GENERAL EXPLANATIONS

- Precursor in a route; or in a branch or section of a route

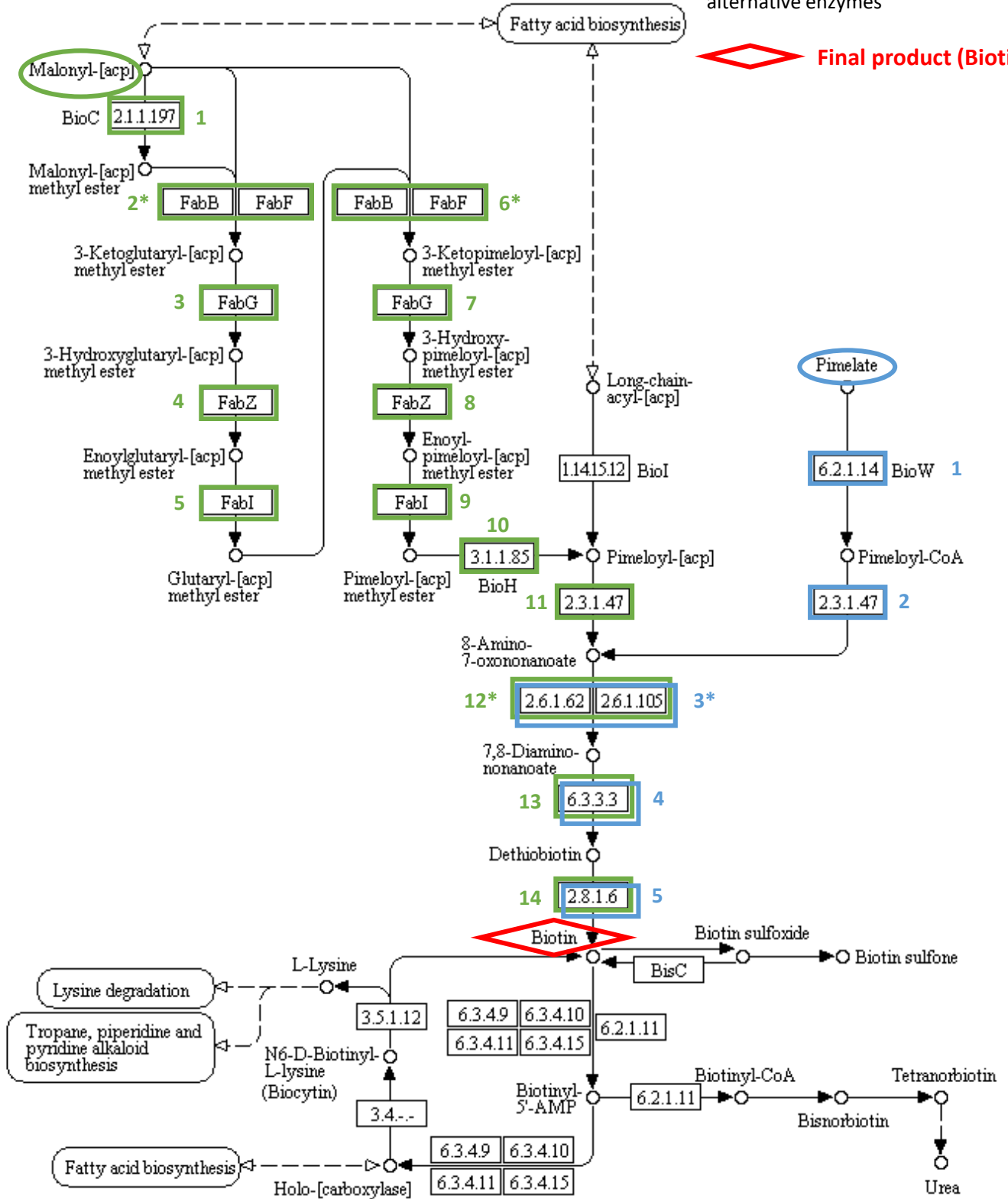- Final product (cofactor) of the route

- Catalytic step

BIOTIN METABOLISM

Main route: Synthesis from Malonyl-[acp]

Alternative route: Synthesis from Pimelate

* Steps that can be catalysed by alternative enzymes

Final product (Biotin)

Fatty acid biosynthesis

Malonyl-[acp]

BioC 2.1.1.197 1

Malonyl-[acp] methyl ester

2* FabB FabF   FabB FabF 6*

3-Ketoglutaryl-[acp] methyl ester   3-Ketopimeloyl-[acp] methyl ester

3 FabG   FabG 7

3-Hydroxyglutaryl-[acp] methyl ester

3-Hydroxy-pimeloyl-[acp] methyl ester

4 FabZ   FabZ 8

Enoylglutaryl-[acp] methyl ester

Enoyl-pimeloyl-[acp] methyl ester

5 FabI   FabI 9

10

Glutaryl-[acp] methyl ester

Pimeloyl-[acp] methyl ester   3.1.1.85

BioH

Pimeloyl-[acp]

