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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:

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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>	$\beta$ -glucosidase
Rv2202c	<i>cbhK</i>	carbohydrate kinase
Rv0727c	<i>fucA</i>	L-fucose 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>mraA</i>	phosphoglucosyltransferase or phosphomannosyltransferase
Rv0118c	<i>oxoA</i>	oxalyl-CoA decarboxylase
Rv3068c	<i>pgmA</i>	phosphoglucosyltransferase
Rv3257c	<i>pmmA</i>	phosphomannosyltransferase
Rv3308	<i>pmmB</i>	phosphomannosyltransferase
Rv2702	<i>ppgK</i>	polyphosphate glucokinase
Rv0408	<i>pta</i>	phosphate acetyltransferase
Rv0729	<i>xytB</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 $\gamma$ subunit
Rv1849	<i>ureB</i>	urease $\beta$ subunit
Rv1850	<i>ureC</i>	urease $\alpha$ 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, $\alpha$ subunit
Rv0973c	<i>accA2</i>	acetyl/propionyl-CoA carboxylase, $\alpha$ subunit
Rv2502c	<i>accD1</i>	acetyl/propionyl-CoA carboxylase, $\beta$ subunit
Rv0974c	<i>accD2</i>	acetyl/propionyl-CoA carboxylase, $\beta$ 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>echH</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>	superfamily enoyl-CoA hydratase/isomerase
Rv3374	<i>echA18'</i>	superfamily, N-term enoyl-CoA hydratase/isomerase
Rv3516	<i>echA19</i>	superfamily, C-term enoyl-CoA hydratase/isomerase
Rv3550	<i>echA20</i>	superfamily enoyl-CoA hydratase/isomerase
Rv3774	<i>echA21</i>	superfamily enoyl-CoA hydratase/isomerase
Rv0859	<i>fadA</i>	superfamily $\beta$ oxidation complex, $\beta$ 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>	$\beta$ oxidation complex, $\alpha$ 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>mor</i>	$\alpha$ -methyl acyl-CoA racemase
Rv1492	<i>mutA</i>	methylmalonyl-CoA mutase, $\beta$ subunit
Rv1493	<i>mutB</i>	methylmalonyl-CoA mutase, $\alpha$ subunit
Rv2504c	<i>scoA</i>	3-oxo acid:CoA transferase, $\alpha$ subunit
Rv2503c	<i>scoB</i>	3-oxo acid:CoA transferase, $\beta$ 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 $\alpha$ subunit
Rv2496c	<i>pdhB</i>	pyruvate dehydrogenase E1 component $\beta$ 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 $\beta$ chain
Rv1098c	<i>fum</i>	fumarate
Rv1131	<i>glitA1</i>	citrate synthase 3
Rv0896	<i>glitA2</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 $\beta$ chain
Rv0952	<i>sucD</i>	succinyl-CoA synthase $\alpha$ chain

**4. Glyoxylate bypass**

Rv0467	<i>aceA</i>	isocitrate lyase
Rv1915	<i>aceAa</i>	isocitrate lyase, $\alpha$ module
Rv1916	<i>aceAb</i>	isocitrate lyase, $\beta$ 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

Rv2436 *rbkK* ribokinase  
Rv1408 *rpe* ribulose-phosphate 3-epimerase  
Rv2465c *rpi* phosphopentose isomerase  
Rv1448c *tal* transaldolase  
Rv1449c *tkl* transketolase  
Rv1121 *zwf* glucose-6-phosphate 1-dehydrogenase  
Rv1447c *zwf2* glucose-6-phosphate 1-dehydrogenase

#### 6. Respiration

*a. aerobic*  
Rv0527 *ccsA* cytochrome *c*-type biogenesis protein  
Rv0529 *ccsB* cytochrome *c*-type biogenesis protein  
Rv1451 *ctaB* cytochrome *c* oxidase assembly factor  
Rv2200c *ctaC* cytochrome *c* oxidase chain II  
Rv3043c *ctaD* cytochrome *c* oxidase polypeptide I  
Rv2193 *ctaE* cytochrome *c* oxidase polypeptide III  
Rv1542c *glbN* hemoglobin-like, oxygen carrier  
Rv2470 *glbO* hemoglobin-like, oxygen carrier  
Rv2249c *glpD1* glycerol-3-phosphate dehydrogenase  
Rv3302c *glpD2* glycerol-3-phosphate dehydrogenase  
Rv0694 *lldD1* L-lactate dehydrogenase (cytochrome)  
Rv1872c *lldD2* L-lactate dehydrogenase  
Rv1854c *ndh* probable NADH dehydrogenase  
Rv3145 *nuoA* NADH dehydrogenase chain A  
Rv3146 *nuoB* NADH dehydrogenase chain B  
Rv3147 *nuoC* NADH dehydrogenase chain C  
Rv3148 *nuoD* NADH dehydrogenase chain D  
Rv3149 *nuoE* NADH dehydrogenase chain E  
Rv3150 *nuoF* NADH dehydrogenase chain F  
Rv3151 *nuoG* NADH dehydrogenase chain G  
Rv3152 *nuoH* NADH dehydrogenase chain H  
Rv3153 *nuoI* NADH dehydrogenase chain I  
Rv3154 *nuoJ* NADH dehydrogenase chain J  
Rv3155 *nuoK* NADH dehydrogenase chain K  
Rv3156 *nuoL* NADH dehydrogenase chain L  
Rv3157 *nuoM* NADH dehydrogenase chain M  
Rv3158 *nuoN* NADH dehydrogenase chain N  
Rv2195 *qcrA* Rieske iron-sulphur component of *ubiQ*-*cytB* reductase  
Rv2196 *qcrB* cytochrome  $\beta$  component of *ubiQ*-*cytB* reductase  
Rv2194 *qcrC* cytochrome *b/c* component of *ubiQ*-*cytB* reductase

#### *b. anaerobic*

Rv2392 *cysH* 3'-phosphoadenylylsulfate (PAPS) reductase  
Rv2899c *fdhD* affects formate dehydrogenase-N molybdopterin-containing oxidoreductase  
Rv2900c *fdhF*  
Rv1552 *frdA* fumarate reductase flavoprotein subunit  
Rv1553 *frdB* fumarate reductase iron sulphur protein  
Rv1554 *frdC* fumarate reductase 15kD anchor protein  
Rv1555 *frdD* fumarate reductase 13kD anchor protein  
Rv1161 *narG* nitrate reductase  $\alpha$  subunit  
Rv1162 *narH* nitrate reductase  $\beta$  chain  
Rv1164 *narI* nitrate reductase  $\gamma$  chain  
Rv1163 *narJ* nitrate reductase  $\delta$  chain  
Rv1736c *narX* fused nitrate reductase  
Rv2391 *nirA* probable nitrite reductase/sulphite reductase  
Rv0252 *nirB* nitrite reductase flavoprotein  
Rv0253 *nirD* probable nitrite reductase small subunit

#### *c. Electron transport*

Rv0409 *ackA* acetate kinase  
Rv1623c *appC* cytochrome *bd-II* oxidase subunit I  
Rv1622c *cydB* cytochrome *d* ubiquinol oxidase subunit II  
Rv1620c *cydC* ABC transporter  
Rv1621c *cydD* ABC transporter  
Rv2007c *fdxA* ferredoxin  
Rv3554 *fdxB* ferredoxin  
Rv1177 *fdxC* ferredoxin 4Fe-4S  
Rv3503c *fdxD* probable ferredoxin  
Rv3029c *fixA* electron transfer flavoprotein  $\beta$  subunit  
Rv3028c *fixB* electron transfer flavoprotein  $\alpha$  subunit  
Rv3106 *fprA* adrenodoxin and NADPH ferredoxin reductase  
Rv0886 *fprB* ferredoxin, ferredoxin-NADP reductase  
Rv3251c *rubA* rubredoxin A

Rv3250c *rubB* rubredoxin B

#### 7. Miscellaneous oxidoreductases and oxygenases 171

#### 8. ATP-proton motive force

Rv1308 *atpA* ATP synthase  $\alpha$  chain  
Rv1304 *atpB* ATP synthase  $\alpha$  chain  
Rv1311 *atpC* ATP synthase  $\epsilon$  chain  
Rv1310 *atpD* ATP synthase  $\beta$  chain  
Rv1305 *atpE* ATP synthase  $\gamma$  chain  
Rv1306 *atpF* ATP synthase  $\gamma$  chain  
Rv1309 *atpG* ATP synthase  $\gamma$  chain  
Rv1307 *atpH* ATP synthase  $\delta$  chain

#### C. Central intermediary metabolism

##### 1. General

Rv2589 *gabT* 4-aminobutyrate aminotransferase  
Rv3432c *gadB* glutamate decarboxylase  
Rv1832 *gcvB* glycine decarboxylase  
Rv1826 *gcvH* glycine cleavage system H protein  
Rv2211c *gcvT* T protein of glycine cleavage system  
Rv1213 *glgC* glucose-1-phosphate adenylyltransferase  
Rv3842c *glpQ1* glycerophosphoryl diester phosphodiesterase  
Rv0317c *glpQ2* glycerophosphoryl diester phosphodiesterase  
Rv3566c *nhoA* N-hydroxyarylamino  $\alpha$ -acetyltransferase  
Rv0155 *pntAA* pyridine transhydrogenase subunit  $\alpha$ 1  
Rv0156 *pntAB* pyridine transhydrogenase subunit  $\alpha$ 2  
Rv0157 *pntB* pyridine transhydrogenase subunit  $\beta$   
Rv1127c *ppdK* similar to pyruvate, phosphate dikinase

##### 2. Gluconeogenesis

Rv0211 *pckA* phosphoenolpyruvate carboxykinase  
Rv0069c *sdaA* L-serine dehydratase 1

##### 3. Sugar nucleotides

Rv1512 *epiA* nucleotide sugar epimerase  
Rv3784 *epiB* probable UDP-galactose 4-epimerase  
Rv1511 *gmdA* GDP-mannose 4,6 dehydratase  
Rv0334 *rmlA* glucose-1-phosphate thymidyltransferase  
Rv3264c *rmlA2* glucose-1-phosphate thymidyltransferase  
Rv3464 *rmlB* dTDP-glucose 4,6-dehydratase  
Rv3634c *rmlB2* dTDP-glucose 4,6-dehydratase  
Rv3468c *rmlB3* dTDP-glucose 4,6-dehydratase  
Rv3465 *rmlC* dTDP-4-dehydrorhamnose 3,5-epimerase  
Rv3266c *rmlD* dTDP-4-dehydrorhamnose reductase  
Rv0322 *udgA* UDP-glucose dehydrogenase/GDP-mannose 6-dehydrogenase  
Rv3265c *wbbL* dTDP-rhamnosyl transferase  
Rv1525 *wbbL2* dTDP-rhamnosyl transferase  
Rv3400 - probable  $\beta$ -phosphoglucosyltransferase

##### 4. Amino sugars

Rv3436c *glmS* glucosamine-fructose-6-phosphate aminotransferase

##### 5. Sulphur metabolism

Rv0711 *atsA* arylsulfatase  
Rv3299c *atsB* probable arylsulfatase  
Rv0663 *atsD* probable arylsulfatase  
Rv3077 *atsF* probable arylsulfatase  
Rv0296c *atsG* probable arylsulfatase  
Rv3796 *atsH* probable arylsulfatase  
Rv1285 *cysD* ATP:sulphurylase subunit 2  
Rv1286 *cysN* ATP:sulphurylase subunit 1  
Rv2131c *cysQ* homologue of *M.leprae* *cysQ*  
Rv3248c *sahH* adenosylhomocysteinase  
Rv3283 *sseA* thiosulfate sulfurtransferase  
Rv2291 *sseB* thiosulfate sulfurtransferase  
Rv3118 *sseC* thiosulfate sulfurtransferase  
Rv0814c *sseC2* thiosulfate sulfurtransferase  
Rv3762c - probable alkyl sulfatase

#### D. Amino acid biosynthesis

##### 1. Glutamate family

Rv1654 *argB* acetylglutamate kinase  
Rv1652 *argC* N-acetyl- $\gamma$ -glutamyl-phosphate reductase  
Rv1655 *argD* acetylornithine aminotransferase  
Rv1656 *argF* ornithine carbamoyltransferase  
Rv1658 *argG* arginosuccinate synthase  
Rv1659 *argH* arginosuccinate lyase  
Rv1653 *argJ* glutamate N-acetyltransferase  
Rv2220 *glnA1* glutamine synthase class I  
Rv2222c *glnA2* glutamine synthase class II

Rv1878 *glnA3* probable glutamine synthase  
Rv2860c *glnA4* probable glutamine synthase  
Rv2918c *glnD* uridylyltransferase  
Rv2221c *glnE* glutamate-ammonia-ligase  
Rv3859c *gltB* adenylyltransferase  
Rv3858c *gltD* ferredoxin-dependent glutamate synthase  
Rv3704c *gshA* small subunit of NADH-dependent glutamate synthase  
Rv2427c *proA* possible  $\gamma$ -glutamylcysteine synthase  
Rv2439c *proB*  $\gamma$ -glutamyl phosphate reductase  
Rv0500 *proC* glutamate 5-kinase  
pyrroline-5-carboxylate reductase

##### 2. Aspartate family

Rv3708c *asd* aspartate semialdehyde dehydrogenase  
Rv3709c *ask* aspartokinase  
Rv2201 *asnB* asparagine synthase B  
Rv3565 *aspB* aspartate aminotransferase  
Rv0337c *aspC* aspartate aminotransferase  
Rv2753c *dapA* dihydrodipicolinate synthase  
Rv2773c *dapB* dihydrodipicolinate reductase  
Rv1202 *dapE* succinyl-diaminopimelate desuccinylase  
Rv2141c *dapE2* ArgE/DapE/Acy1/Cpg2/yscS family  
Rv2726c *dapF* diaminopimelate epimerase  
Rv1293 *lysA* diaminopimelate decarboxylase  
Rv3341 *metA* homoserine  $\alpha$ -acetyltransferase  
Rv1079 *metB* cystathionine  $\gamma$ -synthase  
Rv3340 *metC* cystathionine  $\beta$ -lyase  
Rv1133c *metE* 5-methyltetrahydropteroylglutamate-homocysteine methyltransferase  
Rv2124c *metH* 5-methyltetrahydrofolate-homocysteine methyltransferase  
Rv1392 *metK* S-adenosylmethionine synthase  
Rv0391 *metZ* o-succinylhomoserine sulphydrylase  
Rv1294 *thrA* homoserine dehydrogenase  
Rv1296 *thrB* homoserine kinase  
Rv1295 *thrC* homoserine synthase

