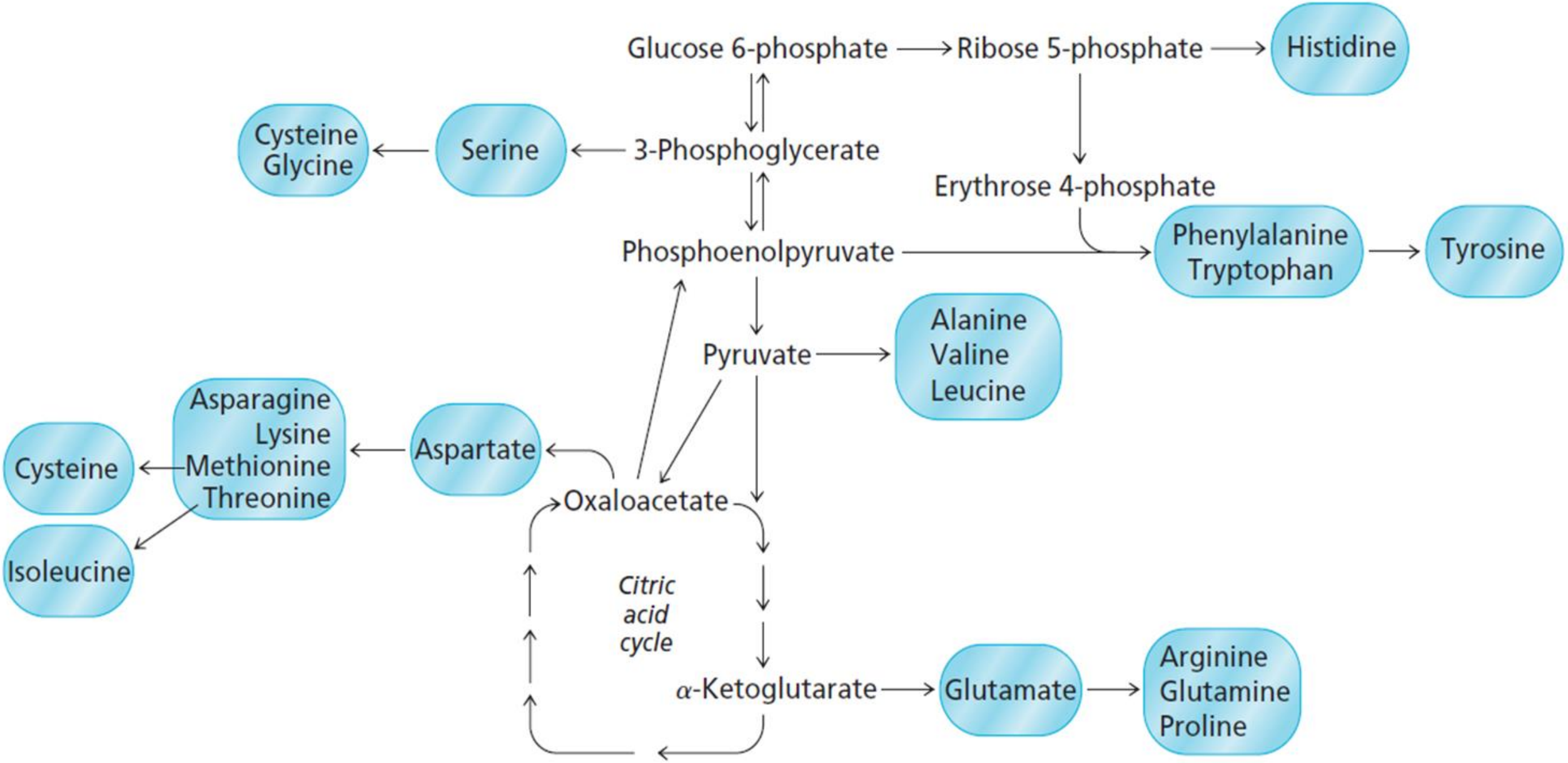
Assist. Prof. Dr. Shakir .F. Tuleab
Ph. D. Biochemistry
University of Anbar
College Of Education For Pure Sciences
Chemistry department

