

## Pathway analyses

A. **Pathway Analyses on BioCyc** ([www.biocyc.com](http://www.biocyc.com), Karp *et al.* 2019; Paley and Karp, 2021).

Pathway coverage analyses were carried out on BioCyc using the metabolomics pathway coverage tool..

Here, the annotation for each of the significant pathways in Xp91-118 in both positive and negative ion phases are presented. Annotation of gene loci in Xp91-118 are also available on BioCyc ([www.biocyc.org](http://www.biocyc.org)).

- a. Positive ion phase: Metabolic pathway coverage report identified of 18 pathways for metabolites in the positive phase. The table below shows the pathways and metabolites.

Supplementary Table S3. Positive Phase Pathways and metabolites covered in each pathway. Only the underlined compounds are the significant metabolites from our metabolomics annotation.

Pathways	Covered Compounds
adenosylcobalamin salvage from cobinamide I	GMP phosphate nicotinate
biotin-carboxyl carrier protein assembly	phosphate biotin AMP
L-arginine biosynthesis I (via L-ornithine)	L-ornithine phosphate L-glutamine AMP
L-asparagine biosynthesis II	L-asparagine AMP
L-cysteine biosynthesis VI (from L-methionine)	L-cysteine L-cystathionine L-serine L-methionine phosphate
L-histidine degradation II	urocanate
L-lysine biosynthesis I	phosphate L-lysine
L-tryptophan degradation I (via anthranilate)	L-kynurenine anthranilate
proline to cytochrome bo oxidase electron transfer	L-proline
putrescine degradation II	putrescine phosphate
pyridoxal 5'-phosphate salvage I	pyridoxine
pyrimidine ribonucleosides salvage II	uridine uracil cytidine
superpathway of L-isoleucine biosynthesis I	L-isoleucine phosphate
superpathway of L-serine and glycine biosynthesis I	L-serine glycine phosphate

Supplementary Table S3 (continued).

Pathways	Covered Compounds
superpathway of pyrimidine deoxyribonucleoside salvage	2'-deoxycytidine
superpathway of pyrimidine ribonucleotides de novo biosynthesis	L-glutamine phosphate UMP orotate
taurine degradation IV	taurine
tetrapyrrole biosynthesis I (from glutamate)	AMP 5-aminolevulinate

- b. Negative ion phase: A pathway covering set of 48 pathways covers significant metabolites in the negative phase. The table below shows the pathways and metabolites in each pathway. While 24 metabolites originally cover pathways of Xp91-118, the different forms of the metabolites are also included.

Supplementary Table S4. Negative Phase Pathways and metabolites covered in each pathway. Only the underlined compounds are the significant metabolites from our metabolomics annotation.

Pathways	Covered Compounds
2-oxopentenoate degradation	(S)-4-hydroxy-2-oxopentanoate pyruvate 2-oxopent-4-enoate
biotin biosynthesis I	S-adenosyl-L-methionine S-adenosyl-4-methylthio-2-oxobutanoate  L-methionine L-alanine S-adenosyl-L-homocysteine
CMP-2-deoxy-D-manno-octulosonate biosynthesis	phosphoenolpyruvate 2-deoxy- $\alpha$ -D-manno-2-octulosonate
D-galactonate degradation	D-galactonate 2-dehydro-2-deoxy-D-galactonate pyruvate
glycerol and glycerophosphodiester degradation	glycerol
glycine betaine biosynthesis I (Gram-negative bacteria)	glycine betaine
glycolysis III (from glucose)	2-phospho-D-glycerate 2-phospho-D-glycerate pyruvate phosphoenolpyruvate 2-phospho-D-glyceroyl-phosphate 2,2-diphospho-D-glycerate
glyoxylate cycle	(S)-malate oxaloacetate <i>cis</i> -aconitate D- <i>threo</i> -isocitrate glyoxylate succinate
indole-2-acetate biosynthesis V (bacteria and fungi)	(indol-2-yl)acetate

Supplementary Table S4 (continued).

Pathways	Covered Compounds
L-arginine biosynthesis I (via L-ornithine)	N-acetyl-L-ornithine L-ornithine acetate 2-oxoglutarate L-glutamate  <i>N</i> -acetyl-L-glutamate L-glutamine L-citrulline L-arginine fumarate  L-aspartate AMP
L-asparagine degradation I	L-asparagine L-aspartate
L-cysteine biosynthesis VI (from L-methionine)	L-cysteine  O-succinyl-L-homoserine L-cystathionine succinate L-homocysteine L-serine <i>S</i> -adenosyl-L-methionine <i>S</i> -adenosyl-L-homocysteine L-methionine <i>S</i> -ribosyl-L-homocysteine
L-histidine degradation II	N-formyl-L-glutamate L-glutamate formate <i>N</i> -formimino-L-glutamate  urocanate L-histidine

Supplementary Table S4 (continued).

Pathways	Covered Compounds
L-lysine biosynthesis I	L-aspartate L-aspartyl-4-phosphate L-aspartate-semialdehyde pyruvate 2-oxoglutarate  L-glutamate L,L-diaminopimelate succinate <i>meso</i> -diaminopimelate L-lysine
L-lysine degradation VI	L-2-aminoadipate L-lysine 2-oxoglutarate L-glutamate
L-phenylalanine biosynthesis I	chorismate  <i>keto</i> -phenylpyruvate L-glutamate L-phenylalanine 2-oxoglutarate
L-proline biosynthesis I	L-glutamate L-glutamate-5-semialdehyde L-proline (S)-1-pyrroline-5-carboxylate
L-threonine degradation II	glycine L-2-amino-2-oxobutanoate L-threonine
L-tryptophan degradation I (via anthranilate)	L-tryptophan L-kynurenine  formate L-alanine

Supplementary Table S4 (continued).

Pathways	Covered Compounds
L-tyrosine degradation I	2-oxoglutarate L-tyrosine 4-hydroxyphenylpyruvate L-glutamate fumarate  acetoacetate
L-valine degradation I	(S)-2-amino-2-methylpropanoate 2-oxoglutarate L-glutamate 2-methyl-2-oxobutanoate  L-valine
levulinate degradation	4-hydroxypentanoate AMP 4-oxopentanoate
methylglyoxal degradation I	(R)-lactate  pyruvate
octane oxidation	octanoate AMP
palmitate biosynthesis II (bacteria and plants)	laurate AMP palmitate
palmitoleate biosynthesis I (from (5Z)-dodec-5-enoate)	palmitoleate
phosphopantothenate biosynthesis I	2-methyl-2-oxobutanoate (R)-pantoate $\beta$ -alanine AMP

Supplementary Table S4 (continued).

Pathways	Covered Compounds
protocatechuate degradation I (meta-cleavage pathway)	2-hydroxy-4-oxobutane-1,2,4-tricarboxylate  pyruvate oxaloacetate (1E)-4-oxobut-1-ene-1,2,4-tricarboxylate (1E,2E)-4-hydroxybuta-1,2-diene-1,2,4-tricarboxylate  protocatechuate
protocatechuate degradation II (ortho-cleavage pathway)	2-oxoadipate 2-carboxy- <i>cis,cis</i> -muconate protocatechuate
purine nucleotides degradation II (aerobic)	xanthine  GMP AMP hypoxanthine
purine ribonucleosides degradation	D-ribose 5-phosphate  hypoxanthine  xanthine
pyridoxal 5'-phosphate salvage I	pyridoxine
pyrimidine nucleobases salvage I	UMP uracil
S-methyl-5-thio- $\alpha$ -D-ribose 1-phosphate degradation	2-oxoglutaramate 2-oxoglutarate L-methionine 4-(methylsulfanyl)-2-oxobutanoate L-glutamine formate
sorbitol biosynthesis II	D-gluconate keto-D-fructose

Supplementary Table S4 (continued).



Pathways	Covered Compounds
stearate biosynthesis II (bacteria and plants)	stearate AMP
superpathway of $\beta$ -D-glucuronosides degradation	aldehydo-D-glucuronate pyruvate 2-dehydro-2-deoxy-D-gluconate  D-mannonate
superpathway of branched chain amino acid biosynthesis	2-oxobutanoate L-threonine pyruvate (S)-2-aceto-2-hydroxybutanoate  2-oxoglutarate L-isoleucine L-glutamate (S)-2-methyl-2-oxopentanoate  (S)-2-acetolactate  (2R)-2,2-dihydroxy-2-methylbutanoate L-valine 2-methyl-2-oxobutanoate 4-methyl-2-oxopentanoate L-leucine
superpathway of L-isoleucine biosynthesis I	2-oxobutanoate L-threonine pyruvate (S)-2-aceto-2-hydroxybutanoate 2-oxoglutarate L-isoleucine L-glutamate (S)-2-methyl-2-oxopentanoate  O-phospho-L-homoserine  L-homoserine L-aspartate-semialdehyde L-aspartyl-4-phosphate L-aspartate, oxaloacetate

Supplementary Table S4 (continued).

Pathways	Covered Compounds
superpathway of L-methionine biosynthesis (by sulfhydrylation)	sulfate L-homocysteine L-methionine L-homoserine <i>O</i> -acetyl-L-homoserine  acetate L-aspartate-semialdehyde L-aspartyl-4-phosphate L-aspartate 2-oxoglutarate  oxaloacetate L-glutamate
superpathway of pyrimidine deoxyribonucleotides de novo biosynthesis	L-glutamine L-glutamate  UMP  orotate <i>N</i> -carbamoyl-L-aspartate L-aspartate
superpathway of sulfate assimilation and cysteine biosynthesis	2-phospho-L-serine L-serine 2-phospho-D-glycerate 2-oxoglutarate L-glutamate <i>O</i> -acetyl-L-serine L-cysteine acetate sulfate

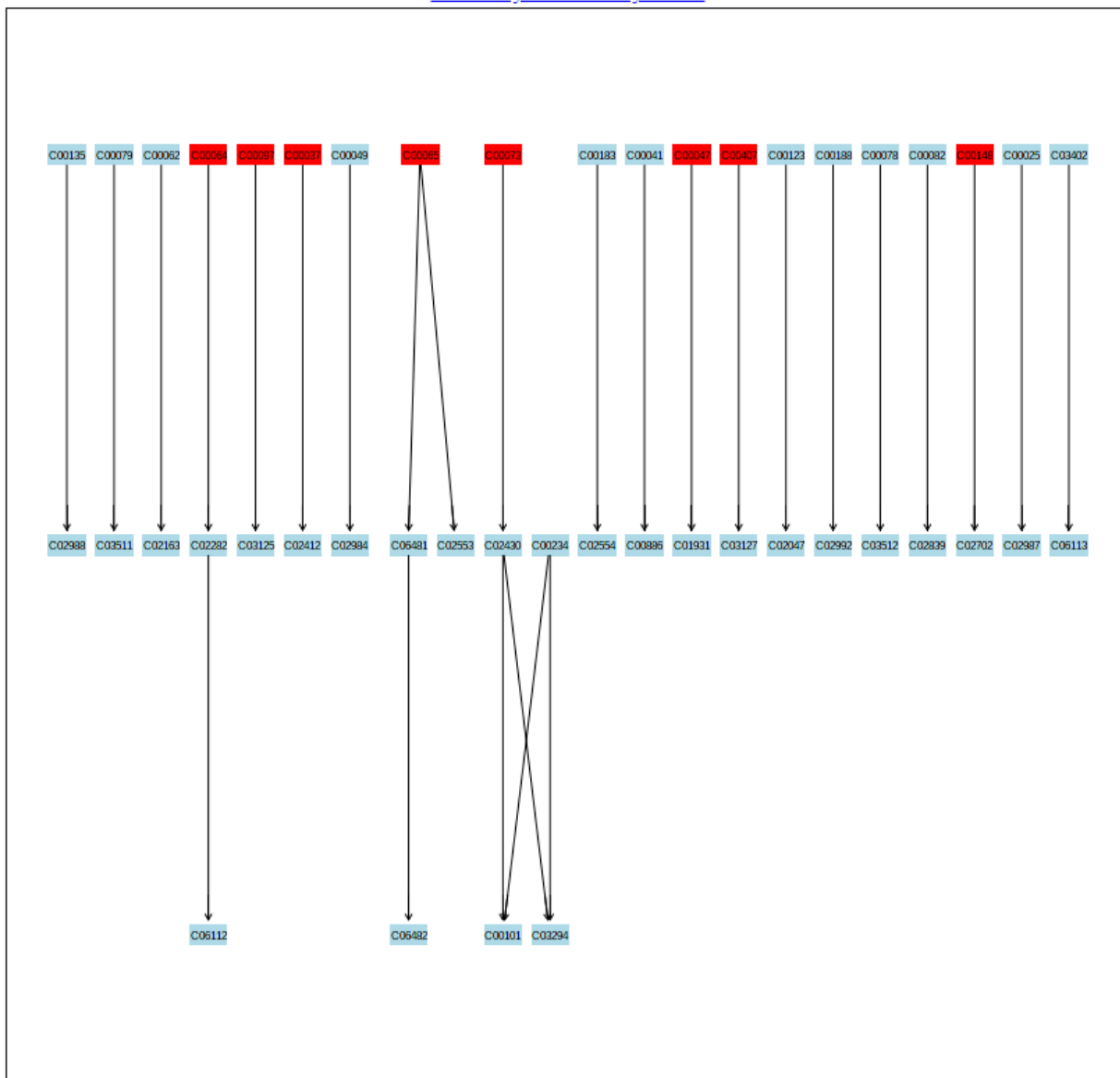
Supplementary Table S4 (continued).

