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Genome of *Streptococcus oralis* Strain Uo5▽

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***Streptococcus oralis*, a commensal species of the human oral cavity, belongs to the Mitis group of streptococci, which includes one of the major human pathogens as well, *S. pneumoniae*. We report here the first complete genome sequence of this species. *S. oralis* Uo5, a high-level penicillin- and multiple-antibiotic-resistant isolate from Hungary, is competent for genetic transformation under laboratory conditions. Comparative and functional genomics of Uo5 will be important in understanding the evolution of pathogenesis among Mitis streptococci and their potential to engage in interspecies gene transfer.**

The Mitis phylogenetic group of streptococci consists of members of the commensal flora of the upper respiratory tract of humans (1, 2, 9). It includes *Streptococcus pneumoniae*, one of the major human pathogens and resident in the nasopharynx, and its closest relatives, *S. mitis* and *S. oralis*. A detailed *in silico* comparison of the *S. mitis* B6 genome with six *S. pneumoniae* genomes supported the suggestion that *S. pneumoniae* is a specialized *S. mitis* clone (3), whereas *S. oralis* is a well-separated group consisting of many unrelated lineages (1, 2, 9).

Species that belong to the Mitis group are naturally competent for genetic transformation (8). Gene transfer events between different species can be recognized by the mosaic structure of gene sequences such as those for penicillin-binding proteins (PBPs) (4). However, estimations of the extent of interspecies gene transfer on the genomic scale are limited since mainly *S. pneumoniae* genomes are available (currently 23; http://www.ncbi.nlm.nih.gov/genomes/lproks.cgi), with only one finished *S. mitis* genome (3).

S. oralis Uo5 (Hu5 [13] or Hu-o5 [7]) has been chosen since it had been specified to be *S. oralis* by comparative genomic hybridization (7) and multilocus sequence typing (2). It is a high-level penicillin- and multiple-antibiotic-resistant strain isolated in Hungary in the early 1980s (13), a phenotype which is also prevalent among the main *S. pneumoniae* clone from Hungary, Hu19A^{-6} (12, 14). Moreover, it is naturally transformable and thus is susceptible to genetic manipulation.

The Uo5 genome was sequenced using a combination of Roche GS-FLX (Roche Diagnostics, Basel, Switzerland) (11) and Solexa (Illumina GA IIx, Illumina, CA) paired-end sequencing technologies. Library preparation, sequencing reaction, and the sequencing run were carried out according to Illumina's instructions. The *S. mitis* B6 genome was used as a reference genome for the alignment of contigs (3). Gap closures were performed by combinatorial PCR and Sanger sequencing of the PCR products using an ABI 3100 capillary sequencer.

Annotation was performed using the Glimmer (15), tRNAscan-SE (10), and Rfam (6) software programs and software predicting transcriptional terminators (5) and finalized by manual review as described for the *S. mitis* B6 genome (3). The Uo5 chromosome is 1,958,690 bp in length, which is smaller than the *S. pneumoniae* and *S. mitis* B6 genomes, and has a G+C content of 41.14% and a coding percentage of 89.7. There are 1,909 predicted protein coding sequences (CDSs), with an average length of 921 bp, 61 tRNAs, 4 rRNA loci, and another 9 RNA coding genes. Similar to the *S. mitis* B6 genome, that of Uo5 shows a striking X alignment compared to *S. pneumoniae* genomes.

Only the main pneumococcal pathogenicity factors are missing in *S. oralis* Uo5, similar to the case with *S. mitis* B6 (3). It contains genetic islands and antibiotic resistance determinants that are representatives of the accessory genome of *S. pneumoniae* and/or other streptococcal species and which are likely to be capable in modulation of the virulence potential. The availability of the first finished *S. oralis* genome will be helpful for comparative genomics to understand host interaction and pathogenicity within the Mitis group of streptococci.

Nucleotide sequence accession number. The complete genome sequence has been deposited in the EMBL database under accession no. FR720602.

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REFERENCES

1. **Bishop, C. J., et al.** 2009. Assigning strains to bacterial species via the internet. BMC Biol. **7:**3.
2. **Chi, F., O. Nolte, C. Bergmann, M. Ip, and R. Hakenbeck.** 2007. Crossing the barrier: evolution and spread of a major class of mosaic *pbp2x* in *S. pneumoniae*, *S. mitis* and *S. oralis*. Int. J. Med. Microbiol. **297:**503–512.

3. **Denapaite, D., et al.** 2010. The genome of *Streptococcus mitis* B6—what is a commensal? PLoS One **5:**e9426.
4. **Denapaite, D., F. Chi, P. Maurer, O. Nolte, and R. Hakenbeck.** 2007. Mechanism of penicillin resistance in *Streptococcus pneumoniae*: targets, gene transfer, and mutations, p. 290–303. *In* R. Hakenbeck and G. S. Chhatwal (ed.), Molecular biology of streptococci. Horizon Bioscience, Wymondham, United Kingdom.
5. **Ermolaeva, M. D., H. G. Khalak, O. White, H. O. Smith, and S. L. Salzberg.** 2000. Prediction of transcription terminators in bacterial genomes. J. Mol. Biol. **301:**27–33.
6. **Griffiths-Jones, S., et al.** 2005. Rfam: annotating non-coding RNAs in complete genomes. Nucleic Acids Res. **33:**D121–D124.
7. **Hakenbeck, R., et al.** 2001. Mosaic genes and mosaic chromosomes: intra- and interspecies variation of *Streptococcus pneumoniae*. Infect. Immun. **69:** 2477–2486.
8. **Johnsborg, O., V. Eldholm, and L. S. Havarstein.** 2007. Natural genetic transformation: prevalence, mechanisms and function. Res. Microbiol. **158:** 767–778.
9. **Kilian, M., et al.** 2008. Evolution of *Streptococcus pneumoniae* and its close commensal relatives. PLoS One **3:**e2683.
10. **Lowe, T. M., and S. R. Eddy.** 1997. tRNAscan-SE: a program for improved detection of transfer RNA genes in genomic sequence. Nucleic Acids Res. **25:**955–964.
11. **Margulies, M., et al.** 2005. Genome sequencing in microfabricated high-density picolitre reactors. Nature **437:**376–380.
12. **Marton, A.** 1995. Epidemiology of resistant pneumococci in Hungary. Microb. Drug Resist. **1:**127–130.
13. **Reichmann, P., et al.** 1997. A global gene pool for high-level cephalosporin resistance in commensal *Streptococcus* spp. and *Streptococcus pneumoniae.* J. Infect. Dis. **176:**1001–1012.
14. **Reichmann, P., et al.** 1995. Penicillin-resistant *Streptococcus pneumoniae* in Germany: genetic relationship to clones from other European countries. J. Med. Microbiol. **43:**377–385.
15. **Salzberg, S. L., A. L. Delcher, S. Kasif, and O. White.** 1998. Microbial gene identification using interpolated Markov models. Nucleic Acids Res. **26:**544–548.