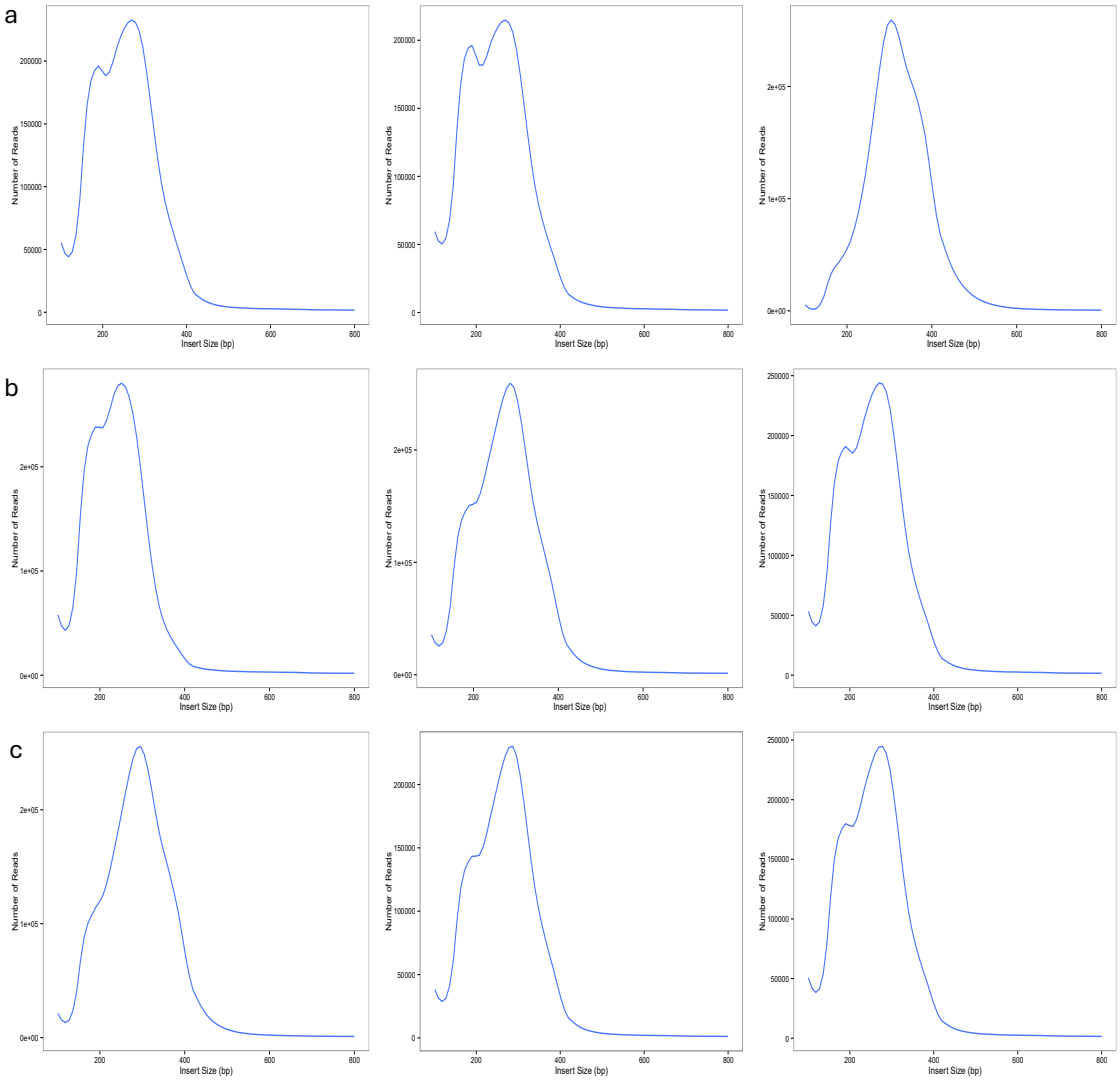
Chalcone and Trans-Chalcone Induce Transcriptomic Changes in Caenorhabsitis elegans Compatible with a Novel Cumulative Damage Mode of Action

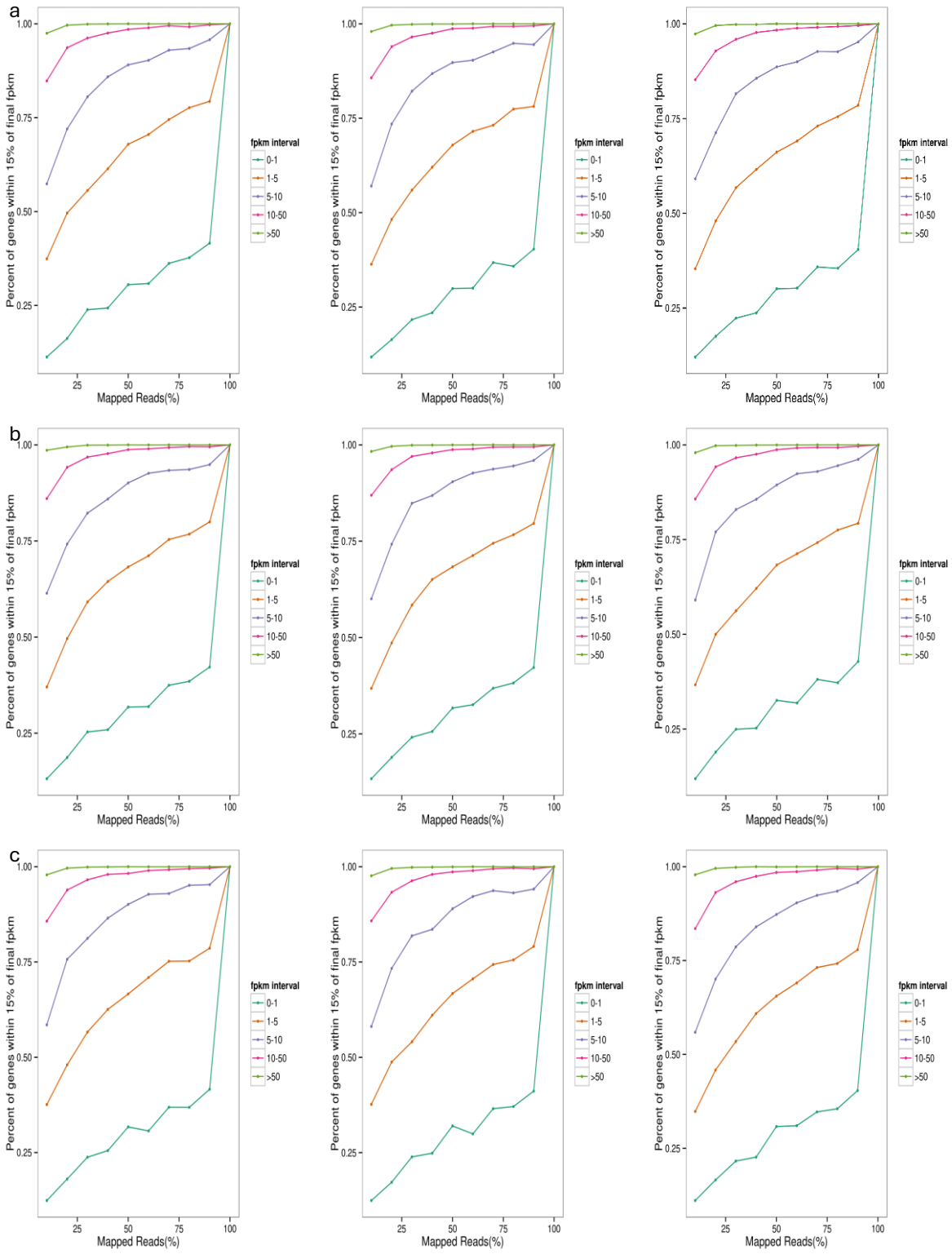
Giulio Galli [1], Carl S. Bruun [2], Carlos García-Estrada [1,3], Rafael Balaña-Fouce [1,3,*], María Martinez-Valladares [4] and Tina V. A. Hansen [2,*]

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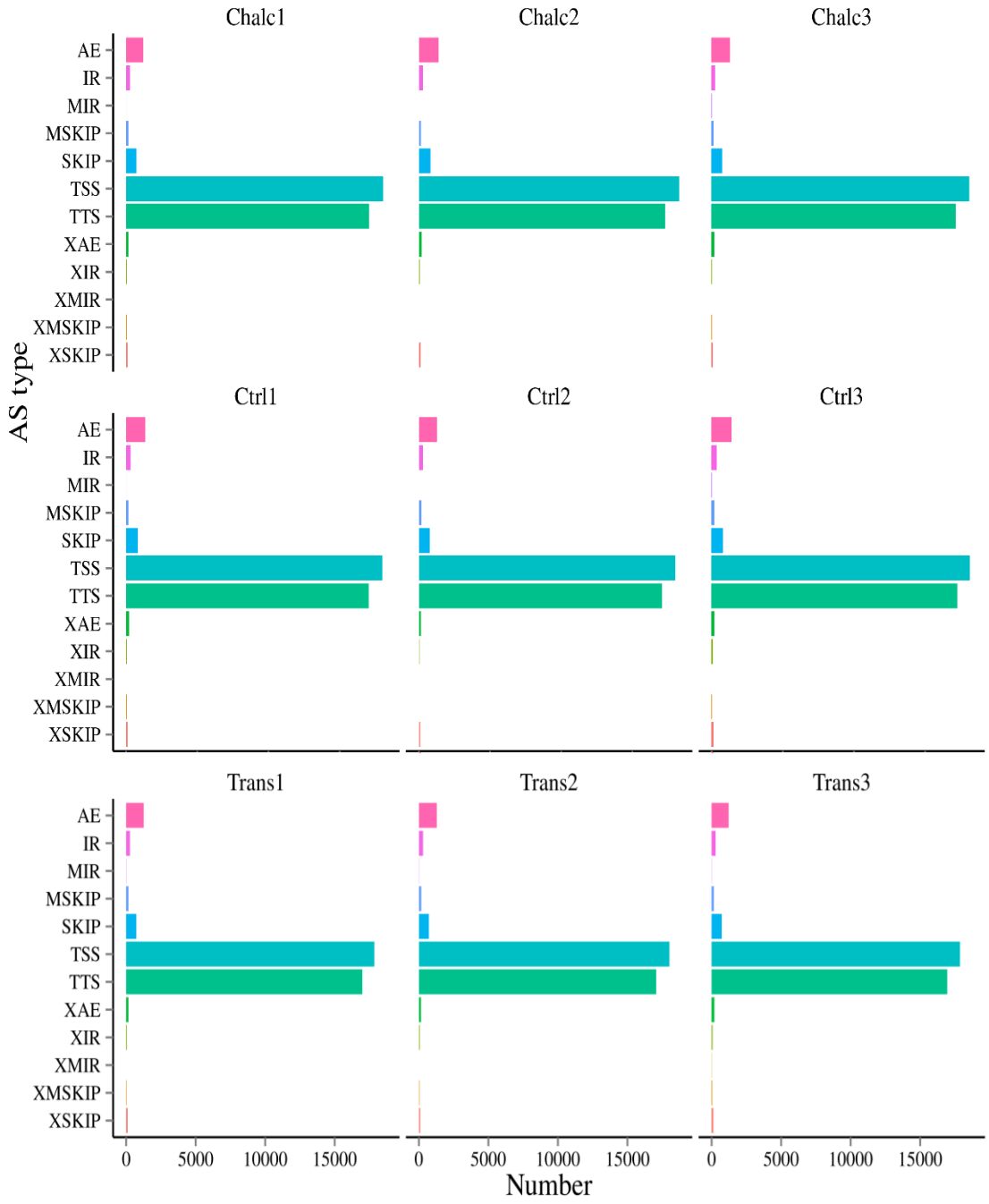
* Correspondence: rbalf@unileon.es (R.B.-F.); alstrup@sund.ku.dk (T.V.A.H.)



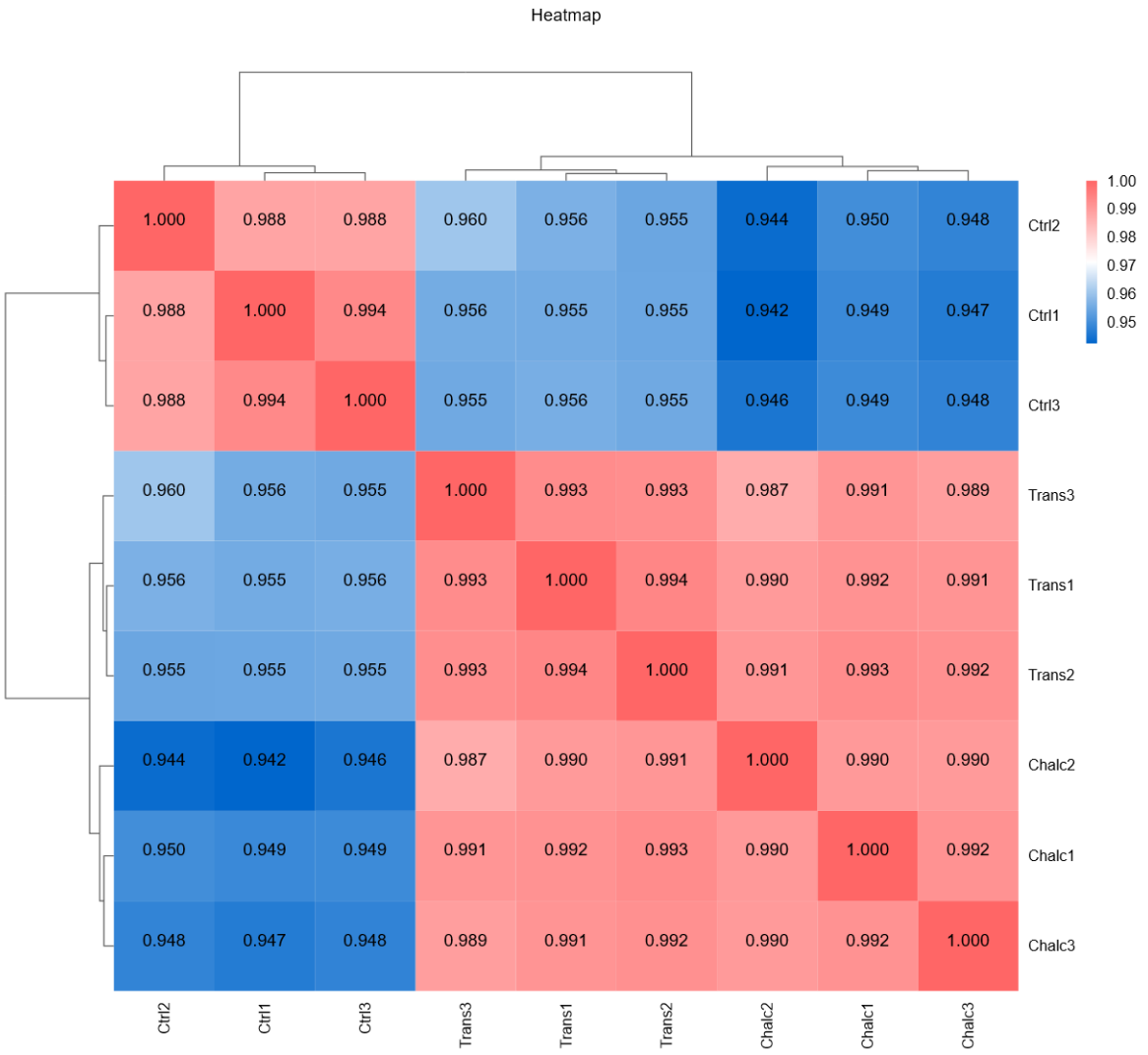
Supplementary Figure S1. Distribution of insert lengths across each sample for each condition in triplicate. The lack of multiple peaks suggests high-quality mature mRNA sequencing. a) control samples b) chalcone-exposed sample c) *trans*-chalcone-exposed sample.



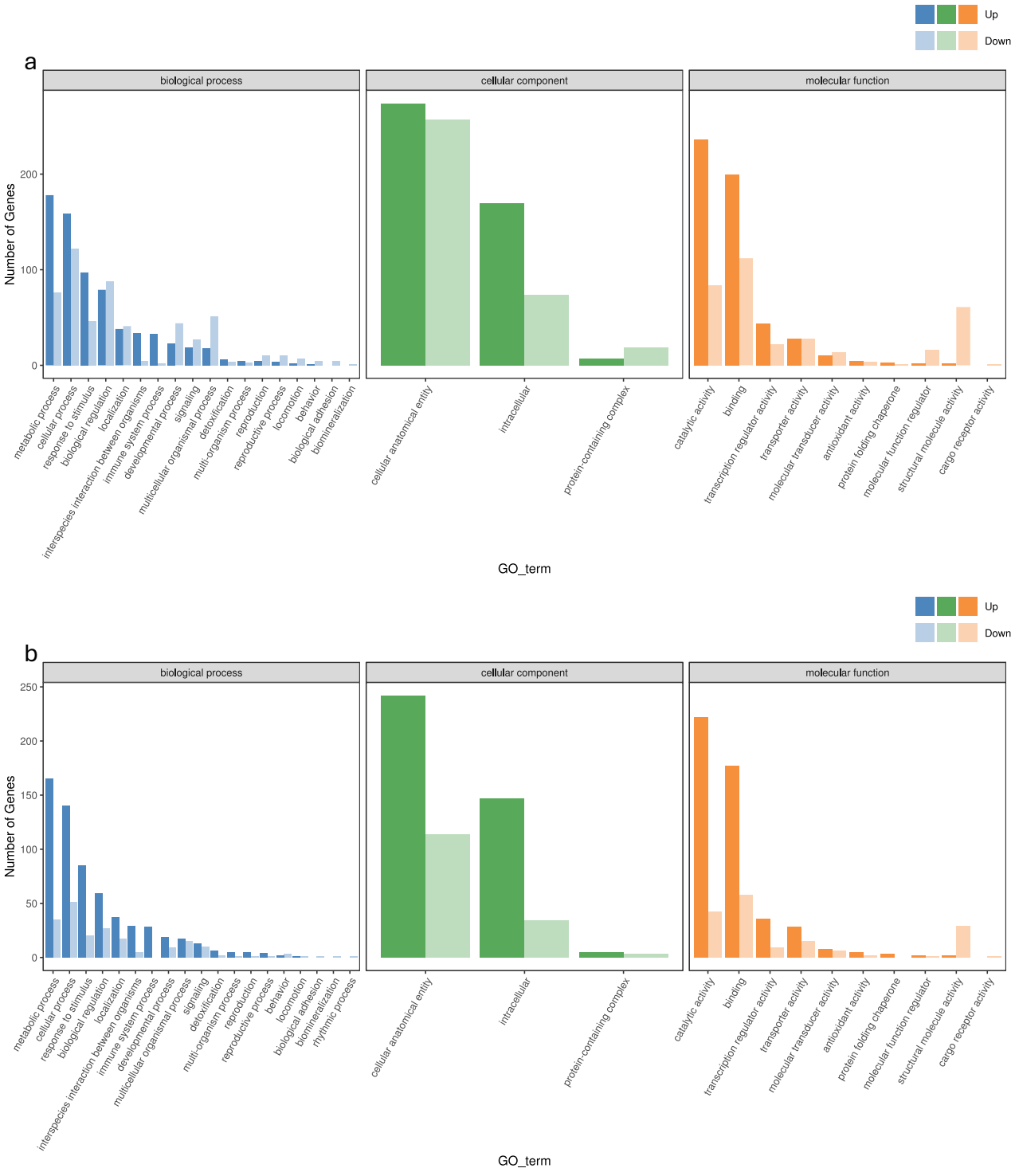
Supplementary Figure S2. Saturation test for library volume adequacy demonstrating extensive transcript coverage. a) control samples b) chalcone-exposed sample c) *trans*-chalcone-exposed sample, each line corresponding to triplicates.



