

Table S1. *M. leprae* ORFs transcribed during infection in nude mouse foot pads as detected by cross-species DNA microarray and RT-PCR analyses.

| ML Number^a | Gene | Gene Product |
|---|--------------|---|
| I. Small-molecule metabolism | | |
| I.A Degradation | | |
| I.A.1 Carbon compounds | | |
| ML1023 | <i>ppgK</i> | polyphosphate glucokinase (Rv2702) ^b |
| ML1950 ^c | --- | carbohydrate degrading enzyme (Rv1096) |
| I.A.2 Amino acids and amines | | |
| ML0524 ^c | <i>adi</i> | putative amino acid decarboxylase (Rv2531c) |
| I.A.3 Fatty acids | | |
| ML0120 | <i>echA1</i> | putative enoyl-CoA hydratase (Rv3774) |
| ML2461 | <i>fadB2</i> | 3-hydroxyacyl-CoA dehydrogenase (Rv0468) |
| ML2563 | <i>fadE5</i> | acyl-CoA dehydrogenase (Rv0244c) |
| ML2564 | <i>fadA2</i> | acetyl-CoA C-acetyltransferase (Rv0243) |
| I.A.4 Phosphorous compounds | | |
| ML0210 | <i>ppa</i> | putative inorganic pyrophosphatase (Rv3628) |
| ML0627 | <i>phoH</i> | PhoH-family protein (Rv2372c) |
| ML1681 | --- | possible polyphosphate kinase (Rv2984) |
| ML1951 | <i>phoH2</i> | PhoH-like protein (Rv1095) |
| I.B Energy Metabolism | | |
| I.B.1 Glycolysis | | |
| ML0079 | --- | putative phosphoglycerate mutase (Rv3837c) |
| ML0150 | <i>pgi</i> | glucose-6-phosphate isomerase (Rv0946c) |
| ML0255 | <i>eno</i> | putative enolase (Rv1023) |
| ML0286 ^c | <i>fba</i> | putative fructose biphosphate aldolase (Rv0363c) |
| ML0570 | <i>gap</i> | glyceraldehyde3-phosphate dehydrogenase (Rv1436) |
| ML0571 | <i>pgk</i> | phosphoglycerate kinase (Rv1437) |
| ML0572 | <i>tpi</i> | triosephosphate isomerase (Rv1438) |
| ML1277 | <i>pykA</i> | pyruvate kinase (Rv1617) |
| ML1701 | <i>pfkA</i> | 6-phosphofructokinase (Rv3010c) |
| ML2441 | <i>gpm</i> | phosphoglycerate mutase (Rv0489) |
| I.B.4 Glyoxylate bypass | | |
| ML1985 | <i>aceA</i> | isocitrate lyase (Rv1915) |
| ML2069 | <i>glcB</i> | malate synthase (Rv1837) |
| I.B.6a Aerobic respiration | | |
| ML0881 | <i>qcrC</i> | cytochrome C reductase/component (Rv2194) |
| I.B.7 Miscellaneous oxidoreductases and oxygenases | | |
| ML2501 ^c | --- | probable iron-sulphur-binding reductase (Rv0338c) |
| I.C Central Intermediary Metabolism | | |
| I.C.1 General intermediary metabolism | | |
| ML0955 | <i>ppdK</i> | pyruvate, phosphate dikinase (Rv1127c) |
| I.C.2 Gluconeogenesis | | |
| ML1755 | <i>sdaA</i> | L-serine dehydratase (Rv0069) |
| ML2624 | <i>pckA</i> | phosphoenolpyruvate carboxykinase (Rv0211) |
| I.C.5 Sulfur metabolism | | |
| ML0771 | <i>sahH</i> | S-adenosyl-L-homocysteine hydrolase (Rv3248c) |
| I.D Amino Acid Biosynthesis | | |
| I.D.1 Glutamate family | | |
| ML1630 ^c | <i>glnE</i> | glutamate-ammonia-ligase adenylyltransferase (Rv2221c) |
| I.D.2 Aspartate family | | |
| ML1307 | <i>metH</i> | 5-methyltetrahydrofolate-homocysteine methyltransferase |

(Rc2124c)

