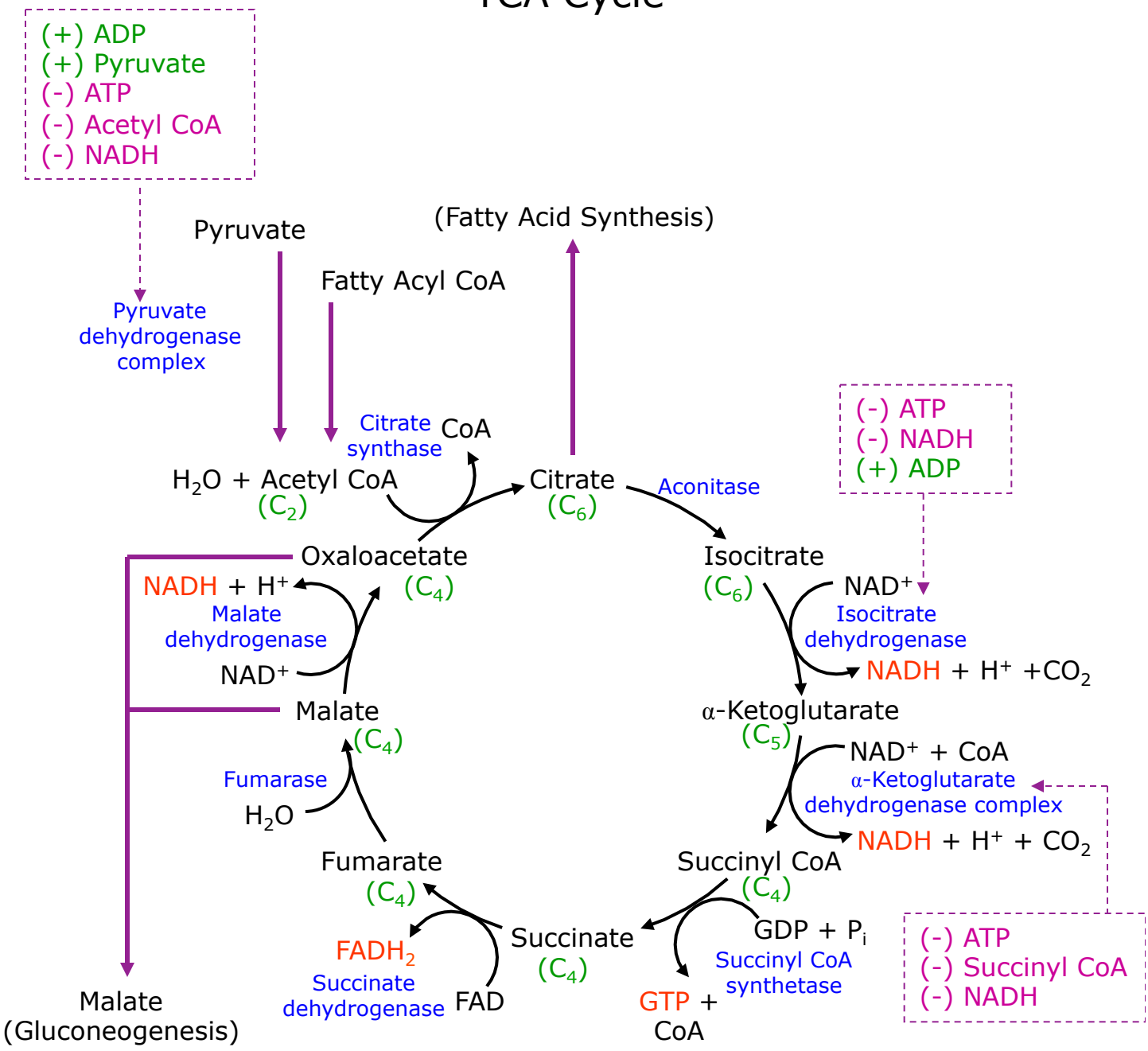
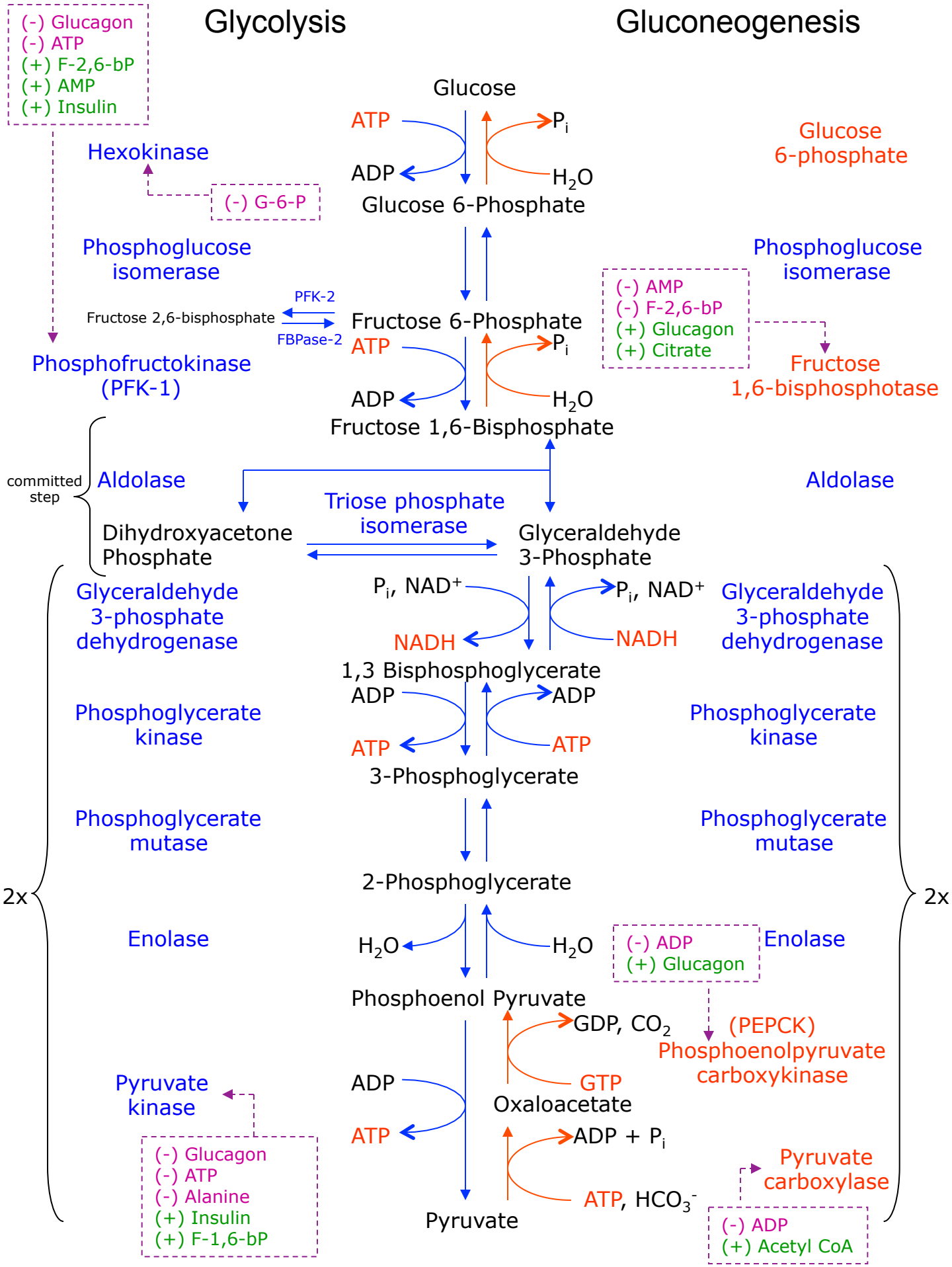
TCA Cycle


(+) ADP
(+) Pyruvate
(-) ATP
(-) Acetyl CoA
(-) NADH
Pyruvate
Pyruvate dehydrogenase complex
(Fatty Acid Synthesis)
Fatty Acyl CoA
Citrate synthase
CoA
H2O + Acetyl CoA
(C2)
Citrate
(C6)
Aconitase
(-) ATP
(-) NADH
(+) ADP
Oxaloacetate
(C4)
NADH + H+
Malate dehydrogenase
NAD+
Isocitrate
(C6)
NAD+
Isocitrate dehydrogenase
NADH + H+ +CO2
Malate
(C4)
α-Ketoglutarate
(C5)
NAD+ + CoA
α-Ketoglutarate dehydrogenase complex
NADH + H+ + CO2
Fumarase
H2O
Fumarate
(C4)
Succinyl CoA
(C4)
FADH2
Succinate dehydrogenase
FAD
Succinate
(C4)
GDP + Pi
Succinyl CoA synthetase
GTP + CoA
(-) ATP
(-) Succinyl CoA
(-) NADH
Malate
(Gluconeogenesis)


Glycolysis
Gluconeogenesis
(-) Glucagon
(-) ATP
(+) F-2,6-bP
(+) AMP
(+) Insulin
Glucose
ATP
ADP
P_i
H_2O
Glucose 6-Phosphate
Glucose 6-phosphate
Hexokinase
(-) G-6-P
Phosphoglucose isomerase
PFK-2
Fructose 2,6-bisphosphate
FBPase-2
Fructose 6-Phosphate
(-) AMP
(-) F-2,6-bP
(+) Glucagon
(+) Citrate
Phosphofructokinase (PFK-1)
Fructose 1,6-bisphosphotase
Fructose 1,6-Bisphosphate
committed step
Aldolase
Triose phosphate isomerase
Dihydroxyacetone Phosphate
Glyceraldehyde 3-Phosphate
Glyceraldehyde 3-phosphate dehydrogenase
P_i, NAD^+
NADH
1,3 Bisphosphoglycerate
Phosphoglycerate kinase
3-Phosphoglycerate
Phosphoglycerate mutase
2-Phosphoglycerate
Enolase
H_2O
(-) ADP
(+) Glucagon
Phosphoenol Pyruvate
GDP, CO_2
GTP
(PEPCK)
Phosphoenolpyruvate carboxykinase
Oxaloacetate
Pyruvate kinase
(-) Glucagon
(-) ATP
(-) Alanine
(+) Insulin
(+) F-1,6-bP
$ADP + P_i$
ATP, HCO_3^-
Pyruvate carboxylase
(-) ADP
(+) Acetyl CoA
Pyruvate
2x
2x

