Draft Genome Sequences of Three *Mycobacterium chimaera* Respiratory Isolates

Michéal Mac Aogáin,a Emma Roycroft,a,b Philomena Raftery,b Simone Mok,a Margaret Fitzgibbon,b Thomas R. Rogersa,b

Department of Clinical Microbiology, School of Medicine, Trinity College Dublin, St. James’s Hospital, Dublin, Ireland; Irish Mycobacteria Reference Laboratory, LabMed Directorate, St. James’s Hospital, Dublin, Ireland

*Mycobacterium chimaera* is an opportunistic human pathogen implicated in both pulmonary and cardiovascular infections. Here, we report the draft genome sequences of three strains isolated from human respiratory specimens.

Comparative analysis of *M. chimaera* genome assemblies revealed an average nucleotide identity (ANI) of 99.9% between strains, consistent with their assignment to a common species (9). In contrast, a lower ANI of 97.7% was obtained when assemblies were compared to *M. intracellularum*—a closely related yet distinct species of the MAC. The observed ANI values correlate with observed divergence in the 16S *rRNA* gene and ITS regions relative to *M. intracellularum* and lend credence to the use of the 16S RNA gene and ITS sequence analysis to distinguish *M. chimaera* clinically (1, 2, 5).

Analysis of reciprocal BLAST hits among non-pseudogene-coding sequences revealed a set of 4,951 genes common to all three *M. chimaera* isolates (10). Strains MCIMRL2 and MCIMRL6 exhibited a higher degree of similarity to each other than to MCIMRL4, sharing 5,230 genes, whereas MCIMRL4 shared 4,993 and 5,044 genes with MCIMRL2 and MCIMRL6, respectively. MCIMRL4 divergence was also reflected in comparative analysis of the 4,951 common gene sequences; MCIMRL4 diverged from MCIMRL2 and MCIMRL6 by 2,763 and 2,825 “core” single nucleotide variants (SNVs), respectively, whereas only 242 SNVs separated MCIMRL2 and MCIMRL6. Among the common genes shared by all three strains were putative host-interaction factors, including several conserved type-VII secretion systems and multiple PE/PE-GRS-family proteins, which represent important virulence determinants in other pathogenic mycobacteria (11).

This report represents the first whole-genome sequencing study of *M. chimaera*—an emerging opportunistic pathogen of the MAC. The data will serve as a useful reference for *M. chimaera*.  

Table 1: Genomic sequence assembly overview

| Strain | Yr isolated | Specimen type | Total reads | Assembly size | Fold coverage | % G+C | Contigs (≥2 kb) | N₅₀ (bp) | Largest contig (bp) | No. of ORFs | GenBank accession no. |
|--------|-------------|--------------|-------------|---------------|--------------|-------|----------------|----------|---------------------|------------|----------------------|
| MCIMRL2 | 2009 | Sputum | 3,466,168 | 6,087,047 | 50X | 67.7 | 247 | 46,281 | 161,388 | 5,632 | LIHL00000000 |
| MCIMRL4 | 2013 | Sputum | 4,040,276 | 6,020,776 | 77X | 67.7 | 210 | 89,969 | 201,826 | 5,553 | LIHN00000000 |
| MCIMRL6 | 2014 | BALa | 3,334,536 | 6,451,412 | 67X | 67.6 | 150 | 71,588 | 195,331 | 5,983 | LIHN00000000 |

a ORFs, open reading frames.
b Bronchoalveolar lavage.

© 2015 Mac Aogáin et al. This is an open-access article distributed under the terms of the Creative Commons Attribution 3.0 Unported license.

Address correspondence to Michéal Mac Aogáin, m.macaoagain@tcd.ie.

Received 9 October 2015 Accepted 16 October 2015 Published 3 December 2015

Citation Mac Aogáin M, Roycroft E, Raftery P, Mok S, Fitzgibbon M, Rogers TR. 2015. Draft genome sequences of three *Mycobacterium chimaera* respiratory isolates. Genome Announc. 3(6):e01409-15. doi:10.1128/genomeA.01409-15.
genomic epidemiology and provide the first insights into the potential virulence determinants of this pathogen.

**Nucleotide sequence accession numbers.** This whole-genome shotgun project has been deposited at DDBJ/EMBL/GenBank under the accession numbers listed in Table 1.

