

## The metabolic building blocks of a minimal cell

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Supplementary material.

**Table S1.** List of enzymes and reactions modified from Gabaldon et. al. (2007). n.i.: non identified.

E.C. number	Name	Reaction	Gil <i>et. al.</i> 2004	Glass <i>et. al.</i> 2006
2.7.1.69	phosphotransferase system	glc + pep → g6p + pyr	PTS	MG041, 069, 429
5.3.1.9	glucose-6-phosphate isomerase	g6p ↔ f6p	PGI	MG111
2.7.1.11	6-phosphofructokinase	f6p + atp → fbp + adp	PFK	MG215
4.1.2.13	fructose-1,6-bisphosphate aldolase	fbp ↔ gdp + dhp	FBA	MG023
5.3.1.1	triose-phosphate isomerase	gdp ↔ dhp	TPI	MG431
1.2.1.12	glyceraldehyde-3-phosphate dehydrogenase	gdp + nad + p ↔ bpg + nadh	GAP	MG301
2.7.2.3	phosphoglycerate kinase	bpg + adp ↔ 3pg + atp	PGK	MG300
5.4.2.1	phosphoglycerate mutase	3pg ↔ 2pg	GPM	MG430
4.2.1.11	enolase	2pg ↔ pep	ENO	MG407
2.7.1.40	pyruvate kinase	pep + adp → pyr + atp	PYK	MG216
1.1.1.27	lactate dehydrogenase	pyr + nadh ↔ lac + nad	LDH	MG460
1.1.1.94	sn-glycerol-3-phosphate dehydrogenase	dhp + nadh → g3p + nad	GPS	n.i.
2.3.1.15	sn-glycerol-3-phosphate acyltransferase	g3p + pal → mag	PLSb	n.i.
2.3.1.51	1-acyl-sn-glycerol-3-phosphate	mag + pal → dag	PLSc	MG212

	acyltransferase			
2.7.7.41	phosphatidate cytidyltransferase	$\text{dag} + \text{ctp} \rightarrow \text{cdp-dag} + \text{pp}$	CDS	MG437
2.7.8.8	phosphatidylserine synthase	$\text{cdp-dag} + \text{ser} \rightarrow \text{pser} + \text{cmp}$	PSS	n.i.
4.1.1.65	phosphatidylserine decarboxylase	$\text{pser} \rightarrow \text{peta}$	PSD	n.i.
4.1.2.13	fructose-1,6-bisphosphate aldolase	$\text{gdp} + \text{e4p} \leftrightarrow \text{sbp}$	FBA2	MG023
3.1.3.37	sedoheptulose-1,7-bisphosphatase	$\text{sbp} \rightarrow \text{s7p} + \text{p}$	SPH	n.i.
2.2.1.1	transketolase	$\text{gdp} + \text{s7p} \leftrightarrow \text{rip} + \text{xip}$	TKT	MG066
2.2.1.1	transketolase	$\text{e4p} + \text{xip} \leftrightarrow \text{f6p} + \text{gdp}$	TKT2	MG066
5.1.3.1	ribulose-phosphate 3-epimerase	$\text{xip} \leftrightarrow \text{rup}$	RPE	MG112
5.3.1.6	ribose-5-phosphate isomerase	$\text{rup} \leftrightarrow \text{rip}$	RPI	MG396
2.7.6.1	phosphoribosylpyrophosphate synthetase	$\text{rip} + \text{atp} \rightarrow \text{prpp} + \text{amp}$	PRS	MG058
2.4.2.8	hypoxanthine phosphoribosyltransferase	$\text{prpp} + \text{ade} \rightarrow \text{amp} + \text{pp}$	HPT	MG276
2.4.2.8	hypoxanthine phosphoribosyltransferase	$\text{prpp} + \text{gua} \rightarrow \text{gmp} + \text{pp}$	HPT2	MG458
2.4.2.9	uracil phosphoribosyltransferase	$\text{prpp} + \text{ura} \rightarrow \text{ump} + \text{pp}$	UPP	MG030
3.6.1.1	inorganic pyrophosphatase	$\text{pp} \rightarrow 2\text{p}$	PPA	MG351
2.7.4.3	adenylate kinase	$\text{amp} + \text{atp} \rightarrow 2\text{adp}$	ADK	MG171
2.7.4.8	guanylate kinase	$\text{gmp} + \text{atp} \rightarrow \text{gdp} + \text{adp}$	GMK	MG107
2.7.4.14	cytidylate kinase	$\text{ump} + \text{atp} \rightarrow \text{udp} + \text{adp}$	CMK	MG330
2.7.4.14	cytidylate kinase	$\text{cmp} + \text{atp} \rightarrow \text{cdp} + \text{adp}$	CMK2	MG330
2.7.4.6	nucleoside diphosphate kinase	$\text{gdp} + \text{atp} \leftrightarrow \text{gtp} + \text{adp}$	NDK	MG216

2.7.4.6	nucleoside diphosphate kinase	$udp + atp \leftrightarrow utp + adp$	NDK2	
2.7.4.6	nucleoside diphosphate kinase	$dadp + atp \leftrightarrow datp + adp$	NDK3	MG216
2.7.4.6	nucleoside diphosphate kinase	$dgdp + atp \leftrightarrow dgtp + adp$	NDK4	MG216
2.7.4.6	nucleoside diphosphate kinase	$ctp + adp \leftrightarrow cdp + atp$	NDK5	
2.7.4.6	nucleoside diphosphate kinase	$dcdp + atp \leftrightarrow dctp + adp$	NDK6	
2.7.4.6	nucleoside diphosphate kinase	$dutp + adp \leftrightarrow dudp + atp$	NDK7	
2.7.4.6	nucleoside diphosphate kinase	$tdp + adp \leftrightarrow ttp + adp$	NDK8	MG034
1.17.4.1	ribonucleoside diphosphate reductase	$adp + nadh \rightarrow dadp + nad$	NRD	MG229–MG231
1.17.4.1	ribonucleoside diphosphate reductase	$gdp + nadh \rightarrow dgdp + nad$	NRD2	MG229–MG231
1.17.4.1	ribonucleoside diphosphate reductase	$cdp + nadh \rightarrow dcdp + nad$	NRD3	MG229–MG231
6.3.4.2	CTP synthase	$utp \rightarrow ctp$	PYR	n.i.
3.5.4.13	dCTP deaminase	$dctp \rightarrow dutp$	DCD	n.i.
2.7.4.9	thymidylate kinase	$dudp + adp \leftrightarrow dump + atp$	TMK	MG006
2.7.4.9	thymidylate kinase	$tmp + atp \leftrightarrow tdp + adp$	TMK2	MG006
2.1.1.45	thymidylate synthase	$dump + mthf \rightarrow dhf + tmp$	THY	MG227
1.5.1.3	dihydrofolate reductase	$dhf + nadh \leftrightarrow thf + nad$	DFR	MG228
2.1.2.1	glycine hydroxymethyltransferase	$ser + thf \leftrightarrow gly + mthf$	GHT	MG394

**Table S2.** Reactions, and compounds that make up *Ca. Nasuia deltocephalinicola*'s m-DAG. Reversible reactions are denoted by the superscript *r*.

Substrate KEGG id	ReactionID (E.C.number)	Definition	Product KEGG id
C00002	R00435 <sup>r</sup> (2.7.7.6)	ATP + RNA ↔ Diphosphate + RNA	C00046
C00131	R00375 <sup>r</sup> (2.7.7.7)	dATP + DNA ↔ Diphosphate + DNA	C00039
C00044	R00441 <sup>r</sup> (2.7.7.6)	GTP + RNA ↔ Diphosphate + RNA	C00046
C00286	R00376 <sup>r</sup> (2.7.7.7)	dGTP + DNA ↔ Diphosphate + DNA	C00039
C00075	R00443 (2.7.7.6)	UTP + RNA → Diphosphate + RNA	C00046
C00063	R00442 (2.7.7.6)	CTP + RNA → Diphosphate + RNA	C00046
C00458	R00377 (2.7.7.7)	dCTP + DNA → Diphosphate + DNA	C00039
C00459	R00378 (2.7.7.7)	dTTP + DNA → Diphosphate + DNA	C00039
C01118+C00283	R01288 (2.5.1.48)	O-Succinyl-L-homoserine + Hydrogen sulfide → L-Homocysteine + Succinate	C00155 + C00042
C00155	R04405 (2.1.1.14)	5-Methyltetrahydropteroyltri-L-glutamate + L-Homocysteine → Tetrahydropteroyltri-L-glutamate + L-Methionine	C00073
C02739	R01071 <sup>r</sup> (2.4.2.17)	1- (5-Phospho-D-ribosyl)-ATP + Diphosphate ↔ ATP + 5-Phospho-alpha-D-ribose 1-diphosphate	C00119
C01929	R01163 (1.1.1.23)	L-Histidinal + H <sub>2</sub> O + NAD <sup>+</sup> → L-Histidine + NADH + H <sup>+</sup>	C00135
C00860	R03012 (1.1.1.23)	L-Histidinal + NAD <sup>+</sup> → L-Histidinal + NADH + H <sup>+</sup>	C01929
C01100	R03243 <sup>r</sup> (2.6.1.9)	L-Histidinal phosphate + 2-Oxoglutarate ↔ 3- (Imidazol-4-yl)-2-oxopropyl phosphate + L-Glutamate	C01267
C04666	R03457 (4.2.1.19)	D-erythro-1- (Imidazol-4-yl)glycerol 3-phosphate → 3- (Imidazol-4-yl)-2-oxopropyl phosphate + H <sub>2</sub> O	C01267
C04896	R04640 (5.3.1.16)	5- (5-Phospho-D-ribosylaminoformimino)-1- (5-phosphoribosyl)-imidazole-4-carboxamide → N- (5'-Phospho-D-1'-ribulosylformimino)-5-amino-1- (5'-phospho-D-ribosyl)-4-imidazolecarboxamide	C04916
C02741	R04037 (3.5.4.19)	Phosphoribosyl-AMP + H <sub>2</sub> O → 5- (5-Phospho-D-ribosylaminoformimino)-1- (5-phosphoribosyl)-imidazole-4-carboxamide	C04916
C04916	R04558 (-.-.-)	N- (5'-Phospho-D-1'-ribulosylformimino)-5-amino-1- (5"-phospho-D-ribosyl)-4-imidazolecarboxamide + L-Glutamine → D-erythro-1- (Imidazol-4-yl)glycerol 3-phosphate + 1- (5'-Phosphoribosyl)-5-amino-4-imidazolecarboxamide + L-Glutamate	C04666 + C04677
C00166	R00694 <sup>r</sup> (2.6.1.9)	Phenylpyruvate + L-Glutamate ↔ L-Phenylalanine + 2-Oxoglutarate	C00079
C00082	R00734 <sup>r</sup> (2.6.1.9)	L-Tyrosine + 2-Oxoglutarate ↔ 3- (4-Hydroxyphenyl)pyruvate + L-Glutamate	C01179

