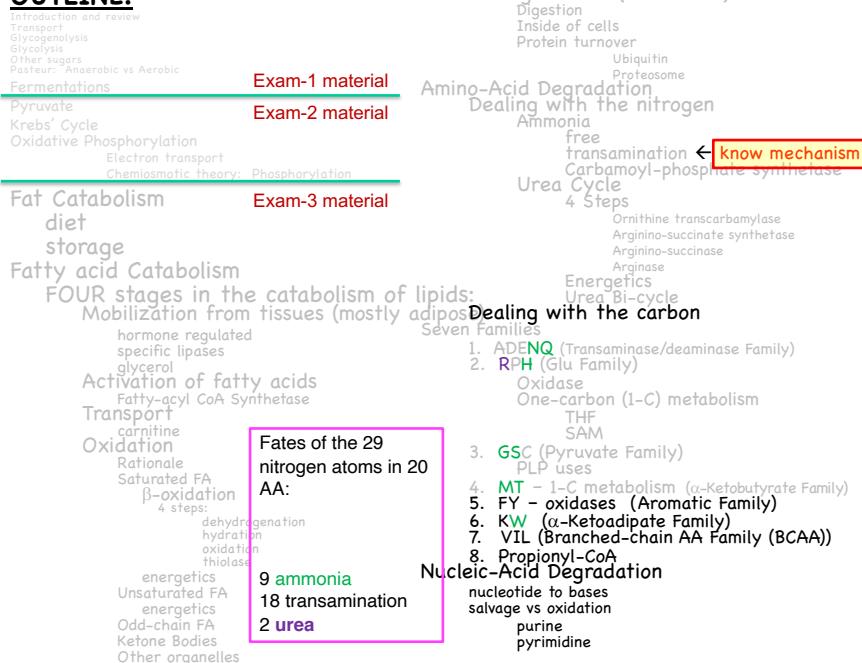


BI/CH 422/622

OUTLINE:



Fates of the 29 nitrogen atoms in 20 AA:

9 ammonia	Nucleic-Acid Degradation
18 transamination	nucleotide to bases salvage vs oxidation
2 urea	purine pyrimidine

Amino Acid Degradation: the carbon “skeletons”

A. Concepts

1. Convergent

2. ketogenic/glucogenic

3. Reactions seen before

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

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-Ketoacidic Family (K,W)

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

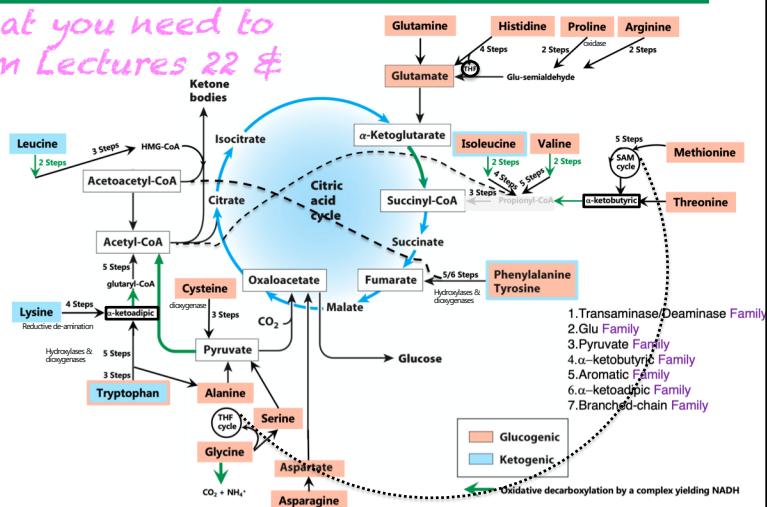
E. Convergence with Fatty Acids: propionyl-CoA

