ARTIFICIAL LYMPHOCYTES

BY

VISHAL SAXENA
TOM MONK
DILRAJ SARVAIYA

PASS

RESEARCH PAPER
BASED ON
PATHOLOGY LECTURES
AT MEDLINK 2010

Abstract

Nanotechnology offers powerful new prospects for the treament of many conditions. This paper proposes a theoretical device dubbed a mechanical lymphocyte, which is intended to be used primarily as an immune system supplement to enhance immune response. Other uses of such a device are proposed and many more probably possible. This artificial lymphocyte's main advantage would be that it can produce antibodies complementary in shape to *any* antigen, menaing the humoral immune response would be much faster and in some cases the pathogen may be destroyed before it even begins to introduce symptoms in the sufferer.

Introduction

Nanotechnology is work based on the manipulation of matter on an atomic scale. At the moment the work of nanotechnology is about making computers and machines extremely small, in particular into a few nanometres and even smaller.

Nanomedicine is seen as the basis for the next revolutionary step in medicine, since the very basic building-blocks of life around us are cells. These by their nature are extremely tiny and tend to be usually not more than 10 micrometres. Nanomedicine would allow doctors to inject tiny robots into a sick person, and these robots would actually repair cells on a molecular level, something that is not possible at the moment. This would change the very basis of medicine, and there are hundreds of possibilities, like treating cancer without the need of chemotherapy or radiotherapy.

The idea of nanotechnology was first conceived in December 1959 in a talk by the physicist Richard Feynman while at the California Institute of Technology. Since then the interest in nantechnology has increased dramatically. Certain key events, like the 1986 Engines of Creation:The Coming Era of Nanotechnology by K. Eric Drexler was controversial in some eyes, but raised questions about the many applications of nanoscience, in particularly molecular nanotechnology. Possibly the most famous discovery related to nanotechnology was the Buckminsterfullerene or the 'buckyball' in the late 1980's and 1990's. These fullerenes were under debate regarding the possible function of binding certain antibiotics to the atoms to target pathogens and harmful substances. At the moment, current research is trying to determine the possible uses of carbon nanotubes, reducing the size of microprocessors and creating synthetic molecular motors.

The possibility of treating diseases within actual cells is now a very real prospect.

Our initial idea of an artificial lymphocyte arose when reading a paper by Robert Freaitas, in which he proposed an idea for an artificial phagocyte called a microbivore [1]. Although a microbivore would provide some defense from pathogens, the specific immune response would still be slow. So in order to speed up immune response, we propose an artificial component to the specific immune response; an artificial B lymphocyte.

A microbivore is an oblate spheroidal nanomedical device which consists of 610 billion of precisely arranged structural atoms; in practice it is the equivalent of an artificial phagocyte or white blood cell. It would also contain 150 billion atoms of water or gas molecules in operation. The idea behind its design was the guarantee of a safe, easy and quick eradication of pathogens.

This nanorobot measures 3.4 microns in diameter at its greatest point and 2.0 microns in at its smallest point. It has a gross geometric volume of 12.1 cubic microns. The size would guarantee that the machine would be able to fit in a capillary. Our artificial lymphocyte would be similar in size to Freitas' microbivore, and ideally would work together with it in the body and potentially artificial T lymphocytes too to quell any infection before symptoms have even arisen.

Discussion

Our idea is in essence an artificial B lymphocyte. Whereas the human body's B lymphocytes are each specific to one particular antigen, our mechanical lymphocyte will be able to produce antibodies complementary in shape to all antigens. This is what makes it unique.

The size and structure of the lymphocyte will be similar to Robert Freitas' [1] 'Microbivore', which is essentially an artificial phagocyte constructed from 610 billion arranged atoms. Although it would seem impossible to manufacture enough artificial lymphocytes to have an effect in the human body considering each one consists of so many atoms, an important part of nanotechnology is that of self replication; that is molecules or indeed robots that assemble themselves or each other in a 'bottom up' fashion according to the chemical properties of the nanoparticles involved.