C05698	R09365 (2.1.1.13 2.1.1.14)	Selenohomocysteine + 5-Methyltetrahydropteroyltri-L-glutamate → L-Selenomethionine + Tetrahydropteroyltri-L-glutamate	C05335
C18902	R09372 (1.8.1.9)	2 NADPH + 2 H+ + Methylselenic acid → 2 NADP+ + 2 H2O + Methaneselenol	C05703
C06148	R04639 (3.5.4.16)	2,5-Diamino-6- (5'-triphosphoryl-3',4'-trihydroxy-2'-oxopentyl)-amino-4-oxopyrimidine → 7,8-Dihydronoopterin 3'-triphosphate + H2O	C04895
C05923	R05048 (3.5.4.16)	2,5-Diaminopyrimidine nucleoside triphosphate → 2,5-Diamino-6- (5'-triphosphoryl-3',4'-trihydroxy-2'-oxopentyl)-amino-4-oxopyrimidine	C06148
C05922	R05046 (3.5.4.16)	Formamidopyrimidine nucleoside triphosphate + H2O → 2,5-Diaminopyrimidine nucleoside triphosphate + Formate	C05923
C00044	R00428 (3.5.4.16)	GTP + H2O → Formamidopyrimidine nucleoside triphosphate	C05922
C00283	R00858r (1.8.1.2)	Hydrogen sulfide + 3 NADP+ + 3 H2O ↔ Sulfite + 3 NADPH + 3 H+	C00094
C00053	R02021 (1.8.4.8)	Thioredoxin + 3'-Phosphoadenyl sulfate → Thioredoxin disulfide + Sulfite + Adenosine 3',5'-bisphosphate	C00094
C00082	R02918 (6.1.1.1)	ATP + L-Tyrosine + tRNA (Tyr) → AMP + Diphosphate + L-Tyrosyl-tRNA (Tyr)	C02839
C02282	R03905 (6.3.5.7)	Glutaminyl-tRNA + L-Glutamate + Orthophosphate + ADP → L-Glutamyl-tRNA (Gln) + L-Glutamine + ATP + H2O	C06112
C03402	R04212 (6.3.5.6)	L-Asparaginyl-tRNA (Asn) + L-Glutamate + Orthophosphate + ADP ↔ L-Aspartyl-tRNA (Asn) + L-Glutamine + ATP + H2O	C06113

**Table S3.** Reactions included in the reconstruction of the JCVI-syn3.0 reaction graph and the minimal organism constructed for this work and the pathways in which each reaction (can) participates.

Reacción	JCVI-syn3.0	This work	Pathways in which they can participate
R02691(2.4.1.46)	Yes	No	1,2-diacylglycerol 3-beta-galactosyltransferase [EC:2.4.1.46]
R02241(2.3.1.51)	Yes	Yes	1-acyl-sn-glycerol-3-phosphate acyltransferase [EC:2.3.1.51]///lysophosphatidate acyltransferase [EC:2.3.1.51]///lysocardiolipin and lysophospholipid acyltransferase [EC:2.3.1.- 2.3.1.51]///lysophospholipid acyltransferase 1/2 [EC:2.3.1.51 2.3.1.-]///lysophospholipid acyltransferase [EC:2.3.1.51 2.3.1.23 2.3.1.-]///lysophosphatidic acid acyltransferase / lysophosphatidylinositol acyltransferase [EC:2.3.1.51 2.3.1.-]///TAG lipase / steryl ester hydrolase / phospholipase A2 / LPA acyltransferase [EC:3.1.1.3 3.1.1.13 3.1.1.4 2.3.1.51]///lysophosphatidate acyltransferase [EC:2.3.1.51]///1-acylglycerol-3-phosphate O-acyltransferase [EC:2.3.1.51]
R00508(3.1.3.7)	Yes	No	3'(2'), 5'-bisphosphate nucleotidase [EC:3.1.3.7]///bifunctional oligoribonuclease and PAP phosphatase NrnA [EC:3.1.3.7 3.1.13.3]///3'(2'), 5'-bisphosphate nucleotidase / inositol polyphosphate 1-phosphatase [EC:3.1.3.7 3.1.3.57]///inositol monophosphatase 3 [EC:3.1.3.25 3.1.3.7]
R01968(3.1.3.5)	Yes	No	5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]//2',3'-cyclic-nucleotide 2'-phosphodiesterase / 3'-nucleotidase / 5'-nucleotidase [EC:3.1.4.16 3.1.3.6 3.1.3.5]///5'-deoxynucleotidase [EC:3.1.3.89]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase / UDP-sugar diphosphatase [EC:3.1.3.5 3.6.1.45]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]
R02088(3.1.3.5)	Yes	No	5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]//2',3'-cyclic-nucleotide 2'-phosphodiesterase / 3'-nucleotidase / 5'-nucleotidase [EC:3.1.4.16 3.1.3.6 3.1.3.5]///5'-deoxynucleotidase [EC:3.1.3.89]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase / UDP-sugar diphosphatase [EC:3.1.3.5 3.6.1.45]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]
R01569(3.1.3.5)	Yes	No	5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]//2',3'-cyclic-nucleotide 2'-phosphodiesterase / 3'-nucleotidase / 5'-nucleotidase [EC:3.1.4.16 3.1.3.6 3.1.3.5]///5'-deoxynucleotidase [EC:3.1.3.89]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase / UDP-sugar diphosphatase [EC:3.1.3.5 3.6.1.45]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]
R01664(3.1.3.5)	Yes	No	5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]//2',3'-cyclic-nucleotide 2'-phosphodiesterase / 3'-nucleotidase / 5'-nucleotidase [EC:3.1.4.16 3.1.3.6 3.1.3.5]///5'-deoxynucleotidase [EC:3.1.3.89]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase / UDP-sugar diphosphatase [EC:3.1.3.5 3.6.1.45]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]
R02102(3.1.3.5)	Yes	No	5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]//2',3'-cyclic-nucleotide 2'-phosphodiesterase / 3'-nucleotidase / 5'-nucleotidase [EC:3.1.4.16 3.1.3.6 3.1.3.5]///5'-deoxynucleotidase [EC:3.1.3.89]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase / UDP-sugar diphosphatase [EC:3.1.3.5 3.6.1.45]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]
R00183(3.1.3.5)	Yes	No	5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]//2',3'-cyclic-nucleotide 2'-phosphodiesterase / 3'-nucleotidase / 5'-nucleotidase [EC:3.1.4.16 3.1.3.6 3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase / UDP-sugar diphosphatase [EC:3.1.3.5 3.6.1.45]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]
R01126(3.1.3.5)	Yes	No	5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]//2',3'-cyclic-nucleotide 2'-phosphodiesterase / 3'-nucleotidase / 5'-nucleotidase [EC:3.1.4.16 3.1.3.6 3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase / UDP-sugar diphosphatase [EC:3.1.3.5 3.6.1.45]///IMP and pyridine-specific 5'-nucleotidase [EC:3.1.3.99 3.1.3.-]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]

R01227(3.1.3.5)	Yes	No	5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]//2',3'-cyclic-nucleotide 2'-phosphodiesterase / 3'-nucleotidase / 5'-nucleotidase [EC:3.1.4.16 3.1.3.6 3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase / UDP-sugar diphosphatase [EC:3.1.3.5 3.6.1.45]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]
R02719(3.1.3.5)	Yes	No	5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]//2',3'-cyclic-nucleotide 2'-phosphodiesterase / 3'-nucleotidase / 5'-nucleotidase [EC:3.1.4.16 3.1.3.6 3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase / UDP-sugar diphosphatase [EC:3.1.3.5 3.6.1.45]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]
R00511(3.1.3.5)	Yes	No	5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]//2',3'-cyclic-nucleotide 2'-phosphodiesterase / 3'-nucleotidase / 5'-nucleotidase [EC:3.1.4.16 3.1.3.6 3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase / UDP-sugar diphosphatase [EC:3.1.3.5 3.6.1.45]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]
R00963(3.1.3.5)	Yes	No	5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]//2',3'-cyclic-nucleotide 2'-phosphodiesterase / 3'-nucleotidase / 5'-nucleotidase [EC:3.1.4.16 3.1.3.6 3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase / UDP-sugar diphosphatase [EC:3.1.3.5 3.6.1.45]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]
R02323(3.1.3.5)	Yes	No	5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]//5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase / UDP-sugar diphosphatase [EC:3.1.3.5 3.6.1.45]///IMP and pyridine-specific 5'-nucleotidase [EC:3.1.3.99 3.1.3.-]///pyrimidine and pyridine-specific 5'-nucleotidase [EC:3.1.3.-]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]
R03346(3.1.3.5)	Yes	No	5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]//5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase / UDP-sugar diphosphatase [EC:3.1.3.5 3.6.1.45]///IMP and pyridine-specific 5'-nucleotidase [EC:3.1.3.99 3.1.3.-]///pyrimidine and pyridine-specific 5'-nucleotidase [EC:3.1.3.-]///5'-nucleotidase [EC:3.1.3.5]
R01569(3.1.3.89)	Yes	No	5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]//2',3'-cyclic-nucleotide 2'-phosphodiesterase / 3'-nucleotidase / 5'-nucleotidase [EC:3.1.4.16 3.1.3.6 3.1.3.5]///5'-deoxynucleotidase [EC:3.1.3.89]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase / UDP-sugar diphosphatase [EC:3.1.3.5 3.6.1.45]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]
R01664(3.1.3.89)	Yes	No	5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]//2',3'-cyclic-nucleotide 2'-phosphodiesterase / 3'-nucleotidase / 5'-nucleotidase [EC:3.1.4.16 3.1.3.6 3.1.3.5]///5'-deoxynucleotidase [EC:3.1.3.89]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase / UDP-sugar diphosphatase [EC:3.1.3.5 3.6.1.45]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]
R02102(3.1.3.89)	Yes	No	5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]//2',3'-cyclic-nucleotide 2'-phosphodiesterase / 3'-nucleotidase / 5'-nucleotidase [EC:3.1.4.16 3.1.3.6 3.1.3.5]///5'-deoxynucleotidase [EC:3.1.3.89]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase / UDP-sugar diphosphatase [EC:3.1.3.5 3.6.1.45]///5'-nucleotidase [EC:3.1.3.5]///5'-nucleotidase [EC:3.1.3.5]
R04779(2.7.1.11)	Yes	Yes	6-phosphofructokinase 1 [EC:2.7.1.11]///6-phosphofructokinase 2 [EC:2.7.1.11]//ATP-dependent phosphofructokinase / diphosphate-dependent phosphofructokinase [EC:2.7.1.11 2.7.1.90]///6-phosphofructokinase [EC:2.7.1.11]
R00315(2.7.2.1)	Yes	No	acetate kinase [EC:2.7.2.1]
R01353(2.7.2.1)	Yes	No	acetate kinase [EC:2.7.2.1]///propionate kinase [EC:2.7.2.15]///propionate kinase [EC:2.7.2.15]
R04378(2.4.2.7)	Yes	No	adenine phosphoribosyltransferase [EC:2.4.2.7]
R00190(2.4.2.7)	Yes	Yes	adenine phosphoribosyltransferase [EC:2.4.2.7]//hypoxanthine phosphoribosyltransferase [EC:2.4.2.8]
R01229(2.4.2.7)	Yes	Yes	adenine phosphoribosyltransferase [EC:2.4.2.7]//hypoxanthine phosphoribosyltransferase [EC:2.4.2.8]//xanthine phosphoribosyltransferase [EC:2.4.2.22]//xanthine phosphoribosyltransferase [EC:2.4.2.22]//bifunctional protein

