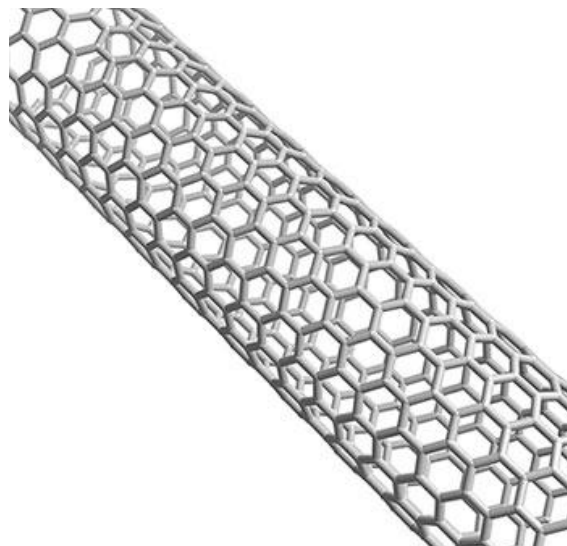


THE MEDICAL APPLICATIONS OF NANOTECHNOLOGY:
DEVELOPMENT OF TISSUE ENGINEERING AND CONTROLLED
DRUG DELIVERY

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PASS



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ABSTRACT

Nanotechnology is a relatively new science, barely 50 years old. Scientists, whilst still not fully understanding the way materials behave at less than 100nm, strive to apply this promising form of technology to almost all disciplines. This paper looks briefly at how nanotechnology can help solve current issues such as Bioterrorism and Global Warming. However, its main focus will be on the medical applications of nanotechnology, leading on to two specific areas; tissue engineering and controlled drug delivery. Providing examples of some of the latest research and developments, this paper aims to provide suitable proposals for advancements, taking into consideration the ethical implications surrounding this new technology and the limitations that exist.

INTRODUCTION

Richard Feynman, who would go on to win the Nobel Prize in Physics, gave a talk on December 29, 1959 entitled, "There's plenty of room at the bottom." This is often credited as being the starting point for research and development in nanotechnology. However it was not until 1974 that the word, nanotechnology, was first used. Nori Taniguchi of the Tokyo Science University used the term to refer to "production technology to get the extra high accuracy and ultra fine dimensions, i.e. the preciseness and fineness on the order of 1 nanometre".

By definition, nanotechnology is the science of designing, producing, and using structures and devices of 100 nanometres or less (see Figure 1). Nature operates at this nanoscale, and scientists are acquiring an increasing understanding of natural processes at this scale, enabled by a new generation of scientific instruments.

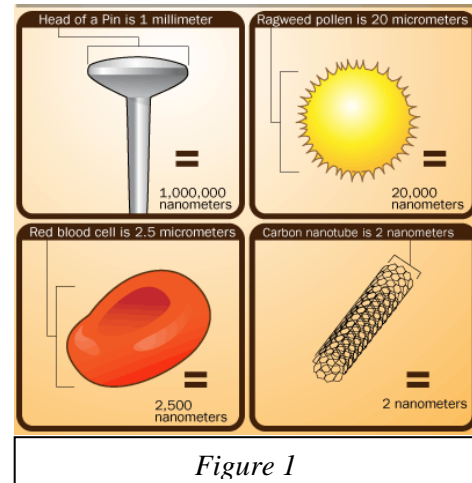


Figure 1

Nanotechnology can be applied to numerous research subjects, however it generally leads to advancements in four main areas; security, environment, energy and medicine. Emerging nanotechnologies are expected to play a critical role in helping to maintain national security. They include new and powerful biodetection schemes that can analyse a potential bioterrorism threat at the point-of-care, materials that can detoxify an area or a human that has been exposed to a set of toxins, and ways of encoding structures that can then be used to secure computer systems.