The SEVEN (7) Families

Before FY

Amino Acid Degradation

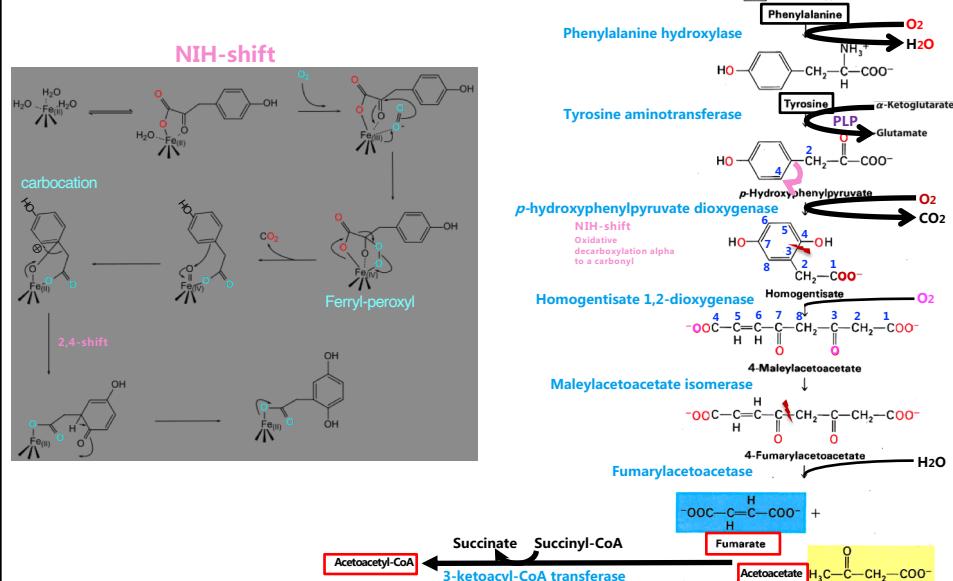
This is what you need to Know from Lectures 22 & 23



Amino Acid Degradation

F,Y

Aromatic Family

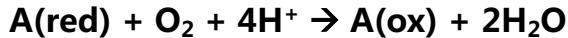


Amino Acid Degradation: Oxidases

Nomenclature

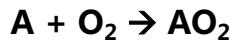
Oxidases – use molecular oxygen as an electron acceptor, but no atoms into substrate

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

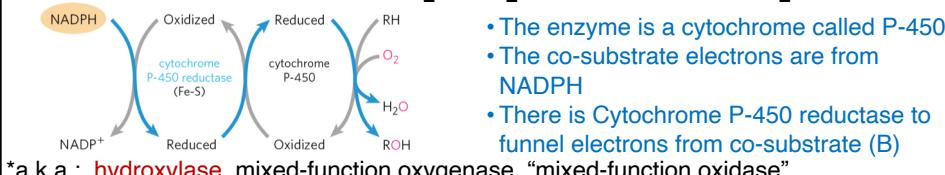


Oxygenase* – use of molecular oxygen to put into the substrate

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



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



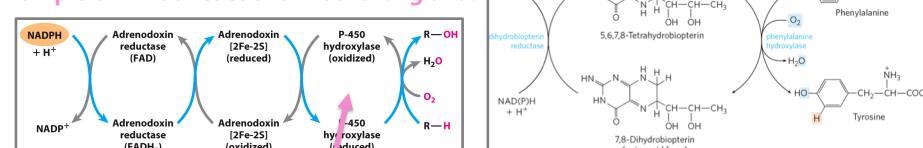
*a.k.a.: **hydroxylase**, mixed-function oxygenase, “mixed-function oxidase”

Amino Acid Degradation: Oxidases



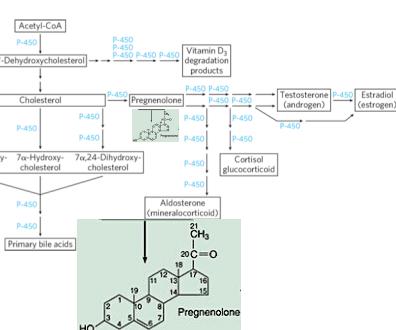
Hydroxylases

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

Called CYP
(CYtochrome P-450)



Amino Acid Degradation

F,Y

- 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

- Glucogenic amino acids can be converted to glucose.