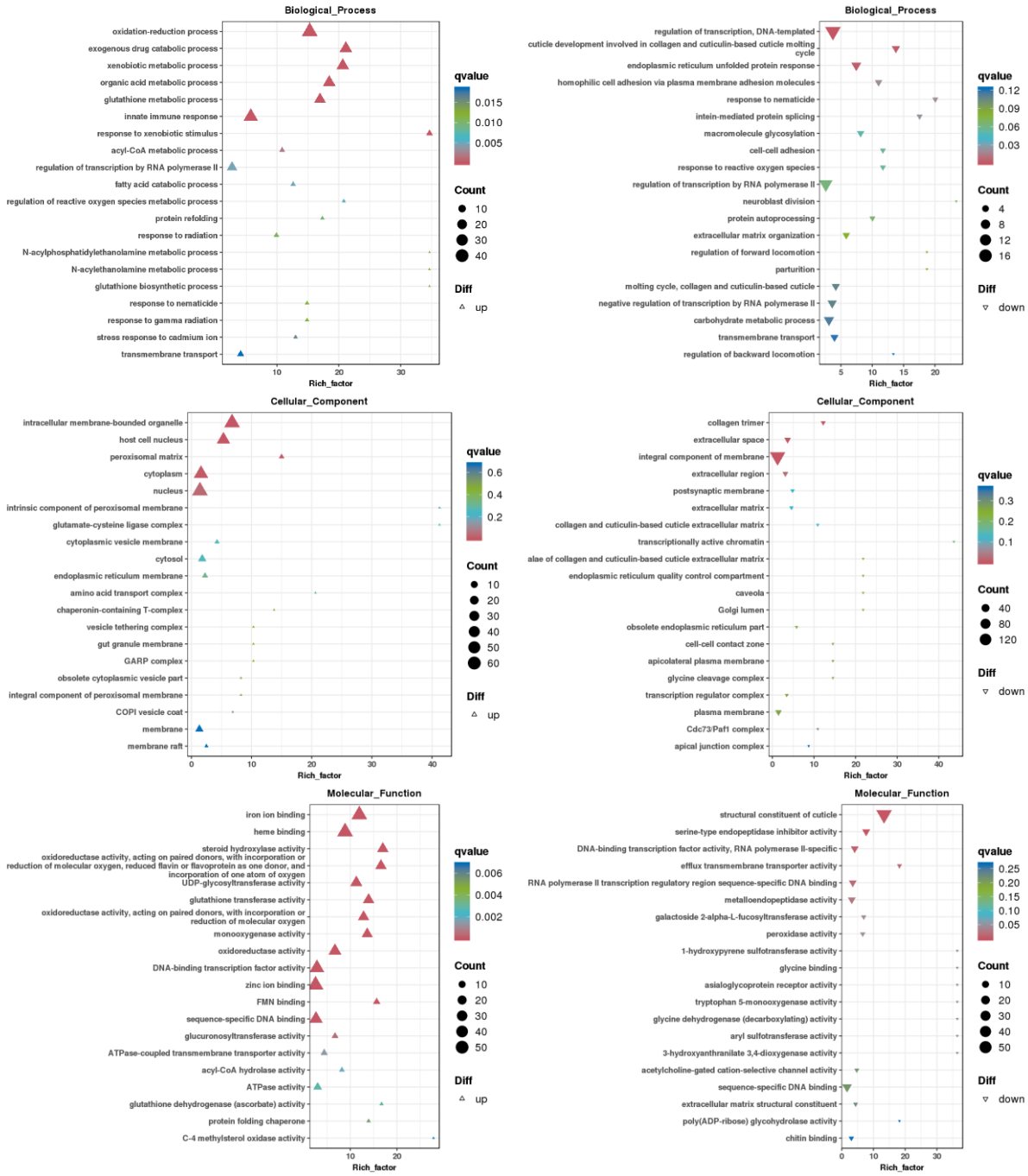
Supplementary Figure S3. Alternative splicing was predicted using Asprofile, highlighting differences among prediction models. Chalc = chalcone, ctrl = controls, trans = *trans*-chalcone, each line representing triplicates of the same sample.



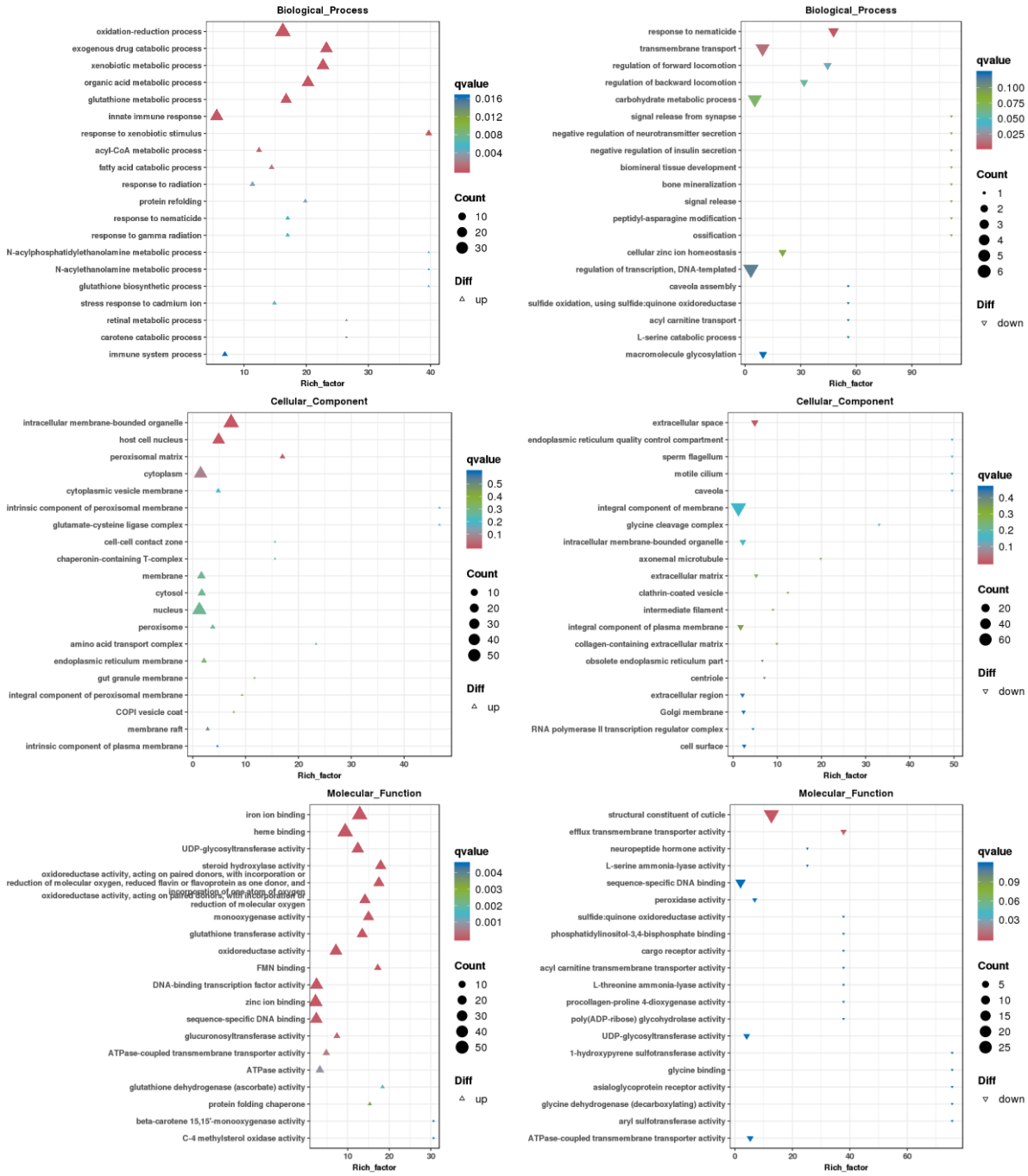
Supplementary Figure S4. Pearson correlation heatmap of transcriptomic profiles from *C. elegans* L4 larvae exposed to DMSO (controls, Ctrl), chalcone (Chalc), or *trans*-chalcone (Trans). A clear separation in transcriptomic profiles is observed between the DMSO-exposed larvae and those exposed to chalcone or *trans*-chalcone, indicating distinct global expression patterns, while more subtle differences are evident between the two chalcone isoforms.



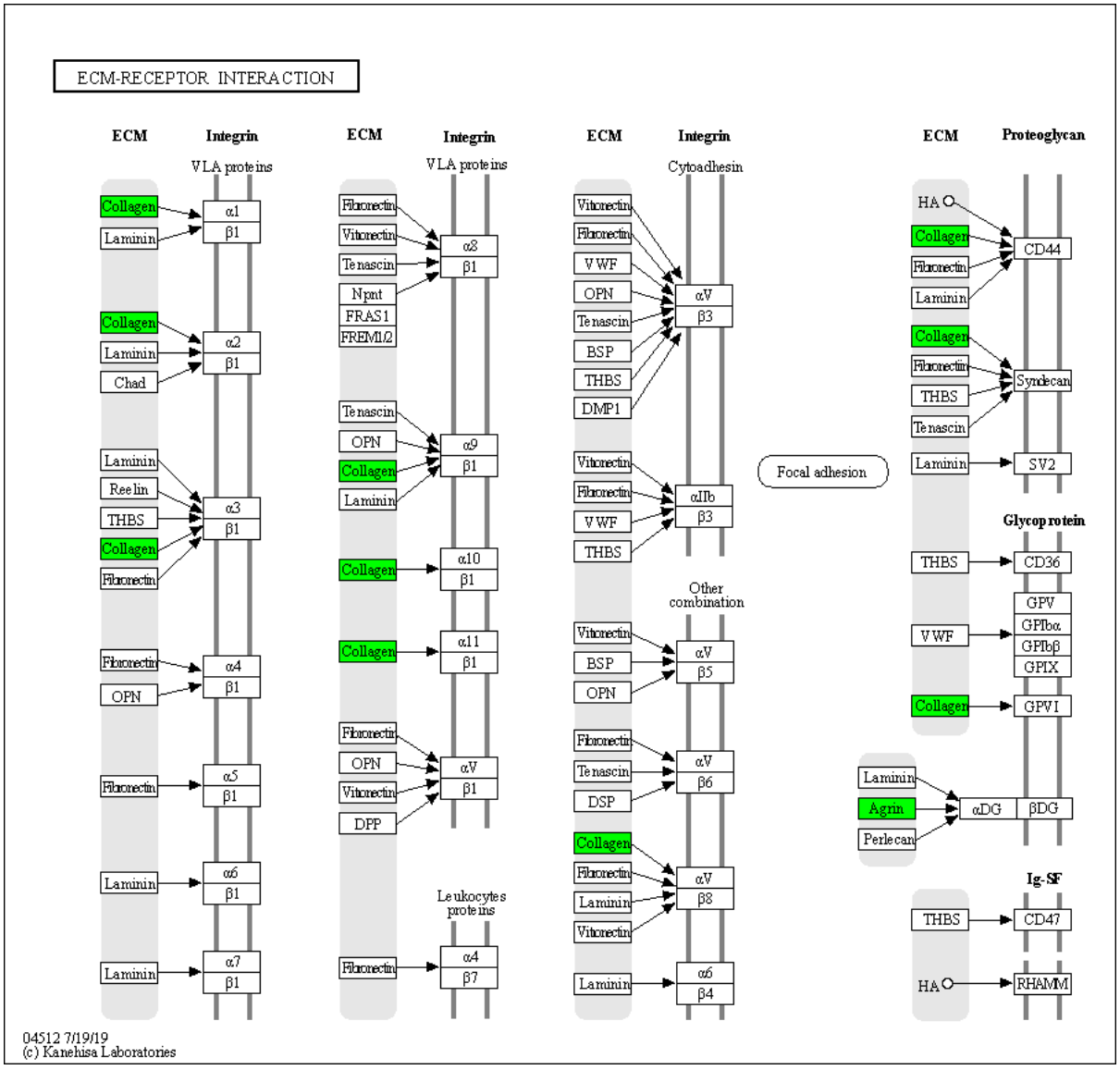
Supplementary Figure S5. Gene Ontology classification of differentially expressed genes (DEGs) in chalcone- or *trans*-chalcone-exposed *C. elegans* L4 larvae compared with DMSO-exposed control *C. elegans*, showing reduced enrichment of structural molecule activity and increased enrichment of metabolic and cellular processes. a) chalcone-exposed L4 larvae, b) *trans*-chalcone-exposed L4 larvae.

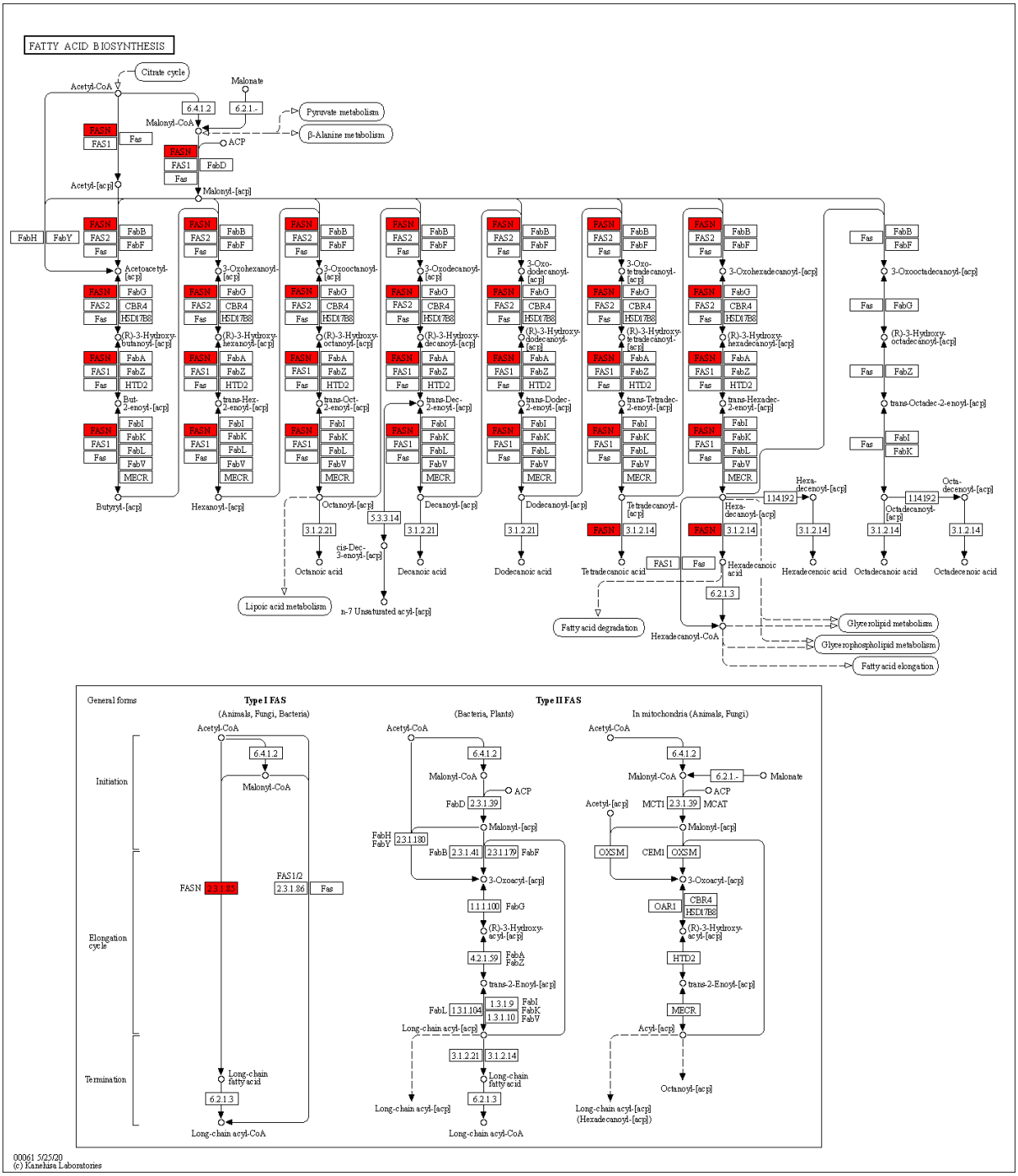


Supplementary Figure S6. Enriched KEGG pathways of chalcone-exposed *C. elegans* L4 larvae compared to DMSO-exposed control L4 larvae. Red: upregulated, green: downregulated, blue: both upregulated and downregulated.

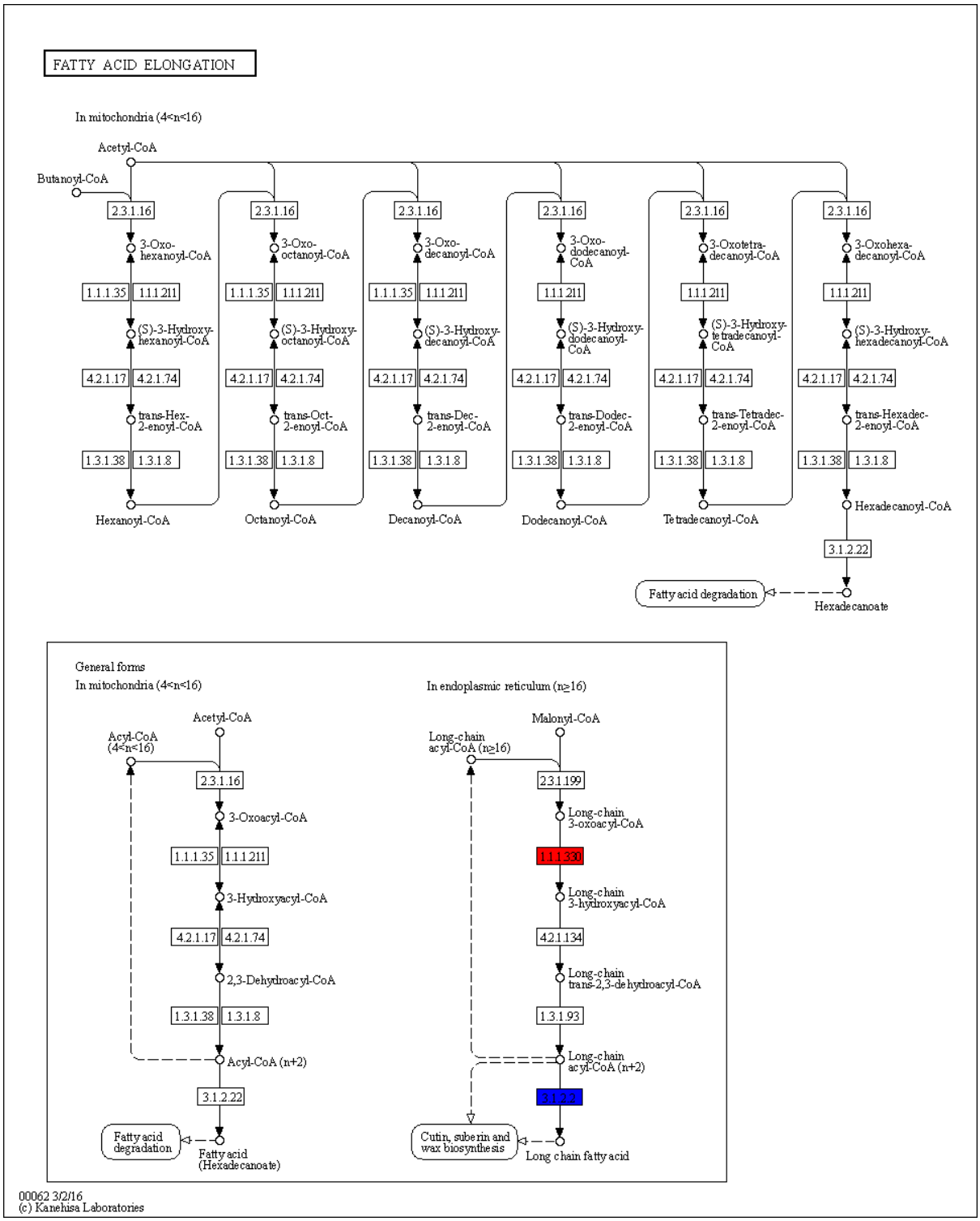


Supplementary Figure S7. Enriched KEGG pathways of *trans*-chalcone-exposed *C. elegans* L4 larvae compared to DMSO-exposed control L4 larvae. Red: upregulated, green: downregulated, blue: both upregulated and downregulated.