Other Sugars

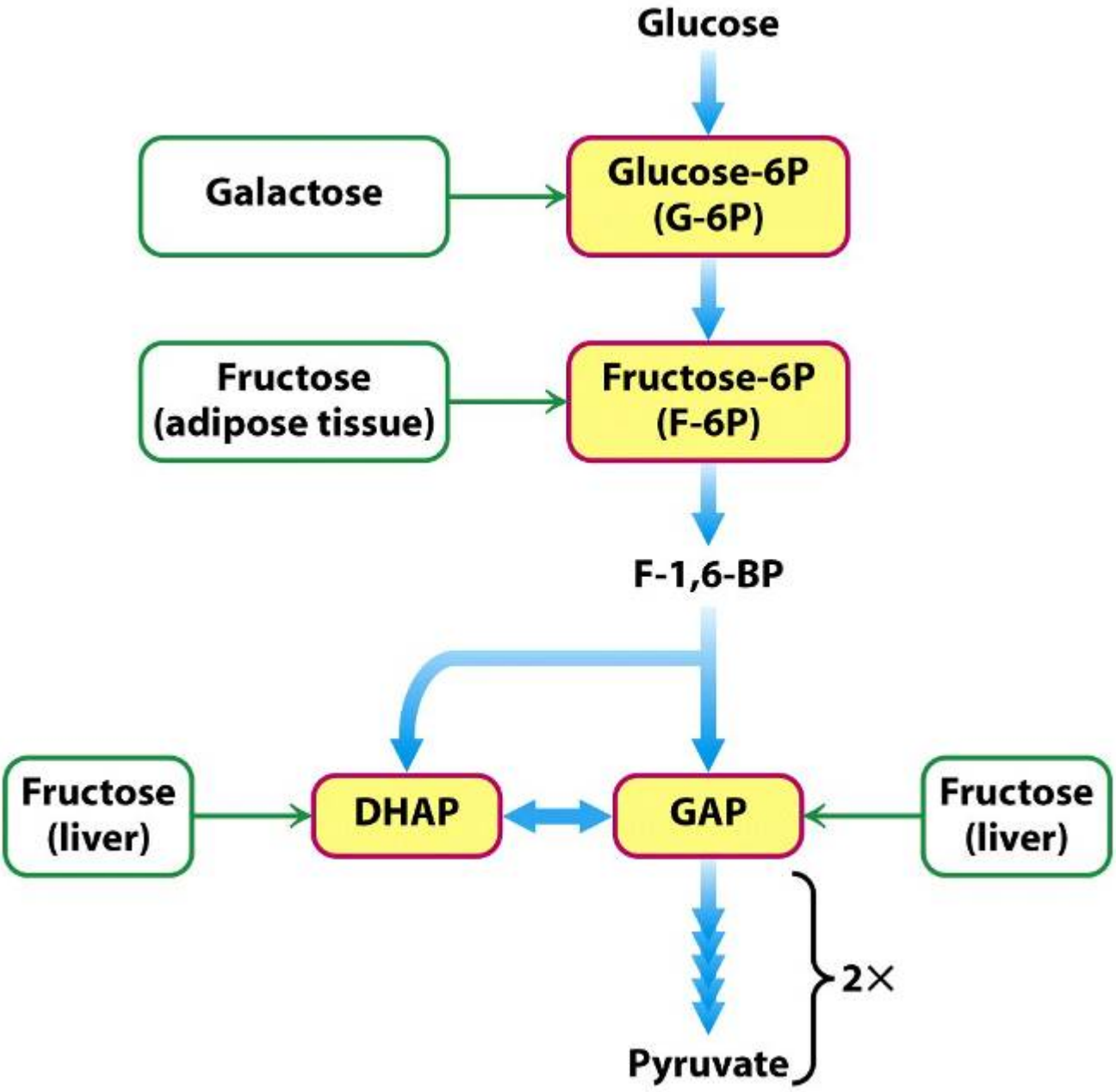
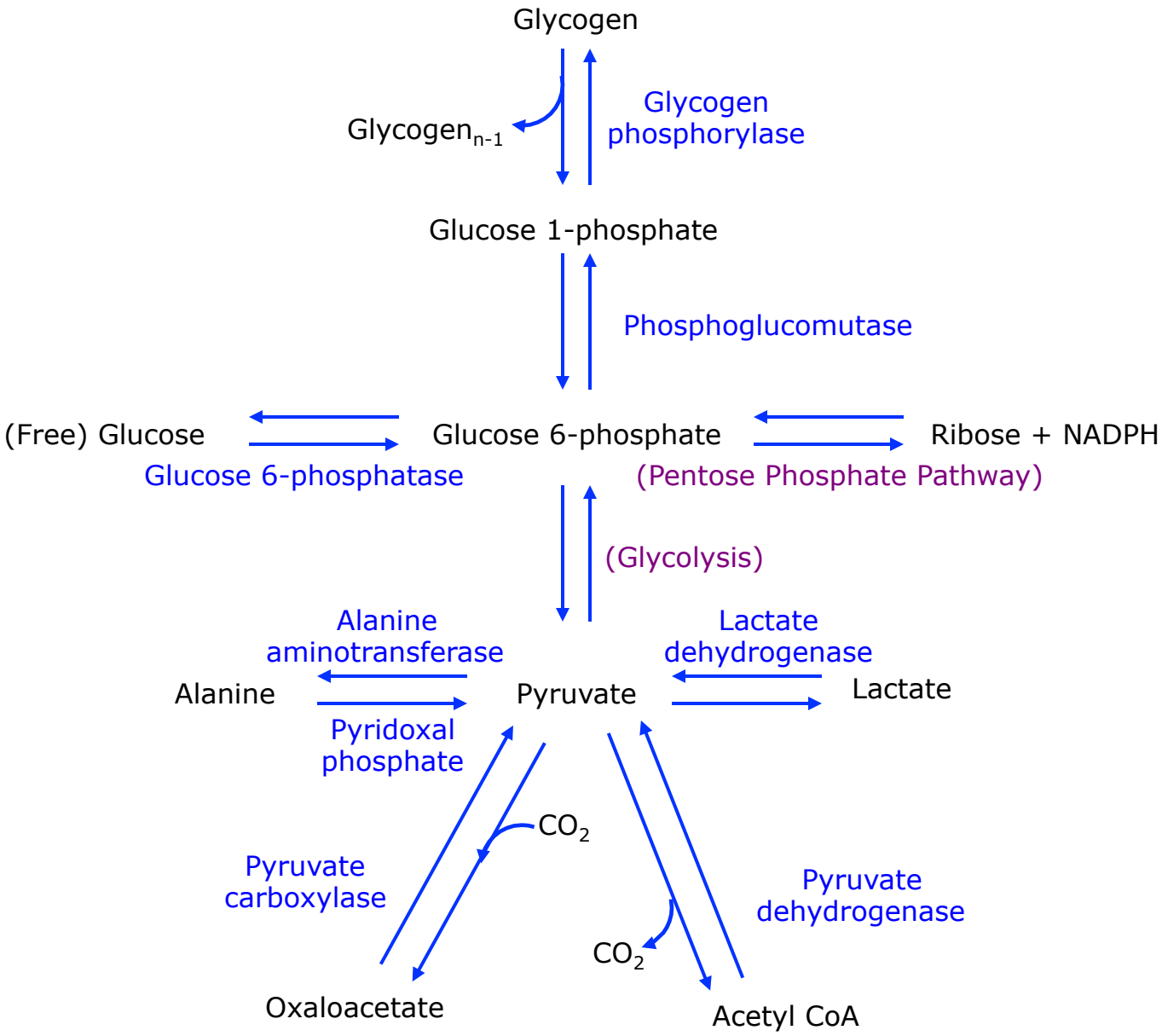
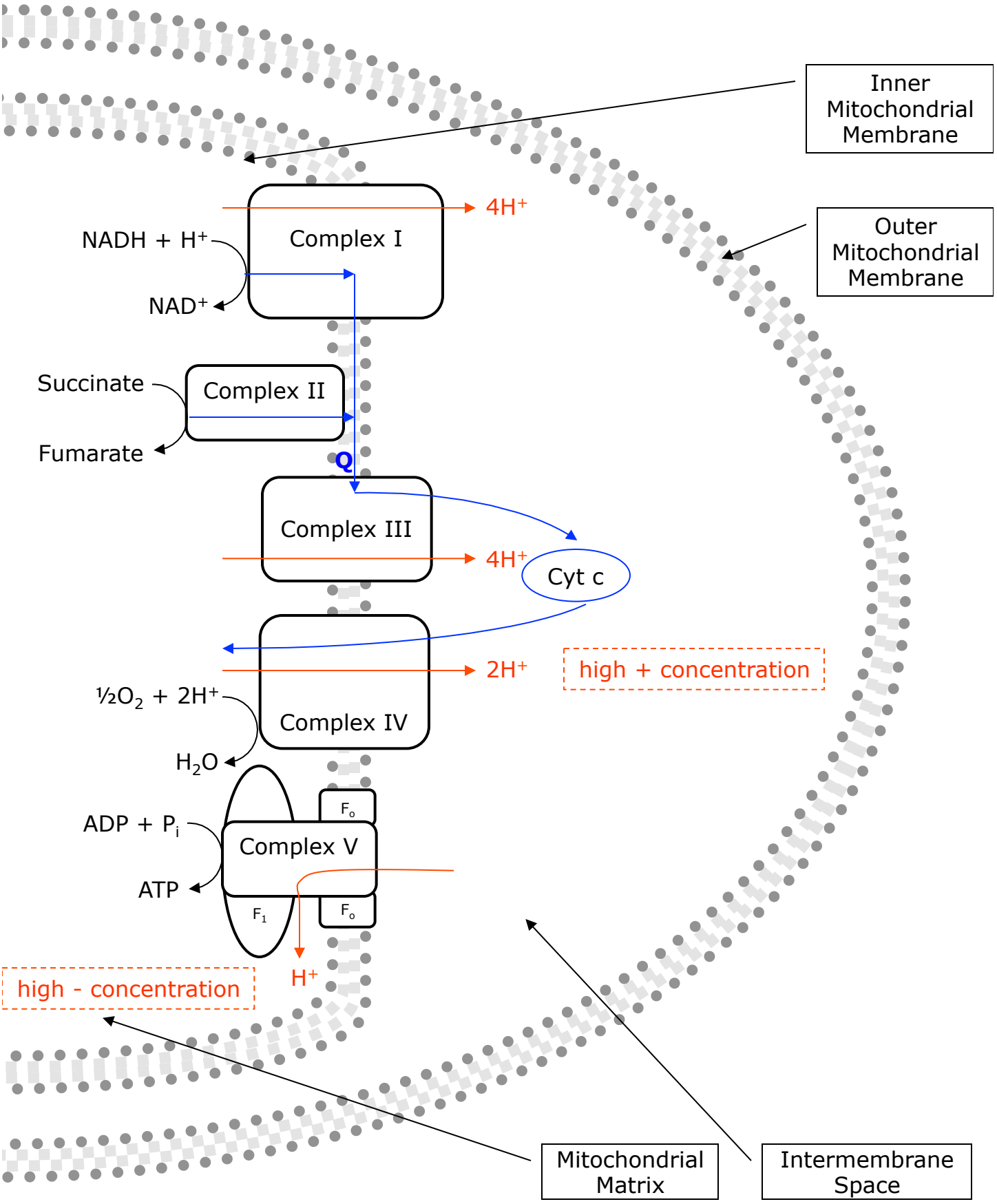


Figure 16-13
Biochemistry, Sixth Edition

Carbohydrate Connections



Oxidative Phosphorylation
(electron transport chain)



Glycogen Synthesis

- Glycogen is an alpha 1,4 chain of UDP-Glucose with alpha 1,6 branches
  - Uridine diphosphate glucose (UDP-Glucose) – activated form of glucose
  - C1 is reducing end
  - C4 is nonreducing end

- Phosphoglucomutase
  - Changes Glucose 6-phosphate to Glucose 1-phosphate
  - Normal cellular glucose is Glucose 6-phosphate
  - Glycogen synthesis requires Glucose 1-phosphate

- UDP-glucose pyrophosphorylase
  - Converts G-1-P to UDP-Glucose using UTP (uridine triphosphate)
  - PPi is a product driving this step toward UDP-G

- Glycogenin – protein bound to reducing end of primer
  - Adds first 8 glucose residues to itself

- Glycogen synthase (regulated step)
  - Takes over after 8 glucose residues, then adds linearly to chain
  - Regulated (inactivated) by Protein Kinase A (PKA) and Glycogen Synthase Kinase (GSK) – glucagon, epinephrine
  - Regulated (activated) by Protein phosphatase 1 (PP1)
  - a = active (R)
  - b-P = inactive (T)
  - Glucose 6-P (+) forces b-P into an (R) active state
  - Insulin (+) stimulates (Glucagon and epinephrine inhibit)

- Branching enzyme
  - Acts after chain is 11+ residues long
  - Clips the chain 7 residues from the end
  - Moves 4 residues farther up the chain
  - Creates the alpha 1,6 branch point

Glycogen Breakdown

- Glucose 1-Phosphate is the major product of Glycogen breakdown
  - Minor Product is free glucose