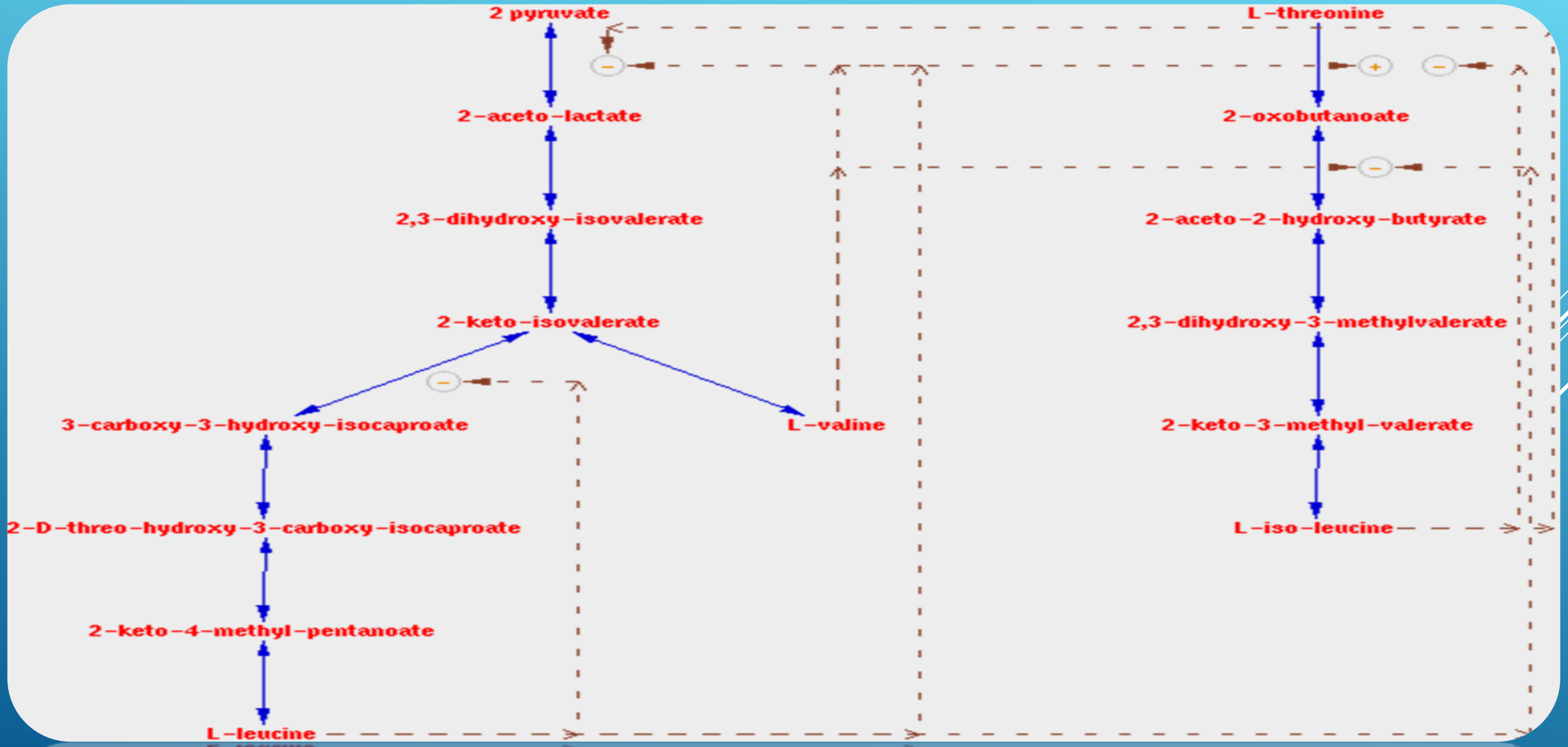
Biosynthesis of essential amino acids

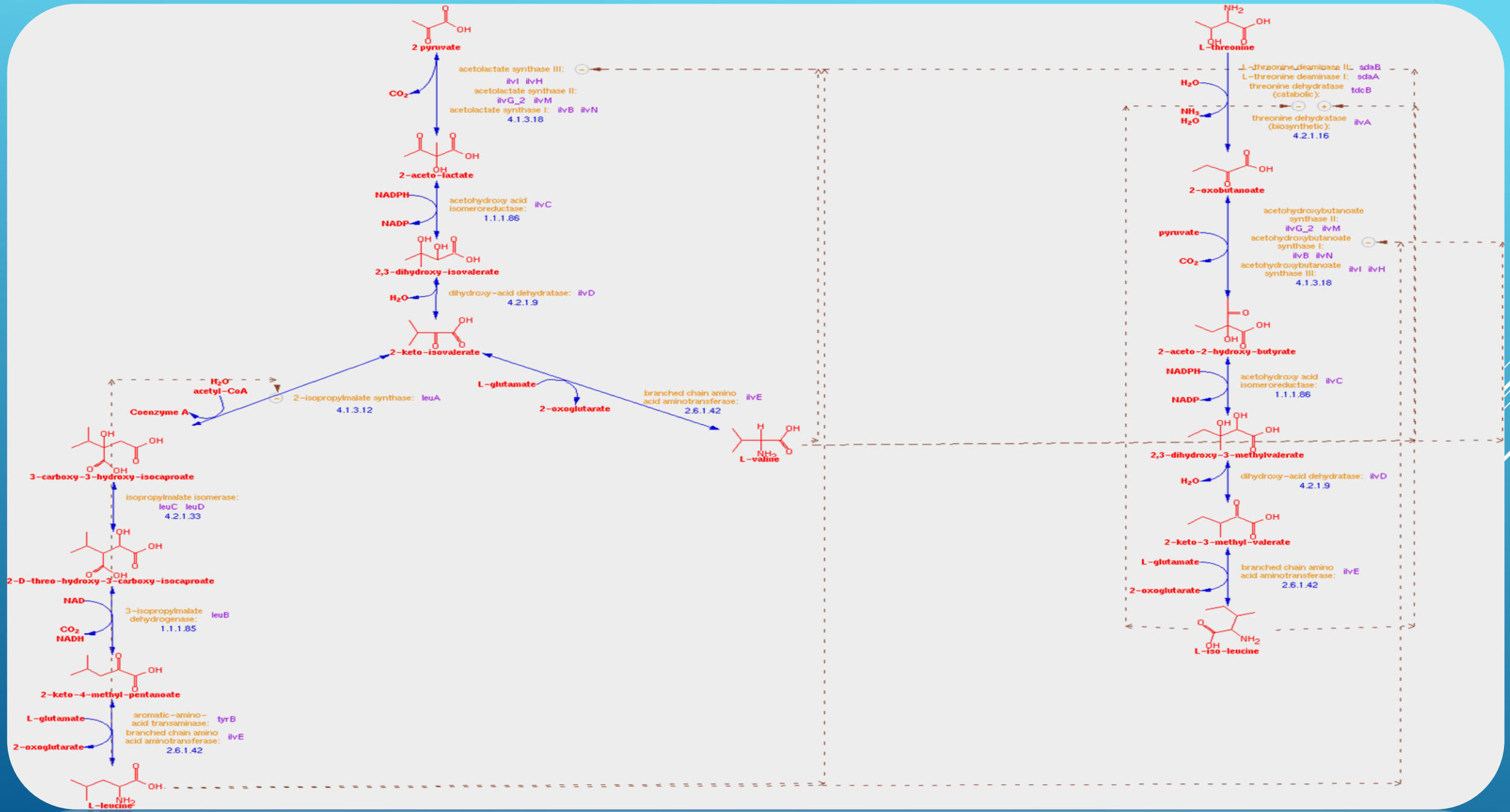
Biosynthesis of amino acids

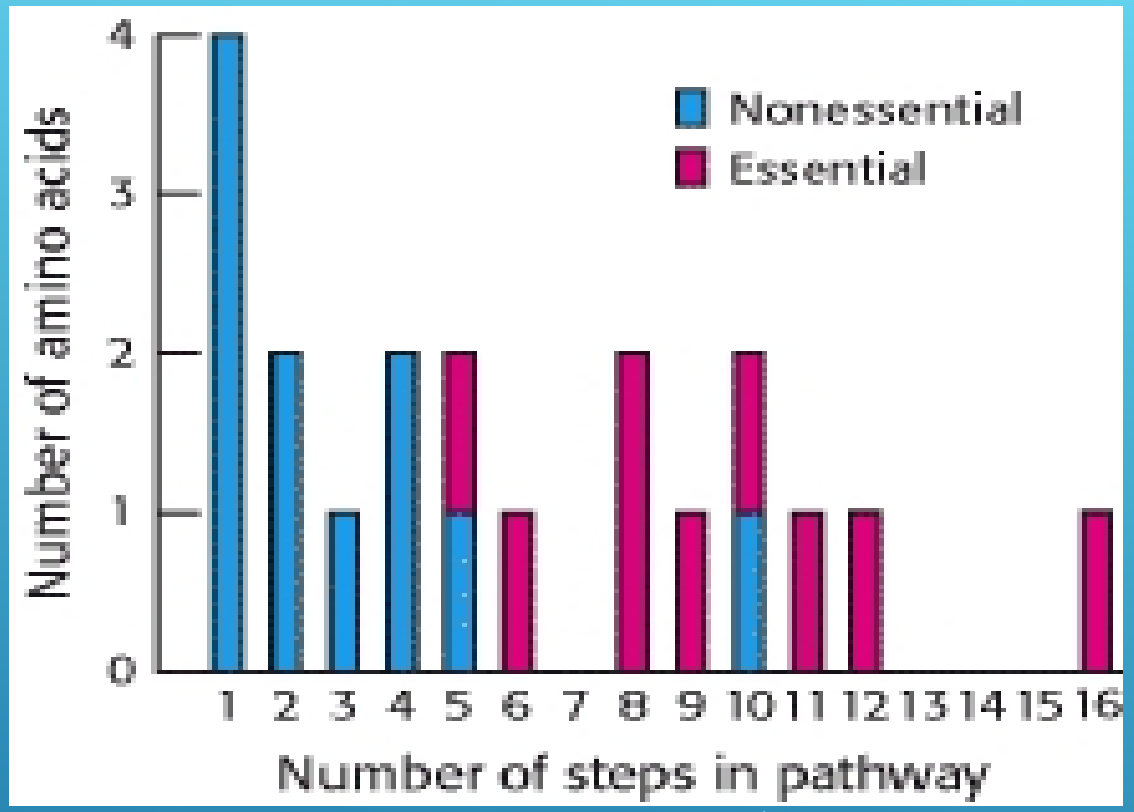


- Plants and bacteria synthesize all 20 common amino acids. Mammals can synthesize about half; the others are required in the diet (essential amino acids ——Leu、Trp、Phe、Val、Met、Leu、Thr、Ile).