Pathways	Covered Compounds
superpathway of tetrahydrofolate biosynthesis	4-aminobenzoate pyruvate L-glutamine chorismate L-glutamate  formate AMP
taurine degradation IV	2-oxoglutarate taurine succinate
tetrapyrrole biosynthesis I (from glutamate)	L-glutamate AMP 5-aminolevulinate
trehalose degradation VI (periplasmic)	$\alpha$ -D-glucopyranose  $\beta$ -D-glucopyranose
UDP-N-acetylmuramoyl-pentapeptide biosynthesis I (meso-diaminopimelate containing)	D-alanine <i>meso</i> -diaminopimelate L-glutamate D-glutamate L-alanine phosphoenolpyruvate
UTP and CTP dephosphorylation I	CMP UMP cytidine uridine L-glutamine L-glutamate

## B. Pathway Analyses on MetaboAnalyst

The additional pathways identified in *Pseudomonas putida* KT2440 using annotated metabolites in our study are shown in the figures below (Please see figure 3 in main paper for additional details).

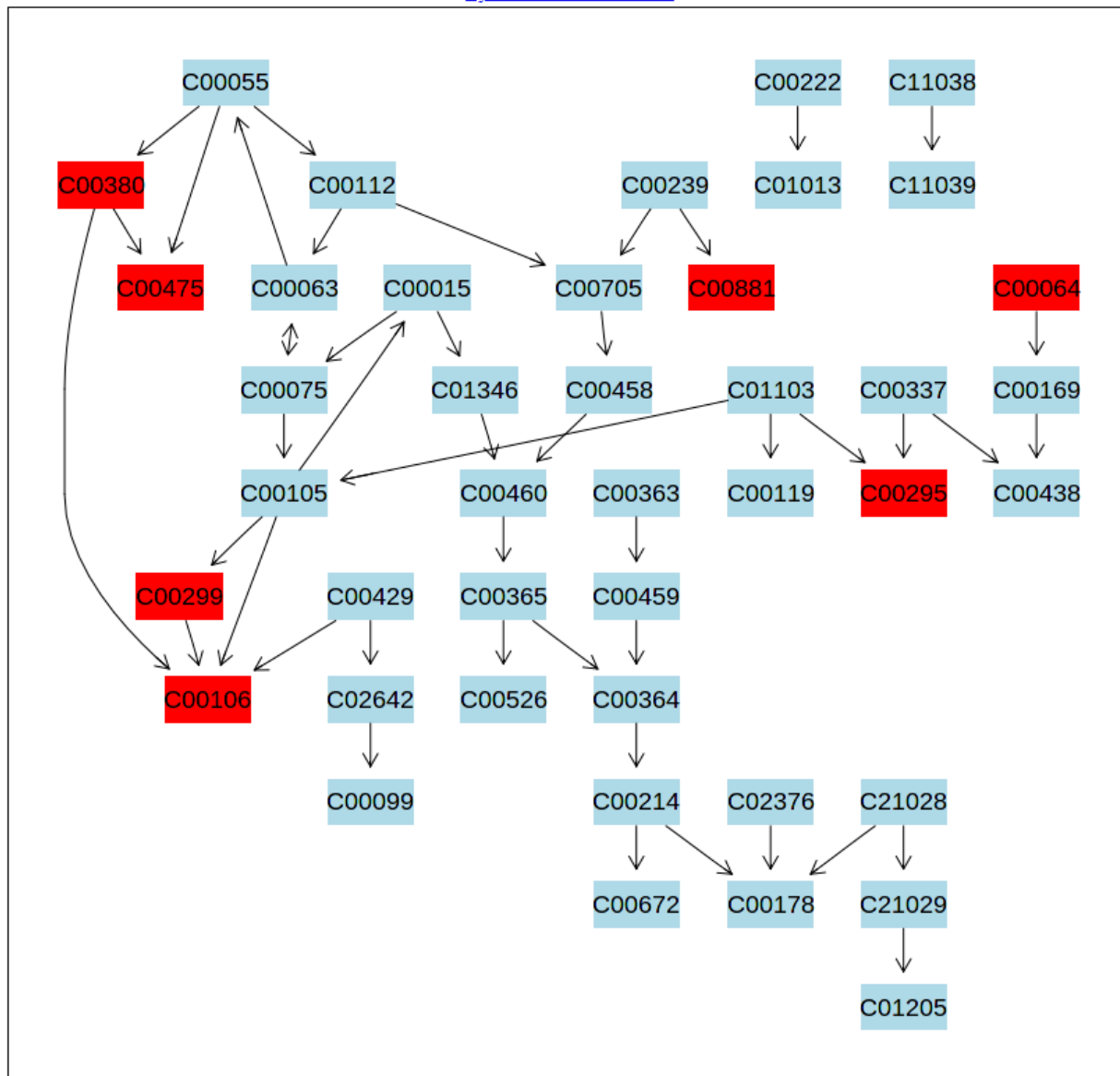
### Aminoacyl-tRNA biosynthesis



C00064: L-Glutamine; C00097: L-Cysteine; C00027: Glycine; C00065: L-Serine; C00072: L-Methionine; C00047: Lysine; C00407: Isoleucine; C00148: L-Proline

Supplementary Figure S2a(i). Metabolites putatively identified in *X. perforans* that are involved in aminoacyl tRNA biosynthesis

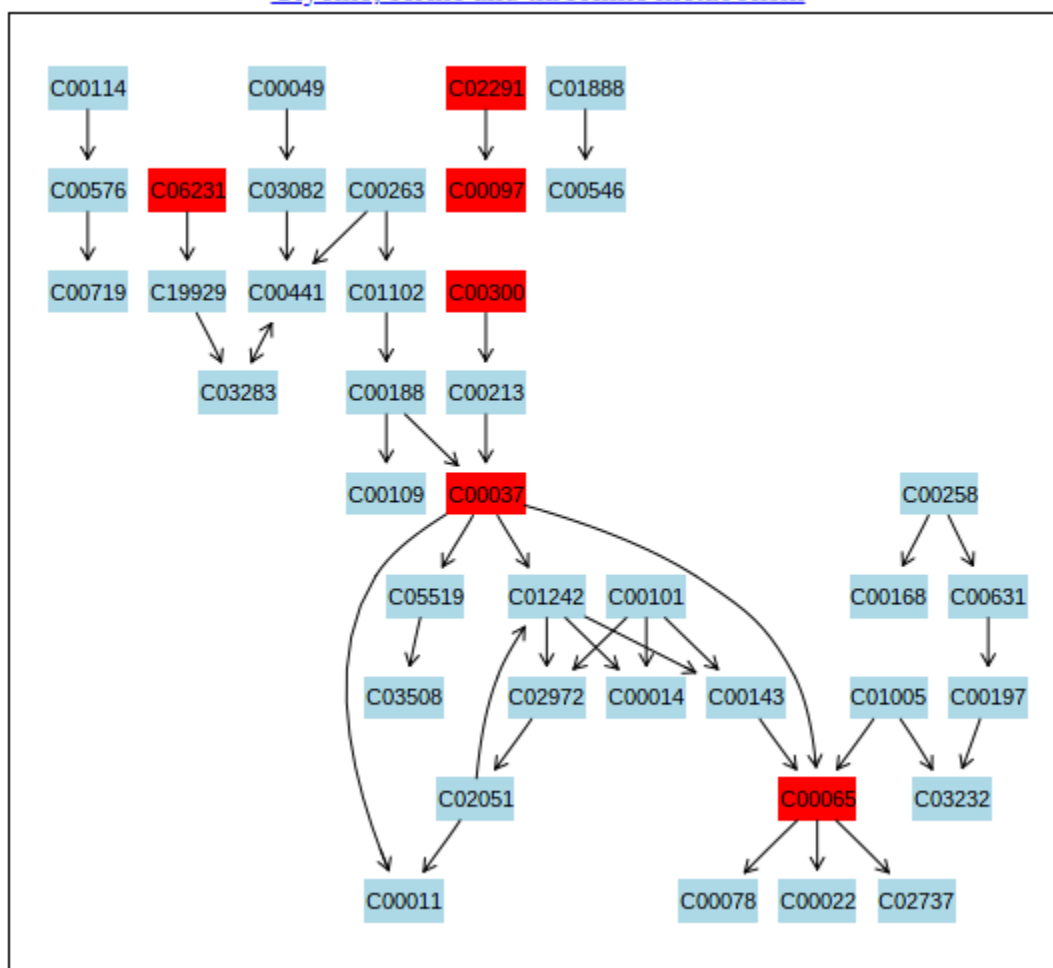
Pyrimidine metabolism



C00280: Cytosine, C00475: Cytidine; C00881: Deoxycitidine; C00064: L-Glutamine; C00295: Orotate; C00299: Uridine, C00106: Uracil

Supplementary Figure S2a(ii). Metabolites putatively identified in *X. perforans* that are involved in pyrimidine metabolism

