

**Supporting Information:**

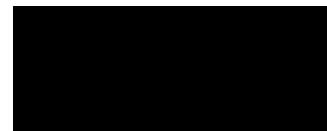
The global *Microcystis* interactome

Cook, K.V.,<sup>1,2</sup> C. Li,<sup>3</sup>, H. Cai<sup>1</sup>, L.R. Krumholz,<sup>3</sup> K.D. Hambright,<sup>1,2,\*</sup> H.W. Paerl,<sup>4</sup> M.M. Steffen,<sup>5</sup> A.E. Wilson,<sup>6</sup> M.A. Burford,<sup>7</sup> H.-P. Grossart,<sup>8</sup> D. P. Hamilton,<sup>7,9</sup> H. Jiang,<sup>10</sup> A. Sukenik,<sup>11</sup> D. Latour,<sup>12</sup> E.I. Meyer,<sup>13</sup> J. Padisák,<sup>14</sup> B. Qin,<sup>10</sup> R.M. Zamor,<sup>15,a</sup> and G. Zhu<sup>10</sup>

**Table S1.** Summary of metagenome data for each lake.

Lake	category	contigs number	contigs bases(Mbp)	N50(bp)	Max length(bp)	protein-coding gene number
Belső-tó	Bacteria	33496	27.1	765	74324	26699
	<i>Microcystis</i>	890	4.7	16388	81696	4267
Chaohu	Bacteria	23682	19.8	794	36145	18385
	<i>Microcystis</i>	5258	7.8	1944	54606	6268
Clarendon	Bacteria	82636	104.8	1392	321729	102844
	<i>Microcystis</i>	6740	10.9	2336	38246	9427
FP23	Bacteria	155545	19.5	1454	49139	28976
	<i>Microcystis</i>	4816	7.9	2248	35883	6825
Grand	Bacteria	73551	92.3	1418	105344	89141
	<i>Microcystis</i>	9312	11.1	1418	57431	8881
Kinneret	Bacteria	26202	37.0	1817	101729	37307
	<i>Microcystis</i>	4943	9.1	2627	55640	8028
Aasee	Bacteria	36892	57.9	2441	299862	56457
	<i>Microcystis</i>	1122	5.5	19101	77987	5191
Rotoehu	Bacteria	26009	31.1	1368	41132	32313
	<i>Microcystis</i>	503	4.3	16710	49814	4098
Villerest	Bacteria	30454	40.5	1691	97662	36391
	<i>Microcystis</i>	2619	6.7	5702	54900	5927

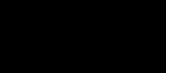
**Table S2.** KEGG orthology numbers and functional pathways found in *Microcystis* and the microbiome bacteria, indicating involvement in C, N, P, or S cycling. Complete pathways are indicated by black fill  , while modules with no more than one pathway missing, are indicated by blue fill  . Empty cells indicate missing or partial (>1 missing) pathways.

