

Draft Genome Sequence of an Extensively Drug-Resistant *Mycobacterium tuberculosis* Clinical Isolate of the Ural Strain OSDD493

Shamsudheen Karuthedath Vellarikkal,^a Ajay Vir Singh,^c Pravin Kumar Singh,^c Parul Garg,^c Viswa Mohan Katoch,^c Kiran Katoch,^c Open Source Drug Discovery Consortium,^d D. S. Chauhan,^c Vinod Scaria,^b Sridhar Sivasubbu^a

Genomics and Molecular Medicine, CSIR Institute of Genomics and Integrative Biology, Delhi, India^a; GN Ramachandran Knowledge Center for Genome Informatics, CSIR Institute of Genomics and Integrative Biology, Delhi, India^b; National JALMA Institute of Leprosy and Other Mycobacterial Diseases, Tajganj, Agra, India^c; CSIR Open Source Drug Discovery Unit, Anusandhan Bhavan, New Delhi, India^d

We describe the genome sequencing and analysis of a clinical isolate of *Mycobacterium tuberculosis* belonging to the Ural strain OSDD493 from India.

Received 2 October 2013 Accepted 4 October 2013 Published 7 November 2013

Citation Karuthedath Vellarikkal S, Vir Singh A, Kumar Singh P, Garg P, Mohan Katoch V, Katoch K, Open Source Drug Discovery Consortium, Chauhan DS, Scaria V, Sivasubbu S. 2013. Draft genome sequence of an extensively drug-resistant *Mycobacterium tuberculosis* clinical isolate of the Ural strain OSDD493. *Genome Announc*. 1(6):e00928-13. doi: 10.1128/genomeA.00928-13.

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

Address correspondence to Sridhar Sivasubbu, s.sivasubbu@igib.res.in, or Vinod Scaria, vinods@igib.res.in.

Tuberculosis is caused by a closely related group of pathogenic organisms known as the *Mycobacterium tuberculosis* complex. Distinct lineages of *Mycobacterium tuberculosis* have been reported and have been characterized and classified based on spoligotype patterns. The six major distinct lineages are the Indo-Oceanic (EAI), East Asian (Beijing), East African-Indian (CAS), Euro-American (Haarlem, LAM, T, X), West African I (AFRI1), and West African lineage II (AFRI2) lineages (1). The Ural spoligotype was initially identified from the Ural region in Russia, which has one of the highest incidences of tuberculosis in the country. Nevertheless, the Ural spoligotype forms a minority of genotypes of *M. tuberculosis* strains isolated from this region (2). The genotype has also been reported from across Eurasia and Central Asia and forms a significant proportion of genotypes observed in some of these regions. The Ural genotype is thought to be associated with significantly low transmissibility, pathogenicity, and frequency of drug resistance (3, 4).

Understanding the genome sequence of the Ural strain of *Mycobacterium tuberculosis* would provide immense insights into the genomic architecture associated with low pathogenicity. In this paper, we describe the draft genome sequence of an extensively drug-resistant clinical isolate of *Mycobacterium tuberculosis* conforming to a novel spoligotype clustering within the Ural spoligotype. The clinical isolate OSDD493 was obtained from the strain repository maintained at the National JALMA Institute of Leprosy and other Mycobacterial Diseases, which is part of the Open Source Drug Discovery Open Access Repository. Spoligotyping was performed and drug sensitivity was evaluated per standard protocols (5–7). Drug sensitivity analysis revealed the isolate to be resistant to streptomycin, rifampin, isoniazid, ethambutol, ofloxacin, kanamycin, and ethionamide and sensitive to amikacin, pyrazinamide, capreomycin, cycloserine, and *para*-aminosalicylate sodium (PAS). DNA was isolated per standard protocols. The raw sequence data were generated after library preparation on Ion Torrent PGM according to protocols recommended by the manufacturers. Draft genomes were assembled de novo using

CLC Genomics Workbench 6. The assembly resulted in 193 contigs at N_{50} values of 42,650 bp and a total assembly of 4,227,747 bp. Further, automated gene prediction on the draft genomes was performed using the RAST server (8). Analysis revealed 4,223 genes, including 42 RNA genes.

Nucleotide sequence accession numbers. This whole-genome shotgun project has been deposited at DDBJ/EMBL/GenBank under the accession number [AVQJ00000000](https://www.ncbi.nlm.nih.gov/nuccore/AVQJ00000000). The version described in this paper is version AVQJ01000000.

