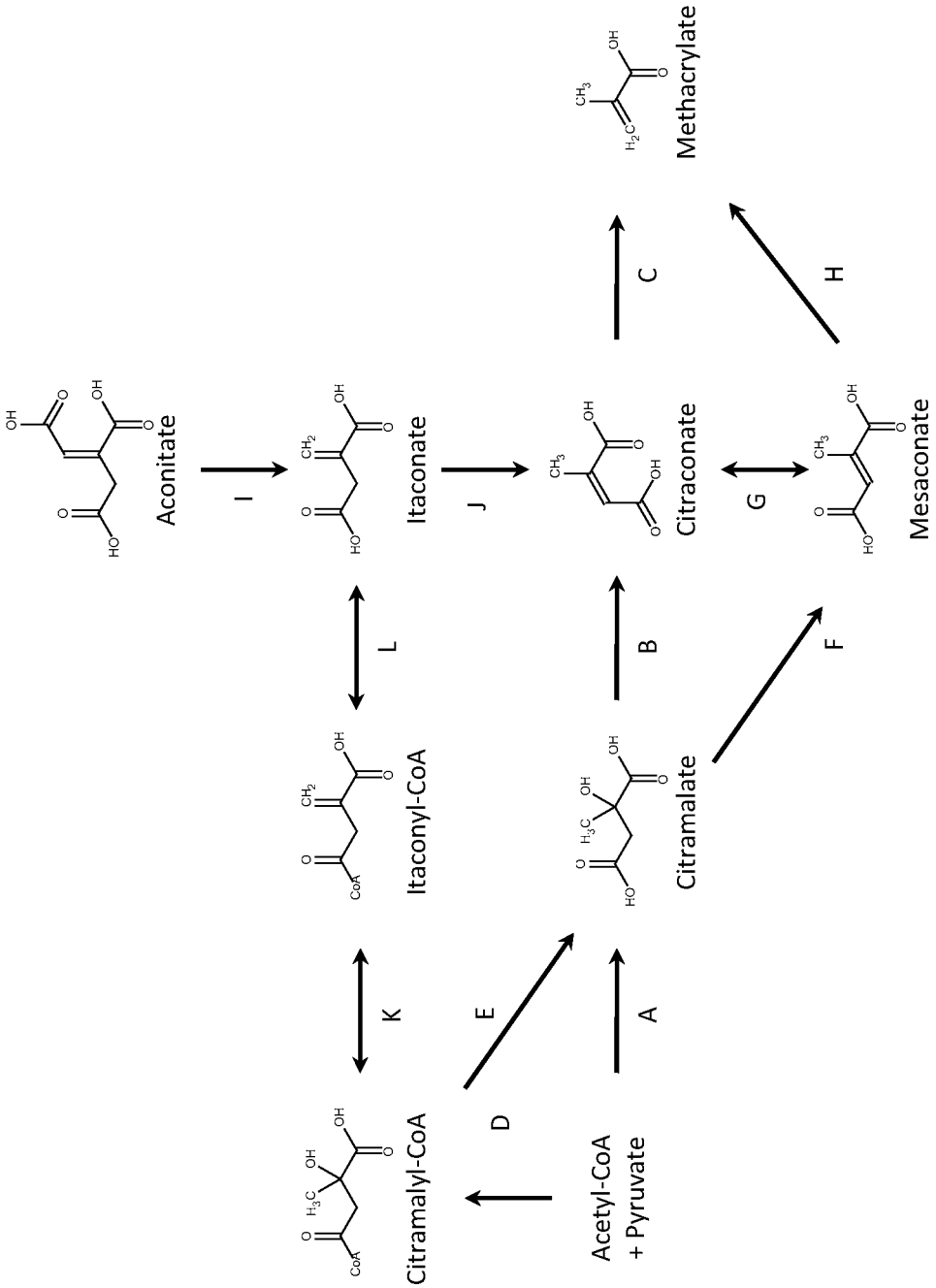

Aconitate
Itaconate
Citraconate
Mesaconate
Methacrylate
Itaconyl-CoA
Citramalate
Citramalyl-CoA
Acetyl-CoA
+ Pyruvate
I
J
C
H
G
L
B
F
K
E
A
D

Figure 1

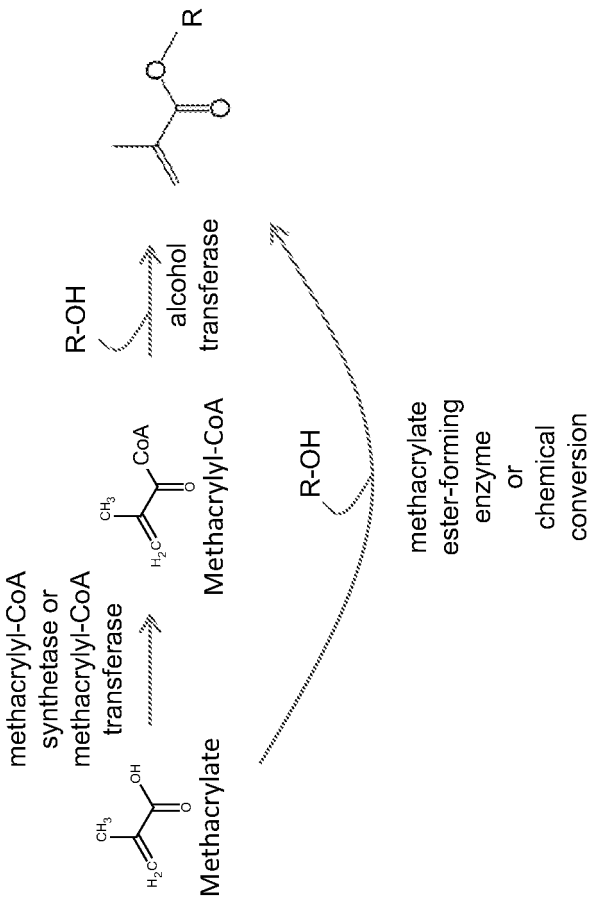

methacrylyl-CoA synthetase or methacrylyl-CoA transferase
Methacrylate
Methacrylyl-CoA
R-OH
alcohol transferase
R
R-OH
methacrylate ester-forming enzyme or chemical conversion

Figure 2

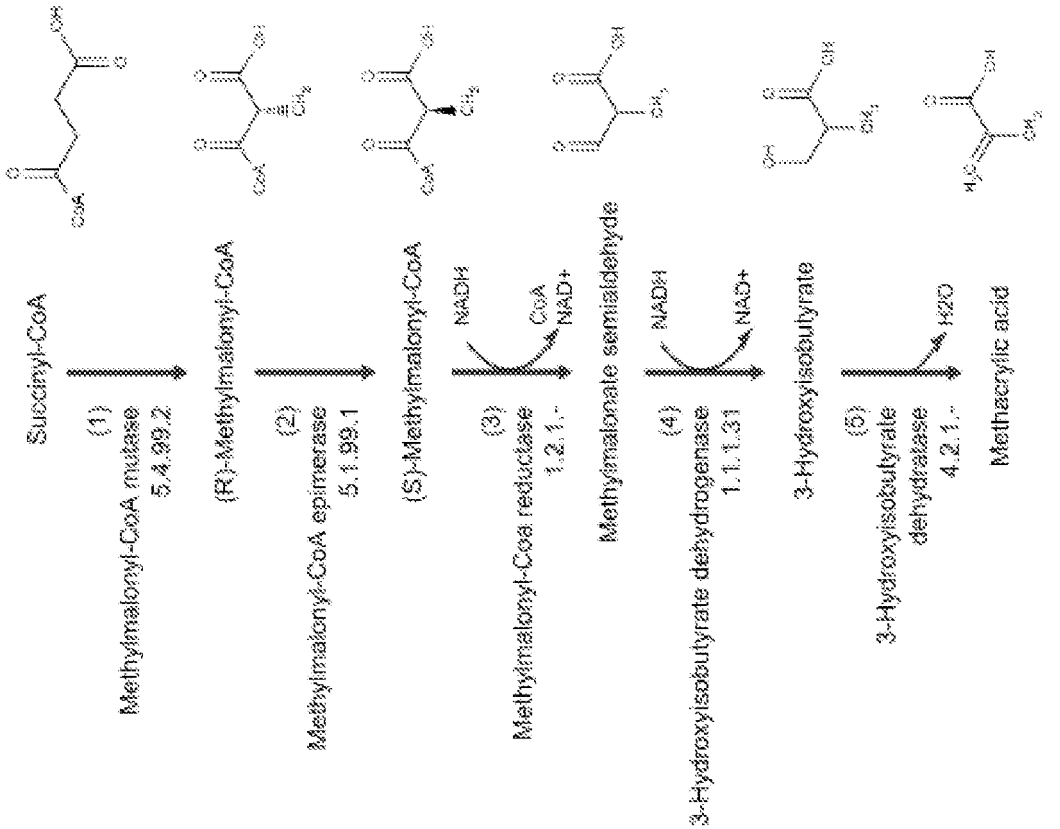

Succinyl-CoA
(1)
Methylmalonyl-CoA mutase
5.4.99.2
(R)-Methylmalonyl-CoA
(2)
Methylmalonyl-CoA epimerase
5.1.99.1
(S)-Methylmalonyl-CoA
NADH
(3)
Methylmalonyl-Coa reductase
1.2.1.-
CoA
NAD+
Methylmalonate semialdehyde
NADH
(4)
3-Hydroxyisobutyrate dehydrogenase
1.1.1.31
NAD+
3-Hydroxyisobutyrate
(5)
3-Hydroxyisobutyrate dehydratase
4.2.1.-
H2O
Methacrylic acid

Figure 3

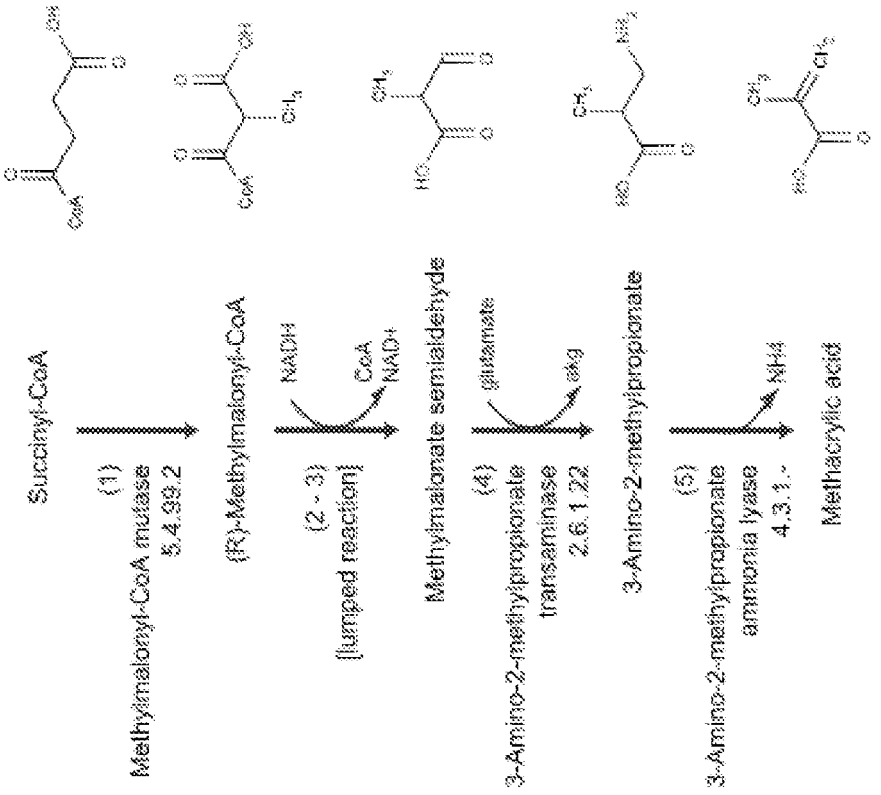

Succinyl-CoA
(1)
Methylmalonyl-CoA mutase
5.4.99.2
(R)-Methylmalonyl-CoA
NADH
CoA
(2 - 3)
[lumped reaction]
NAD+
Methylmalonate semialdehyde
(4)
glutamate
3-Amino-2-methylpropionate
transaminase
2.6.1.22
αKG
3-Amino-2-methylpropionate
(5)
3-Amino-2-methylpropionate
ammonia lyase
4.3.1.-
NH4
Methacrylic acid

Figure 4

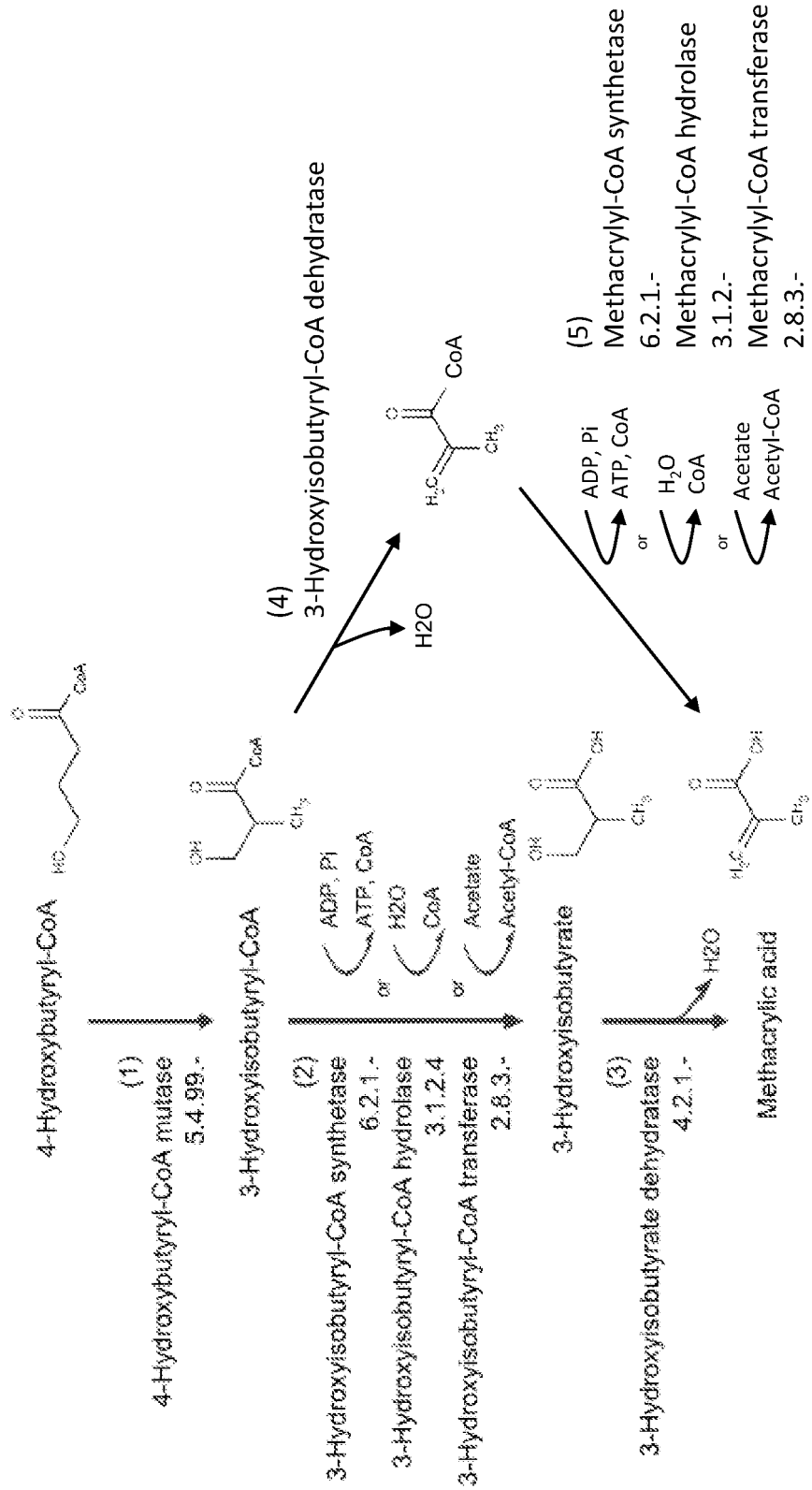

4-Hydroxybutyryl-CoA
(1)
4-Hydroxybutyryl-CoA mutase
5.4.99.-
3-Hydroxyisobutyryl-CoA
(2)
3-Hydroxyisobutyryl-CoA synthetase
6.2.1.-
ADP, Pi
ATP, CoA
or
3-Hydroxyisobutyryl-CoA hydrolase
3.1.2.4
H2O
CoA
or
3-Hydroxyisobutyryl-CoA transferase
2.8.3.-
Acetate
Acetyl-CoA
3-Hydroxyisobutyrate
(3)
3-Hydroxyisobutyrate dehydratase
4.2.1.-
H2O
Methacrylic acid
(4)
3-Hydroxyisobutyryl-CoA dehydratase
H2O
(5)
Methacrylyl-CoA synthetase
6.2.1.-
ADP, Pi
ATP, CoA
or
Methacrylyl-CoA hydrolase
3.1.2.-
H2O
CoA
or
Methacrylyl-CoA transferase
2.8.3.-
Acetate
Acetyl-CoA