superpathway of leucine, valine, and isoleucine biosynthesis



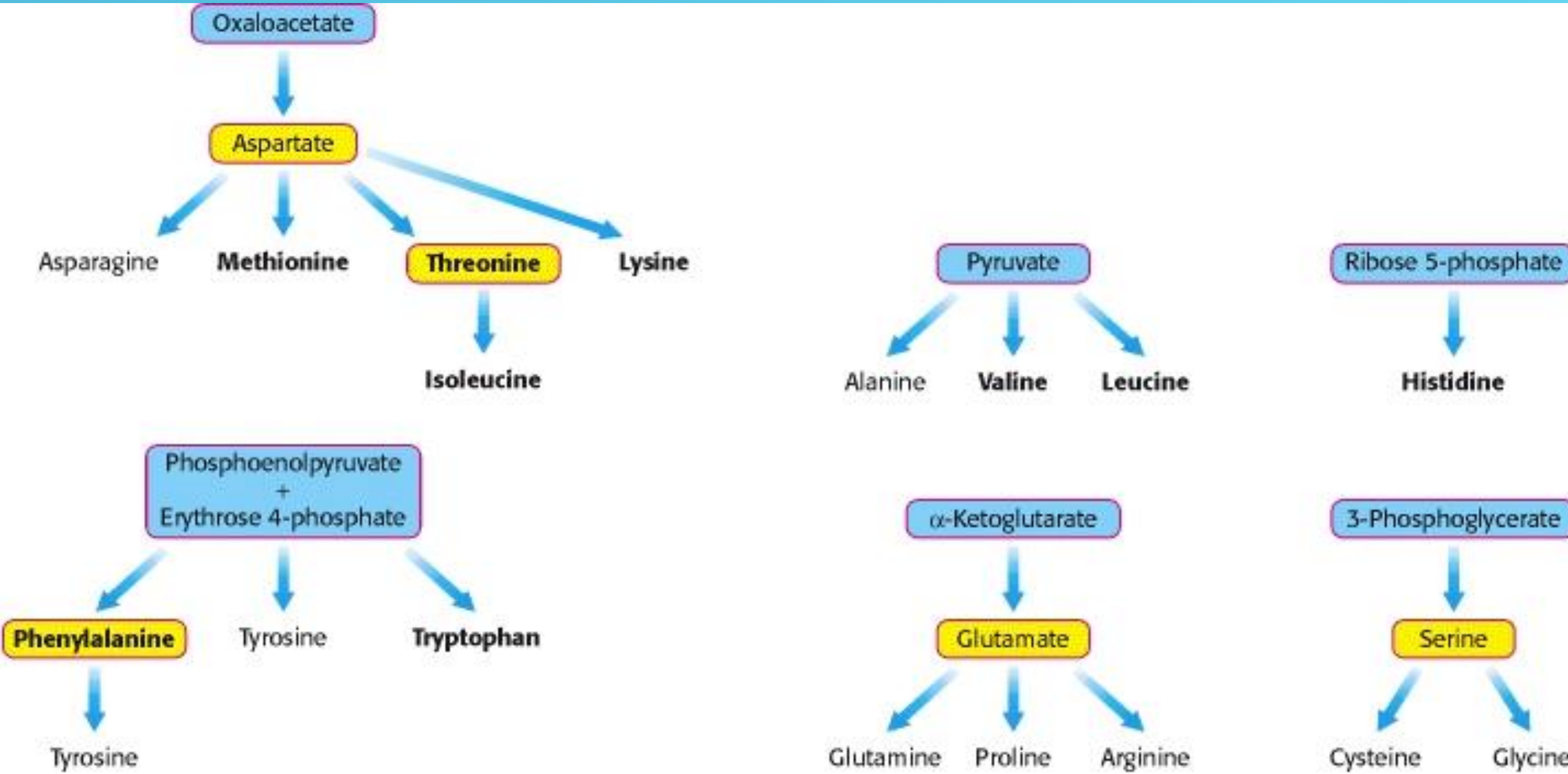

2 pyruvate
acetolactate synthase III:
ilvI ilvH
acetolactate synthase II:
ilvG_2 ilvM
acetolactate synthase I: ilvB ilvN
4.1.3.18
CO2
2-aceto-lactate
NADPH
NADP
acetohydroxy acid isomeroreductase: ilvC
1.1.1.86
2,3-dihydroxy-isovalerate
H2O
dihydroxy-acid dehydratase: ilvD
4.2.1.9
2-keto-isovalerate
H2O
acetyl-CoA
Coenzyme A
2-isopropylmalate synthase: leuA
4.1.3.12
L-glutamate
2-oxoglutarate
branched chain amino acid aminotransferase: ilvE
2.6.1.42
L-valine
3-carboxy-3-hydroxy-isocaproate
isopropylmalate isomerase:
leuC leuD
4.2.1.33
2-D-threo-hydroxy-3-carboxy-isocaproate
NAD
CO2
NADH
3-isopropylmalate dehydrogenase: leuB
1.1.1.85
2-keto-4-methyl-pentanoate
L-glutamate
2-oxoglutarate
aromatic-amino-acid transaminase: tyrB
branched chain amino acid aminotransferase: ilvE
2.6.1.42
L-leucine
L-threonine
L-threonine deaminase II: sdaB
L-threonine deaminase I: sdaA
threonine dehydratase (catabolic): tdcB
H2O
NH3
H2O
threonine dehydratase (biosynthetic): ilvA
4.2.1.16
2-oxobutanoate
pyruvate
CO2
acetohydroxybutanoate synthase II:
ilvG_2 ilvM
acetohydroxybutanoate synthase I:
ilvB ilvN
acetohydroxybutanoate synthase III: ilvI ilvH
4.1.3.18
2-aceto-2-hydroxy-butyrate
NADPH
NADP
acetohydroxy acid isomeroreductase: ilvC
1.1.1.86
2,3-dihydroxy-3-methylvalerate
H2O
dihydroxy-acid dehydratase: ilvD
4.2.1.9
2-keto-3-methyl-valerate
L-glutamate
2-oxoglutarate
branched chain amino acid aminotransferase: ilvE
2.6.1.42
L-iso-leucine



- In general, humans can’t synthesize amino acids that require more than 5 steps.

THIS ONE IS ARGININE

▸Six biosynthetic families (**bold** = essential):



Amino acid biosynthesis

Essential

Nonessential

His

Pentose → Tetrose + triose (PEP) → **Tyr/Trp/Phe**

(pentose phosphate shunt) (aromatics)

(glycolysis)

3PG → **Ser** → **Cys/Gly**

Pyruvate → 1. → **Ala/Val/Leu/Ile**

2. → α-KG → **Glu** → **Gln/Pro**

(urea cycle)

Ornithine → Arg

3. OA → **Asp** → **Lys/Asn/Met/Thr**

▶ Regulation

Typically, first enzyme in a pathway is allosterically inhibited by the end product (allosteric feedback inhibition).