**ACKNOWLEDGMENTS**

We acknowledge support and funding received from the Clinical Microbiology Department, Trinity College, Dublin, and the Irish Mycobacteria Reference Laboratory and Microbiology Department, LabMed Directorate, St. James’ Hospital, Dublin.

**REFERENCES**

1. Tortoli E, Rindi L, Garcia MJ, Chiaradonna P, Dei R, Garzelli C, Kroppenstedt RM, Lari N, Mattei R, Mariottini A, Mazzarelli G, Murcia MI, Nanetti A, Piccoli P, Scarparo C. 2004. Proposal to elevate the genetic variant MAC-A, included in the *Mycobacterium avium* complex, to species rank as *Mycobacterium chimaera* sp. nov. Int J Syst Evol Microbiol 54:1277–1285. http://dx.doi.org/10.1099/ijs.0.02777-0.

2. Sax H, Bloemberg G, Hasse B, Sommerstein R, Kohler P, Achermann Y, Rössle M, Falk V, Kuster SP, Böttger EC, Weber R. 2015. Prolonged outbreak of *Mycobacterium chimaera* infection after open-chest heart surgery. Clin Infect Dis 61:67–75. http://dx.doi.org/10.1093/cid/civ198.

3. Kohler P, Kuster SP, Bloemberg G, Schulthess B, Frank M, Tanner FC, Rössle M, Böni C, Falk V, Wilhelm MJ, Sommerstein R, Achermann Y, Ten Oever J, Debast SB, Wolfhagen MJHM, Brandon Bravo Bruinsma GJ, Vos MC, Bogers A, Serr A, Beyersdorf F, Sax H, Böttger EC, Weber R, van Ingen J, Wagner D, Hasse B. 2015. Healthcare-associated prosthetic heart valve, aortic vascular graft, and disseminated *Mycobacterium chimaera* infections subsequent to open heart surgery. Eur Heart J [Epub ahead of print.] http://dx.doi.org/10.1093/eurheartj/ehv342.

4. Roth A, Fischer M, Hamid ME, Michalke S, Ludwig W, Mauch H. 1998. Differentiation of phylogenetically related slowly growing mycobacteria based on 16S-23S rRNA gene internal transcribed spacer sequences. J Clin Microbiol 36:139–147.

5. Roth A, Reischl U, Streubel A, Naumann L, Kroppenstedt RM, Habicht M, Fischer M, Mauch H. 2000. Novel diagnostic algorithm for identification of mycobacteria using genus-specific amplification of the 16S-23S rRNA gene spacer and restriction endonucleases. J Clin Microbiol 38:1094–1104.

6. Bolger AM, Lohse M, Usadel B. 2014. Trimomatic: a flexible trimmer for Illumina sequence data. Bioinformatics 30:2114–2120. http://dx.doi.org/10.1093/bioinformatics/btu170.

7. Bankevich A, Nurk S, Antipov D, Gurevich AA, Dvorkin M, Kulikov AS, Lesin VM, Nikolenko SI, Pham S, Prjibelski AD, Pyshkin AV, Sirotkin AV, Vyahhi N, Tesler G, Alekseyev MA, Pevzner PA. 2012. SPAdes: a new genome assembly algorithm and its applications to single-cell sequencing. J Comput Biol 19:455–477. http://dx.doi.org/10.1089/cmb.2012.0021.

8. Assefa S, Keane TM, Otto TD, Newbold C, Berriman M. 2009. ABACAS: algorithm-based automatic contiguation of assembled sequences. Bioinformatics 25:1968–1969. http://dx.doi.org/10.1093/bioinformatics/btp347.

9. Konstantinidis KT, Ramette A, Tiedje JM. 2006. The bacterial species definition in the genomic era. Philos Trans R Soc Lond B Biol Sci 361:1929–1940.

10. Altschul S, Madden TL, Schaffer AA, Zhang J, Zhang Z, Miller W, Lipman DJ. 1997. Gapped BLAST and psi-blast: a new generation of protein database search programs. Nucleic Acids Res 25:3389–3402. http://dx.doi.org/10.1093/nar/25.17.3389.

11. Houben ENG, Korotkov KV, Bitter W. 2014. Take five—type VII secretion systems of mycobacteria. Biochim Biophys Acta 1843:1707–1716. http://dx.doi.org/10.1016/j.bbamcr.2013.11.003.