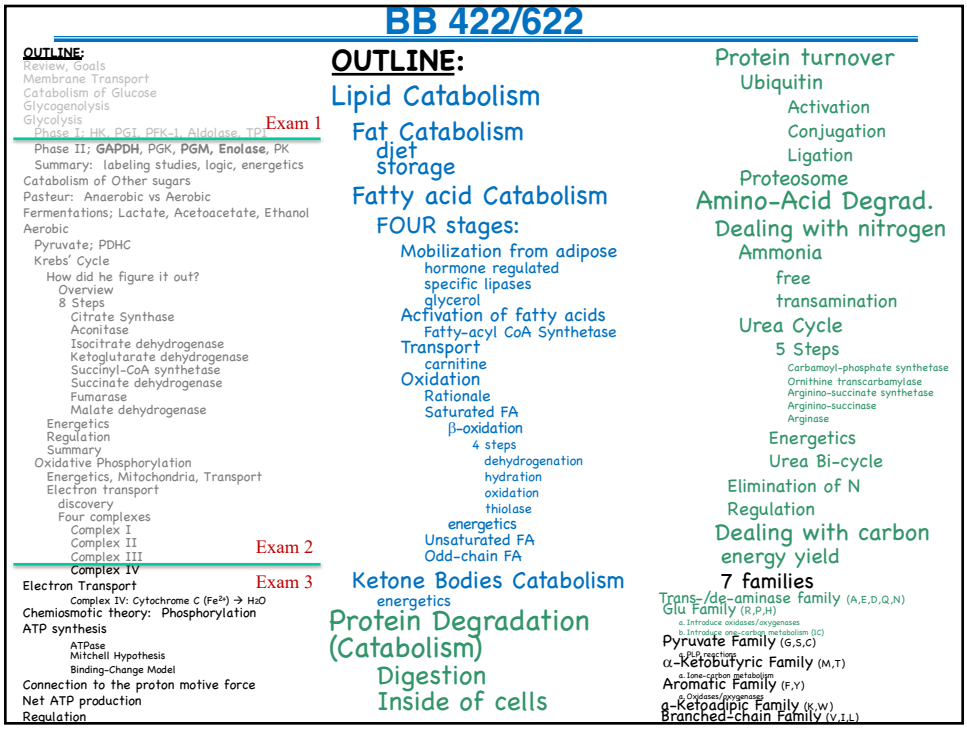


87

Amino Acid Degradation: the carbon "skeletons"

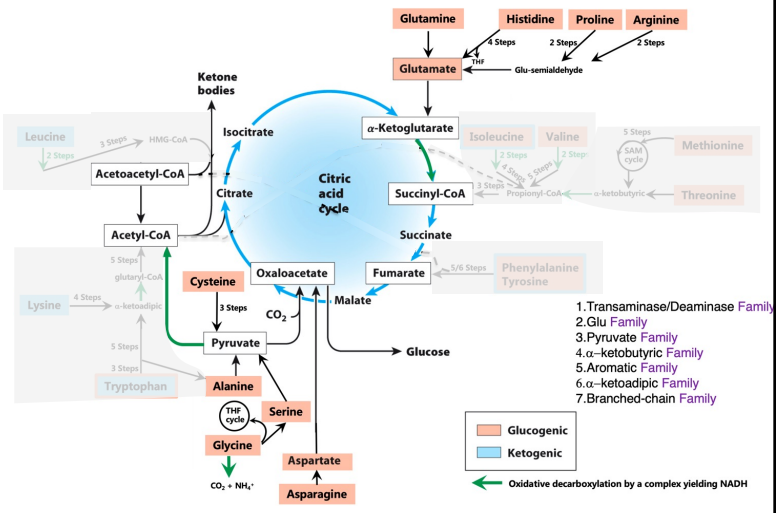
A. Concepts
   1. Convergent
   2. ketogenic/glucogenic
   3. Reactions seen before

The SEVEN (7) Families

B. Transaminase (A,D,E) / Deaminase (Q,N) Family (5)
C. Related to biosynthesis (8)
   1. Glu Family (R,P,H)
      a. Introduce oxidases/oxygenases
      b. Introduce one-carbon metabolism (1C)
   2. Pyruvate Family (G,S,C)
      a. PLP reactions
   3. α–Ketobutyric Family (M,T)
      a. 1-C metabolism
D. Dedicated (7)
   1. Aromatic Family (F,Y)
      a. oxidases/oxygenases
   2. α–Ketoadipic Family (K,W)
   3. Branched-chain Family (V,I,L)
E. Convergence with Fatty Acids: propionyl-CoA

