

Received 7 July; accepted 21 September 1998.

1. Dalbey, R. E., Lively, M. O., Bron, S. & van Dijl, J. M. The chemistry and enzymology of the type 1 signal peptidases. *Protein Sci.* **6**, 1129–1138 (1997).
2. Kuo, D. W. *et al.* *Escherichia coli* leader peptidase: production of an active form lacking a requirement for detergent and development of peptide substrates. *Arch. Biochem. Biophys.* **303**, 274–280 (1993).
3. Tschantz, W. R. *et al.* Characterization of a soluble, catalytically active form of *Escherichia coli* leader peptidase: requirement of detergent or phospholipid for optimal activity. *Biochemistry* **34**, 3935–3941 (1995).
4. Allsop, A. E. *et al.* in *Anti-Infectives, Recent Advances in Chemistry and Structure-Activity Relationships* (eds Bentley, P. H. & O'Hanlon, P. J.) 61–72 (R. Soc. Chem., Cambridge, 1997).
5. Black, M. T. & Bruton, G. Inhibitors of bacterial signal peptidases. *Curr. Pharm. Des.* **4**, 133–154 (1998).
6. Date, T. Demonstration by a novel genetic technique that leader peptidase is an essential enzyme in *Escherichia coli*. *J. Bacteriol.* **154**, 76–83 (1983).
7. Whitley, P. & von Heijne, G. The DsbA-DsbB system affects the formation of disulfide bonds in periplasmic but not in intramembraneous protein domains. *FEBS Lett.* **332**, 49–51 (1993).
8. Peat, T. S. *et al.* Structure of the UmuD' protein and its regulation in response to DNA damage. *Nature* **380**, 727–730 (1996).
9. Paetzel, M. *et al.* Crystallization of a soluble, catalytically active form of *Escherichia coli* leader peptidase. *Proteins Struct. Funct. Genet.* **23**, 122–125 (1995).
10. van Klompenburg, W. *et al.* Phosphatidylethanolamine mediated insertion of the catalytic domain of leader peptidase in membranes. *FEBS Lett.* **431**, 75–79 (1998).
11. Kim, Y. T., Muramatsu, T. & Takahashi, K. Identification of Trp 300 as an important residue for *Escherichia coli* leader peptidase activity. *Eur. J. Biochem.* **234**, 358–362 (1995).
12. Landolt-Marticorena, C., Williams, K. A., Deber, C. M. & Reithmeier, R. A. Non-random distribution of amino acids in the transmembrane segments of human type I single span membrane proteins. *J. Mol. Biol.* **229**, 602–608 (1993).
13. James, M. N. G. in *Proteolysis and Protein Turnover* (eds Bond, J. S. & Barrett, A. J.) 1–8 (Portland, Brookfield, VT, 1994).
14. Strynadka, N. C. J. *et al.* Molecular structure of the acyl-enzyme intermediate in  $\beta$ -lactamase at 1.7 Å resolution. *Nature* **359**, 393–400 (1992).
15. Manard, R. & Storer, A. C. Oxyanion hole interactions in serine and cysteine proteases. *Biol. Chem. Hoppe-Seyler* **373**, 393–400 (1992).
16. Nicolas, A. *et al.* Contribution of cutinase Ser 42 side chain to the stabilization of the oxyanion transition state. *Biochemistry* **35**, 398–410 (1996).
17. Paetzel, M. *et al.* Use of site-directed chemical modification to study an essential lysine in *Escherichia coli* leader peptidase. *J. Biol. Chem.* **272**, 9994–10003 (1997).
18. Paetzel, M. & Dalbey, R. E. Catalytic hydroxyl/amine dyads with serine proteases. *Trends Biochem. Sci.* **22**, 28–31 (1997).
19. von Heijne, G. Signal sequences. The limits of variation. *J. Mol. Biol.* **184**, 99–105 (1985).
20. Izard, J. W. & Kendall, D. A. Signal peptides: exquisitely designed transport promoters. *Mol. Microbiol.* **13**, 765–773 (1994).
21. Matthews, B. W. Solvent content of protein crystals. *J. Mol. Biol.* **33**, 491–497 (1968).
22. Otwinowski, Z. in *DENZO* (eds Sawyer, L., Isaacs, N. & Bailly, S.) 56–62 (SERC Daresbury Laboratory, Warrington, UK, 1993).
23. Collaborative Computational Project No. 4 The CCP4 suite: programs for protein crystallography. *Acta Crystallogr. D* **50**, 760–763 (1994).
24. Jones, T. A., Zou, J. Y., Cowan, S. W. & Kjeldgaard, M. Improved methods for building protein models in electron density maps and the location of errors in these models. *Acta Crystallogr. A* **47**, 110–119 (1991).
25. Brunger, A. T. *X-PLOR: A System for X-ray Crystallography and NMR (Version 3.1)* (Yale Univ. Press, New Haven, 1987).

26. Tronrud, D. E. Conjugate-direction minimization: an improved method for the refinement of macromolecules. *Acta Crystallogr. A* **48**, 912–916 (1992).
27. Wolfe, P. B., Wickner, W. & Goodman, J. M. Sequence of the leader peptidase gene of *Escherichia coli* and the orientation of leader peptidase in the bacterial envelope. *J. Biol. Chem.* **258**, 12073–12080 (1983).
28. Kraulis, P. G. Molscript: a program to produce both detailed and schematic plots of protein structures. *J. Appl. Crystallogr.* **24**, 946–950 (1991).
29. Nicholls, A., Sharp, K. A. & Honig, B. Protein folding and association: insights from the interfacial and the thermodynamic properties of hydrocarbons. *Proteins Struct. Funct. Genet.* **11**, 281–296 (1991).
30. Meritt, E. A. & Bacon, D. J. Raster3D: photorealistic molecular graphics. *Methods Enzymol.* **277**, 505–524 (1997).

**Acknowledgements.** We thank SmithKlineBeecham Pharmaceuticals for penem inhibitor; R. M. Sweet for use of beamline X12C (NSLS, Brookhaven National Laboratory); G. Petsko for the ethylmercury phosphate; M. N. G. James for access to equipment for characterization of earlier crystal forms of SPase; and S. Mosimann and S. Ness for discussions. This work was supported by the Medical Research Council of Canada, the Canadian Bacterial Diseases Network of Excellence, and British Columbia Medical Research Foundation grants to N.C.J.S. M.P. is funded by an MRC of Canada post-doctoral fellowship, N.C.J.S. by an MRC of Canada scholarship, and R.E.D. by the NIH and the American Heart Association.

Correspondence and requests for materials should be addressed to N.C.J.S. (e-mail: natalie@byron.biochem.ubc.ca).

errata

Reconciling the spectrum of *Sagittarius A\** with a two-temperature plasma model

Rohan Mahadevan

*Nature* **394**, 651–653 (1998)

A misleading typographical error was introduced into the second sentence of the bold introductory paragraph of this Letter: the word “infrared” should be “inferred”. □

Deciphering the biology of *Mycobacterium tuberculosis* from the complete genome sequence

S. T. Cole, R. Brosch, J. Parkhill, T. Garnier, C. Churcher, D. Harris, S. V. Gordon, K. Eiglmeier, S. Gas, C. E. Barry III, F. Tekaia, K. Badcock, D. Basham, D. Brown, T. Chillingworth, R. Connor, R. Davies, K. Devlin, T. Feltwell, S. Gentles, N. Hamlin, S. Holroyd, T. Hornsby, K. Jagels, A. Krogh, J. McLean, S. Moule, L. Murphy, K. Oliver, J. Osborne, M. A. Quail, M.-A. Rajandream, J. Rogers, S. Rutter, K. Seeger, J. Skelton, R. Squares, S. Squares, J. E. Sulston, K. Taylor, S. Whitehead & B. G. Barrell

*Nature* **393**, 537–544 (1998)

As a result of an error during film output, Table 1 was published with some symbols missing. The correct version can be found at <http://www.sanger.ac.uk> and is reproduced again here (following pages).

Also, in Fig. 2, we incorrectly labelled Rv0649 as *fadD37* instead of *fabD2*. Two of the genes for mycolyl transferases were inverted: Rv0129c encodes antigen 85C and not 85C' as stated, whereas Rv3803c codes for the secreted protein MPT51 and not antigen 85C (*Infect. Immun.* **59**, 372–382; 1991); Rv3803c is now designated *fbpD*. We thank Morten Harboe and Harald Wiker for drawing this to our attention.

The sequence of Rv0746 from *M. bovis* BCG-Pasteur presented in Fig. 5b was incorrect and should have shown a 16-codon deletion instead of 29, as indicated here:

```
H37Rv . . . . . GSGAPGGAGGAAGLWGTGGAGGAGGSSAGGGGAGGAGGAGGWLGDGGAGGIGGAST . . .
. . . . . : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :
BCG . . . . . GSGAPGGAGGAAGLWGTGGA-----GGAGGWLGDGGAGGIGGAST . . .
```

**Table 1. Functional classification of *Mycobacterium tuberculosis* protein-coding genes**

**I. Small-molecule metabolism**

**A. Degradation**

**1. Carbon compounds**

Rv0186	<i>bglS</i>	β-glucosidase
Rv2202c	<i>cbhK</i>	carbohydrate kinase
Rv0727c	<i>fucA</i>	L-fuculose phosphate aldolase
Rv1731	<i>gabD1</i>	succinate-semialdehyde dehydrogenase
Rv0234c	<i>gabD2</i>	succinate-semialdehyde dehydrogenase
Rv0501	<i>galE1</i>	UDP-glucose 4-epimerase
Rv0536	<i>galE2</i>	UDP-glucose 4-epimerase
Rv0620	<i>galK</i>	galactokinase
Rv0619	<i>galT</i>	galactose-1-phosphate uridylyltransferase C-term
Rv0618	<i>galT'</i>	galactose-1-phosphate uridylyltransferase N-term
Rv0993	<i>galU</i>	UTP-glucose-1-phosphate uridylyltransferase
Rv3696c	<i>glpK</i>	ATP:glycerol 3-phosphotransferase
Rv3255c	<i>manA</i>	mannose-6-phosphate isomerase
Rv3441c	<i>mrsA</i>	phosphoglucomutase or phosphomannomutase
Rv0118c	<i>oxcA</i>	oxalyl-CoA decarboxylase
Rv3068c	<i>pgmA</i>	phosphoglucomutase
Rv3257c	<i>pmmA</i>	phosphomannomutase
Rv3308	<i>pmmB</i>	phosphomannomutase
Rv2702	<i>ppgK</i>	polyphosphate glucokinase
Rv0408	<i>pta</i>	phosphate acetyltransferase
Rv0729	<i>xyfB</i>	xylulose kinase
Rv1096	-	carbohydrate degrading enzyme

**2. Amino acids and amines**

Rv1905c	<i>aaO</i>	D-amino acid oxidase
Rv2531c	<i>adi</i>	ornithine/arginine decarboxylase
Rv2780	<i>ald</i>	L-alanine dehydrogenase
Rv1538c	<i>ansA</i>	L-asparaginase
Rv1001	<i>arcA</i>	arginine deiminase
Rv0753c	<i>mmsA</i>	methylmalmonate semialdehyde dehydrogenase
Rv0751c	<i>mmsB</i>	methylmalmonate semialdehyde oxidoreductase
Rv1187	<i>rocA</i>	pyrroline-5-carboxylate dehydrogenase
Rv2322c	<i>rocD1</i>	ornithine aminotransferase
Rv2321c	<i>rocD2</i>	ornithine aminotransferase
Rv1848	<i>ureA</i>	urease γ subunit
Rv1849	<i>ureB</i>	urease β subunit
Rv1850	<i>ureC</i>	urease α subunit
Rv1853	<i>ureD</i>	urease accessory protein
Rv1851	<i>ureF</i>	urease accessory protein
Rv1852	<i>ureG</i>	urease accessory protein
Rv2913c	-	probable D-amino acid aminohydrolase
Rv3551	-	possible glutamate CoA-transferase

**3. Fatty acids**

Rv2501c	<i>accA1</i>	acetyl/propionyl-CoA carboxylase, α subunit
Rv0973c	<i>accA2</i>	acetyl/propionyl-CoA carboxylase, α subunit
Rv2502c	<i>accD1</i>	acetyl/propionyl-CoA carboxylase, β subunit
Rv0974c	<i>accD2</i>	acetyl/propionyl-CoA carboxylase, β subunit
Rv3667	<i>acs</i>	acetyl-CoA synthase
Rv3409c	<i>choD</i>	cholesterol oxidase
Rv0222	<i>echA1</i>	enoyl-CoA hydratase/isomerase superfamily
Rv0456c	<i>echA2</i>	enoyl-CoA hydratase/isomerase superfamily
Rv0632c	<i>echA3</i>	enoyl-CoA hydratase/isomerase superfamily
Rv0673	<i>echA4</i>	enoyl-CoA hydratase/isomerase superfamily
Rv0675	<i>echA5</i>	enoyl-CoA hydratase/isomerase superfamily
Rv0905	<i>echA6</i>	enoyl-CoA hydratase/isomerase superfamily (aka <i>ecch</i> )
Rv0971c	<i>echA7</i>	enoyl-CoA hydratase/isomerase superfamily
Rv1070c	<i>echA8</i>	enoyl-CoA hydratase/isomerase superfamily
Rv1071c	<i>echA9</i>	enoyl-CoA hydratase/isomerase superfamily
Rv1142c	<i>echA10</i>	enoyl-CoA hydratase/isomerase superfamily
Rv1141c	<i>echA11</i>	enoyl-CoA hydratase/isomerase superfamily
Rv1472	<i>echA12</i>	enoyl-CoA hydratase/isomerase superfamily
Rv1935c	<i>echA13</i>	enoyl-CoA hydratase/isomerase superfamily
Rv2486	<i>echA14</i>	enoyl-CoA hydratase/isomerase superfamily
Rv2679	<i>echA15</i>	enoyl-CoA hydratase/isomerase superfamily

Rv2831	<i>echA16</i>	superfamily enoyl-CoA hydratase/isomerase
Rv3039c	<i>echA17</i>	superfamily enoyl-CoA hydratase/isomerase
Rv3373	<i>echA18</i>	enoyl-CoA hydratase/isomerase superfamily, N-term
Rv3374	<i>echA18'</i>	enoyl-CoA hydratase/isomerase superfamily, C-term
Rv3516	<i>echA19</i>	enoyl-CoA hydratase/isomerase superfamily
Rv3550	<i>echA20</i>	enoyl-CoA hydratase/isomerase superfamily
Rv3774	<i>echA21</i>	enoyl-CoA hydratase/isomerase superfamily
Rv0859	<i>fadA</i>	β oxidation complex, β subunit (acetyl-CoA C-acetyltransferase)
Rv0243	<i>fadA2</i>	acetyl-CoA C-acetyltransferase
Rv1074c	<i>fadA3</i>	acetyl-CoA C-acetyltransferase
Rv1323	<i>fadA4</i>	acetyl-CoA C-acetyltransferase (aka <i>thiL</i> )
Rv3546	<i>fadA5</i>	acetyl-CoA C-acetyltransferase
Rv3556c	<i>fadA6</i>	acetyl-CoA C-acetyltransferase
Rv0860	<i>fadB</i>	β oxidation complex, α subunit (multiple activities)
Rv0468	<i>fadB2</i>	3-hydroxyacyl-CoA dehydrogenase
Rv1715	<i>fadB3</i>	3-hydroxyacyl-CoA dehydrogenase
Rv3141	<i>fadB4</i>	3-hydroxyacyl-CoA dehydrogenase
Rv1912c	<i>fadB5</i>	3-hydroxyacyl-CoA dehydrogenase
Rv1750c	<i>fadD1</i>	acyl-CoA synthase
Rv0270	<i>fadD2</i>	acyl-CoA synthase
Rv3561	<i>fadD3</i>	acyl-CoA synthase
Rv0214	<i>fadD4</i>	acyl-CoA synthase
Rv0166	<i>fadD5</i>	acyl-CoA synthase
Rv1206	<i>fadD6</i>	acyl-CoA synthase
Rv0119	<i>fadD7</i>	acyl-CoA synthase
Rv0551c	<i>fadD8</i>	acyl-CoA synthase
Rv2590	<i>fadD9</i>	acyl-CoA synthase
Rv0099	<i>fadD10</i>	acyl-CoA synthase
Rv1550	<i>fadD11</i>	acyl-CoA synthase, N-term
Rv1549	<i>fadD11'</i>	acyl-CoA synthase, C-term
Rv1427c	<i>fadD12</i>	acyl-CoA synthase
Rv3089	<i>fadD13</i>	acyl-CoA synthase
Rv1058	<i>fadD14</i>	acyl-CoA synthase
Rv2187	<i>fadD15</i>	acyl-CoA synthase
Rv0852	<i>fadD16</i>	acyl-CoA synthase
Rv3506	<i>fadD17</i>	acyl-CoA synthase
Rv3513c	<i>fadD18</i>	acyl-CoA synthase
Rv3515c	<i>fadD19</i>	acyl-CoA synthase
Rv1185c	<i>fadD21</i>	acyl-CoA synthase
Rv2948c	<i>fadD22</i>	acyl-CoA synthase
Rv3826	<i>fadD23</i>	acyl-CoA synthase
Rv1529	<i>fadD24</i>	acyl-CoA synthase
Rv1521	<i>fadD25</i>	acyl-CoA synthase
Rv2930	<i>fadD26</i>	acyl-CoA synthase
Rv0275c	<i>fadD27</i>	acyl-CoA synthase
Rv2941	<i>fadD28</i>	acyl-CoA synthase
Rv2950c	<i>fadD29</i>	acyl-CoA synthase
Rv0404	<i>fadD30</i>	acyl-CoA synthase
Rv1925	<i>fadD31</i>	acyl-CoA synthase
Rv3801c	<i>fadD32</i>	acyl-CoA synthase
Rv1345	<i>fadD33</i>	acyl-CoA synthase
Rv0035	<i>fadD34</i>	acyl-CoA synthase
Rv2505c	<i>fadD35</i>	acyl-CoA synthase
Rv1193	<i>fadD36</i>	acyl-CoA synthase
Rv0131c	<i>fadE1</i>	acyl-CoA dehydrogenase
Rv0154c	<i>fadE2</i>	acyl-CoA dehydrogenase
Rv0215c	<i>fadE3</i>	acyl-CoA dehydrogenase
Rv0231	<i>fadE4</i>	acyl-CoA dehydrogenase
Rv0244c	<i>fadE5</i>	acyl-CoA dehydrogenase
Rv0271c	<i>fadE6</i>	acyl-CoA dehydrogenase
Rv0400c	<i>fadE7</i>	acyl-CoA dehydrogenase
Rv0672	<i>fadE8</i>	acyl-CoA dehydrogenase (aka <i>aidB</i> )
Rv0752c	<i>fadE9</i>	acyl-CoA dehydrogenase
Rv0873	<i>fadE10</i>	acyl-CoA dehydrogenase
Rv0972c	<i>fadE12</i>	acyl-CoA dehydrogenase
Rv0975c	<i>fadE13</i>	acyl-CoA dehydrogenase
Rv1346	<i>fadE14</i>	acyl-CoA dehydrogenase
Rv1467c	<i>fadE15</i>	acyl-CoA dehydrogenase
Rv1679	<i>fadE16</i>	acyl-CoA dehydrogenase
Rv1934c	<i>fadE17</i>	acyl-CoA dehydrogenase
Rv1933c	<i>fadE18</i>	acyl-CoA dehydrogenase
Rv2500c	<i>fadE19</i>	acyl-CoA dehydrogenase (aka <i>mmgC</i> )
Rv2724c	<i>fadE20</i>	acyl-CoA dehydrogenase
Rv2789c	<i>fadE21</i>	acyl-CoA dehydrogenase
Rv3061c	<i>fadE22</i>	acyl-CoA dehydrogenase
Rv3140	<i>fadE23</i>	acyl-CoA dehydrogenase
Rv3139	<i>fadE24</i>	acyl-CoA dehydrogenase
Rv3274c	<i>fadE25</i>	acyl-CoA dehydrogenase
Rv3504	<i>fadE26</i>	acyl-CoA dehydrogenase
Rv3505	<i>fadE27</i>	acyl-CoA dehydrogenase
Rv3544c	<i>fadE28</i>	acyl-CoA dehydrogenase

Rv3543c	<i>fadE29</i>	acyl-CoA dehydrogenase
Rv3560c	<i>fadE30</i>	acyl-CoA dehydrogenase
Rv3562	<i>fadE31</i>	acyl-CoA dehydrogenase
Rv3563	<i>fadE32</i>	acyl-CoA dehydrogenase
Rv3564	<i>fadE33</i>	acyl-CoA dehydrogenase
Rv3573c	<i>fadE34</i>	acyl-CoA dehydrogenase
Rv3797	<i>fadE35</i>	acyl-CoA dehydrogenase
Rv3761c	<i>fadE36</i>	acyl-CoA dehydrogenase
Rv1175c	<i>fadH</i>	2,4-Dienoyl-CoA Reductase
Rv0855	<i>far</i>	fatty acyl-CoA racemase
Rv1143	<i>mcr</i>	α-methyl acyl-CoA racemase
Rv1492	<i>mutA</i>	methylmalonyl-CoA mutase, β subunit
Rv1493	<i>mutB</i>	methylmalonyl-CoA mutase, α subunit
Rv2504c	<i>scoA</i>	3-oxo acid:CoA transferase, α subunit
Rv2503c	<i>scoB</i>	3-oxo acid:CoA transferase, β subunit
Rv1136	-	probable carnitine racemase
Rv1683	-	possible acyl-CoA synthase

**4. Phosphorous compounds**

Rv2368c	<i>phoH</i>	ATP-binding <i>pho</i> regulon component
Rv1095	<i>phoH2</i>	PhoH-like protein
Rv3628	<i>ppa</i>	probable inorganic pyrophosphatase
Rv2984	<i>ppk</i>	polyphosphate kinase

**B. Energy metabolism**

**1. Glycolysis**

Rv1023	<i>eno</i>	enolase
Rv0363c	<i>fba</i>	fructose bisphosphate aldolase
Rv1436	<i>gap</i>	glyceraldehyde 3-phosphate dehydrogenase
Rv0489	<i>gpm</i>	phosphoglycerate mutase I
Rv3010c	<i>pfkA</i>	phosphofructokinase I
Rv2029c	<i>pfkB</i>	phosphofructokinase II
Rv0946c	<i>pgi</i>	glucose-6-phosphate isomerase
Rv1437	<i>pgk</i>	phosphoglycerate kinase
Rv1617	<i>pykA</i>	pyruvate kinase
Rv1438	<i>tpi</i>	triosephosphate isomerase
Rv2419c	-	putative phosphoglycerate mutase
Rv3837c	-	putative phosphoglycerate mutase

**2. Pyruvate dehydrogenase**

Rv2241	<i>aceE</i>	pyruvate dehydrogenase E1 component
Rv3303c	<i>lpdA</i>	dihydrolipoamide dehydrogenase
Rv2497c	<i>pdhA</i>	pyruvate dehydrogenase E1 component α subunit
Rv2496c	<i>pdhB</i>	pyruvate dehydrogenase E1 component β subunit
Rv2495c	<i>pdhC</i>	dihydrolipoamide acetyltransferase
Rv0462	-	probable dihydrolipoamide dehydrogenase

**3. TCA cycle**

Rv1475c	<i>acon</i>	aconitate hydratase
Rv0889c	<i>citA</i>	citrate synthase 2
Rv2498c	<i>citE</i>	citrate lyase β chain
Rv1098c	<i>fum</i>	fumarase
Rv1131	<i>glfA1</i>	citrate synthase 3
Rv0896	<i>glfA2</i>	citrate synthase 1
Rv3339c	<i>icd1</i>	isocitrate dehydrogenase
Rv0066c	<i>icd2</i>	isocitrate dehydrogenase
Rv0794c	<i>lpdB</i>	dihydrolipoamide dehydrogenase
Rv1240	<i>mdh</i>	malate dehydrogenase
Rv2967c	<i>pca</i>	pyruvate carboxylase
Rv3318	<i>sdhA</i>	succinate dehydrogenase A
Rv3319	<i>sdhB</i>	succinate dehydrogenase B
Rv3316	<i>sdhC</i>	succinate dehydrogenase C subunit
Rv3317	<i>sdhD</i>	succinate dehydrogenase D subunit
Rv1248c	<i>sucA</i>	2-oxoglutarate dehydrogenase
Rv2215	<i>sucB</i>	dihydrolipoamide succinyltransferase
Rv0951	<i>sucC</i>	succinyl-CoA synthase β chain
Rv0952	<i>sucD</i>	succinyl-CoA synthase α chain

**4. Glyoxylate bypass**

Rv0467	<i>aceA</i>	isocitrate lyase
Rv1915	<i>aceAa</i>	isocitrate lyase, α module
Rv1916	<i>aceAb</i>	isocitrate lyase, β module
Rv1837c	<i>glcB</i>	malate synthase
Rv3323c	<i>gphA</i>	phosphoglycolate phosphatase

**5. Pentose phosphate pathway**

Rv1445c	<i>devB</i>	glucose-6-phosphate 1-dehydrogenase
Rv1844c	<i>gnd</i>	6-phosphogluconate dehydrogenase (Gram -)
Rv1122	<i>gnd2</i>	6-phosphogluconate dehydrogenase (Gram +)
Rv1446c	<i>opcA</i>	unknown function, may aid G6PDH





