

GENETICS

Replacement Genome Gives Microbe New Identity

For decades, molecular biologists have genetically modified microbes and other kinds of cells by adding short DNA sequences, whole genes, and even large pieces of chromosomes. Now, in a feat reported in a paper published online by *Science* this week (www.sciencemag.org/cgi/content/abstract/1144622), one group has induced a bacterium to take up an entire 1.08-million-base genome in one gulp. In doing so, microbiologist John Glass and his colleagues at the J. Craig Venter Institute in Rockville, Maryland, have transformed one bacterial species into another.

"This is a significant and unexpected advance," says molecular biologist Robert Holt of the Michael Smith Genome Sciences Centre in Vancouver, Canada. But the advance remains somewhat mysterious. Glass says he doesn't fully understand why the genome transplant succeeded, and it's not clear how applicable their technique will be to other microbes. Nonetheless, "it's a necessary step toward creating artificial life," says microbiologist Frederick Blattner of the University of Wisconsin, Madison.

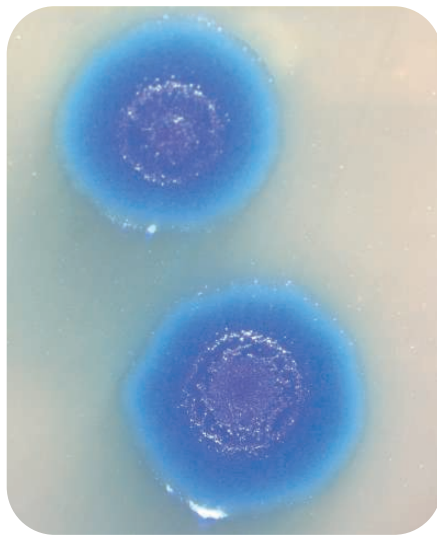
Glass and his colleagues are among several groups trying to build a microbe with the minimal gene set needed for life, with the goal of then adding other useful genes, such as ones for making biofuels. In anticipation, Glass and colleagues wanted to develop a way to move a complete genome into a living cell.

As a proof of principle, they tried transplanting the single, circular chromosome of *Mycoplasma mycoides* large colony (LC) into a close relative, *M. capricolum*. Both of these innocuous goat pathogens lack the cell walls typical of many other bacteria, eliminating a possible impediment to genome transfer.

At the Venter Institute, Carole Lartigue and her colleagues first added two genes to *M. mycoides* LC that would provide proof if the transfer of its genome worked. One gene conferred antibiotic resistance, and the other caused bacteria expressing it to turn blue. Lartigue removed the modified chromosome from *M. mycoides* LC, checked to make sure she had stripped off all proteins from the DNA, and then added the naked genome to a tube of *M. capricolum*. Within 4 days, blue colonies appeared, indicating that *M. capricolum* had taken up the foreign DNA. When they analyzed these blue bacteria for sequences specific to either mycoplasma, the researchers found no evidence of the host bacterium's DNA.

Microbial geneticist Antoine Danchin of the Pasteur Institute in Paris calls the experiment "an exceptional technical feat." Yet, he laments, "many controls are missing." And that has prevented Glass's team, as well as independent scientists, from truly understanding how the introduced DNA takes over the host cell.

Glass suspects that at first, both genomes are present in *M. capricolum*. But when one of those double-genomed microbes divides, one genome somehow goes to one daughter cell and the other to the second. By exposing the growing colony to an antibiotic, the researchers selected for cells that contain only the *M. mycoides* LC genome.



Species makeover. Blue signals successful genome transfer in these bacterial colonies.

Other researchers are not sure the strategy will work on bacteria with cell walls. And Danchin expects it will be difficult to swap genomes among bacteria that aren't as closely related. Regardless, George Church of Harvard University questions the need for genome transplantation; instead of starting with a minimal genome, he's making useful chemicals by simply adding customized genes to existing species' genomes.

Nonetheless, Markus Schmidt of the Organisation for International Dialogue and Conflict Management in Vienna, Austria, predicts that the mycoplasma genome swap will force more discussions about the societal and security issues related to synthetic biology. "We are one step closer to synthetic organisms," he says.

—ELIZABETH PENNISI

Dealing With Mesopotamia

When U.S. troops invaded Iraq in 2003, they received a deck of playing cards showing the faces of Saddam Hussein and other top Baathists as a guide to capturing Iraq's most wanted criminals. Now, the Pentagon intends to use the same approach to educate troops about Iraq's endangered archaeological heritage.



The 40,000 decks depict four different aspects of that heritage: diamonds for artifacts, spades for archaeological sites, hearts for encouraging soldiers to win over the locals, and clubs for preservation. Archaeologists say raising such awareness is critical: Thousands of ancient sites, mostly unguarded, have been damaged in the past 3 years, while artifacts continue to be smuggled out of the country in unknown numbers. Archaeologist Elizabeth Stone of Stony Brook University in New York state says the cards "seem like a good idea, but [the program] also seems to me to be too little, too late."

—ANDREW LAWLER

Bioenergy Centers Are Not Corny

The Department of Energy (DOE) has named the winners in a competition to run three \$125 million bioenergy research centers. The 5-year awards go to teams led by Lawrence Berkeley National Laboratory in California, the University of Wisconsin, Madison, and Oak Ridge National Laboratory (ORNL) in Tennessee to manage the facilities, set to open in 2009.

The centers, intended to be as flexible as start-up companies, are a new departure for DOE. Officials had originally proposed large-scale bioenergy institutes focused on themes such as proteomics or genomics. But last year, heeding advice from the National Research Council, DOE created more nimble centers focused directly on natural microbes that could break down lignin, a protein that blocks access to cellulose from grasses, waste, or woody plants, which DOE wants to tap to make biofuels instead of corn, the standard current feedstock. The Oak Ridge team, for example, includes two national labs, four universities, and three biotech companies coordinating work at ORNL on plant genomics, cell imaging, entomology, and molecular biology. Researchers have focused on many of these problems before, says center director Martin Keller, but not "integrated at this level."

—ELI KINTISCH