Figure 5

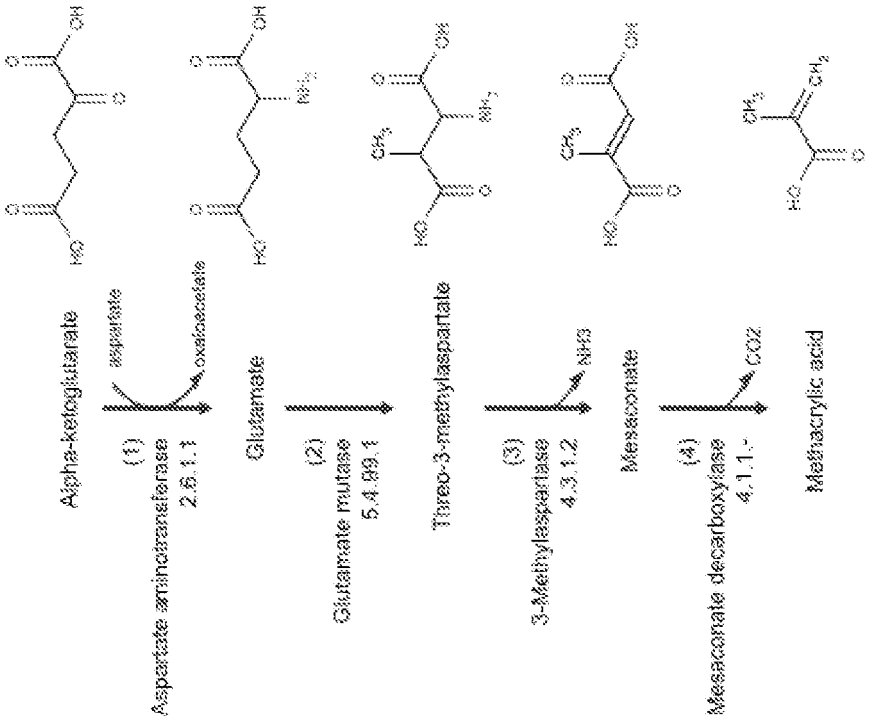

Alpha-ketoglutarate
aspartate
(1)
Aspartate aminotransferase
2.6.1.1
oxaloacetate
Glutamate
(2)
Glutamate mutase
5.4.99.1
Threo-3-methylaspartate
(3)
3-Methylaspartase
4.3.1.2
NH3
Mesaconate
(4)
Mesaconate decarboxylase
4.1.1.-
CO2
Methacrylic acid

Figure 6

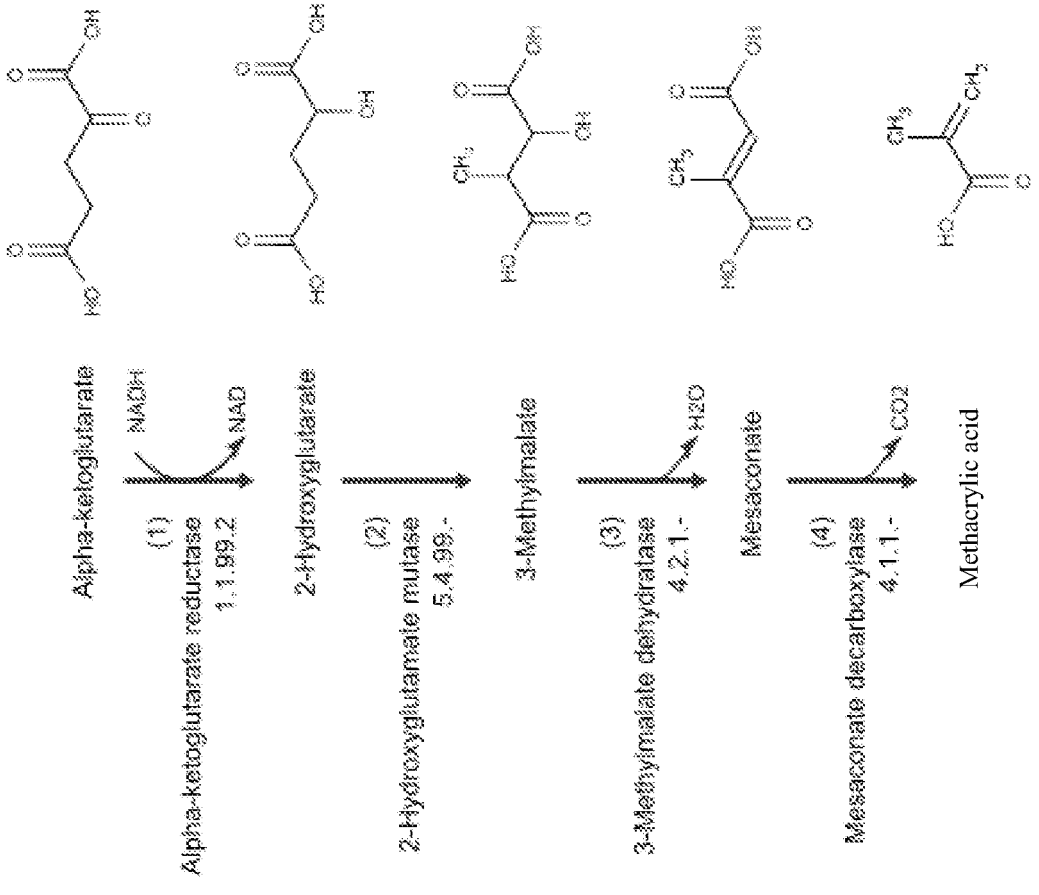

Alpha-ketoglutarate
NADH
(1)
Alpha-ketoglutarate reductase
1.1.99.2
NAD
2-Hydroxyglutarate
(2)
2-Hydroxyglutaramate mutase
5.4.99.-
3-Methylmalate
(3)
3-Methylmalate dehydratase
4.2.1.-
H2O
Mesaconate
(4)
Mesaconate decarboxylase
4.1.1.-
CO2
Methacrylic acid

Figure 7

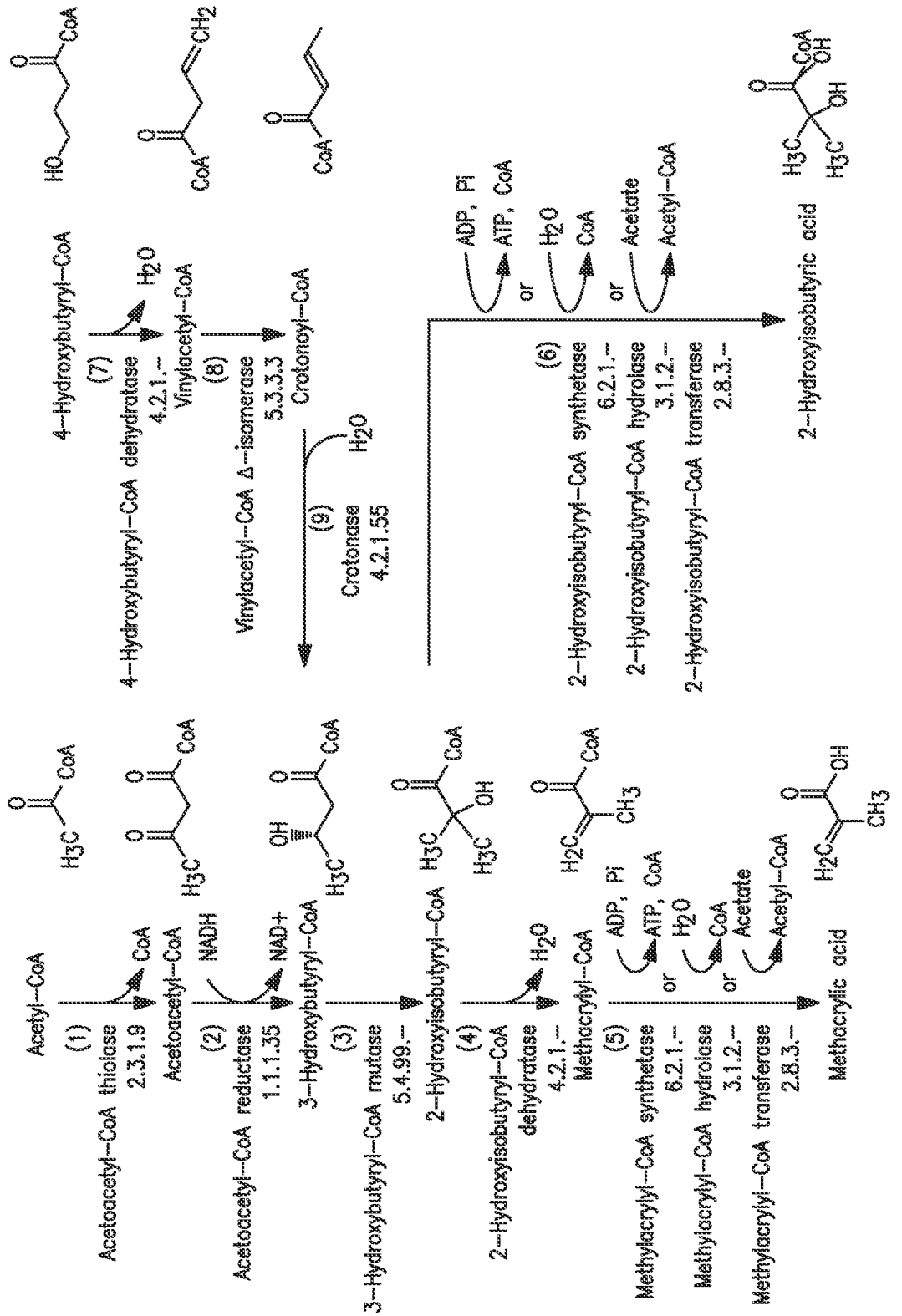

Acetyl–CoA
(1)
Acetoacetyl–CoA thiolase
2.3.1.9
CoA
Acetoacetyl–CoA
(2)
NADH
Acetoacetyl–CoA reductase
1.1.1.35
NAD+
3–Hydroxybutyryl–CoA
(3)
3–Hydroxybutyryl–CoA mutase
5.4.99.–
2–Hydroxyisobutyryl–CoA
(4)
2–Hydroxyisobutyryl–CoA dehydratase
4.2.1.–
H2O
Methacrylyl–CoA
(5)
Methylacrylyl–CoA synthetase
6.2.1.–
ADP, Pi
ATP, CoA
or
Methylacrylyl–CoA hydrolase
3.1.2.–
H2O
CoA
or
Methylacrylyl–CoA transferase
2.8.3.–
Acetate
Acetyl–CoA
Methacrylic acid
4–Hydroxybutyryl–CoA
(7)
4–Hydroxybutyryl–CoA dehydratase
4.2.1.–
H2O
Vinylacetyl–CoA
(8)
Vinylacetyl–CoA Δ–isomerase
5.3.3.3
Crotonoyl–CoA
(9)
Crotonase
4.2.1.55
H2O
(6)
2–Hydroxyisobutyryl–CoA synthetase
6.2.1.–
ADP, Pi
ATP, CoA
or
2–Hydroxyisobutyryl–CoA hydrolase
3.1.2.–
H2O
CoA
or
2–Hydroxyisobutyryl–CoA transferase
2.8.3.–
Acetate
Acetyl–CoA
2–Hydroxyisobutyric acid

Figure 8

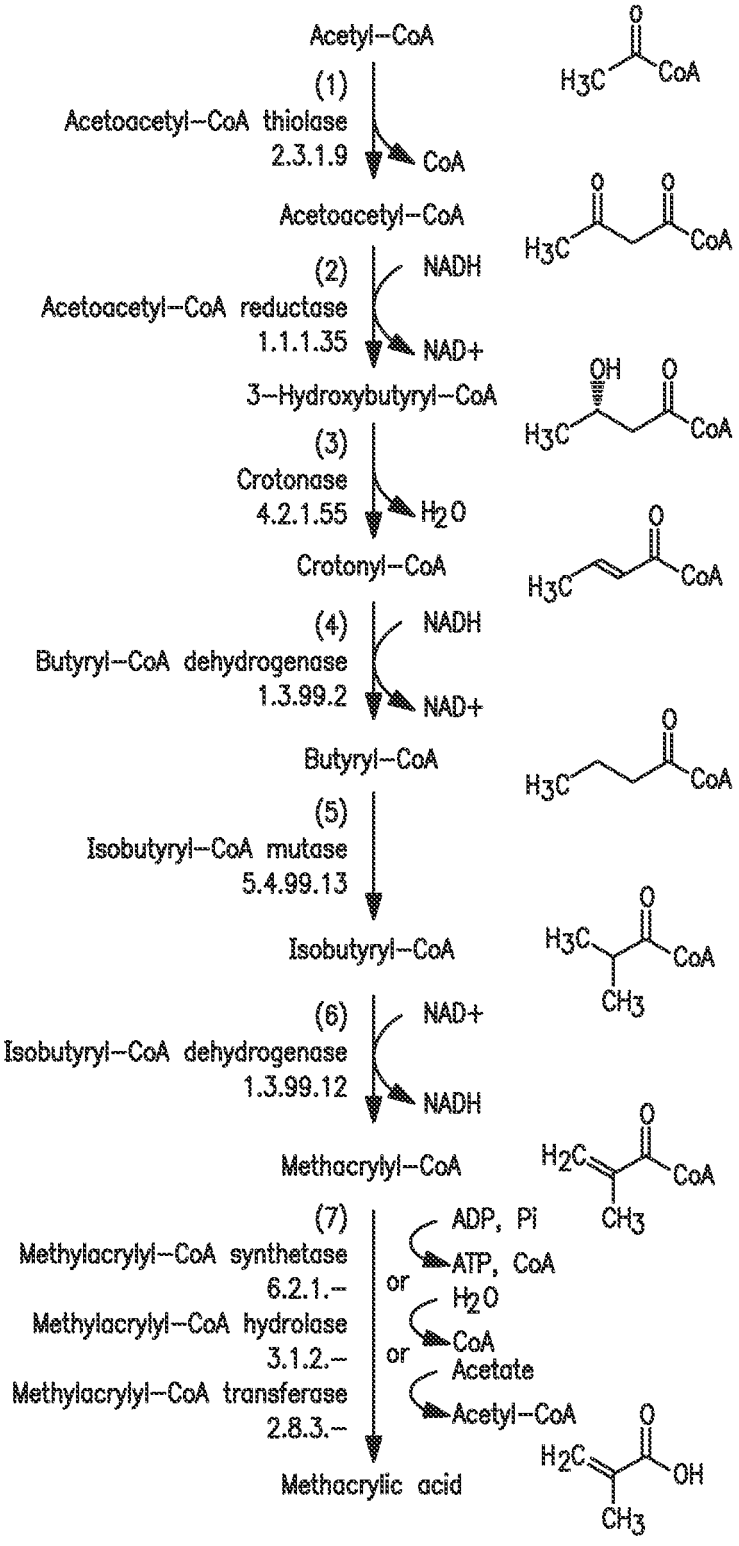

Acetyl-CoA
(1)
Acetoacetyl-CoA thiolase
2.3.1.9
CoA
Acetoacetyl-CoA
(2)
Acetoacetyl-CoA reductase
1.1.1.35
NADH
NAD+
3-Hydroxybutyryl-CoA
(3)
Crotonase
4.2.1.55
H2O
Crotonyl-CoA
(4)
Butyryl-CoA dehydrogenase
1.3.99.2
NADH
NAD+
Butyryl-CoA
(5)
Isobutyryl-CoA mutase
5.4.99.13
Isobutyryl-CoA
(6)
Isobutyryl-CoA dehydrogenase
1.3.99.12
NAD+
NADH
Methacrylyl-CoA
(7)
Methylacrylyl-CoA synthetase
6.2.1.-
ADP, Pi
ATP, CoA
or
Methylacrylyl-CoA hydrolase
3.1.2.-
H2O
CoA
or
Methylacrylyl-CoA transferase
2.8.3.-
Acetate
Acetyl-CoA
Methacrylic acid