88

Amino Acid Degradation



90

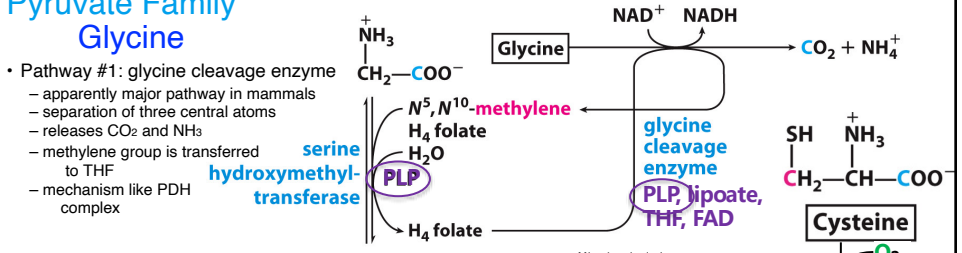
Amino Acid Degradation

G,S,C

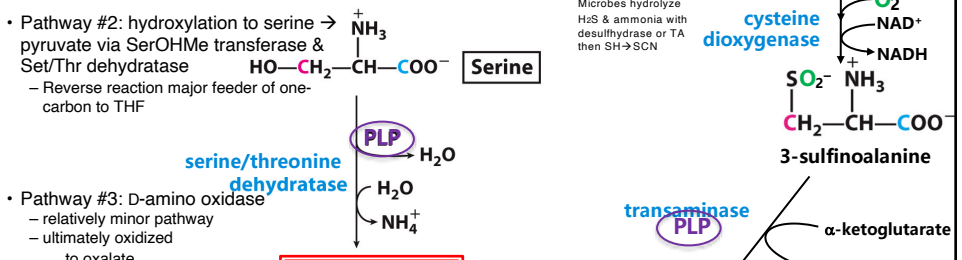
Pyruvate Family

Glycine

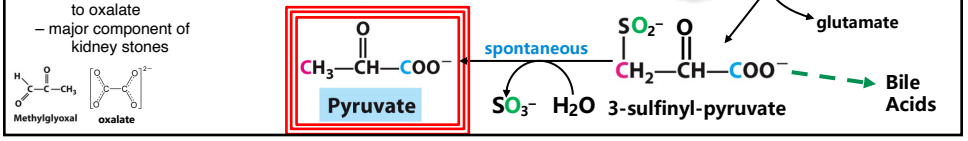
- Pathway #1: glycine cleavage enzyme
  - apparently major pathway in mammals
  - separation of three central atoms
  - releases CO_2 and NH_3
  - methylene group is transferred to THF
  - mechanism like PDH complex



- Pathway #2: hydroxylation to serine → pyruvate via SerOHMe transferase & Set/Thr dehydratase
  - Reverse reaction major feeder of one-carbon to THF



- Pathway #3: D-amino oxidase
  - relatively minor pathway
  - ultimately oxidized to oxalate
  - major component of kidney stones



92

Amino Acid Degradation

G,S,C

Pyruvate Family
Glycine

- Pathway #1: glycine cleavage enzyme
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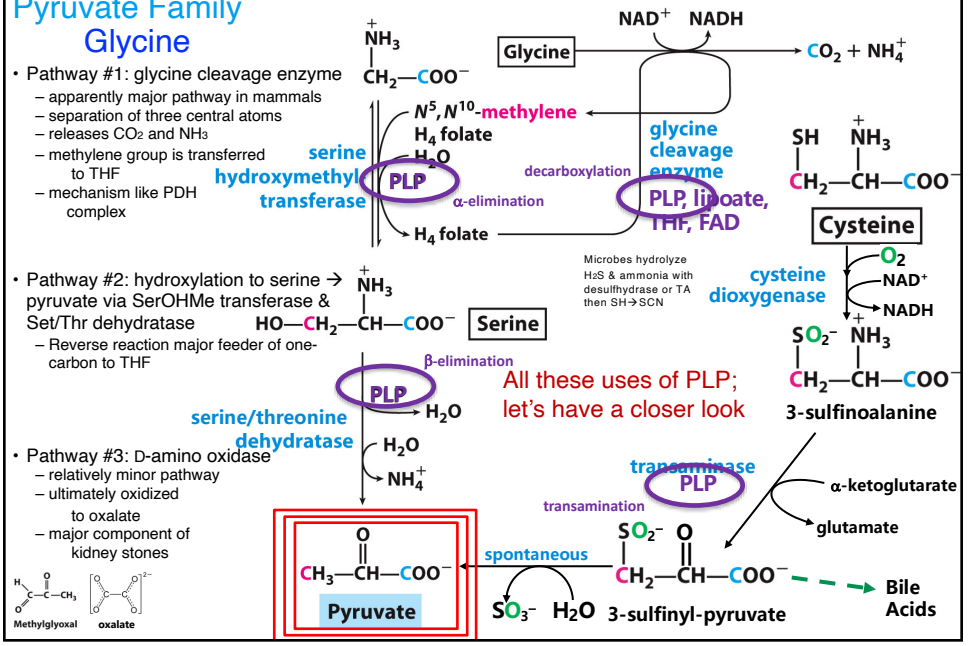


94

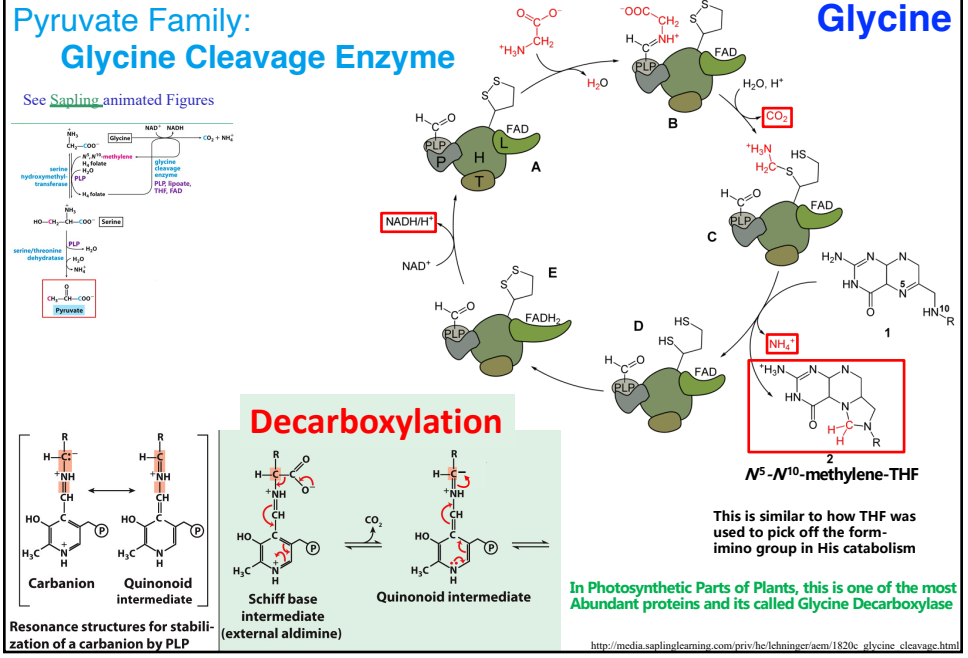
Amino Acid Degradation

G,S,C

Pyruvate Family:
Glycine Cleavage Enzyme

Glycine

See Sapling animated Figures



Resonance structures for stabilization of a carbanion by PLP

This is similar to how THF was used to pick off the formimino group in His catabolism

In Photosynthetic Parts of Plants, this is one of the most Abundant proteins and its called Glycine Decarboxylase

http://media.saplinglearning.com/priv/hc/lehninger/acm/1820c_glycine_cleavage.html