I.F Purines, Pyrimidines, Nucleosides and Nucleotides

I.F.1 Purine ribonucleotide biosynthesis

| | | |
|---------------------|-------------|--|
| ML2205 ^c | <i>purM</i> | 5'phosphoribosyl-5-aminoimidazol synthase (Rv0809) |
| ML2230 | <i>purB</i> | adenylosuccinate lyase (Rv0777) |
| ML2235 | <i>purD</i> | phosphoribosylamine-glycine ligase (Rv0772) |

I.F.2 Pyrimidine ribonucleotide biosynthesis

| | | |
|--------|-------------|--|
| ML0532 | <i>pyrB</i> | putative aspartate carbamoyltransferase (Rv1380) |
|--------|-------------|--|

I.F.4 Salvage of nucleosides and nucleotides

| | | |
|---------------------|-------------|---|
| ML2451 ^c | <i>deoC</i> | deoxyribose-phosphate aldolase (Rv0478) |
|---------------------|-------------|---|

I.F.5 Miscellaneous nucleoside/nucleotide reactions

| | | |
|---------------------|-------------|--|
| ML0491 | <i>relA</i> | putative GTP pyrophosphokinase (Rv2583c) |
| ML0831 | <i>dgt</i> | putative dGTP hydrolase (Rv2344c) |
| ML1465 ^c | --- | GTP1/Obg- family GTP-binding protein (Rv2440c) |

I.G Biosynthesis of Cofactors, Prosthetic Groups and Carriers

I.G.1 Biotin biosynthesis

| | | |
|---------------------|-------------|-------------------------------------|
| ML0732 ^c | <i>birA</i> | biotin apo-protein ligase (Rv3279c) |
|---------------------|-------------|-------------------------------------|

I.G.2 Folic acid biosynthesis

| | | |
|---------------------|--------------|---|
| ML0224 | <i>folP</i> | dihydropteroate synthase (Rv3608c) |
| ML0674 ^c | <i>folD</i> | methylenetetrahydrofolate dehydrogenase (Rv3356c) |
| ML1063 | <i>folP2</i> | dihydropteroate synthase (Rv1207) |

I.G.7 Pyridine nucleotide biosynthesis

| | | |
|--------|-------------|--|
| ML0294 | <i>thiC</i> | putative thiamine biosynthesis protein (Rv0423c) |
|--------|-------------|--|

I.G.8 Thiamine biosynthesis

| | | |
|--------|-------------|---|
| ML0295 | <i>thiD</i> | phosphomethylpyrimidine kinase (Rv0422c) |
| ML0297 | <i>thiG</i> | putative thiamine biosynthesis protein (Rv0417) |
| ML0300 | <i>thiE</i> | thiamine-phosphate pyrophosphorylase (Rv0414c) |
| ML1676 | <i>thiL</i> | thiamine-monophosphate kinase (Rv2977c) |

I.G.11 Menaquinone, PQQ, ubiquinone and other terpenoids biosynthesis

| | | |
|---------------------|------------|--|
| ML1038 | <i>dxs</i> | 1-deoxy-D-xylulose 5-phosphate synthase (Rv2682c) |
| ML2406 ^c | --- | 4-dihydroxy-2-naphthoate octaprenyl- transferase (Rv0534c) |

I.G.14 Iron utilization

| | | |
|--------|-------------|--|
| ML0808 | <i>entC</i> | putative isochorismate synthase (Rv3215) |
| ML2038 | <i>bfrA</i> | bacterioferritin (Rv1876) |

I.H Lipid Biosynthesis

I.H.1 Synthesis of fatty and mycolic acids

| | | |
|--------|-------------|--|
| ML1191 | <i>fas</i> | fatty acid synthase (Rv2524c) |
| ML1655 | <i>kasA</i> | 3-oxoacyl-[acyl-carrier-protein] synthase (Rv2245) |
| ML1806 | <i>inhA</i> | enoyl-[ACP] reductase (Rv1484) |

I.H.3 Acyltransferases, mycolyltransferases, and phospholipid synthases

| | | |
|---------------------|--------------|--|
| ML0097 | <i>fbpA</i> | antigen 85A, mycolyltransferase (Rv3804c) |
| ML0098 | <i>fbpC</i> | antigen 85C, mycolyltransferase (Rv0129c) |
| ML2028 | <i>fbpB</i> | antigen 85A, mycolyltransferase (Rv1886c) |
| ML2655 | <i>fbpC2</i> | secreted antigen 85A, mycolyltransferase (Rv3803c) |
| ML1417 ^c | --- | CDP-diacylglycerol pyrophosphatase (Rv2289) |