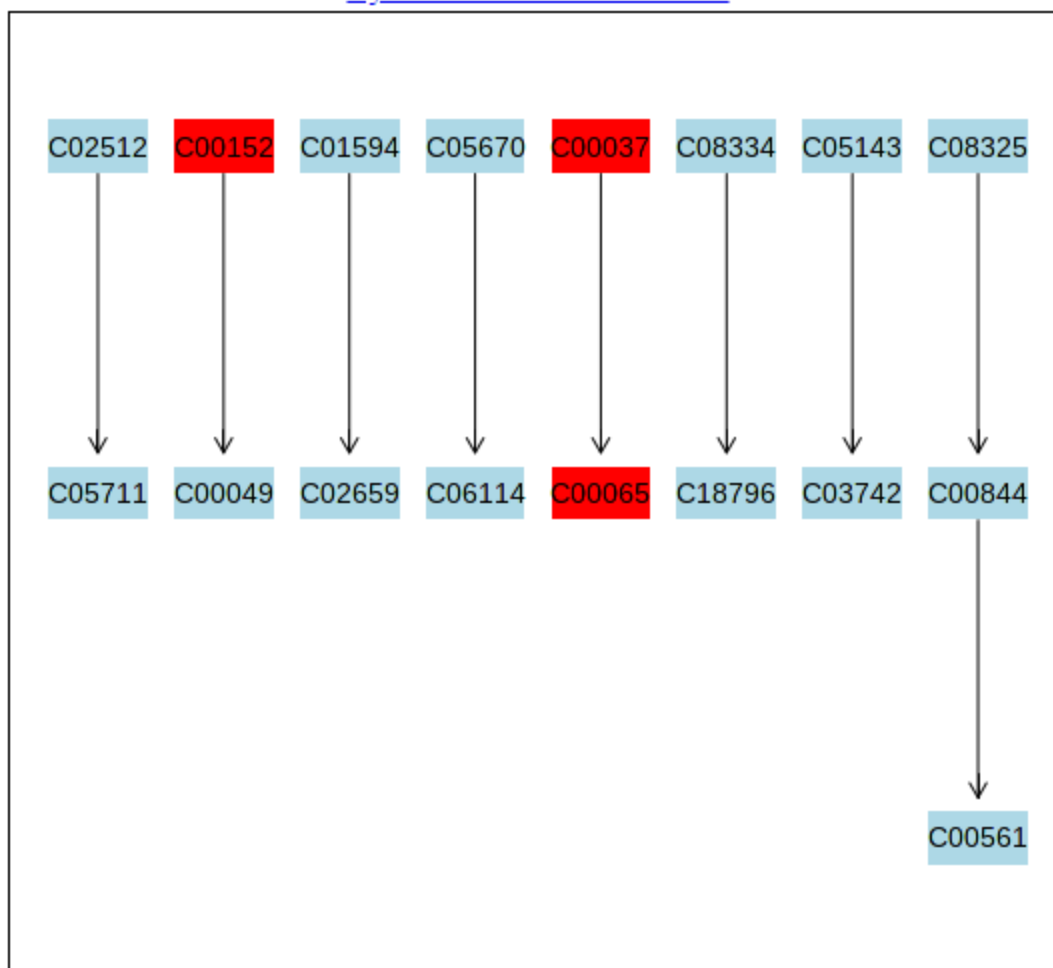
### Glycine, serine and threonine metabolism



C02291: L-cystathionine, C06221: Ectoine, C00097: Cysteine, C00200: Creatine, C00065: L-Serine

Supplementary Figure S2a(iii). Metabolites putatively identified in *X. perforans* that are involved in glycine, serine and threonine metabolism

### Cyanoamino acid metabolism

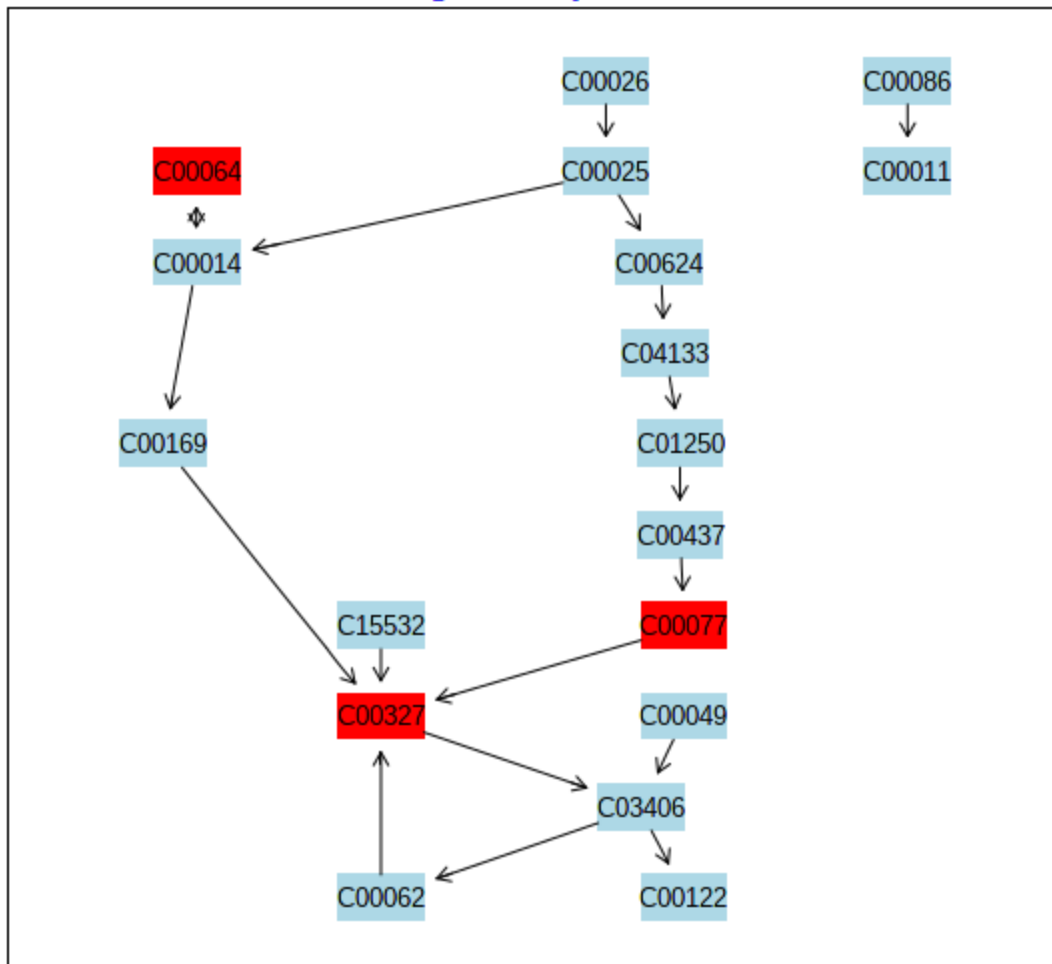


C00152: L-Asparagine, C00027: Glycine, C00065: L-serine

Supplementary Figure S2a(iv). Metabolites putatively identified in *X. perforans* that are involved in cyanoamino acid metabolism



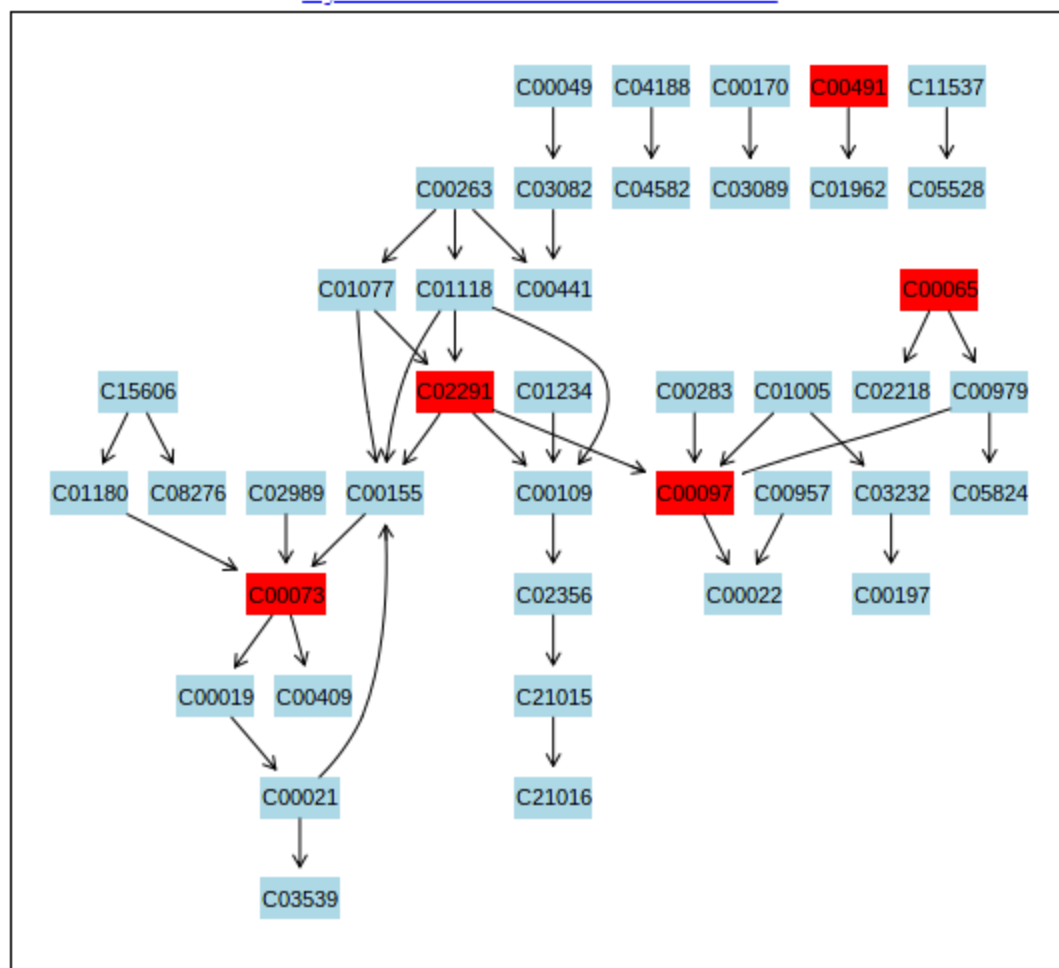
### Arginine biosynthesis



C0064: L-Glutamine, C00227: L-Citrulline, C00077: L-Ornithine

Supplementary Figure S2a (v). Metabolites putatively identified in *X. perforans* that are involved in arginine biosynthesis

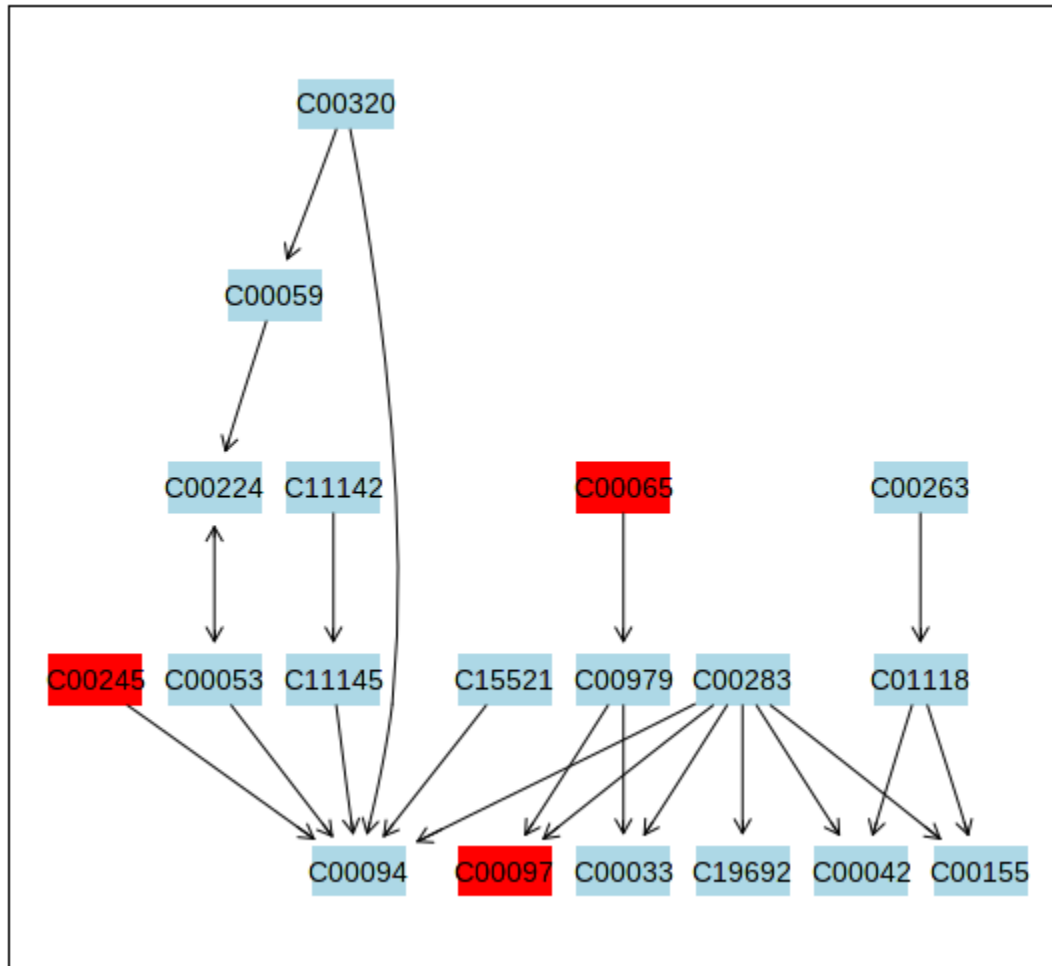
### Cysteine and methionine metabolism



C00491: L-Cystine, C00065: L-Serine, C02291: L-Cystathionine, C00097: L-Cysteine, C00072: L-Methionine