Long-chain-acyl-[acp]

1.14.15.12 BioI

Pimelate

6.2.1.14 BioW 1

Pimeloyl-CoA

11 2.3.1.47   2.3.1.47 2

8-Amino-7-oxononanoate

12* 2.6.1.62 2.6.1.105 3*

7,8-Diamino-nonanoate

13 6.3.3.3 4

Dethiobiotin

14 2.8.1.6 5

Biotin sulfoxide

Biotin   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)

3.4.-.-

Biotinyl-5'-AMP   6.2.1.11

Biotinyl-CoA   Tetranorbiotin

Bisnorbiotin

Fatty acid biosynthesis

Holo-[carboxylase]   6.3.4.9 6.3.4.10
                       6.3.4.11 6.3.4.15

Urea

00780 9/1/15
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Branch 1: Synthesis of Adenosyl cobyrinate hexaamide
    — **Section 1: Formation of ALA**
    — **Section 2: Formation of Adenosyl cobyrinate hexaamide**
Branch 2: Transformation of Adenosyl cobyrinate hexaamide into Adenosine-GDP-cobinamide
    — **Section 1: Formation of Adenosyl cobinamide phosphate**
    — **Section 2: Transformation of Adenosyl cobinamide phosphate to Adenosine-GDP-cobinamide**
— **Branch 3: Synthesis of α-Ribazole from 5-Aminoimidazole ribotide (based on Hazra et al., PNAS 112: 10792 (2015)**
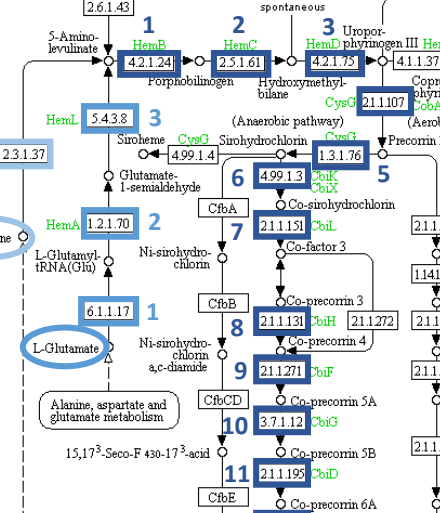— **Branch 4: Merge of Adenosine-GDP-cobinamide with α-Ribazole to form B12 coenzyme**
◇ **Final product (Adenosylcobalamin – B12 coenzyme)**
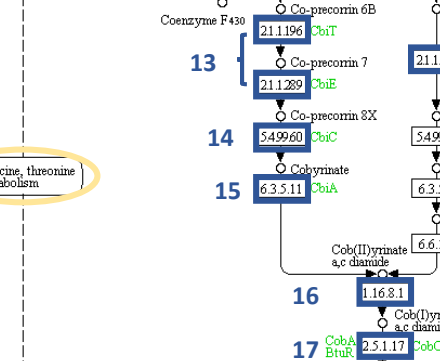
ADENOSYLCOBALAMIN PATHWAY