Renewable energy technologies are often referred to as clean energy because they are far less harmful to the environment than conventional energy sources. Nanotech researchers are working on the development of a solar panel/fuel cell combination that can collect excess energy, convert it to hydrogen, and store it. Nanotechnology could also provide cost-effective solutions to nuclear decontamination and other challenging environmental cleanup problems.

There is a limited supply of fossil fuels and at the moment they are being used up faster than they are being found. Researchers are exploring ways in which nanotechnology could help us accomplish two main goals; to be able to access and use fossil fuels more efficiently in order to get more energy out of current reserves and to develop new ways in which to generate energy. One of the processes being developed to use fossil fuels more efficiently is the current research to design zeolite catalysts at the nanoscale. New energy sources such as hydro or solar can be expensive and difficult to harness. Researchers, like

those at the University of California, hope to use nanotechnology to develop nano solar cells that would be energy-intensive and far less expensive to make.

When applied to medicine, nanotechnology can be used to design devices that can either directly interact with, or influence, the behaviour of living cells. Currently the main areas of nanotechnology in medicine are detection and diagnosis, biological markers, regeneration and treatment.

Some diseases do not exhibit recognisable symptoms until they are well advanced. The earlier a disease is detected the more likely treatment will be successful. Sensors based upon nanoscale materials have the potential to be millions of times more sensitive than their macro scale counterparts. For example, doctors would like to be able to diagnose breast cancer when the tumour mass is 100-1000 cells but at the moment, with techniques like mammography, a tumour mass needs to be more than a million cells before an accurate clinical diagnosis can be made. Nanotechnology could also be used to detect hundreds of diseases at the same time.

Researchers have discovered that there are biological markers in the body for diseases, but most of these biological markers are at such small concentrations that current methods cannot sense them. Recently researchers identified a biological marker for Alzheimer's disease and have been able to detect minute concentrations of it using nanotechnology (the bio-barcode process developed by C. Mirkin and colleagues). If successful, this could be the first tool for early diagnosis of Alzheimer's. Experiments are also underway to use this process for other diseases like AIDS and many forms of cancer.

Nanotechnology can be used to engineer a gel that spurs the growth of nerve cells. This gel fills the space between existing cells and encourages new cells to grow. While still in the experimental stage, this process could eventually be used to re-grow lost or damaged spinal cord or brain cells. Researchers are also investigating the use of nanotechnology to keep the body from rejecting artificial parts, and to stimulate the body to re-grow bone and other types of tissue.

Disease is mainly caused by damage and destruction at the molecular and cellular level. Unfortunately, many current treatments cause damage to healthy tissue as well as diseased tissue. Controlled and targeted drug delivery could be the way forward. At the moment researchers are investigating the use of nanoparticles as drug carriers. These nanoscale drug carriers could be coated with nano-sensors, which could recognise diseased tissues and attach to them, releasing a drug exactly where needed. Nanoparticles could also be used to enter damaged cells and release enzymes that tell the cells to auto-destruct, or they could release enzymes to try to repair the cell and return it to normal functioning.

Though there are many applications of nanotechnology in medicine, for this research paper I have chosen to focus on two specific areas, controlled drug delivery and tissue engineering. At the nanometre scale, many materials display very different physical, chemical and biological properties, compared to the very same material, in bulk form. The properties of nanoparticles include increased chemical activity and the ability to cross tissue barriers. These properties are leading to new drug targeting and delivery techniques. Nanotechnology is also making the stimulation of the body's own mechanisms to successfully repair diseased or damaged tissues possible, replacing the need for transplants and artificial organs.

DISCUSSION

Recent discoveries of various forms of carbon nanostructures have stimulated research on their applications, particularly in medicine. Carbon nanotubes (see Figure 2) have the potential to carry drugs in organisms, as they are hollow and far smaller than blood cells. Methods have been developed to attach DNA and protein molecules to the inside and outside of nanotubes, enabling them to target and destroy individual cells that may be cancerous or infected with a virus. Nanotubes with attached enzymes may be able to be used as enzymatic biosensors that could both detect and measure a variety of biological molecules.