96

Mechanism of Glycine Decarboxylase

- In plants, this same ortholog of Gly-clevage enzyme is called Gly decarboxylase
- Flux through rubisco reaction and glycolate pathway can be high in bright sun, so plants need a lot of glycine decarboxylase.
  - makes up 50% of protein in some plant leaves
  - but non-photosynthetic parts of plants (tubers, etc.) have *little* glycine decarboxylase

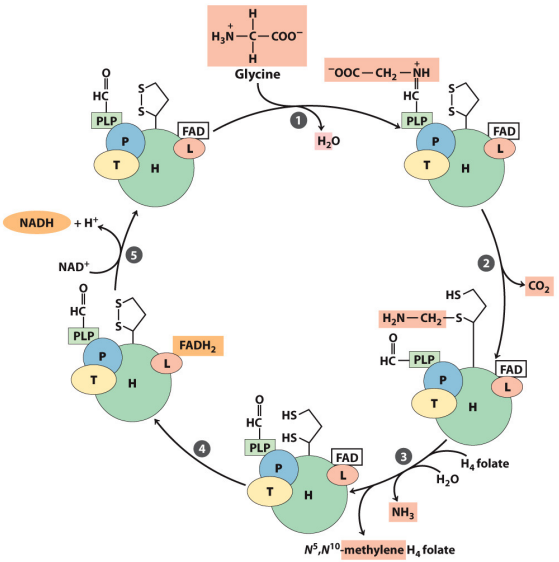


Figure 20-49

Glycine Decarboxylase Is Abundant in Photosynthetic Parts of Plants

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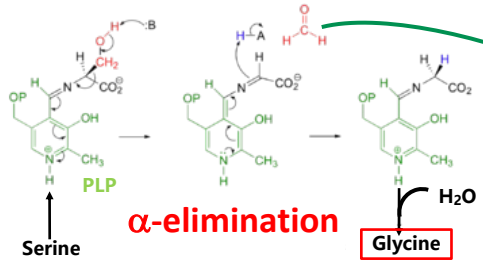
Amino Acid Degradation G,S,C

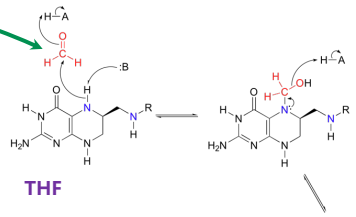
Pyruvate Family:

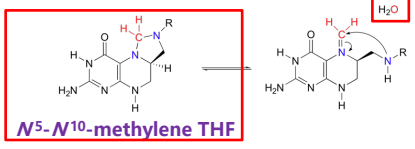
Serine hydroxymethyl transferase

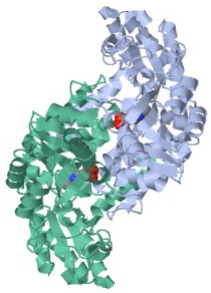
Serine/Glycine

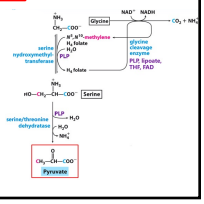
See Sapling animated Figure (shows Gly→Ser)











99

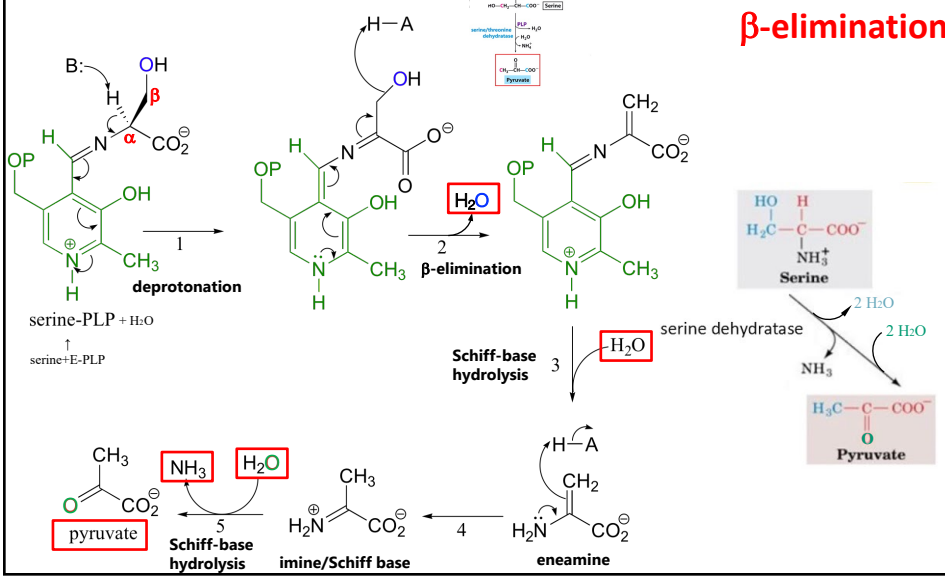
Amino Acid Degradation G,S,C

Pyruvate Family:
Ser/Thr dehydratase

Serine

See Sapling animated Figures (shows a concerted mech)

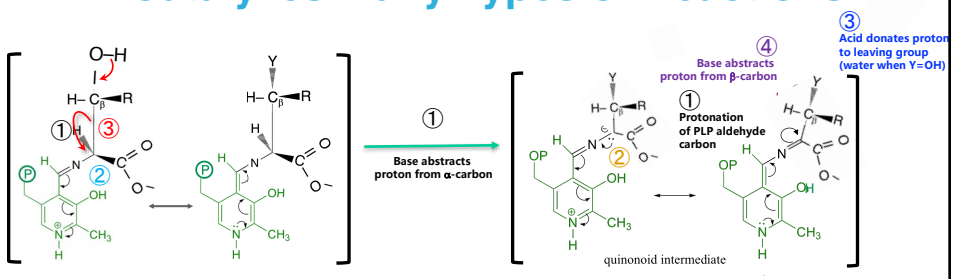
β-elimination



101

Amino Acid Degradation

PLP Catalyzes Many Types of Reactions

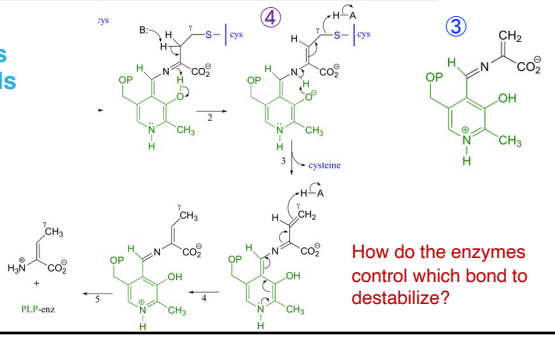


Cα-bond:

① Transamination of Amino Acids
② Decarboxylation of Amino Acids
③ α-elimination of Amino Acids

After Cα-H abstracted ① :

② Racemization of Amino Acids
③ β-elimination of Amino Acids
④ γ-elimination of Amino Acids

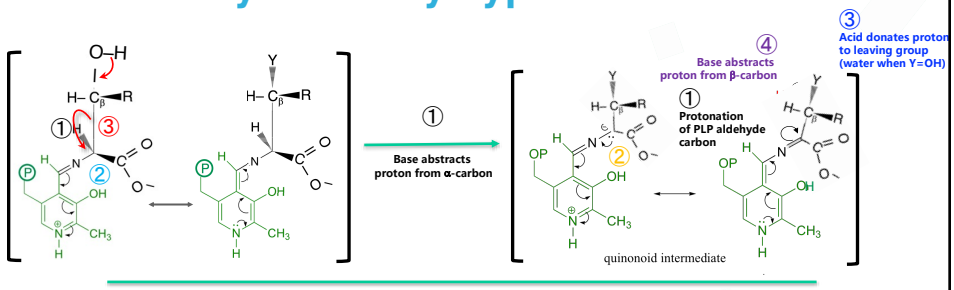


How do the enzymes control which bond to destabilize?

102

Amino Acid Degradation

PLP Catalyzes Many Types of Reactions



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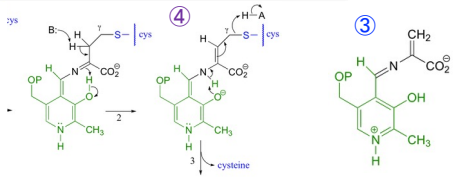

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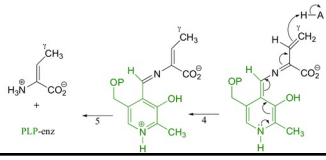

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103

Amino Acid Degradation

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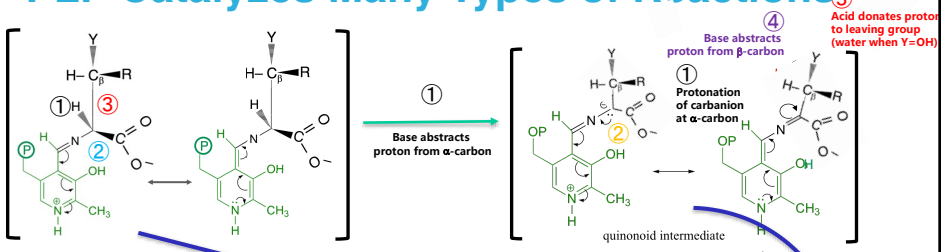

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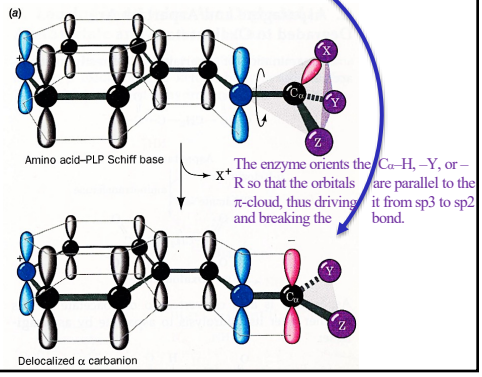

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② Racemization of Amino Acids
③ β-elimination of Amino Acids
④ γ-elimination of Amino Acids

104

Amino Acid Degradation

G,S,C

- 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,[7] Ile,[7] *Thr*, Lys,[6] Trp,[6] Phe,[5] Tyr[5]

- Glucogenic amino acids can be converted to glucose.

Six to pyruvate[3,1]	*Thr*, Trp
Five to α-ketoglutarate[2,1]	
Four to succinyl-CoA[7,4]	Ile, Met, **Thr**, Val
Two to fumarate[5]	Phe, Tyr
Two to oxaloacetate[1]	

✓[1]Trans-/de-aminase family
✓[2]Glu family
✓[3]Pyruvate family
[4]Alpha-keto butyric family
[5]Aromatic family
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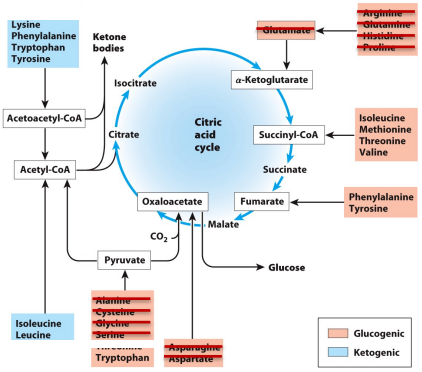
[7]Branched-chain family



105

Amino Acid Degradation: the carbon "skeletons"

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 (8)
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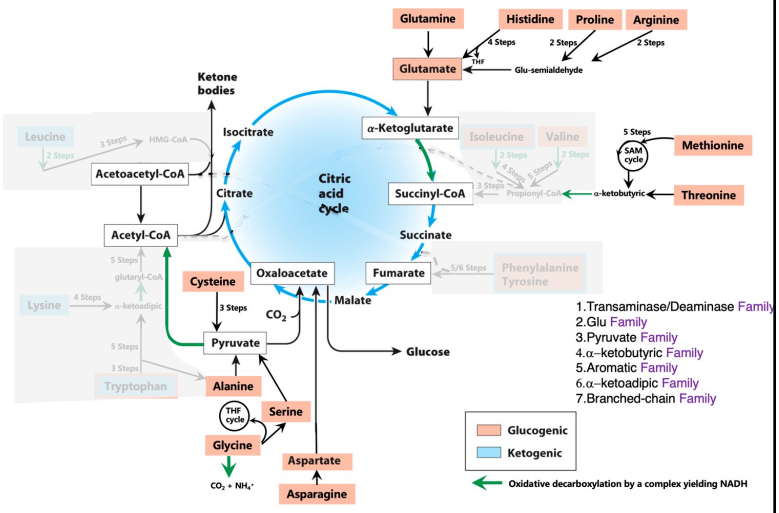
    b. Introduce one-carbon metabolism (1C)
  2. Pyruvate Family (G,S,C)
    a. PLP reactions
  3. α–Ketobutyric Family (M,T)
    a. 1-C metabolism
D. Dedicated (7)
  1. Aromatic Family (F,Y)
    a. oxidases/oxygenases
  2. α–Ketoadipic Family (K,W)
  3. Branched-chain Family (V,I,L)
E. Convergence with Fatty Acids: propionyl-CoA

