A consolidated analysis of the physiologic and molecular responses induced under acid stress in the legume-symbiont model-soil bacterium *Sinorhizobium meliloti*.

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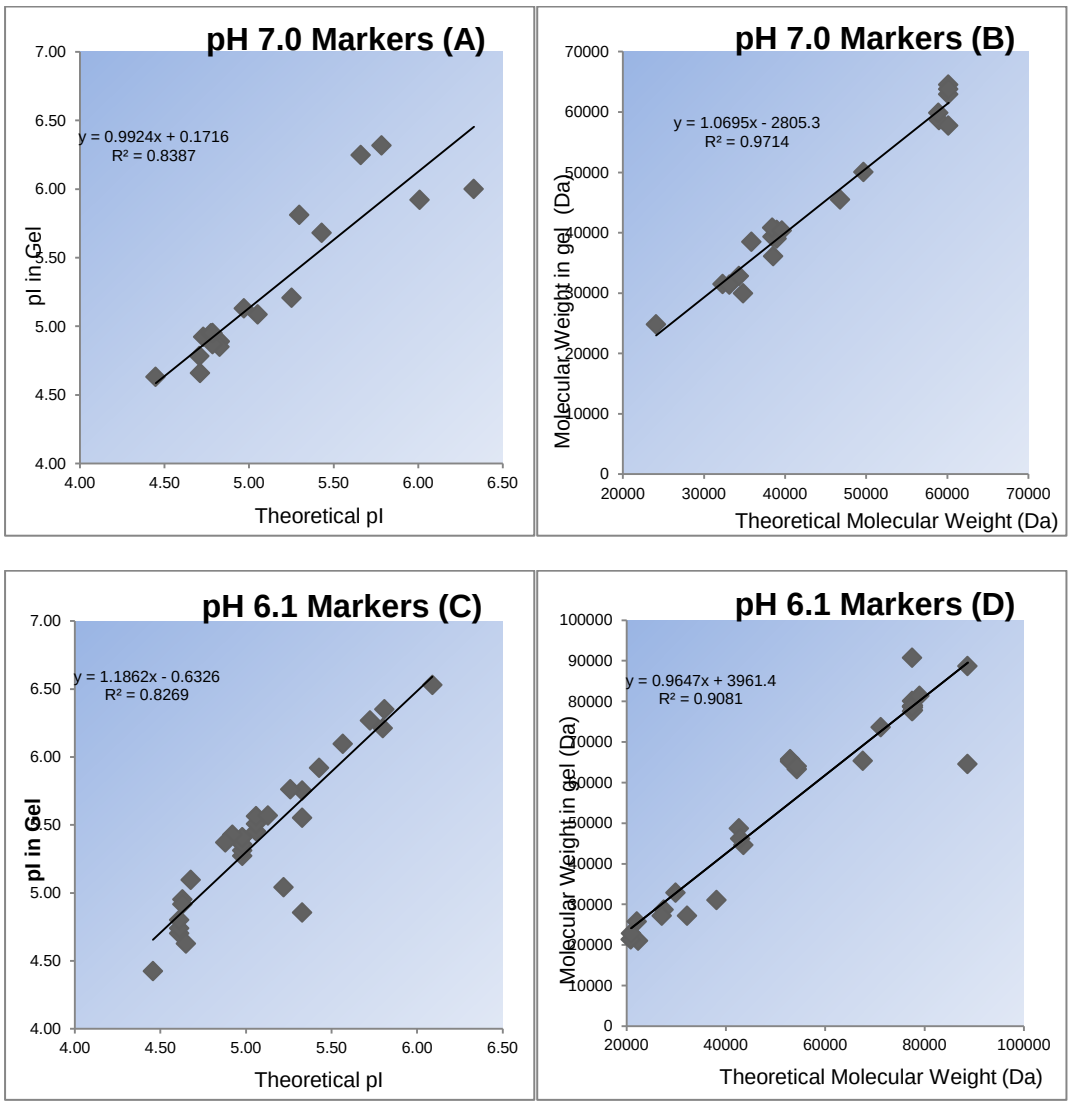
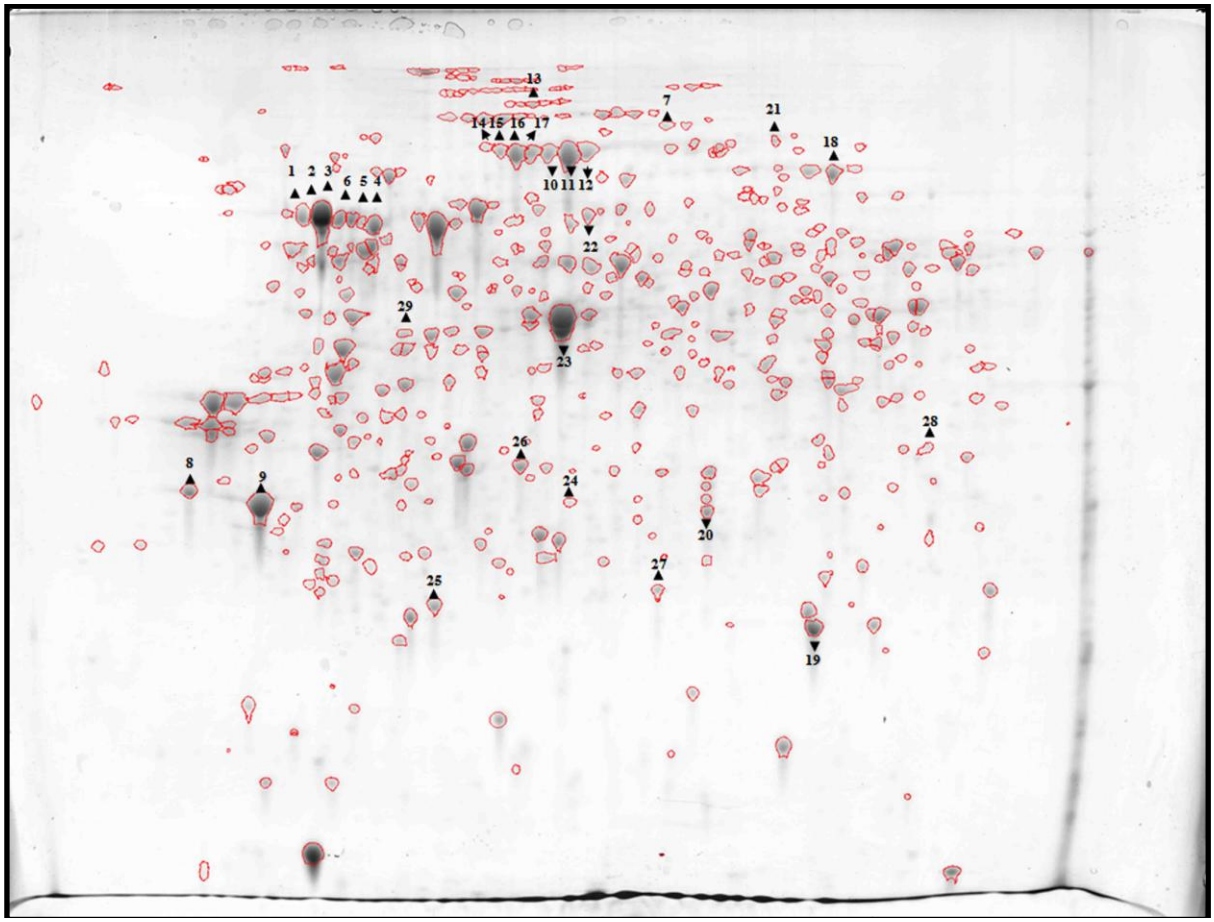
SUPPLEMENTARY DATA

Fig. S1. Correlation analysis between the experimental and the expected (calculated) values of molecular weight (Panel B, pH 7.0 and Panel D, pH 6.1) and isolectric point (Panel A, pH 7.0 and Panel C, pH 6.1) of the protein markers identified by PMF in the gels shown in Figs. 1 and 2. The molecular weight and isoelectric-point (pI) values for each individual polypeptide were calculated from the corresponding amino-acid sequence (abscissa). Experimental values were inferred from the position in the 2-D gels by means of the *Image Master*™ software (*ordinate*). For most polypeptides a good correlation was obtained between the observed and the expected molecular weight and pI values.



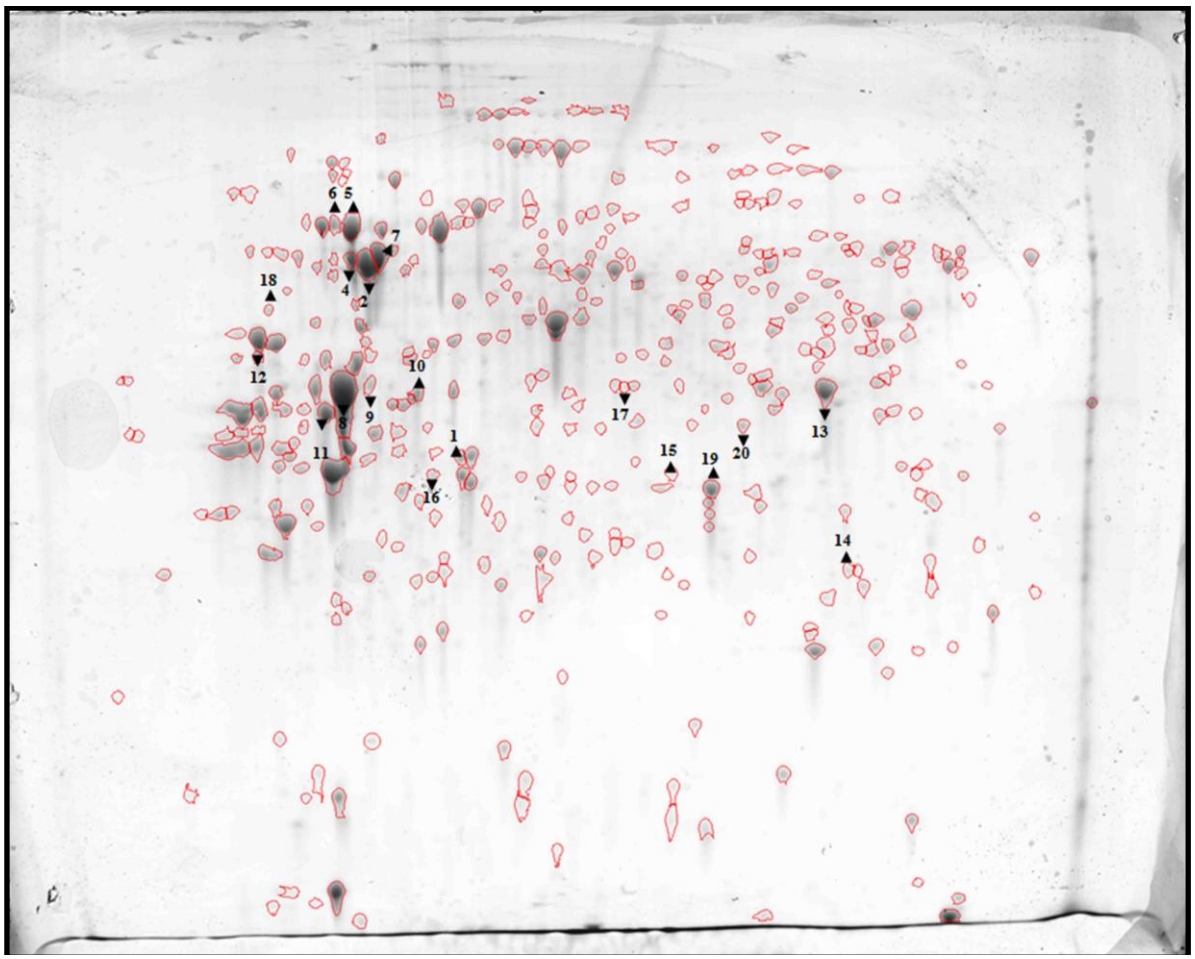
SUPPLEMENTARY DATA

Fig. S2. Image-Master detection of induced polypeptides in the cytosolic proteome of *S. meliloti* 2011 grown in chemostat at pH 6.1 compared to the expression of the corresponding polypeptides in the proteome of the same rhizobia grown at pH 7.0. The ratio of homologous polypeptides in one pH condition compared to the other was estimated by the ratio of the spot volumes (Image Master) after each one was normalized to the total intensity (all spots) from the corresponding gel. For each pH condition four independent gels were analyzed, including those from Figs.1 and 2. The numerical codes (in black) for each red-outlined spot in the figure (differentially expressed polypeptides) correspond to the respective numbers in the first column of Table 2.



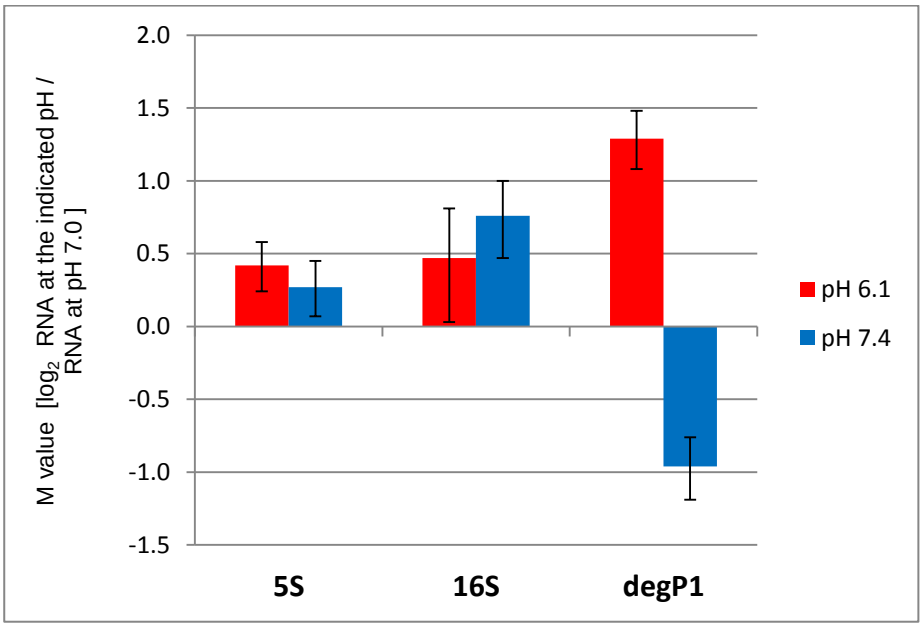
SUPPLEMENTARY DATA

Fig. S3. Image-Master detection of induced polypeptides in the cytosolic proteome of *S. meliloti* 2011 grown in chemostat at pH 7.0 compared to the expression of the corresponding polypeptides in the proteome of the same rhizobia grown at pH 6.1. The ratio of homologous polypeptides in one pH condition compared to the other was estimated by the ratio of the spot volumes (Image Master) after each one was normalized to the total intensity (all spots) from the corresponding gel. For each pH condition four independent gels were analyzed, including those from Figs.1 and 2. The numerical codes (in black) for each red-outlined spot in the figure (differentially expressed polypeptides) correspond to the respective numbers in the first column of Table 3.



