

Table S2. Reactions manually removed from the automatic reconstruction of the small-molecule metabolism of *B. cicadellincola*. **GR:** generic reaction; **IR:** isolated reactions; **ES:** enzyme specificity misannotations; **MM:** reactions involving macromolecules out of the scope of the study; **NC:** reactions not corresponding to carbon atom transfers

Reaction BioCyc ID	Name	Formula	Evidence to remove it
MALATE-DEHYDROGENASE-ACCEPTOR-RXN	Malate dehydrogenase (acceptor)	malate + an oxidized electron acceptor → a reduced electron acceptor + oxaloacetate	GR
RXN-6401	NA	pantoyl lactone + beta-alanine ↔ pantothenate	ES, IR
2.8.1.8-RXN	Lipoyl synthase	a protein 6-N-(octanoyl)lysine + 2 S0 + 2 S-adenosyl-L-methionine ↔ a protein 6-N-(lipoyl)lysine + 2 L-methionine + 2 D'-deoxyadenosine	MM
QUINOLINATE-SYNTHETASE-MULTI-RXN	quinolinate synthetase	L-aspartate + dihydroxy-acetone phosphate + O2 ↔ quinolinate + phosphate + H2O2 + 2 H2O	ES
PTAALT-RXN	NA	phosphate + propionyl-CoA → coenzyme A + propionyl-P	IR
UPPSYN-RXN	NA	isopentenyl diphosphate + a cis,trans-polyisoprenyl-PP ↔ diphosphate + a cis,trans-polyisoprenyl-PP	GR, IR
DECAPCISTRANSFER-RXN	di-trans-poly-cis-decaprenylcistransferase	di-trans,poly-cis-decaprenyl diphosphate + isopentenyl diphosphate ↔ diphosphate + di-trans,poly-cis-undecaprenyl diphosphate	ES, IR
1.17.1.2-RXN	4-hydroxy-3-methylbut-2-enyl diphosphate reductase	Isopentenyl diphosphate + NAD(P) ⁺ + H2O ↔ (E)-4-hydroxy-3-methyl but2-en-1-yl diphosphate + NAD(P)H	ES
6.3.2.10-RXN	UDP-N-acetylmuramoyl alanine-D-glutamyl-lysine--D-alanyl-D-alanine ligase	D-alanyl-D-alanine + UDP-N-acetylmuramoyl-L-alanyl-D-glutamyl-L-lysine + ATP → H ⁺ + ADP + phosphate + UDP-N-acetylmuramoyl-L-alanyl-D-glutamyl-L-lysyl-D-alanyl-D-alanine	ES, IR
RXN-8975	Phospho-N-acetylmuramoyl-pentapeptide-transferase	UDP-N-acetylmuramoyl-L-alanyl-D-glutamyl-L-lysyl-D-alanyl-D-alanine + di-trans,poly-cis-undecaprenyl phosphate → N-acetylmuramoyl-L-alanyl-D-glutamyl-L-lysyl-D-alanyl-D-alanine-diphosphoundecaprenol + uridine-5'-phosphate	ES, IR
NUCLEOSIDE-DIP-KIN-RXN	Nucleoside-diphosphate kinase	ATP + a ribonucleoside diphosphate ↔ ADP + a ribonucleoside triphosphate	GR
RXN0-1	NA	H2O + a 2'-deoxyribonucleoside diphosphate + an oxidized electron acceptor ↔ a reduced electron acceptor + a ribonucleoside diphosphate	GR
RXN-7241	NA	H2O + phytate → phosphate + D-myo-inositol (1,2,3,5,6) pentakisphosphate	IR
6-PHYT-RXN	6-phytase	H2O + phytate → D-myo-inositol (1,2,3,4,5)-pentakisphosphate + phosphate	IR
DIHYDLIPOXN-RXN	NA	Dihydrolipoamide + NAD ⁺ ↔ lipoamide + NADH	IR, ES
2-6-1-57-RXN	aromatic amino acid aminotransferase	an aromatic amino acid + 2-ketoglutarate ↔ an aromatic oxo-acid + L-glutamate	IR, GR

