

## Amino Acid Metabolism

1. Explain the role of glutamate in amino acid biosynthesis and degradation.
2. How is it possible for the amino group of some amino acids to end up in urea without first being converted to ammonium?
3. Glyphosate, also known as Round-Up, is an herbicide that kills plants by inhibiting an enzyme in the amino acid biosynthetic pathway responsible for phenylalanine synthesis. Would it be safe to use glyphosate in areas where farm animals may accidentally eat plants that have been sprayed? Explain.
4. Why does it take up to 7 days before there is any noticeable herbicidal effect of glyphosate?
5. Individuals with the disease phenylketonuria (PKU) lack the enzyme phenylalanine hydroxylase which is required to convert phenylalanine to tyrosine. Albinism is a disease characterized by lack of skin pigments due to a deficiency in the enzyme tyrosinase which converts tyrosine to melanin-based pigments. What biomolecule is found at very high levels in the blood of PKU sufferers and how are the severe neurological symptoms of the disease avoided when PKU is diagnosed at birth?
6. Why are individuals with the disease phenylketonuria restricted from drinking sodas or eating foods that contain NutraSweet (aspartame)?
7. Since individuals with PKU cannot synthesize tyrosine from phenylalanine, do they also suffer from albinism? Explain.
8. Tay Sachs Disease and Phenylketonuria are due to deficiencies in enzymes required for normal metabolism, and both can cause severe neurological dysfunction and death. What characteristic do they share with regard to the underlying cause of the disease symptoms in terms of the substrates and products of these enzymatic reactions?
9. Explain why individuals born with Phenylketonuria can survive with proper treatment, whereas, children born with Tay Sachs Disease die early in life.
10. The enzyme glutamate dehydrogenase catalyzes the oxidative deamination of glutamate to produce  $\text{NH}_4^+$  and alpha-ketoglutarate. Name the enzyme that interconverts aspartate to oxaloacetate and in the process produces glutamate from alpha-ketoglutarate.
11. Explain why tyrosine is considered a non-essential amino acid even though humans lack the enzymes required for de novo tyrosine biosynthesis.
12. Name the two enzymes in amino acid catabolism that together catalyze the following net reaction



## Answers

1. Glutamate dehydrogenase plays a key role in fixing ammonia into organic nitrogen. The amino group of glutamate can then be used to convert a wide variety of keto acids into the corresponding amino acid. During amino acid degradation, the amino groups of amino acids are transferred to alpha-ketoglutarate to form glutamate. Glutamate is converted to alpha-ketoglutarate and ammonia, and this ammonia then enters the urea cycle.

2. The amino group can be transferred to glutamate which in turn can be the source of nitrogen for the formation of aspartate from OAA. The amino group from aspartate is used in the urea cycle.

AA ----> glutamate + OAA ---> aspartate + alpha-ketoglutarate ---> urea cycle

3. Yes it would be safe because animals do not have the enzyme pathway to synthesize phenylalanine (unlike plants) and would therefore be unaffected by glyphosate. (Animals obtain phenylalanine from their diet).

4. Because it takes that long before the plant uses up all available phenylalanine and becomes dependent on the de novo pathway for phenylalanine biosynthesis. Since the Shikimate pathway is blocked, plant cells cannot continue to make new proteins as they lack all 20 amino acids.

5. Phenylalanine and phenylpyruvate are found at high levels (20x higher) in the blood. Individuals with PKU are put on phenylalanine-restricted diets.

6. Aspartame is a dipeptide of aspartate and phenylalanine. Individuals with phenylketonuria lack the enzyme phenylalanine hydroxylase that is required to metabolize phenylalanine. A build-up of phenylalanine and phenylpyruvate leads to severe neurological symptoms including mental retardation.

7. Phenylketonurians are not albinos because they obtain tyrosine from the diet and are not dependent on tyrosine production from phenylalanine.

8. Tay Sachs Disease and Phenylketonuria are both diseases in which a build-up of unreacted substrates leads to the production of harmful metabolites.

9. Phenylketonurians can avoid the disease symptoms by restricting phenylalanine in their diets which prevents the build-up of phenylalanine metabolites. Individuals with Tay Sachs Disease suffer neurological consequences during development. Currently, there is no treatment that successfully removes excess GM2 from the brain.

10. The enzyme aspartate aminotransferase interconverts aspartate to oxaloacetate, thus producing glutamate and alpha-ketoglutarate.

11. Tyrosine is considered a non-essential amino acid because humans contain an enzyme (phenylalanine hydroxylase) that converts the essential amino acid phenylalanine to tyrosine.

12. The two enzymes are aspartate aminotransferase and glutamate dehydrogenase.