Draft genome sequence of *Coxiella burnetii* Dog Utad, a strain isolated from a dog-related outbreak of Q fever

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**Abstract**

*Coxiella burnetii* Dog Utad, with a 2 008 938 bp genome is a strain isolated from a parturient dog responsible for a human familial outbreak of acute Q fever in Nova Scotia, Canada. Its genotype, determined by multispacer typing, is 21; the only one found in Canada that includes Q212, which causes endocarditis. Only 107 single nucleotide polymorphisms and 16 INDELs differed from Q212, suggesting a recent clonal radiation.

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*Coxiella burnetii* is a Gram-negative bacterium with a complex intracellular cycle belonging to the γ-proteobacteria [1]. To date, 13 genomes are available from the NCBI [2]. Our strain, Dog Utad, was isolated in Marseille from a dog responsible for a Q fever familial outbreak in Nova Scotia, Canada [3]. This female dog was a hound that had caught rabbits during its pregnancy and gave birth to four pups. All of them died within 24 h after birth. All three family members (mother, father and son) who were present during the delivery, developed pneumonia in the 2 weeks following parturition. Index case was the mother, who helped with the delivery and cleaned up afterward. Serological data confirmed acute Q fever in the mother and the son and *C. burnetii* was isolated by shell vial technique [4] from the dog uterus, which was removed 70 days after parturition, frozen and shipped to our laboratory [5].

Genotyping was performed on the strain using multi-spacer sequence typing (MST) [6], a technique based on the variability of ten intergenic sequences. The genotype MST 21 was identified and confirmed by BLAST of the genome [7] against *Cox* sequences [10]. We compared the Dog Utad strain to the seven available strains. A comparison of the COG categories showed that Dog Utad follows the same trend as the other available *C. burnetii* genomes, but with more similarities with CbuG_Q212, a genome previously deposited in GenBank corresponding to a strain from a Canadian man presenting with Q fever endocarditis and having the same genotype (MST21).

*Coxiella burnetii* Dog Utad reads best covered (98%) the *Coxiella burnetii* CbuG_Q212 genome with a maximum coverage of 1482 and an average coverage of 173. Moreover, the final Dog Utad sequence was the same size as CbuG_Q212 (2 Mb) and there were only 80 gaps (for a total of 52 047 bp). The genome is characterized by a consensus sequence of 2 008 938 bp (G+C content 44%). It encodes 1896 proteins and carries 44 tRNA and one ribosomal operon.

To the best of our knowledge after analysing 335 strains with available MST from around the world, MST21 was the only genotype identified in Canada. Two other strains from humans presenting with Q fever endocarditis, two from cats and one other from a dog from Canada were also identified as MST21. The uniformity of geographical and genotypic criteria allows us to define the Canadian genotype, which corresponds to the genotype MST21, infects cats, dogs and humans and is responsible for acute Q fever and endocarditis in the Canadian population. It was also found in two French patients [6] and in Alberta, Canada.

We found only 123 mutations (70 of them in putative open reading frames (ORF)) when compared with CbuG_Q212: 107 single nucleotide polymorphisms (SNPs; 67 in ORF), eight insertions (one ORF) and eight deletions (two in ORF). Forty-seven of the 70 are non-synonymous mutations, corresponding to 44 mutated genes. These genes encode for 17 proteins involved in metabolism, five transporters, three membrane proteins, three proteins of signal transduction, three translation proteins, two transcription proteins, two chaperone proteins, three hypothetical proteins, one type IV secretion system protein, one DNA replication protein, one protein involved in cellular processes, one organic solvent tolerance protein, one isomerase and one stress protein (Table 1). This very low number of SNPs suggests a very short genetic distance between these two genomes, suggesting a recent clonal radiation of *C. burnetii* MST21 in Canada.
TABLE 1. Non-synonymous point mutations in Coxiella burnetii Dog Utad compared with Coxiella burnetii Q212