Before MT

106

Amino Acid Degradation

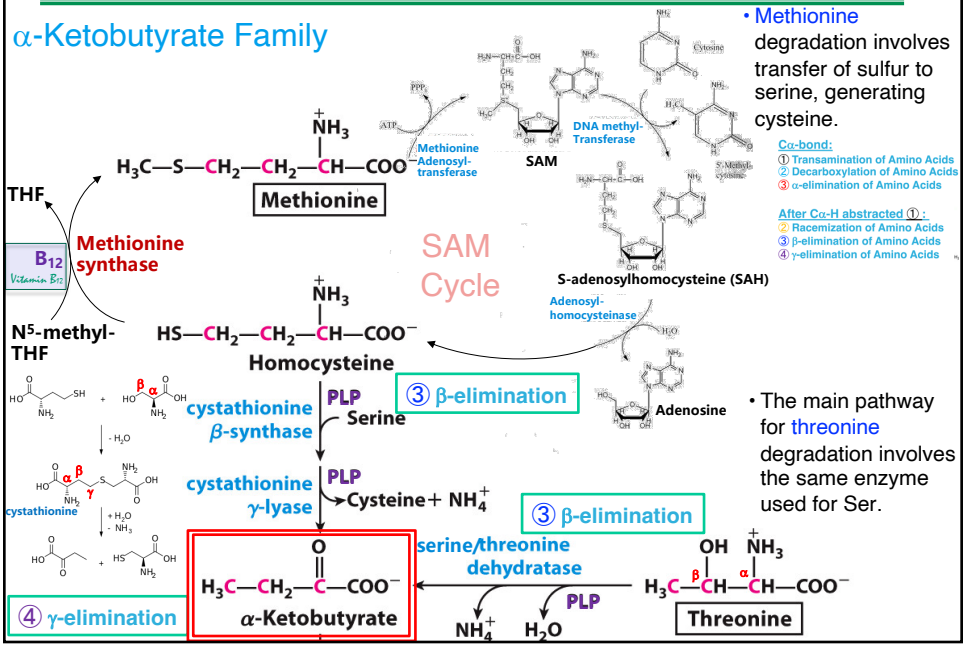


109

Amino Acid Degradation

M,T

α-Ketobutyrate Family



- Methionine degradation involves transfer of sulfur to serine, generating cysteine.

Cα-bond:
① Transamination of Amino Acids
② Decarboxylation of Amino Acids
③ α-elimination of Amino Acids

After Cα-H abstracted ① :
② Racemization of Amino Acids
③ β-elimination of Amino Acids
④ γ-elimination of Amino Acids

- The main pathway for threonine degradation involves the same enzyme used for Ser.

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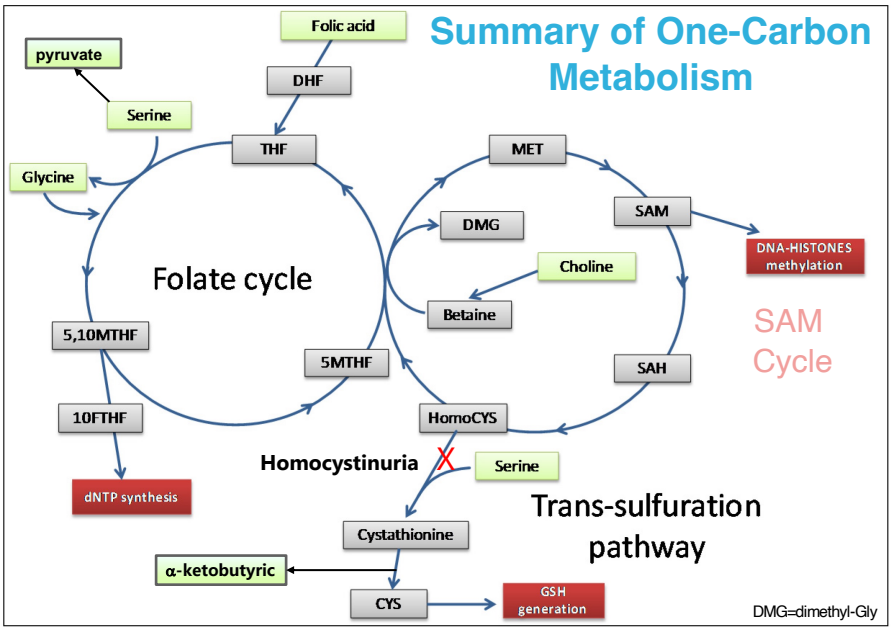
Amino Acid Degradation: One Carbon



112

Amino Acid Degradation

M,T

- 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,[7] Ile,[7] Lys,[6] Trp,[6] Phe,[5] Tyr[5]

- Glucogenic amino acids can be converted to glucose.