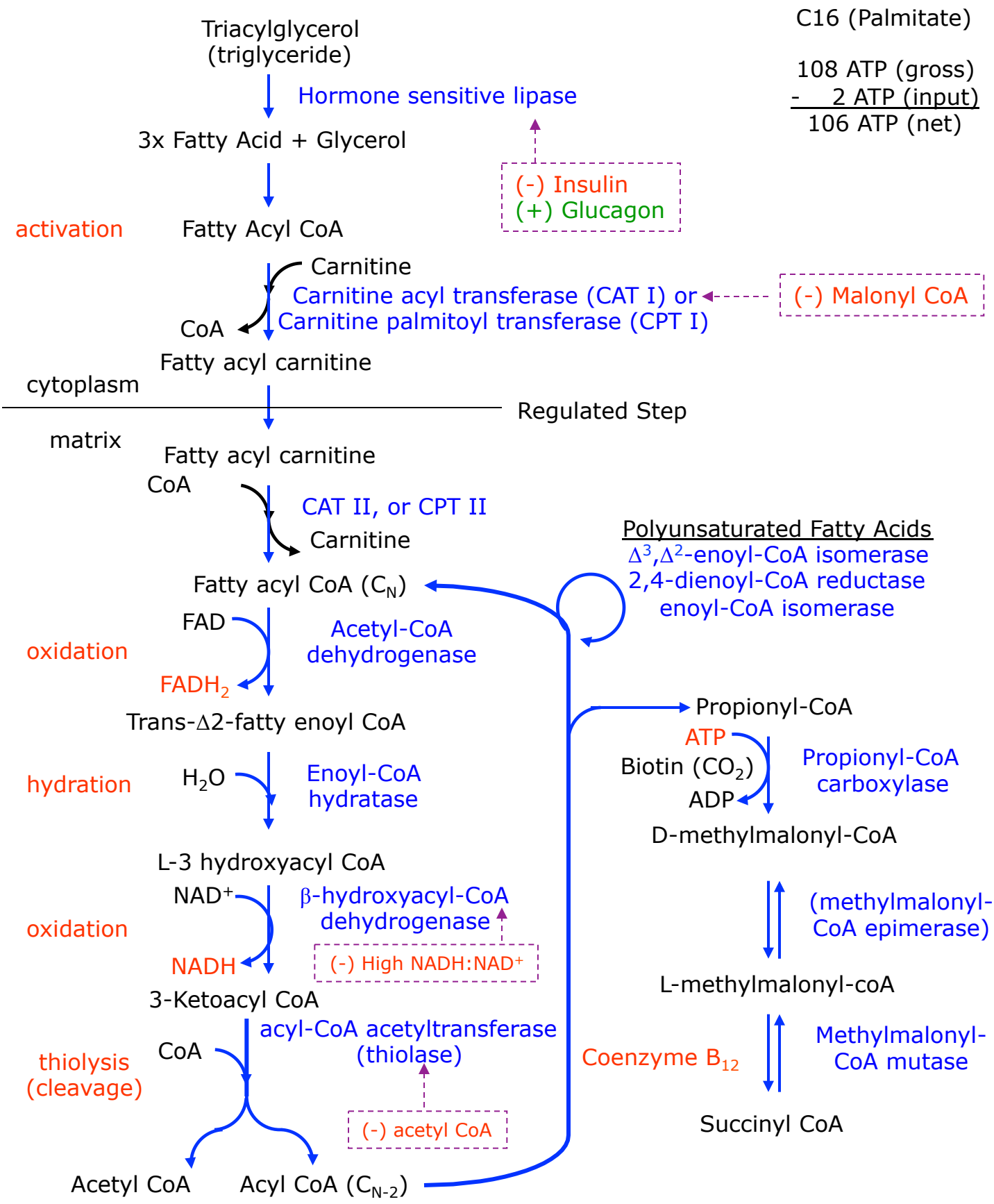
- Glycogen phosphorylase (regulated step)
  - Clips off a single glucose without adding water across the bond
  - Glucose residue is left unphosphorylated very transiently, so it won't leave the cell
  - Glycogen phosphorylase cannot clip within 4 residues of a branch point
  - Regulated (activated) by: (glucagon and epinephrine)
    - Protein Kinase A (PKA) phosphorylation
    - Increase in [Ca^{++}]
    - Can be super-stimulated by both increased [Ca^{++}] and phosphorylation (PKA)
  - Regulated (inactivated) by Protein phosphatase 1 (PP1)
  - a-P = active (R)
  - b = inactive (T)
  - Liver
    - Glucose (-) forces a-P to a (T) inactive state
    - Glucagon (+) stimulates (insulin inhibits)
  - Muscle
    - AMP (+) forces b into an (R) active state
    - ATP (-) holds b in a (T) inactive state
    - Glucose 6-P (-) holds b in a (T) inactive
    - Epinephrine (+) stimulates (insulin inhibits)

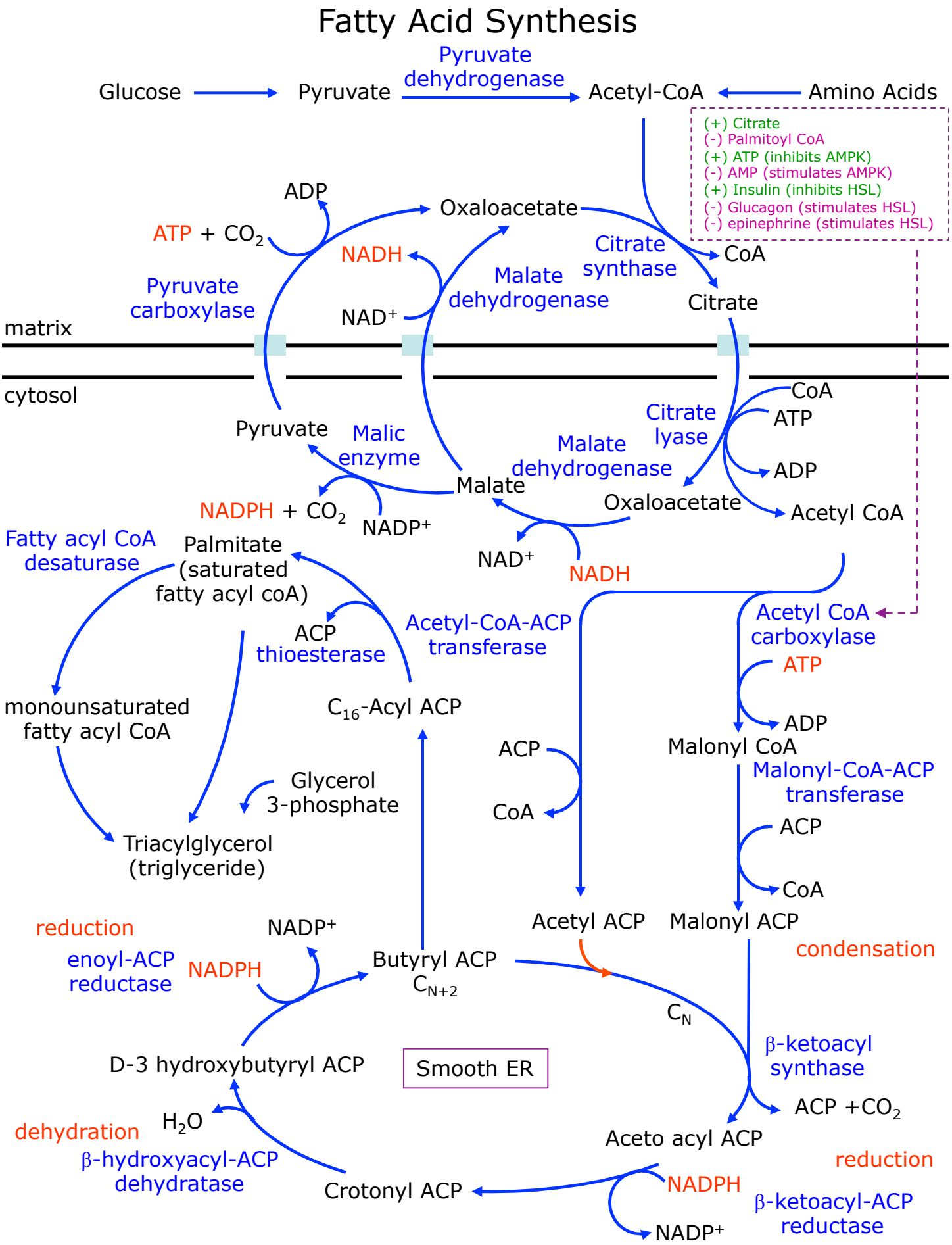
- Transferase (same polypeptide as debranching enzyme)
  - Clips off 3 of the last 4 glucose residues on a branch, then attaches them to the end of the next major chain

- Debranching enzyme (a.k.a. alpha-1,6-glucosidase)
  - Clips off the final glucose residue (uses hydrolysis)
  - Can lose this glucose unless it is phosphorylated by hexokinase

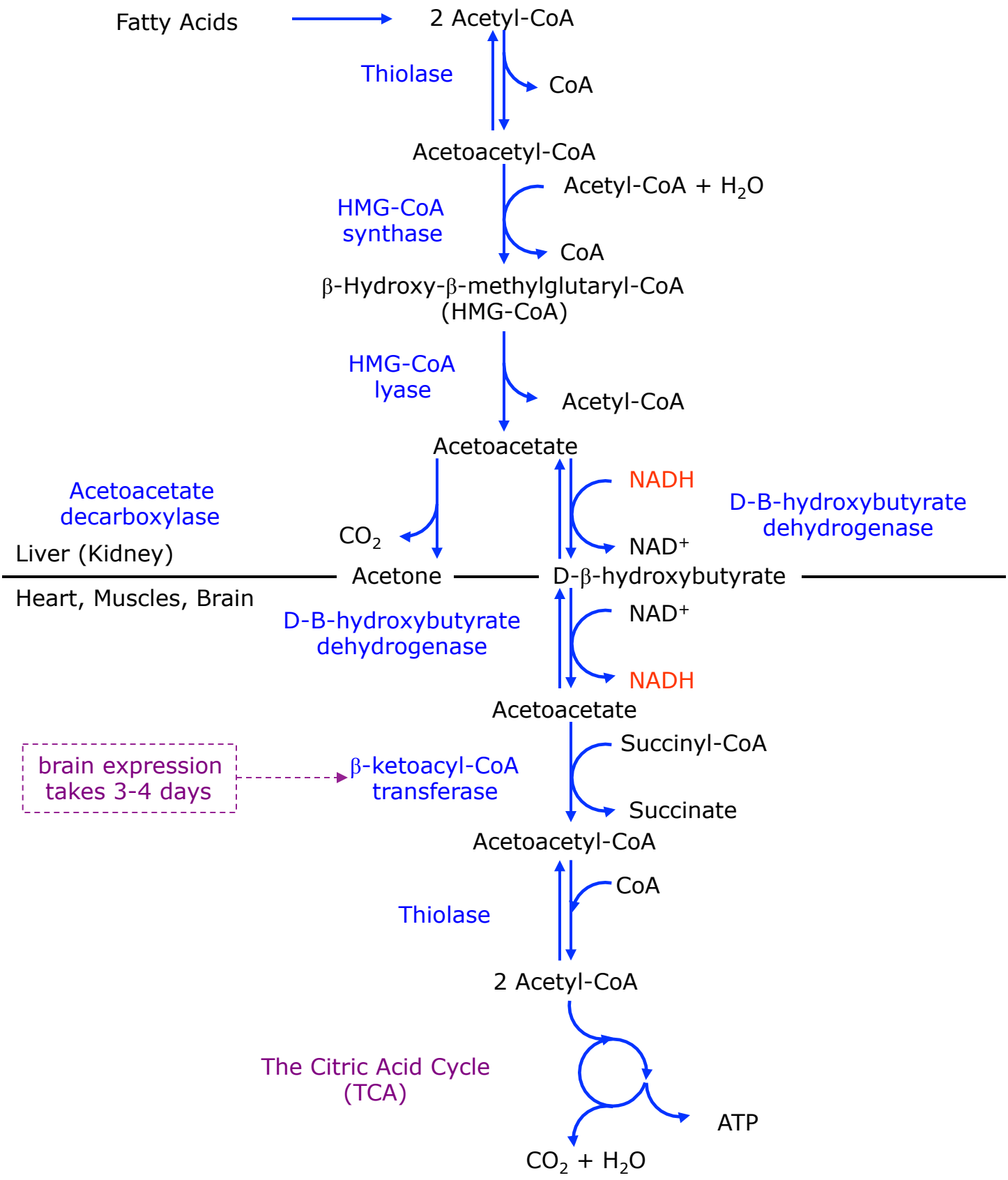
- Phosphoglucomutase
  - Converts Glucose 1-Phosphate to Glucose 6-Phosphate for use in the cell

Fatty Acid β-Oxidation (Degradation)