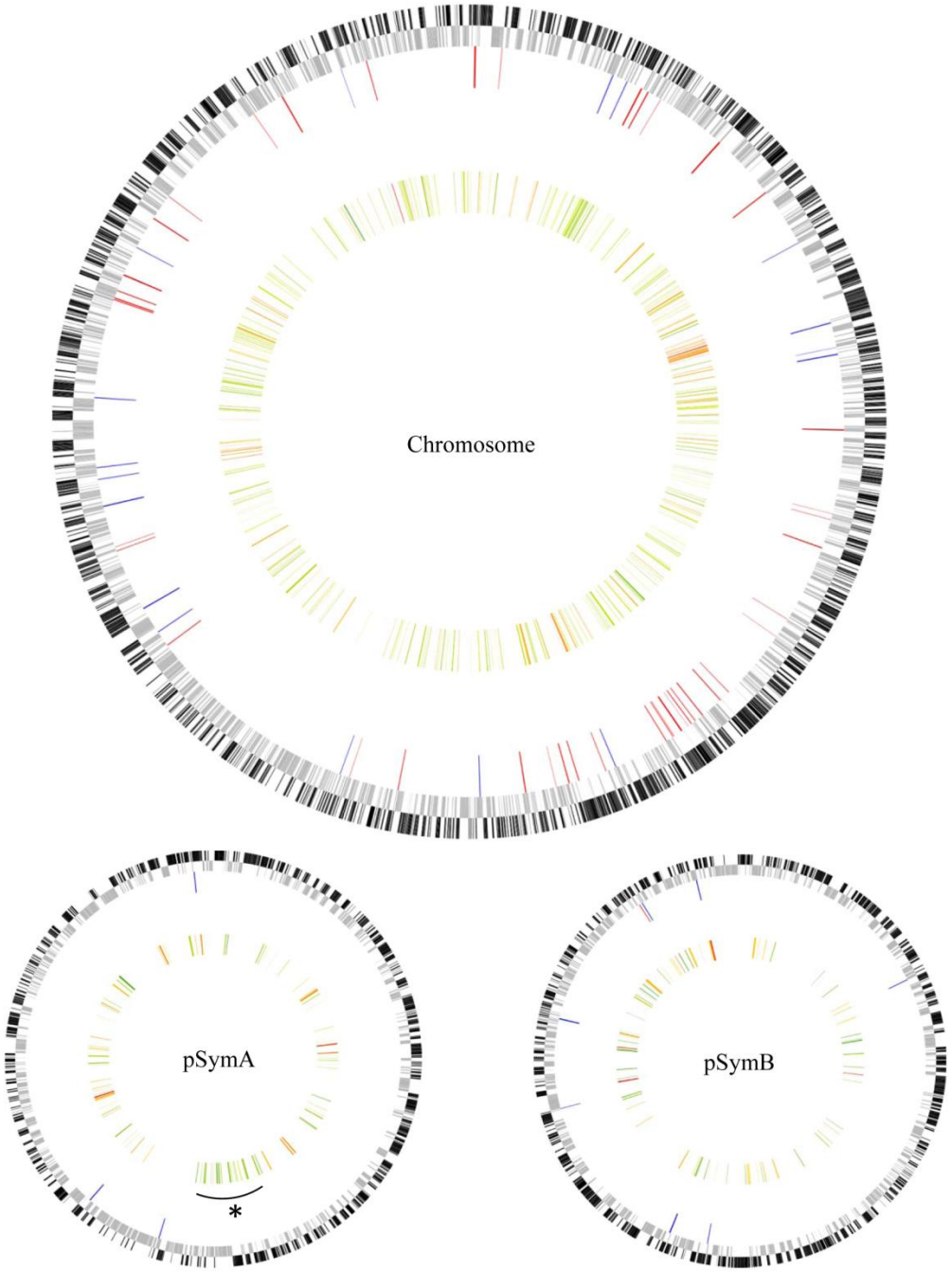
SUPPLEMENTARY DATA

Fig. S4. qRT-PCR estimation of 5S and 16S rRNAs in *S. meliloti* cells grown in the chemostat under steady state at pH 7.0, and at pH 6.1. The quantification of specific RNA species was carried out by quantitative reverse-transcription PCR using a KAPA SYBR FAST One-Step qRT-PCR kit (Kapa Biosystems Inc. Wilmington, MA, USA) according to the manufacturer's instructions. Analyses were performed using a same normalized amount of total RNA for all samples. M values represent the $\log_2$ of the fold change of the indicated RNA species at pH 6.1 (red bars) and 7.4 (blue bars) both with respect to their corresponding amounts at pH 7.0 (reference condition). 5S and 16S correspond to the analysis of 5S and 16S rRNA. *degP1* (SMc02365) corresponds to the analysis of the mRNA of an acid-induced gene used as positive control ($M^{\text{pH 6.1 / pH 7.0}}$ from the microarrays = 1.98). The DegP1 polypeptide was also induced in the proteome of acid-grown rhizobia (fold change *ca.* 4.8 in Table 2, so with an estimated $M^{\text{pH 6.1 / pH 7.0}}$ from the proteome = 2.26). The M values are the means calculated from three technical qRT-PCR replicas. The bars represent the standard deviations.



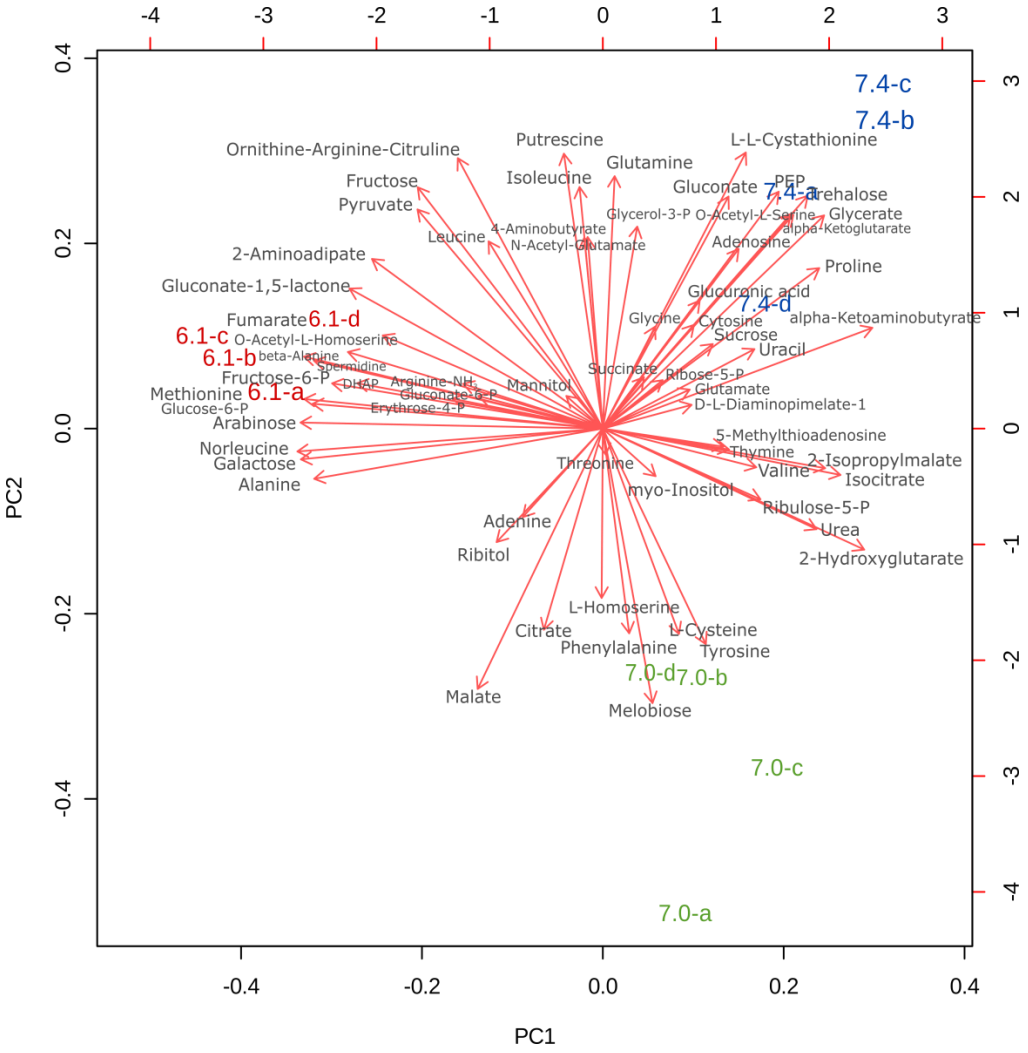
SUPPLEMENTARY DATA

Fig. S5. Genomic distribution of proteome and transcriptome markers differentially overexpressed at pH 6.1 *versus* 7.0. The two outermost circular array of lines on each replicon show—in black and in gray—the respective positions of open reading frames within the two complementary DNA strands. The next array inside shows—with red and blue lines—the genomic position of genes encoding polypeptides that were observed to be induced under acidic and neutral extracellular conditions, respectively (from the proteomic data). The innermost array marks—with green and orange lines—the genomic position of genes encoding RNAs that were also observed to be induced under acidic and neutral extracellular conditions, respectively (from the transcriptome data). The pSymA region characterized by a high density of overexpressed genes at pH 6.1 (*cf*. the text) is outlined and marked by an asterisk.


Chromosome
pSymA
*
pSymB

SUPPLEMENTARY DATA

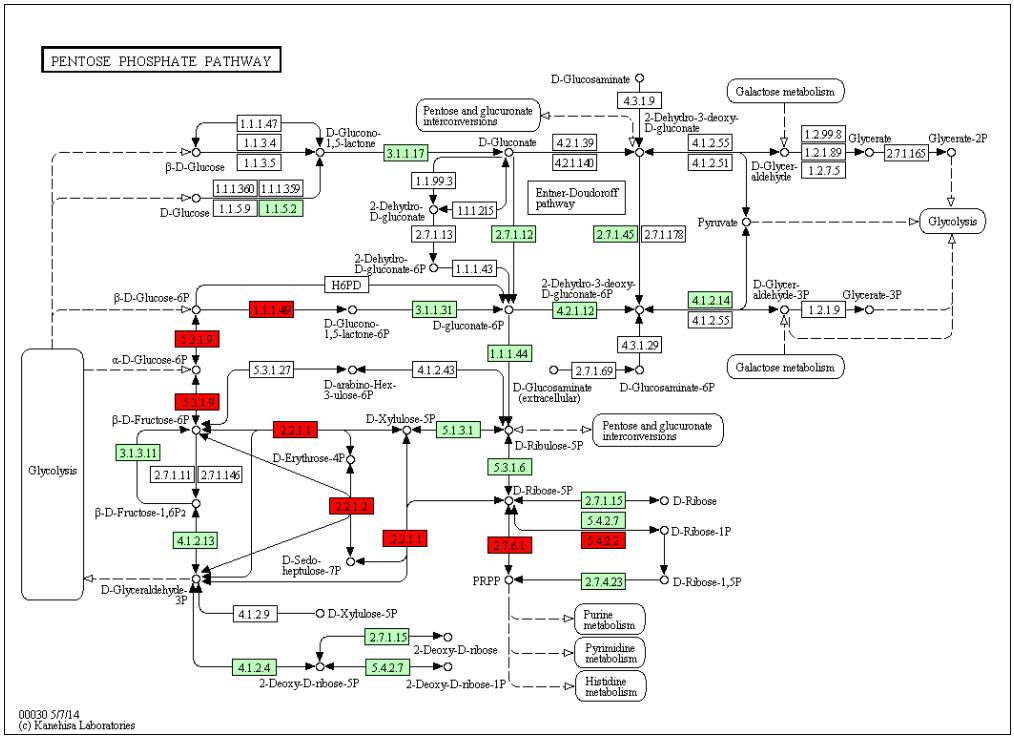
Fig. S6. Vector-correlation plot between the variables examined (*i. e.*, the amount of metabolites) and the PC1 and PC2 spaces of PCA. The direction and length of the vectors are indicative of the positive contribution of each individual metabolite to the position of each sample analyzed in the plot (*i. e.*, from rhizobia grown at pH 6.1, pH 7.0, or pH 7.4).



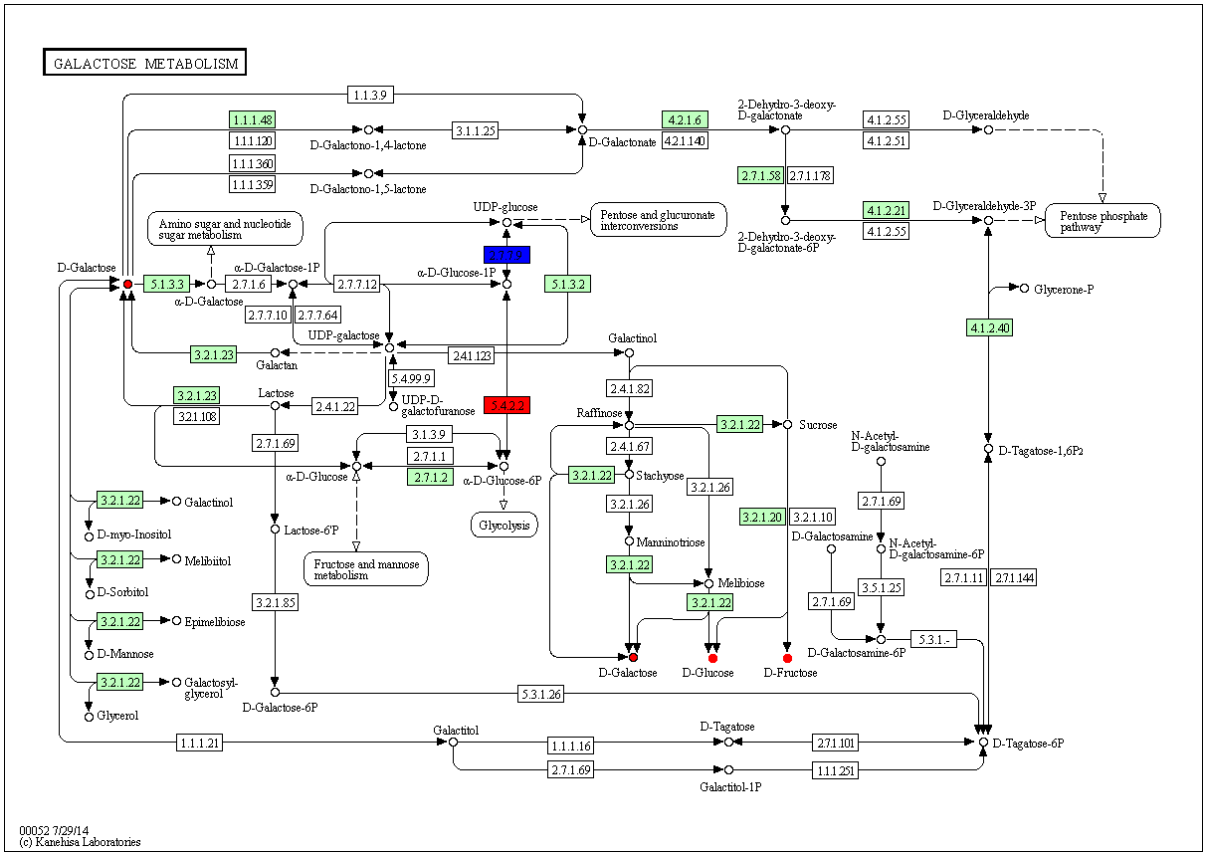
SUPPLEMENTARY DATA

Fig. S7. Graphical maps indicating significant increases of specific RNAs, polypeptides, or metabolites on different *S. meliloti* metabolic pathways (KEGG format); and also changes in RNAs/polypeptides related to cellular macromolecular complexes (transport, energy, translation). Colored rectangles: correspond to increased RNAs or polypeptides (i.e. RNAs listed in Supplementary Table 1, and polypeptides listed in the main Tables 1 and 2). Colored circles: correspond to increased metabolites (i.e. those listed in Supplementary Table 2, and also presented in the volcano plot from Fig. 3). **Red** and **blue** colors indicate increased amount of the corresponding species at **pH 6.1** and **pH 7.0**, respectively. References to panels are as follows: **A.** Pentose phosphate pathway; **B.** Galactose metabolism; **C.** Starch and sucrose metabolism; **D.** Carbon metabolism; **E.** Arginine and proline metabolism; **F.** Cysteine and methionine metabolism; **G.** Glutathione metabolism; **H.** Aminoacids biosynthesis; **I.** Purine metabolism; **J.** Pyrimidine metabolism; **K.** Biotin metabolism; **L.** Ribosome components; **M.** RNA degradation; **N.** O xidative phosphorylation; **O.** Flagellar assembly; **P.** Secretion systems; **Q.** Two-component systems; and **R.** ABC transporters.

