Species Distribution and Macrolide Susceptibility

of *Mycobacterium fortuitum* Complex Clinical Isolates

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Lee, Seung Heon Lee, Sung Jae Shin, Shannon Kasperbauer, Gwen A. Huitt, Charles L.

Daley, Won-Jung Koh

Species designations

M. fortuitum. Isolates designated as *M. fortuitum* had *rpoB* sequences with 99.0% identity to those of the *M. fortuitum* type strain ATCC 6841 (GenBank accession no. CP014258) and strain CT6 (CP011269); the *hsp65* and 16S rRNA gene sequences of the isolates were 100% identical to those of *M. fortuitum* strain CT6 (CP011269); and the ITS sequences of the isolates showed 99.4% identity with that of *M. fortuitum* strain CT6 (CP011269).

M. peregrinum. Isolates designated as *M. peregrinum* had *rpoB* and 16S rRNA gene sequences that were 100% identical to those of the *M. peregrinum* type strain CIP 105382 (AY147166 and NR042915, respectively).

M. porcinum. Isolates designated as *M. porcinum* had *rpoB* and 16S rRNA gene sequences with 100% identity to those of the *M. porcinum* type strain CIP 105392 (AY262737 and NR114657, respectively), and the ITS sequences of the isolates showed 100% and 99.0% identity with those of *M. porcinum* strain WH500 (KR995212) and the type strain CIP 105392 (AJ291598), respectively.

M. septicum. Isolates designated as *M. septicum* had *rpoB* sequences with 100%, 99.9%, and 98.7% identity with those of *M. septicum* strain 43MF (KY400689), strain D13 (AY772165), and the *M. septicum* type strain ATCC 700731 (AT147167); the 16S rRNA gene sequences of the isolates were 100% identical to that of the type strain ATCC 700731 (NR042916); and the ITS sequences of isolates showed 97.5% identity with that of the type strain ATCC 700731 (AM421289).

M. conceptionense. Isolates designated as *M. conceptionense* had 16S rRNA gene sequences with 100% identity to those of the *M. conceptionense* type strain CIP 108544 (NR043239), the *M. senegalense* type strain ATCC 35796 (NR114660), and the *M. farcinogenes* strain ATCC 35753 (NR114440); and the *rpoB* and ITS sequences of isolates were 100% identical to those of *M. conceptionense* strain M137 (HM536982 and HM536981, respectively).

FIGURE S1. Alignment of the nucleotide sequences of *erm*(39) (A) and the peptide sequences of Erm(39) (B) from 44 *M. fortuitum* clinical isolates investigated in this study. Clarithromycin-susceptible (S) or -resistant (R) isolates are indicated by the "-S" or "-R", respectively, after the isolate number. Sequences of *M. fortuitum* DSM46621 (=ATCC 6841) were used as the reference, and dots represent identical nucleotides or amino acids. CT6, *M. fortuitum* strain CT6 (GenBank accession no. CP011269).

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                         10        20        30        40        50        60        70        80
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fortuitum_DSM46621  GTGTCTTCAGTTCATCACGGCCGGCATGAGAACGGCCAGAATTTTCTGCGCGACCGTCGAGTGGTCGGCGACATCGTGAG
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CT6                 ................................................................................
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18-S                ................A...............................................................
32-S                .........C......................................................................
2-R                 .........C.............................................................A.C..
21-R                .........C.............................................................A.C..
22-R                .........C.............................................................A.C..
25-R                .........C.............................................................A.C..
28-R                .........C.............................................................A.C..
39                  .........C..........................................................A...........

                         90        100       110       120       130       140       150       160
                    ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
fortuitum_DSM46621  GATGGTCTCGCACACAGCGGGTCCCATCGTCGAGATCGGGGCCGGAGACGGCGCCCTCACCCTGCCGTTACAGCGGCTGG
33                  ................................................................................
CT6                 ................A...............................................................
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18-S               ...............A.................................................................
32-S               ...............A..C..............................................................
2-R                ...............A.................................................................
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22-R               ...............A.................................................................
25-R               ...............A.................................................................
28-R               ...............A.................................................................
39                 ...............A.........................................C.......................