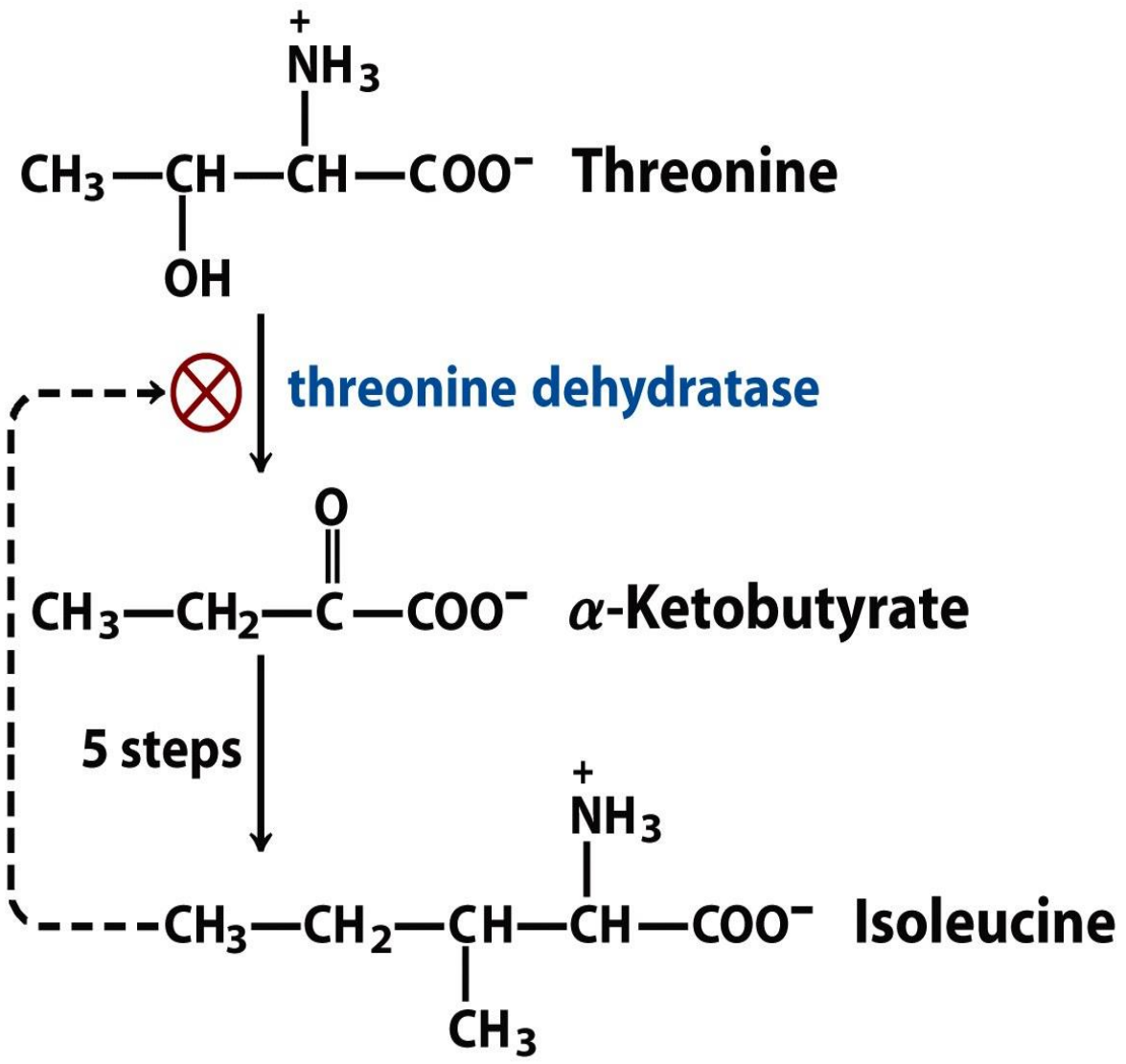


Figure 22-21
Lehninger Principles of Biochemistry, Fifth Edition
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Regulation

Interlocking regulatory mechanisms ensure that amino acids are synthesized in the correct proportions for protein synthesis.

E. coli **regulation of various amino acids derived from Asp.**

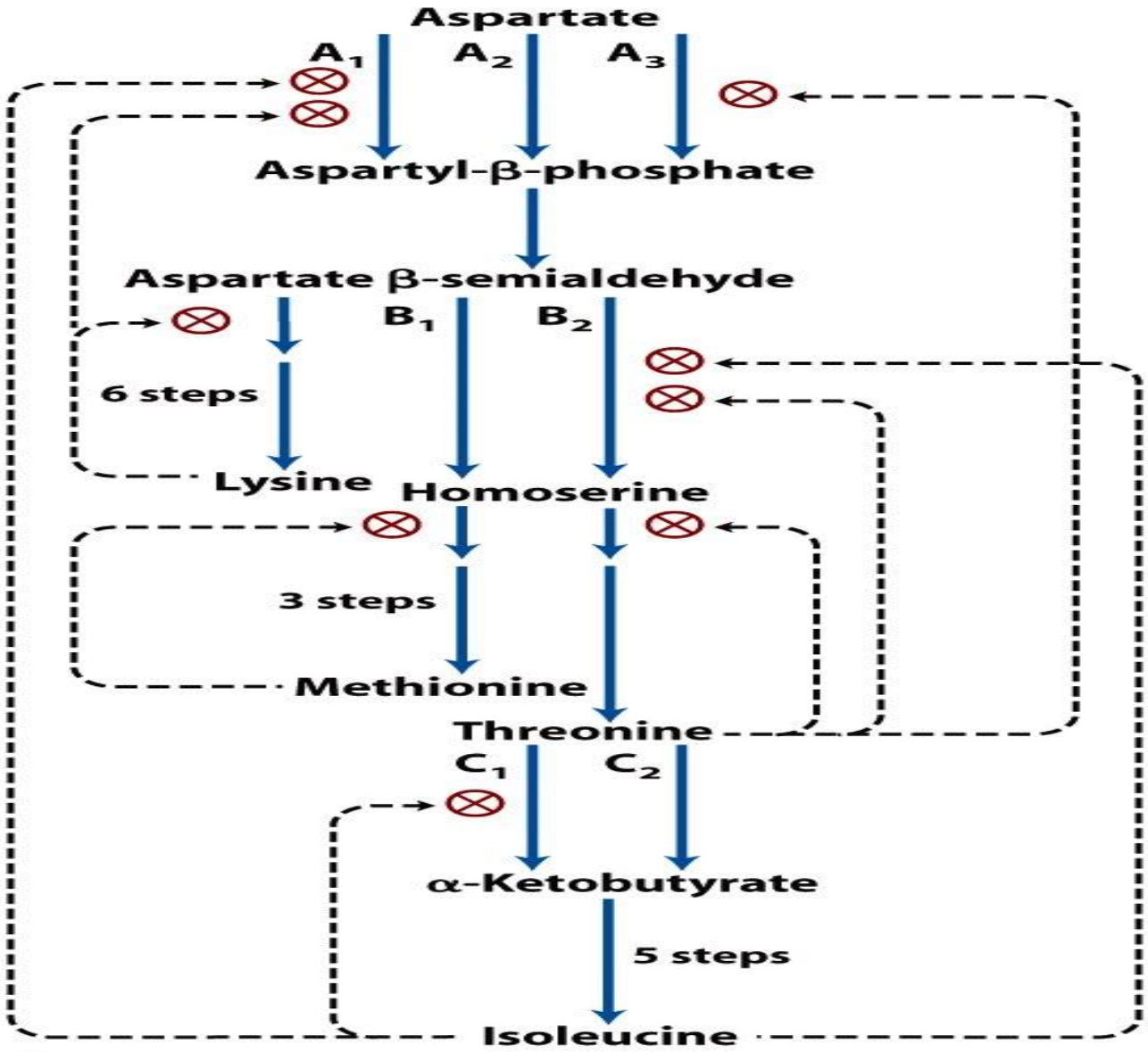

Figure 22-22
Lehninger Principles of Biochemistry, Fifth Edition
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- Plants and microbes synthesize all 20 amino acids
- The amino group is derived from glutamate via transamination of the corresponding a-keto acid
- Mammals can sythesize only 10 of the 20 amino acids

- PEP and Erythrose-4-P Family
- Phenylalanine Tyrosine Tryptophan
- Histidine is derived from PRPP (phosphoribosylpyrophosphate)