A



B


GALACTOSE METABOLISM
D-Galactose
α-D-Galactose
α-D-Galactose-1P
α-D-Glucose-1P
UDP-glucose
UDP-galactose
Amino sugar and nucleotide sugar metabolism
Pentose and glucuronate interconversions
D-Galactono-1,4-lactone
D-Galactono-1,5-lactone
D-Galactonate
2-Dehydro-3-deoxy-D-galactonate
2-Dehydro-3-deoxy-D-galactonate-6P
D-Glyceraldehyde
D-Glyceraldehyde-3P
Pentose phosphate pathway
Glycerone-P
Galactan
Galactinol
Lactose
UDP-D-galactofuranose
Raffinose
Sucrose
Stachyose
Manninotriose
Melibiose
N-Acetyl-D-galactosamine
N-Acetyl-D-galactosamine-6P
D-Tagatose-1,6P2
D-myo-Inositol
Melibiitol
D-Sorbitol
Epimelibiose
D-Mannose
Galactosyl-glycerol
Glycerol
Lactose-6'P
α-D-Glucose
α-D-Glucose-6P
Glycolysis
Fructose and mannose metabolism
D-Galactosamine
D-Galactosamine-6P
D-Galactose
D-Glucose
D-Fructose
D-Galactose-6P
Galactitol
D-Tagatose
D-Tagatose-6P
Galactitol-1P
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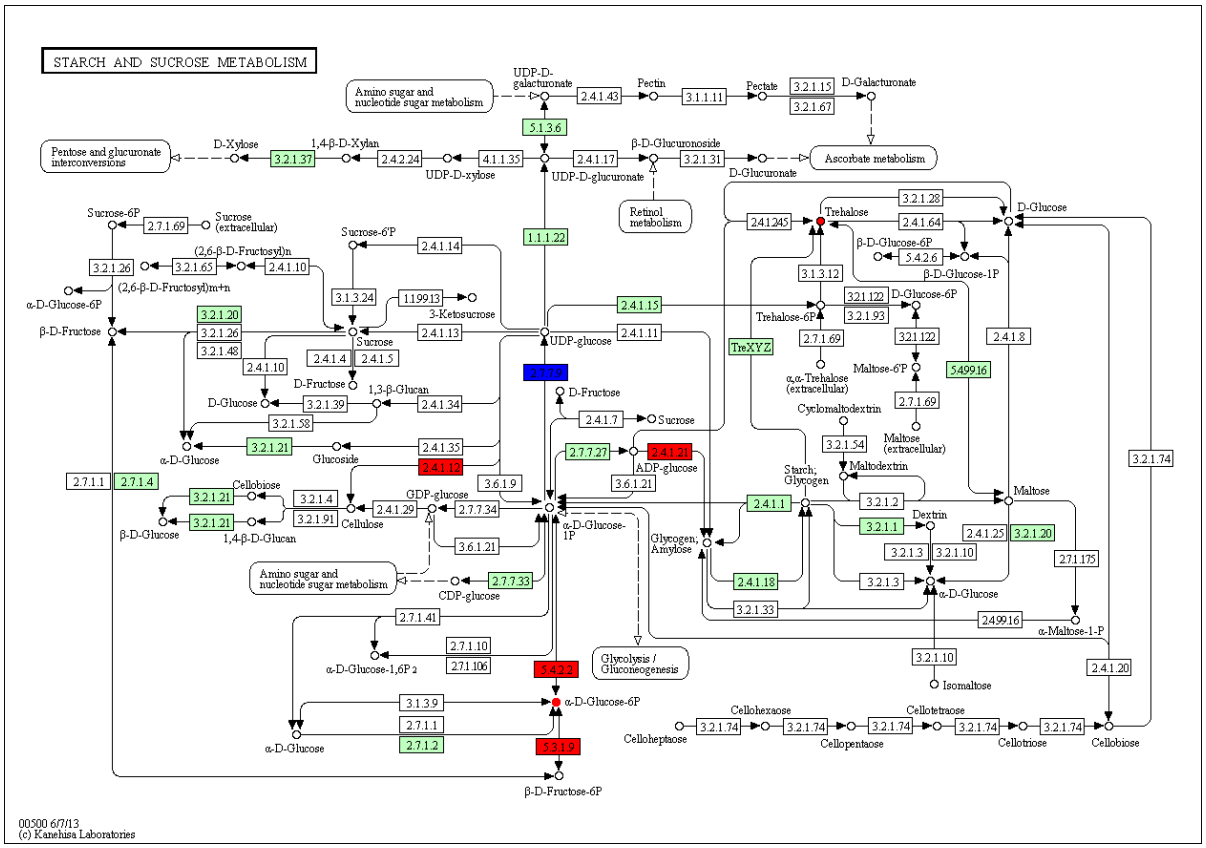
C


STARCH AND SUCROSE METABOLISM
Amino sugar and nucleotide sugar metabolism
Pentose and glucuronate interconversions
Ascorbate metabolism
Retinol metabolism
UDP-D-galacturonate
Pectin
Pectate
D-Galacturonate
D-Xylose
1,4-β-D-Xylan
UDP-D-xylose
UDP-D-glucuronate
β-D-Glucuronoside
D-Glucuronate
Sucrose-6P
Sucrose (extracellular)
Sucrose-6'P
(2,6-β-D-Fructosyl)n
(2,6-β-D-Fructosyl)m+n
α-D-Glucose-6P
β-D-Fructose
Sucrose
3-Ketosucrose
UDP-glucose
D-Fructose
D-Glucose
1,3-β-Glucan
Glucoside
α-D-Glucose
Cellobiose
β-D-Glucose
1,4-β-D-Glucan
Cellulose
GDP-glucose
CDP-glucose
ADP-glucose
α-D-Glucose-1P
Glycogen; Amylose
Starch; Glycogen
Maltodextrin
Maltose
Dextrin
Isomaltose
α-D-Glucose-1,6P 2
α-D-Glucose-6P
β-D-Fructose-6P
Trehalose
Trehalose-6P
β-D-Glucose-6P
β-D-Glucose-1P
D-Glucose-6P
α,α-Trehalose (extracellular)
Cyclomaltodextrin
Maltose (extracellular)
Maltose-6P
α-D-Glucose
α-Maltose-1-P
Cellohexaose
Cellotetraose
Cellopentaose
Cellotriose
Cellobiose
Cellobiose
00500 6/7/13
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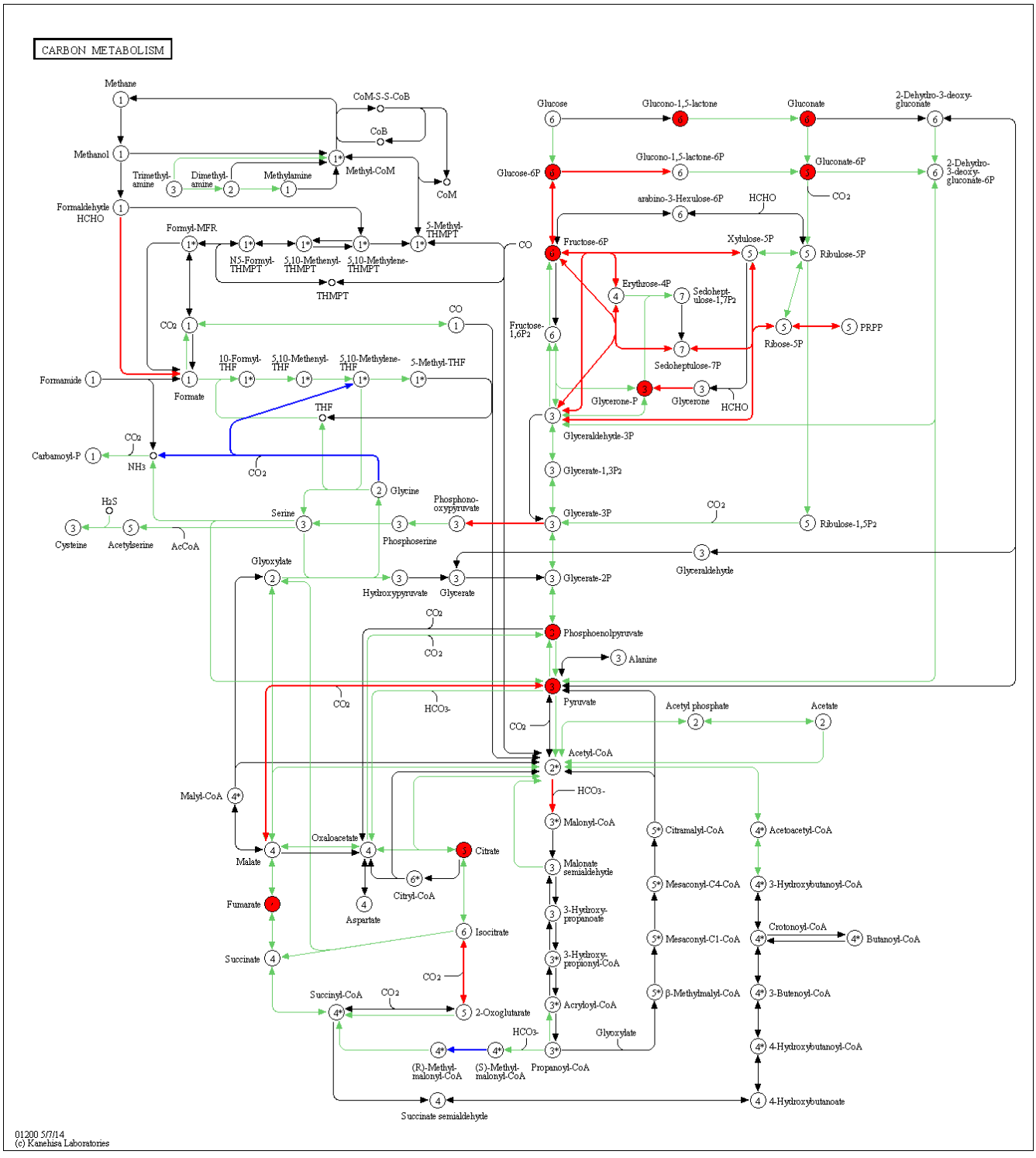
D


CARBON METABOLISM
Methane
CoM-S-S-CoB
CoB
Methanol
Methyl-CoM
CoM
Trimethyl-amine
Dimethyl-amine
Methylamine
Formaldehyde HCHO
Formyl-MFR
5-Methyl-THMPT
N5-Formyl-THMPT
5,10-Methenyl-THMPT
5,10-Methylene-THMPT
THMPT
CO
CO2
Formamide
Formate
10-Formyl-THF
5,10-Methenyl-THF
5,10-Methylene-THF
5-Methyl-THF
THF
Carbamoyl-P
NH3
Glycine
H2S
Cysteine
Acetylserine
AcCoA
Serine
Phosphono-oxypyruvate
Phosphoserine
Glyoxylate
Hydroxypyruvate
Glycerate
Glycerate-2P
Glycerate-3P
Glycerate-1,3P2
Glyceraldehyde-3P
Glyceraldehyde
Glycerone-P
Glycerone
HCHO
Fructose-1,6P2
Fructose-6P
Erythrose-4P
Sedohept-ulose-1,7P2
Sedoheptulose-7P
Ribose-5P
PRPP
Ribulose-5P
Xylulose-5P
Ribulose-1,5P2
arabino-3-Hexulose-6P
Glucose
Glucose-6P
Glucono-1,5-lactone
Glucono-1,5-lactone-6P
Gluconate
Gluconate-6P
2-Dehydro-3-deoxy-gluconate
2-Dehydro-3-deoxy-gluconate-6P
Phosphoenolpyruvate
Alanine
Pyruvate
HCO3-
Acetyl phosphate
Acetate
Acetyl-CoA
Malyl-CoA
Malonyl-CoA
Malonate semialdehyde
3-Hydroxy-propanoate
3-Hydroxy-propionyl-CoA
Acryloyl-CoA
Propanoyl-CoA
Citramalyl-CoA
Mesaconyl-C4-CoA
Mesaconyl-C1-CoA
β-Methylmalyl-CoA
Acetoacetyl-CoA
3-Hydroxybutanoyl-CoA
Crotonoyl-CoA
Butanoyl-CoA
3-Butenoyl-CoA
4-Hydroxybutanoyl-CoA
4-Hydroxybutanoate
Oxaloacetate
Malate
Citrate
Citryl-CoA
Aspartate
Fumarate
Isocitrate
Succinate
Succinyl-CoA
2-Oxoglutarate
Succinate semialdehyde
(R)-Methyl-malonyl-CoA
(S)-Methyl-malonyl-CoA
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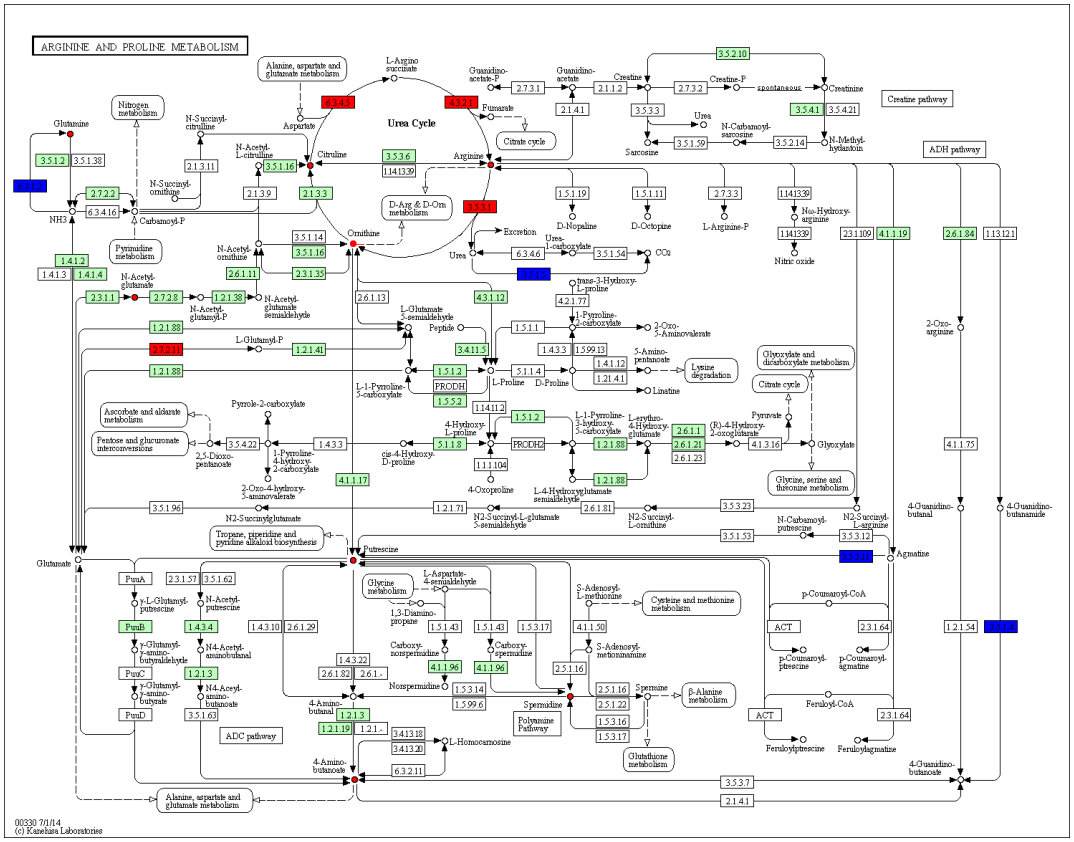
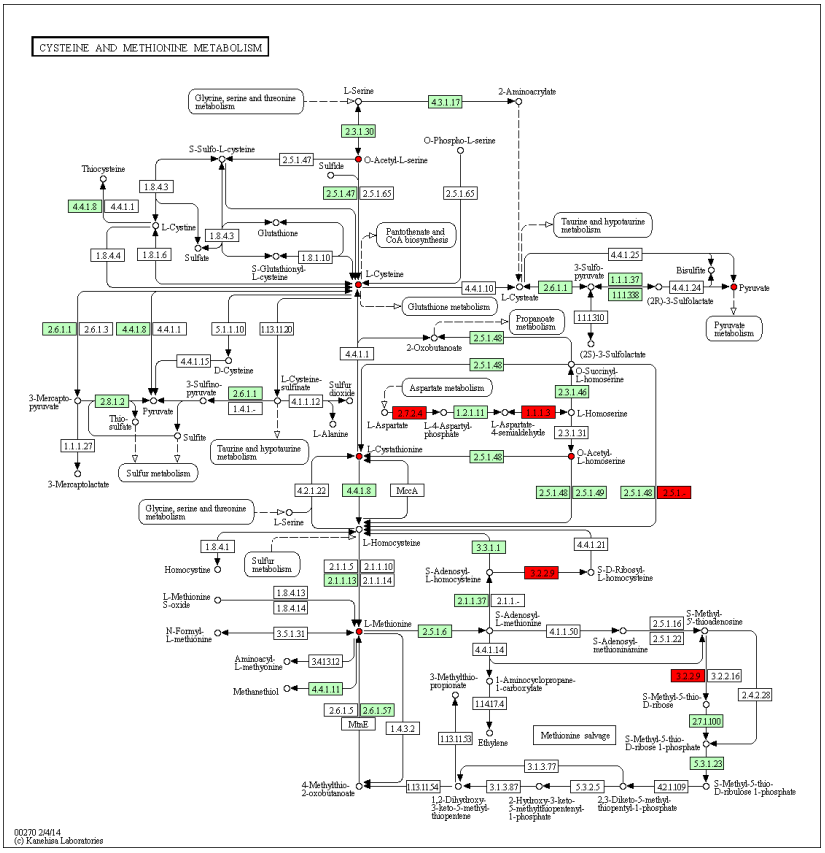
(c) Kanehisa Laboratories