			TilS/HprT [EC:6.3.4.19 2.4.2.8]///hypoxanthine phosphoribosyltransferase [EC:2.4.2.8]
R01229(2.4.2.8)	Yes	Yes	adenine phosphoribosyltransferase [EC:2.4.2.7]///hypoxanthine phosphoribosyltransferase [EC:2.4.2.8]///xanthine phosphoribosyltransferase [EC:2.4.2.22]///xanthine phosphoribosyltransferase [EC:2.4.2.22]///bifunctional protein TilS/HprT [EC:6.3.4.19 2.4.2.8]///hypoxanthine phosphoribosyltransferase [EC:2.4.2.8]
R00185(2.7.1.74)	Yes	No	adenosine kinase [EC:2.7.1.20]///deoxycitidine kinase [EC:2.7.1.74]///deoxyadenosine/deoxycytidine kinase [EC:2.7.1.76 2.7.1.74]
R00086(3.6.1.15)	Yes	No	adenosinetriphosphatase [EC:3.6.1.3]///apyrase [EC:3.6.1.5]///nucleoside triphosphate diphosphatase [EC:3.6.1.9]//nucleoside-triphosphatase [EC:3.6.1.15]//apyrase [EC:3.6.1.5]///golgi apyrase [EC:3.6.1.5]
R11319(2.7.4.3)	Yes	No	adenylate kinase [EC:2.7.4.3]
R01547(2.7.4.11)	Yes	No	adenylate kinase [EC:2.7.4.3]//adenylate kinase [EC:2.7.4.3]//adenylate/nucleoside-diphosphate kinase [EC:2.7.4.3 2.7.4.6]
R01547(2.7.4.3)	Yes	No	adenylate kinase [EC:2.7.4.3]//adenylate kinase [EC:2.7.4.3]//adenylate/nucleoside-diphosphate kinase [EC:2.7.4.3 2.7.4.6]
R01801(2.7.8.5)	Yes	No	CDP-diacylglycerol---glycerol-3-phosphate 3-phosphatidyltransferase [EC:2.7.8.5]
R01800(2.7.8.8)	No	Yes	CDP-diacylglycerol---serine O-phosphatidyltransferase [EC:2.7.8.8]//CDP-diacylglycerol---serine O-phosphatidyltransferase [EC:2.7.8.8]
R00512(2.7.4.25)	Yes	Yes	CMP/dCMP kinase [EC:2.7.4.25]//pantoate ligase / CMP/dCMP kinase [EC:6.3.2.1 2.7.4.25]//UMP-CMP kinase [EC:2.7.4.14]//UMP-CMP kinase 2, mitochondrial [EC:2.7.4.14]
R01665(2.7.4.25)	Yes	No	CMP/dCMP kinase [EC:2.7.4.25]//pantoate ligase / CMP/dCMP kinase [EC:6.3.2.1 2.7.4.25]//UMP-CMP kinase [EC:2.7.4.14]//UMP-CMP kinase 2, mitochondrial [EC:2.7.4.14]
R00158(2.7.4.22)	Yes	Yes	CMP/dCMP kinase [EC:2.7.4.25]//uridylylate kinase [EC:2.7.4.22]//pantoate ligase / CMP/dCMP kinase [EC:6.3.2.1 2.7.4.25]//UMP-CMP kinase [EC:2.7.4.14]//UMP-CMP kinase 2, mitochondrial [EC:2.7.4.14]
R00571(6.3.4.2)	Yes	Yes	CTP synthase [EC:6.3.4.2]
R00573(6.3.4.2)	Yes	Yes	CTP synthase [EC:6.3.4.2]
R01663(3.5.4.12)	Yes	No	dCMP deaminase [EC:3.5.4.12]
R02325(3.5.4.13)	No	Yes	dCTP deaminase [EC:3.5.4.13]
R01667(3.6.1.12)	Yes	No	dCTP diphosphatase [EC:3.6.1.12]
R01668(3.6.1.12)	Yes	No	dCTP diphosphatase [EC:3.6.1.12]
R02089(2.7.1.76)	Yes	No	deoxyadenosine kinase [EC:2.7.1.76]///deoxyadenosine/deoxycytidine kinase [EC:2.7.1.76 2.7.1.74]
R01666(2.7.1.74)	Yes	No	deoxycytidine kinase [EC:2.7.1.74]///deoxyadenosine/deoxycytidine kinase [EC:2.7.1.76 2.7.1.74]//cytidine kinase [EC:2.7.1.213]
R01967(2.7.1.113)	Yes	No	deoxyguanosine kinase [EC:2.7.1.113]//deoxyguanosine kinase [EC:2.7.1.113]
R02235(1.5.1.3)	No	Yes	dihydrofolate reductase [EC:1.5.1.3]//dihydrofolate reductase / thymidylate synthase [EC:1.5.1.3 2.1.1.45]//dihydrofolate

			reductase (trimethoprim resistance protein) [EC:1.5.1.3]//dihydrofolate reductase (trimethoprim resistance protein) [EC:1.5.1.3]
R02094(2.7.4.9)	Yes	Yes	dTMP kinase [EC:2.7.4.9]
R02098(2.7.4.9)	Yes	Yes	dTMP kinase [EC:2.7.4.9]
R11896(3.6.1.23)	Yes	No	dUTP pyrophosphatase [EC:3.6.1.23]
R00161(2.7.7.2)	Yes	No	FAD synthetase [EC:2.7.7.2]//riboflavin kinase / FMN adenylyltransferase [EC:2.7.1.26 2.7.7.2]//FAD synthetase [EC:2.7.7.2]//FAD synthetase [EC:2.7.7.2]
R00942(6.3.2.17)	Yes	No	folylpolyglutamate synthase [EC:6.3.2.17]///dihydrofolate synthase / folylpolyglutamate synthase [EC:6.3.2.12 6.3.2.17]///dihydrofolate synthase / folylpolyglutamate synthase [EC:6.3.2.12 6.3.2.17]
R04241(6.3.2.17)	Yes	No	folylpolyglutamate synthase [EC:6.3.2.17]///dihydrofolate synthase / folylpolyglutamate synthase [EC:6.3.2.12 6.3.2.17]///dihydrofolate synthase / folylpolyglutamate synthase [EC:6.3.2.12 6.3.2.17]
R02237(6.3.2.17)	Yes	No	folylpolyglutamate synthase [EC:6.3.2.17]///dihydrofolate synthase / folylpolyglutamate synthase [EC:6.3.2.12 6.3.2.17]///dihydrofolate synthase [EC:6.3.2.12]//dihydrofolate synthase / folylpolyglutamate synthase [EC:6.3.2.12 6.3.2.17]///dihydrofolate synthase / dihydropteroate synthase [EC:6.3.2.12 2.5.1.15]
R00765(3.5.99.6)	Yes	No	glucosamine-6-phosphate deaminase [EC:3.5.99.6]
R02301(6.3.3.2)	Yes	No	glutamate formiminotransferase / 5-formyltetrahydrofolate cyclo-ligase [EC:2.1.2.5 6.3.3.2]//5-formyltetrahydrofolate cyclo-ligase [EC:6.3.3.2]
R01058(1.2.1.9)	Yes	No	glyceraldehyde-3-phosphate dehydrogenase (NADP+) [EC:1.2.1.9]///glyceraldehyde-3-phosphate dehydrogenase [NAD(P)+] [EC:1.2.1.90]
R00847(2.7.1.30)	Yes	No	glycerol kinase [EC:2.7.1.30]
R00851(2.3.1.15)	No	Yes	glycerol-3-phosphate O-acyltransferase 1/2 [EC:2.3.1.15]//glycerol-3-phosphate O-acyltransferase [EC:2.3.1.15]//glycerol-3-phosphate O-acyltransferase [EC:2.3.1.15]///glycerol-3-phosphate O-acyltransferase 3/4 [EC:2.3.1.15]//glycerol-3-phosphate O-acyltransferase / dihydroxyacetone phosphate acyltransferase [EC:2.3.1.15 2.3.1.42]//glycerol-3-phosphate acyltransferase [EC:2.3.1.15 2.3.1.198]
R00945(2.1.2.1)	Yes	Yes	glycine hydroxymethyltransferase [EC:2.1.2.1]
R09099(2.1.2.1)	Yes	No	glycine hydroxymethyltransferase [EC:2.1.2.1]
R00332(2.7.4.8)	Yes	Yes	guanylate kinase [EC:2.7.4.8]
R02090(2.7.4.8)	Yes	No	guanylate kinase [EC:2.7.4.8]
R01625(2.7.8.7)	Yes	No	holo-[acyl-carrier protein] synthase [EC:2.7.8.7]///4'-phosphopantetheinyl transferase [EC:2.7.8.-]
R08237(2.4.2.8)	Yes	No	hypoxanthine phosphoribosyltransferase [EC:2.4.2.8]
R08238(2.4.2.8)	Yes	No	hypoxanthine phosphoribosyltransferase [EC:2.4.2.8]