- Arginine biosynthesis involves steps that are part of the urea cycle and depends on the formation of ornithine. Ornithine has three metabolic roles:
- **1) as a precursor to arginine.**
- **2) as an intermediate in the urea cycle.**
- **3) as an intermediate in Arginine degradation.**

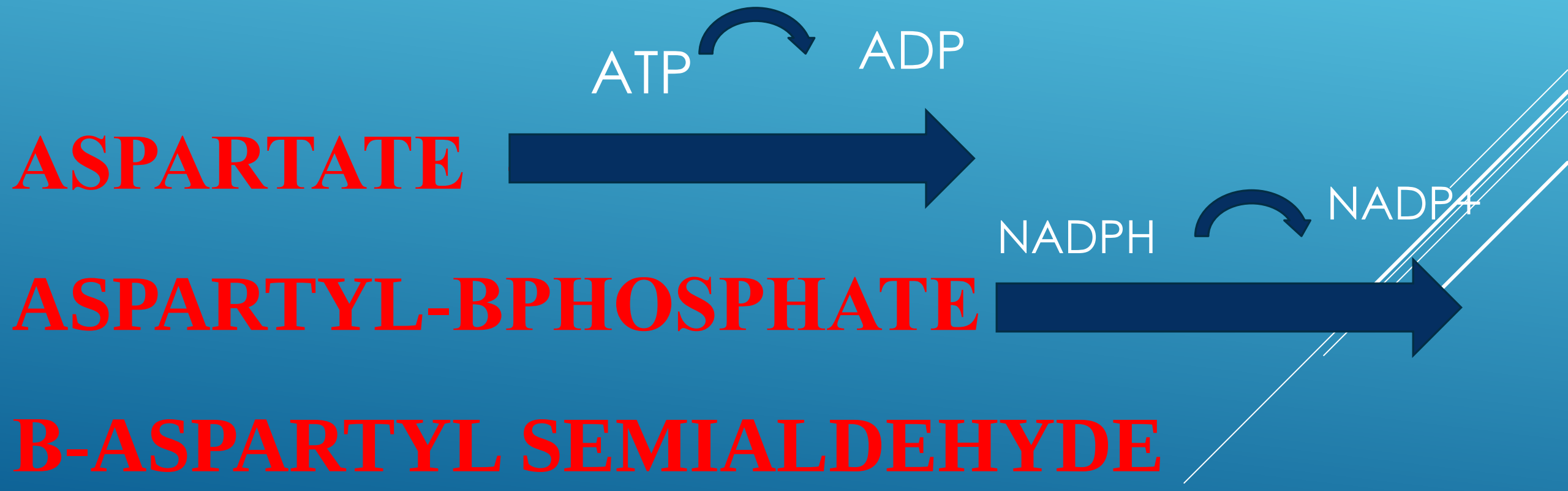
- Lysine biosynthesis in fungi stems from α-Kg; in other organisms it comes from aspartate.
- Starting from a-Kg, the carbon chain is lengthened by one Carbon in a series of steps reminiscent of the TCA cycle: Acetyl CoA is condensed with a-Kg to form homocitrate; homoisocitrate is formed.
- oxidative decarboxylation removed one carbon leaving the intermediate a-ketoadipate; 5 additional steps then form lysine

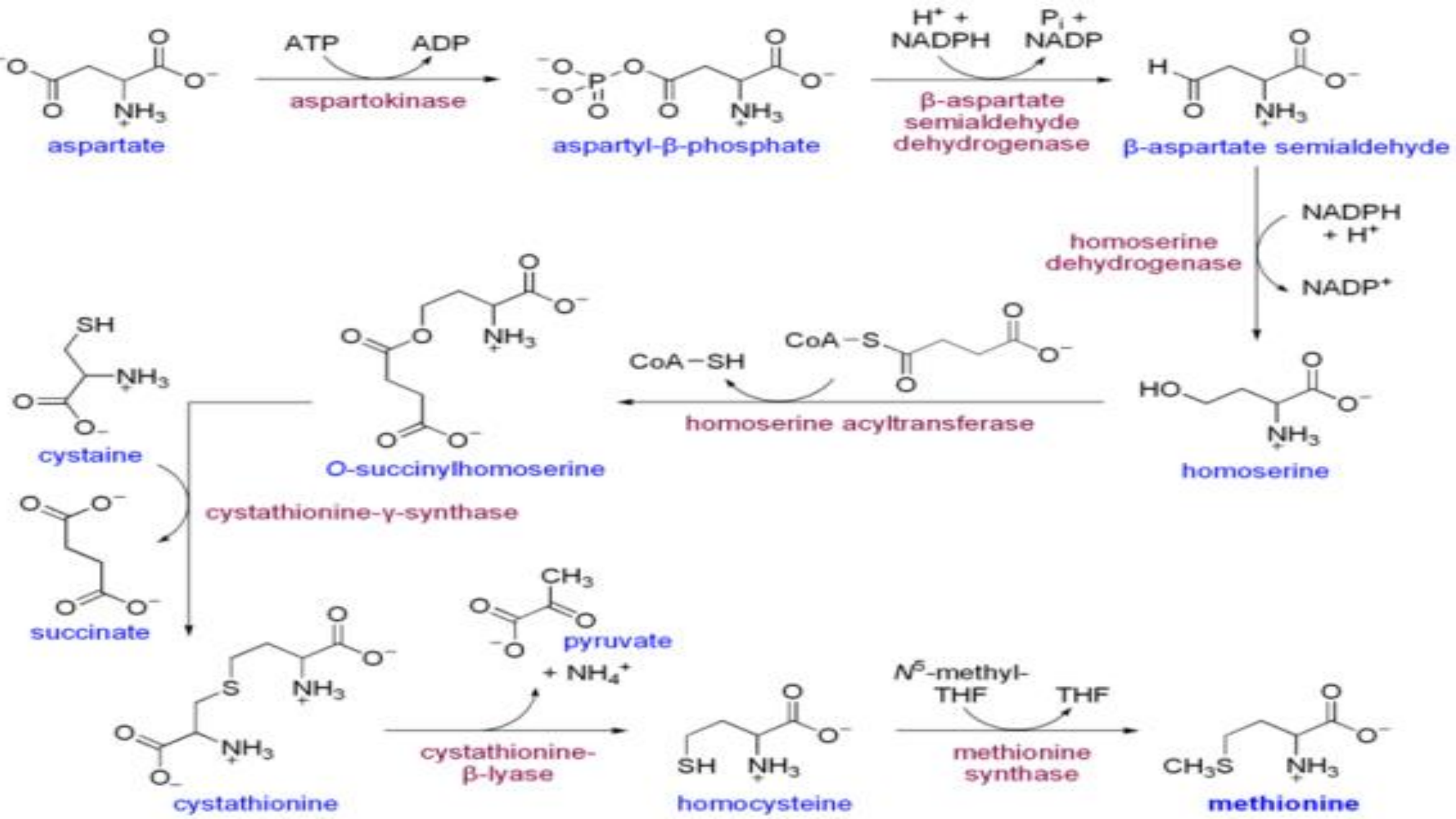
α-Kg → Homocitrate → Homoisocitrate → α-ketoadipate

