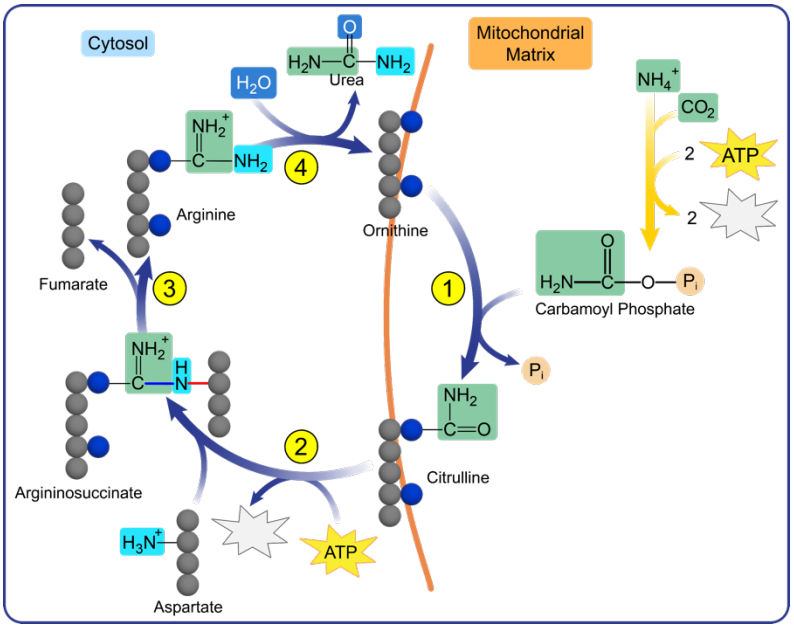
CONCEPT: THE UREA CYCLE

Overview of the Urea Cycle

- The urea cycle converts NH_4^+ to urea using ornithine as a _____.
  - □ C atom source: CO_2
  - □ N atom source: NH_4^+ and _____.
  - □ The energy cost of the process is ___ ATP.



EXAMPLE: Give the number of ATP molecules consumed in the urea cycle and the actual energy cost of the process.

a) 4, 3

b) 3, 3

c) 2, 3

d) 3, 4

PRACTICE: Which amino acid provides the NH_4^+ for the formation of carbamoyl phosphate?

a) α-ketoglutarate

b) Glutamine

c) Glutamate

d) Aspartate

PRACTICE: Which of the following amino acids is not a part of the urea cycle?

a) Asparagine

b) Argininosuccinate

c) Arginine

d) Ornithine

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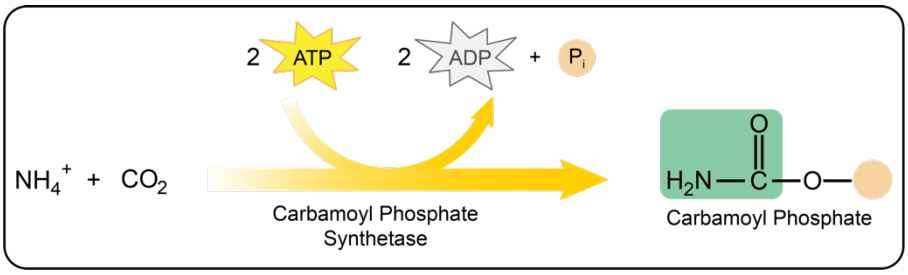
Phase A – Preparation

- Synthesis of carbamoyl phosphate (CP) from NH_4^+ and CO_2 is an energy-consuming step.
  - □ The enzyme _____ phosphate synthetase catalyzes the reaction.
  - □ ___ ATP molecules are hydrolyzed to ___ ADP and ___ P_i.

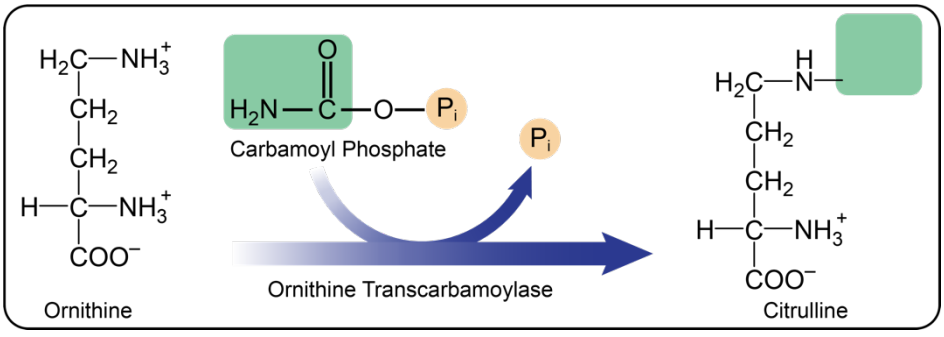


Phase B – Conversion

- The urea cycle is a cyclic pathway consisting of ___ reactions.
  - □ Reaction 1 inside mitochondrial matrix.
  - □ Reactions 2, 3, and 4 inside cytosol.
  - □ Cycle utilizes 3 _____ amino acids.