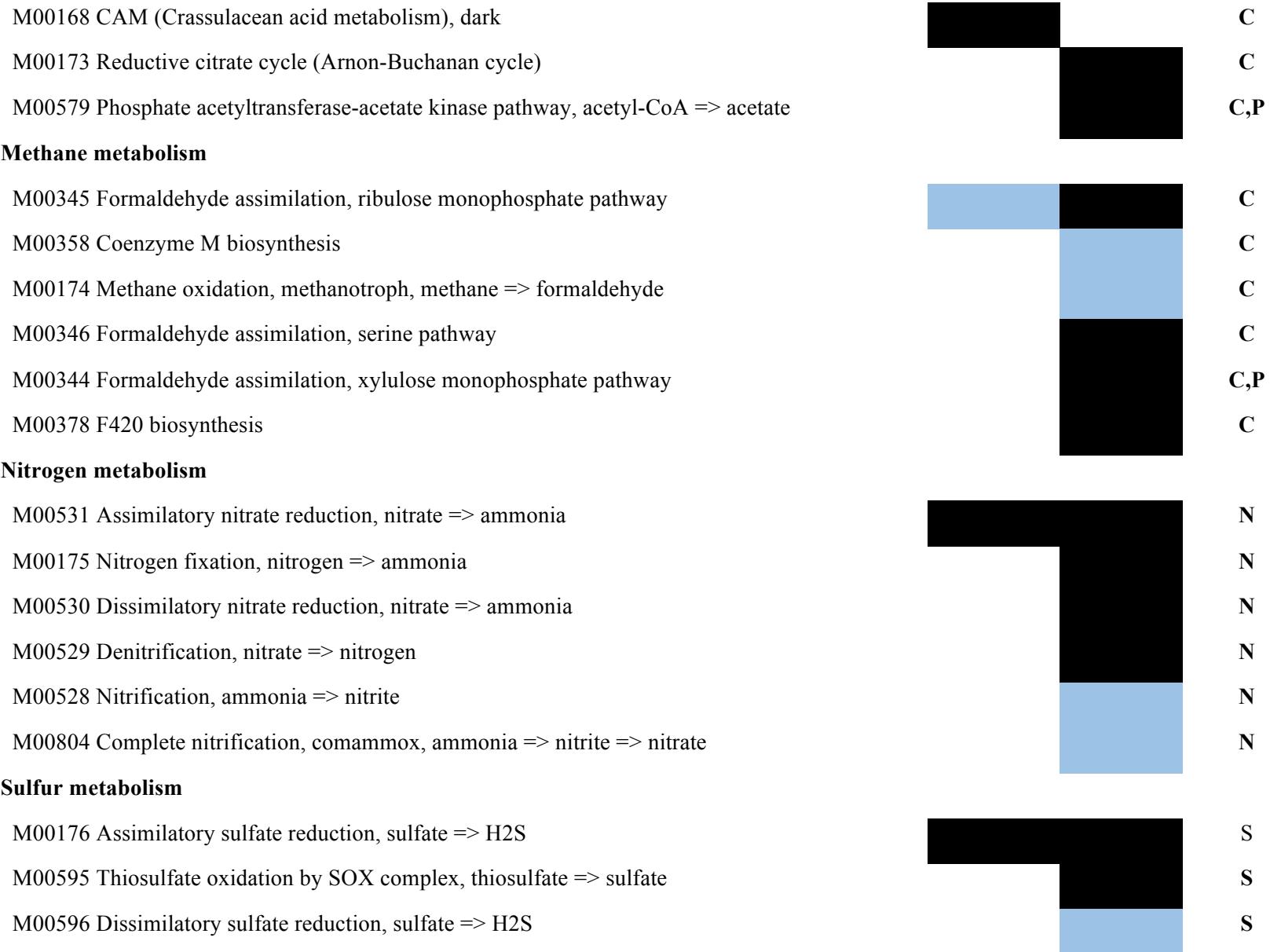
Pathway	<i>Microcystis</i>	Bacteria	Biogeochemical cycle
<b>Carbohydrate metabolism</b>			
M00001 Glycolysis (Embden-Meyerhof pathway), glucose => pyruvate			C
M00002 Glycolysis, core module involving three-carbon compounds			C
M00003 Gluconeogenesis, oxaloacetate => fructose-6P			C, P
M00307 Pyruvate oxidation, pyruvate => acetyl-CoA			C
M00009 Citrate cycle (TCA cycle, Krebs cycle)			C
M00010 Citrate cycle, first carbon oxidation, oxaloacetate => 2-oxoglutarate			C, S
M00011 Citrate cycle, second carbon oxidation, 2-oxoglutarate => oxaloacetate			C
M00004 Pentose phosphate pathway (Pentose phosphate cycle)			C, P
M00006 Pentose phosphate pathway, oxidative phase, glucose 6P => ribulose 5P			C,P
M00007 Pentose phosphate pathway, non-oxidative phase, fructose 6P => ribose 5P			C,P
M00580 Pentose phosphate pathway, archaea, fructose 6P => ribose 5P			C,P
M00005 PRPP biosynthesis, ribose 5P => PRPP			C,P
M00008 Entner-Doudoroff pathway, glucose-6P => glyceraldehyde-3P + pyruvate			C,P
M00308 Semi-phosphorylative Entner-Doudoroff pathway, gluconate => glycerate-3P			C,P