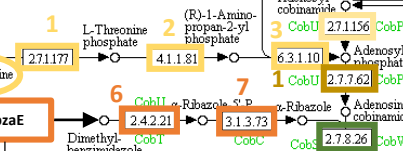PORPHYRIN AND CHLOROPHYLL METABOLISM

Branch 1

Section 1

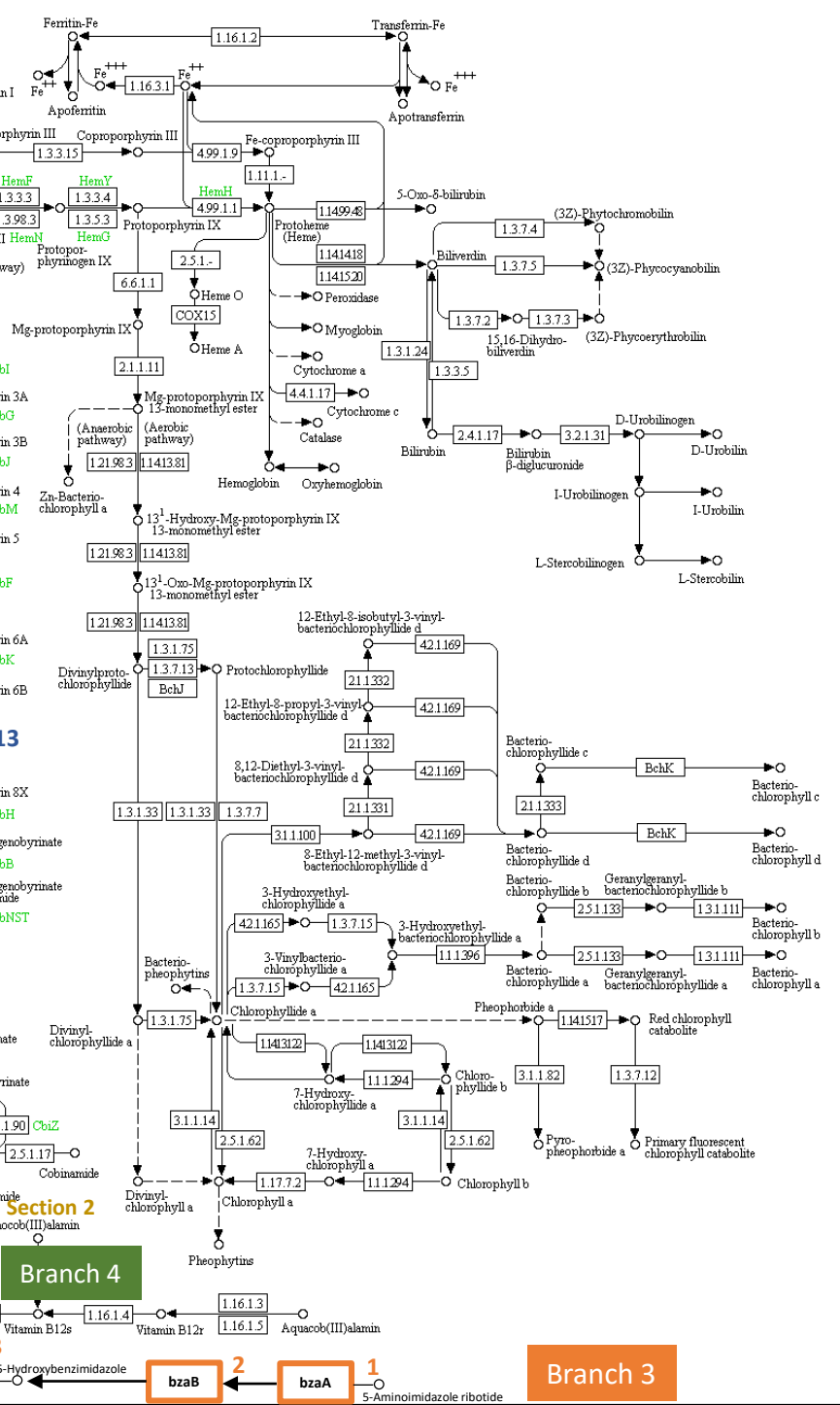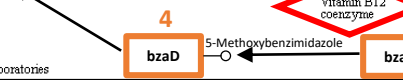4,5-Dioxopentanoate

Uroporphyrin I
Uroporphyrinogen I — 4.1.1.37 — Coproporphyrin I
Coproporphyrinogen I
Ferritin-Fe — 1.16.1.2 — Transferrin-Fe
Fe^{+++} Fe^{++} Fe^{+++}
Apoferritin — 1.16.3.1 — Apotransferrin
Fe^{++} Fe^{+++}

2.6.1.43

spontaneous

Uroporphyrin III — Coproporphyrin III — Fe-coproporphyrin III
1.3.3.15 4.99.1.9 1.11.1.-

5-Oxo-δ-bilirubin
5-Amino-levulinate
1 HemB 4.2.1.24
2 HemC 2.5.1.61
3 HemD 4.2.1.75
Uropor-phyrinogen III HemE 4.1.1.37
Uropor-phyrinogen III HemN
CysG 2.1.1.107 **4** CobA
Coproporphyrinogen III
HemF 1.3.3.3 / 1.3.98.3
HemY 1.3.3.4 / 1.3.5.3
HemG
Protoporphyrinogen IX
HemH 4.99.1.1
Protoheme (Heme)
Protoporphyrin IX
1.14.99.48
1.14.14.18
1.14.15.20
Peroxidase
(3Z)-Phytochromobilin
Biliverdin 1.3.7.4
1.3.7.5 (3Z)-Phycocyanobilin
1.3.7.2 1.3.7.3
15,16-Dihydro-biliverdin (3Z)-Phycoerythrobilin

Porphobilinogen
Hydroxymethyl-bilane
CysG CysG
3 HemL 5.4.3.8
Siroheme CysG 4.99.1.4 Sirohydrochlorin 1.3.1.76
Precorrin 2
1 2.3.1.37
Glutamate-1-semialdehyde
6 4.99.1.3 CbiK CbiX **5**
Co-sirohydrochlorin
Myoglobin
1.3.1.24
1.3.3.5
D-Urobilinogen
2.4.1.17 — 3.2.1.31 — D-Urobilin

Glycine
CfbA
2 HemA 1.2.1.70
Ni-sirohydro-chlorin
7 2.1.1.151 CbiL
Co-factor 3
Mg-protoporphyrin IX
2.1.1.11
2.1.1.130 CobI
1.14.13.83 CobG
Precorrin 3A
Heme O COX15
Heme A
Cytochrome a
Cytochrome c
4.4.1.17
Bilirubin
Bilirubin β-diglucuronide
I-Urobilinogen — I-Urobilin