##### 3. Serine family

Rv0815c *cysA2* thiosulfate sulfurtransferase  
Rv3117 *cysA3* thiosulfate sulfurtransferase  
Rv2335 *cysE* serine acetyltransferase  
Rv0511 *cysG* uroporphyrin-III  $\alpha$ -methyltransferase  
Rv2847c *cysG2* multifunctional enzyme, siroheme synthase  
Rv2334 *cysK* cysteine synthase A  
Rv1336 *cysM* cysteine synthase B  
Rv1077 *cysM2* cystathionine  $\beta$ -synthase  
Rv0848 *cysM3* putative cysteine synthase  
Rv1093 *glyA* serine hydroxymethyltransferase  
Rv0070c *glyA2* serine hydroxymethyltransferase  
Rv2996c *serA* D-3-phosphoglycerate dehydrogenase  
Rv0505c *serB* probable phosphoserine phosphatase  
Rv3042c *serB2* C-term similar to phosphoserine phosphatase  
Rv0884c *serC* phosphoserine aminotransferase

##### 4. Aromatic amino acid family

Rv3227 *aroA* 3-phosphoshikimate 1-carboxyvinyl transferase  
Rv2538c *aroB* 3-dehydroquinate synthase  
Rv2537c *aroD* 3-dehydroquinate dehydratase  
Rv2552c *aroE* shikimate 5-dehydrogenase  
Rv2540c *aroF* chorismate synthase  
Rv2178c *aroG* DAHP synthase  
Rv2539c *aroK* shikimate kinase I  
Rv3838c *pheA* prephenate dehydratase  
Rv1613 *trpA* tryptophan synthase  $\alpha$  chain  
Rv1612 *trpB* tryptophan synthase  $\beta$  chain  
Rv1611 *trpC* indole-3-glycerol phosphate synthase  
Rv2192c *trpD* anthranilate phosphoribosyltransferase  
Rv1609 *trpE* anthranilate synthase component I  
Rv2386c *trpE2* anthranilate synthase component I  
Rv3754 *tyrA* prephenate dehydrogenase

##### 5. Histidine

Rv1603 *hisA* phosphoribosylformimino-5-aminoimidazole carboxamide ribonucleotide isomerase  
Rv1601 *hisB* imidazole glycerol-phosphate dehydratase  
Rv1600 *hisC* histidinol-phosphate aminotransferase  
Rv3772 *hisC2* histidinol-phosphate aminotransferase  
Rv1599 *hisD* histidinol dehydrogenase

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>	subunit 2 molybdopterin-converting factor
Rv1602	<i>hisH</i>	amidotransferase	Rv3052c	<i>nrdI</i>	NrdI/YgaO/YmaA family	Rv3322c	<i>moaE3</i>	subunit 2 molybdopterin-converting factor
Rv2122c	<i>hisI</i>	phosphoribosyl-AMP cyclohydrolase	Rv3247c	<i>tmk</i>	thymidylate kinase	Rv0994	<i>moaA</i>	subunit 2 molybdopterin biosynthesis
Rv1606	<i>hisI2</i>	probable phosphoribosyl-AMP 1,6 cyclohydrolase	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>moaV</i>	molybdopterin biosynthesis
			Rv3752c	-	probable cytidine/deoxycytidylate deaminase	Rv1681	<i>moaX</i>	weak similarity to <i>E. coli</i> MoaA
						Rv1355c	<i>moaY</i>	weak similarity to <i>E. coli</i> MoaB
6. Pyruvate family						Rv3206c	<i>moaZ</i>	probably involved in molybdopterin biosynthesis
Rv3423c	<i>alr</i>	alanine racemase	4. Salvage of nucleosides and nucleotides			Rv0865	<i>mog</i>	molybdopterin biosynthesis
7. Branched amino acid family			Rv3313c	<i>add</i>	probable adenosine deaminase	5. Pantothenate		
Rv1559	<i>ilvA</i>	threonine deaminase	Rv2584c	<i>apt</i>	adenine phosphoribosyltransferase	Rv1092c	<i>coaA</i>	pantothenate kinase
Rv3003c	<i>ilvB</i>	acetolactate synthase I large subunit	Rv3315c	<i>cdd</i>	probable cytidine deaminase	Rv2225	<i>panB</i>	3-methyl-2-oxobutanoate hydroxymethyltransferase
Rv3470c	<i>ilvB2</i>	acetolactate synthase large subunit	Rv3314c	<i>deoA</i>	thymidine phosphorylase	Rv3602c	<i>panC</i>	pantoate-β-alanine ligase
Rv3001c	<i>ilvC</i>	ketol-acid reductoisomerase	Rv0478	<i>deoC</i>	deoxyribose-phosphate aldolase	Rv3601c	<i>panD</i>	aspartate 1-decarboxylase
Rv0189c	<i>ilvD</i>	dihydroxy-acid dehydratase	Rv3307	<i>deoD</i>	probable purine nucleoside phosphorylase			
Rv2210c	<i>ilvE</i>	branched-chain-amino-acid transaminase	Rv3624c	<i>hpt</i>	probable hypoxanthine-guanine phosphoribosyltransferase			
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>	α-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
			Rv2344c	<i>dgt</i>	probable deoxyguanosine triphosphate hydrolase	8. Thiamine		
<i>E. Polyamine synthesis</i>			Rv2404c	<i>lepA</i>	GTP-binding protein LepA	Rv0422c	<i>thiD</i>	phosphomethylpyrimidine kinase
Rv2601	<i>speE</i>	spermidine synthase	Rv2727c	<i>miaA</i>	tRNA 8(2)-isopentenylpyrophosphate transferase	Rv0414c	<i>thiE</i>	thiamine synthesis, thiazole moiety
<i>F. Purines, pyrimidines, nucleosides and nucleotides</i>			Rv2445c	<i>ndkA</i>	nucleoside diphosphate kinase	Rv0417	<i>thiG</i>	thiamine synthesis, thiazole moiety
1. Purine ribonucleotide biosynthesis			Rv2440c	<i>obg</i>	Obg GTP-binding protein	Rv2977c	<i>thiL</i>	probable thiamine-monophosphate kinase
Rv1389	<i>gmk</i>	putative guanylate kinase	Rv2583c	<i>relA</i>	(p)ppGpp synthase I			
Rv3396c	<i>guaA</i>	GMP synthase				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>	riboflavin synthase α 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 β 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			
Rv0808	<i>purF</i>	amidophosphoribosyltransferase	Rv0089	-	possible <i>bioC</i> biotin synthesis gene	10. Thioredoxin, glutaredoxin and mycothiol		
Rv0957	<i>purH</i>	phosphoribosylaminoimidazole-carboxamide formyltransferase	2. Folic acid			Rv0773c	<i>ggtA</i>	putative γ-glutamyl transpeptidase
Rv3276c	<i>purK</i>	phosphoribosylaminoimidazole carboxylase ATPase subunit	Rv2763c	<i>dfra</i>	dihydrofolate reductase	Rv2394	<i>ggtB</i>	γ-glutamyltranspeptidase precursor
Rv0803	<i>purL</i>	phosphoribosylformylglycinamide synthase II	Rv2447c	<i>foIC</i>	folypolyglutamate synthase	Rv2855	<i>gorA</i>	glutathione reductase homologue
Rv0809	<i>purM</i>	5'-phosphoribosyl-5-aminoimidazole synthase	Rv3356c	<i>foID</i>	methylene tetrahydrofolate dehydrogenase	Rv0816c	<i>thiX</i>	equivalent to <i>M. leprae</i> ThiX
Rv0956	<i>purN</i>	phosphoribosylglycinamide formyltransferase I	Rv3609c	<i>foIE</i>	GTP cyclohydrolase I	Rv1470	<i>trxA</i>	thioredoxin
Rv0788	<i>purQ</i>	phosphoribosylformylglycinamide synthase I	Rv3606c	<i>foIK</i>	7,8-dihydro-6-hydroxymethylpterin pyrophosphokinase	Rv1471	<i>trxB</i>	thioredoxin reductase
Rv0389	<i>purT</i>	phosphoribosylglycinamide formyltransferase II	Rv3608c	<i>foIP</i>	dihydropterate synthase	Rv3913	<i>trxB2</i>	thioredoxin reductase
Rv2964	<i>purU</i>	formyltetrahydrofolate deformylase	Rv1207	<i>foIP2</i>	dihydropterate synthase	Rv3914	<i>trxC</i>	thioredoxin
			Rv3607c	<i>foIX</i>	may be involved in folate biosynthesis	11. Menaquinone, PQQ, ubiquinone and other terpenoids		
2. Pyrimidine ribonucleotide biosynthesis			Rv0013	<i>pabA</i>	p-aminobenzoate synthase glutamine amidotransferase	Rv2682c	<i>dxs</i>	1-deoxy-D-xylulose 5-phosphate synthase
Rv1383	<i>carA</i>	carbamoyl-phosphate synthase subunit	Rv1005c	<i>pabB</i>	p-aminobenzoate synthase	Rv0562	<i>groC1</i>	heptaprenyl diphosphate synthase II
Rv1384	<i>carB</i>	carbamoyl-phosphate synthase subunit	Rv0812	<i>pabC</i>	aminodeoxychorismate lyase	Rv0989c	<i>groC2</i>	heptaprenyl diphosphate synthase II
Rv1380	<i>pyrB</i>	aspartate carbamoyltransferase	3. Lipote			Rv3398c	<i>idsA</i>	geranylgeranyl pyrophosphate synthase
Rv1381	<i>pyrC</i>	dihydroorotase	Rv2218	<i>lipA</i>	lipote biosynthesis protein A	Rv2173	<i>idsA2</i>	geranylgeranyl pyrophosphate synthase
Rv2139	<i>pyrD</i>	dihydroorotate dehydrogenase	Rv2217	<i>lipB</i>	lipote biosynthesis protein B	Rv3383c	<i>idsB</i>	transfergeranyl, similar geranyl pyrophosphate synthase
Rv1385	<i>pyrF</i>	orotidine 5'-phosphate decarboxylase	4. Molybdopterin			Rv0534c	<i>menA</i>	4-dihydroxy-2-naphthoate octaprenyltransferase
Rv1699	<i>pyrG</i>	CTP synthase	Rv3109	<i>moaA</i>	molybdenum cofactor biosynthesis, protein A	Rv0548c	<i>menB</i>	naphthoate synthase
Rv2883c	<i>umpH</i>	uridylylate kinase	Rv0869c	<i>moaA2</i>	molybdenum cofactor biosynthesis, protein A	Rv0553	<i>menC</i>	o-succinylbenzoate-CoA synthase
Rv0382c	<i>umpA</i>	probable uridine 5'-monophosphate synthase	Rv0438c	<i>moaA3</i>	molybdenum cofactor biosynthesis, protein A	Rv0555	<i>menD</i>	2-succinyl-6-hydroxy-2,4-cyclohexadiene-1-carboxylate synthase
3. 2'-deoxyribonucleotide metabolism			Rv3110	<i>moaB</i>	molybdenum cofactor biosynthesis, protein B	Rv0542c	<i>menE</i>	o-succinylbenzoate-coA-CoA ligase
Rv0321	<i>dcd</i>	deoxycytidine triphosphate deaminase	Rv0984	<i>moaB2</i>	molybdenum cofactor biosynthesis, protein B	Rv3853	<i>menG</i>	S-adenosylmethionine: 2-demethylmenaquinone
Rv2697c	<i>dut</i>	deoxyuridine triphosphatase	Rv3111	<i>moaC</i>	molybdenum cofactor biosynthesis, protein C	Rv3397c	<i>phyA</i>	phytoene synthase
Rv0233	<i>nrdB</i>	ribonucleoside-diphosphate reductase B2 (eukaryotic-like)	Rv0864	<i>moaC2</i>	molybdenum cofactor biosynthesis, protein C	Rv0693	<i>pqqE</i>	coenzyme PQQ synthesis
Rv3051c	<i>nrdE</i>	ribonucleoside diphosphate reductase α chain	Rv3324c	<i>moaC3</i>	molybdenum cofactor biosynthesis, protein C	Rv0558	<i>ubiE</i>	ubiquinone/menaquinone biosynthesis methyltransferase
Rv1981c	<i>nrdF</i>	ribonucleotide reductase small	Rv3112	<i>moaD</i>	molybdopterin converting factor subunit 1	12. Heme and porphyrin		
			Rv0868c	<i>moaD2</i>	molybdopterin converting factor	Rv0509	<i>hemA</i>	glutamyl-tRNA reductase