Rv1300	<i>hemK</i>	protoporphyrinogen oxidase	transferase	Rv2931	<i>ppsA</i>	phenolphthiocerol synthesis ( <i>ppsB</i> )
Rv0524	<i>hemL</i>	glutamate-1-semialdehyde amino-transferase		Rv2932	<i>ppsB</i>	phenolphthiocerol synthesis ( <i>ppsC</i> )
Rv2388c	<i>hemN</i>	oxygen-independent coproporphyrinogen III oxidase	3. Acyltransferases, mycolyltransferases and phospholipid synthesis	Rv2933	<i>ppsC</i>	phenolphthiocerol synthesis ( <i>ppsD</i> )
Rv2677c	<i>hemY'</i>	protoporphyrinogen oxidase	Rv2289	<i>cdh</i>	<i>ppsD</i>	phenolphthiocerol synthesis ( <i>ppsE</i> )
Rv1485	<i>hemZ</i>	ferrochelatase	Rv2881c	<i>cdsA</i>	<i>ppsE</i>	phenolphthiocerol synthesis ( <i>ppsF</i> )
13. Cobalamin			Rv3804c	<i>fbpA</i>	<i>tesA</i>	thioesterase
Rv2849c	<i>cobA</i>	cob(I)alamin adenosyltransferase	Rv1886c	<i>fbpB</i>	Rv1544	probable ketoacyl reductase
Rv2848c	<i>cobB</i>	cobyrinic acid $\alpha,\gamma$ -diamide synthase	Rv0129c	<i>fbpC</i>		
Rv2231c	<i>cobC</i>	aminotransferase	Rv3803c	<i>fbpD</i>		
Rv2236c	<i>cobD</i>	cobinamide synthase	Rv0564c	<i>gpdA1</i>		
Rv2064	<i>cobG</i>	percorrin reductase	Rv2982c	<i>gpdA2</i>		
Rv2065	<i>cobH</i>	percorrin isomerase	Rv2612c	<i>pgsA</i>		
Rv2066	<i>cobI</i>	CobI-CobJ fusion protein	Rv1822	<i>pgsA2</i>		
Rv2070c	<i>cobK</i>	percorrin reductase	Rv2746c	<i>pgsA3</i>		
Rv2072c	<i>cobL</i>	probable methyltransferase	Rv1551	<i>plsB1</i>		
Rv2071c	<i>cobM</i>	percorrin-3 methylase	Rv2482c	<i>plsB2</i>		
Rv2062c	<i>cobN</i>	cobalt insertion	Rv0437c	<i>psd</i>		
Rv2208	<i>cobS</i>	cobalamin (5'-phosphate) synthase	Rv0436c	<i>psaA</i>		
Rv2207	<i>cobT</i>	nicotinate-nucleotide-dimethylbenzimidazole transferase	Rv0045c	-		
Rv0254c	<i>cobU</i>	cobinamide kinase	Rv0914c	-		
Rv0255c	<i>cobQ</i>	cobyrinic acid synthase	Rv1543	-		
Rv3713	<i>cobQ2</i>	possible cobyrinic acid synthase	Rv1627c	-		
Rv0306	-	similar to BluB cobalamin synthesis protein <i>R. capsulatus</i>	Rv1814	-		
14. Iron utilization			Rv1867	-		
Rv1876	<i>bfrA</i>	bacterioferritin	Rv2261c	-		
Rv3841	<i>bfrB</i>	bacterioferritin	Rv2262c	-		
Rv3215	<i>entC</i>	probable isochorismate synthase	Rv3523	-		
Rv3214	<i>entD</i>	weak similarity to many phosphoglycerate mutases	Rv3720	-		
Rv2895c	<i>viuB</i>	similar to proteins involved in vibriobactin uptake				
Rv3525c	-	similar to ferrityochelin binding protein				
H. Lipid biosynthesis						
1. Synthesis of fatty and mycolic acids						
Rv3285	<i>accA3</i>	acetyl/propionyl CoA carboxylase $\alpha$ subunit				
Rv0904c	<i>accD3</i>	acetyl/propionyl CoA carboxylase $\beta$ subunit				
Rv3799c	<i>accD4</i>	acetyl/propionyl CoA carboxylase $\beta$ subunit				
Rv3280	<i>accD5</i>	acetyl/propionyl CoA carboxylase $\beta$ subunit				
Rv2247	<i>accD6</i>	acetyl/propionyl CoA carboxylase $\beta$ subunit				
Rv2244	<i>acpM</i>	acyl carrier protein (meromycolate extension)				
Rv2523c	<i>acpS</i>	CoA:apo-[ACP] pantethienophosphotransferase				
Rv2243	<i>fabD</i>	malonyl CoA-[ACP] transacylase				
Rv0649	<i>fabD2</i>	malonyl CoA-[ACP] transacylase				
Rv1483	<i>fabG1</i>	3-oxoacyl-[ACP] reductase (aka MabA)				
Rv1350	<i>fabG2</i>	3-oxoacyl-[ACP] reductase				
Rv2002	<i>fabG3</i>	3-oxoacyl-[ACP] reductase				
Rv0242c	<i>fabG4</i>	3-oxoacyl-[ACP] reductase				
Rv2766c	<i>fabG5</i>	3-oxoacyl-[ACP] reductase				
Rv0533c	<i>fabH</i>	$\beta$ -ketoacyl-ACP synthase III				
Rv2524c	<i>fas</i>	fatty acid synthase				
Rv1484	<i>inhA</i>	enoyl-[ACP] reductase				
Rv2245	<i>kasA</i>	$\beta$ -ketoacyl-ACP synthase (meromycolate extension)				
Rv2246	<i>kasB</i>	$\beta$ -ketoacyl-ACP synthase (meromycolate extension)				
Rv1618	<i>tesB1</i>	thioesterase II				
Rv2605c	<i>tesB2</i>	thioesterase II				
Rv0033	-	possible acyl carrier protein				
Rv1344	-	possible acyl carrier protein				
Rv1722	-	possible biotin carboxylase				
Rv3221c	-	resembles biotin carboxyl carrier				
Rv3472	-	possible acyl carrier protein				
2. Modification of fatty and mycolic acids						
Rv3391	<i>acrA1</i>	fatty acyl-CoA reductase				
Rv3392c	<i>cmaA1</i>	cyclopropane mycolic acid synthase 1				
Rv0503c	<i>cmaA2</i>	cyclopropane mycolic acid synthase 2				
Rv0824c	<i>desA1</i>	acyl-[ACP] desaturase				
Rv1094	<i>desA2</i>	acyl-[ACP] desaturase				
Rv3229c	<i>desA3</i>	acyl-[ACP] desaturase				
Rv0645c	<i>mmaA1</i>	methoxymycolic acid synthase 1				
Rv0644c	<i>mmaA2</i>	methoxymycolic acid synthase 2				
Rv0643c	<i>mmaA3</i>	methoxymycolic acid synthase 3				
Rv0642c	<i>mmaA4</i>	methoxymycolic acid synthase 4				
Rv0447c	<i>ufaA1</i>	unknown fatty acid methyltransferase				
Rv3538	<i>ufaA2</i>	unknown fatty acid methyltransferase				
Rv0469	<i>umaA1</i>	unknown mycolic acid methyltransferase				
Rv0470c	<i>umaA2</i>	unknown mycolic acid methyltransferase				
Rv2934	<i>ppsD</i>	phenolphthiocerol synthesis ( <i>ppsE</i> )				
Rv2928	<i>ppsE</i>	phenolphthiocerol synthesis ( <i>ppsF</i> )				
Rv2925	<i>tesA</i>	thioesterase				
J. Broad regulatory functions						
1. Repressors/activators						
Rv1657	<i>argR</i>	arginine repressor				
Rv1267c	<i>embR</i>	regulator of <i>embAB</i> genes ( <i>AisR/DndI/RedD</i> family)				
Rv1909c	<i>furA</i>	ferric uptake regulatory protein				
Rv2359	<i>furB</i>	ferric uptake regulatory protein				
Rv2919c	<i>glnB</i>	nitrogen regulatory protein				
Rv2711	<i>ideR</i>	iron dependent repressor, IdeR				
Rv2720	<i>lexA</i>	LexA, SOS repressor protein				
Rv1479	<i>maxR</i>	transcriptional regulator, MoxR homologue				
Rv3692	<i>maxR2</i>	transcriptional regulator, MoxR homologue				
Rv3164c	<i>maxR3</i>	transcriptional regulator, MoxR homologue				
Rv0212c	<i>nadR</i>	similar to <i>E. coli</i> NadR				
Rv0117	<i>oxyS</i>	transcriptional regulator ( <i>LysR</i> family)				
Rv1379	<i>pyrR</i>	regulatory protein pyrimidine biosynthesis				
Rv2788	<i>sirR</i>	iron-dependent transcriptional repressor				
Rv3082c	<i>virS</i>	putative virulence regulating protein ( <i>AraC/XylS</i> family)				
Rv3219	<i>whiB1</i>	WhiB transcriptional activator homologue				
Rv3260c	<i>whiB2</i>	WhiB transcriptional activator homologue				
Rv3416	<i>whiB3</i>	WhiB transcriptional activator homologue				
Rv3681c	<i>whiB4</i>	WhiB transcriptional activator homologue				
Rv0023	-	putative transcriptional regulator				
Rv0043c	-	transcriptional regulator ( <i>GntR</i> family)				
Rv0067c	-	transcriptional regulator ( <i>TetR/AcrR</i> family)				
Rv0078	-	transcriptional regulator ( <i>TetR/AcrR</i> family)				
Rv0081	-	transcriptional regulator ( <i>ArsR</i> family)				
Rv0135c	-	putative transcriptional regulator				
Rv0144	-	putative transcriptional regulator				
Rv0158	-	transcriptional regulator ( <i>TetR/AcrR</i> family)				
Rv0165c	-	transcriptional regulator ( <i>GntR</i> family)				
Rv0195	-	transcriptional regulator ( <i>LuxR/UhpA</i> family)				
Rv0196	-	transcriptional regulator ( <i>TetR/AcrR</i> family)				
Rv0232	-	transcriptional regulator ( <i>TetR/AcrR</i> family)				
Rv0238	-	transcriptional regulator ( <i>TetR/AcrR</i> family)				
Rv0273c	-	putative transcriptional regulator				
Rv0302	-	transcriptional regulator ( <i>TetR/AcrR</i> family)				
Rv0324	-	putative transcriptional regulator				
Rv0328	-	transcriptional regulator ( <i>TetR/AcrR</i> family)				
Rv0348	-	putative transcriptional regulator				
Rv0377	-	transcriptional regulator ( <i>LysR</i> family)				
Rv0386	-	transcriptional regulator ( <i>LuxR/UhpA</i> family)				
Rv0452	-	putative transcriptional regulator				
Rv0465c	-	transcriptional regulator ( <i>PbsX/Xre</i> family)				
Rv0472c	-	transcriptional regulator ( <i>TetR/AcrR</i> family)				
Rv0474	-	transcriptional regulator ( <i>PbsX/Xre</i> family)				
Rv0485	-	transcriptional regulator ( <i>ROK</i> family)				
Rv0494	-	transcriptional regulator ( <i>GntR</i> family)				
Rv0552	-	putative transcriptional regulator				
Rv0576	-	putative transcriptional regulator				
Rv0586	-	transcriptional regulator ( <i>GntR</i> family)				
Rv0650	-	transcriptional regulator ( <i>ROK</i> family)				
Rv0653c	-	putative transcriptional regulator				
Rv0681	-	transcriptional regulator ( <i>TetR/AcrR</i> family)				
Rv0691c	-	transcriptional regulator ( <i>TetR/AcrR</i> family)				
Rv0737	-	putative transcriptional regulator				
Rv0744c	-	putative transcriptional regulator				
Rv0792c	-	transcriptional regulator ( <i>GntR</i> family)				



Rv1650	<i>pheT</i>	phenylalanyl-tRNA synthase $\beta$ subunit	Rv2090	-	partially similar to DNA polymerase I	2. DNA		
Rv2845c	<i>proS</i>	prolyl-tRNA synthase	Rv2191	-	similar to both PolC and UvrC proteins	Rv0670	<i>end</i>	endonuclease IV (apurinase)
Rv3834c	<i>serS</i>	seryl-tRNA synthase	Rv2464c	-	probable DNA glycosylase, endonuclease VIII	Rv1108c	<i>xseA</i>	exonuclease VII large subunit
Rv2614c	<i>thrS</i>	threonyl-tRNA synthase	Rv3201c	-	probable ATP-dependent DNA helicase	Rv1107c	<i>xseB</i>	exonuclease VII small subunit
Rv2906c	<i>trmD</i>	tRNA (guanine-N1)-methyltransferase	Rv3202c	-	similar to UvrD proteins			3. Proteins, peptides and glycopeptides
Rv3336c	<i>trpS</i>	tryptophanyl tRNA synthase	Rv3263	-	probable DNA methylase	Rv3305c	<i>amiA</i>	probable aminohydrolase
Rv1689	<i>tyrS</i>	tyrosyl-tRNA synthase	Rv3644c	-	similar in N-term to DNA polymerase III	Rv3306c	<i>amiB</i>	probable aminohydrolase
Rv2448c	<i>valS</i>	valyl-tRNA synthase				Rv3596c	<i>clpC</i>	ATP-dependent Clp protease
						Rv2461c	<i>clpP</i>	ATP-dependent Clp protease proteolytic subunit
						Rv2460c	<i>clpP2</i>	ATP-dependent Clp protease proteolytic subunit
						Rv2457c	<i>clpX</i>	ATP-dependent Clp protease
						Rv2667	<i>clpX'</i>	ATP-binding subunit ClpX similar to ClpC from <i>M. leprae</i> but shorter
						Rv3419c	<i>gcp</i>	glycoprotease
						Rv2725c	<i>htrX</i>	GTP-binding protein
						Rv1223	<i>htrA</i>	serine protease
						Rv2861c	<i>mapA1</i>	methionine aminopeptidase
						Rv0734	<i>mapA2</i>	probable methionine aminopeptidase
						Rv0319	<i>ppp</i>	pyrrolidone-carboxylate peptidase
						Rv0125	<i>pepA</i>	probable serine protease
						Rv2213	<i>pepB</i>	aminopeptidase A/I
						Rv0800	<i>pepC</i>	aminopeptidase I
						Rv2467	<i>pepD</i>	probable aminopeptidase
						Rv2089c	<i>pepE</i>	cytoplasmic peptidase
						Rv2535c	<i>pepQ</i>	cytoplasmic peptidase
						Rv2782c	<i>pepR</i>	protease/peptidase, M16 family (insulinase)
						Rv2109c	<i>prcA</i>	proteasome $\alpha$ -type subunit 1
						Rv2110c	<i>prcB</i>	proteasome $\beta$ -type subunit 2
						Rv0782	<i>ptrBa</i>	protease II, $\alpha$ subunit
						Rv0781	<i>ptrBb</i>	protease II, $\beta$ subunit
						Rv0724	<i>sppA</i>	protease IV, signal peptide peptidase
						Rv0198c	-	probable zinc metalloprotease
						Rv0457c	-	probable peptidase
						Rv0840c	-	probable proline iminopeptidase
						Rv0983	-	probable serine protease
						Rv1977	-	probable zinc metallopeptidase
						Rv3668c	-	probable alkaline serine protease
						Rv3671c	-	probable serine protease
						Rv3883c	-	probable secreted protease
						Rv3886c	-	protease
								4. Polysaccharides, lipopolysaccharides and phospholipids
						Rv0062	<i>celA</i>	cellulase/endoglucanase
						Rv3915	<i>cwIM</i>	hydrolase
						Rv0315	-	probable $\beta$ -1,3-glucanase
						Rv1090	-	probable inactivated cellulase/endoglucanase
						Rv1327c	-	probable glycosyl hydrolase, $\alpha$ -amylase family
						Rv1333	-	probable hydrolase
						Rv3463	-	probable neuraminidase
						Rv3717	-	possible N-acetylmuramoyl-L-alanine amidase
								5. Esterases and lipases
						Rv0220	<i>lipC</i>	probable esterase
						Rv1923	<i>lipD</i>	probable esterase
						Rv3775	<i>lipE</i>	probable hydrolase
						Rv3487c	<i>lipF</i>	probable esterase
						Rv0646c	<i>lipG</i>	probable hydrolase
						Rv1399c	<i>lipH</i>	probable lipase
						Rv1400c	<i>lipI</i>	probable lipase
						Rv1900c	<i>lipJ</i>	probable esterase
						Rv2385	<i>lipK</i>	probable acetyl-hydrolase
						Rv1497	<i>lipL</i>	esterase
						Rv2284	<i>lipM</i>	probable esterase
						Rv2970c	<i>lipN</i>	probable lipase/esterase
						Rv1426c	<i>lipO</i>	probable esterase
						Rv2463	<i>lipP</i>	probable esterase
						Rv2485c	<i>lipQ</i>	probable carboxylesterase
						Rv3084	<i>lipR</i>	probable acetyl-hydrolase
						Rv3176c	<i>lipS</i>	probable esterase/lipase
						Rv2045c	<i>lipT</i>	probable carboxylesterase
						Rv1076	<i>lipU</i>	probable esterase
						Rv3203	<i>lipV</i>	probable lipase
						Rv0217c	<i>lipW</i>	probable esterase
						Rv2351c	<i>plcA</i>	phospholipase C precursor
						Rv2350c	<i>plcB</i>	phospholipase C precursor
						Rv2349c	<i>plcC</i>	phospholipase C precursor
						Rv1755c	<i>plcD</i>	partial CDS for phospholipase C
						Rv1104	-	probable esterase pseudogene
						Rv1105	-	probable esterase pseudogene
								6. Aromatic hydrocarbons
						Rv3469c	<i>mhpE</i>	probable 4-hydroxy-2-oxovalerate aldolase
						Rv0316	-	probable muconolactone isomerase
						Rv0771	-	probable 4-carboxymuconolactone decarboxylase
						Rv0939	-	probable dehydrase
						Rv1723	-	6-aminohexanoate-dimer hydro-

Rv2715 - lase  
2-hydroxymuconic semialdehyde  
hydrolase  
Rv3530c - probable *cis*-diol dehydrogenase  
Rv3534c - 4-hydroxy-2-oxovalerate aldolase  
Rv3536c - aromatic hydrocarbon degradation

*C. Cell envelope*

1. Lipoproteins (*lppA-lppO*) 65

2. Surface polysaccharides, lipopolysaccharides, proteins and antigens

Rv0806c *cpsY* probable UDP-glucose-4-epimerase  
Rv3811 *csp* secreted protein  
Rv1677 *dsbF* highly similar to C-term Mpt53  
Rv3794 *embA* involved in arabinogalactan synthesis  
Rv3795 *embB* involved in arabinogalactan synthesis  
Rv3793 *embC* involved in arabinogalactan synthesis  
Rv3875 *esat6* early secretory antigen target  
Rv0112 *gca* probable GDP-mannose dehydratase  
Rv0113 *gmhA* phosphoheptose isomerase  
Rv2965c *kdtB* lipopolysaccharide core biosynthesis protein  
Rv2878c *mpt53* secreted protein Mpt53  
Rv1980c *mpt64* secreted immunogenic protein Mpb64/Mpt64  
Rv2875 *mpt70* major secreted immunogenic protein Mpt70 precursor  
Rv2873 *mpt83* surface lipoprotein Mpt83  
Rv0899 *ompA* member of OmpA family  
Rv3810 *pirG* cell surface protein precursor (Eip protein)  
Rv3782 *rfbE* similar to rhamnosyl transferase  
Rv1302 *rfe* undecaprenyl-phosphate  $\alpha$ -N-acetylglucosaminyltransferase antigen 84 (aka wag31)  
Rv2145c *wag31* tuberculin related peptide (AT103)  
Rv0431 - cell envelope antigen  
Rv0954 - involved in polysaccharide synthesis  
Rv1514c - involved in exopolysaccharide synthesis  
Rv1758 - partial cutinase  
Rv1910c - probable secreted protein  
Rv1919c - weak similarity to pollen antigens  
Rv1984c - probable secreted protein  
Rv1987 - probable secreted protein  
Rv2223c - probable exported protease  
Rv2224c - probable exported protease  
Rv2301 - probable cutinase  
Rv2345 - precursor of probable membrane protein  
Rv2672 - putative exported protease  
Rv3019c - similar to Esat6  
Rv3036c - probable secreted protein  
Rv3449 - probable precursor of serine protease  
Rv3451 - probable cutinase  
Rv3452 - probable cutinase precursor  
Rv3724 - probable cutinase precursor

5. Other membrane proteins 211

Rv1367c - probable penicillin binding protein  
Rv1730c - probable penicillin binding protein  
Rv1922 - probable penicillin binding protein  
Rv2864c - probable penicillin binding protein  
Rv3330 - probable penicillin binding protein  
Rv3627c - probable penicillin binding protein

4. Conserved membrane proteins

Rv0402c *mmpL1* conserved large membrane protein  
Rv0507 *mmpL2* conserved large membrane protein  
Rv0206c *mmpL3* conserved large membrane protein  
Rv0450c *mmpL4* conserved large membrane protein  
Rv0676c *mmpL5* conserved large membrane protein  
Rv1557 *mmpL6* conserved large membrane protein  
Rv2942 *mmpL7* conserved large membrane protein  
Rv3823c *mmpL8* conserved large membrane protein  
Rv2339 *mmpL9* conserved large membrane protein  
Rv1183 *mmpL10* conserved large membrane protein  
Rv0202c *mmpL11* conserved large membrane protein  
Rv1522c *mmpL12* conserved large membrane protein  
Rv0403c *mmpS1* conserved small membrane protein  
Rv0506 *mmpS2* conserved small membrane protein  
Rv2198c *mmpS3* conserved small membrane protein  
Rv0451c *mmpS4* conserved small membrane protein  
Rv0677c *mmpS5* conserved small membrane protein

III. Cell processes

A. Transport/binding proteins

1. Amino acids

Rv2127 *ansP* L-asparagine permease  
Rv0346c *aroP2* probable aromatic amino acid permease  
Rv0917 *betP* glycine betaine transport  
Rv1704c *cycA* transport of D-alanine, D-serine and glycine  
Rv3666c *dppA* probable peptide transport system permease  
Rv3665c *dppB* probable peptide transport system permease  
Rv3664c *dppC* probable peptide transport system permease  
Rv3663c *dppD* probable ABC-transporter  
Rv0522 *gabP* probable 4-amino butyrate transporter  
Rv0411c *glnH* putative glutamine binding protein  
Rv2564 *glnQ* probable ATP-binding transport protein  
Rv1280c *oppA* probable oligopeptide transport protein  
Rv1283c *oppB* oligopeptide transport protein  
Rv1282c *oppC* oligopeptide transport system permease  
Rv1281c *oppD* probable peptide transport protein  
Rv2320c *rocE* arginine/ornithine transporter  
Rv3253c - probable cationic amino acid transport  
Rv3454 - possible proline permease

2. Cations

Rv2920c *amt* putative ammonium transporter  
Rv1607 *chaA* putative calcium/proton antiporter  
Rv1239c *corA* probable magnesium and cobalt transport protein  
Rv0092 *ctpA* cation-transporting ATPase  
Rv0103c *ctpB* cation transport ATPase  
Rv3270 *ctpC* cation transport ATPase  
Rv1469 *ctpD* probable cadmium-transporting ATPase  
Rv0908 *ctpE* probable cation transport ATPase  
Rv1997 *ctpF* probable cation transport ATPase  
Rv1992c *ctpG* probable cation transport ATPase  
Rv0425c *ctpH* C-terminal region putative cation-transporting ATPase  
Rv0107c *ctpl* probable magnesium transport ATPase  
Rv0969 *ctpV* cation transport ATPase  
Rv3044 *fecB* putative Fe(III)-dicitrate transporter  
Rv0265c *fecB2* iron transport protein Fe(III) dicitrate transporter  
Rv1029 *kdpA* potassium-transporting ATPase A chain

Rv1030 *kdpB* potassium-transporting ATPase B chain  
Rv1031 *kdpC* potassium-transporting ATPase C chain  
Rv3236c *ketB* probable glutathione-regulated potassium-efflux protein  
Rv2877c *merT* possible mercury resistance transport system  
Rv1811 *mgtC* probable magnesium transport ATPase protein C  
Rv0362 *mgtE* putative magnesium ion transporter  
Rv2856 *nicT* probable nickel transport protein  
Rv0924c *nramp* transmembrane protein belonging to Nramp family  
Rv2691 *trkA* probable potassium uptake protein  
Rv2692 *trkB* probable potassium uptake protein  
Rv2287 *yjcE* probable Na<sup>+</sup>/H<sup>+</sup> exchanger  
Rv2723 - probable membrane protein, tellurium resistance  
Rv3162c - probable membrane protein  
Rv3237c - possible potassium channel protein  
Rv3743c - probable cation-transporting ATPase

3. Carbohydrates, organic acids and alcohols

Rv2443 *dctA* C4-dicarboxylate transport protein  
Rv3476c *kgtP* sugar transport protein  
Rv1902c *nanT* probable sialic acid transporter  
Rv1236 *sugA* membrane protein probably involved in sugar transport  
Rv1237 *sugB* sugar transport protein  
Rv1238 *sugC* ABC transporter component of sugar uptake system  
Rv3331 *sugI* probable sugar transport protein  
Rv2835c *ugpA* *sn*-glycerol-3-phosphate permease  
Rv2833c *ugpB* *sn*-glycerol-3-phosphate-binding periplasmic lipoprotein  
Rv2832c *ugpC* *sn*-glycerol-3-phosphate transport ATP-binding protein  
Rv2834c *ugpE* *sn*-glycerol-3-phosphate transport system protein  
Rv2316 *uspA* sugar transport protein  
Rv2318 *uspC* sugar transport protein  
Rv2317 *uspE* sugar transport protein  
Rv1200 - probable sugar transporter  
Rv2038c - probable ABC sugar transporter  
Rv2039c - probable sugar transporter  
Rv2040c - probable sugar transporter  
Rv2041c - probable sugar transporter

4. Anions

Rv2684 *arsA* probable arsenical pump  
Rv2685 *arsB* probable arsenical pump  
Rv3578 *arsB2* probable arsenical pump  
Rv2643 *arsC* probable arsenical pump  
Rv2397c *cysA* sulphate transport ATP-binding protein  
Rv2399c *cysT* sulphate transport system permease protein  
Rv2398c *cysW* sulphate transport system permease protein  
Rv1857 *modA* molybdate binding protein  
Rv1858 *modB* transport system permease, molybdate uptake  
Rv1859 *modC* molybdate uptake ABC-transporter  
Rv1860 *modD* precursor of Apa (45/47 kD secreted protein)  
Rv2329c *narK1* probable nitrite extrusion protein  
Rv1737c *narK2* nitrite extrusion protein  
Rv0261c *narK3* nitrite extrusion protein  
Rv0267 *narU* similar to nitrite extrusion protein 2  
Rv0934 *phoS1* PstS component of phosphate uptake  
Rv0928 *phoS2* PstS component of phosphate uptake  
Rv0820 *phoT* phosphate transport system ABC transporter  
Rv3301c *phoY1* phosphate transport system regulator  
Rv0821c *phoY2* phosphate transport system regulator  
Rv0545c *pitA* low-affinity inorganic phosphate transporter  
Rv2281 *pitB* phosphate permease  
Rv0930 *pstA1* PstA component of phosphate uptake  
Rv0936 *pstA2* PstA component of phosphate uptake  
Rv0933 *pstB* ABC transport component of phosphate uptake  
Rv0935 *pstC* PstC component of phosphate uptake  
Rv0929 *pstC2* membrane-bound component of