                             170       180       190       200       210       220       230       240
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fortuitum_DSM46621 GCCGACCGTTGACCGCCATCGAGATCGACCTCCACCGTGCCCGACGGCTCGCCGACCGAACCACTGCCGAGGTGATCGCA
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25-R               ......................................................................C.........G.....
28-R               ......................................................................C.........G.....
39                 ......................................................................C.........G.....

                             250       260       270       280       290       300       310       320
                   ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
fortuitum_DSM46621 ACCGACTTCCTGCGGTACCGGCTGCCGCGCACGCCGCACGTGGTGGTGGGCAACCTGCCGTTCCATCTGACCACCGCCAT
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39                      ...................................................G........................

                                  330       340       350       360       370       380       390       400
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fortuitum_DSM46621      CCTCCGGCGCCTACTGCACGAGAACGGCTGGACCGATGCGATCCTGTTGGTGCAGTGGGAGGTGGCTCGACGGCGGGCCG
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                                410       420       430       440       450       460       470       480
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fortuitum_DSM46621 GTGTCGGCGGCGCCACCATGATGACCGCCCAGTGGTGGCCGTGGTTCGAATTCGGCCTGGCGCGAAAGGTTTCGGCCGAC
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                                490       500       510       520       530       540       550       560
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fortuitum_DSM46621 GCGTTCCGGCCGCGGCCGAGTGTGGATGCCGGGCTGCTGACCATTCAGCGCCGAGCTGAGCCGCTACTCCCGTGGGCCGA
33                 ..............................................A.................................
CT6                ................................................................................
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18-S              ......A...............................................................................
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28-R              .............................................................A.......G..................
39                ......A.......................................T.........A...........................


                          570       580       590       600       610       620       630       640
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fortuitum_DSM46621 CCGTCGTGCGTATCAGGCGCTGGTCCACAGGGTTTTCACCGGGCGCGGGCGTGGTCTGGCCCAGATTCTGCGGCCCCACG
33                ................A.........................................C.....................
CT6               ................A.....T......................................................T....
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38                ................A.....T......................................................T....
41                ................A.....T......................................................T....
42                ................A.....T......................................................T....
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44                 ..................A....T........................................................T....
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18-S               ...........................................................C...............T....
32-S               ...........................................................C...............T....
2-R                ..................A............................................................A....
21-R               ..................A............................................................A....
22-R               ..................A............................................................A....
25-R               ..A...............A.............................................................
28-R               ...C.....A........A.................................A...........................
39                 ..................A....................................................T.....

                             650       660       670       680       690       700       710       720
                   ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
fortuitum_DSM46621 TGCACCCACGGTGGCTGTCTGCCAACGGAATTCACCCGTCGGCTCTGCCCAGAGCGCTGACGGCTCGACAGTGGGTGGCG
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CT6                ...............................................................................
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2-R                ......................A..................................A...A.................
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28-R               ......................A..............................C..C...A.................
39                 .........................................A.....................................

                             730       740
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fortuitum_DSM46621 TTGTTCGATGCCGCCGGCTAG
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CT6                ....................
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32-S                    ....................
2-R                     .......A............
21-R                    .......A............
22-R                    .......A............
25-R                    .......A............
28-R                    ........A............
39                      ....................
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                         10        20        30        40        50        60        70        80
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fortuitum_DSM46621 VSSVHHGRHENGQNFLRDRRVVGDIVRMVSHTAGPIVEIGAGDGALTLPLQRLGRPLTAIEIDLHRARRLADRTTAEVIA
33                 ................................................................................
CT6                ..............................T.............................................V.
1                  ..............................T.............................................V.
3                  ..............................T.............................................V.
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27                 ..............................T.............................................V.
18-S               ......S.......................T.............................................V.
32-S               ...A..........................TA............................................V.
2-R                ...A...............I.....T..................................................V.
21-R               ...A...............I.....T..................................................V.
22-R               ...A...............I.....T..................................................V.
25-R               ...A...............I.....T..................................................V.
28-R               ...A...............I.....T..................................................V.
39                 ...A................I.........T.............................................V.


                         90       100       110       120       130       140       150       160
                   ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
fortuitum_DSM46621 TDFLRYRLPRTPHVVVGNLPFHLTTAILRRLLHENGWTDAILLVQWEVARRRAGVGGATMMTAQWWPWFEFGLARKVSAD
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CT6                ................................................................................
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39                  ...............V...................................................R.P..