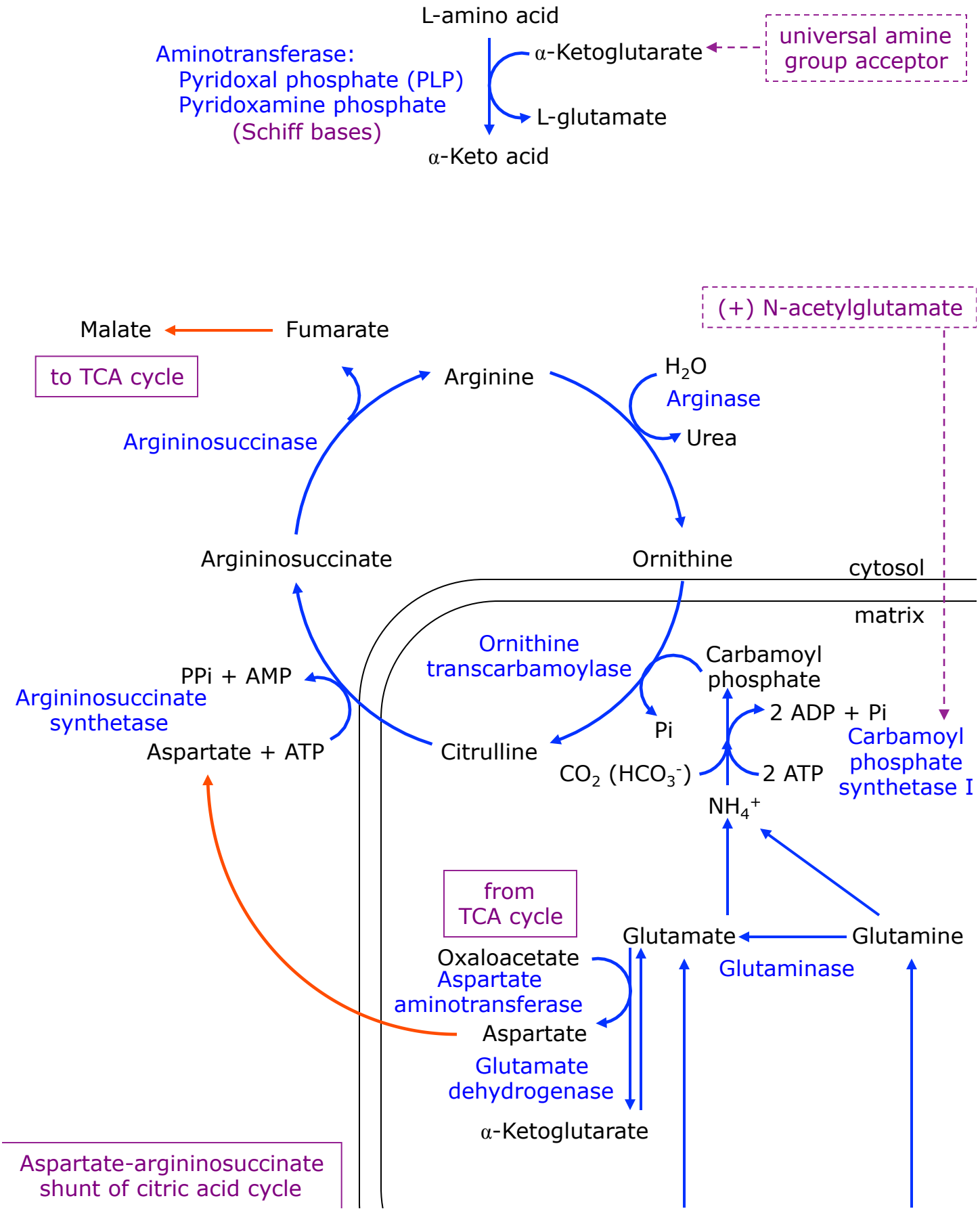



Fatty Acid Synthesis
Glucose
Pyruvate
Pyruvate dehydrogenase
Acetyl-CoA
Amino Acids
(+) Citrate
(-) Palmitoyl CoA
(+) ATP (inhibits AMPK)
(-) AMP (stimulates AMPK)
(+) Insulin (inhibits HSL)
(-) Glucagon (stimulates HSL)
(-) epinephrine (stimulates HSL)
ADP
ATP + CO2
Oxaloacetate
NADH
Citrate synthase
CoA
Pyruvate carboxylase
NAD+
Malate dehydrogenase
Citrate
matrix
cytosol
CoA
Citrate lyase
ATP
Pyruvate
Malic enzyme
Malate dehydrogenase
ADP
Malate
NADPH + CO2
NADP+
Oxaloacetate
Acetyl CoA
Fatty acyl CoA desaturase
Palmitate (saturated fatty acyl coA)
NAD+
NADH
Acetyl CoA carboxylase
ACP thioesterase
Acetyl-CoA-ACP transferase
ATP
monounsaturated fatty acyl CoA
C16-Acyl ACP
ADP
ACP
Malonyl CoA
Malonyl-CoA-ACP transferase
Glycerol 3-phosphate
CoA
ACP
Triacylglycerol (triglyceride)
CoA
reduction
NADP+
Acetyl ACP
Malonyl ACP
condensation
enoyl-ACP reductase
NADPH
Butyryl ACP
CN+2
CN
β-ketoacyl synthase
D-3 hydroxybutyryl ACP
Smooth ER
ACP +CO2
H2O
dehydration
Aceto acyl ACP
reduction
β-hydroxyacyl-ACP dehydratase
Crotonyl ACP
NADPH
β-ketoacyl-ACP reductase
NADP+