Six to pyruvate^{3,1}

Five to α -ketoglutarate^{2,1}

Four to succinyl-CoA^{7,4} Ile, Val

Two to fumarate⁵

Two to oxaloacetate¹

✓¹Trans-/de-aminase family

✓²Glu family

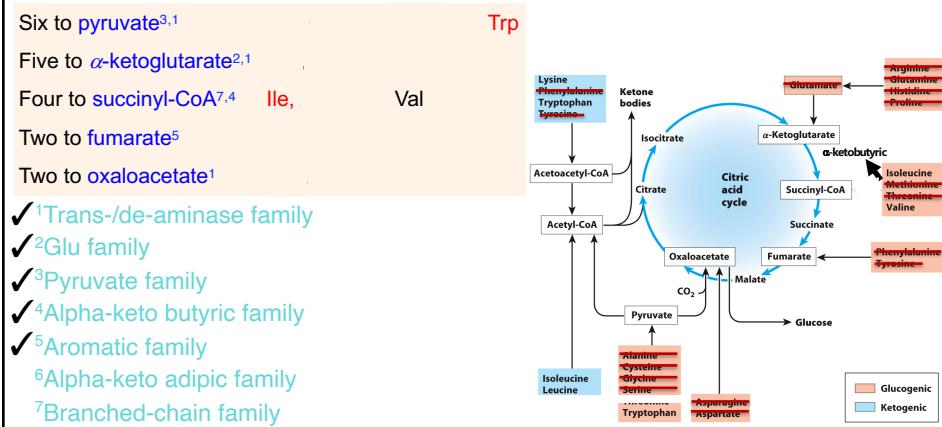
✓³Pyruvate family

✓⁴ α -Keto butyric family

✓⁵Aromatic family

⁶Alpha-keto adipic family

⁷Branched-chain family



Amino Acid Degradation: the carbon “skeletons”

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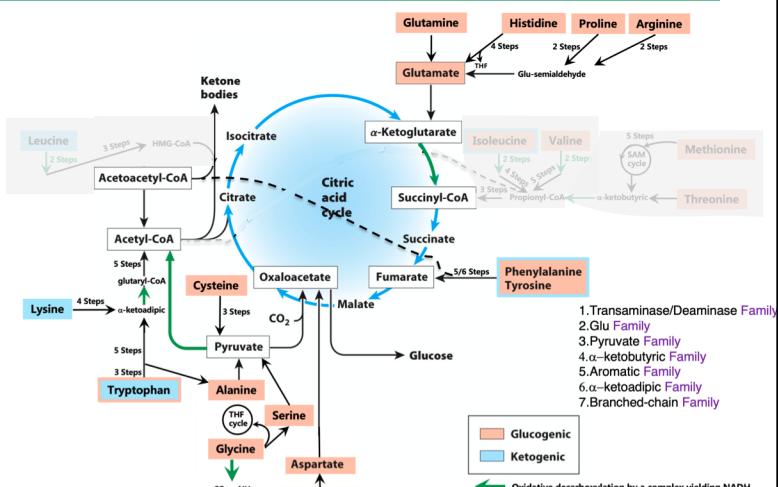
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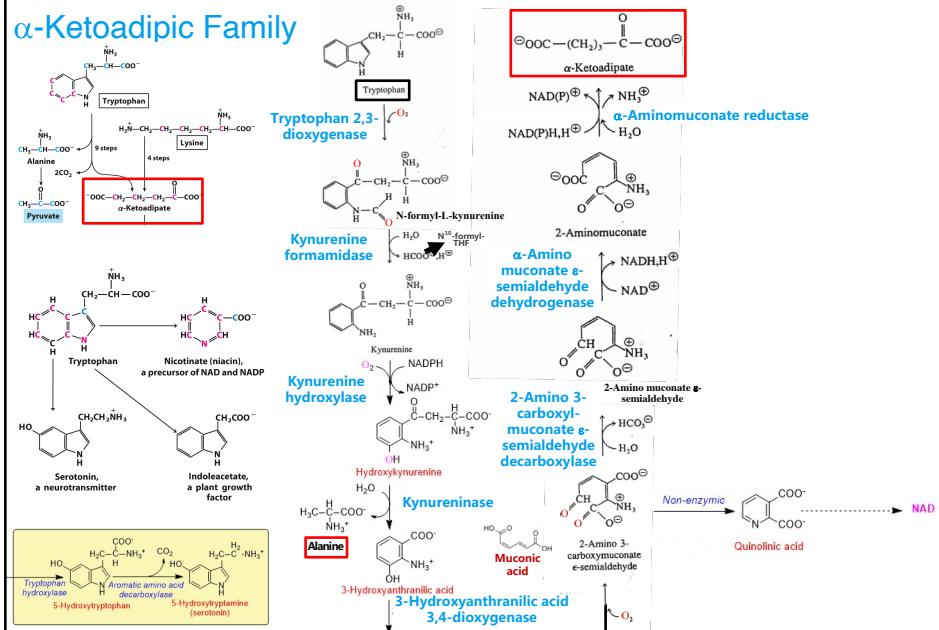
Before KW