Rv0932c	<i>pstS</i>	phosphate transport system PstS component of phosphate uptake
Rv2400c	<i>subI</i>	sulphate binding precursor
Rv0143c	-	probable chloride channel
Rv1707	-	probable sulphate permease
Rv1739c	-	possible sulphate transporter
Rv3679	-	possible anion transporter
Rv3680	-	probable anion transporter
5. Fatty acid transport		
Rv2790c	<i>ltp1</i>	non-specific lipid transport protein
Rv3540c	<i>ltp2</i>	non-specific lipid transport protein
6. Efflux proteins		
Rv2936	<i>drvA</i>	similar daunorubicin resistance ABC-transporter
Rv2937	<i>drvB</i>	similar daunorubicin resistance transmembrane protein
Rv2938	<i>drvC</i>	similar daunorubicin resistance transmembrane protein
Rv2846c	<i>efpA</i>	putative efflux protein
Rv3065	<i>emrE</i>	resistance to ethidium bromide
Rv0783c	-	multidrug resistance protein
Rv0849	-	possible quinolone efflux pump
Rv1145	-	probable drug transporter
Rv1146	-	probable drug transporter
Rv1250	-	probable drug efflux protein
Rv1258c	-	probable multidrug resistance pump
Rv1410c	-	probable drug efflux protein
Rv1634	-	probable drug efflux protein
Rv1819c	-	probable multidrug resistance pump
Rv2136c	-	putative bacitracin resistance protein
Rv2209	-	probable drug efflux protein
Rv2333c	-	probable tetracycline C resistance protein
Rv2994	-	probable fluoroquinolone efflux protein
Rv1877	-	probable drug efflux protein
Rv2459	-	probable drug efflux protein
B. Chaperones/Heat shock		
Rv0384c	<i>clpB</i>	heat shock protein
Rv0352	<i>dnaJ</i>	acts with GrpE to stimulate DnaK ATPase
Rv2373c	<i>dnaJ2</i>	DnaJ homologue
Rv0350	<i>dnaK</i>	70 kD heat shock protein, chromosome replication
Rv3417c	<i>groEL1</i>	60 kD chaperonin 1
Rv0440	<i>groEL2</i>	60 kD chaperonin 2
Rv3418c	<i>groES</i>	10 kD chaperone
Rv0351	<i>grpE</i>	stimulates DnaK ATPase activity
Rv2374c	<i>hrcA</i>	heat-inducible transcription repressor
Rv0251c	<i>hsp</i>	possible heat shock protein
Rv0353	<i>hspR</i>	heat shock regulator
Rv2031c	<i>hspX</i>	14kD antigen, heat shock protein Hsp20 family
Rv2299c	<i>htpG</i>	heat shock protein Hsp90 family
Rv0563	<i>htpX</i>	probable (transmembrane) heat shock protein
Rv2701c	<i>suhB</i>	putative extragenic suppressor protein
Rv3269	-	probable heat shock protein
C. Cell division		
Rv3641c	<i>fic</i>	possible cell division protein
Rv3102c	<i>ftsE</i>	membrane protein
Rv3610c	<i>ftsH</i>	inner membrane protein, chaperone
Rv2748c	<i>ftsK</i>	chromosome partitioning
Rv2151c	<i>ftsQ</i>	ingrowth of wall at septum
Rv2154c	<i>ftsW</i>	membrane protein (shape determination)
Rv3101c	<i>ftsX</i>	membrane protein
Rv2921c	<i>ftsY</i>	cell division protein FtsY
Rv2150c	<i>ftsZ</i>	circumferential ring, GTPase
Rv3919c	<i>gid</i>	glucose inhibited division protein B
Rv3625c	<i>mesJ</i>	probable cell cycle protein
Rv3917c	<i>parA</i>	chromosome partitioning; DNA-binding
Rv3918c	<i>parB</i>	possibly involved in chromosome partitioning
Rv2922c	<i>smc</i>	member of Smc1/Cut3/Cut14 family
Rv0012	-	possible cell division protein
Rv0435c	-	ATPase of AAA-family
Rv2115c	-	ATPase of AAA-family
Rv3213c	-	possible role in chromosome segregation
Rv1708	-	possible role in chromosome partitioning
D. Protein and peptide secretion		
Rv2916c	<i>ffh</i>	signal recognition particle protein
Rv2903c	<i>lepB</i>	signal peptidase I
Rv1614	<i>lgt</i>	prolipoprotein diacylglycerol transferase
Rv1539	<i>lspA</i>	lipoprotein signal peptidase
Rv0379	<i>sec</i>	probable transport protein SecE/Sec61- $\gamma$ family
Rv3240c	<i>secA</i>	SecA, preprotein translocase sub-

Rv1821	<i>secA2</i>	unit SecA, preprotein translocase sub-unit
Rv2587c	<i>secD</i>	protein-export membrane protein
Rv0638	<i>secE</i>	SecE preprotein translocase
Rv2586c	<i>secF</i>	protein-export membrane protein
Rv1440	<i>secG</i>	protein-export membrane protein
Rv0732	<i>secY</i>	SecY subunit of preprotein translocase
Rv2462c	<i>tig</i>	chaperone protein, similar to trigger factor
Rv2813	-	probable general secretion pathway protein
E. Adaptations and atypical conditions		
Rv1901	<i>cinA</i>	competence damage protein
Rv3648c	<i>cspA</i>	cold shock protein, transcriptional regulator
Rv0871	<i>cspB</i>	probable cold shock protein
Rv3063	<i>cstA</i>	starvation-induced stress response protein
Rv3490	<i>otsA</i>	probable $\alpha$ , $\alpha$ -trehalose-phosphate synthase
Rv2006	<i>otsB</i>	trehalose-6-phosphate phosphatase
Rv3372	<i>otsB2</i>	trehalose-6-phosphate phosphatase
Rv3758c	<i>proV</i>	osmoprotection ABC transporter
Rv3757c	<i>proW</i>	transport system permease
Rv3759c	<i>proX</i>	similar to osmoprotection proteins
Rv3756c	<i>proZ</i>	transport system permease
Rv1026	-	probable pppGpp-5'phosphohydrolyase
F. Detoxification		
Rv2428	<i>ahpC</i>	alkyl hydroperoxide reductase
Rv2429	<i>ahpD</i>	member of AhpC/TSA family
Rv2238c	<i>ahpE</i>	member of AhpC/TSA family
Rv2521	<i>bcp</i>	bacterioferritin comigratory protein
Rv1608c	<i>bcpB</i>	probable bacterioferritin comigratory protein
Rv3473c	<i>bpoA</i>	probable non-heme bromoperoxidase
Rv1123c	<i>bpoB</i>	probable non-heme bromoperoxidase
Rv0554	<i>bpoC</i>	probable non-heme bromoperoxidase
Rv3617	<i>ephA</i>	probable epoxide hydrolase
Rv1938	<i>ephB</i>	probable epoxide hydrolase
Rv1124	<i>ephC</i>	probable epoxide hydrolase
Rv2214c	<i>ephD</i>	probable epoxide hydrolase
Rv3670	<i>ephE</i>	probable epoxide hydrolase
Rv0134	<i>ephF</i>	probable epoxide hydrolase
Rv3171c	<i>hpx</i>	probable non-heme haloperoxidase
Rv1908c	<i>katG</i>	catalase-peroxidase
Rv3846	<i>sodA</i>	superoxide dismutase
Rv0432	<i>sodC</i>	superoxide dismutase precursor - (Cu-Zn)
Rv1932	<i>tpx</i>	thiol peroxidase
Rv0634c	-	putative glyoxylase II
Rv2581c	-	putative glyoxylase II
Rv3177	-	probable non-heme haloperoxidase
IV. Other		
A. Virulence		
Rv0169	<i>mce1</i>	cell invasion protein
Rv0589	<i>mce2</i>	cell invasion protein
Rv1966	<i>mce3</i>	cell invasion protein
Rv3499c	<i>mce4</i>	cell invasion protein
Rv3100c	<i>smgB</i>	probable small protein b
Rv1694	<i>tya</i>	cytotoxin/hemolysin homologue
Rv0024	-	putative p60 homologue
Rv0167	-	part of <i>mce1</i> operon
Rv0168	-	part of <i>mce1</i> operon
Rv0170	-	part of <i>mce1</i> operon
Rv0171	-	part of <i>mce1</i> operon
Rv0172	-	part of <i>mce1</i> operon
Rv0174	-	part of <i>mce1</i> operon
Rv0587	-	part of <i>mce2</i> operon
Rv0588	-	part of <i>mce2</i> operon
Rv0590	-	part of <i>mce2</i> operon
Rv0591	-	part of <i>mce2</i> operon
Rv0592	-	part of <i>mce2</i> operon
Rv0594	-	part of <i>mce2</i> operon
Rv1085c	-	possible hemolysin
Rv1477	-	putative exported p60 protein homologue
Rv1478	-	putative exported p60 protein homologue
Rv1566c	-	putative exported p60 protein homologue
Rv1964	-	part of <i>mce3</i> operon
Rv1965	-	part of <i>mce3</i> operon
Rv1967	-	part of <i>mce3</i> operon
Rv1968	-	part of <i>mce3</i> operon
Rv1969	-	part of <i>mce3</i> operon
Rv1971	-	part of <i>mce3</i> operon
Rv2190c	-	putative p60 homologue
Rv3494c	-	part of <i>mce4</i> operon
Rv3496c	-	part of <i>mce4</i> operon
Rv3497c	-	part of <i>mce4</i> operon
Rv3498c	-	part of <i>mce4</i> operon

Rv3500c	-	part of <i>mce4</i> operon
Rv3501c	-	part of <i>mce4</i> operon
Rv3896c	-	putative p60 homologue
Rv3922c	-	possible hemolysin
B. IS elements, Repeated sequences, and Phage		
1. IS elements		
IS6110	-	16 copies
IS1081	-	6 copies
Others	-	34 copies
2. REP13E12 family		
7 copies		
3. Phage-related functions		
Rv2894c	<i>xerC</i>	integrase/recombinase
Rv1701	<i>xerD</i>	integrase/recombinase
Rv1054	-	integrase-a
Rv1055	-	integrase-b
Rv1573	-	phiRV1 phage related protein
Rv1574	-	phiRV1 phage related protein
Rv1575	-	phiRV1 phage related protein
Rv1576c	-	phiRV1 phage related protein
Rv1577c	-	phiRV1 possible prohead protease
Rv1578c	-	phiRV1 phage related protein
Rv1579c	-	phiRV1 phage related protein
Rv1580c	-	phiRV1 phage related protein
Rv1581c	-	phiRV1 phage related protein
Rv1582c	-	phiRV1 phage related protein
Rv1583c	-	phiRV1 phage related protein
Rv1584c	-	phiRV1 phage related protein
Rv1585c	-	phiRV1 phage related protein
Rv1586c	-	phiRV1 integrase
Rv2309c	-	integrase
Rv2310	-	excisionase
Rv2646	-	phiRV2 integrase
Rv2647	-	phiRV2 phage related protein
Rv2650c	-	phiRV2 phage related protein
Rv2651c	-	phiRV2 prohead protease
Rv2652c	-	phiRV2 phage related protein
Rv2653c	-	phiRV2 phage related protein
Rv2654c	-	phiRV2 phage related protein
Rv2655c	-	phiRV2 phage related protein
Rv2656c	-	phiRV2 phage related protein
Rv2657c	-	similar to gp36 of mycobacteriophage L5
Rv2658c	-	phiRV2 phage related protein
Rv2659c	-	phiRV2 integrase
Rv2830c	-	similar to phage P1 <i>phd</i> gene
Rv3750c	-	excisionase
Rv3751	-	putative integrase
C. PE and PPE families		
1. PE family		
PE subfamily	-	38 members
PE_PGRS subfamily	-	61 members
2. PPE family		
68 members		
D. Antibiotic production and resistance		
Rv2068c	<i>blaC</i>	class A $\beta$ -lactamase
Rv3290c	<i>lat</i>	lysine-c aminotransferase
Rv2043c	<i>pncA</i>	pyrazinamide resistance/sensitivity
Rv0133	-	possible puromycin N-acetyltransferase
Rv0262c	-	aminoglycoside 2'-N-acetyltransferase
Rv0802c	-	acetyltransferase
Rv1082	-	similar to <i>S. lincolnensis</i> <i>lmbE</i>
Rv1170	-	similar to <i>S. lincolnensis</i> <i>lmbE</i>
Rv1347c	-	possible aminoglycoside 6'-N-acetyltransferase
Rv2036	-	similar to lincomycin production genes
Rv2303c	-	similar to <i>S. griseus</i> macrotetrolide resistance protein
Rv3225c	-	probable aminoglycoside 3'-phosphotransferases
Rv3700c	-	probable acetyltransferase
Rv3817	-	probable aminoglycoside 3'-phosphotransferase
E. Bacteriocin-like proteins		
3		
F. Cytochrome P450 enzymes		
22		
G. Coenzyme F420-dependent enzymes		
3		
H. Miscellaneous transferases		
61		
I. Miscellaneous phosphatases, lyases, and hydrolases		
18		
J. Cyclases		
6		
K. Chelataes		
2		
V. Conserved hypotheticals		
912		
VI. Unknowns		
606		
TOTAL	-	3924

# Deciphering the biology of *Mycobacterium tuberculosis* from the complete genome sequence

S. T. Cole\*, R. Brosch\*, J. Parkhill, T. Garnier\*, C. Churcher, D. Harris, S. V. Gordon\*, K. Eiglmeier\*, S. Gas\*, C. E. Barry III†, F. Tekaia‡, K. Badcock, D. Basham, D. Brown, T. Chillingworth, R. Connor, R. Davies, K. Devlin, T. Feltwell, S. Gentles, N. Hamlin, S. Holroyd, T. Hornsby, K. Jagels, A. Krogh§, J. McLean, S. Moule, L. Murphy, K. Oliver, J. Osborne, M. A. Quail, M.-A. Rajandream, J. Rogers, S. Rutter, K. Seeger, J. Skelton, R. Squares, S. Squares, J. E. Sulston, K. Taylor, S. Whitehead & B. G. Barrell

Sanger Centre, Wellcome Trust Genome Campus, Hinxton CB10 1SA, UK

\* Unité de Génétique Moléculaire Bactérienne, and ‡ Unité de Génétique Moléculaire des Levures, Institut Pasteur, 28 rue du Docteur Roux, 75724 Paris Cedex 15, France

† Tuberculosis Research Unit, Laboratory of Intracellular Parasites, Rocky Mountain Laboratories, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Hamilton, Montana 59840, USA

§ Center for Biological Sequence Analysis, Technical University of Denmark, Lyngby, Denmark

**Countless millions of people have died from tuberculosis, a chronic infectious disease caused by the tubercle bacillus. The complete genome sequence of the best-characterized strain of *Mycobacterium tuberculosis*, H37Rv, has been determined and analysed in order to improve our understanding of the biology of this slow-growing pathogen and to help the conception of new prophylactic and therapeutic interventions. The genome comprises 4,411,529 base pairs, contains around 4,000 genes, and has a very high guanine + cytosine content that is reflected in the biased amino-acid content of the proteins. *M. tuberculosis* differs radically from other bacteria in that a very large portion of its coding capacity is devoted to the production of enzymes involved in lipogenesis and lipolysis, and to two new families of glycine-rich proteins with a repetitive structure that may represent a source of antigenic variation.**

Despite the availability of effective short-course chemotherapy (DOTS) and the Bacille Calmette-Guérin (BCG) vaccine, the tubercle bacillus continues to claim more lives than any other single infectious agent<sup>1</sup>. Recent years have seen increased incidence of tuberculosis in both developing and industrialized countries, the widespread emergence of drug-resistant strains and a deadly synergy with the human immunodeficiency virus (HIV). In 1993, the gravity of the situation led the World Health Organisation (WHO) to declare tuberculosis a global emergency in an attempt to heighten public and political awareness. Radical measures are needed now to prevent the grim predictions of the WHO becoming reality. The combination of genomics and bioinformatics has the potential to generate the information and knowledge that will enable the conception and development of new therapies and interventions needed to treat this airborne disease and to elucidate the unusual biology of its aetiological agent, *Mycobacterium tuberculosis*.

The characteristic features of the tubercle bacillus include its slow growth, dormancy, complex cell envelope, intracellular pathogenesis and genetic homogeneity<sup>2</sup>. The generation time of *M. tuberculosis*, in synthetic medium or infected animals, is typically ~24 hours. This contributes to the chronic nature of the disease, imposes lengthy treatment regimens and represents a formidable obstacle for researchers. The state of dormancy in which the bacillus remains quiescent within infected tissue may reflect metabolic shutdown resulting from the action of a cell-mediated immune response that can contain but not eradicate the infection. As immunity wanes, through ageing or immune suppression, the dormant bacteria reactivate, causing an outbreak of disease often many decades after the initial infection<sup>3</sup>. The molecular basis of dormancy and reactivation remains obscure but is expected to be genetically programmed and to involve intracellular signalling pathways.

The cell envelope of *M. tuberculosis*, a Gram-positive bacterium with a G + C-rich genome, contains an additional layer beyond the peptidoglycan that is exceptionally rich in unusual lipids, glycolipids and polysaccharides<sup>4,5</sup>.

Novel biosynthetic pathways generate cell-wall components such as mycolic acids, mycocerosic acid, phenolthiocerol, lipoarabinomannan and arabinogalactan, and several of these may contribute to mycobacterial longevity, trigger inflammatory host reactions and act in pathogenesis. Little is known about the mechanisms involved in life within the macrophage, or the extent and nature of the virulence factors produced by the bacillus and their contribution to disease.

It is thought that the progenitor of the *M. tuberculosis* complex, comprising *M. tuberculosis*, *M. bovis*, *M. bovis* BCG, *M. africanum* and *M. microti*, arose from a soil bacterium and that the human bacillus may have been derived from the bovine form following the domestication of cattle. The complex lacks interstrain genetic diversity, and nucleotide changes are very rare<sup>6</sup>. This is important in terms of immunity and vaccine development as most of the proteins will be identical in all strains and therefore antigenic drift will be restricted. On the basis of the systematic sequence analysis of 26 loci in a large number of independent isolates<sup>6</sup>, it was concluded that the genome of *M. tuberculosis* is either unusually inert or that the organism is relatively young in evolutionary terms.

Since its isolation in 1905, the H37Rv strain of *M. tuberculosis* has found extensive, worldwide application in biomedical research because it has retained full virulence in animal models of tuberculosis, unlike some clinical isolates; it is also susceptible to drugs and amenable to genetic manipulation. An integrated map of the 4.4 megabase (Mb) circular chromosome of this slow-growing pathogen had been established previously and ordered libraries of cosmids and bacterial artificial chromosomes (BACs) were available<sup>7,8</sup>.

## Organization and sequence of the genome

**Sequence analysis.** To obtain the contiguous genome sequence, a combined approach was used that involved the systematic sequence analysis of selected large-insert clones (cosmids and BACs) as well as

random small-insert clones from a whole-genome shotgun library. This culminated in a composite sequence of 4,411,529 base pairs (bp) (Figs 1, 2), with a G + C content of 65.6%. This represents the second-largest bacterial genome sequence currently available (after that of *Escherichia coli*)<sup>9</sup>. The initiation codon for the *dnaA* gene, a hallmark for the origin of replication, *oriC*, was chosen as the start point for numbering. The genome is rich in repetitive DNA, particularly insertion sequences, and in new multigene families and duplicated housekeeping genes. The G + C content is relatively constant throughout the genome (Fig. 1) indicating that horizontally transferred pathogenicity islands of atypical base composition are probably absent. Several regions showing higher than average G + C content (Fig. 1) were detected; these correspond to sequences belonging to a large gene family that includes the polymorphic G + C-rich sequences (PGRSs).

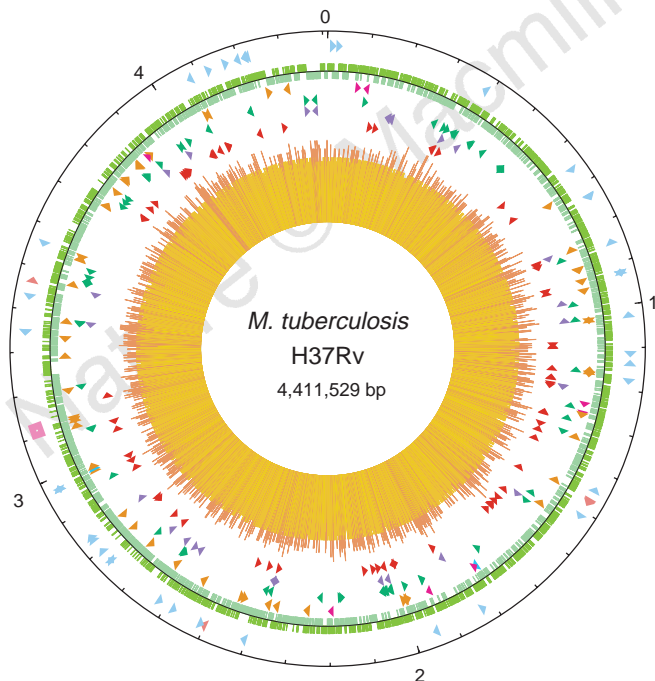
**Genes for stable RNA.** Fifty genes coding for functional RNA molecules were found. These molecules were the three species produced by the unique ribosomal RNA operon, the 10Sa RNA involved in degradation of proteins encoded by abnormal messenger RNA, the RNA component of RNase P, and 45 transfer RNAs. No 4.5S RNA could be detected. The *rrn* operon is situated unusually as it occurs about 1,500 kilobases (kb) from the putative *oriC*; most eubacteria have one or more *rrn* operons near to *oriC* to exploit the gene-dosage effect obtained during replication<sup>10</sup>. This arrangement may be related to the slow growth of *M. tuberculosis*. The genes encoding tRNAs that recognize 43 of the 61 possible sense codons were distributed throughout the genome and, with one

exception, none of these uses A in the first position of the anticodon, indicating that extensive wobble occurs during translation. This is consistent with the high G + C content of the genome and the consequent bias in codon usage. Three genes encoding tRNAs for methionine were found; one of these genes (*metV*) is situated in a region that may correspond to the terminus of replication (Figs 1, 2). As *metV* is linked to defective genes for integrase and excisionase, perhaps it was once part of a phage or similar mobile genetic element.

**Insertion sequences and prophages.** Sixteen copies of the promiscuous insertion sequence IS6110 and six copies of the more stable element IS1081 reside within the genome of H37Rv<sup>8</sup>. One copy of IS1081 is truncated. Scrutiny of the genomic sequence led to the identification of a further 32 different insertion sequence elements, most of which have not been described previously, and of the 13E12 family of repetitive sequences which exhibit some of the characteristics of mobile genetic elements (Fig. 1). The newly discovered insertion sequences belong mainly to the IS3 and IS256 families, although six of them define a new group. There is extensive similarity between IS1561 and IS1552 with insertion sequence elements found in *Nocardia* and *Rhodococcus* spp., suggesting that they may be widely disseminated among the actinomycetes.

Most of the insertion sequences in *M. tuberculosis* H37Rv appear to have inserted in intergenic or non-coding regions, often near tRNA genes (Fig. 1). Many are clustered, suggesting the existence of insertional hot-spots that prevent genes from being inactivated, as has been described for *Rhizobium*<sup>11</sup>. The chromosomal distribution of the insertion sequences is informative as there appears to have been a selection against insertions in the quadrant encompassing *oriC* and an overrepresentation in the direct repeat region that contains the prototype IS6110. This bias was also observed experimentally in a transposon mutagenesis study<sup>12</sup>.

At least two prophages have been detected in the genome sequence and their presence may explain why *M. tuberculosis* shows persistent low-level lysis in culture. Prophages phiRv1 and phiRv2 are both ~10 kb in length and are similarly organized, and some of their gene products show marked similarity to those encoded by certain bacteriophages from *Streptomyces* and saprophytic mycobacteria. The site of insertion of phiRv1 is intriguing as it corresponds to part of a repetitive sequence of the 13E12 family that itself appears to have integrated into the biotin operon. Some strains of *M. tuberculosis* have been described as requiring biotin as a growth supplement, indicating either that phiRv1 has a polar effect on expression of the distal *bio* genes or that aberrant excision, leading to mutation, may occur. During the serial attenuation of *M. bovis* that led to the vaccine strain *M. bovis* BCG, the phiRv1 prophage was lost<sup>13</sup>. In a systematic study of the genomic diversity of prophages and insertion sequences (S.V.G. *et al.*, manuscript in preparation), only IS1532 exhibited significant variability, indicating that most of the prophages and insertion sequences are currently stable. However, from these combined observations, one can conclude that horizontal transfer of genetic material into the free-living ancestor of the *M. tuberculosis* complex probably occurred in nature before the tubercle bacillus adopted its specialized intracellular niche.



**Figure 1** Circular map of the chromosome of *M. tuberculosis* H37Rv. The outer circle shows the scale in Mb, with 0 representing the origin of replication. The first ring from the exterior denotes the positions of stable RNA genes (tRNAs are blue, others are pink) and the direct repeat region (pink cube); the second ring inward shows the coding sequence by strand (clockwise, dark green; anticlockwise, light green); the third ring depicts repetitive DNA (insertion sequences, orange; 13E12 REP family, dark pink; prophage, blue); the fourth ring shows the positions of the PPE family members (green); the fifth ring shows the PE family members (purple, excluding PGRS); and the sixth ring shows the positions of the PGRS sequences (dark red). The histogram (centre) represents G + C content, with <65% G + C in yellow, and >65% G + C in red. The figure was generated with software from DNASTAR.

