

Complete Genome Sequence of *Methanomassiliicoccus luminyensis*, the Largest Genome of a Human-Associated Archaea Species

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The present study describes the complete and annotated genome sequence of *Methanomassiliicoccus luminyensis* strain B10 (DSM 24529^T, CSUR P135), which was isolated from human feces. The 2.6-Mb genome represents the largest genome of a methanogenic euryarchaeon isolated from humans. The genome data of *M. luminyensis* reveal unique features and horizontal gene transfer events, which might have occurred during its adaptation and/or evolution in the human ecosystem.

Methanomassiliicoccus luminyensis strain B10 was isolated from human feces by enrichment culture studies that were conducted to isolate new human-associated *Archaea* species (4). The strictly anaerobic strain B10 grows optimally at 37°C, pH 7.6, with 1% NaCl, and is able to produce methane by reducing methanol with hydrogen as an electron donor.

A phylogenetic analysis using 16S rRNA gene sequences showed that strain B10 is most closely related to the nonmethanogen *Aciduliprofundum boonei* (4). Strain B10, only the fourth euryarchaeote to be successfully cultivated and isolated from humans (5), represents the first species of a novel genus (4).

The complete genome of *M. luminyensis* was sequenced with a combination of shotgun and 3-kb paired-end libraries using high-throughput 454 pyrosequencing by 454 Life Sciences (Roche, Boulogne Billancourt, France). Sequence reads were assembled using a Newbler assembler (Roche), 26 contigs were generated into one scaffold, and gaps were closed by PCR on genomic DNA. A preliminary open reading frame (ORF) prediction was conducted by automated annotation with Glimmer (<http://www.cbc.umd.edu/software/glimmer/>) and RAST (2). The annotation was manually cured using BLAST and the nr database of NCBI. The CRISPRfinder (<http://crispr.u-psud.fr/Server/>) was used to detect and identify CRISPR repeat and spacer sequences in the genome.

The *M. luminyensis* genome consists of a circular chromosome of 2,637,810 bp (with a high GC content of 60.5%), which is much larger than the genomes of other methanogenic *Archaea* isolated from humans: *Methanobrevibacter smithii* (1.8 Mb) (10) and *Methanosphaera stadtmanae* (1.77 Mb) (6).

The genome of *M. luminyensis* contains, surprisingly, a single 16S-23S rRNA cluster (rarely observed for methanogenic *Archaea*) and two copies of 5S and 42 tRNA genes. A total of 2,613 ORFs were recovered, and most of them presumably encode proteins involved in DNA/RNA metabolism, synthesis and degradation of proteins, biosynthesis of nucleotides/amino acids/fatty acids/vitamins and cofactors, and energy metabolism.

As for *M. stadtmanae*, the *M. luminyensis* genome carries a restricted methanogenesis pathway, which could explain why *M. luminyensis* reduces only methanol in the presence of H₂ for methane formation.

Among the proteins involved in DNA metabolism, the DNA replication machinery of *M. luminyensis* is strongly conserved with proteins of archaeal origin such as ORC1/CDC6, RFA, Pri-1, Pri-2, MCM, RFC, PCNA, FEN, RNase H, DNA polymerase B, and DNA polymerase D (which is specific to *Euryarchaea*) (3). In contrast, the repair system of *M. luminyensis* contains proteins of nonarchaeal origin. The genome

contains several genes encoding bacterial proteins such as UvrD helicase or DinG helicase, suggesting horizontal gene transfers from *Bacteria* found in the gut (1).

Moreover, the *M. luminyensis* genome contains 3 CRISPR loci and the associated proteins (Cas), which could confer a resistance against the intrusion of mobile elements such as viruses and plasmids (9). The distribution of the CRISPR/Cas systems in *Archaea* genomes shows an important horizontal gene transfer from *Bacteria* driven by mobile elements (7, 8).

These horizontal gene acquisitions from *Bacteria* might have contributed to the evolution and adaptation of *M. luminyensis* to the host niche.

Nucleotide sequence accession numbers. The *Methanomassiliicoccus luminyensis* strain B10 genome sequence has been deposited in EMBL under the accession numbers CAJE01000001 to CAJE01000026.

ACKNOWLEDGMENT

This work was funded by Fondation Méditerranée Infection.

We have no conflicts of interest to declare.

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Received 31 May 2012 Accepted 12 June 2012

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doi:10.1128/JB.00956-12