Amino Acid Degradation



Amino Acid Degradation K,W

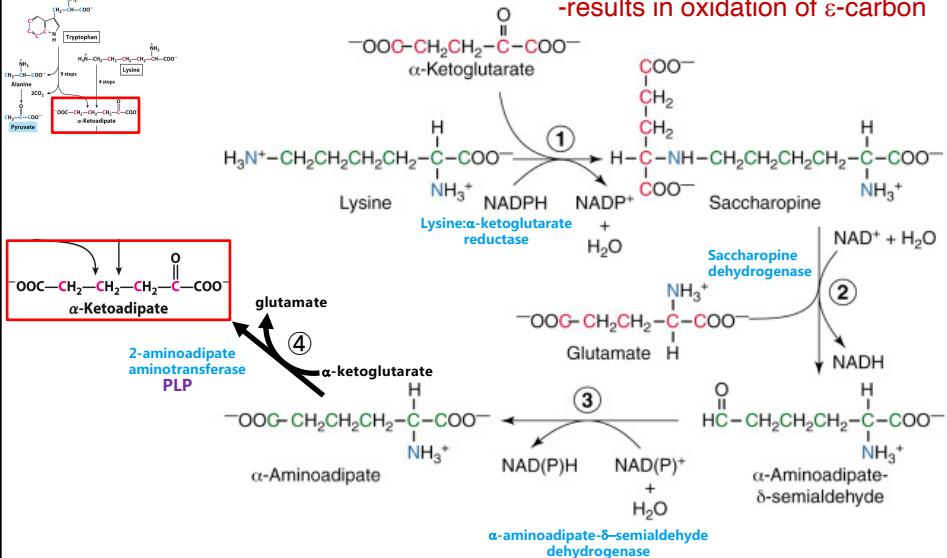
α-Ketoacidic Family



Amino Acid Degradation

α -Ketoacidic Family

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



Amino Acid Degradation

K,W

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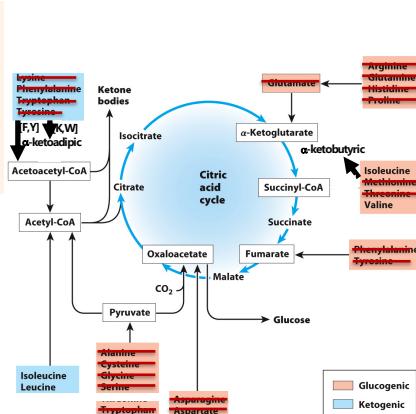
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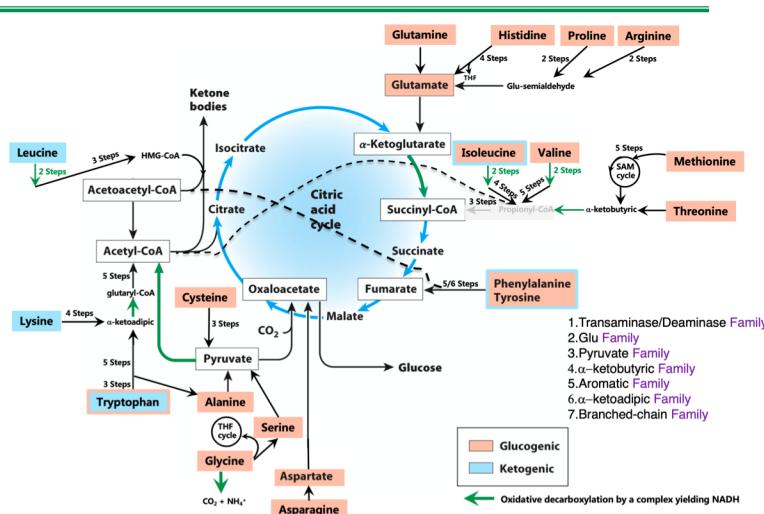
