Supplementary information to:

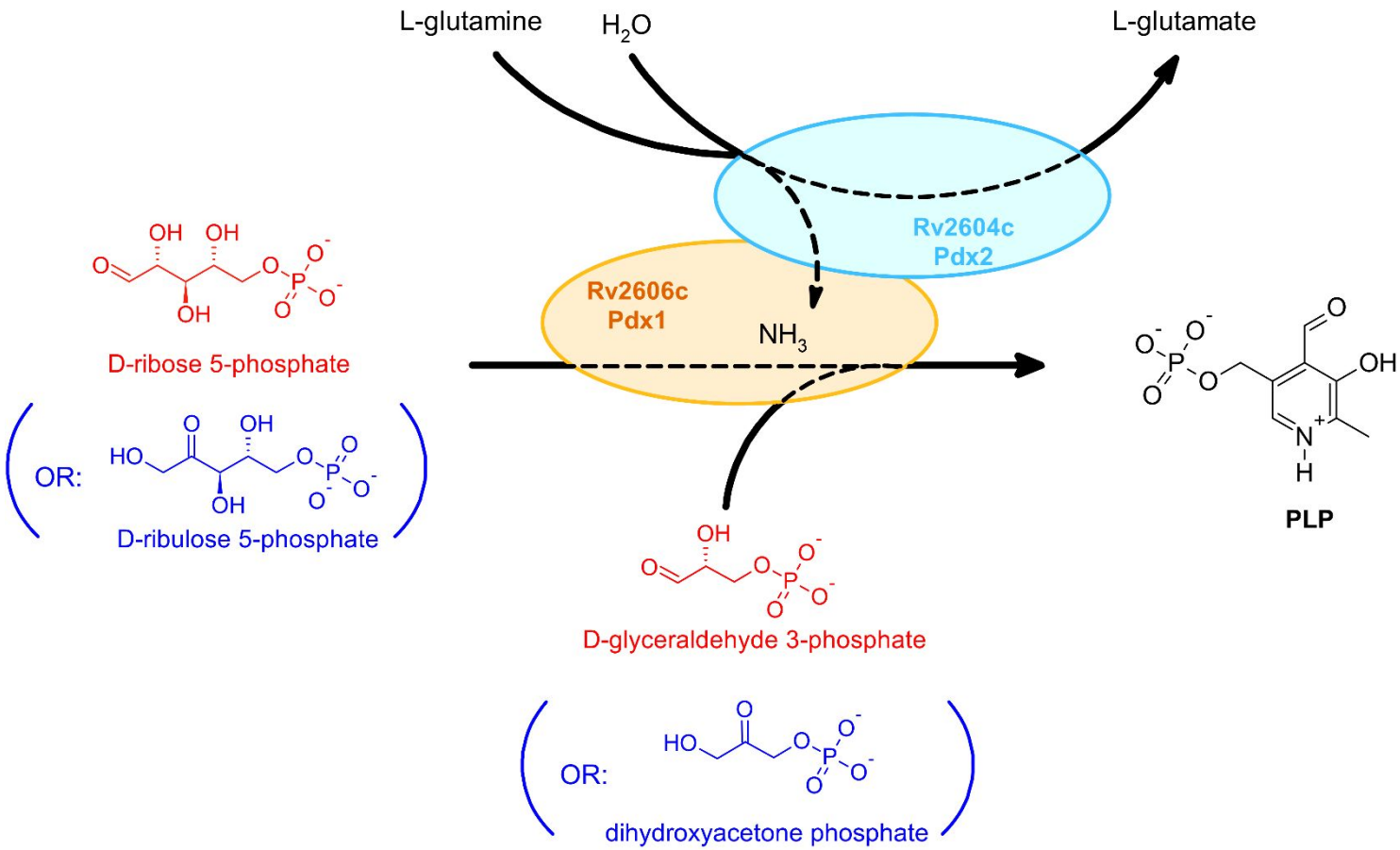
The pyridoxal-5'-phosphate dependent enzymes of *Mycobacterium tuberculosis*

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Supplementary figure 1 – Biosynthesis of vitamin B6 in *M. tuberculosis*. *Mtb* produces vitamin B6 via the so-called deoxyxylulose 5-phosphate-(DXP-) independent pathway [1], which is widespread among archaea, plants, fungi and a variety of bacteria (whereas a different, DXP-dependent pathway, which was extensively studied in *Escherichia coli*, is found in a smaller subset of bacteria)[2,3]. In this pathway, the biosynthesis of PLP from simple phosphorylated sugars is accomplished thanks to the activity of just two enzymes, termed Pdx1 and Pdx2 (Rv2606c and Rv2604c) [1] that together form a PLP synthase complex. The complex can employ either ribose 5-phosphate and glyceraldehyde-3-phosphate or ribulose 5-phosphate and dihydroxyacetone phosphate as carbon sources [1], whereas the PLP nitrogen atom derives from glutamine. The structure of Rv2606c (Pdx1) has been determined experimentally [4]. *Mtb* also possesses a salvage pathway for reconversion of pyridoxamine 5'-phosphate (or pyridoxine 5'-phosphate) into PLP, thanks to the FMN-dependent oxidase PdxH (Rv2607) [5,6].

