Shining a light on nanoparticle therapy

Creative new approaches to cancer therapy deserve to be publicly celebrated. But steering the right course between simplistic talk of 'wonder drugs' and baffling readers with unnecessary scientific detail can be tricky. **Mark Henderson**, of the UK national daily *The Times*, won a Best Cancer Reporter Award for his story about a novel nanoparticle therapy, which is reprinted below.

A nanotechnology therapy that targets cancer with a 'stealth smart bomb' is to begin patient trials next year in the first clinical test of a pioneering approach to medicine.

The nanoparticle, which targets tumour cells while evading the body's immune system, promises to deliver larger and more effective doses of drugs to cancers, while simultaneously sparing patients many of the distressing side-effects of chemotherapy.

Animal studies have indicated that the treatment can shrink tumours "essentially to zero", while being better tolerated than conventional cancer treatments. Final toxicology studies are about to begin.

A trial involving about 25 cancer patients is scheduled to start within a year. If successful, it could lead to a licensed drug within five years.

Although the therapy was originally designed for prostate cancer, it is expected to be effective against other solid tumours, such as forms of breast, lung and brain cancer. Patients with some of these cancers, as well as prostate cancer, may be included in the first trial.

The technology, developed by BIND Biosciences, a company based in Cambridge, Massachusetts, should also be suitable for delivering drugs for treating other conditions, as well as for the chemotherapy agents that it has been set up to carry.

"This should be the first targeted nanoparticle delivering a chemotherapeutic to enter clinical trials," Jeff Hrkach, the company's vice-president of pharmaceutical sciences, said. "We're then looking to develop this as a broad platform that could also be used to treat cardiovascular disease, inflammation, even infectious disease."

The nanoparticle, known as BIND 014, is designed to solve three of the major challenges in drug delivery: how to ensure therapeutic molecules get to the right place in the body, how to release them slowly over several days, and how to keep the body's immune system from recognising them as foreign and destroying them.

It does this by packing drugs inside a 'special delivery parcel' developed by Robert Langer, of the Massachusetts Institute of Technology, and Omid Farokhzad, of Harvard University, who founded BIND Biosciences.

Mark Henderson

THE TIMES

The science behind the therapy. Well-written articles explaining potentially important developments in treating cancer promote public understanding of the disease and help build confidence in, and support for, the research effort


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How it works

This nanoparticle's diameter is 1000 times smaller than that of a human hair, measuring about 100 nanometres – or one ten-millionth of a metre – across. It has four elements, the first of which is its payload, a common chemotherapy drug called docetaxel or Taxotere.

The docetaxel molecules are enclosed in a matrix made of a biodegradable polymer known as polylactic acid, which breaks down slowly over several days so that the drug is released gradually. This means that a single injection of nanoparticles can have a long-lasting effect.

This drug-filled 'warhead' is then covered with a 'stealth coating' of polyethylene glycol, which helps the particle to hide so that it is not attacked by elements of the body's immune system such as antibodies and macrophage cells. Normally, nanoparticles for drug delivery risk being recognised by the immune system and destroyed.

"Regular nanoparticles struggle to get through to tumours," Professor Langer said. "They get eaten by macrophages. By containing the drug within this molecule, we can avoid the macrophages."

The final element of the particle is its smart targeting system, in the form of special enzymes attached to the outer coating known as targeting ligands. These are designed to bind to a molecule found on prostate cancer cells called prostate-specific membrane antigen (PSMA), so that the particles accumulate at the site of tumours before releasing their drugs.

"It's an anchor, rather than a homing beacon," Dr Hrkach said. "If we do things right and get it to the tumour, when the particles get there they stay there.

"What's different about this delivery system is that we believe we can very explicitly target the disease site, while also protecting the nanoparticle from the body's immune system. You can get a high concentration at the site of the tumour and a lower concentration everywhere else.

"By virtue of doing that you're not exposing the body to the side-effects of chemotherapy so much, while at the same time getting larger doses of drug to the tumour."

It promises to deliver larger doses of drugs to cancers, while sparing patients many of the side-effects

Professor Langer said, "We've created a nanoparticle decorated with two molecules, one of which helps it to dodge the immune system, while the other helps it to target cancer cells."

The drug has been successfully tested against human prostate tumours grown under the skin of mice, in studies that have shown both that the drug accumulates around tumours and reduces them in size. "It's shrunk tumours in animals essentially to zero," Professor Langer said.

As the PMSA molecule targeted by the nanoparticle is also found in the blood vessels grown by many other solid tumours, it should be suitable for treating other cancers.

"We think that going after that same target with that same drug, we can not only go after prostate cancer but a considerably long list of other solid tumours," Dr Hrkach said. "The plan is to start clinical trials in the third quarter of next year. We're now transferring our efforts to manufacturing enough material for a clinical study."

The clinical trials are now scheduled to start by the end of 2010
This article was first published in *The Times* on 5 November 2009 under the title 'New attack on cancer with nano-weapon', and is reprinted here with permission

BATTLE AGAINST A COMMON KILLER

- Prostate cancer is the most common cancer among men in Britain; it was diagnosed in 35,000 men in 2006
- About 10,200 men die of the disease each year
- Seventy per cent of men with newly diagnosed prostate cancer survive for at least five years
- About 60 per cent of cases occur in men over the age of 70
- It is usually diagnosed by digital rectal examination and/or a test for prostate-specific antigen, a protein, followed by a biopsy
- Treatments include surgery, chemotherapy, radiotherapy and hormone therapy
- Scientists have identified about two dozen genes that affect the risk of prostate cancer
- Sufferers have included François Mitterrand, the former President of France; Rudy Giuliani, the former Mayor of New York; Dennis Hopper, the actor; Frank Zappa, the singer; John Kerry, the former US presidential candidate; Linus Pauling, the scientist; and Nelson Mandela

Sources: Cancer Research UK, *Times* database