I.I Polyketide and Non-ribosomal Peptide Synthesis

| | | |
|--------|-----|------------------------------|
| ML2354 | --- | polyketide synthase (Rv2934) |
|--------|-----|------------------------------|

I.J Broad Regulatory Functions

I.J.1 Repressors/activators

| | | |
|---------------------|---------------|--|
| ML0382 | <i>whiB3</i> | putative transcriptional regulator (Rv3416) |
| ML0565 ^c | --- | putative transcriptional regulator (Rv1423) |
| ML0639 | <i>whiB7</i> | putative transcriptional regulator (Rv1021c) |
| ML0760 | <i>whiB2</i> | putative transcriptional regulator (Rv3260c) |
| ML0804 | <i>whiB1</i> | putative transcriptional regulator (Rv3219) |
| ML1013 | <i>(IdeR)</i> | iron-dependent repressor (Rv2711) |
| ML2156 ^c | --- | possible DNA-binding protein (Rv2538) |

II Macromolecule Metabolism

II.A Synthesis and Modification of Macromolecules

II.A.1 Ribosomal protein synthesis and modification

| | | |
|---------------------|-------------|-------------------------------------|
| ML1133 | <i>rpmE</i> | 50S ribosomal protein L31 (Rv1298) |
| ML1842 ^c | <i>rpsE</i> | 30S ribosomal protein S5 (Rv0721) |
| ML1845 ^c | <i>rpsH</i> | 30S ribosomal protein S8 (Rv0718) |
| ML1904 ^c | <i>rplA</i> | 50S ribosomal protein L1 (Rv0641) |
| ML1960 | <i>rpsM</i> | 30S ribosomal protein S13 (Rv3460c) |

II.A.2 Ribosome modification and maturation

| | | |
|--------|-------------|---|
| ML0241 | <i>ksgA</i> | putative dimethyladenosine transferase (Rv1010) |
| ML1370 | --- | possible pseudouridine synthase (Rv1711) |
| ML1616 | <i>rimM</i> | 16S rRNA processing protein (Rv2907c) |

II.A.3 Aminoacyl tRNA synthetases and their modification

| | | |
|---------------------|-------------|--|
| ML0494 ^c | <i>hisS</i> | histidyl-tRNA synthase (Rv2580c) |
| ML1402 | <i>pheT</i> | phenylalanyl-tRNA synthase-[beta]subunit (Rv1649) |
| ML1700 ^c | <i>gatB</i> | glutamyl-tRNA(Gln) amidotransferase, subunit B (Rv3009c) |

II.A.5 DNA replication, repair, recombination, and restriction/modification

| | | |
|---------------------|--------------|--|
| ML0001 | <i>dnaA</i> | chromosomal replication initiator protein (Rv0001) |
| ML0002 | <i>dnaN</i> | DNA polymerase III, [beta] subunit (Rv0002) |
| ML0003 | <i>recF</i> | DNA replication, SOS induction protein (Rv0003) |
| ML0005 | <i>gyrB</i> | DNA gyrase, subunit B (Rv0005) |
| ML0006 | <i>gyrA</i> | DNA gyrase, subunit A (Rv0006) |
| ML0153 | <i>uvrD</i> | putative ATP-dependent DNA helicase (Rv0949) |
| ML0200 | <i>topA</i> | putative DNA topoisomerase I (Rv3646c) |
| ML0252 | <i>mfd</i> | transcription-repair coupling factor (Rv1020) |
| ML0833 | <i>dnaG</i> | DNA primase (Rv2343c) |
| ML1333 ^c | <i>helY</i> | probable helicase, Ski2 subfamily (Rv2092c) |
| ML1705 ^c | <i>ligA</i> | DNA ligase (Rv3014c) |
| ML2335 | <i>dnaZX</i> | DNA polymerase III, subunit [gamma/tau] (Rv3721c) |

