Bacterial Infections Diagnosed in Hours With New DNA Test

Ricki Lewis, PhD | May 10, 2013

A nanoparticle DNA hybridization device described in separate articles published online May 5 in *Nature Nanotechnology* and in the April issue of *Nature Communications* identifies bacterial pathogens in less than 2.5 hours.

Millions of people die from bacterial infections annually, despite the availability of treatments, largely because of delayed diagnosis. Traditional microbiological techniques can take days to provide results, and although polymerase chain reaction (PCR)-based techniques are faster, they are not optimized for resource-limited settings.

Ralph Weissleder, MD, and colleagues at Massachusetts General Hospital in Boston, have pioneered 2 related approaches for rapidly identifying bacteria. Both techniques rely on DNA hybridization and detection with a miniaturized nuclear magnetic resonance (NMR) device the size of a microscope slide.

In the article published in *Nature Nanotechnology*, Hyun Jung Chung, PhD, from the Center for Systems Biology, Massachusetts General Hospital, and colleagues describe their generic platform for rapid identification of bacterial pathogens, using 16S rRNA sequences, including sequences both common to many species and specific to particular species.

Using the device, the researchers were able to correctly identify 13 bacterial pathogens in clinical specimens within 2 hours, with sensitivity reaching a single bacterium.

On this 2.5- by 7.5-cm cartridge, DNA extracted from sputum samples is amplified in the chambers on the left. TB-specific sequences are magnetically labeled in the microfluidic mixing channels in the center and detected by passage through the micro-NMR coil on the right. *Source: Center for Systems Biology, Massachusetts General Hospital*

Selected rRNAs are reverse-transcribed and amplified into single-stranded DNA molecules, to which 2 types of oligonucleotide probes bind: one on polystyrene beads and the other on magnetic nanoparticles (MNPs).

The binding of amplified bacterial DNA to the MNPs shortens the transverse relaxation rate, which the NMR device picks up. From 300,000 to 800,000 probes are found on each capture bead, and 16 to 29 probes are found on each MNP. Approximately 300,000 MNPs bind each capture bead.

The researchers tested the approach, using *Staphylococcus aureus*, and then tested for a dozen bacterial pathogens, including *Streptococcus*, *Enterococcus*, *Pseudomonas*, *Klebsiella*, and *Lactobacillus*, in clinical specimens. The assay took up to 2 hours, and "showed excellent accuracy, detecting all bacterial species identified by standard culture," the researchers write.

The technique also identified 2 species (*Citrobacter* and *Acinetobacter*) that conventional microbiology tests missed and that are resistant to cephalosporins. The researchers call for further investigation of the ability of the new technique to detect bacterial species that are not easily cultured.

In the article published in *Nature Communications*, Monty Liong, PhD, also from the Center for Systems Biology, Massachusetts General Hospital, and colleagues describe a related magnetic barcode assay to diagnose *Mycobacterium tuberculosis* infection in patient specimens within 2.5 hours. The test discriminated single nucleotide polymorphism differences in target genes, therefore making it possible to detect drug-resistant strains.

The barcode system was adapted from a technique created to detect cancer biomarkers. "Combined with portable systems, the magnetic barcode assay holds promise to become a sensitive, high-throughput and low-cost platform for point-of-care diagnostics," the researchers conclude.

"Chung and colleagues have reported the development of an elegant technology that helps us move closer to realizing the promise of time-critical infection diagnosis that could lead to a more rational use of antimicrobial therapy and better healthcare outcomes," Paul Dark, PhD, from the Academic Health Sciences Centre, University of Manchester, United Kingdom, told *Medscape Medical News*. "There remains, however, a pressing need to establish the clinical effectiveness and cost utility of these and other emerging diagnostic technologies to judge how best to improve patient care within available budgets."

Dr. Weissleder consults for T2 Biosystems. Dr. Dark and the other authors have disclosed no relevant financial relationships. Massachusetts General Hospital has applied for patents on the new technology.

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