Supplementary Figure S2a (vi). Metabolites putatively identified in *X. perforans* that are involved in cysteine and methionine metabolism

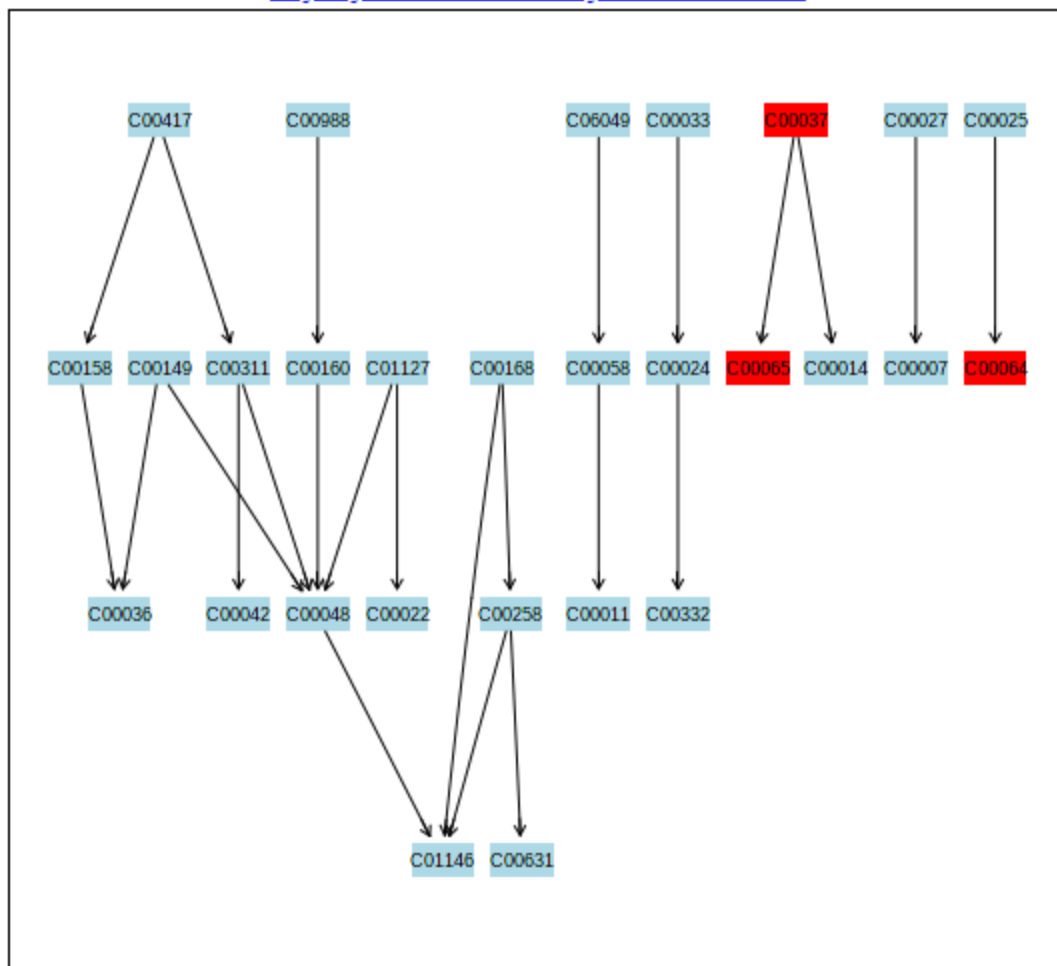
### Sulfur metabolism



C00065: L-Serine, C00245: Taurine, C00097: L-Cysteine.

Supplementary Figure S2a(vii). Metabolites putatively identified in *X. perforans* that are involved in sulfur metabolism

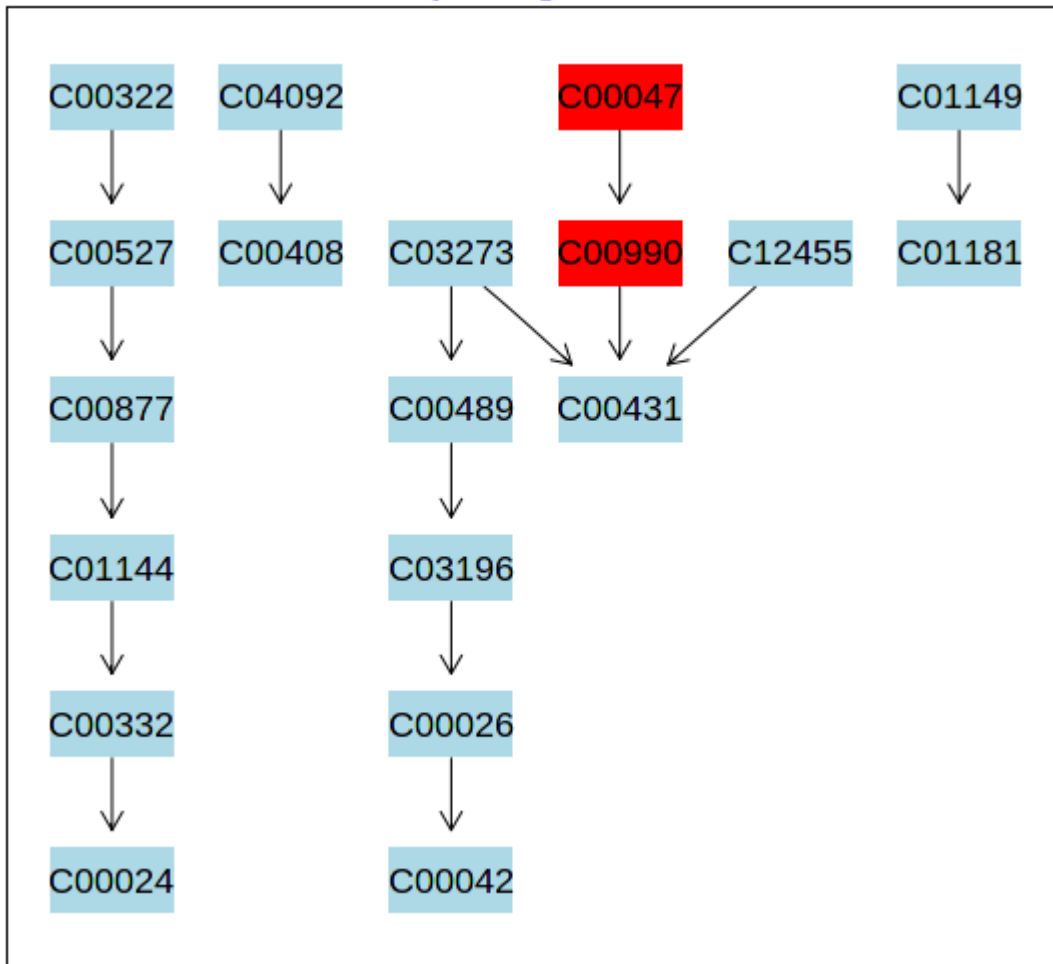
### Glyoxylate and dicarboxylate metabolism



C00027: Glycine, C00065: L-Serine, C00064: L-Glutamine.

Supplementary Figure S2a(viii). Metabolites putatively identified in *X. perforans* that are involved in glyoxylate and dicarboxylate metabolism

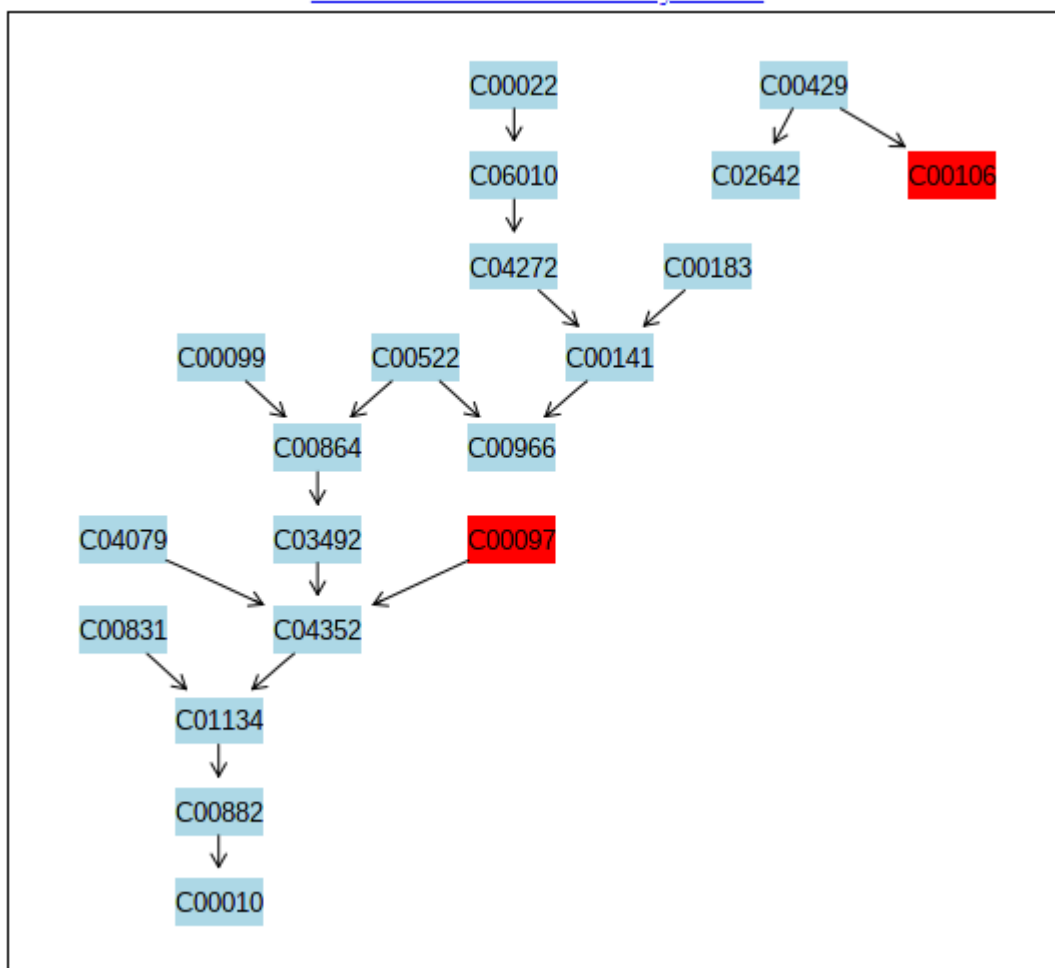
### Lysine degradation



C00047: L-Lysine, C00990: 5-Aminopentanamide.

Supplementary Figure S2a(ix). Metabolites putatively identified in *X. perforans* that are involved in lysine degradation.