ECM-RECEPTOR INTERACTION
ECM
Integrin
VLA proteins
Collagen
Laminin
α1
β1
Collagen
Laminin
Chad
α2
β1
Laminin
Reelin
THBS
Collagen
Fibronectin
α3
β1
Fibronectin
OPN
α4
β1
Fibronectin
α5
β1
Laminin
α6
β1
Laminin
α7
β1
ECM
Integrin
VLA proteins
Fibronectin
Vitronectin
Tenascin
Npnt
FRAS1
FREM1/2
α8
β1
Tenascin
OPN
Collagen
Laminin
α9
β1
Collagen
α10
β1
Collagen
α11
β1
Fibronectin
OPN
Vitronectin
DPP
αV
β1
Leukocytes proteins
Fibronectin
α4
β7
ECM
Integrin
Cytoadhesin
Vitronectin
Fibronectin
VWF
OPN
Tenascin
BSP
THBS
DMP1
αV
β3
Vitronectin
Fibronectin
VWF
THBS
αIIb
β3
Other combination
Vitronectin
BSP
OPN
αV
β5
Fibronectin
Tenascin
DSP
αV
β6
Collagen
Fibronectin
Laminin
Vitronectin
αV
β8
Laminin
α6
β4
Focal adhesion
ECM
Proteoglycan
HA
Collagen
Fibronectin
Laminin
CD44
Collagen
Fibronectin
THBS
Tenascin
Syndecan
Laminin
SV2
Glycoprotein
THBS
CD36
VWF
GPV
GPIbα
GPIbβ
GPIX
Collagen
GPVI
Laminin
Agrin
Perlecan
αDG
βDG
Ig-SF
THBS
CD47
HA
RHAMM
04512 7/19/19
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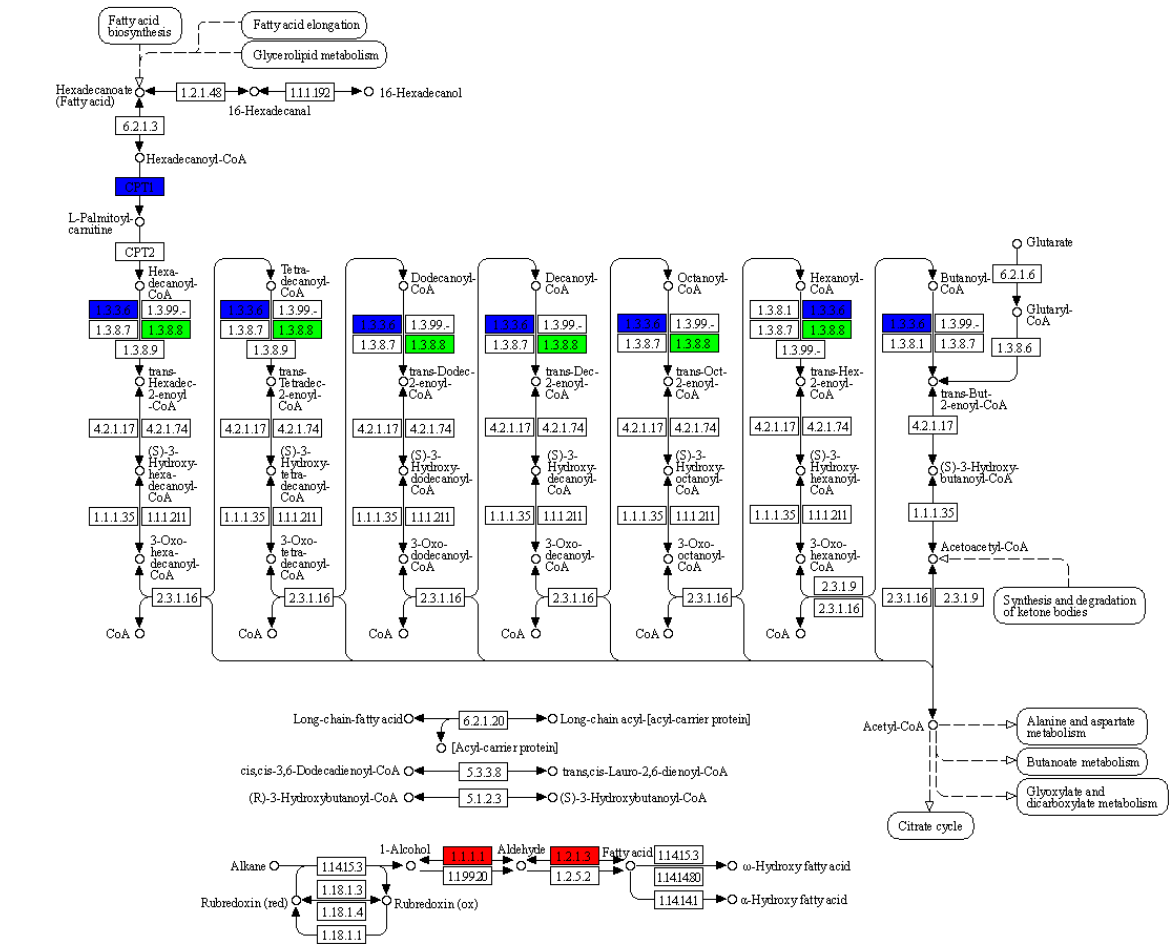


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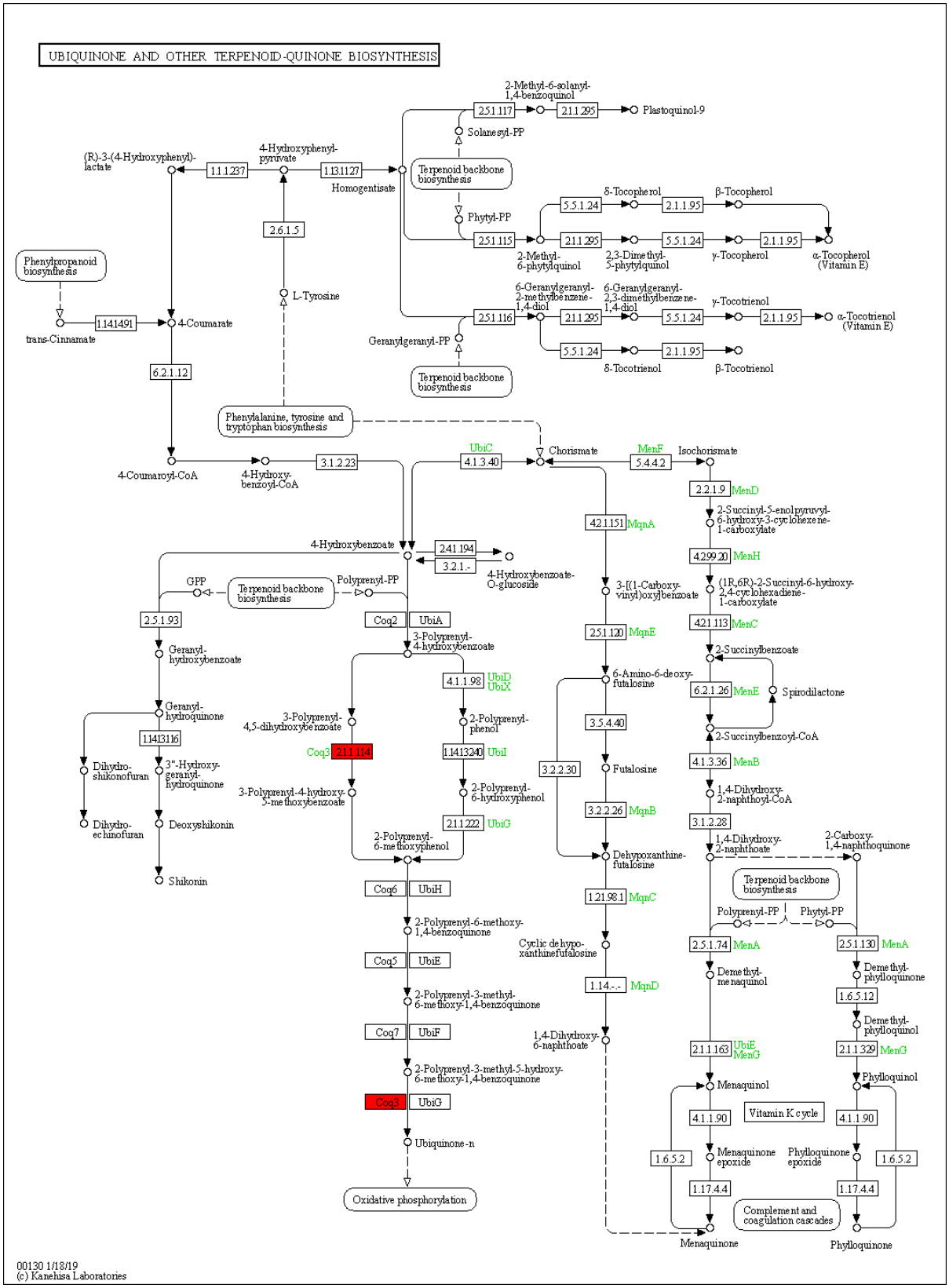


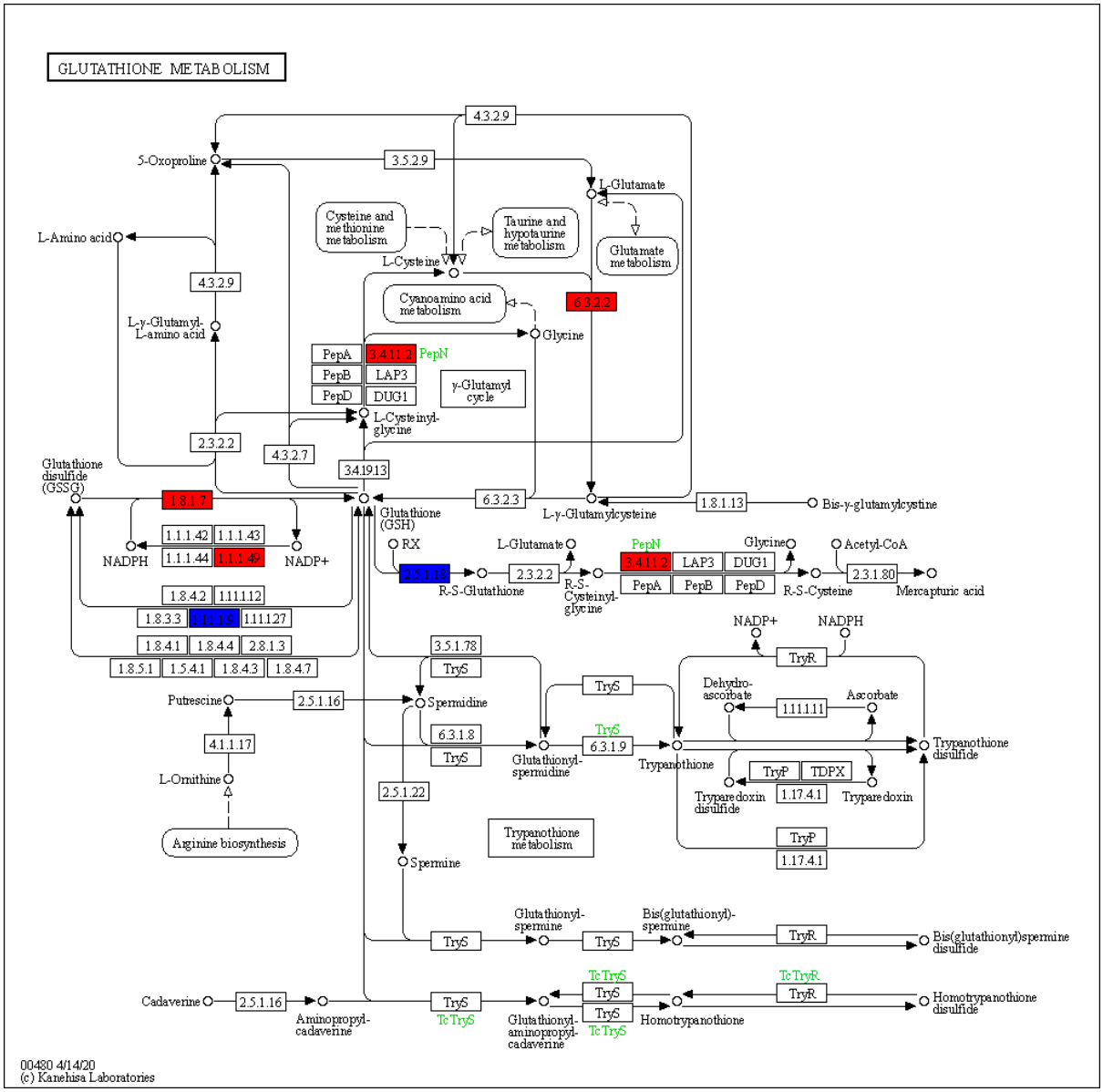
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FATTY ACID DEGRADATION

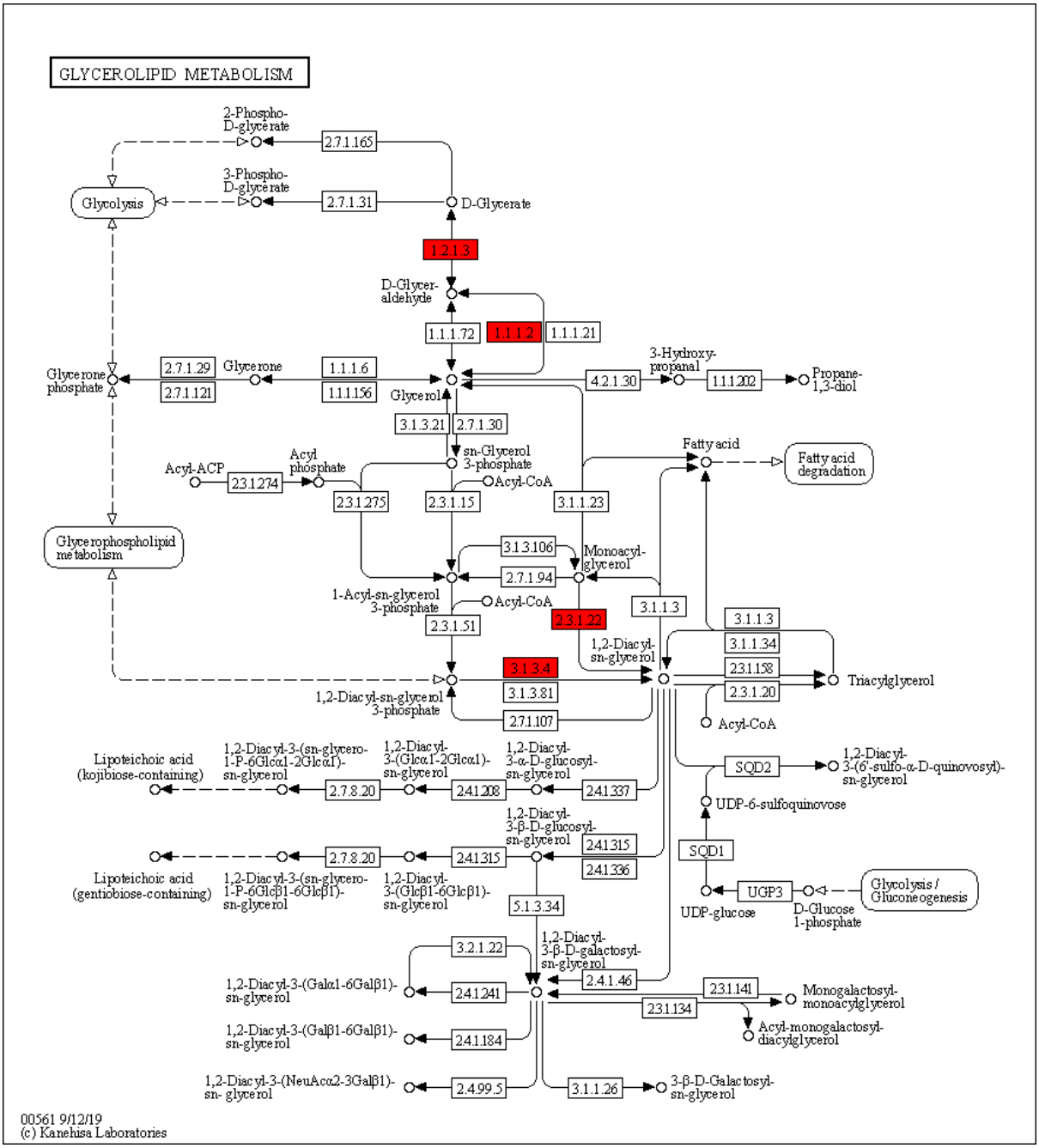


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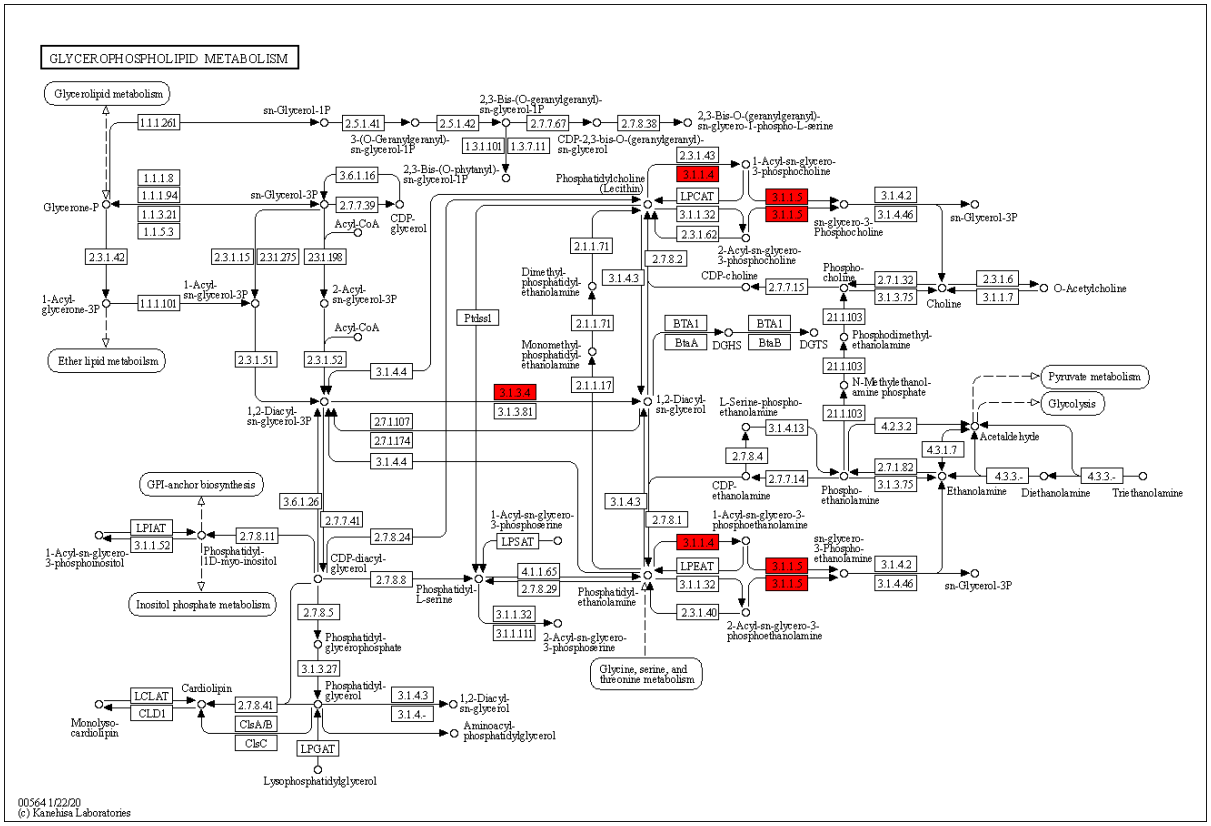