Supplementary Table 1 – An extended overview of the PLP-dependent enzymes encoded in the *M. tuberculosis* H37Rv genome. This table extends and integrates Table 1 in the main text, by providing information about (1) the structural family ('fold-type') to which the enzyme belongs; (2) the NCBI refseqs corresponding to each gene product; (3) the occurrence of orthologs (>65% identical) of the *Mtb* genes in *Mycolicibacterium smegmatis*, which is commonly used as a nonpathogenic and fast-growing model organism to study mycobacteria; (4) the occurrence of structural homologs (arbitrarily defined as sequences showing >30% identity to the *Mtb* enzyme) encoded in the human genome and (5) the occurrence of functional homologs (that is, enzymes that are known to catalyze the same reaction) in the human metabolism, irrespective of their structure.

Gene locus	Gene name	Established or putative catalytic function	Validation	Ref.	Essential?	Fold type	NCBI refseq	Ortholog in *M. smegmatis* MC2 155	Homolog in *H. sapiens*	
									Sequence	Function
Rv0032	*bioF2*	Serine C-palmitoyltransferase (EC 2.3.1.50) ?	-	-	1/4	I	NP_214546	-	GCAT	SPTLC2 ? SPTLC3 ?
Rv0070c	*glyA2*	Serine hydroxymethyltransferase (EC 2.1.2.1)	B	[7]	0/4	I	NP_214584	-	SHMT2	SHMT1, SHMT2
Rv0075	-	L-cysteine desulfidase (C-S lyase) (EC 4.4.1.28) ?	-	-	0/4	I	NP_214589	-	-	?
Rv0337c	*aspC*	Alanine aminotransferase (EC 2.6.1.2)	B	[8]	3/4	I	NP_214851	WP_003892107	GPT2	GPT, GPT2
Rv0391	*metZ*	O-succinylhomoserine sulfhydrylase (2.5.1.-)	G	[9]	1/4	I	NP_214905	WP_011727178	CTH	-
Rv0524	*hemL*	Glutamate-1-semialdehyde 2,1-aminomutase (EC 5.4.3.8)	-	-	4/4	I	NP_215038	WP_003892395	-	-
Rv0812	*pabC*	4-amino-4-deoxychorismate lyase / D-amino acid transaminase (EC 4.1.3.38/ 2.6.1.21) [g]	B	[10]	1/3	IV	YP_177757	WP_029104397	-	-
Rv0848	*cysK2*	S-sulfo-L-cysteine synthase (EC 2.8.5.1)	B	[11]	0/4	II	YP_177762	-	CBS	-
Rv0858c	*dapC*	Glutamine transaminase (EC 2.6.1.64/2.6.1.117)	-	-	0/4	I	NP_215373	WP_011730742	KYAT3	KIAT1, KYAT3
Rv0884c	*serC*	Phosphoserine aminotransferase (EC 2.6.1.52)	B	[12]	3/3	I	NP_215399	WP_003897096	-	PSAT1
Rv1077	*cysM2*	Cystathionine beta-synthase (EC 4.2.1.22)	B	[13]	0/4	II	YP_177782	WP_011730431	CBS	CBS
Rv1079	*metB*	Cystathionine gamma-lyase (EC 4.4.1.1)	B	[14,15]	0/3	I	NP_215595	WP_011730426	CTH	CTH
Rv1093	*glyA1*	Serine hydroxymethyltransferase (EC 2.1.2.1)	B	[7]	3/3	I	YP_177787	WP_011730415	SHMT2	SHMT1, SHMT2
Rv1178	-	Succinyldiaminopimelate transaminase (EC 2.6.1.17) [i]	B	[16]	0/4		NP_215694	WP_011730331	-	-
Rv1293	*lysA*	Diaminopimelate decarboxylase (EC 4.1.1.20)	B	[17,18]	4/4	III	NP_215809	WP_011730213	-	-

