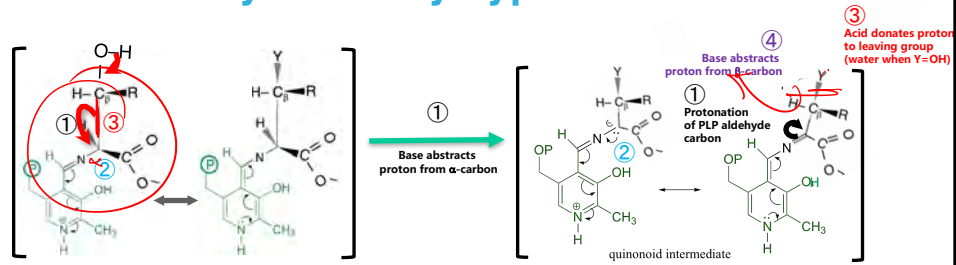


Amino Acid Degradation

PLP Catalyzes Many Types of Reactions

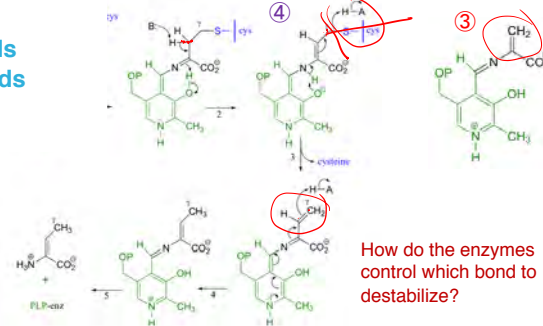


α -bond:

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

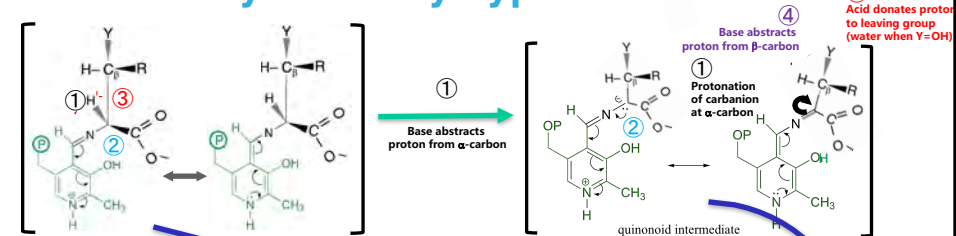
After α -H abstracted ①:

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



Amino Acid Degradation

PLP Catalyzes Many Types of Reactions

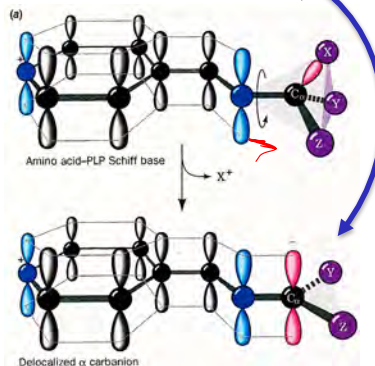


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Amino Acid Degradation

S,G,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, **Ile**, **Thr**, Lys, **Phe**, Tyr, Trp

- Glucogenic amino acids can be converted to glucose.

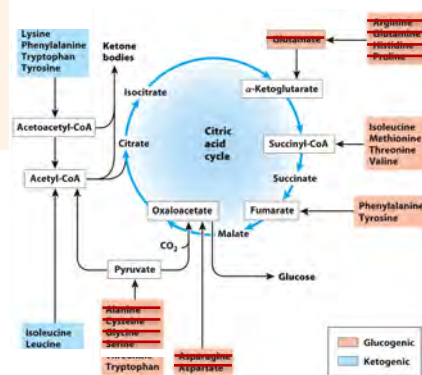
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Four to **succinyl-CoA** **Ile**, Met, **Thr**, Val

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. 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 (V,I,L)

- a. oxidases/oxygenases

2. α -ketoadipic Family (K,W)

3. Branched-chain Family (V,I,L)

M,T

[illegible]