                            170       180       190       200       210       220       230       240
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fortuitum_DSM46621  AFRPRPSVDAGLLTIQRRAEPLLPWADRRAYQALVHRVFTGRGRGLAQILRPHVHPRWLSANGIHPSALPRALTARQWVA
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22-R                ..........................................................T..............Q....
25-R                ....................H.....................................T..............Q....
28-R                ...............D.........................T.................T..............Q....
39                  .............I......................................S.........................

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fortuitum_DSM46621  LFDAAG*
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18-S                    ......*
32-S                    ......*
2-R                     ..E...*
21-R                    ..E...*
22-R                    ..E...*
25-R                    ..E...*
28-R                    ..E...*
39                      ......*
```

FIGURE S2. Alignment of the nucleotide sequences of *erm*(39) (A) and the peptide sequences of Erm(39) (B) from 10 *M. porcinum* clinical isolates investigated in this study. The clarithromycin-resistant (R) isolate is indicated by the "-R" after the isolate number. Sequences of the *M. porcinum* type strain ATCC 33776 (GenBank accession no. DQ447745) were used as the reference, and dots represent identical nucleotides or amino acids.

A

```
                  10        20        30        40        50        60        70        80
                  ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
porcinum_DQ447745 GTGCCTTCAACTCATCACGGCCGTCACGAGTACGGCCAGAACTTCCTGTGCGACCGACGAGTGATCGCCGACATCGTCAC
51                ...............T................................................................
54                ...............T................................................................
50-R              ...............T................................................................
46                ...............T................................................................
45                ...............T................................................................
49                ...............T................................................................
53                ...............T................................................................
47                ...............T................................................................
48                ...............T................................................................
52                ...............T................................................................


                  90        100       110       120       130       140       150       160
                  ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
porcinum_DQ447745 AATCGTTTCGCGCACAACAGGTCCCATCATCGAAATCGGCGCCGGCGACGGTGCGCTCACCCTGCCACTGCAACGGTTGA
51                ................................................................................
54                ................................................................................
50-R              ................................................................................
46                ................................................................................
45                ................................................................................
49                ................................................................................
53                ................................................................................
47                ................................................................................
48                ................................................................................
52                ................................................................................


                  170       180       190       200       210       220       230       240
                  ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
porcinum_DQ447745 ACCGGCAGCTGACCGCCATCGAGATCGACCGGCGGCGGGCGCGACGATTGGCGGACCGAACTTCAGCCGAAGTGGTCAGT
51                ....................................................................C...................
54                ....................................................................C...................
50-R              ....................................................................C...................
46                ....................................................................C...................
45                ....................................................................C...................
49                ....................................................................C...................
53                ....................................................................C...................
47                ....................................................................C...................
48                ....................................................................C...................
52                ....................................................................C...................


                  250       260       270       280       290       300       310       320
                  ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
porcinum_DQ447745 GCGGATTTTCTGAAGTACCGCCTCCCCACTGCGCCGCATGTGGTGGTGGGCAATCTGCCCTTTCACCTGACCACCGCGAT
51                ...........CG..-.................................T...............................
54                ...........CG....................................T...............................
50-R              ...........CG....................................T...............................
46                ...........CG....................................T...............................
45                ...........CG....................................T...............................
49                ..A.............................................................................
53                ..A.............................................................................
47                ................................................................................
48                ................................................................................
52                ................................................................................