Six to pyruvate[3,1] Trp
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Four to succinyl-CoA[7,4] Ile, Val
Two to fumarate[5] Phe, Tyr
Two to oxaloacetate[1]

✓[1]Trans-/de-aminase family
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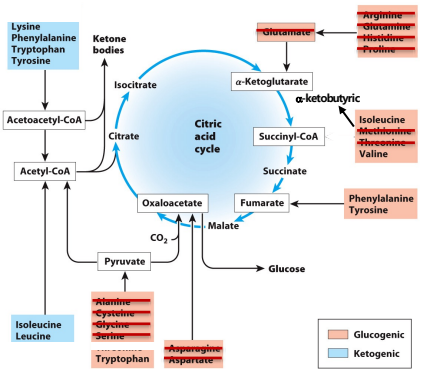

113

Amino Acid Degradation: the carbon "skeletons"

A. Concepts
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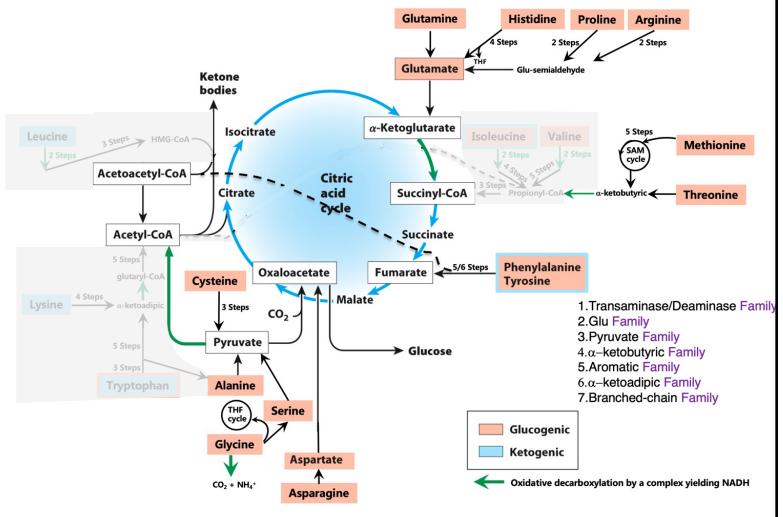
E. Convergence with Fatty Acids: propionyl-CoA

Before FY

115

Amino Acid Degradation



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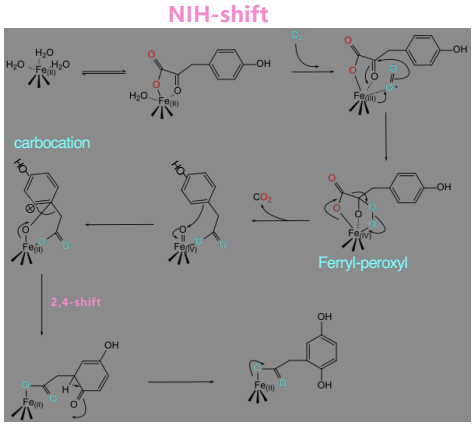
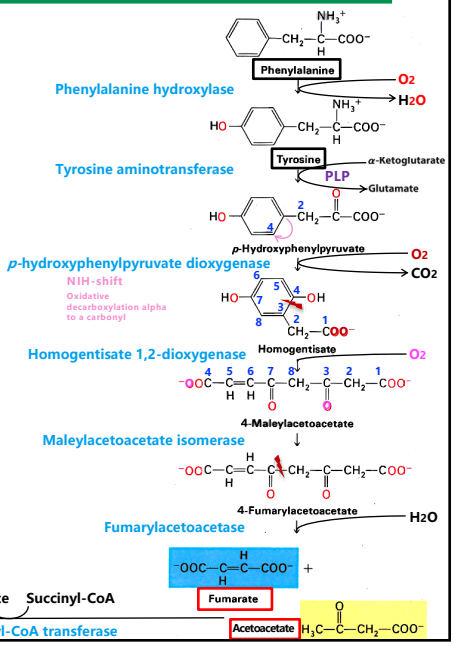
Amino Acid Degradation

F,Y

Aromatic Family





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Amino Acid Degradation: Oxidases

Nomenclature

Oxidases – use molecular oxygen as an electron acceptor, but no atoms into substrate

- e.g., cytochrome oxidase, proline oxidase
- usually have water or hydrogen peroxide as product

$$A(red) + O_2 + 4H^+ \rightarrow A(ox) + 2H_2O$$

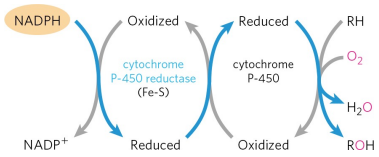
Oxygenase* – use of molecular oxygen to put into the substrate

- dioxygenases – use both atoms; e.g., cysteine dioxygenase

$$A + O_2 \rightarrow AO_2$$

- mono-oxygenases – one atom in substrate, one atom as water

$$RH + BH_2 + O_2 \rightarrow ROH + B + H_2O$$



- The enzyme is a cytochrome called P-450
- The co-substrate electrons are from NADPH
- There is Cytochrome P-450 reductase to funnel electrons from co-substrate (B)

*a.k.a.: hydroxylase, mixed-function oxygenase, "mixed-function oxidase"

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F,Y

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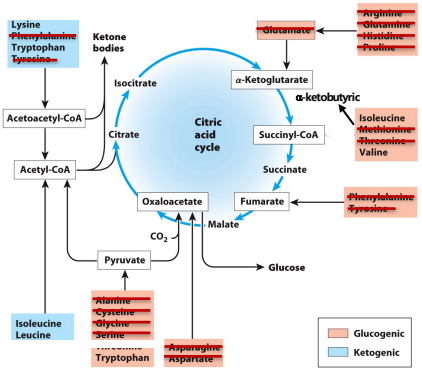

125

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Before KW

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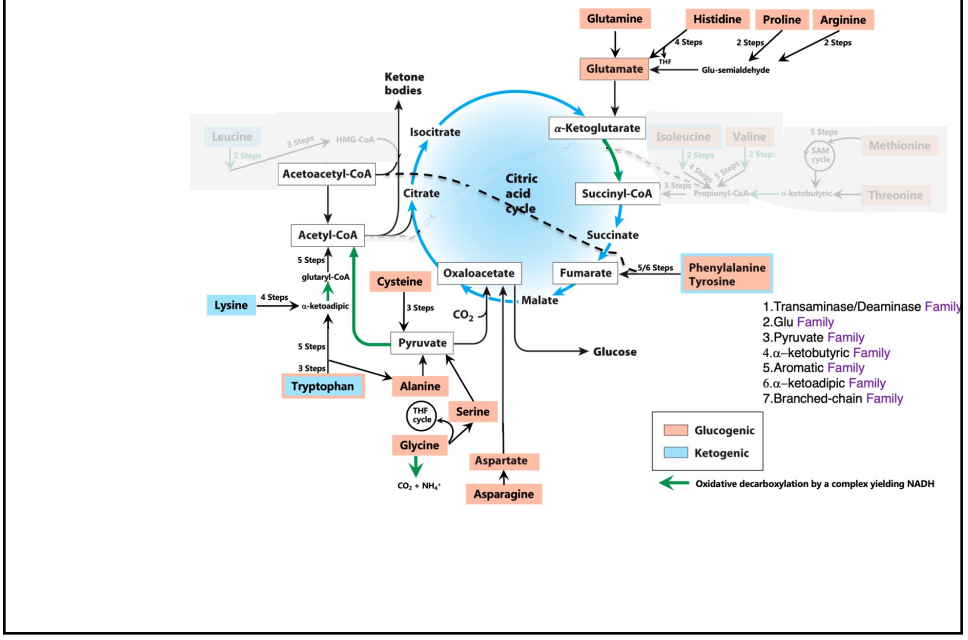
Amino Acid Degradation



