

Urea Cycle

The urea cycle is a process for excess nitrogen to be broken down and excreted by the kidneys. This biochemical pathway converts ammonia to urea, and takes place in both the liver and the kidneys.



PLAY PICMONIC

Mitochondria

N-Acetylglutamate

[Seagull-glue-tomato](#)

The urea cycle begins in the mitochondrial matrix. Here, N-acetylglutamate serves as an activator for this process, working to allosterically activate carbamoyl phosphate synthetase I.

Carbamoyl Phosphate Synthetase I

[Cardboard-mole Synthesizer](#)

Carbamoyl phosphate synthetase is the first enzyme involved in the urea cycle. It takes ammonia (NH_3), bicarbonate (HCO_3^-), and two molecules of ATP, using them to eventually form carbamoyl phosphate. Of note, during this reaction, the bicarbonate is converted to CO_2 and H_2O , so other interpretations of this first step can also show $\text{NH}_3 + \text{CO}_2$ being converted by this enzyme.

$\text{NH}_3 + \text{CO}_2$

[Ammo and \$\text{CO}_2\$ Molecule](#)

Carbamoyl phosphate synthetase I takes NH_3 and CO_2 (Converted to CO_2 and H_2O from HCO_3^-), as well as two ATP molecules to produce carbamoyl phosphate.

Carbamoyl Phosphate

[Cardboard-mole](#)

Carbamoyl phosphate enters the urea cycle as a substrate for ornithine transcarbamylase, which converts this substrate and ornithine into citrulline.

Ornithine Transcarbamylase

[Hornet-Train made of cardboard](#)

Ornithine transcarbamylase synthesizes citrulline with the help of ornithine which accepts the substrate carbamoyl phosphate in this reaction.

Citrulline

[Citrus-Crystals](#)

Citrulline is synthesized from carbamoyl phosphate and ornithine. Citrulline can then react with aspartate in an ATP-dependent step.

Cytosol

Aspartate

[Ass-potato](#)

The amine group in aspartate attacks the carbonyl carbon group on citrulline, working to form argininosuccinate, but can only do so with ATP and the enzyme argininosuccinate synthetase. Of note, this portion of the reaction occurs after transportation out of the mitochondrial matrix to the cytosol of liver cells.

Argininosuccinate

[Orange-suckers](#)

Argininosuccinate is formed by citrulline and aspartate in a reaction requiring ATP. The enzyme argininosuccinase promotes the breakdown of argininosuccinate into arginine and fumarate.

Fumarate

[Fuming](#)

Argininosuccinate is cleaved into arginine and fumarate. Fumarate is then used in the citric acid cycle, helping to form malate and later, oxaloacetate.

Arginine

[Orange-in-jeans](#)

The arginine produced in the earlier step is then broken down by arginase to produce urea and ornithine, with the addition of water.

H₂O to Urea

[Water changing into U-rainbow colors](#)

The enzyme arginase combines H₂O and arginine, synthesizing urea and ornithine. This urea is excreted out of the body in urine via the kidney.

Ornithine

[Hornets](#)

The ornithine produced in the previous step is recycled back to the mitochondria to be used in the next urea cycle.