Making germs glow: New test helps save lives and cuts costs

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A clinical microbiologist examines microbe colonies grown on an agar culture plate. (Photo: Beatriz Verdugo/UANews)

(Medical Xpress) -- Replacing conventional laboratory tests with a new DNA sequence-based technology to identify pathogens causing bloodstream infections dramatically lowered mortality and health-care costs, a clinical study conducted by an interdisciplinary UA research team found.

Unlike conventional laboratory tests, a new technology called PNA-FISH is designed to rapidly identify bloodstream pathogens by their genetic code. Results are available within hours instead of days providing pharmacists and physicians with information they can use to rapidly customize antimicrobial treatment for patients with infections.

PNA-FISH is an abbreviation for “peptide nucleic acid fluorescence in situ hybridization.” Rapid reporting of PNA FISH results to pharmacists and physicians cut the mortality of ICU patients with enterococcus or streptococcus bloodstream infections by almost half and slashed mortality from yeast infections by 86 percent. In addition, the intervention resulted in healthcare cost reduction of almost $5 million per year.

The interdisciplinary research team recently presented its results at the 51st Interscience Conference on Antimicrobial Agents and Chemotherapy in Chicago.

"Our goal was to decrease mortality for patients with bloodstream infections, and we achieved that goal through a strong collaboration among research scientists at the UA's BIO5 Institute, clinical microbiology laboratory scientists at University of Arizona Medical Center, and an interdepartmental collaboration among the clinical laboratory, infectious disease pharmacy and physicians," said Donna Wolk, an associate professor at the UA's College of Medicine, who led the study. Wolk is division chief of clinical and molecular microbiology in the department of pathology at the UA.

Every year, more than 875,000 patients are diagnosed with bloodstream infections in the U.S., resulting in more than 90,000 deaths and significant costs to the health-care system.

According to Wolk, bloodstream infections can be difficult to treat because conventional diagnostic laboratory methods often require days to identify slow-growing bacteria and confirm which antimicrobials will work best. That lag-time forces physicians to prescribe broad-spectrum antibiotics until laboratory results can confirm the pathogen identity and antibiotic effectiveness patterns.

Overuse of antibiotics can lead to toxic side effects and disruption of the body's normal flora or beneficial bacteria, which can also lead to other infections.

The study assessed patients with positive blood cultures admitted to UA Medical Center-University Campus between August 2007 and March 2011. Outcomes and costs for 722 patients were analyzed, of which, 344 had PNA FISH performed. Board certified clinical microbiologists tested blood cultures and reported PNA FISH results to infectious disease pharmacists and physicians.

In conventional tests for bloodstream infections, clinical microbiologists typically take a blood sample from the patient, mix it with a liquid growth medium and incubate it to stimulate microbial growth.

Once the microbes present in the sample have multiplied to large numbers, some of the liquid is transferred to a petri dish filled with solid agar growth medium and placed into an incubator to allow the growth of distinct and recognizable microbe colonies.

"It's a bit like a gardener waiting to pick the flowers," Wolk explained.

"It takes about a day to cultivate the fluid and at least another day to see the individual bacteria colonies on the agar. Once we see them growing, we can pick one to perform a biochemical profile, which identifies the pathogen and the best antibiotics to use, but that process wastes precious time."

PNA-FISH, on the other hand, bypasses this process. It uses fluorescent molecules tagged to genetic sequences that match those in the microbe. When added to a dried drop of blood culture containing pathogens, sequences that find their match inside the microbe stick, while those that don't are washed away. The process is not unlike placing a key into a

lock – only the right key will fit.

Once the tagged genetic sequences link up, a clinical scientist views the slide under a special microscope that makes the fluorescent tags visible. The microbes' identity is confirmed by the color of their fluorescence.

"The tagged pathogens will glow, different colors for different microbes – it's like fireworks under our microscope," Wolk said, "and we feel a Fourth of July excitement because we know our laboratory is helping to save the lives of people in our community."

Wolk recognizes the importance of a university-based bench to bedside translational research approach to diagnosis of infections. With a vision that began in late 2006, she directs the BIO5's Infectious Disease Research Core Laboratory, or IDRC, where research scientists participate in clinical trials to verify the accuracy of new technology.

The IDRC works with bioindustry sponsors like AdvanDX, the manufacturer of PNA FISH, to obtain approval from the U.S. Food and Drug Administration to use the technology for patient care. Since its inception, IDRC has participated in more than 16 clinical trials in which research staff focus on developing faster and more precise diagnostic tests aimed at detecting and preventing infectious diseases and public health threats.

After a clinical trial, the next step in the translational pipeline is to assess which technology is most likely to benefit critically ill patients and move that technology from the research to the highly standardized and regulated hospital setting at UAMC. There, medically board-certified clinical laboratory scientists perform testing to quickly identify pathogens and relay information to pharmacists and physicians.

"The collaboration between the UA's pathology department and UA's

BIO5 Institute was essential for us to establish a national model of bench-to-bedside laboratory practices," Wolk added. "Our collective translational capabilities are very unique and provide a long-awaited missing link for translating molecular microbiology methods into clinical microbiology laboratories for improving patient care."

"At the IDRC, our motto is simple," she said: "'Advancing diagnostics, saving lives.' We are very proud of the contribution our team makes, helping to improve the quality and efficiency of health care in our community and across the globe."

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