M00309 Non-phosphorylative Entner-Doudoroff pathway, gluconate/galactonate => glycerate		C
M00854 Glycogen biosynthesis, glucose-1P => glycogen/starch		C,P
M00855 Glycogen degradation, glycogen => glucose-6P		C,P
M00565 Trehalose biosynthesis, D-glucose 1P => trehalose		C,P
M00549 Nucleotide sugar biosynthesis, glucose => UDP-glucose		C,P
M00631 D-Galacturonate degradation, D-galacturonate => pyruvate + D glyceraldehyde 3P		C,P
M00061 D-Glucuronate degradation, D-glucuronate => pyruvate + D-glyceraldehyde 3P		C,P
M00632 Galactose degradation, Leloir pathway, galactose => alpha-D-glucose-1P		C,P
M00552 D-galactonate degradation, De Ley-Doudoroff pathway, D-galactonate => glycerate-3P		C,P
M00554 Nucleotide sugar biosynthesis, galactose => UDP-galactose		C,P
M00012 Glyoxylate cycle		C
M00373 Ethylmalonyl pathway		C
M00013 Malonate semialdehyde pathway, propanoyl-CoA => acetyl-CoA		C
M00741 Propanoyl-CoA metabolism, propanoyl-CoA => succinyl-CoA		C
M00130 Inositol phosphate metabolism, PI=>PIP2 => Ins(1,4,5)P3 => Ins(1,3,4,5)P4		C,P
M00132 Inositol phosphate metabolism, Ins(1,3,4)P3 => phytate		C

## Energy metabolism

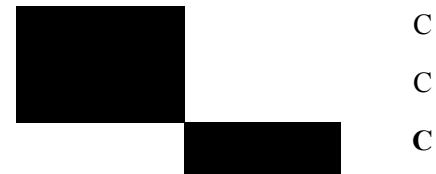
### Carbon fixation

M00165 Reductive pentose phosphate cycle (Calvin cycle)		C
M00166 Reductive pentose phosphate cycle, ribulose-5P => glyceraldehyde-3P		C,P
M00167 Reductive pentose phosphate cycle, glyceraldehyde-3P => ribulose-5P		C,P



## Photosynthesis

M00161 Photosystem II



M00163 Photosystem I

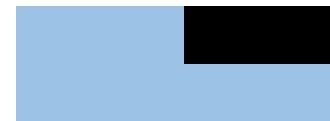


M00597 Anoxygenic photosystem II



## ATP synthesis (Structural complex)

M00144 NADH:quinone oxidoreductase, prokaryotes



M00146 NADH dehydrogenase (ubiquinone) 1 alpha subcomplex



M00145 NAD(P)H:quinone oxidoreductase, chloroplasts and cyanobacteria



M00149 Succinate dehydrogenase, prokaryotes



M00162 Cytochrome b6f complex



M00154 Cytochrome c oxidase



M00155 Cytochrome c oxidase, prokaryotes



M00153 Cytochrome bd ubiquinol oxidase



M00157 F-type ATPase, prokaryotes and chloroplasts



M00150 Fumarate reductase, prokaryotes



M00162 Cytochrome b6f complex



M00151 Cytochrome bc1 complex respiratory unit



M00152 Cytochrome bc1 complex



M00154 Cytochrome c oxidase



M00155 Cytochrome c oxidase, prokaryotes



M00153 Cytochrome bd ubiquinol oxidase



M00417 Cytochrome o ubiquinol oxidase



M00156 Cytochrome c oxidase, cbb3-type

M00159 V-type ATPase, prokaryotes

## Lipid metabolism

### Fatty acid metabolism

M00082 Fatty acid biosynthesis, initiation



C

M00083 Fatty acid biosynthesis, elongation

C

M00086 beta-Oxidation, acyl-CoA synthesis

C

M00087 beta-Oxidation

C

M00861 beta-Oxidation, peroxisome, VLCFA

C

### Sterol biosynthesis

M00862 beta-Oxidation, peroxisome, tri/dihydroxycholestanyl-CoA => cholooyl/chenodeoxycholooyl-CoA



C

M00107 Steroid hormone biosynthesis, cholesterol => pregnenolone => progesterone

C

M00110 C19/C18-Steroid hormone biosynthesis, pregnenolone => androstenedione => estrone

C

## Lipid metabolism

M00098 Acylglycerol degradation



C

M00088 Ketone body biosynthesis, acetyl-CoA => acetoacetate/3-hydroxybutyrate/acetone