Many steps ↓

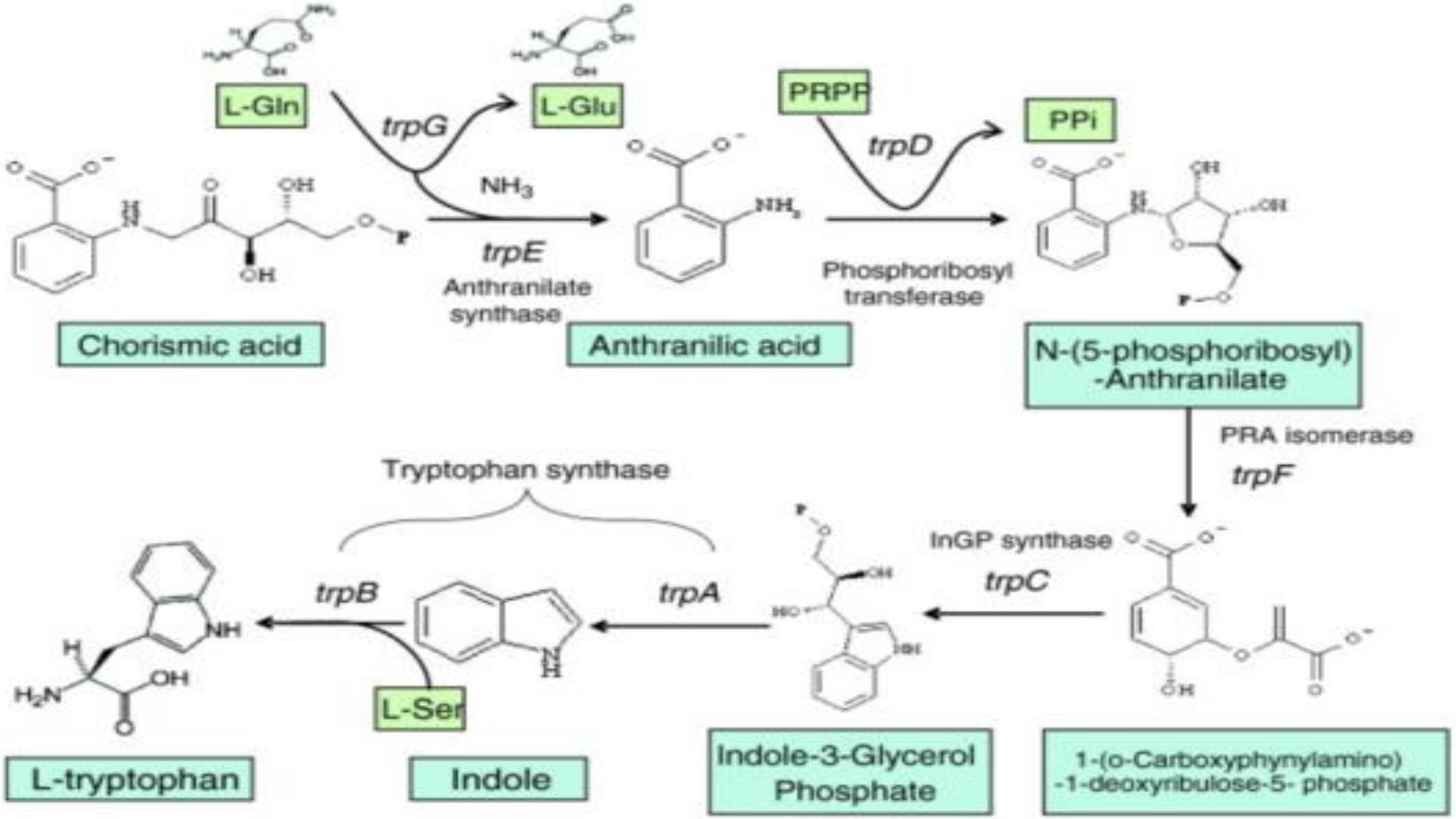
lysine

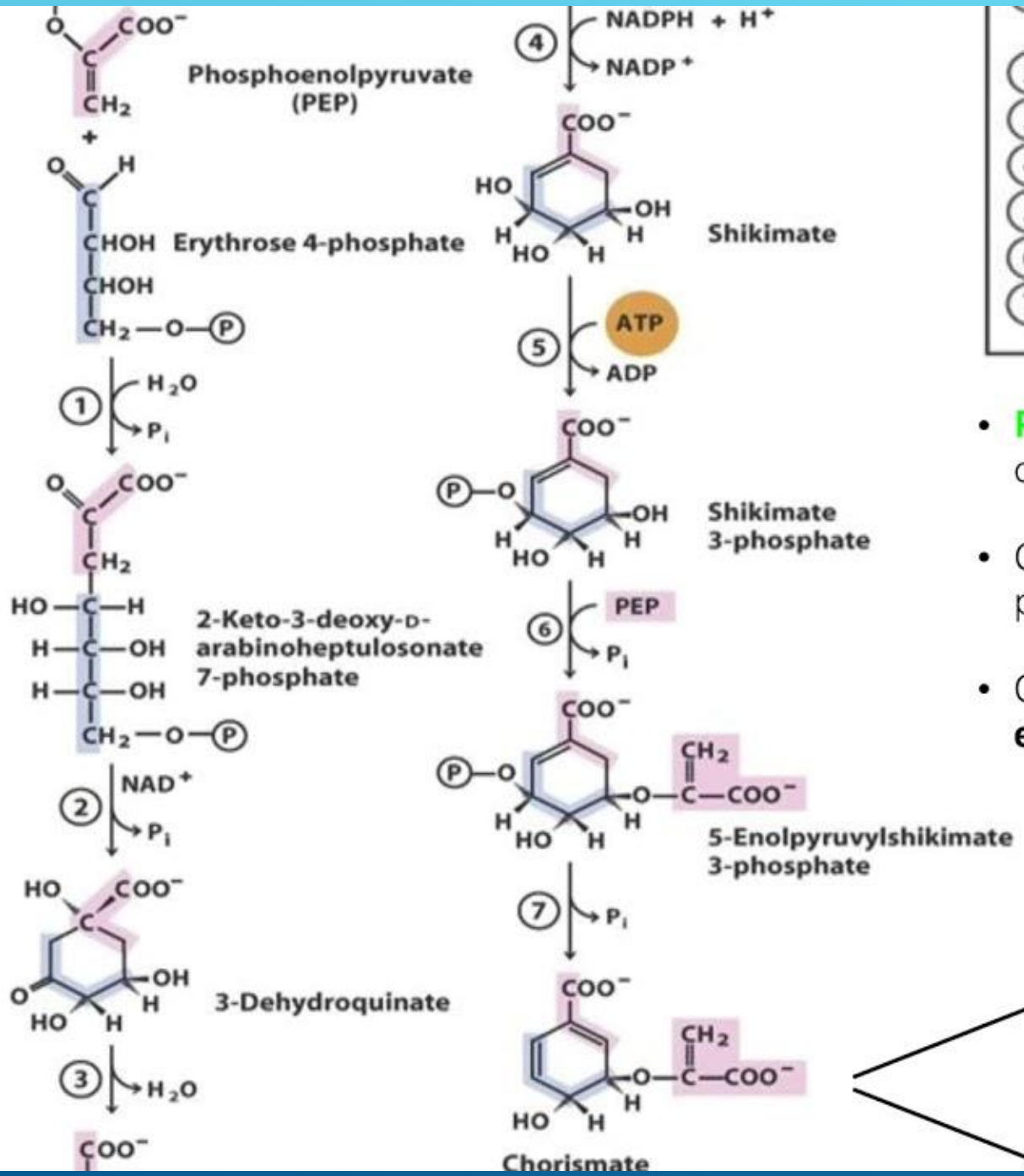
Threonine, methionine and lysine biosynthesis in bacteria arises from the common precursor aspartate via the intermediate β -aspartyl semialdehyde




aspartate
ATP
ADP
aspartokinase
aspartyl-β-phosphate
H+ + NADPH
Pi + NADP
β-aspartate semialdehyde dehydrogenase
β-aspartate semialdehyde
NADPH + H+
NADP+
homoserine dehydrogenase
homoserine
CoA–S
CoA–SH
homoserine acyltransferase
O-succinylhomoserine
cystaine
succinate
cystathionine-γ-synthase
cystathionine
pyruvate
+ NH4+
cystathionine-β-lyase
homocysteine
N5-methyl-THF
THF
methionine synthase
methionine