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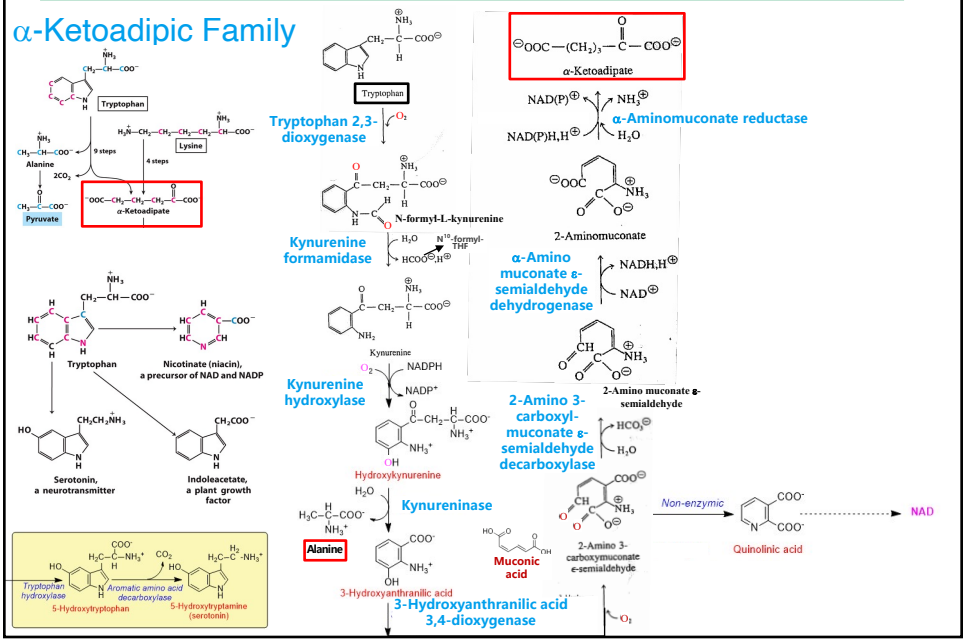
Amino Acid Degradation

K,W



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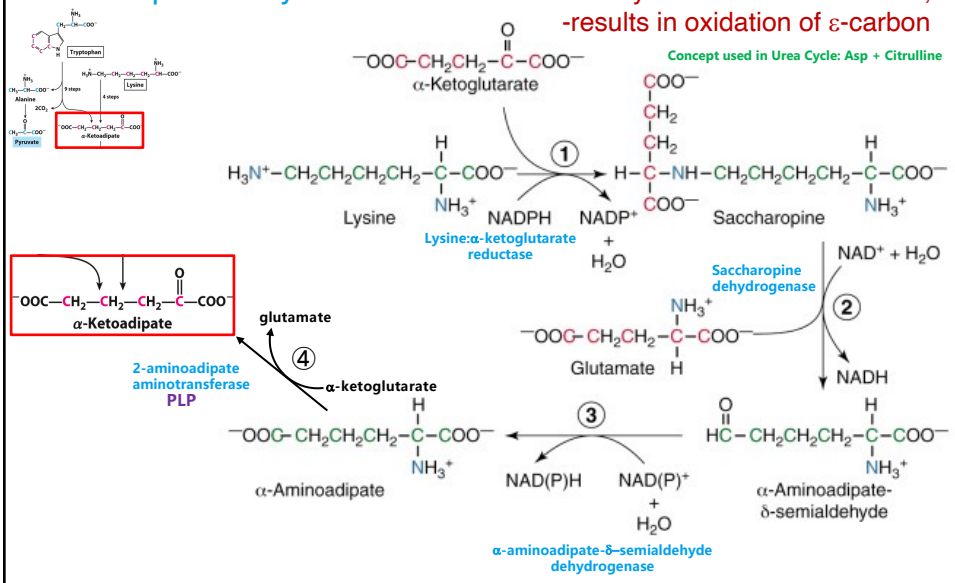
Amino Acid Degradation

α-Ketoadipic Family

-removal of ε-amino by reductive de-amination;
-results in oxidation of ε-carbon



132

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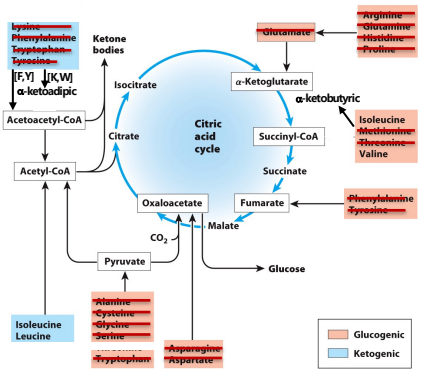
✓[4]Alpha-keto butyric family
✓[5]Aromatic family
✓[6]Alpha-keto adipic family
[7]Branched-chain family



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Amino Acid Degradation: the carbon "skeletons"

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; M,T)
   1. Glu Family
      a. Introduce oxidases/oxygenases
      b. Introduce one-carbon metabolism (1C)
   2. Pyruvate Family
      a. PLP reactions
   3. α–Ketobutyric Family (M,T)
      a. 1-C metabolism

D. Dedicated
   1. Aromatic Family (F,Y)
      a. oxidases/oxygenases
   2. α–Ketoadipic Family (K,W)
   3. Branched-chain Family (V,I,L)