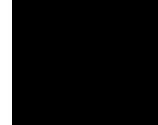


C

M00089 Triacylglycerol biosynthesis

C

M00090 Phosphatidylcholine (PC) biosynthesis, choline => PC



C,P

M00091 Phosphatidylcholine (PC) biosynthesis, PE => PC

C,P

M00092 Phosphatidylethanolamine (PE) biosynthesis, ethanolamine => PE



C,P

M00093 Phosphatidylethanolamine (PE) biosynthesis, PA => PS => PE



C,P

M00094 Ceramide biosynthesis



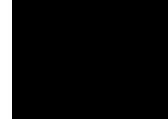
C

M00066 Lactosylceramide biosynthesis



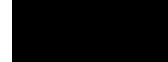
C

M00099 Sphingosine biosynthesis



C

M00100 Sphingosine degradation



C

## Nucleotide metabolism

### Purine metabolism

M00048 Inosine monophosphate biosynthesis, PRPP + glutamine => IMP



C,P

M00049 Adenine ribonucleotide biosynthesis, IMP => ADP,ATP



C,P

M00050 Guanine ribonucleotide biosynthesis IMP => GDP,GTP



C,P

M00546 Purine degradation, xanthine => urea



C,N

### Pyrimidine metabolism

M00051 Uridine monophosphate biosynthesis, glutamine (+ PRPP) => UMP



C,P

M00052 Pyrimidine ribonucleotide biosynthesis, UMP => UDP/UTP,CDP/CTP



C,P

M00053 Pyrimidine deoxyribonucleotide biosynthesis, CDP/CTP => dCDP/dCTP,dTDP/dTTP



C,P

M00046 Pyrimidine degradation, uracil => beta-alanine, thymine => 3-aminoisobutanoate



C,P

## Amino acid metabolism

### Serine and threonine metabolism

M00018 Threonine biosynthesis, aspartate => homoserine => threonine



C,N

M00555 Betaine biosynthesis, choline => betaine



C,N

M00020 Serine biosynthesis, glycerate-3P => serine



C,N

M00033 Ectoine biosynthesis, aspartate => ectoine

C,N

### Cysteine and methionine metabolism

M00021 Cysteine biosynthesis, serine => cysteine



C,N

M00338 Cysteine biosynthesis, homocysteine + serine => cysteine

C,N

M00034 Methionine salvage pathway

C,N

M00035 Methionine degradation

C,N

M00017 Methionine biosynthesis, apartate => homoserine => methionine

C,N

M00368 Ethylene biosynthesis, methionine => ethylene

C,N

### Branched-chain amino acid metabolism

M00019 Valine/isoleucine biosynthesis, pyruvate => valine / 2-oxobutanoate => isoleucine



C,N

M00535 Isoleucine biosynthesis, pyruvate => 2-oxobutanoate

C,N

M00570 Isoleucine biosynthesis, threonine => 2-oxobutanoate => isoleucine

C,N

M00432 Leucine biosynthesis, 2-oxoisovalerate => 2-oxoisocaproate

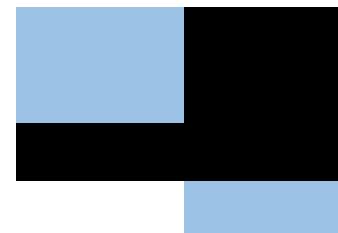
C,N

M00036 Leucine degradation, leucine => acetoacetate + acetyl-CoA

C,N

### Lysine metabolism

M00016 Lysine biosynthesis, succinyl-DAP pathway, aspartate => lysine



C,N

M00526 Lysine biosynthesis, DAP dehydrogenase pathway, aspartate => lysine

C,N

M00527 Lysine biosynthesis, DAP aminotransferase pathway, aspartate => lysine

C,N

M00433 Lysine biosynthesis, 2-oxoglutarate => 2-oxoadipate

C,N

### Arginine and proline metabolism

M00028 Ornithine biosynthesis, glutamate => ornithine



C,N

M00844 Arginine biosynthesis, ornithine => arginine

C,N

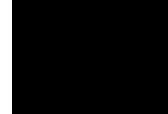
M00015 Proline biosynthesis, glutamate => proline

C,N

M00845 Arginine biosynthesis, glutamate => acetylcitrulline => arginine

C,N

M00047 Creatine pathway



C,N

### Polyamine biosynthesis

M00133 Polyamine biosynthesis, arginine => agmatine => putrescine => spermidine



C,N

M00134 Polyamine biosynthesis, arginine => ornithine => putrescine

C,N

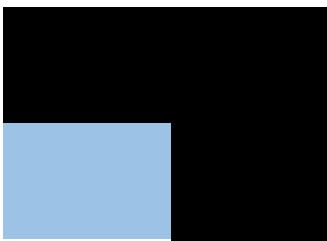
M00136 GABA biosynthesis, prokaryotes, putrescine => GABA