- PEP and Erythrose-4-P Family:
- The aromatic amino acids are synthesized in a shared pathway that has chorismate as the key intermediate. Chorismate is common to the synthesis of compounds with benzene rings including amino acids, Q, Qb, Vitamins E and K, and lignin.
- Chorismate is synthesized via the shikimate pathway; and the precursors to shikimate are PEP and erythrose-4-P

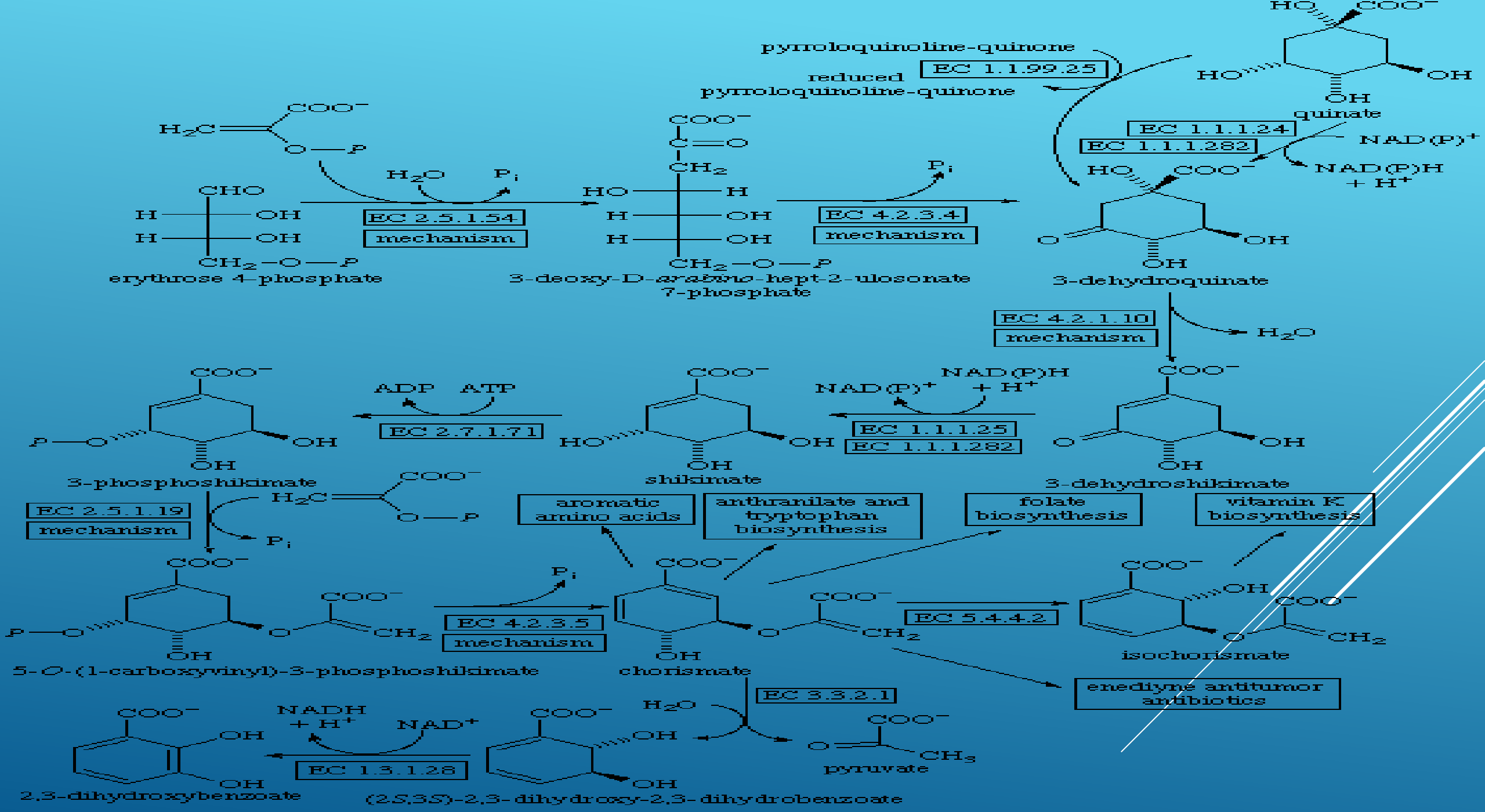

L-Gln
trpG
L-Glu
NH3
trpE
Anthranilate synthase
PRPP
trpD
PPi
Phosphoribosyl transferase
Chorismic acid
Anthranilic acid
N-(5-phosphoribosyl) -Anthranilate
PRA isomerase
trpF
InGP synthase
trpC
Tryptophan synthase
trpB
trpA
L-Ser
L-tryptophan
Indole
Indole-3-Glycerol Phosphate
1-(o-Carboxyphynylamino) -1-deoxyribulose-5- phosphate



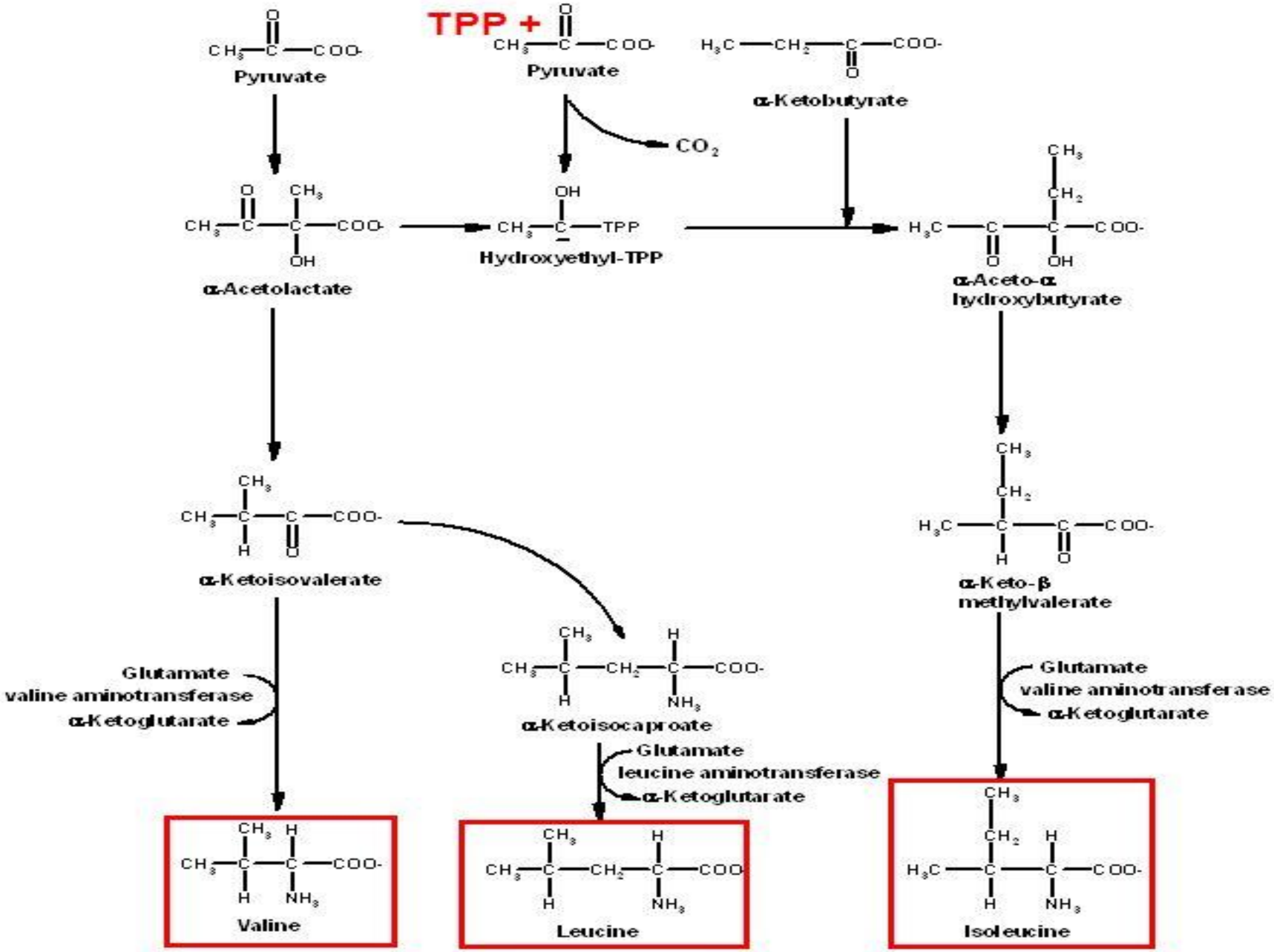
synthase
2. dehydroquinate synthase
3. 3-dehydroquinate dehydratase
4. shikimate dehydrogenase
5. shikimate kinase
6. 5-enolpyruvylshikimate 3-phosphate synthase
7. chorismate synthase

