Team develops 'logic gates' to program bacteria as computers

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A team of UCSF researchers has engineered E. coli with the key molecular circuitry that will enable genetic engineers to program cells to communicate and perform computations.

The work builds into cells the same logic gates found in electronic computers and creates a method to create circuits by "rewiring" communications between cells. This system can be harnessed to turn cells into miniature computers, according to findings that will be reported in an upcoming issue of *Nature* and appear today in the advanced online edition.

That, in turn, will enable cells to be programmed with more intricate functions for a variety of purposes, including agriculture and the production of pharmaceuticals, materials and industrial chemicals, according to Christopher A. Voigt, PhD, a synthetic biologist and associate professor in the UCSF School of Pharmacy's Department of Pharmaceutical Chemistry who is senior author of the paper.

The most common electronic computers are digital, he explained; that is, they apply logic operations to streams of 1's and 0's to produce more complex functions, ultimately producing the software with which most people are familiar. These logic operations are the basis for cellular computation, as well.

"We think of electronic currents as doing computation, but any substrate can act like a computer, including gears, pipes of water, and cells," Voigt said. "Here, we've taken a colony of bacteria that are receiving two chemical signals from their neighbors, and have created the same logic gates that form the basis of silicon computing."

Applying this to biology will enable researchers to move beyond trying to understand how the myriad parts of cells work at the molecular level, to actually use those cells to perform targeted functions, according to Mary Anne Koda-Kimble, dean of the UCSF School of Pharmacy.

"This field will be transformative in how we harness biology for biomedical advances," said Koda-Kimble, who championed Voigt's recruitment to lead this field at UCSF in 2003. "It's an amazing and exciting relationship to watch cellular systems and synthetic biology unfold before our eyes."

The *Nature* paper describes how the Voigt team built simple logic gates out of genes and inserted them into separate E. coli strains. The gate controls the release and sensing of a chemical signal, which allows the gates to be connected among bacteria much the way electrical gates would be on a circuit board.

"The purpose of programming cells is not to have them overtake electronic computers," explained Voigt, whom Scientist magazine named a "scientist to watch" in 2007 and whose work is included among the Scientist's Top 10 Innovations of 2009. "Rather, it is to be able to access all of the things that biology can do in a reliable, programmable way."

The research already has formed the basis of an industry partnership with Life Technologies, in Carlsbad, Cal., in which the genetic circuits and design algorithms developed at UCSF will be integrated into a professional software package as a tool for genetic engineers, much as computer-aided design is used in architecture and the development of advanced computer chips.

The automation of these complex operations and design choices will advance basic and applied research in synthetic biology. In the future, Voigt said the goal is to be able to program cells using a formal language that is similar to the programming languages currently used to write computer code.

Provided by University of California - San Francisco

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