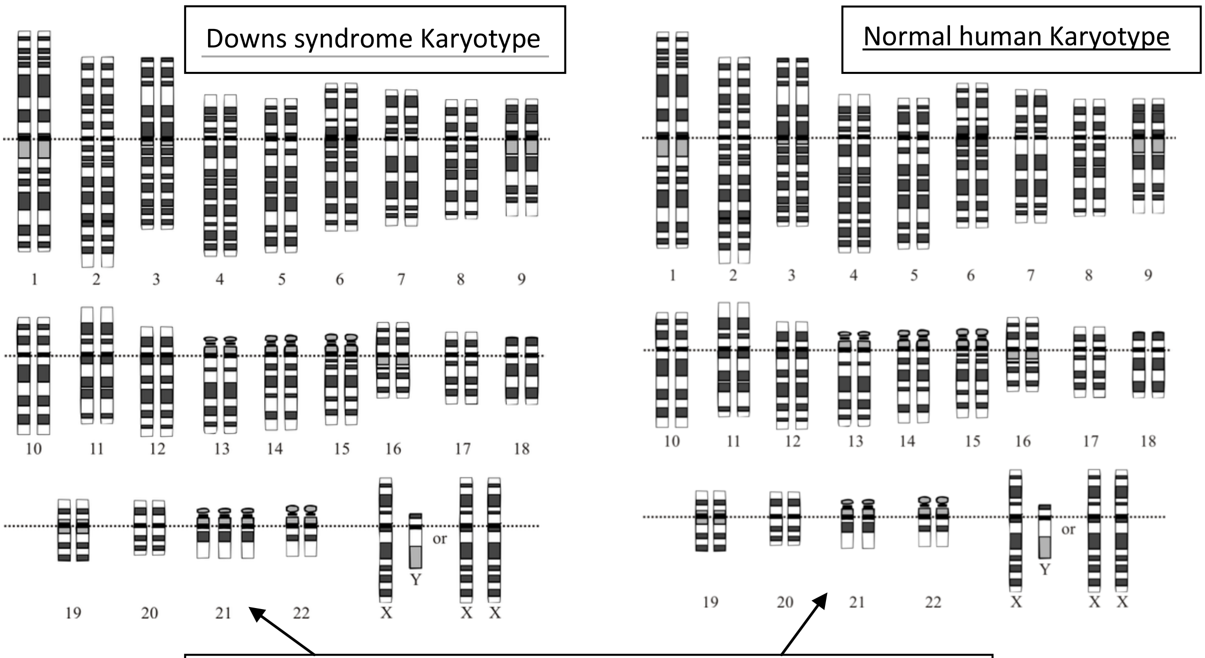

Figure 9
In the Down syndrome Karyotype Chromosome 21 has an extra copy; this would be present in the new chromatin, eradicating the syndrome. Chromallocytes will completely replace chromatin on the left with that on the right.

Nanofactories and the development of Nanotechnology

Nanotechnology will be dependent on the development of Nanofactories and this development would make Chromallocytes more accessible. A Nanofactory involves Nanomachines, resembling molecular assemblers or industrial robot arms, to produce larger atomically precise objects.

The Nanofactory is a proposed compact molecular manufacturing system, possibly small enough to sit on a desktop. As the size of the Nanofactory is so small, precision and design is vital. A Nanofactory could build a divergent selection of large-scale molecularly precise products. Nanofactories pose the potential for being extremely low cost, high quality and extremely flexible.

The products formed in Nanofactories have the same the intricacy and sophistication that is found in nature, but with increased power, speed and reliability. Nanofactories will be under human control, so that humans can hopefully control what is created, unlike in nature.

The Ethics and Safety of the Use of Nanotechnology and Chromallocytes

Science is always moving forward and as a result fantastic new understandings and inventions are always coming to light. The invention of chromallocytes by Robert Freitus is one of the giant leaps forward, not only in Nanotechnology, but in science over the last decade. However, although scientific advances may appear to be exciting and something we should push for, because we live in a moral society we cannot afford to leave the ethics of what we are developing behind.

Nanotechnology as a concept is openly opposed by groups such as ‘Angels against Nanotech’. People oppose it because they believe that it is unnatural to interfere with the assembly of nature. Even when the Nanotechnology being used is not directly linked with humans (for example, in sunscreens, zinc oxide or titanium oxide is used to absorb harmful U.V rays) some people still object.