E


ARGININE AND PROLINE METABOLISM
Urea Cycle
Ornithine
Arginine
Citrulline
Aspartate
Fumarate
Citrate cycle
Creatine pathway
ADH pathway
Glutamine
Glutamate
Nitrogen metabolism
Pyrimidine metabolism
Carbamoyl-P
Putrescine
Agmatine
Proline
Glycine, serine and threonine metabolism
Glyoxylate and dicarboxylate metabolism
Lysine degradation
Ascorbate and aldarate metabolism
Pentose and glucuronate interconversions
Tropane, piperidine and pyridine alkaloid biosynthesis
Glycine metabolism
Cysteine and methionine metabolism
Spermine
Spermidine
Polyamine Pathway
β-Alanine metabolism
Glutathione metabolism
ADC pathway
Alanine, aspartate and glutamate metabolism
00330 7/1/14
(c) Kanehisa Laboratories

F


CYSTEINE AND METHIONINE METABOLISM
Glycine, serine and threonine metabolism
L-Serine
2-Aminoacrylate
O-Acetyl-L-serine
O-Phospho-L-serine
S-Sulfo-L-cysteine
Thiocysteine
Sulfide
L-Cystine
Glutathione
Sulfate
S-Glutathionyl-L-cysteine
L-Cysteine
Pantothenate and CoA biosynthesis
Taurine and hypotaurine metabolism
Glutathione metabolism
Propanoate metabolism
Pyruvate metabolism
Bisulfite
Pyruvate
(2R)-3-Sulfolactate
(2S)-3-Sulfolactate
2-Oxobutanoate
Aspartate metabolism
L-Aspartate
L-Aspartyl-phosphate
L-Aspartate-4-semialdehyde
L-Homoserine
O-Succinyl-L-homoserine
O-Acetyl-L-homoserine
L-Cystathionine
L-Alanine
Sulfite
Sulfur dioxide
3-Sulfino-pyruvate
3-Mercapto-pyruvate
Thio-sulfate
3-Mercaptolactate
Sulfur metabolism
Taurine and hypotaurine metabolism
MccA
L-Homocysteine
Homocysteine
Sulfur metabolism
S-Adenosyl-L-homocysteine
S-D-Ribosyl-L-homocysteine
L-Methionine
S-oxide
N-Formyl-L-methionine
S-Adenosyl-L-methionine
S-Adenosyl-methioninamine
S-Methyl-5'-thioadenosine
Aminoacyl-L-methionine
Methanethiol
3-Methylthio-propionate
1-Aminocyclopropane-1-carboxylate
S-Methyl-5-thio-D-ribose
Ethylene
Methionine salvage
S-Methyl-5-thio-D-ribose 1-phosphate
4-Methylthio-2-oxobutanoate
1,2-Dihydroxy-3-keto-5-methyl-thiopentene
2-Hydroxy-3-keto-5-methylthiopentenyl-1-phosphate
2,3-Diketo-5-methyl-thiopentyl-1-phosphate
S-Methyl-5-thio-D-ribulose 1-phosphate
00270 2/4/14
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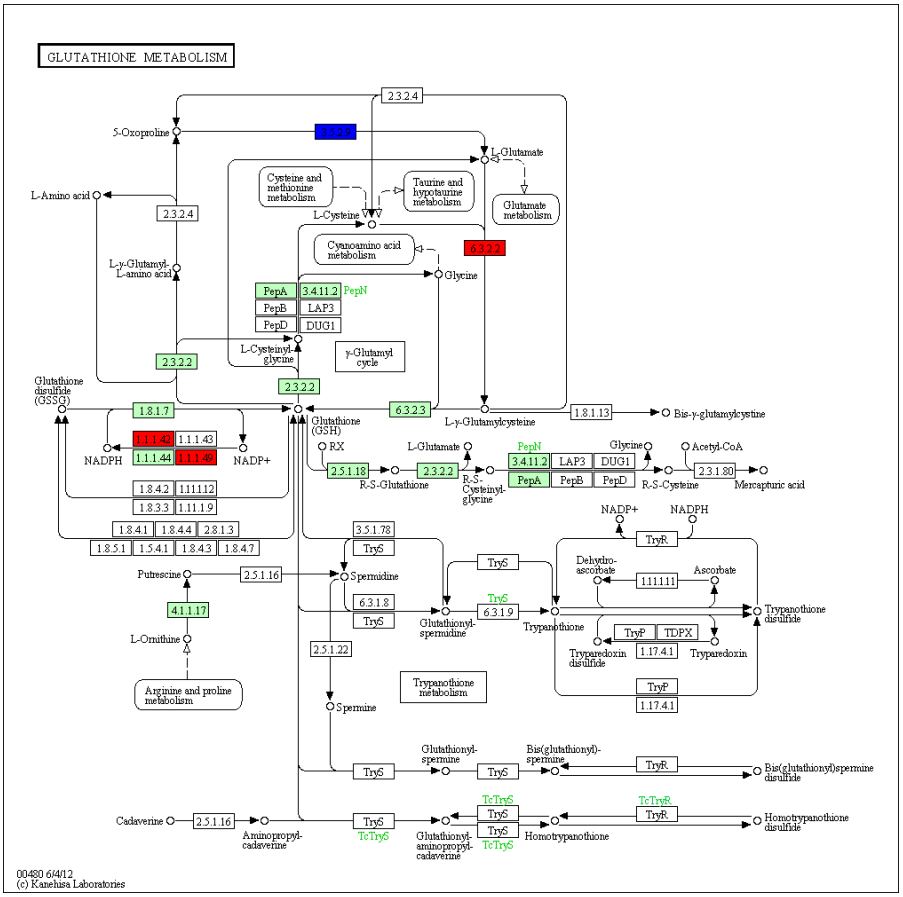
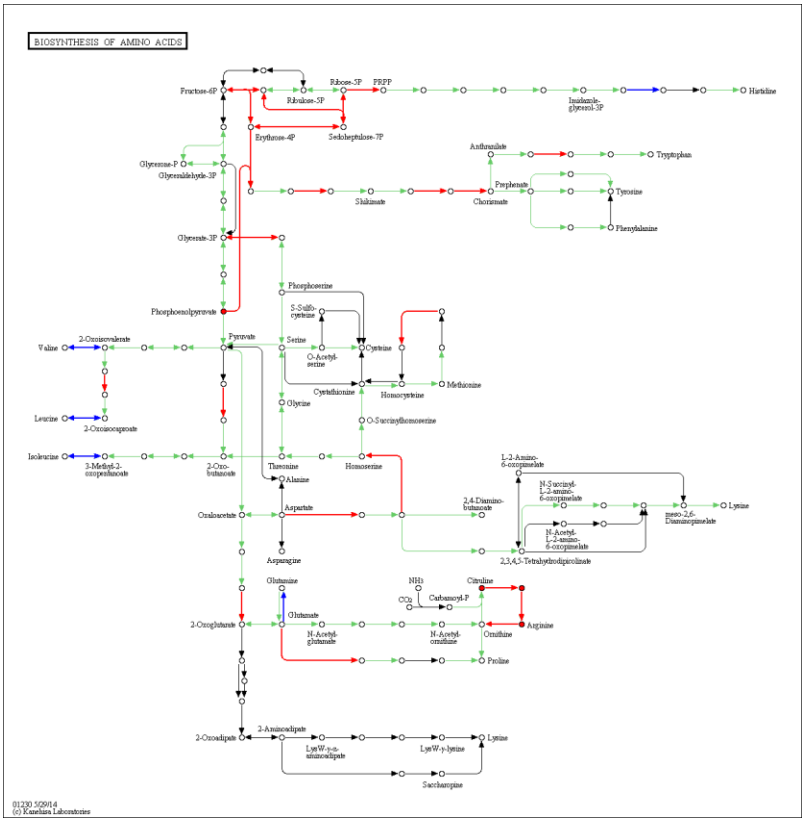
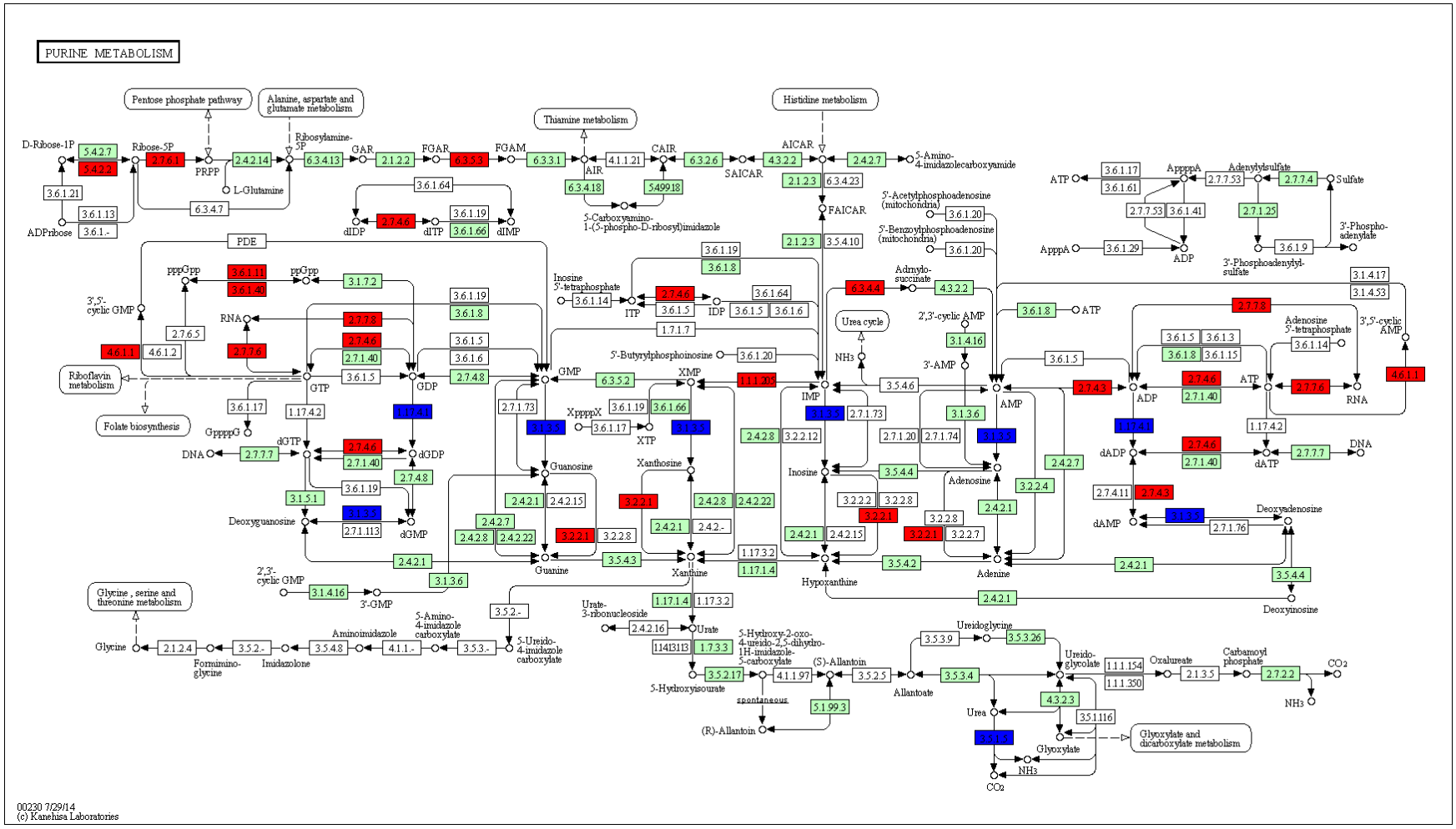
G


GLUTATHIONE METABOLISM
5-Oxoproline
L-Glutamate
L-Amino acid
Cysteine and methionine metabolism
Taurine and hypotaurine metabolism
Glutamate metabolism
L-Cysteine
Cyanoamino acid metabolism
Glycine
L-γ-Glutamyl-L-amino acid
PepA
PepB
PepD
LAP3
DUG1
PepN
L-Cysteinyl-glycine
γ-Glutamyl cycle
Glutathione disulfide (GSSG)
Glutathione (GSH)
L-γ-Glutamylcysteine
Bis-γ-glutamylcystine
NADPH
NADP+
RX
R-S-Glutathione
R-S-Cysteinyl-glycine
R-S-Cysteine
Acetyl-CoA
Mercapturic acid
Putrescine
Spermidine
Glutathionyl-spermidine
Trypanothione
Dehydro-ascorbate
Ascorbate
Tryparedoxin disulfide
Tryparedoxin
Trypanothione disulfide
TryS
TryR
TryP
TDPX
L-Ornithine
Arginine and proline metabolism
Trypanothione metabolism
Spermine
Glutathionyl-spermine
Bis(glutathionyl)-spermine
Bis(glutathionyl)spermine disulfide
Cadaverine
Aminopropyl-cadaverine
Glutathionyl-aminopropyl-cadaverine
Homotrypanothione
Homotrypanothione disulfide
TcTryS
TcTryR
00480 6/4/12
(c) Kanehisa Laboratories

H


BIOSYNTHESIS OF AMINO ACIDS
Fructose-6P
Ribose-5P
PRPP
Ribulose-5P
Histidine
Erythrose-4P
Sedoheptulose-7P
Glycerone-P
Glyceraldehyde-3P
Anthranilate
Tryptophan
Shikimate
Prephenate
Chorismate
Tyrosine
Phenylalanine
Glycerate-3P
Phosphoserine
Phosphoenolpyruvate
S-Sulfo-cysteine
Valine
2-Oxoisovalerate
Pyruvate
Serine
O-Acetyl-serine
Cysteine
Cystathionine
Homocysteine
Methionine
Glycine
Leucine
2-Oxoisocaproate
O-Succinylhomoserine
Isoleucine
3-Methyl-2-oxopentanoate
2-Oxo-butanoate
Threonine
Homoserine
Alanine
Oxaloacetate
Aspartate
L-2-Amino-6-oxopimelate
N-Succinyl-L-2-amino-6-oxopimelate
2,4-Diamino-butanoate
meso-2,6-Diaminopimelate
Lysine
N-Acetyl-L-2-amino-6-oxopimelate
2,3,4,5-Tetrahydrodipicolinate
Asparagine
Glutamine
NH3
CO2
Carbamoyl-P
Citrulline
2-Oxoglutarate
Glutamate
N-Acetyl-glutamate
N-Acetyl-ornithine
Ornithine
Arginine
Proline
2-Oxoadipate
2-Aminoadipate
LysW-γ-2-aminoadipate
LysW-γ-lysine
Saccharopine