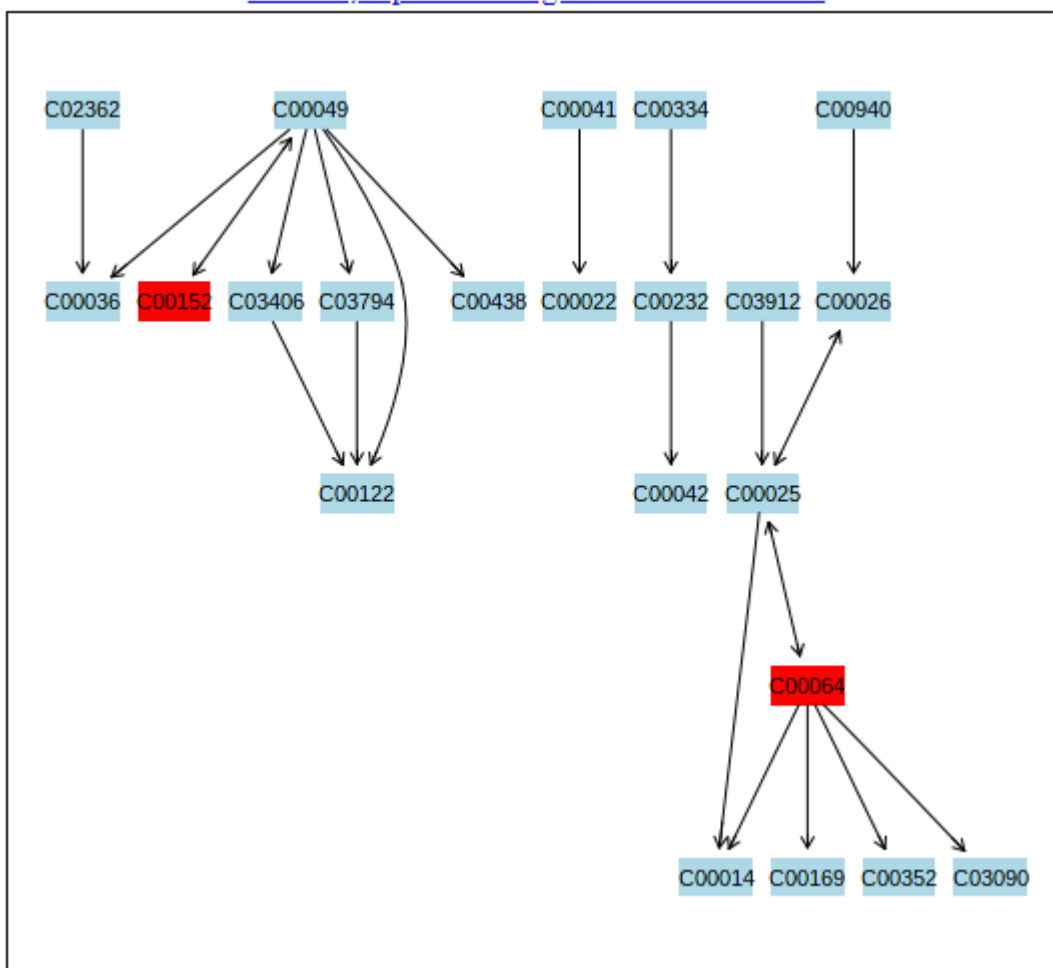
### Pantothenate and CoA biosynthesis



C00106: Uracil, C00097: L-Cysteine

Supplementary Figure S2a (x). Metabolites putatively identified in *X. perforans* that are involved in pantothenate and CoA biosynthesis.

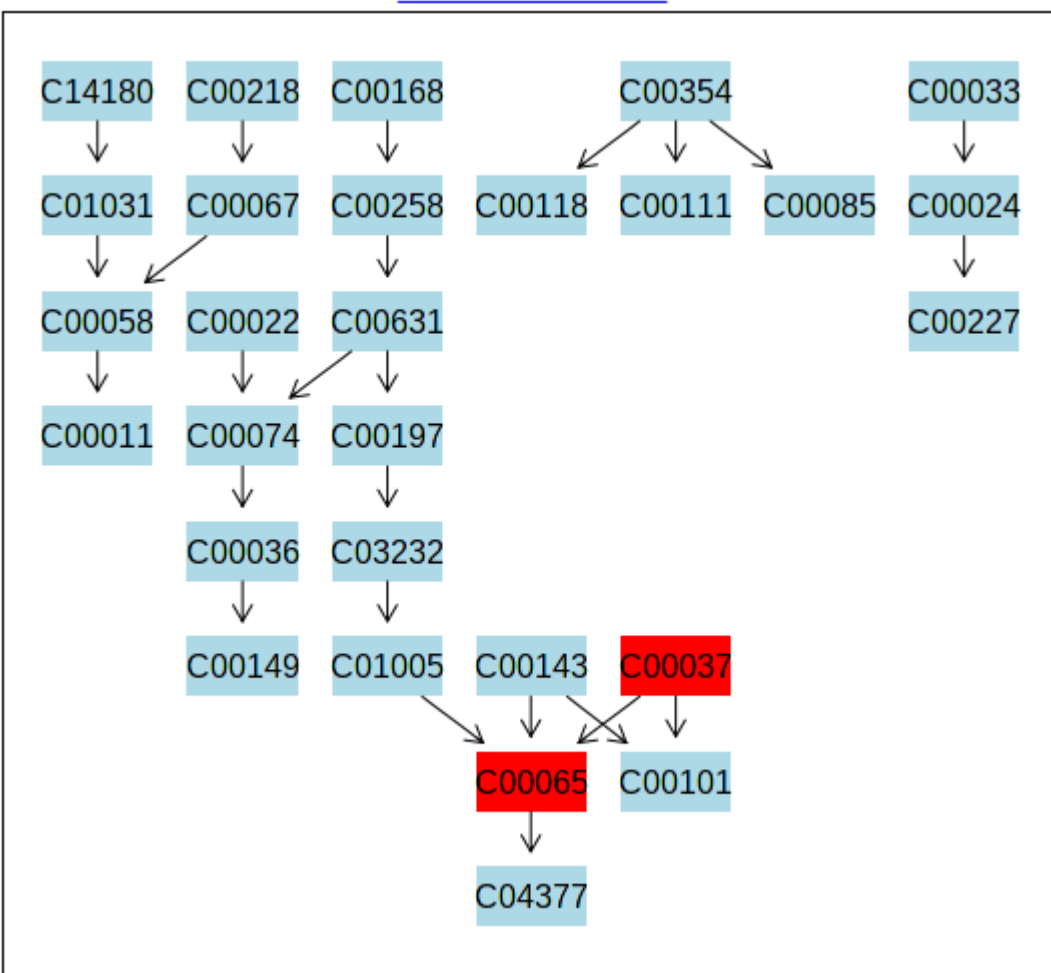
### Alanine, aspartate and glutamate metabolism



C00152: L-Asparagine, C00064: L-Glutamine

Supplementary Figure S2a(xii). Metabolites putatively identified in *X. perforans* that are involved in alanine, aspartate and glutamate metabolism.

### Methane metabolism



C00027: Glycine, C00065: L-Serine

Supplementary Figure S2a (xii). Metabolites putatively identified in *X. perforans* that are involved in methane metabolism.

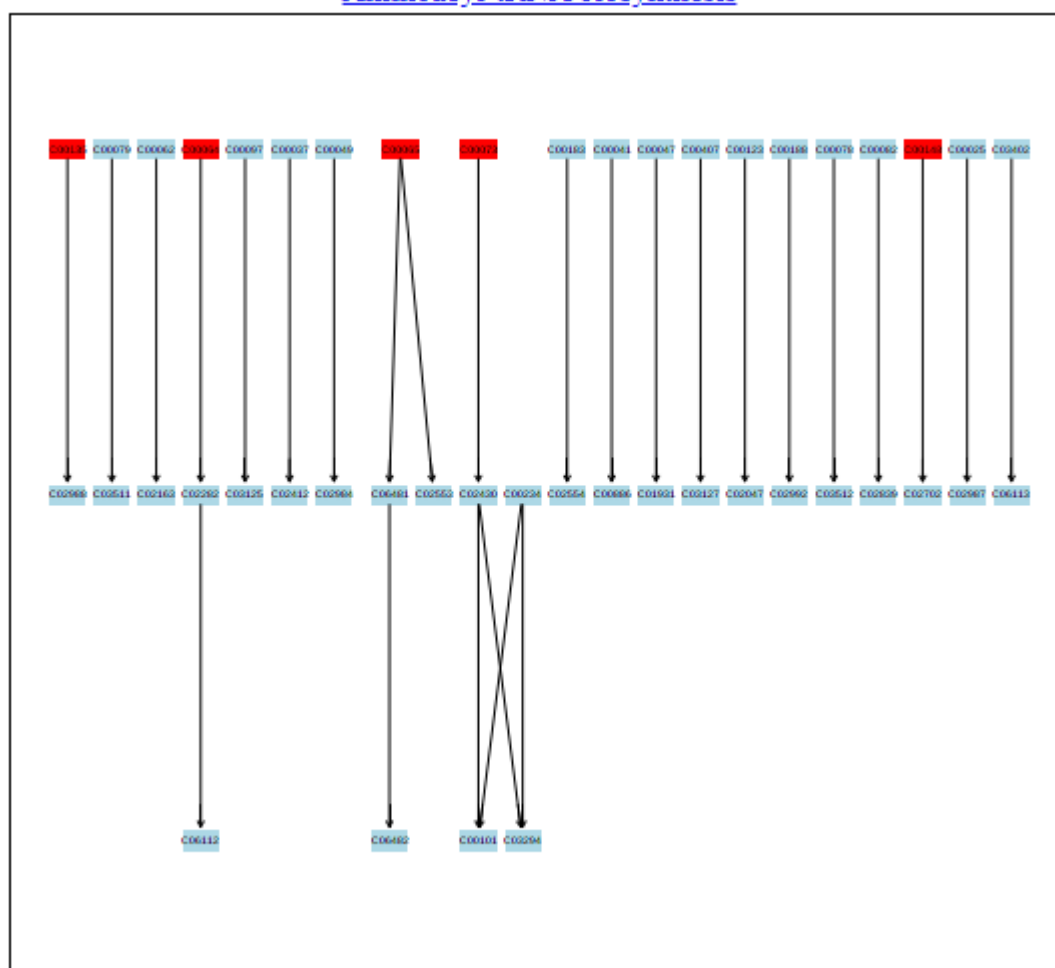


## NEGATIVE PHASE SIGNIFICANT METABOLITES AND PATHWAYS

Metabolites putatively identified in *X. perforans* that are involved

Metabolites putatively identified in *X. perforans* that are involved

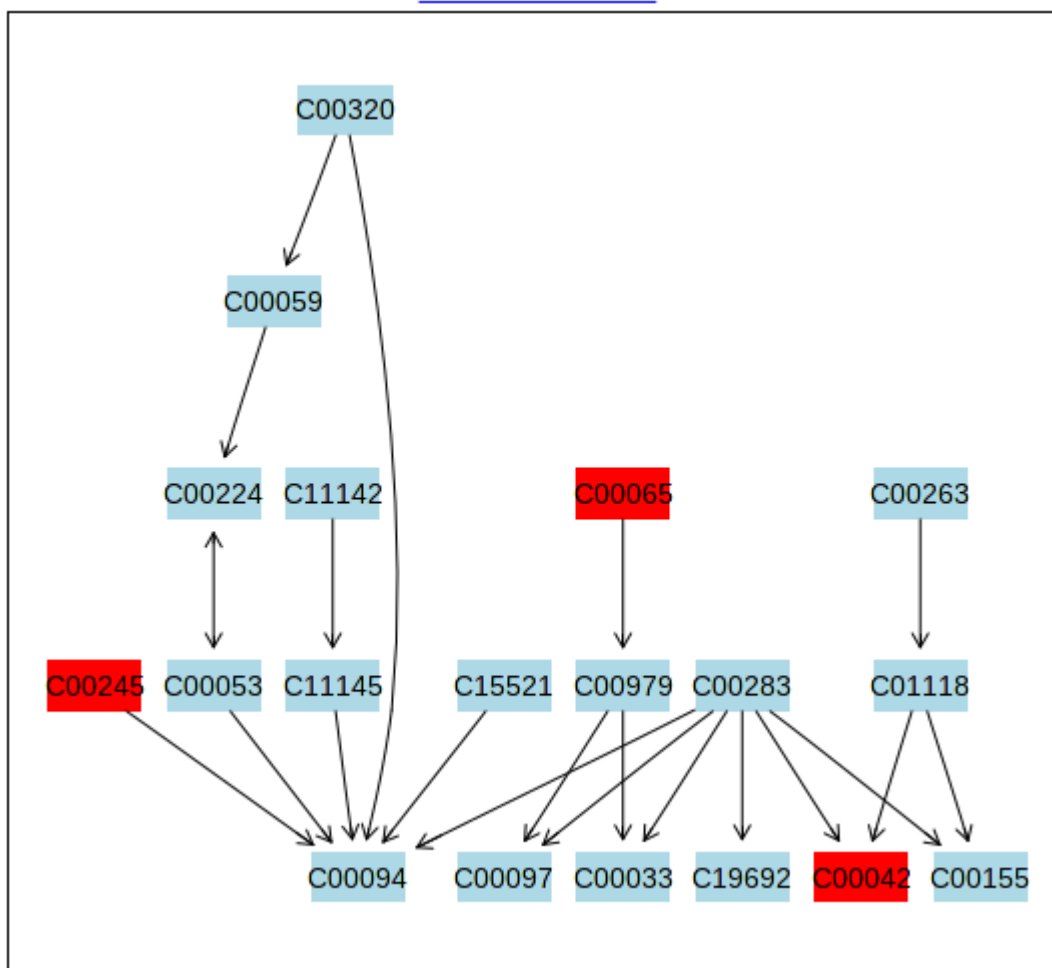
## Aminoacyl-tRNA biosynthesis



C00125: L-Histamine; C00064: L-Glutamine; C00065: L-Serine; C00072: L-Methionine; C00148: L-Proline