13. Cobalamin		14. Iron utilization		H. Lipid biosynthesis		J. Broad regulatory functions		
Rv2849c	<i>cobA</i>	cob(I)lamina adenosyltransferase	Rv1860c	<i>fbpC</i>	antigen 85B, mycolyltransferase	Rv1657	<i>argR</i>	arginine repressor
Rv2848c	<i>cobB</i>	cobyrinic acid a,c-diamide synthase	Rv0129c	<i>fbpC</i>	antigen 85C, mycolyltransferase	Rv1267c	<i>embR</i>	regulator of <i>embAB</i> genes (AisR/DndI/RedD family)
Rv2231c	<i>cobC</i>	aminotransferase	Rv3803c	<i>fbpD</i>	antigen MPT51, mycolyltransferase			
Rv2236c	<i>cobD</i>	cobinamide synthase				Rv1909c	<i>furA</i>	ferric uptake regulatory protein
Rv2064	<i>cobG</i>	percorrin reductase	Rv0564c	<i>gpdA1</i>	glycerol-3-phosphate dehydrogenase	Rv2359	<i>furB</i>	ferric uptake regulatory protein
Rv2065	<i>cobH</i>	percorrin isomerase	Rv2982c	<i>gpdA2</i>	glycerol-3-phosphate dehydrogenase	Rv2919c	<i>glnB</i>	nitrogen regulatory protein
Rv2066	<i>cobI</i>	CobI-CobJ fusion protein				Rv2711	<i>ideR</i>	iron dependent repressor, IdeR
Rv2070c	<i>cobK</i>	percorrin reductase	Rv2612c	<i>pgsA</i>	CDP-diacylglycerol-glycerol-3-phosphate phosphatidyltransferase	Rv2720	<i>lexA</i>	LexA, SOS repressor protein
Rv2072c	<i>cobL</i>	probable methyltransferase				Rv1479	<i>maxR</i>	transcriptional regulator, MoxR
Rv2071c	<i>cobM</i>	percorrin-3 methylase						homologue
Rv2062c	<i>cobN</i>	cobalt insertion	Rv1822	<i>pgsA2</i>	CDP-diacylglycerol-glycerol-3-phosphate phosphatidyltransferase	Rv3692	<i>maxR2</i>	transcriptional regulator, MoxR
Rv2208	<i>cobS</i>	cobalamin (5'-phosphate) synthase						homologue
Rv2207	<i>cobT</i>	nicotinate-nucleotide-dimethylbenzimidazole transferase	Rv2746c	<i>pgsA3</i>	CDP-diacylglycerol-glycerol-3-phosphate phosphatidyltransferase	Rv3164c	<i>maxR3</i>	transcriptional regulator, MoxR
								homologue
Rv0254c	<i>cobU</i>	cobinamide kinase	Rv1551	<i>plsB1</i>	glycerol-3-phosphate acyltransferase	Rv0212c	<i>nadR</i>	similar to <i>E. coli</i> NadR
Rv0255c	<i>cobQ</i>	cobryic acid synthase				Rv0117	<i>oxyS</i>	transcriptional regulator (LysR family)
Rv3713	<i>cobQ2</i>	possible cobryic acid synthase	Rv2482c	<i>plsB2</i>	glycerol-3-phosphate acyltransferase	Rv1379	<i>pyrR</i>	regulatory protein pyrimidine biosynthesis
Rv0306	-	similar to BluB cobalamin synthesis protein <i>R. capsulatus</i>				Rv2788	<i>sirR</i>	iron-dependent transcriptional repressor
			Rv0437c	<i>psd</i>	putative phosphatidylserine decarboxylase			
			Rv0436c	<i>pssA</i>	CDP-diacylglycerol-serine o-phosphatidyltransferase	Rv3082c	<i>virS</i>	putative virulence regulating protein (AraC/XylS family)
			Rv0045c	-	possible dihydrolipoamide acetyltransferase	Rv3219	<i>whiB1</i>	WhiB transcriptional activator
			Rv0914c	-	lipid transfer protein			homologue
			Rv1543	-	probable fatty-acyl CoA reductase	Rv3260c	<i>whiB2</i>	WhiB transcriptional activator
			Rv1627c	-	lipid carrier protein			homologue
			Rv1814	-	possible C-5 sterol desaturase	Rv3416	<i>whiB3</i>	WhiB transcriptional activator
			Rv1867	-	similar to acetyl CoA synthase/lipid carriers			homologue
						Rv3681c	<i>whiB4</i>	WhiB transcriptional activator
			Rv2261c	-	apolipoprotein N-acyltransferase-a			homologue
			Rv2262c	-	apolipoprotein N-acyltransferase-b	Rv0023	-	putative transcriptional regulator
			Rv3523	-	lipid carrier protein	Rv0043c	-	transcriptional regulator (GntR family)
			Rv3720	-	C-term similar to cyclopropane fatty acid synthases	Rv0067c	-	transcriptional regulator (TetR/AcrR family)
						Rv0078	-	transcriptional regulator (TetR/AcrR family)
						Rv0081	-	transcriptional regulator (ArsR family)
						Rv0135c	-	putative transcriptional regulator
						Rv0144	-	putative transcriptional regulator
						Rv0158	-	transcriptional regulator (TetR/AcrR family)
						Rv0165c	-	transcriptional regulator (GntR family)
						Rv0195	-	transcriptional regulator (LuxR/UhpA family)
						Rv0196	-	transcriptional regulator (TetR/AcrR family)
						Rv0232	-	transcriptional regulator (TetR/AcrR family)
						Rv0238	-	transcriptional regulator (TetR/AcrR family)
						Rv0273c	-	putative transcriptional regulator
						Rv0302	-	transcriptional regulator (TetR/AcrR family)
						Rv0324	-	putative transcriptional regulator
						Rv0328	-	transcriptional regulator (TetR/AcrR family)
						Rv0348	-	putative transcriptional regulator
						Rv0377	-	transcriptional regulator (LysR family)
						Rv0386	-	transcriptional regulator (LuxR/UhpA family)
						Rv0452	-	putative transcriptional regulator
						Rv0465c	-	transcriptional regulator (PbsX/Xre family)
						Rv0472c	-	transcriptional regulator (TetR/AcrR family)
						Rv0474	-	transcriptional regulator (PbsX/Xre family)
						Rv0485	-	transcriptional regulator (ROK family)
						Rv0494	-	transcriptional regulator (GntR family)
						Rv0552	-	putative transcriptional regulator
						Rv0576	-	putative transcriptional regulator
						Rv0586	-	transcriptional regulator (GntR family)
						Rv0650	-	transcriptional regulator (ROK family)
						Rv0653c	-	putative transcriptional regulator
						Rv0681	-	transcriptional regulator (TetR/AcrR family)
						Rv0691c	-	transcriptional regulator (TetR/AcrR family)
						Rv0737	-	putative transcriptional regulator
						Rv0744c	-	putative transcriptional regulator
						Rv0792c	-	transcriptional regulator (GntR family)

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> <b>A. Synthesis and modification of macromolecules</b> <b>1. Ribosomal protein synthesis and modification</b> Rv3420c <i>rimI</i> ribosomal protein S18 acetyl transferase Rv0995 <i>rimJ</i> acetylation of 30S S5 subunit Rv0641 <i>rplA</i> 50S ribosomal protein L1 Rv0704 <i>rplB</i> 50S ribosomal protein L2 Rv0701 <i>rplC</i> 50S ribosomal protein L3 Rv0702 <i>rplD</i> 50S ribosomal protein L4 Rv0716 <i>rplE</i> 50S ribosomal protein L5 Rv0719 <i>rplF</i> 50S ribosomal protein L6 Rv0056 <i>rplI</i> 50S ribosomal protein L9 Rv0651 <i>rplJ</i> 50S ribosomal protein L10 Rv0640 <i>rplK</i> 50S ribosomal protein L11 Rv0652 <i>rplL</i> 50S ribosomal protein L7/L12 Rv3443c <i>rplM</i> 50S ribosomal protein L13 Rv0714 <i>rplN</i> 50S ribosomal protein L14 Rv0723 <i>rplO</i> 50S ribosomal protein L15 Rv0708 <i>rplP</i> 50S ribosomal protein L16 Rv3456c <i>rplQ</i> 50S ribosomal protein L17 Rv0720 <i>rplR</i> 50S ribosomal protein L18 Rv2904c <i>rplS</i> 50S ribosomal protein L19 Rv1643 <i>rplT</i> 50S ribosomal protein L20 Rv2442c <i>rplU</i> 50S ribosomal protein L21 Rv0706 <i>rplV</i> 50S ribosomal protein L22 Rv0703 <i>rplW</i> 50S ribosomal protein L23 Rv0715 <i>rplX</i> 50S ribosomal protein L24 Rv1015c <i>rplY</i> 50S ribosomal protein L25 Rv2441c <i>rpmA</i> 50S ribosomal protein L27 Rv1050c <i>rpmB</i> 50S ribosomal protein L28 Rv2058c <i>rpmB2</i> 50S ribosomal protein L28 Rv0709 <i>rpmC</i> 50S ribosomal protein L29 Rv0722 <i>rpmD</i> 50S ribosomal protein L30 Rv1298 <i>rpmE</i> 50S ribosomal protein L31 Rv2057c <i>rpmG</i> 50S ribosomal protein L33 Rv3924c <i>rpmH</i> 50S ribosomal protein L34 Rv1642 <i>rpmI</i> 50S ribosomal protein L35 Rv3461c <i>rpmJ</i> 50S ribosomal protein L36 Rv1630 <i>rpsA</i> 30S ribosomal protein S1 Rv2890c <i>rpsB</i> 30S ribosomal protein S2 Rv0707 <i>rpsC</i> 30S ribosomal protein S3 Rv3458c <i>rpsD</i> 30S ribosomal protein S4 Rv0721 <i>rpsE</i> 30S ribosomal protein S5 Rv0053 <i>rpsF</i> 30S ribosomal protein S6 Rv0683 <i>rpsG</i> 30S ribosomal protein S7 Rv0718 <i>rpsH</i> 30S ribosomal protein S8 Rv3442c <i>rpsI</i> 30S ribosomal protein S9 Rv0700 <i>rpsJ</i> 30S ribosomal protein S10 Rv3459c <i>rpsK</i> 30S ribosomal protein S11 Rv0682 <i>rpsL</i> 30S ribosomal protein S12 Rv3460c <i>rpsM</i> 30S ribosomal protein S13 Rv0717 <i>rpsN</i> 30S ribosomal protein S14 Rv2056c <i>rpsN2</i> 30S ribosomal protein S14 Rv2785c <i>rpsO</i> 30S ribosomal protein S15 Rv2909c <i>rpsP</i> 30S ribosomal protein S16 Rv0710 <i>rpsQ</i> 30S ribosomal protein S17 Rv0055 <i>rpsR</i> 30S ribosomal protein S18 Rv2055c <i>rpsR2</i> 30S ribosomal protein S18 Rv0705 <i>rpsS</i> 30S ribosomal protein S19 Rv2412 <i>rpsT</i> 30S ribosomal protein S20 Rv3241c - member of S30AE ribosomal protein family		
Rv0894	-	putative transcriptional regulator	Rv3208	-	transcriptional regulator (TetR/AcrR family)			
Rv1019	-	transcriptional regulator (TetR/AcrR family)	Rv3249c	-	transcriptional regulator (TetR/AcrR family)			
Rv1049	-	transcriptional regulator (MarR family)	Rv3291c	-	transcriptional regulator (Lrp/AsnC family)			
Rv1129c	-	transcriptional regulator (PbsX/Xre family)	Rv3295	-	transcriptional regulator (TetR/AcrR family)			
Rv1151c	-	putative transcriptional regulator	Rv3334	-	transcriptional regulator (MerR family)			
Rv1152	-	transcriptional regulator (GntR family)	Rv3405c	-	putative transcriptional regulator			
Rv1167c	-	putative transcriptional regulator	Rv3522	-	putative transcriptional regulator			
Rv1219c	-	putative transcriptional regulator	Rv3557c	-	transcriptional regulator (TetR/AcrR family)			
Rv1255c	-	transcriptional regulator (TetR/AcrR family)	Rv3574	-	transcriptional regulator (TetR/AcrR family)			
Rv1332	-	putative transcriptional regulator	Rv3575c	-	transcriptional regulator (LacI family)			
Rv1353c	-	transcriptional regulator (TetR/AcrR family)	Rv3583c	-	putative transcriptional regulator			
Rv1358	-	transcriptional regulator (LuxR/UhpA family)	Rv3676	-	transcriptional regulator (Crp/Fnr family)			
Rv1359	-	putative transcriptional regulator	Rv3678c	-	transcriptional regulator (LysR family)			
Rv1395	-	transcriptional regulator (AraC/XylS family)	Rv3736	-	transcriptional regulator (AraC/XylS family)			
Rv1404	-	transcriptional regulator (MarR family)	Rv3744	-	transcriptional regulator (ArsR family)			
Rv1423	-	putative transcriptional regulator	Rv3830c	-	transcriptional regulator (TetR/AcrR family)			
Rv1460	-	putative transcriptional regulator	Rv3833	-	transcriptional regulator (AraC/XylS family)			
Rv1474c	-	transcriptional regulator (TetR/AcrR family)	Rv3840	-	putative transcriptional regulator			
Rv1534	-	transcriptional regulator (TetR/AcrR family)	Rv3855	-	putative transcriptional regulator			
Rv1556	-	putative transcriptional regulator	<b>2. Two component systems</b> Rv1028c <i>kdpD</i> sensor histidine kinase Rv1027c <i>kdpE</i> two-component response regulator Rv3246c <i>mtrA</i> two-component response regulator Rv3245c <i>mtrB</i> sensor histidine kinase Rv0844c <i>narL</i> two-component response regulator Rv0757 <i>phoP</i> two-component response regulator Rv0758 <i>phoR</i> sensor histidine kinase Rv0491 <i>regX3</i> two-component response regulator Rv0490 <i>senX3</i> sensor histidine kinase Rv0602c <i>tcrA</i> two-component response regulator Rv0260c - two-component response regulator Rv0600c - sensor histidine kinase Rv0601c - sensor histidine kinase Rv0818 - two-component response regulator Rv0845 - sensor histidine kinase Rv0902c - sensor histidine kinase Rv0903c - two-component response regulator Rv0981 - two-component response regulator Rv0982 - sensor histidine kinase Rv1032c - sensor histidine kinase Rv1033c - two-component response regulator Rv1626 - two-component response regulator Rv2027c - sensor histidine kinase Rv2884 - two-component response regulator Rv3132c - sensor histidine kinase Rv3133c - two-component response regulator Rv3143 - putative sensory transduction protein Rv3220c - sensor histidine kinase Rv3764c - sensor histidine kinase Rv3765c - two-component response regulator					
Rv1674c	-	putative transcriptional regulator						
Rv1675c	-	putative transcriptional regulator						
Rv1719	-	transcriptional regulator (IclR family)						
Rv1773c	-	transcriptional regulator (IclR family)						
Rv1776c	-	putative transcriptional regulator						
Rv1816	-	putative transcriptional regulator						
Rv1846c	-	putative transcriptional regulator						
Rv1931c	-	transcriptional regulator (AraC/XylS family)						
Rv1956	-	putative transcriptional regulator						
Rv1963c	-	putative transcriptional regulator						
Rv1985c	-	transcriptional regulator (LysR family)						
Rv1990c	-	putative transcriptional regulator						
Rv1994c	-	transcriptional regulator (MerR family)						
Rv2017	-	putative transcriptional regulator (PbsX/Xre family)						
Rv2021c	-	putative transcriptional regulator						
Rv2034	-	transcriptional regulator (ArsR family)						
Rv2175c	-	putative transcriptional regulator						
Rv2250c	-	putative transcriptional regulator						
Rv2258c	-	putative transcriptional regulator						
Rv2282c	-	transcriptional regulator (LysR family)						
Rv2308	-	putative transcriptional regulator						
Rv2324	-	transcriptional regulator (Lrp/AsnC family)						
Rv2358	-	transcriptional regulator (ArsR family)						
Rv2488c	-	transcriptional regulator (LuxR/UhpA family)						
Rv2506	-	transcriptional regulator (TetR/AcrR family)						
Rv2621c	-	putative transcriptional regulator						
Rv2640c	-	transcriptional regulator (ArsR family)						
Rv2642	-	transcriptional regulator (ArsR family)						
Rv2669	-	putative transcriptional regulator						
Rv2745c	-	putative transcriptional regulator						
Rv2779c	-	transcriptional regulator (Lrp/AsnC family)						
Rv2887	-	transcriptional regulator (MarR family)						
Rv2912c	-	transcriptional regulator (TetR/AcrR family)						
Rv2989	-	transcriptional regulator (IclR family)						
Rv3050c	-	putative transcriptional regulator						
Rv3055	-	putative transcriptional regulator						
Rv3058c	-	putative transcriptional regulator						
Rv3060c	-	transcriptional regulator (GntR family)						
Rv3066	-	putative transcriptional regulator						
Rv3095	-	putative transcriptional regulator						
Rv3124	-	transcriptional regulator (AraC/XylS family)						
<b>3. Serine-threonine protein kinases and phosphoprotein phosphatases</b> Rv0015c <i>pknA</i> serine-threonine protein kinase Rv0014c <i>pknB</i> serine-threonine protein kinase Rv0931c <i>pknD</i> serine-threonine protein kinase Rv1743 <i>pknE</i> serine-threonine protein kinase Rv1746 <i>pknF</i> serine-threonine protein kinase Rv0410c <i>pknG</i> serine-threonine protein kinase Rv1266c <i>pknH</i> serine-threonine protein kinase Rv2914c <i>pknI</i> serine-threonine protein kinase Rv2088 <i>pknJ</i> serine-threonine protein kinase Rv3080c <i>pknK</i> serine-threonine protein kinase Rv2176 <i>pknL</i> serine-threonine protein kinase			<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> alanyl-tRNA synthase Rv1292 <i>argS</i> arginyl-tRNA synthase Rv2572c <i>aspS</i> aspartyl-tRNA synthase Rv3580c <i>cysS</i> cysteinyl-tRNA synthase Rv2130c <i>cysS2</i> cysteinyl-tRNA synthase Rv1406 <i>fmrT</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					