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

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

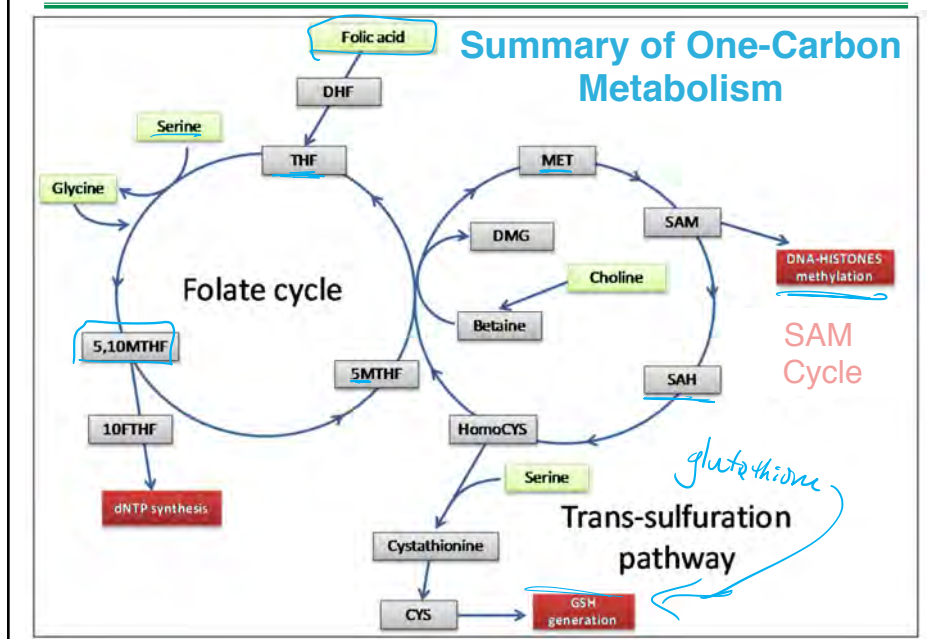
M,T

[illegible]

- **Methionine**
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Amino Acid Degradation: One Carbon



Amino Acid Degradation

M,T

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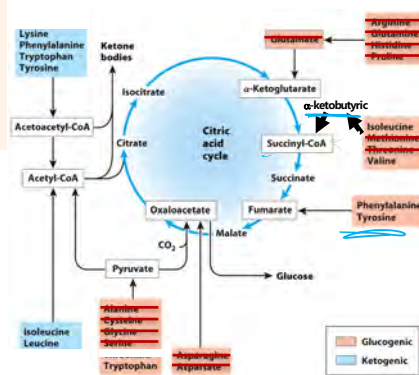
Two to **oxaloacetate**⁴ Asp, Asn

¹Pyruvate family

²Glu family

³Aromatic family

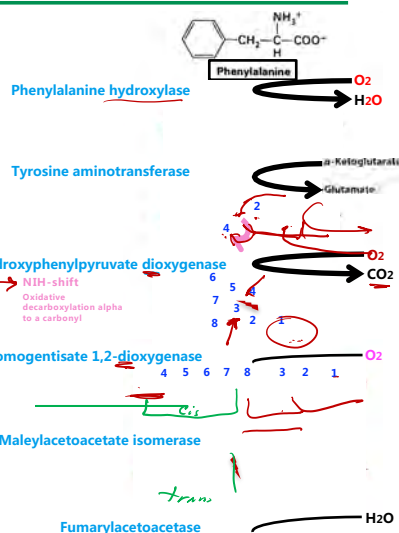
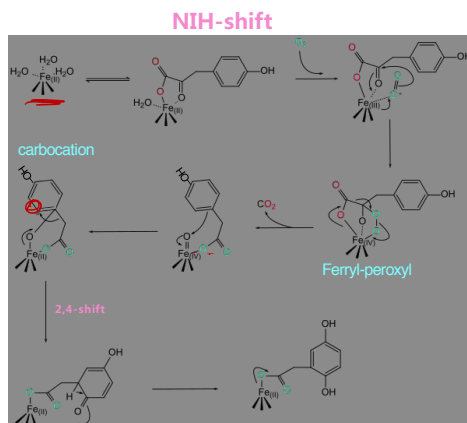
⁴Trans-/de-aminase family



