

25.6: Biosynthesis of Nonessential Amino Acids

Learning Objectives

- Objective 1
- Objective 2

In humans, only half of the standard amino acids (Glu, Gln, Pro, Asp, Asn, Ala, Gly, Ser, Tyr, Cys) can be synthesized (Figure 25.6.12 and 13), and are thus classified the **nonessential amino acids**. Within this group, the first three, glutamate, glutamine, and proline, have a shared anabolic pathway. It begins with glutamate dehydrogenase, which adds ammonia to α -ketoglutarate in the presence of NADPH to form glutamate. This is a key reaction for all amino acid synthesis: glutamate is a nitrogen (amino group) donor for the production of all the other amino acids.

Glutamine synthetase catalyzes the formation of glutamine from glutamate and ammonia. This is an important biochemical reaction for a completely different reason: it is the primary route for ammonia detoxification.

Proline is synthesized from glutamate in a two-step process that begins with the reduction of glutamate to a semialdehyde form that spontaneously cyclizes to D-pyrroline-5-carboxylate. This is reduced by pyrroline carboxylate reductase to proline.

Alanine and Aspartate are the products of glutamate-based transamination of pyruvate and oxaloacetate, respectively.

Asparagine is synthesized through one of two known pathways. In bacteria, an asparagine synthetase combines aspartate and ammonia. However, in mammals, the aspartate gets its amino group from glutamine.

The synthesis of serine begins with the metabolic intermediate 3-phosphoglycerate (glycolysis). Phosphoglycerate dehydrogenase oxidizes it to 3-phosphohydroxypyruvate. An amino group is donated by glutamate in a reaction catalyzed by phosphoserine transaminase, forming 3-phosphoserine, and finally the phosphate is removed by phosphoserine phosphatase to produce serine.

Serine is the immediate precursor to glycine, which is formed by serine hydroxymethyltransferase. This enzyme requires the coenzyme tetrahydrofolate (THF), which is a derivative of vitamin B₉ (folic acid).

Serine is also a precursor for cysteine, although the synthesis of cysteine actually begins with the essential amino acid methionine. Methionine is converted to S-adenosylmethionine by methionine adenosyltransferase. This is then converted to S-adenosylhomocysteine by a member of the SAM-dependent methylase family. The sugar is removed by adenosylhomocysteinase, and the resultant homocysteine is connected by cystathionine synthase to the serine molecule to form cystathionine. Finally, cystathionine- γ -lyase catalyzes the production of cysteine.

Tyrosine is another amino acid that depends on an essential amino acid as a precursor. In this case, phenylalanine oxygenase reduces phenylalanine to produce the tyrosine.

In general, the synthesis of essential amino acids, usually in microorganisms, is much more complex than for the nonessential amino acids and is best left to a full-fledged biochemistry course.

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