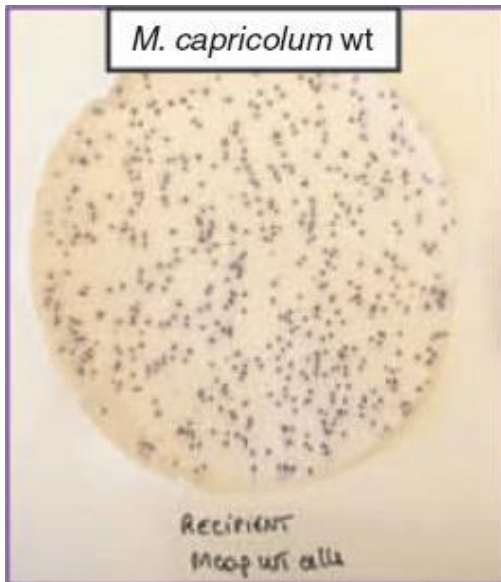


First genome transplant changes one species into another



Colony of *M. Capricolum*, the recipient cells, in one of the experiments. Image credit: Lartigue, et al. ©2007 Science.

For the first time, scientists have completely transformed a species of bacteria into another species by transplanting its complete set of DNA. The achievement marks a significant step toward the construction of synthetic life, with applications including the production of clean fuel in as little as a decade.

Scientists Carole Lartigue and colleagues from the J. Craig Venter Institute in Rockville, Maryland, have published their results in a recent issue of *Science*. In addition to being a proof-of-concept experiment, the researchers hope that genome transplantation will enable the production of synthetic microbes for green energy sources, pharmaceuticals, chemicals and textiles.

The scientists' results show that it is possible to transplant the complete set of DNA—the genome—from one species into the genome of a different species, so that the recipient organism is phenotypically and genotypically identical to the donor organism.

In their experiment, the researchers used two species of bacteria that belong to a group of organisms called mycoplasmas due to their small genomes (making them easier to handle) and lack of a cell wall (enabling easier insertion of DNA). In the experiment, *Mycoplasma mycoides* Large Colony (LC) served as the donor, and *Mycoplasma capricolum* the receiver. Both bacteria are mild pathogens of goats, and are genetically similar, sharing about 75% of their genomic material.

The researchers explained that the transplantation method is simple in concept, though complicated to execute. First, the proteins were stripped from the *M. mycoides* LC cells, resulting in “naked” DNA that can be passed between cells. Then this intact DNA was incubated briefly with *M. capricolum* cells, soaking in a solution that caused the *M. capricolum* cells to fuse together. As two of these recipient cells fused, they sometimes encapsulated a donor DNA chromosome.

Then, the scientists treated all the cells with the antibiotic tetracycline, which is toxic to *M. capricolum* cells. However, since the researchers used a strain of *M. mycoides* LC that was resistant to tetracycline, any *M. capricolum* that contained the *M. mycoides* LC DNA survived, which was about 1 in 150,000 cells. The researchers then performed tests to confirm the identities of the new organism.

“While one success in 150,000 attempts would be unacceptable in most human endeavors such as shooting free throws, in most microbiology applications such efficiency is completely OK,” Glass explained to *PhysOrg.com*. “It is very easy for us to attempt to transplant donor genomes into 15 million or more recipient cells, which would yield hundreds on transplants. Still, we are exploring approaches that are more efficient, but our current method is completely tractable for our current plans.”

The scientists aren't sure of the mechanism behind the transplant, but they have ruled out natural methods of DNA transformation, such as recombination. They suspect that cell fusion may play an important role in mediating the transplant due to the optimal concentrations of fusion solution. However, they do not know if other species will be able to transfer their complete DNA using the same method.

The researchers are excited about the success of the first genome transplantation because it marks a step toward the propagation of synthetic genomes. In previous studies, Craig Venter and his colleagues have defined a minimal genome of approximately 400 genes required to sustain cellular life. The scientists want to synthesize this genome, called *Mycoplasma genitalium*, using only simple chemicals.

The longest piece of DNA synthesized so far is 35,000 units, while the *M. genitalium* is 580,000 units, making the synthesis a realistic goal. After synthesizing complete genomes, the scientists hope to make the genomes take control of living cells, with a genome transplant like the one in the current study.

“To better enable rational design of new species of microbes capable of efficiently producing molecules that can solve human needs for energy, health and bioremediation, we believe we first need to better understand more fully how cells work,” Glass said. “We will use our genome transplantation technology to enliven this genome [*M. genitalium*] by transferring it into a suitable recipient cell. From that first ‘synthetic cell’ we will iteratively remake the genome in ever smaller simpler forms by deleting non-essential genes. Eventually we will produce cells containing only the essential set of genes necessary for life under laboratory conditions. These cells will be invaluable platforms for discovery of the biological roles of cellular components we currently can ascribe no function to or to components we may not even be aware of.”

Synthetic biologists predict this research will have many applications, including production of clean alternative fuel in as little as 10 years. Venter has also set up a company called Synthetic Genomics to create alternative fuels, which could potentially be used in the same infrastructure as petroleum and be used in today's vehicles.

“We envision engineering bacteria to convert cellulosic material to ethanol, butanol, or perhaps long chain alcohols,” Glass explained. “Some microbes have the capacity to convert the carbohydrate polymers that comprise cellulose into glucose and other simple sugars. Other bacteria have the capacity to convert simple sugars into various fuels. We envision synthesizing new chimeric bacterial species that can efficiently do both.”

Citation: Lartigue, Carole, Glass, John I., Alperovich, Nina, Pieper, Rembert, Parmar, Prashanth P., Hutchison III, Clyde A., Smith, Hamilton O., and Venter, J. Craig. “Genome Transplantation in Bacteria: Changing One Species to Another.” 3 August 2007, Vo. 317, *Science*.

Copyright 2007 PhysOrg.com.

All rights reserved. This material may not be published, broadcast, rewritten or redistributed in whole or part without the express written permission of PhysOrg.com.

This document is subject to copyright. Apart from any fair dealing for the purpose of private study, research, no part may be reproduced without the written permission. The content is provided for information purposes only.