R08245(2.4.2.8)	Yes	No	hypoxanthine phosphoribosyltransferase [EC:2.4.2.8]
R01132(2.4.2.8)	Yes	No	hypoxanthine phosphoribosyltransferase [EC:2.4.2.8]///bifunctional protein TilS/HprT [EC:6.3.4.19 2.4.2.8]///hypoxanthine phosphoribosyltransferase [EC:2.4.2.8]
R02142(2.4.2.8)	Yes	No	hypoxanthine phosphoribosyltransferase [EC:2.4.2.8]///xanthine phosphoribosyltransferase [EC:2.4.2.22]///xanthine phosphoribosyltransferase [EC:2.4.2.22]///bifunctional protein TilS/HprT [EC:6.3.4.19 2.4.2.8]///hypoxanthine phosphoribosyltransferase [EC:2.4.2.8]
R02100(3.6.1.23)	Yes	No	inosine triphosphate pyrophosphatase [EC:3.6.1.-]///dUTP pyrophosphatase [EC:3.6.1.23]///XTP/dITP diphosphohydrolase [EC:3.6.1.66]
R00703(1.1.1.27)	No	Yes	L-lactate dehydrogenase [EC:1.1.1.27]
R03940(2.1.2.9)	Yes	No	methionyl-tRNA formyltransferase [EC:2.1.2.9]
R01655(3.5.4.9)	Yes	No	methylene tetrahydrofolate dehydrogenase (NADP+) / methenyltetrahydrofolate cyclohydrolase / formyltetrahydrofolate synthetase [EC:1.5.1.5 3.5.4.9 6.3.4.3]///methylene tetrahydrofolate dehydrogenase (NADP+) / methenyltetrahydrofolate cyclohydrolase [EC:1.5.1.5 3.5.4.9]///methenyltetrahydrofolate cyclohydrolase [EC:3.5.4.9]///methylene tetrahydrofolate dehydrogenase(NAD+) / 5,10-methenyltetrahydrofolate cyclohydrolase [EC:1.5.1.15 3.5.4.9]
R01220(1.5.1.5)	Yes	No	methylene tetrahydrofolate dehydrogenase (NADP+) / methenyltetrahydrofolate cyclohydrolase / formyltetrahydrofolate synthetase [EC:1.5.1.5 3.5.4.9 6.3.4.3]///methylene tetrahydrofolate/methylenetetrahydromethanopterin dehydrogenase (NADP+) [EC:1.5.1.5 1.5.1.-]//methylene tetrahydrofolate dehydrogenase (NADP+) / methenyltetrahydrofolate cyclohydrolase [EC:1.5.1.5 3.5.4.9]
R05168(3.5.1.25)	Yes	No	N-acetylgalactosamine-6-phosphate deacetylase [EC:3.5.1.25]
R02059(3.5.1.25)	Yes	No	N-acetylglucosamine-6-phosphate deacetylase [EC:3.5.1.25]
R02705(2.7.1.60)	Yes	No	N-acylmannosamine kinase [EC:2.7.1.60]///bifunctional UDP-N-acetylglucosamine 2-epimerase / N-acetylmannosamine kinase [EC:3.2.1.183 2.7.1.60]//N-acetylmannosamine-6-phosphate 2-epimerase / N-acetylmannosamine kinase [EC:5.1.3.9 2.7.1.60]
R00104(2.7.1.23)	Yes	No	NAD+ kinase [EC:2.7.1.23]
R00189(6.3.1.5)	Yes	No	NAD+ synthase [EC:6.3.1.5]
R01271(2.4.2.12)	Yes	No	nicotinamide phosphoribosyltransferase [EC:2.4.2.12]
R00137(2.7.7.18)	Yes	No	nicotinamide-nucleotide adenylyltransferase [EC:2.7.7.1]///nicotinate-nucleotide adenylyltransferase [EC:2.7.7.18]///nicotinamide mononucleotide adenylyltransferase [EC:2.7.7.1 2.7.7.18]///HTH-type transcriptional regulator, transcriptional repressor of NAD biosynthesis genes [EC:2.7.7.1 2.7.1.22]///bifunctional NMN adenylyltransferase/nudix hydrolase [EC:2.7.7.1 3.6.1.-]//nicotinamide-nucleotide adenylyltransferase [EC:2.7.7.1]
R03005(2.7.7.18)	Yes	No	nicotinamide-nucleotide adenylyltransferase [EC:2.7.7.1]///nicotinate-nucleotide adenylyltransferase [EC:2.7.7.18]///nicotinamide mononucleotide adenylyltransferase [EC:2.7.7.1 2.7.7.18]///HTH-type transcriptional regulator, transcriptional repressor of NAD biosynthesis genes [EC:2.7.7.1 2.7.1.22]///bifunctional NMN adenylyltransferase/nudix hydrolase [EC:2.7.7.1 3.6.1.-]//nicotinamide-nucleotide adenylyltransferase [EC:2.7.7.1]

R00615(3.6.1.15)	Yes	No	nucleoside-triphosphatase [EC:3.6.1.15]///ribosome biogenesis GTPase / thiamine phosphate phosphatase [EC:3.6.1.-3.1.3.100]
R00921(2.3.1.8)	Yes	No	phosphate acetyltransferase [EC:2.3.1.8]///phosphate acetyltransferase [EC:2.3.1.8]///phosphate propanoyltransferase [EC:2.3.1.222]///putative phosphotransacetylase [EC:2.3.1.8]
R00230(2.3.1.8)	Yes	No	phosphate acetyltransferase [EC:2.3.1.8]///phosphotransacetylase//phosphate acetyltransferase [EC:2.3.1.8]///putative phosphotransacetylase [EC:2.3.1.8]
R01799(2.7.7.41)	Yes	Yes	phosphatidate cytidylyltransferase [EC:2.7.7.41]
R04162(3.1.3.4)	Yes	No	phosphatidate phosphatase [EC:3.1.3.4]
R02029(3.1.3.27)	Yes	No	phosphatidylglycerophosphatase GEP4 [EC:3.1.3.27]///phosphatidylglycerophosphatase A [EC:3.1.3.27]///phosphatidylglycerophosphatase B [EC:3.1.3.27 3.1.3.81 3.1.3.4 3.6.1.27]///phosphatidylglycerophosphatase C [EC:3.1.3.27]
R01512(2.7.2.3)	Yes	Yes	phosphoglycerate kinase [EC:2.7.2.3]
R01969(2.4.2.1)	Yes	No	purine-nucleoside phosphorylase [EC:2.4.2.1]///purine-nucleoside phosphorylase [EC:2.4.2.1]
R02557(2.4.2.1)	Yes	No	purine-nucleoside phosphorylase [EC:2.4.2.1]///purine-nucleoside phosphorylase [EC:2.4.2.1]
R02748(2.4.2.1)	Yes	No	purine-nucleoside phosphorylase [EC:2.4.2.1]///purine-nucleoside phosphorylase [EC:2.4.2.1]
R02294(2.4.2.1)	Yes	No	purine-nucleoside phosphorylase [EC:2.4.2.1]///purine-nucleoside phosphorylase [EC:2.4.2.1]
R02295(2.4.2.1)	Yes	No	purine-nucleoside phosphorylase [EC:2.4.2.1]///purine-nucleoside phosphorylase [EC:2.4.2.1]
R01561(2.4.2.1)	Yes	No	purine-nucleoside phosphorylase [EC:2.4.2.1]///purine-nucleoside phosphorylase [EC:2.4.2.1]///purine/pyrimidine-nucleoside phosphorylase [EC:2.4.2.1 2.4.2.2]
R01863(2.4.2.1)	Yes	No	purine-nucleoside phosphorylase [EC:2.4.2.1]///purine-nucleoside phosphorylase [EC:2.4.2.1]///purine/pyrimidine-nucleoside phosphorylase [EC:2.4.2.1 2.4.2.2]
R02147(2.4.2.1)	Yes	No	purine-nucleoside phosphorylase [EC:2.4.2.1]///purine-nucleoside phosphorylase [EC:2.4.2.1]///purine/pyrimidine-nucleoside phosphorylase [EC:2.4.2.1 2.4.2.2]
R02297(2.4.2.1)	Yes	No	purine-nucleoside phosphorylase [EC:2.4.2.1]///purine-nucleoside phosphorylase [EC:2.4.2.1]///xanthosine phosphorylase [EC:2.4.2.-]///purine/pyrimidine-nucleoside phosphorylase [EC:2.4.2.1 2.4.2.2]
R02484(2.4.2.1)	Yes	No	pyrimidine-nucleoside phosphorylase [EC:2.4.2.2]///uridine phosphorylase [EC:2.4.2.3]///thymidine phosphorylase [EC:2.4.2.4]///purine-nucleoside phosphorylase [EC:2.4.2.1]///purine-nucleoside phosphorylase [EC:2.4.2.1]
R00200(2.7.1.40)	Yes	Yes	pyruvate kinase [EC:2.7.1.40]//pyruvate kinase isozymes R/L [EC:2.7.1.40]
R00430(2.7.1.40)	Yes	Yes	pyruvate kinase [EC:2.7.1.40]//pyruvate kinase isozymes R/L [EC:2.7.1.40]
R01138(2.7.1.40)	Yes	Yes	pyruvate kinase [EC:2.7.1.40]//pyruvate kinase isozymes R/L [EC:2.7.1.40]
R01858(2.7.1.40)	Yes	Yes	pyruvate kinase [EC:2.7.1.40]//pyruvate kinase isozymes R/L [EC:2.7.1.40]

R00549(2.7.1.26)	Yes	No	riboflavin kinase [EC:2.7.1.26]///riboflavin kinase / FMN adenylyltransferase [EC:2.7.1.26 2.7.7.2]///riboflavin kinase / FMN hydrolase [EC:2.7.1.26 3.1.3.102]
R08363(1.17.4.1)	Yes	No	ribonucleoside-diphosphate reductase subunit M1 [EC:1.17.4.1]///ribonucleoside-diphosphate reductase subunit M2 [EC:1.17.4.1]
R11893(1.17.4.1)	Yes	No	ribonucleoside-diphosphate reductase subunit M1 [EC:1.17.4.1]///ribonucleoside-diphosphate reductase subunit M2 [EC:1.17.4.1]
R02018(1.17.4.1)	Yes	No	ribonucleotide reductase, class II [EC:1.17.4.1]///ribonucleoside-diphosphate reductase alpha chain [EC:1.17.4.1]///ribonucleoside-diphosphate reductase beta chain [EC:1.17.4.1]
R02017(1.17.4.1)	Yes	Yes	ribonucleotide reductase, class II [EC:1.17.4.1]///ribonucleoside-diphosphate reductase alpha chain [EC:1.17.4.1]///ribonucleoside-diphosphate reductase beta chain [EC:1.17.4.1]///ribonucleoside-diphosphate reductase subunit M1 [EC:1.17.4.1]///ribonucleoside-diphosphate reductase subunit M2 [EC:1.17.4.1]
R02019(1.17.4.1)	Yes	Yes	ribonucleotide reductase, class II [EC:1.17.4.1]///ribonucleoside-diphosphate reductase alpha chain [EC:1.17.4.1]///ribonucleoside-diphosphate reductase beta chain [EC:1.17.4.1]///ribonucleoside-diphosphate reductase subunit M1 [EC:1.17.4.1]///ribonucleoside-diphosphate reductase subunit M2 [EC:1.17.4.1]
R02024(1.17.4.1)	Yes	Yes	ribonucleotide reductase, class II [EC:1.17.4.1]///ribonucleoside-diphosphate reductase alpha chain [EC:1.17.4.1]///ribonucleoside-diphosphate reductase beta chain [EC:1.17.4.1]///ribonucleoside-diphosphate reductase subunit M1 [EC:1.17.4.1]///ribonucleoside-diphosphate reductase subunit M2 [EC:1.17.4.1]
R01049(2.7.6.1)	Yes	Yes	ribose-phosphate pyrophosphokinase [EC:2.7.6.1]
R07618(1.8.1.4)	Yes	No	rn00010: Glycolysis / Gluconeogenesis///rn00020: Citrate cycle (TCA cycle)///rn00280: Valine, leucine and isoleucine degradation///rn00620: Pyruvate metabolism///rn00640: Propionate metabolism///rn01100: Metabolic pathways///rn01110: Biosynthesis of secondary metabolites
R03270(1.2.4.1)	Yes	No	rn00010: Glycolysis / Gluconeogenesis///rn00020: Citrate cycle (TCA cycle)///rn00620: Pyruvate metabolism
R00014(1.2.4.1)	Yes	No	rn00010: Glycolysis / Gluconeogenesis///rn00020: Citrate cycle (TCA cycle)///rn00620: Pyruvate metabolism
R02569(2.3.1.12)	Yes	No	rn00010: Glycolysis / Gluconeogenesis///rn00020: Citrate cycle (TCA cycle)///rn00620: Pyruvate metabolism
R01070(4.1.2.13)	Yes	Yes	rn00010: Glycolysis / Gluconeogenesis///rn00030: Pentose phosphate pathway///rn00051: Fructose and mannose metabolism///rn01100: Metabolic pathways///rn01110: Biosynthesis of secondary metabolites///rn01120: Microbial metabolism in diverse environments///rn01200: Carbon metabolism///rn01230: Biosynthesis of amino acids
R02740(5.3.1.9)	Yes	Yes	rn00010: Glycolysis / Gluconeogenesis///rn00030: Pentose phosphate pathway///rn00520: Amino sugar and nucleotide sugar metabolism///rn01100: Metabolic pathways///rn01110: Biosynthesis of secondary metabolites///rn01120: Microbial metabolism in diverse environments///rn01200: Carbon metabolism
R02739(5.3.1.9)	Yes	No	rn00010: Glycolysis / Gluconeogenesis///rn00030: Pentose phosphate pathway///rn01100: Metabolic pathways///rn01110: Biosynthesis of secondary metabolites///rn01120: Microbial metabolism in diverse environments
R01015(5.3.1.1)	Yes	No	rn00010: Glycolysis / Gluconeogenesis///rn00051: Fructose and mannose metabolism///rn00562: Inositol phosphate metabolism///rn00710: Carbon fixation in photosynthetic organisms///rn01100: Metabolic pathways///rn01110: Biosynthesis of secondary metabolites///rn01120: Microbial metabolism in diverse environments///rn01200: Carbon