FIGURE 9

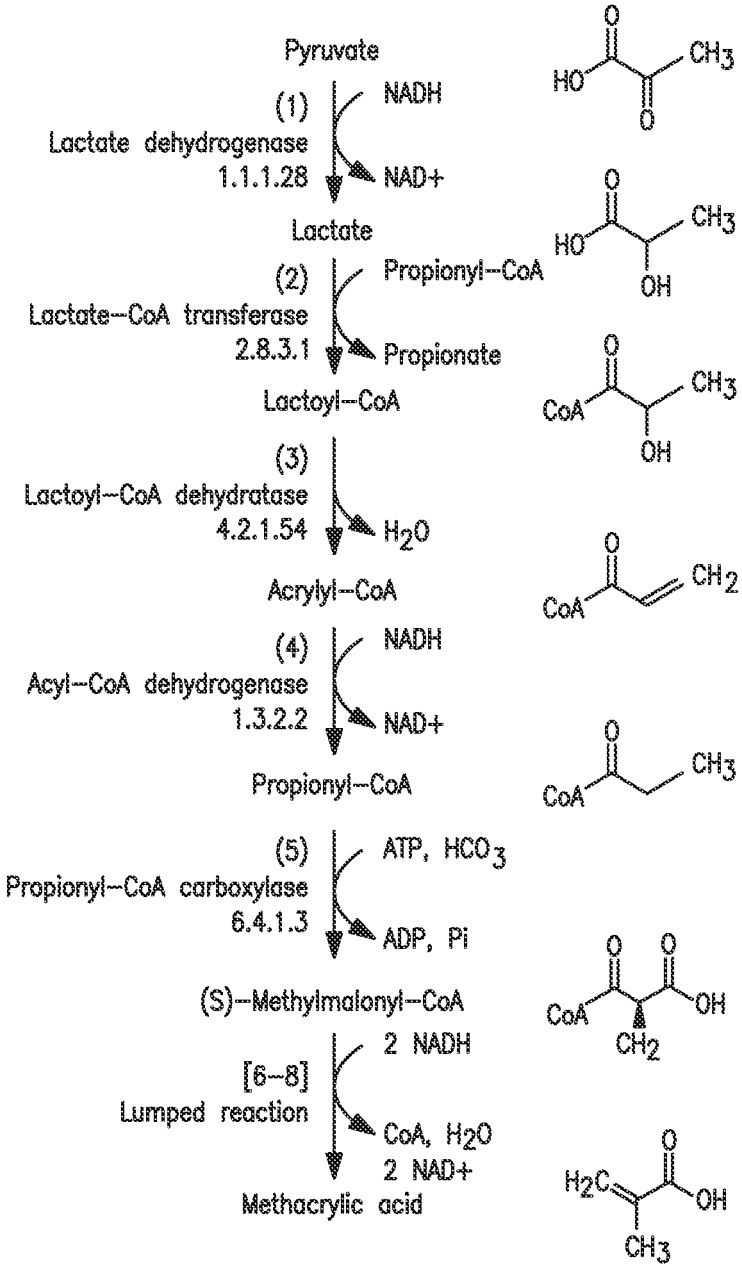

Pyruvate
(1)
Lactate dehydrogenase
1.1.1.28
NADH
NAD+
Lactate
(2)
Lactate–CoA transferase
2.8.3.1
Propionyl–CoA
Propionate
Lactoyl–CoA
(3)
Lactoyl–CoA dehydratase
4.2.1.54
H2O
Acrylyl–CoA
(4)
Acyl–CoA dehydrogenase
1.3.2.2
NADH
NAD+
Propionyl–CoA
(5)
Propionyl–CoA carboxylase
6.4.1.3
ATP, HCO3
ADP, Pi
(S)–Methylmalonyl–CoA
[6–8]
Lumped reaction
2 NADH
CoA, H2O
2 NAD+
Methacrylic acid

FIGURE 10

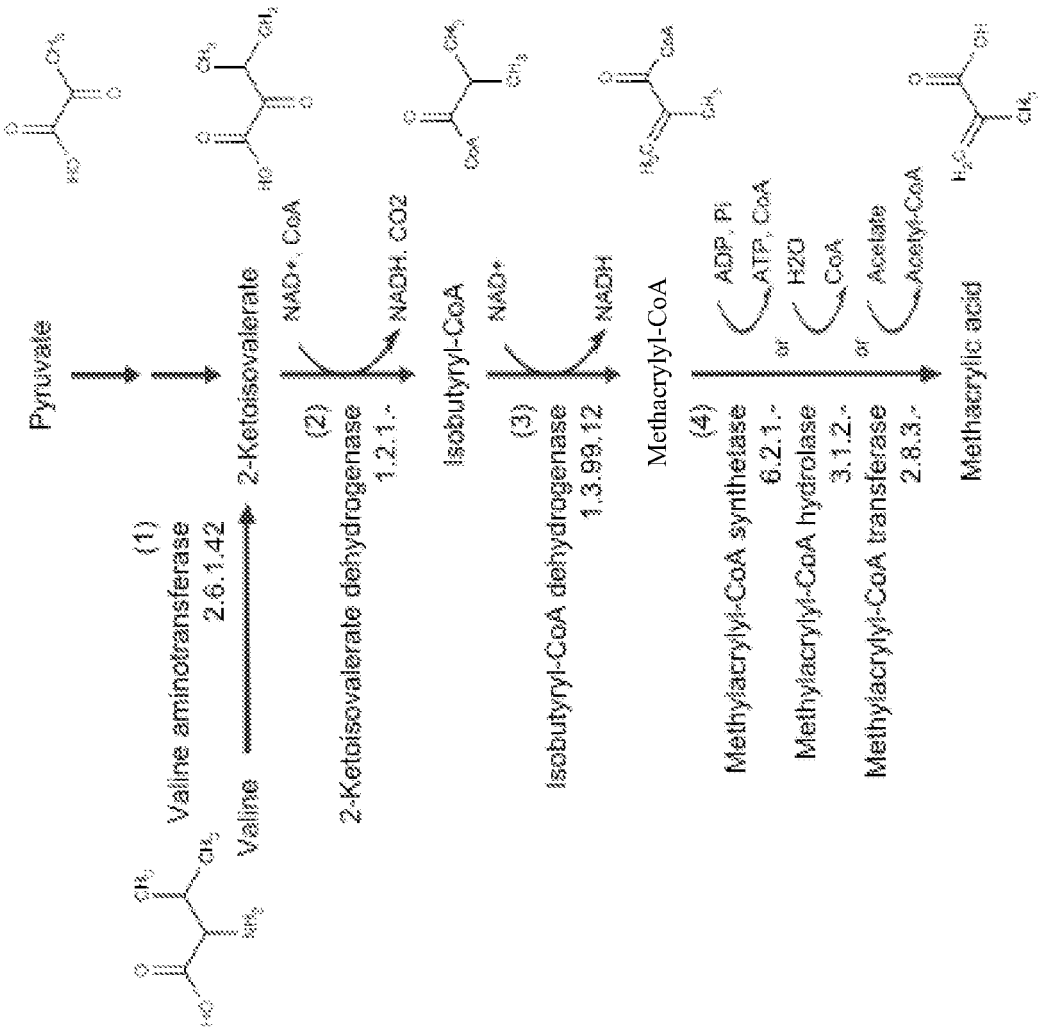

Pyruvate
(1)
Valine aminotransferase
2.6.1.42
Valine
2-Ketoisovalerate
(2)
2-Ketoisovalerate dehydrogenase
1.2.1.-
NAD+, CoA
NADH, CO2
Isobutyryl-CoA
(3)
Isobutyryl-CoA dehydrogenase
1.3.99.12
NAD+
NADH
Methacrylyl-CoA
(4)
Methylacrylyl-CoA synthetase
6.2.1.-
ADP, Pi
ATP, CoA
or
Methylacrylyl-CoA hydrolase
3.1.2.-
H2O
CoA
or
Methylacrylyl-CoA transferase
2.8.3.-
Acetate
Acetyl-CoA
Methacrylic acid

Figure 11

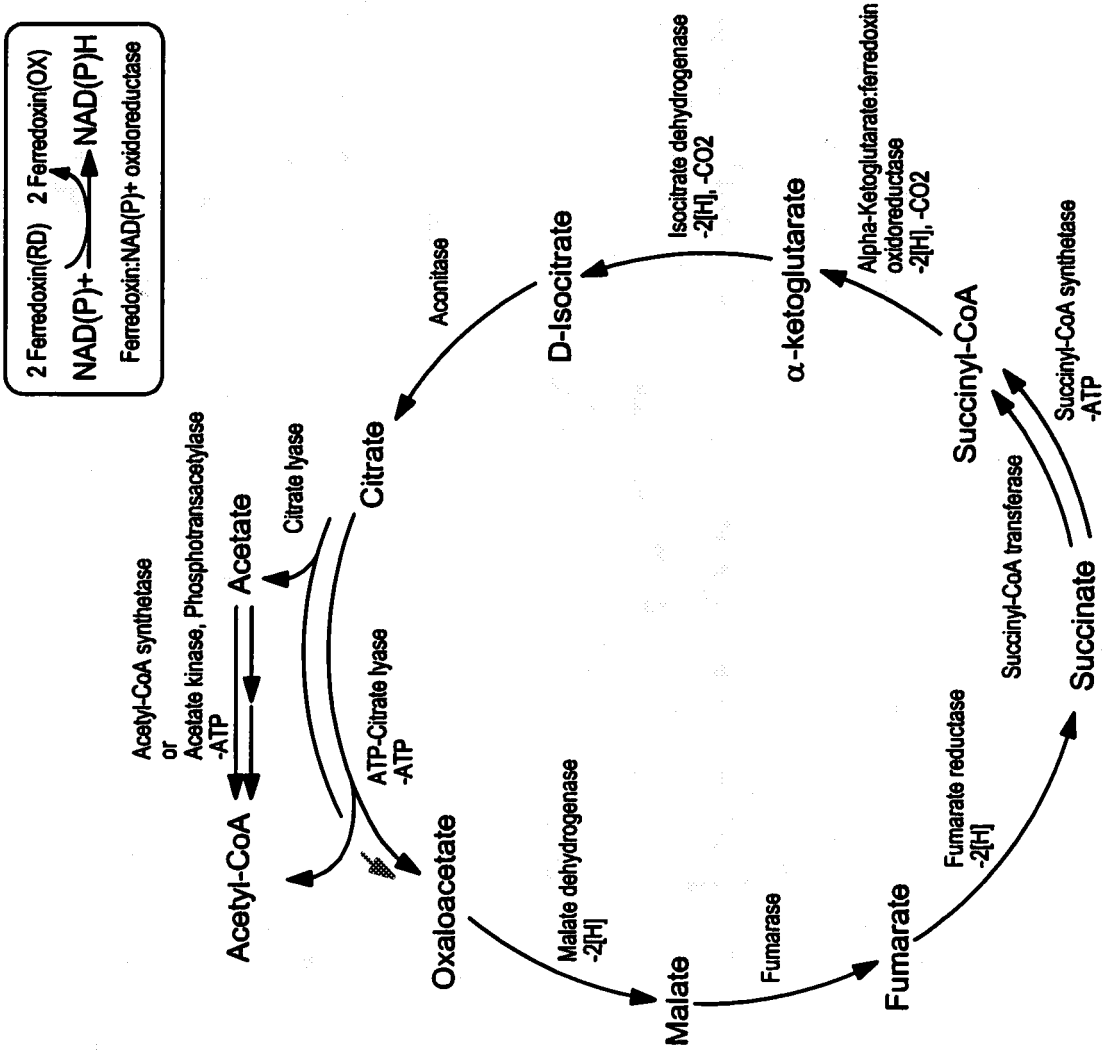

2 Ferredoxin(RD)
2 Ferredoxin(OX)
NAD(P)+
NAD(P)H
Ferredoxin:NAD(P)+ oxidoreductase
Acetyl-CoA synthetase
or
Acetate kinase, Phosphotransacetylase
-ATP
Acetate
Citrate lyase
Citrate
Aconitase
D-Isocitrate
Isocitrate dehydrogenase
-2[H], -CO2
α-ketoglutarate
Alpha-Ketoglutarate:ferredoxin
oxidoreductase
-2[H], -CO2
Succinyl-CoA
Succinyl-CoA synthetase
-ATP
Succinate
Succinyl-CoA transferase
Fumarate reductase
-2[H]
Fumarate
Fumarase
Malate
Malate dehydrogenase
-2[H]
Oxaloacetate
ATP-Citrate lyase
-ATP
Acetyl-CoA

Figure 12

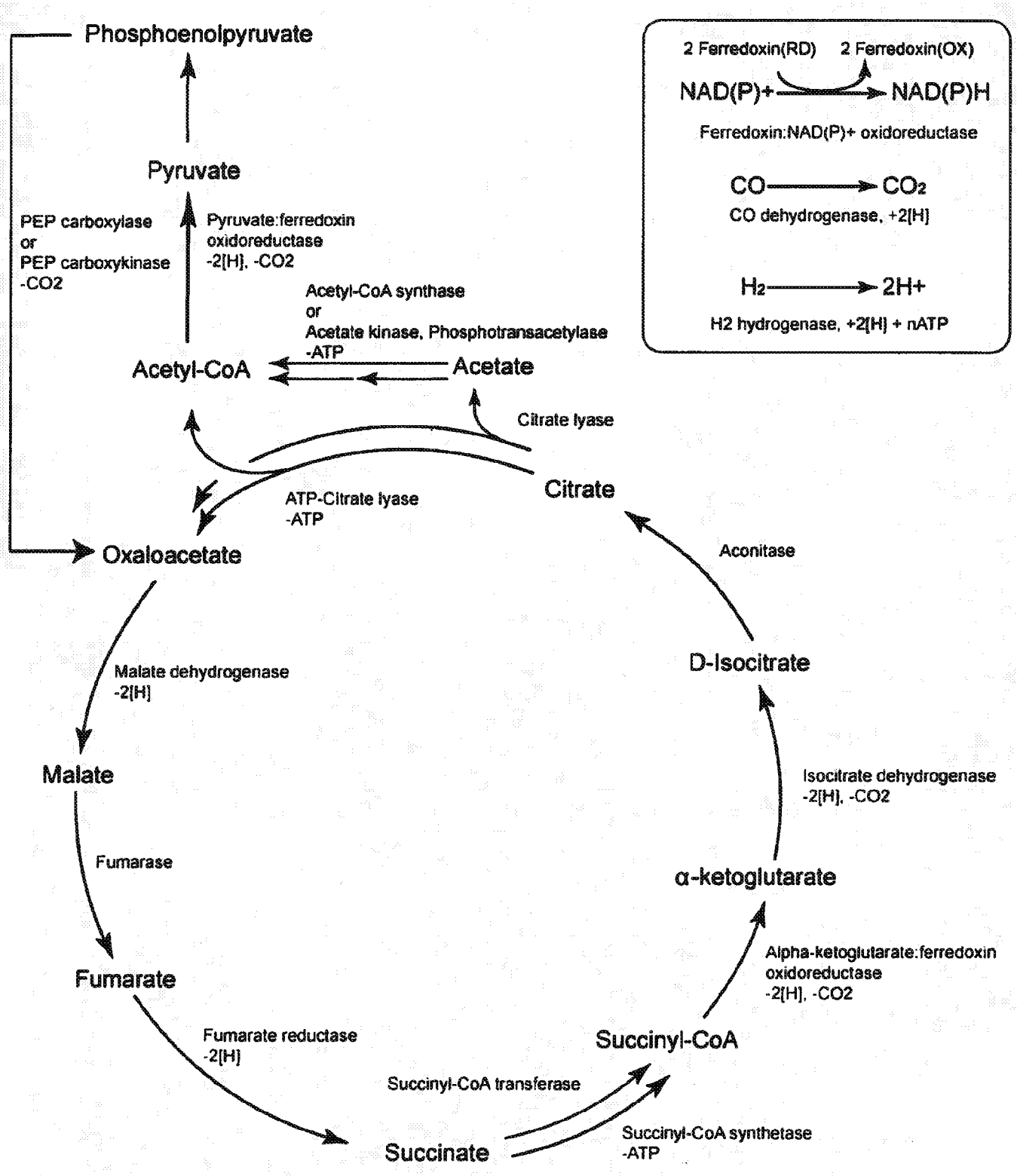

Phosphoenolpyruvate
Pyruvate
PEP carboxylase
or
PEP carboxykinase
-CO2
Pyruvate:ferredoxin
oxidoreductase
-2[H], -CO2
Acetyl-CoA synthase
or
Acetate kinase, Phosphotransacetylase
-ATP
Acetyl-CoA
Acetate
Citrate lyase
Citrate
ATP-Citrate lyase
-ATP
Oxaloacetate
Aconitase
D-Isocitrate
Malate dehydrogenase
-2[H]
Malate
Isocitrate dehydrogenase
-2[H], -CO2
Fumarase
α-ketoglutarate
Fumarate
Alpha-ketoglutarate:ferredoxin
oxidoreductase
-2[H], -CO2
Fumarate reductase
-2[H]
Succinyl-CoA
Succinyl-CoA transferase
Succinate
Succinyl-CoA synthetase
-ATP
2 Ferredoxin(RD)
2 Ferredoxin(OX)
NAD(P)+
NAD(P)H
Ferredoxin:NAD(P)+ oxidoreductase
CO
CO2
CO dehydrogenase, +2[H]
H2
2H+
H2 hydrogenase, +2[H] + nATP