L-Glutamyl-tRNA(Glu)
CfbB
1 6.1.1.17
Ni-sirohydro-chlorin a,c-diamide
8 2.1.1.131 CbiH 2.1.1.272
Co-precorrin 3
Precorrin 3B
Mg-protoporphyrin IX 13-monomethyl ester
2.1.1.131 CobJ
Precorrin 4
(Anaerobic pathway) 1.21.98.3
(Aerobic pathway) 1.14.13.81
Hemoglobin Oxyhemoglobin

Alanine, aspartate and glutamate metabolism
CfbCD
9 2.1.1.271 CbiF
Co-precorrin 4
2.1.1.133 CobM
Precorrin 5
Zn-Bacterio-chlorophyll a
13^1-Hydroxy-Mg-protoporphyrin IX 13-monomethyl ester
1.21.98.3 1.14.13.81
L-Stercobilinogen — L-Stercobilin

15,17^3-Seco-F 430-17^3-acid
10 3.7.1.12 CbiG
Co-precorrin 5A
CfbE
11 2.1.1.195 CbiD
Co-precorrin 5B
2.1.1.152 CobF
Precorrin 6A
13^1-Oxo-Mg-protoporphyrin IX 13-monomethyl ester
1.21.98.3 1.14.13.81

Coenzyme F430
Section 2
12 1.3.1.106 CbiJ
Co-precorrin 6A
1.3.1.54 CobK
Precorrin 6B
1.3.1.75 1.3.7.13 BchJ
Protochlorophyllide
12-Ethyl-8-isobutyl-3-vinyl-bacteriochlorophyllide d
42.1.169

2.1.1.196 CbiT
Co-precorrin 6B
12-Ethyl-8-propyl-3-vinyl-bacteriochlorophyllide d
2.1.1.332 42.1.169
Bacterio-chlorophyllide c
2.1.1.332

13 2.1.1.196 CbiT
2.1.1.289 CbiE
Co-precorrin 7
2.1.1.132 **13**
Precorrin 8X
8,12-Diethyl-3-vinyl-bacteriochlorophyllide d
2.1.1.331 42.1.169 BchK
Bacterio-chlorophyllide c

14 5.4.99.60 CbiC
Co-precorrin 8X
Cobyrinate
5.4.99.61 CobH
Precorrin 8X
Hydrogenobyrinate
1.3.1.33 1.3.1.33 1.3.7.7
3.1.1.100
8-Ethyl-12-methyl-3-vinyl-bacteriochlorophyllide d
2.1.1.333
Bacterio-chlorophyllide d BchK Bacterio-chlorophyll d

15 6.3.5.11 CbiA
6.3.5.9 CobB
Hydrogenobyrinate a,c diamide
Bacterio-chlorophyllide b Geranylgeranyl-bacteriochlorophyllide b
2.5.1.133 — 1.3.1.111

Glycine, threonine metabolism
Cob(II)yrinate a,c diamide
6.6.1.2 CobNST
3-Hydroxyethyl-chlorophyllide a
42.1.165 1.3.7.15 3-Hydroxyethyl-bacteriochlorophyllide a
1.1.1.396
2.5.1.133 — 1.3.1.111
Bacterio-chlorophyllide b Geranylgeranyl-bacteriochlorophyllide b

16 1.16.8.1
Cob(I)yrinate a,c diamide
3-Vinylbacterio-chlorophyllide a
1.3.7.15 42.1.165
Bacterio-chlorophyllide a Geranylgeranyl-bacteriochlorophyllide a

17 CobA BtuR 2.5.1.17 CobO
Adenosyl cobyrinate a,c diamide
Bacterio-pheophytins
Chlorophyllide a
1.3.1.75
Divinyl-chlorophyllide a
Pheophorbide a 1.14.15.17 Red chlorophyll catabolite

18 CbiP 6.3.5.10 CobQ
Adenosyl cobyrinate hexaamide
1.14.13.122 1.14.13.122
3.1.1.82 1.3.7.12

Branch 2
(R)-1-Amino-propan-2-ol
CobB CobC CobD protein α 6.3.1.10 3.5.1.90 CbiZ
Adenosyl cobinamide
7-Hydroxy-chlorophyllide a
3.1.1.14 2.5.1.62
7-Hydroxy-chlorophyllide a
Chlorophyll b
1.17.7.2 1.1.1.294
Pyro-pheophorbide a Primary fluorescent chlorophyll catabolite

Section 1
1 2.7.1.177
L-Threonine phosphate
2 4.1.1.81
(R)-1-Amino-propan-2-yl phosphate
3 CobU 6.3.1.10
4 2.7.1.156 CobP **5**
Adenosyl cobinamide phosphate
Cobinamide
2.5.1.17
L-Threonine
Divinyl-chlorophyllide a
3.1.1.14 2.5.1.62
Chlorophyll a Chlorophyll b