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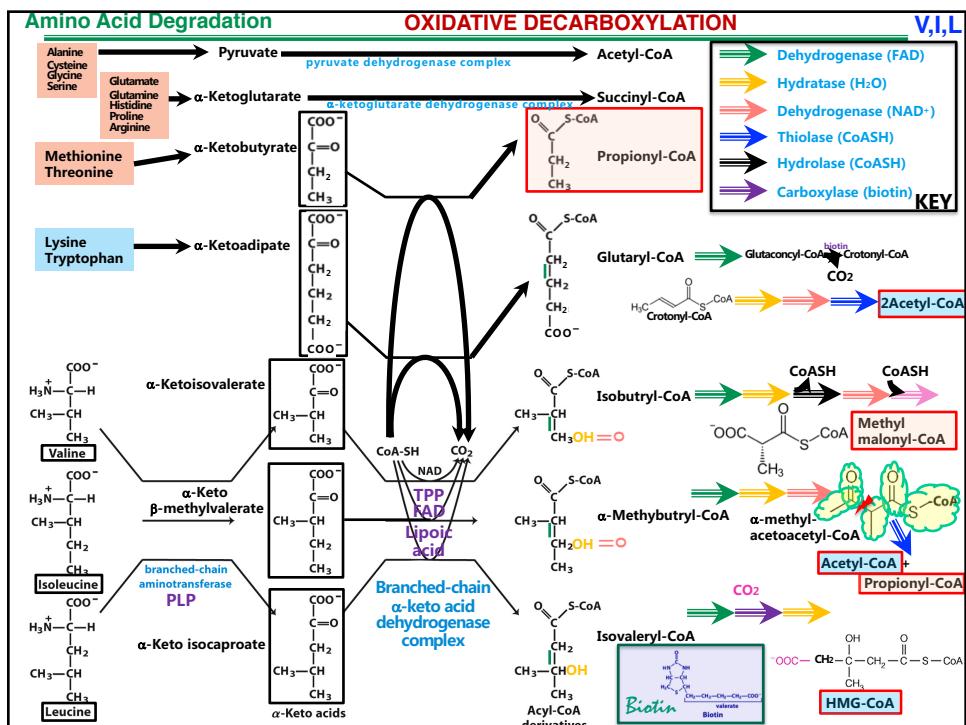
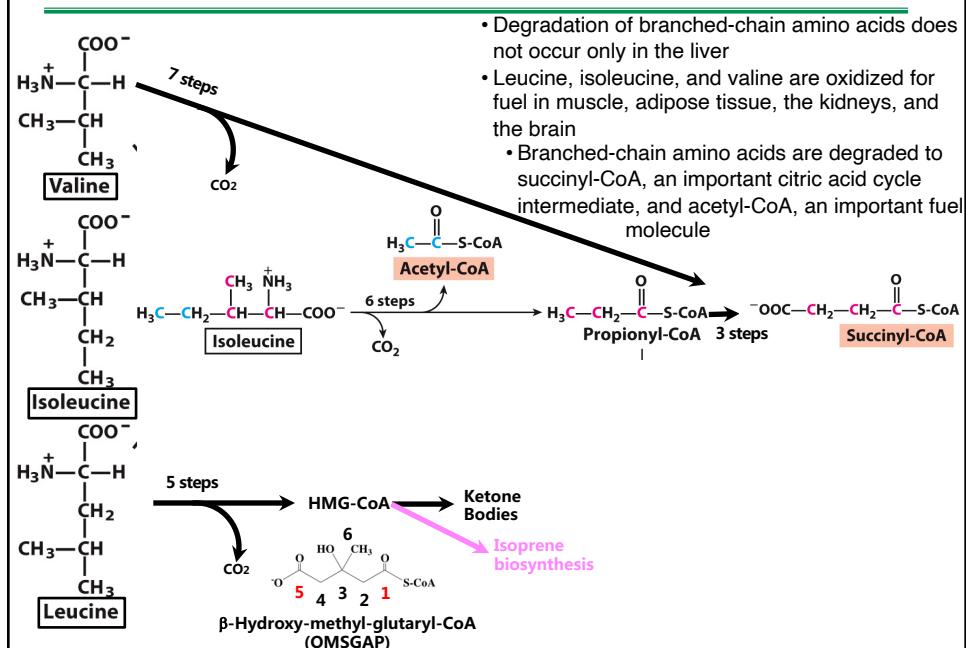
Before VIL

Amino Acid Degradation



Amino Acid Degradation

V,I,L



Amino Acid Degradation

V,I,L

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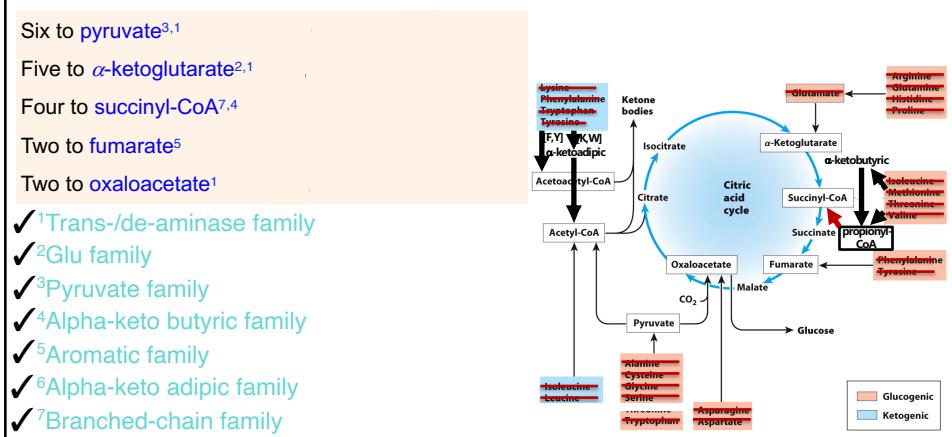
✓ ²Glu family