Amino Acid Degradation

F,Y

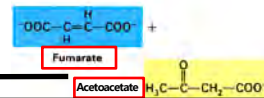
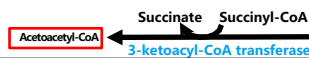
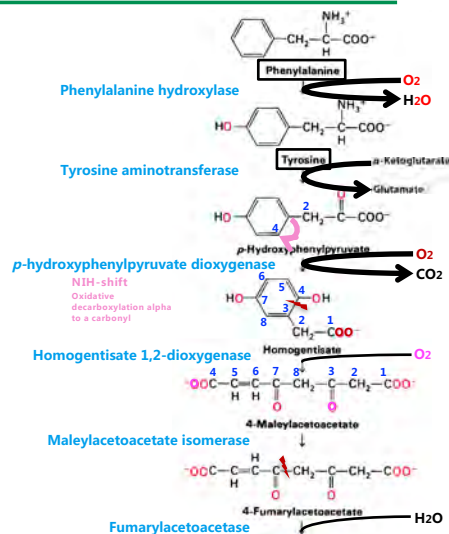
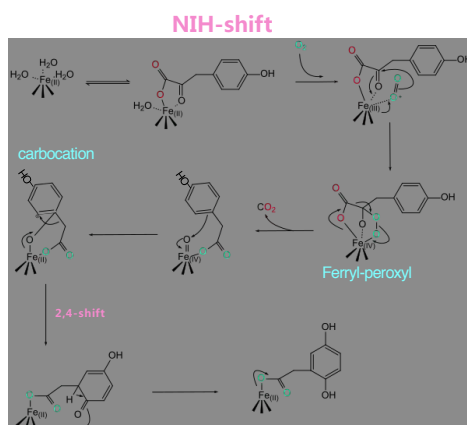
Aromatic Family



