

Draft Genome Sequence of *Streptomyces globisporus* C-1027, Which Produces an Antitumor Antibiotic Consisting of a Nine-Membered Enediyne with a Chromoprotein

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Streptomyces globisporus C-1027 is the producer of antitumor antibiotic C-1027, a nine-membered enediyne-containing compound. Here we present a draft genome sequence of *S. globisporus* C-1027 containing the intact biosynthetic gene cluster for this antibiotic. The genome also carries numerous sets of genes for the biosynthesis of diverse secondary metabolites.

S*treptomyces globisporus* C-1027, isolated from a soil sample collected in the Qian-jiang area of China (2), produces an extremely potent antitumor antibiotic, C-1027. As a member of enediyne family, C-1027 is currently undergoing phase II clinical trial in China (8). Here, we present a draft genome sequence of S. globisporus C-1027.

The nucleotide sequencing was performed by BGI (Shenzhen, China) using an illumina/GA sequencer. Short reads were assembled by SOAP *de novo* (3), and protein coding sequences (CDSs) were predicted by Glimmer, version 3.0 (1). Gene functional annotation was based on BLASTP results determined with the KEGG, COG, Swiss-Prot, NT, and NR databases. tRNA genes were predicted with tRNAscan-SE (7), and rRNA sequences were found by alignment with an rRNA pool.

A total of 1,242.47 Mb of data were generated, which represented 169.37-fold coverage of the genome. The draft genome sequence of S. globisporus C-1027 contains 7,693,617 bp with a GC content of 71.63% distributed over 84 scaffolds containing 278 contigs. We identified 7,231 putative protein CDSs, accounting for 88.22% of the genome, as well as 56 tRNA genes and five rRNA operons in our draft genome. The intact biosynthetic gene cluster for C-1027, which had been cloned and sequenced previously (4), was located on scaffold 34, with 99% identity to the sequence of the reported C-1027 biosynthetic genes. In addition, scaffold 34 disclosed a further 6,264 bp upstream of the C-1027 gene cluster in which a pair of genes composing a primase/helicase-like gene and a putative replication initiation gene were predicted. Together with three other pairs of these genes previously annotated adjacent to the C-1027 gene cluster, there are a total of four pairs of genes involved in the linear plasmid replication. The coding proteins of these genes are highly homologous to the plasmid-type DNA primase/replication proteins of plasmid pSLA2-L from S. rochei (5) and plasmid SCP1 from S. coelicolor (6), suggesting that the biosynthetic gene cluster of C-1027 is possibly located on a giant linear plasmid at least 92 kb in length. Genome analysis also revealed a number of genes related to biosynthesis of diverse secondary metabolites besides C-1027, including putative nonribosomal peptide synthetase (NRPS) genes, polyketide synthase (PKS) genes, NRPS-PKS hybrid genes, terpene cyclase genes, and genes for lantibiotic biosynthesis. The genome sequence of S. globisporus C-1027 will aid our further analysis and understanding of C-1027 biosynthesis-regulatory mechanisms and discovery of new natural products by uncovering cryptic metabolic pathways.

Nucleotide sequence accession numbers. This whole-genome shotgun project has been deposited at DDBJ/EMBL/GenBank under accession no. AJUO00000000. The version described in this paper is the first version, deposited under AJUO01000000.

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REFERENCES

- Delcher AL, Bratke KA, Powers EC, Salzberg SL. 2007. Identifying bacterial genes and endosymbiont DNA with Glimmer. Bioinformatics 23: 673–679.
- Hu JL, et al. 1988. A new macromolecular antitumor antibiotic, C-1027. I. Discovery, taxonomy of producing organism, fermentation and biological activity. J. Antibiot. (Tokyo) 41:1575–1579.
- 3. Li R, et al. 2010. De novo assembly of human genomes with massively parallel short read sequencing. Genome Res. 20:265–272.
- Liu W, Shen B. 2000. Genes for production of the enediyne antitumor antibiotic C-1027 in *Streptomyces globisporus* are clustered with the *cagA* gene that encodes the C-1027 apoprotein. Antimicrob. Agents Chemother. 44:382–392.
- Mochizuki S, et al. 2003. The large linear plasmid pSLA2-L of *Streptomyces rochei* has an unusually condensed gene organization for secondary metabolism. Mol. Microbiol. 48:1501–1510.
- Redenbach M, Bibb M, Gust B, Seitz B, Spychaj A. 1999. The linear plasmid SCP1 of *Streptomyces coelicolor* A3(2) possesses a centrally located replication origin and shows significant homology to the transposon Tn4811. Plasmid 42:174–185.
- 7. Schattner P, Brooks AN, Lowe TM. 2005. The tRNAscan-SE, snoscan and snoGPS web servers for the detection of tRNAs and snoRNAs. Nucleic Acids Res. 33:W686–W689.
- Shao RG, Zhen YS. 2008. Enediyne anticancer antibiotic lidamycin: chemistry, biology and pharmacology. Anticancer Agents Med. Chem. 8:123– 131.

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