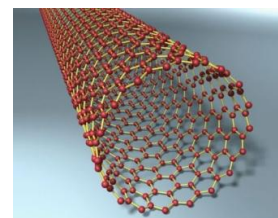


Figure 2

Carbon nanofibres and nanotubes grow through or from the surface of certain metal catalyst particles (for example, Fe, Co or Ni). A combination of carbon nanofibres/nanotubes and the magnetic, metal catalyst particles may allow carbon nanofibres/nanotubes to be used for magnetically guided drug delivery. However, the successful application of this would depend on the physical, chemical and biological properties of the material used. The particles would have to be biologically inert and biodegradable, have a high sorption capacity that has an adjustable selectivity, be able to conveniently bind with antibodies and have a high magnetization and magnetic susceptibility in the relatively weak magnetic fields. Iron particles combined with different carbon nanostructures meet all of these requirements and are therefore a likely candidate for future medical applications.

Researchers have demonstrated the possible use of nanotechnology to accelerate the repair of cells within the human body. Unlike other cells in the body, once cells in the central nervous system (spinal cord or brain cells) are mature, they cannot reproduce themselves like other cells can. If these cells are damaged through accident or disease, patients must learn to live with the impact.

However, an experiment conducted at Northwestern University, showed that after laboratory mice were paralysed with spinal cord injuries they were able to regain full mobility within six weeks of being injected with nanomaterials. The nanomaterials were molecules that self assembled into nanofibres in the spinal tissue, and then aided in repairing the damaged neurons. While still in the experimental stage, this process could eventually be used to re-grow lost or damaged spinal cord or brain cells.

Damaged cartilage (see Figure 3) occurs in many people, especially athletes and older adults. Over time, symptoms can become extremely painful and may lead to loss of physical function. Currently, there is no therapy to effectively treat damaged cartilage, but researchers now hope nanotechnology holds the answers for regenerative treatment.

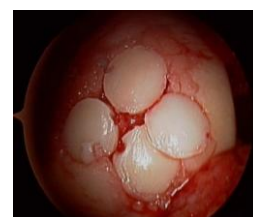


Figure 3

So far, scientists (led by Ramille N. Shah, assistant professor of materials science and engineering at the McCormick School of Engineering and Applied Science, and assistant professor of orthopaedic surgery at the Feinberg School of Medicine) have developed a new nanofibre gel that promotes the growth of cartilage in damaged joints. The nanoscopic material is injected into the joint where it stimulates bone marrow cells to produce cartilage containing type II collagen, which is the major protein in articular cartilage (the white connective tissue that cushions bones within the joint).

Currently, a procedure called microfracture is the most common technique used by doctors. This procedure involves drilling small holes in the bone beneath the damaged cartilage to create a new blood supply in order to stimulate the growth of new cartilage.

However this tends to produce a cartilage consisting of mainly type I collagen, which is more like scar tissue. Recent tests in lab animals showed that the nanoscopic material produced far better results than the microfracture procedure alone.

Bones are vital parts of the body and, whenever partially damaged, they have the ability to heal themselves. However, when seriously damaged, bone takes a far longer time to regenerate. Engineers in bone tissue are working towards a material that can induce and accelerate bone re-growth as well as being able to disappear as soon as the bone has recovered.

New porous compounds (such as those found by Beatriz Olade, research scholar at the Health unit of Tecnalia) have been developed, which are capable of chemically and electrically interacting with bone cells. Carbon nanotubes are used to enhance mechanical properties, along with polymer polylactic acid, for its widely used biodegradable properties and bioceramic hydroxyapatite which provides enough calcium to facilitate growth.

Trials carried out by those at the Health unit of Tecnalia provided promising results for both in vitro (in an artificial environment) and in vivo (inside a living organism). Encouraging amounts of bone growth were observed after 3 weeks and after 16 weeks. The bone formed had properties hugely similar to healthy bone tissue.