UBIQUINONE AND OTHER TERPENOID-QUINONE BIOSYNTHESIS
2-Methyl-6-solanyl-1,4-benzoquinol
2.5.1.117
2.1.1.295
Plastoquinol-9
Solanesyl-PP
(R)-3-(4-Hydroxyphenyl)-lactate
1.1.1.237
4-Hydroxyphenyl-pyruvate
1.13.11.27
Homogentisate
Terpenoid backbone biosynthesis
δ-Tocopherol
β-Tocopherol
5.5.1.24
2.1.1.95
Phytyl-PP
2.5.1.115
2-Methyl-6-phytylquinol
2,3-Dimethyl-5-phytylquinol
γ-Tocopherol
α-Tocopherol (Vitamin E)
2.6.1.5
Phenylpropanoid biosynthesis
L-Tyrosine
6-Geranylgeranyl-2-methylbenzene-1,4-diol
6-Geranylgeranyl-2,3-dimethylbenzene-1,4-diol
γ-Tocotrienol
α-Tocotrienol (Vitamin E)
2.5.1.116
trans-Cinnamate
1.14.14.91
4-Coumarate
Geranylgeranyl-PP
δ-Tocotrienol
β-Tocotrienol
6.2.1.12
Terpenoid backbone biosynthesis
Phenylalanine, tyrosine and tryptophan biosynthesis
UbiC
4.1.3.40
Chorismate
MenF
5.4.4.2
Isochorismate
4-Coumaroyl-CoA
4-Hydroxybenzoyl-CoA
3.1.2.23
2.2.1.9
MenD
2-Succinyl-5-enolpyruvyl-6-hydroxy-3-cyclohexene-1-carboxylate
4.2.1.151
MqnA
4-Hydroxybenzoate
2.4.1.194
3.2.1.-
4-Hydroxybenzoate-O-glucoside
4.2.99.20
MenH
3-[(1-Carboxyvinyl)oxy]benzoate
(1R,6R)-2-Succinyl-6-hydroxy-2,4-cyclohexadiene-1-carboxylate
GPP
Terpenoid backbone biosynthesis
Polyprenyl-PP
2.5.1.93
Coq2
UbiA
3-Polyprenyl-4-hydroxybenzoate
2.5.1.120
MqnE
4.2.1.113
MenC
2-Succinylbenzoate
Geranyl-hydroxybenzoate
4.1.1.98
UbiD
UbiX
6-Amino-6-deoxyfutalosine
6.2.1.26
MenE
Spirodilactone
Geranyl-hydroxyquinone
3-Polyprenyl-4,5-dihydroxybenzoate
2-Polyprenyl-phenol
3.5.4.40
2-Succinylbenzoyl-CoA
1.14.13.116
Coq3
2.1.1.114
1.14.13.240
UbiI
3.2.2.30
Futalosine
4.1.3.36
MenB
Dihydro-shikonofuran
3"-Hydroxy-geranyl-hydroquinone
3-Polyprenyl-4-hydroxy-5-methoxybenzoate
2-Polyprenyl-6-hydroxyphenol
3.2.2.26
MqnB
1,4-Dihydroxy-2-naphthoyl-CoA
3.1.2.28
Dihydro-echinofuran
Deoxyshikonin
2.1.1.222
UbiG
1,4-Dihydroxy-2-naphthoate
2-Carboxy-1,4-naphthoquinone
2-Polyprenyl-6-methoxyphenol
Dehypoxanthine-futalosine
Terpenoid backbone biosynthesis
Shikonin
Coq6
UbiH
1.21.98.1
MqnC
Polyprenyl-PP
Phytyl-PP
2-Polyprenyl-6-methoxy-1,4-benzoquinone
Cyclic dehypoxanthinefutalosine
2.5.1.74
MenA
2.5.1.130
MenA
Coq5
UbiE
Demethyl-menaquinol
Demethyl-phylloquinone
1.14.-.-
MqnD
1.6.5.12
2-Polyprenyl-3-methyl-6-methoxy-1,4-benzoquinone
Demethyl-phylloquinol
Coq7
UbiF
1,4-Dihydroxy-6-naphthoate
2.1.1.163
UbiE
MenG
2.1.1.329
MenG
2-Polyprenyl-3-methyl-5-hydroxy-6-methoxy-1,4-benzoquinone
Phylloquinol
Menaquinol
Coq3
UbiG
4.1.1.90
Vitamin K cycle
4.1.1.90
Ubiquinone-n
1.6.5.2
Menaquinone epoxide
Phylloquinone epoxide
1.6.5.2
Oxidative phosphorylation
1.17.4.4
1.17.4.4
Complement and coagulation cascades
Menaquinone
Phylloquinone
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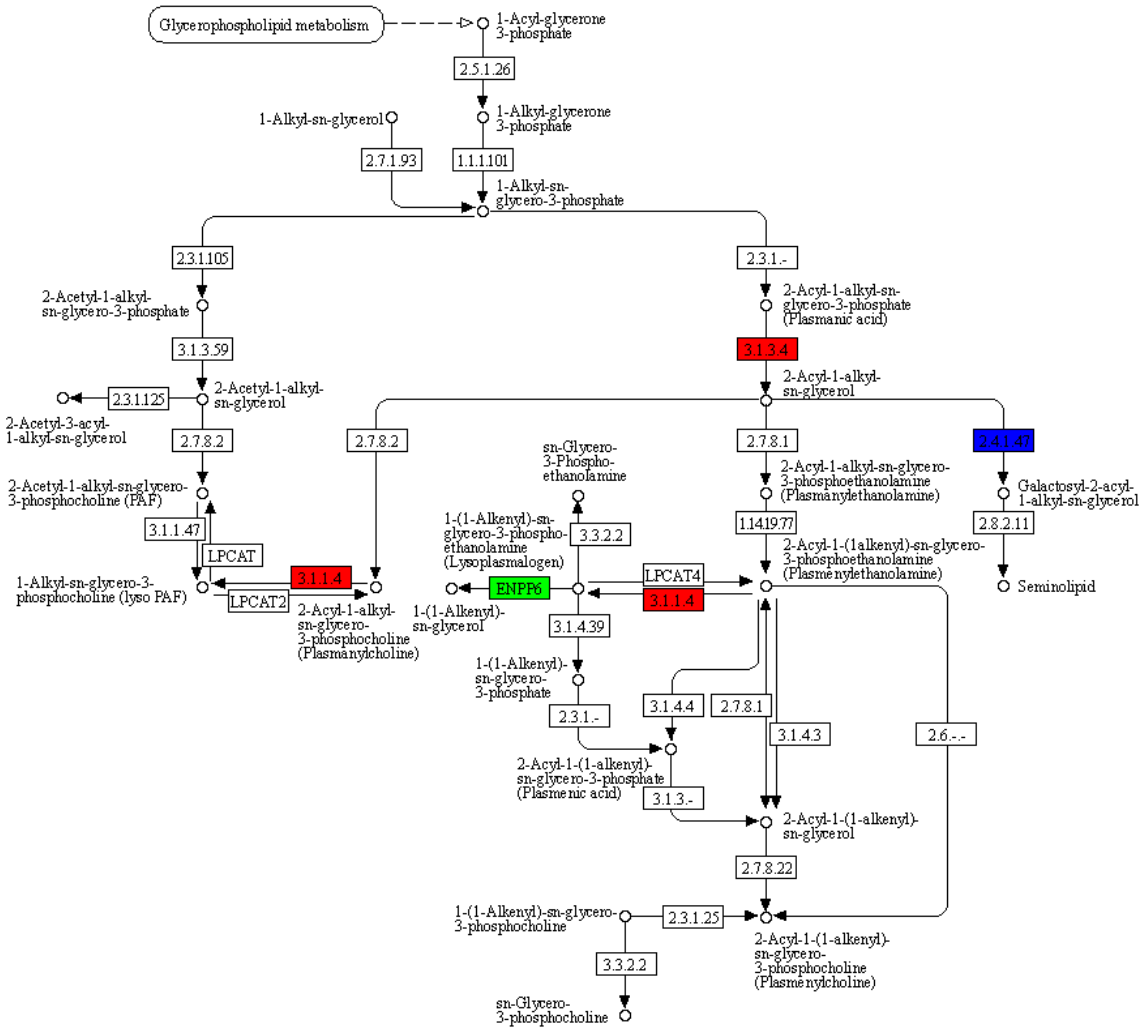
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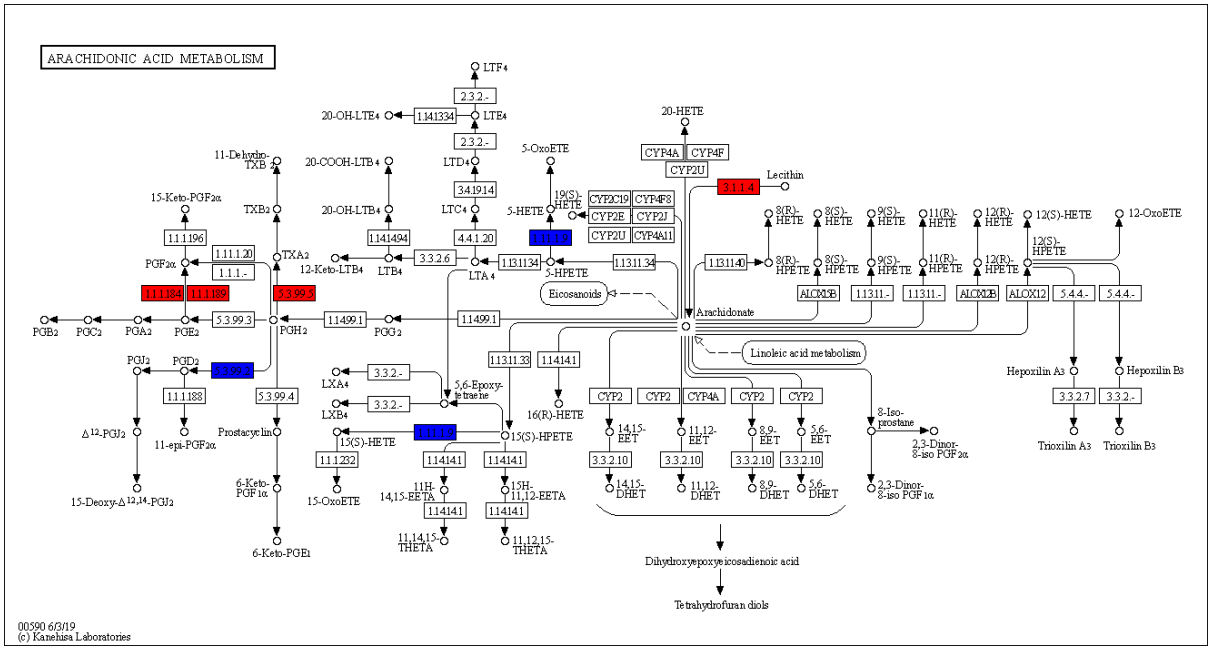
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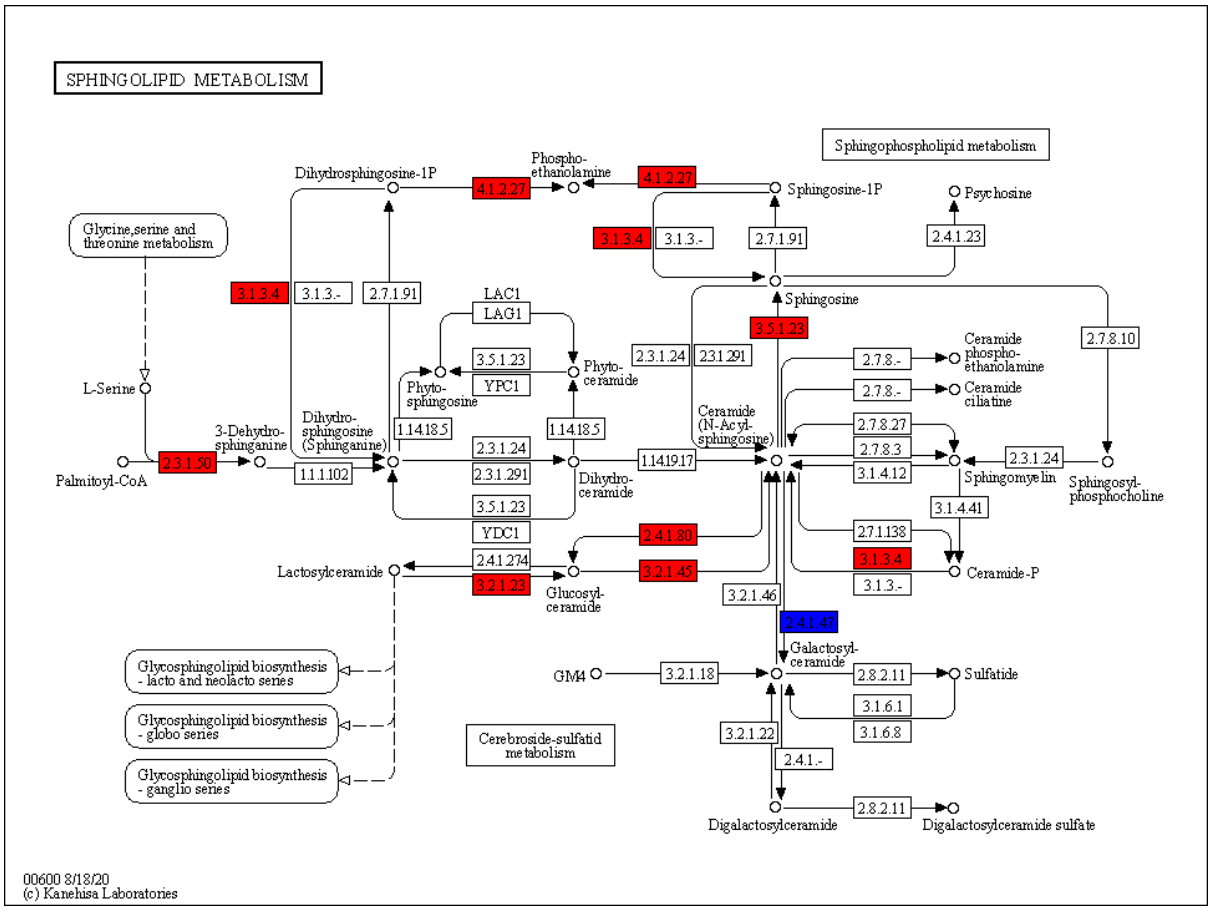

GLYCEROPHOSPHOLIPID METABOLISM
Glycerolipid metabolism
Glycerone-P
sn-Glycerol-3P
Acyl-CoA
CDP-glycerol
1-Acyl-glycerone-3P
1-Acyl-sn-glycerol-3P
2-Acyl-sn-glycerol-3P
Ether lipid metabolism
1,2-Diacyl-sn-glycerol-3P
1,2-Diacyl-sn-glycerol
sn-Glycerol-1P
3-(O-Geranylgeranyl)-sn-glycerol-1P
2,3-Bis-(O-geranylgeranyl)-sn-glycerol-1P
2,3-Bis-(O-phytanyl)-sn-glycerol-1P
CDP-2,3-bis-O-(geranylgeranyl)-sn-glycerol
2,3-Bis-O-(geranylgeranyl)-sn-glycero-1-phospho-L-serine
Phosphatidylcholine (Lecithin)
1-Acyl-sn-glycero-3-phosphocholine
2-Acyl-sn-glycero-3-phosphocholine
sn-glycero-3-Phosphocholine
Dimethyl-phosphatidyl-ethanolamine
Monomethyl-phosphatidyl-ethanolamine
CDP-choline
Phospho-choline
Choline
O-Acetylcholine
Ptdss1
BTA1
BtaA
DGHS
BtaB
DGTS
Phosphodimethyl-ethanolamine
N-Methylethanol-amine phosphate
L-Serine-phospho-ethanolamine
CDP-ethanolamine
Phospho-ethanolamine
Ethanolamine
Diethanolamine
Triethanolamine
Acetaldehyde
Pyruvate metabolism
Glycolysis
GPI-anchor biosynthesis
1-Acyl-sn-glycero-3-phosphoinositol
Phosphatidyl-1D-myo-inositol
Inositol phosphate metabolism
CDP-diacyl-glycerol
Phosphatidyl-L-serine
1-Acyl-sn-glycero-3-phosphoserine
Phosphatidyl-ethanolamine
1-Acyl-sn-glycero-3-phosphoethanolamine
2-Acyl-sn-glycero-3-phosphoethanolamine
sn-glycero-3-Phospho-ethanolamine
Phosphatidyl-glycerophosphate
Phosphatidyl-glycerol
Cardiolipin
Monolyso-cardiolipin
Aminoacyl-phosphatidylglycerol
Lysophosphatidylglycerol
Glycine, serine, and threonine metabolism
LPIAT
LCLAT
CLD1
ClsA/B
ClsC
LPGAT
LPCAT
LPSAT
LPEAT
Ptdss1
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ETHER LIPID METABOLISM