ACKNOWLEDGMENTS

We thank Swati Subodh (TCGA) and Nupur Mehrotra (Premas Biotech) for scientific discussions and help in maintaining the strains. We also acknowledge S. Ramachandran for valuable input.

The project was funded by CSIR India through the Open Source Drug Discovery Programme (HCP001). The sequencing facility is supported through grants SIP006 and FAC002 from CSIR, India, and the computational analysis was performed at the CSIR Center for *In Silico* Biology at CSIR-IGIB.

REFERENCES

1. Brudey K, Driscoll JR, Rigouts L, Prodinger WM, Gori A, Al-Hajj SA, Allix C, Aristimuño L, Arora J, Baumanis V, Binder L, Cafrune P, Cataldi A, Cheong S, Diel R, Ellermeier C, Evans JT, Fauville-Dufaux M, Ferdinand S, Garcia de Viedma D, Garzelli C, Gazzola L, Gomes HM, Guttierrez MC, Hawkey PM, van Helden PD, Kadival GV, Kreiswirth BN, Kremer K, Kubin M, Kulkarni SP, Liens B, Lillebaek T, Ho ML, Martin C, Martin C, Mokrousov I, Narvskaia O, Ngeow YF, Naumann L, Niemann S, Parwati I, Rahim Z, Rasolof-Razanamparany V, Rasolonalonana T, Rossetti ML, Rüsche-Gerdes S, Sajduda A, Samper S, Shemyakin IG, Singh UB, Somoskovi A, Skuce RA, van Soolingen D, Streicher EM, Suffys PN, Tortoli E, Tracevska T, Vincent V, Victor TC, Warren RM, Yap SF, Zaman K, Portaels F, Rastogi N, Sola C. 2006. *Mycobacterium tuberculosis* complex genetic diversity: mining the fourth international spoligotyping database (SpolDB4) for classification, population genetics and epidemiology. *BMC Microbiol*. 6:23.
2. Kovalev SY, Kamaev EY, Kravchenko MA, Kurepina NE, Skorniakov SN.

2005. Genetic analysis of *Mycobacterium tuberculosis* strains isolated in Ural region, Russian Federation, by MIRU-VNTR genotyping. *Int. J. Tuberc. Lung Dis.* 9:746–752.
3. Mokrousov I. 2012. The quiet and controversial: Ural family of *Mycobacterium tuberculosis*. *Infect. Genet. Evol.* 12:619–629.
 4. Mokrousov I, Vyazovaya A, Otten T, Zhuravlev V, Pavlova E, Tarashevich L, Krishevich V, Vishnevsky B, Narvskaya O. 2012. *Mycobacterium tuberculosis* population in northwestern Russia: an update from Russian-EU/Latvian border region. *PLoS One* 7:e41318.
 5. Kamerbeek J, Schouls L, Kolk A, van Agterveld M, van Soolingen D, Kuijper S, Bunschoten A, Molhuizen H, Shaw R, Goyal M, van Embden J. 1997. Simultaneous detection and strain differentiation of *Mycobacterium tuberculosis* for diagnosis and epidemiology. *J. Clin. Microbiol.* 35:907–914.
 6. National Committee for Clinical Laboratory Standards. 2002. Susceptibility testing of mycobacteria, *Nocardia*, and other aerobic actinomycetes. Tentative standard M24T2, 2nd ed. National Committee for Clinical Laboratory Standards, Wayne, PA.
 7. Canetti G, Fox W, Khomenko A, Mahler HT, Menon NK, Mitchison DA, Rist N, Smelev NA. 1969. Advances in techniques of testing mycobacterial drug sensitivity, and the use of sensitivity tests in tuberculosis control programmes. *Bull. World Health Organ.* 41:21–43.
 8. Aziz RK, Bartels D, Best AA, DeJongh M, Disz T, Edwards RA, Formsma K, Gerdes S, Glass EM, Kubal M, Meyer F, Olsen GJ, Olson R, Osterman AL, Overbeek RA, McNeil LK, Paarmann D, Paczian T, Parrello B, Pusch GD, Reich C, Stevens R, Vassieva O, Vonstein V, Wilke A, Zagnitko O. 2008. The RAST server: rapid annotations using subsystems technology. *BMC Genomics* 9:1471–2164.