Figure 13

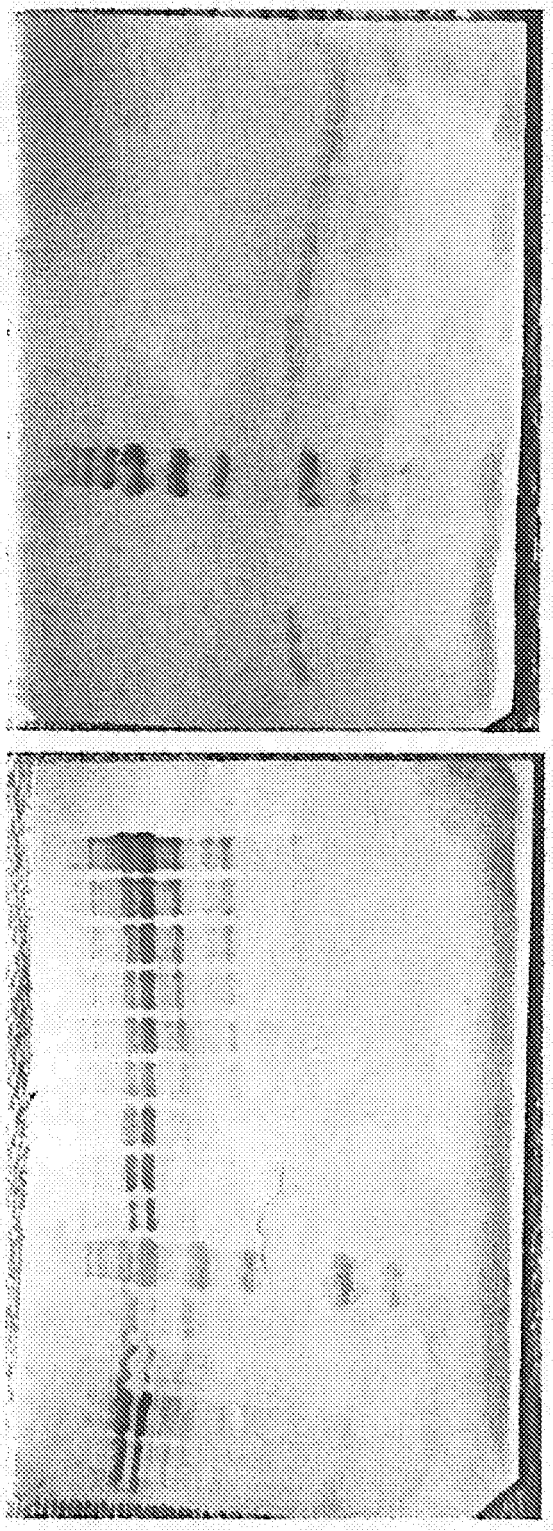
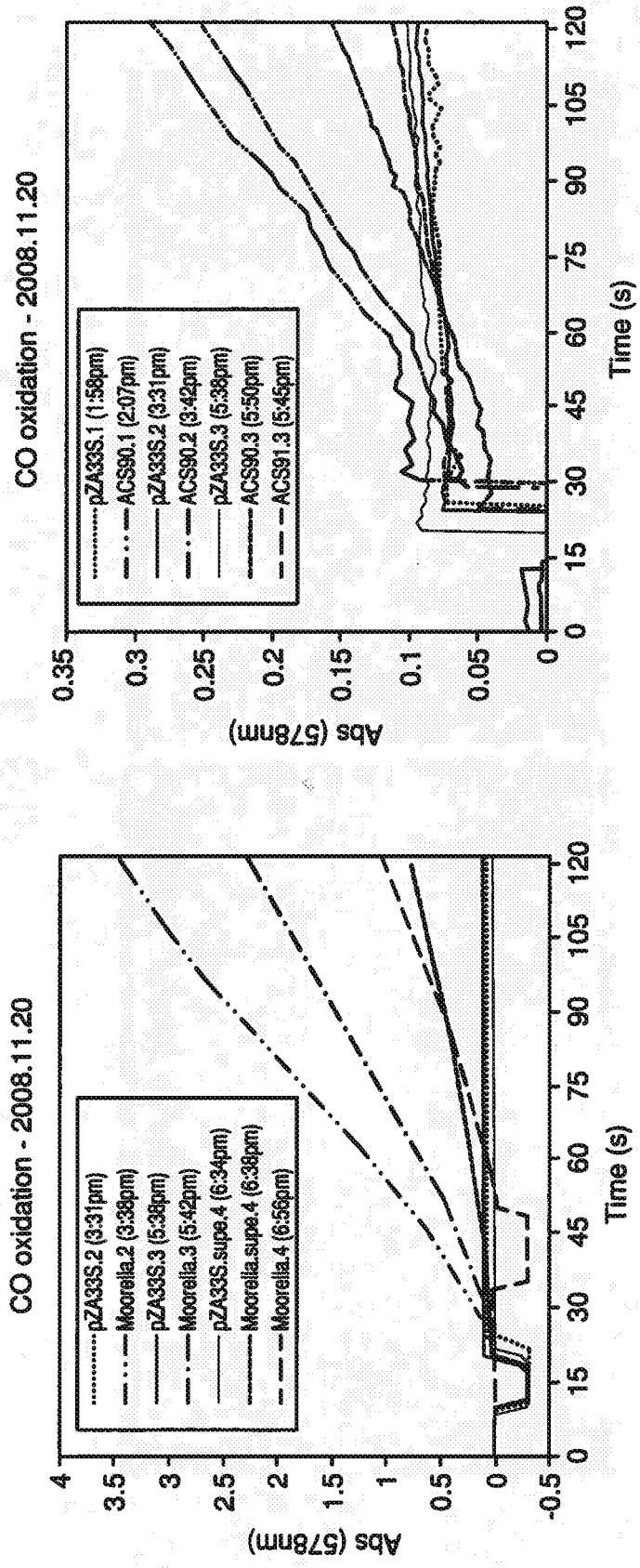
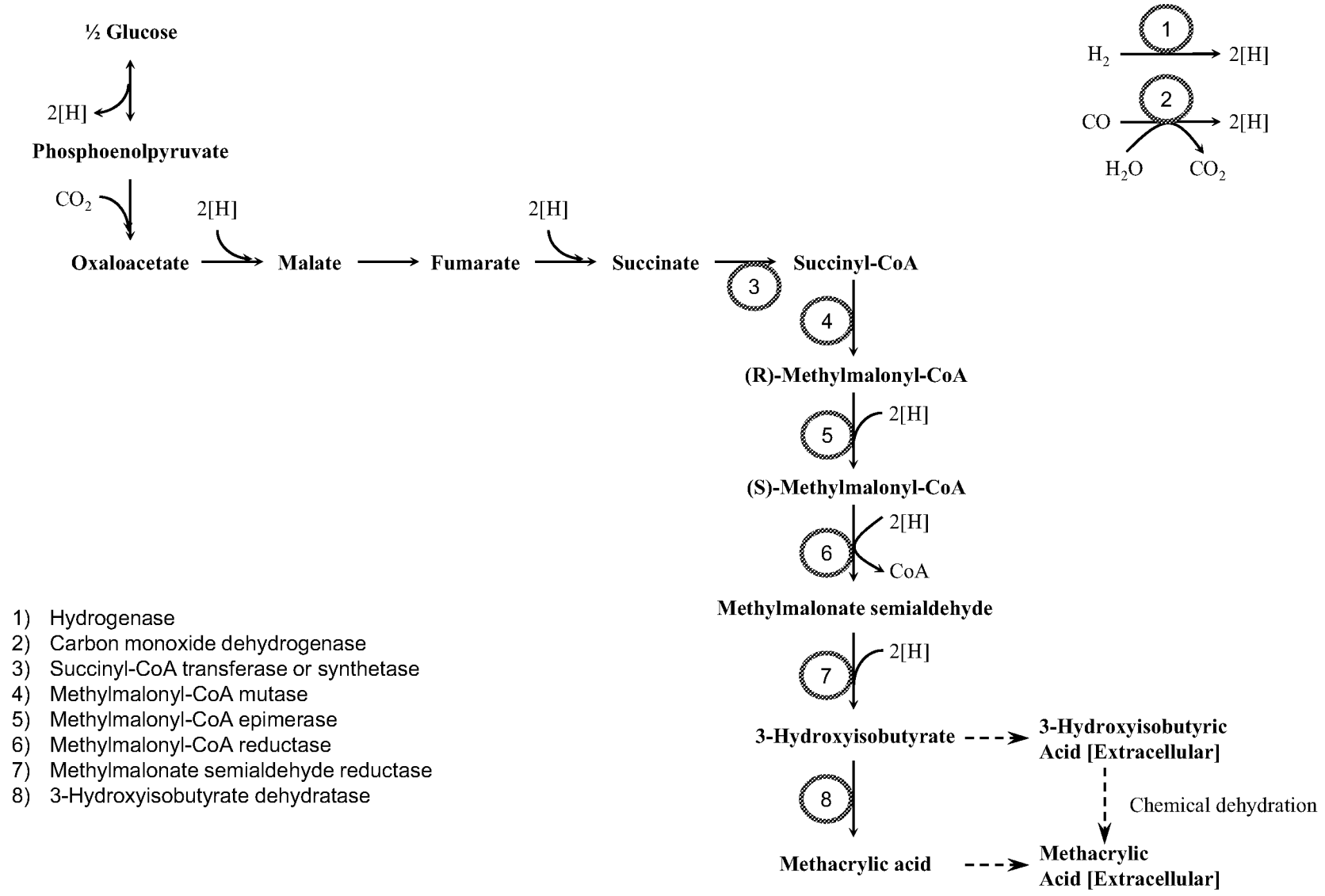


FIGURE 14

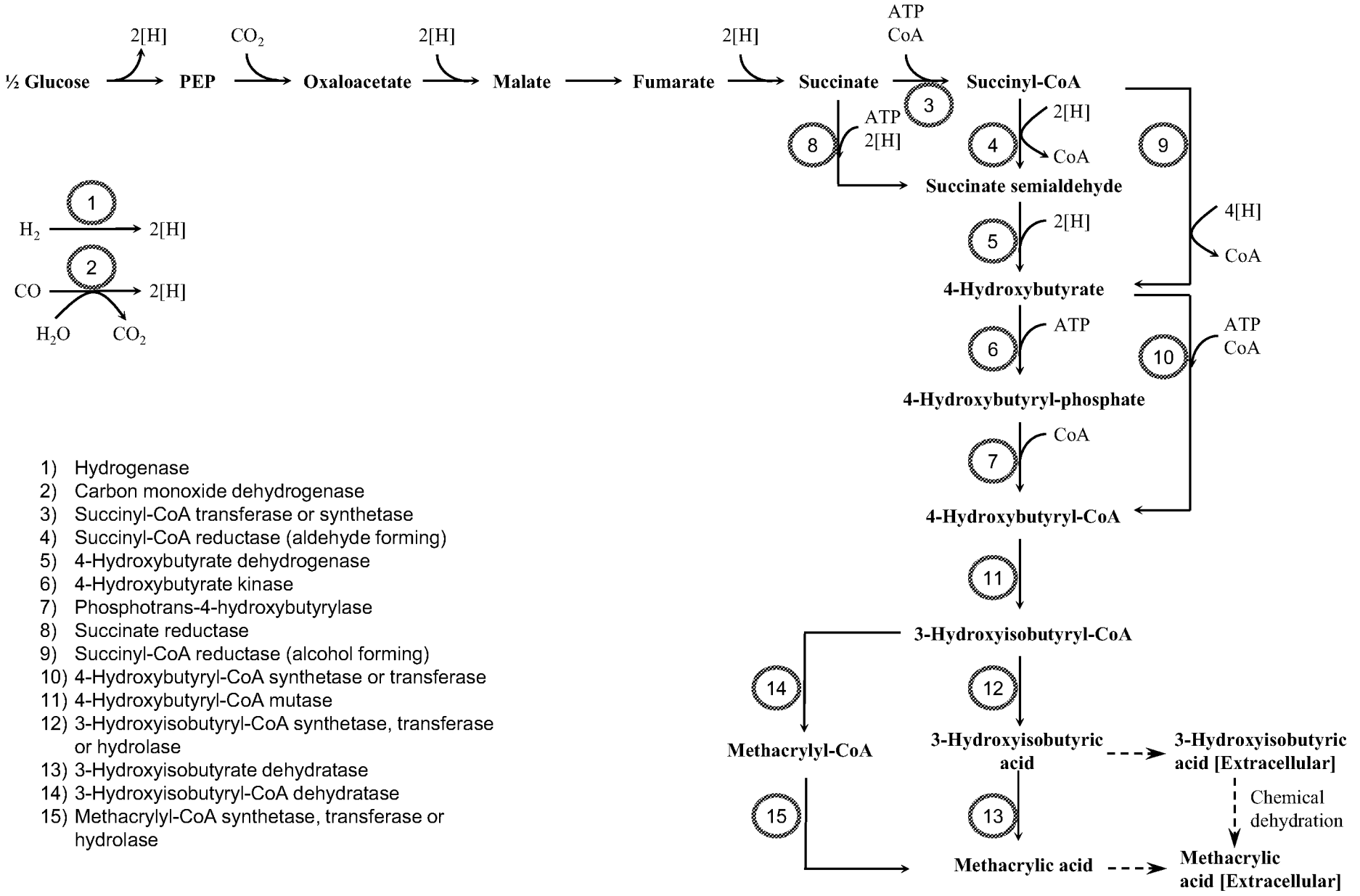
FIGURE 15


CO oxidation - 2008.11.20
pZA33S.2 (3:31pm)
Moorella.2 (3:39pm)
pZA33S.3 (5:38pm)
Moorella.3 (5:42pm)
pZA33S.supe.4 (6:34pm)
Moorella.supe.4 (6:38pm)
Moorella.4 (6:56pm)
Abs (578nm)
Time (s)
CO oxidation - 2008.11.20
pZA33S.1 (1:58pm)
ACS90.1 (2:07pm)
pZA33S.2 (3:31pm)
ACS90.2 (3:42pm)
pZA33S.3 (5:38pm)
ACS90.3 (5:50pm)
ACS91.3 (5:45pm)
Abs (578nm)
Time (s)