**Figure 2** Linear map of the chromosome of *M. tuberculosis* H37Rv showing the position and orientation of known genes and coding sequences (CDS). We used the following functional categories (adapted from ref. 20): lipid metabolism (black); intermediary metabolism and respiration (yellow); information pathways (pink); regulatory proteins (sky blue); conserved hypothetical proteins (orange); proteins of unknown function (light green); insertion sequences and phage-related functions (blue); stable RNAs (purple); cell wall and cell processes (dark green); PE and PPE protein families (magenta); virulence, detoxification and adaptation (white). For additional information about gene functions, refer to <http://www.sanger.ac.uk>.

**Genes encoding proteins.** 3,924 open reading frames were identified in the genome (see Methods), accounting for ~91% of the potential coding capacity (Figs 1, 2). A few of these genes appear to have in-frame stop codons or frameshift mutations (irrespective of the source of the DNA sequenced) and may either use frameshifting during translation or correspond to pseudogenes. Consistent with the high G + C content of the genome, GTG initiation codons (35%) are used more frequently than in *Bacillus subtilis* (9%) and *E. coli* (14%), although ATG (61%) is the most common translational start. There are a few examples of atypical initiation codons, the most notable being the ATC used by *infC*, which begins with ATT in both *B. subtilis* and *E. coli*<sup>9,14</sup>. There is a slight bias in the orientation of the genes (Fig. 1) with respect to the direction of replication as ~59% are transcribed with the same polarity as replication, compared with 75% in *B. subtilis*. In other bacteria, genes transcribed in the same direction as the replication forks are believed to be expressed more efficiently<sup>9,14</sup>. Again, the more even distribution in gene polarity seen in *M. tuberculosis* may reflect the slow growth and infrequent replication cycles. Three genes (*dnaB*, *recA* and *Rv1461*) have been invaded by sequences encoding inteins (protein introns) and in all three cases their counterparts in *M. leprae* also contain inteins, but at different sites<sup>15</sup> (S.T.C. *et al.*, unpublished observations).

**Protein function, composition and duplication.** By using various database comparisons, we attributed precise functions to ~40% of the predicted proteins and found some information or similarity for another 44%. The remaining 16% resembled no known proteins and may account for specific mycobacterial functions. Examination of the amino-acid composition of the *M. tuberculosis* proteome by correspondence analysis<sup>16</sup>, and comparison with that of other microorganisms whose genome sequences are available, revealed a statistically significant preference for the amino acids Ala, Gly, Pro, Arg and Trp, which are all encoded by G + C-rich codons, and a comparative reduction in the use of amino acids encoded by A + T-rich codons such as Asn, Ile, Lys, Phe and Tyr (Fig. 3). This approach also identified two groups of proteins rich in Asn or Gly that belong to new families, PE and PPE (see below). The fraction of the proteome that has arisen through gene duplication is similar to that seen in *E. coli* or *B. subtilis* (~51%; refs 9, 14), except that the level of sequence conservation is considerably higher, indicating that there may be extensive redundancy or differential production of the corresponding polypeptides. The apparent lack of divergence following gene duplication is consistent with the hypothesis that *M. tuberculosis* is of recent descent<sup>6</sup>.

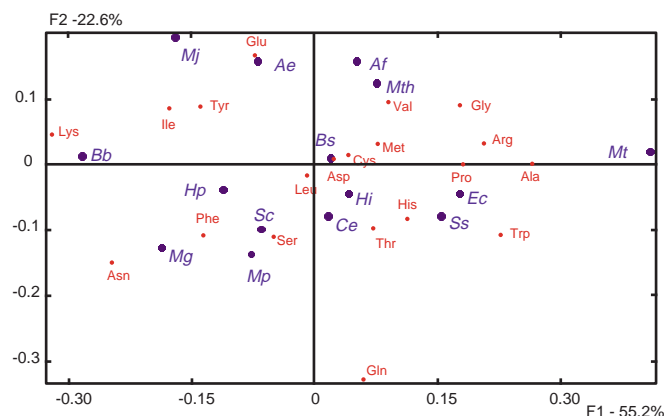
**General metabolism, regulation and drug resistance**

**Metabolic pathways.** From the genome sequence, it is clear that the tubercle bacillus has the potential to synthesize all the essential amino acids, vitamins and enzyme co-factors, although some of the pathways involved may differ from those found in other bacteria. *M. tuberculosis* can metabolize a variety of carbohydrates, hydrocarbons, alcohols, ketones and carboxylic acids<sup>2,17</sup>. It is apparent from genome inspection that, in addition to many functions involved in lipid metabolism, the enzymes necessary for glycolysis, the pentose phosphate pathway, and the tricarboxylic acid and glyoxylate cycles are all present. A large number (~200) of oxidoreductases, oxygenases and dehydrogenases is predicted, as well as many oxygenases containing cytochrome P450, that are similar to fungal proteins involved in sterol degradation. Under aerobic growth conditions, ATP will be generated by oxidative phosphorylation from electron transport chains involving a ubiquinone cytochrome *b* reductase complex and cytochrome *c* oxidase. Components of several anaerobic phosphorylative electron transport chains are also present, including genes for nitrate reductase (*narGHJI*), fumarate reductase (*frdABCD*) and possibly nitrite reductase (*nirBD*), as well as a new reductase (*narX*) that results from a rearrangement of a homologue of the *narGHJI* operon. Two genes encoding haemoglobin-like

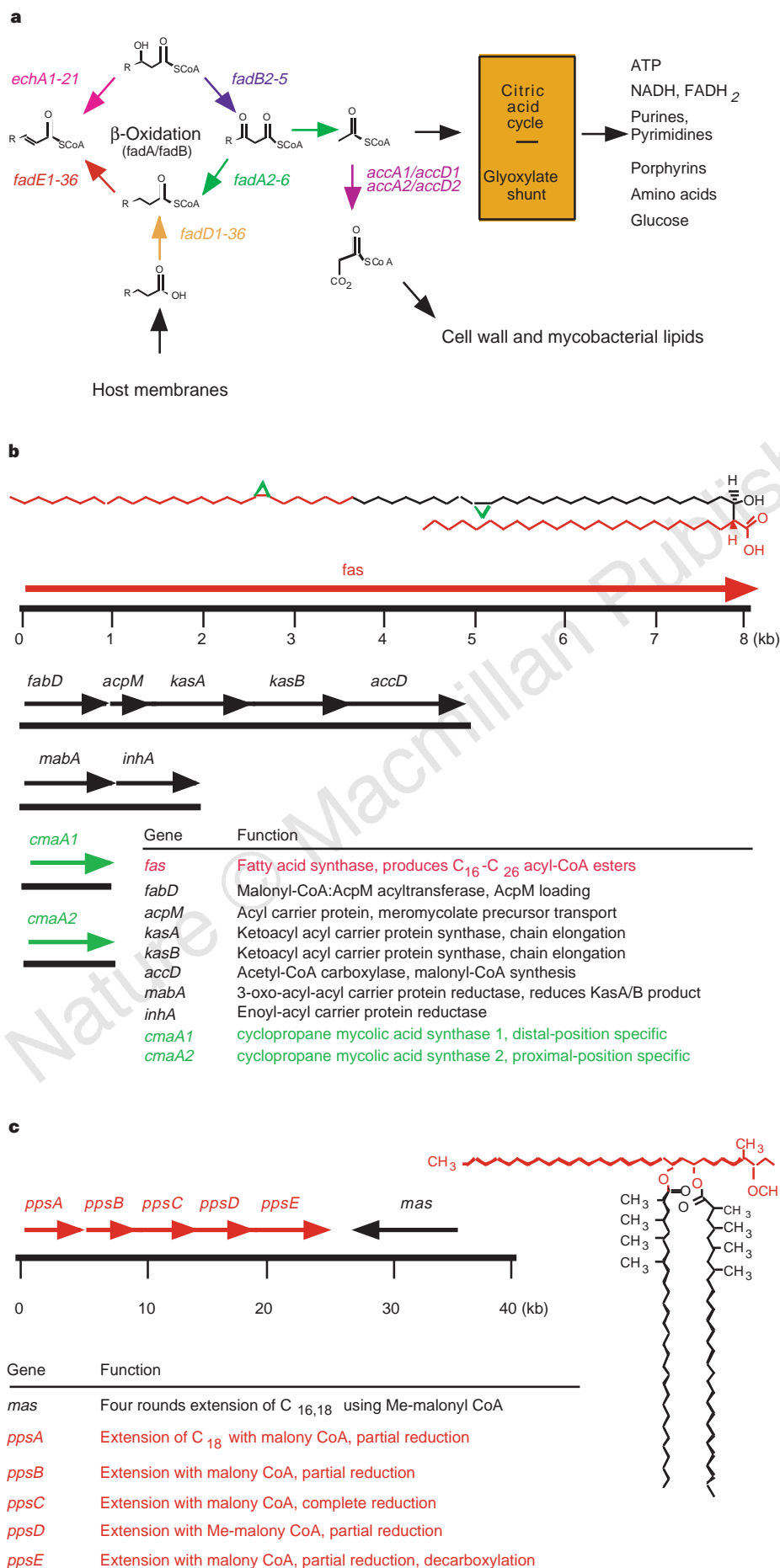
proteins, which may protect against oxidative stress or be involved in oxygen capture, were found. The ability of the bacillus to adapt its metabolism to environmental change is significant as it not only has to compete with the lung for oxygen but must also adapt to the microaerophilic/anaerobic environment at the heart of the burgeoning granuloma.

**Regulation and signal transduction.** Given the complexity of the environmental and metabolic choices facing *M. tuberculosis*, an extensive regulatory repertoire was expected. Thirteen putative sigma factors govern gene expression at the level of transcription initiation, and more than 100 regulatory proteins are predicted (Table 1). Unlike *B. subtilis* and *E. coli*, in which there are >30 copies of different two-component regulatory systems<sup>14</sup>, *M. tuberculosis* has only 11 complete pairs of sensor histidine kinases and response regulators, and a few isolated kinase and regulatory genes. This relative paucity in environmental signal transduction pathways is probably offset by the presence of a family of eukaryotic-like serine/threonine protein kinases (STPKs), which function as part of a phosphorelay system<sup>18</sup>. The STPKs probably have two domains: the well-conserved kinase domain at the amino terminus is predicted to be connected by a transmembrane segment to the carboxy-terminal region that may respond to specific stimuli. Several of the predicted envelope lipoproteins, such as that encoded by *lppR* (Rv2403), show extensive similarity to this putative receptor domain of STPKs, suggesting possible interplay. The STPKs probably function in signal transduction pathways and may govern important cellular decisions such as dormancy and cell division, and although their partners are unknown, candidate genes for phosphoprotein phosphatases have been identified.

**Drug resistance.** *M. tuberculosis* is naturally resistant to many antibiotics, making treatment difficult<sup>19</sup>. This resistance is due mainly to the highly hydrophobic cell envelope acting as a permeability barrier<sup>4</sup>, but many potential resistance determinants are also encoded in the genome. These include hydrolytic or drug-modifying enzymes such as  $\beta$ -lactamases and aminoglycoside acetyl transferases, and many potential drug-efflux systems, such as 14 members of the major facilitator family and numerous ABC transporters. Knowledge of these putative resistance mechanisms will promote better use of existing drugs and facilitate the conception of new therapies.



**Figure 3** Correspondence analysis of the proteomes from extensively sequenced organisms as a function of amino-acid composition. Note the extreme position of *M. tuberculosis* and the shift in amino-acid preference reflecting increasing G + C content from left to right. Abbreviations used: Ae, *Aquifex aeolicus*; Af, *Archaeoglobus fulgidis*; Bb, *Borrelia burgdorferi*; Bs, *B. subtilis*; Ce, *Caenorhabditis elegans*; Ec, *E. coli*; Hi, *Haemophilus influenzae*; Hp, *Helicobacter pylori*; Mg, *Mycoplasma genitalium*; Mj, *Methanococcus jannaschi*; Mp, *Mycoplasma pneumoniae*; Mt, *M. tuberculosis*; Mth, *Methanobacterium thermoautotrophicum*; Sc, *Saccharomyces cerevisiae*; Ss, *Synechocystis* sp. strain PCC6803. F1 and F2, first and second factorial axes<sup>16</sup>.



**Figure 4** Lipid metabolism. **a**, Degradation of host-cell lipids is vital in the intracellular life of *M. tuberculosis*. Host-cell membranes provide precursors for many metabolic processes, as well as potential precursors of mycobacterial cell-wall constituents, through the actions of a broad family of  $\beta$ -oxidative enzymes encoded by multiple copies in the genome. These enzymes produce acetyl CoA, which can be converted into many different metabolites and fuel for the bacteria through the actions of the enzymes of the citric acid cycle and the glyoxylate shunt of this cycle. **b**, The genes that synthesize mycolic acids, the dominant lipid component of the mycobacterial cell wall, include the type I fatty acid synthase (*fas*) and a unique type II system which relies on extension of a precursor bound to an acyl carrier protein to form full-length (~80-carbon) mycolic acids. The *cma* genes are responsible for cyclopropanation. **c**, The genes that produce phthiocerol dimycocerosate form a large operon and represent type I (*mas*) and type II (the *pps* operon) polyketide synthase systems. Functions are colour coordinated.

**Lipid metabolism**

Very few organisms produce such a diverse array of lipophilic molecules as *M. tuberculosis*. These molecules range from simple fatty acids such as palmitate and tuberculostearate, through isoprenoids, to very-long-chain, highly complex molecules such as mycolic acids and the phenolphthiocerol alcohols that esterify with mycocerosic acid to form the scaffold for attachment of the mycosides. Mycobacteria contain examples of every known lipid and polyketide biosynthetic system, including enzymes usually found in mammals and plants as well as the common bacterial systems. The biosynthetic capacity is overshadowed by the even more remarkable radiation of degradative, fatty acid oxidation systems and, in total, there are ~250 distinct enzymes involved in fatty acid metabolism in *M. tuberculosis* compared with only 50 in *E. coli*<sup>20</sup>.

**Fatty acid degradation.** *In vivo*-grown mycobacteria have been suggested to be largely lipolytic, rather than lipogenic, because of the variety and quantity of lipids available within mammalian cells and the tubercle<sup>2</sup> (Fig. 4a). The abundance of genes encoding components of fatty acid oxidation systems found by our genomic approach supports this proposition, as there are 36 acyl-CoA synthases and a family of 36 related enzymes that could catalyse the first step in fatty acid degradation. There are 21 homologous enzymes belonging to the enoyl-CoA hydratase/isomerase superfamily of enzymes, which rehydrate the nascent product of the acyl-CoA dehydrogenase. The four enzymes that convert the 3-hydroxy fatty acid into a 3-keto fatty acid appear less numerous, mainly

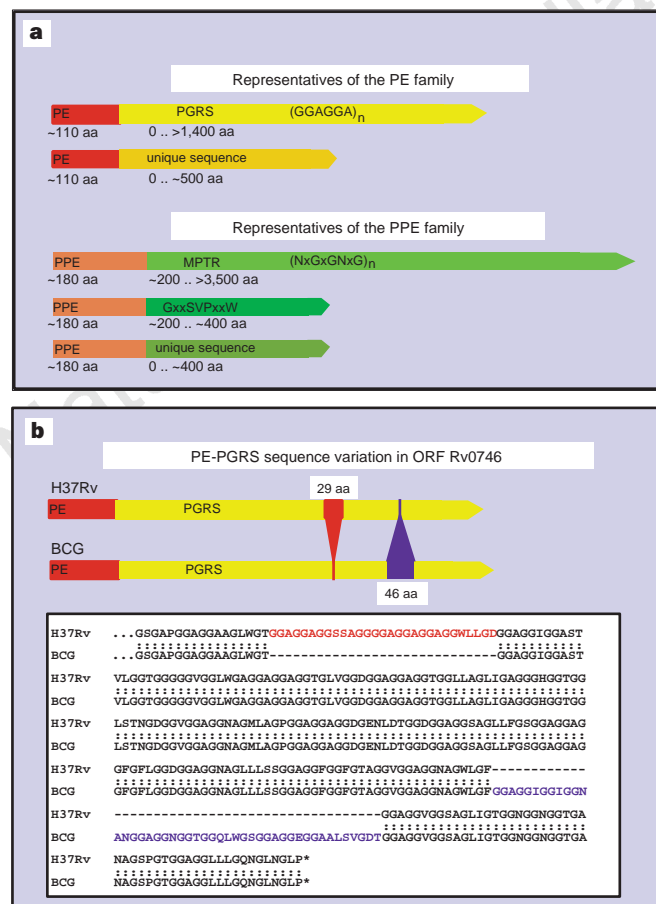
because they are difficult to distinguish from other members of the short-chain alcohol dehydrogenase family on the basis of primary sequence. The five enzymes that complete the cycle by thiolysis of the  $\beta$ -ketoester, the acetyl-CoA C-acetyltransferases, do indeed appear to be a more limited family. In addition to this extensive set of dissociated degradative enzymes, the genome also encodes the canonical FadA/FadB  $\beta$ -oxidation complex (Rv0859 and Rv0860). Accessory activities are present for the metabolism of odd-chain and multiply unsaturated fatty acids.

**Fatty acid biosynthesis.** At least two discrete types of enzyme system, fatty acid synthase (FAS) I and FAS II, are involved in fatty acid biosynthesis in mycobacteria (Fig. 4b). FAS I (Rv2524, *fas*) is a single polypeptide with multiple catalytic activities that generates several shorter CoA esters from acetyl-CoA primers<sup>5</sup> and probably creates precursors for elongation by all of the other fatty acid and polyketide systems. FAS II consists of dissociable enzyme components which act on a substrate bound to an acyl-carrier protein (ACP). FAS II is incapable of *de novo* fatty acid synthesis but instead elongates palmitoyl-ACP to fatty acids ranging from 24 to 56 carbons in length<sup>17,21</sup>. Several different components of FAS II may be targets for the important tuberculosis drug isoniazid, including the enoyl-ACP reductase *InhA*<sup>22</sup>, the ketoacyl-ACP synthase *KasA* and the ACP *AcpM*<sup>21</sup>. Analysis of the genome shows that there are only three potential ketoacyl synthases: *KasA* and *KasB* are highly related, and their genes cluster with *acpM*, whereas *KasC* is a more distant homologue of a ketoacyl synthase III system. The number of ketoacyl synthase and ACP genes indicates that there is a single FAS II system. Its genetic organization, with two clustered ketoacyl synthases, resembles that of type II aromatic polyketide biosynthetic gene clusters, such as those for actinorhodin, tetracycline and tetracenomycin in *Streptomyces* species<sup>23</sup>. *InhA* seems to be the sole enoyl-ACP reductase and its gene is co-transcribed with a *fabG* homologue, which encodes 3-oxoacyl-ACP reductase. Both of these proteins are probably important in the biosynthesis of mycolic acids.

Fatty acids are synthesized from malonyl-CoA and precursors are generated by the enzymatic carboxylation of acetyl (or propionyl)-CoA by a biotin-dependent carboxylase (Fig. 4b). From study of the genome we predict that there are three complete carboxylase systems, each consisting of an  $\alpha$ - and a  $\beta$ -subunit, as well as three  $\beta$ -subunits without an  $\alpha$ -counterpart. As a group, all of the carboxylases seem to be more related to the mammalian homologues than to the corresponding bacterial enzymes. Two of these carboxylase systems (*accA1*, *accD1* and *accA2*, *accD2*) are probably involved in degradation of odd-numbered fatty acids, as they are adjacent to genes for other known degradative enzymes. They may convert propionyl-CoA to succinyl-CoA, which can then be incorporated into the tricarboxylic acid cycle. The synthetic carboxylases (*accA3*, *accD3*, *accD4*, *accD5* and *accD6*) are more difficult to understand. The three extra  $\beta$ -subunits might direct carboxylation to the appropriate precursor or may simply increase the total amount of carboxylated precursor available if this step were rate-limiting.

Synthesis of the paraffinic backbone of fatty and mycolic acids in the cell is followed by extensive postsynthetic modifications and unsaturations, particularly in the case of the mycolic acids<sup>24,25</sup>. Unsaturation is catalysed either by a FabA-like  $\beta$ -hydroxyacyl-ACP dehydrase, acting with a specific ketoacyl synthase, or by an aerobic terminal mixed function desaturase that uses both molecular oxygen and NADPH. Inspection of the genome revealed no obvious candidates for the FabA-like activity. However, three potential aerobic desaturases (encoded by *desA1*, *desA2* and *desA3*) were evident that show little similarity to related vertebrate or yeast enzymes (which act on CoA esters) but instead resemble plant desaturases (which use ACP esters). Consequently, the genomic data indicate that unsaturation of the meromycolate chain may occur while the acyl group is bound to AcpM.

Much of the subsequent structural diversity in mycolic acids is



**Figure 5** The PE and PPE protein families. **a**, Classification of the PE and PPE protein families. **b**, Sequence variation between *M. tuberculosis* H37Rv and *M. bovis* BCG-Pasteur in the PE-PGRS encoded by open reading frame (ORF) Rv0746.

generated by a family of *S*-adenosyl-L-methionine-dependent enzymes, which use the unsaturated meromycolic acid as a substrate to generate *cis* and *trans* cyclopropanes and other mycolates. Six members of this family have been identified and characterized<sup>25</sup> and two clustered, convergently transcribed new genes are evident in the genome (*umaA1* and *umaA2*). From the functions of the known family members and the structures of mycolic acids in *M. tuberculosis*, it is tempting to speculate that these new enzymes may introduce the *trans* cyclopropanes into the meromycolate precursor. In addition to these two methyltransferases, there are two other unrelated lipid methyltransferases (*Ufa1* and *Ufa2*) that share homology with cyclopropane fatty acid synthase of *E. coli*<sup>25</sup>. Although cyclopropanation seems to be a relatively common modification of mycolic acids, cyclopropanation of plasma-membrane constituents has not been described in mycobacteria. Tuberculostearic acid is produced by methylation of oleic acid, and may be synthesized by one of these two enzymes.

Condensation of the fully functionalized and preformed meromycolate chain with a 26-carbon  $\alpha$ -branch generates full-length mycolic acids that must be transported to their final location for attachment to the cell-wall arabinogalactan. The transfer and subsequent transesterification is mediated by three well-known immunogenic proteins of the antigen 85 complex<sup>26</sup>. The genome encodes a fourth member of this complex, antigen 85C' (*fbpC2*, *Rv0129*), which is highly related to antigen 85C. Further studies are needed to show whether the protein possesses mycolyltransferase activity and to clarify the reason behind the apparent redundancy. **Polyketide synthesis.** Mycobacteria synthesize polyketides by several different mechanisms. A modular type I system, similar to that involved in erythromycin biosynthesis<sup>23</sup>, is encoded by a very large operon, *ppsABCDE*, and functions in the production of phenolphthiocerol<sup>5</sup>. The absence of a second type I polyketide synthase suggests that the related lipids phthiocerol A and B, phthiodiolone A and phthiotriol may all be synthesized by the same system, either from alternative primers or by differential postsynthetic modification. It is physiologically significant that the *pps* gene cluster occurs immediately upstream of *mas*, which encodes the multifunctional enzyme mycocerosic acid synthase (MAS), as their products phthiocerol and mycocerosic acid esterify to form the very abundant cell-wall-associated molecule phthiocerol dimycocerosate (Fig. 4c).

Members of another large group of polyketide synthase enzymes are similar to MAS, which also generates the multiply methyl-branched fatty acid components of mycosides and phthiocerol dimycocerosate, abundant cell-wall-associated molecules<sup>5</sup>. Although some of these polyketide synthases may extend type I FAS CoA primers to produce other long-chain methyl-branched fatty acids such as mycolipenic, mycolipodienic and mycolipanic acids or the phthioceranic and hydroxyphthioceranic acids, or may even show functional overlap<sup>5</sup>, there are many more of these enzymes than there are known metabolites. Thus there may be new lipid and polyketide metabolites that are expressed only under certain conditions, such as during infection and disease.

A fourth class of polyketide synthases is related to the plant enzyme superfamily that includes chalcone and stilbene synthase<sup>23</sup>. These polyketide synthases are phylogenetically divergent from all other polyketide and fatty acid synthases and generate unreduced polyketides that are typically associated with anthocyanin pigments and flavonoids. The function of these systems, which are often linked to apparent type I modules, is unknown. An example is the gene cluster spanning *pk10*, *pk7*, *pk8* and *pk9*, which includes two of the chalcone-synthase-like enzymes and two modules of an apparent type I system. The unknown metabolites produced by these enzymes are interesting because of the potent biological activities of some polyketides such as the immunosuppressor rapamycin.

**Siderophores.** Peptides that are not ribosomally synthesized are

made by a process that is mechanistically analogous to polyketide synthesis<sup>23,27</sup>. These peptides include the structurally related iron-scavenging siderophores, the mycobactins and the exochelins<sup>2,28</sup>, which are derived from salicylate by the addition of serine (or threonine), two lysines and various fatty acids and possible polyketide segments. The *mbt* operon, encoding one apparent salicylate-activating protein, three amino-acid ligases, and a single module of a type I polyketide synthase, may be responsible for the biosynthesis of the mycobacterial siderophores. The presence of only one non-ribosomal peptide-synthesis system indicates that this pathway may generate both siderophores and that subsequent modification of a single  $\epsilon$ -amino group of one lysine residue may account for the different physical properties and function of the siderophores<sup>28</sup>.

### Immunological aspects and pathogenicity

Given the scale of the global tuberculosis burden, vaccination is not only a priority but remains the only realistic public health intervention that is likely to affect both the incidence and the prevalence of the disease<sup>29</sup>. Several areas of vaccine development are promising, including DNA vaccination, use of secreted or surface-exposed proteins as immunogens, recombinant forms of BCG and rational attenuation of *M. tuberculosis*<sup>29</sup>. All of these avenues of research will benefit from the genome sequence as its availability will stimulate more focused approaches. Genes encoding ~90 lipoproteins were identified, some of which are enzymes or components of transport systems, and a similar number of genes encoding preproteins (with type I signal peptides) that are probably exported by the Sec-dependent pathway. *M. tuberculosis* seems to have two copies of *secA*. The potent T-cell antigen Esat-6 (ref. 30), which is probably secreted in a Sec-independent manner, is encoded by a member of a multigene family. Examination of the genetic context reveals several similarly organized operons that include genes encoding large ATP-hydrolysing membrane proteins that might act as transporters. One of the surprises of the genome project was the discovery of two extensive families of novel glycine-rich proteins, which may be of immunological significance as they are predicted to be abundant and potentially polymorphic antigens.