II.A.6 Protein translation and modification

| | | |
|--------|-------------|----------------------------------|
| ML1962 | <i>infA</i> | initiation factor IF-1 (Rv3462c) |
|--------|-------------|----------------------------------|

II.A.7 RNA synthesis, RNA modification, and DNA transcription

| | | |
|---------------------|--------------------|---|
| ML1957 | <i>rpoA</i> | [alpha] subunit RNA polymerase (Rv3457c) |
| ML1891 ^c | <i>rpoB</i> | [beta] subunit RNA polymerase (Rv0667) |
| ML1890 | <i>rpoC</i> | [beta'] subunit RNA polymerase (Rv0668) |
| ML1022 | <i>rpoT (sigA)</i> | RNA polymerase sigma factor (Rv2703) |
| ML1014 | <i>sigB</i> | RNA polymerase sigma factor (Rv2710) |
| ML1448 ^c | <i>sigC</i> | ECF subfamily sigma factor (Rv2069) |
| ML1076 | <i>sigE</i> | ECF subfamily sigma subunit (Rv1221) |
| ML1132 | <i>rho</i> | transcription termination factor Rho (Rv1297) |
| ML1558 | <i>nusA</i> | transcription termination/anti-termination factor (Rv2841c) |
| ML0523 | <i>nusB</i> | transcription termination protein (Rv2533c) |
| ML1906 | <i>nusG</i> | transcription anti-termination protein NusG (Rv0639) |
| ML2697 | <i>pcnA</i> | putative polynucleotide polymerase (Rv3907c) |

II.B Degradation of Macromolecules

II.B.1 RNA degradation

| | | |
|--------|-------------|----------------------------|
| ML1611 | <i>rnhB</i> | ribonuclease HII (Rv2902c) |
|--------|-------------|----------------------------|

II.B.2 DNA

| | | |
|--------|-------------|---|
| ML1889 | --- | putative endonuclease IV (apurinase) (Rv0670) |
| ML1940 | <i>xseA</i> | exonuclease VII large subunit (Rv1108c) |
| ML1941 | <i>xseB</i> | exonuclease VII small subunit (Rv1107c) |

II.B.3 Proteins, peptides, and glycopeptides

| | | |
|--------|-------------|--|
| ML0041 | --- | probable secreted protease (Rv3883c) |
| ML0176 | --- | possible secreted serine protease (Rv0983) |
| ML0235 | <i>clpC</i> | ATP-dependent Clp protease (Rv3596c) |
| ML0379 | <i>gcp</i> | putative O-sialoglycoprotein endopeptidase (Rv3419c) |