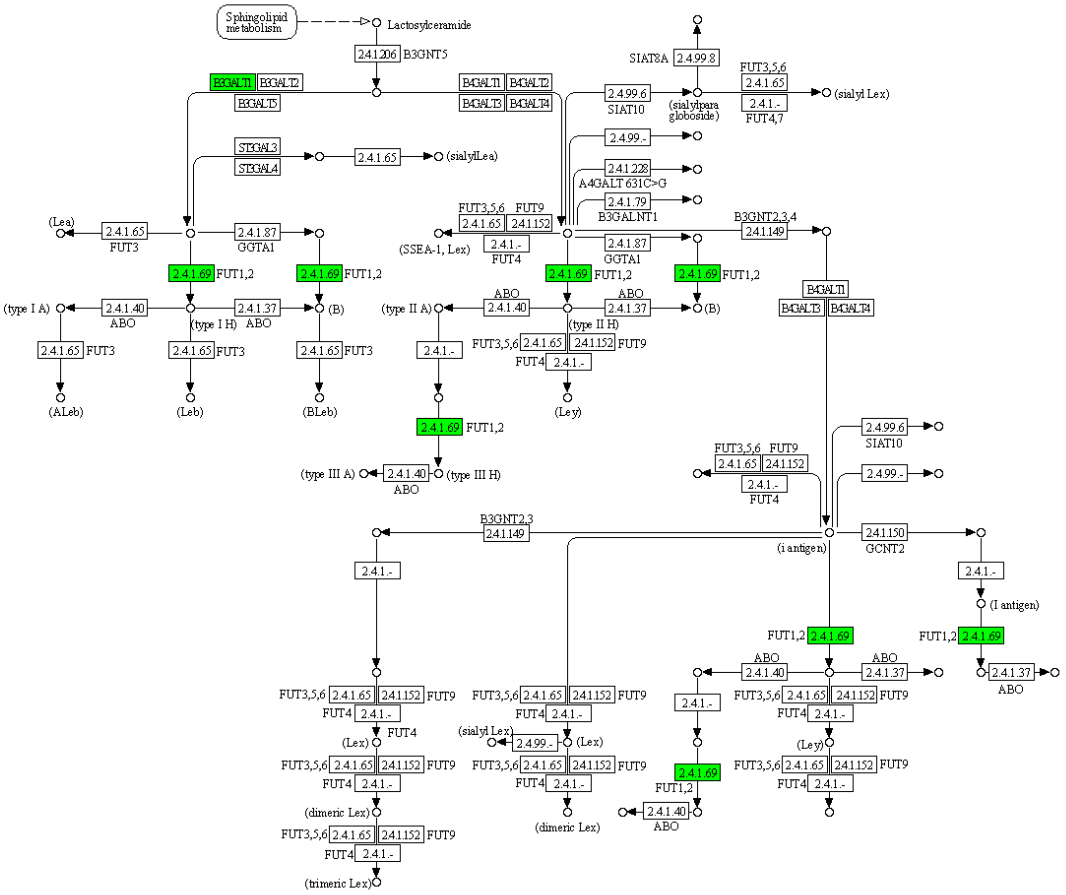


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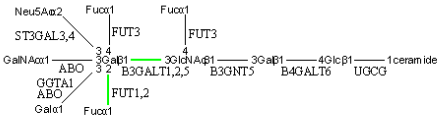

ARACHIDONIC ACID METABOLISM
LTF4
20-OH-LTE4
LTE4
20-HETE
11-Dehydro-TXB2
20-COOH-LTB4
5-OxoETE
CYP4A
CYP4F
CYP2U
Lecithin
15-Keto-PGF2α
TXB2
20-OH-LTB4
LTC4
5-HETE
CYP2C19
CYP4F8
CYP2E
CYP2J
CYP2U
CYP4A11
8(R)-HETE
8(S)-HETE
9(S)-HETE
11(R)-HETE
12(R)-HETE
12(S)-HETE
12-OxoETE
PGF2α
TXA2
12-Keto-LTB4
LTB4
LTA4
5-HPETE
8(R)-HPETE
8(S)-HPETE
9(S)-HPETE
11(R)-HPETE
12(R)-HPETE
12(S)-HPETE
Eicosanoids
ALOX5B
ALOX12B
ALOX12
PGB2
PGC2
PGA2
PGE2
PGH2
PGG2
Arachidonate
Linoleic acid metabolism
PGJ2
PGD2
LXA4
LXB4
5,6-Epoxy-tetraene
16(R)-HETE
15(S)-HETE
15(S)-HPETE
CYP2
CYP4A
14,15-EET
11,12-EET
8,9-EET
5,6-EET
8-Iso-prostane
Hepoxilin A3
Hepoxilin B3
Trioxilin A3
Trioxilin B3
Δ12-PGJ2
11-epi-PGF2α
Prostacyclin
15-Deoxy-Δ12,14-PGJ2
6-Keto-PGF1α
15-OxoETE
14,15-EETA
11H-14,15-EETA
15H-11,12-EETA
14,15-DHET
11,12-DHET
8,9-DHET
5,6-DHET
2,3-Dinor-8-iso PGF2α
2,3-Dinor-8-iso PGF1α
6-Keto-PGE1
11,14,15-THETA
11,12,15-THETA
Dihydroxyepoxyeicosadienoic acid
Tetrahydrofuran diols
00590 6/3/19
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SPHINGOLIPID METABOLISM
Sphingophospholipid metabolism
Dihydrosphingosine-1P
Phospho-ethanolamine
Sphingosine-1P
Psychosine
Glycine,serine and threonine metabolism
Sphingosine
LAC1
LAG1
Phyto-sphingosine
Phyto-ceramide
Ceramide phospho-ethanolamine
Ceramide ciliatine
L-Serine
3-Dehydro-sphinganine
Dihydro-sphingosine (Sphinganine)
Ceramide (N-Acyl-sphingosine)
Palmitoyl-CoA
Dihydro-ceramide
Sphingomyelin
Sphingosyl-phosphocholine
Ceramide-P
Lactosylceramide
Glucosyl-ceramide
Galactosyl-ceramide
GM4
Sulfatide
Glycosphingolipid biosynthesis - lacto and neolacto series
Glycosphingolipid biosynthesis - globo series
Glycosphingolipid biosynthesis - ganglio series
Cerebroside-sulfatid metabolism
Digalactosylceramide
Digalactosylceramide sulfate
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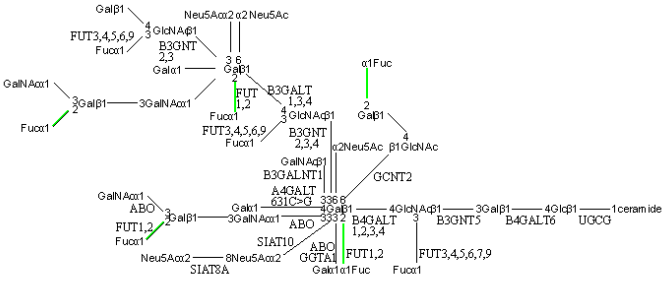
GLYCOSPHINGOLIPID BIOSYNTHESIS - LACTO AND NEOLACTO SERIES



Lacto series

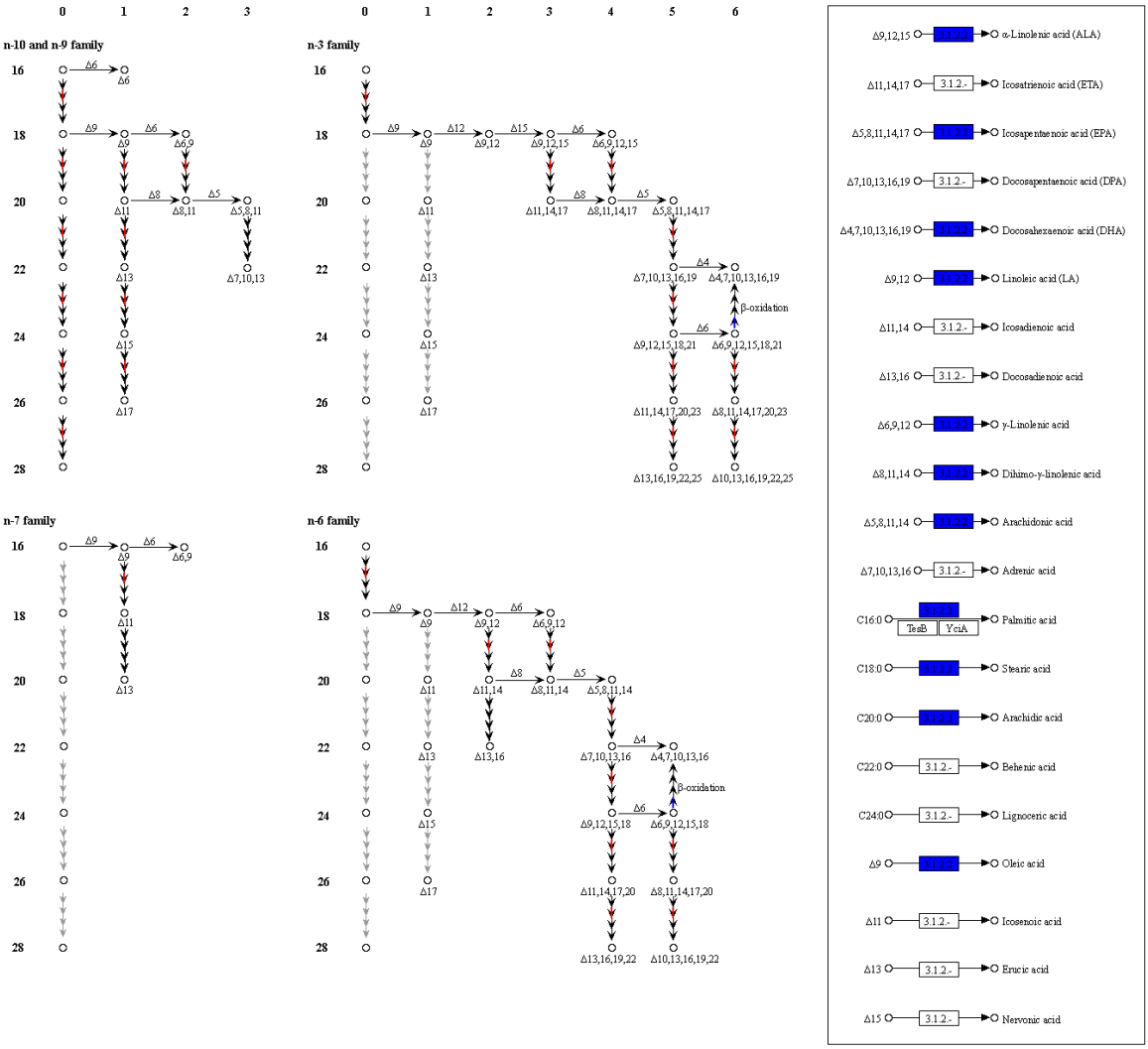


Neolacto series

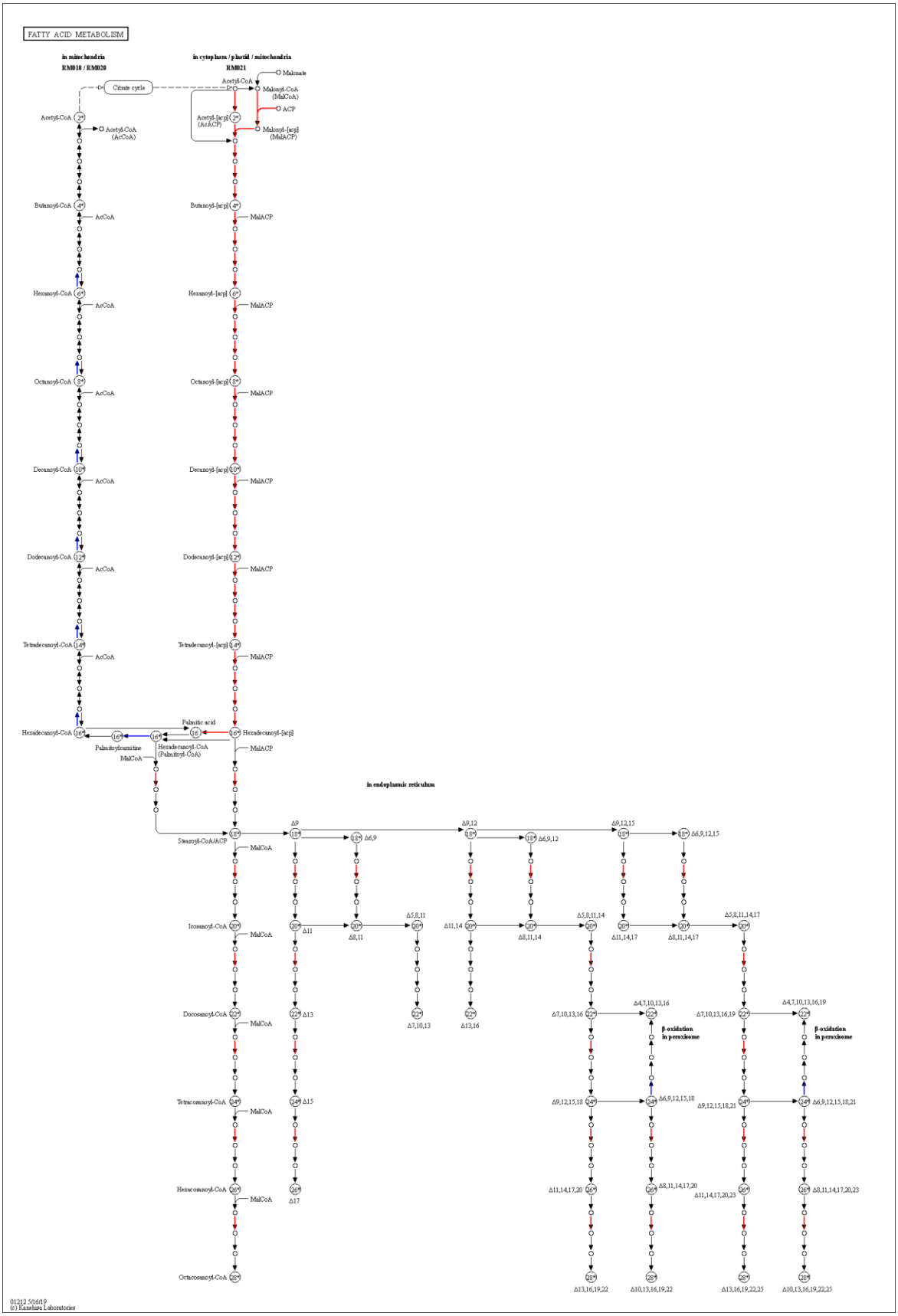


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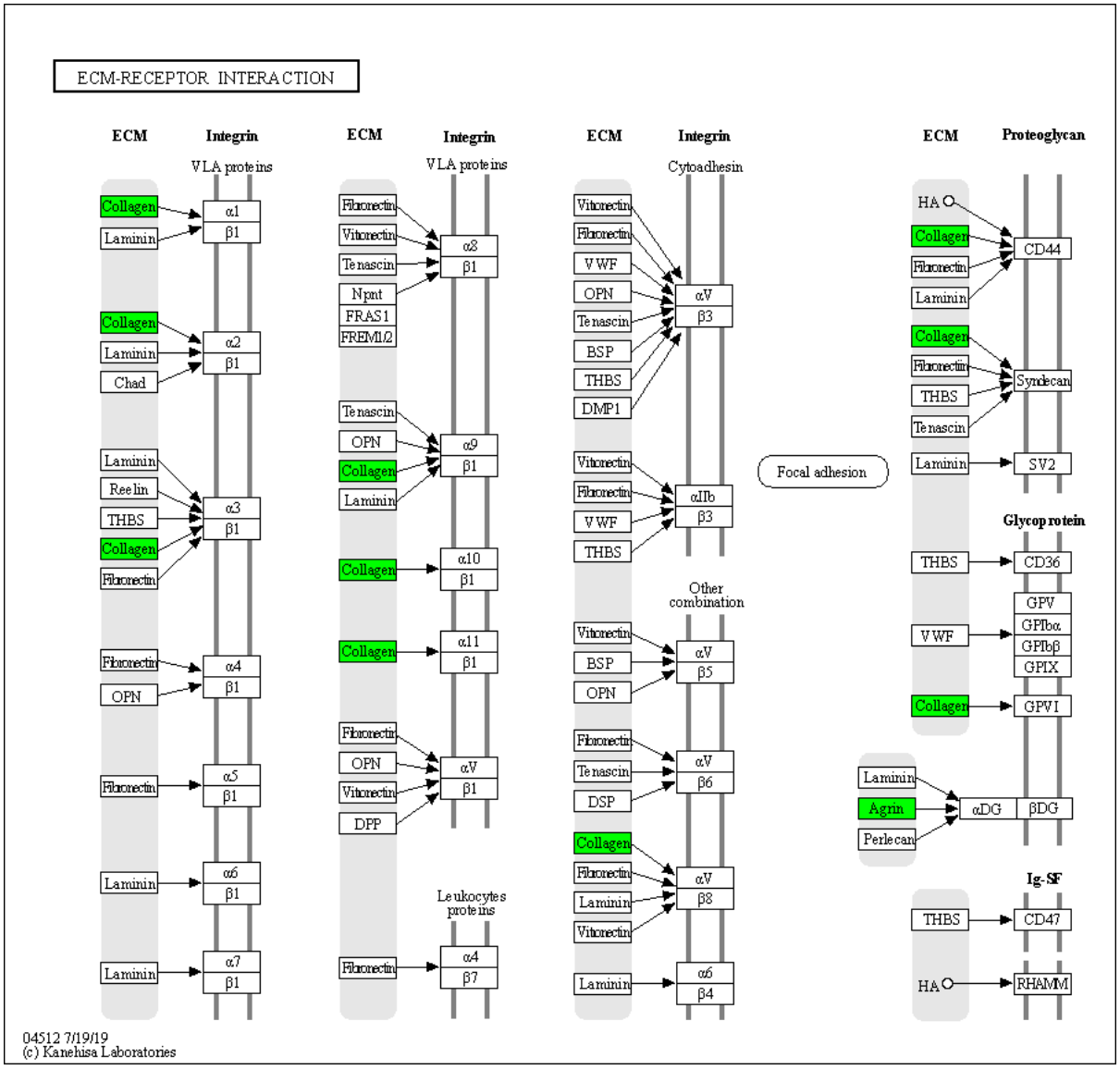
BIOSYNTHESIS OF UNSATURATED FATTY ACIDS

