

High-Quality Draft Genome Sequence of *Babesia divergens*, the Etiological Agent of Cattle and Human Babesiosis

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***Babesia divergens* causes significant morbidity and mortality in cattle and splenectomized or immunocompromised individuals. Here, we present a 10.7-Mb high-quality draft genome of this parasite close to chromosome resolution that will enable comparative genome analyses and synteny studies among related parasites.**

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Babesia divergens is a tick-borne, intraerythrocytic apicomplexan parasite that causes severe hemolytic anemia in cattle and recently has become a significant zoonotic human pathogen (1). Infection by blood transfusion is possible as well, as the infected erythrocytes are optimum vehicles for the parasite (2, 3). Erythrocytic invasion is a critical component of the *B. divergens* asexual life cycle, ensuring continual parasite replication in red blood cells (RBCs) (4) and producing a malaria-like disease. Despite the veterinary and zoonotic importance of this parasite, relatively little research has been carried out on *Babesia*, and many questions regarding the parasite's biology remain unanswered. A better understanding of the species' biology and host-parasite interactions may lead to improved control mechanisms and new trends in vaccine and antibabesial drug development. To facilitate these studies, we sequenced the genome of *B. divergens* human isolate (Rouen 1987) combining three different sequencing platforms to produce a high-quality draft genome.

Genomic DNA was isolated (5, 6) from *B. divergens* human RBC cultures (7). The genome was assembled in three stages. First, a total of 34,182,568 reads, representing 310× coverage, produced with the Illumina HiSeq 2000 platform, were assembled using ALLPATHS-LG (8). Second, 829,056 reads, representing a 23× coverage produced by 454, were assembled using Newbler v. 2.8 and adding the Illumina scaffolds as overlapping “fake” Sanger reads. Third, 109,329 PacBio reads from one SMRT cell run (P4/C2 chemistry) were used to close gaps or extend contig ends in the Illumina+454 hybrid assembly using PBjelly (9). Finally, ICORN2 (10) was used for platform-specific base error corrections. The final assembly had 10,797,556 bp in 514 scaffolds, with N_{50}/N_{90} values of 1,084,746/6,917 bp, respectively. The GC content was 40%, similar to other *Babesia* genomes (11, 12). However, the estimated genome size read k-mer content (~11.5 Mbp) exceeded the observed size in other *Babesia* species and in other *B. divergens* strains (~9 Mbp) (11–13). This could be due to a different repeat content (~30%) or small contigs containing genes

with several haplotypes that were not resolved by the assemblers. While this work was in progress, the genomes of *B. divergens* strains (Rouen 1987 and 1802 A strains) were published (12). The Rouen 1987 sequence was reported as a very fragmented assembly with an arbitrary scaffold ordering. In contrast, our assembly contained very large scaffolds where a high number of telomeric repeats are found, indicating reconstruction of almost complete chromosomes. Using CEGMA v. 2.5 (14), we obtained 80% completeness of the genome. Protein-coding genes (3,741) predicted using Augustus (15) and the CEGMA completion level obtained were very similar to those for the recently published *B. divergens* genome (12), although the degree of continuity obtained in our study is superior, as presented in the assembly statistics.

Therefore, the *B. divergens* genome presented here can be used as a reference to study its genome structure in order to understand the regulation of its genes and probe shared synteny with other Apicomplexan species.

Nucleotide sequence accession numbers. This genome shotgun project has been deposited at the European Nucleotide Archive under the accession numbers [CCSG01000001](https://www.ebi.ac.uk/ena/record/CCSG01000001) to [CCSG01000514](https://www.ebi.ac.uk/ena/record/CCSG01000514).

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