Chem 352 - Lecture 10
Lipid, Amino Acid, and
Nucleotide Metabolism
Part II: Amino Acid Metabolism

1

Introduction

Amino acid metabolism is complex

We will focus on a couple of important themes:

- 17.1 Nitrogen fixation and the nitrogen cycle
- 17.2 Assimilation of ammonia
- 17.3 Synthesis of amino acids (Ala, Asp, Asn, Glu, Gln, Arg, Pro, Ser, Gly)
- 17.4 Amino acids as precursors
- 17.7 The urea cycle

2

Nitrogen Fixation

Inorganic sources of nitrogen include

- N_2 from the atmosphere
- NO_2^- (nitrite) and NO_3^- (nitrate) ions

Both are reduced to NH_3 for assimilation into living systems.

Most animals get their nitrogen from amino acids.

3-1

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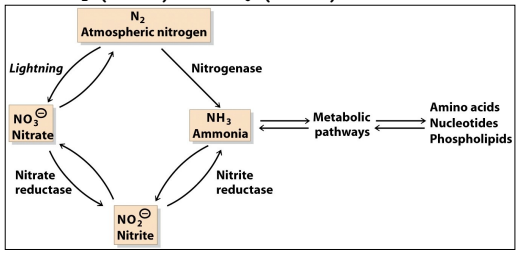


3-2

Nitrogen Fixation

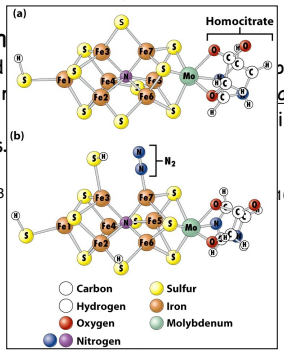
Nitrogen fixation.

- Carried out by a limited number of bacteria
  - Most notably, the symbiotic Rhizobacteria found in the root nodules of leguminous plants.

$N_2 + 8\,H^+ + 8\,e^- + 16\,ATP \longrightarrow 2\,NH_3 + H_2 + 16\,ADP + 16\,P_i$

4-1

Nitrogen Fixation



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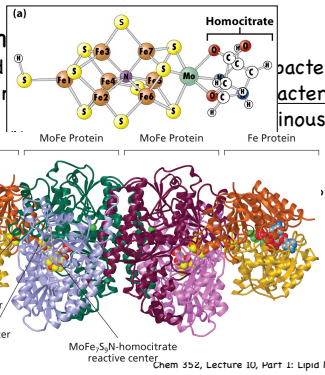
Nitrogen Fixation



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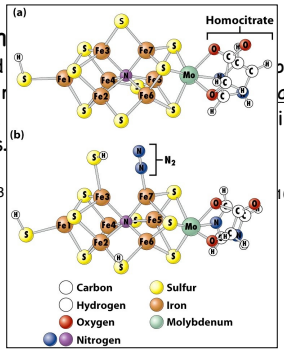
Nitrogen Fixation



4-4

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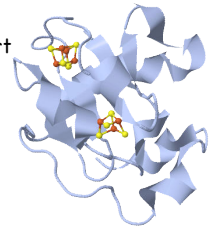
4-5

Nitrogen Fixation

Nitrogen fixation.

- The source of electrons are the electron tranport proteins **ferredoxin** and **flavodoxin**
- We saw ferredoxin in in the light reactions of photosynthesis



Ferredoxin

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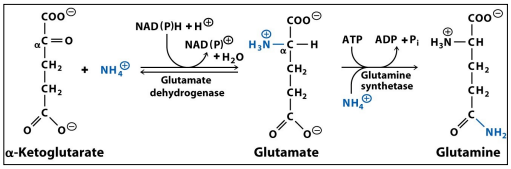
Assimilation of Ammonia

Ammonia is assimilated primarily through the amino acids glutamate and glutamine.

- Mammals do not assimilate much NH_3 directly.



6-1

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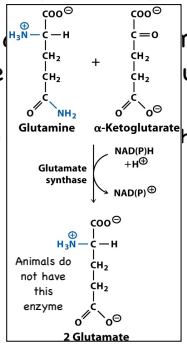

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Assimilation of Ammonia

Nitrogen can then transferred to other amino acids using the transamination reaction.

