Nanomedicine
Science that is changing our lives

29.04.13 | The Guardian | How nanotechnology can improve our health | guardian.co.uk/nanopinion

Nanomedicines are revolutionising healthcare – they could end the need for surgery and chemotherapy and ultimately work as medical ‘nanorobots’ in the body. Holly Cave reports

Good things come in small packages, or so they say. But there’s more – things so tiny that they are almost impossible to imagine. Anaesthetists just a millimetre in size could become a vital weapon in our arsenal to combat a disease. And yet we’re rapidly learning more about how to create and manipulate these tiny objects to improve diagnosis, targeting and treatment of diseases.

There’s no doubt that we need improvements to treatments for a wide variety of diseases, ranging from cancer to tuberculosis, says Vicki Stone, director of NanoSafety at Heriot-Watt University. “Nano-medicines offer lots of exciting opportunities to improve diagnosis, targeting and treatment of these diseases.”

Sometimes, however, molecular engineers just like to show off. In 2013, IBM created the smallest ever three-dimensional map of Earth, featuring a replica of the Matterhorn measuring just 25 nanometres high.

Part of everyday life
Nanotechnology is already a reality in many areas of our lives – from the food we eat to the cosmetics we rub into our skin and, while development is slower, medicine is no exception. There are approved nanomedicines that treat certain types of cancer, high cholesterol, fungal infections, hepatitis and more. Nanoparticles and nanomedicines – and even, perhaps, even nanorobots – could be used not just for treatment and drug delivery, but for vaccinations, imaging the body,spotting infections, andengineering new tissues.

We could tackle disease on the same scale at which it occurs, says chemist and Nobel laureate Richard Smalley: “Human health has always been determined on the nanometer scale; this is where the structure and properties of the machines of life work in every one of the cells in every living thing. The practical impact of nanoscience on human health will be huge.”

Take cancer, which the vast majority of nanomedicines in development are designed to treat. Almost two decades ago, the chemotherapy medication Doxil was approved for treating Kaposi’s sarcoma – a rare cancer often found in people with AIDS – and it is now used to treat some other cancers. Doxil uses nanotechnology knowledge to carry the drug doxorubicin to the cancer cell,encapsulating it inside globules of fat (liposomes) about 100 nanometres wide. This nanoformulation, and others like it in development, may not only better target the drug to the tumour, but could reduce unpleasant and destructive side effects such as bone marrow breakdown and damage to heart muscle.

Conventional methods of cancer diagnosis - typically biopsy and surgery - are invasive and often come too late, while treatment with chemotherapy is a scattergun approach – dosing the whole body with toxic chemicals without directly targeting the tumour. Nanoparticles have the potential to change this by offering earlier, non-invasive diagnosis and more targeted treatments that avoid side-effects. Their size helps. Nanoparticles can be selected by size and fine-tuned to slip easily into the unusually leaky blood vessels of tumours. A peculiar effect they have - known as the enhanced permeability and retention (EPR) effect - is to then stay there, accumulating where they are most needed.

Start from scratch
But it’s not just about being tiny. Nanomedicines can be engineered from scratch, piecing together nanoparticles to create multifunctional complexes. This means that nanomedicines would be tailored to target a certain part of the body. They could be made magnetic or responsive to light so that they could be activated by a remote trigger. They could even carry both drugs and tags which would show up in scans – offering imaging and treatment from a single injection.

The ultimate aim of all medicine is to make it smarter and more responsive to real-time changes in the human body. “Doctors still chiefly rely on the body’s ability to repair itself,” says Roberto Freitas Jr, senior research fellow at the Institute for Molecular Manufacturing in California. “But in the future we’ll develop tools for working at the molecular level; precisely and with three-dimensional control. With these tools we’ll be able to place the components parts of human cells exactly where they should be, and restructure them as they should be, to ensure an almost ideal state.”

Nanomedicines are blurring the lines between drugs and devices. It may only be a matter of time before we start calling nanomedicines “smart”, in recognising potential of these potential to respond in real-time to changes in the body, acting like tiny computer to fix problems and possibly even manufacture drugs where they are needed. Some researchers, including Freitas, believe that as they hone these skills of manufacturing precise, nano-structured right down to the level of individual atoms, it will become possible to create molecular machines – medical nanorobots the size of a virus or bacteria. Flip to the back page of this supplement to get a glimpse into Freitas’ vision for medical nanorobots. Could this be the future of medicine?
INTERCEPTING INFECTIONS

Easily you might think of a swimming kit for replacing
small-dose antibiotics. They are not envisaged to be as
large-dose antibiotics. They are not envisaged to be as
difficult to use as large-dose antibiotics. They are not envisaged to be as
difficult to use as large-dose antibiotics. They are not envisaged to be as
difficult to use as large-dose antibiotics. They are not envisaged to be as
difficult to use as large-dose antibiotics. They are not envisaged to be as

DELIVERING DRUGS

might be easier to inject or to delivery, but the
facility is not envisaged to be as small-dose antibiotics. They are not envisaged to be as
difficult to use as large-dose antibiotics. They are not envisaged to be as
difficult to use as large-dose antibiotics. They are not envisaged to be as

CONTROLLING CELLS

might be easier to inject or to delivery, but the
facility is not envisaged to be as small-dose antibiotics. They are not envisaged to be as
difficult to use as large-dose antibiotics. They are not envisaged to be as