C,N

### Aromatic amino acid metabolism

M00022 Shikimate pathway, phosphoenolpyruvate + erythrose-4P => chorismate



C,N

M00023 Tryptophan biosynthesis, chorismate => tryptophan

C,N

M00024 Phenylalanine biosynthesis, chorismate => phenylalanine

C,N

M00040 Tyrosine biosynthesis, prephanate => pretyrosine => tyrosine

C,N

M00025 Tyrosine biosynthesis, chorismate => tyrosine

C,N

M00042 Catecholamine biosynthesis, tyrosine => dopamine => noradrenaline => adrenaline

C,N

M00044 Tyrosine degradation, tyrosine => homogentisate

C,N

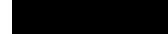
M00533 Homoprotocatechuate degradation, homoprotocatechuate => 2-oxohept-3-enedioate

C,N

M00545 Trans-cinnamate degradation, trans-cinnamate => acetyl-CoA

C,N

M00038 Tryptophan metabolism, tryptophan => kynurenine => 2-aminomuconate



C,N

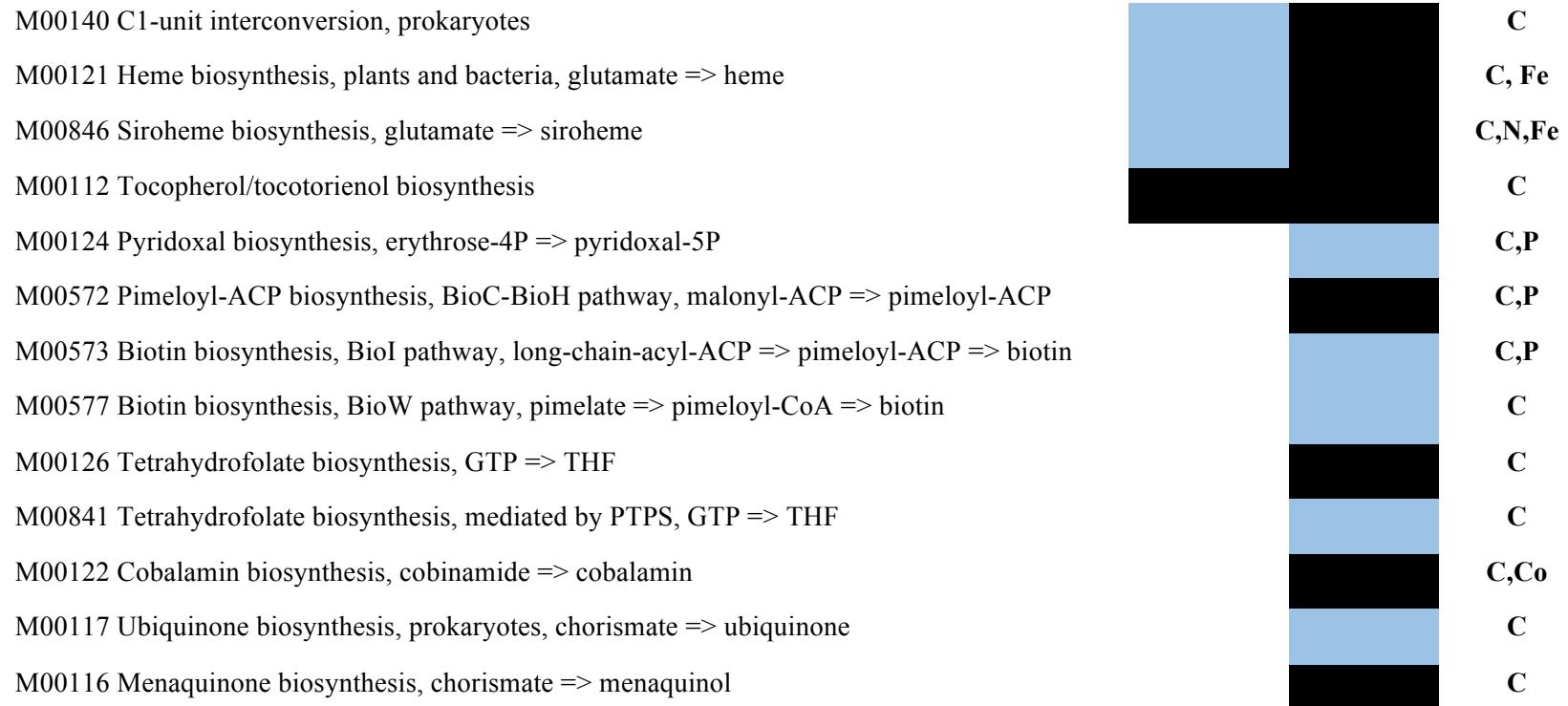
### Glycan metabolism

## Lipopolysaccharide metabolism

M00064 ADP-L-glycero-D-manno-heptose biosynthesis	C
M00072 N-glycosylation by oligosaccharyltransferase	C
