Amino Acid Metabolism

Biosynthesis of

Nonessential Amino Acid :

From Krebs Cycle Intermediates

Usman Sumo Friend Tambunan

Arli Aditya Parikesit

Ersi Yuliantika

Bioinformatics Group

Department of Chemistry

Faculty of Mathematics and Science

University of Indonesia

Essential vs Nonessential Amino Acids

- **Essential Amino acid**

Arginine

Methionine

Threonine

Histidine

Isoleucine

Lysine

Phenylalanine

Valine

Tyrptophan

Leucine

Essential vs Nonessential Amino Acids

- **NonEssential Amino Acid**

Alanine

Asparagine

Aspartate

Cysteine

Glutamate

Glutamine

Glycine

Proline

Serine

Tyrosine

Biosynthesis of NonEssential Amino Acid

- The pathways for the biosynthesis of amino acid are diverse.
- The carbon skeletons for all nonessential amino acid are derived from metabolic intermediates from glycolysis, the pentose phosphate pathway, and the krebs cycle.

Biosynthesis of NonEssential Amino Acid

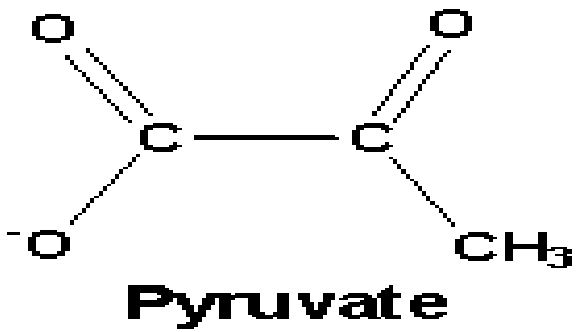
- Transamination is process by which an amino group is transferred from an amino acid to the α-carbon of a ketoacid is catalyzed by an aminotransferase.

Biosynthesis of NonEssential Amino Acid

- Three very common α-ketoacids can be transaminated in one step to their corresponding amino acid:
  - Pyruvate (glycolytic end product) → alanine
  - Oxaloacetate (citric acid cycle intermediate) → aspartate
  - α-ketoglutarate (citric acid cycle intermediate) → glutamate

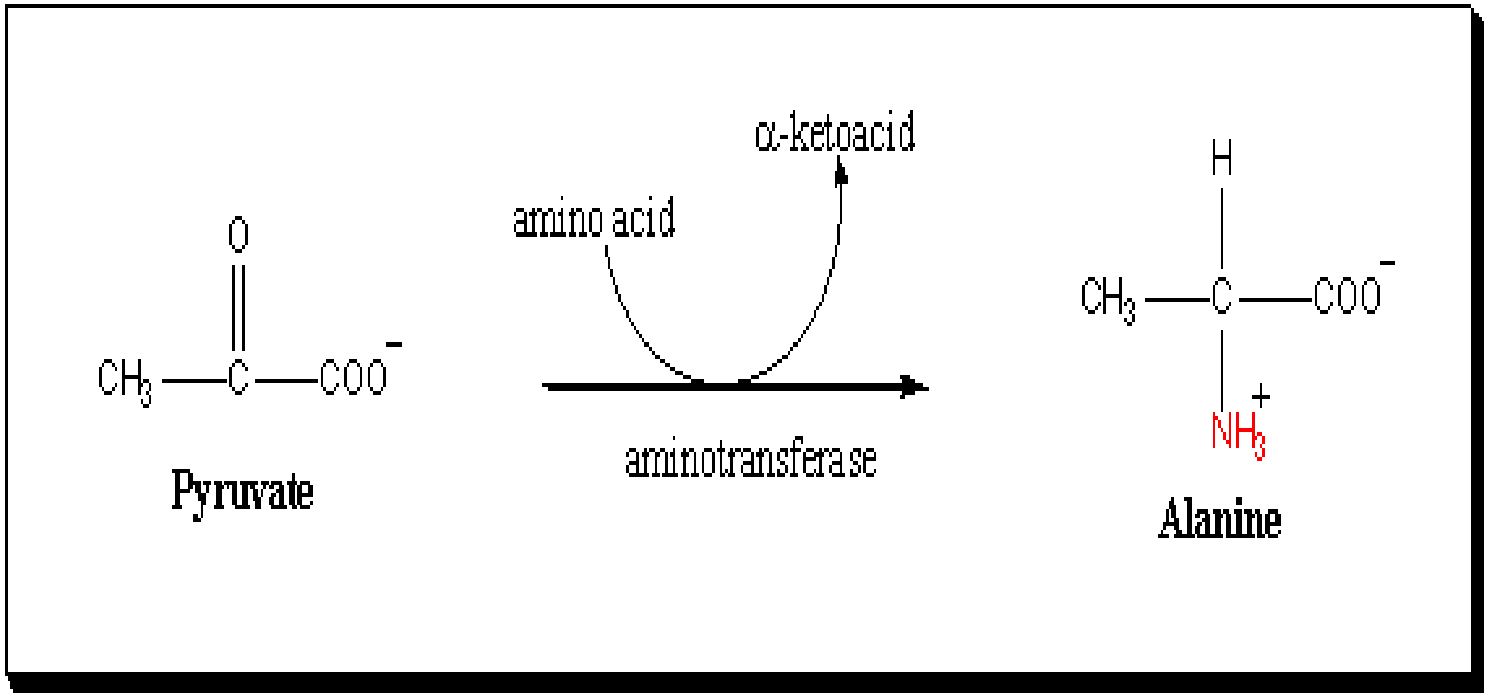
Pyruvate

- **Pyruvate** is the final product of **glycolysis** and a starting point for **gluconeogenesis**.