| | | |
|--|---------------|---|
| ML2659 | --- | probable secreted serine protease (Rv1088) |
| II.C Cell Envelope | | |
| II.C.1 Lipoproteins (lppA-lprO) | | |
| ML1966 | <i>lpqH</i> | possible lipoprotein (Rv3763) |
| II.C.2 Surface polysaccharides, lipopolysaccharides, proteins, and antigens | | |
| ML0049 | --- | possible secreted protein (Rv3875) |
| ML0050 | --- | possible secreted protein (Rv3874) |
| ML0091 | --- | 28 kDa antigen precursor (Rv3810) |
| ML0234 ^c | <i>lsr2</i> | <i>lsr2</i> protein (15 kDa antigen) |
| ML0620 | <i>mtb12</i> | putative secreted protein (Rv2376c) |
| ML0715 | <i>lpqC</i> | putative secreted hydrolase (Rv3298c) |
| ML1339 | --- | putative secreted protease (Rv2672) |
| ML1632 ^c | --- | possible hydrolase (Rv2223c) |
| ML1633 | --- | possible secreted hydrolase (Rv2223c) |
| ML1923 | <i>lpqF</i> | probable secreted protein (Rv3593) |
| ML2274 | --- | putative secreted protein (Rv0559c) |
| ML2331 | --- | possible secreted protein (Rv3717) |
| ML2380 | --- | possible secreted protein (Rv0455c) |
| ML2450 | --- | possible secreted protein (Rv0479c) |
| ML2522 | --- | putative secreted protein (Rv0309) |
| ML2569A | --- | putative secreted protein (Rv0236A) |
| ML2590 | <i>mce1B</i> | putative secreted protein (Rv0170) |
| ML2591 | <i>mce1C</i> | putative secreted protein (Rv0171) |
| ML2592 | <i>mce1D</i> | putative secreted protein (Rv0172) |
| ML2594 | <i>mce1F</i> | putative secreted protein (Rv0174) |
| ML2598 | --- | putative secreted protein (Rv0178) |
| II.C.3 Murein sacculus and peptidoglycan | | |
| ML0019 | <i>rodA</i> | putative cell-division protein (Rv0017c) |
| ML0908 ^c | <i>pbpB</i> | penicillin-binding protein 2 (Rv2163c) |
| II.C.4 Conserved membrane proteins | | |
| ML0007 | --- | putative membrane protein (Rv0007) |
| ML0073 ^c | --- | putative membrane protein (Rv3843c) |
| ML0256 ^c | --- | putative membrane protein (Rv1024) |
| ML0644 ^c | --- | putative integral membrane protein (Rv3193c) |
| ML0904 ^c | --- | putative membrane protein (Rv2424c) |
| ML1892 ^c | --- | ABC transporter ATP-binding protein (Rv0655) |
| ML2710 ^c | --- | putative conserved membrane protein (Rv3921c) |
| III Cell Processes | | |
| III.A.1 Amino acids | | |
| ML0303 ^c | <i>glnH</i> | putative glutamine-binding protein (Rv0144c) |
| III.A.2 Cations | | |
| ML1267 ^c | --- | putative antiporter (Rv1607) |
| ML1729 | <i>fecB</i> | FeIII-dicitrate transporter lipoprotein (Rv3044) |
| ML2098 | <i>mntH</i> | probable manganese transport protein (Rv0107c) |
| ML2671 ^c | --- | probable cation transport ATPase (Rv3743c) |
| III.A.4 Anions | | |
| ML0615 | <i>subl</i> | putative sulphate-binding protein (Rv2400c) |
| III.A.6 Efflux proteins | | |
| ML1756 ^c | --- | probable multidrug resistance protein (Rv1819c) |
| III.B Chaperones/heat shock | | |
| ML0317 | <i>groEL2</i> | 60 kDa chaperonin 2 (Rv0440) |
| ML0380 | <i>groES</i> | 10 kDa chaperonin (Rv3418c) |
| ML0381 | <i>groEL1</i> | 60 kDa chaperonin 1 (Rv3417c) |
| ML0624 | <i>hrcA</i> | heat-inducible transcription repressor (Rv2374c) |
| ML1623 | <i>htpG</i> | heat shock protein Hsp90 family (Rv2299c) |
| ML1795 | <i>hsp18</i> | 18 kDa heat shock protein antigen (Hsp16.7) (Rv0251c) |