One objection is that, because Nanotechnology is still a fairly new concept that has not been around for long, the full long term effects may not yet be known. Moreover it is not just the long term effects on the humans that are unknown, but the impact on the environment. In March 2004, environmental toxicologist, Eva Oberdörster, led an investigation in which fish were exposed to fullerenes over a 48 hour period. After this time they were found to have extensive brain damage. This troubles people because we cannot always predict the properties of the Nanomaterials we create.

When we apply these unknowns to chromallocytes it becomes apparent why it will take years of rigorous testing and observation before doctors can even think about introducing them to a patient. Nanorobots are larger than Nanoparticles, but they are still at a scale where the effects could be different to what the developers might expect and introducing these tiny machines into the human body could cause an undesirable or even fatal outcome.

It cannot be ignored that we live in a largely religious society (86% of the world's population classify themselves as religious). The introduction of Nanorobots to treat diseases such as cancer is one thing, but to intentionally go on to alter the genetic makeup of a person, to many seems wrong. Religious people may argue that it is their God's plan for us to be affected with whatever disease we inherit and to interfere is sacrilegious. It could be argued that we are not just interfering with God's will, but are trying to "play God". Some people feel that, our society should not engage in science such as this, as the intentions of some are not always for the good of the population and the use of Chromallocytes could be exploited. By accepting the idea of Chromallocytes society could eventually reject any 'abnormal' people and we could generate a culture where perfection is necessary.

A further concern is the age at which patients would be allowed to undergo the treatment. Parents may be considered unloving if they allow their children to have the treatment, because they are "changing" their children. But they may also be considered unloving if they do not allow their children to have the treatment, because they may be forcing their children to live with an uncomfortable or disfiguring disability.

It may also be difficult deciding which conditions are suitable for the treatment to be used. For example if a child had a birthmark, some may consider it essential that it is removed and others may not agree. If there is no regulation we may end up with a “designer baby” culture, where parents decide eye colour, hair colour and much more. However, the removal of some genes may be beneficial to society as a whole. For example the so called “fat gene”. The UK has a highly increasing obesity rate, especially within children, and it is costing the NHS a considerable sum each year to deal with the health conditions caused by obesity (for example heart disease) so some may argue that any opportunity to remove the gene should be taken. On the other hand, people may consider it unacceptable that people’s individuality could be affected like this, and suggest that if society ever accepts any types of genetic manipulation, then we could end up with a new generation of “perfect” clones, with no individuality.

Legality of Chromallocytes

Having discussed the possibilities that the use of Chromallocytes can bring, they seem like an exciting advancement in Nanotechnology. However, there are hindrances that may block the way for such future developments.

The legality of gene replacement therapy is something that must always be approached with caution. The legal system varies in different countries, so, for instance, if the use of Chromallocytes in humans were accepted in the United States it does not necessarily follow that they would be accepted in the UK. At this moment, it is illegal in the U.K to carry out chromosome replacement such as this, but who knows where we shall be in 10 years time? Especially as the practise is seen as largely therapeutic. Laws and attitudes may change. Nevertheless ethical laws and restrictions play a part in hindering the development of such ideas.

We may develop easier routes to gene replacement therapy. Chromallocytes are proof that medical science is always moving forward and it is possible that, while Chromallocytes are still being developed, someone may come up with a better way of tackling the issue of genetic diseases. There are already alternative routes, such as the use of viruses, which sidesteps the necessity of Nanotechnology altogether. In Vitro Fertilisation babies can have gene line therapy which sidesteps the need for Chromallocytes later.

Conclusion

To summarise, there are many obvious positives to the eradication of genetic diseases: for example the extension of age and a more pleasurable old life or; the removal of a diseases that will affect future generations. However, we must be aware of our humanity and ignorance. There will always be many grey areas in the definition of a genetic disease and this could be exploited, for example height alleles may be altered so that a child grows up tall or short depending on what society at the time views as ‘the norm’. There are an infinite number of unknown consequences of Chromallocytes and effects of chromosome replacement therapy may cause defect genes further down the family line or lead to exploitation of knowledge. The positives must be weighed out against the negatives. It cannot be disputed that many significant advances in science would not have been achieved without significant risks.

Having researched the use of Nanotechnology extensively, we feel that there are many positives that we can gain from investing in the production of Nanotechnology. As long as the ethical side is monitored then developing these Chromallocytes will have a positive impact on society. The eradication of genetic disorders will allow many people to live better lives that they always had the potential to live, but have been hindered because of a genetic defect.

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