Pyruvate

Alanine Biosynthesis

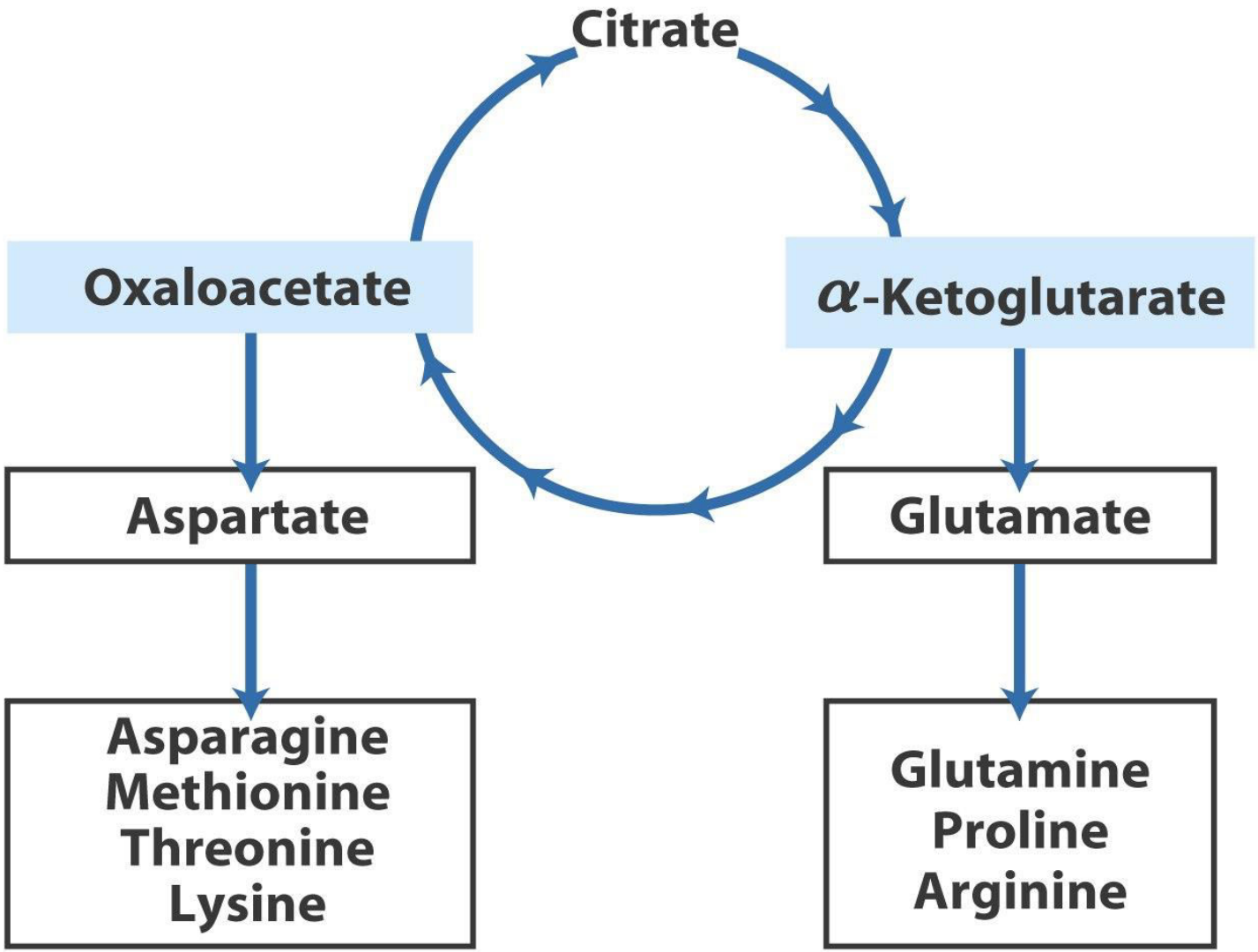


The functions of Alanine

- Alanine is used by the body to build protein.
- Alanine is readily converted to glucose when blood sugar levels fall to provide energy.
- Alanine stimulates lymphocyte production and strengthens the immune system by producing antibodies.

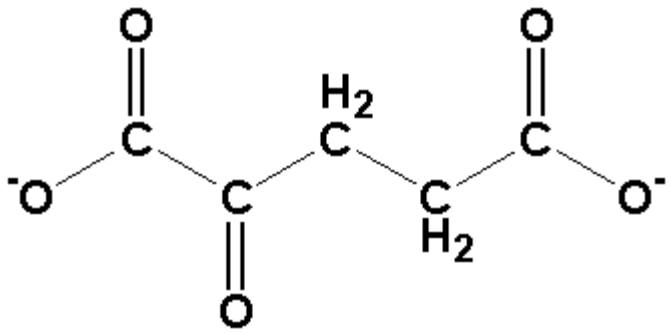
Alanine Deficiency

- Because the body easily constructs alanine from other sources, it is difficult to become deficient in alanine.
- Alanine deficiency has been seen in hypoglycemia.


Citrate
Oxaloacetate
α-Ketoglutarate
Aspartate
Glutamate
Asparagine
Methionine
Threonine
Lysine
Glutamine
Proline
Arginine