                  330       340       350       360       370       380       390       400
                  ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
porcinum_DQ447745 GCTGCGGCGACTGCTACACGGCCCGGGGTGGACCGACGCCGTCCTGCTGATGCAATGGGAGGTGGCCCGCCGACGAGCCG
51                C...............................................................................
54                C...............................................................................
50-R              C...............................................................................
46                C...............................................................................
45                C...............................................................................
49                C...............................................................................
53                C...............................................................................
47                C...............................................................................
48                C...............................................................................
52                C...............................................................................
```

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                        410       420       430       440       450       460       470       480
                   ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
porcinum_DQ447745  CCATCGGCGGCGCCACCATGATGACCGCGCAGTGGTGGCCATGGTTCGAATTCGGTCTGGCACGAAAGGTTTCCGCAGAT
51                 ..G.............................................................................
54                 ..G.............................................................................
50-R               ..G.............................................................................
46                 ..G.............................................................................
45                 ..G.............................................................................
49                 ................................................................................
53                 ................................................................................
47                 ................................................................................
48                 ................................................................................
52                 ................................................................................


                        490       500       510       520       530       540       550       560
                   ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
porcinum_DQ447745  GCCTTCCGGCCCAGACCCGGTGTGGACGCCGGGCTGTTGACCATCACACGCCGTGGTGAACCCCTGGTCCCCACGGCCGA
51                 ...............................................G................................
54                 ...............................................G................................
50-R               ...............................................G................................
46                 ...............................................G................................
45                 ...............................................G................................
49                 .....................................A..........................................
53                 .....................................A..........................................
47                 .....................................A..........................................
48                 .....................................A..........................................
52                 .....................................A..........................................


                        570       580       590       600       610       620       630       640
                   ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
porcinum_DQ447745  CCGACGCAGGTATCAGGCCCTCGCACACGAGGTGTTCACCGGGCGGGGCCACGGCATGGCGCAGATCCTGCGCCATCACG
51                 ...G...C..................................................................G.....
54                 ...G...C........................................................................
50-R               ...G...C........................................................................
46                 ...G...C........................................................................
45                 ...G...C........................................................................
49                 ................................................................................
53                 ................................................................................
47                 ................................................................................
48                 ................................................................................
52                 ................................................................................


                        650       660       670       680       690       700       710       720
                   ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
porcinum_DQ447745  TGGATCGTCGGTGGTTGCAGGCCAACGGAATTCATCCCTCGGCGCTGCCGCGTGACCTGTCCGCACAACAGTGGGCCGCC
51                 ...G............................................................................
54                 ................................................................................
50-R               ................................................................................
46                 ................................................................................
45                 ................................................................................
49                 ................................................................................
53                 ................................................................................
47                 ................................................................................
48                 ................................................................................
52                 ................................................................................


                        730       740
                   ....|....|....|....|.
porcinum_DQ447745  CTGTTCGATGCGGTCCGCTAA
51                 .....................
54                 .....................
50-R               .....................
46                 .....................
45                 .....................
49                 .....................
53                 .....................
47                 .....................
48                 .....................
52                 .....................
```

B

```
                          10        20        30        40        50        60        70        80
                   ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
porcinum_DQ447745  VPSTHHGRHEYGQNFLCDRRVIADIVTIVSRTTGPIIEIGAGDGALTLPLQRLNRQLTAIEIDRRRARRLADRTSAEVVS
51                 ................................................................................
54                 ................................................................................
50-R               ................................................................................
46                 ................................................................................
45                 ................................................................................
49                 ................................................................................
53                 ................................................................................
47                 ................................................................................
48                 ................................................................................
52                 ................................................................................


                          90       100       110       120       130       140       150       160
                   ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
porcinum_DQ447745  ADFLKYRLPTAPHVVVGNLPFHLTTAMLRRLLHGPGWTDAVLLMQWEVARRRAAIGGATMMTAQWWPWFEFGLARKVSAD
51                 ....RX...................I...........................V...........................
54                 ....R....................I...........................V...........................
50-R               ....R....................I...........................V...........................
46                 ....R....................I...........................V...........................
45                 ....R....................I...........................V...........................
49                 .........................I......................................................
53                 .........................I......................................................
47                 .........................I......................................................
48                 .........................I......................................................
52                 .........................I......................................................


                         170       180       190       200       210       220       230       240
                   ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
porcinum_DQ447745  AFRPRPGVDAGLLTITRRGEPLVPTADRRRYQALAHEVFTGRGHGMAQILRHHVDRRWLQANGIHPSALPRDLSAQQWAA
51                 ..............................................................R..G...............
54                 ................................................................................
50-R               ................................................................................
46                 ................................................................................
45                 ................................................................................
49                 ................................................................................
53                 ................................................................................
47                 ................................................................................
48                 ................................................................................
52                 ................................................................................


                   ....|..
porcinum_DQ447745  LFDAVR*
51                 ......*
54                 ......*
50-R               ......*
46                 ......*
45                 ......*
49                 ......*
53                 ......*
47                 ......*
48                 ......*
52                 ......*
```