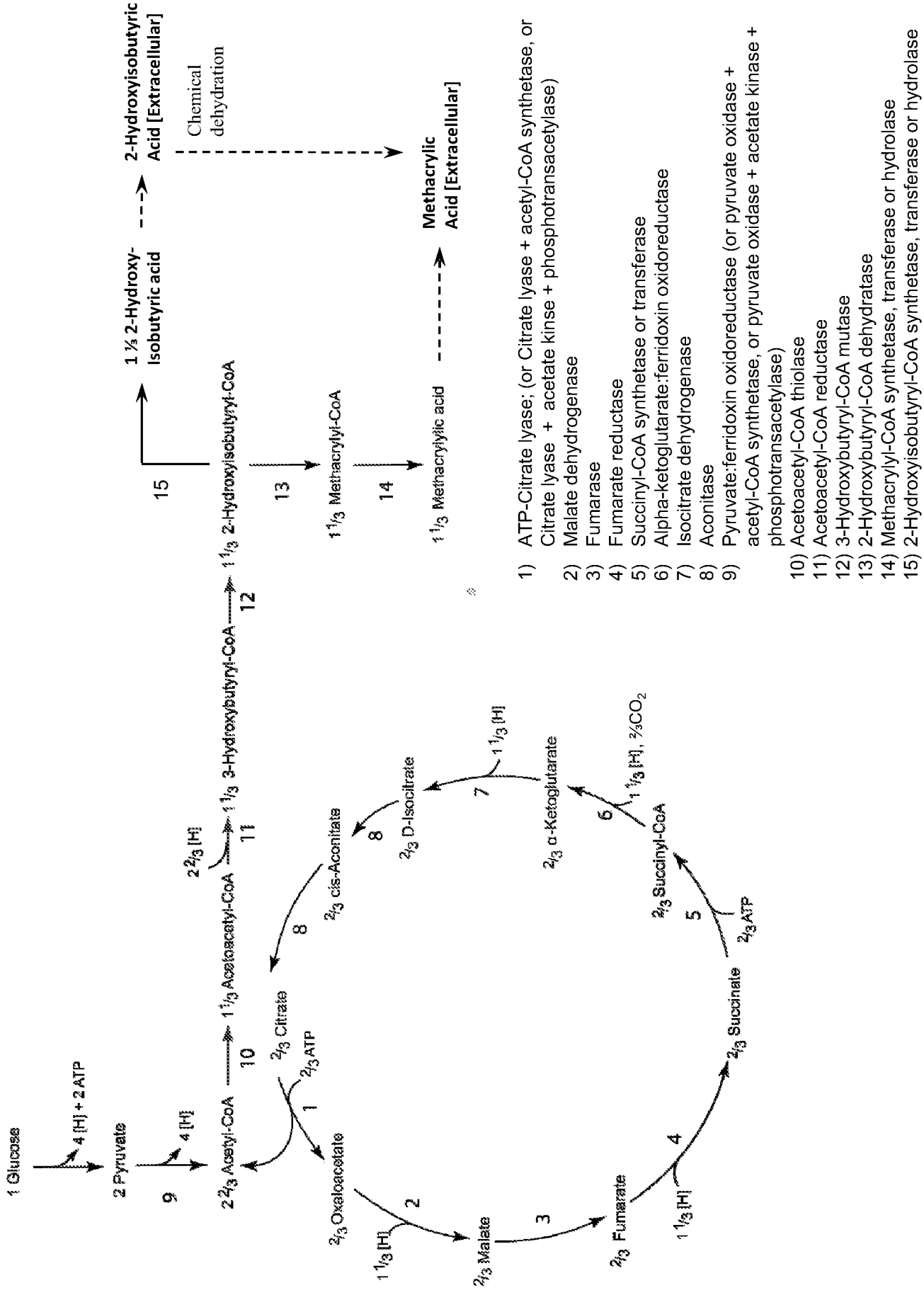
1) Hydrogenase
2) Carbon monoxide dehydrogenase
3) Succinyl-CoA transferase or synthetase
4) Methylmalonyl-CoA mutase
5) Methylmalonyl-CoA epimerase
6) Methylmalonyl-CoA reductase
7) Methylmalonate semialdehyde reductase
8) 3-Hydroxyisobutyrate dehydratase

Figure 16A



1) Hydrogenase
2) Carbon monoxide dehydrogenase
3) Succinyl-CoA transferase or synthetase
4) Succinyl-CoA reductase (aldehyde forming)
5) 4-Hydroxybutyrate dehydrogenase
6) 4-Hydroxybutyrate kinase
7) Phosphotrans-4-hydroxybutyrylase
8) Succinate reductase
9) Succinyl-CoA reductase (alcohol forming)
10) 4-Hydroxybutyryl-CoA synthetase or transferase
11) 4-Hydroxybutyryl-CoA mutase
12) 3-Hydroxyisobutyryl-CoA synthetase, transferase or hydrolase
13) 3-Hydroxyisobutyrate dehydratase
14) 3-Hydroxyisobutyryl-CoA dehydratase
15) Methacrylyl-CoA synthetase, transferase or hydrolase

Figure 16B



1) ATP-Citrate lyase; (or Citrate lyase + acetyl-CoA synthetase, or Citrate lyase + acetate kinse + phosphotransacetylase)
2) Malate dehydrogenase
3) Fumarase
4) Fumarate reductase
5) Succinyl-CoA synthetase or transferase
6) Alpha-ketoglutarate:ferridoxin oxidoreductase
7) Isocitrate dehydrogenase
8) Aconitase
9) Pyruvate:ferridoxin oxidoreductase (or pyruvate oxidase + acetyl-CoA synthetase, or pyruvate oxidase + acetate kinase + phosphotransacetylase)
10) Acetoacetyl-CoA thiolase
11) Acetoacetyl-CoA reductase
12) 3-Hydroxybutyryl-CoA mutase
13) 2-Hydroxybutyryl-CoA dehydratase
14) Methacrylyl-CoA synthetase, transferase or hydrolase
15) 2-Hydroxyisobutyryl-CoA synthetase, transferase or hydrolase

Figure 16C

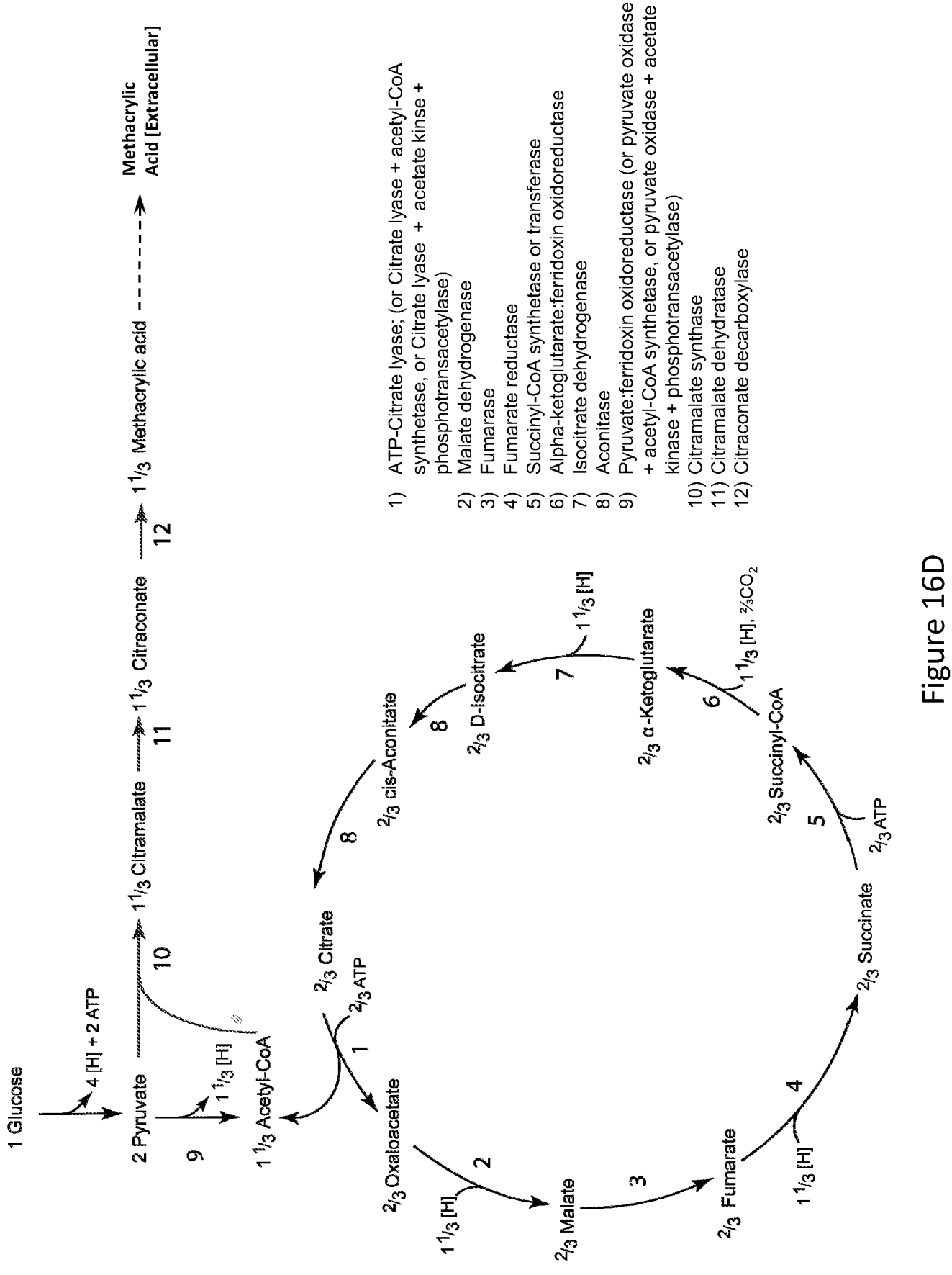
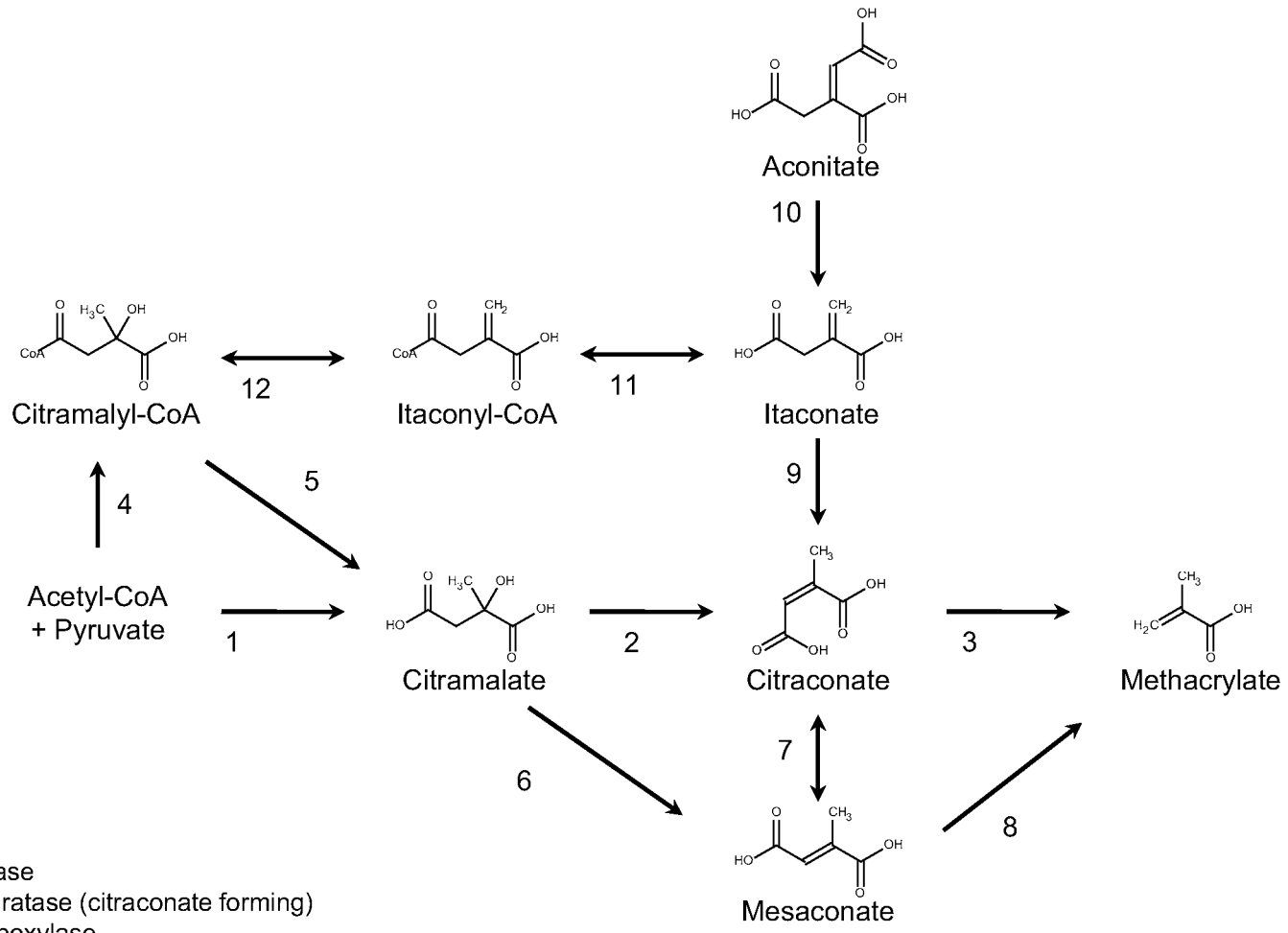

1 Glucose
4 [H] + 2 ATP
2 Pyruvate
1 1/3 [H]
1 1/3 Acetyl-CoA
1 1/3 Citramalate
1 1/3 Citraconate
1 1/3 Methacrylic acid
Methacrylic Acid [Extracellular]
2/3 Citrate
2/3 ATP
2/3 Oxaloacetate
1 1/3 [H]
2/3 Malate
2/3 Fumarate
1 1/3 [H]
2/3 Succinate
2/3 ATP
2/3 Succinyl-CoA
1 1/3 [H], 2/3CO2
2/3 α-Ketoglutarate
1 1/3 [H]
2/3 D-Isocitrate
2/3 cis-Aconitate
1) ATP-Citrate lyase; (or Citrate lyase + acetyl-CoA synthetase, or Citrate lyase + acetate kinse + phosphotransacetylase)
2) Malate dehydrogenase
3) Fumarase
4) Fumarate reductase
5) Succinyl-CoA synthetase or transferase
6) Alpha-ketoglutarate:ferridoxin oxidoreductase
7) Isocitrate dehydrogenase
8) Aconitase
9) Pyruvate:ferridoxin oxidoreductase (or pyruvate oxidase + acetyl-CoA synthetase, or pyruvate oxidase + acetate kinase + phosphotransacetylase)
10) Citramalate synthase
11) Citramalate dehydratase
12) Citraconate decarboxylase

Figure 16D



1. Citramalate synthase
2. Citramalate dehydratase (citraconate forming)
3. Citraconate decarboxylase
4. Citramalyl-CoA lyase
5. Citramalyl-CoA transferase, synthetase or hyrolase
6. Citramalate dehydratase (mesaconate forming)
7. Citraconate isomerase
8. Mesaconate decarboxylase
9. Aconitate decarboxylase
10. Itaconate isomerase
11. Itaconyl-CoA transferase or synthetase
12. Itaconyl-CoA hydratase