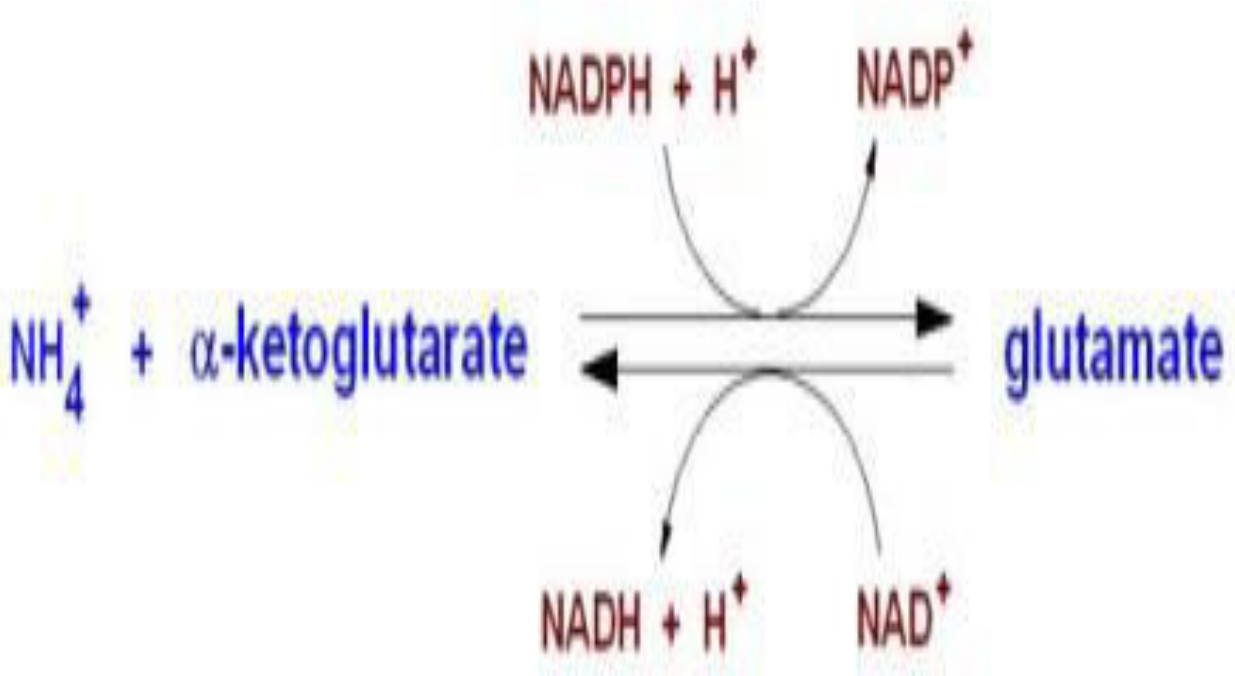
α-Ketoglutarate

- α-Ketoglutarate is a citric acid cycle intermediate and an important compound in amino acid metabolism and transamination reaction.



Alpha-keto-glutarate

Glutamate Biosynthesis



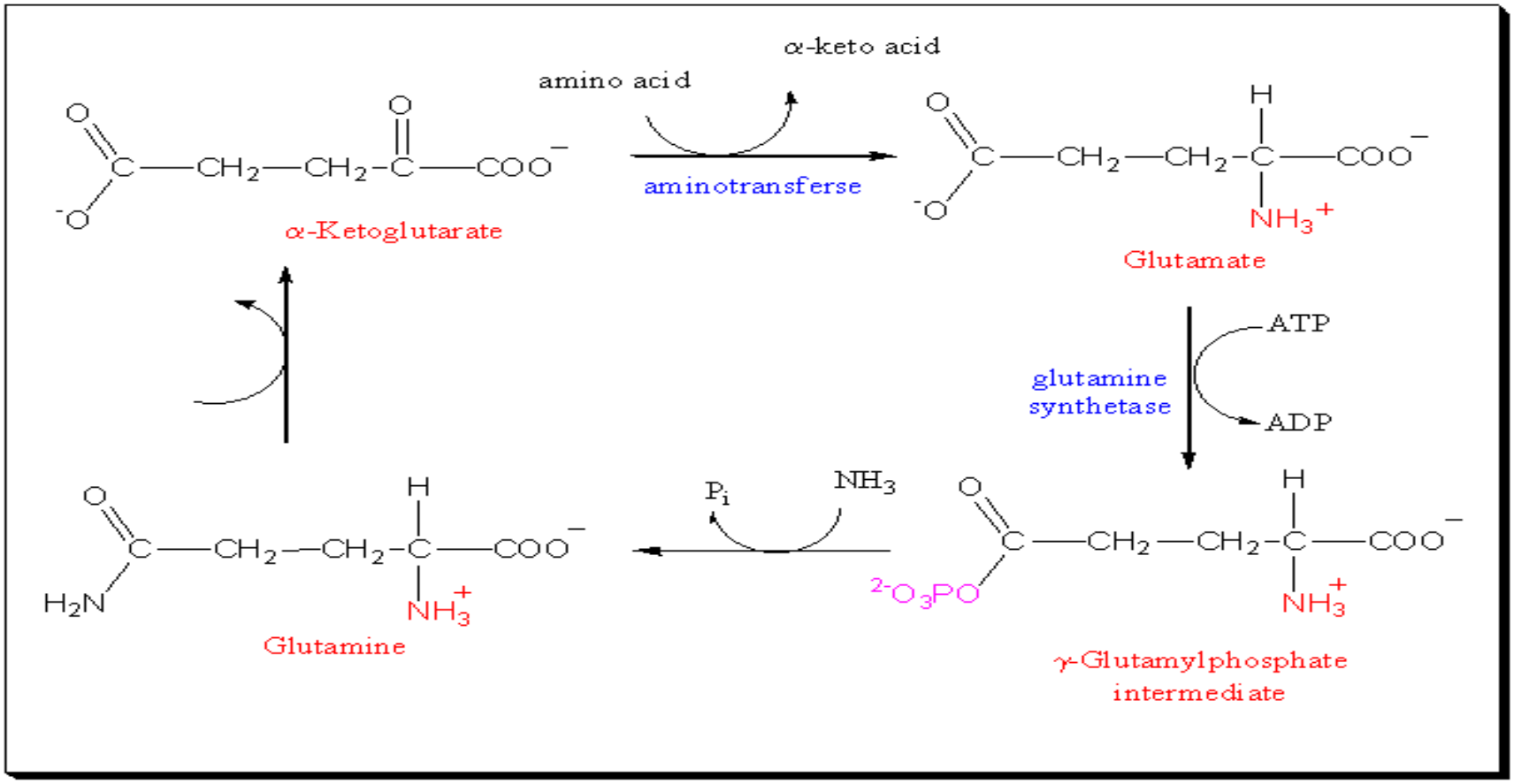
The functions of Glutamate

- Glutamine precursor
- A component of folic acid and a precursor of glutathioine an antioxidant
- Neurotransmitter
- Fuel in the brain

Glutamate Deficiency

- Excitotoxicity
- Excitotoxicity due to glutamate occurs as part of the ischemic cascade and is associated with stroke and diseases like amyotrophic lateral sclerosis, lathyrism, and Alzheimer's disease.