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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  
secreted protein  
Rv3811 *csp* highly similar to C-term Mpt53  
Rv1677 *dsbF* involved in arabinogalactan synthesis  
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 (Erp protein)  
Rv3782 *rfbE* similar to rhamnosyl transferase  
Rv1302 *rfe* undecaprenyl-phosphate  $\alpha$ -N-acetylglucosaminyltransferase  
Rv2145c *wag31* antigen 84 (aka wag31)  
Rv0431 - tuberculin related peptide (AT103)  
Rv0954 - cell envelope antigen  
Rv1514c - involved in polysaccharide synthesis  
Rv1518 - 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

#### 3. Murein sacculus and peptidoglycan

Rv2911 *dacB* penicillin binding protein  
Rv2981c *dala* D-alanine-D-alanine ligase A  
Rv3809c *glf* UDP-galactopyranose mutase  
Rv1018c *glmU* UDP-N-acetylglucosamine pyrophosphorylase  
Rv3382c *lytB1* LytB protein homologue  
Rv1110 *lytB2* very similar to LytB  
Rv1315 *murA* UDP-N-acetylglucosamine-1-carboxyvinyltransferase  
Rv0482 *murB* UDP-N-acetylenolpyruvylglucosamine reductase  
Rv2152c *murC* UDP-N-acetyl-muramate-alanine ligase  
Rv2155c *murD* UDP-N-acetylmuramoylalanine-D-glutamate ligase  
Rv2158c *murE* meso-diaminopimelate-adding enzyme  
Rv2157c *murF* D-alanine:D-alanine-adding enzyme  
Rv2153c *murG* transferase in peptidoglycan synthesis  
Rv1338 *murI* glutamate racemase  
Rv2156c *murX* phospho-N-acetylmuramoyl-pentapeptide transferase  
Rv3332 *nagA* N-acetylglucosamine-6-P-deacetylase  
Rv0016c *pbpA* penicillin-binding protein  
Rv2163c *pbpB* penicillin-binding protein 2  
Rv0050 *ponA1* penicillin-binding protein  
Rv3682 *ponA2* class A penicillin binding protein  
Rv0017c *rodA* FtsW/RodA/SpvE family  
Rv0907 - probable penicillin binding protein

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

#### 5. Other membrane proteins 211

### 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(II)-dicitrate transporter  
Rv0265c *fecB2* iron transport protein Fe(II) dicitrate transporter  
Rv1029 *kdpA* potassium-transporting ATPase A chain

Rv1030 *kdpB* potassium-transporting ATPase B chain  
Rv1031 *kdpC* potassium-transporting ATPase C chain  
Rv3236c *kefB* 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 *pstS* phosphate transport system  
PstS component of phosphate uptake  
Rv2400c *subI* 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 *ltp1* non-specific lipid transport protein  
Rv3540c *ltp2* non-specific lipid transport protein

6. Efflux proteins  
Rv2936 *drfA* similar daunorubicin resistance ABC-transporter  
Rv2937 *drfB* similar daunorubicin resistance transmembrane protein  
Rv2938 *drfC* 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 *hspG* heat shock protein Hsp90 family  
Rv0563 *hspX* probable (transmembrane) heat shock protein  
Rv2701c *subB* putative extragenic suppressor protein  
Rv3269 - probable heat shock protein

C. *Cell division*  
Rv3641c *fts* 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-

unit  
Rv1821 *secA2* SecA, preprotein translocase sub-unit  
Rv2587c *secD* protein-export membrane protein  
Rv0638 *secE* SecE preprotein translocase  
Rv2586c *secF* protein-export membrane protein  
Rv1440 *secG* protein-export membrane protein  
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 *smvB* probable small protein b  
Rv1694 *tlvA* 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 34 copies

2. *REP 13E12 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'-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, mycosteric 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).

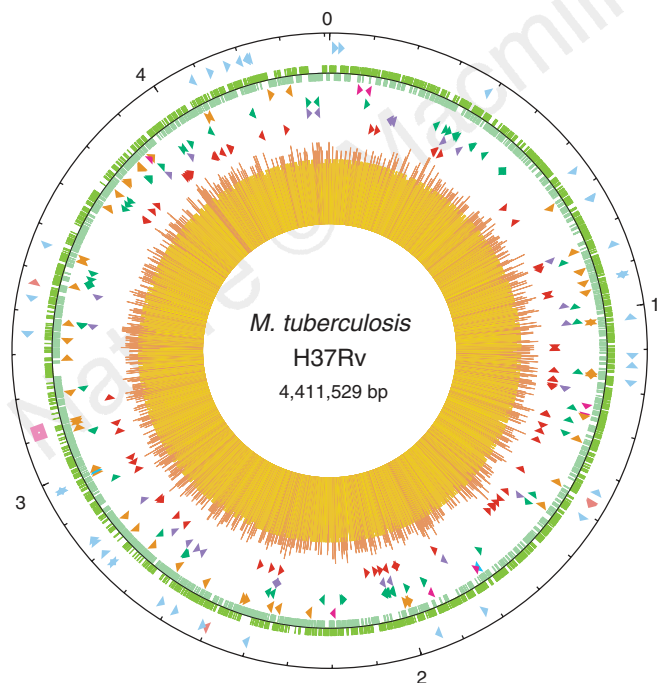
**Genes for stable RNA.** Fifty genes coding for functional RNA molecules were found. These molecules were the three species produced by the unique ribosomal RNA operon, the 16S rRNA involved in degradation of proteins encoded by abnormal messenger RNA, the RNA component of RNase P, and 45 transfer RNAs. 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 inwards 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>.

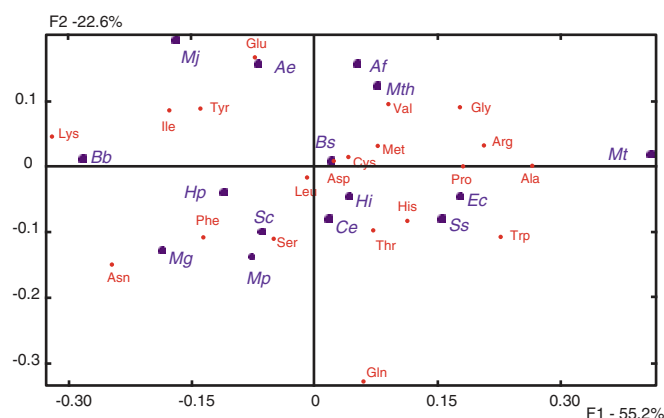
## General metabolism, regulation and drug resistance

**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

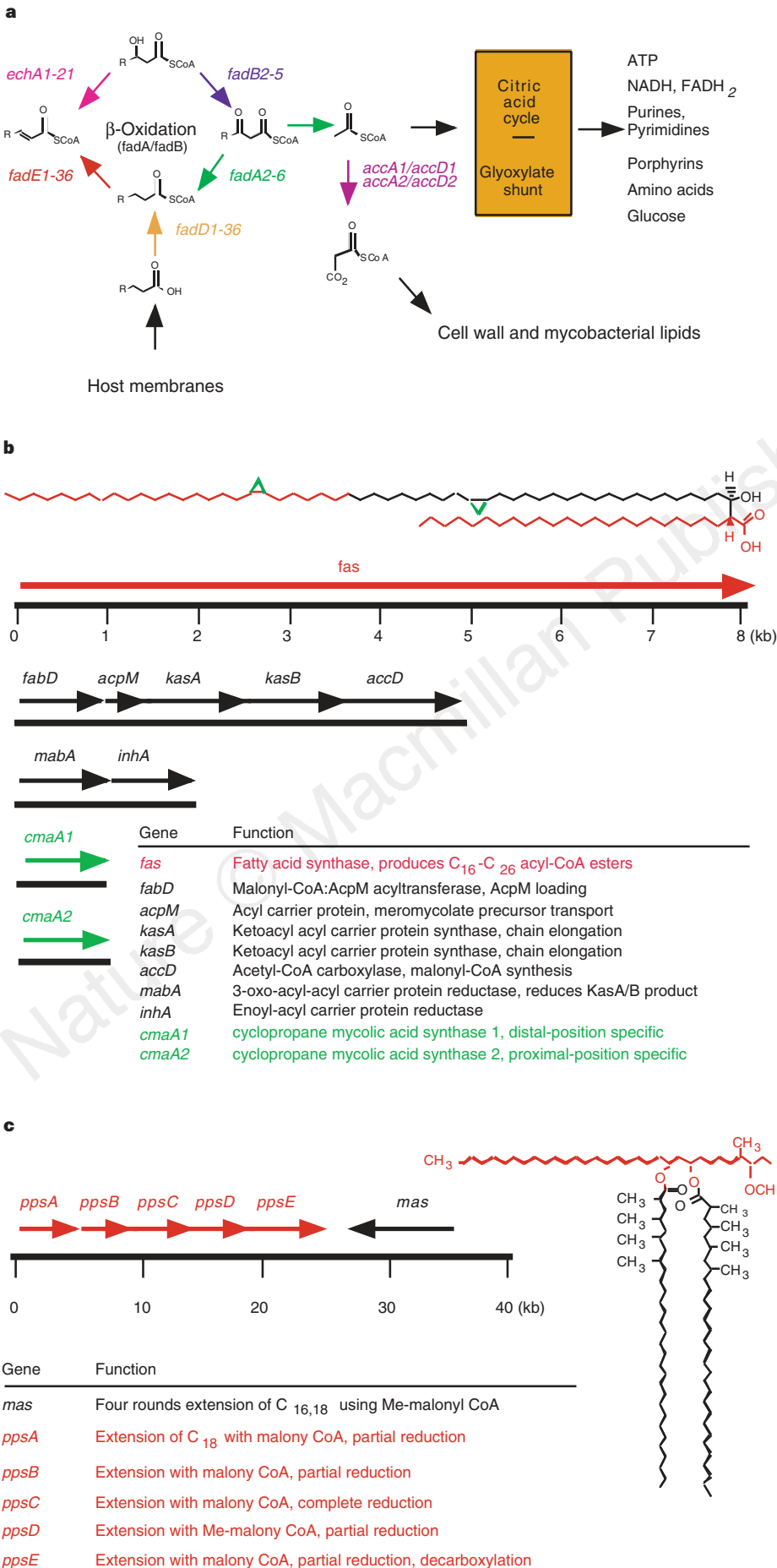
proteins, which may protect against oxidative stress or be involved in oxygen capture, were found. The ability of the bacillus to adapt its metabolism to environmental change is significant as it not only has to compete with the lung for oxygen but must also adapt to the microaerophilic/anaerobic environment 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 fulgidus*; Bb, *Borrelia burgdorferi*; Bs, *B. subtilis*; Ce, *Caenorhabditis elegans*; Ec, *E. coli*; Hi, *Haemophilus influenzae*; Hp, *Helicobacter pylori*; Mg, *Mycoplasmag genitalium*; Mj, *Methanococcus jannaschii*; Mp, *Mycoplasmag 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 mycosteric 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

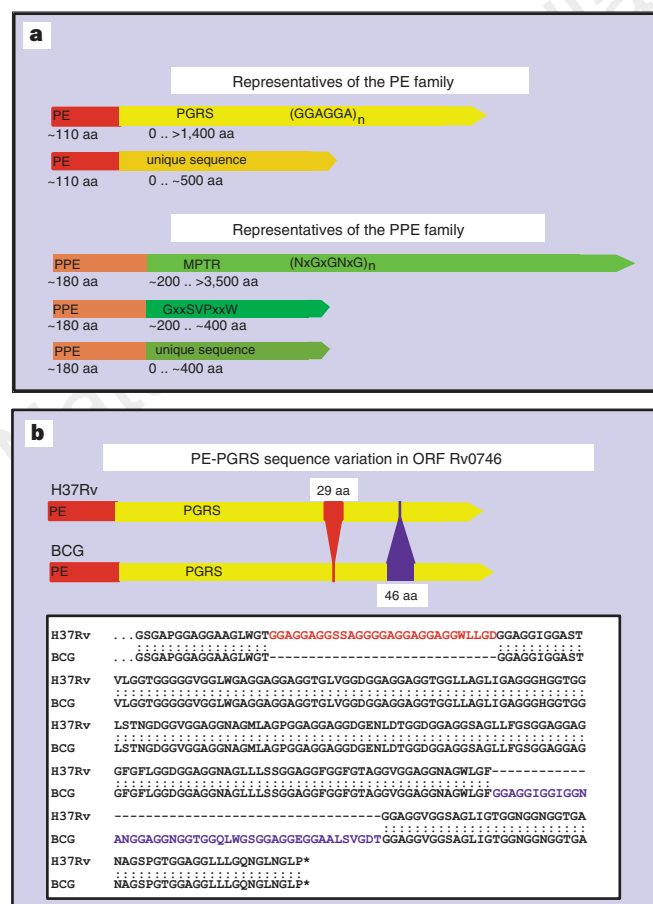
because they are difficult to distinguish from other members of the short-chain alcohol dehydrogenase family on the basis of primary sequence. The five enzymes that complete the cycle by thiolysis of the  $\beta$ -ketoester, the acetyl-CoA C-acetyltransferases, do indeed appear to be a more limited family. 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. Tuberculoheptanoic 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/>).