7-1

Assimilation of Ammonia

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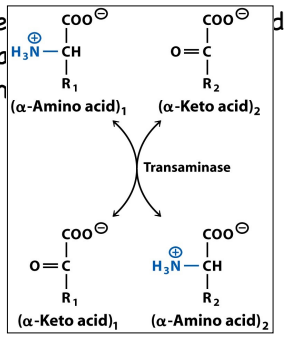

7-2

Assimilation of Ammonia

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7-3

Assimilation of Ammonia

Nitrogen is then transferred to other amino acids by the transamination reaction.

- The transamination reactions uses the coenzyme **pyridoxal phosphate (PLP, Chapter 7.8)**

8-1

Assimilation of Ammonia

Nit…r
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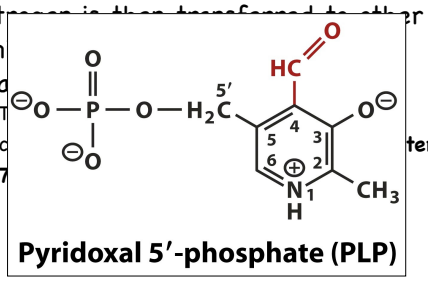

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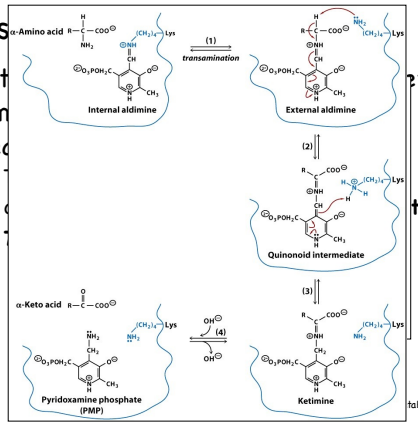

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8-3

As…

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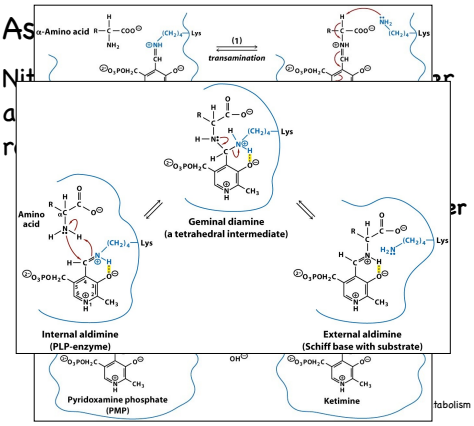

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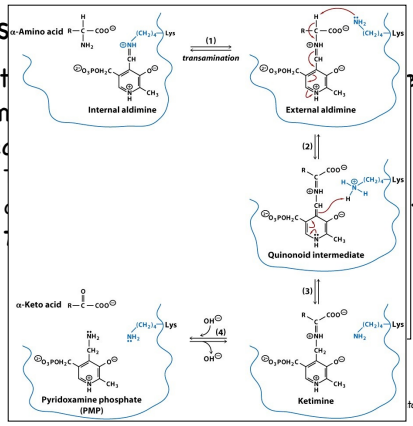

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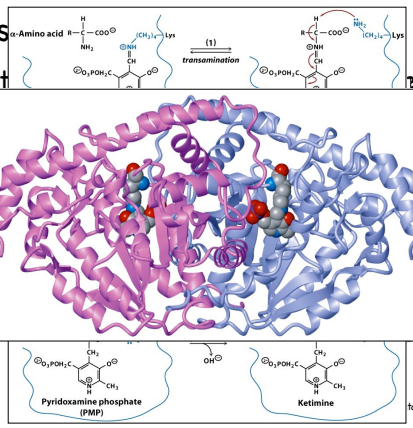

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Assimilation of Ammonia

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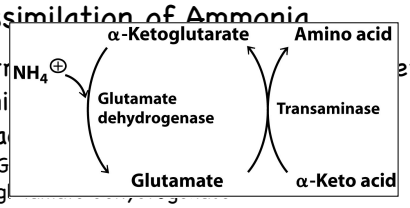
8-7