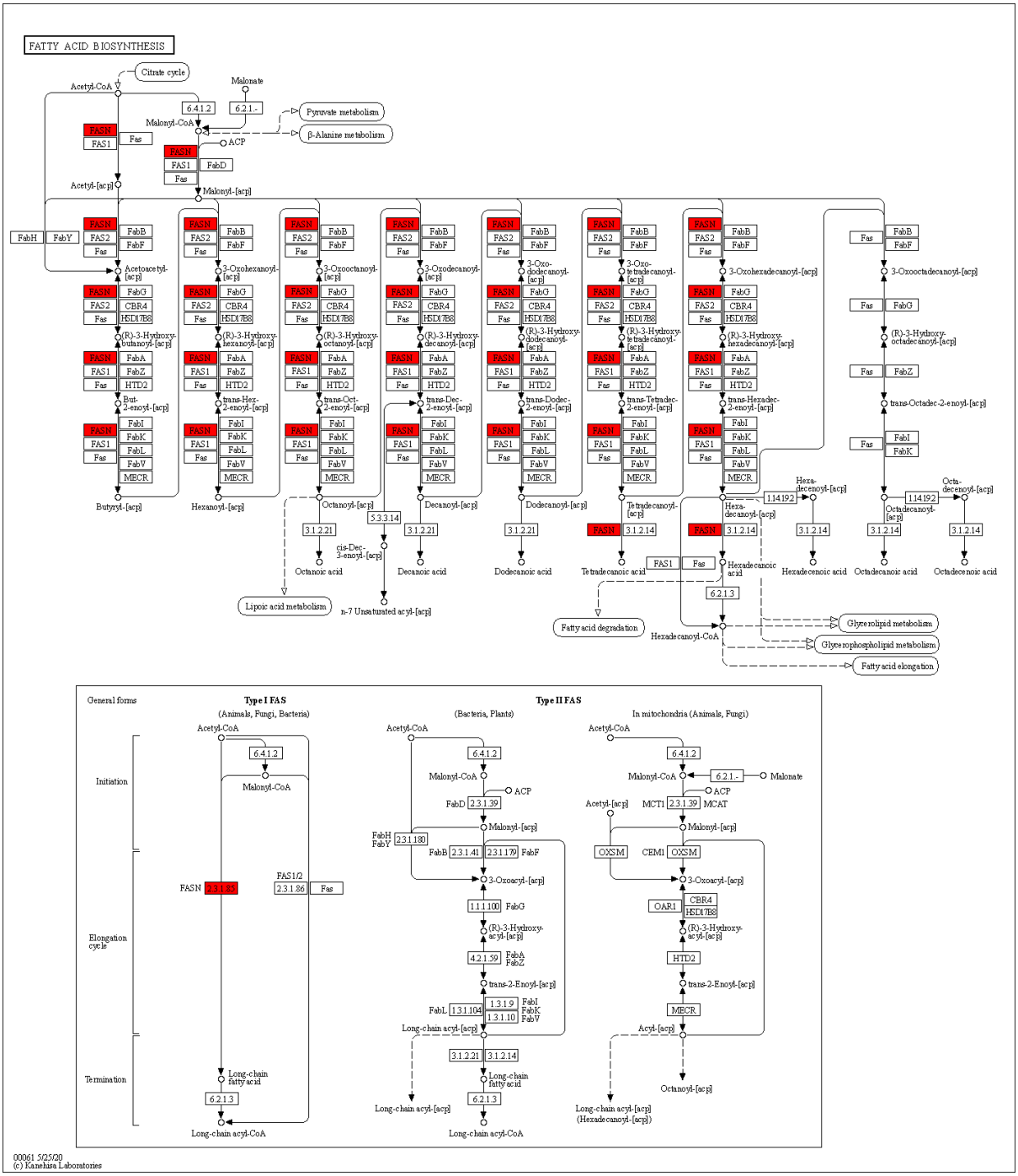


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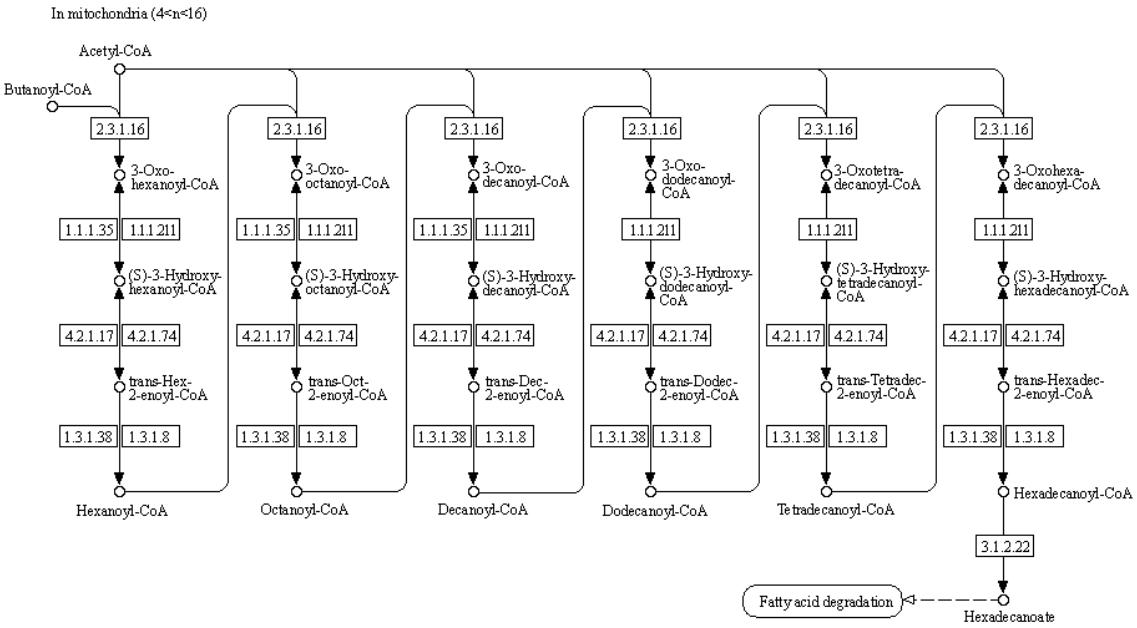
Supplementary Figure S8. Enriched KEGG pathways of chalcone-exposed worms compared to controls. Red: indicates pathways with predominantly upregulated genes, green: indicates predominantly downregulated genes, blue: indicates pathways containing both upregulated and underregulated genes.

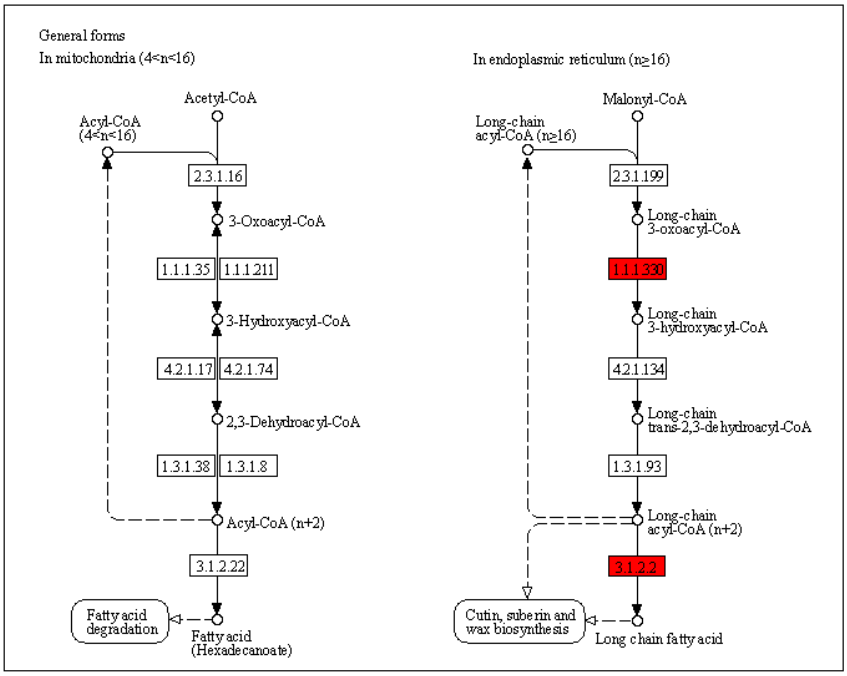

ECM-RECEPTOR INTERACTION
ECM
Integrin
VLA proteins
Collagen
Laminin
α1
β1
Collagen
Laminin
Chad
α2
β1
Laminin
Reelin
THBS
Collagen
Fibronectin
α3
β1
Fibronectin
OPN
α4
β1
Fibronectin
α5
β1
Laminin
α6
β1
Laminin
α7
β1
ECM
Integrin
VLA proteins
Fibronectin
Vitronectin
Tenascin
Npnt
FRAS1
FREM1/2
α8
β1
Tenascin
OPN
Collagen
Laminin
α9
β1
Collagen
α10
β1
Collagen
α11
β1
Fibronectin
OPN
Vitronectin
DPP
αV
β1
Leukocytes proteins
Fibronectin
α4
β7
ECM
Integrin
Cytoadhesin
Vitronectin
Fibronectin
VWF
OPN
Tenascin
BSP
THBS
DMP1
αV
β3
Vitronectin
Fibronectin
VWF
THBS
αIIb
β3
Other combination
Vitronectin
BSP
OPN
αV
β5
Fibronectin
Tenascin
DSP
αV
β6
Collagen
Fibronectin
Laminin
Vitronectin
αV
β8
Laminin
α6
β4
Focal adhesion
ECM
Proteoglycan
HA
Collagen
Fibronectin
Laminin
CD44
Collagen
Fibronectin
THBS
Tenascin
Syndecan
Laminin
SV2
Glycoprotein
THBS
CD36
VWF
GPV
GPIbα
GPIbβ
GPIX
Collagen
GPVI
Laminin
Agrin
Perlecan
αDG
βDG
Ig-SF
THBS
CD47
HA
RHAMM
04512 7/19/19
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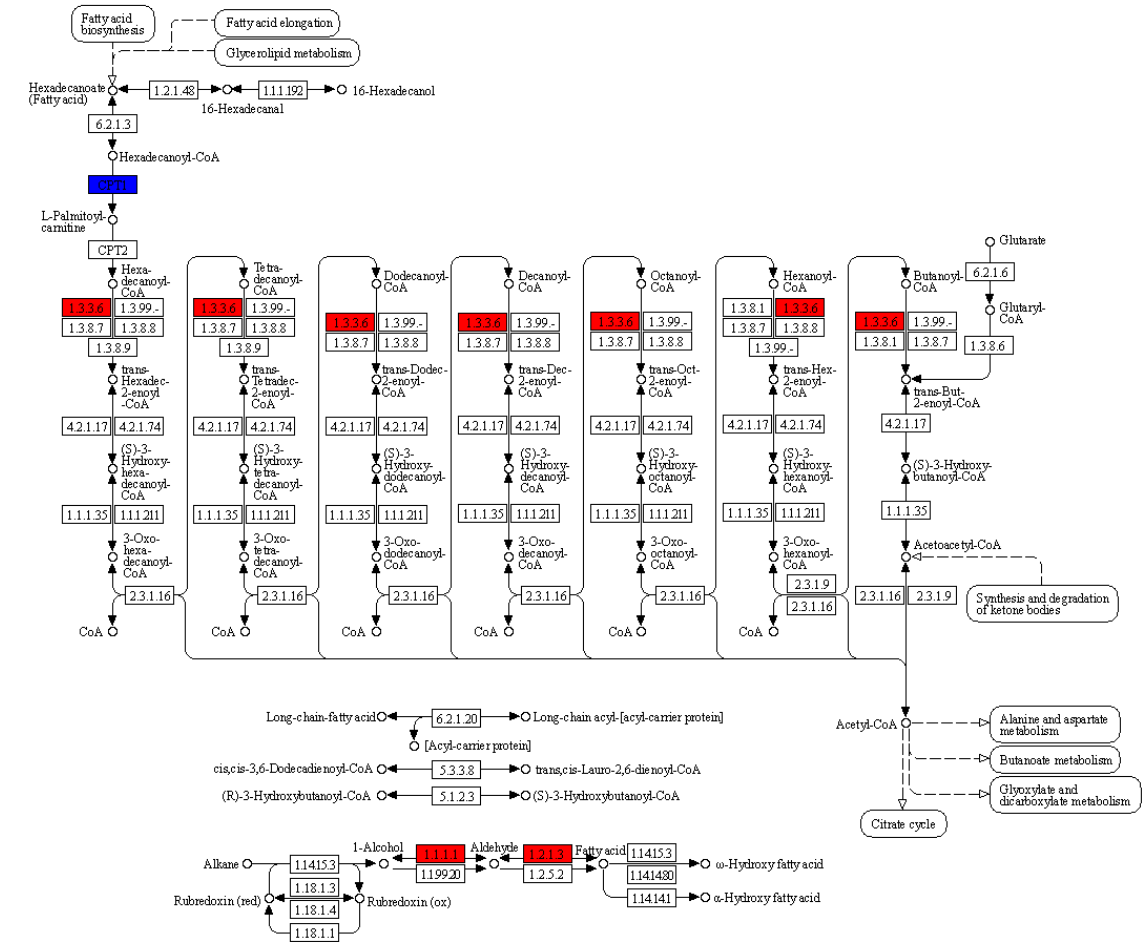
FATTY ACID ELONGATION



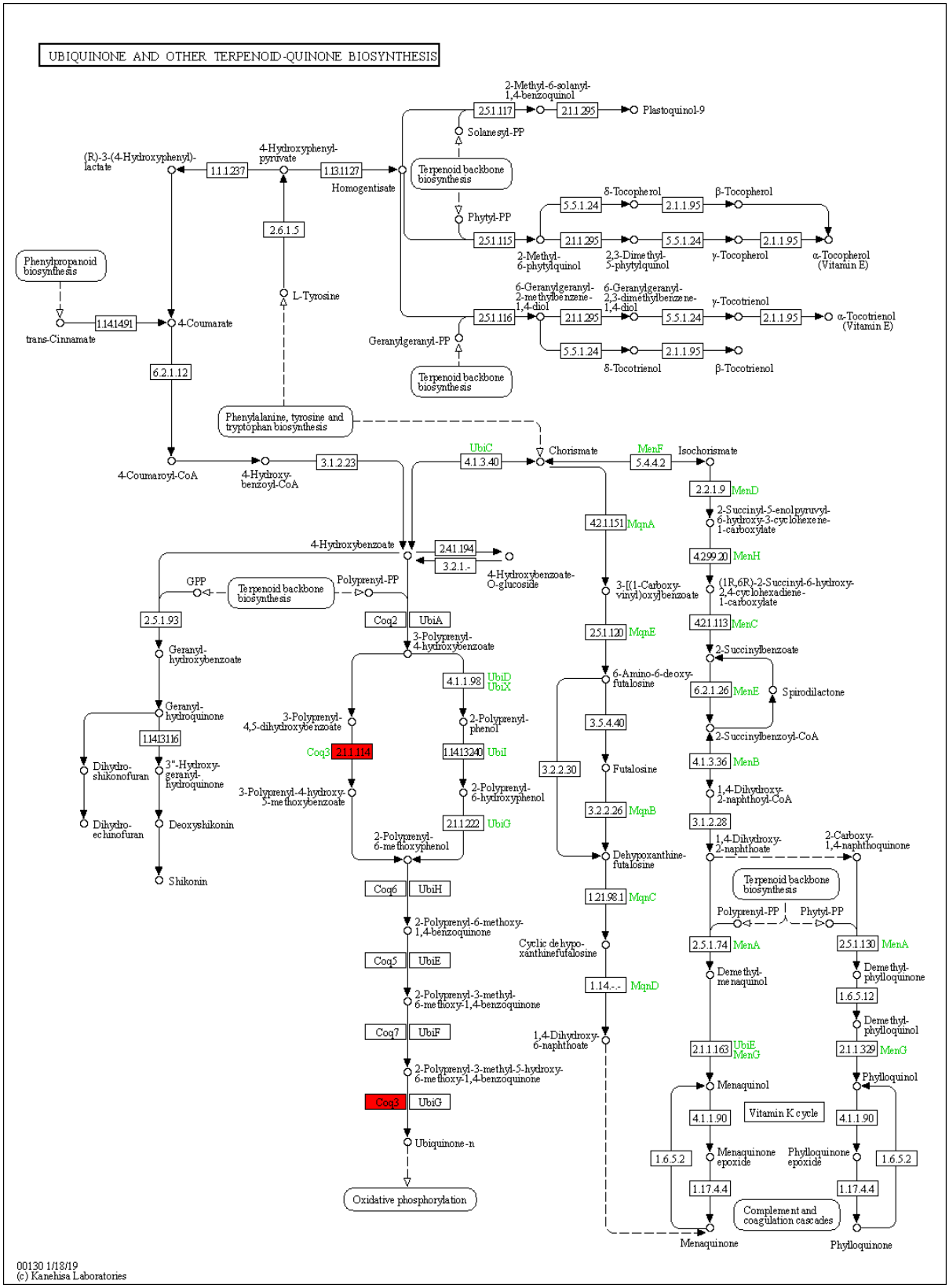


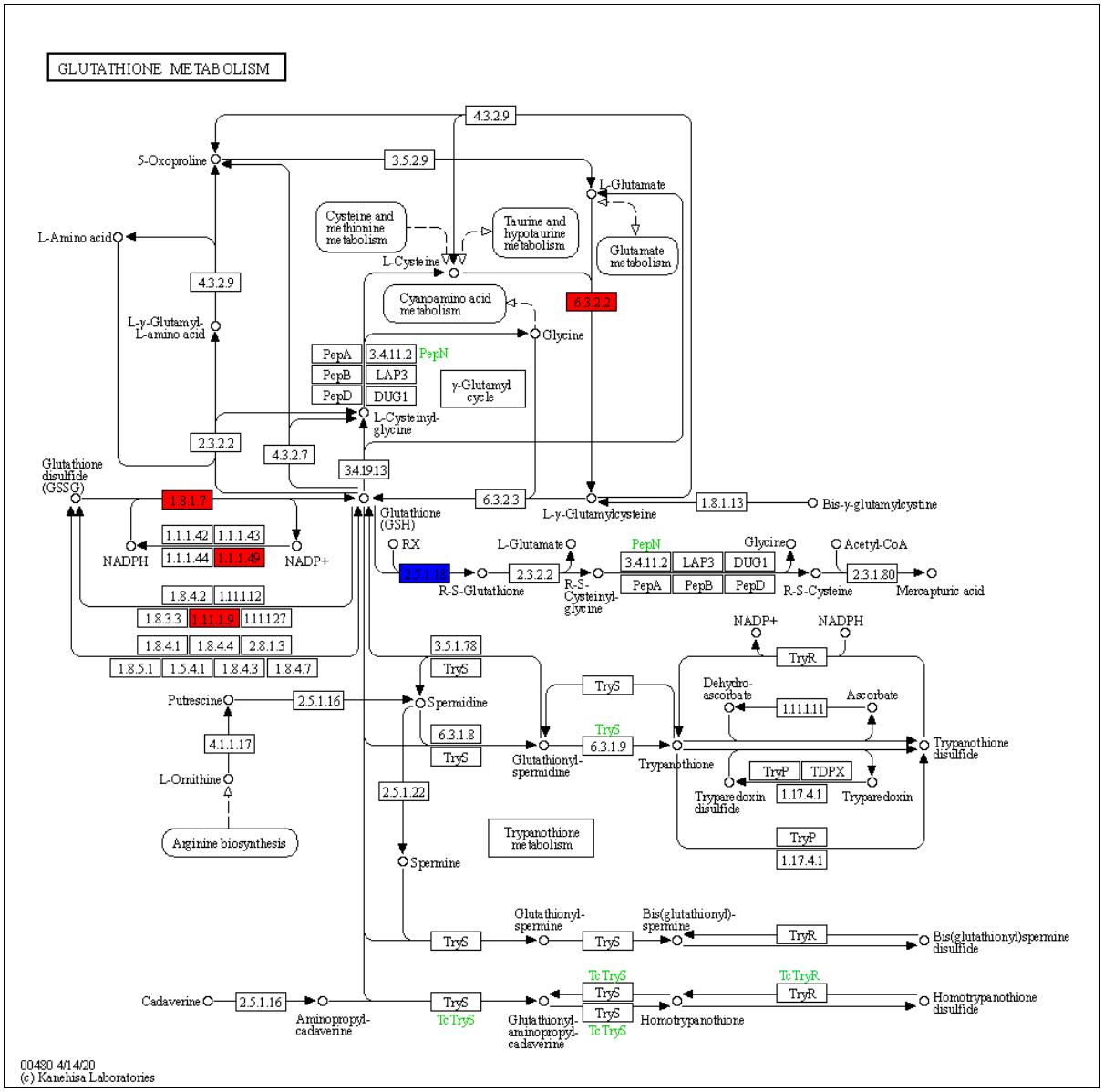
00062 3/2/16
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FATTY ACID DEGRADATION