			metabolism///rn01230: Biosynthesis of amino acids
R00959(5.4.2.5)	Yes	No	rn00010: Glycolysis / Gluconeogenesis///rn00052: Galactose metabolism///rn00520: Amino sugar and nucleotide sugar metabolism///rn01100: Metabolic pathways///rn01110: Biosynthesis of secondary metabolites///rn01120: Microbial metabolism in diverse environments
R01518(5.4.2.12)	Yes	Yes	rn00010: Glycolysis / Gluconeogenesis///rn00260: Glycine, serine and threonine metabolism///rn00680: Methane metabolism///rn01100: Metabolic pathways///rn01110: Biosynthesis of secondary metabolites///rn01120: Microbial metabolism in diverse environments///rn01200: Carbon metabolism///rn01230: Biosynthesis of amino acids
R00658(4.2.1.11)	Yes	Yes	rn00010: Glycolysis / Gluconeogenesis///rn00680: Methane metabolism///rn01100: Metabolic pathways///rn01110: Biosynthesis of secondary metabolites///rn01120: Microbial metabolism in diverse environments///rn01200: Carbon metabolism///rn01230: Biosynthesis of amino acids
R01061(1.2.1.12)	Yes	Yes	rn00010: Glycolysis / Gluconeogenesis///rn00710: Carbon fixation in photosynthetic organisms///rn01100: Metabolic pathways///rn01110: Biosynthesis of secondary metabolites///rn01120: Microbial metabolism in diverse environments///rn01200: Carbon metabolism///rn01230: Biosynthesis of amino acids
R03321(5.3.1.9)	Yes	No	rn00010: Glycolysis / Gluconeogenesis///rn01100: Metabolic pathways///rn01110: Biosynthesis of secondary metabolites///rn01120: Microbial metabolism in diverse environments
R01529(5.1.3.1)	Yes	Yes	rn00030: Pentose phosphate pathway///rn00040: Pentose and glucuronate interconversions///rn00710: Carbon fixation in photosynthetic organisms///rn01100: Metabolic pathways///rn01110: Biosynthesis of secondary metabolites///rn01120: Microbial metabolism in diverse environments///rn01200: Carbon metabolism///rn01230: Biosynthesis of amino acids
R01057(5.4.2.7)	Yes	No	rn00030: Pentose phosphate pathway///rn00230: Purine metabolism///rn01100: Metabolic pathways
R01641(2.2.1.1)	Yes	Yes	rn00030: Pentose phosphate pathway///rn00710: Carbon fixation in photosynthetic organisms///rn01100: Metabolic pathways///rn01110: Biosynthesis of secondary metabolites///rn01120: Microbial metabolism in diverse environments///rn01200: Carbon metabolism///rn01230: Biosynthesis of amino acids
R01056(5.3.1.6)	Yes	Yes	rn00030: Pentose phosphate pathway///rn00710: Carbon fixation in photosynthetic organisms///rn01100: Metabolic pathways///rn01110: Biosynthesis of secondary metabolites///rn01120: Microbial metabolism in diverse environments///rn01200: Carbon metabolism///rn01230: Biosynthesis of amino acids
R01066(4.1.2.4)	Yes	No	rn00030: Pentose phosphate pathway///rn01100: Metabolic pathways
R02749(5.4.2.7)	Yes	No	rn00030: Pentose phosphate pathway///rn01100: Metabolic pathways
R01819(5.3.1.8)	Yes	No	rn00051: Fructose and mannose metabolism///rn00520: Amino sugar and nucleotide sugar metabolism///rn01100: Metabolic pathways///rn01110: Biosynthesis of secondary metabolites
R02568(4.1.2.13)	Yes	No	rn00051: Fructose and mannose metabolism///rn01100: Metabolic pathways///rn01120: Microbial metabolism in diverse environments
R09030(5.3.1.6)	Yes	No	rn00051: Fructose and mannose metabolism///rn01100: Metabolic pathways///rn01120: Microbial metabolism in diverse environments
R00291(5.1.3.2)	Yes	No	rn00052: Galactose metabolism///rn00520: Amino sugar and nucleotide sugar metabolism///rn01100: Metabolic pathways

R00505(5.4.99.9)	Yes	No	rn00052: Galactose metabolism//rn00520: Amino sugar and nucleotide sugar metabolism//rn01100: Metabolic pathways
R00127(2.7.4.3)	Yes	Yes	rn00230: Purine metabolism//rn01100: Metabolic pathways///rn01110: Biosynthesis of secondary metabolites
R03815(1.8.1.4)	Yes	No	rn00260: Glycine, serine and threonine metabolism
R00192(3.3.1.1)	Yes	No	rn00270: Cysteine and methionine metabolism//rn01100: Metabolic pathways
R00177(2.5.1.6)	Yes	No	rn00270: Cysteine and methionine metabolism///rn01100: Metabolic pathways//rn01110: Biosynthesis of secondary metabolites///rn01230: Biosynthesis of amino acids
R08364(1.17.4.1)	Yes	No	rn00480: Glutathione metabolism
R00771(5.3.1.9)	Yes	No	rn00500: Starch and sucrose metabolism//rn01100: Metabolic pathways//rn01110: Biosynthesis of secondary metabolites
R02087(5.1.3.9)	Yes	No	rn00520: Amino sugar and nucleotide sugar metabolism//rn01100: Metabolic pathways
R02239(3.1.3.4)	Yes	No	rn00561: Glycerolipid metabolism//rn00564: Glycerophospholipid metabolism//rn01100: Metabolic pathways///rn01110: Biosynthesis of secondary metabolites
R02055(4.1.1.65)	No	Yes	rn00564: Glycerophospholipid metabolism//rn01100: Metabolic pathways///rn01110: Biosynthesis of secondary metabolites
R00842(1.1.1.94)	No	Yes	rn00564: Glycerophospholipid metabolism//rn01110: Biosynthesis of secondary metabolites
R06522(3.1.3.4)	Yes	No	rn00600: Sphingolipid metabolism
R06520(3.1.3.4)	Yes	No	rn00600: Sphingolipid metabolism//rn01100: Metabolic pathways
R06521(3.1.3.4)	Yes	No	rn00600: Sphingolipid metabolism//rn01100: Metabolic pathways
R00939(1.5.1.3)	No	Yes	rn00670: One carbon pool by folate//rn00790: Folate biosynthesis//rn01100: Metabolic pathways
R01068(4.1.2.13)	Yes	No	rn00680: Methane metabolism//rn00710: Carbon fixation in photosynthetic organisms//rn01100: Metabolic pathways//rn01120: Microbial metabolism in diverse environments//rn01200: Carbon metabolism
R01829(4.1.2.13)	Yes	Yes	rn00710: Carbon fixation in photosynthetic organisms//rn01100: Metabolic pathways//rn01120: Microbial metabolism in diverse environments//rn01200: Carbon metabolism
R06590(2.2.1.1)	Yes	No	rn01051: Biosynthesis of ansamycins//rn01110: Biosynthesis of secondary metabolites
R03596(1.8.1.9)	Yes	No	thioredoxin reductase (NADPH) [EC:1.8.1.9]///thioredoxin reductase (NADPH) [EC:1.8.1.9]
R09372(1.8.1.9)	Yes	No	thioredoxin reductase (NADPH) [EC:1.8.1.9]///thioredoxin reductase (NADPH) [EC:1.8.1.9]
R01567(2.7.1.21)	Yes	No	thymidine kinase [EC:2.7.1.21]
R02099(2.7.1.21)	Yes	No	thymidine kinase [EC:2.7.1.21]
R08233(2.7.1.21)	Yes	No	thymidine kinase [EC:2.7.1.21]
R02101(2.1.1.45)	No	Yes	thymidylate synthase [EC:2.1.1.45]///dihydrofolate reductase / thymidylate synthase [EC:1.5.1.3 2.1.1.45]
R01827(2.2.1.2)	Yes	No	transaldolase [EC:2.2.1.2]///transaldolase / glucose-6-phosphate isomerase [EC:2.2.1.2 5.3.1.9]