1 Transfer: The carbamoyl group is transferred from CP to ornithine to produce citrulline.

- □ Catalyzed by enzyme ornithine transcarbamoylase (OTC).



- □ Citrulline is transported _____ the mitochondria.

EXAMPLE: Name the amino acid formed when ornithine reacts with carbamoyl phosphate.

a) Glutamate

b) Citrulline

c) Aspartate

d) Glycine

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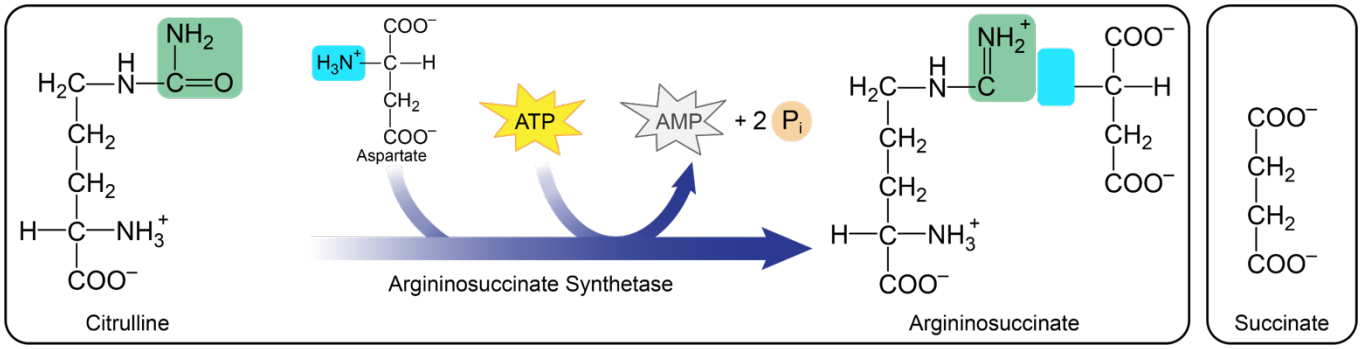
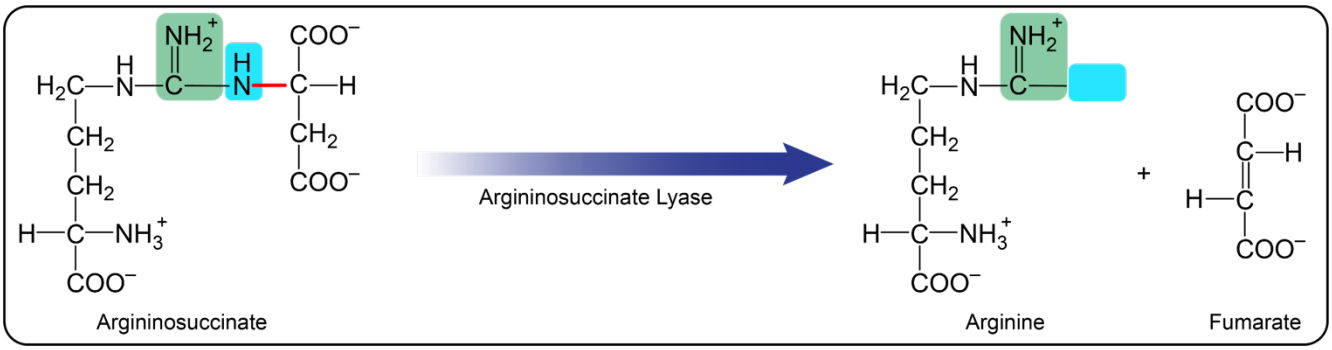
2 Condensation: Citrulline undergoes condensation with _____ to produce argininosuccinate.

- □ Catalyzed by enzyme argininosuccinate _____.
- □ 1 ATP is hydrolyzed to 1 _____ and 2 P_i (equivalent to __ ATP ⟶ __ ADP)