Supplementary Figure S2b(i). Metabolites putatively identified in *X. perforans* that are involved in aminoacyl-tRNA biosynthesis

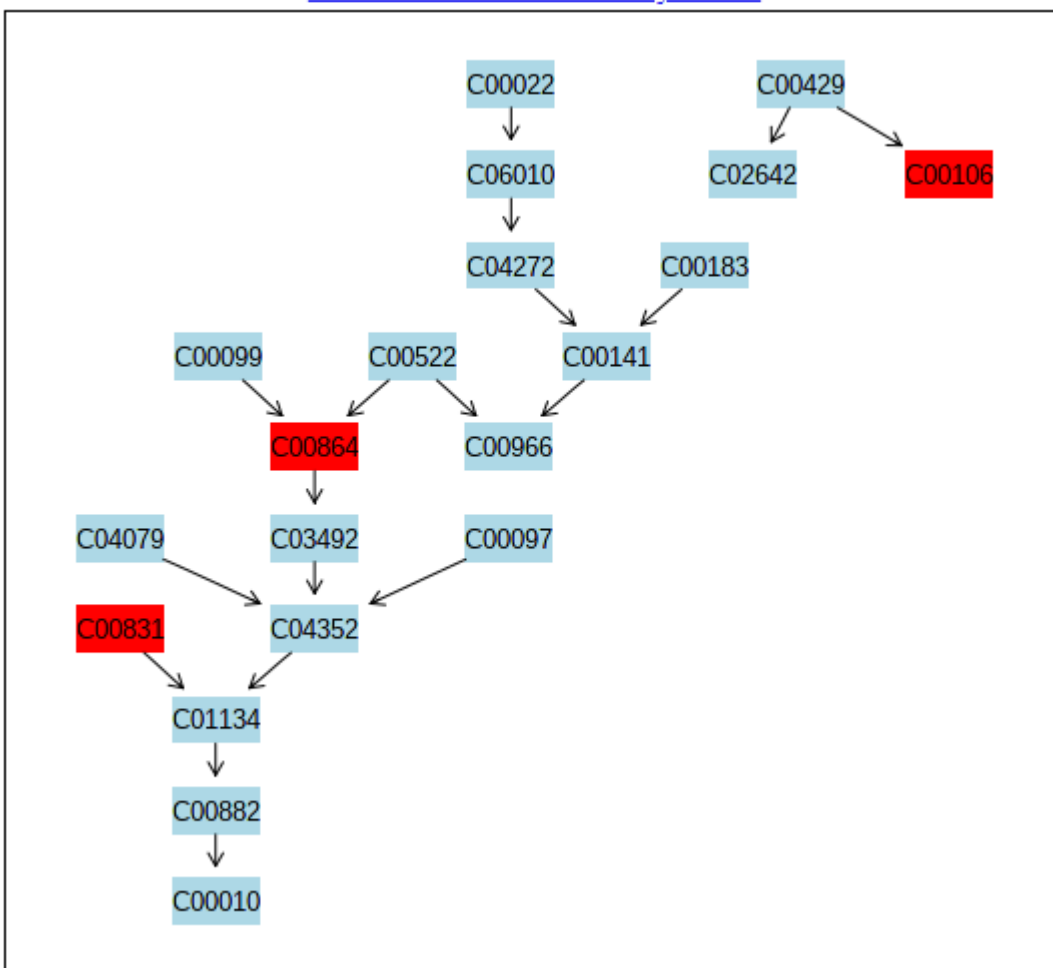
### Sulfur metabolism



C00065: L-Serine, C00245: Taurine, C00042: Succinate.

Supplementary Figure S2b(ii). Metabolites putatively identified in *X. perforans* that are involved in sulfur metabolism

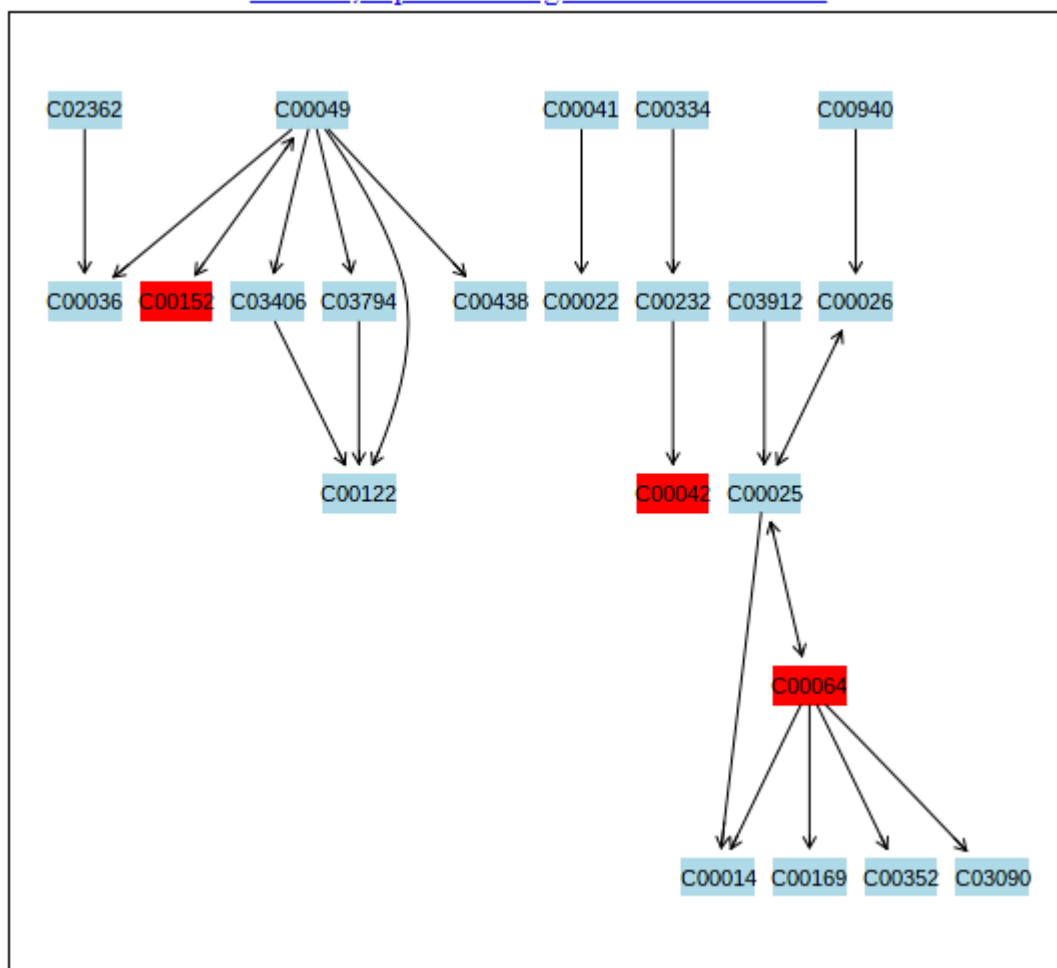
### Pantothenate and CoA biosynthesis



C00106: Uracil, C00864: Pantothenate C00821: Pantetheine

Supplementary Figure S2b(iii). Metabolites putatively identified in *X. perforans* that are involved in pantothenate and CoA biosynthesis

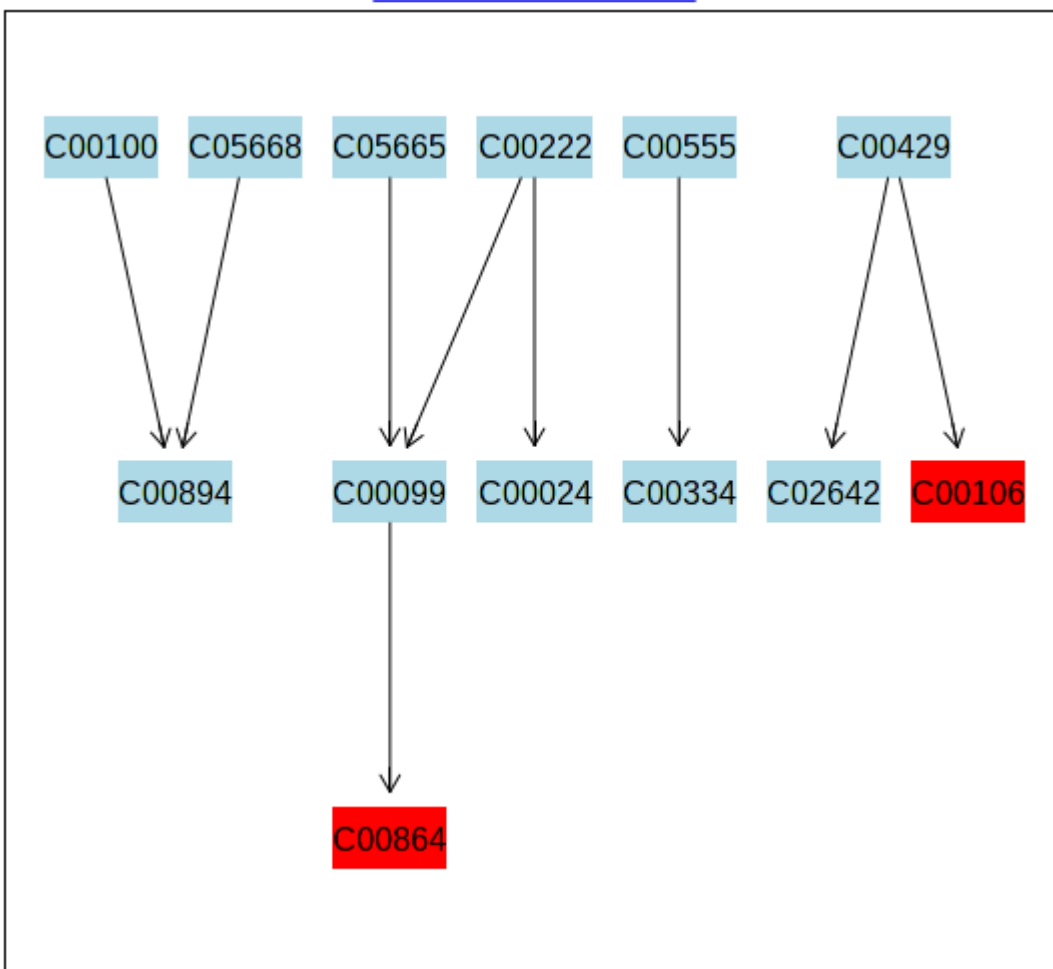
### Alanine, aspartate and glutamate metabolism