For the lymphocyte to work, it will need to contain some form of artificial memory so it knows which antigens are self, and which are foreign and need to have antibodies produced against them. In theory, the process of our lymphocyte should be as follows: The lymphocyte collides with an antigen which has a shape it does not recognise. The lymphocyte acknowledges that this antigen is foreign. It then produces antibodies with a complementary shape to the antigen and releases them into the bloodstream. At the same time, it sends an electromagnetic signal to other artificial lymphocytes in the body which can then also produce antibodies.

The first major question that arises is how can they produce antibodies? Well there are two methods we have considered. The first is actually constructing antibodies from plastic. [2] An American research team actually did this and tested them in mice and found they were successful. These plastic antibodies are made by 'molecular imprinting', a process which uses melittin mixed with a monomer solution, causing a chemical reaction to occur which makes the solution solidify. The melittin is removed, leaving solid plastic and fully functioning antibodies.

The second method of constructing these antibodies is artificially joining a sequence of amino acids to form a protein which will in turn form into the correct antibody. [3]. Although this method is not developed in such a way that it enables us to produce antibodies to any antigen, it has been useful for producing some antibodies, for example one that binds to a protein linked to aging, and could in the future provide a reliable method of mass producing antibodies.

A lymphocyte which can produce antibodies to any foreign antigen would have amazing potential in the body. It's primary use would be speeding up the immune response, as time does not have to be taken to find the correct lymphocyte each time the body is infected. Ailments such as the common cold and influenza would not have time to develop and produce symptoms, as well as many more serious infections which would also be brought under control quickly. There are multiple other uses a lymphocyte like this could serve; for example it could also be used to destroy cancerous tumours. [4] This could be achieved by attaching gold nanoparticles to the antibodies it produces, and then if it collides with a cancerous tumour it will send out antibodies with the gold nanoparticles attached, and these will in turn bind with the tumour antigens. Once the antibody-antigen complex is formed, we can fire a near infrared laser at the site of the tumour which will cause the gold nanoparticles on the antibodies to heat up and consequently destroy surrounding tissues, namely the tumour.

If it is too complicated a process to use such an artificial lymphocyte inside the body in large numbers, then they could also be used outside the body in much smaller numbers for purposes such as producing monoclonal antibodies. Because they are artificial they will make this process easier than it would be if B lymphocytes are used, as these must first be combined with tumour cells so they divide outside the body. An artificial lymphocyte would not need to divide outside the body and could just produce the antibodies needed when stimulated by a particular antigen, or maybe even when programmed to do so without even needing stimulation.

Other uses of the lymphocyte could be in detection of substances. A sample of blood or urine or other substance is placed in a dish with a number of artificial lymphocytes. If the antibodies the lymphocyte produces have a particular enzyme attached, then when the lymphocyte is stimulated to produce antibodies by an antigen, the antibodies will bind with the antigens and form an antibody-antigen complex. It will of course have to have been programmed to ignore antigens on materials we aren't looking for. After rinsing the surface, a substrate is poured over and will change colour if the original antigen we were searching for is present. This method could be used in drug detection, pregnancy tests etc. The advantage this method has over the current method involving monoclonal antibodies is that in this method the antibodies do not need to be created first, the test sample can simply be mixed with some artificial lymphocytes.

Numerous ethical arguments also surround this area, particularly when it comes to enhancement versus therapy. In some ways, the utilisation of artificial lymphocytes in an already functional immune system could be seen as transhumanism, and simply as a way to better ourselves when it is not needed, particularly when there are much more serious conditions that the use of artificial lymphocytes would not affect. However, if they were used in patients with a dysfunctional immune system, then this would simply be therapy rather than a needless attempt to give ourselves mechanical immune systems.