Figure 16E

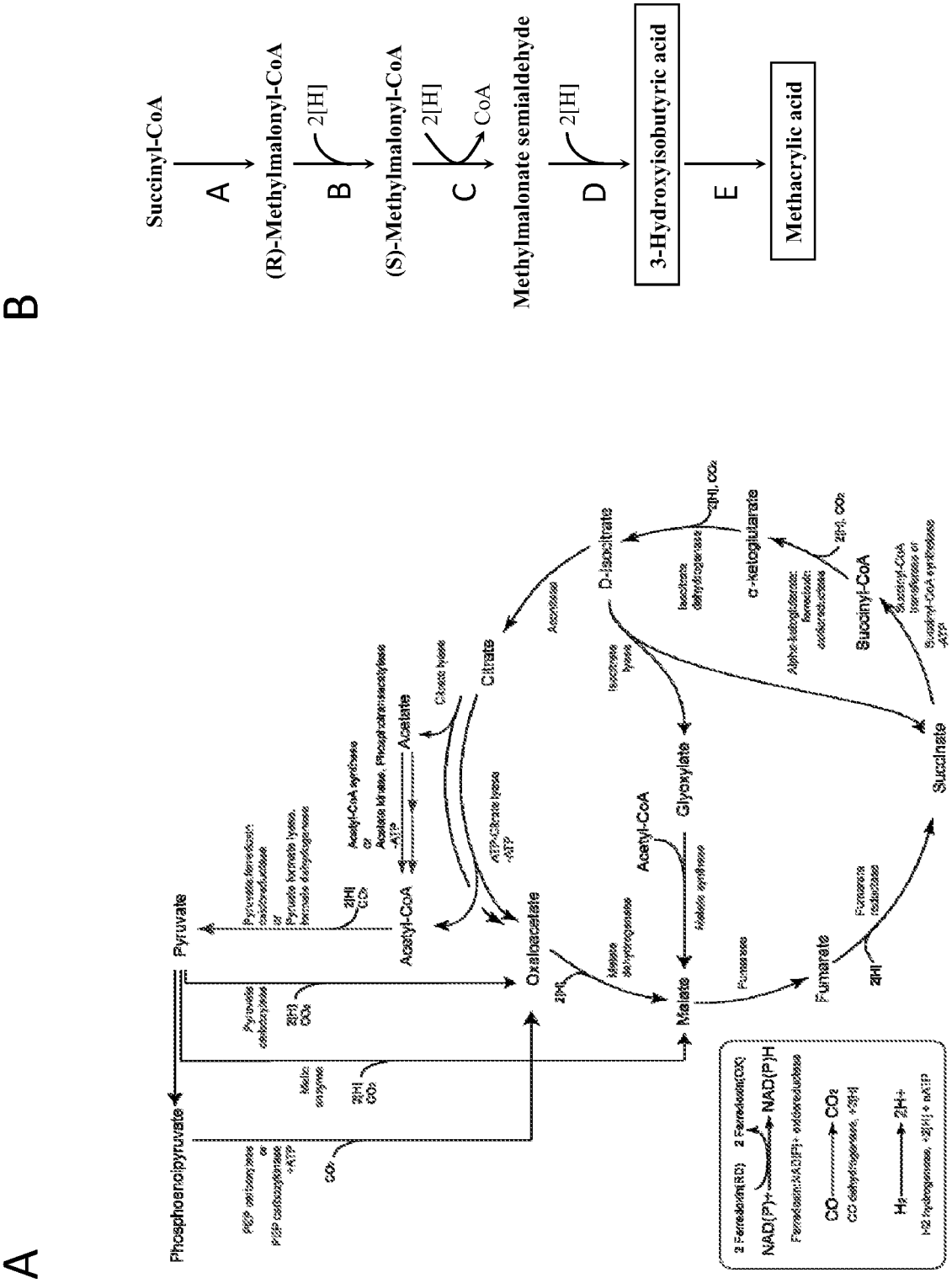

A
B
Succinyl-CoA
A
(R)-Methylmalonyl-CoA
2[H]
B
(S)-Methylmalonyl-CoA
2[H]
C
CoA
Methylmalonate semialdehyde
2[H]
D
3-Hydroxyisobutyric acid
E
Methacrylic acid
Phosphoenolpyruvate
Pyruvate
Oxaloacetate
Malate
Fumarate
Succinate
Citrate
Acetyl-CoA
Acetate
D-Isocitrate
α-ketoglutarate
Succinyl-CoA
Glyoxylate

Figure 17

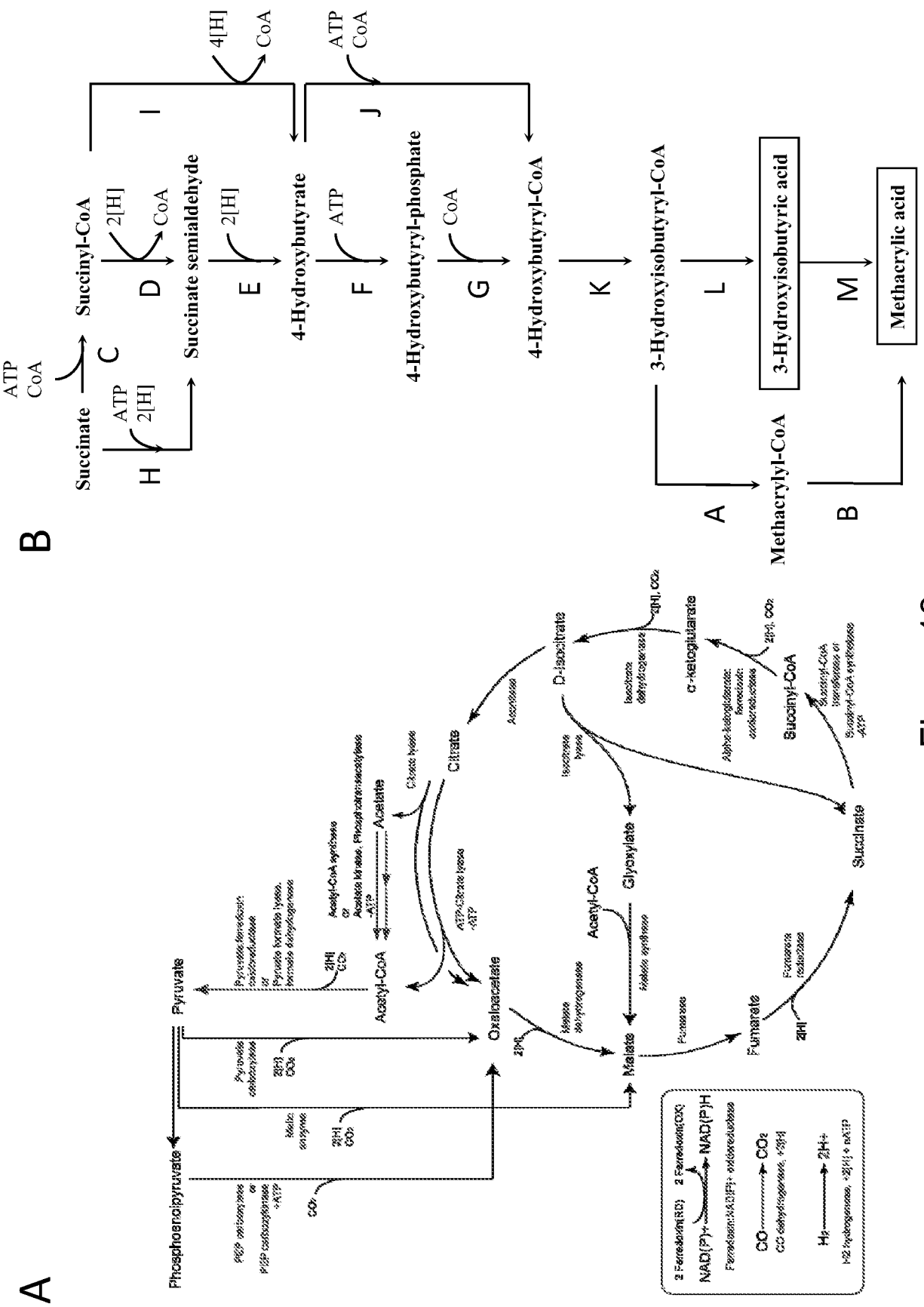

A
B
Succinate
Succinyl-CoA
Succinate semialdehyde
4-Hydroxybutyrate
4-Hydroxybutyryl-phosphate
4-Hydroxybutyryl-CoA
3-Hydroxyisobutyryl-CoA
3-Hydroxyisobutyric acid
Methacrylic acid
Methacrylyl-CoA
ATP
CoA
2[H]
4[H]
H
C
D
E
F
G
I
J
K
L
M
A
B
Phosphoenolpyruvate
Pyruvate
Oxaloacetate
Malate
Fumarate
Acetyl-CoA
Citrate
Acetate
Glyoxylate
D-Isocitrate
α-ketoglutarate
Succinyl-CoA
Succinate

Figure 18

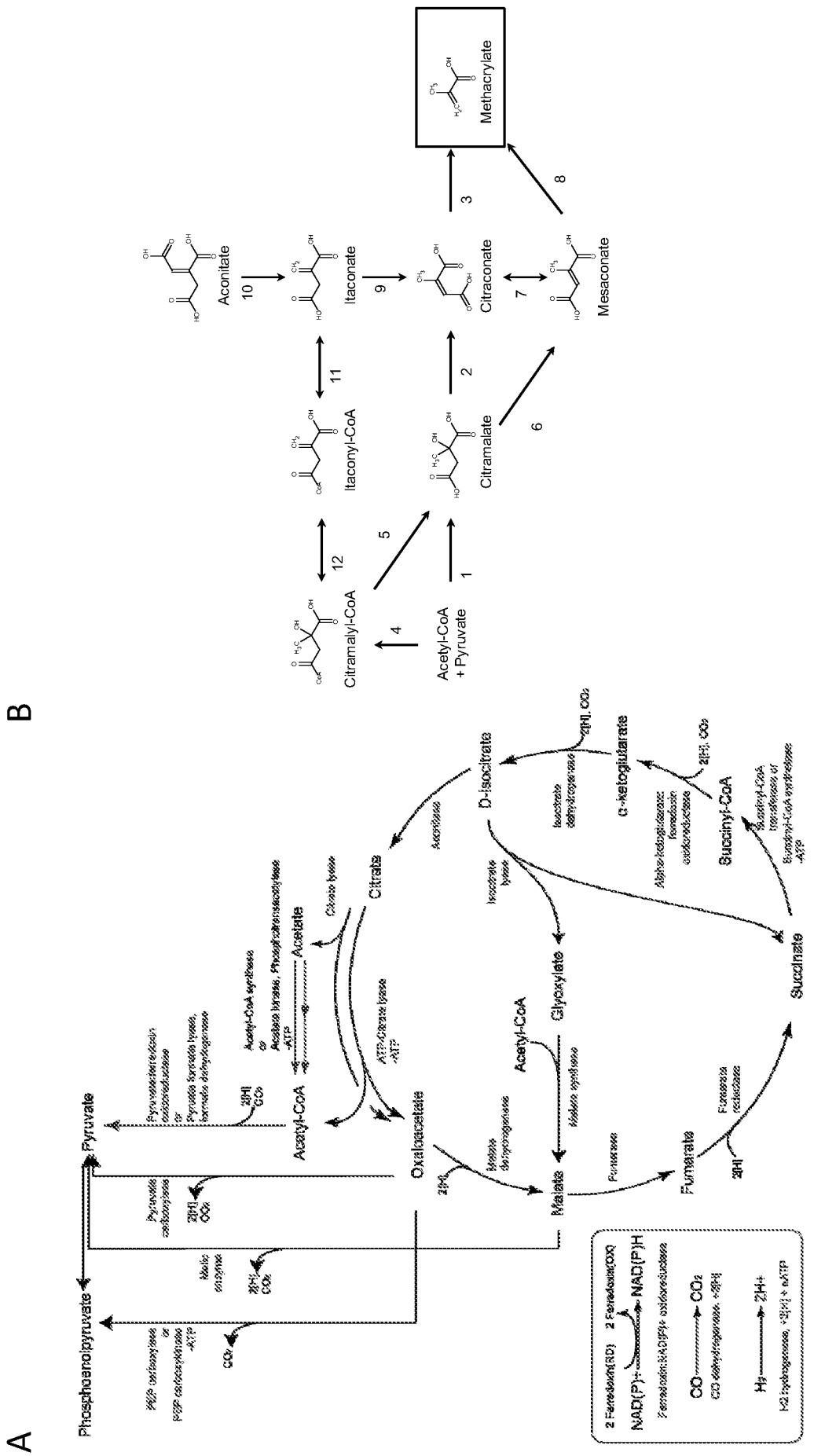

A
Phosphoenolpyruvate
Pyruvate
Acetyl-CoA
Acetate
Oxaloacetate
Citrate
Malate
Fumarate
Acetyl-CoA
Glyoxylate
D-isocitrate
α-ketoglutarate
Succinyl-CoA
Succinate
B
Acetyl-CoA + Pyruvate
Citramalyl-CoA
Citramalate
Itaconyl-CoA
Itaconate
Aconitate
Citraconate
Mesaconate
Methacrylate

Figure 19

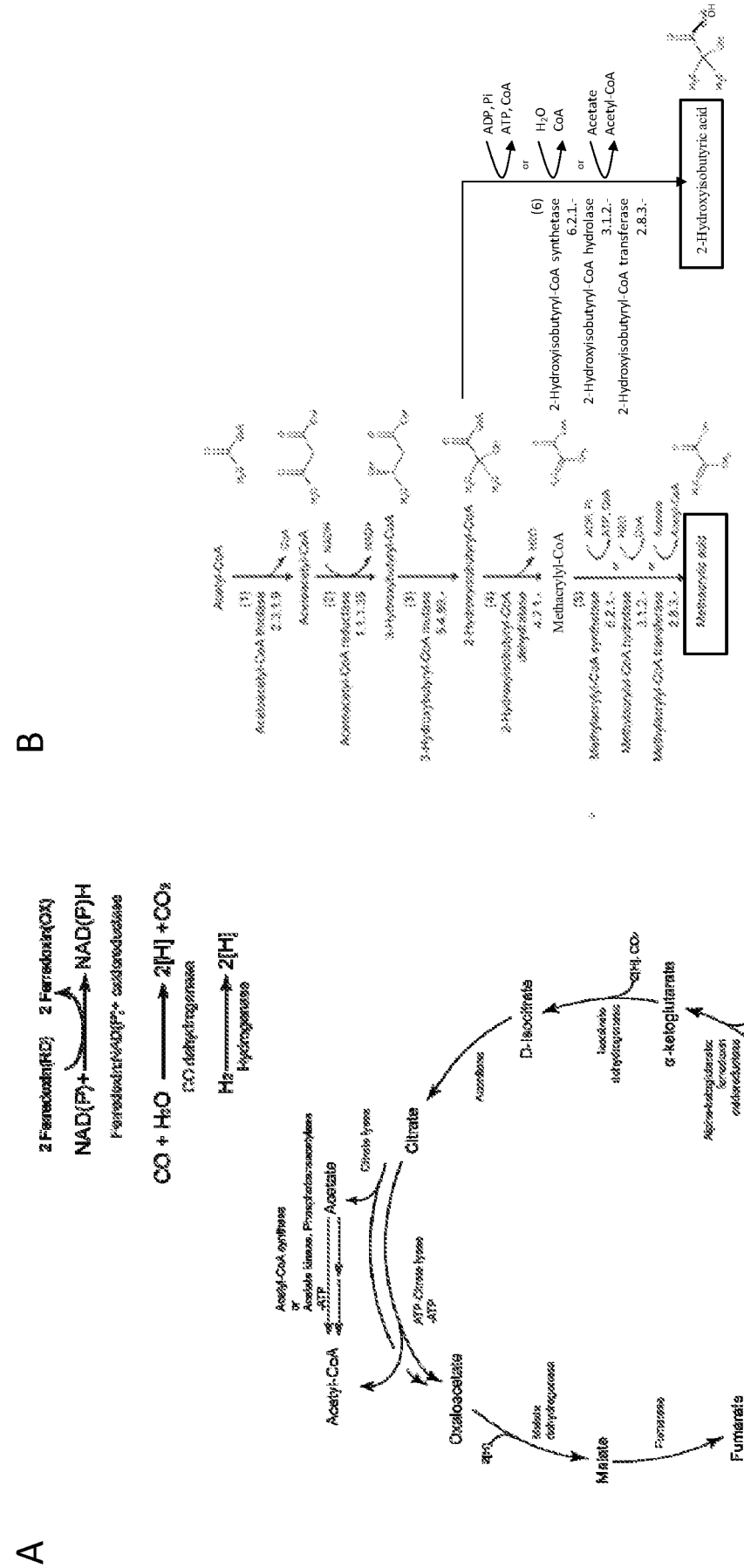

A
2 Ferredoxin(Red)
2 Ferredoxin(OX)
NAD(P)+
NAD(P)H
Ferredoxin:NAD(P)+ oxidoreductase
CO + H2O
2[H] +CO2
CO dehydrogenase
H2
2[H]
Hydrogenase
Acetyl-CoA synthase or Acetate kinase, Phosphotransacetylase
ATP
ADP
Acetate
Acetyl-CoA
Citrate lyase
ATP Citrate lyase
ATP
Citrate
Aconitase
D-Isocitrate
Isocitrate dehydrogenase
2[H], CO2
α-ketoglutarate
Alpha-ketoglutarate ferredoxin oxidoreductase
ADP, CO2
Succinyl-CoA
Succinyl-CoA synthetase or Succinyl-CoA synthetase ATP
Succinate
Fumarase
Fumarate reductase
2[H]
Fumarate
Fumarase
Malate
Malate dehydrogenase
ADP
Oxaloacetate
B
Acetyl-CoA
(1)
Acetoacetyl-CoA
(2)
3-Hydroxybutyryl-CoA
(3)
2-Hydroxyisobutyryl-CoA
(4)
Methacrylyl-CoA
(5)
Methacrylic acid
(6)
2-Hydroxyisobutyryl-CoA synthetase 6.2.1.-
2-Hydroxyisobutyryl-CoA hydrolase 3.1.2.-
2-Hydroxyisobutyryl-CoA transferase 2.8.3.-
ADP, Pi
ATP, CoA
or
H2O
CoA
or
Acetate
Acetyl-CoA
2-Hydroxyisobutyric acid
OH