| Position* | Type       | Gene ID          | Annotation                                      | Nucleotide change (Q212 → Dog Utad) | Amino acid change (Q212 → Dog Utad) |
|-----------|------------|------------------|------------------------------------------------|------------------------------------|-------------------------------------|
| 26219     | SNP        | ChuG_0030        | Hypothetical protein                            | C→A                               | Ala→Glu                             |
| 57338     | SNP        | ChuG_0066        | Thioredoxin peroxidase                         | A→C                               | Ser→Ala                             |
| 77850     | SNP        | ChuG_0091        | Transporter-sodium dependent                   | A→C                               | Thr→Pro                             |
| 100854    | SNP        | ChuG_0107        | Biotin carboxylase                              | G→C                               | Gly→Ala                             |
| 329943    | SNP        | ChuG_0357        | Ribosomal protein α-6 glutamate ligase         | G→A                               | Gly→Glu                             |
| 366913    | SNP        | ChuG_0400        | lcnj                                           | G→A                               | Glu→Lys                             |
| 366926    | SNP        | ChuG_0400        | lcnj                                           | A→G                               | Glu→Gly                             |
| 393251    | SNP        | ChuG_0426        | Sodium/proton antiporter protein                | T→C                               | DEL20aa                             |
| 503017    | SNP        | ChuG_0540        | Exported membrane spanning protein             | T→A                               | Phe→Tyr                             |
| 504897    | SNP        | ChuG_0540        | Exported membrane spanning protein             | A→G                               | Thr→Ala                             |
| 543181    | SNP        | ChuG_0577        | Bacterial protein translation initiation factor 2 | G→A                               | Val→Met                             |
| 610658    | SNP        | ChuG_0645        | Outer membrane lipoprotein                     | C→T                               | Met→Leu                             |
| 719445    | SNP        | ChuG_0753        | N2,4-H4 antipporter                            | T→C                               | Gin→Arg                             |
| 736723    | SNP        | ChuG_0769        | Malate dehydrogenase                           | G→A                               | Arg→Gln                             |
| 763310    | SNP        | ChuG_0791        | Phosphoglycolate phosphatase                    | T→C                               | Phe→Ser                             |
| 803836    | SNP        | ChuG_0828        | Glycine-rich RNA-binding protein                | T→C                               | Met→Leu                             |
| 836313    | SNP        | ChuG_0860        | Transcription-repair coupling factor           | G→T                               | Ser→Tyr                             |
| 894420    | SNP        | ChuG_0919        | Two component system histidine kinase          | T→G                               | Ile→Ser                             |
| 914733    | SNP        | ChuG_0941        | ABC transporter                                 | T→G                               | Leu→Phe                             |
| 928574    | SNP        | ChuG_0953        | Aspartokinase                                   | C→T                               | Pro→Leu                             |
| 974371    | SNP        | ChuG_1002        | Carboxylesterase                               | A→T                               | Glu→Asp                             |
| 1006992   | SNP        | ChuG_1039        | Cytochrome c ubiquinol oxidase subunit I       | T→C                               | Ser→Ala                             |
| 1050734   | SNP        | ChuG_1088        | Endonuclease/exonuclease/phosphatase family protein | C→G                               | Ala→Pro                             |
| 1052481   | SNP        | ChuG_1090        | UDP-N-acetyl glucosamine 6 dehydrogenase       | C→T                               | Ala→Val                             |
| 1065901   | SNP        | ChuG_1106        | Calcin V production protein                    | A→C                               | Leu→Trp                             |
| 1076084   | SNP        | ChuG_1117        | Aminoglycoside N-6′ acetytransferase           | G→A                               | Ala→Val                             |
| 1164183   | SNP        | ChuG_1199        | Ribosomal-protein-51β-alanine acetyltransferase | T→C                               | Asn→Asp                             |
| 1199449   | SNP        | ChuG_1231        | Response regulator                             | A→C                               | Val→Gly                             |
| 1292064   | SNP        | ChuG_1336        | NAD-dependent epimerase/dehydroxytransferase   | G→T                               | Thr→Lys                             |
| 1314367   | SNP        | ChuG_1357        | GTP cyclohydrolase II                          | T→G                               | Glu→Ala                             |
| 1349656   | SNP        | ChuG_1395        | ATP-dependent DNA helicase Rec G               | G→T                               | Ser→Arg                             |
| 1615472   | SNP        | ChuG_1668        | Membrane alamine aminopeptidase                | A→G                               | Leu→Pro                             |
| 1662811   | SNP        | ChuG_1713        | Hypothetical protein                            | T→C                               | Phe→Xaa                             |
| 1790891   | SNP        | ChuG_1860        | Type 4 pil biogenesis protein (nucleotide-binding protein) | G→A                               | Glu→Lys                             |
| 1802885   | SNP        | ChuG_1874        | UDP-3-O-[3-hydroxymyristoyl] N-acetylglucosamine desacetylase | C→T                               | Gln→Glu                             |
| 1807467   | SNP        | ChuG_1879        | UDP-N-acetylenylpyruvoylglucosamine reductase   | T→G                               | Asn→His                             |
| 1899207   | SNP        | ChuG_1975        | Multidrug resistance protein D                 | G→T                               | Glu→Cys                             |
| 1902387   | SNP        | ChuG_1983        | Carboxylesterase                               | T→G                               | Ser→Ala                             |
| 1903042   | SNP        | ChuG_1985        | Organic solvent tolerance protein              | A→C                               | Thr→Cys                             |
| 1906869   | SNP        | ChuG_1985        | Organic solvent tolerance protein              | A→C                               | Glu→Asp                             |
| 1907022   | SNP        | ChuG_1987        | PepDyl-d-prolyl cis-trans isomerase            | G→A                               | Val→Ile                             |
| 1910250   | SNP        | ChuG_1990        | Universal stress protein A                     | G→A                               | Ala→Thr                             |
| 1933346   | SNP        | ChuG_2020        | ATP-dependent endopeptidase hsl proteolytic subunit | C→G                               | Phe→Leu                             |
| 1934809   | SNP        | ChuG_2021        | ATP-dependent endopeptidase hsl ATP-binding subunit | T→C                               | Met→Thr                             |
| 118600    | Insertion  | ChuG_1215        | CoA-transferase family III protein             | TG→GG                            | inc-HIS                             |
| 479266    | Deletion   | ChuG_0513        | NADH quinone oxidoreductase subunit L          | G→A                               | DEL5aa                              |
| 491265    | Deletion   | ChuG_0526        | Hypothetical protein                            | T→A                               | DEL1aa                              |

*Position in C. burnetii Cbu_Q212.

Nucleotide Sequence Accession Numbers

Strain Dog Utad has been deposited in GenBank under the project accession number PRJEB4294. The version described in this article is the first version, PRJEB4294.

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Conflict of Interest

None declared.

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