DISAPPEARING DEVICES

might be easier to inject or to delivery, but the
facility is not envisaged to be as small-dose antibiotics. They are not envisaged to be as
difficult to use as large-dose antibiotics. They are not envisaged to be as

VISUALISING VIRUSES

might be easier to inject or to delivery, but the
facility is not envisaged to be as small-dose antibiotics. They are not envisaged to be as
difficult to use as large-dose antibiotics. They are not envisaged to be as
Medical intervention usually involves risk. You only have to look on the leaflet listing potential side-effects inside any pill packet. For all treatments, the big decision to be made is whether the benefits (even outweigh the risks (side-effects, toxicity). We’re relatively well versed in predicting and testing how drugs behave in the body, but nanomedicines come with an added level of complexity.

Why? Because the ways in which nanomedicines enter cells and spread around the body are different to drugs, and their tiny size means detection is tricky. Medical researchers are making use of the ability of nanomedicines to permeate blood vessel walls to improve drug delivery to a specific target.

However, the immune system, which is particularly adept at recognising and taking up bacteria and viruses - also accumulates large amounts of nanomedicines particles. This leads either to the death of immune cells or their activation (resulting in inflammation), and the desired target is unlikely to receive enough of the nanomedicine for it to be effective. Thankfully, scientists are getting better at manipulating the behaviour of nanomedicines in the body in order to overcome these problems.

**Inflammation concerns**

Nanoparticles can have properties which are relatively different to larger particles of the same substance. A common one - higher surface reactivity - can be hugely beneficial when trying to increase the effectiveness of a treatment - to reduce toxicity, cost and the dose required. But too much surface reactivity may come at a price. As mentioned above, the cells of the immune system can only gather up foreign particles, leading to inflammation. If brief and controlled in size, inflammation is important for removing foreign particles from the body - indeed, without it the body could not defend itself against infection or pollutant particles. But many diseases are driven by inflammation, including asthma, cardiovascular disease, diabetes and cancer. Additional inflammation in such patients could make their symptoms even worse.

Since these groups of patients are key candidates for treatment with nanomedicines, it will be really important to figure out how potential treatments might exacerbate their existing condition as well as treat it. Getting the right balance will be essential.

**The licensing of nanomedicines, especially those that contain metals such as iron, is critical - and will need a different approach than conventional medicines**

For all new treatments, potential side-effects usually involve risk - you only have to look on the leaflet listing potential side-effects inside any pill packet. For all treatments, the big decision to be made is whether the benefits (even outweigh the risks (side-effects, toxicity). We’re relatively well versed in predicting and testing how drugs behave in the body, but nanomedicines come with an added level of complexity.

Why? Because the ways in which nanomedicines enter cells and spread around the body are different to drugs, and their tiny size means detection is tricky. Medical researchers are making use of the ability of nanomedicines to permeate blood vessel walls to improve drug delivery to a specific target.

However, the immune system, which is particularly adept at recognising and taking up bacteria and viruses - also accumulates large amounts of nanomedicines particles. This leads either to the death of immune cells or their activation (resulting in inflammation), and the desired target is unlikely to receive enough of the nanomedicine for it to be effective. Thankfully, scientists are getting better at manipulating the behaviour of nanomedicines in the body in order to overcome these problems.

**Inflammation concerns**

Nanoparticles can have properties which are relatively different to larger particles of the same substance. A common one - higher surface reactivity - can be hugely beneficial when trying to increase the effectiveness of a treatment - to reduce toxicity, cost and the dose required. But too much surface reactivity may come at a price. As mentioned above, the cells of the immune system can only gather up foreign particles, leading to inflammation. If brief and controlled in size, inflammation is important for removing foreign particles from the body - indeed, without it the body could not defend itself against infection or pollutant particles. But many diseases are driven by inflammation, including asthma, cardiovascular disease, diabetes and cancer. Additional inflammation in such patients could make their symptoms even worse.

Since these groups of patients are key candidates for treatment with nanomedicines, it will be really important to figure out how potential treatments might exacerbate their existing condition as well as treat it. Getting the right balance will be essential.

**Nanorobots**

Nanorobots are machines as they can to antibiotics. When a nanorobot, for example, could act as a “soft” nanomedicine that is easily replaced with non-defective base-pairs. They may be composed of a strong, diamond-like material. A nanorobot will need motors to make things move, and manipulate arms or mechanical legs. It will need a power supply, sensors to guide it, and an onboard computer to control its behaviour. But unlike a regular robot, a nanorobot will be smaller than our red blood cells and able to squeeze through our body’s narrowest capillaries.

**A vision of the future – nanorobots get to grips with red and white (in yellow) blood cells**

Researcher at the Welsh School of Pharmacy at Cardiff University are investigating using nanoscale technology to tackle breast cancer cells.

In contrast, imaging contrast agents (used predominantly for diagnosis), which include metals such as iron, are likely to be more biocompatible to the body, requiring greater consideration of their impacts on inflammation as well as their long-term effects on patients.

There’s no doubt we need new medicines, including nanomedicines – for a range of diseases. But considerations of their risks will become greater and will need a change of approach to that used for traditional medicines.

Vicki Stone and Helinor Johnston, director and deputy director of nano-safety at Heriot-Watt University