

Amino Acid Degradation

A. Concepts

1. Convergent
2. ketogenic/glucogenic
3. Reactions seen before

The SEVEN (7) Families

B. Transaminase (A,D,E) / Deaminase (Q,N) Family

C. Related to biosynthesis (R,P,H; C,G,S; T,M)

1. Glu Family

- a. Introduce oxidases/oxygenases
- b. Introduce one-carbon metabolism (1C)

2. Pyruvate Family

- a. PLP reactions

3. α -ketobutyric Family

- a. 1-C metabolism

D. Dedicated (F,Y; K,W; V,I,L)

1. Aromatic Family

- a. oxidases/oxygenases

2. α -ketoadipic Family

3. Branched-chain Family

Amino Acid Degradation

- Intermediates of the **central metabolic pathway**
- Some amino acids result in more than one intermediate.
- Ketogenic amino acids can be converted to ketone bodies.

Seven to **Acetyl-CoA** Leu, **Ile**, **Thr**, Lys, **Phe**, **Tyr**, **Trp**

- Glucogenic amino acids can be converted to glucose.

Six to **pyruvate**¹ Ala, Cys, Gly, Ser, **Thr**, **Trp**

Five to **α -ketoglutarate**² Arg, Glu, Gln, His, Pro

Four to **succinyl-CoA** **Ile**, Met, **Thr**, Val

Two to **fumarate**³ **Phe**, **Tyr**

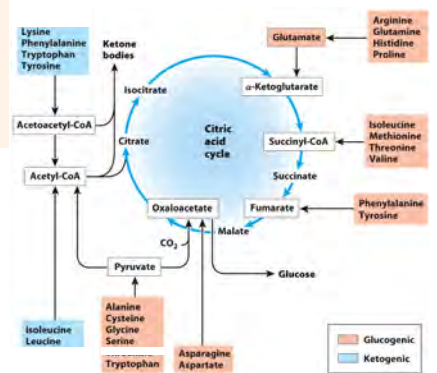
Two to **oxaloacetate**⁴ Asp, Asn

¹Pyruvate family

²Glu family

³Aromatic family

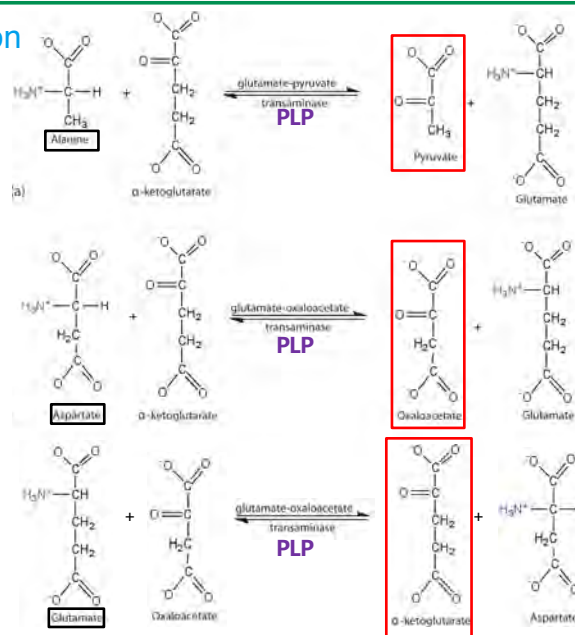
⁴Trans-/de-aminase family



Amino Acid Degradation

A,D,E

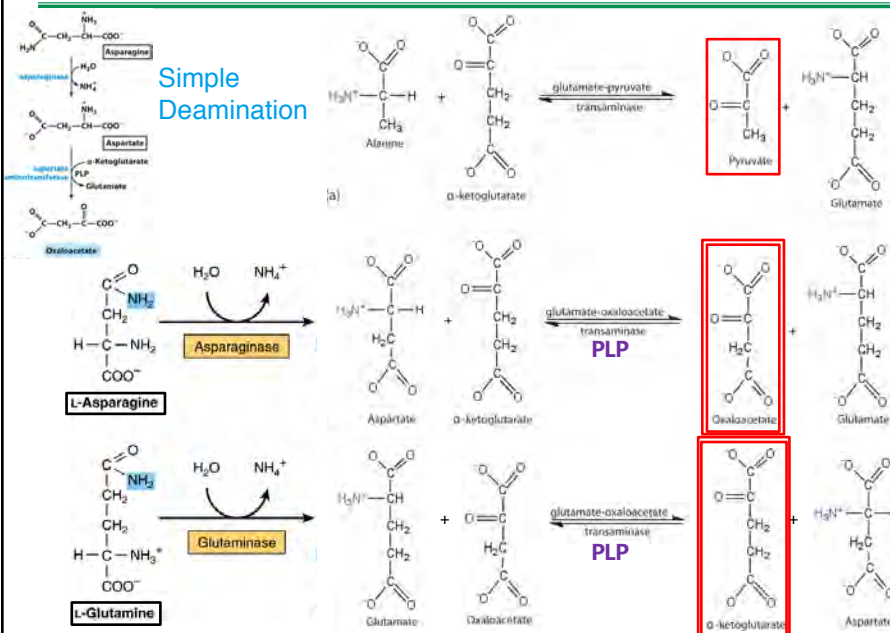
Simple Transamination



Amino Acid Degradation

N,Q

Simple Deamination



Amino Acid Degradation

A,D,E,N,Q

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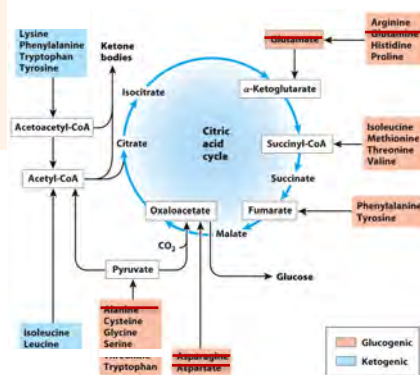
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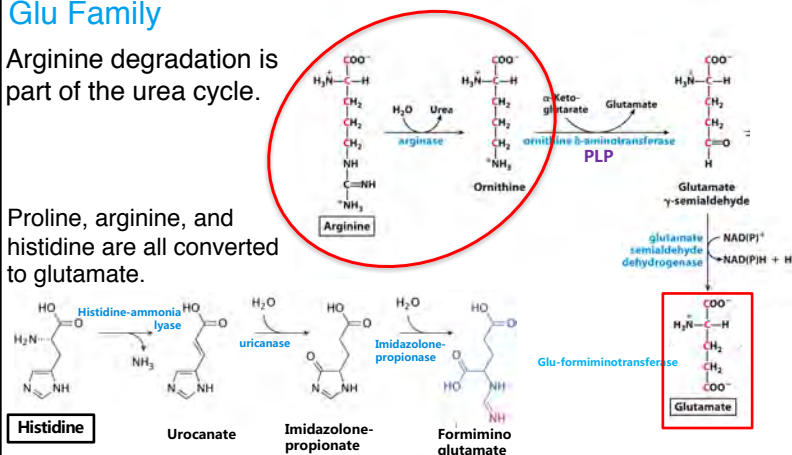
Amino Acid Degradation

R,P,H

Glu Family

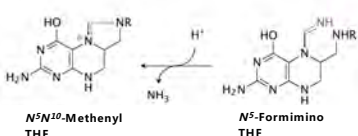
Arginine degradation is part of the urea cycle.

Proline, arginine, and histidine are all converted to glutamate.



Two new metabolic concepts used:

- Oxidase
- One-carbon metabolism



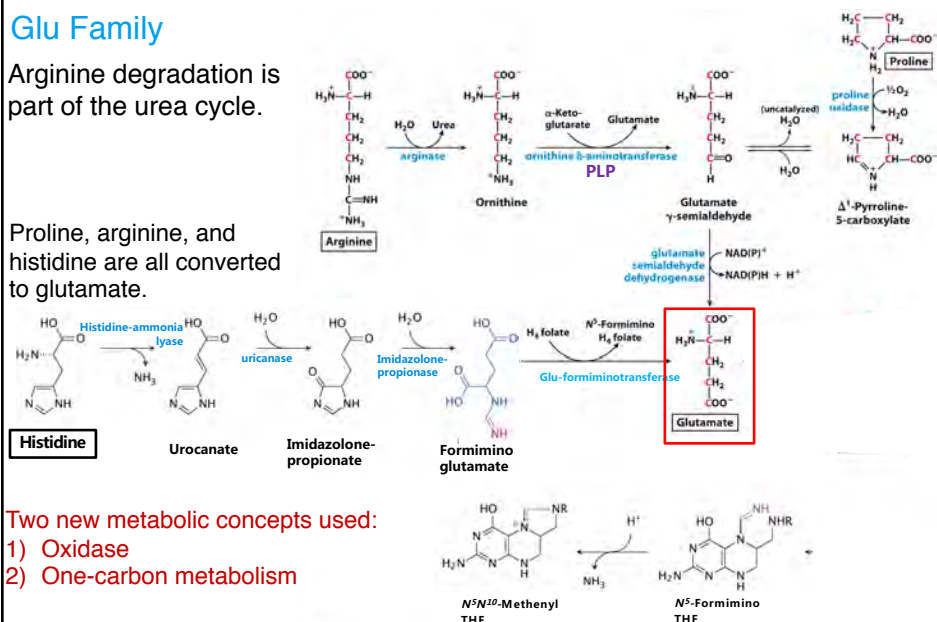
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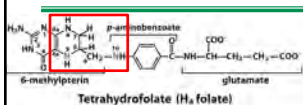
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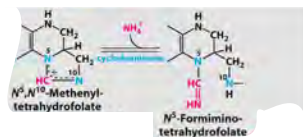
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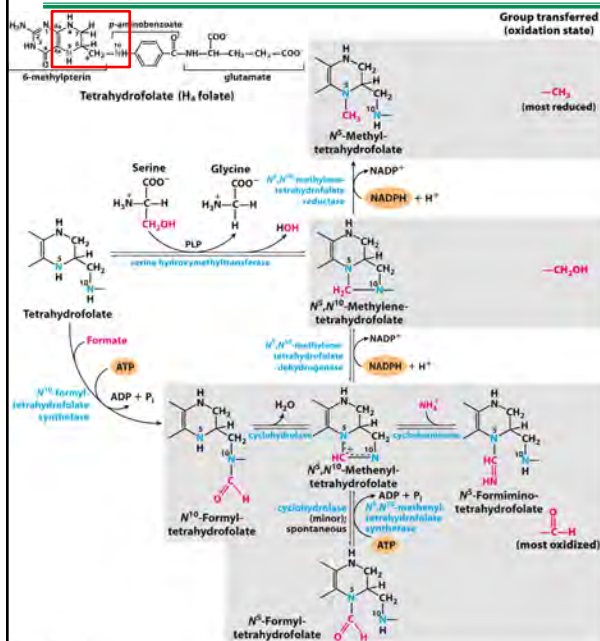
- 1) Oxidase
- 2) One-carbon metabolism

Amino Acid Degradation: One Carbon



- Tetrahydrofolate is formed from folate.
 - an essential vitamin
 - Folate is reduced to dihydrofolate, then to tetrahydrofolate (THF)
- It is used in a wide variety of metabolic reactions.
- THF can transfer 1-carbon in different oxidation states.
 - CH₃, CH₂OH, and CHO
- Carbon generally comes from serine.
- Forms are interconverted on THF before use.

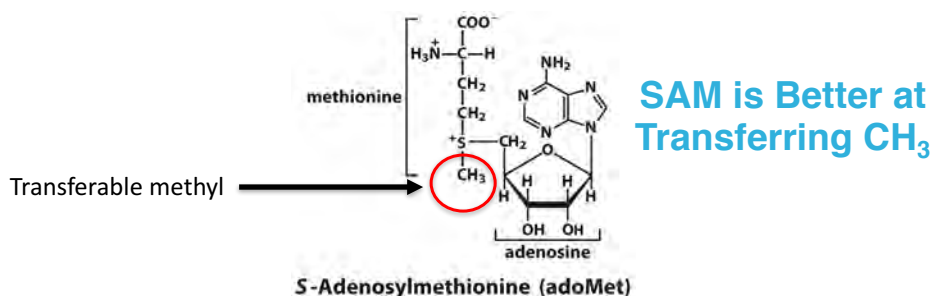




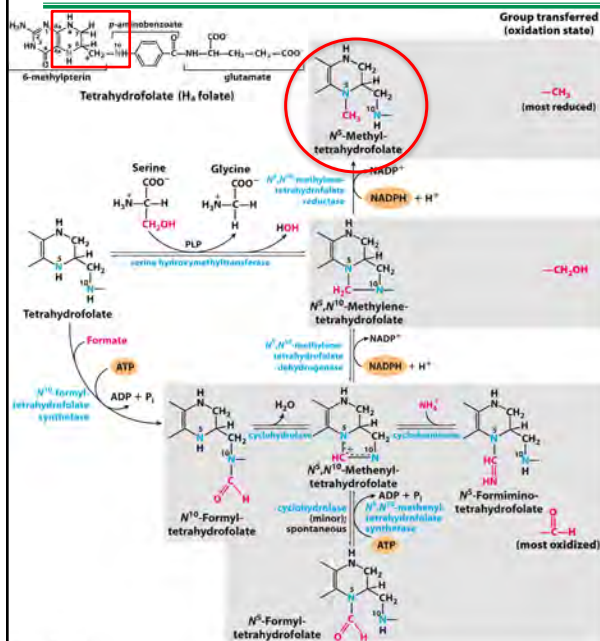
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Amino Acid Degradation: One Carbon