Reaction BioCyc ID	Name	Formula	Evidence to remove it
R343-RXN	Cob(II)yrinic acid a,c-diamide reductase	$H^+ + FMN + \text{cob(II)yrinate a,c-diamide} \rightarrow FMNH_2 + \text{cob(I)yrinate a,c-diamide}$	IR
2.6.1.7-RXN	Kynurenine--oxoglutarate aminotransferase	$2\text{-oxoglutarate} + \text{kynurenine} \leftrightarrow 4\text{-(2-aminophenyl)-2,4-dioxobutanoate} + \text{L-glutamate}$	IR, ES
MYO-INOSITOL-1OR-4-MONOPHOSPHATASE-RXN	Myo-inositol-1(or 4)-monophosphatase	$H_2O + \text{D-myoinositol (3)-monophosphate} \rightarrow \text{phosphate} + \text{myoinositol}$	IR
RXN0-5063	NA	$\text{N-6-isopentyl adenosine-37 tRNA} + \text{S-adenosyl-L-methionine} \leftrightarrow \text{S-adenosyl-L-homocysteine} + 2\text{-methylthio-N-6-isopentyl adenosine-37 tRNA} + 5'\text{-deoxyadenosine} + \text{L-methionine}$	IR
1-7-1-13-RXN	queuine synthase	$\text{queuine} + 2 \text{NADP}^+ \leftrightarrow 7\text{-cyano-7-carbaguanine}$	IR
2-HEXADECENAL-REDUCTASE-RXN	2-hexadecenal reductase	$2\text{-trans-Hexadecenal} + H^+ + \text{NADPH} \rightarrow \text{palmitaldehyde} + \text{NADP}^+$	IR
3-1-13-1-RXN	Exoribonuclease II	$\text{an RNA} \leftrightarrow \text{a nucleoside-5'-phosphate} + \text{an RNA}$	IR
PSERTRANSAM-RXN	Phosphoserine aminotransferase	$\text{L-glutamate} + 3\text{-phospho-hydroxypyruvate} \rightarrow 2\text{-oxoglutarate} + 3\text{-phospho-serine}$	IR
RXN-7958	NA	$\text{ATP} + \text{propionate} \leftrightarrow \text{ADP} + \text{propionyl-P}$	IR
RXN0-4022	NA	$H^+ + 7\text{-cyano-7-deazaguanine} + \text{NADPH} \leftrightarrow 7\text{-aminomethyl-7-deazaguanine} + \text{NADP}^+$	IR
NADH-DEHYDROGENASE-QUINONE-RXN	NADH dehydrogenase (quinone)	$\text{NADH} + \text{a quinone} \leftrightarrow \text{a hydroquinone} + \text{NAD}^+$	IR, GR
CARBOXYLESTERASE-RXN	carboxylesterase	$H_2O + \text{a carboxylic ester} \leftrightarrow \text{an alcohol} + \text{a carboxylate}$	IR, GR
RXN0-5225		$H_2O + \text{GlcNAc-1,6-anhMurNAc-L-Ala-gamma-D-Glu-DAP-D-Ala} \leftrightarrow \text{L-Ala-gamma-D-Glu-DAP-D-Ala} + \text{GlcNAc-1,6-anhMurNAc}$	IR
POLYPHOSPHATE-KINASE-RXN	Polyphosphate kinase	$\text{long chain polyphosphate} + \text{ATP} \leftrightarrow \text{long chain polyphosphate} + \text{ADP}$	IR
PEPTIDYLPROLYL-ISOMERASE-RXN	Peptidylprolyl isomerase	$\text{peptidylproline (omega} = 180) \leftrightarrow \text{peptidylproline (omega} = 0)$	IR
RXN0-5063	NA	$\text{N-6-isopentyl adenosine-37 tRNA} + \text{S-adenosyl-L-methionine} \leftrightarrow \text{S-adenosyl-L-homocysteine} + 2\text{-methylthio-N-6-isopentyl adenosine-37 tRNA} + 5'\text{-deoxyadenosine} + \text{L-methionine}$	IR
RXN-7919	NA	$\text{S-(2-hydroxyacyl)glutathione} + H_2O \leftrightarrow \text{glutathione} + \text{a 2-hydroxy carboxylate}$	IR, GR
GLYOXII-RXN	Hydroxy acylglutathione hydrolase	$H_2O + \text{S-lactoyl-glutathione} \rightarrow H^+ + \text{D-lactate} + \text{glutathione}$	IR
DNA-LIGASE-NAD43-RXN	DNA ligase (NAD ⁺)	$\text{a deoxynucleotide} + \text{NAD}^+ + (\text{deoxynucleotides})(m) \leftrightarrow \text{a deoxynucleotide} + \text{nicotinamide mononucleotide} + \text{adenosine-5'-phosphate}$	IR

