

# Draft Genome Sequence of the Oxytetracycline-Producing Bacterium *Streptomyces rimosus* ATCC 10970

Florence E. Pethick,<sup>a</sup> Alison C. MacFadyen,<sup>a</sup> Zhenyu Tang,<sup>a,b</sup> Vartul Sangal,<sup>a</sup> Tze-Tze Liu,<sup>c</sup> Ju Chu,<sup>b</sup> Gregor Kosec,<sup>d</sup> Hrvoje Petkovic,<sup>d</sup> Meijin Guo,<sup>b</sup> Ralph Kirby,<sup>e</sup> Paul A. Hoskisson,<sup>a</sup> Paul R. Herron,<sup>a</sup> Iain S. Hunter<sup>a</sup>

Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, United Kingdom<sup>a</sup>; State Key Laboratory of Bioreactor Engineering, East China University of Science and Technology, Shanghai, China<sup>b</sup>; Genome Research Center, National Yang-Ming University, Taipei, Taiwan<sup>c</sup>; Acies Bio, Ltd., Ljubljana, Slovenia<sup>d</sup>; Department of Life Sciences, Institute of Genome Science, National Yang-Ming University, Taipei, Taiwan<sup>e</sup>

**We report the draft genome of *Streptomyces rimosus* (ATCC 10970), a soil isolate that produces oxytetracycline, a commercially important and clinically useful antibiotic.**

Received 28 January 2013 Accepted 6 February 2013 Published 7 March 2013

**Citation** Pethick FE, MacFadyen AC, Tang Z, Sangal V, Liu T-T, Chu J, Kosec G, Petkovic H, Guo M, Kirby R, Hoskisson PA, Herron PR, Hunter IS. 2013. Draft genome sequence of the oxytetracycline-producing bacterium *Streptomyces rimosus* ATCC 10970. *Genome Announc.* 1(2):e00063-13. doi:10.1128/genomeA.00063-13.

**Copyright** © 2013 Pethick et al. This is an open-access article distributed under the terms of the [Creative Commons Attribution 3.0 Unported license](http://creativecommons.org/licenses/by/3.0/).

Address correspondence to Iain S. Hunter, i.s.hunter@strath.ac.uk.

*Streptomyces rimosus* is a Gram-positive, aerobic, filamentous actinobacterium. It was reported in 1950 and was patented (1) as the founder strain for the production of the antibiotic oxytetracycline (OTC) (2). Recombination was recognized (3) and a rudimentary genetic map was deduced (4). The pharmaceutical industry set out to improve the commercial productivity of OTC, deriving higher-titer genealogies that led to the contemporary industrial strains that are now responsible for the production of >10<sup>8</sup> kg of OTC annually. Stimulated by commercial interest over the years, a sophisticated genetics and molecular biology has been developed for *S. rimosus* (5). This announcement reports the derivation of data to enable the generation of a scaffold genome sequence for this important industrial species.

Genome sequencing of the *S. rimosus* type strain ATCC 10970 was carried out using a whole-genome shotgun sequencing approach performed on a Roche 454 GS Junior apparatus. Using three single-ended runs, we obtained 440,253 reads. The reads were assembled using Genome Sequencer *de novo* Assembler (version 2.7, Roche), which led to a final assembly of 453 contigs of >500 bp. The total size of the assembly was 9.5 Mbp, with a mean contig size of 21 kbp (average, 17× coverage) and a G+C content of 71.88%. Automatic functional annotation results were obtained using the NCBI Prokaryotic Genome Annotation Pipeline (<http://www.ncbi.nlm.nih.gov/genomes/static/Pipeline.html>).

The draft genome of *S. rimosus* is estimated to have a total of 8,416 protein-coding genes, along with 66 tRNAs. The overall genome size is consistent with the physical map of *S. rimosus*, derived by pulsed-field gel electrophoresis (6). It is also within the range of other published streptomycete genome sequences. Three gene clusters associated with the production of previously reported secondary metabolites [OTC (7), rimocidin (8), and desferrioxamine C (9)] are readily identified within the sequence, in addition to around 45 other putative secondary metabolite biosynthetic clusters whose functions remain to be elucidated (10). The strain is lysogenic for phages RP2 and RP3, with the DNA sequences corresponding to the restriction maps published previously (11). The genome sequence is also likely to include at least

one giant (387 kb) linear plasmid known to be present in *S. rimosus* (12).