Section 2
1 CobU 2.7.7.62 CobP
Cyanocob(III)alamin
Adenosine-GDP-cobinamide

6 CobU 2.4.2.21 CobT
Ribazole 5'-P
7 3.1.3.73
α-Ribazole
bzaE
Dimethyl-benzimidazole
Branch 4
1 Cob5 2.7.8.26 CobV
Vitamin B12 coenzyme ◇
2.5.1.17
Vitamin B12s Vitamin B12r 1.16.1.3 / 1.16.1.5 Aquacob(III)alamin
1.16.1.4

5-Methoxy-6-methylbenzimidazole
5
4 bzaD
5-Methoxybenzimidazole
3 bzaC
5-Hydroxybenzimidazole
2 bzaB
1 bzaA
5-Aminoimidazole ribotide
Branch 3

Pheophytins

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FOLATE BIOSYNTHESIS

Branch 1

Branch 2

Branch 3

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NICOTINATE AND NICOTINAMIDE METABOLISM

NADP+

2.4.9.20

3.2.2.5
3.2.2.6
3.5.1.-

1a
2.4.2.12
3.2.2.14

1.6.1.1 1.6.1.2

3.1.3.- 2.7.1.23

N1-Methyl-2-pyridone-5-carboxamide
1.2.3.1

1b
2.4.2.1
N-Ribosyl-nicotinamide
3.2.2.1
3.2.2.3

1b
2.7.1.22
Nicotinamide D-ribonucleotide
3.1.3.5
3.1.3.-

2*
2.7.7.1
2.7.7.18

NAD+

3*
6.3.1.5 6.3.5.1

5*

1.2.3.1
N1-Methyl-4-pyridone-5-carboxamide

Nicotinamide
2.1.1.1
N1-Methyl-nicotinamide

3.6.1.9
3.6.1.22

3.5.1.19

3.5.1.42

Tropane, piperidine and pyridine alkaloid biosynthesis

1a
6.3.4.21

Nicotinate
1b
2.4.2.1
3.2.2.3

Nicotinate D-ribonucleoside

1b
2.7.1.173

Nicotinate D-ribonucleotide
3.1.3.5
3.1.3.-

2*
2.7.7.1
2.7.7.18

4*

Deamino-NAD+

3.6.1.9
3.6.1.22

Nicotine

1.5.99.4 1.5.99.4

1.5.3.-

Pseudooxy-nicotine
1.4.3.24

NS

1-Methyl pyrrolinium

3-Succinoyl-semialdehyde-pyridine

2.4.2.19
3

Tryptophan metabolism

Quinolinate

(S)-6-Hydroxy-nicotine
1.5.3.5

(R)-6-Hydroxy-nicotine
1.5.3.6

6-Hydroxy-N-methylmyosmine

N-Methylmyosmine
NicA1
1.2.1.83

3-Succinoylpyridine

Nicotinurate

1.17.2.1 1.17.1.5

2.1.1.7

Trigonelline

6-oxo-1,4,5,6-Tetrahydro-nicotinate

1.3.7.1
6-Hydroxy-nicotinate
3.5.2.18
2-Formyl-glutarate

NadA
2
Glycerone-P
Iminoaspartate

6-Hydroxy-pseudooxynicotine
1.5.99.14

Spm

6-Hydroxy-3-succinoylpyridine
1.14.13.163

2,5-Dihydroxy-pyridine

1.1.1.291

Methylitaconate
5.4.99.4
2-Methylene-glutarate

(S)-2-Hydroxy-methylglutarate

2,6-Dihydroxy-pseudooxynicotine
3.7.1.19

2,6-Dihydroxy-N-methylmyosmine

1.5.3.21

1.14.13.10

4-Methyl-aminobutyrate

1.5.3.19

4-Amino-butanoate

2,3,6-Trihydroxypyridine

Succinate-semialdehyde
1.2.1.16
1.2.1.24
1.2.1.79

Succinate

Citrate cycle

Alanine metabolism

1.17.3.3

5.3.3.6

2,3-Dimethyl-maleate

4.2.1.85

(2R,3S)-2,3-Dimethylmalate

4.1.3.32

Propanoate

Pyruvate

1.4.3.16 1.4.1.21
1*

L-Aspartate

1.13.11.9

N-formyl maleamate

3.5.1.106

2,6-Dihydroxy-nicotinate

Pyruvate metabolism

C5-Branched dibasic acid metabolism

Alanine, aspartate and glutamate metabolism

Maleamate
3.5.1.107
Maleate
5.2.1.1
Fumarate

2,6-Dihydroxy-pyridine

Blue pigment
1.1.1.328
3,3'-Bipyridine-2,2',5,5',6,6'-hexol

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Branch 1: Synthesis of (R)-Pantoate

─── **Section 1: Synthesis of 3-Methyl-2-oxobutanoate (from Pyruvate or** from L-Valine**)**