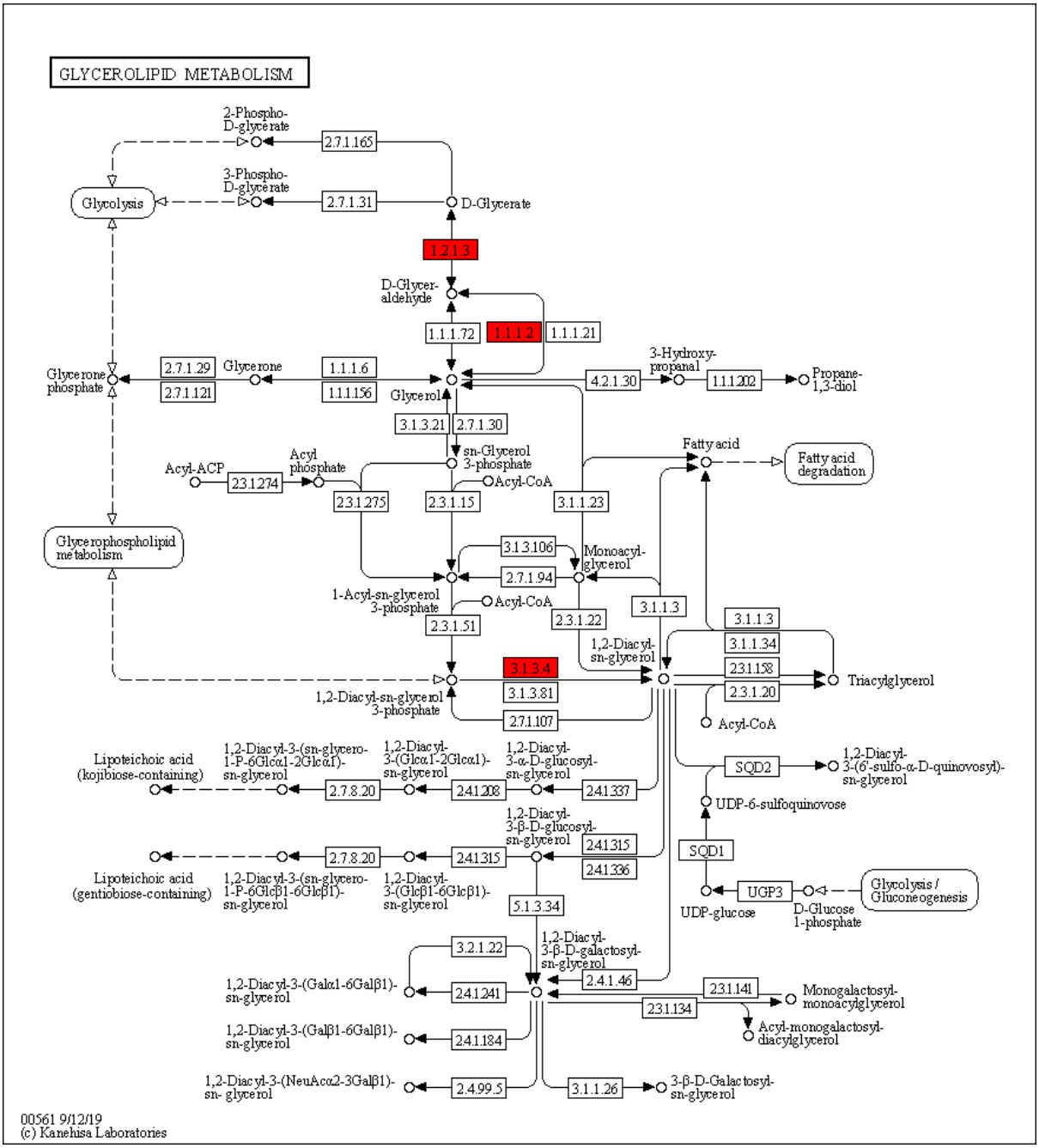


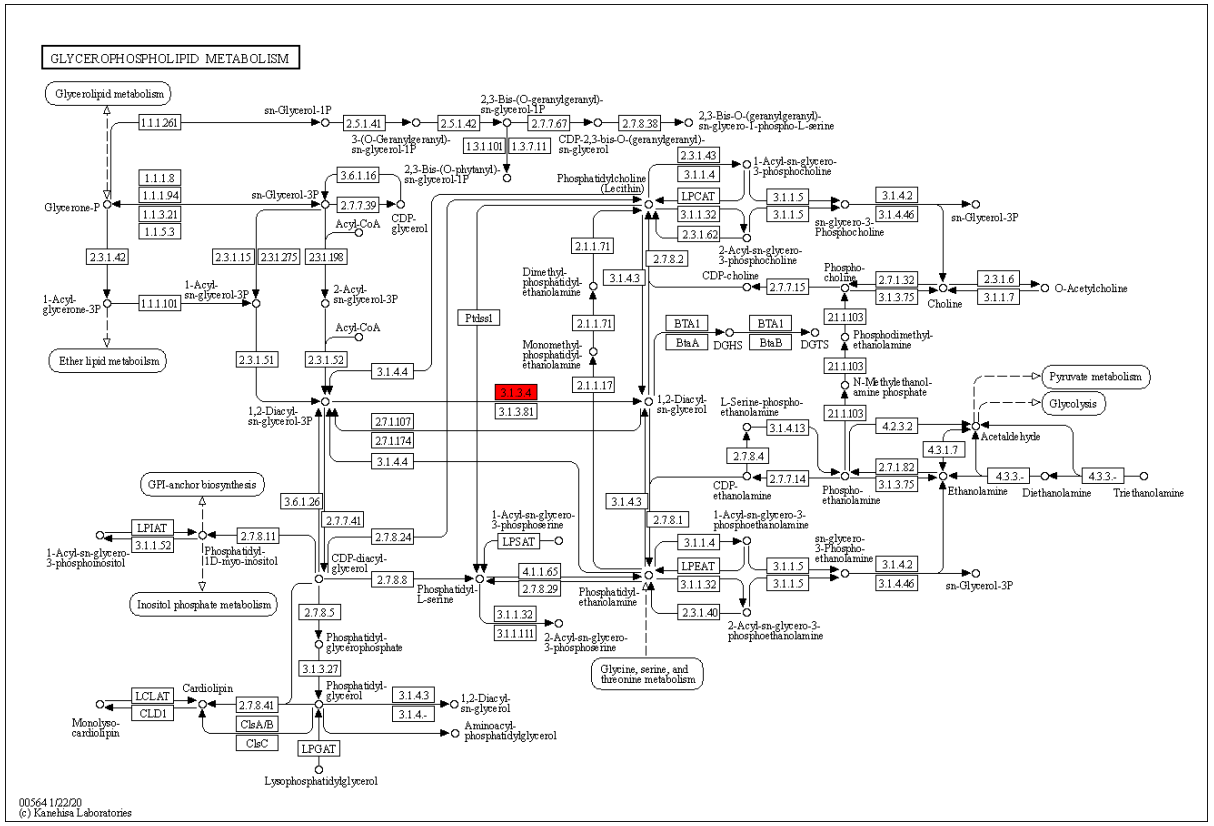
00071 5/25/20
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UBIQUINONE AND OTHER TERPENOID-QUINONE BIOSYNTHESIS
2-Methyl-6-solanyl-1,4-benzoquinol
2.5.1.117
2.1.1.295
Plastoquinol-9
Solanesyl-PP
(R)-3-(4-Hydroxyphenyl)-lactate
1.1.1.237
4-Hydroxyphenyl-pyruvate
1.13.11.27
Homogentisate
Terpenoid backbone biosynthesis
δ-Tocopherol
β-Tocopherol
5.5.1.24
2.1.1.95
Phytyl-PP
2.5.1.115
2-Methyl-6-phytylquinol
2,3-Dimethyl-5-phytylquinol
γ-Tocopherol
α-Tocopherol (Vitamin E)
2.6.1.5
Phenylpropanoid biosynthesis
L-Tyrosine
6-Geranylgeranyl-2-methylbenzene-1,4-diol
6-Geranylgeranyl-2,3-dimethylbenzene-1,4-diol
γ-Tocotrienol
α-Tocotrienol (Vitamin E)
2.5.1.116
trans-Cinnamate
1.14.14.91
4-Coumarate
Geranylgeranyl-PP
δ-Tocotrienol
β-Tocotrienol
6.2.1.12
Terpenoid backbone biosynthesis
Phenylalanine, tyrosine and tryptophan biosynthesis
UbiC
4.1.3.40
Chorismate
MenF
5.4.4.2
Isochorismate
4-Coumaroyl-CoA
4-Hydroxybenzoyl-CoA
3.1.2.23
2.2.1.9
MenD
2-Succinyl-5-enolpyruvyl-6-hydroxy-3-cyclohexene-1-carboxylate
4.2.1.151
MqnA
4-Hydroxybenzoate
2.4.1.194
3.2.1.-
4-Hydroxybenzoate-O-glucoside
4.2.99.20
MenH
3-[(1-Carboxyvinyl)oxy]benzoate
(1R,6R)-2-Succinyl-6-hydroxy-2,4-cyclohexadiene-1-carboxylate
GPP
Terpenoid backbone biosynthesis
Polyprenyl-PP
2.5.1.93
Coq2
UbiA
3-Polyprenyl-4-hydroxybenzoate
2.5.1.120
MqnE
4.2.1.113
MenC
2-Succinylbenzoate
Geranyl-hydroxybenzoate
4.1.1.98
UbiD
UbiX
6-Amino-6-deoxyfutalosine
6.2.1.26
MenE
Spirodilactone
Geranyl-hydroxyquinone
3-Polyprenyl-4,5-dihydroxybenzoate
2-Polyprenyl-phenol
3.5.4.40
2-Succinylbenzoyl-CoA
1.14.13.116
Coq3
2.1.1.114
1.14.13.240
UbiI
3.2.2.30
Futalosine
4.1.3.36
MenB
Dihydro-shikonofuran
3"-Hydroxy-geranyl-hydroquinone
3-Polyprenyl-4-hydroxy-5-methoxybenzoate
2-Polyprenyl-6-hydroxyphenol
3.2.2.26
MqnB
1,4-Dihydroxy-2-naphthoyl-CoA
3.1.2.28
Dihydro-echinofuran
Deoxyshikonin
2.1.1.222
UbiG
1,4-Dihydroxy-2-naphthoate
2-Carboxy-1,4-naphthoquinone
2-Polyprenyl-6-methoxyphenol
Dehypoxanthine-futalosine
Terpenoid backbone biosynthesis
Shikonin
Coq6
UbiH
1.21.98.1
MqnC
Polyprenyl-PP
Phytyl-PP
2-Polyprenyl-6-methoxy-1,4-benzoquinone
Cyclic dehypoxanthinefutalosine
2.5.1.74
MenA
2.5.1.130
MenA
Coq5
UbiE
Demethyl-menaquinol
Demethyl-phylloquinone
1.14.-.-
MqnD
1.6.5.12
2-Polyprenyl-3-methyl-6-methoxy-1,4-benzoquinone
Demethyl-phylloquinol
Coq7
UbiF
1,4-Dihydroxy-6-naphthoate
2.1.1.163
UbiE
MenG
2.1.1.329
MenG
2-Polyprenyl-3-methyl-5-hydroxy-6-methoxy-1,4-benzoquinone
Phylloquinol
Menaquinol
Coq3
UbiG
4.1.1.90
Vitamin K cycle
4.1.1.90
Ubiquinone-n
1.6.5.2
Menaquinone epoxide
Phylloquinone epoxide
1.6.5.2
Oxidative phosphorylation
1.17.4.4
1.17.4.4
Complement and coagulation cascades
Menaquinone
Phylloquinone
00130 1/18/19
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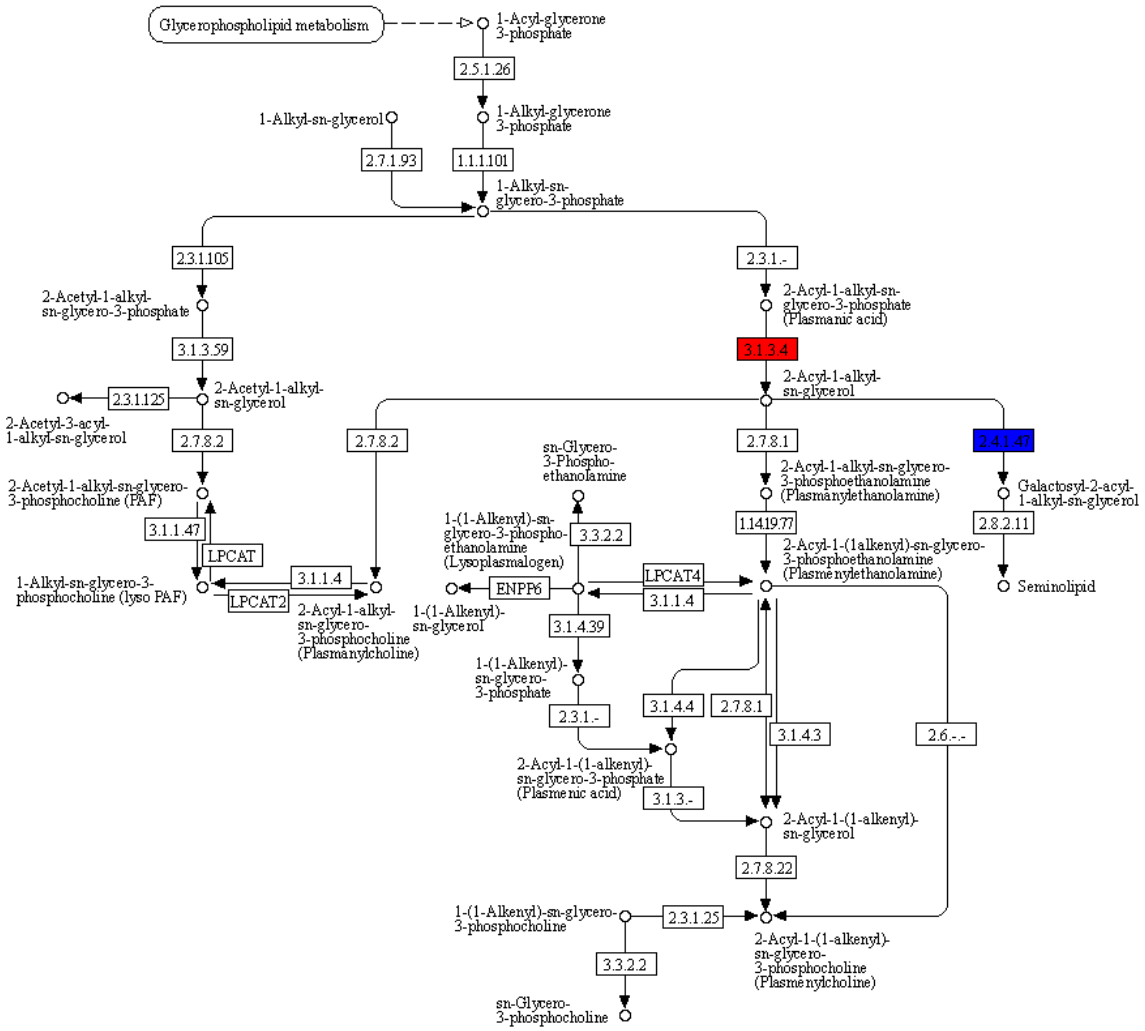


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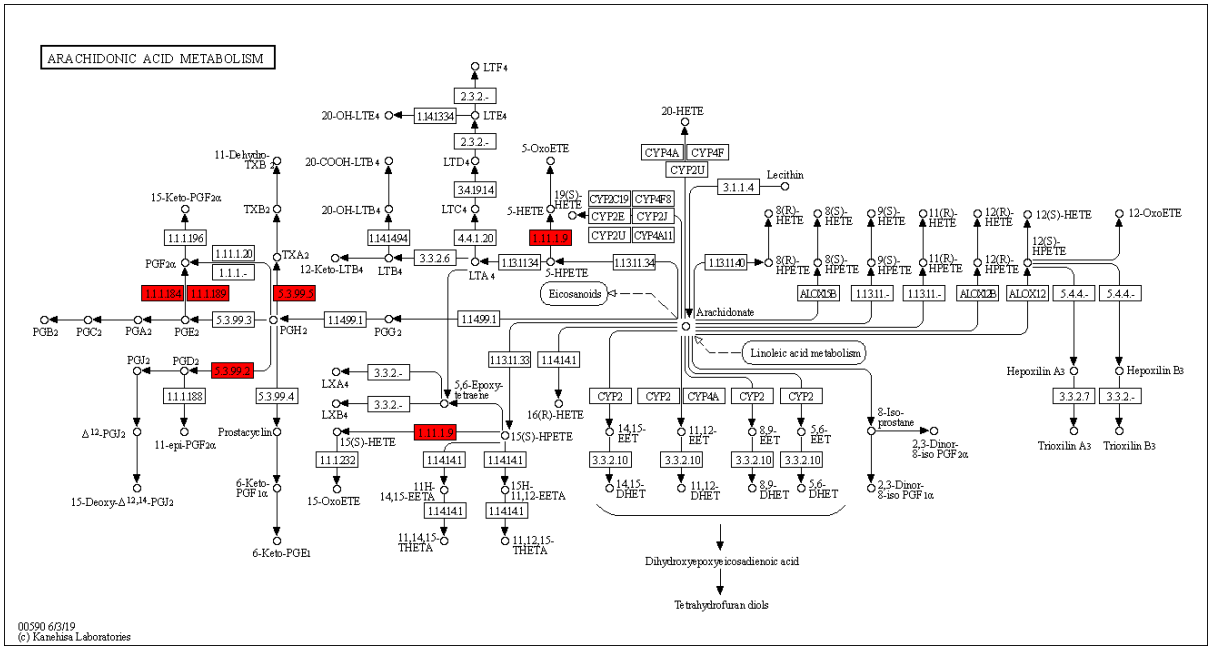