**The PE and PPE multigene families.** About 10% of the coding capacity of the genome is devoted to two large unrelated families of acidic, glycine-rich proteins, the PE and PPE families, whose genes are clustered (Figs 1, 2) and are often based on multiple copies of the polymorphic repetitive sequences referred to as PGRSs, and major polymorphic tandem repeats (MPTRs), respectively<sup>31,32</sup>. The names PE and PPE derive from the motifs Pro-Glu (PE) and Pro-Pro-Glu (PPE) found near the N terminus in most cases<sup>33</sup>. The 99 members of the PE protein family all have a highly conserved N-terminal domain of ~110 amino-acid residues that is predicted to have a globular structure, followed by a C-terminal segment that varies in size, sequence and repeat copy number (Fig. 5). Phylogenetic analysis separated the PE family into several subfamilies. The largest of these is the highly repetitive PGRS class, which contains 61 members; members of the other subfamilies, share very limited sequence similarity in their C-terminal domains (Fig. 5). The predicted molecular weights of the PE proteins vary considerably as a few members contain only the N-terminal domain, whereas most have C-terminal extensions ranging in size from 100 to 1,400 residues. The PGRS proteins have a high glycine content (up to 50%), which is the result of multiple tandem repetitions of Gly-Gly-Ala or Gly-Gly-Asn motifs, or variations thereof.

The 68 members of the PPE protein family (Fig. 5) also have a conserved N-terminal domain that comprises ~180 amino-acid residues, followed by C-terminal segments that vary markedly in sequence and length. These proteins fall into at least three groups, one of which constitutes the MPTR class characterized by the presence of multiple, tandem copies of the motif Asn-X-Gly-X-Gly-Asn-X-Gly. The second subgroup contains a characteristic, well-conserved motif around position 350, whereas the third contains

proteins that are unrelated except for the presence of the common 180-residue PPE domain.

The subcellular location of the PE and PPE proteins is unknown and in only one case, that of a lipase (Rv3097), has a function been demonstrated. On examination of the protein database from the extensively sequenced *M. leprae*<sup>15</sup>, no PGRS- or MPTR-related polypeptides were detected but a few proteins belonging to the non-MPTR subgroup of the PPE family were found. These proteins include one of the major antigens recognized by leprosy patients, the serine-rich antigen<sup>34</sup>. Although it is too early to attribute biological functions to the PE and PPE families, it is tempting to speculate that they could be of immunological importance. Two interesting possibilities spring to mind. First, they could represent the principal source of antigenic variation in what is otherwise a genetically and antigenically homogeneous bacterium. Second, these glycine-rich proteins might interfere with immune responses by inhibiting antigen processing.

Several observations and results support the possibility of antigenic variation associated with both the PE and the PPE family proteins. The PGRS member Rv1759 is a fibronectin-binding protein of relative molecular mass 55,000 (ref. 35) that elicits a variable antibody response, indicating either that individuals mount different immune responses or that this PGRS protein may vary between strains of *M. tuberculosis*. The latter possibility is supported by restriction fragment length polymorphisms for various PGRS and MPTR sequences in clinical isolates<sup>33</sup>. Direct support for genetic variation within both the PE and the PPE families was obtained by comparative DNA sequence analysis (Fig. 5). The gene for the PE-PGRS protein Rv0746 of BCG differs from that in H37Rv by the deletion of 29 codons and the insertion of 46 codons. Similar variation was seen in the gene for the PPE protein Rv0442 (data not shown). As these differences were all associated with repetitive sequences they could have resulted from intergenic or intragenic recombinational events or, more probably, from strand slippage during replication<sup>32</sup>. These mechanisms are known to generate antigenic variability in other bacterial pathogens<sup>36</sup>.

There are several parallels between the PGRS proteins and the Epstein-Barr virus nuclear antigens (EBNAs). Members of both polypeptide families are glycine-rich, contain extensive Gly-Ala repeats, and exhibit variation in the length of the repeat region between different isolates. The Gly-Ala repeat region of EBNA1 functions as a *cis*-acting inhibitor of the ubiquitin/proteasome antigen-processing pathway that generates peptides presented in the context of major histocompatibility complex (MHC) class I molecules<sup>37,38</sup>. MHC class I knockout mice are very susceptible to *M. tuberculosis*, underlining the importance of a cytotoxic T-cell response in protection against disease<sup>3,39</sup>. Given the many potential effects of the PPE and PE proteins, it is important that further studies are performed to understand their activity. If extensive antigenic variability or reduced antigen presentation were indeed found, this would be significant for vaccine design and for understanding protective immunity in tuberculosis, and might even explain the varied responses seen in different BCG vaccination programmes<sup>40</sup>.

**Pathogenicity.** Despite intensive research efforts, there is little information about the molecular basis of mycobacterial virulence<sup>41</sup>. However, this situation should now change as the genome sequence will accelerate the study of pathogenesis as never before, because other bacterial factors that may contribute to virulence are becoming apparent. Before the completion of the genome sequence, only three virulence factors had been described<sup>41</sup>: catalase-peroxidase, which protects against reactive oxygen species produced by the phagocyte; *mce*, which encodes macrophage-colonizing factor<sup>42</sup>; and a sigma factor gene, *sigA* (aka *rpoV*), mutations in which can lead to attenuation<sup>41</sup>. In addition to these single-gene virulence factors, the mycobacterial cell wall<sup>4</sup> is also important in pathology,

but the complex nature of its biosynthesis makes it difficult to identify critical genes whose inactivation would lead to attenuation.

On inspection of the genome sequence, it was apparent that four copies of *mce* were present and that these were all situated in operons, comprising eight genes, organized in exactly the same manner. In each case, the genes preceding *mce* code for integral membrane proteins, whereas *mce* and the following five genes are all predicted to encode proteins with signal sequences or hydrophobic stretches at the N terminus. These sets of proteins, about which little is known, may well be secreted or surface-exposed; this is consistent with the proposed role of Mce in invasion of host cells<sup>42</sup>. Furthermore, a homologue of *smpB*, which has been implicated in intracellular survival of *Salmonella typhimurium*, has also been identified<sup>43</sup>. Among the other secreted proteins identified from the genome sequence that could act as virulence factors are a series of phospholipases C, lipases and esterases, which might attack cellular or vacuolar membranes, as well as several proteases. One of these phospholipases acts as a contact-dependent haemolysin (N. Stoker, personal communication). The presence of storage proteins in the bacillus, such as the haemoglobin-like oxygen captors described above, points to its ability to stockpile essential growth factors, allowing it to persist in the nutrient-limited environment of the phagosome. In this regard, the ferritin-like proteins, encoded by *bfrA* and *bfrB*, may be important in intracellular survival as the capacity to acquire enough iron in the vacuole is very limited. □

## Methods

**Sequence analysis.** Initially, ~3.2 Mb of sequence was generated from cosmids<sup>8</sup> and the remainder was obtained from selected BAC clones<sup>7</sup> and 45,000 whole-genome shotgun clones. Sheared fragments (1.4–2.0 kb) from cosmids and BACs were cloned into M13 vectors, whereas genomic DNA was cloned in pUC18 to obtain both forward and reverse reads. The PGRS genes were grossly underrepresented in pUC18 but better covered in the BAC and cosmid M13 libraries. We used small-insert libraries<sup>44</sup> to sequence regions prone to compression or deletion and, in some cases, obtained sequences from products of the polymerase chain reaction or directly from BACs<sup>7</sup>. All shotgun sequencing was performed with standard dye terminators to minimize compression problems, whereas finishing reactions used dRhodamine or BigDye terminators (<http://www.sanger.ac.uk>). Problem areas were verified by using dye primers. Thirty differences were found between the genomic shotgun sequences and the cosmids; twenty of which were due to sequencing errors and ten to mutations in cosmids (1 error per 320 kb). Less than 0.1% of the sequence was from areas of single-clone coverage, and <0.2% was from one strand with only one sequencing chemistry.

**Informatics.** Sequence assembly involved PHRAP, GAP4 (ref. 45) and a customized perl script that merges sequences from different libraries and generates segments that can be processed by several finishers simultaneously. Sequence analysis and annotation was managed by DIANA (B.G.B. *et al.*, unpublished). Genes encoding proteins were identified by TB-parse<sup>46</sup> using a hidden Markov model trained on known *M. tuberculosis* coding and non-coding regions and translation-initiation signals, with corroboration by positional base preference. Interrogation of the EMBL, TrEMBL, SwissProt, PROSITE<sup>47</sup> and in-house databases involved BLASTN, BLASTX<sup>48</sup>, DOTTER (<http://www.sanger.ac.uk>) and FASTA<sup>49</sup>. tRNA genes were located and identified using tRNAscan and tRNAscan-SE<sup>50</sup>. The complete sequence, a list of annotated cosmids and linking regions can be found on our website (<http://www.sanger.ac.uk>) and in MycDB (<http://www.pasteur.fr/mycdb/>).

Received 15 April; accepted 8 May 1998.

- Snider, D. E. Jr, Ravighione, M. & Kochi, A. in *Tuberculosis: Pathogenesis, Protection, and Control* (ed. Bloom, B. R.) 2–11 (Am. Soc. Microbiol., Washington DC, 1994).
- Wheeler, P. R. & Ratledge, C. in *Tuberculosis: Pathogenesis, Protection, and Control* (ed. Bloom, B. R.) 353–385 (Am. Soc. Microbiol., Washington DC, 1994).
- Chan, J. & Kaufmann, S. H. E. in *Tuberculosis: Pathogenesis, Protection, and Control* (ed. Bloom, B. R.) 271–284 (Am. Soc. Microbiol., Washington DC, 1994).
- Brennan, P. J. & Draper, P. in *Tuberculosis: Pathogenesis, Protection, and Control* (ed. Bloom, B. R.) 271–284 (Am. Soc. Microbiol., Washington DC, 1994).
- Kolattukudy, P. E., Fernandes, N. D., Azad, A. K., Fitzmaurice, A. M. & Sirakova, T. D. *Biochemistry*



and molecular genetics of cell-wall lipid biosynthesis in mycobacteria. *Mol. Microbiol.* **24**, 263–270 (1997).

6. Sreevatsan, S. *et al.* Restricted structural gene polymorphism in the *Mycobacterium tuberculosis* complex indicates evolutionarily recent global dissemination. *Proc. Natl Acad. Sci. USA* **94**, 9869–9874 (1997).
7. Brosch, R. *et al.* Use of a *Mycobacterium tuberculosis* H37Rv bacterial artificial chromosome library for genome mapping, sequencing and comparative genomics. *Infect. Immun.* **66**, 2221–2229 (1998).
8. Philipp, W. J. *et al.* An integrated map of the genome of the tubercle bacillus, *Mycobacterium tuberculosis* H37Rv, and comparison with *Mycobacterium leprae*. *Proc. Natl Acad. Sci. USA* **93**, 3132–3137 (1996).
9. Blattner, F. R. *et al.* The complete genome sequence of *Escherichia coli* K-12. *Science* **277**, 1453–1462 (1997).
10. Cole, S. T. & Saint-Girons, I. Bacterial genomics. *FEMS Microbiol. Rev.* **14**, 139–160 (1994).
11. Freiberg, C. *et al.* Molecular basis of symbiosis between *Rhizobium* and legumes. *Nature* **387**, 394–401 (1997).
12. Bardarov, S. *et al.* Conditionally replicating mycobacteriophages: a system for transposon delivery to *Mycobacterium tuberculosis*. *Proc. Natl Acad. Sci. USA* **94**, 10961–10966 (1997).
13. Mahairas, G. G., Sabo, P. J., Hickey, M. J., Singh, D. C. & Stover, C. K. Molecular analysis of genetic differences between *Mycobacterium bovis* BCG and virulent *M. bovis*. *J. Bacteriol.* **178**, 1274–1282 (1996).
14. Kunst, F. *et al.* The complete genome sequence of the gram-positive bacterium *Bacillus subtilis*. *Nature* **390**, 249–256 (1997).
15. Smith, D. R. *et al.* Multiplex sequencing of 1.5 Mb of the *Mycobacterium leprae* genome. *Genome Res.* **7**, 802–819 (1997).
16. Greenacre, M. *Theory and Application of Correspondence Analysis* (Academic, London, 1984).
17. Ratledge, C. R. in *The Biology of the Mycobacteria* (eds Ratledge, C. & Stanford, J.) 53–94 (Academic, San Diego, 1982).
18. Av-Gay, Y. & Davies, J. Components of eukaryotic-like protein signaling pathways in *Mycobacterium tuberculosis*. *Microb. Comp. Genomics* **2**, 63–73 (1997).
19. Cole, S. T. & Telenti, A. Drug resistance in *Mycobacterium tuberculosis*. *Eur. Resp. Rev.* **8**, 701S–713S (1995).
20. Riley, M. & Labeledan, B. in *Escherichia coli and Salmonella* (ed. Neidhardt, F. C.) 2118–2202 (ASM, Washington, 1996).
21. Mdluli, K. *et al.* Inhibition of a *Mycobacterium tuberculosis*  $\beta$ -ketoacyl ACP synthase by isoniazid. *Science* **280**, 1607–1610 (1998).
22. Banerjee, A. *et al.* *inhA*, a gene encoding a target for isoniazid and ethionamide in *Mycobacterium tuberculosis*. *Science* **263**, 227–230 (1994).
23. Hopwood, D. A. Genetic contributions to understanding polyketide synthases. *Chem. Rev.* **97**, 2465–2497 (1997).
24. Minnikin, D. E. in *The Biology of the Mycobacteria* (eds Ratledge, C. & Stanford, J.) 95–184 (Academic, London, 1982).
25. Barry, C. E. III *et al.* Mycolic acids: structure, biosynthesis, and physiological functions. *Prog. Lipid Res.* (in the press).
26. Belisle, J. T. *et al.* Role of the major antigen of *Mycobacterium tuberculosis* in cell wall biogenesis. *Science* **276**, 1420–1422 (1997).
27. Marahiel, M. A., Stachelhaus, T. & Mootz, H. D. Modular peptide synthetases involved in nonribosomal peptide synthesis. *Chem. Rev.* **97**, 2651–2673 (1997).
28. Gobin, J. *et al.* Iron acquisition by *Mycobacterium tuberculosis*: isolation and characterization of a family of iron-binding exochelins. *Proc. Natl Acad. Sci. USA* **92**, 5189–5193 (1995).
29. Young, D. B. & Fruth, U. in *New Generation Vaccines* (eds Levine, M., Woodrow, G., Kaper, J. & Cobon, G. S.) 631–645 (Marcel Dekker, New York, 1997).
30. Sorensen, A. L., Nagai, S., Houen, G., Andersen, P. & Anderson, A. B. Purification and characterization of a low-molecular-mass T-cell antigen secreted by *Mycobacterium tuberculosis*. *Infect. Immun.* **63**,

- 1710–1717 (1995).
31. Hermans, P. W. M., van Soolingen, D. & van Embden, J. D. A. Characterization of a major polymorphic tandem repeat in *Mycobacterium tuberculosis* and its potential use in the epidemiology of *Mycobacterium kansasii* and *Mycobacterium goodii*. *J. Bacteriol.* **174**, 4157–4165 (1992).
32. Poulet, S. & Cole, S. T. Characterisation of the polymorphic GC-rich repetitive sequence (PGRS) present in *Mycobacterium tuberculosis*. *Arch. Microbiol.* **163**, 87–95 (1995).
33. Cole, S. T. & Barrell, B. G. in *Genetics and Tuberculosis* (eds Chadwick, D. J. & Cardew, G., *Novartis Foundation Symp.* 217) 160–172 (Wiley, Chichester, 1998).
34. Vega-Lopez, F. *et al.* Sequence and immunological characterization of a serine-rich antigen from *Mycobacterium leprae*. *Infect. Immun.* **61**, 2145–2153 (1993).
35. Abou-Zeid, C. *et al.* Genetic and immunological analysis of *Mycobacterium tuberculosis* fibronectin-binding proteins. *Infect. Immun.* **59**, 2712–2718 (1991).
36. Robertson, B. D. & Meyer, T. F. Genetic variation in pathogenic bacteria. *Trends Genet.* **8**, 422–427 (1992).
37. Levitskaya, J. *et al.* Inhibition of antigen processing by the internal repeat region of the Epstein-Barr virus nuclear antigen-1. *Nature* **375**, 685–688 (1995).
38. Levitskaya, J., Sharipo, A., Leonchiks, A., Ciechanover, A. & Masucci, M. G. Inhibition of ubiquitin/proteasome-dependent protein degradation by the Gly-Ala repeat domain of the Epstein-Barr virus nuclear antigen 1. *Proc. Natl Acad. Sci. USA* **94**, 12616–12621 (1997).
39. Flynn, J. L., Goldstein, M. A., Treibold, K. J., Koller, B. & Bloom, B. R. Major histocompatibility complex class-I restricted T cells are required for resistance to *Mycobacterium tuberculosis* infection. *Proc. Natl Acad. Sci. USA* **89**, 12013–12017 (1992).
40. Bloom, B. R. & Fine, P. E. M. in *Tuberculosis: Pathogenesis, Protection, and Control* (ed. Bloom, B. R.) 531–557 (Am. Soc. Microbiol., Washington DC, 1994).
41. Collins, D. M. In search of tuberculosis virulence genes. *Trends Microbiol.* **4**, 426–430 (1996).
42. Arruda, S., Bomfim, G., Knights, R., Huima-Byron, T. & Riley, L. W. Cloning of an *M. tuberculosis* DNA fragment associated with entry and survival inside cells. *Science* **261**, 1454–1457 (1993).
43. Baumber, A. J., Kusters, J. G., Stojkovic, I. & Heffron, F. *Salmonella typhimurium* loci involved in survival within macrophages. *Infect. Immun.* **62**, 1623–1630 (1994).
44. McMurray, A. A., Sulston, J. E. & Quail, M. A. Short-insert libraries as a method of problem solving in genome sequencing. *Genome Res.* **8**, 562–566 (1998).
45. Bonfield, J. K., Smith, K. F. & Staden, R. A new DNA sequence assembly program. *Nucleic Acids Res.* **24**, 4992–4999 (1995).
46. Krogh, A., Mian, I. S. & Haussler, D. A hidden Markov model that finds genes in *E. coli* DNA. *Nucleic Acids Res.* **22**, 4768–4778 (1994).
47. Bairoch, A., Bucher, P. & Hofmann, K. The PROSITE database, its status in 1997. *Nucleic Acids Res.* **25**, 217–221 (1997).
48. Altschul, S., Gish, W., Miller, W., Myers, E. & Lipman, D. A basic local alignment search tool. *J. Mol. Biol.* **215**, 403–410 (1990).
49. Pearson, W. & Lipman, D. Improved tools for biological sequence comparisons. *Proc. Natl Acad. Sci. USA* **85**, 2444–2448 (1988).
50. Lowe, T. M. & Eddy, S. R. tRNAscan-SE: a program for improved detection of transfer RNA genes in genomic DNA. *Nucleic Acids Res.* **25**, 955–964 (1997).

**Acknowledgements.** We thank Y. Av-Gay, F.-C. Bange, A. Danchin, B. Dujon, W. R. Jacobs Jr, L. Jones, M. McNeil, I. Moszer, P. Rice and J. Stephenson for advice, reagents and support. This work was supported by the Wellcome Trust. Additional funding was provided by the Association Française Raoul Follereau, the World Health Organisation and the Institut Pasteur. S.V.G. received a Wellcome Trust travelling research fellowship.

Correspondence and requests for materials should be addressed to B.G.B. (barrell@sanger.ac.uk) or S.T.C. (stcole@pasteur.fr). The complete sequence has been deposited in EMBL/GenBank/DDJB as MTBH37RV, accession number AL123456.


# YOURS TO HAVE AND TO HOLD BUT NOT TO COPY

The publication you are reading is protected by copyright law.

Photocopying copyright material without permission is no different from stealing a magazine from a newsagent, only it doesn't seem like theft.

If you take photocopies from books, magazines and periodicals at work your employer should be licensed with CLA.

Make sure you are protected by a photocopying licence.



**The Copyright Licensing Agency Limited**  
 90 Tottenham Court Road, London W1P 0LP  
 Telephone: 0171 436 5931 Fax: 0171 436 3986

**Table 1. Functional classification of *Mycobacterium tuberculosis* protein-coding genes**

**I. Small-molecule metabolism**

**A. Degradation**

**1. Carbon compounds**

Rv0186 *bgIS* β-glucosidase  
 Rv2202c *cbhK* carboxylate kinase  
 Rv0727c *fucA* L-fucose phosphate aldolase  
 Rv1731 *gabD1* succinate-semialdehyde dehydrogenase  
 Rv0234c *gabD2* succinate-semialdehyde dehydrogenase  
 Rv0501 *galE1* UDP-glucose 4-epimerase  
 Rv0536 *galE2* UDP-glucose 4-epimerase  
 Rv0620 *galK* galactokinase  
 Rv0619 *galT* galactose-1-phosphate uridylyltransferase C-term  
 Rv0618 *galT'* galactose-1-phosphate uridylyltransferase N-term  
 Rv0993 *galU* UTP-glucose-1-phosphate uridylyltransferase  
 Rv3696c *glpK* ATP:glycerol 3-phosphotransferase  
 Rv3255c *manA* mannose-6-phosphate isomerase  
 Rv3441c *mrsA* phosphoglucomutase or phosphomannomutase  
 Rv0118c *oxcA* oxalyl-CoA decarboxylase  
 Rv3068c *pgmA* phosphoglucomutase  
 Rv3257c *pmmA* phosphomannomutase  
 Rv3308 *pmmB* phosphomannomutase  
 Rv2702 *ppgK* polyphosphate glucokinase  
 Rv0408 *pta* phosphate acetyltransferase  
 Rv0729 *xyiB* xylose kinase  
 Rv1096 - carbohydrate degrading enzyme

**2. Amino acids and amines**

Rv1905c *ao* D-amino acid oxidase  
 Rv2531c *adi* ornithine/arginine decarboxylase  
 Rv2780 *ald* L-alanine dehydrogenase  
 Rv1538c *ansA* L-asparaginase  
 Rv1001 *arcA* arginine deiminase  
 Rv0753c *mmsA* methylmalonate semialdehyde dehydrogenase  
 Rv0751c *mmsB* methylmalonate semialdehyde oxidoreductase  
 Rv1187 *rocA* pyrroline-5-carboxylate dehydrogenase  
 Rv2322c *rocD1* ornithine aminotransferase  
 Rv2321c *rocD2* ornithine aminotransferase  
 Rv1848 *ureA* urease γ subunit  
 Rv1849 *ureB* urease β subunit  
 Rv1850 *ureC* urease α subunit  
 Rv1853 *ureD* urease accessory protein  
 Rv1851 *ureF* urease accessory protein  
 Rv1852 *ureG* urease accessory protein  
 Rv2913c - probable D-amino acid aminohydrolase  
 Rv3551 - possible glutaconate CoA-transferase

**3. Fatty acids**

Rv2501c *accA1* acetyl/propionyl-CoA carboxylase, α subunit  
 Rv0973c *accA2* acetyl/propionyl-CoA carboxylase, α subunit  
 Rv2502c *accD1* acetyl/propionyl-CoA carboxylase, β subunit  
 Rv0974c *accD2* acetyl/propionyl-CoA carboxylase, β subunit  
 Rv3667 *acs* acetyl-CoA synthase  
 Rv3409c *choD* cholesterol oxidase  
 Rv0222 *echA1* enoyl-CoA hydratase/isomerase superfamily  
 Rv0456c *echA2* enoyl-CoA hydratase/isomerase superfamily  
 Rv0632c *echA3* enoyl-CoA hydratase/isomerase superfamily  
 Rv0673 *echA4* enoyl-CoA hydratase/isomerase superfamily  
 Rv0675 *echA5* enoyl-CoA hydratase/isomerase superfamily  
 Rv0905 *echA6* enoyl-CoA hydratase/isomerase superfamily (aka *ecchH*)  
 Rv0971c *echA7* enoyl-CoA hydratase/isomerase superfamily  
 Rv1070c *echA8* enoyl-CoA hydratase/isomerase superfamily  
 Rv1071c *echA9* enoyl-CoA hydratase/isomerase superfamily  
 Rv1142c *echA10* enoyl-CoA hydratase/isomerase superfamily  
 Rv1141c *echA11* enoyl-CoA hydratase/isomerase superfamily  
 Rv1472 *echA12* enoyl-CoA hydratase/isomerase superfamily  
 Rv1935c *echA13* enoyl-CoA hydratase/isomerase superfamily  
 Rv2486 *echA14* enoyl-CoA hydratase/isomerase superfamily  
 Rv2679 *echA15* enoyl-CoA hydratase/isomerase