9-1

Assimilation of Ammonia

Nitr… …er
ami…
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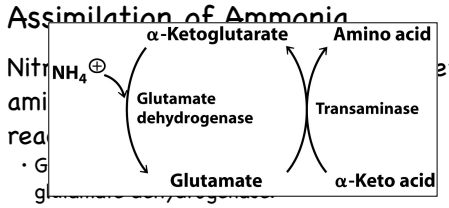
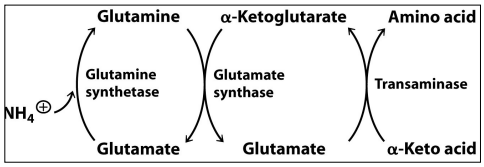
- G…





9-2

Assimilation of Ammonia

Nitrogen is then transferred to other amino acids by the transamination reaction.

- Glutamine synthetase has a lower K_m than glutamate dehydrogenase.

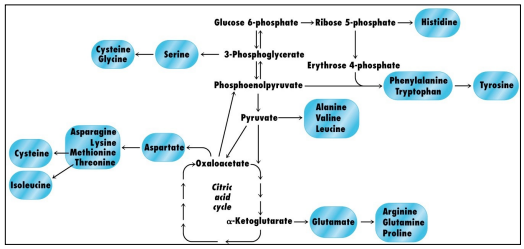
10

Assimilation of Ammonia

Nitrogen is then transferred to other amino acids by by additional transamination reactions.

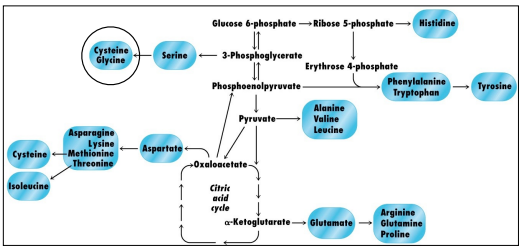
11

Synthesis of Amino Acids



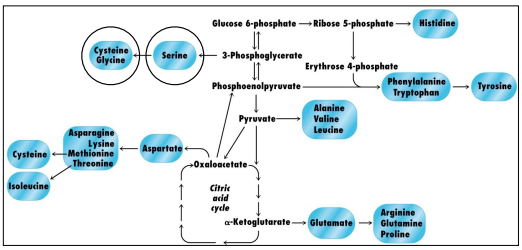
12-1

Synthesis of Amino Acids



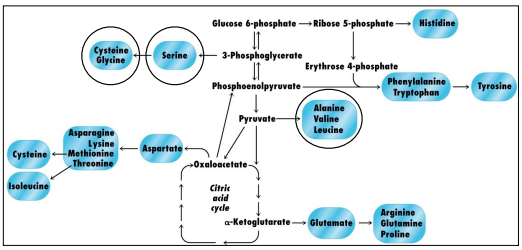
12-2

Synthesis of Amino Acids



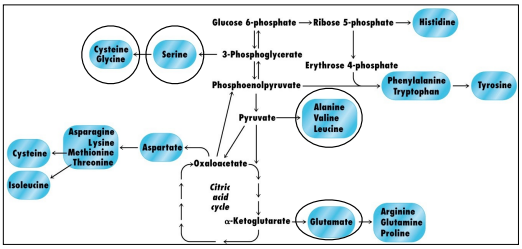
12-3

Synthesis of Amino Acids



12-4

Synthesis of Amino Acids



12-5

Synthesis of Amino Acids

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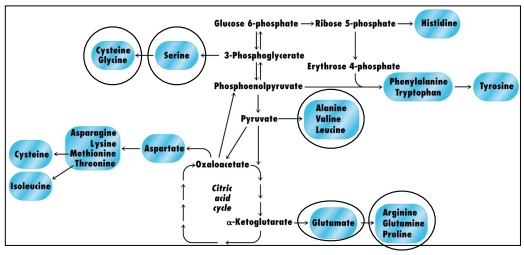
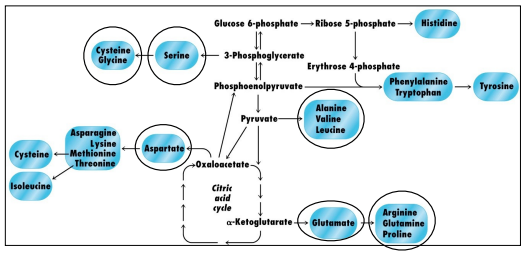


