Medical Xpress

Synthetic biology: Engineered cells detect diabetes and cancer

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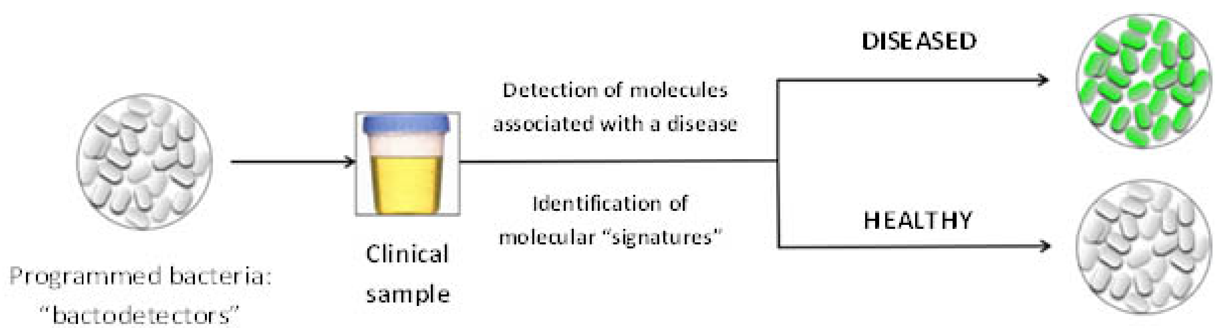

The principle of the use of modified bacteria for medical diagnosis. Credit: ©J. Bonnet/ Inserm.

A Stanford-designed project has built a startling new tool for diagnostic medicine: living biosensors made of bacteria that glow a particular color when they detect trouble.

The team rewired the genetic circuitry inside bacterial cells so that the cells recognized abnormal glucose levels in urine, signaling diabetes.

The custom-designed bacteria show the practical promise of the fledgling field of synthetic biology, which designs and builds organisms unlike anything made by Mother Nature.

"We are showing that we can begin to use engineering tools to systematically program cells for use as human medical diagnostics," said Drew Endy of Stanford's School of Engineering, where the project had its start before moving with its lead investigator Jerome Bonnet to France's Institut de Genetique Moleculaire de Montpellier.

The cells, tested in patients' urine samples, performed almost as well as the conventional diabetes dipstick, Bonnet reported.

While there are still technical hurdles to be overcome, bacterial biosensors could be faster, cheaper and more durable than traditional tests, Bonnet reported in last week's issue of the journal *Science Translational Medicine*.

"It is a very exciting initial foray into this fairly novel field. There is a need for better faster diagnosis of metabolic perturbations in people with diabetes," said Dr. Samuel Dagogo-Jack, president of medicine and science for the American Diabetes Association.

Diabetes is a serious disease that affects the body's ability to produce or respond properly to insulin, a hormone that allows blood glucose to enter the cells of the body and be used for energy.

This approach could aid earlier detection of upward or downward swings of blood glucose levels, said Dagogo-Jack, chief of the Division of Endocrinology, Diabetes and Metabolism at the University of Tennessee Health Science Center in Memphis. It could also help identify subtle signs of complications of the disease.

While synthetic biology cannot yet create artificial life from scratch, projects like this one show that it's possible to swap out a cell's original operating system for a lab-designed one. Then these made-to-order creations can be put to work.

The cells can respond and adapt to their surroundings in ways that current diagnostic devices cannot. They are very sensitive detectors of foreign substances. They live a long time, even in harsh environments. And because cells multiply, it is very simple to create enough for thousands of tests.

"Our work could be a steppingstone toward future applications that use living cells to perform diagnostics," Bonnet wrote in the paper.

The news is an outgrowth of Stanford's 2013 landmark success in building a "biological computer." This approach relies on the same concept as electronics, where a transistor controls the flow of electrons along a circuit. But instead of silicon, it uses a transistor-like device composed of genetic material, called a transcriptor, which controls the flow of an important protein as it travels along a strand of DNA, like an electron on a copper wire.

This genetic material serves as a biological version of electrical engineers' "logic gates" - the building blocks of digital circuits that send and receive signals.

The internal computer communicates by engineering a cell to change color.

In this experiment, when integrated inside E. coli bacteria cells and suspended inside gel-like balls, they delivered true-false answers to this biological question: Do you detect glucose?

The bacteria emitted a glow from a red fluorescent protein to reveal the presence of abnormal glucose levels in the urine from 12 different diabetic patients.

"Since the late '70s and early '80s, techniques in molecular biology and genetic engineering have allowed us to utilize lower forms of life, like bacteria, for therapeutic purposes," such as production of synthetic human insulin," said Dagogo-Jack. "The role of bacteria as useful allies in the war against disease is well-established."

"However, the current urine-based work" of the Stanford study "will need to be refined," he added. "What is needed are detection systems that operate in the body, instead of in excreted urine," which signals trouble too late. "Blood levels are more informative, in real time."

Stanford has turned over its "biological computer" insights to the public domain, rather than privatizing it, which is speeding its adoption at other universities.

"We wish to enable everyone to work together to create a free-to-use tool kit for medical diagnostics powered by engineered cells," Endy said.

Someday, he hopes, medical devices with built-in biological computers could monitor - or even alter - cellular behaviors from inside a patient's body.

In a separate study in the journal that also showed the promise of synthetic biology, scientists at the University of California, San Diego, and the Massachusetts Institute of Technology programmed bacteria that can find and signal the presence of metastatic cancer in urine.

Cancer metastases are difficult to detect with conventional imaging - but if they are found early, patients can be treated and live longer.

The team engineered E. coli bacteria to produce an enzyme when it encountered a tumor cell in the livers of mice. The enzyme then breaks down an injected compound, releasing a light-emitting molecule that can be seen in urine.

They fed the bacteria to mice, where it detected cancer that had spread to the liver from tumors of the colon, lung, ovaries and pancreas.

Although further testing is needed before such biosensors move into the clinic, scientists hope that cells can be repurposed for the simple detection of many cancers.

"Much of medicine depends on hardware, software and chemistry - such as stethoscopes, X-ray imaging and drug molecules," Endy said. "But medicine is really about understanding and treating biology.

"Why not make our medicines from biology directly? We foresee that global health can be practically and affordably realized using biology. If you need more medicine somewhere, people can simply grow it where and when it is needed."

More information: *Science Translational Medicine*, dx.doi.org/10.1126/scitranslmed.aaa3601