E. Convergence with Fatty Acids: propionyl-CoA

Before VIL

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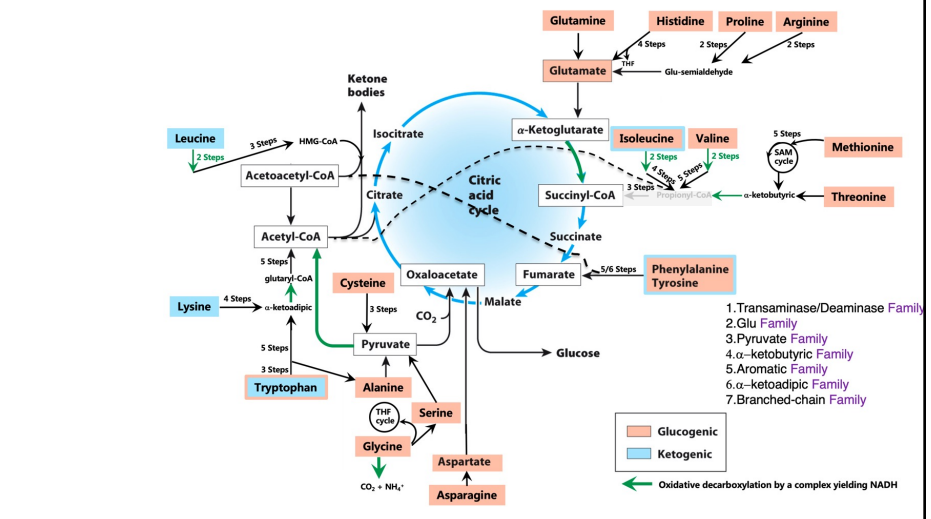
Amino Acid Degradation



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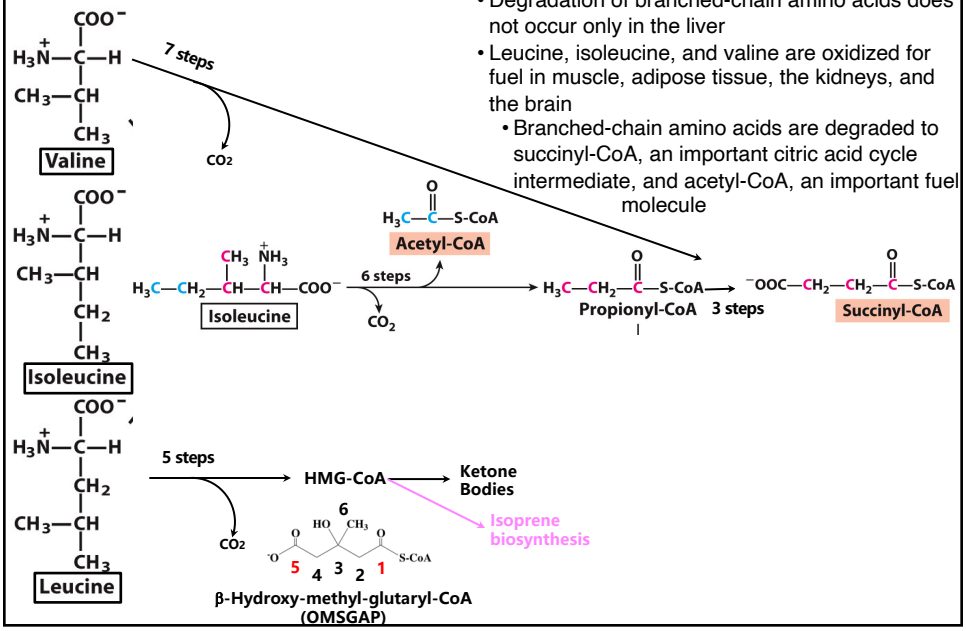
Amino Acid Degradation

V,I,L

- Degradation of branched-chain amino acids does not occur only in the liver
- Leucine, isoleucine, and valine are oxidized for fuel in muscle, adipose tissue, the kidneys, and the brain
  - Branched-chain amino acids are degraded to succinyl-CoA, an important citric acid cycle intermediate, and acetyl-CoA, an important fuel molecule



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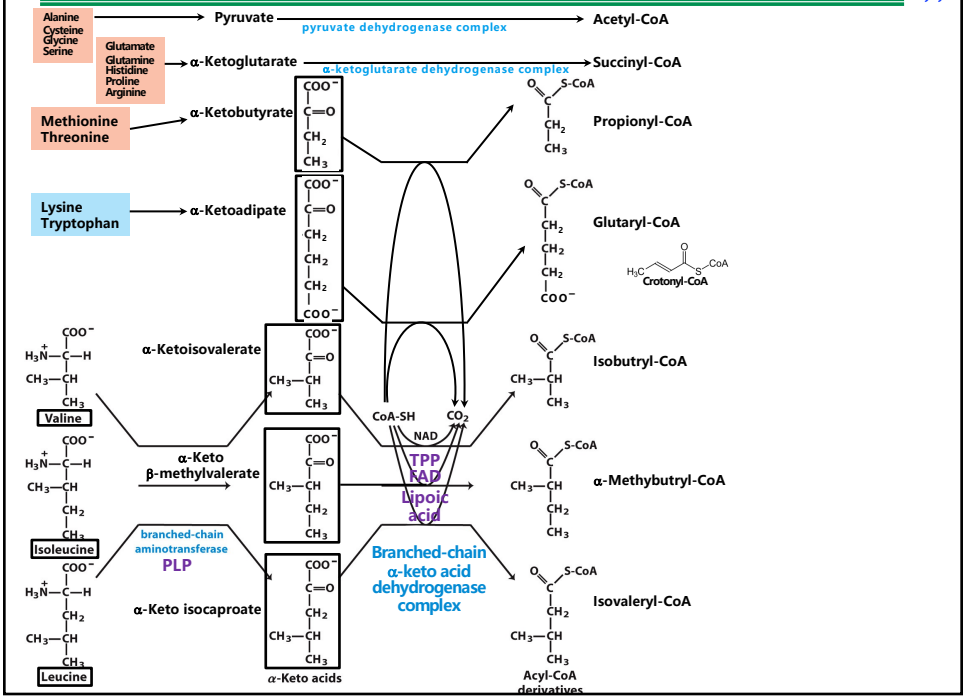
Amino Acid Degradation — OXIDATIVE DECARBOXYLATION — V,I,L



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