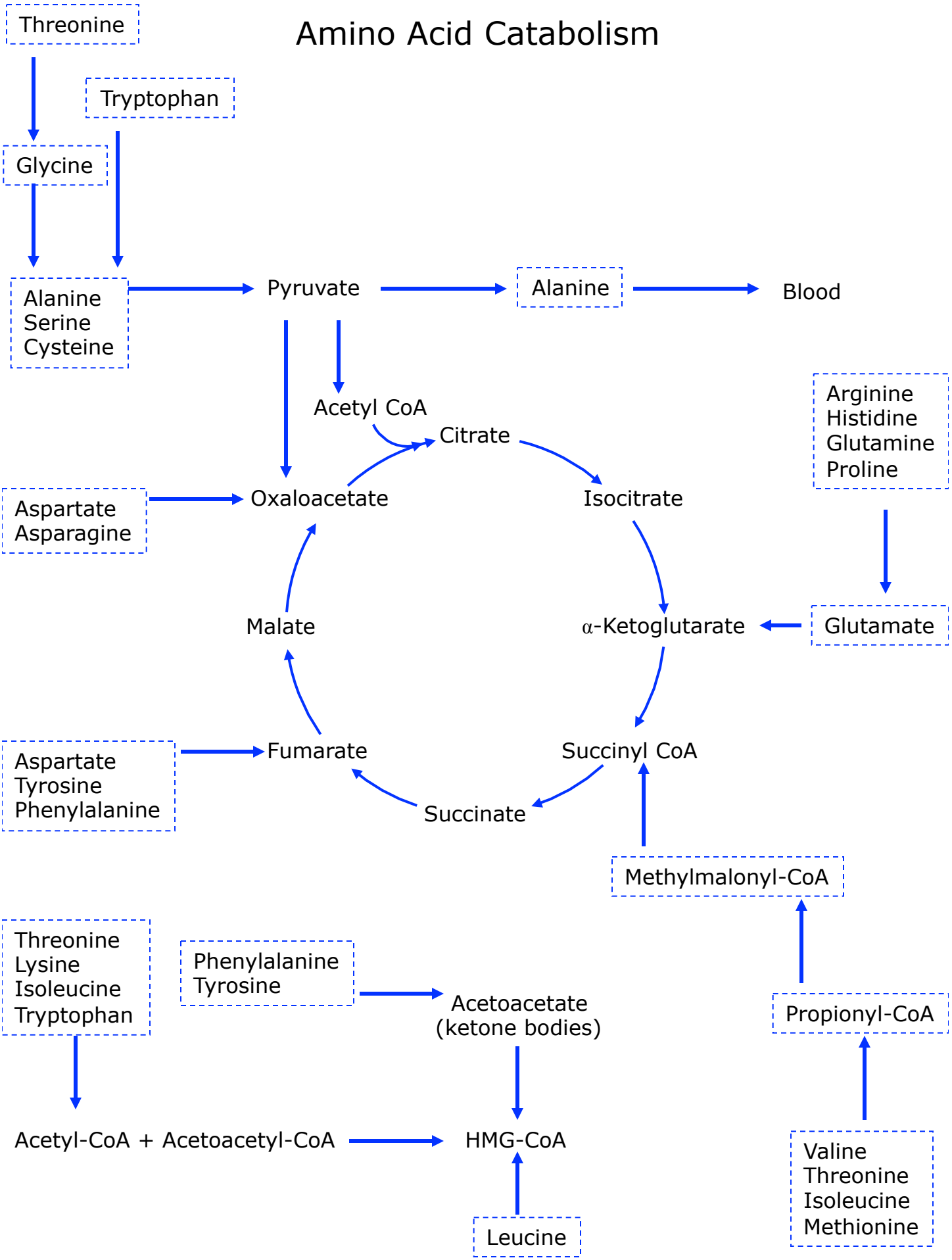
Ketone Body Metabolism

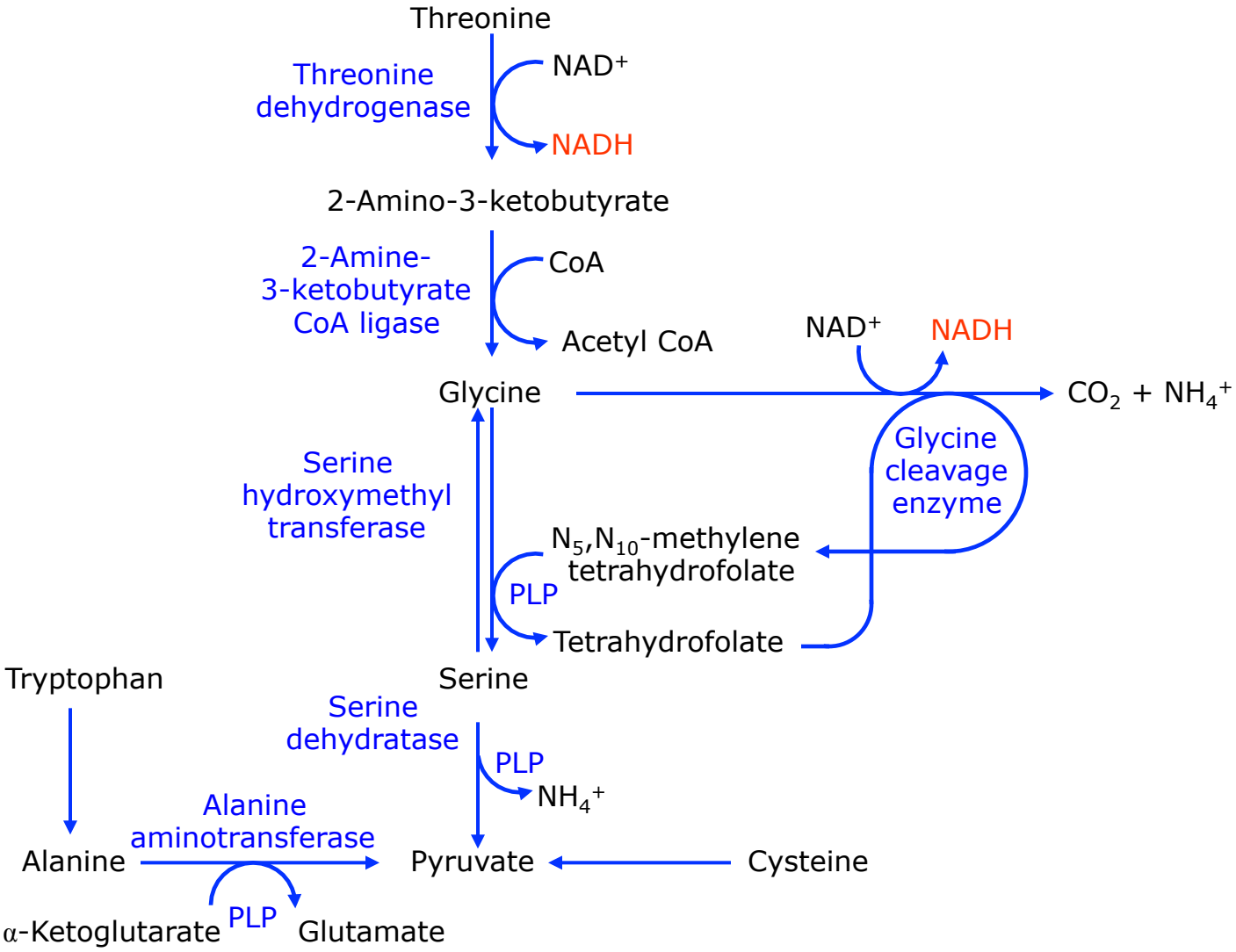


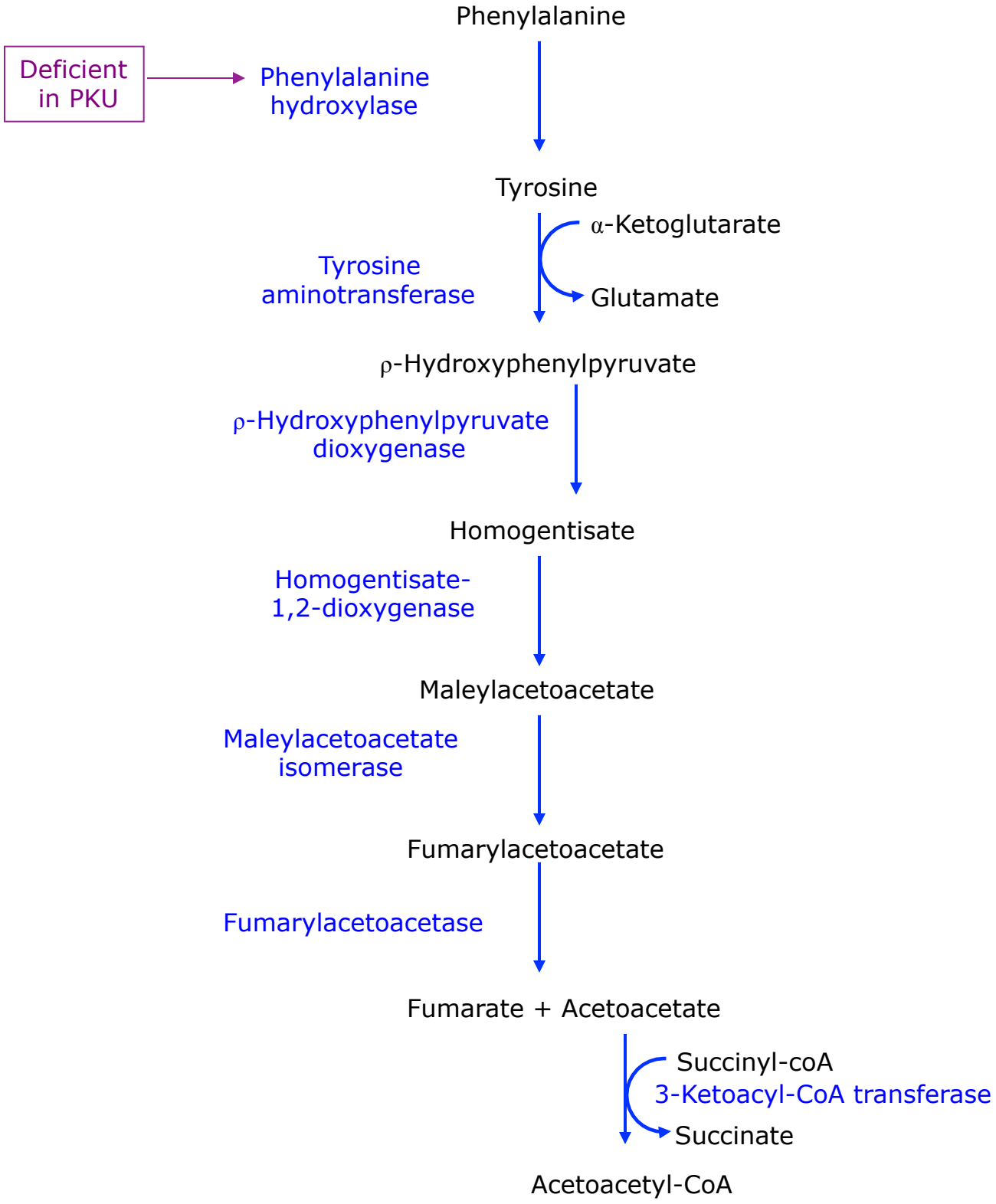
Urea Cycle

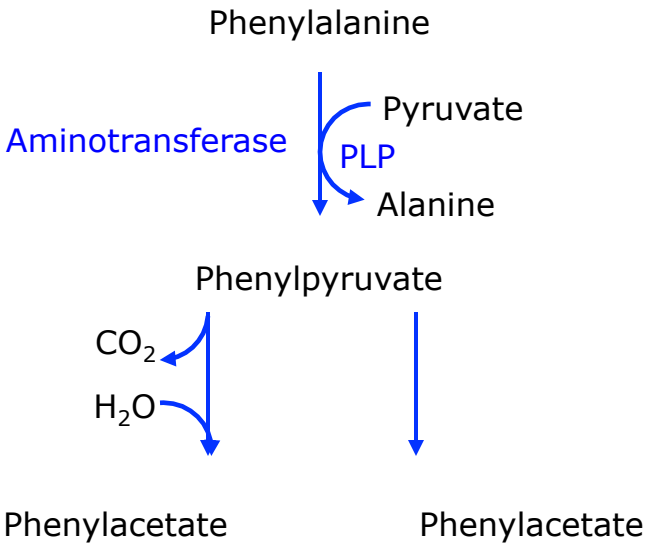

L-amino acid
Aminotransferase:
Pyridoxal phosphate (PLP)
Pyridoxamine phosphate
(Schiff bases)
α-Ketoglutarate
universal amine group acceptor
L-glutamate
α-Keto acid
(+) N-acetylglutamate
Malate
Fumarate
to TCA cycle
Arginine
H_2O
Arginase
Urea
Argininosuccinase
Argininosuccinate
Ornithine
cytosol
matrix
Ornithine transcarbamoylase
Carbamoyl phosphate
PPi + AMP
Argininosuccinate synthetase
Aspartate + ATP
Citrulline
Pi
2 ADP + Pi
Carbamoyl phosphate synthetase I
CO_2 (HCO_3^-)
2 ATP
NH_4^+
from TCA cycle
Glutamate
Glutamine
Oxaloacetate
Glutaminase
Aspartate aminotransferase
Aspartate
Glutamate dehydrogenase
α-Ketoglutarate
Aspartate-argininosuccinate shunt of citric acid cycle

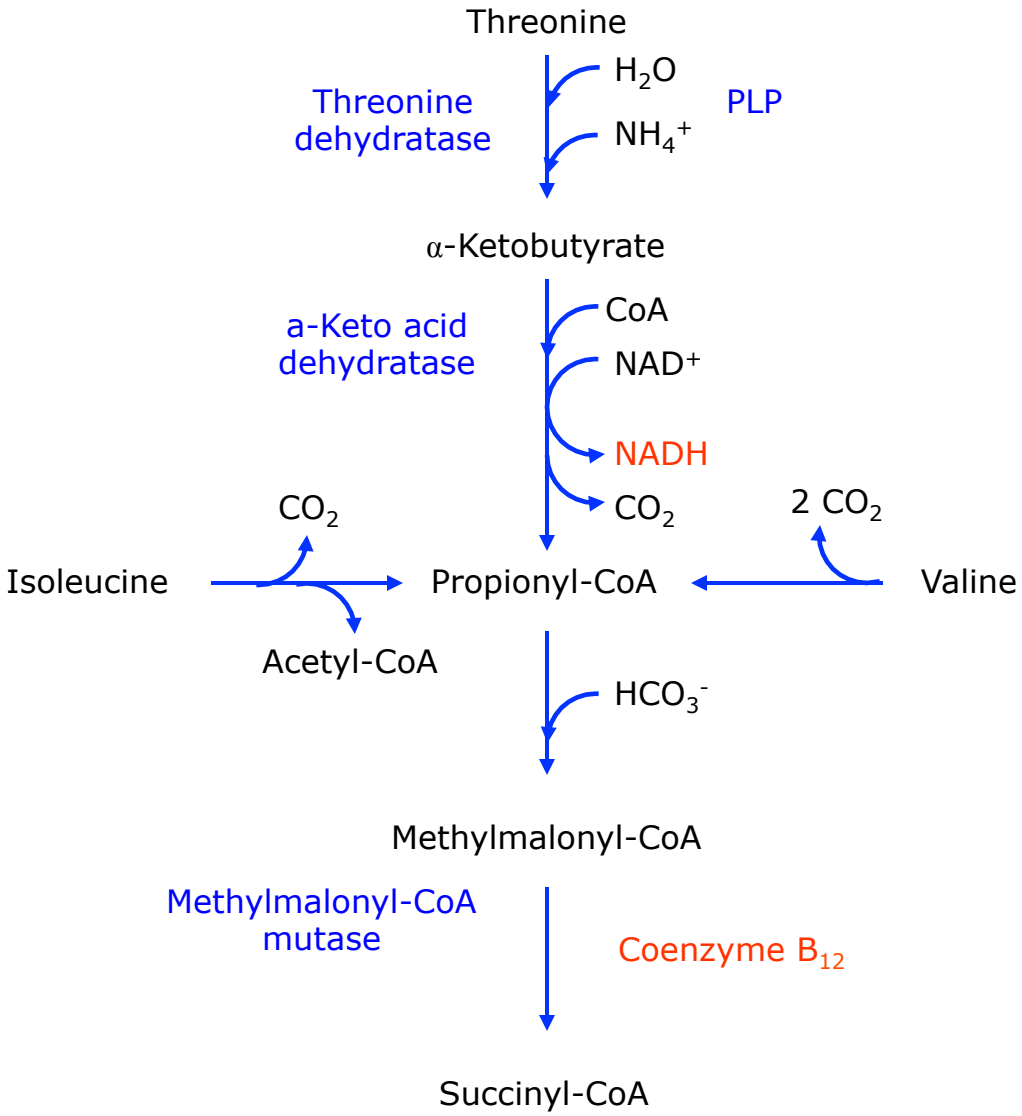
Amino Acid Catabolism



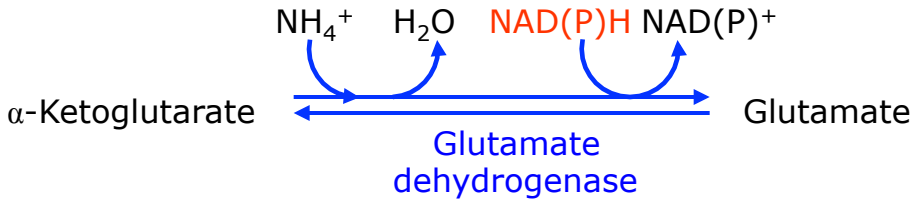

Threonine
Threonine dehydrogenase
NAD+
NADH
2-Amino-3-ketobutyrate
2-Amine-3-ketobutyrate CoA ligase
CoA
Acetyl CoA
NAD+
NADH
Glycine
CO2 + NH4+
Glycine cleavage enzyme
Serine hydroxymethyl transferase
N5,N10-methylene tetrahydrofolate
PLP
Tetrahydrofolate
Tryptophan
Serine
Serine dehydratase
PLP
NH4+
Alanine aminotransferase
Alanine
Pyruvate
Cysteine
PLP
α-Ketoglutarate
Glutamate


Phenylalanine
Deficient in PKU
Phenylalanine hydroxylase
Tyrosine
α-Ketoglutarate
Tyrosine aminotransferase
Glutamate
ρ-Hydroxyphenylpyruvate
ρ-Hydroxyphenylpyruvate dioxygenase
Homogentisate
Homogentisate-1,2-dioxygenase
Maleylacetoacetate
Maleylacetoacetate isomerase
Fumarylacetoacetate
Fumarylacetoacetase
Fumarate + Acetoacetate
Succinyl-coA
3-Ketoacyl-CoA transferase
Succinate
Acetoacetyl-CoA

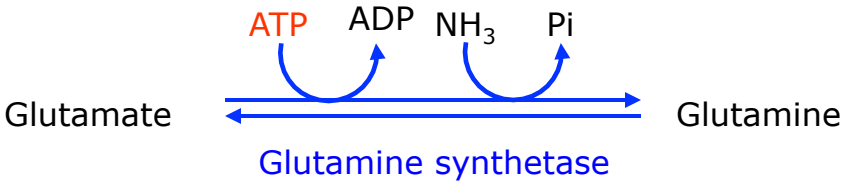

Phenylalanine
Aminotransferase
Pyruvate
PLP
Alanine
Phenylpyruvate
CO_2
H_2O
Phenylacetate
Phenylacetate

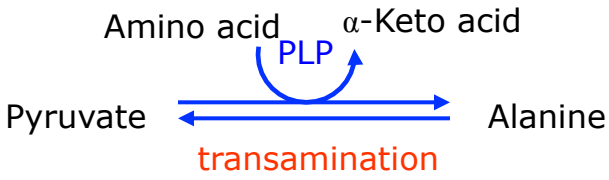

Threonine
Threonine dehydratase
H_2O
NH_4^+
PLP
α-Ketobutyrate
a-Keto acid dehydratase
CoA
NAD^+
NADH
CO_2
CO_2
$2\ CO_2$
Isoleucine
Propionyl-CoA
Valine
Acetyl-CoA
HCO_3^-
Methylmalonyl-CoA
Methylmalonyl-CoA mutase
Coenzyme B_{12}
Succinyl-CoA