C00152: L-Asparagine, C00042: Succinate C00064: L-Glutamine

Supplementary Figure S2b(iv). Metabolites putatively identified in *X. perforans* that are involved in alanine, aspartate and glutamate metabolism

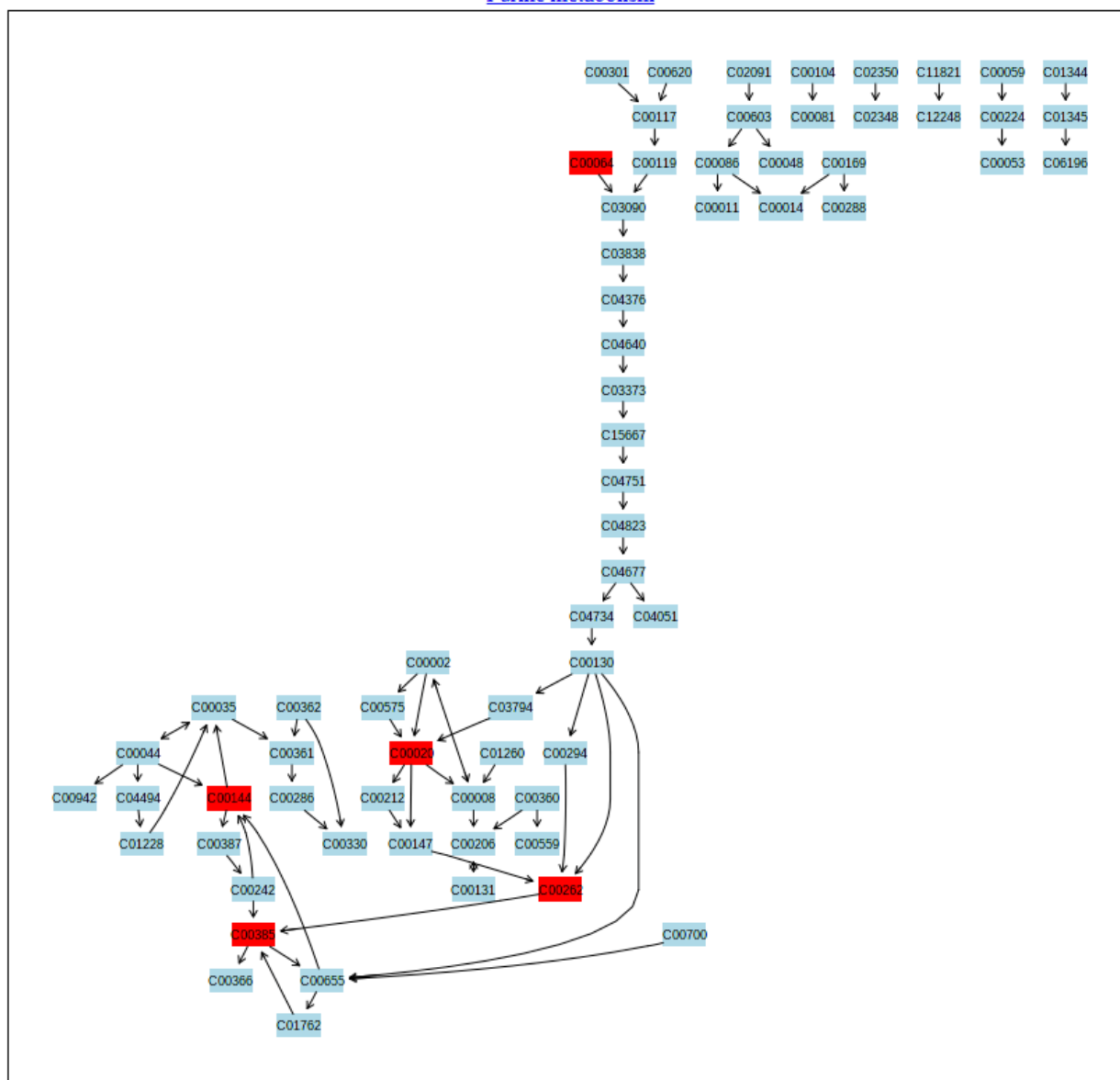
beta-Alanine metabolism



C00106: Uracil, C00864: Pantothenate

Supplementary Figure S2b(v). Metabolites putatively identified in *X. perforans* that are involved in beta-Alanine metabolism

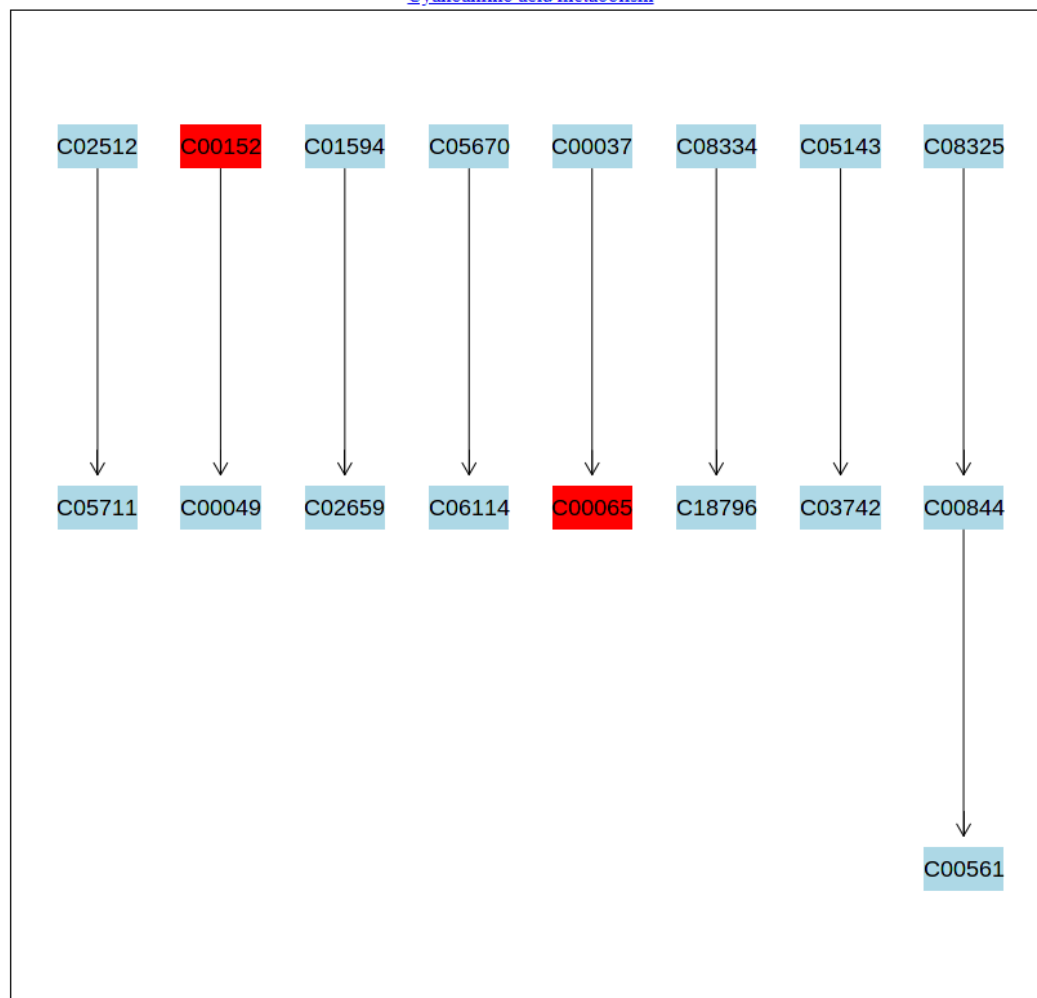
# Purine metabolism



C00064: L-Glutamine, C00020: AMP, C00144: GMP C00262: Hypoxanthine; C00285: Xanthine

Supplementary Figure S2b(vi). Metabolites putatively identified in *X. perforans* that are involved in purine metabolism

Cyanoamino acid metabolism

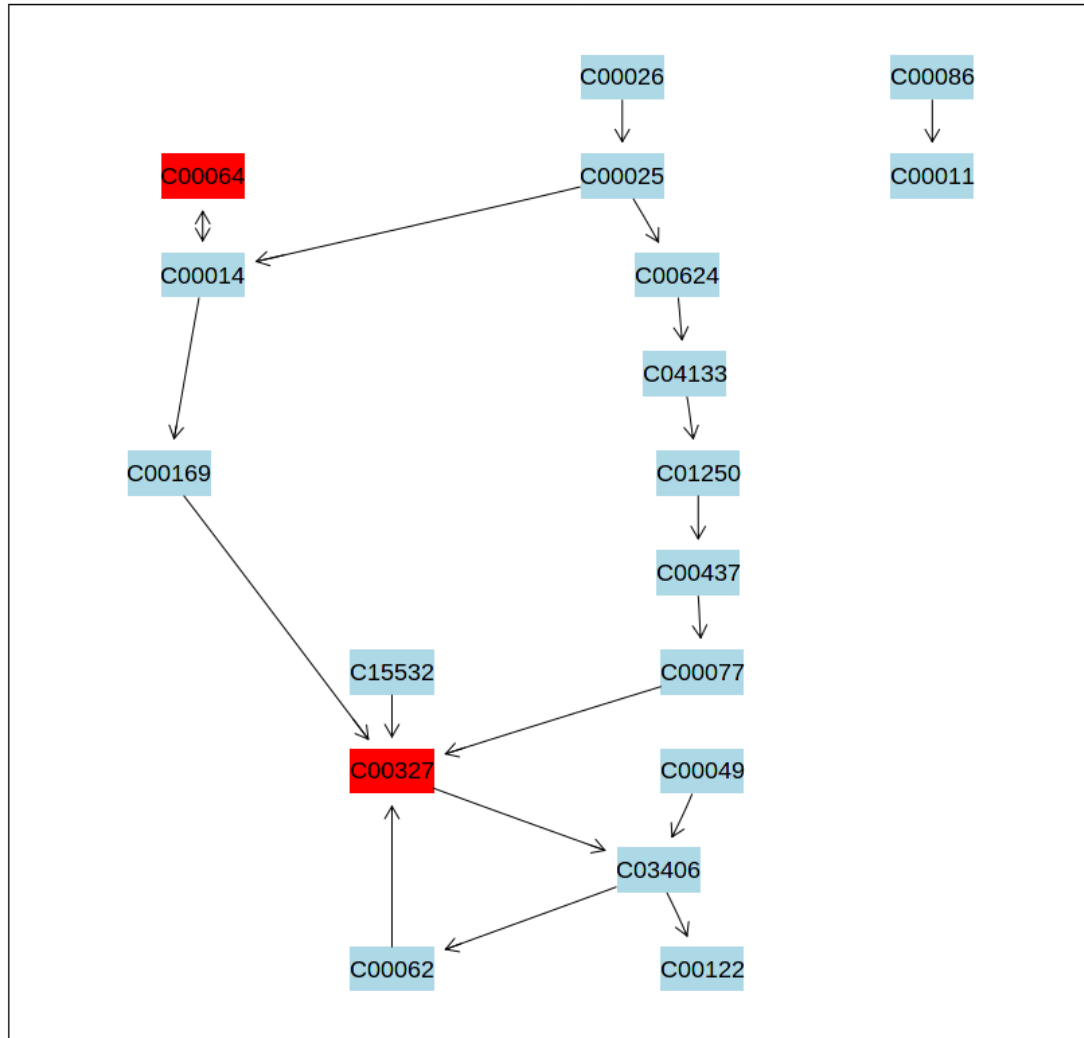


C00152: L-Asparagine, C00065: L-Serine

Supplementary Figure S2b(vii). Metabolites putatively identified in *X. perforans* that are involved in cyanoamino acid metabolism