Rv2831 *echA16* enoyl-CoA hydratase/isomerase superfamily  
 Rv3039c *echA17* enoyl-CoA hydratase/isomerase superfamily  
 Rv3373 *echA18* enoyl-CoA hydratase/isomerase superfamily, N-term  
 Rv3374 *echA18'* enoyl-CoA hydratase/isomerase superfamily, C-term  
 Rv3516 *echA19* enoyl-CoA hydratase/isomerase superfamily  
 Rv3550 *echA20* enoyl-CoA hydratase/isomerase superfamily  
 Rv3774 *echA21* enoyl-CoA hydratase/isomerase superfamily  
 Rv0859 *fadA* β oxidation complex, β subunit (acetyl-CoA C-acetyltransferase)  
 Rv0243 *fadA2* acetyl-CoA C-acetyltransferase  
 Rv1074c *fadA3* acetyl-CoA C-acetyltransferase  
 Rv1323 *fadA4* acetyl-CoA C-acetyltransferase (aka *thiL*)  
 Rv3546 *fadA5* acetyl-CoA C-acetyltransferase  
 Rv3556c *fadA6* acetyl-CoA C-acetyltransferase  
 Rv0860 *fadB* β oxidation complex, α subunit (multiple activities)  
 Rv0468 *fadB2* 3-hydroxyacyl-CoA dehydrogenase  
 Rv1715 *fadB3* 3-hydroxyacyl-CoA dehydrogenase  
 Rv3141 *fadB4* 3-hydroxyacyl-CoA dehydrogenase  
 Rv1912c *fadB5* 3-hydroxyacyl-CoA dehydrogenase  
 Rv1750c *fadD1* acyl-CoA synthase  
 Rv0270 *fadD2* acyl-CoA synthase  
 Rv3561 *fadD3* acyl-CoA synthase  
 Rv0214 *fadD4* acyl-CoA synthase  
 Rv0166 *fadD5* acyl-CoA synthase  
 Rv1206 *fadD6* acyl-CoA synthase  
 Rv0119 *fadD7* acyl-CoA synthase  
 Rv0551c *fadD8* acyl-CoA synthase  
 Rv2590 *fadD9* acyl-CoA synthase  
 Rv0099 *fadD10* acyl-CoA synthase  
 Rv1550 *fadD11* acyl-CoA synthase, N-term  
 Rv1549 *fadD11'* acyl-CoA synthase, C-term  
 Rv1427c *fadD12* acyl-CoA synthase  
 Rv3089 *fadD13* acyl-CoA synthase  
 Rv1058 *fadD14* acyl-CoA synthase  
 Rv2187 *fadD15* acyl-CoA synthase  
 Rv0852 *fadD16* acyl-CoA synthase  
 Rv3506 *fadD17* acyl-CoA synthase  
 Rv3513c *fadD18* acyl-CoA synthase  
 Rv3515c *fadD19* acyl-CoA synthase  
 Rv1185c *fadD21* acyl-CoA synthase  
 Rv2948c *fadD22* acyl-CoA synthase  
 Rv3826 *fadD23* acyl-CoA synthase  
 Rv1529 *fadD24* acyl-CoA synthase  
 Rv1521 *fadD25* acyl-CoA synthase  
 Rv2930 *fadD26* acyl-CoA synthase  
 Rv0275c *fadD27* acyl-CoA synthase  
 Rv2941 *fadD28* acyl-CoA synthase  
 Rv2950c *fadD29* acyl-CoA synthase  
 Rv0404 *fadD30* acyl-CoA synthase  
 Rv1925 *fadD31* acyl-CoA synthase  
 Rv3801c *fadD32* acyl-CoA synthase  
 Rv1345 *fadD33* acyl-CoA synthase  
 Rv0035 *fadD34* acyl-CoA synthase  
 Rv2505c *fadD35* acyl-CoA synthase  
 Rv1193 *fadD36* acyl-CoA synthase  
 Rv0131c *fadE1* acyl-CoA dehydrogenase  
 Rv0154c *fadE2* acyl-CoA dehydrogenase  
 Rv0215c *fadE3* acyl-CoA dehydrogenase  
 Rv0231 *fadE4* acyl-CoA dehydrogenase  
 Rv0244c *fadE5* acyl-CoA dehydrogenase  
 Rv0271c *fadE6* acyl-CoA dehydrogenase  
 Rv0400c *fadE7* acyl-CoA dehydrogenase  
 Rv0672 *fadE8* acyl-CoA dehydrogenase (aka *aidB*)  
 Rv0752c *fadE9* acyl-CoA dehydrogenase  
 Rv0873 *fadE10* acyl-CoA dehydrogenase  
 Rv0972c *fadE12* acyl-CoA dehydrogenase  
 Rv0975c *fadE13* acyl-CoA dehydrogenase  
 Rv1346 *fadE14* acyl-CoA dehydrogenase  
 Rv1467c *fadE15* acyl-CoA dehydrogenase  
 Rv1679 *fadE16* acyl-CoA dehydrogenase  
 Rv1934c *fadE17* acyl-CoA dehydrogenase  
 Rv1933c *fadE18* acyl-CoA dehydrogenase  
 Rv2500c *fadE19* acyl-CoA dehydrogenase (aka *mmgC*)  
 Rv2724c *fadE20* acyl-CoA dehydrogenase  
 Rv2789c *fadE21* acyl-CoA dehydrogenase  
 Rv3061c *fadE22* acyl-CoA dehydrogenase  
 Rv3140 *fadE23* acyl-CoA dehydrogenase  
 Rv3139 *fadE24* acyl-CoA dehydrogenase  
 Rv3274c *fadE25* acyl-CoA dehydrogenase  
 Rv3504 *fadE26* acyl-CoA dehydrogenase  
 Rv3505 *fadE27* acyl-CoA dehydrogenase  
 Rv3544c *fadE28* acyl-CoA dehydrogenase

Rv3543c *fadE29* acyl-CoA dehydrogenase  
 Rv3560c *fadE30* acyl-CoA dehydrogenase  
 Rv3562 *fadE31* acyl-CoA dehydrogenase  
 Rv3563 *fadE32* acyl-CoA dehydrogenase  
 Rv3564 *fadE33* acyl-CoA dehydrogenase  
 Rv3573c *fadE34* acyl-CoA dehydrogenase  
 Rv3797 *fadE35* acyl-CoA dehydrogenase  
 Rv3761c *fadE36* acyl-CoA dehydrogenase  
 Rv1175c *fadH* 2,4-Dienoyl-CoA Reductase  
 Rv0855 *far* fatty acyl-CoA racemase  
 Rv1143 *mcr* α-methyl acyl-CoA racemase  
 Rv1492 *mutA* methylmalonyl-CoA mutase, β subunit  
 Rv1493 *mutB* methylmalonyl-CoA mutase, α subunit  
 Rv2504c *scoA* 3-oxo acid:CoA transferase, α subunit  
 Rv2503c *scoB* 3-oxo acid:CoA transferase, β subunit  
 Rv1136 - probable carnitine racemase  
 Rv1683 - possible acyl-CoA synthase

**4. Phosphorous compounds**

Rv2368c *phoH* ATP-binding *pho* regulon component  
 Rv1095 *phoH2* PhoH-like protein  
 Rv3628 *ppa* probable inorganic pyrophosphatase  
 Rv2984 *ppk* polyphosphate kinase

**B. Energy metabolism**

**1. Glycolysis**

Rv1023 *eno* enolase  
 Rv0363c *fba* fructose bisphosphate aldolase  
 Rv1436 *gap* glyceraldehyde 3-phosphate dehydrogenase  
 Rv0489 *gpm* phosphoglycerate mutase I  
 Rv3010c *pfkA* phosphofructokinase I  
 Rv2029c *pfkB* phosphofructokinase II  
 Rv0946c *pgi* glucose-6-phosphate isomerase  
 Rv1437 *pgk* phosphoglycerate kinase  
 Rv1617 *pykA* pyruvate kinase  
 Rv1438 *tpi* triosephosphate isomerase  
 Rv2419c - putative phosphoglycerate mutase  
 Rv3837c - putative phosphoglycerate mutase

**2. Pyruvate dehydrogenase**

Rv2241 *aceE* pyruvate dehydrogenase E1 component  
 Rv3303c *lpdA* dihydroliipoamide dehydrogenase  
 Rv2497c *pdhA* pyruvate dehydrogenase E1 component α subunit  
 Rv2496c *pdhB* pyruvate dehydrogenase E1 component β subunit  
 Rv2495c *pdhC* dihydroliipoamide acetyltransferase  
 Rv0462 - probable dihydroliipoamide dehydrogenase

**3. TCA cycle**

Rv1475c *acn* aconitate hydratase  
 Rv0889c *citA* citrate synthase 2  
 Rv2498c *citE* citrate lyase β chain  
 Rv1098c *fum* fumarase  
 Rv1131 *glitA1* citrate synthase 3  
 Rv0896 *glitA2* citrate synthase 1  
 Rv3339c *icd1* isocitrate dehydrogenase  
 Rv0066c *icd2* isocitrate dehydrogenase  
 Rv0794c *lpdB* dihydroliipoamide dehydrogenase  
 Rv1240 *mdh* malate dehydrogenase  
 Rv2967c *pca* pyruvate carboxylase  
 Rv3318 *sdhA* succinate dehydrogenase A  
 Rv3319 *sdhB* succinate dehydrogenase B  
 Rv3316 *sdhC* succinate dehydrogenase C subunit  
 Rv3317 *sdhD* succinate dehydrogenase D subunit  
 Rv1248c *sucA* 2-oxoglutarate dehydrogenase  
 Rv2215 *sucB* dihydroliipoamide succinyltransferase  
 Rv0951 *sucC* succinyl-CoA synthase β chain  
 Rv0952 *sucD* succinyl-CoA synthase α chain

**4. Glyoxylate bypass**

Rv0467 *aceA* isocitrate lyase  
 Rv1915 *aceAa* isocitrate lyase, α module  
 Rv1916 *aceAb* isocitrate lyase, β module  
 Rv1837c *glcB* malate synthase  
 Rv3233c *gphA* phosphoglycolate phosphatase

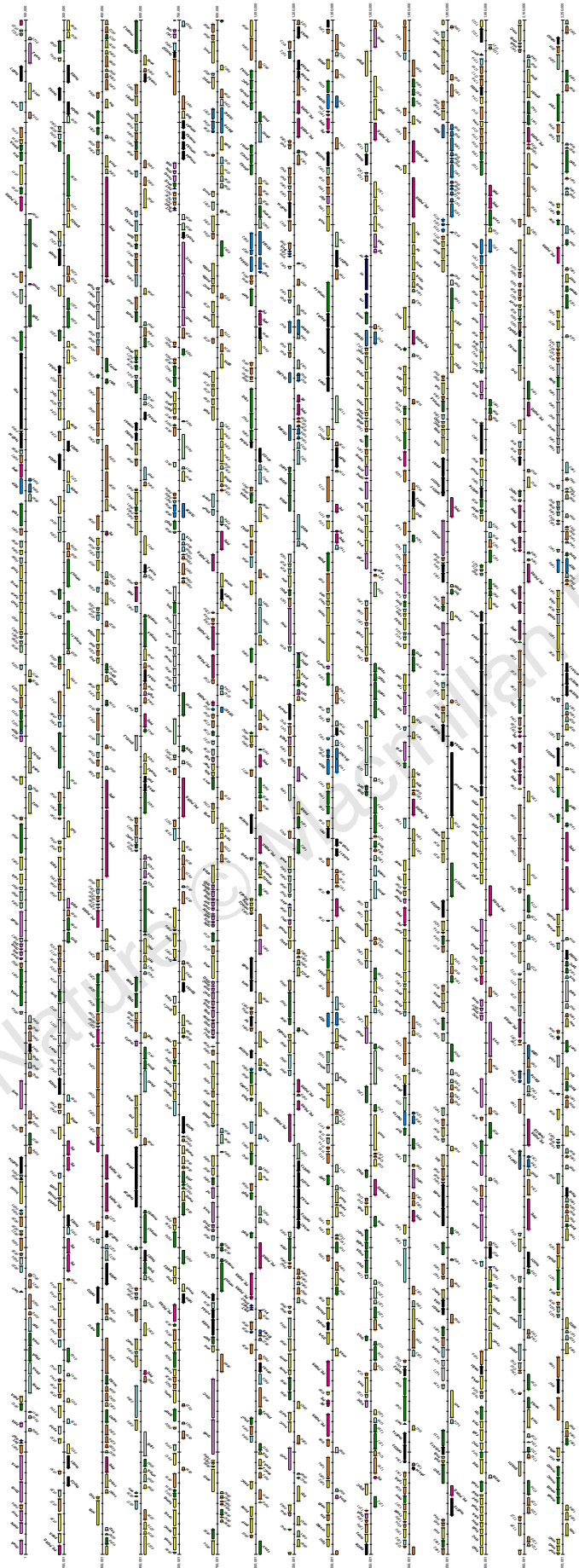
**5. Pentose phosphate pathway**

Rv1445c *devB* glucose-6-phosphate 1-dehydrogenase  
 Rv1844c *gnd* 6-phosphogluconate dehydrogenase (Gram -)  
 Rv1122 *gnd2* 6-phosphogluconate dehydrogenase (Gram +)  
 Rv1446c *opcA* unknown function, may aid G6PDH



Rv1605	<i>hisF</i>	imidazole glycerol-phosphate synthase	Rv3048c	<i>nrdG</i>	subunit ribonucleoside-diphosphate small subunit	Rv3119	<i>moaE</i>	subunit 1 molybdopterin-converting factor
Rv2121c	<i>hisG</i>	ATP phosphoribosyltransferase	Rv3053c	<i>nrdH</i>	glutaredoxin electron transport component of NrdEF system	Rv0866	<i>moaE2</i>	molybdopterin-converting factor subunit 2
Rv1602	<i>hisH</i>	amidotransferase	Rv3052c	<i>nrdI</i>	NrdI/YgaO/YmaA family thymidylate kinase	Rv3322c	<i>moaE3</i>	molybdopterin-converting factor subunit 2
Rv2122c	<i>hisI</i>	phosphoribosyl-AMP cyclohydro-lase	Rv3247c	<i>tmk</i>	thymidylate kinase	Rv0994	<i>moaA</i>	molybdopterin biosynthesis
Rv1606	<i>hisI2</i>	probable phosphoribosyl-AMP 1,6 cyclohydrolyase	Rv2764c	<i>thyA</i>	thymidylate synthase	Rv3116	<i>moaB</i>	molybdopterin biosynthesis
Rv0114	-	similar to HisB	Rv0570	<i>nrdZ</i>	ribonucleotide reductase, class II	Rv2338c	<i>moaW</i>	molybdopterin biosynthesis
6. Pyruvate family			Rv3752c	-	probable cytidine/deoxycytidylate deaminase	Rv1681	<i>moaX</i>	weak similarity to <i>E. coli</i> MoaA
Rv3423c	<i>alr</i>	alanine racemase	4. Salvage of nucleosides and nucleotides			Rv1355c	<i>moaY</i>	weak similarity to <i>E. coli</i> MoeB
7. Branched amino acid family			Rv3313c	<i>add</i>	probable adenosine deaminase	Rv3206c	<i>moaZ</i>	probably involved in molybdopterin biosynthesis
Rv1559	<i>ilvA</i>	threonine deaminase	Rv2584c	<i>apt</i>	adenine phosphoribosyltransferases	Rv0865	<i>mog</i>	molybdopterin biosynthesis
Rv3003c	<i>ilvB</i>	acetolactate synthase I large subunit	Rv3315c	<i>cdd</i>	probable cytidine deaminase	5. Pantothenate		
Rv3470c	<i>ilvB2</i>	acetolactate synthase large subunit	Rv3314c	<i>deoA</i>	thymidine phosphorylase	Rv1092c	<i>coaA</i>	pantothenate kinase
Rv3001c	<i>ilvC</i>	ketol-acid reductoisomerase	Rv0478	<i>deoC</i>	deoxyribose-phosphate aldolase	Rv2225	<i>panB</i>	3-methyl-2-oxobutanoate hydroxymethyltransferase
Rv0189c	<i>ilvD</i>	dihydroxy-acid dehydratase	Rv3307	<i>deoD</i>	probable purine nucleoside phosphorylase	Rv3602c	<i>panC</i>	pantoate- $\beta$ -alanine ligase
Rv2210c	<i>ilvE</i>	branched-chain-amino-acid transaminase	Rv3624c	<i>hpt</i>	probable hypoxanthine-guanine phosphoribosyltransferase	Rv3601c	<i>panD</i>	aspartate 1-decarboxylase
Rv1820	<i>ilvG</i>	acetolactate synthase II	Rv3393	<i>iunH</i>	probable inosine-uridine preferring nucleoside hydrolase	6. Pyridoxine		
Rv3002c	<i>ilvN</i>	acetolactate synthase I small subunit	Rv0535	<i>pnp</i>	phosphorylase from Pnp/MtaP family 2	Rv2607	<i>pdxH</i>	pyridoxamine 5'-phosphate oxidase
Rv3509c	<i>ilvX</i>	probable acetohydroxyacid synthase I large subunit	Rv3309c	<i>upp</i>	uracil phosphoribosyltransferase	7. Pyridine nucleotide		
Rv3710	<i>leuA</i>	$\alpha$ -isopropyl malate synthase	5. Miscellaneous nucleoside/nucleotide reactions			Rv1594	<i>nadA</i>	quinolinate synthase
Rv2995c	<i>leuB</i>	3-isopropylmalate dehydrogenase	Rv0733	<i>adk</i>	probable adenylate kinase	Rv1595	<i>nadB</i>	L-aspartate oxidase
Rv2988c	<i>leuC</i>	3-isopropylmalate dehydratase large subunit	Rv2364c	<i>bex</i>	GTP-binding protein of Era/ThdF family	Rv1596	<i>nadC</i>	nicotinate-nucleotide pyrophosphatase
Rv2987c	<i>leuD</i>	3-isopropylmalate dehydratase small subunit	Rv1712	<i>cmk</i>	cytidylate kinase	Rv0423c	<i>thiC</i>	thiamine synthesis, pyrimidine moiety
<i>E. Polyamine synthesis</i>			Rv2344c	<i>dgt</i>	probable deoxyguanosine triphosphate hydrolase	8. Thiamine		
Rv2601	<i>speE</i>	spermidine synthase	Rv2404c	<i>lepA</i>	GTP-binding protein LepA	Rv0422c	<i>thiD</i>	phosphomethylpyrimidine kinase
<i>F. Purines, pyrimidines, nucleosides and nucleotides</i>			Rv2727c	<i>miaA</i>	tRNA $\delta$ (2)-isopentenylpyrophosphate transferase	Rv0414c	<i>thiE</i>	thiamine synthesis, thiazole moiety
1. Purine ribonucleotide biosynthesis			Rv2445c	<i>ndkA</i>	nucleoside diphosphate kinase	Rv0417	<i>thiG</i>	thiamine synthesis, thiazole moiety
Rv1389	<i>gmk</i>	putative guanylate kinase	Rv2440c	<i>obg</i>	Obg GTP-binding protein	Rv2977c	<i>thiL</i>	probable thiamine-monophosphate kinase
Rv3396c	<i>guaA</i>	GMP synthase	Rv2583c	<i>relA</i>	(p)ppGpp synthase I	9. Riboflavin		
Rv1843c	<i>guaB1</i>	inosine-5'-monophosphate dehydrogenase	<i>G. Biosynthesis of cofactors, prosthetic groups and carriers</i>			Rv1940	<i>ribA</i>	GTP cyclohydrolase II
Rv3411c	<i>guaB2</i>	inosine-5'-monophosphate dehydrogenase	1. Biotin			Rv1415	<i>ribA2</i>	probable GTP cyclohydrolase II
Rv3410c	<i>guaB3</i>	inosine-5'-monophosphate dehydrogenase	Rv1568	<i>bioA</i>	adenosylmethionine-8-amino-7-oxononanoate aminotransferase	Rv1412	<i>ribC</i>	probable riboflavin synthase $\alpha$ chain
Rv1017c	<i>prsA</i>	ribose-phosphate pyrophosphokinase	Rv1589	<i>bioB</i>	biotin synthase	Rv2671	<i>ribD</i>	probable riboflavin deaminase
Rv0357c	<i>purA</i>	adenylosuccinate synthase	Rv1570	<i>bioD</i>	dethiobiotin synthase	Rv2786c	<i>ribF</i>	riboflavin kinase
Rv0777	<i>purB</i>	adenylosuccinate lyase	Rv1569	<i>bioF</i>	8-amino-7-oxononanoate synthase	Rv1409	<i>ribG</i>	riboflavin biosynthesis
Rv0780	<i>purC</i>	phosphoribosylaminoimidazole-succinocarboxamide synthase	Rv0032	<i>bioF2</i>	C-terminal similar to <i>B. subtilis</i> BioF	Rv1416	<i>ribH</i>	riboflavin synthase $\beta$ chain
Rv0772	<i>purD</i>	phosphoribosylamine-glycine ligase	Rv3279c	<i>birA</i>	biotin apo-protein ligase	Rv3300c	-	probable deaminase, riboflavin synthesis
Rv3275c	<i>purE</i>	phosphoribosylaminoimidazole carboxylase	Rv1442	<i>bisC</i>	biotin sulfoxide reductase	10. Thioredoxin, glutaredoxin and mycothiol		
Rv0808	<i>purF</i>	amidophosphoribosyltransferase	Rv0089	-	possible <i>bioC</i> biotin synthesis gene	Rv0773c	<i>ggtA</i>	putative $\gamma$ -glutamyl transpeptidase
Rv0957	<i>purH</i>	phosphoribosylaminoimidazole-carboxamide formyltransferase	2. Folic acid			Rv2394	<i>ggtB</i>	$\gamma$ -glutamyltranspeptidase precursor
Rv3276c	<i>purK</i>	phosphoribosylaminoimidazole carboxylase ATPase subunit	Rv2763c	<i>dfrA</i>	dihydrofolate reductase	Rv2855	<i>gorA</i>	glutathione reductase homologue
Rv0803	<i>purL</i>	phosphoribosylformylglycinamide synthase II	Rv2447c	<i>folC</i>	folypolyglutamate synthase	Rv0816c	<i>thiX</i>	equivalent to <i>M. leprae</i> ThiX
Rv0809	<i>purM</i>	5'-phosphoribosyl-5-aminoimidazole synthase	Rv3356c	<i>folD</i>	methylene tetrahydrofolate dehydrogenase	Rv1470	<i>trxA</i>	thioredoxin
Rv0956	<i>purN</i>	phosphoribosylglycinamide formyltransferase I	Rv3609c	<i>folE</i>	GTP cyclohydrolase I	Rv1471	<i>trxB</i>	thioredoxin reductase
Rv0788	<i>purQ</i>	phosphoribosylformylglycinamide synthase I	Rv3606c	<i>folK</i>	7,8-dihydro-6-hydroxymethylpterin pyrophosphokinase	Rv3913	<i>trxB2</i>	thioredoxin reductase
Rv0389	<i>purT</i>	phosphoribosylglycinamide formyltransferase II	Rv3608c	<i>folP</i>	dihydropterate synthase	Rv3914	<i>trxC</i>	thioredoxin
Rv2964	<i>purU</i>	formyltetrahydrofolate deformylase	Rv1207	<i>folP2</i>	dihydropterate synthase	11. Menaquinone, PQQ, ubiquinone and other terpenoids		
2. Pyrimidine ribonucleotide biosynthesis			Rv3607c	<i>folX</i>	may be involved in folate biosynthesis	Rv2682c	<i>dxs</i>	1-deoxy-D-xylulose 5-phosphate synthase
Rv1383	<i>carA</i>	carbamoyl-phosphate synthase subunit	Rv0013	<i>pabA</i>	<i>p</i> -aminobenzoate synthase	Rv0562	<i>grcC1</i>	heptaprenyl diphosphate synthase II
Rv1384	<i>carB</i>	carbamoyl-phosphate synthase subunit	Rv1005c	<i>pabB</i>	glutamine amidotransferase	Rv0989c	<i>grcC2</i>	heptaprenyl diphosphate synthase II
Rv1380	<i>pyrB</i>	aspartate carbamoyltransferase	Rv0812	<i>pabC</i>	<i>p</i> -aminobenzoate synthase	Rv3398c	<i>idsA</i>	geranylgeranyl pyrophosphate synthase
Rv1381	<i>pyrC</i>	dihydroorotase	3. Lipoate			Rv2173	<i>idsA2</i>	geranylgeranyl pyrophosphate synthase
Rv2139	<i>pyrD</i>	dihydroorotase dehydrogenase	Rv2218	<i>lipA</i>	lipoate biosynthesis protein A	Rv3383c	<i>idsB</i>	transfergeranyl, similar geranyl pyrophosphate synthase
Rv1385	<i>pyrF</i>	orotidine 5'-phosphate decarboxylase	Rv2217	<i>lipB</i>	lipoate biosynthesis protein B	Rv0534c	<i>menA</i>	pyrophosphate synthase
Rv1699	<i>pyrG</i>	CTP synthase	4. Molybdopterin			Rv0548c	<i>menB</i>	4-dihydroxy-2-naphthoate octaprenyltransferase
Rv2883c	<i>pyrH</i>	uridylylase	Rv3109	<i>moaA</i>	molybdenum cofactor biosynthesis, protein A	Rv0553	<i>menC</i>	naphthoate synthase
Rv0382c	<i>umpA</i>	probable uridine 5'-monophosphate synthase	Rv0869c	<i>moaA2</i>	molybdenum cofactor biosynthesis, protein A	Rv0555	<i>menD</i>	<i>o</i> -succinylbenzoate-CoA synthase
3. 2'-deoxyribonucleotide metabolism			Rv0438c	<i>moaA3</i>	molybdenum cofactor biosynthesis, protein A	Rv0542c	<i>menE</i>	2-succinyl-6-hydroxy-2,4-cyclohexadiene-1-carboxylate synthase
Rv0321	<i>dcd</i>	deoxycytidine triphosphate deaminase	Rv3110	<i>moaB</i>	molybdenum cofactor biosynthesis, protein B	Rv3853	<i>menG</i>	<i>o</i> -succinylbenzoic acid-CoA ligase
Rv2697c	<i>dut</i>	deoxyuridine triphosphatase	Rv0984	<i>moaB2</i>	molybdenum cofactor biosynthesis, protein B	Rv3397c	<i>phyA</i>	<i>S</i> -adenosylmethionine: 2-demethylmenaquinone phytoene synthase
Rv0233	<i>nrdB</i>	ribonucleoside-diphosphate reductase B2 (eukaryotic-like)	Rv3111	<i>moaC</i>	molybdenum cofactor biosynthesis, protein C	Rv0693	<i>pqqE</i>	coenzyme PQQ synthesis protein E
Rv3051c	<i>nrdE</i>	ribonucleoside diphosphate reductase $\alpha$ chain	Rv0864	<i>moaC2</i>	molybdenum cofactor biosynthesis, protein C	Rv0558	<i>ubiE</i>	ubiquinone/menaquinone biosynthesis methyltransferase
Rv1981c	<i>nrdF</i>	ribonucleotide reductase small subunit	Rv3324c	<i>moaC3</i>	molybdenum cofactor biosynthesis, protein C	12. Heme and porphyrin		
			Rv3112	<i>moaD</i>	molybdopterin converting factor subunit 1	Rv0509	<i>hema</i>	glutamyl-tRNA reductase
			Rv0868c	<i>moaD2</i>	molybdopterin converting factor	Rv0512	<i>hemB</i>	$\delta$ -aminolevulinic acid dehydratase
						Rv0510	<i>hemC</i>	porphobilinogen deaminase
						Rv2678c	<i>hemE</i>	uroporphyrinogen decarboxylase