M00073 N-glycan precursor trimming	C
M00056 O-glycan biosynthesis, mucin type core	C
M00070 Glycosphingolipid biosynthesis, lacto-series, LacCer => Lc4Cer	C
M00068 Glycosphingolipid biosynthesis, globo-series, LacCer => Gb4Cer	C
M00060 KDO2-lipid A biosynthesis, Raetz pathway, LpxL-LpxM type	C
M00866 KDO2-lipid A biosynthesis, Raetz pathway, non-LpxL-LpxM type	C
M00063 CMP-KDO biosynthesis	C
M00064 ADP-L-glycero-D-manno-heptose biosynthesis	C

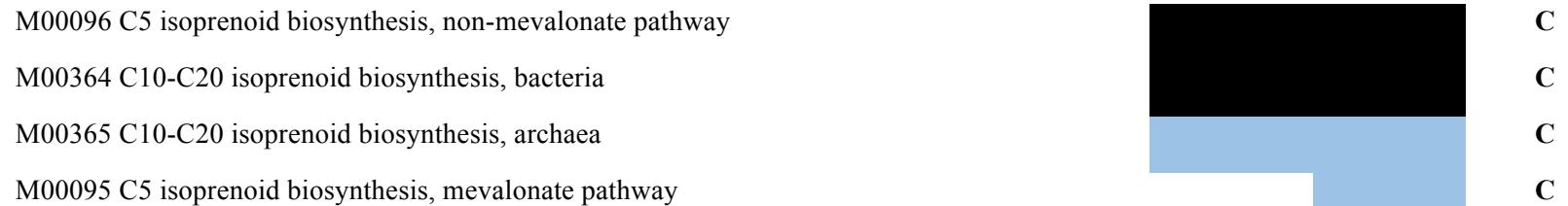
## Metabolism of cofactors and vitamins

Cofactor and vitamin metabolism	C,P
M00127 Thiamine biosynthesis, AIR => thiamine-P/thiamine-2P	C,P
M00125 Riboflavin biosynthesis, GTP => riboflavin/FMN/FAD	C,P
M00115 NAD biosynthesis, aspartate => NAD	C,N
M00119 Pantothenate biosynthesis, valine/L-aspartate => pantothenate	C
M00120 Coenzyme A biosynthesis, pantothenate => CoA	C
M00123 Biotin biosynthesis, pimeloyl-ACP/CoA => biotin	C
M00842 Tetrahydrobiopterin biosynthesis, GTP => BH4	C
M00843 L-threo-Tetrahydrobiopterin biosynthesis, GTP => L-threo-BH4	C