Glutamine Biosynthesis



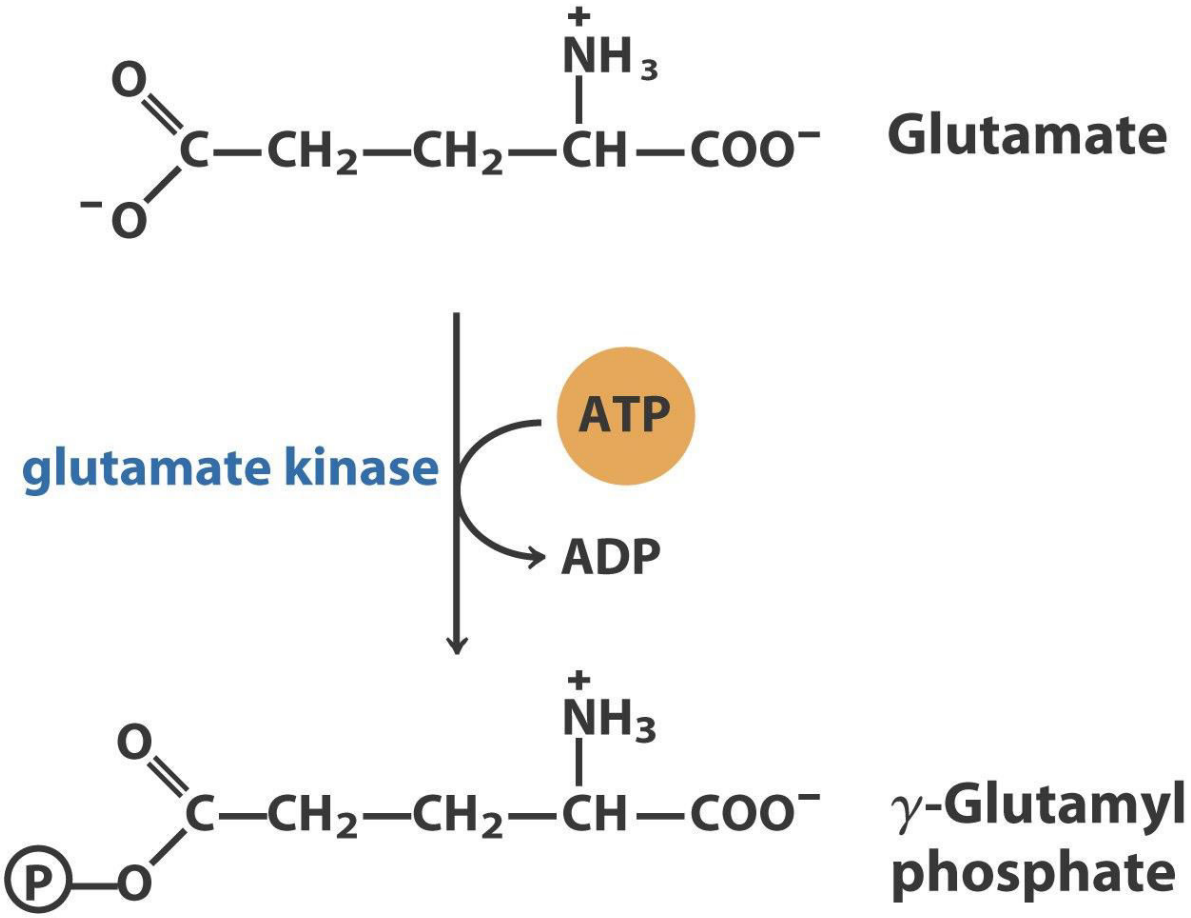
The functions of Glutamine

- Glutamine is converted to glucose as an energy source
- Important for immune function
- Basis of the building blocks for the synthesis of RNA and DNA
- Increases the body's ability to secrete human growth hormone (HGH)
- Removing excess ammonia

