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# Methanogenic archaeon sequenced

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#### Summary

Determination of the complete genome sequence of the methanogen *Methanosarcina acetivorans* reveals unusual metabolic versatility

# Significance and context

An estimated 900 million tonnes of methane are produced annually by biological systems. Methane is a greenhouse gas and contributes significantly to global warming. It is produced by the activities of anaerobic microorganisms, known collectively as methanogens, and most is generated by the reduction of acetate. The genome sequence of the acetate-using methanogen *Methanosarcina acetivorans* C2A has now been determined by Galagan *et al.* Exceptionally, *M. acetivorans* also has the two other pathways of methanogenesis: the reduction of CO2 using electrons derived from the oxidation of H2 (hydrogenotrophic pathway); and the use of methanol, methylamines or methyl sulfides as substrates (methylotrophic pathway). *M. acetivorans* has been identified in a variety of environments, including freshwater and marine sediments, decaying leaves, soils, lagoons, and the feces of herbivores. Depending on growth stage and environmental factors, different morphological forms of *M. acetivorans* were observed, including single cells that lack the cell envelope and multicellular aggregates. The genome sequence of *M. acetivorans* and powerful analytic genetic techniques can now be used to understand this extraordinary and important form of life.

# Key results

The genome of *M. acetivorans* is 5,751,492 bp in size and has a G+C content of 42.7%. On analysis, 4,524 potential protein-encoding genes were identified, with an average size of approximately 936 bp per gene. Of these, 69% had significant similarity either to known proteins or to conserved hypothetical proteins, and 31% had no similarity to any database sequences. Interestingly, the proteome of *M. acetivorans* is most similar to that of *Archaeoglobus fulgidus*, in contrast to the small-subunit rRNA sequence-based taxonomic classification which relates *Halobacterium* most closely to *M. acetivorans*. The genome contains 539 multigene families: the largest ones encode ATP-binding cassette (ABC) transporters, surface proteins, sensory transduction histidine kinases, methyltransferases, and oligopeptide ABC transporters. *M. acetivorans* contains approximately 200 genes involved in methanogenesis, the only energy-generating process known so far in methanogenic bacteria. Many of

those genes are present in several copies. For example, there are two copies - 95% identical to each other - of a six-gene operon encoding the acetyl-CoA decarbonylase/synthase complex required for the production of methane from acetate. Methanogens are very sensitive to even small concentrations of oxygen. It was therefore surprising to identify a copy of the *cydAB* genes, which encode cytochrome *d* oxidase in *Escherichia coli*, a key enzyme in oxygen-dependent respiration. Although its function in *M. acetivorans* is not yet known, it is possible that cytochrome *d* oxidase may act as a protection against oxygen by removing it and thus lowering the cellular concentration. Genes encoding three different nitrogenase complexes were found in *M. acetivorans*, suggesting the importance of nitrogen fixation in this methanogen.

*M. acetivorans* can undergo morphological changes, including the formation of multicellular structures, in which each cell contains a cell envelope of protein subunits, called the S-layer, present in a sacculus-like structure. They can also grow in multicellular bodies embedded within an extracellular matrix. Genes putatively involved in the synthesis of extracellular polysaccharides, and S-layer glycoproteins were identified. Furthermore, genes encoding environmental stimuli-sensing two-component systems were present. These normally consist of a sensory transduction histidine kinase and a response-regulator protein in a one to one ratio. In *M. acetivorans*, however, there are 50 histidine kinase-encoding genes and only 18 response-regulator-encoding genes. This suggests a different mode of action of two-component systems in archaea.

### Links

The genome sequence of *M. acetivorans* and other archaea are available at the Deambulum:%20Archaea website.

# Reporter's comments

Having the complete genome sequence of the *M. acetivorans* will be useful for studying metabolic pathways, adaptations to changed environmental conditions, and the morphology of this archaeon during different stages of growth and/or changes in the environment. A mutagenesis program and in-depth biochemical studies should be part of future work to reach this goal.

### Table of links

Genome%20Research

Deambulum: %20 Archaea

#### References

1. Galagan JE, Nusbaum C, Roy A, Endrizzi MG, Macdonald P, FitzHugh W, Calvo S, Engels R, Smirnov S, Atnoor D, et al: The genome of *M. acetivorans* reveals extensive metabolic and physiological diversity. Genome Res. 2002, 12: 532-542.

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