- Phenylalanine, Tyrosine, and Tryptophan all possess 1 or 2 aromatic rings.
- Generating the aromatic ring requires a common precursor: **chorismate**
- Chorismate is generated from **PEP** (glycolysis, step 9) and **erythrose-4-phosphate** (hexose monophosphate shunt).

Phenylalanine
Tyrosine → ***Catecholamines***

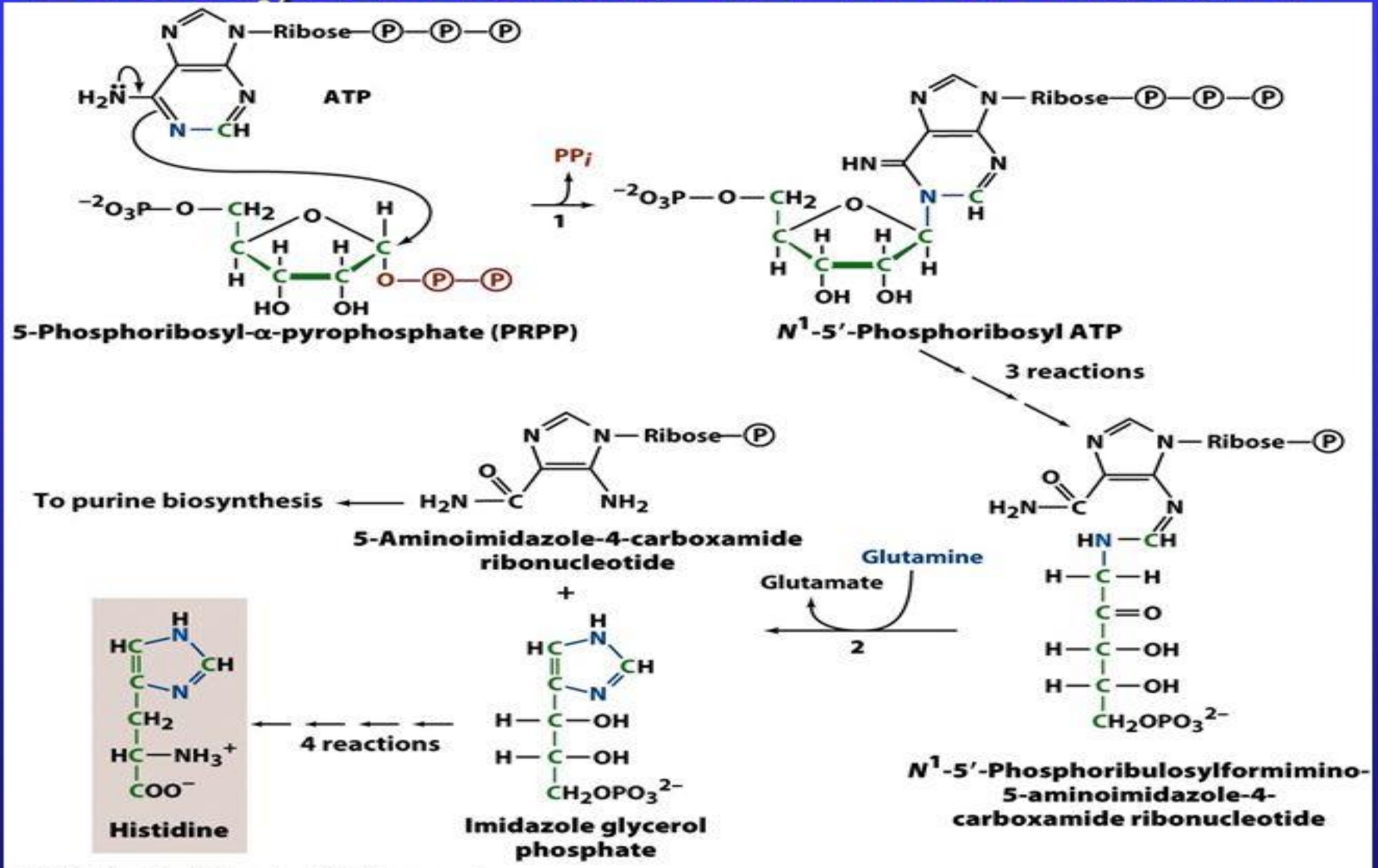

pyrroloquinoline-quinone
EC 1.1.99.25
reduced pyrroloquinoline-quinone
quinate
EC 1.1.1.24
EC 1.1.1.282
NAD(P)+
NAD(P)H + H+
H2O
Pi
EC 2.5.1.54
mechanism
erythrose 4-phosphate
3-deoxy-D-arabino-hept-2-ulosonate 7-phosphate
EC 4.2.3.4
mechanism
3-dehydroquinate
EC 4.2.1.10
mechanism
3-dehydroshikimate
EC 1.1.1.25
EC 1.1.1.282
shikimate
ADP
ATP
EC 2.7.1.71
3-phosphoshikimate
EC 2.5.1.19
mechanism
aromatic amino acids
anthranilate and tryptophan biosynthesis
folate biosynthesis
vitamin K biosynthesis
5-O-(1-carboxyvinyl)-3-phosphoshikimate
EC 4.2.3.5
mechanism
chorismate
EC 5.4.4.2
isochorismate
enediyne antitumor antibiotics
EC 3.3.2.1
pyruvate
NADH + H+
NAD+
EC 1.3.1.28
2,3-dihydroxybenzoate
(2S,3S)-2,3-dihydroxy-2,3-dihydrobenzoate

Synthesis of Valine, Leucine, and Isoleucine



Willmore 2003

Biosynthesis of Histidine



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Voet, Voet & Pratt 2008 Fig 21.36

Many thanks for attention