✓ Pyruvate family

✓ Alpha-keto aldehydes

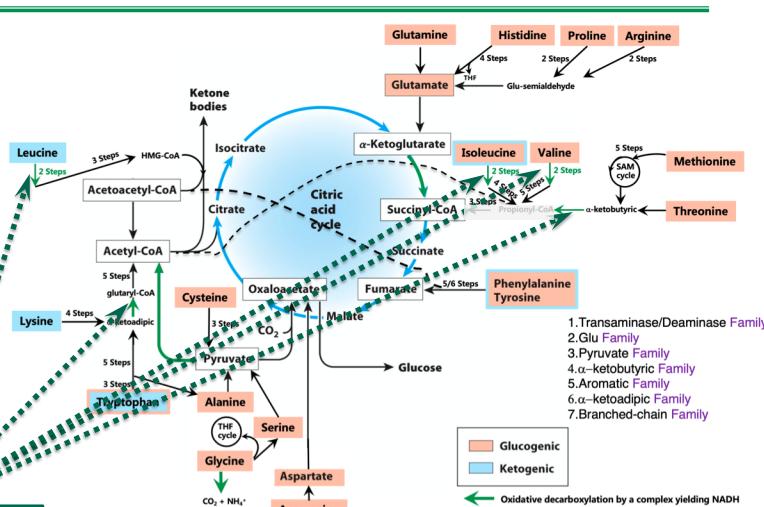
✓ ⁶Alpha-keto adipic f...

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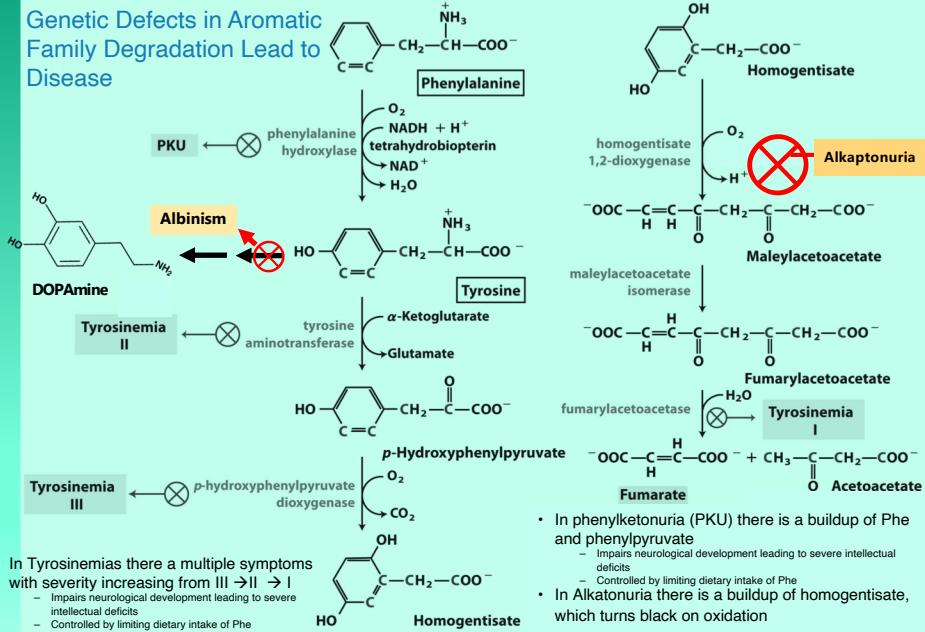
Amino Acid Degradation

Same Complex



Clinical Correlations

Genetic Defects in Aromatic Family Degradation Lead to Disease



- In Tyrosinemias there are multiple symptoms with severity increasing from III → II → I
 - Impairs neurological development leading to severe intellectual deficits
 - Controlled by limiting dietary intake of Phe

- 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