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Genomes of Two Chronological Isolates (*Helicobacter pylori* 2017 and 2018) of the West African *Helicobacter pylori* Strain 908 Obtained from a Single Patient▽

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The diverse clinical outcomes of colonization by *Helicobacter pylori* reflect the need to understand the genomic rearrangements enabling the bacterium to adapt to host niches and exhibit varied colonization/virulence potential. We describe the genome sequences of the two serial isolates, *H. pylori* 2017 and 2018 (the chronological subclones of *H. pylori* 908), cultured in 2003 from the antrum and corpus, respectively, of an African patient who suffered from recrudescent duodenal ulcer disease. When compared with the genome of the parent strain, 908 (isolated from the antrum of the same patient in 1994), the genome sequences revealed genomic alterations relevant to virulence optimization or host-specific adaptation.

The high genetic variability of *Helicobacter pylori* (1–4) points to its capacity toward adaptive evolution (6, 9, 12, 16, 17). DNA profiling reveals minor differences in clinical or related strains, suggestive of microevolution (5, 18, 19, 22, 25, 28), although such methods do not explain the underlying rearrangements. Multiple genome sequences of *H. pylori* better explain its lifestyle and evolution (7, 11, 15, 21, 24, 27). However, chronological isolates, especially those obtained from single patients (18, 19, 25) or single families (28), have not been sequenced.

H. pylori isolates 2017 and 2018 represent chronological subclones of strain 908 recovered after a decade of the original isolation of the parent strain from a West African duodenal ulcer disease patient in France (8, 25). Recently, strain 908 was completely sequenced by our group (15). Herein, we report full genome sequences of the subsequent isolates, 2017 and 2018.

Genomes were determined by Illumina Genome Analyzer (GA2x, pipeline version l.6) and comprised of sequence reads equivalent to 60 Mb for each isolate, encompassing 101-bp paired-end reads with an insert size of 300 bp, and the genome coverage achieved was 50X (15). The sequence reads were assembled using Velvet (29) with the hash length set to 21 (15). In view of the phylogenetic relatedness of 908 to *H. pylori* J99 (8, 15), the assembled contigs were ordered with respect to the best-aligned positions when compared to the genome of reference strain J99 using BLAT (20). The genomes were annotated with the help of the RAST server (10), and putative coding sequences (CDSs) were identified by comparing outputs from Glimmer (14), Genemark (13), and EasyGene (23). Finally, manual curation was carried out. Artemis (26) was used to glean the following details of the two genomes.

The sizes of the 2017 and 2018 draft genomes were 1,548,238 and 1,562,832 bp, respectively, with G+C contents of 39.3 and 39.29%, respectively. The genomes of 2017 and 2018 revealed coding percentages of 91.5 and 91.6, respectively, and contained 1,593 and 1,603 protein coding sequences, respectively, with average lengths of 894 and 896 bp, respectively. Each of the genomes had 36 tRNA and 3 rRNA genes, and a few pseudogenes and putative phagelike products were identified. Both the genomes displayed a conserved repertoire of housekeeping genes corresponding to various metabolic pathways, a largely intact *cag*PAI, the genomic island *tfs3*, and virulence-associated alleles of *vacA*, as also described earlier (25), and revealed the presence of several plasticity zone open reading frames (ORFs) and putative virulence factors. Comparative genomic analysis of the 2017 and 2018 genomes revealed that they are almost identical and descended from that of strain 908 (15).

In conclusion, the genome sequences prove the clonal origin of the three isolates (908, 2017, and 2018) and thus reinforce our stance that the patient under study did in fact harbor only a single strain which survived eradication therapy (25) and that the subclones, 2017 and 2018, did not represent exogenous reinfection by a new source.

Nucleotide sequence accession numbers. The genome sequences for 2017 and 2018 are deposited in GenBank under accession numbers CP002571 and CP002572, respectively.

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