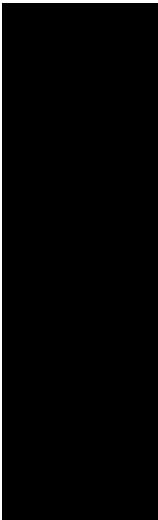
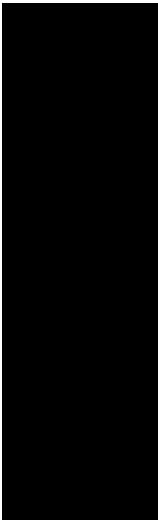
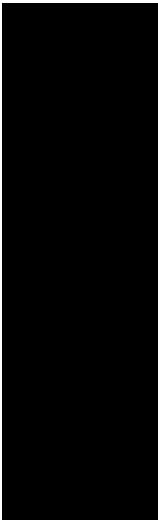
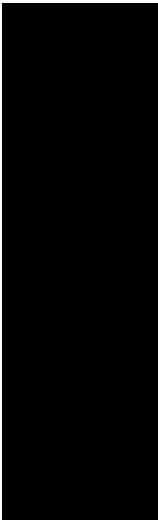
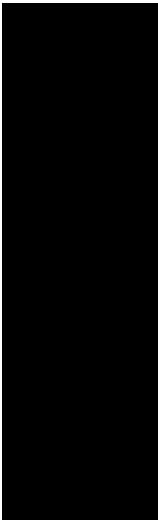
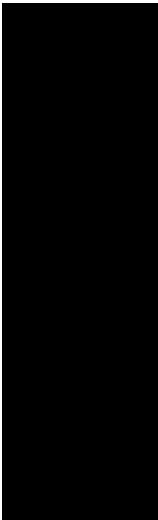
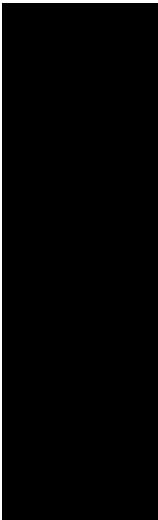
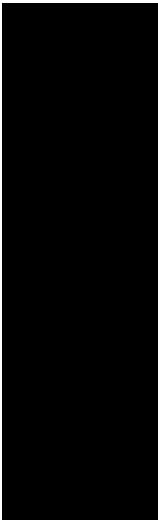
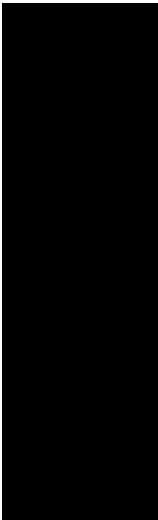
### Biosynthesis of terpenoids and polyketides

#### Terpenoid backbone biosynthesis

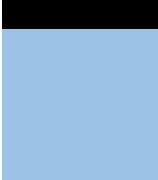
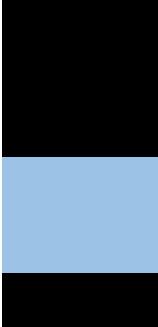
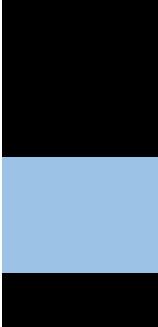
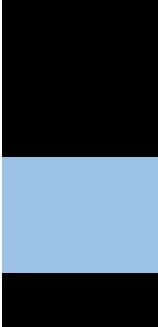
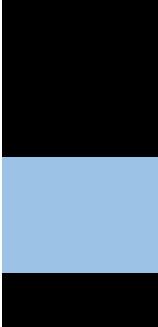
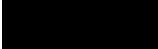


### Xenobiotics biodegradation

#### Aromatics degradation

M00538 Toluene degradation, toluene => benzoate		C
M00537 Xylene degradation, xylene => methylbenzoate		C
M00551 Benzoate degradation, benzoate => catechol / methylbenzoate => methylcatechol (ete)		C
M00637 Anthranilate degradation, anthranilate => catechol		C
M00568 Catechol ortho-cleavage, catechol => 3-oxoadipate		C
M00569 Catechol meta-cleavage, catechol => acetyl-CoA / 4-methylcatechol => propanoyl-CoA		C
M00540 Benzoate degradation, cyclohexanecarboxylic acid =>pimeloyl-CoA		C
M00638 Salicylate degradation, salicylate => gentisate		C
M00623 Phthalate degradation, phthalate => protocatechuate		C

### Drug resistance

M00627 beta-Lactam resistance, Bla system	
M00745 Imipenem resistance, repression of porin OprD (13)	
M00651 Vancomycin resistance, D-Ala-D-Lac type	
M00726 Cationic antimicrobial peptide (CAMP) resistance, lysyl-phosphatidylglycerol (L-PG) synthase MprF	
M00744 Cationic antimicrobial peptide (CAMP) resistance, protease PgtE	
M00718 Multidrug resistance, efflux pump MexAB-OprM	
M00642 Multidrug resistance, efflux pump MexJK-OprM	
M00643 Multidrug resistance, efflux pump MexXY-OprM	
M00769 Multidrug resistance, efflux pump MexPQ-OpmE	
M00649 Multidrug resistance, efflux pump AdeABC	

M00696 Multidrug resistance, efflux pump AcrEF-TolC

M00697 Multidrug resistance, efflux pump MdtEF-TolC

M00698 Multidrug resistance, efflux pump BpeEF-OprC

M00700 Multidrug resistance, efflux pump AbcA

M00714 Multidrug resistance, efflux pump QacA

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