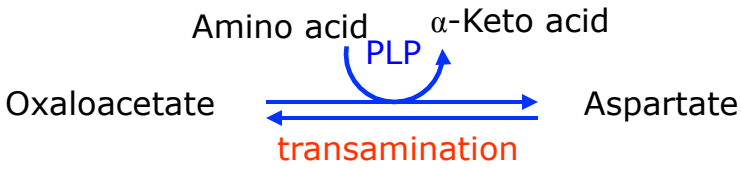
Amino Acid Synthesis

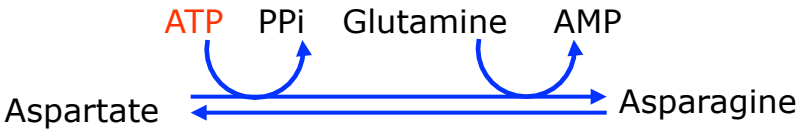


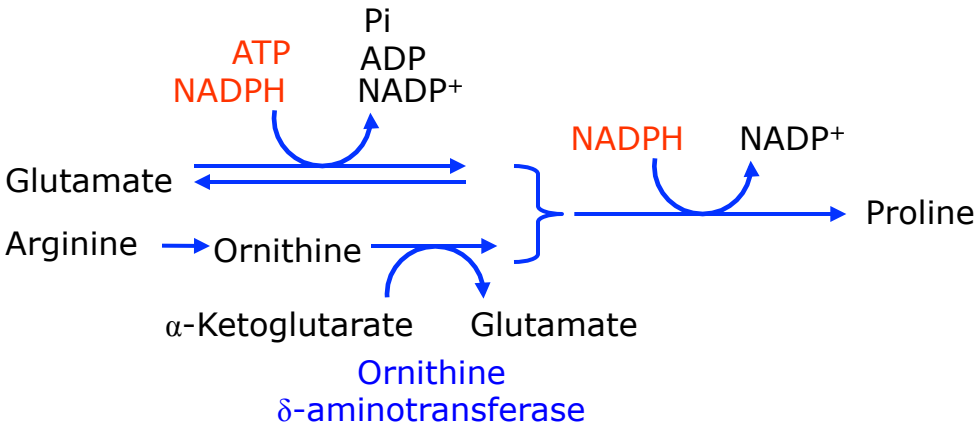
reductive amination



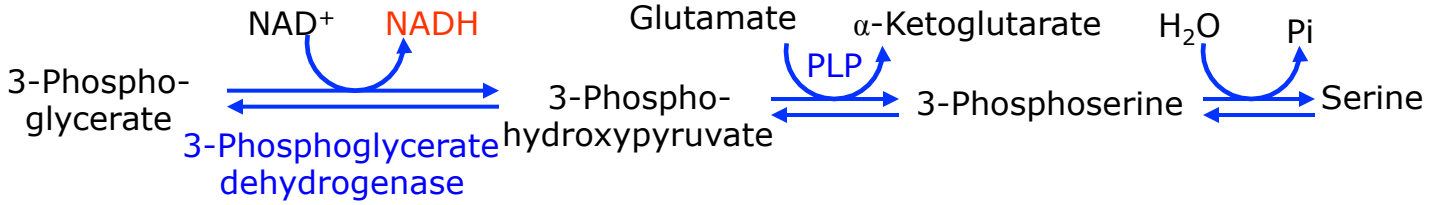


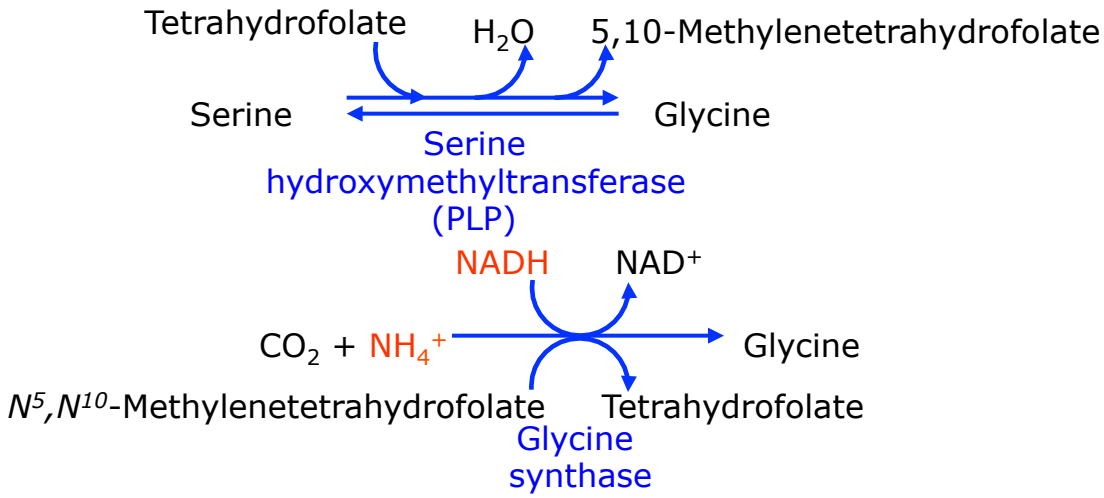


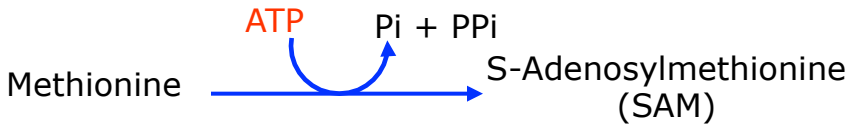


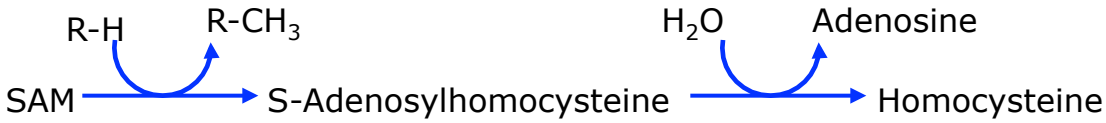


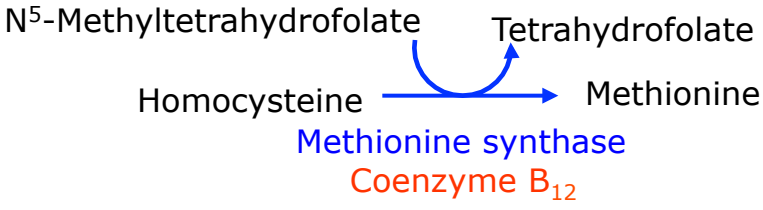
Amino Acid Synthesis

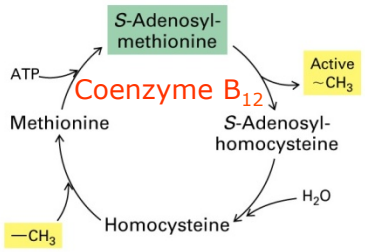


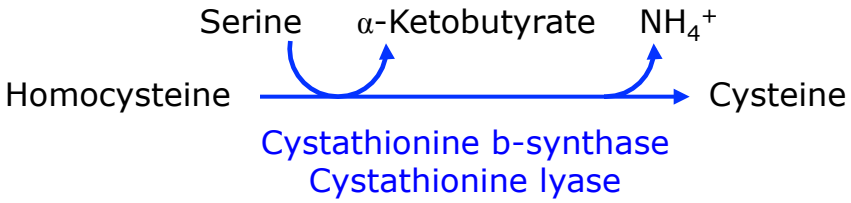




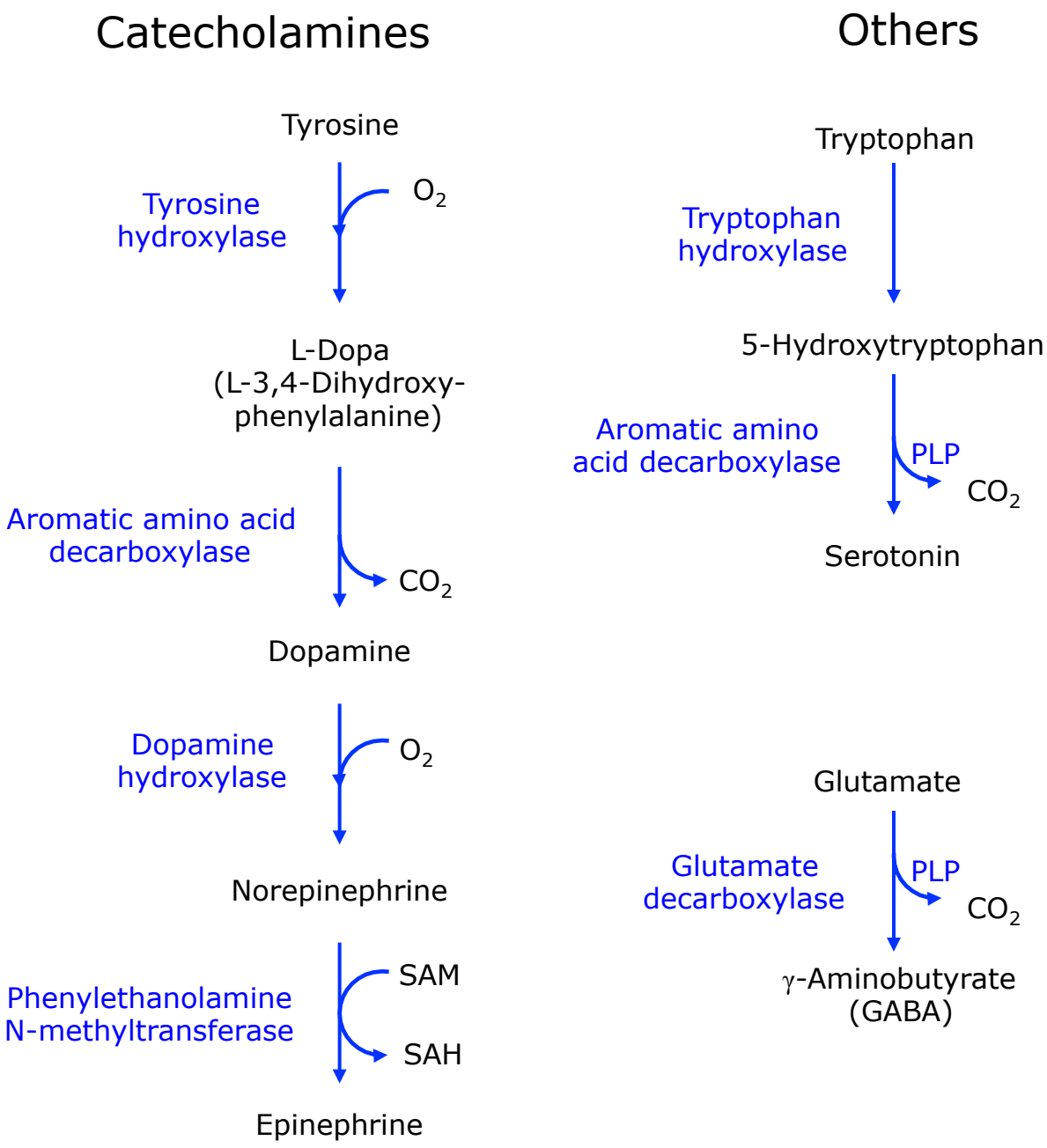


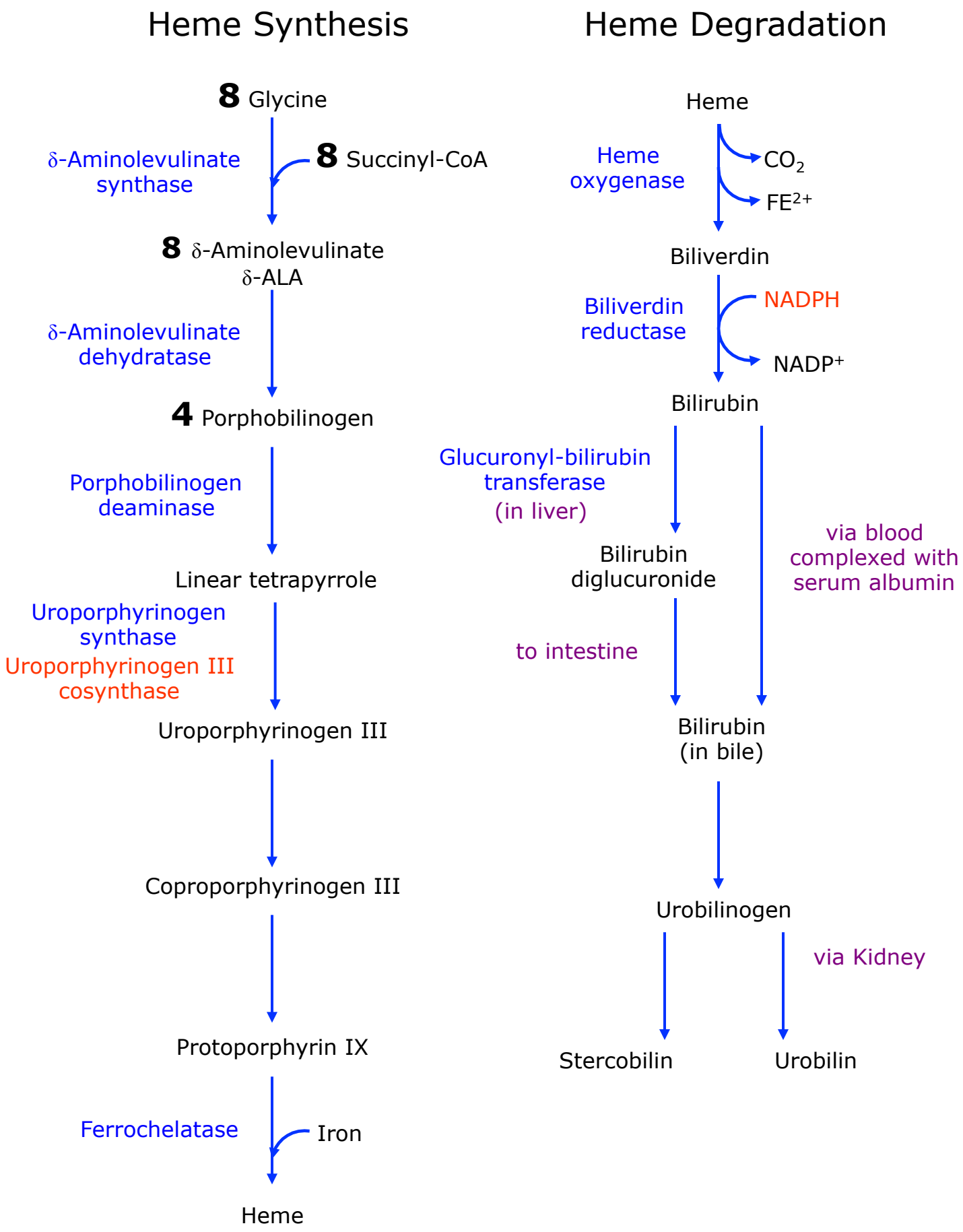




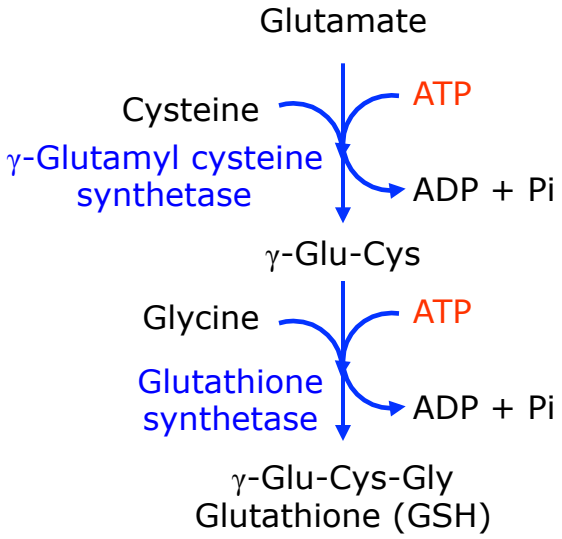


Neurotransmitter Synthesis

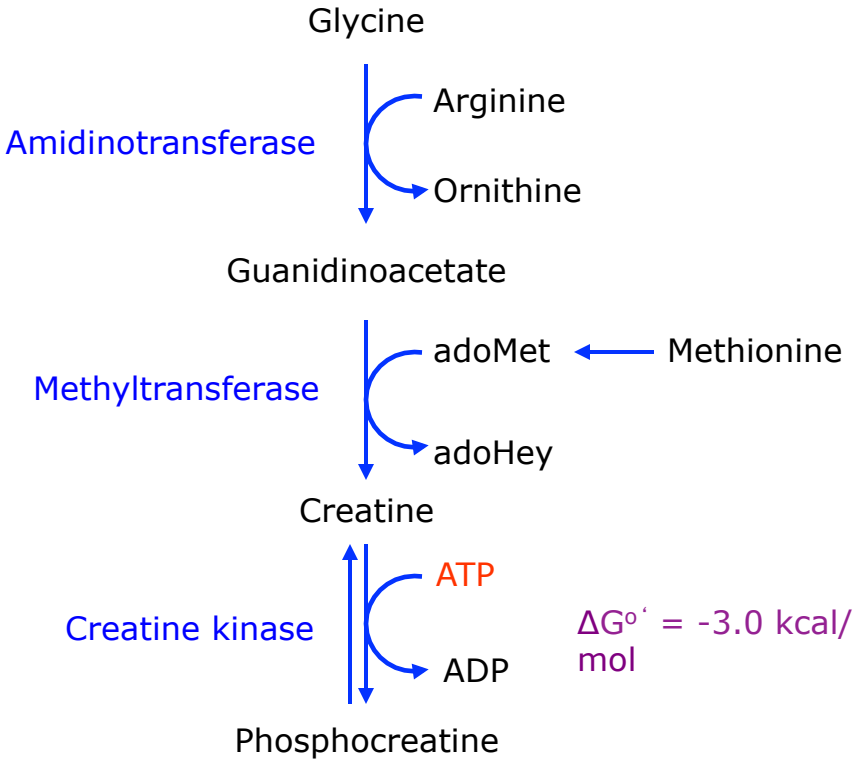



Heme Synthesis
8 Glycine
δ-Aminolevulinate synthase
8 Succinyl-CoA
8 δ-Aminolevulinate
δ-ALA
δ-Aminolevulinate dehydratase
4 Porphobilinogen
Porphobilinogen deaminase
Linear tetrapyrrole
Uroporphyrinogen synthase