Amino Acid Degradation

F,Y

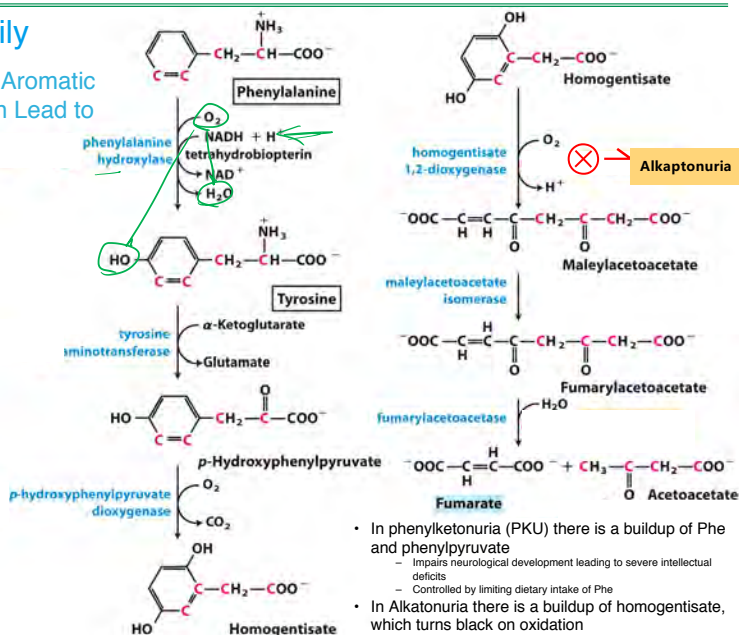
Aromatic Family



Amino Acid Degradation

Aromatic Family

Genetic Defects in Aromatic Family Degradation Lead to Disease

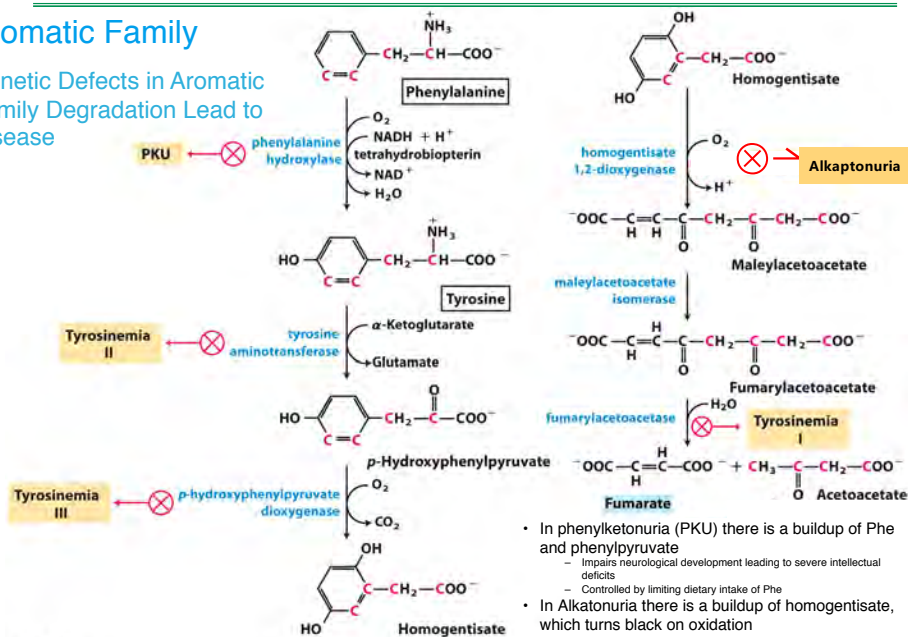


- In phenylketonuria (PKU) there is a buildup of Phe and phenylpyruvate
 - Impairs neurological development leading to severe intellectual deficits
 - Controlled by limiting dietary intake of Phe
- In Alkaptonuria there is a buildup of homogentisate, which turns black on oxidation

Amino Acid Degradation

Aromatic Family

Genetic Defects in Aromatic Family Degradation Lead to Disease



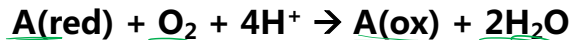
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Amino Acid Degradation: Oxidases

Nomenclature

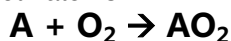
Oxidases – use molecular oxygen as an electron acceptor, but no atoms into substrate

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

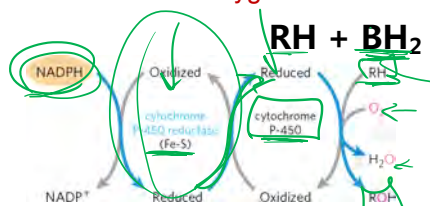


Oxygenase* – use of molecular oxygen to put into the substrate

- dioxygenases – use both atoms



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



- 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

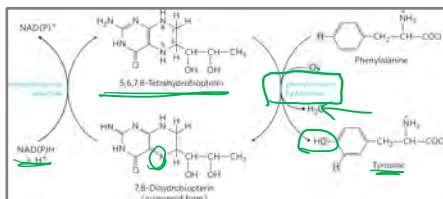
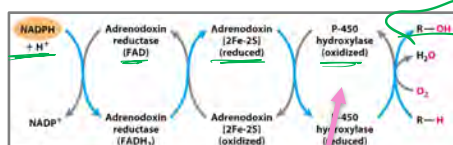
*a.k.a.: **hydroxylase**, mixed-function oxygenase, “mixed-function oxidase”

Amino Acid Degradation: Oxidases

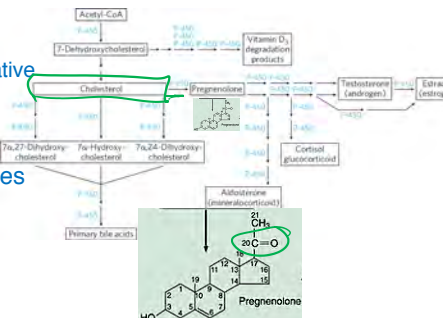


Hydroxylases

Example of P-450 reactions in adrenal gland:



- 1) Source of reducing electrons are most often NADPH (the co-substrate)
- 2) Other co-substrates
 - a) FAD, FeS clusters, α -ketoglutarate (oxidative decarboxylation to succinate)
 - b) Others: tetrahydrobiopterin (Phe hydroxylase)
- 3) Major class are the P-450 heme hydroxylases
 - a) Expressed in liver and adrenal glands
 - b) Steroids & fatty acids
 - c) Xenobiotics (drugs)
 - i. Specific
 - ii. Non-specific
 - iii. Inducible
 - iv. Drug-drug interactions



F,Y

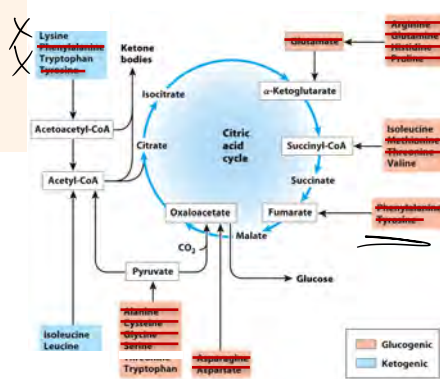
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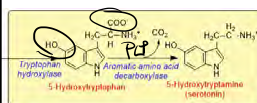
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4Trans-/de-aminase family