Figure 20

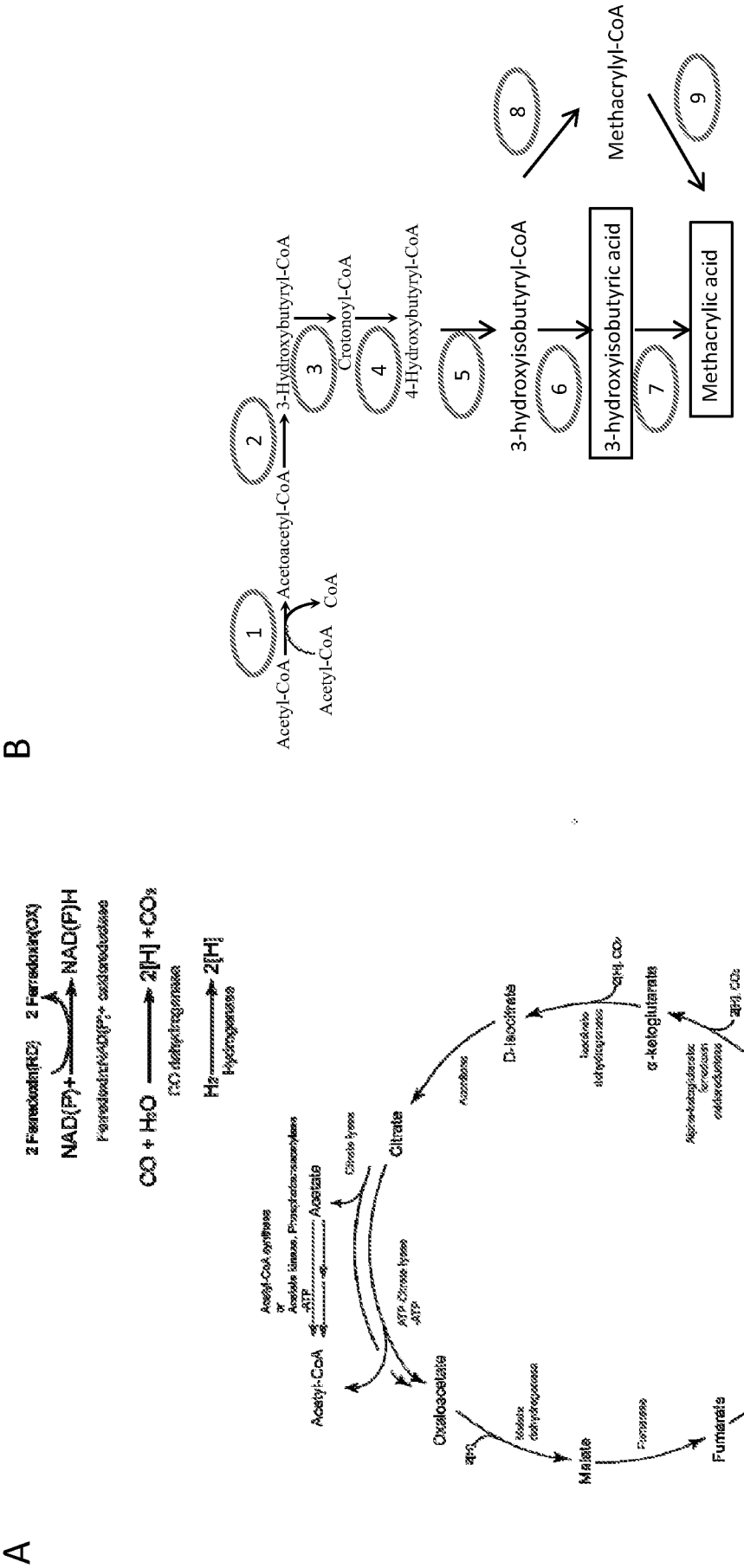

A
B
Acetyl-CoA
Acetoacetyl-CoA
CoA
3-Hydroxybutyryl-CoA
Crotonoyl-CoA
4-Hydroxybutyryl-CoA
3-hydroxyisobutyryl-CoA
3-hydroxyisobutyric acid
Methacrylyl-CoA
Methacrylic acid
1
2
3
4
5
6
7
8
9

Figure 21

ATGGCAGTGGATTCACCGGATGAGCGGCTACAGCGCCGCATTGCACAGTTGTTTGCAGAAGATG
AGCAGGTCAAGGCCGCACGTCCGCTCGAAGCGGTGAGCGCGGCGGTGAGCGCGCCCGGTATGCG
GCTGGCGCAGATCGCCGCCACTGTTATGGCGGGTTACGCCGACCGCCCGGCCGCCGGGCAGCGT
GCGTTCGAACTGAACACCGACGACGCGACGGGCCGCACCTCGCTGCGGTTACTTCCCCGATTCG
AGACCATCACCTATCGCGAACTGTGGCAGCGAGTCGGCGAGGTTGCCGCGGCCTGGCATCATGA
TCCCGAGAACCCCTTGCGCGCAGGTGATTTCGTCGCCCTGCTCGGCTTCACCAGCATCGACTAC
GCCACCCTCGACCTGGCCGATATCCACCTCGGCGCGGTTACCGTGCCGTTGCAGGCCAGCGCGG
CGGTGTCCCAGCTGATCGCTATCCTCACCGAGACTTCGCCGCGGCTGCTCGCCTCGACCCCGGA
GCACCTCGATGCGGCGGTCGAGTGCCTACTCGCGGGCACCACACCGGAACGACTGGTGGTCTTC
GACTACCACCCCGAGGACGACGACCAGCGTGCGGCCTTCGAATCCGCCCGCCGCCGCCTTGCCG
ACGCGGGCAGCTTGGTGATCGTCGAAACGCTCGATGCCGTGCGTGCCCGGGGCCGCGACTTACC
GGCCGCGCCACTGTTCGTTCCCGACACCGACGACGACCCGCTGGCCCTGCTGATCTACACCTCC
GGCAGCACCGGAACGCCGAAGGGCGCGATGTACACCAATCGGTTGGCCGCCACGATGTGGCAGG
GGAACTCGATGCTGCAGGGGAACTCGCAACGGGTCGGGATCAATCTCAACTACATGCCGATGAG
CCACATCGCCGGTCGCATATCGCTGTTCGGCGTGCTCGCTCGCGGTGGCACCGCATACTTCGCG
GCCAAGAGCGACATGTCGACACTGTTCGAAGACATCGGCTTGGTACGTCCCACCGAGATCTTCT
TCGTCCCGCGCGTGTGCGACATGGTCTTCCAGCGCTATCAGAGCGAGCTGGACCGGCGCTCGGT
GGCGGGCGCCGACCTGGACACGCTCGATCGGGAAGTGAAAGCCGACCTCCGGCAGAACTACCTC
GGTGGGCGCTTCCTGGTGGCGGTCGTCGGCAGCGCGCCGCTGGCCGCGGAGATGAAGACGTTCA
TGGAGTCCGTCCTCGATCTGCCACTGCACGACGGGTACGGGTCGACCGAGGCGGGCGCAAGCGT
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CGATTCCGGGCTACTACAAGCGGCCCGAGGTCACCGCGGAGATCTTCGACGAGGACGGCTTCTA
CAAGACCGGCGATATCGTGGCCGAGCTCGAGCACGATCGGCTGGTCTATGTCGACCGTCGCAAC
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CCCCAATCTGAAGGAACGCTACGGCGCTCAGCTGGAGCAGATGTACACCGATCTCGCGACAGGC
CAGGCCGATGAGCTGCTCGCCCTGCGCCGCGAAGCCGCCGACCTGCCGGTGCTCGAAACCGTCA
GCCGGGCAGCGAAAGCGATGCTCGGCGTCGCCTCCGCCGATATGCGTCCCGACGCGCACTTCAC
CGACCTGGGCGGCGATTCCCTTTCCGCGCTGTCGTTCTCGAACCTGCTGCACGAGATCTTCGGG
GTCGAGGTGCCGGTGGGTGTCGTCGTCAGCCCGGCGAACGAGCTGCGCGATCTGGCGAATTACA
TTGAGGCGGAACGCAACTCGGGCGCGAAGCGTCCCACCTTCACCTCGGTGCACGGCGGCGGTTC
CGAGATCCGCGCCGCCGATCTGACCCTCGACAAGTTCATCGATGCCCGCACCCTGGCCGCCGCC
GACAGCATTCCGCACGCGCCGGTGCCAGCGCAGACGGTGCTGCTGACCGGCGCGAACGGCTACC
TCGGCCGGTTCCTGTGCCTGGAATGGCTGGAGCGGCTGGACAAGACGGGTGGCACGCTGATCTG
CGTCGTGCGCGGTAGTGACGCGGCCGCGGCCCGTAAACGGCTGGACTCGGCGTTCGACAGCGGC
GATCCCGGCCTGCTCGAGCACTACCAGCAACTGGCCGCACGGACCCTGGAAGTCCTCGCCGGTG
ATATCGGCGACCCGAATCTCGGTCTGGACGACGCGACTTGGCAGCGGTTGGCCGAAACCGTCGA
CCTGATCGTCCATCCCGCCGCGTTGGTCAACCACGTCCTTCCCTACACCCAGCTGTTCGGCCCC

FIGURE 22A

AATGTCGTCGGCACCGCCGAAATCGTCCGGTTGGCGATCACGGCGCGGCGCAAGCCGGTCACCT
ACCTGTCGACCGTCGGAGTGGCCGACCAGGTCGACCCGGCGGAGTATCAGGAGGACAGCGACGT
CCGCGAGATGAGCGCGGTGCGCGTCGTGCGCGAGAGTTACGCCAACGGCTACGGCAACAGCAAG
TGGGCGGGGGAGGTCCTGCTGCGCGAAGCACACGATCTGTGTGGCTTGCCGGTCGCGGTGTTCC
GTTCGGACATGATCCTGGCGCACAGCCGGTACGCGGGTCAGCTCAACGTCCAGGACGTGTTCAC
CCGGCTGATCCTCAGCCTGGTCGCCACCGGCATCGCGCCGTACTCGTTCTACCGAACCGACGCG
GACGGCAACCGGCAGCGGGCCCACTATGACGGCTTGCCGGCGGACTTCACGGCGGCGGCGATCA
CCGCGCTCGGCATCCAAGCCACCGAAGGCTTCCGGACCTACGACGTGCTCAATCCGTACGACGA
TGGCATCTCCCTCGATGAATTCGTCGACTGGCTCGTCGAATCCGGCCACCCGATCCAGCGCATC
ACCGACTACAGCGACTGGTTCCACCGTTTCGAGACGGCGATCCGCGCGCTGCCGGAAAAGCAAC
GCCAGGCCTCGGTGCTGCCGTTGCTGGACGCCTACCGCAACCCCTGCCCGGCGGTCCGCGGCGC
GATACTCCCGGCCAAGGAGTTCCAAGCGGCGGTGCAAACAGCCAAAATCGGTCCGGAACAGGAC
ATCCCGCATTTGTCCGCGCCACTGATCGATAAGTACGTCAGCGATCTGGAACTGCTTCAGCTGC
TCTAA

FIGURE 22A CONT.

mavdspderlqrriaqlfaedeqvkaarpleavsaavsapgmrlaqiaatvmagyadrpaagqr
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tdysdwfhrfetairalpekqrqasvlplldayrnpcpavrgailpakefqaavqtakigpeqd
iphlsaplidkyvsdlellqll*

FIGURE 22B

FIGURE 23A

ATGATTGAAACCATTCTGCCTGCAGGCGTTGAAAGCGCAGAACTGCTGGAATATCCGGAAGATC
TGAAAGCACATCCGGCAGAAGAACATCTGATTGCCAAAAGCGTTGAAAAACGTCGTCGTGATTT
TATTGGTGCACGTCATTGTGCACGTCTGGCACTGGCAGAACTGGGTGAACCTCCGGTTGCAATT
GGTAAAGGTGAACGTGGTGCACCGATTTGGCCTCGTGGTGTTGTTGGTAGCCTGACCCATTGTG
ATGGTTATCGTGCAGCAGCAGTTGCACATAAAATGCGCTTTCGCAGCATTGGTATTGATGCAGA
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ATAAAGCCTGGTGGCCGCTGACAGCACGTTGGCTGGGTTTTGAAGAAGCCCATATTACCTTTGA
AATTGAAGATGGTAGCGCAGATAGCGGTAATGGCACCTTTCATAGCGAACTGCTGGTTCCGGGT
CAGACCAATGATGGTGGTACACCGCTGCTGAGCTTTGATGGTCGTTGGCTGATTGCAGATGGTT
TTATTCTGACCGCAATTGCCTATGCCTAA

FIGURE 23B

mietilpagvesaelleypedlkahpaeehliaksvekrrrdfigarhcarlalaelgeppvai
gkgergapiwprgvvgslthcdgyraaavahkmrfrsigidaephatlpegvldsvslpperew
lkttdsalhldrllfcakeatykawwpltarwlgfeeahitfeiedgsadsgngtfhsellvpg
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FIGURE 24A

FIGURE 24B

MTSDVHDATDGVTETALDDEQSTRRIAELYATDPEFAAAAPLPAVVDAAHKPGLRLAEILQTLFTGYGDRPALGYRA
RELATDEGGRTVTRLLPRFDTLTYAQVWSRVQAVAAALRHNFAQPIYPGDAVATIGFASPDYLTLDLVCAYLGLVSV
PLQHNAPVSRLAPILAEVEPRILTVSAEYLDLAVESVRDVNSVSQLVVFDHHPEVDDHRDALARAREQLAGKGIAVT
TLDAIADEGAGLPAEPIYTADHDQRLAMILYTSGSTGAPKGAMYTEAMVARLWTMSFITGDPTPVINVNFMPLNHLG
GRIPISTAVQNGGTSYFVPESDMSTLFEDLALVRPTELGLVPRVADMLYQHHLATVDRLVTQGADELTAEKQAGAEL
REQVLGGRVITGFVSTAPLAAEMRAFLDITLGAHIVDGYGLTETGAVTRDGVIVRPPVIDYKLIDVPELGYFSTDKP
YPRGELLVRSQTLTPGYYKRPEVTASVFDRDGYYHTGDVMAETAPDHLVYVDRRNNVLKLAQGEFVAVANLEAVFSG
AALVRQIFVYGNSERSFLLAVVVPTPEALEQYDPAALKAALADSLQRTARDAELQSYEVPADFIVETEPFSAANGLL
SGVGKLLRPNLKDRYGQRLEQMYADIAATQANQLRELRRAAATQPVIDTLTQAAATTLGTGSEVASDAHFTDLGGDS
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ADRHLRVVAGDIGDPNLGLTPEIWHRLAAEVDLVVHPAALVNHVLPYRQLFGPNVVGTAEVIKLALTERIKPVTYLS
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DMFTRLLLSLLITGVAPRSFYIGDGERPRAHYPGLTVDFVAEAVTTLGAQQREGYVSYDVMNPHDDGISLDVFVDWL
IRAGHPIDRVDDYDDWVRRFETALTALPEKRRAQTVLPLLHAFRAPQAPLRGAPEPTEVFHAAVRTAKVGPGDIPHL
DEALIDKYIRDLREFGLI

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cgatagctcccaccgacgtgttccgggcagcggtgcaggaggcgaaaatcggccccgacaaagacattccgcacgtg
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FIGURE 25A