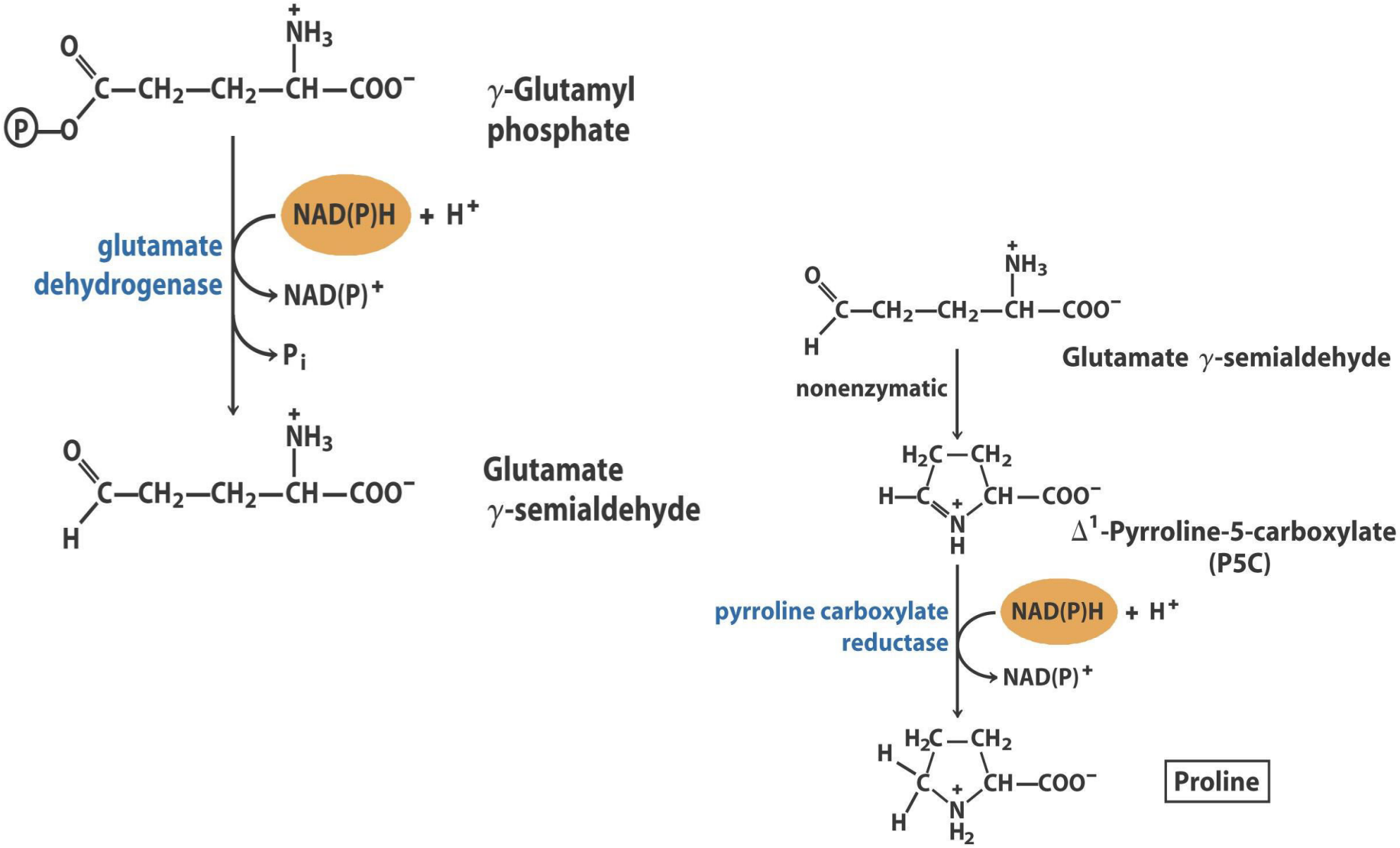
Glutamine Deficiency

- Glutamine deficiency develops during periods of fasting, starvation, strict dieting, cirrhosis, and weight loss associated with AIDS and cancer.
- Deficiencies cause increased permeability of the intestines to allergens and toxins inflammation of the intestines, food allergies, inflammatory arthritis, fatigue, impaired immune function, poor wound healing and slow recovery from illness.
- HIV infection appears to induce glutamine deficiency

Proline Biosynthesis



Proline Biosynthesis



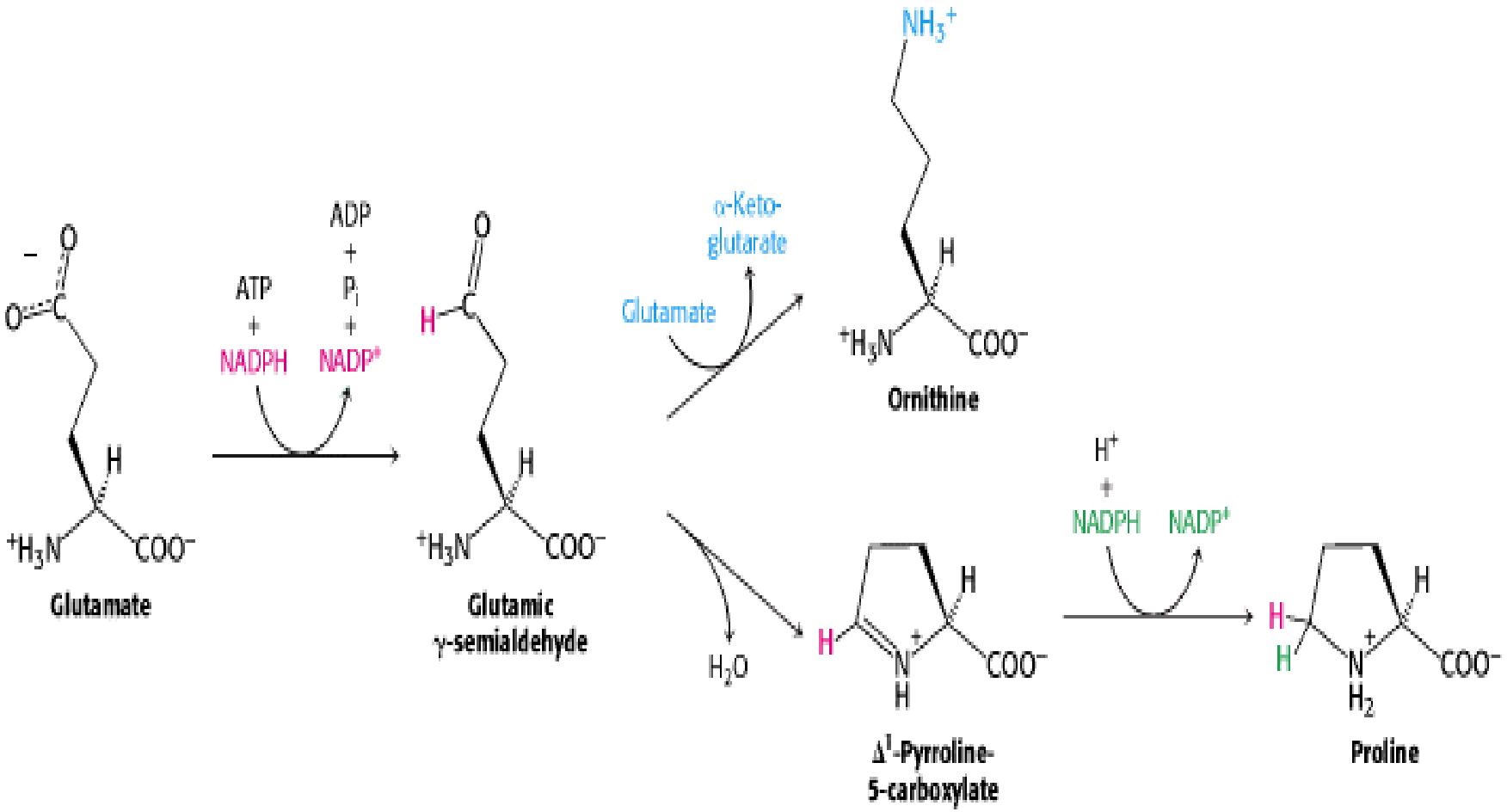
The functions of Proline

- Proline is needed for the production of collagen. Collagen is a building block of tendons, ligaments, arteries, veins and muscles.
- The body needs proline to maintain muscle tissue as well.
- Proline is important in wound healing, cartilage building, and in flexible joints and muscle support.
- It also helps reduce the sagging, wrinkling, and aging of skin resulting from exposure to the sun.