PURINE METABOLISM
Pentose phosphate pathway
Alanine, aspartate and glutamate metabolism
Thiamine metabolism
Histidine metabolism
D-Ribose-1P
Ribose-5P
PRPP
L-Glutamine
Ribosylamine-5P
GAR
FGAR
FGAM
AIR
CAIR
AICAR
SAICAR
FAICAR
5-Amino-4-imidazolecarboxyamide
5-Carboxyamino-1-(5-phospho-D-ribosyl)imidazole
ADPribose
dIDP
dITP
dIMP
PDE
pppGpp
ppGpp
3',5'-cyclic GMP
RNA
Riboflavin metabolism
Folate biosynthesis
GTP
GDP
GMP
GppppG
dGTP
dGDP
DNA
Deoxyguanosine
dGMP
Inosine 5'-tetraphosphate
ITP
IDP
IMP
5'-Butyrylphosphoinosine
XpppX
XTP
XMP
Guanosine
Xanthosine
Inosine
Adenosine
Guanine
Xanthine
Hypoxanthine
Adenine
Urea cycle
NH3
Adenylo-succinate
2',3'-cyclic AMP
3'-AMP
AMP
ADP
ATP
RNA
dADP
dATP
DNA
dAMP
Deoxyadenosine
Deoxyinosine
5'-Acetylphosphoadenosine (mitochondria)
5'-Benzoylphosphoadenosine (mitochondria)
ATP
ADP
ApppA
AppppA
Adenylylsulfate
Sulfate
3'-Phospho-adenylate
3'-Phosphoadenylyl-sulfate
Adenosine 5'-tetraphosphate
3',5'-cyclic AMP
2',3'-cyclic GMP
3'-GMP
Glycine , serine and threonine metabolism
Glycine
Formimino-glycine
Imidazolone
Aminoimidazole
5-Amino-4-imidazole carboxylate
5-Ureido-4-imidazole carboxylate
Urate-3-ribonucleoside
Urate
5-Hydroxy-2-oxo-4-ureido-2,5-dihydro-1H-imidazole-5-carboxylate
5-Hydroxyisourate
(S)-Allantoin
(R)-Allantoin
spontaneous
Allantoate
Ureidoglycine
Ureido-glycolate
Oxalureate
Carbamoyl phosphate
CO2
NH3
Urea
Glyoxylate
Glyoxylate and dicarboxylate metabolism
00230 7/29/14
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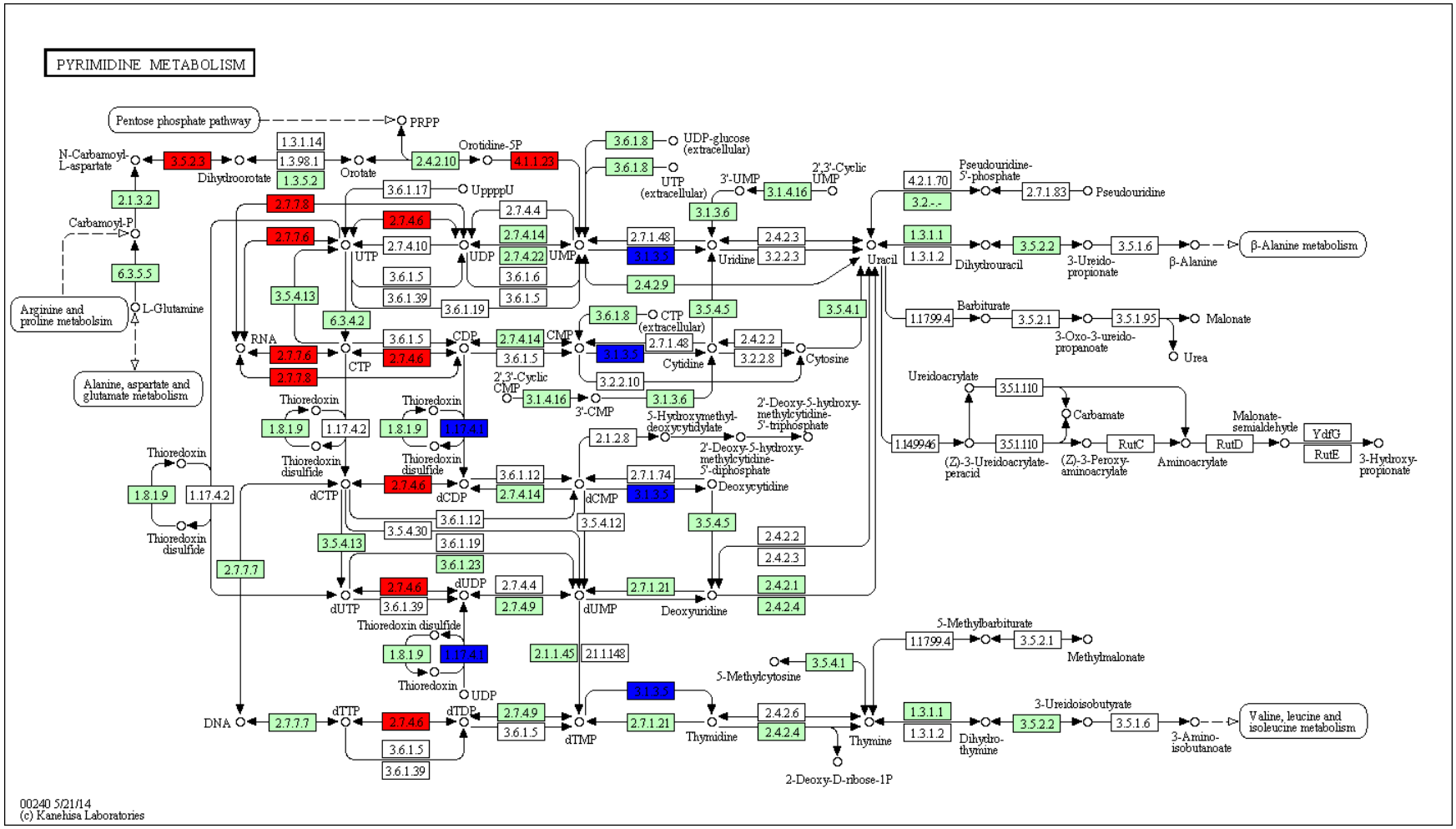
J


PYRIMIDINE METABOLISM
Pentose phosphate pathway
PRPP
N-Carbamoyl-L-aspartate
Dihydroorotate
Orotate
Orotidine-5P
UDP-glucose (extracellular)
UTP (extracellular)
3'-UMP
2',3'-Cyclic UMP
Pseudouridine-5'-phosphate
Pseudouridine
Carbamoyl-P
Arginine and proline metabolism
L-Glutamine
Alanine, aspartate and glutamate metabolism
UppppU
UTP
UDP
UMP
Uridine
Uracil
Dihydrouracil
3-Ureido-propionate
β-Alanine
β-Alanine metabolism
RNA
CTP
CDP
CMP
CTP (extracellular)
Cytidine
Cytosine
2',3'-Cyclic CMP
3'-CMP
Barbiturate
3-Oxo-3-ureido-propanoate
Malonate
Urea
Ureidoacrylate
Carbamate
(Z)-3-Ureidoacrylate-peracid
(Z)-3-Peroxy-aminoacrylate
Aminoacrylate
Malonate-semialdehyde
YdfG
RutE
RutC
RutD
3-Hydroxy-propionate
5-Hydroxymethyl-deoxycytidylate
2'-Deoxy-5-hydroxy-methylcytidine-5'-triphosphate
2'-Deoxy-5-hydroxy-methylcytidine-5'-diphosphate
Deoxycytidine
Thioredoxin
Thioredoxin disulfide
dCTP
dCDP
dCMP
dUTP
dUDP
dUMP
Deoxyuridine
Thioredoxin disulfide
DNA
dTTP
dTDP
dTMP
Thymidine
Thymine
2-Deoxy-D-ribose-1P
5-Methylcytosine
5-Methylbarbiturate
Methylmalonate
3-Ureidoisobutyrate
Dihydro-thymine
3-Amino-isobutanoate
Valine, leucine and isoleucine metabolism
00240 5/21/14
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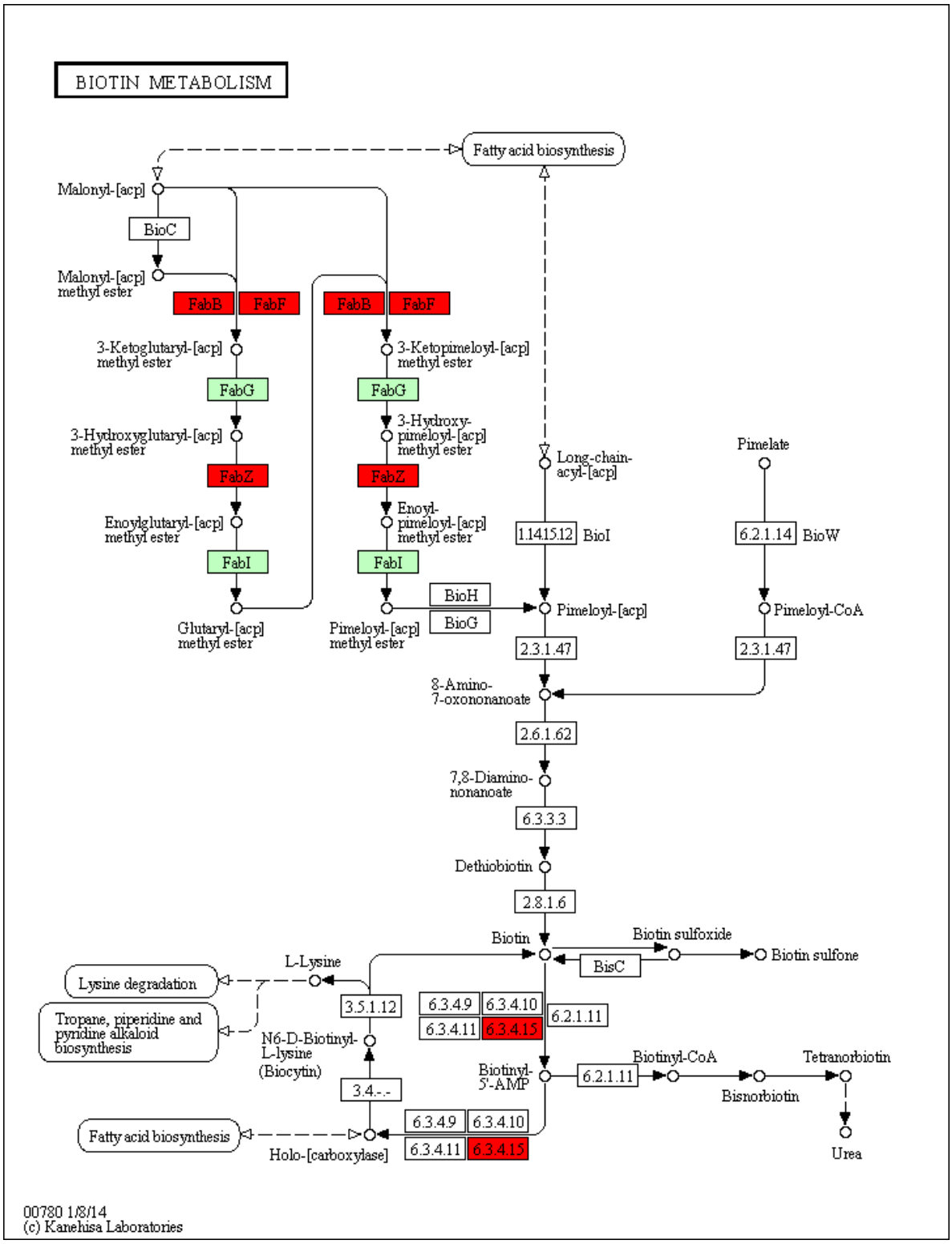
K


BIOTIN METABOLISM
Fatty acid biosynthesis
Malonyl-[acp]
BioC
Malonyl-[acp] methyl ester
FabB
FabF
FabB
FabF
3-Ketoglutaryl-[acp] methyl ester
3-Ketopimeloyl-[acp] methyl ester
FabG
FabG
3-Hydroxyglutaryl-[acp] methyl ester
3-Hydroxy-pimeloyl-[acp] methyl ester
FabZ
FabZ
Enoylglutaryl-[acp] methyl ester
Enoyl-pimeloyl-[acp] methyl ester
FabI
FabI
Long-chain-acyl-[acp]
Pimelate
1.14.15.12
BioI
6.2.1.14
BioW
BioH
BioG
Glutaryl-[acp] methyl ester
Pimeloyl-[acp] methyl ester
Pimeloyl-[acp]
Pimeloyl-CoA
2.3.1.47
2.3.1.47
8-Amino-7-oxononanoate
2.6.1.62
7,8-Diamino-nonanoate
6.3.3.3
Dethiobiotin
2.8.1.6
Biotin
Biotin sulfoxide
BisC
Biotin sulfone
L-Lysine
Lysine degradation
Tropane, piperidine and pyridine alkaloid biosynthesis
3.5.1.12
6.3.4.9
6.3.4.10
6.3.4.11
6.3.4.15
6.2.1.11
N6-D-Biotinyl-L-lysine (Biocytin)
Biotinyl-5'-AMP
6.2.1.11
Biotinyl-CoA
Tetranorbiotin
Bisnorbiotin
3.4.-.-
6.3.4.9
6.3.4.10
6.3.4.11
6.3.4.15
Fatty acid biosynthesis
Holo-[carboxylase]
Urea
00780 1/8/14
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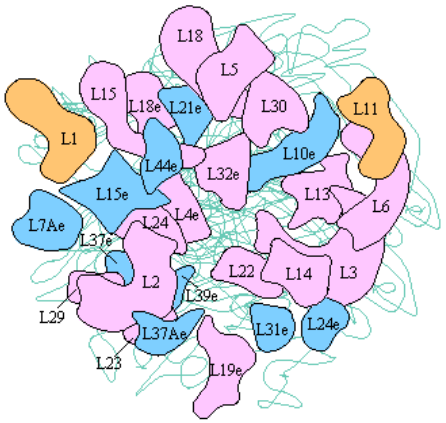
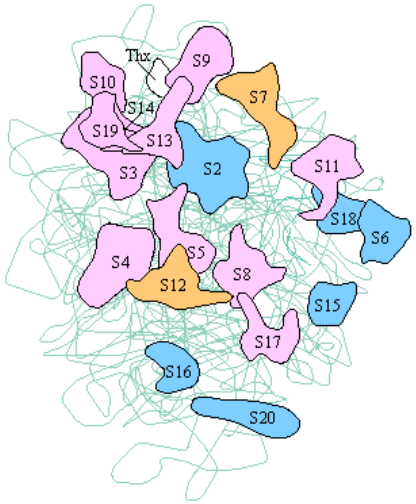
L

RIBOSOME



Large subunit (Haloarcula marismortui)



Small subunit (Thermus aquaticus)

Ribosomal RNAs

Bacteria / Archaea	23S	5S		16S	
Eukaryotes	25S	5S	5.8S	18S	

Ribosomal proteins

EF-Tu	S10	L3	L4	L23	L2	S19	L22	S3	RP-L16	L29					
	S20e	L3e	L4e	L23Ae	L8e	S15e	L17e	S3e	L10e	L35e					

