Gold nanoparticles: A new delivery for cancer drugs

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(Phys.org) —The protein tumor necrosis factor-alpha (TNF-alpha) is a powerful weapon in the arsenal to control cancer. Unfortunately, as is the case with many potent cancer therapies, the use of TNF-alpha as an anti-cancer therapy has been severely limited. "It was so toxic that it caused death," and researchers gave up on it, explains Scott McNeil, director of the Nanotechnology Characterization Lab at the Frederick National Laboratory for Cancer Research.

That was back in the 1990s. Today, TNF-alpha is a prime example of how to safely and effectively deliver toxic substances to cancer cells through the use of nanotechnology.

McNeil's lab, part of the federally funded research and development center operated by SAIC-Frederick for the National Cancer Institute, worked with a drug company to reformulate TNF-alpha by coupling it with gold nanoparticles. Using the nanotechnology-enhanced protein, it appears possible to safely inject up to three times the amount that had been lethal with previous versions. The modified drug has been through a Phase 1 clinical trial and is entering Phase 2.

In McNeil's lab, and for other scientists using nanotechnology for drug delivery, stories like this one are increasingly common. Researchers are looking to accelerate the development of potential nanotechnology drugs for cancer by exploring ways to reduce side effects and make treatments hit their targets more effectively. This can mean using nanotechnology to reformulate drugs that may have failed in previous clinical trials. In

some cases, by attaching a nanoparticle to an existing drug, researchers may not only be able to lower its toxicity, but they may also see significant life expectancy gains for patients.

Many cancer drugs are approved based on how long they delay the progression of disease. Some drugs on the market "only improve life expectancy by maybe five weeks," says McNeil. He sees nanomedicine as a potential game-changer for cancer drugs in the future.

McNeil, both a chemist and biologist, has spent the majority of his career working in nanotechnology, but when he was asked to apply his expertise to find better drugs for cancer, he was skeptical. "My professional career was mostly military," says the former Army officer. "I was using nanotech for military applications at SAIC, using quantum dots to see if you scatter things, where they land. I got a call out of the blue in December of 2003 and the message was, 'We want to use nanotech for cancer applications.' I thought, 'What are they thinking? You are going to put a cadmium quantum dot in a human? There is no way!' I discounted it at first and I actually ignored the emails, hoping it would go away."

But it did not go away. In fact, much has changed in the last 10 years. Now, nanopharmaceuticals are beginning to demonstrate their capacity to place the drugs directly in the tumor, where they will do the most good, rather than let them roam freely in the body. A drug is attached to a nanoparticle, which is often a tiny little sphere. To put it in perspective, a nanometer is one billionth of a meter; the width of a single strand of hair is about 10,000 nanometers. The nanoparticle is small enough to flow through blood vessels and into a tumor, where the particle dissociates, and the drug is released. In the end, the goal of nanomedicine is that the only part of the body affected by the drug is the tumor, the area of need.

McNeil's Nanotechnology Characterization Lab was founded in 2004 in collaboration with the Food and Drug Administration and the National Institute of Standards and Technology. There is one thing the lab does not do: develop nanotechnology drugs. Instead, researchers there—ranging in expertise from cancer biology and toxicology to chemistry, immunology, and physics—help investigators from around the world create the best drugs possible. "We help investigators get from proof of concept, where they are generating a few tens of milligrams of material and get into clinical trials, where they are going to need kilograms of materials," say McNeil. "That translational research, as we call it, is absolutely germane to getting into clinical trials."

The majority of scientists who apply for assistance from the NCL are seeking FDA approval for their nanotech drugs but they don't have the resources to optimize their formula. The NCL can help. "We help them understand what is involved with their particle because they don't have the tools that we have to be able to characterize," says McNeil. "They may have a nice picture or cartoon of it but until they see our electron micrographs, they don't know what it looks like."

The Nanotechnology Characterization Lab serves two purposes. After a molecule has been through the NCL's assay cascade which consists of a set of tests that evaluate the preclinical toxicology, pharmacology, and efficacy of nanoparticles, the NCL is able to offer an evaluation. "The investigator is going to need $40 million dollars to get into Phase 2 trials. Investigators need to justify the investment. We help them generate data they need to further their work and then we serve as a third-party evaluation." That is crucial, McNeil says, for an investigator seeking funding. "A venture capital company can come to us and say, 'Well, what do you really think of this? Let's see your data, and explain it and defend it.' We, obviously, cannot endorse it but we can discuss the data in the context of what they are trying to do. That really holds a lot of weight."

Consider the example of Abraxane (paclitaxel), which was approved for use by the FDA in 2005. Abraxane, a variably toxic but widely prescribed cancer drug, has been enhanced by attaching it to a nanoparticle, thereby creating a new, targeted treatment. "Because of the size and the binding to a different receptor, that drug now has decreased toxicity compared to the former drug. For the nanoparticle-Abraxane conjugate toxicity is very marginal, at least for immunotoxicity and hypersensitivity," says McNeil.

Since 2005, the Nanotechnology Characterization Lab has characterized nearly 300 different particles. Six of them are in clinical trials. "Depending upon what community you are from, either that is a terrific ratio or that is a poor ratio," explains McNeil. "We view it as a super terrific ratio. A pharmaceutical company can make hundreds of thousands of different drugs and only about one out of 100,000 gets into clinical trials."

Nanotechnology's place in the cancer treatment arsenal also appears secure. A new report from Infiniti Research Limited, a marketing research firm specializing in pharmaceuticals and health care, forecasts that the nanotechnology drug delivery market is on track to double within the next five years.

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