GLYCEROLIPID METABOLISM
2-Phospho-D-glycerate
2.7.1.165
3-Phospho-D-glycerate
Glycolysis
2.7.1.31
D-Glycerate
1.2.1.3
D-Glycer-aldehyde
1.1.1.72
1.1.1.2
1.1.1.21
Glycerone phosphate
2.7.1.29
2.7.1.121
Glycerone
1.1.1.6
1.1.1.156
Glycerol
4.2.1.30
3-Hydroxy-propanal
1.1.1.202
Propane-1,3-diol
3.1.3.21
2.7.1.30
sn-Glycerol 3-phosphate
Acyl-ACP
2.3.1.274
Acyl phosphate
2.3.1.275
2.3.1.15
Acyl-CoA
3.1.1.23
Fatty acid
Fatty acid degradation
Glycerophospholipid metabolism
3.1.3.106
Monoacyl-glycerol
2.7.1.94
1-Acyl-sn-glycerol 3-phosphate
Acyl-CoA
2.3.1.51
2.3.1.22
3.1.1.3
1,2-Diacyl-sn-glycerol
3.1.1.3
3.1.1.34
2.3.1.158
2.3.1.20
Triacylglycerol
Acyl-CoA
3.1.3.4
3.1.3.81
1,2-Diacyl-sn-glycerol 3-phosphate
2.7.1.107
Lipoteichoic acid (kojibiose-containing)
1,2-Diacyl-3-(sn-glycero-1-P-6Glcα1-2Glcα1)-sn-glycerol
2.7.8.20
1,2-Diacyl-3-(Glcα1-2Glcα1)-sn-glycerol
2.4.1.208
1,2-Diacyl-3-α-D-glucosyl-sn-glycerol
2.4.1.337
SQD2
1,2-Diacyl-3-(6'-sulfo-α-D-quinovosyl)-sn-glycerol
UDP-6-sulfoquinovose
1,2-Diacyl-3-β-D-glucosyl-sn-glycerol
2.4.1.315
2.4.1.336
SQD1
Lipoteichoic acid (gentiobiose-containing)
1,2-Diacyl-3-(sn-glycero-1-P-6Glcβ1-6Glcβ1)-sn-glycerol
1,2-Diacyl-3-(Glcβ1-6Glcβ1)-sn-glycerol
5.1.3.34
UGP3
Glycolysis / Gluconeogenesis
UDP-glucose
D-Glucose 1-phosphate
3.2.1.22
1,2-Diacyl-3-β-D-galactosyl-sn-glycerol
2.4.1.46
1,2-Diacyl-3-(Galα1-6Galβ1)-sn-glycerol
2.4.1.241
2.3.1.141
2.3.1.134
Monogalactosyl-monoacylglycerol
Acyl-monogalactosyl-diacylglycerol
1,2-Diacyl-3-(Galβ1-6Galβ1)-sn-glycerol
2.4.1.184
1,2-Diacyl-3-(NeuAcα2-3Galβ1)-sn- glycerol
2.4.99.5
3.1.1.26
3-β-D-Galactosyl-sn-glycerol
00561 9/12/19
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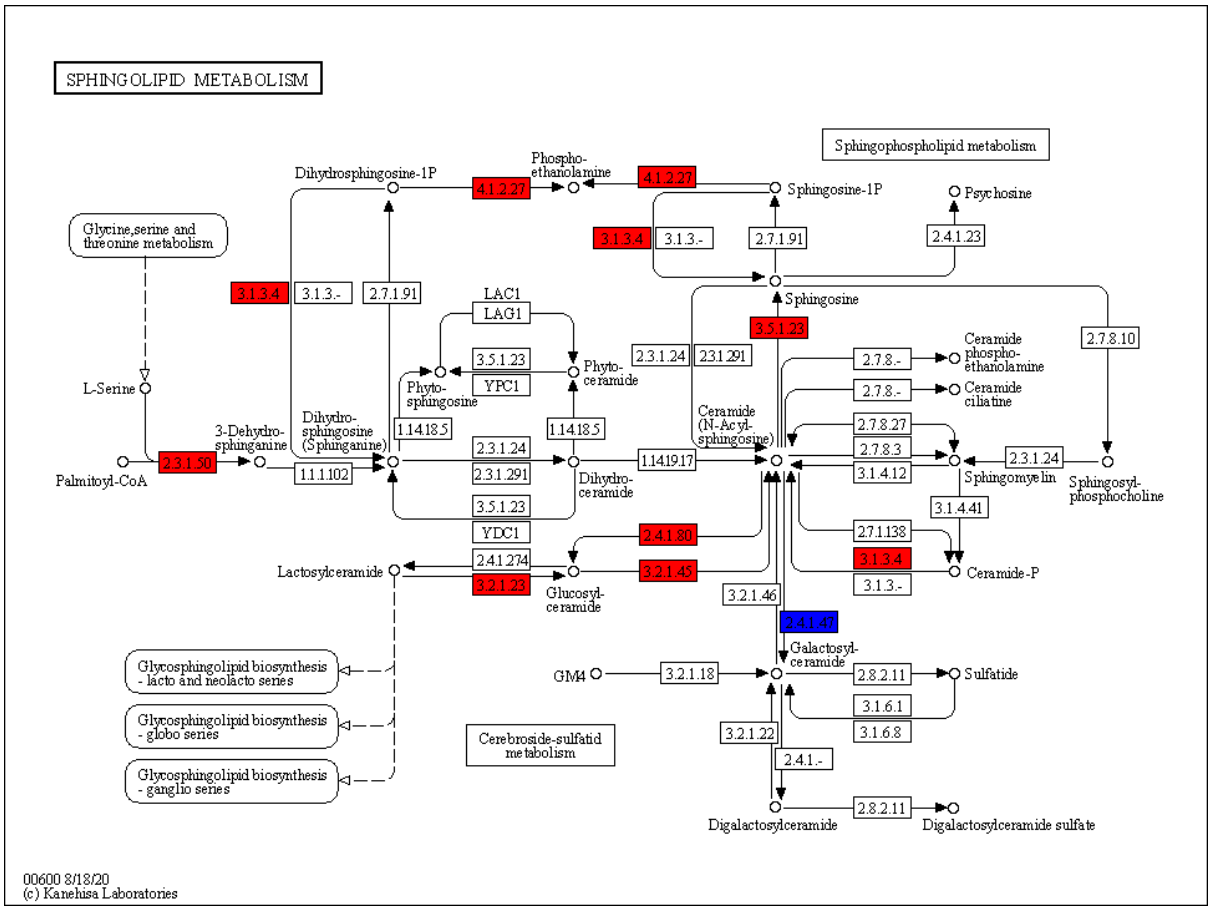

GLYCEROPHOSPHOLIPID METABOLISM
Glycerolipid metabolism
Glycerone-P
sn-Glycerol-3P
Acyl-CoA
CDP-glycerol
1-Acyl-glycerone-3P
1-Acyl-sn-glycerol-3P
2-Acyl-sn-glycerol-3P
Ether lipid metabolism
1,2-Diacyl-sn-glycerol-3P
1,2-Diacyl-sn-glycerol
sn-Glycerol-1P
3-(O-Geranylgeranyl)-sn-glycerol-1P
2,3-Bis-(O-geranylgeranyl)-sn-glycerol-1P
2,3-Bis-(O-phytanyl)-sn-glycerol-1P
CDP-2,3-bis-O-(geranylgeranyl)-sn-glycerol
2,3-Bis-O-(geranylgeranyl)-sn-glycero-1-phospho-L-serine
Phosphatidylcholine (Lecithin)
1-Acyl-sn-glycero-3-phosphocholine
2-Acyl-sn-glycero-3-phosphocholine
sn-glycero-3-Phosphocholine
Dimethyl-phosphatidyl-ethanolamine
Monomethyl-phosphatidyl-ethanolamine
CDP-choline
Phospho-choline
Choline
O-Acetylcholine
Ptdss1
BTA1
BtaA
BtaB
DGHS
DGTS
Phosphodimethyl-ethanolamine
N-Methylethanol-amine phosphate
L-Serine-phospho-ethanolamine
CDP-ethanolamine
Phospho-ethanolamine
Ethanolamine
Diethanolamine
Triethanolamine
Acetaldehyde
Pyruvate metabolism
Glycolysis
GPI-anchor biosynthesis
1-Acyl-sn-glycero-3-phosphoinositol
Phosphatidyl-1D-myo-inositol
Inositol phosphate metabolism
CDP-diacyl-glycerol
Phosphatidyl-L-serine
1-Acyl-sn-glycero-3-phosphoserine
2-Acyl-sn-glycero-3-phosphoserine
Phosphatidyl-ethanolamine
1-Acyl-sn-glycero-3-phosphoethanolamine
2-Acyl-sn-glycero-3-phosphoethanolamine
sn-glycero-3-Phospho-ethanolamine
Phosphatidyl-glycerophosphate
Phosphatidyl-glycerol
Cardiolipin
Monolyso-cardiolipin
1,2-Diacyl-sn-glycerol
Aminoacyl-phosphatidylglycerol
Lysophosphatidylglycerol
Glycine, serine, and threonine metabolism
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ETHER LIPID METABOLISM

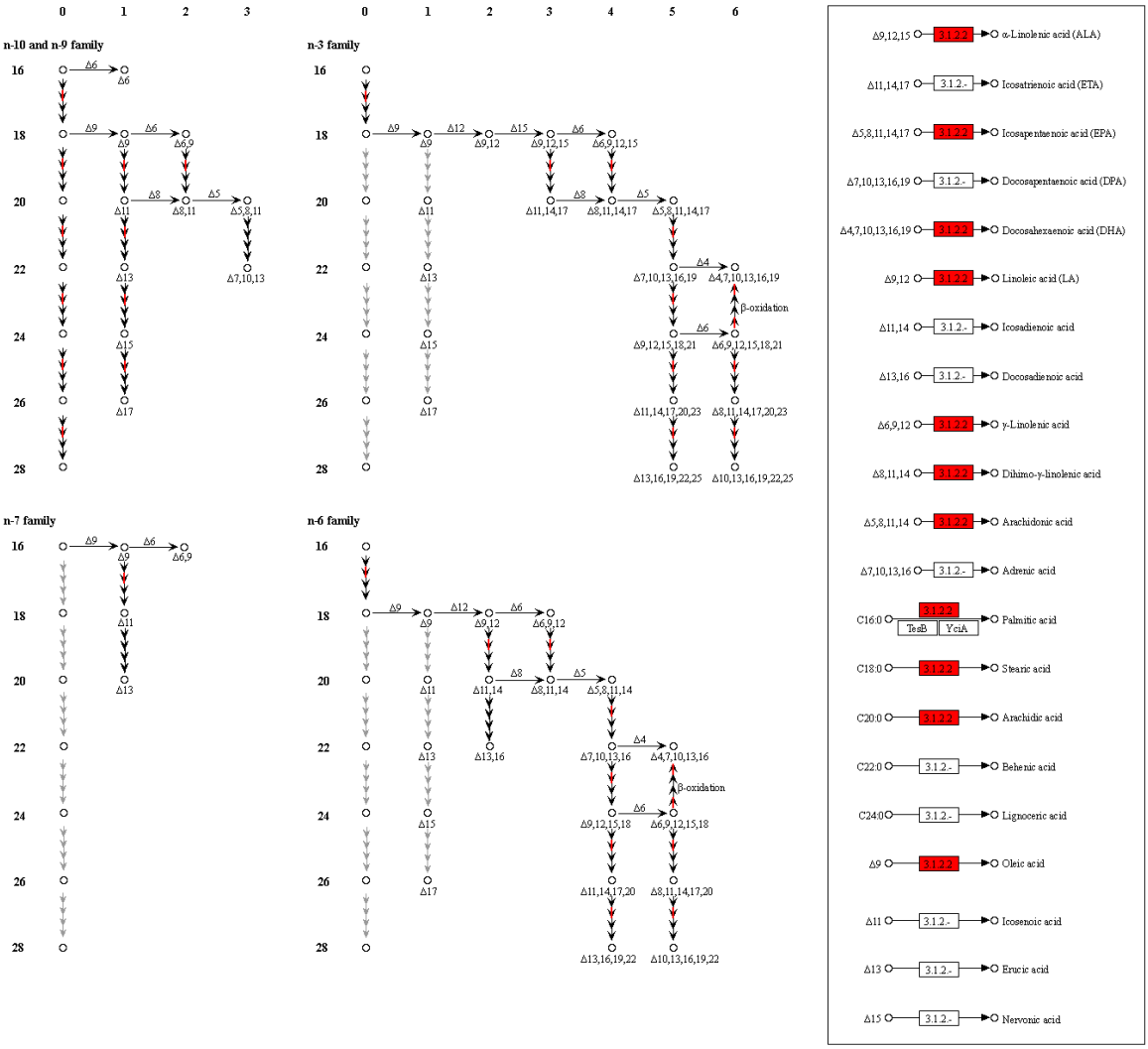


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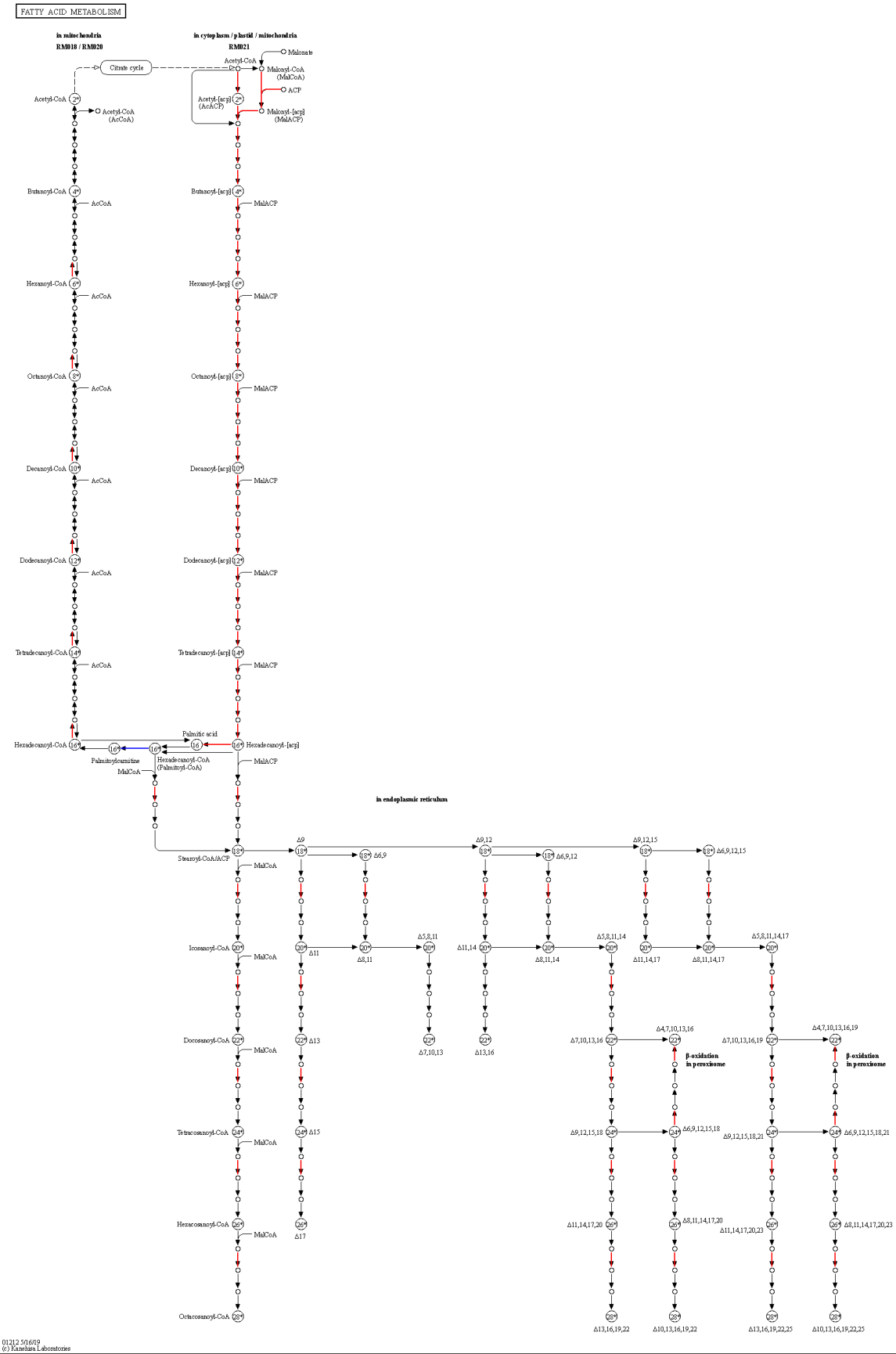

ARACHIDONIC ACID METABOLISM
LTF4
20-OH-LTE4
LTE4
20-HETE
11-Dehydro-TXB2
20-COOH-LTB4
5-OxoETE
CYP4A
CYP4F
CYP2U
Lecithin
15-Keto-PGF2α
TXB2
20-OH-LTB4
LTC4
5-HETE
CYP2C19
CYP4F8
CYP2E
CYP2J
CYP2U
CYP4A11
8(R)-HETE
8(S)-HETE
9(S)-HETE
11(R)-HETE
12(R)-HETE
12(S)-HETE
12-OxoETE
PGF2α
TXA2
12-Keto-LTB4
LTB4
LTA4
5-HPETE
8(R)-HPETE
8(S)-HPETE
9(S)-HPETE
11(R)-HPETE
12(R)-HPETE
12(S)-HPETE
Eicosanoids
Arachidonate
ALOX5B
ALOX12B
ALOX12
PGB2
PGC2
PGA2
PGE2
PGH2
PGG2
Linoleic acid metabolism
PGJ2
PGD2
LXA4
LXB4
5,6-Epoxy-tetraene
16(R)-HETE
8-Iso-prostane
Hepoxilin A3
Hepoxilin B3
Δ12-PGJ2
11-epi-PGF2α
Prostacyclin
15(S)-HETE
15(S)-HPETE
14,15-EET
11,12-EET
8,9-EET
5,6-EET
2,3-Dinor-8-iso PGF2α
Trioxilin A3
Trioxilin B3
15-Deoxy-Δ12,14-PGJ2
6-Keto-PGF1α
15-OxoETE
14,15-EETA
11H-14,15-EETA
15H-11,12-EETA
14,15-DHET
11,12-DHET
8,9-DHET
5,6-DHET
2,3-Dinor-8-iso PGF1α
6-Keto-PGE1
11,14,15-THETA
11,12,15-THETA
Dihydroxyepoxyeicosadienoic acid
Tetrahydrofuran diols
00590 6/3/19
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SPHINGOLIPID METABOLISM
Sphingophospholipid metabolism
Dihydrosphingosine-1P
Phospho-ethanolamine
Sphingosine-1P
Psychosine
Glycine,serine and threonine metabolism
Sphingosine
LAC1
LAG1
Ceramide phospho-ethanolamine
Ceramide ciliatine
L-Serine
Phyto-sphingosine
Phyto-ceramide
3-Dehydro-sphinganine
Dihydro-sphingosine (Sphinganine)
Ceramide (N-Acyl-sphingosine)
Palmitoyl-CoA
Dihydro-ceramide
Sphingomyelin
Sphingosyl-phosphocholine
Lactosylceramide
Glucosyl-ceramide
Ceramide-P
Galactosyl-ceramide
GM4
Sulfatide
Glycosphingolipid biosynthesis - lacto and neolacto series
Glycosphingolipid biosynthesis - globo series
Glycosphingolipid biosynthesis - ganglio series
Cerebroside-sulfatid metabolism
Digalactosylceramide
Digalactosylceramide sulfate
00600 8/18/20
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BIOSYNTHESIS OF UNSATURATED FATTY ACIDS



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FATTY ACID METABOLISM
in mitochondria
RM018 / RM020
in cytoplasm / plastid / mitochondria
RM021
Malonate
Citrate cycle
Acetyl-CoA
Malonyl-CoA
(MalCoA)
ACP
Acetyl-[acp]
(AcACP)
Malonyl-[acp]
(MalACP)
Acetyl-CoA
(AcCoA)
Butanoyl-CoA
Butanoyl-[acp]
AcCoA
MalACP
Hexanoyl-CoA
Hexanoyl-[acp]
Octanoyl-CoA
Octanoyl-[acp]
Decanoyl-CoA
Decanoyl-[acp]
Dodecanoyl-CoA
Dodecanoyl-[acp]
Tetradecanoyl-CoA
Tetradecanoyl-[acp]
Palmitic acid
Hexadecanoyl-CoA
Hexadecanoyl-[acp]
Palmitoylcarnitine
Hexadecanoyl-CoA
(Palmitoyl-CoA)
MalCoA
in endoplasmic reticulum
Stearoyl-CoA/ACP
Δ9
Δ6,9
Δ9,12
Δ6,9,12
Δ9,12,15
Δ6,9,12,15
Icosanoyl-CoA
Δ11
Δ8,11
Δ5,8,11
Δ11,14
Δ8,11,14
Δ5,8,11,14
Δ11,14,17
Δ8,11,14,17
Δ5,8,11,14,17
Docosanoyl-CoA
Δ13
Δ7,10,13
Δ13,16
Δ7,10,13,16
Δ4,7,10,13,16
Δ7,10,13,16,19
Δ4,7,10,13,16,19
β-oxidation
in peroxisome
Tetracosanoyl-CoA
Δ15
Δ9,12,15,18
Δ6,9,12,15,18
Δ9,12,15,18,21
Δ6,9,12,15,18,21
Hexacosanoyl-CoA
Δ17
Δ11,14,17,20
Δ8,11,14,17,20
Δ11,14,17,20,23
Δ8,11,14,17,20,23
Octacosanoyl-CoA
Δ13,16,19,22
Δ10,13,16,19,22
Δ13,16,19,22,25
Δ10,13,16,19,22,25
01212 5/16/12
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Supplementary Figure S9. Enriched KEGG pathways of trans-chalcone-exposed worms compared to controls. Red: indicates pathways with predominantly upregulated genes, green: indicates predominantly downregulated genes, blue: indicates pathways containing both upregulated and underregulated genes.