

Genome Sequence of Coxiella burnetii 109, a Doxycycline-Resistant Clinical Isolate

Laetitia Rouli, Jean-Marc Rolain, Adil El Filali, Catherine Robert, and Didier Raoult

Aix Marseille Université, URMITE, UM63, CNRS 7278, IRD 198, Inserm 1095, Marseille, France

Coxiella burnetii 109, with a 2.03-Mb genome, is a doxycycline-resistant human isolate that was isolated from the cardiac valve of a German male patient with Q fever endocarditis who died during the course of the treatment due to the bacterium's resistance to doxycycline. This new genome can be useful for future comparative genomic or Q fever studies.

oxiella burnetii is a human pathogen causing Q fever (7). It is a Gram-negative bacterium belonging to the gammaproteobacteria and having a complex intracellular cycle (7). Actually, five genomes are available from the NCBI: Dugway 5J108-111 (1), CbuG_Q212 (1, 2), CbuK_Q154 (1), RSA 331, and RSA 493 (1, 9).

Our strain, 109, is a human isolate of C. burnetii resistant to doxycycline (MIC = $8 \mu g/ml$), isolated from the cardiac valve of a German male patient with Q fever endocarditis who died during the course of the treatment despite the use of an increased-doxycycline regimen (400 mg/day) but a low serum doxycycline concentration (3.5 μ g/ml \pm 0.6 μ g/ml after 1 year of treatment) (8). Its genome was sequenced by shotgun, 454 pyrosequencing and use of the SOLiD system, for a total of 7,654,293 reads, and assembled using the software program GS Assembler and CLC bio software. We finally obtained 236 large contigs and 4 scaffolds. The finishing is in progress. We used the Prodigal software program (3) to annotate the DNA sequences; tRNAs were predicted using the software program tRNAScan-SE (6), rRNAs were predicted using the RNAmmer program (4), and COG and KEGG analysis were done thanks to CAMERA (10).

The 2.03-Mb genome of strain 109 (42.5% GC content) encodes 1,846 proteins and carries 42 tRNAs and one ribosomal operon. Among the 1,846 proteins, 88% own a COG (Cluster of Orthologous Groups) category, 208 are split, and 177 are hypothetical. Strain 109 contains a QpH1-type plasmid of 0.037 Mb (39.3% GC content).

We compared strain 109 to the five available strains. A comparison of the COG categories shows that 109 follows the same trend as the other strains. It is the same for the KEGG classes. All the strains follow the same trend, with a high number of proteins implied to be in the metabolism category (amino acid metabolism and carbohydrate metabolism in the majority) and with some proteins belonging to genetic information and processing (translation, replication, and repair in the majority). Moreover, based on a study published in 2011 (5), there are 35 deleted open reading frames (ORFs) in strain 109.

Availability of the strain 109 genome could help in understanding the resistant profile of this strain. The added sequences are also interesting for a later pangenomic study.

Nucleotide sequence accession numbers. Strain 109 has been deposited in GenBank under the project accession number AKYP00000000. The version described in this article is the first version, AKYP01000000.

ACKNOWLEDGMENTS

This work was supported by the Mediterranean Infection Foundation. We have no conflict of interest to declare.

REFERENCES

- 1. Beare PA, et al. 2009. Comparative genomics reveal extensive transposon-mediated genomic plasticity and diversity among potential effector proteins within the genus Coxiella. Infect. Immun. 77:642-656.
- 2. Boccard F, Baulcombe D. 1993. Mutational analysis of cis-acting sequences and gene function in RNA3 of cucumber mosaic virus. Virology
- 3. Hyatt D, et al. 2010. Prodigal: prokaryotic gene recognition and translation initiation site identification. BMC Bioinformatics 11:119. doi: 10.1186/1471-2105-11-119.
- 4. Lagesen K, et al. 2007. RNAmmer: consistent and rapid annotation of ribosomal RNA genes. Nucleic Acids Res. 35:3100-3108.
- 5. Leroy Q, Armougom F, Barbry P, Raoult D. 2011. Genomotyping of Coxiella burnetii using microarrays reveals a conserved genomotype for hard tick isolates. PLoS One. 6:e25781. doi:10.1371/journal.pone.0025781.
- 6. Lowe TM, Eddy SR. 1997. tRNAscan-SE: a program for improved detection of transfer RNA genes in genomic sequence. Nucleic Acids Res. 25:
- 7. Maurin M, Raoult D. 1999. Q fever. Clin. Microbiol. Rev. 12:518-553.
- 8. Rolain JM, Boulos A, Mallet MN, Raoult D. 2005. Correlation between ratio of serum doxycycline concentration to MIC and rapid decline of antibody levels during treatment of Q fever endocarditis. Antimicrob. Agents Chemother. 49:2673-2676.
- 9. Seshadri R, et al. 2003. Complete genome sequence of the Q-fever pathogen Coxiella burnetii. Proc. Natl. Acad. Sci. U. S. A. 100:5455-5460.
- Sun S, et al. 2011. Community Cyberinfrastructure for Advanced Microbial and Ecological Research and Analysis: the CAMERA resource. Nucleic Acids Res. 39:D546-D551.

Received 26 September 2012 Accepted 1 October 2012 Address correspondence to Didier Raoult, didier.raoult@gmail.com. Copyright © 2012, American Society for Microbiology. All Rights Reserved. doi:10.1128/JB.01856-12