Breakthrough test screens for all known bacterial infections

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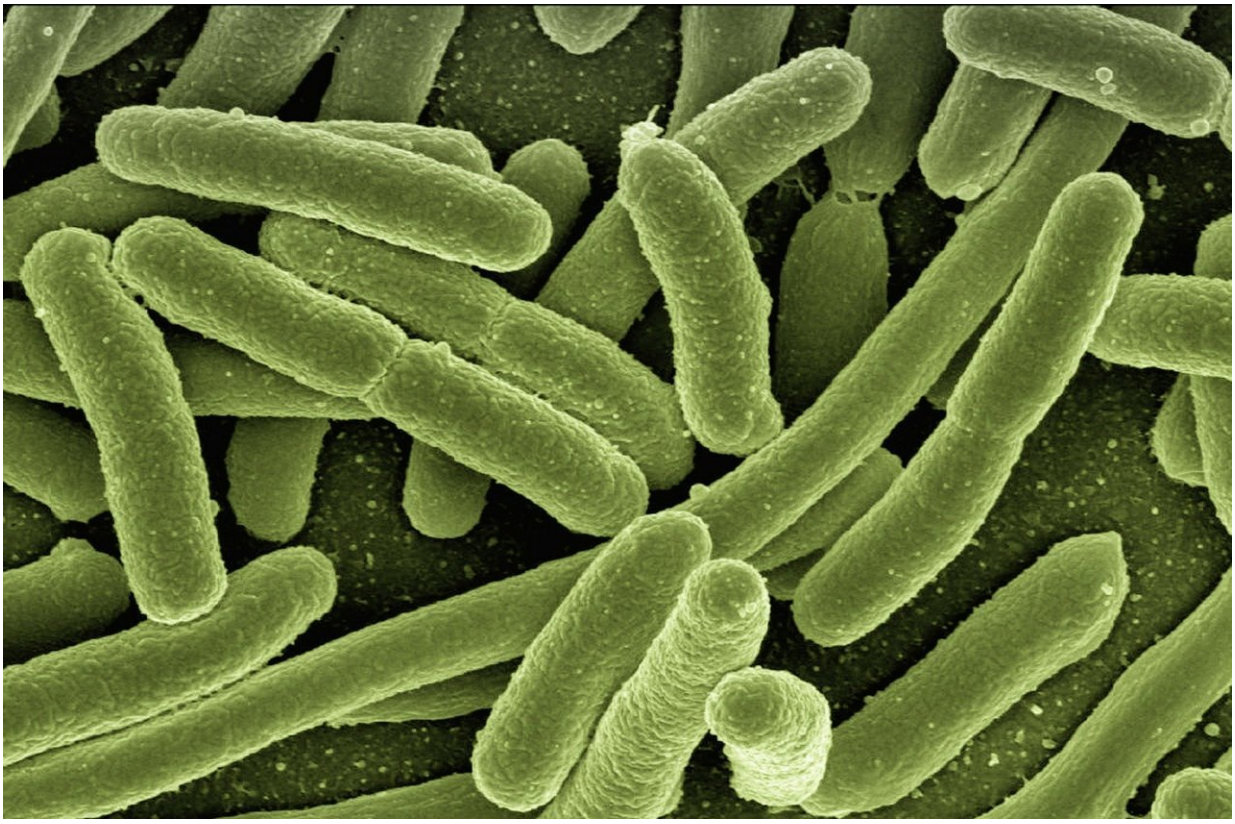

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Scientists at the Center for Infection and Immunity (CII) in the Columbia University Mailman School of Public Health have developed the first diagnostic platform that can simultaneously screen for all known

human pathogenic bacteria as well as markers for virulence and antibiotic resistance. A study in the journal *mBio* provides details on the performance of the BacCapSeq platform.

"Once approved for clinical use, BacCapSeq will give physicians a powerful tool to quickly and precisely screen for all known pathogenic bacteria, including those that cause sepsis, the third leading cause of death in the United States," says first author Orchid M. Allicock, Ph.D., a post-doctoral researcher at CII. "This platform is 1,000 times more sensitive than traditional unbiased testing, at a level comparable to tests that screen one bacterium at a time."

Currently, the most common method used to test for sepsis can take as long as three days, and even longer to provide information on antibiotic resistance. While physicians wait for a result, they usually prescribe broad spectrum antibiotics, a practice that contributes to the growth of antibiotic resistance. BacCapSeq provides results in 70 hours, but the researchers believe that the platform will become faster with advances in computing power.

Each year, antibiotic-resistant infections claim 100,000 lives in the United States, and 700,000 globally, with the highest burden in the developing world, according to World Economic Forum estimates. The direct annual impact of antibiotic resistance in the U.S. is $20-35 billion with an additional $35 billion in lost productivity, according to the U.S. Center for Disease Control and Prevention. Absent an effective response to limit further growth in antimicrobial resistance, the challenge will continue to increase. The World Bank issued a report in 2017 projecting an impact on the GDP between $1.1 trillion and $3.4 trillion.

BacCapSeq contains 4.2 million genetic probes used to detect the signature DNA of all 307 pathogenic bacteria, as well as biomarkers for antibiotic resistance and virulence. Each probe binds to a corresponding

sequence; when a particular bacterium and biomarker is present in a sample, a magnetic process "pulls out" its unique sequences, which can then be used to identify the bacterium and its characteristics. To date, even the most advanced multiplexed polymerase chain reaction systems are only able to screen for up to 19 pathogenic bacteria, and none can assess virulence and antimicrobial resistance.

In the study, the researchers assess the performance of BacCapSeq in several ways: using nucleic acid from blood spiked with DNA from several different bacteria, blood spiked with bacterial cells, blood culture samples, and blood samples from patients with unexplained sepsis. In each case, the platform performance exceeded traditional methods, sometimes detecting infections that were missed by the alternative method. In one case, the test implicated the bacterium Gardnerella vaginalis, which is only rarely associated with significant disease, as the cause of unexplained sepsis in an individual with HIV/AIDS.

BacCapSeq is a complement to VirCapSeq, a similar test developed at CII that screens for all known human viral infections. Recent published studies have reported on that test's performance in Tanzania and Uganda. A test for differential diagnosis of fungal infections is in development.

"Microbiological intelligence must be an integral component of precision medicine,"says W. Ian Lipkin, MD, director of CII and the John Snow Professor of Epidemiology at Columbia Public Health. "Accurate, early differential diagnosis of infectious diseases and knowledge of drug sensitivity profiles will reduce mortality, morbidity, and health care costs."

Provided by Columbia University's Mailman School of Public Health