─── **Section 2: Conversion of 3-Methyl-2-oxobutanoate to (R)-Pantoate**

Branch 2: Synthesis of β-Alanine

─── **Alternative a: From L-Aspartate**

─── **Alternative b: From Uracil**

─── **Alternative c: From Propanoate metabolism**

Branch 3: Merge of (R)-Pantoate and β-Alanine

─── **Section 1: Synthesis of (R)-4'-Phospho-pantothenate**

─── **Section 2: Merge of D-4'-Phospho-pantothenate with L-Cysteine to produce CoA**

Salvage route: Use of Pantetheine

─── **Alternative A: Shortcut route through 4'-Phospho-pantetheine**

─── **Alternative B: Route through (R)-Pantothenate**

⬦ **Final product (Coenzyme A)**

* Steps that can be catalysed by alternative enzymes

PANTOTHENATE AND CoA BIOSYNTHESIS

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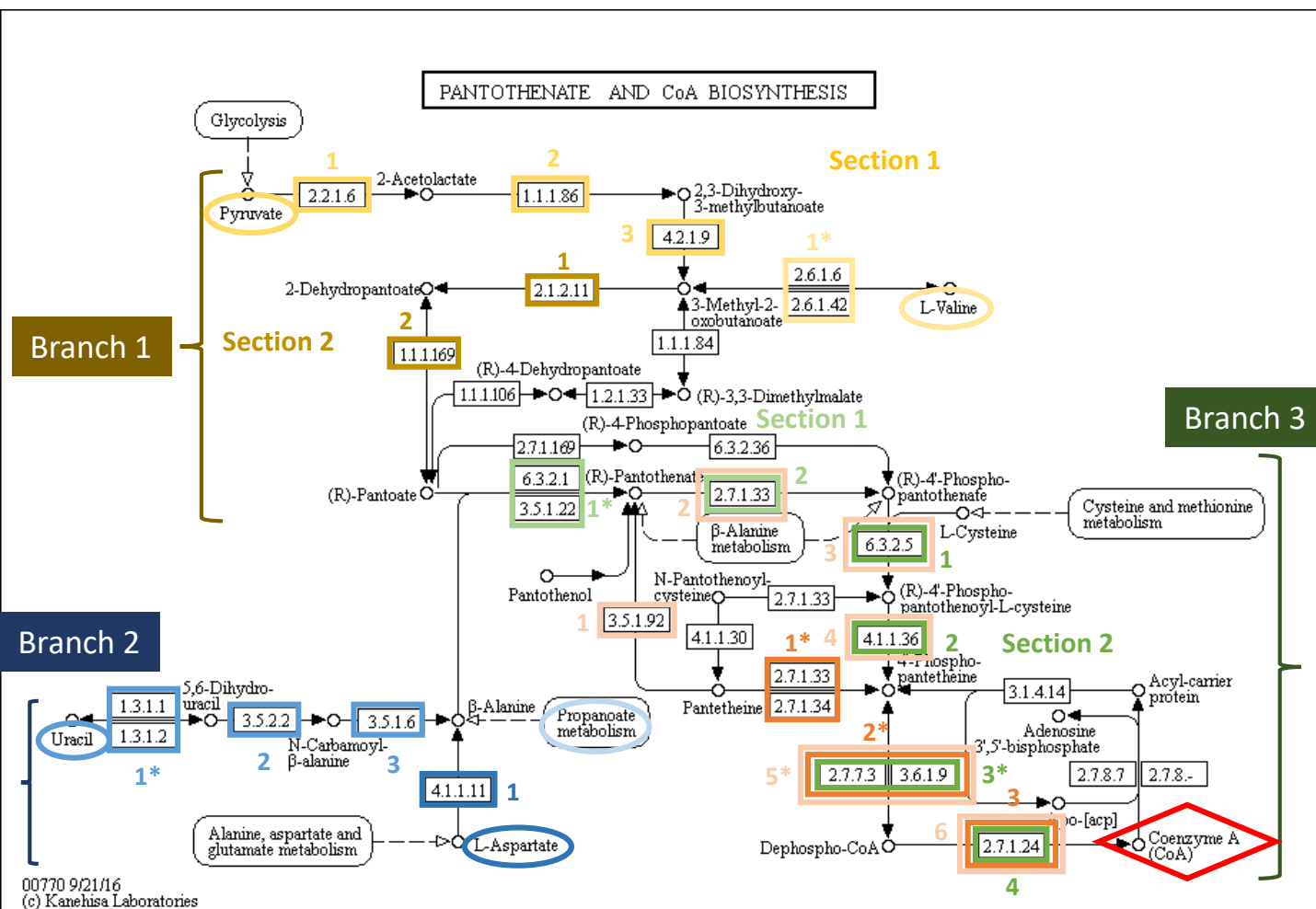
Main route: Synthesis from D-Erythrose 4-phosphate

Alternative route: Synthesis from Ribulose 5-phosphate + Glyceraldehyde 3-phosphate

