

Technology

AN MIT ENTERPRISE

Review

Speeding Up Diagnosis

A new nanoparticle-based tool could provide a faster, easier way to identify infections.

A STARTUP BASED IN CAMBRIDGE, MA, is commercializing a new kind of rapid diagnostic technology that relies on magnetic nanoparticles and a technique similar to magnetic resonance imaging (MRI). The nanoparticles can be designed to signal the presence of specific viruses and bacteria, particular strands of DNA and proteins including those found on cancer cells, and other molecules such as glucose. The technique can use blood, spit, or any other samples with no preparation. The researchers hope the tool will help doctors identify treatments faster and allow for better monitoring of cancer treatments.

The company, T2 Biosystems, expects to begin marketing diagnostics for infectious diseases in two years, and it's developing implantable sensors and handheld readers for monitoring diseases such as diabetes and cancer. Prominent researchers from MIT, Harvard, and Massachusetts General Hospital founded the company. Tyler Jacks, director of the MIT Center for Cancer Research and a cofounder of T2, says that the company is developing "more rapid, accurate, portable, and cheaper diagnostics."

The new diagnostic is based on iron-oxide nanoparticles

that generate a strong magnetic signal when exposed to a magnetic field. Each nanoparticle resembles a spiky ball and is coated with molecules like antibodies or single strands of DNA that bind to a specific target. The researchers can design nanoparticles to target just about any molecule. In the absence of the target, the nanoparticles float freely in solution. When the nanoparticles are put in a solution containing the target molecule, they aggregate,

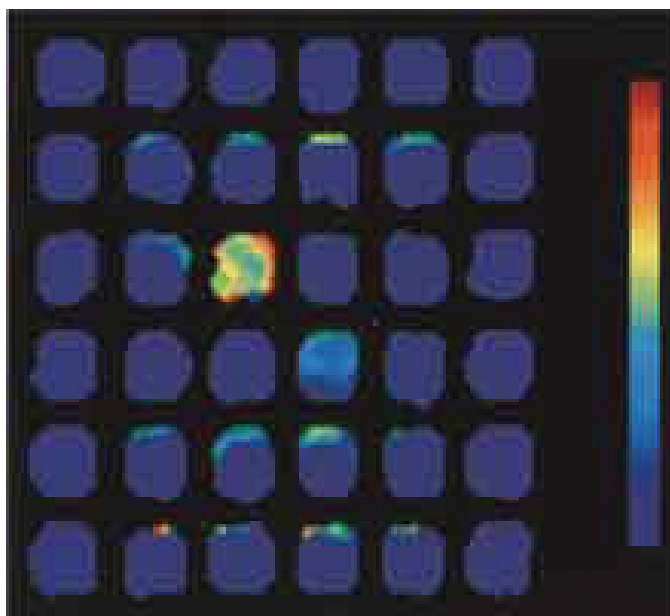
each nanoparticle binding to multiple target molecules and creating tangled clumps. The nanoparticles make a different kind of magnetic signal when clumped. This signal can be read in an MRI machine or in a relaxometer, a desktop-sized device.

The nanoparticles were developed by company cofounders Ralph Weissleder, director of the Center for Molecular Imaging Research at Harvard, and Lee Josephson, associate professor of radiology at Harvard

Medical School. Josephson says that the key advantage to T2 Biosystems' diagnostic is that it doesn't rely on optical signals. Traditional biochemical diagnostic techniques all require extensive sample processing because light doesn't travel well through the body or through opaque liquids like blood, which must therefore be purified. The signal created by the magnetic nanoparticles does.

No preparation is necessary for T2 Biosystems' tests. A sample is simply combined with the nanoparticles and put in the relaxometer to take a reading. (Relaxometers are commercially available and could be incorporated into hospital laboratories.)

Josephson expects the nanoparticle diagnostic to have a "very large advantage over the state of the art" in the area of infectious disease. He and



COURTESY OF RALPH WEISSELER, HARVARD CENTER FOR MOLECULAR IMAGING RESEARCH

Detecting disease: A new diagnostic system uses magnetic nanoparticles to detect biomarkers, bacteria, and viruses. The wells of liquid in this MRI image contain nanoparticles targeted to particular strands of RNA. The greenish well shows a signal resulting from the detection of a brain-cancer cell. The additional wells contain sensing nanoparticles and other cancer cells.

Weissleder have used the nanoparticles to identify, among other pathogens, common viruses including herpes simplex and adenoviruses, as well as the bacteria that cause tuberculosis. Identifying the cause of a patient's infection using traditional means, such as culturing bacteria, can require a great deal of time, says Josephson. Genomic techniques for identifying viruses and bacterial strains, such as PCR, also require sample preparation. The sooner the pathogen is identified, the sooner the patient can be given the right antibiotic or isolated and prevented from infecting other people. This is especially important in the case of a viral outbreak like SARS or influenza, or when a patient harboring drug-resistant bacteria enters a hospital.

Weissleder is currently testing the nanoparticle sensors using a research tool called a micro-NMR. Ultimately, he and

the other T2 Biosystems researchers hope to develop a portable, commercial, handheld system that could be used at a patient's bedside or in an ambulance. The system works the same way as MRI but with much smaller components, says David Lee, another of the company's cofounders and the director of engineering at Analog Devices. "Instead of having coils for [radio-frequency] detection and magnets on the centimeter scale, the idea is to build them on the micrometer scale," he says. "The electronics in a cell phone are not too different from what you'd want in a detector." Lee says that making such a small detector is a matter of design, not basic research.

Developing a smaller detecting system is key to the company's long-term goal of enlisting the nanoparticles to monitor cancer and chronic diseases like diabetes using implantable devices, says Jacks. Michael

Cima, also a T2 Biosystems cofounder, is developing small silicone implants that contain the magnetic nanoparticles and are permeable to biomarkers circulating in the body. Such an implant could be inserted into a tumor during a needle biopsy.

A cancer patient's progress is currently monitored with infrequent MRI scans to determine if tumors are shrinking. With an implant, clinicians could take readings frequently and easily using a handheld device that could provide information including how metabolically active a tumor is and whether the drugs are reaching it. After a tumor seems to have gone away, the implant could be monitored for molecular signs that it might be recurring. Or a diabetes patient with an implant could use a handheld device to monitor her glucose levels without having to prick a finger.

Katherine Bourzac



286 Cardinal Medeiros Avenue
Cambridge, MA 02141
617-661-8282
www.T2biosystems.com