R01830(2.2.1.1)	Yes	Yes	transketolase [EC:2.2.1.1]
R01067(2.2.1.1)	Yes	No	transketolase [EC:2.2.1.1]
R00966(2.4.2.9)	Yes	Yes	uracil phosphoribosyltransferase [EC:2.4.2.9]///pyrimidine operon attenuation protein / uracil phosphoribosyltransferase [EC:2.4.2.9]
R00289(2.7.7.9)	Yes	No	UTP--glucose-1-phosphate uridylyltransferase [EC:2.7.7.9]///UDP-sugar pyrophosphorylase [EC:2.7.7.64]///UTP---glucose-1-phosphate uridylyltransferase [EC:2.7.7.9]
R00156(2.7.4.6)	No	Yes	rn00240: Pyrimidine metabolism///rn01100: Metabolic pathways
R00570(2.7.4.6)	No	Yes	rn00240: Pyrimidine metabolism///rn01100: Metabolic pathways
R02326(2.7.4.6)	No	Yes	rn00240: Pyrimidine metabolism///rn01100: Metabolic pathways
R02331(2.7.4.6)	No	Yes	rn00240: Pyrimidine metabolism///rn01100: Metabolic pathways
R02093(2.7.4.6)	No	Yes	rn00240: Pyrimidine metabolism///rn01100: Metabolic pathways
R02738(2.7.1.199)	Yes	Yes	rn00010: Glycolysis / Gluconeogenesis///rn00520: Amino sugar and nucleotide sugar metabolism///rn01100: Metabolic pathways
R01843(2.7.1.11)	Yes	Yes	
R02324	No	Yes	rn00760: Nicotinate and nicotinamide metabolism///rn01100: Metabolic pathways
R00137	No	Yes	rn00760: Nicotinate and nicotinamide metabolism///rn01100: Metabolic pathways
R00549	No	Yes	rn00740: Riboflavin metabolism///rn01100: Metabolic pathways///rn01110: Biosynthesis of secondary metabolites
R00161	No	Yes	rn00740: Riboflavin metabolism///rn01100: Metabolic pathways///rn01110: Biosynthesis of secondary metabolites
R00619	No	Yes	rn00730: Thiamine metabolism///rn01100: Metabolic pathways
R00177	No	Yes	rn00270: Cysteine and methionine metabolism///rn01100: Metabolic pathways///rn01110: Biosynthesis of secondary metabolites///rn01230: Biosynthesis of amino acids
R00173	No	Yes	rn00750: Vitamin B6 metabolism///rn01100: Metabolic pathways
R02971	No	Yes	rn00770: Pantothenate and CoA biosynthesis
R03035	No	Yes	rn00770: Pantothenate and CoA biosynthesis///rn01100: Metabolic pathways
R00130	No	Yes	rn00770: Pantothenate and CoA biosynthesis///rn01100: Metabolic pathways
R03018	No	Yes	rn00770: Pantothenate and CoA biosynthesis///rn01100: Metabolic pathways
R04391	No	Yes	rn00770: Pantothenate and CoA biosynthesis
R04231	No	Yes	rn00770: Pantothenate and CoA biosynthesis///rn01100: Metabolic pathways

**Table S4.** Names of the enzymes and definition of each reaction involved in the comparison of the MBBs of the three networks under study.

Reaction	Enzyme name	Definition
R00156	ATP:UDP phosphotransferase	ATP + UDP ↔ ADP + UTP
R00158	ATP:UMP phosphotransferase	ATP + UMP ↔ ADP + UDP
R00332	ATP:GMP phosphotransferase	ATP + GMP ↔ ADP + GDP
R00430	GTP:pyruvate 2-O-phosphotransferase	GTP + Pyruvate ↔ GDP + Phosphoenolpyruvate
R00658	2-phospho-D-glycerate hydro-lyase (phosphoenolpyruvate-forming)	2-Phospho-D-glycerate ↔ Phosphoenolpyruvate + H <sub>2</sub> O
R00842	sn-Glycerol-3-phosphate:NAD+ 2-oxidoreductase	sn-Glycerol 3-phosphate + NAD+ ↔ Glycerone phosphate + NADH + H+
R00844	sn-Glycerol-3-phosphate:NADP+ 2-oxidoreductase	sn-Glycerol 3-phosphate + NADP+ ↔ Glycerone phosphate + NADPH + H+
R00966	UMP:diphosphate phospho-alpha-D-ribosyltransferase	UMP + Diphosphate ↔ Uracil + 5-Phospho-alpha-D-ribose 1-diphosphate
R01049	ATP:D-ribose-5-phosphate diphosphotransferase	ATP + D-Ribose 5-phosphate ↔ AMP + 5-Phospho-alpha-D-ribose 1-diphosphate
R01056	D-ribose-5-phosphate aldose-ketose-isomerase	D-Ribose 5-phosphate ↔ D-Ribulose 5-phosphate
R01061	D-glyceraldehyde-3-phosphate:NAD+ oxidoreductase (phosphorylating)	D-Glyceraldehyde 3-phosphate + Orthophosphate + NAD+ ↔ 3-Phospho-D-glyceroyl phosphate + NADH + H+
R01070	beta-D-fructose-1,6-bisphosphate D-glyceraldehyde-3-phosphate-lyase (glycerone-phosphate-forming)	beta-D-Fructose 1,6-bisphosphate ↔ Glycerone phosphate + D-Glyceraldehyde 3-phosphate
R01229	GMP:diphosphate 5-phospho-alpha-D-ribosyltransferase	GMP + Diphosphate ↔ Guanine + 5-Phospho-alpha-D-ribose 1-diphosphate
R01512	ATP:3-phospho-D-glycerate 1-phosphotransferase	ATP + 3-Phospho-D-glycerate ↔ ADP + 3-Phospho-D-glyceroyl phosphate
R01518	D-phosphoglycerate 2,3-phosphomutase	2-Phospho-D-glycerate ↔ 3-Phospho-D-glycerate
R01529	D-Ribulose-5-phosphate 3-epimerase	D-Ribulose 5-phosphate ↔ D-Xylulose 5-phosphate
R01641	sedoheptulose-7-phosphate:D-glyceraldehyde-3-phosphate glycolaldehyde transferase	Sedoheptulose 7-phosphate + D-Glyceraldehyde 3-phosphate ↔ D-Ribose 5-phosphate + D-Xylulose 5-phosphate
R01829	sedoheptulose 1,7-bisphosphate D-glyceraldehyde-3-phosphate-lyase	Sedoheptulose 1,7-bisphosphate ↔ Glycerone phosphate + D-Erythrose 4-phosphate
R01830	beta-D-Fructose 6-phosphate:D-glyceraldehyde-3-phosphate glycolaldehyde transferase	beta-D-Fructose 6-phosphate + D-Glyceraldehyde 3-phosphate ↔ D-Erythrose 4-phosphate + D-Xylulose 5-phosphate
R01843	ATP:Sedoheptulose 7-phosphate 1-phosphotransferase	ATP + Sedoheptulose 7-phosphate ↔ ADP + Sedoheptulose 1,7-bisphosphate
R02740	alpha-D-Glucose 6-phosphate ketol-isomerase	alpha-D-Glucose 6-phosphate ↔ beta-D-Fructose 6-phosphate

R04779	ATP:D-fructose-6-phosphate 1-phosphotransferase	ATP + beta-D-Fructose 6-phosphate ↔ ADP + beta-D-Fructose 1,6-bisphosphate
R02098	ATP:dUMP phosphotransferase	ATP + dUMP ↔ ADP + dUDP
R02331	ATP:dUDP phosphotransferase	ATP + dUDP ↔ ADP + dUTP
R00512	ATP: CMP phosphotransferase	ATP + CMP ↔ ADP + CDP
R00570	ATP: CDP phosphotransferase	ATP + CDP ↔ ADP + CTP
R02019	2'-Deoxyguanosine 5'-diphosphate: oxidized-thioredoxin 2'-oxidoreductase	dGDP + Thioredoxin disulfide + H2O ↔ GDP + Thioredoxin
R00127	ATP:AMP phosphotransferase	ATP + AMP ↔ 2 ADP
R00190	AMP: diphosphate phospho-D-ribosyltransferase	AMP + Diphosphate ↔ Adenine + 5-Phospho-alpha-D-ribose 1-diphosphate
R01138	dATP: pyruvate 2-O-phosphotransferase	dATP + Pyruvate ↔ dADP + Phosphoenolpyruvate
R02017	2'-Deoxyadenosine 5'-diphosphate: oxidized-thioredoxin 2'-oxidoreductase	dADP + Thioredoxin disulfide + H2O ↔ Thioredoxin + ADP
R00936	5,6,7,8-tetrahydrofolate: NAD+ oxidoreductase	Tetrahydrofolate + NAD+ ↔ Dihydrofolate + NADH + H+
R00939	5,6,7,8-tetrahydrofolate: NADP+ oxidoreductase	Tetrahydrofolate + NADP+ ↔ Dihydrofolate + NADPH + H+
R00945	5,10-Methylenetetrahydrofolate: glycine hydroxymethyltransferase	5,10-Methylenetetrahydrofolate + Glycine + H2O ↔ Tetrahydrofolate + L-Serine
R02101	5,10-Methylenetetrahydrofolate: dUMP C-methyltransferase	dUMP + 5,10-Methylenetetrahydrofolate ↔ Dihydrofolate + dTMP
R02235	dihydrofolate: NAD+ oxidoreductase	Dihydrofolate + NAD+ ↔ Folate + NADH + H+
R02236	dihydrofolate: NADP+ oxidoreductase	Dihydrofolate + NADP+ ↔ Folate + NADPH + H+
R00137	ATP: nicotinamide-nucleotide adenylyltransferase	ATP + Nicotinamide D-ribonucleotide ↔ Diphosphate + NAD+
R02093	ATP: dTDP phosphotransferase	ATP + dTDP ↔ ADP + dTTP
R02094	ATP: dTMP phosphotransferase	ATP + dTMP ↔ ADP + dTDP
R00014	pyruvate: thiamin diphosphate acetaldehydetransferase (decarboxylating)	Pyruvate + Thiamin diphosphate ↔ 2-(alpha-Hydroxyethyl)thiamine diphosphate + CO2
R00230	acetyl-CoA: phosphate acetyltransferase	Acetyl-CoA + Orthophosphate ↔ CoA + Acetyl phosphate
R00315	ATP: acetate phosphotransferase	ATP + Acetate ↔ ADP + Acetyl phosphate
R02569	acetyl-CoA: enzyme N6-(dihydrolipoyl)lysine S-acetyltransferase	Acetyl-CoA + Enzyme N6-(dihydrolipoyl)lysine ↔ CoA + [Dihydrolipoyllysine-residue acetyltransferase] S-acetyldihydrolipoyllysine
R03270	pyruvate dehydrogenase	2-(alpha-Hydroxyethyl)thiamine diphosphate + Enzyme N6-(lipoyl)lysine ↔ [Dihydrolipoyllysine-residue acetyltransferase] S-acetyldihydrolipoyllysine + Thiamin diphosphate