Nature © Macmillan Publishers Ltd 1998



Rv0823c	-	family) transcriptional regulator (NifR3/Smm1 family)	Rv3160c	-	putative transcriptional regulator	Rv0018c	<i>ppp</i>	truncated putative phosphoprotein phosphatase
Rv0827c	-	transcriptional regulator (ArsR family)	Rv3167c	-	putative transcriptional regulator	Rv2234	<i>ptpA</i>	low molecular weight protein-tyrosine-phosphatase
Rv0890c	-	transcriptional regulator (LuxR/UhpA family)	Rv3173c	-	transcriptional regulator (TetR/AcrR family)	Rv0153c	-	putative protein-tyrosine-phosphatase
Rv0891c	-	putative transcriptional regulator	Rv3183	-	putative transcriptional regulator	<b>II. Macromolecule metabolism</b>		
Rv0894	-	putative transcriptional regulator	Rv3208	-	transcriptional regulator (TetR/AcrR family)			
Rv1019	-	transcriptional regulator (TetR/AcrR family)	Rv3249c	-	transcriptional regulator (TetR/AcrR family)	<b>A. Synthesis and modification of macromolecules</b>		
Rv1049	-	transcriptional regulator (MarR family)	Rv3291c	-	transcriptional regulator (Lrp/AsnC family)			
Rv1129c	-	transcriptional regulator (PbsX/Xre family)	Rv3295	-	transcriptional regulator (TetR/AcrR family)	<b>1. Ribosomal protein synthesis and modification</b>		
Rv1151c	-	putative transcriptional regulator	Rv3334	-	transcriptional regulator (MerR family)			
Rv1152	-	transcriptional regulator (GntR family)	Rv3405c	-	putative transcriptional regulator	Rv3420c	<i>rimI</i>	ribosomal protein S18 acetyltransferase
Rv1167c	-	putative transcriptional regulator	Rv3522	-	putative transcriptional regulator	Rv0995	<i>rimJ</i>	acetylation of 30S S5 subunit
Rv1219c	-	putative transcriptional regulator	Rv3557c	-	transcriptional regulator (TetR/AcrR family)	Rv0641	<i>rplA</i>	50S ribosomal protein L1
Rv1255c	-	transcriptional regulator (TetR/AcrR family)	Rv3574	-	transcriptional regulator (TetR/AcrR family)	Rv0704	<i>rplB</i>	50S ribosomal protein L2
Rv1332	-	putative transcriptional regulator	Rv3575c	-	transcriptional regulator (LacI family)	Rv0701	<i>rplC</i>	50S ribosomal protein L3
Rv1353c	-	transcriptional regulator (TetR/AcrR family)	Rv3583c	-	putative transcriptional regulator	Rv0702	<i>rplD</i>	50S ribosomal protein L4
Rv1358	-	transcriptional regulator (LuxR/UhpA family)	Rv3676	-	transcriptional regulator (Crp/Fnr family)	Rv0716	<i>rplE</i>	50S ribosomal protein L5
Rv1359	-	putative transcriptional regulator	Rv3678c	-	transcriptional regulator (LysR family)	Rv0719	<i>rplF</i>	50S ribosomal protein L6
Rv1395	-	transcriptional regulator (AraC/XylS family)	Rv3736	-	transcriptional regulator (AraC/XylS family)	Rv0056	<i>rplI</i>	50S ribosomal protein L9
Rv1404	-	transcriptional regulator (MarR family)	Rv3744	-	transcriptional regulator (ArsR family)	Rv0651	<i>rplJ</i>	50S ribosomal protein L10
Rv1423	-	putative transcriptional regulator	Rv3830c	-	transcriptional regulator (TetR/AcrR family)	Rv0640	<i>rplK</i>	50S ribosomal protein L11
Rv1460	-	putative transcriptional regulator	Rv3833	-	transcriptional regulator (AraC/XylS family)	Rv0652	<i>rplL</i>	50S ribosomal protein L7/L12
Rv1474c	-	transcriptional regulator (TetR/AcrR family)	Rv3840	-	putative transcriptional regulator	Rv3443c	<i>rplM</i>	50S ribosomal protein L13
Rv1534	-	transcriptional regulator (TetR/AcrR family)	Rv3855	-	putative transcriptional regulator	Rv0714	<i>rplN</i>	50S ribosomal protein L14
Rv1556	-	putative transcriptional regulator	<b>2. Two component systems</b>			Rv0723	<i>rplO</i>	50S ribosomal protein L15
Rv1674c	-	putative transcriptional regulator	Rv1028c	<i>kdpD</i>	sensor histidine kinase	Rv0708	<i>rplP</i>	50S ribosomal protein L16
Rv1675c	-	putative transcriptional regulator	Rv1027c	<i>kdpE</i>	two-component response regulator	Rv3456c	<i>rplQ</i>	50S ribosomal protein L17
Rv1719	-	transcriptional regulator (IclR family)	Rv3246c	<i>mtrA</i>	two-component response regulator	Rv0720	<i>rplR</i>	50S ribosomal protein L18
Rv1773c	-	transcriptional regulator (IclR family)	Rv3245c	<i>mtrB</i>	sensor histidine kinase	Rv2904c	<i>rplS</i>	50S ribosomal protein L19
Rv1776c	-	putative transcriptional regulator	Rv0844c	<i>narL</i>	two-component response regulator	Rv1643	<i>rplT</i>	50S ribosomal protein L20
Rv1816	-	putative transcriptional regulator	Rv0757	<i>phoP</i>	two-component response regulator	Rv2442c	<i>rplU</i>	50S ribosomal protein L21
Rv1846c	-	putative transcriptional regulator	Rv0758	<i>phoR</i>	sensor histidine kinase	Rv0706	<i>rplV</i>	50S ribosomal protein L22
Rv1931c	-	transcriptional regulator (AraC/XylS family)	Rv0491	<i>regX3</i>	two-component response regulator	Rv0703	<i>rplW</i>	50S ribosomal protein L23
Rv1956	-	putative transcriptional regulator	Rv0490	<i>senX3</i>	sensor histidine kinase	Rv0715	<i>rplX</i>	50S ribosomal protein L24
Rv1963c	-	putative transcriptional regulator	Rv0602c	<i>trcA</i>	two-component response regulator	Rv1015c	<i>rplY</i>	50S ribosomal protein L25
Rv1985c	-	transcriptional regulator (LysR family)	Rv0260c	-	two-component response regulator	Rv2441c	<i>rpmA</i>	50S ribosomal protein L27
Rv1990c	-	putative transcriptional regulator	Rv0600c	-	sensor histidine kinase	Rv0105c	<i>rpmB</i>	50S ribosomal protein L28
Rv1994c	-	transcriptional regulator (MerR family)	Rv0601c	-	sensor histidine kinase	Rv2058c	<i>rpmB2</i>	50S ribosomal protein L28
Rv2017	-	putative transcriptional regulator (PbsX/Xre family)	Rv0818	-	two-component response regulator	Rv0709	<i>rpmC</i>	50S ribosomal protein L29
Rv2021c	-	putative transcriptional regulator	Rv0845	-	sensor histidine kinase	Rv0722	<i>rpmD</i>	50S ribosomal protein L30
Rv2034	-	transcriptional regulator (ArsR family)	Rv0902c	-	sensor histidine kinase	Rv1298	<i>rpmE</i>	50S ribosomal protein L31
Rv2175c	-	putative transcriptional regulator	Rv0903c	-	two-component response regulator	Rv2057c	<i>rpmG</i>	50S ribosomal protein L33
Rv2250c	-	putative transcriptional regulator	Rv0981	-	two-component response regulator	Rv3924c	<i>rpmH</i>	50S ribosomal protein L34
Rv2258c	-	putative transcriptional regulator	Rv0982	-	sensor histidine kinase	Rv1642	<i>rpmI</i>	50S ribosomal protein L35
Rv2282c	-	transcriptional regulator (LysR family)	Rv1032c	-	sensor histidine kinase	Rv3461c	<i>rpmJ</i>	50S ribosomal protein L36
Rv2308	-	putative transcriptional regulator	Rv1033c	-	two-component response regulator	Rv1630	<i>rpsA</i>	30S ribosomal protein S1
Rv2324	-	transcriptional regulator (Lrp/AsnC family)	Rv1626	-	two-component response regulator	Rv2890c	<i>rpsB</i>	30S ribosomal protein S2
Rv2358	-	transcriptional regulator (ArsR family)	Rv2027c	-	sensor histidine kinase	Rv0707	<i>rpsC</i>	30S ribosomal protein S3
Rv2488c	-	transcriptional regulator (LuxR/UhpA family)	Rv2884	-	two-component response regulator	Rv3458c	<i>rpsD</i>	30S ribosomal protein S4
Rv2506	-	transcriptional regulator (TetR/AcrR family)	Rv3132c	-	sensor histidine kinase	Rv0721	<i>rpsE</i>	30S ribosomal protein S5
Rv2621c	-	putative transcriptional regulator	Rv3133c	-	two-component response regulator	Rv0053	<i>rpsF</i>	30S ribosomal protein S6
Rv2640c	-	transcriptional regulator (ArsR family)	Rv3143	-	putative sensory transduction protein	Rv0683	<i>rpsG</i>	30S ribosomal protein S7
Rv2642	-	transcriptional regulator (ArsR family)	Rv3220c	-	sensor histidine kinase	Rv0718	<i>rpsH</i>	30S ribosomal protein S8
Rv2669	-	putative transcriptional regulator	Rv3764c	-	sensor histidine kinase	Rv3442c	<i>rpsI</i>	30S ribosomal protein S9
Rv2745c	-	putative transcriptional regulator	Rv3765c	-	two-component response regulator	Rv0700	<i>rpsJ</i>	30S ribosomal protein S10
Rv2779c	-	transcriptional regulator (Lrp/AsnC family)	<b>3. Serine-threonine protein kinases and phosphoprotein phosphatases</b>			Rv3459c	<i>rpsK</i>	30S ribosomal protein S11
Rv2887	-	transcriptional regulator (MarR family)	Rv0015c	<i>pknA</i>	serine-threonine protein kinase	Rv0682	<i>rpsL</i>	30S ribosomal protein S12
Rv2912c	-	transcriptional regulator (TetR/AcrR family)	Rv0014c	<i>pknB</i>	serine-threonine protein kinase	Rv3460c	<i>rpsM</i>	30S ribosomal protein S13
Rv2989	-	transcriptional regulator (IclR family)	Rv0931c	<i>pknD</i>	serine-threonine protein kinase	Rv0717	<i>rpsN</i>	30S ribosomal protein S14
Rv3050c	-	putative transcriptional regulator	Rv1743	<i>pknE</i>	serine-threonine protein kinase	Rv2056c	<i>rpsN2</i>	30S ribosomal protein S14
Rv3055	-	putative transcriptional regulator	Rv1746	<i>pknF</i>	serine-threonine protein kinase	Rv2785c	<i>rpsO</i>	30S ribosomal protein S15
Rv3058c	-	putative transcriptional regulator	Rv0410c	<i>pknG</i>	serine-threonine protein kinase	Rv2909c	<i>rpsP</i>	30S ribosomal protein S16
Rv3060c	-	transcriptional regulator (GntR family)	Rv1266c	<i>pknH</i>	serine-threonine protein kinase	Rv0710	<i>rpsQ</i>	30S ribosomal protein S17
Rv3066	-	putative transcriptional regulator	Rv2914c	<i>pknI</i>	serine-threonine protein kinase	Rv0055	<i>rpsR</i>	30S ribosomal protein S18
Rv3095	-	putative transcriptional regulator	Rv2088	<i>pknJ</i>	serine-threonine protein kinase	Rv2055c	<i>rpsR2</i>	30S ribosomal protein S18
Rv3124	-	transcriptional regulator (AisR/DndI/RedD family)	Rv3080c	<i>pknK</i>	serine-threonine protein kinase	Rv0705	<i>rpsS</i>	30S ribosomal protein S19
			Rv2176	<i>pknL</i>	serine-threonine protein kinase,	Rv2412	<i>rpsT</i>	30S ribosomal protein S20
						Rv3241c	-	member of S30AE ribosomal protein family
						<b>2. Ribosome modification and maturation</b>		
						Rv1010	<i>ksgA</i>	16S rRNA dimethyltransferase
						Rv2838c	<i>rbfA</i>	ribosome-binding factor A
						Rv2907c	<i>rimM</i>	16S rRNA processing protein
						<b>3. Aminoacyl tRNA synthetases and their modification</b>		
						Rv2555c	<i>alaS</i>	alanine-tRNA synthase
						Rv1292	<i>argS</i>	arginyl-tRNA synthase
						Rv2572c	<i>aspS</i>	aspartyl-tRNA synthase
						Rv3580c	<i>cysS</i>	cysteine-tRNA synthase
						Rv2130c	<i>cysS2</i>	cysteine-tRNA synthase
						Rv1406	<i>fmt</i>	methionyl-tRNA formyltransferase
						Rv3011c	<i>gatA</i>	glu-tRNA-gln amidotransferase, subunit B
						Rv3009c	<i>gatB</i>	glu-tRNA-gln amidotransferase, subunit A
						Rv3012c	<i>gatC</i>	glu-tRNA-gln amidotransferase, subunit C
						Rv2992c	<i>gltS</i>	glutamyl-tRNA synthase
						Rv2357c	<i>glyS</i>	glycyl-tRNA synthase
						Rv2580c	<i>hisS</i>	histidyl-tRNA synthase
						Rv1536	<i>ileS</i>	isoleucyl-tRNA synthase
						Rv0041	<i>leuS</i>	leucyl-tRNA synthase
						Rv3598c	<i>lysS</i>	lysyl-tRNA synthase
						Rv1640c	<i>lysX</i>	C-term lysyl-tRNA synthase
						Rv1007c	<i>metS</i>	methionyl-tRNA synthase
						Rv1649	<i>pheS</i>	phenylalanyl-tRNA synthase $\alpha$ subunit



Rv1650	<i>pheT</i>	phenylalanyl-tRNA synthase $\beta$ subunit	Rv2090	-	partially similar to DNA polymerase I	2. DNA	
Rv2845c	<i>proS</i>	prolyl-tRNA synthase	Rv2191	-	similar to both PolC and UvrC proteins	Rv0670	<i>end</i> endonuclease IV (apurinase)
Rv3834c	<i>serS</i>	seryl-tRNA synthase				Rv1108c	<i>xseA</i> exonuclease VII large subunit
Rv2614c	<i>thrS</i>	threonyl-tRNA synthase	Rv2464c	-	probable DNA glycosylase, endonuclease VIII	Rv1107c	<i>xseB</i> exonuclease VII small subunit
Rv2906c	<i>trmD</i>	tRNA (guanine-N1)-methyltransferase	Rv3201c	-	probable ATP-dependent DNA helicase	3. Proteins, peptides and glycopeptides	
Rv3336c	<i>trpS</i>	tryptophanyl tRNA synthase	Rv3202c	-	similar to UvrD proteins	Rv3305c	<i>amiA</i> probable aminohydrolase
Rv1689	<i>tyrS</i>	tyrosyl-tRNA synthase	Rv3263	-	probable DNA methylase	Rv3306c	<i>amiB</i> probable aminohydrolase
Rv2448c	<i>valS</i>	valyl-tRNA synthase	Rv3644c	-	similar in N-term to DNA polymerase III	Rv3596c	<i>clpC</i> ATP-dependent Clp protease
						Rv2461c	<i>clpP</i> ATP-dependent Clp protease proteolytic subunit
4. Nucleoproteins						Rv2460c	<i>clpP2</i> ATP-dependent Clp protease proteolytic subunit
Rv1407	<i>fmu</i>	similar to Fmu protein				Rv2457c	<i>clpX</i> ATP-dependent Clp protease
Rv3852	<i>hns</i>	HU-histone protein	6. Protein translation and modification				ATP-binding subunit ClpX
Rv2986c	<i>hupB</i>	DNA-binding protein II	Rv0429c	<i>def</i>	polypeptide deformylase	Rv2667	<i>clpX'</i> similar to ClpC from <i>M. leprae</i> but shorter
Rv1388	<i>mIHF</i>	integration host factor	Rv2534c	<i>efp</i>	elongation factor P		
5. DNA replication, repair, recombination and restriction/modification			Rv2882c	<i>frr</i>	ribosome recycling factor	Rv3419c	<i>gcp</i> glycoprotease
Rv1317c	<i>alkA</i>	DNA-3-methyladenine glycosidase II	Rv0684	<i>fusA</i>	elongation factor G	Rv2725c	<i>hflX</i> GTP-binding protein
			Rv0120c	<i>fusA2</i>	elongation factor G	Rv1223	<i>htrA</i> serine protease
Rv2836c	<i>dinF</i>	DNA-damage-inducible protein F	Rv1080c	<i>greA</i>	transcription elongation factor G	Rv2861c	<i>map</i> probable methionine aminopeptidase
Rv1329c	<i>dinG</i>	probable ATP-dependent helicase	Rv3462c	<i>infA</i>	initiation factor IF-1	Rv0734	<i>map'</i> probable methionine aminopeptidase
Rv3056	<i>dinP</i>	DNA-damage-inducible protein	Rv2839c	<i>infB</i>	initiation factor IF-2		
Rv1537	<i>dinX</i>	probable DNA-damage-inducible protein	Rv1641	<i>infC</i>	initiation factor IF-3	Rv0319	<i>pcp</i> pyrrolidone-carboxylate peptidase
			Rv0009	<i>ppiA</i>	peptidyl-prolyl <i>cis-trans</i> isomerase	Rv0125	<i>pepA</i> probable serine protease
Rv0001	<i>dnaA</i>	chromosomal replication initiator protein	Rv2582	<i>ppiB</i>	peptidyl-prolyl <i>cis-trans</i> isomerase	Rv2213	<i>pepB</i> aminopeptidase A/I
			Rv1299	<i>prfA</i>	peptide chain release factor 1	Rv0800	<i>pepC</i> aminopeptidase I
Rv0058	<i>dnaB</i>	DNA helicase (contains intein)	Rv3105c	<i>prfB</i>	peptide chain release factor 2	Rv2467	<i>pepD</i> probable aminopeptidase
Rv1547	<i>dnaE1</i>	DNA polymerase III, $\alpha$ subunit	Rv2889c	<i>tsf</i>	elongation factor EF-Ts	Rv2089c	<i>pepE</i> cytoplasmic peptidase
Rv3370c	<i>dnaE2</i>	DNA polymerase III $\alpha$ chain	Rv0685	<i>tuf</i>	elongation factor EF-Tu	Rv2535c	<i>pepQ</i> cytoplasmic peptidase
Rv2343c	<i>dnaG</i>	DNA primase	7. RNA synthesis, RNA modification and DNA transcription			Rv2782c	<i>pepR</i> protease/peptidase, M16 family (insulinase)
Rv0002	<i>dnaN</i>	DNA polymerase III, $\beta$ subunit	Rv1253	<i>deaD</i>	ATP-dependent DNA/RNA helicase	Rv2109c	<i>prcA</i> proteasome $\alpha$ -type subunit 1
Rv3711c	<i>dnaQ</i>	DNA polymerase III $\epsilon$ chain	Rv2783c	<i>gpsI</i>	pppGpp synthase and polynucleotide phosphorylase	Rv2110c	<i>prcB</i> proteasome $\beta$ -type subunit 2
Rv3721c	<i>dnaX</i>	DNA polymerase III, $\gamma$ (dnaZ) and $\tau$ (dnaX)	Rv2841c	<i>nusA</i>	transcription termination factor	Rv0782	<i>ptrBa</i> protease II, $\alpha$ subunit
			Rv2533c	<i>nusB</i>	N-utilization substance protein B	Rv0781	<i>ptrBb</i> protease II, $\beta$ subunit
Rv2924c	<i>fgp</i>	formamidopyrimidine-DNA glycosylase	Rv0639	<i>nusG</i>	transcription antitermination protein	Rv0724	<i>sppA</i> protease IV, signal peptide peptidase
			Rv3907c	<i>pcnA</i>	polynucleotide polymerase	Rv0198c	-
Rv0006	<i>gyrA</i>	DNA gyrase subunit A	Rv3232c	<i>pvdS</i>	alternative sigma factor for siderophore production	Rv0457c	-
Rv0005	<i>gyrB</i>	DNA gyrase subunit B				Rv0840c	-
Rv2092c	<i>heliY</i>	probable helicase, Ski2 subfamily	Rv3211	<i>rhlE</i>	probable ATP-dependent RNA helicase	Rv0983	-
Rv2101	<i>heliZ</i>	probable helicase, Snf2/Rad54 family	Rv1297	<i>rho</i>	transcription termination factor rho	Rv1977	-
Rv2756c	<i>hsdM</i>	type I restriction/modification system DNA methylase	Rv3457c	<i>rpoA</i>	$\alpha$ subunit of RNA polymerase	Rv3668c	-
Rv2755c	<i>hsdS'</i>	type I restriction/modification system specificity determinant	Rv0667	<i>rpoB</i>	$\beta$ subunit of RNA polymerase	Rv3671c	-
			Rv0668	<i>rpoC</i>	$\beta'$ subunit of RNA polymerase	Rv3883c	-
Rv3296	<i>lhr</i>	ATP-dependent helicase	Rv1364c	<i>rsbU</i>	SigB regulation protein	Rv3886c	-
Rv3014c	<i>ligA</i>	DNA ligase	Rv3287c	<i>rsbW</i>	anti-sigma B factor		
Rv3062	<i>ligB</i>	DNA ligase	Rv2703	<i>sigA</i>	RNA polymerase sigma factor (aka MysA, RpoV)	4. Polysaccharides, lipopolysaccharides and phospholipids	
Rv3731	<i>ligC</i>	probable DNA ligase	Rv2710	<i>sigB</i>	RNA polymerase sigma factor (aka MysB)	Rv0062	<i>celA</i> cellulase/endoglucanase
Rv1020	<i>mfd</i>	transcription-repair coupling factor	Rv2069	<i>sigC</i>	ECF subfamily sigma subunit	Rv3915	<i>cwIM</i> hydrolase
Rv2528c	<i>mrr</i>	restriction system protein	Rv3414c	<i>sigD</i>	ECF subfamily sigma subunit	Rv0315	-
Rv2985	<i>mutT1</i>	MutT homologue	Rv1221	<i>sigE</i>	ECF subfamily sigma subunit	Rv1090	-
Rv1160	<i>mutT2</i>	MutT homologue	Rv3286c	<i>sigF</i>	ECF subfamily sigma subunit		
Rv0413	<i>mutT3</i>	MutT homologue	Rv0182c	<i>sigG</i>	sigma-70 factors ECF subfamily	Rv1327c	-
Rv3589	<i>mutY</i>	probable DNA glycosylase	Rv3223c	<i>sigH</i>	ECF subfamily sigma subunit		
Rv3297	<i>nei</i>	probable endonuclease VIII	Rv1189	<i>sigI</i>	ECF family sigma factor	Rv1333	-
Rv3674c	<i>nth</i>	probable endonuclease III	Rv3328c	<i>sigJ</i>	similar to SigI, ECF family	Rv3463	-
Rv1316c	<i>ogt</i>	methylated-DNA-protein-cysteine methyltransferase	Rv0445c	<i>sigK</i>	ECF-type sigma factor	Rv3717	-
			Rv0735	<i>sigL</i>	sigma-70 factors ECF subfamily		
Rv1629	<i>polA</i>	DNA polymerase I	Rv3911	<i>sigM</i>	probable sigma factor, similar to SigE	5. Esterases and lipases	
Rv1402	<i>priA</i>	putative primosomal protein n' (replication factor Y)	Rv3366	<i>spoU</i>	probable rRNA methylase	Rv0220	<i>lipC</i> probable esterase
			Rv3455c	<i>truA</i>	probable pseudouridylylase	Rv1923	<i>lipD</i> probable esterase
Rv3585	<i>radA</i>	probable DNA repair RadA homologue	Rv2793c	<i>truB</i>	tRNA pseudouridine 55 synthase	Rv3775	<i>lipE</i> probable hydrolase
			Rv1644	<i>tsnR</i>	putative 23S rRNA methyltransferase	Rv3487c	<i>lipF</i> probable esterase
Rv2737c	<i>recA</i>	recombinase (contains intein)	Rv3649	-	ATP-dependent DNA/RNA helicase	Rv0646c	<i>lipG</i> probable hydrolase
Rv0630c	<i>recB</i>	exodeoxyribonuclease V				Rv1399c	<i>lipH</i> probable lipase
Rv0631c	<i>recC</i>	exodeoxyribonuclease V	8. Polysaccharides (cytoplasmic)			Rv1400c	<i>lipI</i> probable lipase
Rv0629c	<i>recD</i>	exodeoxyribonuclease V	Rv1326c	<i>glgB</i>	1,4- $\alpha$ -glucan branching enzyme	Rv1900c	<i>lipJ</i> probable esterase
Rv0003	<i>recF</i>	DNA replication and SOS induction	Rv1328	<i>glgP</i>	probable glycogen phosphorylase	Rv2385	<i>lipK</i> probable acetyl-hydrolase
						Rv1497	<i>lipL</i> esterase
Rv2973c	<i>recG</i>	ATP-dependent DNA helicase	Rv1564c	<i>glgX</i>	probable glycogen debranching enzyme	Rv2284	<i>lipM</i> probable esterase
Rv1696	<i>recN</i>	recombination and DNA repair	Rv1563c	<i>glgY</i>	putative $\alpha$ -amylase	Rv2970c	<i>lipN</i> probable lipase/esterase
Rv3715c	<i>recR</i>	RecBC-Independent process of DNA repair	Rv1562c	<i>glgZ</i>	maltooligosyltrehalose trehalohydrolase	Rv1426c	<i>lipO</i> probable esterase
						Rv2463	<i>lipP</i> probable esterase
Rv2736c	<i>recX</i>	regulatory protein for RecA				Rv2485c	<i>lipQ</i> probable carboxylesterase
Rv2593c	<i>ruvA</i>	Holliday junction binding protein, DNA helicase	Rv0126	-	probable glycosyl hydrolase	Rv3084	<i>lipR</i> probable acetyl-hydrolase
			Rv1781c	-	probable 4- $\alpha$ -glucanotransferase	Rv3176c	<i>lipS</i> probable esterase/lipase
Rv2592c	<i>ruvB</i>	Holliday junction binding protein	Rv2471	-	probable maltase $\alpha$ -glucosidase	Rv2045c	<i>lipT</i> probable carboxylesterase
Rv2594c	<i>ruvC</i>	Holliday junction resolvase, endodeoxyribonuclease				Rv1076	<i>lipU</i> probable esterase
						Rv3203	<i>lipV</i> probable lipase
Rv0054	<i>ssb</i>	single strand binding protein				Rv0217c	<i>lipW</i> probable esterase
Rv1210	<i>tagA</i>	DNA-3-methyladenine glycosidase I				Rv2351c	<i>plcA</i> phospholipase C precursor
						Rv2350c	<i>plcB</i> phospholipase C precursor
Rv3646c	<i>topA</i>	DNA topoisomerase				Rv2349c	<i>plcC</i> phospholipase C precursor
Rv2976c	<i>ung</i>	uracil-DNA glycosylase				Rv1755c	<i>plcD</i> partial CDS for phospholipase C
Rv1638	<i>uvrA</i>	excinuclease ABC subunit A				Rv1104	-
Rv1633	<i>uvrB</i>	excinuclease ABC subunit B				Rv1105	-
Rv1420	<i>uvrC</i>	excinuclease ABC subunit C					
Rv0949	<i>uvrD</i>	DNA-dependent ATPase I and helicase II	B. Degradation of macromolecules				
			1. RNA			6. Aromatic hydrocarbons	
Rv3198c	<i>uvrD2</i>	putative UvrD	Rv1014c	<i>pth</i>	peptidyl-tRNA hydrolase	Rv3469c	<i>mhpE</i> probable 4-hydroxy-2-oxovalerate aldolase
Rv0427c	<i>xthA</i>	exodeoxyribonuclease III	Rv2925c	<i>rnc</i>	RNAse III		
Rv0071	-	group II intron maturase	Rv2444c	<i>rne</i>	similar at C-term to ribonuclease E	Rv0316	-
Rv0861c	-	probable DNA helicase					
Rv0944c	-	possible formamidopyrimidine-DNA glycosylase	Rv2902c	<i>rnhB</i>	ribonuclease HII	Rv0771	-
			Rv3923c	<i>rnpA</i>	ribonuclease P protein component		
Rv1688	-	probable 3-methylpurine DNA glycosylase	Rv1340	<i>rphA</i>	ribonuclease PH	Rv0939	-
						Rv1723	-