Rv1295	*thrC*	Threonine synthase (EC 4.2.3.1)	B	[19]	4/4	II	NP_215811	WP_011730211	-	-
Rv1328	*glgP*	Glycogen (glucan) phosphorylase (EC 2.4.1.1)	-		0/4	V	NP_215844	WP_011730188	-	PYGL, PYGM, PYGB
Rv1336	*cysM*	[CysO]-thiocarboxylate-dependent L-Cys synthase (EC 2.5.1.113)	B	[20,21]	0/4	II	NP_215852	WP_003896302	CBS	-
Rv1464	*csd*	Cysteine desulfurase, SufS-type (EC 2.8.1.7) [h]	B	[22][h]	4/4	I	NP_215980	WP_003894512	NFS1	NFS1
Rv1559	*ilvA*	Threonine ammonia-lyase (EC 4.3.1.19)	B	[23]	2/3	II	NP_216075	WP_003894570	SDS	SDS
Rv1568	*bioA*	S-adenosylmethionine : 8-amino-7-oxononanoate aminotransferase (EC 2.6.1.62)	B	[24]	1/4	I	NP_216084	WP_011728880	-	-
Rv1569	*bioF1*	8-amino-7-oxononanoate synthase (EC 2.3.1.47)	B	[25]	0/3	I	YP_177822	WP_011728881	GCAT	-
Rv1600	*hisC*	Histidinol-phosphate aminotransferase (EC 2.6.1.9)	B	[26]	4/4	I	YP_177823	WP_011728896	-	-
Rv1612	*trpB*	Tryptophan synthase beta subunit (EC 4.2.1.20)	B	[27]	3/3	II	NP_216128	WP_011728904	-	-
Rv1655	*argD*	Acetylornithine aminotransferase (EC 2.6.1.11)	B	[28]	4/4	I	NP_216171	WP_011729315	OAT	-
Rv1832	*gcvB*	Glycine dehydrogenase P protein (EC 1.4.4.2)	-	-	3/4	I	NP_216348	WP_011729226	GLDC	GLDC
Rv2148c	-	PLP-homeostasis protein (YggS family)	-	-	0/3	III	NP_216664	WP_014877975	PLPBP	PLPBP
Rv2210c	*ilvE*	Branched-chain amino acid aminotransferase (EC 2.6.1.42)	B	[29]	3/4	IV	NP_216726	WP_011729696	BCAT1	BCAT1, BCAT2
Rv2231c	*cobC*	Histidinol phosphate aminotransferase (EC 2.6.1.9) ?	B	[30]	1/3	I	NP_216747	-	-	-
Rv2294	-	Cystathionine beta-lyase / L-cysteine desulfidase (EC 4.4.1.8/4.4.1.28) ?	-	-	0/4	I	NP_216810	-	-	-
Rv2334	*cysK1*	O-acetylserine sulfhydrylase (EC 2.5.1.47)	B	[31]	0/3	II	YP_177868	-	-	-
Rv2531c	-	Putative amino acid decarboxylase (4.4.1.-) ?	-	-	0/4	I	YP_177889	-	-	-
Rv2589	*gabT*	4-aminobutyrate aminotransferase (EC 2.6.2.19)	-	-	0/4	I	NP_217105	WP_011728721[a]	OAT	ABAT
Rv3025c	*iscS*	Cysteine desulfurase, NifS-type (EC 2.8.1.7)	B	[32]	3/4	I	NP_217541	WP_011728292	NFS1	NFS1

Rv3290c	*lat*	L-lysine 6-transaminase (EC 2.6.1.36)	B	[33]	0/4	I	NP_217807	WP_003893146	ABAT	-
Rv3329	-	Taurine:pyruvate aminotransferase (EC 2.6.1.77)	-	-[f]	0/4	I	NP_217846	WP_003893069	PHYKPL	-
Rv3340	*metC*	O-acetylhomoserine sulfhydrylase (EC 2.5.1.49)	G	[34]	0/3	I	NP_217857	WP_003893059[b]	CTH	-
Rv3402c	-	dTDP-4-amino-4,6-dideoxy-D-glucose aminotransferase (EC 2.6.1.33)	B	[35]	0/4	I	NP_217919	-	-	-
Rv3423c	*alr*	Alanine racemase (EC 5.1.1.1)	B	[36]	4/4	III	NP_217940	WP_011727747	-	-
Rv3432c	*gadB*	Glutamate decarboxylase (EC 4.1.1.15)	B	[37]	0/4	I	NP_217949	WP_011727746		GAD1, GAD2
Rv3565	*aspB*	Valine:pyruvate aminotransferase (EC 2.6.1.66)	B	[8]	1/2	I	NP_218082	WP_014878528	KYAT1	-
Rv3684	*Cds1*	L-cysteine desulfhydrase (C-S lyase) (EC 4.4.1.28)	B	[38]	0/4	II	NP_218201	WP_011731115	CBS	-
Rv3700c	*egtE*	Hercynylcysteine S-oxide lyase (EC 4.4.1.36)	G	-	0/3	I	NP_218217	WP_011731155	-	-
Rv3722c	-	Aspartate aminotransferase (EC 2.6.1.1)	B	[8]	4/4	I	NP_218239	WP_011731178	-	GOT1, GOT2
Rv3772	*hisC2*	Aromatic amino acid transaminase (EC 2.6.1.57)	B	[26]	0/4	I	NP_218289	WP_011731224	-	TAT

[a] At least three close homologs exist in the *M. smegmatis* MC2 155 genome: in addition to WP_011728721, also WP_003892002 and WP_011731460), the latter of which shows a much lower sequence similarity to Rv2589 as compared to the other two.

[b] Two homologs exist in the *M. smegmatis* MC2 155 genome: WP_003893059 and WP_011726769, the second of which may have a distinct function based on its much lower similarity to Rv3340 and on its occurrence in a distinct genomic context.

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