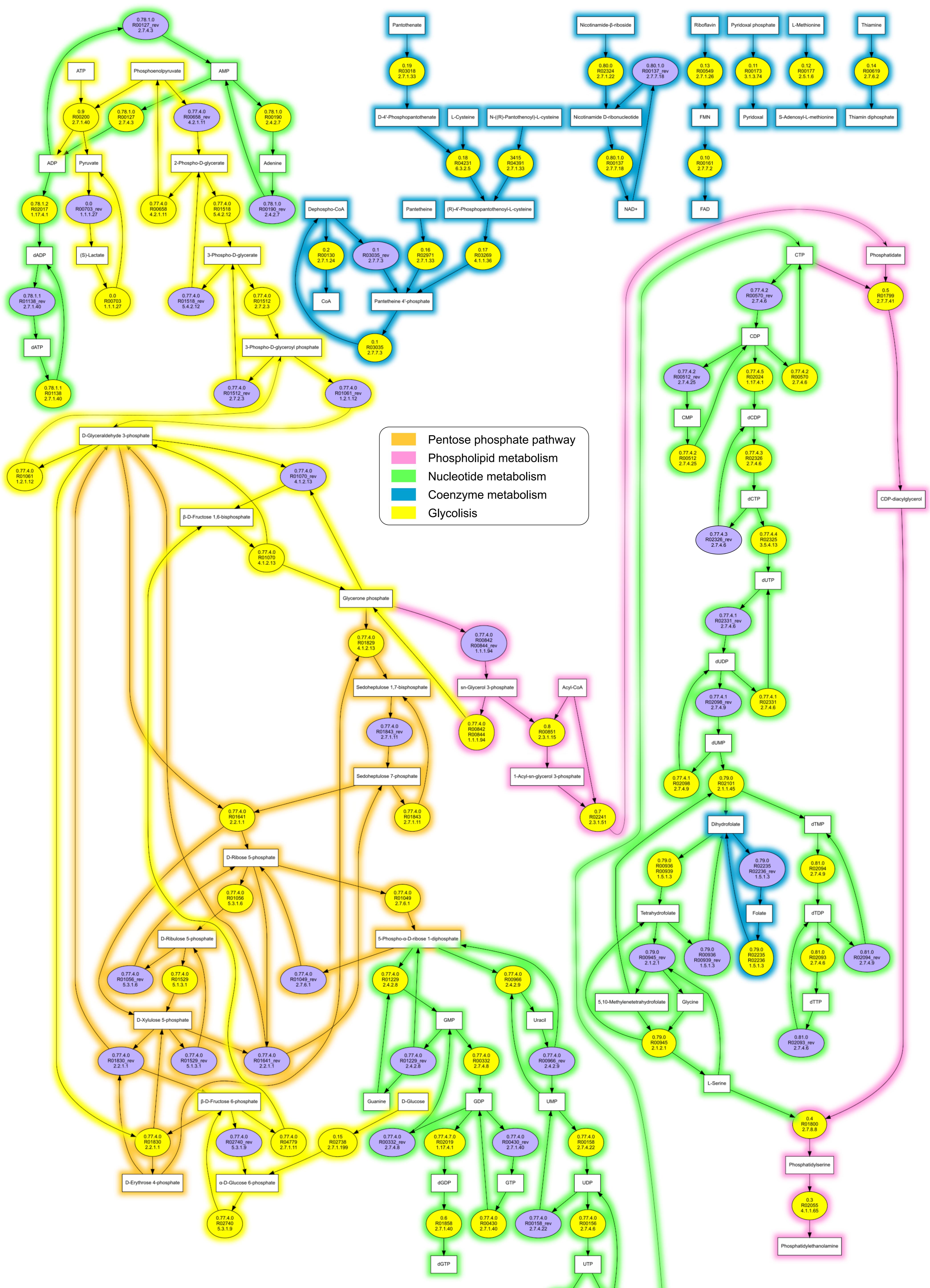
R07618	enzyme N6-(dihydrolipoyl)lysine:NAD <sup>+</sup> oxidoreductase	Enzyme N6-(dihydrolipoyl)lysine + NAD <sup>+</sup> ↔ Enzyme N6-(lipoyl)lysine + NADH + H <sup>+</sup>
R01126	inosine 5'-monophosphate phosphohydrolase	IMP + H <sub>2</sub> O ↔ Inosine + Orthophosphate
R01132	IMP:diphosphate phospho-D-ribosyltransferase	IMP + Diphosphate ↔ Hypoxanthine + 5-Phospho-alpha-D-ribose 1-diphosphate
R01863	inosine:phosphate alpha-D-ribosyltransferase	Inosine + Orthophosphate ↔ Hypoxanthine + alpha-D-Ribose 1-phosphate
R02142	XMP:pyrophosphate phosphoribosyltransferase	Xanthosine 5'-phosphate + Diphosphate ↔ Xanthine + 5-Phospho-alpha-D-ribose 1-diphosphate
R02297	Xanthosine:orthophosphate ribosyltransferase	Xanthosine + Orthophosphate ↔ Xanthine + alpha-D-Ribose 1-phosphate
R02719	xanthosine 5'-phosphate phosphohydrolase	Xanthosine 5'-phosphate + H <sub>2</sub> O ↔ Xanthosine + Orthophosphate
R00921	propanoyl-CoA:phosphate propanoyltransferase	Propanoyl-CoA + Orthophosphate ↔ Propanoyl phosphate + CoA
R01353	ATP:propionate phosphotransferase	ATP + Propionate ↔ ADP + Propanoyl phosphate
R00512	ATP:CMP phosphotransferase	ATP + CMP ↔ ADP + CDP
R00158	ATP:UMP phosphotransferase	ATP + UMP ↔ ADP + UDP
R00289	UTP:alpha-D-glucose-1-phosphate uridylyltransferase	UTP + D-Glucose 1-phosphate ↔ Diphosphate + UDP-glucose
R00291	UDP-glucose 4-epimerase;///UDP-alpha-D-glucose 4-epimerase	UDP-glucose ↔ UDP-alpha-D-galactose
R00332	ATP:GMP phosphotransferase	ATP + GMP ↔ ADP + GDP
R00430	GTP:pyruvate 2-O-phosphotransferase	GTP + Pyruvate ↔ GDP + Phosphoenolpyruvate
R00505	UDP-alpha-D-galactopyranose furanomutase	UDP-alpha-D-galactose ↔ UDP-alpha-D-galactofuranose
R00658	2-phospho-D-glycerate hydro-lyase (phosphoenolpyruvate-forming)	2-Phospho-D-glycerate ↔ Phosphoenolpyruvate + H <sub>2</sub> O
R00959	alpha-D-Glucose 1-phosphate 1,6-phosphomutase	D-Glucose 1-phosphate ↔ alpha-D-Glucose 6-phosphate
R00966	UMP:diphosphate phospho-alpha-D-ribosyltransferase	UMP + Diphosphate ↔ Uracil + 5-Phospho-alpha-D-ribose 1-diphosphate
R01015	D-glyceraldehyde-3-phosphate aldose-ketose-isomerase	D-Glyceraldehyde 3-phosphate ↔ Glycerone phosphate
R01049	ATP:D-ribose-5-phosphate diphosphotransferase	ATP + D-Ribose 5-phosphate ↔ AMP + 5-Phospho-alpha-D-ribose 1-diphosphate
R01056	D-ribose-5-phosphate aldose-ketose-isomerase	D-Ribose 5-phosphate ↔ D-Ribulose 5-phosphate
R01057	D-Ribose 1,5-phosphomutase	alpha-D-Ribose 1-phosphate ↔ D-Ribose 5-phosphate
R01058	D-glyceraldehyde 3-phosphate:NAD <sup>+</sup> oxidoreductase	D-Glyceraldehyde 3-phosphate + NADP <sup>+</sup> + H <sub>2</sub> O ↔ 3-Phospho-D-glycerate + NADPH + H <sup>+</sup>
R01061	D-glyceraldehyde-3-phosphate:NAD <sup>+</sup> oxidoreductase (phosphorylating)	D-Glyceraldehyde 3-phosphate + Orthophosphate + NAD <sup>+</sup> ↔ 3-Phospho-D-glyceroyl phosphate + NADH + H <sup>+</sup>

R01066	2-deoxy-D-ribose-5-phosphate acetaldehyde-lyase (D-glyceraldehyde-3-phosphate-forming)	$2\text{-Deoxy-D-ribose 5-phosphate} \leftrightarrow \text{D-Glyceraldehyde 3-phosphate} + \text{Acetaldehyde}$
R01067	D-Fructose 6-phosphate:D-glyceraldehyde-3-phosphate glycolaldehyde transferase	$\text{D-Fructose 6-phosphate} + \text{D-Glyceraldehyde 3-phosphate} \leftrightarrow \text{D-Erythrose 4-phosphate} + \text{D-Xylulose 5-phosphate}$
R01068	D-fructose-1,6-bisphosphate D-glyceraldehyde-3-phosphate-lyase (glycerone-phosphate-forming)	$\text{D-Fructose 1,6-bisphosphate} \leftrightarrow \text{Glycerone phosphate} + \text{D-Glyceraldehyde 3-phosphate}$
R01070	beta-D-fructose-1,6-bisphosphate D-glyceraldehyde-3-phosphate-lyase (glycerone-phosphate-forming)	$\text{beta-D-Fructose 1,6-bisphosphate} \leftrightarrow \text{Glycerone phosphate} + \text{D-Glyceraldehyde 3-phosphate}$
R01227	guanosine 5'-monophosphate phosphohydrolase	$\text{GMP} + \text{H}_2\text{O} \leftrightarrow \text{Guanosine} + \text{Orthophosphate}$
R01229	GMP:diphosphate 5-phospho-alpha-D-ribosyltransferase	$\text{GMP} + \text{Diphosphate} \leftrightarrow \text{Guanine} + \text{5-Phospho-alpha-D-ribose 1-diphosphate}$
R01229	GMP:diphosphate 5-phospho-alpha-D-ribosyltransferase	$\text{GMP} + \text{Diphosphate} \leftrightarrow \text{Guanine} + \text{5-Phospho-alpha-D-ribose 1-diphosphate}$
R01512	ATP:3-phospho-D-glycerate 1-phosphotransferase	$\text{ATP} + \text{3-Phospho-D-glycerate} \leftrightarrow \text{ADP} + \text{3-Phospho-D-glyceroyl phosphate}$
R01518	D-phosphoglycerate 2,3-phosphomutase	$\text{2-Phospho-D-glycerate} \leftrightarrow \text{3-Phospho-D-glycerate}$
R01529	D-Ribulose-5-phosphate 3-epimerase	$\text{D-Ribulose 5-phosphate} \leftrightarrow \text{D-Xylulose 5-phosphate}$
R01641	sedoheptulose-7-phosphate:D-glyceraldehyde-3-phosphate glycolaldehyde transferase	$\text{Sedoheptulose 7-phosphate} + \text{D-Glyceraldehyde 3-phosphate} \leftrightarrow \text{D-Ribose 5-phosphate} + \text{D-Xylulose 5-phosphate}$
R01819	D-mannose-6-phosphate aldose-ketose-isomerase	$\text{D-Mannose 6-phosphate} \leftrightarrow \text{beta-D-Fructose 6-phosphate}$
R01827	sedoheptulose-7-phosphate:D-glyceraldehyde-3-phosphate glyceronetransferase	$\text{Sedoheptulose 7-phosphate} + \text{D-Glyceraldehyde 3-phosphate} \leftrightarrow \text{D-Erythrose 4-phosphate} + \text{beta-D-Fructose 6-phosphate}$
R01829	sedoheptulose 1,7-bisphosphate D-glyceraldehyde-3-phosphate-lyase	$\text{Sedoheptulose 1,7-bisphosphate} \leftrightarrow \text{Glycerone phosphate} + \text{D-Erythrose 4-phosphate}$
R01830	beta-D-Fructose 6-phosphate:D-glyceraldehyde-3-phosphate glycolaldehyde transferase	$\text{beta-D-Fructose 6-phosphate} + \text{D-Glyceraldehyde 3-phosphate} \leftrightarrow \text{D-Erythrose 4-phosphate} + \text{D-Xylulose 5-phosphate}$
R01843	ATP:Sedoheptulose 7-phosphate 1-phosphotransferase	$\text{ATP} + \text{Sedoheptulose 7-phosphate} \leftrightarrow \text{ADP} + \text{Sedoheptulose 1,7-bisphosphate}$
R01967	ATP:deoxyguanosine 5'-phosphotransferase	$\text{ATP} + \text{Deoxyguanosine} \leftrightarrow \text{ADP} + \text{dGMP}$
R01968	2'-deoxyguanosine 5'-monophosphate phosphohydrolase	$\text{dGMP} + \text{H}_2\text{O} \leftrightarrow \text{Deoxyguanosine} + \text{Orthophosphate}$
R01969	Deoxyguanosine:orthophosphate ribosyltransferase	$\text{Deoxyguanosine} + \text{Orthophosphate} \leftrightarrow \text{Guanine} + \text{2-Deoxy-D-ribose 1-phosphate}$
R02018	2'-Deoxyuridine 5'-diphosphate:oxidized-thioredoxin 2'-oxidoreductase	$\text{dUDP} + \text{Thioredoxin disulfide} + \text{H}_2\text{O} \leftrightarrow \text{Thioredoxin} + \text{UDP}$
R02019	2'-Deoxyguanosine 5'-diphosphate:oxidized-thioredoxin 2'-oxidoreductase	$\text{dGDP} + \text{Thioredoxin disulfide} + \text{H}_2\text{O} \leftrightarrow \text{GDP} + \text{Thioredoxin}$
R02090	ATP:dGMP phosphotransferase	$\text{ATP} + \text{dGMP} \leftrightarrow \text{ADP} + \text{dGDP}$
R02098	ATP:dUMP phosphotransferase	$\text{ATP} + \text{dUMP} \leftrightarrow \text{ADP} + \text{dUDP}$