Salvage route 1: Synthesis from Pyridoxamine

Salvage route 2: Synthesis from Pyridoxal

Salvage route 3: Synthesis from Pyridoxine

Final product (Pyridoxal 5-phosphate)
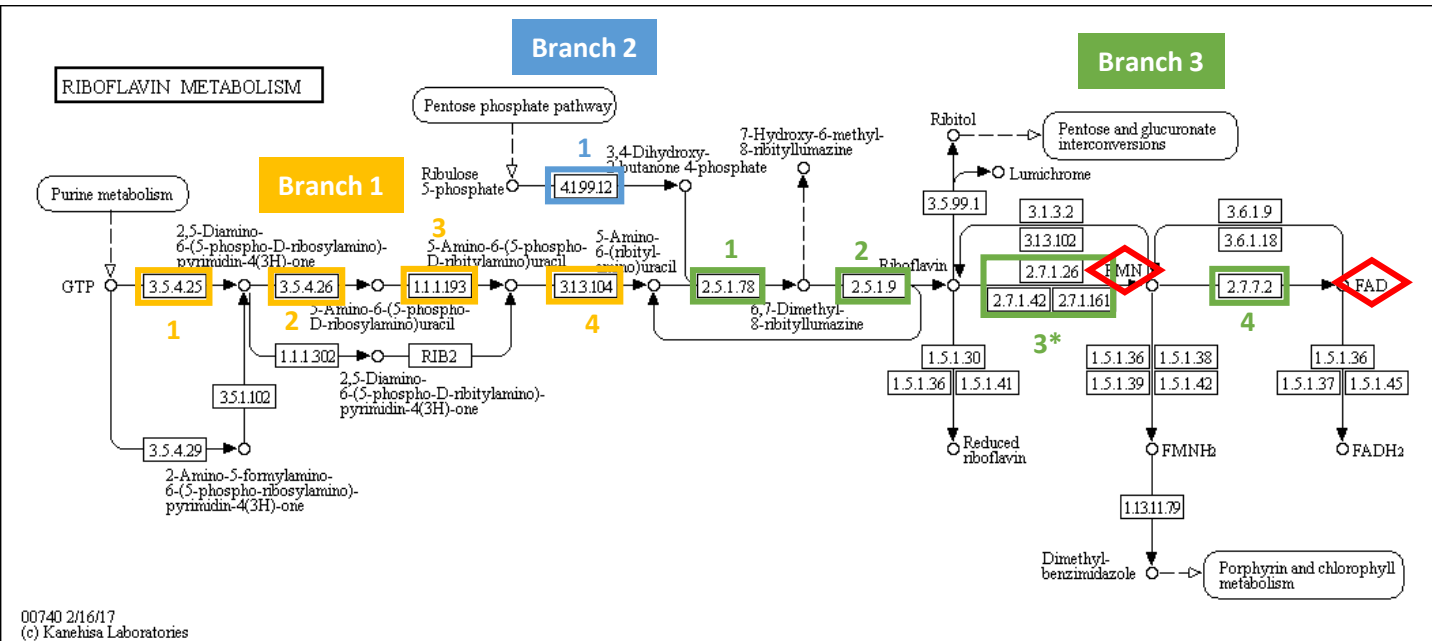
* Steps that can be catalysed by alternative enzymes

VITAMIN B 6 METABOLISM
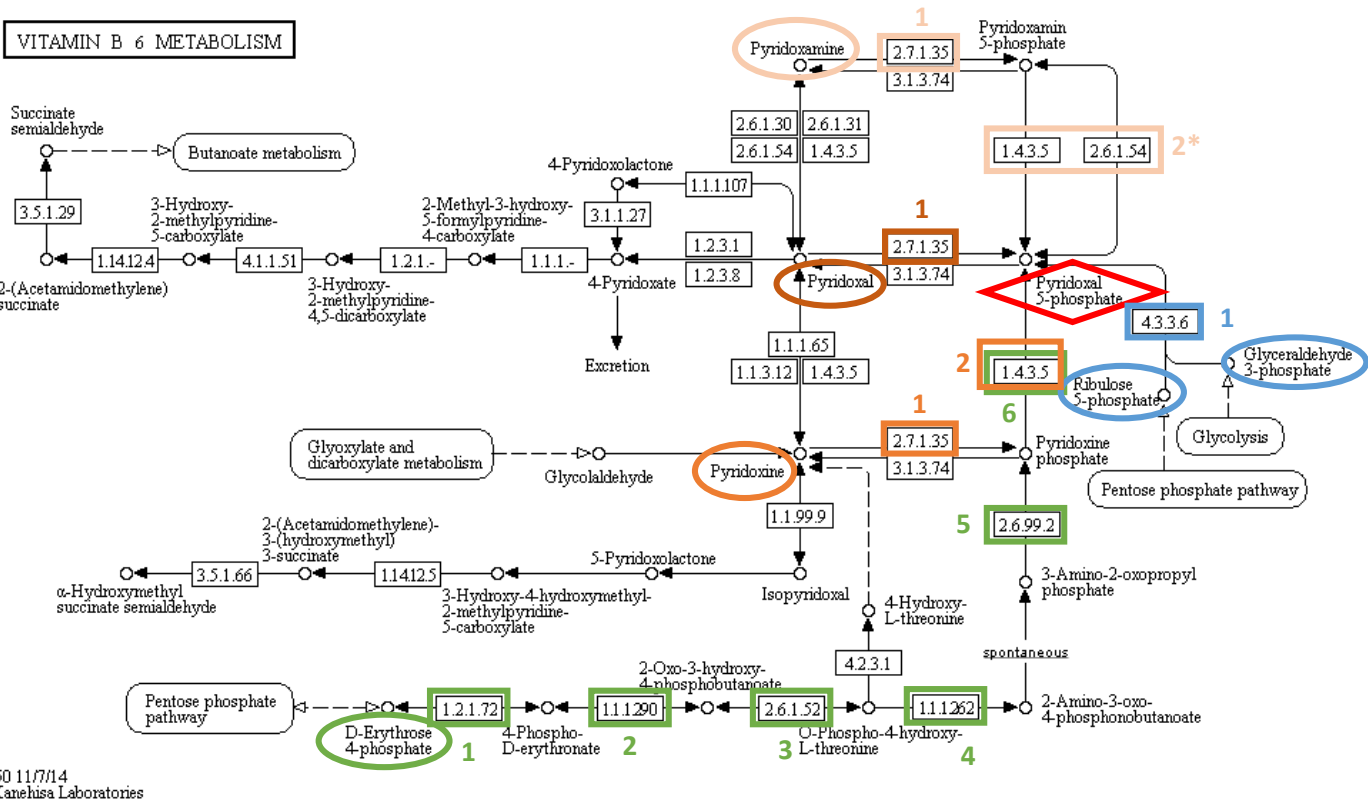
Branch 1: Synthesis of 4-Amino-5-hydroxymethyl-2-methylpyrimidine diphosphate