12-6

Synthesis of Amino Acids

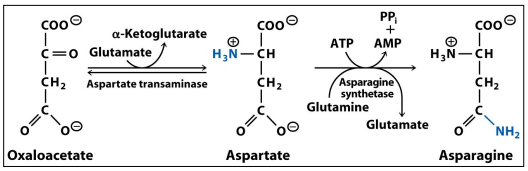


12-7

Synthesis of Amino Acids

Aspartate (Asp) & Asparagine (Asn)

- Start at oxaloacetate

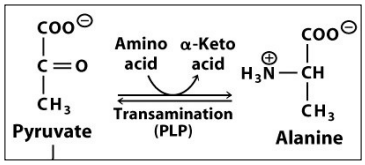


13

Synthesis of Amino Acids

Alanine (Ala)

- Start at pyruvate



14

Synthesis of Amino Acids

Glutamate (Glu) & Glutamine (Gln)

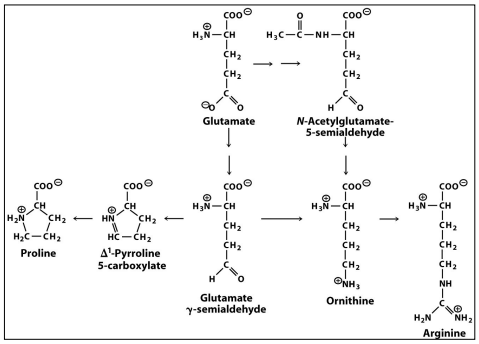
- Start at α-ketoglutarate and transminate

Proline (Pro) & Arginine (Arg)

- Start at Glutamate

15-1

Synthesis of Amino Acids



15-2

Synthesis of Amino Acids

Glutamate (Glu) & Glutamine (Gln)

- Start at α-ketoglutarate and transminate

Proline (Pro) & Arginine (Arg)

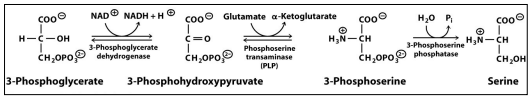
- Start at Glutamate

15-3

Synthesis of Amino Acids

Serine (Ser)

- Start at 3-phosphoglycerate



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Synthesis of Amino Acids

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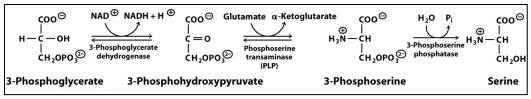
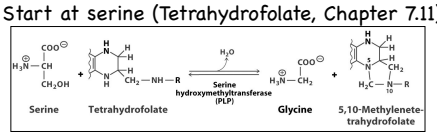


Glycine (Gly)

- Start at serine (Tetrahydrofolate, Chapter 7.11)



17-1

Synthesis of Amino Acids

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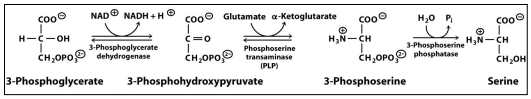

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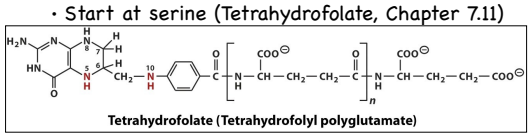


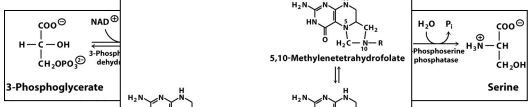
Chem 352, Lecture 10, Part I: Lipid Metabolism 17

17-2

Synthe

Serine (

- Start



Glycine

- Start pter 7.11)

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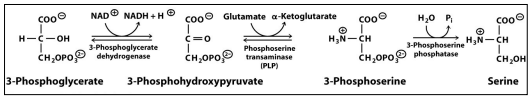
17-3

Synthesis of Amino Acids

Serine (Ser)

- Start at 3-phosphoglycerate



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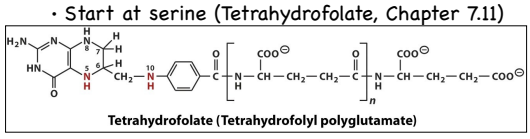