S-Adenosyl-Methionine (SAM or adoMet)



- S-adenosylmethionine is the preferred cofactor for methyl transfer in biological reactions.
 - Methyl in SAM is 1000 times more reactive than THF-methyl group.
- It is synthesized from ATP and methionine in the "SAM Cycle" (part of α -ketobutyrate family (M,T))
- Regeneration uses N⁵-methyl THF.
 - The only known use in mammals



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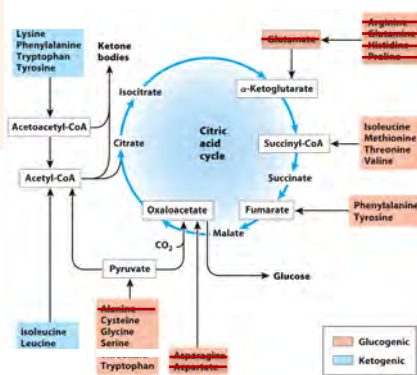
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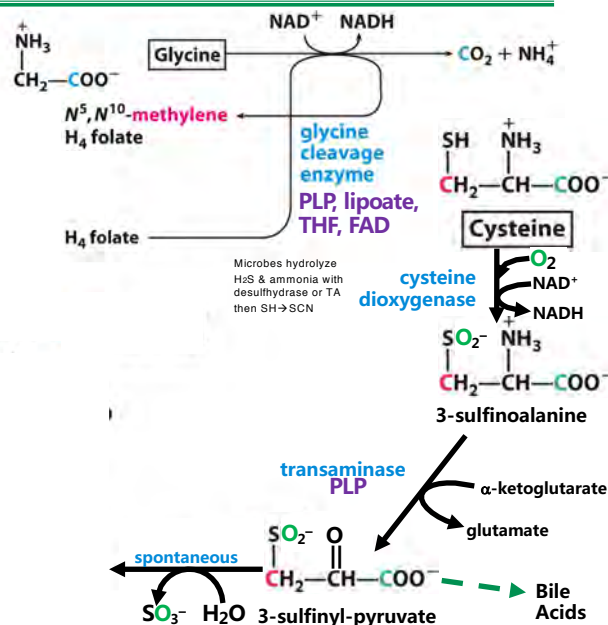
4Trans-/de-aminase family

Amino Acid Degradation

S,G,C

Pyruvate Family

- Pathway #1: glycine cleavage enzyme
 - apparently major pathway in mammals
 - separation of three central atoms
 - releases CO_2 and NH_3
 - methylene group is transferred to THF
 - mechanism like PDH complex
- Pathway #2: hydroxylation to serine \rightarrow pyruvate via SerOHMe transferase & Ser/Thr dehydratase
- Pathway #3: D-amino oxidase
 - relatively minor pathway
 - ultimately oxidized to oxalate
 - major component of kidney stones