Branch 2: Synthesis of 2-(2-Carboxy-4-methylthiazol-5-yl)ethyl phosphate

Section 1: Synthesis of Thiocarboxy-[sulfur-carrier protein]
Section 2: Synthesis of 1-Deoxy-D-Xylulose 5-phosphate
Section 3: Synthesis of Iminoglycine
Section 4: Merge of final products from sections 1, 2 and 3 and synthesis of 2-(2-Carboxy-4-methylthiazol-5-yl)ethyl phosphate

Branch 3: Merge of final compounds from branches 1 and 2 and synthesis of Thiamine diphosphate

Final product (Thiamine diphosphate)

THIAMINE METABOLISM

Branch 1

E.C. 5.3.99.10 in section 4 of the branch 2 is not present in any of the genomes of the project. According to KEGG records, this E.C. has been only identified in certain members of the Order *Bacillales*

Vitamine B6 metabolism
Pyridoxal phosphate
1-(5'-Phospho-ribosyl)-5-aminoimidazole
THI5
Purine metabolism
4.1.99.17 **1**
2.7.1.49
4-Amino-5-hydroxymethyl-2-methylpyrimidine
4-Amino-5-hydroxymethyl-2-methylpyrimidine phosphate
2 2.7.4.7
4-Amino-5-hydroxymethyl-2-methylpyrimidine diphosphate

Cysteine metabolism
L-Cysteine
Tyrosine biosynthesis
Glycine metabolism
Section 1 [IscS]-SH [IscS]-SSH
1 2.8.1.7
2 2.7.7.73 [ThiS]-CO-AMP
3 ThiI [ThiS]-COSH
Section 3
L-Tyrosine Glycine
1a 4.1.99.19 **1b** 1.4.3.19
[ThiS]-COOH
Pyruvate
1-Deoxy-D-xylulose 5-phosphate
Section 2
Glycolysis
2.2.1.7 **1**
Glycer-aldehyde-3P
Iminoglycine
2.8.1.10 **1**

Branch 2
Section 4
2-[(2-Carboxy-4-methyl-thiazol-5(2H)-ylidene]-ethyl phosphate
5.3.99.10 **2 #**

Glycine
ADP-5-ethyl-4-methyl-thiazole-2-carboxylate
THI4
NAD+
2-(2-Carboxy-4-methyl-thiazol-5-yl)ethyl phosphate

Branch 3
1 2.5.1.3
3.6.1.15
3.6.1.-
3.6.1.28
Thiamine phosphate
2 2.7.4.16
2.7.4.15
2.7.4.3
Thiamine triphosphate

5-(2-Hydroxyethyl)-4-methylthiazole
2.7.1.50
5-(2-Hydroxyethyl)-4-methylthiazole phosphate
2.5.1.3
Thiamine diphosphate
3.1.3.1 3.1.3.2
3.1.3.100 2.7.1.89

2.5.1.2
3.5.99.2
Thiamine
2.7.6.2

3.5.99.2
YlmB
TenA_E TenA_E
4-Amino-5-aminomethyl-2-methylpyrimidine
FAMP
1.1.3.23 1.1.3.23
Thiamine aldehyde
Thiamine acetic acid

00730 2/1/17
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