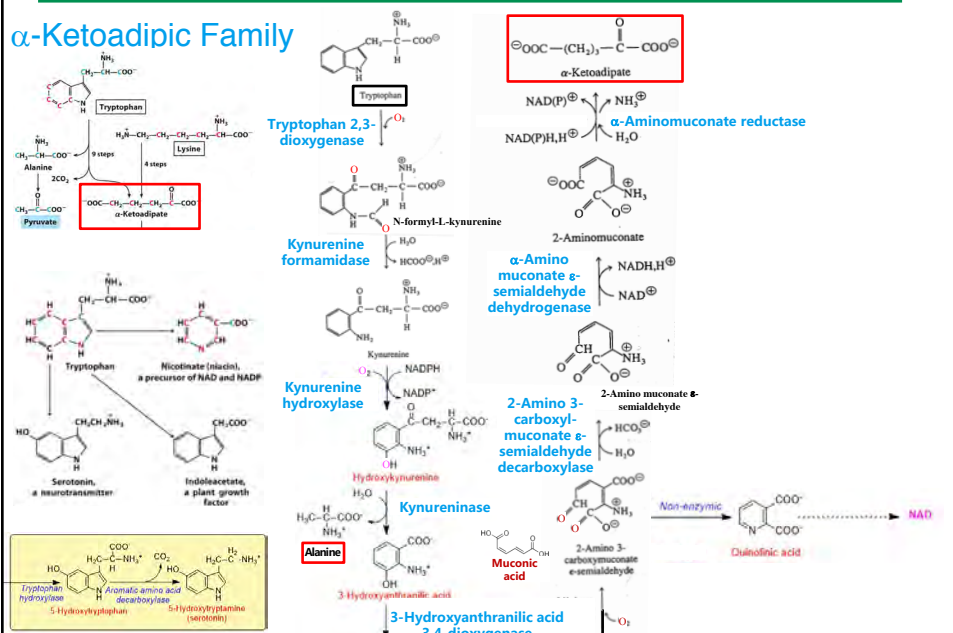
K,W



Amino Acid Degradation

K,W

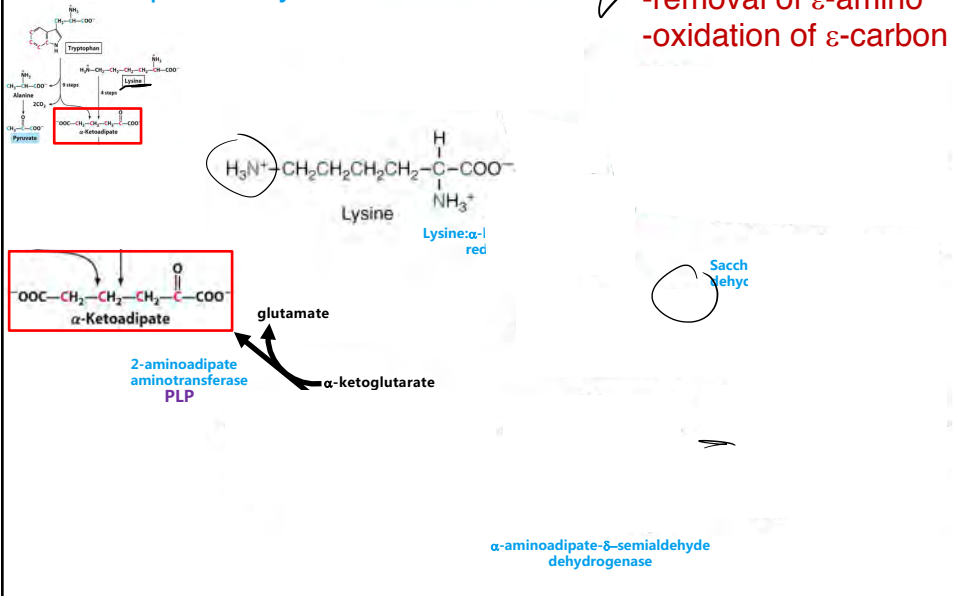
α -Ketoadipic Family



Amino Acid Degradation

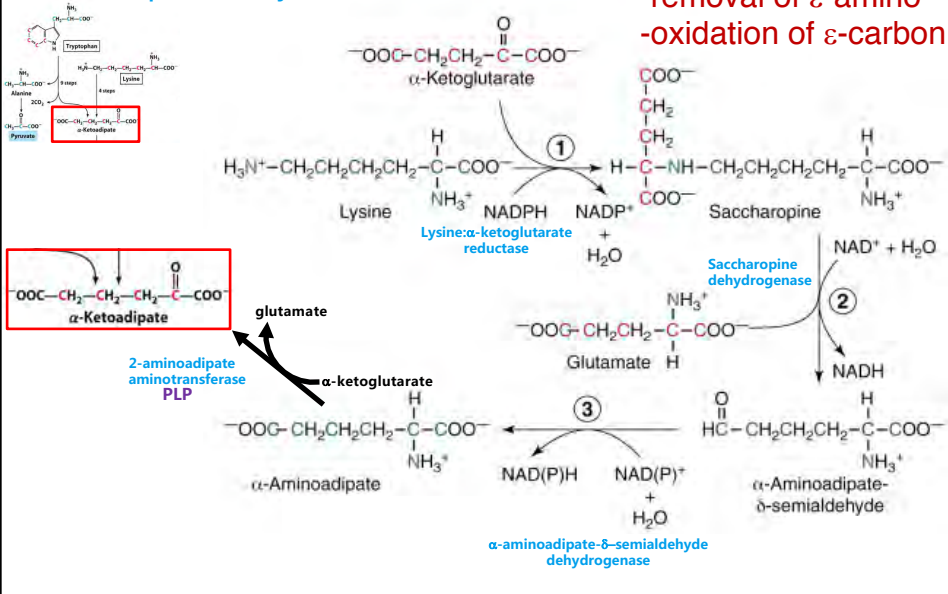
α -Ketoadipic Family

✓ -removal of ϵ -amino
-oxidation of ϵ -carbon



Amino Acid Degradation

α -Ketoadipic Family



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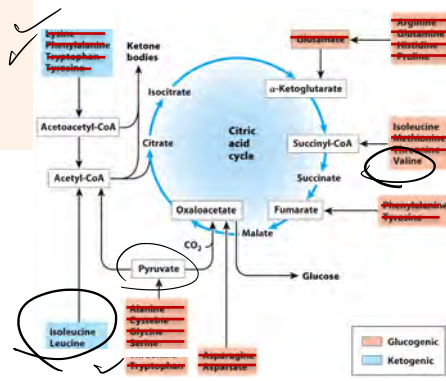
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