Complete genome sequence of the strong mutator Salmonella enterica subsp. enterica serotype Heidelberg strain B182.

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GENOME ANNOUNCEMENT

Complete Genome Sequence of the Strong Mutator *Salmonella enterica* subsp. *enterica* Serotype Heidelberg Strain B182

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In bacteria, normal mutation frequencies are mostly around 10^{-10} per base pair. However, there exists natural isolates, called "mutators," that exhibit permanent mutation occurrences up to 1,000-fold greater than usual. As mutations play essential roles, particularly in the evolution of antibiotic resistance, bacteria showing elevated mutation rates could have an important responsibility in the emergence of antibiotic resistance, especially in the clinical background. In this announcement, we report the first complete genome sequence of the *Salmonella enterica* subsp. *enterica* serotype Heidelberg B182 mutator strain, isolated from bovine feces (France), which consists of a 4,750,465-bp circular chromosome (cB182_4750; GC, 52.2%) and one circular plasmid of 37,581 bp (pB182_37; GC, 42.8%).

Salmonella enterica subsp. *enterica* serotype Heidelberg is a common food-borne pathogen that ranks fourth among the *Salmonella* serotypes isolated from human sources between 1970 and 2009 in the United States (1). During this period, *Salmonella* Heidelberg has been identified as the causative agent in more than 100 outbreaks, which were mostly attributed to consumption of poultry or egg-related food (2). This serotype has been associated with a significantly higher proportion of invasive disease than the well-known *S. enterica* serovar Typhimurium (4), but no serotype-specific virulence factor has yet been identified. However, there are geographical differences since this serotype is not among the 20 most common serotypes in France (3). In 1996, Leclerc et al. (5) detected a high incidence (over 1%) of mutators among pathogenic *Salmonella* and suggested that a high rate of mutation permits rapid adaptation to an unstable environment (5). Within the Heidelberg serotype, only the genome of the strain SL476 (NCBI accession no. NC_011083) has been completely sequenced and annotated to date. The draft genome of strain SL486 (NCBI accession no. NZ_ABEL00000000) is also available as scaffolds. Both SL476 and SL486 are normomutators (rifampin resistance mutation rates of $1 \times 10^{-8} \pm 5.6 \times 10^{-8}$ and $1.9 \times 10^{-8} \pm 1.8 \times 10^{-8}$, respectively, measured as described previously [5]).

Here, we report the complete genome sequence of *Salmonella enterica* subsp. *enterica* serotype Heidelberg strain B182, isolated from bovine feces (departmental veterinary laboratory, Rennes, France). This strain is a strong mutator (rifampin resistance mutation rate of $3.95 \times 10^{-6} \pm 5.6 \times 10^{-6}$) and contains a 12-bp deletion in *mutS*, generating a defective methyl-mismatch repair (MMR) system (6) as is frequently observed in mutator strains (5).

The *Salmonella* Heidelberg B182 genome was sequenced using a Roche/454 pyrosequencing method (Genome Sequencer FLX system with titanium chemistry) at the Functional Genomics and Environmental Platform (Biogenouest, Rennes, France). The assembly of the 436,832 reads, performed using the de Bruijn method (7) and Phrap (http://www.phrap.org/phredphrap/phrap.html), provides 2 circular contigs, one 4,750,465-bp circular chromosome (cB182_4750; GC, 52.2%) and one 37,581-bp circular plasmid (pB182_37; GC, 42.8%).

After assembly, we annotated genes encoding proteins, tRNAs, rRNAs, small noncoding RNAs (ncRNAs), CRISPRs, and genomic islands (insertion sequences [IS], phage, pathogenic islands [PAI]) using an integrated procedure combining numerous tools. This process was manually compared by an expert biocurator against the RAST annotation server results (rast.nmpdr.org/). This annotation resulted, for the chromosome, in 4,287 protein-encoding genes, 86 tRNAs, 22 rRNAs, 143 other ncRNAs, and 51 genomic islands (15 IS, 6 phages, and 30 PAI). The plasmid encompasses 44 protein-encoding genes and three replication origins.

Comparative genome analysis of *Salmonella* Heidelberg strains B182, SL476, and SL486 shows interesting differences that had to be further studied. The three strains differ by both their chromosome and plasmid contents. Further detailed comparative genomics are ongoing to identify factors that might explain the high prevalence of strong mutators among pathogenic strains of *Salmonella* and improve understanding of infections due to *Salmonella enterica* subsp. *enterica* serotype Heidelberg.

Nucleotide sequence accession numbers. The genome sequence of *Salmonella enterica* subsp. *enterica* serotype Heidelberg strain B18 has been deposited in GenBank under accession no. CP003416 for the chromosome and CP003417 for the plasmid.

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