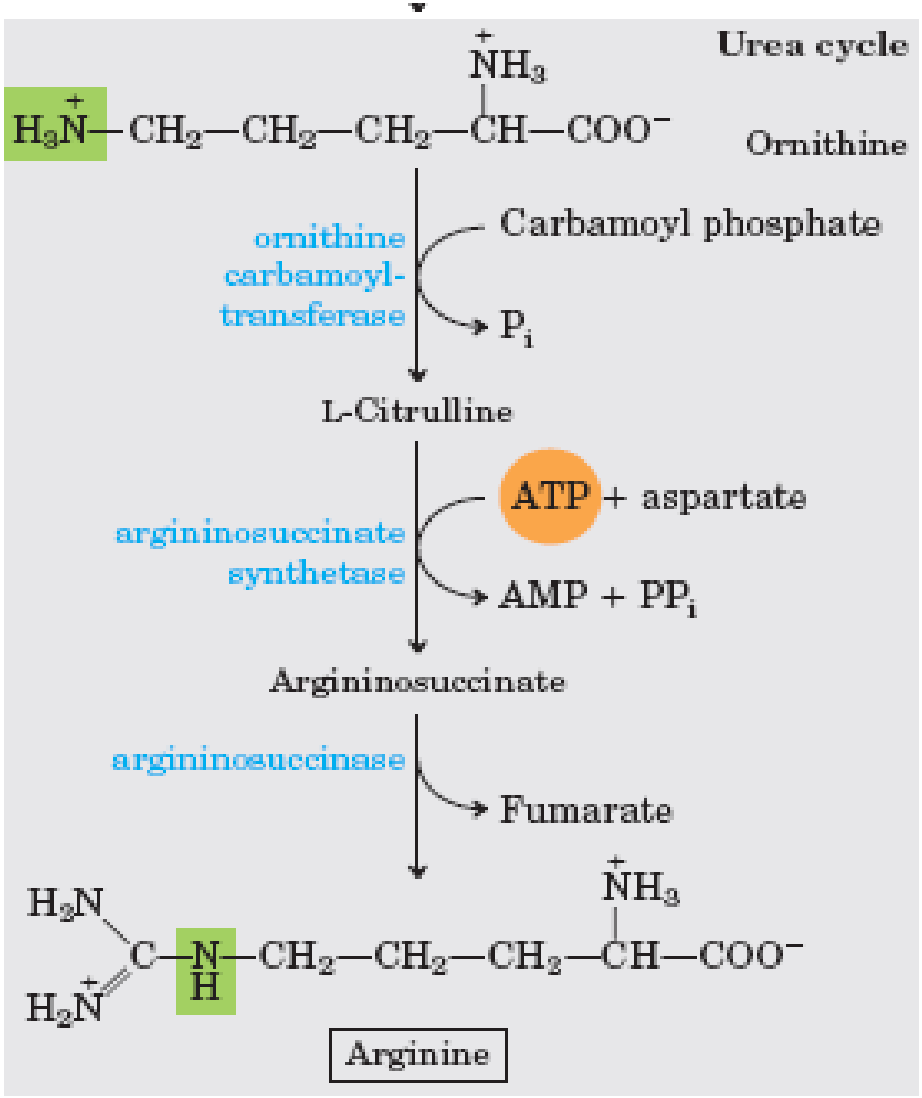
Proline Deficiency

- Proline deficiencies may occur in endurance runners and others who do prolonged exercises.
- Those who have suffered from traumatic injuries in particular, skin injuries, and severe burns and people with pain resulting from insufficient cartilage or collagen formation could also be Proline deficient.