Uroporphyrinogen III cosynthase
Uroporphyrinogen III
Coproporphyrinogen III
Protoporphyrin IX
Ferrochelatase
Iron
Heme
Heme Degradation
Heme
Heme oxygenase
CO2
FE2+
Biliverdin
Biliverdin reductase
NADPH
NADP+
Bilirubin
Glucuronyl-bilirubin transferase
(in liver)
Bilirubin diglucuronide
via blood complexed with serum albumin
to intestine
Bilirubin (in bile)
Urobilinogen
via Kidney
Stercobilin
Urobilin

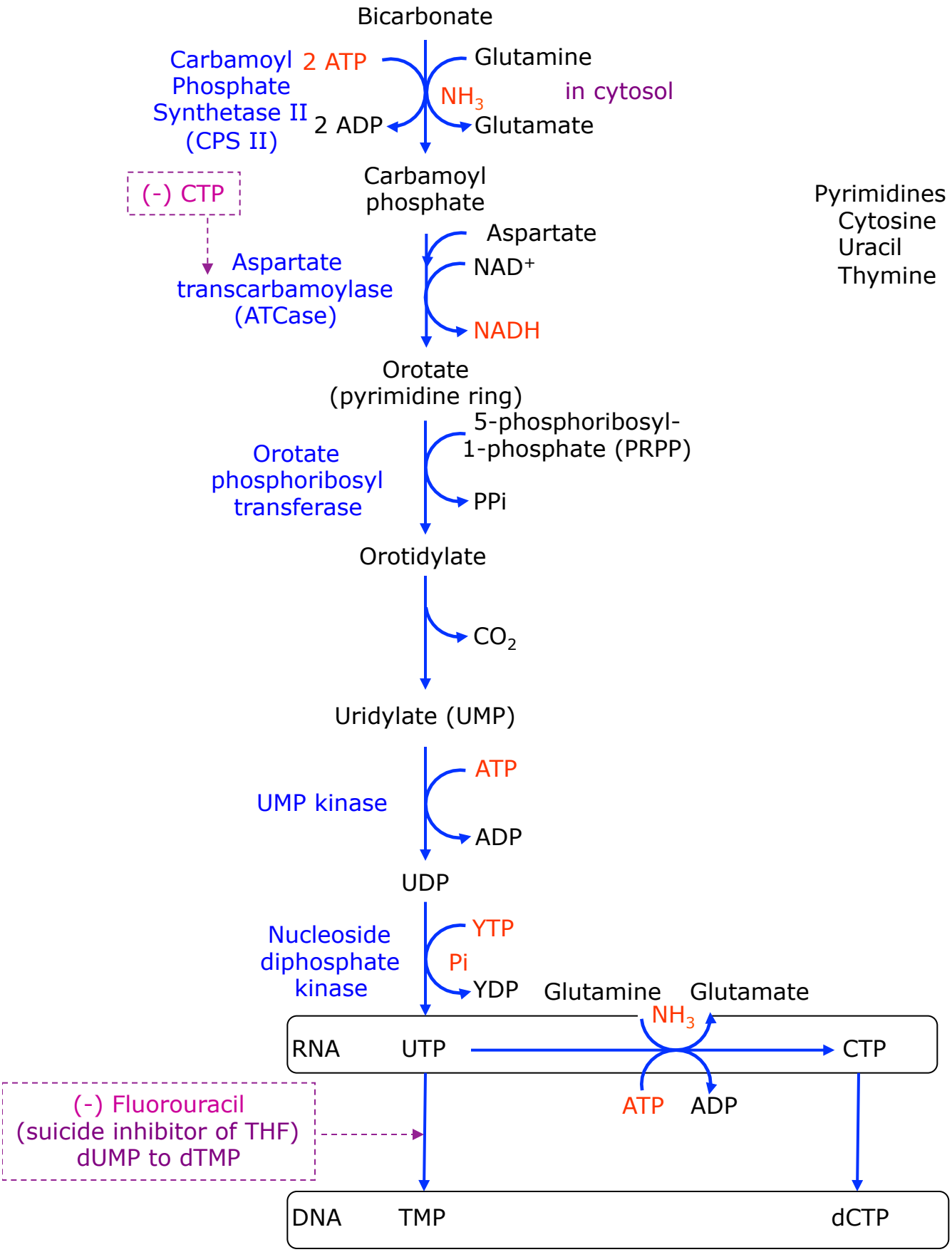
Glutathione Synthesis



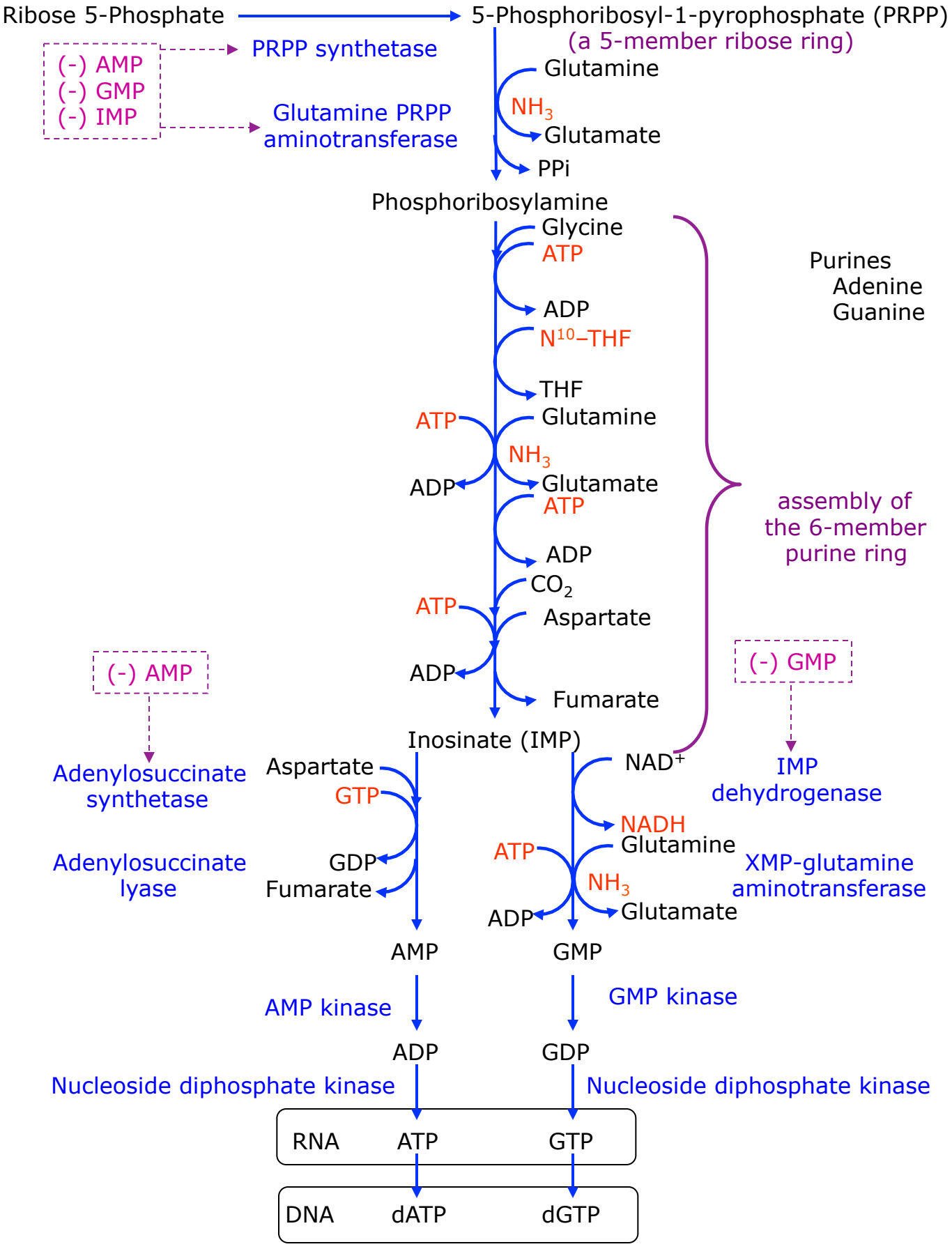
Creatine Phosphate Synthesis



Nucleotide Synthesis - Pyrimidines



Nucleotide Synthesis - Purines



Purine Salvage Pathway

Adenine + PRPP → Adenylate (AMP) + PPi

Adenine phosphoribosyltransferase

Hypoxanthine + PRPP → Inosinate (IMP) + PPi

Guanine + PRPP → Guanylate (GMP) + PPi

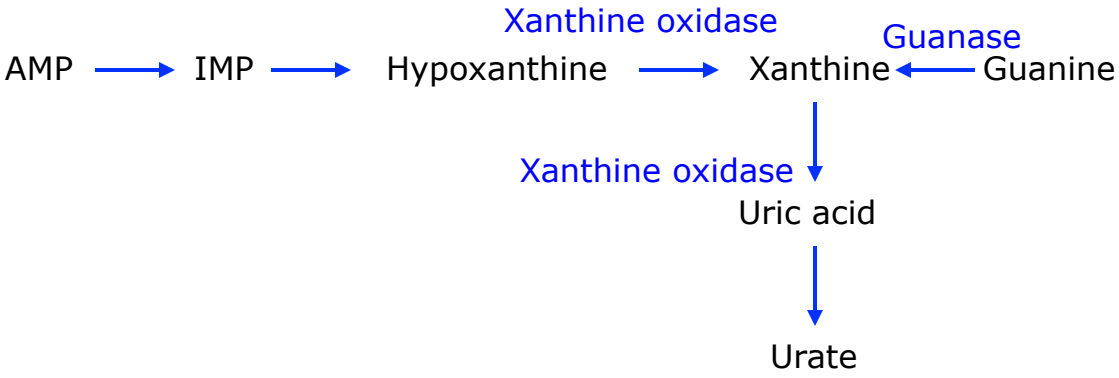
Hypoxanthine-guanine phosphoribosyltransferase

