Research Could Help Prevent Catheter Infections

(PRNewswire-USNewswire) Researchers at the University of Maryland's A. James Clark School of Engineering, backed by funding from the Robert W. Deutsch Foundation, are developing tools that promise powerful new ways to combat catheter-based and other infections without provoking bacterial resistance to antibiotics.

"Finding new ways to treat infections is a key area in which engineers can assist physicians," stated William Bentley, Robert E. Fischell Distinguished Professor and chair of the Clark School's Fischell Department of Bioengineering. "We anticipate that our Deutsch Foundation-funded infection research will one day give physicians new drugs, new drug development systems and new in vivo bacteria sensors and treatment systems that will help improve life for millions of people."

The challenge is enormous. According to Jeffrey D. Hasday, M.D., professor of Medicine and Head of Pulmonary and Critical Care Medicine at the University of Maryland Medical School in Baltimore, catheter infections are a major concern. Bloodstream infection rates are, according to Hasday, about 0.5 percent for each day a catheter is in place, and when infection occurs, it increases mortality by 35 percent and hospitalization costs by more than $35,000; prolonged ICU stays and hospitalization lead in turn to prolonged post-hospitalization rehabilitation. Traditional treatment is by antibiotics, with researchers constantly working to produce new drugs to deal with emerging resistant strains of bacteria.

To offer physicians new treatments, Clark School researchers are pioneering a new approach for combating bacterial infections. Bacteria cells create an infection by communicating their presence to each other using a signaling molecule called autoinducer 2 (AI-2). At a certain point, the cells sense a "quorum," which leads to the formation of a "biofilm" or mass of communicating cells-the first stage of an infection. A team of researchers from the Clark School and other University of Maryland units seeks to control cells' quorum-sensing (QS) response so that the cells never perceive that they have achieved a quorum and fail to produce an infection.

Bentley, with Assistant Professor Herman Sintim, Professor Gregory Payne, Professor Reza Ghodssi and Deutsch Fellow graduate students Mariana Meyer and Varnika Roy, as well as chemistry graduate student Jacqueline Smith, has developed synthetic analogs of AI-2 called C-1 alkyl AI-2, with an ethyl version that strengthens the QS response, and a propyl version that quenches it. They have shown that their prototype drug can control QS response in a three-species synthetic ecosystem comprised of the bacteria E. coli, S. typhimurium and V. harveyi, working in the individual species and across the species. E. coli is a common source of infection in urinary catheters.

"Today we have shown that C-1 alkyl AI-2 in its two forms lets us control QS response in the laboratory," Bentley stated. "Our next step is to test these compounds in environments and conditions more akin to the body's own. The hydrogel and 'lab-on-a-chip' technologies being developed here will enable us to do so."

When a biofilm grows and thickens, it becomes less translucent. Researchers are taking advantage of this fact to create a microfluidic "lab on a chip" that uses light to monitor biofilm formation and biofilm response to drugs such as C-1 alkyl AI-2. Researchers have built a chip containing tiny channels into which fluids can be pumped under highly controlled conditions. On one side of a channel they place light-emitting diodes (LEDs) and on the other photodiodes that detect light.

They pump fluid containing E. coli into the channel, and continuously shine light through it; as a biofilm grows, less light is captured by the photodiodes. They can then introduce a drug such as C-1 alkyl AI-2; if it interrupts the QS response, the biofilm begins to shrink and more light is detected by the photodiodes.

In addition to improving development of drugs to combat infections, Clark School researchers are building sensors to detect, at very early stages, E. coli and other biofilms growing in catheters and implanted devices, such as artificial joints. Early detection will permit physicians to apply drugs more rapidly, increasing chances that the infection can be defeated before it goes on to require extensive treatment. This is being researched via the use of a surface acoustic wave (SAW) sensor for real-time biofilm growth monitoring.

The SAW sensor is an extremely thin piezoelectric film made of zinc oxide that may be placed on the surface of a medical device. So when a biofilm grows on the film, the sensor's resonant frequency changes, creating an electrical signal that the sensor transmits wirelessly to a physician or patient notification system. The sensor is highly sensitive and biocompatible and its operational frequency meets wireless medical device regulations set by the Federal Communication Commission.

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