

Genome Sequence of the Lantibiotic Bacteriocin Producer Streptococcus salivarius Strain K12

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Streptococcus salivarius is a prevalent commensal species of the oropharyngeal tract. *S. salivarius* strain K12 is an isolate from the saliva of a healthy child, used as an oral probiotic. Here, we report its genome sequence, i.e., the full sequence of the 190-kb megaplasmid pSsal-K12 and a high-quality draft 2.2-Gb chromosomal sequence.

S*treptococcus salivarius* is an early colonizer of the human oral cavity and remains a prominent member of the oropharyngeal tract of "healthy" humans (13). *S. salivarius* is a heterogeneous species, and rare cases of strains associated with human infections have been reported (4, 16). Some commensal strains of *S. salivarius* are also used as probiotics for oral and upper respiratory tract health (9, 17, 18), since they are producers of a particularly diverse range of lantibiotic bacteriocins with a broad spectrum against several streptococcal pathogens (18).

Streptococcus salivarius strain K12 (Blis Technologies Ltd.) was isolated from the saliva of a healthy child (repository reference ATCC BAA-1024). It was reported to be a colonizer of the oral mucosa of infants and adults (11, 15), to be effective against halitosis (1), and to downregulate the innate immune responses of human epithelial cells (5). Its safety and human tolerance were also assessed (2, 3), and it received self-affirmed generally recognized as safe (GRAS) status from the United States Food and Drug Administration in 2011. Here, we make available its genome sequence, i.e., the full sequence of the megaplasmid coding for two salivaricins (12) and a high-quality draft chromosomal sequence.

The genome sequence of *S. salivarius* strain K12 was determined using the 454 GS-FLX sequencer (Roche Diagnostics) and Solexa HiSeq (Illumina, Inc.). The chromosome reads were assembled into 95 contigs with Newbler (14), providing 44-fold coverage. Contigs were aligned with the complete genome sequence of *S. salivarius* strain JIM8777 (8) using the mummer package (6). Gaps were closed by PCR, followed by Sanger sequencing of the products and primer walking. The K12 chromosome sequence currently comprises six contigs. The remaining genomic gaps contain copies of highly repetitive serine-rich motifs of putative transmembrane proteins. The estimated length of the chromosome is 2,241,913 bp, with a GC content of 38.9%. The length of the plasmid is 185,045 bp, with a GC content of 34.4%.

Automated annotation carried out by IG Assets using a proprietary pipeline revealed 6 rRNA operons and 57 tRNA genes. It indicated 2,089 protein-coding sequences (CDS) on the chromosome, of which 1,710 (82%) were annotated with known biological functions and 379 (18%) encode hypothetical proteins. The megaplasmid pSsal-K12 contains 164 CDS, of which 69 (42%) were annotated with known biological functions and 95 (68%) encode hypothetical proteins.

Comparative genomics within *S. salivarius* showed that out of 2,089 genes predicted on the chromosome of K12, 1,801, 1,777, and 1,760 align with the genome of the commensals JIM8777 (8) and M18 (10) and the clinical isolate CCHSS3 (7), respectively.

Comparative analysis of pSsal-K12 and the only previously characterized *S. salivarius* megaplasmid, pSsal-M18, isolated from the probiotic strain M18 (10), revealed 54% alignment of the predicted genes. The high-quality draft genome sequence of this probiotic *S. salivarius* strain will contribute to our understanding of the role of this species in the oropharyngeal ecology of human health.

Nucleotide sequence accession numbers. This whole-genome project has been deposited at DDBJ/EMBL/GenBank under the accession number ALIF000000000. The version described in this paper is the first version, ALIF01000000.

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