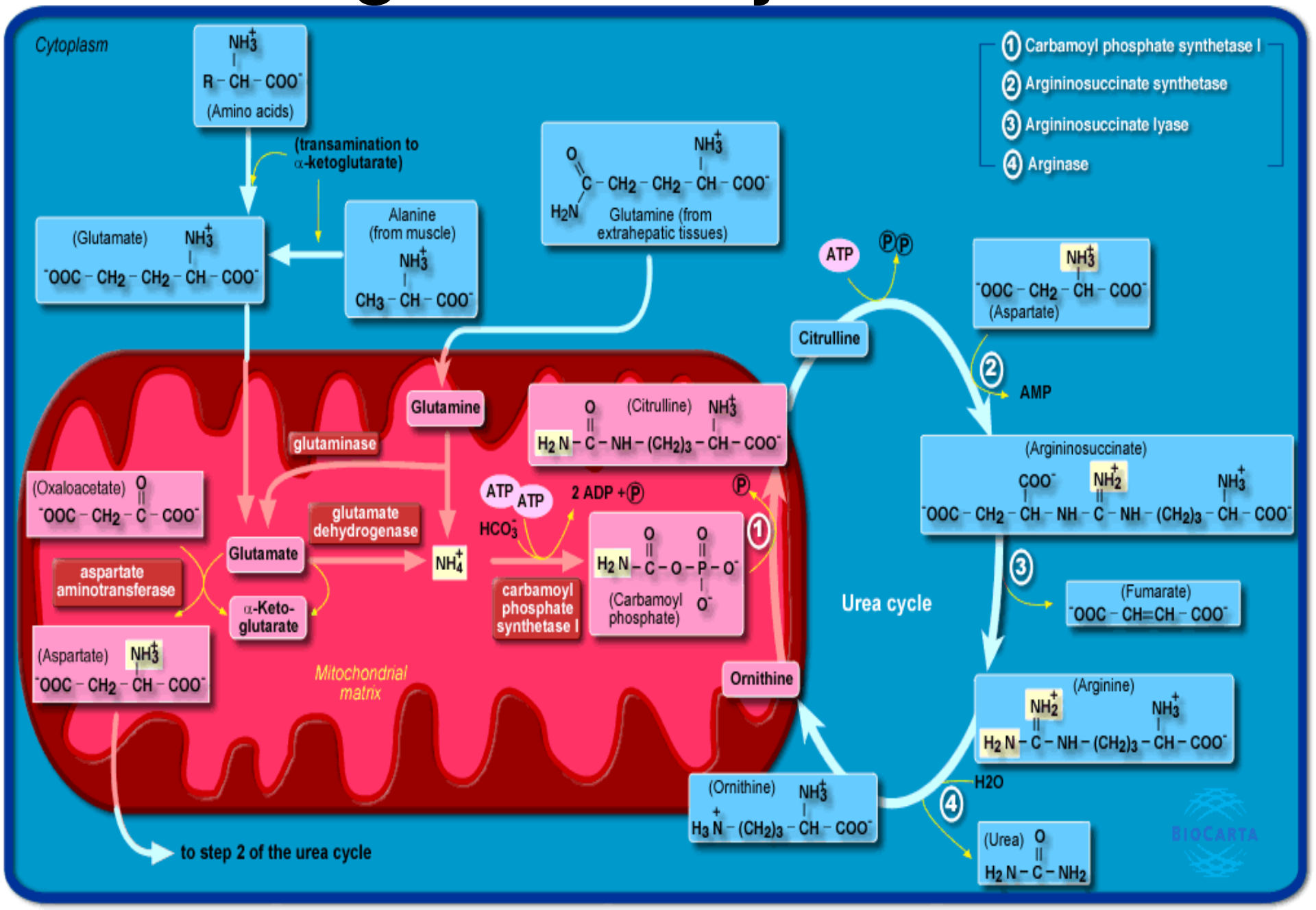
Arginine Biosynthesis



Arginine Biosynthesis



Arginine Biosynthesis



The functions of Arginine

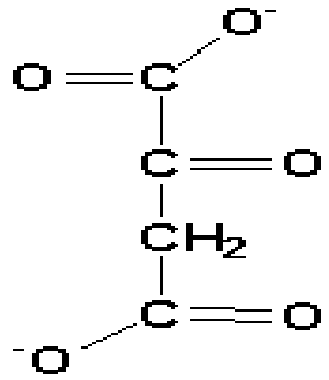
- Removing excess ammonia from the body, immune function, and the release of hormones (glucagon, insulin and growth hormone)
- Increase protein synthesis
- to produce nitric oxide.

Arginine Deficiency

- Because arginine is produced naturally by the body, it is difficult to become deficient in arginine
- However, during times of unusual stress or injury, the body may not be able to produce the necessary amount of arginine.
- Deficiency : muscle weakness, impairs insulin production, glucose production, and liver lipid metabolism.
- deficiencies of arginine are associated with the presence of excessive ammonia in the blood, excessive lysine, rapid growth, pregnancy, trauma, or protein deficiency and malnutrition.
- Arginine deficiency is also associated with rash, hair loss and hair breakage, poor wound healing, constipation, hepatic cirrhosis, and hepatic coma.

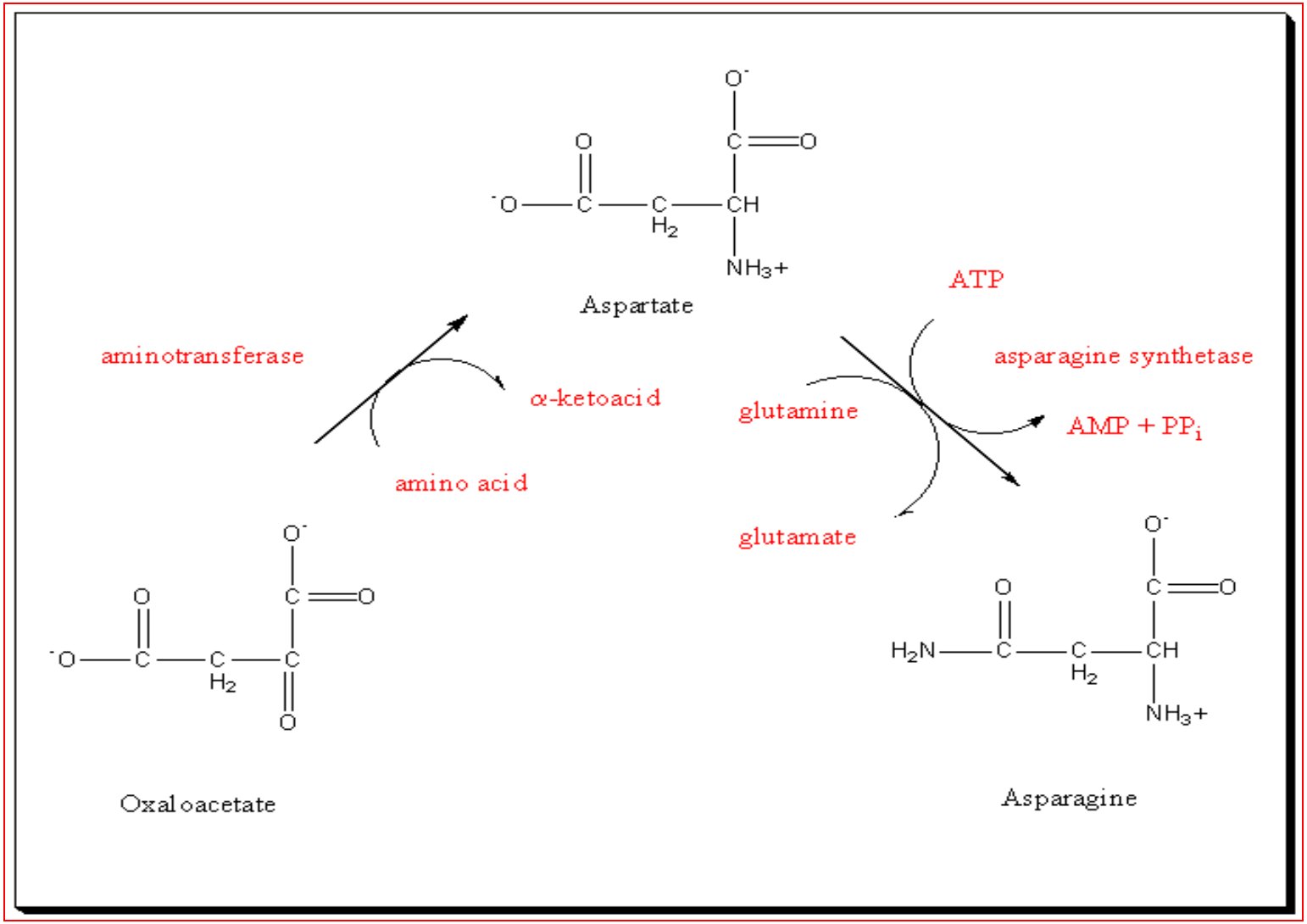
Oxaloacetate

- Oxaloacetate is an intermediate in several pathways, including **gluconeogenesis**, **citric acid cycle**, and amino acid metabolism.