Reaction BioCyc ID	Name	Formula	Evidence to remove it
4.6.1.10-RXN	6-pyruvoyl tetrahydropterin synthase	2-amino-4-oxo-6-(erythro-1',2',3'-trihydroxypropyl)-7,8-dihydroxypteridine triphosphate \leftrightarrow PPPi + 2-amino-4-oxo-6-(1',2'-dioxopropyl)-7,8-dihydroxypteridine	IR, ES
ADPSUGPPHOSPHAT-RXN	ADP-sugar diphosphatase	H ₂ O + an ADP-sugar \leftrightarrow an alpha-D-aldose-1-phosphate + adenosine-5'-phosphate	IR, GR
SELENOCYSTEINE-LYASE-RXN	Selenocysteine lyase	a reduced electron acceptor + L-selenocysteine \leftrightarrow selenide + L-alanine + an oxidized electron acceptor	MM
GMKALT-RXN	T2-induced deoxynucleotide kinase	dGMP + ATP \leftrightarrow H ⁺ + 2'-deoxyguanosine-5'-diphosphate + ADP	ES
RXN0-308	NA	a protein L-cysteine + L-cysteine \rightarrow L-alanine + a protein-S-sulfanylcysteine	MM
TRYPTOPHAN-AMINOTRANSFERASE-RXN	Tryptophan aminotransferase	L-tryptophan + 2-oxoglutarate \rightarrow L-glutamate + indole-3-pyruvate	IR, ES
2-6-1-58-RXN	Phenylalanine (histidine) aminotransferase	L-phenylalanine + pyruvate \rightarrow L-alanine + phenylpyruvate	ES
PHEAMINOTRANS-RXN	Aromatic amino acid transferase	L-glutamate + phenylpyruvate \leftrightarrow L-phenylalanine + 2-oxoglutarate	ES
2-6-1-28-RXN	Tryptophan--phenylpyruvate aminotransferase	L-tryptophan + phenylpyruvate \rightarrow L-phenylalanine + indole-3-pyruvate	ES
TYRAMINOTRANS-RXN	Aromatic amino acid transferase	L-glutamate + 4-hydroxyphenylpyruvate \leftrightarrow L-tyrosine + 2-oxoglutarate	ES
RXN0-2023	NA	L-cysteine + ATP + uridine \leftrightarrow diphosphate + L-alanine + 2-thiouridine + adenosine-5'-phosphate	MM
PSEUDOURIDYLATE-SYNTHASE-RXN	Pseudouridylate synthase	uracil + D-ribose-5-phosphate \leftrightarrow H ₂ O + pseudouridine 5'-phosphate	MM
RXN0-1441	ADP-ribose pyrophosphatase	ADP-ribose + H ₂ O \leftrightarrow H ⁺ + D-ribose-5-phosphate + adenosine-5'-phosphate	MM
RXN-8631	NA	fructose-1-phosphate \leftrightarrow glyceraldehyde + dihydroxyacetone phosphate	ES
GLYCEROL-3-PHOSPHATE-DEHYDROGENASE-RXN	NA	sn-glycerol-3-phosphate + an oxidized electron acceptor \leftrightarrow dihydroxy-acetone phosphate + a reduced electron acceptor	GR
SULFITE-REDUCTASE-RXN	Sulfite reductase	H ₂ O + hydrogen sulfide + an oxidized electron acceptor \leftrightarrow a reduced electron acceptor + sulfite	GR
HEMN-RXN	NA	coproporphyrinogen III + S-adenosyl-L-methionine \rightarrow 5'-deoxyadenosine + L-methionine + protoporphyrinogen IX + CO ₂	IR
3-5-1-88-RXN	Peptide deformylase	H ₂ O + formyl-L-methionyl peptide \leftrightarrow formate + H ⁺ + methionyl peptide	MM
OHMETPYRKIN-RXN	Hydroxymethyl pyrimidine kinase	ATP + hydroxymethylpyrimidine \rightarrow H ⁺ + hydroxymethylpyrimidine phosphate + ADP	IR
RXN-6182	NA	alpha-D-glucose 6-phosphate \rightarrow D-fructose-6-phosphate	ES

Reaction BioCyc ID	Name	Formula	Evidence to remove it
3-6-1-41-RXN	Bis(5'-nucleosyl)-tetraphosphatase (symmetrical)	5',5''-diadenosine tetraphosphate + H ₂ O ↔ H ⁺ + ADP	IR
GLYC3PDEHYDROG-RXN	Glycerol-3-phosphate dehydrogenase	sn-glycerol-3-phosphate + ubiquinone-8 → ubiquinol-8 + dihydroxyacetone phosphate	IR, ES
CYT-UBIQUINOL-OXID-RXN	NA	ubiquinol-8 + oxygen ↔ H ₂ O + ubiquinone-8	IR, ES