New DNA Test Can Identify Bacterial Infections In Under 2.5 Hours

Researchers have developed a novel nanoparticle DNA hybridization device which can identify different species of bacteria in less than 2.5 hours.

The research was reported online May 5 in Nature Nanotechnology and in the April issue of Nature Communications.

Although antibiotics are widely available, many people die annually from sepsis and bacterial infections, which can be related, in some cases, to a delay in diagnosis. Standard available microbiological assays can take days to provide results. While polymerase chain reaction (PCR)-based techniques are more rapid, they are not widely available in smaller institutions.

As a standard practice in patients who are critically ill, medical providers place patients on so-called “broad spectrum antibiotics” in the initial phases of resuscitation to cover a wide array of potential pathogens that may be causing the infection. This is a practice that is widespread so as not to miss any potential pathogens. Having an assay which could provide more specific identification of the offending bacteria, might allow medical providers to select more appropriate antibiotics earlier in the course of their illness.

Researchers at Massachusetts General Hospital in Boston have developed two similar modalities for the rapid identification of bacteria. Both approaches are based on DNA hybridization and detection with a miniaturized nuclear magnetic resonance (NMR) device about the size of a microscope slide.

In the research published in Nature Nanotechnology, investigators developed a methodology for rapid identification of bacterial pathogens using 16S rRNA sequences as well as sequences common to many species and specific to particular species. In the research study, investigators were able to correctly
identify 13 bacterial pathogens in clinical specimens within 2 hours.

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

The NMR device is able to detect binding of amplified bacterial DNA to the MNPs which ultimately reflects a decrease in the transverse relaxation rate. Anywhere from 300,000 to 800,000 probes are found on each capture bead, and 16 to 29 probes are found on each MNP. Nearly 300,000 MNPs can then bind each capture bead.

Investigators evaluated and tested this methodology using *Staphylococcus aureus*, and then conducted additional tests for bacterial pathogens including *Enterococcus*, *Streptococcus*, *Klebsiella*, *Lactobacillus*, *Pseudomonas* in the specimens. The assay took up to 2 hours, and demonstrated high accuracy, detecting all bacterial species identified by standard culture.

The assay also identified two species (*Acinetobacter and Citrobacter*) that standard microbiology tests missed and which are resistant to cephalosporins.

In the article published in *Nature Communications*, investigators describe a similar magnetic “barcode assay” to diagnose *Mycobacterium tuberculosis* infection in patient specimens within 2.5 hours. The test was able to detect single nucleotide polymorphism differences in target genes, therefore making it possible to detect drug-resistant strains.

The barcode system evolved from a technique developed to detect cancer biomarkers. In addition to standard techniques, the magnetic barcode assay likely has the potential to become a sensitive, high performing and economical assay for reliable point-of-care evaluation.

This novel technology using nanoparticles will ideally allow medical providers to diagnose bacterial infections more expediently (or exclude a viral etiology) leading to more targeted antimicrobial therapy and potentially better outcomes such as lower mortality rates and decrease length of stay (LOS) in the hospital.

Further studies will be necessary to establish the efficacy and cost effectiveness of such novel technologies and whether they can lead to tangible gains in quality of care based on cost.

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