R02099	ATP:deoxyuridine 5'-phosphotransferase	ATP + Deoxyuridine $\leftrightarrow$ ADP + dUMP
R02102	2'-deoxyuridine 5'-monophosphate phosphohydrolase	dUMP + H2O $\leftrightarrow$ Deoxyuridine + Orthophosphate
R02102	2'-deoxyuridine 5'-monophosphate phosphohydrolase	dUMP + H2O $\leftrightarrow$ Deoxyuridine + Orthophosphate
R02147	guanosine:phosphate alpha-D-ribosyltransferase	Guanosine + Orthophosphate $\leftrightarrow$ Guanine + alpha-D-Ribose 1-phosphate
R02484	deoxyuridine:orthophosphate 2-deoxy-D-ribosyltransferase;///deoxyuridine:orthophosphate ribosyltransferase	Deoxyuridine + Orthophosphate $\leftrightarrow$ Uracil + 2-Deoxy-D-ribose 1-phosphate
R02568	D-fructose 1-phosphate D-glyceraldehyde-3-phosphate-lyase	D-Fructose 1-phosphate $\leftrightarrow$ Glycerone phosphate + D-Glyceraldehyde
R02739	alpha-D-Glucose 6-phosphate ketol-isomerase	alpha-D-Glucose 6-phosphate $\leftrightarrow$ beta-D-Glucose 6-phosphate
R02740	alpha-D-Glucose 6-phosphate ketol-isomerase	alpha-D-Glucose 6-phosphate $\leftrightarrow$ beta-D-Fructose 6-phosphate
R02749	2-deoxy-D-ribose 1-phosphate 1,5-phosphomutase	2-Deoxy-D-ribose 1-phosphate $\leftrightarrow$ 2-Deoxy-D-ribose 5-phosphate
R03321	beta-D-Glucose 6-phosphate ketol-isomerase	beta-D-Glucose 6-phosphate $\leftrightarrow$ beta-D-Fructose 6-phosphate
R04779	ATP:D-fructose-6-phosphate 1-phosphotransferase	ATP + beta-D-Fructose 6-phosphate $\leftrightarrow$ ADP + beta-D-Fructose 1,6-bisphosphate
R01664	2'-deoxycytidine 5'-monophosphate phosphohydrolase	dCMP + H2O $\leftrightarrow$ Deoxycytidine + Orthophosphate
R01664	2'-deoxycytidine 5'-monophosphate phosphohydrolase	dCMP + H2O $\leftrightarrow$ Deoxycytidine + Orthophosphate
R01665	ATP:dCMP phosphotransferase	ATP + dCMP $\leftrightarrow$ ADP + dCDP
R01666	ATP:deoxycytidine 5'-phosphotransferase	ATP + Deoxycytidine $\leftrightarrow$ ADP + dCMP
R01667	dCDP nucleotidohydrolase	dCDP + H2O $\leftrightarrow$ dCMP + Orthophosphate
R00127	ATP:AMP phosphotransferase	ATP + AMP $\leftrightarrow$ 2 ADP
R00183	adenosine 5'-monophosphate phosphohydrolase	AMP + H2O $\leftrightarrow$ Adenosine + Orthophosphate
R00185	ATP:adenosine 5'-phosphotransferase	ATP + Adenosine $\leftrightarrow$ ADP + AMP
R00190	AMP:diphosphate phospho-D-ribosyltransferase	AMP + Diphosphate $\leftrightarrow$ Adenine + 5-Phospho-alpha-D-ribose 1-diphosphate
R01138	dATP:pyruvate 2-O-phosphotransferase	dATP + Pyruvate $\leftrightarrow$ dADP + Phosphoenolpyruvate
R01547	ATP:dAMP phosphotransferase	ATP + dAMP $\leftrightarrow$ ADP + dADP
R01547	ATP:dAMP phosphotransferase	ATP + dAMP $\leftrightarrow$ ADP + dADP
R01561	adenosine:phosphate alpha-D-ribosyltransferase	Adenosine + Orthophosphate $\leftrightarrow$ Adenine + alpha-D-Ribose 1-phosphate
R02017	2'-Deoxyadenosine 5'-diphosphate:oxidized-thioredoxin 2'-oxidoreductase	dADP + Thioredoxin disulfide + H2O $\leftrightarrow$ Thioredoxin + ADP
R02088	2'-deoxyadenosine 5'-monophosphate phosphohydrolase	dAMP + H2O $\leftrightarrow$ Deoxyadenosine + Orthophosphate

R02089	ATP:deoxyadenosine 5'-phosphotransferase	ATP + Deoxyadenosine $\leftrightarrow$ ADP + dAMP
R02557	Deoxyadenosine:orthophosphate ribosyltransferase	Deoxyadenosine + Orthophosphate $\leftrightarrow$ Adenine + 2-Deoxy-D-ribose 1-phosphate
R00942	Tetrahydrofolate:L-glutamate gamma-ligase (ADP-forming)	ATP + Tetrahydrofolate + L-Glutamate $\leftrightarrow$ ADP + Orthophosphate + THF-L-glutamate
R00945	5,10-Methylenetetrahydrofolate:glycine hydroxymethyltransferase	5,10-Methylenetetrahydrofolate + Glycine + H <sub>2</sub> O $\leftrightarrow$ Tetrahydrofolate + L-Serine
R01220	5,10-methylenetetrahydrofolate:NADP+ oxidoreductase	5,10-Methylenetetrahydrofolate + NADP+ $\leftrightarrow$ 5,10-Methenyltetrahydrofolate + NADPH
R01655	5,10-Methenyltetrahydrofolate 5-hydrolase (decyclizing)	5,10-Methenyltetrahydrofolate + H <sub>2</sub> O $\leftrightarrow$ 10-Formyltetrahydrofolate + H+
R03940	10-Formyltetrahydrofolate:L-methionyl-tRNA N-formyltransferase	L-Methionyl-tRNA + 10-Formyltetrahydrofolate $\leftrightarrow$ Tetrahydrofolate + N-Formylmethionyl-tRNA
R04241	tetrahydropteroyl-gamma-polyglutamate:L-glutamate gamma-ligase (ADP-forming)	ATP + THF-polyglutamate(n) + L-Glutamate $\leftrightarrow$ ADP + Orthophosphate + THF-polyglutamate(n+1)
R00137	ATP:nicotinamide-nucleotide adenylyltransferase	ATP + Nicotinamide D-ribonucleotide $\leftrightarrow$ Diphosphate + NAD+
R01271	nicotinamide-D-ribonucleotide:diphosphate phospho-alpha-D-ribosyltransferase	Nicotinamide D-ribonucleotide + Diphosphate $\leftrightarrow$ Nicotinamide + 5-Phospho-alpha-D-ribose 1-diphosphate
R02294	N-Ribosylnicotinamide:orthophosphate ribosyltransferase	Nicotinamide-beta-riboside + Orthophosphate $\leftrightarrow$ Nicotinamide + alpha-D-Ribose 1-phosphate
R02323	nicotinamide ribonucleotide phosphohydrolase	Nicotinamide D-ribonucleotide + H <sub>2</sub> O $\leftrightarrow$ Nicotinamide-beta-riboside + Orthophosphate
R01567	ATP:thymidine 5'-phosphotransferase	ATP + Thymidine $\leftrightarrow$ ADP + dTMP
R01569	thymidylate 5'-phosphohydrolase	dTMP + H <sub>2</sub> O $\leftrightarrow$ Thymidine + Orthophosphate
R02094	ATP:dTMP phosphotransferase	ATP + dTMP $\leftrightarrow$ ADP + dTDP
R00435	ATP:polynucleotide adenylyltransferase;///ATP:RNA adenylyltransferase	ATP + RNA $\leftrightarrow$ Diphosphate + RNA
R00441	GTP:RNA guanylyltransferase (DNA-directed);///GTP:RNA guanylyltransferase (RNA-directed)	GTP + RNA $\leftrightarrow$ Diphosphate + RNA
R00375	Deoxyadenosine 5'-triphosphate:DNA deoxynucleotidyltransferase (DNA-directed)	dATP + DNA $\leftrightarrow$ Diphosphate + DNA
R00376	Deoxyguanosine 5'-triphosphate:DNA deoxynucleotidyltransferase (DNA-directed)	dGTP + DNA $\leftrightarrow$ Diphosphate + DNA

Figure S1. Full size representation of the reaction graph of the proposed theoretical minimal metabolic network represented in Figure 1



**Figure S2.** The m-DAG of “*Ca. Nasuia deltocephalinicola*”.

