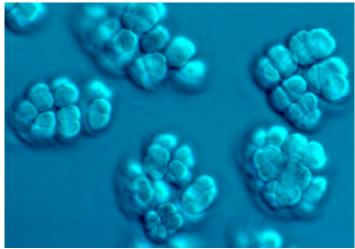
Key player in global warming: M. acetivorans is sequenced

The unsung heroes of the global carbon cycle are methanogens—microbes at the bottom of the food chain who break down the waste products of other organisms and release methane gas into the atmosphere. Scientists have now sequenced one of the most versatile methanogens, an organism called *Methanosarcina acetivorans*.



M. acetivorans is unique among archaea in forming multicellular structures or colonies.

Methanosarcina species live in oil wells, sewage lagoons, trash dumps, decaying leaves, stream sediments, and the stomach of cows, among other places. They subsist on a diverse menu of energy sources, including acetate. With the genome sequenced, researchers have begun to search for genes responsible for the organism's capacity to adapt and break down a variety of waste products.

"This is an incredibly versatile organism," says James Galagan, who led the annotation and analysis effort at the Whitehead Institute Center for Genome Research in Cambridge, Massachusetts. "It is a sink for lots of diverse waste products; the microbe processes these products and then releases methane back into the global carbon cycle."

Methanosarcina acetivorans belongs to the family of archaea, an ancient branch of life that is distinct from plants, animals, and bacteria. The archaea are the least understood domain of life, and researchers will use the sequence to investigate the biology of these organisms, including methanogens. "Methanogens are critical players in the global carbon cycle and have potential uses for addressing human problems," says William W. Metcalf, a microbiologist at the University of Illinois at Urbana-Champaign, and a member of the research team.

Methane is both a potential alternative energy source and a potent greenhouse gas. There is an enormous amount of methane at the bottom of the oceans; and methane reflects heat far better than carbon dioxide does. Metcalf says that methane is both "a staggering untapped source of natural energy" and "a fairly frightening contributor" to global warming.

The biggest surprise of the sequencing project was the size of the genome. Early estimates were either wrong or the researchers did not believe it could be as large as it turned out to be. The genome of *M. acetivorans* C2A is by far the largest of all sequenced archaeal genomes. With 5.7 million base pairs, it is more than three times as large as two previously sequenced methanogens, *Methanobacterium thermoautotrophicum* and *Methanococcus jannaschii*.

"That the genomes of closely related species vary so much in size raises a lot of biological questions," says Galagan. "We are now in a position to answer those questions with the genome sequence." The researchers identified about 4,500 genes of which nearly

200 genes are related to methanogenesis. The findings are published in *Genome Research*.



Courtesy Whitehead Institute Center for Genome Research.

Galagan likens the genome to a rain forest with biodiversity waiting to be explored. Already, the researchers have made some interesting discoveries. For instance, *M. acetivorans* appears to have the capacity to propel itself, although no one has ever seen it do so. The researchers identified genes for flagella and for chemotaxis, the process of moving purposefully toward a chemical. "These genes are pretty strong evidence that the organism is able to move under the right circumstances," says Galagan.

Methanosarcina acetivorans was sequenced in part because genetic tools are available to modify the organism in the laboratory, making it a model species for methanogens. Metcalf's laboratory, among others, created some genetic mutants, and in recent months they have shipped these to researchers interested in testing findings from the sequence.

Despite the genome's size, the sequencing was done relatively quickly. Then the researchers began the process of correcting and annotating the sequence. For two months,

the Whitehead team corresponded with experts around the world about the sequence.

This culminated in a two-day genome analysis meeting at the Whitehead Institute.

"We believe the best way to understand a genome is to bring together as many experts as possible to analyze the sequence," says Galagan. One participant in the two-day meeting told him, "This was the most fun I've had in science in the last decade."

For more information on the M. acetivorans genome, see the M. acetivorans (C2A) acetivorans at the Whitehead Institute.