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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.

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**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-fucose 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>	phosphoglucosylmutase or phosphomannomutase
Rv0118c	<i>oxcA</i>	oxalyl-CoA decarboxylase
Rv3068c	<i>pgmA</i>	phosphoglucosylmutase
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>aoa</i>	D-amino acid oxidase
Rv2313c	<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>	methylmalonate semialdehyde dehydrogenase
Rv0751c	<i>mmsB</i>	methylmalonate 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>echH</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>	enoyl-CoA hydratase/isomerase superfamily
Rv3039c	<i>echA17</i>	enoyl-CoA hydratase/isomerase superfamily
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>	triophosphate 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>acn</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>glitA1</i>	citrate synthase 3
Rv0896	<i>glitA2</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**

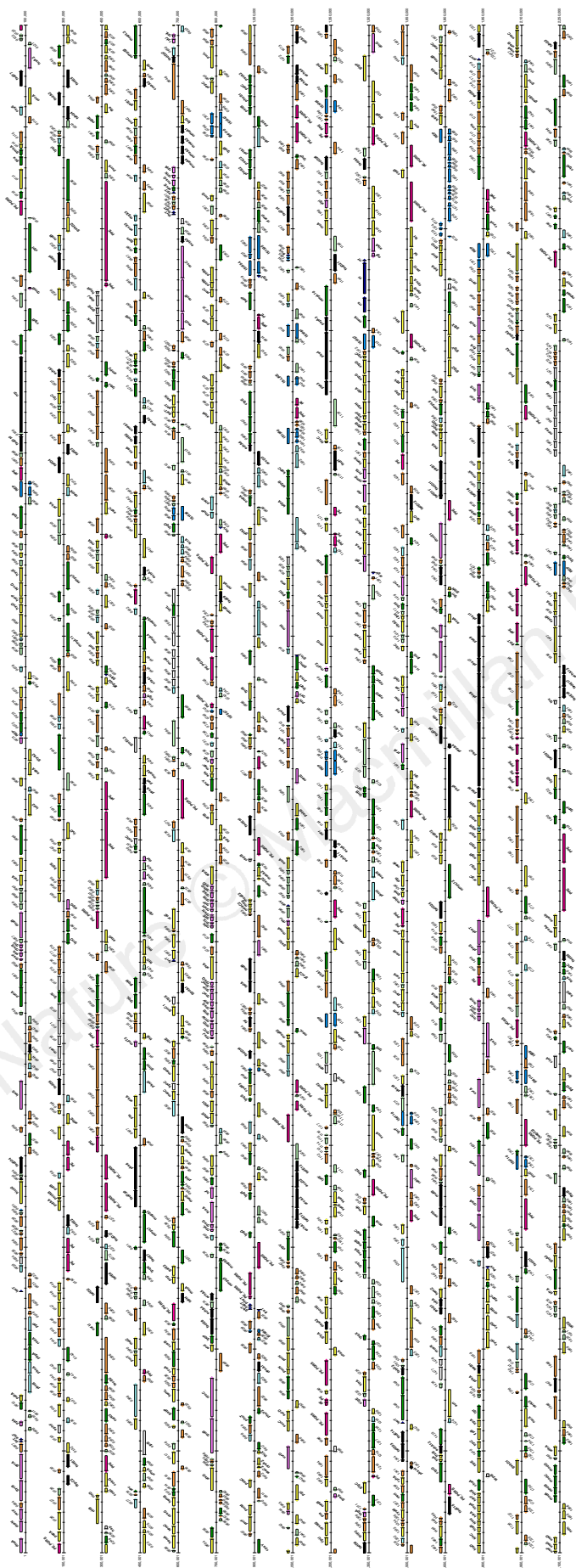
Rv1445c	<i>devB</i>	glucose-6-phosphate 1-dehydrogenase
Rv1844c	<i>gnd</i>	6-phosphogluconate dehydrogenase (Gram -)
Rv1122	<i>gnd2</i>	6-phosphogluconate dehydrogenase (Gram +)
Rv1446c	<i>opcA</i>	unknown function, may aid G6PDH

Rv2436	<i>rbsK</i>	ribokinase	Rv3250c	<i>rubB</i>	rubredoxin B	Rv1878	<i>glnA3</i>	probable glutamine synthase
Rv1408	<i>rpe</i>	ribulose-phosphate 3-epimerase				Rv2860c	<i>glnA4</i>	probable glutamine synthase
Rv2465c	<i>rpi</i>	phosphopentose isomerase	7. Miscellaneous oxidoreductases and oxygenases 171			Rv2918c	<i>glnD</i>	uridylyltransferase
Rv1448c	<i>tal</i>	transaldolase				Rv2221c	<i>glnE</i>	glutamate-ammonia-lyase
Rv1449c	<i>tkl</i>	transketolase	8. ATP-proton motive force					adenyltransferase
Rv1121	<i>zwf</i>	glucose-6-phosphate 1-dehydrogenase	Rv1308	<i>atpA</i>	ATP synthase $\alpha$ chain	Rv3859c	<i>gltB</i>	ferredoxin-dependent glutamate synthase
Rv1447c	<i>zwf2</i>	glucose-6-phosphate 1-dehydrogenase	Rv1304	<i>atpB</i>	ATP synthase $\alpha$ chain	Rv3858c	<i>gltD</i>	small subunit of NADH-dependent glutamate synthase
			Rv1311	<i>atpC</i>	ATP synthase $\epsilon$ chain	Rv3704c	<i>gshA</i>	possible $\gamma$ -glutamylcysteine synthase
			Rv1310	<i>atpD</i>	ATP synthase $\beta$ chain			
			Rv1305	<i>atpE</i>	ATP synthase c chain			
			Rv1306	<i>atpF</i>	ATP synthase b chain	Rv2427c	<i>proA</i>	$\gamma$ -glutamyl phosphate reductase
			Rv1309	<i>atpG</i>	ATP synthase $\gamma$ chain	Rv2439c	<i>proB</i>	glutamate 5-kinase
			Rv1307	<i>atpH</i>	ATP synthase $\delta$ chain	Rv0500	<i>proC</i>	pyrroline-5-carboxylate reductase
6. Respiration								
<i>a. aerobic</i>								
Rv0527	<i>ccsA</i>	cytochrome c-type biogenesis protein	C. Central intermediary metabolism					
Rv0529	<i>ccsB</i>	cytochrome c-type biogenesis protein	1. General			2. Aspartate family		
Rv1451	<i>ctaB</i>	cytochrome c oxidase assembly factor	Rv2589	<i>gabT</i>	4-aminobutyrate aminotransferase	Rv3708c	<i>asd</i>	aspartate semialdehyde dehydrogenase
Rv2200c	<i>ctaC</i>	cytochrome c oxidase chain II	Rv3432c	<i>gabB</i>	glutamate decarboxylase	Rv3709c	<i>ask</i>	aspartokinase
Rv3043c	<i>ctaD</i>	cytochrome c oxidase polypeptide I	Rv1832	<i>gcvB</i>	glycine decarboxylase	Rv2201	<i>asnB</i>	asparagine synthase B
Rv2193	<i>ctaE</i>	cytochrome c oxidase polypeptide III	Rv1826	<i>gcvH</i>	glycine cleavage system H protein	Rv3565	<i>aspB</i>	aspartate aminotransferase
Rv1542c	<i>glbN</i>	hemoglobin-like, oxygen carrier	Rv2211c	<i>gcvT</i>	T protein of glycine cleavage system	Rv0337c	<i>aspC</i>	aspartate aminotransferase
Rv2470	<i>glbO</i>	hemoglobin-like, oxygen carrier	Rv1213	<i>glgC</i>	glucose-1-phosphate adenyltransferase	Rv2753c	<i>dapA</i>	dihydrodipicolinate synthase
Rv2249c	<i>glpD1</i>	glycerol-3-phosphate dehydrogenase	Rv3842c	<i>glpQ1</i>	glycerophosphoryl diester phosphodiesterase	Rv2773c	<i>dapB</i>	dihydrodipicolinate reductase
Rv3302c	<i>glpD2</i>	glycerol-3-phosphate dehydrogenase	Rv0317c	<i>glpQ2</i>	glycerophosphoryl diester phosphodiesterase	Rv1202	<i>dapE</i>	succinyl-diaminopimelate desuccinylase
Rv0694	<i>lldD1</i>	L-lactate dehydrogenase (cytochrome)	Rv3566c	<i>nhoA</i>	N-hydroxyarylamine o-acetyltransferase	Rv2141c	<i>dapE2</i>	ArgE/DapE/Acy1/Cpg2/lycS family
Rv1872c	<i>lldD2</i>	L-lactate dehydrogenase	Rv0155	<i>pntAA</i>	pyridine transhydrogenase subunit $\alpha$ 1	Rv2726c	<i>dapF</i>	diaminopimelate epimerase
Rv1854c	<i>ndh</i>	probable NADH dehydrogenase	Rv0156	<i>pntAB</i>	pyridine transhydrogenase subunit $\alpha$ 2	Rv1293	<i>lysA</i>	diaminopimelate decarboxylase
Rv3145	<i>nuoA</i>	NADH dehydrogenase chain A	Rv0157	<i>pntB</i>	pyridine transhydrogenase subunit $\beta$	Rv3341	<i>metA</i>	homoserine o-acetyltransferase
Rv3146	<i>nuoB</i>	NADH dehydrogenase chain B	Rv1127c	<i>ppdK</i>	similar to pyruvate, phosphate dikinase	Rv1079	<i>metB</i>	cystathionine $\gamma$ -synthase
Rv3147	<i>nuoC</i>	NADH dehydrogenase chain C				Rv3340	<i>metC</i>	cystathionine $\beta$ -lyase
Rv3148	<i>nuoD</i>	NADH dehydrogenase chain D				Rv1133c	<i>metE</i>	5-methyltetrahydropteroyltrimethylhomocysteine methyltransferase
Rv3149	<i>nuoE</i>	NADH dehydrogenase chain E						
Rv3150	<i>nuoF</i>	NADH dehydrogenase chain F						
Rv3151	<i>nuoG</i>	NADH dehydrogenase chain G	2. Gluconeogenesis					
Rv3152	<i>nuoH</i>	NADH dehydrogenase chain H	Rv0211	<i>pckA</i>	phosphoenolpyruvate carboxykinase			
Rv3153	<i>nuoI</i>	NADH dehydrogenase chain I						
Rv3154	<i>nuoJ</i>	NADH dehydrogenase chain J	Rv0069c	<i>sdaA</i>	L-serine dehydratase 1	Rv1294	<i>thrA</i>	homoserine dehydrogenase
Rv3155	<i>nuoK</i>	NADH dehydrogenase chain K				Rv1296	<i>thrB</i>	homoserine kinase
Rv3156	<i>nuoL</i>	NADH dehydrogenase chain L				Rv1295	<i>thrC</i>	homoserine synthase
Rv3157	<i>nuoM</i>	NADH dehydrogenase chain M	3. Sugar nucleotides					
Rv3158	<i>nuoN</i>	NADH dehydrogenase chain N	Rv1512	<i>epiA</i>	nucleotide sugar epimerase			
Rv2195	<i>qcrA</i>	Rieske iron-sulphur component of <i>ubiQ</i> -cytB reductase	Rv3784	<i>epiB</i>	probable UDP-galactose 4-epimerase	3. Serine family		
						Rv0815c	<i>cysA2</i>	thiosulfate sulfurtransferase
Rv2196	<i>qcrB</i>	cytochrome $\beta$ component of <i>ubiQ</i> -cytB reductase	Rv1511	<i>gmdA</i>	GDP-mannose 4,6 dehydratase	Rv3117	<i>cysA3</i>	thiosulfate sulfurtransferase
			Rv0334	<i>rmlA</i>	glucose-1-phosphate thymidyltransferase	Rv2335	<i>cysE</i>	serine acetyltransferase
Rv2194	<i>qcrC</i>	cytochrome <i>b/c</i> component of <i>ubiQ</i> -cytB reductase	Rv3264c	<i>rmlA2</i>	glucose-1-phosphate thymidyltransferase	Rv0511	<i>cysG</i>	uroporphyrin-III C-methyltransferase
			Rv3464	<i>rmlB</i>	dTDP-glucose 4,6-dehydratase	Rv2847c	<i>cysG2</i>	multifunctional enzyme, siroheme synthase
<i>b. anaerobic</i>			Rv3634c	<i>rmlB2</i>	dTDP-glucose 4,6-dehydratase			
Rv2392	<i>cysH</i>	3'-phosphoadenylylsulfate (PAPS) reductase	Rv3468c	<i>rmlB3</i>	dTDP-glucose 4,6-dehydratase	Rv2334	<i>cysK</i>	cysteine synthase A
			Rv3465	<i>rmlC</i>	dTDP-4-dehydrothiamine	Rv1336	<i>cysM</i>	cysteine synthase B
Rv2899c	<i>fdhD</i>	affects formate dehydrogenase-N				Rv1077	<i>cysM2</i>	cystathionine $\beta$ -synthase
Rv2900c	<i>fdhF</i>	molybdopterin-containing oxidoreductase	Rv3266c	<i>rmlD</i>	3,5-epimerase	Rv0848	<i>cysM3</i>	putative cysteine synthase
Rv1552	<i>frdA</i>	fumarate reductase flavoprotein subunit				Rv1093	<i>glyA</i>	serine hydroxymethyltransferase
Rv1553	<i>frdB</i>	fumarate reductase iron sulphur protein	Rv0322	<i>udgA</i>	dTDP-4-dehydrothiamine reductase	Rv0070c	<i>glyA2</i>	serine hydroxymethyltransferase
Rv1554	<i>frdC</i>	fumarate reductase 15kD anchor protein				Rv2996c	<i>serA</i>	D-3-phosphoglycerate dehydrogenase
Rv1555	<i>frdD</i>	fumarate reductase 13kD anchor protein						
						Rv0505c	<i>serB</i>	probable phosphoserine phosphatase
Rv1161	<i>narG</i>	nitrate reductase $\alpha$ subunit	Rv3265c	<i>wbbL</i>	dTDP-rhamnosyl transferase	Rv3042c	<i>serB2</i>	C-term similar to phosphoserine phosphatase
Rv1162	<i>narH</i>	nitrate reductase $\beta$ chain	Rv1525	<i>wbbL2</i>	dTDP-rhamnosyl transferase	Rv0884c	<i>serC</i>	phosphoserine aminotransferase
Rv1164	<i>narI</i>	nitrate reductase $\gamma$ chain	Rv3400	-	probable $\beta$ -phosphoglucosyltransferase			
Rv1163	<i>narJ</i>	nitrate reductase $\delta$ chain						
Rv1736c	<i>narX</i>	fused nitrate reductase	4. Amino sugars					
Rv2391	<i>nirA</i>	probable nitrite reductase/sulphite reductase	Rv3436c	<i>glmS</i>	glucosamine-fructose-6-phosphate aminotransferase	4. Aromatic amino acid family		
Rv0252	<i>nirB</i>	nitrite reductase flavoprotein						
Rv0253	<i>nirD</i>	probable nitrite reductase small subunit						
<i>c. Electron transport</i>								
Rv0409	<i>ackA</i>	acetate kinase	5. Sulphur metabolism					
Rv1623c	<i>appC</i>	cytochrome <i>bd-II</i> oxidase subunit I	Rv0711	<i>atsA</i>	arylsulfatase	Rv3227	<i>aroA</i>	3-phosphoshikimate
Rv1622c	<i>cydB</i>	cytochrome <i>d</i> ubiquinol oxidase subunit II	Rv3299c	<i>atsB</i>	proable arylsulfatase	Rv2538c	<i>aroB</i>	1-carboxyvinyl transferase
Rv1620c	<i>cydC</i>	ABC transporter	Rv0663	<i>atsD</i>	proable arylsulfatase	Rv2537c	<i>aroD</i>	3-dehydroquinate synthase
Rv1621c	<i>cydD</i>	ABC transporter	Rv3077	<i>atsF</i>	proable arylsulfatase	Rv2552c	<i>aroE</i>	3-dehydroquinate dehydratase
Rv2007c	<i>fdxA</i>	ferredoxin	Rv0296c	<i>atsG</i>	proable arylsulfatase	Rv2540c	<i>aroF</i>	shikimate 5-dehydrogenase
Rv3554	<i>fdxB</i>	ferredoxin	Rv3796	<i>atsH</i>	proable arylsulfatase	Rv2178c	<i>aroG</i>	chorismate synthase
Rv1177	<i>fdxC</i>	ferredoxin 4Fe-4S	Rv1285	<i>cysD</i>	ATP:sulphurylase subunit 2	Rv2539c	<i>aroK</i>	DAHPS synthase
Rv3503c	<i>fdxD</i>	probable ferredoxin	Rv1286	<i>cysN</i>	ATP:sulphurylase subunit 1	Rv3838c	<i>pheA</i>	shikimate kinase I
Rv3029c	<i>fixA</i>	electron transfer flavoprotein $\beta$ subunit	Rv2131c	<i>cysQ</i>	homologue of <i>M.leprae</i> <i>cysQ</i>	Rv1613	<i>trpA</i>	prephenate dehydratase
Rv3028c	<i>fixB</i>	electron transfer flavoprotein $\alpha$ subunit	Rv3248c	<i>sahH</i>	adenosylhomocysteinase	Rv1612	<i>trpB</i>	tryptophan synthase $\alpha$ chain
Rv3106	<i>fprA</i>	adrenodoxin and NADPH ferredoxin reductase	Rv3283	<i>sseA</i>	thiosulfate sulfurtransferase	Rv1611	<i>trpC</i>	tryptophan synthase $\beta$ chain
Rv0886	<i>fprB</i>	ferredoxin, ferredoxin-NADP reductase	Rv2291	<i>sseB</i>	thiosulfate sulfurtransferase			
Rv3251c	<i>rubA</i>	rubredoxin A	Rv3118	<i>sseC</i>	thiosulfate sulfurtransferase	Rv2192c	<i>trpD</i>	anthranilate phosphoribosyltransferase
			Rv0814c	<i>sseC2</i>	thiosulfate sulfurtransferase	Rv1609	<i>trpE</i>	anthranilate synthase component I
			Rv3762c	-	probable alkyl sulfatase	Rv2386c	<i>trpE2</i>	anthranilate synthase component I
						Rv3754	<i>tyrA</i>	prephenate dehydrogenase
			D. Amino acid biosynthesis					
			1. Glutamate family			5. Histidine		
			Rv1654	<i>argB</i>	acetylglutamate kinase	Rv1603	<i>hisA</i>	phosphoribosylformimino-5-aminoimidazole carboxamide
			Rv1652	<i>argC</i>	N-acetyl- $\gamma$ -glutamyl-phosphate reductase			ribonucleotide isomerase
			Rv1655	<i>argD</i>	acetylornithine aminotransferase	Rv1601	<i>hisB</i>	imidazole glycerol-phosphate dehydratase
			Rv1656	<i>argF</i>	ornithine carbamoyltransferase			
			Rv1658	<i>argG</i>	arginosuccinate synthase	Rv1600	<i>hisC</i>	histidinol-phosphate aminotransferase
			Rv1659	<i>argH</i>	arginosuccinate lyase			
			Rv1653	<i>argJ</i>	glutamate N-acetyltransferase	Rv3772	<i>hisC2</i>	histidinol-phosphate aminotransferase
			Rv2220	<i>glnA1</i>	glutamine synthase class I			
			Rv2222c	<i>glnA2</i>	glutamine synthase class II	Rv1599	<i>hisD</i>	histidinol dehydrogenase