L7/L12 stalk

S17	L14	L24		L5	S14	S8	L6			L18	S5	L30	L15	SecY	
S11e	L23e	L26e	S4e	L11e	S29e	S15Ae	L9e	L32e	L19e	L5e	S2e	L7e	L27Ae		

		IF1	L36	S13	S11	S4	RpoA		L17	L13	S9				
L34e	L14e			S18e	S14e	S9e		L18e		L13Ae	S16e				

EF-Tu,G	S7	S12		L7A	RpoC,B	L7/L12	L12	L10	L1	L11					
	S5e	S23e	L30e	L7Ae			LP1,LP2	LP0	L10Ae	L12e					

S2	EF-Ts	IF2	S15	IF3	L35	L20	L34	RF1	L31	L32	L9	S18	S6		
SAe			S13e												

L28	L33	L21	L27	FtsY,Ffh	S16	L19	S1	S20	S21	L25					

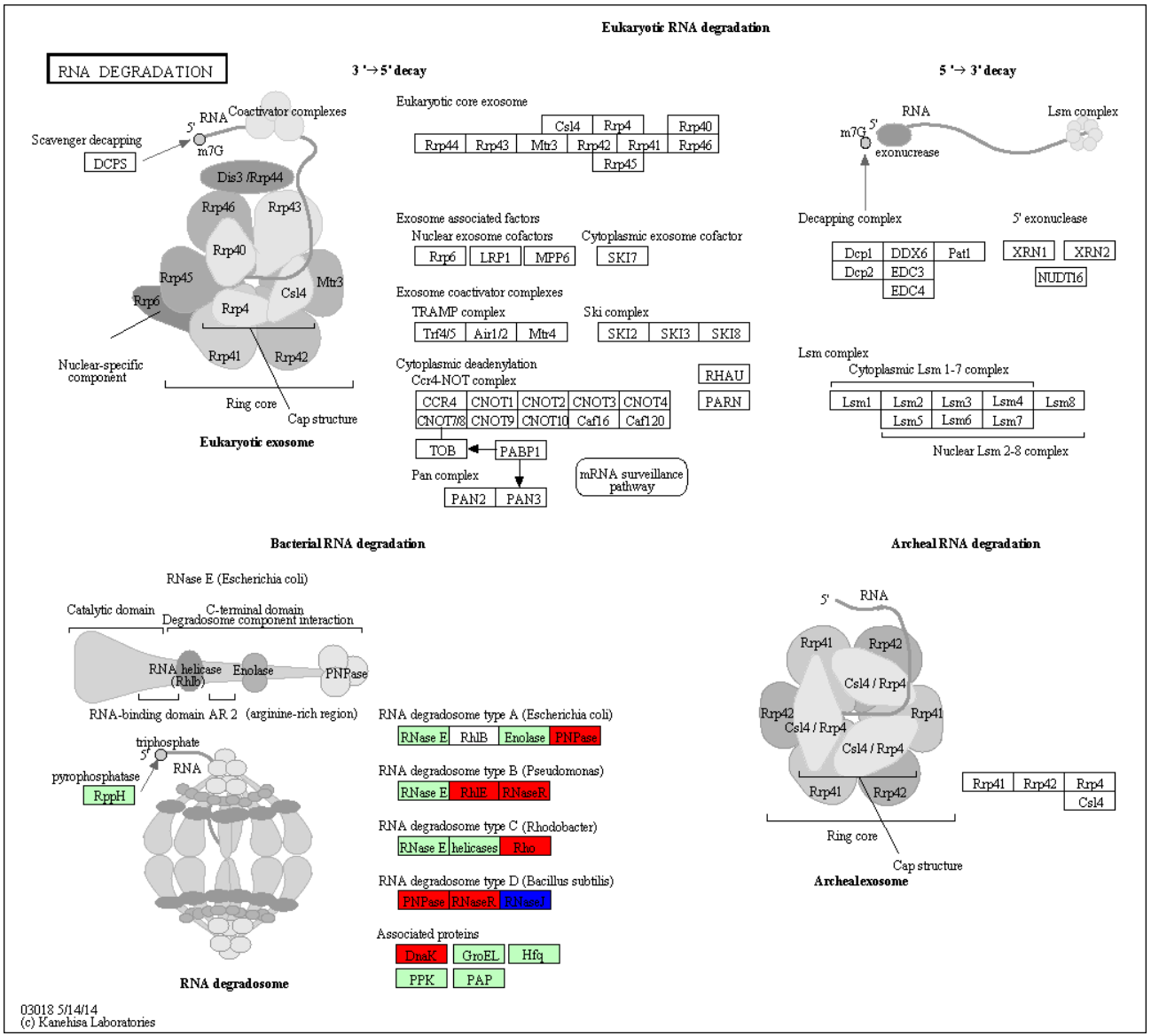
L10e	L13e	L15e	L21e	L24e	L31e	L35Ae	L37e	L37Ae	L39e	L40e	L41e	L44e			

S3Ae	S6e	S8e	S17e	S19e	S24e	S25e	S26e	S27e	S27Ae	S28e	S30e		LX		

L6e	L18Ae	L22e	L27e	L28e	L29e	L36e	L38e

S7e	S10e	S12e	S21e

M


Eukaryotic RNA degradation
RNA DEGRADATION
3 '→ 5' decay
5 '→ 3' decay
RNA
Coactivator complexes
Scavenger decapping
DCPS
m7G
Dis3 /Rrp44
Rrp46
Rrp43
Rrp40
Rrp45
Mtr3
Csl4
Rrp6
Rrp4
Rrp41
Rrp42
Nuclear-specific component
Ring core
Cap structure
Eukaryotic exosome
Eukaryotic core exosome
Csl4
Rrp4
Rrp40
Rrp44
Rrp43
Mtr3
Rrp42
Rrp41
Rrp46
Rrp45
Exosome associated factors
Nuclear exosome cofactors
Cytoplasmic exosome cofactor
Rrp6
LRP1
MPP6
SKI7
Exosome coactivator complexes
TRAMP complex
Ski complex
Trf4/5
Air1/2
Mtr4
SKI2
SKI3
SKI8
Cytoplasmic deadenylation
Ccr4-NOT complex
RHAU
PARN
CCR4
CNOT1
CNOT2
CNOT3
CNOT4
CNOT7/8
CNOT9
CNOT10
Caf16
Caf120
TOB
PABP1
Pan complex
PAN2
PAN3
mRNA surveillance pathway
RNA
Lsm complex
m7G
5'
exonucrease
Decapping complex
5' exonuclease
Dcp1
DDX6
Pat1
Dcp2
EDC3
EDC4
XRN1
XRN2
NUDT16
Lsm complex
Cytoplasmic Lsm 1-7 complex
Lsm1
Lsm2
Lsm3
Lsm4
Lsm8
Lsm5
Lsm6
Lsm7
Nuclear Lsm 2-8 complex
Bacterial RNA degradation
Archeal RNA degradation
RNase E (Escherichia coli)
Catalytic domain
C-terminal domain
Degradosome component interaction
RNA helicase (RhlB)
Enolase
PNPase
RNA-binding domain AR 2 (arginine-rich region)
triphosphate
5'
RNA
pyrophosphatase
RppH
RNA degradosome
RNA degradosome type A (Escherichia coli)
RNase E
RhlB
Enolase
PNPase
RNA degradosome type B (Pseudomonas)
RNase E
RhlE
RNaseR
RNA degradosome type C (Rhodobacter)
RNase E
helicases
Rho
RNA degradosome type D (Bacillus subtilis)
PNPase
RNaseR
RNaseJ
Associated proteins
DnaK
GroEL
Hfq
PPK
PAP
5'
RNA
Rrp41
Rrp42
Csl4 / Rrp4
Rrp42
Rrp41
Csl4 / Rrp4
Csl4 / Rrp4
Rrp41
Rrp42
Ring core
Cap structure
Archealexosome
Rrp41
Rrp42
Rrp4
Csl4
03018 5/14/14
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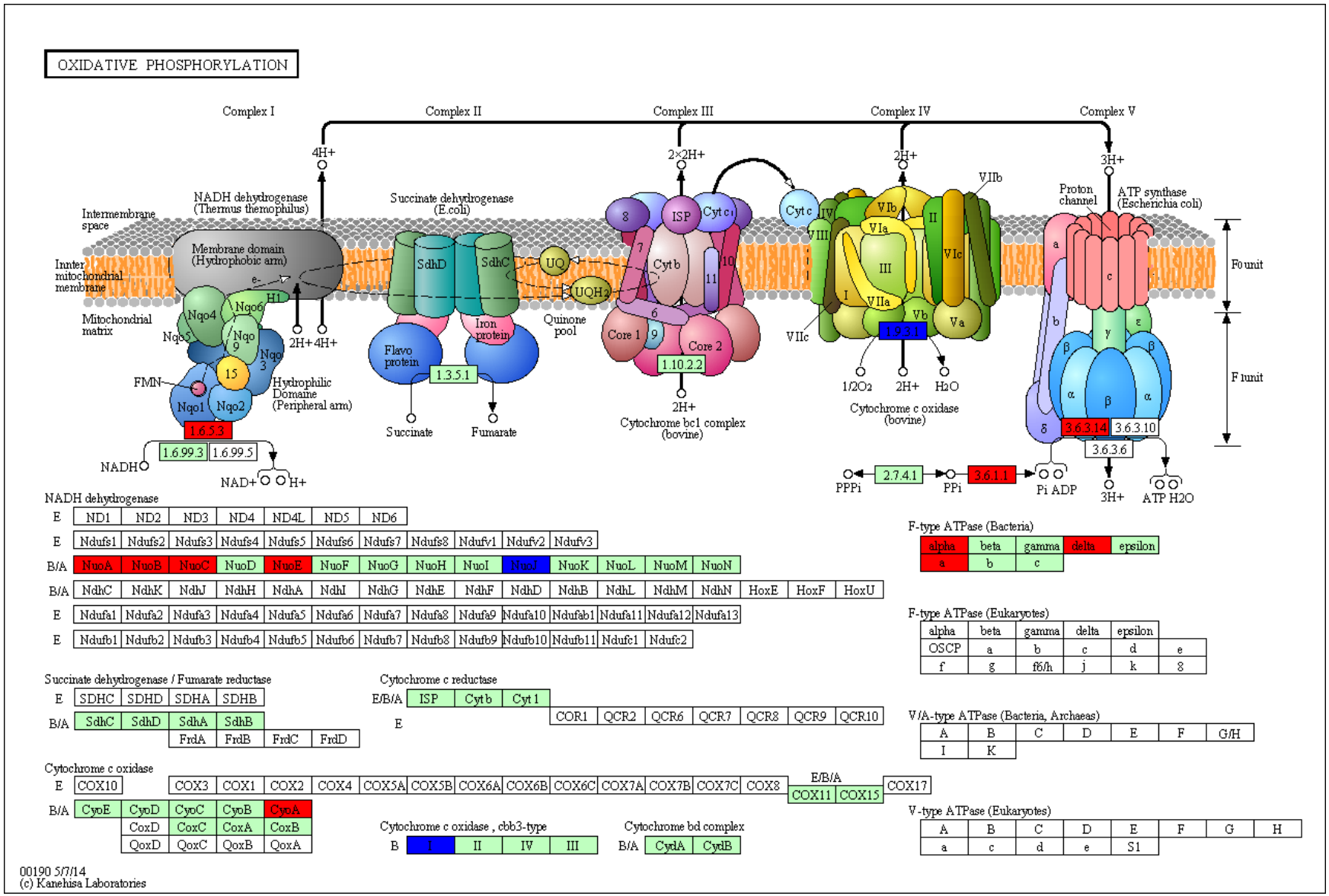
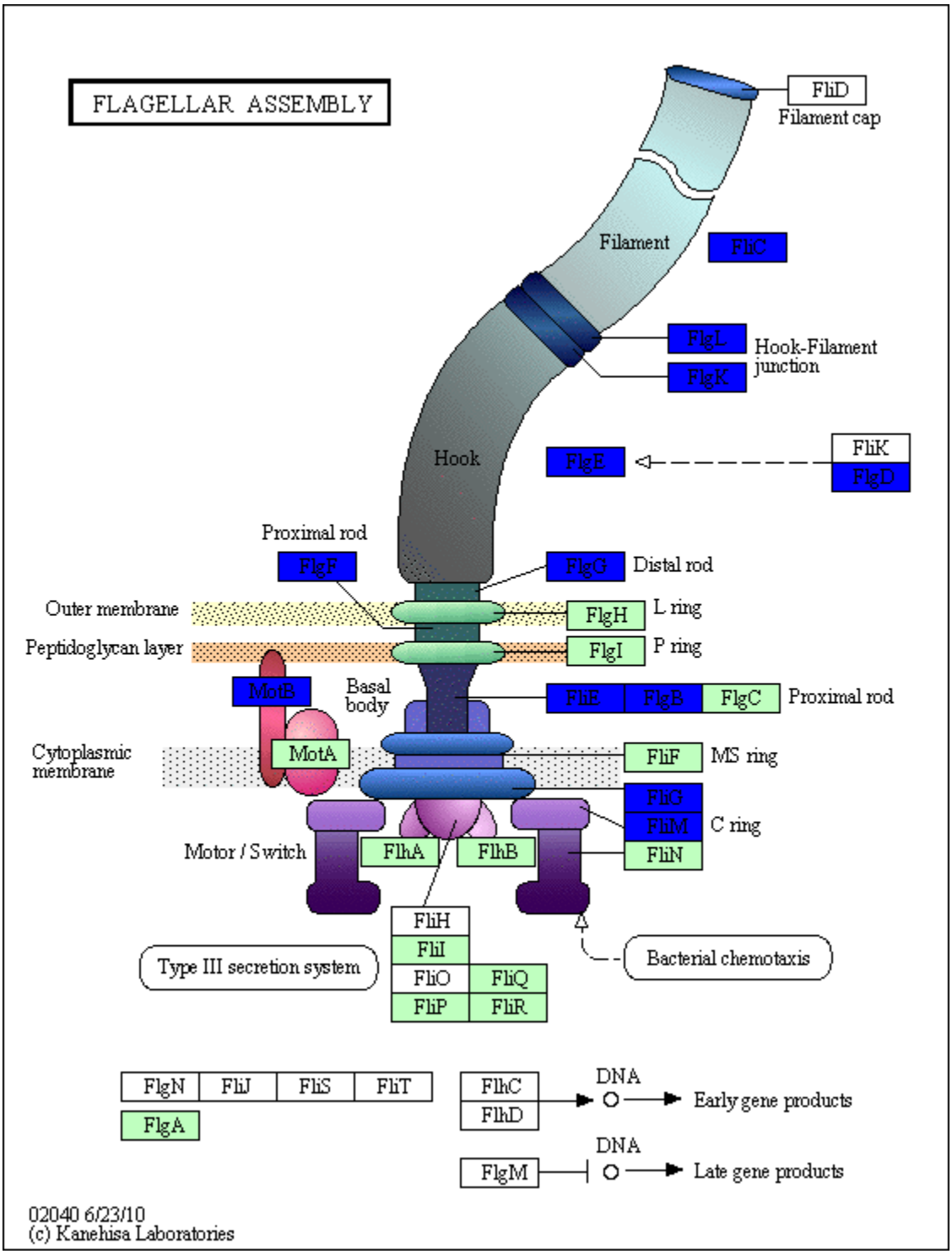
N