Rv2715	-	lase 2-hydroxymuconic semialdehyde hydrolase	Rv1367c	-	probable penicillin binding protein	Rv1030	<i>kdpB</i>	potassium-transporting ATPase B chain
Rv3530c	-	probable <i>cis</i> -diol dehydrogenase	Rv1730c	-	probable penicillin binding protein	Rv1031	<i>kdpC</i>	potassium-transporting ATPase C chain
Rv3534c	-	4-hydroxy-2-oxovalerate aldolase	Rv1922	-	probable penicillin binding protein	Rv3236c	<i>kefB</i>	probable glutathione-regulated potassium-efflux protein
Rv3536c	-	aromatic hydrocarbon degradation	Rv2864c	-	probable penicillin binding protein	Rv2877c	<i>merT</i>	possible mercury resistance transport system
<b>C. Cell envelope</b>			Rv3330	-	probable penicillin binding protein	Rv1811	<i>mgtC</i>	probable magnesium transport ATPase protein C
<b>1. Lipoproteins (<i>lppA-lppO</i>) 65</b>			Rv3627c	-	probable penicillin binding protein	Rv0362	<i>mgtE</i>	putative magnesium ion transporter
<b>2. Surface polysaccharides, lipopolysaccharides, proteins and antigens</b>			<b>4. Conserved membrane proteins</b>			Rv2856	<i>nicT</i>	probable nickel transport protein
Rv0806c	<i>cpsY</i>	probable UDP-glucose-4-epimerase	Rv0402c	<i>mmpL1</i>	conserved large membrane protein	Rv0924c	<i>nramp</i>	transmembrane protein belonging to Nramp family
Rv3811	<i>csp</i>	secreted protein	Rv0507	<i>mmpL2</i>	conserved large membrane protein	Rv2691	<i>trkA</i>	probable potassium uptake protein
Rv1677	<i>dsbF</i>	highly similar to C-term Mpt53	Rv0206c	<i>mmpL3</i>	conserved large membrane protein	Rv2692	<i>trkB</i>	probable potassium uptake protein
Rv3794	<i>embA</i>	involved in arabinogalactan synthesis	Rv0450c	<i>mmpL4</i>	conserved large membrane protein	Rv2287	<i>yjcE</i>	probable Na <sup>+</sup> /H <sup>+</sup> exchanger
Rv3795	<i>embB</i>	involved in arabinogalactan synthesis	Rv0676c	<i>mmpL5</i>	conserved large membrane protein	Rv2723	-	probable membrane protein, tellurium resistance
Rv3793	<i>embC</i>	involved in arabinogalactan synthesis	Rv1557	<i>mmpL6</i>	conserved large membrane protein	Rv3162c	-	probable membrane protein
Rv3875	<i>esat6</i>	early secretory antigen target	Rv2942	<i>mmpL7</i>	conserved large membrane protein	Rv3237c	-	possible potassium channel protein
Rv0112	<i>gca</i>	probable GDP-mannose dehydratase	Rv3823c	<i>mmpL8</i>	conserved large membrane protein	Rv3743c	-	probable cation-transporting ATPase
Rv0113	<i>gmhA</i>	phosphoheptose isomerase	Rv2339	<i>mmpL9</i>	conserved large membrane protein	<b>3. Carbohydrates, organic acids and alcohols</b>		
Rv2965c	<i>kdtB</i>	lipopolysaccharide core biosynthesis protein	Rv1183	<i>mmpL10</i>	conserved large membrane protein	Rv2443	<i>dctA</i>	C4-dicarboxylate transport protein
Rv2878c	<i>mpt53</i>	secreted protein Mpt53	Rv0202c	<i>mmpL11</i>	conserved large membrane protein	Rv3476c	<i>kgtP</i>	sugar transport protein
Rv1980c	<i>mpt64</i>	secreted immunogenic protein Mpb64/Mpt64	Rv1522c	<i>mmpL12</i>	conserved large membrane protein	Rv1902c	<i>nanT</i>	probable salic acid transporter
Rv2875	<i>mpt70</i>	major secreted immunogenic protein Mpt70 precursor	Rv0403c	<i>mmpS1</i>	conserved small membrane protein	Rv1236	<i>sugA</i>	membrane protein probably involved in sugar transport
Rv2873	<i>mpt83</i>	surface lipoprotein Mpt83	Rv0506	<i>mmpS2</i>	conserved small membrane protein	Rv1237	<i>sugB</i>	sugar transport protein
Rv0899	<i>ompA</i>	member of OmpA family	Rv2198c	<i>mmpS3</i>	conserved small membrane protein	Rv1238	<i>sugC</i>	ABC transporter component of sugar uptake system
Rv3810	<i>pirG</i>	cell surface protein precursor (Erp protein)	Rv0451c	<i>mmpS4</i>	conserved small membrane protein	Rv3331	<i>sugI</i>	probable sugar transport protein
Rv3782	<i>rfeE</i>	similar to rhamnosyl transferase	Rv0677c	<i>mmpS5</i>	conserved small membrane protein	Rv2835c	<i>ugpA</i>	sn-glycerol-3-phosphate permease
Rv1302	<i>rfe</i>	undecaprenyl-phosphate $\alpha$ -N-acetylglucosaminyltransferase	<b>5. Other membrane proteins 211</b>			Rv2833c	<i>ugpB</i>	sn-glycerol-3-phosphate-binding periplasmic lipoprotein
Rv2145c	<i>wag31</i>	antigen 84 (aka wag31)	<b>III. Cell processes</b>			Rv2832c	<i>ugpC</i>	sn-glycerol-3-phosphate transport ATP-binding protein
Rv0431	-	tuberculin related peptide (AT103)	<b>A. Transport/binding proteins</b>			Rv2834c	<i>ugpE</i>	sn-glycerol-3-phosphate transport system protein
Rv0954	-	cell envelope antigen	<b>1. Amino acids</b>			Rv2316	<i>uspA</i>	sugar transport protein
Rv1514c	-	involved in polysaccharide synthesis	Rv2127	<i>ansP</i>	L-asparagine permease	Rv2318	<i>uspC</i>	sugar transport protein
Rv1518	-	involved in exopolysaccharide synthesis	Rv0346c	<i>aroF2</i>	probable aromatic amino acid permease	Rv2317	<i>uspE</i>	sugar transport protein
Rv1758	-	partial cutinase	Rv0917	<i>betP</i>	glycine betaine transport	Rv1200	-	probable sugar transporter
Rv1910c	-	probable secreted protein	Rv1704c	<i>cycA</i>	transport of D-alanine, D-serine and glycine	Rv2038c	-	probable ABC sugar transporter
Rv1919c	-	weak similarity to pollen antigens	Rv3666c	<i>dppA</i>	probable peptide transport system permease	Rv2039c	-	probable sugar transporter
Rv1984c	-	probable secreted protein	Rv3665c	<i>dppB</i>	probable peptide transport system permease	Rv2040c	-	probable sugar transporter
Rv1987	-	probable secreted protein	Rv3664c	<i>dppC</i>	probable peptide transport system permease	Rv2041c	-	probable sugar transporter
Rv2223c	-	probable exported protease	Rv3663c	<i>dppD</i>	probable ABC-transporter	<b>4. Anions</b>		
Rv2224c	-	probable exported protease	Rv0522	<i>gabP</i>	probable 4-amino butyrate transporter	Rv2684	<i>arsA</i>	probable arsenical pump
Rv2301	-	probable cutinase	Rv0411c	<i>glnH</i>	putative glutamine binding protein	Rv2685	<i>arsB</i>	probable arsenical pump
Rv2345	-	precursor of probable membrane protein	Rv2564	<i>glnQ</i>	probable ATP-binding transport protein	Rv3578	<i>arsB2</i>	probable arsenical pump
Rv2672	-	putative exported protease	Rv1280c	<i>oppA</i>	probable oligopeptide transport protein	Rv2643	<i>arsC</i>	probable arsenical pump
Rv3019c	-	similar to Esat6	Rv1283c	<i>oppB</i>	oligopeptide transport protein	Rv2397c	<i>cysA</i>	sulphate transport ATP-binding protein
Rv3036c	-	probable secreted protein	Rv1282c	<i>oppC</i>	oligopeptide transport system permease	Rv2399c	<i>cysT</i>	sulphate transport system permease protein
Rv3449	-	probable precursor of serine protease	Rv1281c	<i>oppD</i>	probable peptide transport protein	Rv2398c	<i>cysW</i>	sulphate transport system permease protein
Rv3451	-	probable cutinase	Rv2320c	<i>rocE</i>	probable cationic amino acid transport	Rv1857	<i>modA</i>	molybdate binding protein
Rv3452	-	probable cutinase precursor	Rv3253c	<i>rocE</i>	probable cationic amino acid transport	Rv1858	<i>modB</i>	transport system permease, molybdate uptake
Rv3724	-	probable cutinase precursor	Rv3454	-	possible proline permease	Rv1859	<i>modC</i>	molybdate uptake ABC-transporter
<b>3. Murein sacculus and peptidoglycan</b>			<b>2. Cations</b>			Rv1860	<i>modD</i>	precursor of Apa (45/47 kD secreted protein)
Rv2911	<i>dacB</i>	penicillin binding protein	Rv2920c	<i>amt</i>	putative ammonium transporter	Rv2329c	<i>narK1</i>	probable nitrite extrusion protein
Rv2981c	<i>ddlA</i>	D-alanine-D-alanine ligase A	Rv1607	<i>chaA</i>	putative calcium/proton antiporter	Rv1737c	<i>narK2</i>	nitrite extrusion protein
Rv3809c	<i>glf</i>	UDP-galactopyranose mutase	Rv1239c	<i>corA</i>	probable magnesium and cobalt transport protein	Rv0261c	<i>narK3</i>	nitrite extrusion protein1
Rv1018c	<i>glmU</i>	UDP-N-acetylglucosamine pyrophosphorylase	Rv0092	<i>ctpA</i>	cation-transporting ATPase	Rv0267	<i>narU</i>	similar to nitrite extrusion protein 2
Rv3382c	<i>lytB</i>	LytB protein homologue	Rv0103c	<i>ctpB</i>	cation transport ATPase	Rv0934	<i>phoS1</i>	PstS component of phosphate uptake
Rv1110	<i>lytB'</i>	very similar to LytB	Rv3270	<i>ctpC</i>	cation transport ATPase	Rv0928	<i>phoS2</i>	PstS component of phosphate uptake
Rv1315	<i>murA</i>	UDP-N-acetylglucosamine-1-carboxyvinyltransferase	Rv1469	<i>ctpD</i>	probable cadmium-transporting ATPase	Rv0820	<i>phoT</i>	phosphate transport system ABC transporter
Rv0482	<i>murB</i>	UDP-N-acetylenolpyruvoylglucosamine reductase	Rv0908	<i>ctpE</i>	probable cation transport ATPase	Rv3301c	<i>phoY1</i>	phosphate transport system regulator
Rv2152c	<i>murC</i>	UDP-N-acetyl-muramate-alanine ligase	Rv1997	<i>ctpF</i>	probable cation transport ATPase	Rv0821c	<i>phoY2</i>	phosphate transport system regulator
Rv2155c	<i>murD</i>	UDP-N-acetylmuramoylalanine-D-glutamate ligase	Rv1992c	<i>ctpG</i>	probable cation transport ATPase	Rv0545c	<i>pitA</i>	low-affinity inorganic phosphate transporter
Rv2158c	<i>murE</i>	meso-diaminopimelate-adding enzyme	Rv0425c	<i>ctpH</i>	C-terminal region putative cation-transporting ATPase	Rv2281	<i>pitB</i>	phosphate permease
Rv2157c	<i>murF</i>	D-alanine:D-alanine-adding enzyme	Rv0107c	<i>ctpl</i>	probable magnesium transport ATPase	Rv0930	<i>pstA1</i>	PstA component of phosphate uptake
Rv2153c	<i>murG</i>	transferase in peptidoglycan synthesis	Rv0969	<i>ctpV</i>	cation transport ATPase	Rv0936	<i>pstA2</i>	PstA component of phosphate uptake
Rv1338	<i>murI</i>	glutamate racemase	Rv3044	<i>fecB</i>	putative FellI-dicitrate transporter	Rv0933	<i>pstB</i>	ABC transport component of phosphate uptake
Rv2156c	<i>murX</i>	phospho-N-acetylmuramoyl-pentapeptide transferase	Rv0265c	<i>fecB2</i>	iron transport protein FellII dicitrate transporter	Rv0935	<i>pstC</i>	PstC component of phosphate uptake
Rv3332	<i>nagA</i>	N-acetylglucosamine-6-P-deacetylase	Rv1029	<i>kdpA</i>	potassium-transporting ATPase A chain	Rv0929	<i>pstC2</i>	membrane-bound component of
Rv0016c	<i>pbpA</i>	penicillin-binding protein						
Rv2163c	<i>pbpB</i>	penicillin-binding protein 2						
Rv0050	<i>ponA</i>	penicillin-binding protein class A penicillin binding protein						
Rv3682	<i>ponA'</i>	FtsW/RodA/SpovE family						
Rv0017c	<i>rodA</i>	probable penicillin binding protein						
Rv0907	-							

Rv0932c *pstS* phosphate transport system  
PstS component of phosphate uptake

Rv2400c *subI* sulphate binding precursor

Rv0143c - probable chloride channel

Rv17107 - probable sulphate permease

Rv1739c - possible sulphate transporter

Rv3679 - possible anion transporter

Rv3680 - probable anion transporter

5. Fatty acid transport

Rv2790c *lip1* non-specific lipid transport protein

Rv3540c *lip2* non-specific lipid transport protein

6. Efflux proteins

Rv2936 *draA* similar daunorubicin resistance ABC-transporter

Rv2937 *draB* similar daunorubicin resistance transmembrane protein

Rv2938 *draC* similar daunorubicin resistance transmembrane protein

Rv2846c *efpA* putative efflux protein

Rv3065 *emrE* resistance to ethidium bromide

Rv0783c - multidrug resistance protein

Rv0849 - possible quinolone efflux pump

Rv1145 - probable drug transporter

Rv1146 - probable drug transporter

Rv1250 - probable drug efflux protein

Rv1258c - probable multidrug resistance pump

Rv1410c - probable drug efflux protein

Rv1634 - probable drug efflux protein

Rv1819c - probable multidrug resistance pump

Rv2136c - putative bacitracin resistance protein

Rv2209 - probable drug efflux protein

Rv2333c - probable tetracycline C resistance protein

Rv2994 - probable fluoroquinolone efflux protein

Rv1877 - probable drug efflux protein

Rv2459 - probable drug efflux protein

B. Chaperones/Heat shock

Rv0384c *clpB* heat shock protein

Rv0352 *dnaJ* acts with GrpE to stimulate DnaK ATPase

Rv2373c *dnaJ2* DnaJ homologue

Rv0350 *dnaK* 70 kD heat shock protein, chromosome replication

Rv3417c *groEL1* 60 kD chaperonin 1

Rv0440 *groEL2* 60 kD chaperonin 2

Rv3418c *groES* 10 kD chaperone

Rv0351 *grpE* stimulates DnaK ATPase activity

Rv2374c *hrcA* heat-inducible transcription repressor

Rv0251c *hsp* possible heat shock protein

Rv0353 *hspR* heat shock regulator

Rv2031c *hspX* 14kD antigen, heat shock protein Hsp20 family

Rv2299c *htpG* heat shock protein Hsp90 family

Rv0563 *htpX* probable (transmembrane) heat shock protein

Rv2701c *shhB* putative extragenic suppressor protein

Rv3269 - probable heat shock protein

C. Cell division

Rv3641c *fic* possible cell division protein

Rv3102c *ftsE* membrane protein

Rv3610c *ftsH* inner membrane protein, chaperone

Rv2748c *ftsK* chromosome partitioning

Rv2151c *ftsQ* ingrowth of wall at septum

Rv2154c *ftsW* membrane protein (shape determination)

Rv3101c *ftsX* membrane protein

Rv2921c *ftsY* cell division protein FtsY

Rv2150c *ftsZ* circumferential ring, GTPase

Rv3919c *gid* glucose inhibited division protein B

Rv3625c *mesJ* probable cell cycle protein

Rv3917c *parA* chromosome partitioning; DNA-binding

Rv3918c *parB* possibly involved in chromosome partitioning

Rv2922c *smc* member of Smc1/Cut3/Cut14 family

Rv0012 - possible cell division protein

Rv0435c - ATPase of AAA-family

Rv2115c - ATPase of AAA-family

Rv3213c - possible role in chromosome segregation

Rv1708 - possible role in chromosome partitioning

D. Protein and peptide secretion

Rv2916c *ffh* signal recognition particle protein

Rv2903c *lepB* signal peptidase I

Rv1614 *lgt* prolipoprotein diacylglycerol transferase

Rv1539 *lspA* lipoprotein signal peptidase

Rv0379 *sec* probable transport protein SecE/Sec61- $\gamma$  family

Rv3240c *secA* SecA, preprotein translocase sub-

Rv1821 *secA2* unit SecA, preprotein translocase subunit

Rv2587c *secD* protein-export membrane protein

Rv0638 *secE* SecE preprotein translocase

Rv2586c *secF* protein-export membrane protein

Rv1440 *secG* protein-export membrane protein SecG

Rv0732 *secY* SecY subunit of preprotein translocase

Rv2462c *tig* chaperone protein, similar to trigger factor

Rv2813 - probable general secretion pathway protein

E. Adaptations and atypical conditions

Rv1901 *cinA* competence damage protein

Rv3648c *cspA* cold shock protein, transcriptional regulator

Rv0871 *cspB* probable cold shock protein

Rv3063 *cstA* starvation-induced stress response protein

Rv3490 *otsA* probable  $\alpha$ , $\alpha$ -trehalose-phosphate synthase

Rv2006 *otsB* trehalose-6-phosphate phosphatase

Rv3372 *otsB2* trehalose-6-phosphate phosphatase

Rv3758c *proV* osmoprotection ABC transporter

Rv3757c *proW* transport system permease

Rv3759c *proX* similar to osmoprotection proteins

Rv3756c *proZ* transport system permease

Rv1026 - probable pppGpp-5-phosphohydrolyase

F. Detoxification

Rv2428 *ahpC* alkyl hydroperoxide reductase

Rv2429 *ahpD* member of AhpC/TSA family

Rv2238c *ahpE* member of AhpC/TSA family

Rv2521 *bcp* bacterioferritin comigratory protein

Rv1608c *bcpB* probable bacterioferritin comigratory protein

Rv3473c *bpoA* probable non-heme bromoperoxidase

Rv1123c *bpoB* probable non-heme bromoperoxidase

Rv0554 *bpoC* probable non-heme bromoperoxidase

Rv3617 *ephA* probable epoxide hydrolase

Rv1938 *ephB* probable epoxide hydrolase

Rv1124 *ephC* probable epoxide hydrolase

Rv2214c *ephD* probable epoxide hydrolase

Rv3670 *ephE* probable epoxide hydrolase

Rv0134 *ephF* probable epoxide hydrolase

Rv3171c *hpx* probable non-heme haloperoxidase

Rv1908c *katG* catalase-peroxidase

Rv3846 *sodA* superoxide dismutase

Rv0432 *sodC* superoxide dismutase precursor - (Cu-Zn)

Rv1932 *tpx* thiol peroxidase

Rv0634c - putative glyoxylase II

Rv2581c - putative glyoxylase II

Rv3177 - probable non-heme haloperoxidase

IV. Other

A. Virulence

Rv0169 *mce1* cell invasion protein

Rv0589 *mce2* cell invasion protein

Rv1966 *mce3* cell invasion protein

Rv3499c *mce4* cell invasion protein

Rv3100c *smcB* probable small protein b

Rv1694 *tlyA* cytotoxin/hemolysin homologue

Rv0024 - putative p60 homologue

Rv0167 - part of *mce1* operon

Rv0168 - part of *mce1* operon

Rv0170 - part of *mce1* operon

Rv0171 - part of *mce1* operon

Rv0172 - part of *mce1* operon

Rv0174 - part of *mce1* operon

Rv0587 - part of *mce2* operon

Rv0588 - part of *mce2* operon

Rv0590 - part of *mce2* operon

Rv0591 - part of *mce2* operon

Rv0592 - part of *mce2* operon

Rv0594 - part of *mce2* operon

Rv1085c - possible hemolysin

Rv1477 - putative exported p60 protein homologue

Rv1478 - putative exported p60 protein homologue

Rv1566c - putative exported p60 protein homologue

Rv1964 - part of *mce3* operon

Rv1965 - part of *mce3* operon

Rv1967 - part of *mce3* operon

Rv1968 - part of *mce3* operon

Rv1969 - part of *mce3* operon

Rv1971 - part of *mce3* operon

Rv2190c - putative p60 homologue

Rv3494c - part of *mce4* operon

Rv3496c - part of *mce4* operon

Rv3497c - part of *mce4* operon

Rv3498c - part of *mce4* operon

Rv3500c - part of *mce4* operon

Rv3501c - part of *mce4* operon

Rv3896c - putative p60 homologue

Rv3922c - possible hemolysin

B. IS elements, Repeated sequences, and Phage

1. IS elements

IS6110 16 copies

IS1081 6 copies

Others 37 copies

2. REP13E12 family 7 copies

3. Phage-related functions

Rv2894c *xerC* integrase/recombinase

Rv1701 *xerD* integrase/recombinase

Rv1054 - integrase-a

Rv1055 - integrase-b

Rv1573 - phiRV1 phage related protein

Rv1574 - phiRV1 phage related protein

Rv1575 - phiRV1 phage related protein

Rv1576c - phiRV1 phage related protein

Rv1577c - phiRV1 possible prohead protease

Rv1578c - phiRV1 phage related protein

Rv1579c - phiRV1 phage related protein

Rv1580c - phiRV1 phage related protein

Rv1581c - phiRV1 phage related protein

Rv1582c - phiRV1 phage related protein

Rv1583c - phiRV1 phage related protein

Rv1584c - phiRV1 phage related protein

Rv1585c - phiRV1 phage related protein

Rv1586c - phiRV1 integrase

Rv2309c - integrase

Rv2310 - excisionase

Rv2646 - phiRV2 integrase

Rv2647 - phiRV2 phage related protein

Rv2650c - phiRV2 phage related protein

Rv2651c - phiRV2 prohead protease

Rv2652c - phiRV2 phage related protein

Rv2653c - phiRV2 phage related protein

Rv2654c - phiRV2 phage related protein

Rv2655c - phiRV2 phage related protein

Rv2656c - phiRV2 phage related protein

Rv2657c - similar to gp36 of mycobacteriophage L5

Rv2658c - phiRV2 phage related protein

Rv2659c - phiRV2 integrase

Rv2830c - similar to phage P1 *phd* gene

Rv3750c - excisionase

Rv3751 - putative integrase

C. PE and PPE families

1. PE family

PE subfamily 38 members

PE\_PGRS subfamily 61 members

2. PPE family 68 members

D. Antibiotic production and resistance

Rv2068c *blaC* class A  $\beta$ -lactamase

Rv3290c *lat* lysine- $\epsilon$  aminotransferase

Rv2043c *pncA* pyrazinamide resistance/sensitivity

Rv0133 - possible puromycin N-acetyltransferase

Rv0262c - aminoglycoside 2'-N-acetyltransferase

Rv0802c - acetyltransferase

Rv1082 - similar to *S. lincolnensis* *lmbE*

Rv1170 - similar to *S. lincolnensis* *lmbE*

Rv1347c - possible aminoglycoside 6'-N-acetyltransferase

Rv2036 - similar to lincomycin production genes

Rv2303c - similar to *S. griseus* macrotetrolide resistance protein

Rv3225c - probable aminoglycoside 3'-phosphotransferase

Rv3700c - probable acetyltransferase

Rv3817 - probable aminoglycoside 3'-phosphotransferase

E. Bacteriocin-like proteins 3

F. Cytochrome P450 enzymes 22

G. Coenzyme F420-dependent enzymes 3

H. Miscellaneous transferases 61

I. Miscellaneous phosphatases, lyases, and hydrolases 18

J. Cyclases 6

K. Chelatases 2

V. Conserved hypotheticals 912

VI. Unknowns 606

TOTAL 3924