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











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					
Rv3852	<i>hns</i>	HU-histone protein	6. Protein translation and modification			Rv2457c	<i>clpX</i> ATP-dependent Clp protease
Rv2986c	<i>hupB</i>	DNA-binding protein II	Rv0429c	<i>def</i>	polypeptide deformylase		ATP-binding subunit ClpX
Rv1388	<i>mIHF</i>	integration host factor	Rv2534c	<i>efp</i>	elongation factor P	Rv2667	<i>clpX'</i> similar to ClpC from <i>M. leprae</i> but shorter
5. DNA replication, repair, recombination and restriction/modification			Rv2882c	<i>frr</i>	ribosome recycling factor		
Rv1317c	<i>alkA</i>	DNA-3-methyladenine glycosidase II	Rv0684	<i>fusA</i>	elongation factor G	Rv3419c	<i>gcp</i> glycoprotease
Rv2836c	<i>dinF</i>	DNA-damage-inducible protein F	Rv0120c	<i>fusA2</i>	elongation factor G	Rv2725c	<i>hflX</i> GTP-binding protein
Rv1329c	<i>dinG</i>	probable ATP-dependent helicase	Rv1080c	<i>greA</i>	transcription elongation factor G	Rv1223	<i>htrA</i> serine protease
Rv3056	<i>dinP</i>	DNA-damage-inducible protein	Rv3462c	<i>infA</i>	initiation factor IF-1	Rv2861c	<i>map</i> methionine aminopeptidase
Rv1537	<i>dinX</i>	probable DNA-damage-inducible protein	Rv2839c	<i>infB</i>	initiation factor IF-2	Rv0734	<i>map'</i> probable methionine aminopeptidase
			Rv1641	<i>infC</i>	initiation factor IF-3		
Rv0001	<i>dnaA</i>	chromosomal replication initiator protein	Rv0009	<i>ppiA</i>	peptidyl-prolyl <i>cis-trans</i> isomerase	Rv0319	<i>pcp</i> pyrrolidone-carboxylate peptidase
Rv0058	<i>dnaB</i>	DNA helicase (contains intein)	Rv2582	<i>ppiB</i>	peptidyl-prolyl <i>cis-trans</i> isomerase	Rv0125	<i>pepA</i> probable serine protease
Rv1547	<i>dnaE1</i>	DNA polymerase III, $\alpha$ subunit	Rv1299	<i>prtA</i>	peptide chain release factor 1	Rv2213	<i>pepB</i> aminopeptidase A/I
Rv3370c	<i>dnaE2</i>	DNA polymerase III $\alpha$ chain	Rv3105c	<i>prtB</i>	peptide chain release factor 2	Rv0800	<i>pepC</i> aminopeptidase I
Rv2343c	<i>dnaG</i>	DNA primase	Rv2889c	<i>tsf</i>	elongation factor EF-Ts	Rv2467	<i>pepD</i> probable aminopeptidase
Rv0002	<i>dnaN</i>	DNA polymerase III, $\beta$ subunit	Rv0685	<i>tuf</i>	elongation factor EF-Tu	Rv2089c	<i>pepE</i> cytoplasmic peptidase
Rv3711c	<i>dnaQ</i>	DNA polymerase III $\epsilon$ chain	7. RNA synthesis, RNA modification and DNA transcription			Rv2535c	<i>pepQ</i> cytoplasmic peptidase
Rv3721c	<i>dnaX</i>	DNA polymerase III, $\gamma$ (dnaX) and $\tau$ (dnaX)	Rv1253	<i>deaD</i>	ATP-dependent DNA/RNA helicase	Rv2782c	<i>pepR</i> protease/peptidase, M16 family (insulinase)
Rv2924c	<i>fpg</i>	formamidopyrimidine-DNA glycosylase	Rv2783c	<i>gpsI</i>	pppGpp synthase and polynucleotide phosphorylase		
Rv0006	<i>gyrA</i>	DNA gyrase subunit A	Rv2841c	<i>nusA</i>	transcription termination factor	Rv2109c	<i>prcA</i> proteasome $\alpha$ -type subunit 1
Rv0005	<i>gyrB</i>	DNA gyrase subunit B	Rv2533c	<i>nusB</i>	N-utilization substance protein B	Rv2110c	<i>prcB</i> proteasome $\beta$ -type subunit 2
Rv2092c	<i>heliY</i>	probable helicase, Ski2 subfamily	Rv0639	<i>nusG</i>	transcription antitermination protein	Rv0782	<i>ptrBa</i> protease II, $\alpha$ subunit
Rv2101	<i>heliZ</i>	probable helicase, Snf2/Rad54 family	Rv3907c	<i>pcnA</i>	polynucleotide polymerase	Rv0781	<i>ptrBb</i> protease II, $\beta$ subunit
			Rv3232c	<i>pvdS</i>	alternative sigma factor for siderophore production	Rv0724	<i>sppA</i> protease IV, signal peptide peptidase
Rv2756c	<i>hsdM</i>	type I restriction/modification system DNA methylase	Rv3211	<i>rhlE</i>	probable ATP-dependent RNA helicase		
Rv2755c	<i>hsdS'</i>	type I restriction/modification system specificity determinant	Rv1297	<i>rho</i>	transcription termination factor rho	Rv0198c	- probable zinc metalloprotease
Rv3296	<i>lhr</i>	ATP-dependent helicase				Rv0457c	- probable peptidase
Rv3014c	<i>ligA</i>	DNA ligase	Rv3457c	<i>rpoA</i>	$\alpha$ subunit of RNA polymerase	Rv0840c	- probable proline iminopeptidase
Rv3062	<i>ligB</i>	DNA ligase	Rv0667	<i>rpoB</i>	$\beta$ subunit of RNA polymerase	Rv0983	- probable serine protease
Rv3731	<i>ligC</i>	probable DNA ligase	Rv0668	<i>rpoC</i>	$\beta'$ subunit of RNA polymerase	Rv1977	- probable zinc metallopeptidase
Rv1020	<i>mfd</i>	transcription-repair coupling factor	Rv1364c	<i>rsbU</i>	SigB regulation protein	Rv3668c	- probable alkaline serine protease
Rv2528c	<i>mrr</i>	restriction system protein	Rv3287c	<i>rsbW</i>	anti-sigma B factor	Rv3671c	- probable serine protease
Rv2985	<i>mutT1</i>	MutT homologue	Rv2703	<i>sigA</i>	RNA polymerase sigma factor (aka MysA, RpoV)	Rv3883c	- probable secreted protease
Rv1160	<i>mutT2</i>	MutT homologue				Rv3886c	- protease
Rv0413	<i>mutT3</i>	MutT homologue	Rv2710	<i>sigB</i>	RNA polymerase sigma factor (aka MysB)	4. Polysaccharides, lipopolysaccharides and phospholipids	
Rv3589	<i>mutY</i>	probable DNA glycosylase					
Rv3297	<i>nei</i>	probable endonuclease VIII	Rv2069	<i>sigC</i>	ECF subfamily sigma subunit	Rv0062	<i>celA</i> cellulase/endoglucanase
Rv3674c	<i>nth</i>	probable endonuclease III	Rv3414c	<i>sigD</i>	ECF subfamily sigma subunit	Rv3915	<i>cwlM</i> hydrolase
Rv1316c	<i>ogt</i>	methylated-DNA-protein-cysteine methyltransferase	Rv1221	<i>sigE</i>	ECF subfamily sigma subunit	Rv0315	- probable $\beta$ -1,3-glucanase
			Rv3286c	<i>sigF</i>	ECF subfamily sigma subunit	Rv1090	- probable inactivated cellulase/endoglucanase
Rv1629	<i>polA</i>	DNA polymerase I	Rv0182c	<i>sigG</i>	sigma-70 factors ECF subfamily		
Rv1402	<i>priA</i>	putative primosomal protein n' (replication factor Y)	Rv3223c	<i>sigH</i>	ECF subfamily sigma subunit	Rv1327c	- probable glycosyl hydrolase, $\alpha$ -amylase family
			Rv1189	<i>sigI</i>	ECF family sigma factor		
Rv3585	<i>radA</i>	probable DNA repair RadA homologue	Rv3328c	<i>sigJ</i>	similar to SigI, ECF family	Rv1333	- probable hydrolase
			Rv0445c	<i>sigK</i>	ECF-type sigma factor	Rv3463	- probable neuraminidase
Rv2737c	<i>recA</i>	recombinase (contains intein)	Rv0735	<i>sigL</i>	sigma-70 factors ECF subfamily	Rv3717	- possible N-acetylmuramoyl-L-alanine amidase
Rv0630c	<i>recB</i>	exodeoxyribonuclease V	Rv3911	<i>sigM</i>	probable sigma factor, similar to SigE	5. Esterases and lipases	
Rv0631c	<i>recC</i>	exodeoxyribonuclease V					
Rv0629c	<i>recD</i>	exodeoxyribonuclease V	Rv3366	<i>spoU</i>	probable rRNA methylase	Rv0220	<i>lipC</i> probable esterase
Rv0003	<i>recF</i>	DNA replication and SOS induction	Rv3455c	<i>truA</i>	probable pseudouridylation synthase	Rv1923	<i>lipD</i> probable esterase
						Rv3775	<i>lipE</i> probable hydrolase
Rv2973c	<i>recG</i>	ATP-dependent DNA helicase	Rv2793c	<i>truB</i>	tRNA pseudouridine 55 synthase	Rv3487c	<i>lipF</i> probable esterase
Rv1696	<i>recN</i>	recombination and DNA repair	Rv1644	<i>tsnR</i>	putative 23S rRNA methyltransferase	Rv0646c	<i>lipG</i> probable hydrolase
Rv3715c	<i>recR</i>	RecBC-Independent process of DNA repair				Rv1399c	<i>lipH</i> probable lipase
			Rv3649	-	ATP-dependent DNA/RNA helicase	Rv1400c	<i>lipI</i> probable lipase
Rv2736c	<i>recX</i>	regulatory protein for RecA				Rv1900c	<i>lipJ</i> probable esterase
Rv2593c	<i>ruvA</i>	Holliday junction binding protein, DNA helicase	8. Polysaccharides (cytoplasmic)			Rv2385	<i>lipK</i> probable acetyl-hydrolase
						Rv1497	<i>lipL</i> esterase
Rv2592c	<i>ruvB</i>	Holliday junction binding protein	Rv1326c	<i>glgB</i>	1,4- $\alpha$ -glucan branching enzyme	Rv2284	<i>lipM</i> probable esterase
Rv2594c	<i>ruvC</i>	Holliday junction resolvase, endodeoxyribonuclease	Rv1328	<i>glgP</i>	probable glycogen phosphorylase	Rv2970c	<i>lipN</i> probable lipase/esterase
						Rv1426c	<i>lipO</i> probable esterase
Rv0054	<i>ssb</i>	single strand binding protein	Rv1564c	<i>glgX</i>	probable glycogen debranching enzyme	Rv2463	<i>lipP</i> probable esterase
Rv1210	<i>tagA</i>	DNA-3-methyladenine glycosidase I				Rv2485c	<i>lipQ</i> probable carboxylesterase
			Rv1563c	<i>glgY</i>	putative $\alpha$ -amylase	Rv3084	<i>lipR</i> probable acetyl-hydrolase
Rv3646c	<i>topA</i>	DNA topoisomerase	Rv1562c	<i>glgZ</i>	maltooligosyltrehalose trehalohydrolase	Rv3176c	<i>lipS</i> probable esterase/lipase
Rv2976c	<i>ung</i>	uracil-DNA glycosylase				Rv2045c	<i>lipT</i> probable carboxylesterase
Rv1638	<i>uvrA</i>	excinuclease ABC subunit A	Rv0126	-	probable glycosyl hydrolase	Rv1076	<i>lipU</i> probable esterase
Rv1633	<i>uvrB</i>	excinuclease ABC subunit B	Rv1781c	-	probable 4- $\alpha$ -glucanotransferase	Rv3203	<i>lipV</i> probable lipase
Rv1420	<i>uvrC</i>	excinuclease ABC subunit C	Rv2471	-	probable maltase $\alpha$ -glucosidase	Rv0217c	<i>lipW</i> probable esterase
Rv0949	<i>uvrD</i>	DNA-dependent ATPase I and helicase II				Rv2351c	<i>plcA</i> phospholipase C precursor
						Rv2350c	<i>plcB</i> phospholipase C precursor
Rv3198c	<i>uvrD2</i>	putative UvrD				Rv2349c	<i>plcC</i> phospholipase C precursor
Rv0427c	<i>xthA</i>	exodeoxyribonuclease III	1. RNA			Rv1755c	<i>plcD</i> partial CDS for phospholipase C
Rv0071	-	group II intron maturase	Rv1014c	<i>pth</i>	peptidyl-tRNA hydrolase	Rv1104	- probable esterase pseudogene
Rv0861c	-	probable DNA helicase	Rv2925c	<i>rnc</i>	RNAse III	Rv1105	-
Rv0944	-	possible formamidopyrimidine-DNA glycosylase	Rv2444c	<i>rne</i>	similar at C-term to ribonuclease E	6. Aromatic hydrocarbons	
Rv1688	-	probable 3-methylpurine DNA glycosylase	Rv2902c	<i>rnhB</i>	ribonuclease HII	Rv3469c	<i>mhpE</i> probable 4-hydroxy-2-oxovalerate aldolase
			Rv3923c	<i>rnpA</i>	ribonuclease P protein component		
						Rv0316	- probable muconolactone isomerase
			Rv1340	<i>rphA</i>	ribonuclease PH		
						Rv0771	- probable 4-carboxymuconolactone decarboxylase
						Rv0939	- probable dehydrase
						Rv1723	- 6-aminohexanoate-dimer hydro-