OXIDATIVE PHOSPHORYLATION
Complex I
Complex II
Complex III
Complex IV
Complex V
4H+
2×2H+
2H+
3H+
NADH dehydrogenase (Thermus thermophilus)
Succinate dehydrogenase (E.coli)
Intermembrane space
Inner mitochondrial membrane
Mitochondrial matrix
Membrane domain (Hydrophobic arm)
Hydrophilic Domain (Peripheral arm)
SdhD
SdhC
UQ
UQH2
Quinone pool
Flavo protein
Iron protein
Succinate
Fumarate
Cyt b
Cyt c1
ISP
Core 1
Core 2
Cytochrome bc1 complex (bovine)
Cyt c
Cytochrome c oxidase (bovine)
Proton channel
ATP synthase (Escherichia coli)
F0 unit
F1 unit
FMN
NADH
NAD+
H+
PPPi
PPi
Pi ADP
ATP H2O
1.6.5.3
1.6.99.3
1.6.99.5
1.3.5.1
1.10.2.2
1.9.3.1
2.7.4.1
3.6.1.1
3.6.3.14
3.6.3.10
3.6.3.6
NADH dehydrogenase
E ND1 ND2 ND3 ND4 ND4L ND5 ND6
E Ndufs1 Ndufs2 Ndufs3 Ndufs4 Ndufs5 Ndufs6 Ndufs7 Ndufs8 Ndufv1 Ndufv2 Ndufv3
B/A NuoA NuoB NuoC NuoD NuoE NuoF NuoG NuoH NuoI NuoJ NuoK NuoL NuoM NuoN
B/A NdhC NdhK NdhJ NdhH NdhA NdhI NdhG NdhE NdhF NdhD NdhB NdhL NdhM NdhN HoxE HoxF HoxU
E Ndufa1 Ndufa2 Ndufa3 Ndufa4 Ndufa5 Ndufa6 Ndufa7 Ndufa8 Ndufa9 Ndufa10 Ndufab1 Ndufa11 Ndufa12 Ndufa13
E Ndufb1 Ndufb2 Ndufb3 Ndufb4 Ndufb5 Ndufb6 Ndufb7 Ndufb8 Ndufb9 Ndufb10 Ndufb11 Ndufc1 Ndufc2
Succinate dehydrogenase / Fumarate reductase
E SDHC SDHD SDHA SDHB
B/A SdhC SdhD SdhA SdhB
FrdA FrdB FrdC FrdD
Cytochrome c reductase
E/B/A ISP Cyt b Cyt 1
E COR1 QCR2 QCR6 QCR7 QCR8 QCR9 QCR10
Cytochrome c oxidase
E COX10 COX3 COX1 COX2 COX4 COX5A COX5B COX6A COX6B COX6C COX7A COX7B COX7C COX8
E/B/A COX11 COX15 COX17
B/A CyoE CyoD CyoC CyoB CyoA
CoxD CoxC CoxA CoxB
QoxD QoxC QoxB QoxA
Cytochrome c oxidase , cbb3-type
B I II IV III
Cytochrome bd complex
B/A CydA CydB
F-type ATPase (Bacteria)
alpha beta gamma delta epsilon
a b c
F-type ATPase (Eukaryotes)
alpha beta gamma delta epsilon
OSCP a b c d e
f g f6/h j k 8
V/A-type ATPase (Bacteria, Archaeas)
A B C D E F G/H
I K
V-type ATPase (Eukaryotes)
A B C D E F G H
a c d e S1
00190 5/7/14
(c) Kanehisa Laboratories

O


FLAGELLAR ASSEMBLY
FliD
Filament cap
Filament
FliC
FlgL
FlgK
Hook-Filament junction
Hook
FlgE
FliK
FlgD
Proximal rod
FlgF
FlgG
Distal rod
Outer membrane
FlgH
L ring
Peptidoglycan layer
FlgI
P ring
MotB
Basal body
FliE
FlgB
FlgC
Proximal rod
Cytoplasmic membrane
MotA
FliF
MS ring
FliG
FliM
FliN
C ring
Motor / Switch
FlhA
FlhB
FliH
FliI
FliO
FliP
FliQ
FliR
Type III secretion system
Bacterial chemotaxis
FlgN
FliJ
FliS
FliT
FlgA
FlhC
FlhD
DNA
Early gene products
FlgM
DNA
Late gene products
02040 6/23/10
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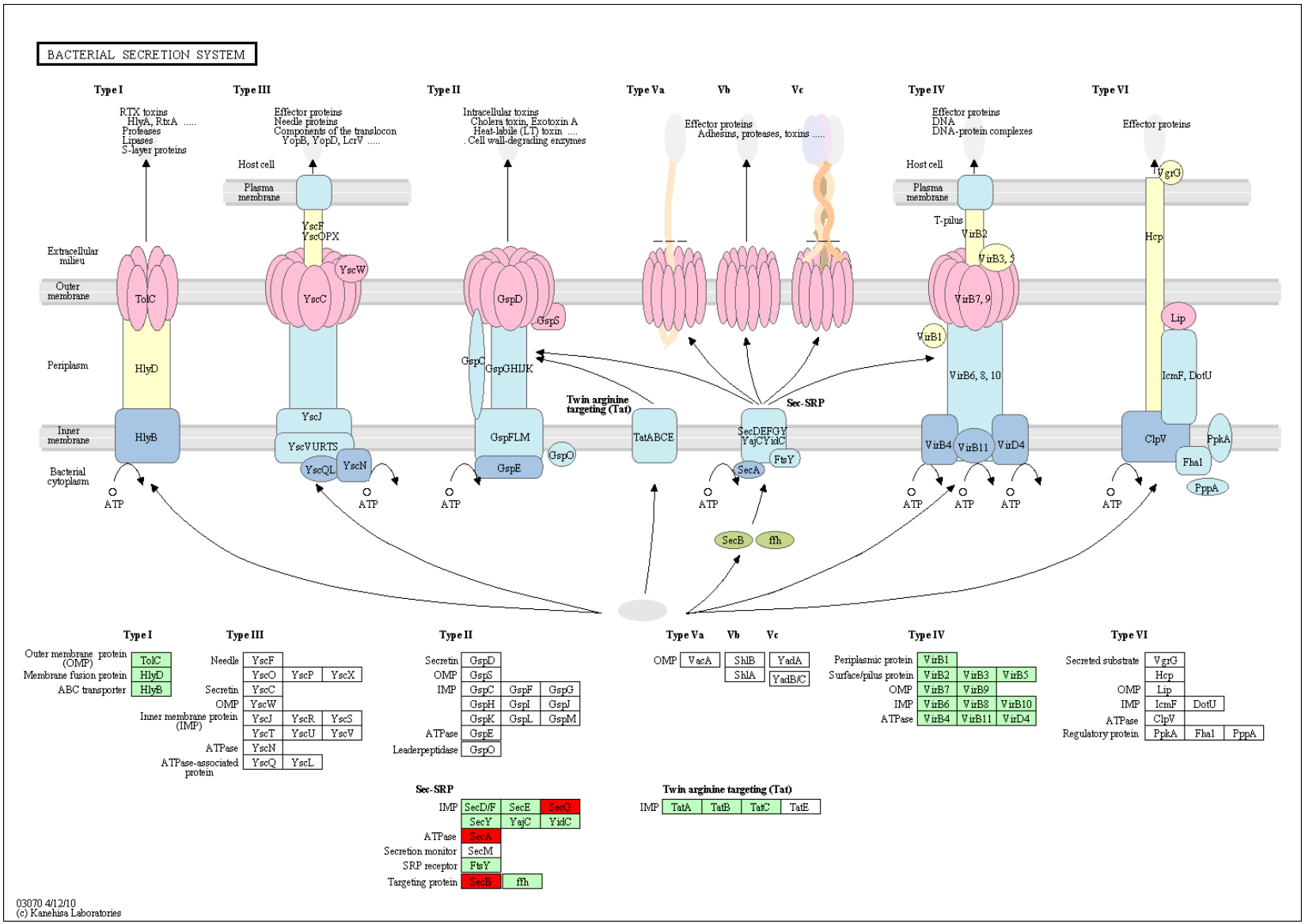
P



Type I	
Outer membrane protein (OMP)	TolC
Membrane fusion protein	HlyD
ABC transporter	HlyB

Type III			
Needle	YscF		
	YscO	YscP	YscX
Secretin	YscC		
OMP	YscW		
Inner membrane protein (IMP)	YscJ	YscR	YscS
	YscT	YscU	YscV
ATPase	YscN		
ATPase-associated protein	YscQ	YscL	

Type II			
Secretin	GspD		
OMP	GspS		
IMP	GspC	GspF	GspG
	GspH	GspI	GspJ
	GspK	GspL	GspM
ATPase	GspE		
Leaderpeptidase	GspO		

Type Va	Vb	Vc
OMP VacA	ShlB	YadA
	ShlA	YadB/C

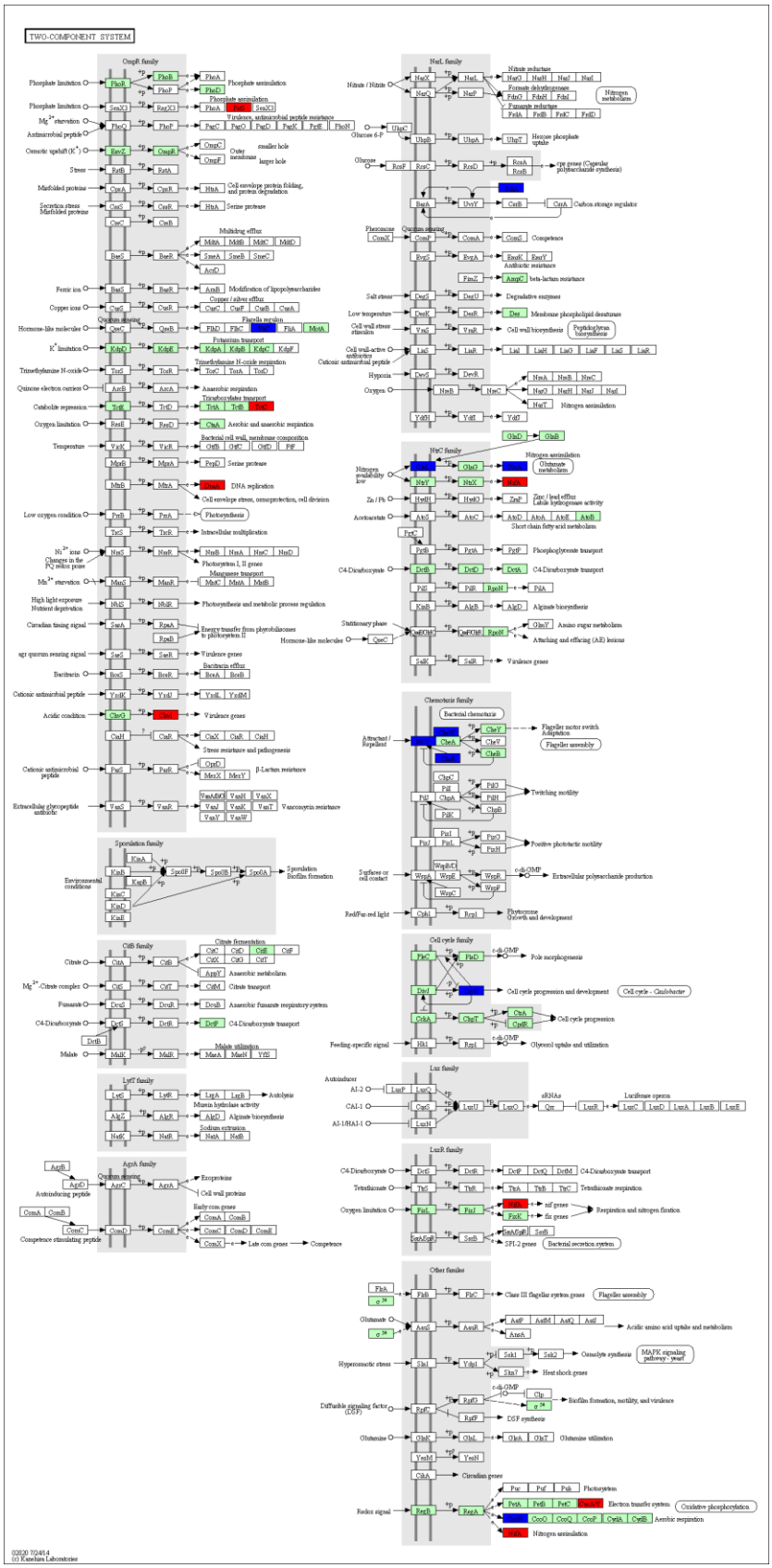
Type IV			
Periplasmic protein	VirB1		
Surface/pilus protein	VirB2	VirB3	VirB5
OMP	VirB7	VirB9	
IMP	VirB6	VirB8	VirB10
ATPase	VirB4	VirB11	VirD4

Type VI		
Secreted substrate	VgrG	
	Hcp	
OMP	Lip	
IMP	IcmF	DotU
ATPase	ClpV	
Regulatory protein	PpkA	Fha1 PppA

Sec-SRP			
IMP	SecD/F	SecE	SecG
	SecY	YajC	YidC
ATPase	SecA		
Secretion monitor	SecM		
SRP receptor	FtsY		
Targeting protein	SecB	ffh	