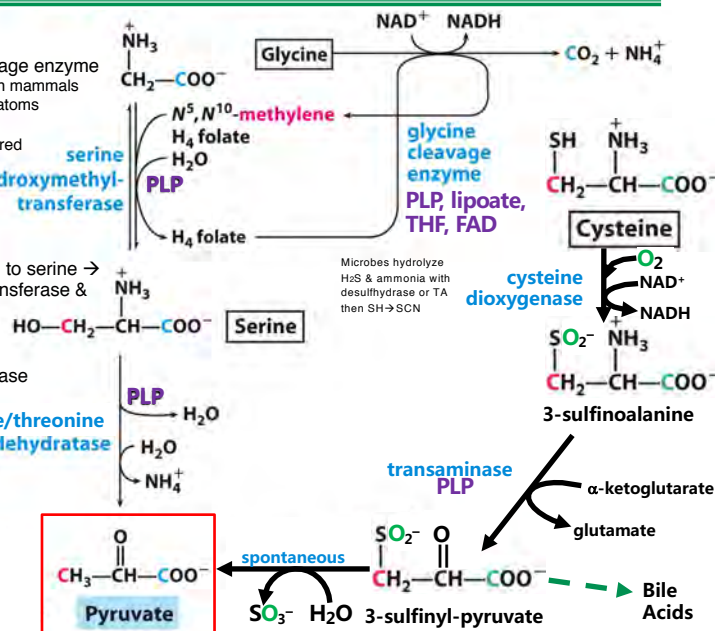


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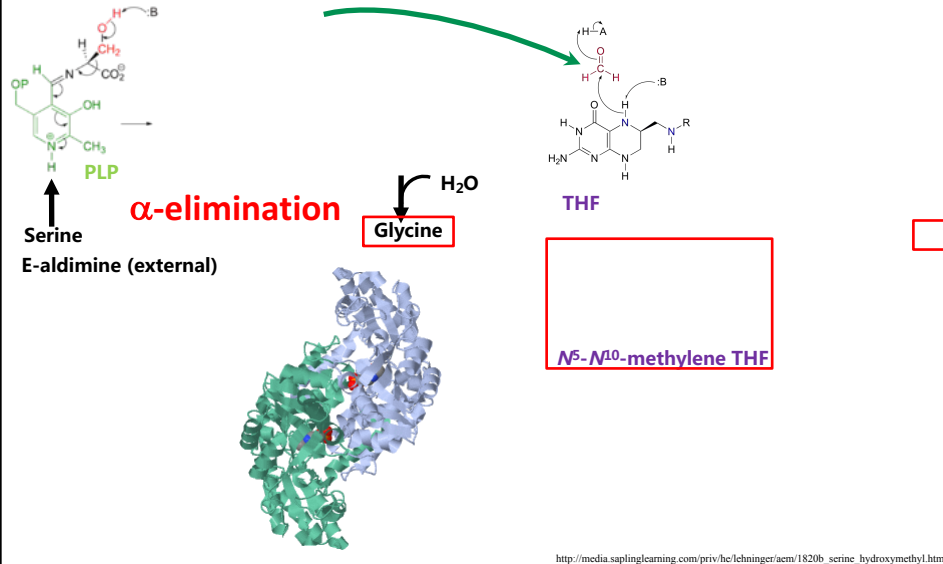
Amino Acid Degradation

Pyruvate Family:

Serine hydroxymethyl transferase

Serine/Glycine

See Sapling animated Figure
(shows Gly→Ser)



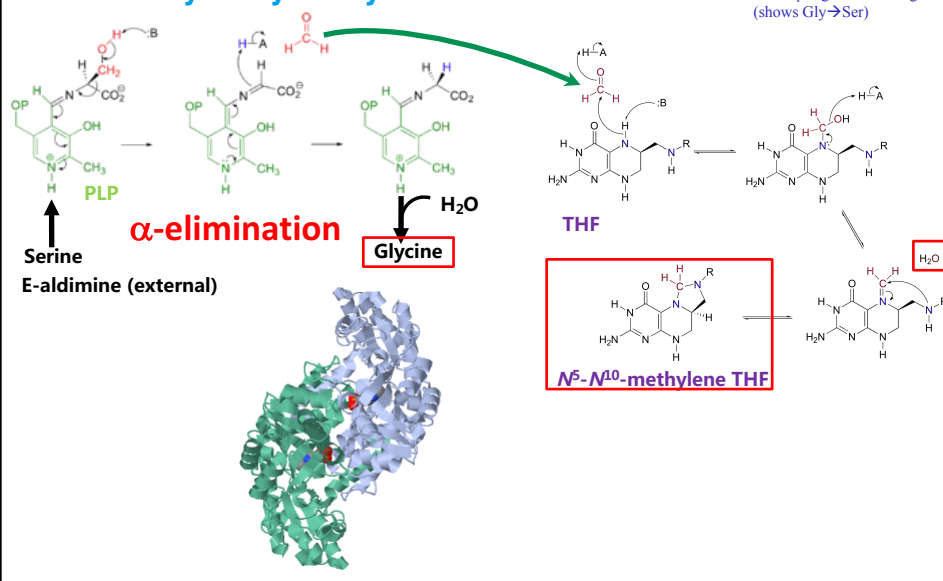
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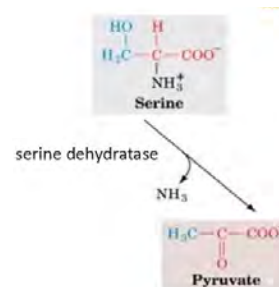
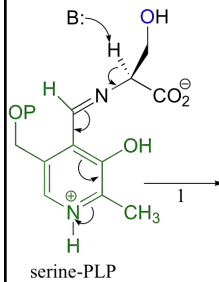
Amino Acid Degradation

Pyruvate Family:
Ser/Thr dehydratase

Serine

See Sapling animated Figures
(shows a concerted mech)

β -elimination



Amino Acid Degradation

Pyruvate Family:
Ser/Thr dehydratase

Serine

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