Chem 352, Lecture 10, Part I: Lipid Metabolism 17

17-4

Synthesis of Amino Acids

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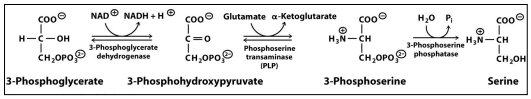

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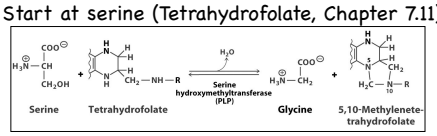
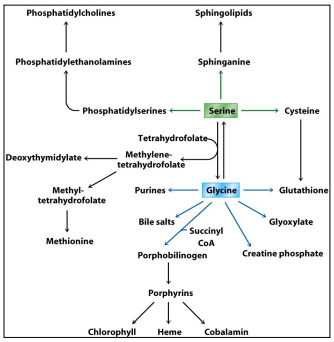


17-5

Amino Acids as Precursors



18

Amino Acids as Precursors

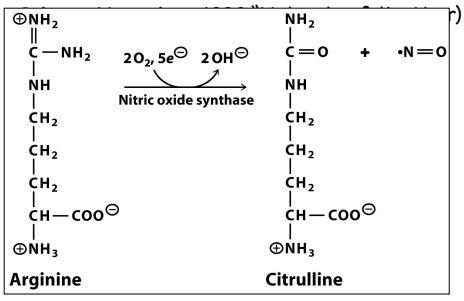
Nitric oxide (NO)

- Science Magazines 1992 "Molecule of the Year)
- Messenger molecule that stimulates the formation of cGMP
- Used by macrophages to kill bacteria
- Smooth muscle relaxant, which lowers blood pressure.

19-1

Amino Acids as Precursors

Nitric oxide (NO)



19-2

Amino Acids as Precursors

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- Smooth muscle relaxant, which lowers blood pressure.

19-3

Amino Acids Degradation

Will focus on the strategies that have evolved for the removal of excess nitrogen.

- NH_3 – aquatic organisms allow ammonia to diffuse into the surroundings.
- Urea – terrestrial animals excrete urea along with other liquid wastes
- Uric acid – avian animals excrete uric acid along with other solid wastes

20-1

Amino Acids Degradation

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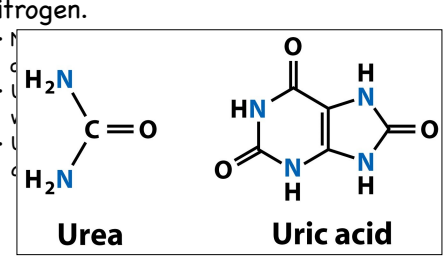

20-2

Amino Acids Degradation

Will focus on the strategies that have evolved for the removal of excess nitrogen.

- NH_3 – aquatic organisms allow ammonia to diffuse into the surroundings.
- Urea – terrestrial animals excrete urea along with other liquid wastes
- Uric acid – avian animals excrete uric acid along with other solid wastes

20-3

The Urea Cycle

Discovered by Hans Krebs in the 1930's shortly before he discovered the citric acid cycle.

- The first step is the synthesis of carbamoyl phosphate I.
  - In the mitochondria of liver cells
- The NH_3 comes from the oxidative deamination of glutamate.

21-1

The Urea Cycle

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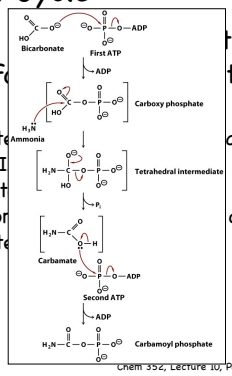
  - In the mit[illegible]
- The NH_3 cor[illegible] deamination of glutamat[illegible]



21-2

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21-3

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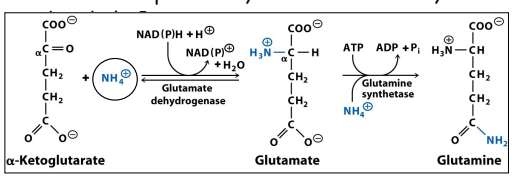

21-4

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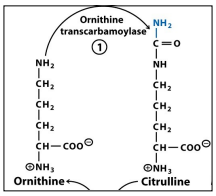
- The NH_3 comes from the oxidative deamination of glutamate.