FIGURE 25B

MSTATHDERLDRRVHELIATDPQFAAAQPDPAITAALEQPGLRLPQIIRTVLDGYADRPALGQRVVEFVTDAKTGRT
SAQLLPRFETITYSEVAQRVSALGRALSDDAVHPGDRVCVLGFNSVDYATIDMALGAIGAVSVPLQTSAAISSLQPI
VAETEPTLIASSVNQLSDAVQLITGAEQAPTRLVVFDYHPQVDDQREAVQDAAARLSSTGVAVQTLAELLERGKDLP
AVAEPPADEDSLALLIYTSGSTGAPKGAMYPQSNVGKMWRRGSKNWFGESAASITLNFMPMSHVMGRSILYGTLGNG
GTAYFAARSDLSTLLEDLELVRPTELNFVPRIWETLYGEFQRQVERRLSEAGDAGERRAVEAEVLAEQRQYLLGGRF
TFAMTGSAPISPELRNWVESLLEMHLMDGYGSTEAGMVLFDGEIQRPPVIDYKLVDVPDLGYFSTDRPHPRGELLLR
TENMFPGYYKRAETTAGVFDEDGYYRTGDVFAEIAPDRLVYVDRRNNVLKLAQGEFVTLAKLEAVFGNSPLIRQIYV
YGNSAQPYLLAVVVPTEEALASGDPETLKPKIADSLQQVAKEAGLQSYEVPRDFIIETTPFSLENGLLTGIRKLAWP
KLKQHYGERLEQMYADLAAGQANELAELRRNGAQAPVLQTVSRAAGAMLGSAASDLSPDAHFTDLGGDSLSALTFGN
LLREIFDVDVPVGVIVSPANDLAAIASYIEAERQGSKRPTFASVHGRDATVVRAADLTLDKFLDAETLAAAPNLPKP
ATEVRTVLLTGATGFLGRYLALEWLERMDMVDGKVIALVRARSDEEARARLDKTFDSGDPKLLAHYQQLAADHLEVI
AGDKGEANLGLGQDVWQRLADTVDVIVDPAALVNHVLPYSELFGPNALGTAELIRLALTSKQKPYTYVSTIGVGDQI
EPGKFVENADIRQMSATRAINDSYANGYGNSKWAGEVLLREAHDLCGLPVAVFRCDMILADTTYAGQLNLPDMFTRL
MLSLVATGIAPGSFYELDADGNRQRAHYDGLPVEFIAAAISTLGSQITDSDTGFQTYHVMNPYDDGVGLDEYVDWLV
DAGYSIERIADYSEWLRRFETSLRALPDRQRQYSLLPLLHNYRTPEKPINGSIAPTDVFRAAVQEAKIGPDKDIPHV
SPPVIVKYITDLQLLGLL

atgtcgccaatcacgcgtgaagagcggctcgagcgccgcatccaggacctctacgccaacgacccgcagttcgccgc
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tgaccggatacgccgatcggccggctctcgctcagcgctcggtcgaattcgtgaccgacgccggcaccggccacacc
acgctgcgactgctcccccacttcgaaaccatcagctacggcgagctttgggaccgcatcagcgcactggccgacgt
gctcagcaccgaacagacggtgaaaccgggcgaccgggtctgcttgttgggcttcaacagcgtcgactacgccacga
tcgacatgactttggcgcggctgggcgcggtggccgtaccactgcagaccagcgcggcgataacccagctgcagccg
atcgtcgccgagacccagcccaccatgatcgcggccagcgtcgacgcactcgctgacgccaccgaattggctctgtc
cggtcagaccgctacccgagtcctggtgttcgaccaccaccggcaggttgacgcacaccgcgcagcggtcgaatccg
cccgggagcgcctggccggctcggcggtcgtcgaaaccctggccgaggccatcgcgcgcggcgacgtgccccgcggt
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gctacgagccgtcgatcacgctgaacttcatgccaatgagccacgtcatgggccgccaaatcctgtacggcacgctg
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FIGURE 26A

FIGURE 26B

MSPITREERLERRIQDLYANDPQFAAAKPATAITAAIERPGLPLPQIIETVMTGYADRPALAQRSVEFVTDAGTGHT
TLRLLPHFETISYGELWDRISALADVLSTEQTVKPGDRVCLLGFNSVDYATIDMTLARLGAVAVPLQTSAAITQLQP
IVAETQPTMIAASVDALADATELALSGQTATRVLVFDHHRQVDAHRAAVESARERLAGSAVVETLAEAIARGDVPRG
ASAGSAPGTDVSDDSLALLIYTSGSTGAPKGAMYPRRNVATFWRKRTWFEGGYEPSITLNFMPMSHVMGRQILYGTL
CNGGTAYFVAKSDLSTLFEDLALVRPTELTFVPRVWDMVFDEFQSEVDRRLVDGADRVALEAQVKAEIRNDVLGGRY
TSALTGSAPISDEMKAWVEELLDMHLVEGYGSTEAGMILIDGAIRRPAVLDYKLVDVPDLGYFLTDRPHPRGELLVK
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ADQIPPSAFTEDADIRVISATRAVDDSYANGYSNSKWAGEVLLREAHDLCGLPVAVFRCDMILADTTWAGQLNVPDM
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FIGURE 27 A

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aa

Figure 27A Cont.

MSTATHDERLDRRVHELIATDPQFAAAQPDPAITAALEQPGLRLPQIIRTVLDGYADRPALGQR
VVEFVTDAKTGRTSAQLLPRFETITYSEVAQRVSALGRALSDDAVHPGDRVCVLGFNSVDYATI
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KGAMYPQSNVGKMWRRGSKNWFGESAASITLNFMPMSHVMGRSILYGTLGNGGTAYFAARSDLS
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VGVIVSPANDLAAIASYIEAERQGSKRPTFASVHGRDATVVRAADLTLDKFLDAETLAAAPNLP
KPATEVRTVLLTGATGFLGRYLALEWLERMDMVDGKVIALVRARSDEEARARLDKTFDSGDPKL
LAHYQQLAADHLEVIAGDKGEANLGLGQDVWQRLADTVDVIVDPAALVNHVLPYSELFGPNALG
TAELIRLALTSKQKPYTYVSTIGVGDQIEPGKFVENADIRQMSATRAINDSYANGYGNSKWAGE
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FIGURE 27B

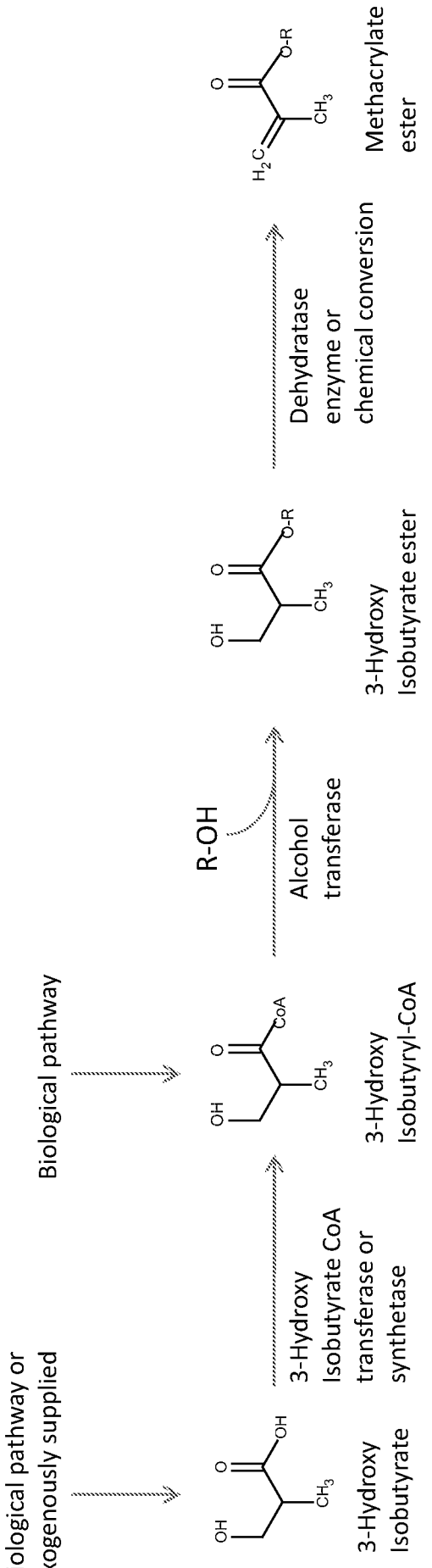

Biological pathway or
Exogenously supplied
3-Hydroxy
Isobutyrate
3-Hydroxy
Isobutyrate CoA
transferase or
synthetase
3-Hydroxy
Isobutyryl-CoA
Biological pathway
R-OH
Alcohol
transferase
3-Hydroxy
Isobutyrate ester
R-OH
3-Hydroxyisobutyrate
ester-forming enzyme
Dehydratase
enzyme or
chemical conversion
Methacrylate
ester

Figure 28

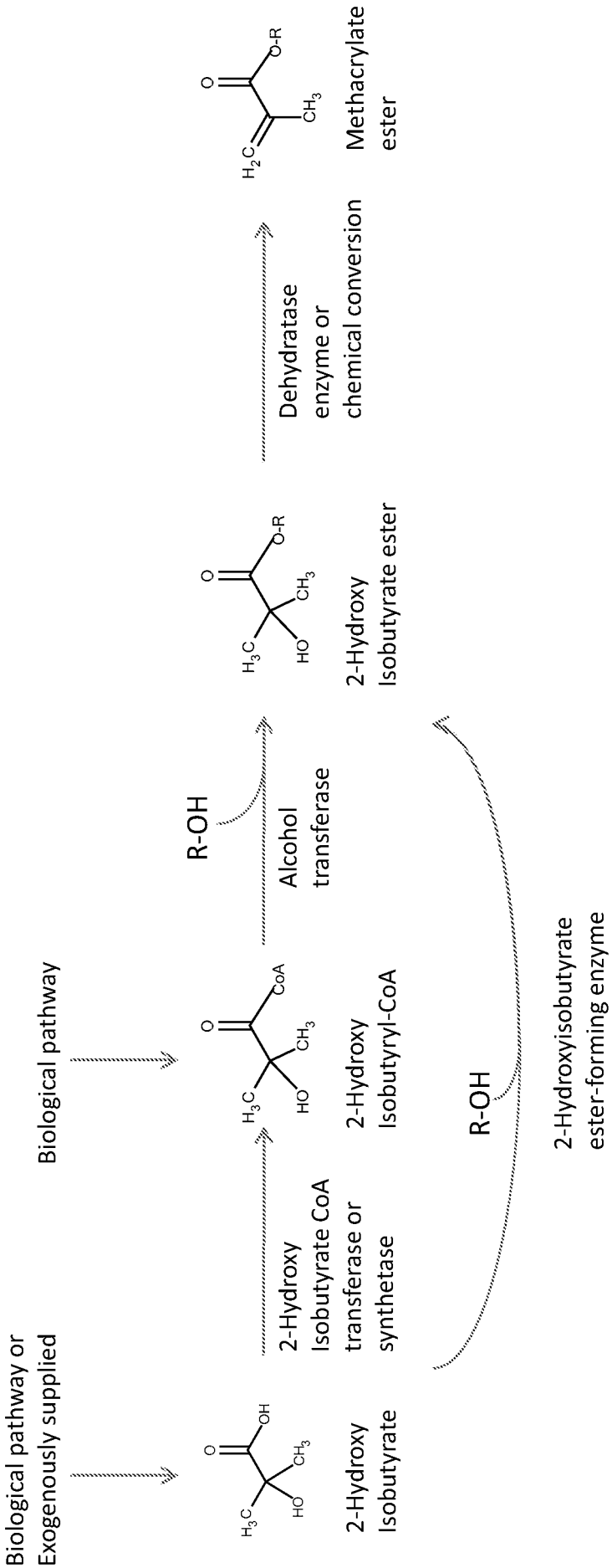

Biological pathway or
Exogenously supplied
2-Hydroxy
Isobutyrate
Biological pathway
2-Hydroxy
Isobutyrate CoA
transferase or
synthetase
2-Hydroxy
Isobutyryl-CoA
R-OH
Alcohol
transferase
2-Hydroxy
Isobutyrate ester
Dehydratase
enzyme or
chemical conversion
Methacrylate
ester
R-OH
2-Hydroxyisobutyrate
ester-forming enzyme

Figure 29

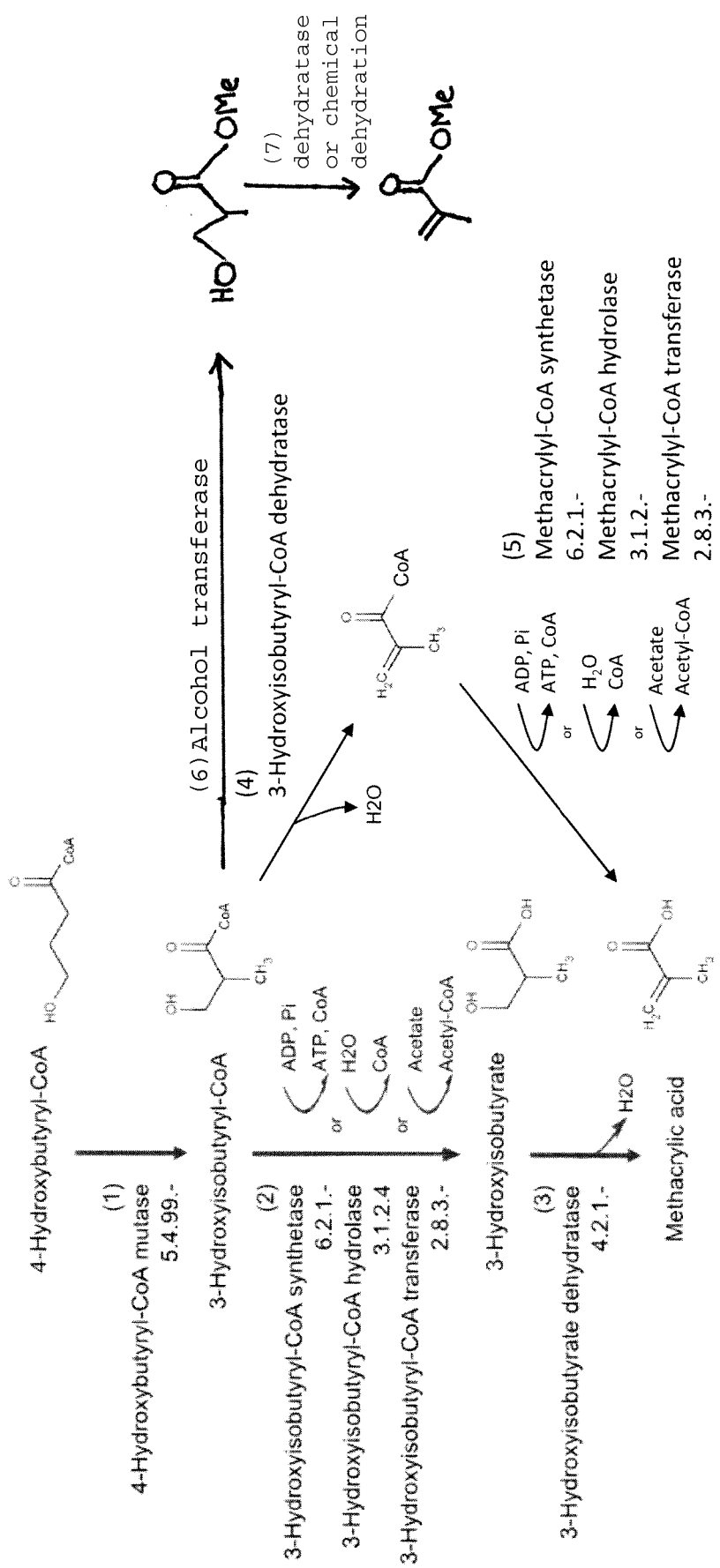

4-Hydroxybutyryl-CoA
(1)
4-Hydroxybutyryl-CoA mutase
5.4.99.-
3-Hydroxyisobutyryl-CoA
(2)
3-Hydroxyisobutyryl-CoA synthetase
6.2.1.-
3-Hydroxyisobutyryl-CoA hydrolase
3.1.2.4
3-Hydroxyisobutyryl-CoA transferase
2.8.3.-
ADP, Pi
ATP, CoA
or
H2O
CoA
or
Acetate
Acetyl-CoA
3-Hydroxyisobutyrate
(3)
3-Hydroxyisobutyrate dehydratase
4.2.1.-
H2O
Methacrylic acid
(6) Alcohol transferase
(4)
3-Hydroxyisobutyryl-CoA dehydratase
H2O
(5)
Methacrylyl-CoA synthetase
6.2.1.-
Methacrylyl-CoA hydrolase
3.1.2.-
Methacrylyl-CoA transferase
2.8.3.-
ADP, Pi
ATP, CoA
or
H2O
CoA
or
Acetate
Acetyl-CoA
(7)
dehydratase
or chemical
dehydration

FIGURE 30