Twin arginine targeting (Tat)				
IMP	TatA	TatB	TatC	TatE

Q


TWO-COMPONENT SYSTEM
OmpR family
PhoB
PhoA
Phosphate assimilation
PhoP
PhoD
Phosphate limitation
SenX3
RegX3
PhoA
PstS
SenX3
Virulence, antimicrobial peptide resistance
Mg2+ starvation
Antimicrobial peptide
PhoQ
PhoP
PqtC
PqtD
PqtE
PqtF
PqtH
Osmotic upshift (K+)
EnvZ
OmpR
OmpC
smaller hole
Outer membrane
OmpF
larger hole
Stress
RstB
RstA
Misfolded protein
CpxA
CpxR
HtrA
Cell envelope protein folding, and protein degradation
Secretion stress, Misfolded proteins
CssS
CssR
HtrA
Serine protease
CseC
CssB
Multidrug efflux
BaeS
BaeR
MdtA
MdtB
MdtC
MdtD
SmeA
SmeB
SmeC
AcrD
Ferric ion
BaeS
BaeR
ArnB
Modification of lipopolysaccharides
Copper ions
CusS
CusR
CusC
CusF
CusB
CusA
Quorum sensing
Hormone-like molecules
QseC
QseB
FliD
FliC
FlgE
FliA
MotA
Flagella regulon
K+ limitation
KdpD
KdpE
KdpA
KdpB
KdpC
KdpF
Potassium transport
Trimethylamine N-oxide
TorS
TorR
TorC
TorA
TorD
Trimethylamine N-oxide respiration
Quinone electron carriers
ArcB
ArcA
Anaerobic respiration
Catabolite repression
TctE
TctD
TctA
TctB
TctC
Tricarboxylates transport
Oxygen limitation
ResE
ResD
CtaA
Aerobic and anaerobic respiration
Temperature
VxrK
VxrR
GtfB
GtfC
GtfD
PilF
Bacterial cell wall, membrane composition
MycB
MycA
PrpD
Serine protease
MtrB
MtrA
DnaA
DNA replication
Cell envelope stress, osmoprotection, cell division
Low oxygen condition
PrrB
PrrA
PsbA
Photosynthesis
TcrC
TcrR
Intracellular multiplication
Ni2+ ions
Changes in the PQ redox pools
NrsS
NrsR
NrsB
NrsA
NrsC
NrsD
Photosystem I, II genes
Mn2+ starvation
MntC
MntR
MntC
MntA
MntB
Manganese transport
High light exposure
Nutrient deprivation
NblS
NblR
Photosynthesis and metabolic process regulation
Circadian timing signal
SasA
RpaA
RpaB
Energy transfer from phycobilisomes to photosystem II
sgr quorum sensing signal
SsrS
SsrR
Virulence genes
Bacitracin
BceS
BceR
BceA
BceB
Bacitracin efflux
Cationic antimicrobial peptide
YxdK
YxdJ
YxdL
YxdM
Acidic condition
ChvG
ChvI
Virulence genes
CssS
CssR
CssX
CssR
CssH
Stress resistance and pathogenesis
Cationic antimicrobial peptide
PmrB
PmrA
CprD
MexX
MexY
β-Lactam resistance
Extracellular glycopeptide antibiotic
VanS
VanR
VanAHX
VanH
VanX
VanA
VanY
VanW
Vancomycin resistance
Sporulation family
KinA
KinB
KapB
KinC
KinD
KinE
Spo0F
Spo0B
Spo0A
Environmental conditions
Sporulation Biofilm formation
CitB family
Citrate
CitA
CitB
Citrate fermentation
CitC
CitD
CitE
CitF
CitX
CitG
CitT
Mg2+-Citrate complex
CitC
CitT
ApbY
Anaerobic metabolism
Fumarate
DcuS
DcuR
CitM
Citrate transport
C4-Dicarboxylate
DctS
DctR
DcuB
Anaerobic fumarate respiratory system
DctB
DctP
C4-Dicarboxylate transport
Malate
MalK
MalR
MaeA
MaeB
YflS
Malate utilization
LytS family
LytS
LytR
LytA
LytB
Autolysis
Murein hydrolase activity
AlgZ
AlgR
AlgD
Alginate biosynthesis
NasK
NasR
NasA
NasB
Sodium extrusion
AgrA family
AgrB
Quorum sensing
AgrD
AgrC
AgrA
Exoproteins
Autoinducing peptide
Cell wall proteins
ComA
ComB
Early com genes
ComC
ComD
ComE
ComX
Late com genes
Competence stimulating peptide
Competence
NtrY family
NtrY
NtrB
Nitrogen availability low
NtrC
NtrX
GlnA
Nitrogen assimilation
Glutamine metabolism
Zn / Pb
HmtH
HmtR
ZnF
Zinc / lead efflux
Cobalt hydrogenase activity
Acetoacetate
AtoS
AtoC
AtoD
AtoA
AtoE
AtoB
Short chain fatty acid metabolism
PrrC
PgtB
PgtA
PgtP
Phosphoglycerate transport
C4-Dicarboxylate
DctB
DctD
DctA
C4-Dicarboxylate transport
PilS
PilR
RpoN
PilA
AlgB
AlgD
Alginate biosynthesis
Stationary phase
Hormone-like molecules
CpxP
CpxR
CpxH
QseC
GlmY
Amino sugar metabolism
Attaching and effacing (AE) lesions
SalK
SalR
Virulence genes
Chemotaxis family
Bacterial chemotaxis
Attractant / Repellent
CheW
CheA
CheR
CheB
CheY
CheV
CheB
Flagellar motor switch
Adaptation
Flagellar assembly
ChpC
PilJ
ChpA
PilG
PilH
PilK
ChpB
Twitching motility
PixI
PixL
PixG
PixH
Positive phototactic motility
WspA
WspB
WspE
WspR
WspF
WspC
Surfaces or cell contact
c-di-GMP
Extracellular polysaccharide production
RedFar-red light
CphI
RcpI
Phytochrome
Growth and development
Cell cycle family
PleC
PleD
c-di-GMP
Pole morphogenesis
DnaA
CtrA
Cell cycle progression and development
Cell cycle - Caulobacter
CckA
ChpT
CtrA
CpdR
Cell cycle progression
Feeding-specific signal
HltI
RpiI
c-di-GMP
Glycerol uptake and utilization
Lux family
Autoinducer
AI-2
CAI-1
AI-1/HAI-1
LuxP
LuxQ
CqsS
LuxU
LuxO
sRNAs
Qrr
LuxR
Luciferase operon
LuxC
LuxD
LuxA
LuxB
LuxE
LuxR family
C4-Dicarboxylate
DctE
DctR
DctP
DctQ
DctM
C4-Dicarboxylate transport
Tetrathionate
ThiS
ThiR
ThiA
ThiB
ThiC
Tetrathionate respiration
Oxygen limitation
FixL
FixJ
nif genes
fix genes
Respiration and nitrogen fixation
FixK
SpiA
SpiR
SPI-2 genes
Bacterial secretion system
Other families
FleA
FliA
FliC
Class III flagellar system genes
Flagellar assembly
Glutamate
AauS
AauR
AatF
AatM
Aat2
Aat1
Acidic amino acid uptake and metabolism
AteA
Hyperosmotic stress
Sln1
Ydp1
Ssk1
Ssk2
Osmolyte synthesis
MAPK signaling pathway - yeast
Sln1
Heat shock genes
Diffusible signaling factor (DSF)
RpfC
RpfG
c-di-GMP
Clp
Biofilm formation, motility, and virulence
RpfF
DSF synthesis
Glutamine
GlnL
GlnA
GlnT
Glutamine utilization
YesM
YesN
CbrA
Circadian genes
Redox signal
RegB
RegA
Puc
Puf
Puh
Photosystem
PetA
PetB
PetC
CcoN
CcoO
CcoQ
CcoP
CydA
CydB
Electron transfer system
Oxidative phosphorylation
Aerobic respiration
NtrA
Nitrogen assimilation
02020 7/24/14
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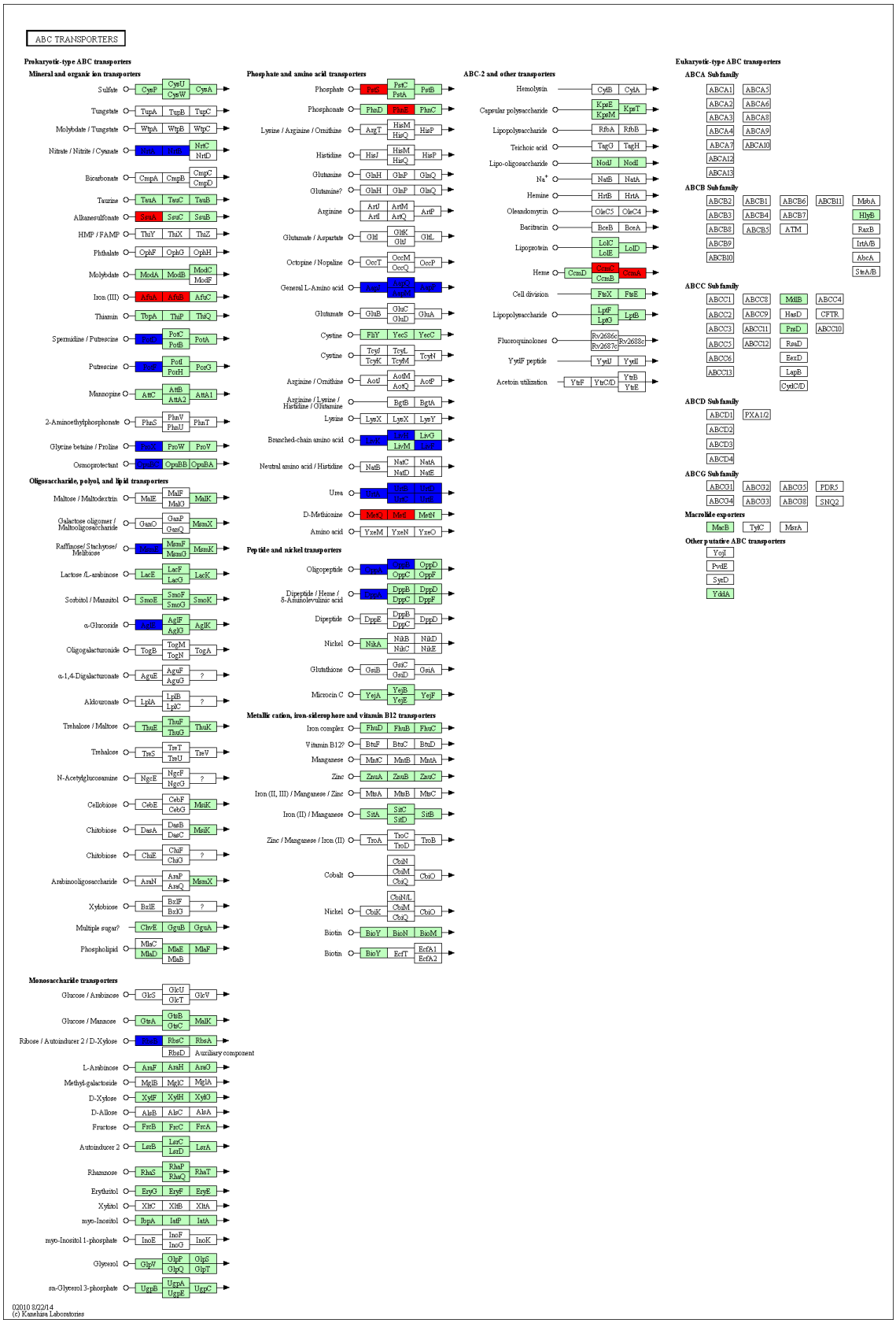
ABC TRANSPORTERS
Prokaryotic-type ABC transporters
Mineral and organic ion transporters
Sulfate CysP CysU CysW CysA
Tungstate TupA TupB TupC
Molybdate / Tungstate WtpA WtpB WtpC
Nitrate / Nitrite / Cyanate NrtA NrtB NrtC NrtD
Bicarbonate CmpA CmpB CmpC CmpD
Taurine TauA TauC TauB
Alkanesulfonate SsuA SsuC SsuB
HMP / FAMP ThiY ThiX ThiZ
Phthalate OphF OphG OphH
Molybdate ModA ModB ModC ModF
Iron (III) AfuA AfuB AfuC
Thiamin TbpA ThiP ThiQ
Spermidine / Putrescine PotC PotB PotA
Putrescine PotI PotH PotG
Mannopine AttC AttB AttA2 AttA1
2-Aminoethylphosphonate PhnS PhnV PhnU PhnT
Glycine betaine / Proline ProX ProW ProV
Osmoprotectant OpuBC OpuBB OpuBA
Oligosaccharide, polyol, and lipid transporters
Maltose / Maltodextrin MalE MalF MalG MalK
Galactose oligomer / Maltooligosaccharide GanO GanP GanQ MsmX
Raffinose/ Stachyose/ Melibiose MsmE MsmF MsmG MsmK
Lactose /L-arabinose LacE LacF LacG LacK
Sorbitol / Mannitol SmoE SmoF SmoG SmoK
α-Glucoside AglE AglF AglG AglK
Oligogalacturonide TogB TogM TogN TogA
α-1,4-Digalacturonate AguE AguF AguG ?
Aldouronate LplA LplB LplC ?
Trehalose / Maltose ThuE ThuF ThuG ThuK
Trehalose TreS TreT TreU TreV
N-Acetylglucosamine NgcE NgcF NgcG ?
Cellobiose CebE CebF CebG MsiK
Chitobiose DasA DasB DasC MsiK
Chitobiose ChiE ChiF ChiG ?
Arabinooligosaccharide AraN AraP AraQ MsmX
Xylobiose BxlE BxlF BxlG ?
Multiple sugar? ChvE GguB GguA
Phospholipid MlaC MlaD MlaE MlaF MlaB
Monosaccharide transporters
Glucose / Arabinose GlcS GlcU GlcT GlcV
Glucose / Mannose GtsA GtsB GtsC MalK
Ribose / Autoinducer 2 / D-Xylose RbsB RbsC RbsD RbsA Auxiliary component
L-Arabinose AraF AraH AraG
Methyl-galactoside MglB MglC MglA
D-Xylose XylF XylH XylG
D-Allose AlsB AlsC AlsA
Fructose FrcB FrcC FrcA
Autoinducer 2 LsrB LsrC LsrD LsrA
Rhamnose RhaS RhaP RhaQ RhaT
Erythritol EryG EryF EryE
Xylitol XltC XltB XltA
myo-Inositol IbpA IatP IatA
myo-Inositol 1-phosphate InoE InoF InoG InoK
Glycerol GlpV GlpP GlpQ GlpS GlpT
sn-Glycerol 3-phosphate UgpB UgpA UgpE UgpC
Phosphate and amino acid transporters
Phosphate PstS PstC PstA PstB
Phosphonate PhnD PhnE PhnC
Lysine / Arginine / Ornithine ArgT HisM HisQ HisP
Histidine HisJ HisM HisQ HisP
Glutamine GlnH GlnP GlnQ
Glutamine? GlnH GlnP GlnQ
Arginine ArtJ ArtM ArtI ArtQ ArtP
Glutamate / Aspartate GltI GltK GltJ GltL
Octopine / Nopaline OccT OccM OccQ OccP
General L-Amino acid AapJ AapQ AapM AapP
Glutamate GluB GluC GluD GluA
Cystine FliY YecS YecC
Cystine TcyJ TcyL TcyK TcyM TcyN
Arginine / Ornithine AotJ AotM AotQ AotP
Arginine / Lysine / Histidine / Glutamine BgtB BgtA
Lysine LysX LysX LysY
Branched-chain amino acid LivK LivF LivG LivM LivH LivJ
Neutral amino acid / Histidine NatB NatC NatD NatA NatE
Urea UrtE UrtD UrtC UrtB
D-Methionine MetQ MetI MetN
Amino acid YxeM YxeN YxeO
Peptide and nickel transporters
Oligopeptide OppA OppB OppC OppD OppF
Dipeptide / Heme / 5-Aminolevulinic acid DppA DppB DppC DppD DppF
Dipeptide DppE DppB DppC DppD
Nickel NikA NikB NikC NikD NikE
Glutathione GsiB GsiC GsiD GsiA
Microcin C YejA YejB YejE YejF
Metallic cation, iron-siderophore and vitamin B12 transporters
Iron complex FhuD FhuB FhuC
Vitamin B12? BtuF BtuC BtuD
Manganese MntC MntB MntA
Zinc ZnuA ZnuB ZnuC
Iron (II, III) / Manganese / Zinc MtsA MtsB MtsC
Iron (II) / Manganese SitA SitC SitD SitB
Zinc / Manganese / Iron (II) TroA TroC TroD TroB
Cobalt CbiN CbiM CbiQ CbiO
Nickel CbiK CbiN/L CbiM CbiQ CbiO
Biotin BioY BioN BioM
Biotin BioY EcfT EcfA1 EcfA2
ABC-2 and other transporters
Hemolysin CylB CylA
Capsular polysaccharide KpsE KpsM KpsT
Lipopolysaccharide RfbA RfbB
Teichoic acid TagG TagH
Lipo-oligosaccharide NodU NodI
Na+ NatB NatA
Hemine HrtB HrtA
Oleandomycin OleC5 OleC4
Bacitracin BceB BceA
Lipoprotein LolC LolE LolD
Heme CcmD CcmC CcmB CcmA
Cell division FtsX FtsE
Lipopolysaccharide LptF LptG LptB
Fluoroquinolones Rv2686c Rv2687c Rv2688c
YxlF peptide YxlU YxlI
Acetoin utilization YtrF YtrC/D YtrB YtrE
Eukaryotic-type ABC transporters
ABCA Subfamily
ABCA1 ABCA5
ABCA2 ABCA6
ABCA3 ABCA8
ABCA4 ABCA9
ABCA7 ABCA10
ABCA12
ABCA13
ABCB Subfamily
ABCB2 ABCB1 ABCB6 ABCB11 MsbA
ABCB3 ABCB4 ABCB7 HlyB
ABCB8 ABCB5 ATM RaxB
ABCB9 IrtA/B
ABCB10 AbcA
SteA/B
ABCC Subfamily
ABCC1 ABCC8 MdlB ABCC4
ABCC2 ABCC9 HasD CFTR
ABCC3 ABCC11 PrsD ABCC10
ABCC5 ABCC12 RsaD
ABCC6 ExcD
ABCC13 LapB
CydC/D
ABCD Subfamily
ABCD1 PXA1/2
ABCD2
ABCD3
ABCD4
ABCG Subfamily
ABCG1 ABCG2 ABCG5 PDR5
ABCG4 ABCG3 ABCG8 SNQ2
Macrolide exporters
MacB TylC MsrA
Other putative ABC transporters
YojI
PvdE
SyrD
YkkA
02010 8/22/14
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