21-5

The Urea Cycle

- The urea cycle involves two new α-amino acids.
  - Ornithine - which is similar to lysine.
  - Citrulline - which is similar to arginine



22-1

The Urea Cycle

- The urea cycle involves two new α-amino acids.
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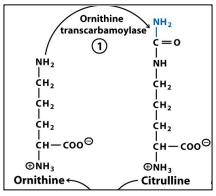
  - Citrulline - which is similar to arginine

Question:

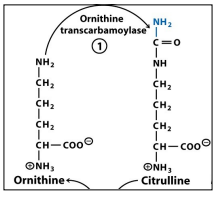
What reaction converts **ornithine** from **lysine**?



22-2

The Urea Cycle

- The urea cycle involves two new α-amino acids.
  - Ornithine - which is similar to lysine.
  - Citrulline - which is similar to arginine



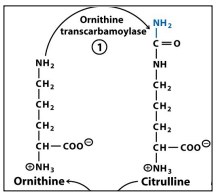
22-3

The Urea Cycle

- The urea cycle involves two new α-amino acids.
  - Ornithine - which is similar to lysine.
  - Citrulline - which is similar to arginine

Question:

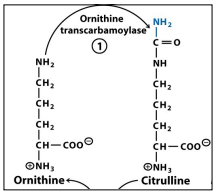
What enzyme catalyzes **citrulline** from **arginine?**



22-4

The Urea Cycle

- The urea cycle involves two new α-amino acids.
  - Ornithine - which is similar to lysine.
  - Citrulline - which is similar to arginine



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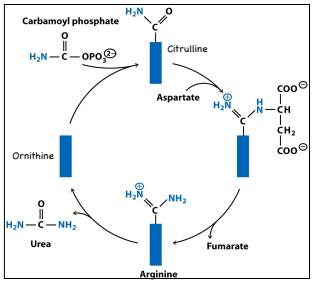
22-5

The Urea Cycle

- The reactions of the urea cycle.



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The Urea Cycle

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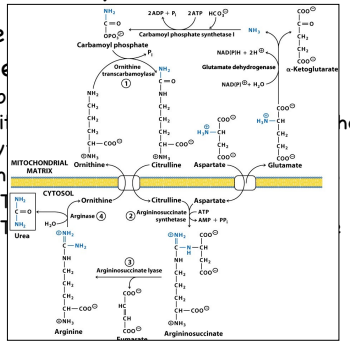

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The Urea Cycle

- The net reaction:

$NH_3 + HCO_3^- + \text{Aspartate} + 3\ ATP \longrightarrow$
$\text{Urea} + \text{Fumarate} + 2\ ADP + 2\ P_i + AMP + PP_i$

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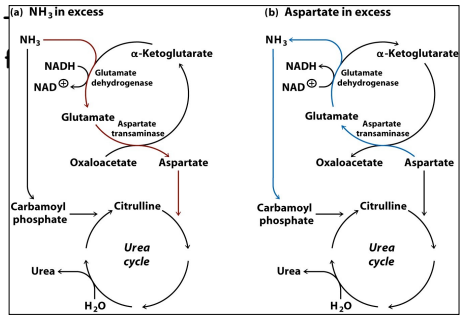
The Urea Cycle

The nitrogen atoms in urea comes from NH_3 and aspartate.

- The needs for these two sources can be balanced by altering the flow material.

26-1

The Urea Cycle



26-2

The Urea Cycle

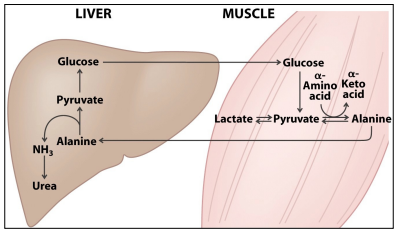
The nitrogen atoms in urea comes from NH_3 and aspartate.

- The needs for these two sources can be balanced by altering the flow material.

26-3

The Urea Cycle

The pyruvate/aspartate shuttles is used to remove excess NH_3 from the muscles.



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Next Up

Lecture 10 - Part III, Nucleotide metabolism (Moran et al, Chapter 18)

Lecture 11 - Nucleic acids

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