The total number of research studies dealing with adverse effects of nanotechnology is small, but growing. However, the most immediate challenge in nanotechnology is that scientists need to learn more about materials and their properties at the nanoscale. Given how little time has elapsed since the inception of nanotechnology, the lack of knowledge about its adverse effects is not surprising.

Because elements at the nanoscale behave differently than they do in their bulk form, there's a concern that some nanoparticles may be toxic. Some doctors worry that because the nanoparticles are so small, that they pose unique problems of exposure. Nanoparticles can potentially penetrate deeply into the lungs when inhaled, be absorbed through the skin and may then be able to be circulated throughout the entire human body once inside. It is also suggested that they could easily cross the blood-brain barrier (a membrane that protects the brain from harmful chemicals in the bloodstream). Some tests on fish have shown toxic, but not lethal, effects. This and other incomplete knowledge of the adverse effects of nanotechnology is undeveloped, but is enough to show that there are potential or actual effects that may warrant concern.

Members of society are also concerned that once nanomaterials are released into the ambient environment they may then be impossible to contain. However, many current commercial applications of nanotechnology involve high exposures, such as cosmetics, clothing and drugs. And as such the concerns regarding exposure are merely hypothetical.

There are also ethical issues to consider when using nanotechnology to further medical advancement. If nanotechnology in medicine will make it possible for humans to enhance themselves physically, is it ethical to do so?

In theory, medical nanotechnology could make the human body smarter, stronger and faster. Not to mention other abilities ranging from rapid healing to night vision. If such goals are pursued, could we continue to call ourselves human, or would we become something else? However, this may be a natural stage in evolution humans must learn how to better themselves on a cellular level before moving on to the next step on Darwin's evolutionary path (see Figure 4).

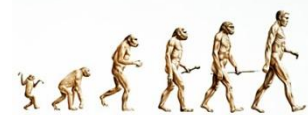


Figure 4

Like all new technologies, nanotechnology would start off as very expensive. Does this mean, that sometime in the future, two races of people would be created; a wealthy race of modified humans and a much poorer population of those who remain unaltered?

CONCLUSION

Over the last 50 years there have been some amazing advancements in the field of nanotechnology. Researchers believe they can now stimulate the human body to re-grow bone and other types of tissue using nanoparticles, such as nanofibres and carbon nanotubes, as well as being able to detect and destroy infected cells by injecting 'smart' drugs. These brilliant developments are still within their experimental stage, however with enough funding for more research and testing, nanotechnology has the potential to revolutionise healthcare for the next generation.

Doctors envision a future where nanotechnology can be harnessed to ultimately provide medicine which operates from a purely preventative state. By identifying and stopping potential sources of disease or illness in the body before they progress. Injuries and damaged or diseased tissue will become insignificant, as nanotechnology stimulates the body's own mechanisms for repair, making the need for transplants and artificial organs obsolete. However, before any of this can be achieved, as with all advancements in science, there are moral, ethical and medical issues that need to be addressed.

Animal testing remains a small but vital part of medical research. In many cases, it is the only way that the effect of a potential new medicine in a living body can be demonstrated before it is used on humans. Whilst some may think it immoral to test new treatments on animals, by safety regulation laws, researchers are required to test all new medicines on animals before they are allowed to be tested in clinical trials. When such animal testing is necessary, researchers are committed to acting morally, providing for the animals health and wellbeing, and practising good animal welfare.

As with other medicines, there are concerns that nanotechnology in healthcare will only be available to the rich, and that poorer members of society will be unable to afford such groundbreaking new treatment. There is also the issue of nanotechnology being used to physically enhance people and whether this is unethical both socially, in everyday life and professionally, in competitive sporting events.

There is also the fear that nanoparticles may be toxic, as scientists are not certain of how materials react at such a minute level. Though studies have shown that there is no real cause for concern, it may be sensible to implement legislative controls on the use of nanomaterials in order to dispel public safety fears.

Despite any of the concerns or reservations highlighted, nanotechnology is indisputably the way forward for the future of medicine.

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