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
			4. Conserved membrane proteins			Rv1811	<i>mgtC</i>	probable magnesium transport ATPase protein C
C. Cell envelope			Rv0402c	<i>mmpL1</i>	conserved large membrane protein	Rv0362	<i>mgtE</i>	putative magnesium ion transporter
1. Lipoproteins ( <i>lppA-lppO</i> ) 65			Rv0507	<i>mmpL2</i>	conserved large membrane protein	Rv2856	<i>nicT</i>	probable nickel transport protein
2. Surface polysaccharides, lipopolysaccharides, proteins and antigens			Rv0206c	<i>mmpL3</i>	conserved large membrane protein	Rv0924c	<i>nramp</i>	transmembrane protein belonging to Nramp family
Rv0806c	<i>cpsY</i>	probable UDP-glucose-4- epimerase	Rv0450c	<i>mmpL4</i>	conserved large membrane protein	Rv2691	<i>trkA</i>	probable potassium uptake pro- tein
Rv3811	<i>csp</i>	secreted protein	Rv0676c	<i>mmpL5</i>	conserved large membrane protein	Rv2692	<i>trkB</i>	probable potassium uptake pro- tein
Rv1677	<i>dsbF</i>	highly similar to C-term Mpt53	Rv1557	<i>mmpL6</i>	conserved large membrane protein	Rv2287	<i>yjcE</i>	probable Na <sup>+</sup> /H <sup>+</sup> exchanger
Rv3794	<i>embA</i>	involved in arabinogalactan syn- thesis	Rv2942	<i>mmpL7</i>	conserved large membrane protein	Rv2723	-	probable membrane protein, tellurium resistance
Rv3795	<i>embB</i>	involved in arabinogalactan syn- thesis	Rv3823c	<i>mmpL8</i>	conserved large membrane protein	Rv3162c	-	probable membrane protein
Rv3793	<i>embC</i>	involved in arabinogalactan syn- thesis	Rv2339	<i>mmpL9</i>	conserved large membrane protein	Rv3237c	-	possible potassium channel protein
Rv3875	<i>esat6</i>	early secretory antigen target	Rv1183	<i>mmpL10</i>	conserved large membrane protein	Rv3743c	-	probable cation-transporting ATPase
Rv0112	<i>gca</i>	probable GDP-mannose dehy- dratase	Rv0202c	<i>mmpL11</i>	conserved large membrane protein	3. Carbohydrates, organic acids and alcohols		
Rv0113	<i>gmhA</i>	phosphoheptose isomerase	Rv1522c	<i>mmpL12</i>	conserved large membrane protein	Rv2443	<i>dctA</i>	C4-dicarboxylate transport protein
Rv2965c	<i>kdtB</i>	lipopolysaccharide core biosyn- thesis protein	Rv0403c	<i>mmpS1</i>	conserved small membrane protein	Rv3476c	<i>kgtP</i>	sugar transport protein
Rv2878c	<i>mpt53</i>	secreted protein Mpt53	Rv0506	<i>mmpS2</i>	conserved small membrane protein	Rv1902c	<i>nanT</i>	probable sialic acid transporter
Rv1980c	<i>mpt64</i>	secreted immunogenic protein Mpb64/Mpt64	Rv2198c	<i>mmpS3</i>	conserved small membrane protein	Rv1236	<i>sugA</i>	membrane protein probably involved in sugar transport
Rv2875	<i>mpt70</i>	major secreted immunogenic pro- tein Mpt70 precursor	Rv0451c	<i>mmpS4</i>	conserved small membrane protein	Rv1237	<i>sugB</i>	sugar transport protein
Rv2873	<i>mpt83</i>	surface lipoprotein Mpt83	Rv0677c	<i>mmpS5</i>	conserved small membrane protein	Rv1238	<i>sugC</i>	ABC transporter component of sugar uptake system
Rv0899	<i>ompA</i>	member of OmpA family	5. Other membrane proteins 211			Rv3331	<i>sugI</i>	probable sugar transport protein
Rv3810	<i>pirG</i>	cell surface protein precursor (Erp protein)	<b>III. Cell processes</b>			Rv2835c	<i>ugpA</i>	sn-glycerol-3-phosphate permease
Rv3782	<i>rfeE</i>	similar to rhamnosyl transferase	A. Transport/binding proteins			Rv2833c	<i>ugpB</i>	sn-glycerol-3-phosphate-binding periplasmic lipoprotein
Rv1302	<i>rfe</i>	undecaprenyl-phosphate $\alpha$ -N- acetylglucosaminyltransferase	1. Amino acids			Rv2832c	<i>ugpC</i>	sn-glycerol-3-phosphate transport ATP-binding protein
Rv2145c	<i>wag31</i>	antigen 84 (aka wag31)	Rv2127	<i>ansP</i>	L-asparagine permease	Rv2834c	<i>ugpE</i>	sn-glycerol-3-phosphate transport system protein
Rv0431	-	tuberculin related peptide (AT103)	Rv0346c	<i>aroP2</i>	probable aromatic amino acid permease	Rv2316	<i>uspA</i>	sugar transport protein
Rv0954	-	cell envelope antigen	Rv0917	<i>betP</i>	glycine betaine transport	Rv2318	<i>uspC</i>	sugar transport protein
Rv1514c	-	involved in polysaccharide syn- thesis	Rv1704c	<i>cycA</i>	transport of D-alanine, D-serine and glycine	Rv2317	<i>uspE</i>	sugar transport protein
Rv1518	-	involved in exopolysaccharide synthesis	Rv3666c	<i>dppA</i>	probable peptide transport system permease	Rv1200	-	probable sugar transporter
Rv1758	-	partial cutinase	Rv3665c	<i>dppB</i>	probable peptide transport system permease	Rv2038c	-	probable ABC sugar transporter
Rv1910c	-	probable secreted protein	Rv3664c	<i>dppC</i>	probable peptide transport system permease	Rv2039c	-	probable sugar transporter
Rv1919c	-	weak similarity to pollen antigens	Rv3663c	<i>dppD</i>	probable ABC-transporter	Rv2040c	-	probable sugar transporter
Rv1984c	-	probable secreted protein	Rv0522	<i>gabP</i>	probable 4-amino butyrate trans- porter	Rv2041c	-	probable sugar transporter
Rv1987	-	probable secreted protein	Rv0411c	<i>glnH</i>	putative glutamine binding protein	4. Anions		
Rv2223c	-	probable exported protease	Rv2564	<i>glnQ</i>	probable ATP-binding transport protein	Rv2684	<i>arsA</i>	probable arsenical pump
Rv2224c	-	probable exported protease	Rv1280c	<i>oppA</i>	probable oligopeptide transport protein	Rv2685	<i>arsB</i>	probable arsenical pump
Rv2301	-	probable cutinase	Rv1283c	<i>oppB</i>	oligopeptide transport protein	Rv3578	<i>arsB2</i>	probable arsenical pump
Rv2345	-	precursor of probable membrane protein	Rv1282c	<i>oppC</i>	oligopeptide transport system per- mease	Rv2643	<i>arsC</i>	probable arsenical pump
Rv2672	-	putative exported protease	Rv1281c	<i>oppD</i>	probable peptide transport protein	Rv2397c	<i>cysA</i>	sulphate transport ATP-binding protein
Rv3019c	-	similar to Esat6	Rv2320c	<i>rocE</i>	probable cationic amino acid transport	Rv2399c	<i>cysT</i>	sulphate transport system perme- ase protein
Rv3036c	-	probable secreted protein	Rv3253c	-	possible proline permease	Rv2398c	<i>cysW</i>	sulphate transport system perme- ase protein
Rv3449	-	probable precursor of serine pro- tease	Rv3454	-		Rv1857	<i>modA</i>	molybdate binding protein
Rv3451	-	probable cutinase	2. Cations			Rv1858	<i>modB</i>	transport system permease, molybdate uptake
Rv3452	-	probable cutinase precursor	Rv2920c	<i>amt</i>	putative ammonium transporter	Rv1859	<i>modC</i>	molybdate uptake ABC- transporter
Rv3724	-	probable cutinase precursor	Rv1607	<i>chaA</i>	putative calcium/proton antiporter	Rv1860	<i>modD</i>	precursor of Apa (45/47 kD secreted protein)
3. Murein sacculus and peptidoglycan			Rv1239c	<i>corA</i>	probable magnesium and cobalt transport protein	Rv2329c	<i>nark1</i>	probable nitrite extrusion protein
Rv2911	<i>dacB</i>	penicillin binding protein	Rv0092	<i>ctpA</i>	cation-transporting ATPase	Rv1737c	<i>nark2</i>	nitrite extrusion protein
Rv2981c	<i>ddlA</i>	D-alanine-D-alanine ligase A	Rv0103c	<i>ctpB</i>	cation transport ATPase	Rv0261c	<i>nark3</i>	nitrite extrusion protein1
Rv3809c	<i>glf</i>	UDP-galactopyranose mutase	Rv1469	<i>ctpD</i>	probable cadmium-transporting ATPase	Rv0267	<i>narU</i>	similar to nitrite extrusion protein 2
Rv1018c	<i>glmU</i>	UDP-N-acetylglucosamine pyrophosphorylase	Rv0908	<i>ctpE</i>	probable cation transport ATPase	Rv0934	<i>phoS1</i>	PstS component of phosphate uptake
Rv3382c	<i>lytB</i>	LytB protein homologue	Rv1997	<i>ctpF</i>	probable cation transport ATPase	Rv0928	<i>phoS2</i>	PstS component of phosphate uptake
Rv1110	<i>lytB'</i>	very similar to LytB	Rv1992c	<i>ctpG</i>	probable cation transport ATPase	Rv0820	<i>phoT</i>	phosphate transport system ABC transporter
Rv1315	<i>murA</i>	UDP-N-acetylglucosamine-1-car- boxyvinyltransferase	Rv0425c	<i>ctpH</i>	C-terminal region putative cation- transporting ATPase	Rv3301c	<i>phoY1</i>	phosphate transport system regulator
Rv0482	<i>murB</i>	UDP-N-acetylenolpyruvoylglu- cosamine reductase	Rv0107c	<i>ctpl</i>	probable magnesium transport ATPase	Rv0821c	<i>phoY2</i>	phosphate transport system regulator
Rv2152c	<i>murC</i>	UDP-N-acetyl-muramate-alanine ligase	Rv0969	<i>ctpV</i>	cation transport ATPase	Rv0545c	<i>pitA</i>	low-affinity inorganic phosphate transporter
Rv2155c	<i>murD</i>	UDP-N-acetylmuramoylalanine-D- glutamate ligase	Rv3044	<i>fecB</i>	putative FeIII-dicitrate transporter	Rv2281	<i>pitB</i>	phosphate permease
Rv2158c	<i>murE</i>	meso-diaminopimelate-adding enzyme	Rv0265c	<i>fecB2</i>	iron transport protein FeIII dici- trate transporter	Rv0930	<i>pstA1</i>	PstA component of phosphate uptake
Rv2157c	<i>murF</i>	D-alanine:D-alanine-adding enzyme	Rv1029	<i>kdpA</i>	potassium-transporting ATPase A chain	Rv0936	<i>pstA2</i>	PstA component of phosphate uptake
Rv2153c	<i>murG</i>	transferase in peptidoglycan syn- thesis				Rv0933	<i>pstB</i>	ABC transport component of phosphate uptake
Rv1338	<i>muri</i>	glutamate racemase				Rv0935	<i>pstC</i>	PstC component of phosphate uptake
Rv2156c	<i>murX</i>	phospho-N-acetylmuramoyl- petapeptide transferase				Rv0929	<i>pstC2</i>	membrane-bound component of
Rv3332	<i>nagA</i>	N-acetylglucosamine-6-P- deacetylase						
Rv0016c	<i>pbpA</i>	penicillin-binding protein						
Rv2163c	<i>pbpB</i>	penicillin-binding protein 2						
Rv0050	<i>ponA</i>	penicillin-binding protein						
Rv3682	<i>ponA'</i>	class A penicillin binding protein						
Rv0017c	<i>rodA</i>	FtsW/RodA/SpovE family						
Rv0907	-	probable penicillin binding protein						