Sequencing of *S. rimosus* ATCC 10970 provides a scaffold from which to investigate and understand how mutation results in higher titers of OTC.

**Nucleotide sequence accession numbers.** The *S. rimosus* ATCC 10970 Whole Genome Shotgun project has been deposited at DDBJ/EMBL/GenBank under the accession no. [ANSJ000000000](https://www.ncbi.nlm.nih.gov/nuccore/ANSJ000000000). The version described in this paper is the first version, [ANSJ010000000](https://www.ncbi.nlm.nih.gov/nuccore/ANSJ010000000).

## ACKNOWLEDGMENTS

We acknowledge financial support from the National Yang-Ming University, Taiwan, for the sequencing project (R.K.), a British Council for Research Projects Network grant (P.A.H. and H.P.), and the British Council/CUC for a Scotland-China Higher Education Research Partnership for PhD Studies (Z.T.).

## REFERENCES

1. Sobin BA, Finlay AC. 1950. Terramycin and its production. US patent 2,516,080.
2. Finlay AC, Hobby GL, P'an SY, Regna PP, Routien JB, Seeley DB, Shull GM, Sobin BA, Solomons IA, Vinson JW, Kane JH. 1950. Terramycin, a new antibiotic. *Science* 111:85.
3. Alikhanian SI, Mindlin SZ. 1957. Recombinations in *Streptomyces rimosus*. *Nature* 180:1208–1209.
4. Friend EJ, Hopwood DA. 1971. The linkage map of *Streptomyces rimosus*. *J. Gen. Microbiol.* 68:187–197.
5. Petković H, Cullum J, Hranueli D, Hunter IS, Perić-Concha N, Pigac J, Thamchaipenet A, Vujaklija D, Long PF. 2006. Genetics of *Streptomyces rimosus*, the oxytetracycline producer. *Microbiol. Mol. Biol. Rev.* 70:704–728.
6. Pandza K, Pfalzer G, Cullum J, Hranueli D. 1997. Physical mapping shows that the unstable oxytetracycline gene cluster of *Streptomyces rimosus* lies close to one end of the linear chromosome. *Microbiology* 143:1493–1501.
7. Zhang W, Ames BD, Tsai SC, Tang Y. 2006. Engineered biosynthesis of a novel amidated polyketide, using the malonamyl-specific initiation module from the oxytetracycline polyketide synthase. *Appl. Environ. Microbiol.* 72:2573–2580.
8. Seco EM, Perez-Zuniga FJ, Rolon MS, Malpartida F. 2004. Starter unit

- choice determines the production of two tetraene macrolides, rimocidin and CE-108, in *Streptomyces diastaticus* var. Chem. Biol. 11:357–366.
9. Barona-Gómez F, Wong U, Giannakopoulos AE, Derrick PJ, Challis GL. 2004. Identification of a cluster of genes that directs desferrioxamine biosynthesis in *Streptomyces coelicolor* M145. J. Am. Chem. Soc. 126: 16282–16283.
  10. Medema MH, Blin K, Cimermancic P, de Jager V, Zakrzewski P, Fischbach MA, Weber T, Takano E, Breitling R. 2011. antiSMASH: rapid identification, annotation and analysis of secondary metabolite biosynthesis gene clusters. Nucleic Acids Res. 29:W339–W346.
  11. Rausch H, Vesligaj M, Pocta D, Biuković G, Pigac J, Cullum J, Schmieger H, Hranueli D. 1993. The temperate phages RP2 and RP3 of *Streptomyces rimosus*. J. Gen. Microbiol. 139:2517–2524.
  12. Gravius B, Glocker D, Pigac J, Pandza K, Hranueli D, Cullum J. 1994. The 387 kb linear plasmid pPZG101 of *Streptomyces rimosus* and its interactions with the chromosome. Microbiology 140:2271–2277.