Another problem with nanobots in general is this idea of self replication, building themselves or others in a bottom up fashion molecule by molecule. It has been speculated [5] that self replicating nanomachines could multiply out of control in a ‘grey goo’ scenario, casing vast swarms of replicating nanobots which cannot be brought under control. Other aspects include the theoretical ‘nanoterrorism’, and the use of nanobots as data collection devices which is of course a massive invasion of privacy [6]. Even if the lymphocytes are constructed and not originally intended to harvest information, or only medically relevant information about a patient, it would not take much for them to be adapted to be used as microscopic spying devices.

The actual development of the lymphocytes for human use will be incredibly difficult. They will need to be tested in so many ways to ensure they are safe for use with different people. First should they be tested on animals, and if they show a positive effect, then the lymphocytes should be tested on around 50 healthy human volunteers. Again if no adverse effects occur, then a larger group of volunteers should be tested, this time testing for the lymphocytes effectiveness rather than it’s compatibility within the body. If it is found to be safe and functions in the body, then it should be tested on a much larger group, around 5000 patients, to test it’s effectiveness in a diverse and varied population. Finally if they are approved for use, they should be continually monitored over the following years to confirm information concerning the lymphocytes risks, benefits and optimal usage.

Conclusion

To conclude, these multiple-antigen-making 'B' cells, if developed, could prove to be extremely beneficial to (nano)medicine and healthcare as they could improve the responsiveness of the immune system to potential life threatening diseases; they could also be linked to the treatment of cancerous tumours, and detection of various substances. There are also a few problems regarding the development of these variations of phagocytes. The first being that the body may launch an immune response against the artificial lymphocyte, but this can be overcome by using monoclonal antibodies to knock out the specific T and B lymphocytes which would be complementary to it’s shape. The second is that phagocytes may try and digest it, but this can be solved by use of a chemorepellent which should cause phagocytes to move away from it. Another big problem is that if somebody with artificial lymphocytes in their blood gets a transplant, the artificial lymphocytes will probably collide with the transplanted organ, recognise it as non self and produce antibodies against it. It would be too difficult to catch and reprogram the lymphocytes once they are in the blood stream, so they would have to be linked wirelessly to one computer which can be reprogrammed as necessary to alter their behaviour towards certain antigens. In the body, T and B lymphocytes work as a team to quell an infection. On their own, it has to be said that these artificial B lymphocytes would not have much effect at all for some infections. The cell mediated response controlled by T lymphocytes would still be slow, as the body needs to find the specific T lymphocyte for the invading pathogen’s antigen. Solutions to this could involve combining it with an artificial T lymphocyte, or using a kind of Microbivore [1].

This theory is based upon, primarily, the use of microbivores to destroy pathogens in the blood using the 'digest and discharge' mechanism. The microbivores are complex and problematic enough to develop, but the artificial phagocytes will surely provide a more challenging and demanding task. Therefore the funds needed for the research to take place are a major obstacle in its development-public awareness is essential in gathering these funds but if enough of these are generated, then the number of deaths from the various diseases that affect the immune system in general could be significantly reduced. As with many technological advances in medicine, this progression will also have various ethical issues and concerns. Some believe that it is unnatural to interfere with God's work, that facing diseases throughout life is a natural process that everyone should accept and leave alone, unaltered. However one can also argue that this research and in effect treatment is being carried out to improve the standard of living of God's work and to try to discard diseases, disorders, and ailments. In the process of the development of these mechanical phagocytes, several tests will need to be carried out including those on animals. These in vivo tests will enable researchers to fully study the effects of these nanorobots so that full benefit can be gained from them in the future.

[1] Microbivores: Artificial mechanical phagocytes using digest and discharge protocol www.rfreitas.com/nano/microbivores.htm

[2]Artificial antibodies made from plastic shown to work in living animals www.nanowerk.com/spotlight/spotid=16668.php

[3]Artificial antibodies hold biomedical promise www.sciencedaily.com/releases/2010/05/100519173100.htm

[4]Nanoshell http://en.wikipedia.org/wiki/Nanoshells

[5]Grey goo http://en.wikipedia.org/wiki/Grey_goo

[6]Thinktank predicts nanotechnology backlash www.guardian.co.uk/education/2003/feb/13/highereducation.uk