Rv0932c	<i>pstS</i>	phosphate transport system PstS component of phosphate uptake	Rv1821	<i>secA2</i>	unit SecA, preprotein translocase sub-unit	Rv3500c	-	part of <i>mce4</i> operon
Rv2400c	<i>subI</i>	sulphate binding precursor	Rv2587c	<i>secD</i>	protein-export membrane protein	Rv3501c	-	part of <i>mce4</i> operon
Rv0143c	-	probable chloride channel	Rv0638	<i>secE</i>	SecE preprotein translocase	Rv3896c	-	putative p60 homologue
Rv1707	-	probable sulphate permease	Rv2586c	<i>secF</i>	protein-export membrane protein	Rv3922c	-	possible hemolysin
Rv1739c	-	possible sulphate transporter	Rv1440	<i>secG</i>	protein-export membrane protein	<i>B. IS elements, Repeated sequences, and Phage</i>		
Rv3679	-	possible anion transporter	Rv0732	<i>secY</i>	SecY subunit of preprotein translocase	1. IS elements		
Rv3680	-	probable anion transporter				IS6110	16 copies	
5. Fatty acid transport			Rv2462c	<i>tig</i>	chaperone protein, similar to trigger factor	IS1081	6 copies	
Rv2790c	<i>lip1</i>	non-specific lipid transport protein	Rv2813	-	probable general secretion pathway protein	Others	37 copies	
Rv3540c	<i>lip2</i>	non-specific lipid transport protein				2. REP13E12 family		
6. Efflux proteins						7 copies		
Rv2936	<i>drvA</i>	similar daunorubicin resistance ABC-transporter	<i>E. Adaptations and atypical conditions</i>			3. Phage-related functions		
Rv2937	<i>drvB</i>	similar daunorubicin resistance transmembrane protein	Rv1901	<i>cinA</i>	competence damage protein	Rv2894c	<i>xerC</i>	integrase/recombinase
Rv2938	<i>drvC</i>	similar daunorubicin resistance transmembrane protein	Rv3648c	<i>cspA</i>	cold shock protein, transcriptional regulator	Rv1701	<i>xerD</i>	integrase/recombinase
Rv2846c	<i>efpA</i>	putative efflux protein	Rv0871	<i>cspB</i>	probable cold shock protein	Rv1054	-	integrase-a
Rv3065	<i>emrE</i>	resistance to ethidium bromide	Rv3063	<i>cstA</i>	starvation-induced stress response protein	Rv1055	-	integrase-b
Rv0783c	-	multidrug resistance protein	Rv3490	<i>otsA</i>	probable $\alpha,\alpha$ -trehalose-phosphate synthase	Rv1573	-	phiRV1 phage related protein
Rv0849	-	possible quinolone efflux pump	Rv2006	<i>otsB</i>	trehalose-6-phosphate phosphatase	Rv1574	-	phiRV1 phage related protein
Rv1145	-	probable drug transporter	Rv3372	<i>otsB2</i>	trehalose-6-phosphate phosphatase	Rv1575	-	phiRV1 phage related protein
Rv1146	-	probable drug transporter	Rv3758c	<i>proV</i>	osmoprotection ABC transporter	Rv1576c	-	phiRV1 phage related protein
Rv1250	-	probable drug efflux protein	Rv3757c	<i>proW</i>	transport system permease	Rv1577c	-	phiRV1 possible prohead protease
Rv1258c	-	probable multidrug resistance pump	Rv3759c	<i>proX</i>	similar to osmoprotection proteins	Rv1578c	-	phiRV1 phage related protein
Rv1410c	-	probable drug efflux protein	Rv3756c	<i>proZ</i>	transport system permease	Rv1579c	-	phiRV1 phage related protein
Rv1819c	-	probable multidrug resistance pump	Rv1026	-	probable pppGpp-5-phosphohydrolyase	Rv1580c	-	phiRV1 phage related protein
Rv2136c	-	putative bacitracin resistance protein	<i>F. Detoxification</i>			Rv1581c	-	phiRV1 phage related protein
Rv2209	-	probable drug efflux protein	Rv2428	<i>ahpC</i>	alkyl hydroperoxide reductase	Rv1582c	-	phiRV1 phage related protein
Rv2333c	-	probable tetracycline C resistance protein	Rv2429	<i>ahpD</i>	member of AhpC/TSA family	Rv1583c	-	phiRV1 phage related protein
Rv2994	-	probable fluoroquinolone efflux protein	Rv2238c	<i>ahpE</i>	member of AhpC/TSA family	Rv1584c	-	phiRV1 phage related protein
Rv1877	-	probable drug efflux protein	Rv2521	<i>bcp</i>	bacterioferritin comigratory protein	Rv1585c	-	phiRV1 phage related protein
Rv2459	-	probable drug efflux protein	Rv1608c	<i>bcpB</i>	probable bacterioferritin comigratory protein	Rv1586c	-	phiRV1 integrase
<i>B. Chaperones/Heat shock</i>			Rv3473c	<i>bpoA</i>	probable non-heme bromoperoxidase	Rv2309c	-	integrase
Rv0384c	<i>clpB</i>	heat shock protein	Rv1123c	<i>bpoB</i>	probable non-heme bromoperoxidase	Rv2310	-	excisionase
Rv0352	<i>dnaJ</i>	acts with GrpE to stimulate DnaK ATPase	Rv0554	<i>bpoC</i>	probable non-heme bromoperoxidase	Rv2646	-	phiRV2 integrase
Rv2373c	<i>dnaJ2</i>	DnaJ homologue	Rv3617	<i>ephA</i>	probable epoxide hydrolase	Rv2647	-	phiRV2 phase related protein
Rv0350	<i>dnaK</i>	70 kD heat shock protein, chromosome replication	Rv1938	<i>ephB</i>	probable epoxide hydrolase	Rv2650c	-	phiRV2 phase related protein
Rv3417c	<i>groEL1</i>	60 kD chaperonin 1	Rv1124	<i>ephC</i>	probable epoxide hydrolase	Rv2651c	-	phiRV2 prohead protease
Rv0440	<i>groEL2</i>	60 kD chaperonin 2	Rv2214c	<i>ephD</i>	probable epoxide hydrolase	Rv2652c	-	phiRV2 phase related protein
Rv3418c	<i>groES</i>	10 kD chaperone	Rv3670	<i>ephE</i>	probable epoxide hydrolase	Rv2653c	-	phiRV2 phase related protein
Rv0351	<i>grpE</i>	stimulates DnaK ATPase activity	Rv0134	<i>ephF</i>	probable epoxide hydrolase	Rv2654c	-	phiRV2 phase related protein
Rv2374c	<i>hrcA</i>	heat-inducible transcription repressor	Rv3171c	<i>hpx</i>	probable non-heme haloperoxidase	Rv2655c	-	phiRV2 phase related protein
Rv0251c	<i>hsp</i>	possible heat shock protein	Rv1908c	<i>katG</i>	catalase-peroxidase	Rv2656c	-	phiRV2 phase related protein
Rv0353	<i>hspR</i>	heat shock regulator	Rv3846	<i>sodA</i>	superoxide dismutase	Rv2657c	-	similar to gp36 of mycobacteriophage L5
Rv2031c	<i>hspX</i>	14kD antigen, heat shock protein	Rv0432	<i>sodC</i>	superoxide dismutase precursor - (Cu-Zn)	Rv2658c	-	phiRV2 phase related protein
Rv2299c	<i>htpG</i>	Hsp20 family	Rv1932	<i>tpx</i>	thiol peroxidase	Rv2659c	-	phiRV2 integrase
Rv0563	<i>htpX</i>	heat shock protein Hsp90 family	Rv0634c	-	putative glyoxylase II	Rv2830c	-	similar to phage P1 <i>phd</i> gene
Rv2701c	<i>uhb</i>	putative extragenic suppressor protein	Rv2581c	-	putative glyoxylase II	Rv3750c	-	excisionase
Rv3269	-	probable heat shock protein	Rv3177	-	probable non-heme haloperoxidase	Rv3751	-	putative integrase
<i>C. Cell division</i>			IV. Other			<i>C. PE and PPE families</i>		
Rv3641c	<i>fic</i>	possible cell division protein	<i>A. Virulence</i>			1. PE family		
Rv3102c	<i>ftsE</i>	membrane protein	Rv0169	<i>mce1</i>	cell invasion protein	PE subfamily	38 members	
Rv3610c	<i>ftsH</i>	inner membrane protein, chaperone	Rv0589	<i>mce2</i>	cell invasion protein	PE_PGRS subfamily	61 members	
Rv2748c	<i>ftsK</i>	chromosome partitioning	Rv1966	<i>mce3</i>	cell invasion protein	2. PPE family		
Rv2151c	<i>ftsQ</i>	ingrowth of wall at septum	Rv3499c	<i>mce4</i>	cell invasion protein	<i>D. Antibiotic production and resistance</i>		
Rv2154c	<i>ftsW</i>	membrane protein (shape determination)	Rv3100c	<i>smfB</i>	probable small protein b	Rv2068c	<i>blaC</i>	class A $\beta$ -lactamase
Rv3101c	<i>ftsX</i>	membrane protein	Rv1694	<i>tlyA</i>	cytotoxin/hemolysin homologue	Rv3290c	<i>lat</i>	lysine- $\epsilon$ aminotransferase
Rv2921c	<i>ftsY</i>	cell division protein FtsY	Rv0024	-	putative p60 homologue	Rv2043c	<i>pncA</i>	pyrazinamide resistance/sensitivity
Rv2150c	<i>ftsZ</i>	circumferential ring, GTPase	Rv0167	-	part of <i>mce1</i> operon	Rv0133	-	possible puromycin N-acetyltransferase
Rv3919c	<i>gid</i>	glucose inhibited division protein B	Rv0168	-	part of <i>mce1</i> operon	Rv0262c	-	aminoglycoside 2'-N-acetyltransferase
Rv3625c	<i>mesJ</i>	probable cell cycle protein	Rv0170	-	part of <i>mce1</i> operon	Rv0802c	-	acetyltransferase
Rv3917c	<i>parA</i>	chromosome partitioning; DNA binding	Rv0171	-	part of <i>mce1</i> operon	Rv1082	-	similar to <i>S. lincolnensis</i> <i>ImbE</i>
Rv3918c	<i>parB</i>	possibly involved in chromosome partitioning	Rv0172	-	part of <i>mce1</i> operon	Rv1170	-	similar to <i>S. lincolnensis</i> <i>ImbE</i>
Rv2922c	<i>smc</i>	member of Smc1/Cut3/Cut14 family	Rv0173	-	part of <i>mce1</i> operon	Rv1347c	-	possible aminoglycoside 6'-N-acetyltransferase
Rv0012	-	possible cell division protein	Rv0587	-	part of <i>mce2</i> operon	Rv2036	-	similar to lincomycin production genes
Rv0435c	-	ATPase of AAA-family	Rv0588	-	part of <i>mce2</i> operon	Rv2303c	-	similar to <i>S. griseus</i> macrotetrolide resistance protein
Rv2115c	-	ATPase of AAA-family	Rv0589	-	part of <i>mce2</i> operon	Rv3225c	-	probable aminoglycoside 3'-phosphotransferases
Rv3213c	-	possible role in chromosome segregation	Rv0590	-	part of <i>mce2</i> operon	Rv3700c	-	probable acetyltransferase
Rv1708	-	possible role in chromosome partitioning	Rv0591	-	part of <i>mce2</i> operon	Rv3817	-	probable aminoglycoside 3'-phosphotransferase
<i>D. Protein and peptide secretion</i>			Rv0592	-	part of <i>mce2</i> operon	<i>E. Bacteriocin-like proteins</i>		
Rv2916c	<i>ffh</i>	signal recognition particle protein	Rv0594	-	part of <i>mce2</i> operon	<i>F. Cytochrome P450 enzymes</i>		
Rv2903c	<i>lepB</i>	signal peptidase I	Rv1085c	-	possible hemolysin	<i>G. Coenzyme F420-dependent enzymes</i>		
Rv1614	<i>lgt</i>	prolipoprotein diacylglycerol transferase	Rv1477	-	putative exported p60 protein homologue	<i>H. Miscellaneous transferases</i>		
Rv1539	<i>lspA</i>	lipoprotein signal peptidase	Rv1478	-	putative exported p60 protein homologue	<i>I. Miscellaneous phosphatases, lyases, and hydrolases</i>		
Rv0379	<i>sec</i>	probable transport protein	Rv1566c	-	putative exported p60 protein homologue	<i>J. Cyclases</i>		
Rv3240c	<i>secA</i>	SecA, preprotein translocase sub-	Rv1964	-	part of <i>mce3</i> operon	<i>K. Chelataes</i>		
			Rv1965	-	part of <i>mce3</i> operon	<i>V. Conserved hypotheticals</i>		
			Rv1967	-	part of <i>mce3</i> operon	<i>VI. Unknowns</i>		
			Rv1968	-	part of <i>mce3</i> operon	TOTAL		
			Rv1969	-	part of <i>mce3</i> operon	3924		
			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			