| | | |
|--|--------------|---|
| ML2490 | <i>clpB</i> | heat shock protein (Rv0384c) |
| ML2493 | <i>hspR</i> | heat shock regulator (Rv0353) |
| ML2494 | <i>dnaJ</i> | Hsp70 cofactor (Rv0352) |
| ML2495 | <i>grpE</i> | Hsp70 cofactor (Rv0351) |
| ML2496 | <i>dnaK</i> | 70 kDa heat shock protein (Rv0350) |
| III.C Cell division | | |
| ML0669 | <i>ftsE</i> | putative cell division ATP-binding protein (Rv3102c) |
| ML0222 | <i>ftsH</i> | putative integral membrane peptidase (Rv3610c) |
| ML0977 | <i>ftsK</i> | cell division protein (Rv2748c) |
| ML0916 | <i>ftsQ</i> | putative FtsQ-family protein (Rv2151c) |
| ML0913 ^c | <i>ftsW</i> | putative cell division protein FtsW (Rv2154c) |
| ML0917 | <i>ftsZ</i> | cell division protein (Rv2150c) |
| ML1629 | <i>smc</i> | possible cell division protein (Rv2922c) |
| ML2707 | <i>parA</i> | putative cell division protein (Rv3917c) |
| ML2706 | <i>parB</i> | putative cell division protein (Rv3918c) |
| ML1600 | <i>xerC</i> | integrase/recombinase (Rv2894c) |
| ML1628 | --- | possible SRP family of GTP-binding proteins (Rv2921c) |
| III.D Protein and peptide secretion | | |
| ML0487 | <i>secD</i> | putative protein-export membrane protein (Rv2587c) |
| ML0488 | <i>secF</i> | putative protein-export membrane protein (Rv2586c) |
| ML0779 | <i>secA</i> | putative preprotein translocase subunit (Rv3240c) |
| ML1833 | <i>secY</i> | SecY subunit of preprotein translocase (Rv0732) |
| ML1907 | <i>secE</i> | SecE preprotein translocase (Rv0638) |
| ML2082 | <i>secA2</i> | SecA preprotein translocase subunit (Rv1821) |
| ML1612 ^c | --- | possible signal peptidase 1 (Rv2903c) |
| III.E Adaptations and atypical conditions | | |
| ML2254 | <i>otsA</i> | probable trehalose-phosphate synthase (Rv3490) |
| III.F Detoxification | | |
| ML0072 | <i>sodA</i> | superoxide dismutase (Rv3846) |
| ML1925 | <i>sodC</i> | superoxide dismutase precursor (Cu-Zn) (Rv0432) |
| ML2042 | <i>ahpC</i> | alkyl hydroperoxide reductase (Rv2428) |
| IV Other | | |
| IV.A Virulence | | |
| ML0885 | --- | putative secreted protein (Rv2190c) |
| ML1214 | --- | putative secreted p60 family protein (Rv1566c) |
| ML1811 | --- | putative exported p60 protein homolog (Rv1478) |
| ML1812 | --- | putative exported p60 protein homolog (Rv1477) |
| ML1358 | <i>tlyA</i> | cytotoxin/hemolysin (Rv1694) |
| ML2055 | <i>modD</i> | cell surface protein (virulence gene) (Rv1860) |
| ML2589 | <i>mce1A</i> | putative cell invasion protein (Rv0169) |
| IV.H Miscellaneous transferases | | |
| ML0324 ^c | --- | putative methyltransferase (Rv3579c) |
| ML1274 ^c | --- | possible prolipoprotein diacylglycerol transferase (Rv1614) |
| IV.I Miscellaneous phosphatases, lyases, and hydrolases | | |
| ML2569 ^c | --- | putative secreted glycosyl hydrolase (Rv0237) |
| V. Conserved hypotheticals | | |
| ML0089 ^c | --- | conserved hypothetical protein (Rv3813c) |
| ML0451 ^c | --- | conserved hypothetical protein (Rv2609c) |
| ML0542 ^c | --- | conserved hypothetical protein (Rv1390) |
| ML0798 ^c | --- | conserved hypothetical protein (Rv2787) |
| ML1067 ^c | --- | conserved hypothetical protein (Rv1211) |
| ML1120 ^c | --- | conserved hypothetical protein (Rv1278) |
| ML1157 ^c | --- | conserved hypothetical protein (Rv1321) |
| ML1254 ^c | --- | conserved hypothetical protein (Rv2469c) |
| ML1536 ^c | --- | conserved hypothetical protein |
| ML1617 ^c | --- | conserved hypothetical protein (Rv2908c) |

| | | |
|---------------------|-----|--|
| ML1720 ^c | --- | conserved hypothetical protein (Rv3035) |
| ML1936 ^c | --- | conserved hypothetical protein (Rv1112) |
| ML2151 ^c | --- | conserved hypothetical protein (Rv1009) |
| ML2204 ^c | --- | conserved hypothetical protein (Rv0810c) |
| ML2708 | --- | conserved hypothetical protein (Rv3919c) |
| ML2709 | --- | conserved hypothetical protein |
| VI. Unknowns | | |
| ML0008 | --- | hypothetical protein |
| ML0126 | --- | hypothetical protein |
| ML0127 | --- | hypothetical protein |
| ML0394 | --- | hypothetical protein |
| ML0678 | --- | hypothetical protein |
| ML0757 | --- | hypothetical protein |
| ML0840 | --- | hypothetical protein |
| ML1057 | --- | hypothetical protein |
| ML2567 | --- | hypothetical protein |
| ML2649 | --- | hypothetical protein |

a. ML numbers (The Wellcome Trust Sanger Institute, 2001). **b.** *M. tuberculosis* homologue (The Wellcome Trust Sanger Institute, 2001). **c.** Gene transcripts observed by cross-species DNA array analysis and confirmed by RT-PCR