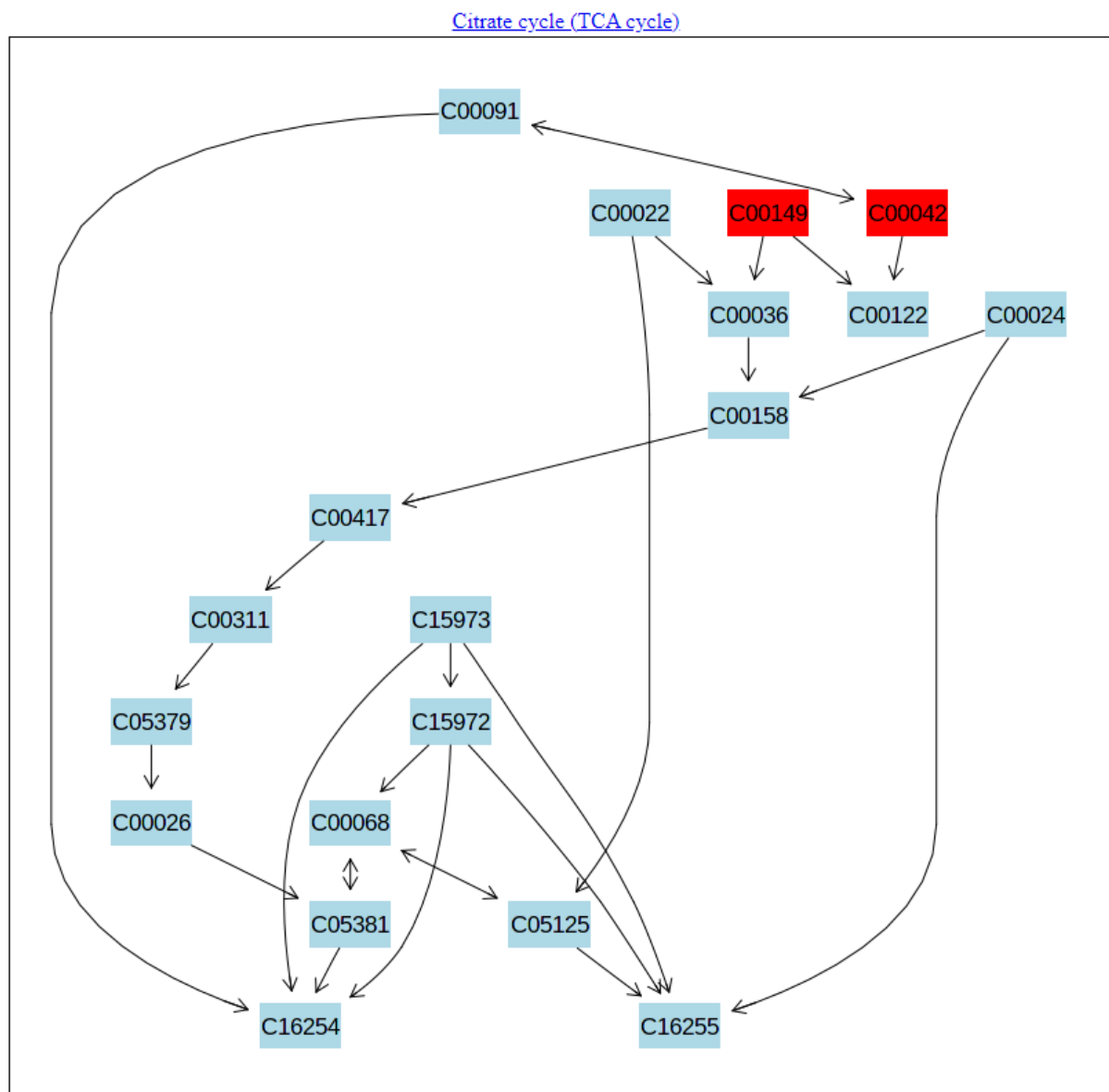


Arginine biosynthesis



C00064: L-Glutamine, C00227: L-Citrulline

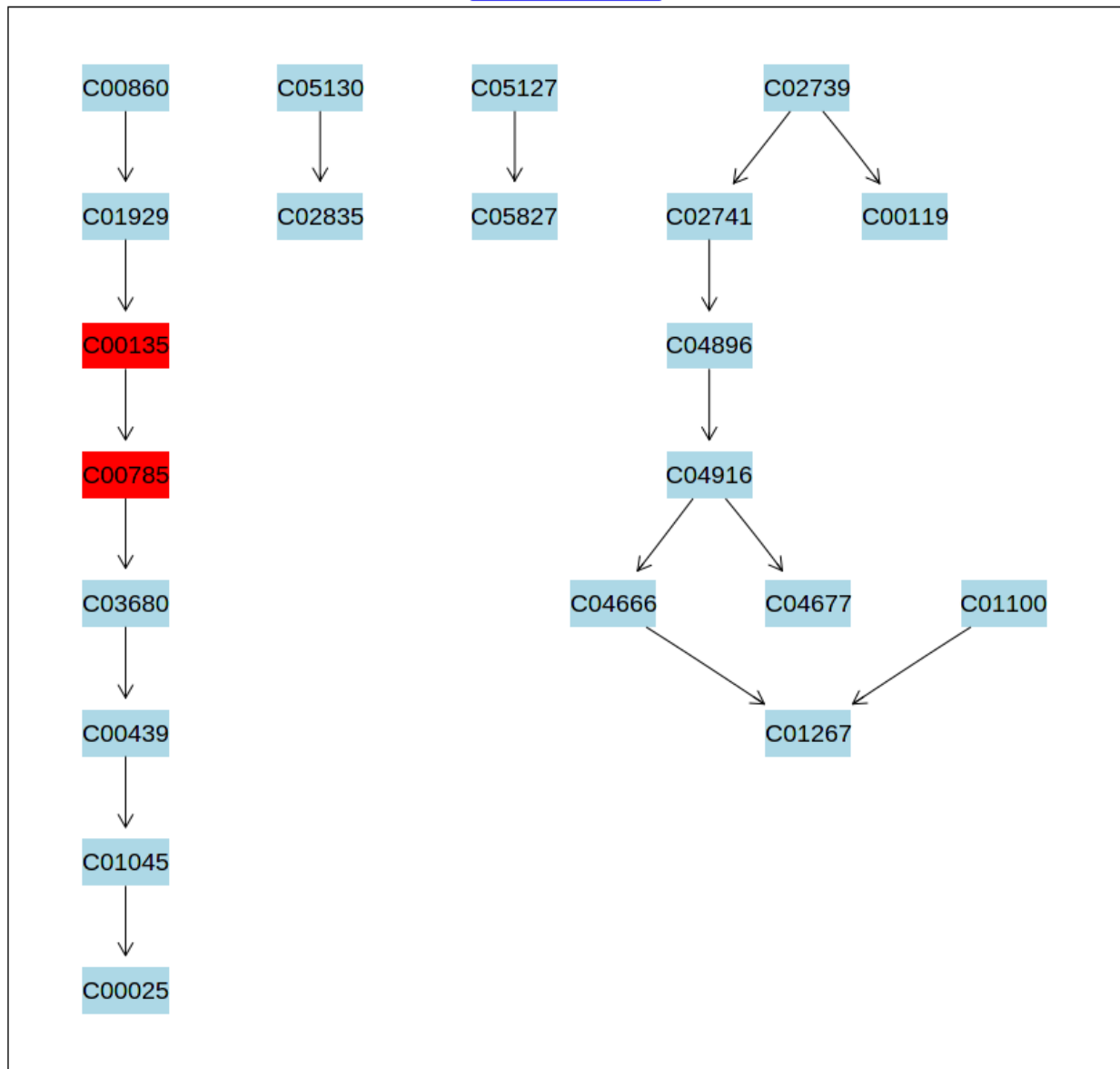
Supplementary Figure S2b(viii). Metabolites putatively identified in *X. perforans* that are involved in arginine biosynthesis



C00149: (S)-Malate, C00042: Succinate

Supplementary Figure S2b(ix). Metabolites putatively identified in *X. perforans* that are involved in TCA cycle.

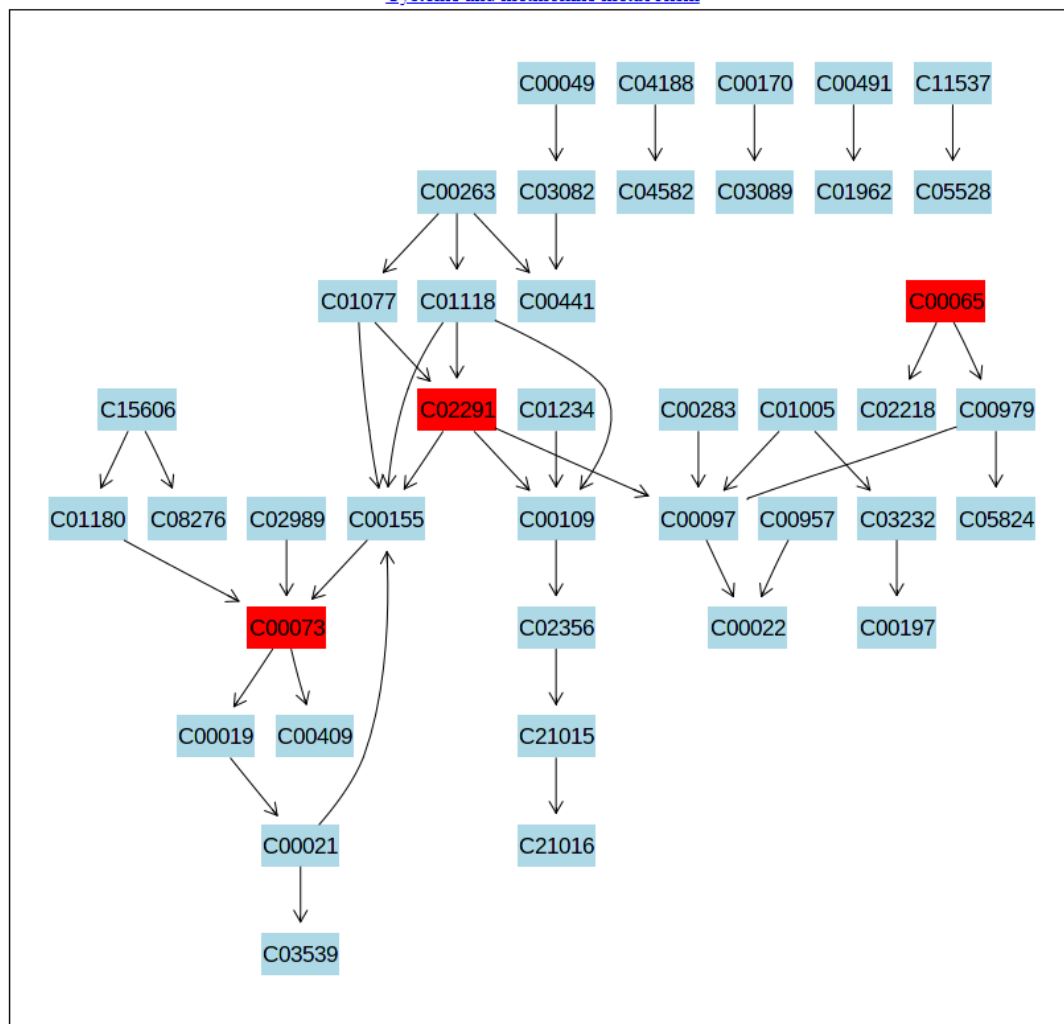
# Histidine metabolism



C00125: L-Histidine, C00785: Urocanate

Supplementary Figure S2b(x). Metabolites putatively identified in *X. perforans* that are involved in histidine metabolism.

Cysteine and methionine metabolism



C00065: L-Serine, C02291: L-Cystathionine, C00073: L-Methionine

Supplementary Figure S2b(xi). Metabolites putatively identified in *X. perforans* that are involved in cysteine and methionine metabolism.