Oxaloacetate

Aspartate Biosynthesis



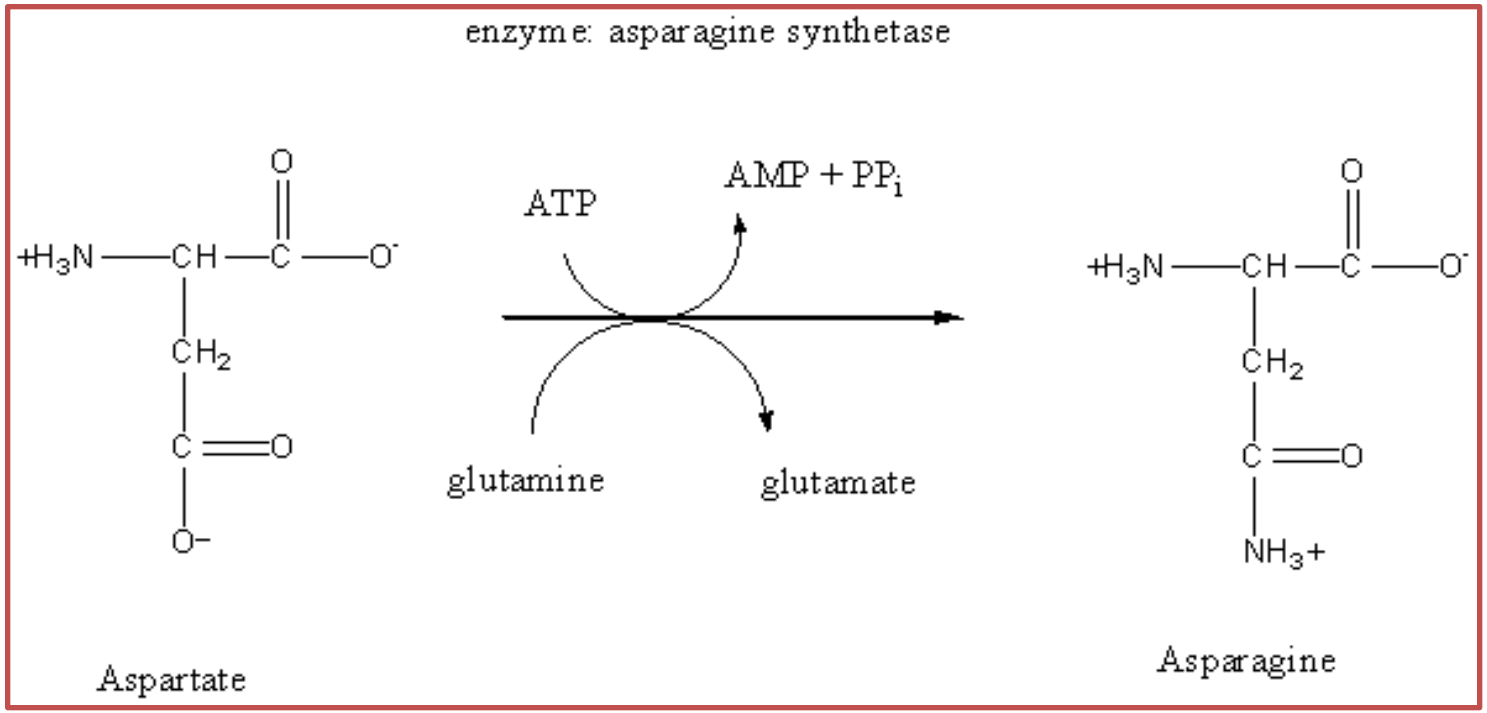
The functions of Aspartate

- **Neurotransmitter**
- It serves as an excitatory neurotransmitter in the brain and is an excitotoxin.
- As a neurotransmitter, aspartic acid may provide resistance to fatigue and thus lead to endurance, although the evidence to support this idea is not strong.

Aspartate Deficiency

- Deficiency of aspartate may occur within certain tissues under stress, but, because the body is able to make its own aspartate to replace depletion, deficiency state do not occur.

Asparagine Biosynthesis



The functions of Asparagine

- Increase protein synthesis
- Asparagine serves as an amino donor in liver transamination processes
- Asparagine is important in the metabolism of toxic ammonia in the body

Asparagine Deficiency

- Asparagine deficiency is rare. However, an asparagine deficiency could be a contributing cause of fatigue and immune system stress including autoimmune disorders, infections and severe allergies

Conclusion

- Plants and bacteria synthesize all of amino acid but human and mammals can synthesize only about half of them.
- Alanine is synthesized by pyruvate with transamination reaction.
- Glutamate is synthesized by α-Ketoglutarate and serves as the precursor of glutamine, proline, and arginine.
- Aspartate is synthesized by oxaloacetate and and serves as the precursor of Asparagine.
- Because the body can be synthesis nonessential amino acid, it is difficult to become deficient in amino acid. However, during times of unusual stress or injury, the body may not be able to produce the necessary amount of amino acid.

References

Lehninger. Principles of Biochemistry. Worth Publishers.1982.

http://www.aw-bc.com/mathews/ch21/c21tcaci.htm

http://www.aw-bc.com/mathews/ch21/fi21p1.htm

http://www.biocarta.com/pathfiles/prolinePathway.asp

http://www.biology.arizona.edu/biochemistry/problem_sets/aa/aa.html

http://www.chempep.com/ChemPep-amino-acids.htm

http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=stryer.section.3345