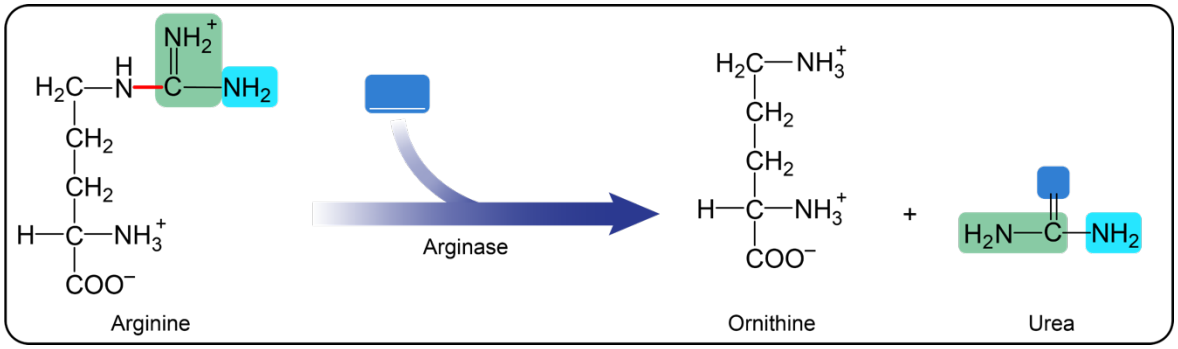


3 Cleavage: Argininosuccinate _____ catalyzes the cleavage of argininosuccinate to produce arginine.

- □ Aspartate C chain is lost as _____.



4 Hydrolysis: The enzyme _____ hydrolyzes arginine to ornithine and urea.



- □ Ornithine is transported back to the mitochondrial matrix.

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EXAMPLE: Which of the following statements explains the structure of carbamoyl group accurately?

a) Two $–NH_2$ groups bonded to a carbonyl group.

b) Two –OH groups bonded to a carbonyl group.

c) An $–NH_2$ group bonded to a carbonyl group.

d) A carbonyl group bonded to one $–NH_2$ and one –OH group.

PRACTICE: What is the function of aspartate in the urea cycle?

a) Produces CO_2 for carbamoyl phosphate synthesis.

b) Provides $–NH_2$ group as ammonium ion.

c) Produces succinate for citrulline formation.

d) Provides the second nitrogen atom for urea.

PRACTICE: Which one of the following sentences is an incorrect description of a reaction in the urea cycle?

a) Citrulline condenses with aspartate to produce argininosuccinate.

b) Hydrolysis of arginine produces urea and regenerates citrulline.

c) Transfer of carbamoyl group from carbamoyl phosphate to ornithine produces citrulline.

d) Argininosuccinate undergoes cleavage to produce arginine and fumarate.

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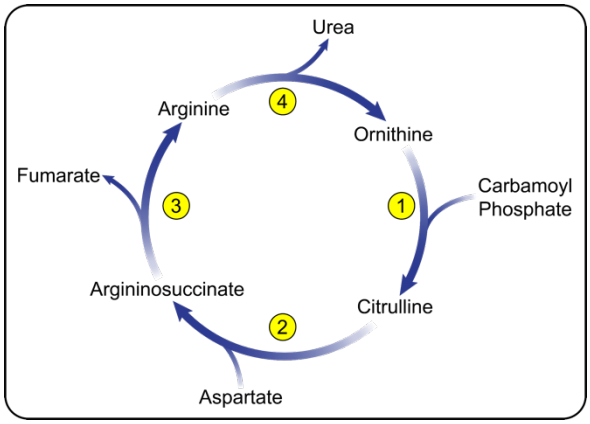
Remembering the Urea Cycle

● Reactions of the urea cycle can be remembered by memorizing the metabolite names.

MEMORY TOOL 1: ① ___dinary _____ooling ____izen,
② ____ires ___ranged-_____ess,
③ ___els ____uments, &
④ __tters __pinions



● The name of the enzyme can be predicted by knowing the substrate and the type of reaction.

Reaction Types: Transfer, Condensation, Cleavage, & Hydrolysis

MEMORY TOOL 2: ____in _____uctor _____ns __ouse

HINT 1: Transfer is catalyzed by ornithine transcarbomylase.

HINT 2: Condensation is catalyzed by a _____.

HINT 3: Cleavage is catalyzed by a _____.

HINT 4: Hydrolysis is catalyzed by _____.

EXAMPLE: What are the products of the third reaction of the urea cycle?

a) Ornithine and urea

b) Fumarate and arginine

c) Aspartate and citrulline

d) Fumarate and aspartate

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PRACTICE: Which of the following metabolites is hydrolyzed in the urea cycle to produce ornithine and urea?

a) Citrulline

b) Arginine

c) Aspartate

d) Argininosuccinate

PRACTICE: Which enzyme catalyzes the reaction of citrulline with aspartate to produce argininosuccinate?

a) Succinate dehydrogenase

b) Argininosuccinate lyase

c) Argininosuccinate synthetase

d) Arginine oxidase

PRACTICE: Write the total number of amino acid metabolites in the urea cycle. How many of those amino acids are not found in proteins?

a) 5, 2

b) 4, 3

c) 4, 2

d) 5, 3