Pyrimidine Salvage Pathway

Orotate + PRPP → Orotidylate (OMP) + PPi

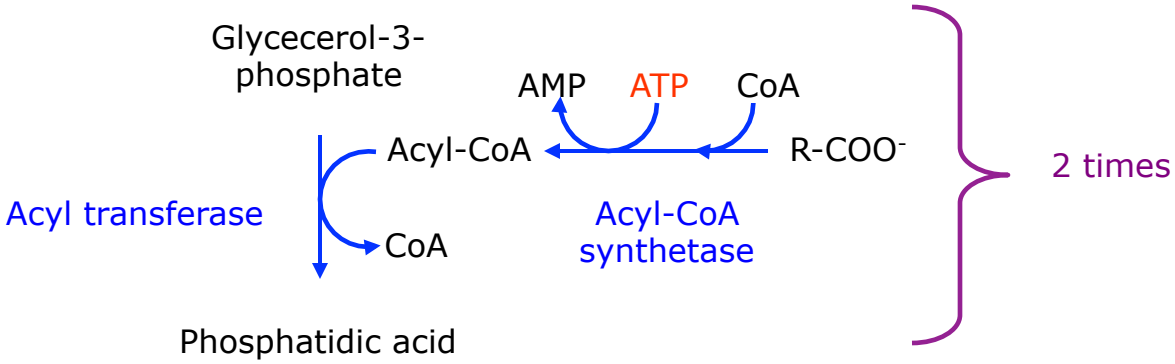
Orotate phosphoribosyl transferase

Purine Degradation



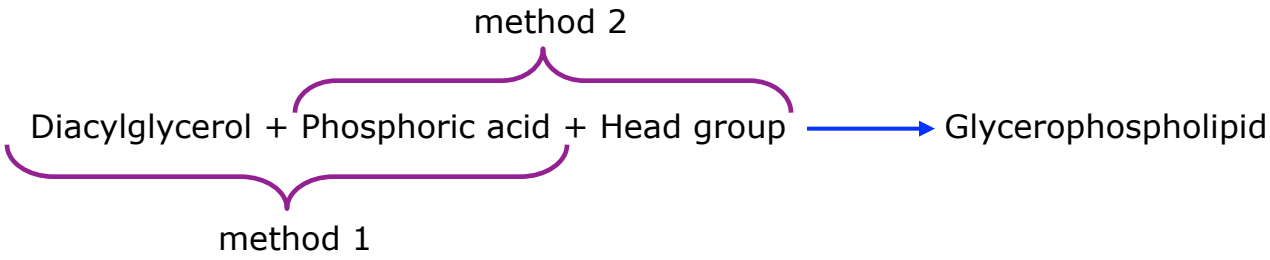
Membrane Lipid Synthesis

PHOSPHATIDATE SYNTHESIS

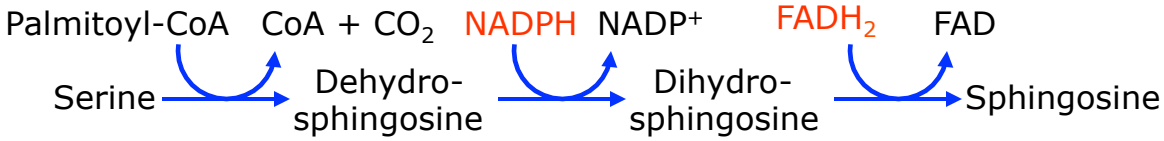


TRIACYLGLYCEROL SYNTHESIS

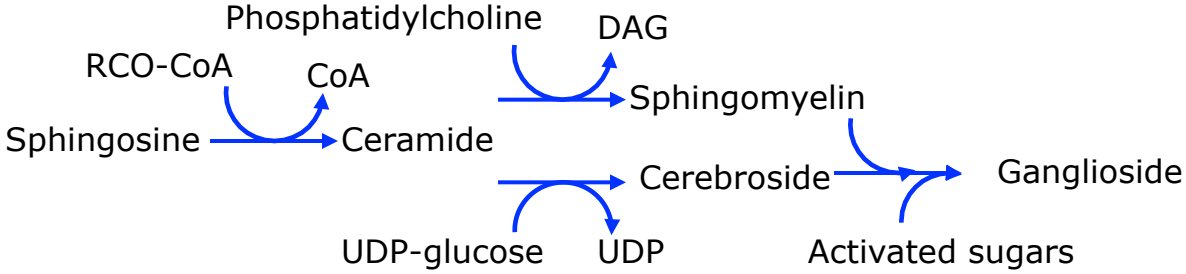
PHOSPHOLIPID ASSEMBLY



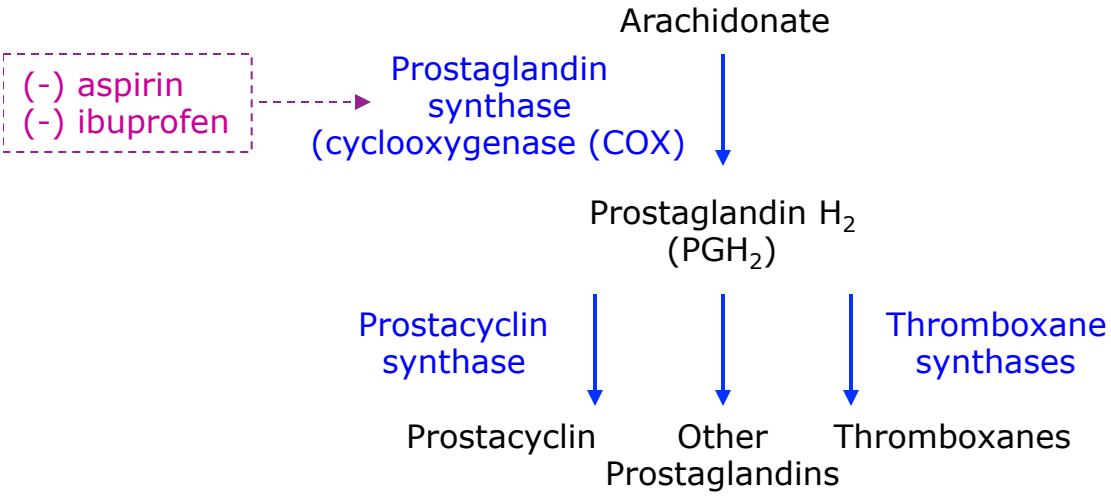
SPHINGOSINE SYNTHESIS



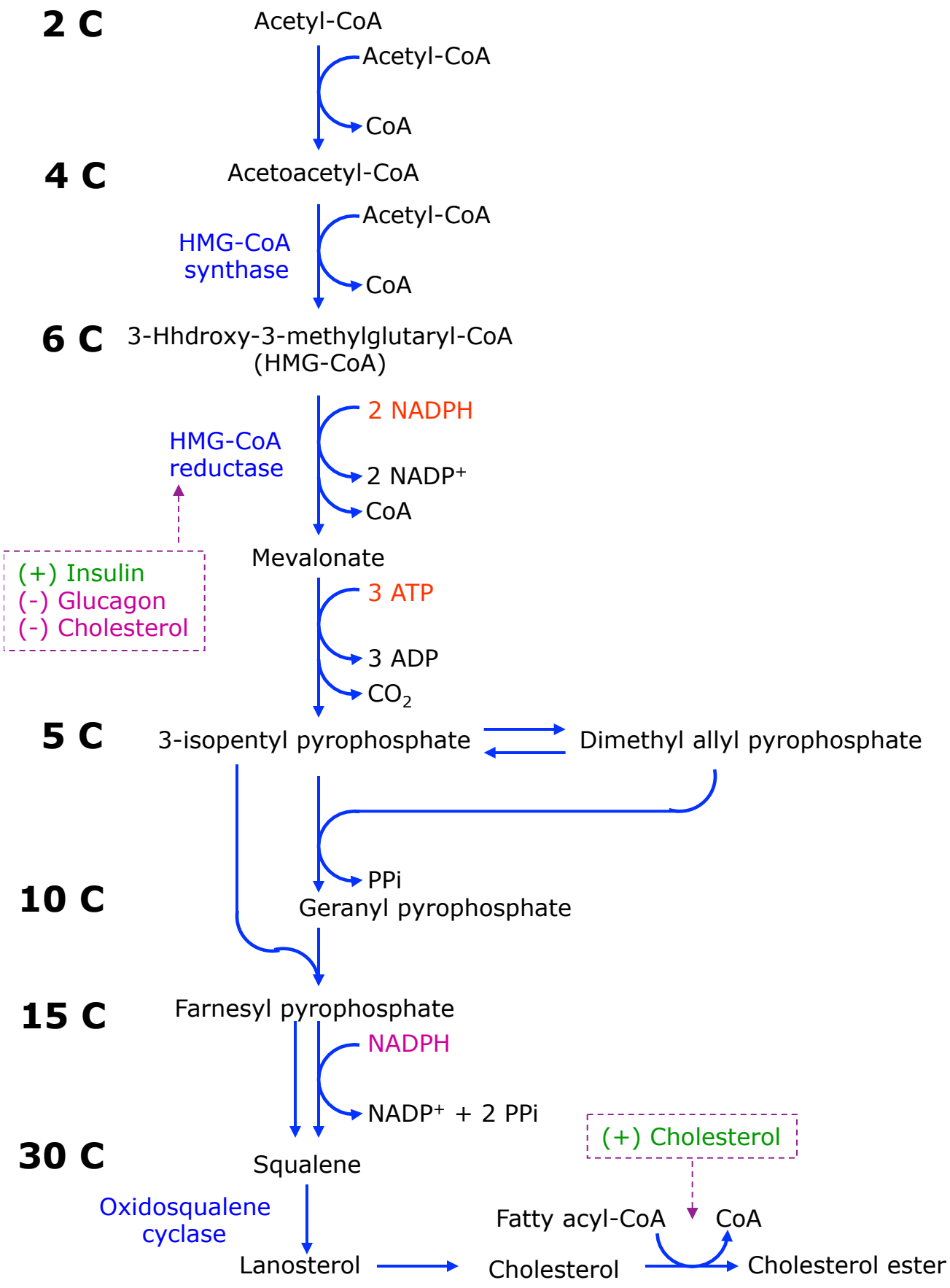
SPHINGOLIPID SYNTHESIS



Eicosanoid Synthesis



Cholesterol Synthesis



Cholesterol Derivatives

SYNTHESIS OF BILE SALTS

Cholesterol

↓

Trihydrocoprostanoate

↓

Cholyl CoA

Glycine → Glycocholate

Taurine → Taurocholate

HORMONE SYNTHESIS

Cholesterol (C_{27})

↓

Pregnenolone (C_{21}) ← Steroid precursor

↓

Progestagens (C_{21})
Progesterone

- → Glucocorticoids (C_{21}) Cortisol
- → Mineralocorticoids (C_{21}) Aldosterone
- → Androgens (C_{19}) Testosterone → Estrogens (C_{18}) Estradiol

VITAMIN D SYNTHESIS

7-Dehydrocholesterol

↓ UV light

Previtamin D_3

↓

Calcitriol

↓

Vitamin D_3
(cholecalciferol)