Biochemistry IN PERSPECTIVE

The Essential Amino Acids

How are the amino acids that are essential for humans and other mammals synthesized in plants and microorganisms? Amino acids essential to mammals are synthesized by elaborate and metabolically expensive pathways, which occur only in plants and some microorganisms. The essential amino acids include members of the aspartate family (lysine, methionine, and threonine), the pyruvate family (valine, leucine, and isoleucine), and the aromatic family (phenylalanine and tryptophan). The biosynthetic pathways for each of these molecules are briefly outlined.

The Aspartate Family

The synthesis of the EAA in the aspartate family (Figure 14A) is initiated by aspartate kinase (often referred to as aspartokinase) in an ATP-requiring reaction in which the side chain carboxyl group is phosphorylated. Aspartate β-semialdehyde, produced by the NADPH-dependent reduction of β-aspartylphosphate, represents an important branch point in plant and bacterial amino acid synthesis. The semialdehyde can either react with pyruvate to form dihydropicolinic acid (a precursor of lysine) or be reduced to homoserine. Lysine is synthesized from dihydropicolinic acid in a series of reactions that is still poorly characterized. Homoserine also occurs at a branch point. It is the precursor in the synthesis of both methionine and threonine.

The Pyruvate Family

The syntheses of valine, leucine, and isoleucine from pyruvate are illustrated in Figure 14B. Valine and isoleucine are synthesized in parallel pathways with the same four enzymes. Valine synthesis begins with the condensation of pyruvate with hydroxyethyl-TPP (a decarboxylation product of a pyruvate-thiamine pyrophosphate intermediate) catalyzed by acetohydroxy acid synthase. The α-acetolactate product is then reduced to form α, β-dihydroxyisovalerate followed by a dehydration to α-ketoisovalerate. Valine is produced in a subsequent transamination reaction from α-ketoisovalerate which is also a precursor of leucine. Isoleucine synthesis also involves hydroxyethyl-TPP, which condenses with α-ketobutyrate to form α-aceto-α-hydroxybutyrate. α-Ketobutyrate is derived from L-threonine in a deamination reaction catalyzed by threonine deaminase. α-Aceto-α-hydroxybutyrate undergoes a reduction reaction and subsequently loses an H_2O molecule, thus forming α-keto-β-methylvalerate. Isoleucine is then produced during a transamination reaction. In the first step of leucine biosynthesis from α-ketoisovalerate, acetyl-CoA donates a two-carbon unit. Leucine is formed after isomerization, reduction, and transamination reactions.

The Aromatic Family

The aromatic family includes phenylalanine, tyrosine, and tryptophan. Tyrosine is not an EAA because it is synthesized from phenylalanine in a hydroxylation reaction. The benzene ring of the aromatic amino acids is formed by the *shikimate pathway* (Figure 14C). The carbons in the benzene ring are derived from erythrose-4-phosphate and phosphoenolpyruvate. These two molecules condense to form a molecule that is subsequently converted to chorismate. Chorismate is the branch point in the syntheses of various aromatic compounds.

Figure 14D illustrates the syntheses of phenylalanine, tyrosine, and tryptophan from chorismate. (Chorismate is also a precursor in the synthesis of the aromatic rings in the mixed terpenoids, e.g., the tocopherols, the ubiquinones, and plastoquinone.)

SUMMARY Biosynthesis of amino acids that are essential to humans and other mammals requires enzymes that are found only in plants and microorganisms. EAA must, therefore, be acquired in the diet.

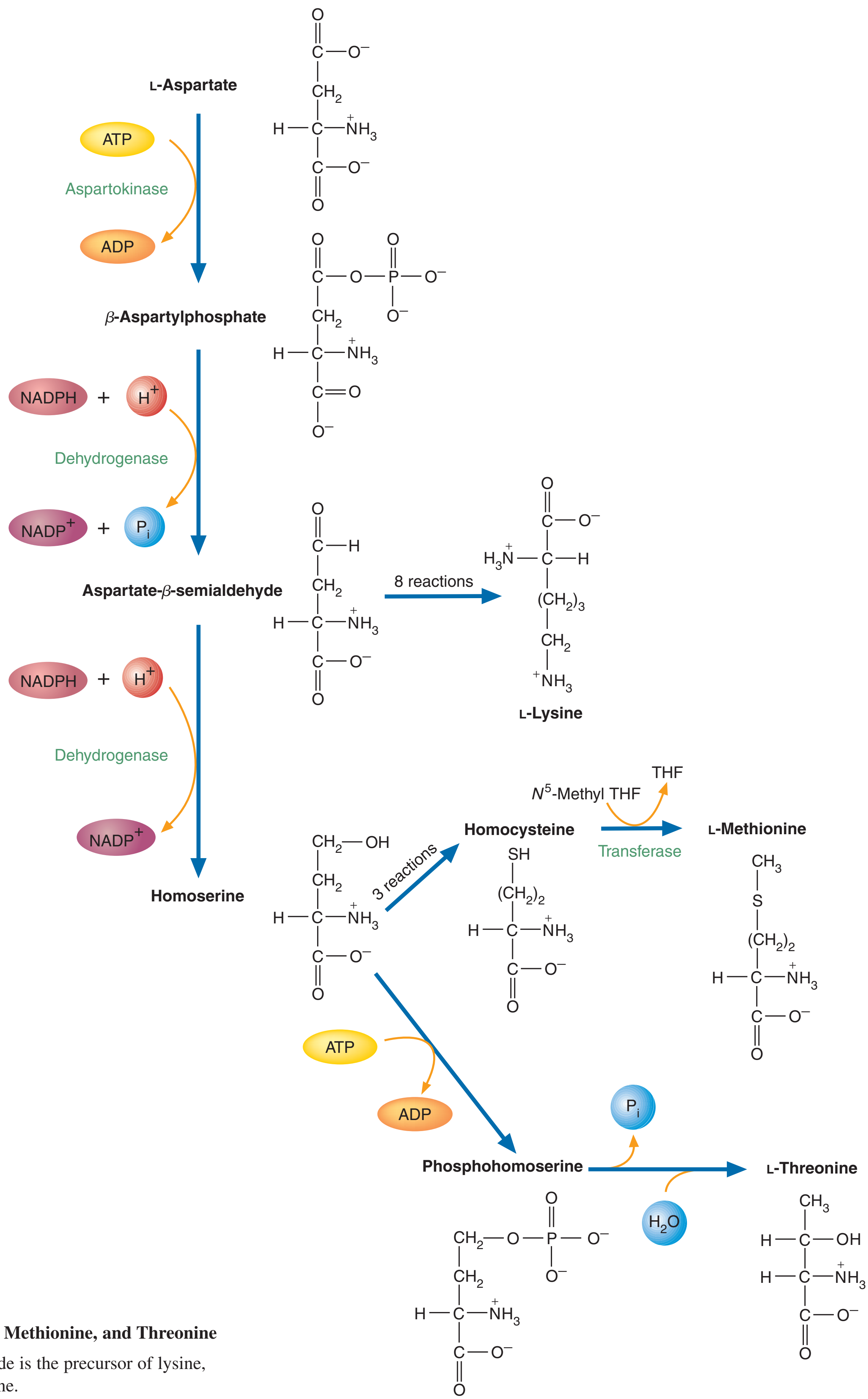


FIGURE 14A

Biosynthesis of Lysine, Methionine, and Threonine

Aspartate β-semialdehyde is the precursor of lysine, methionine, and threonine.

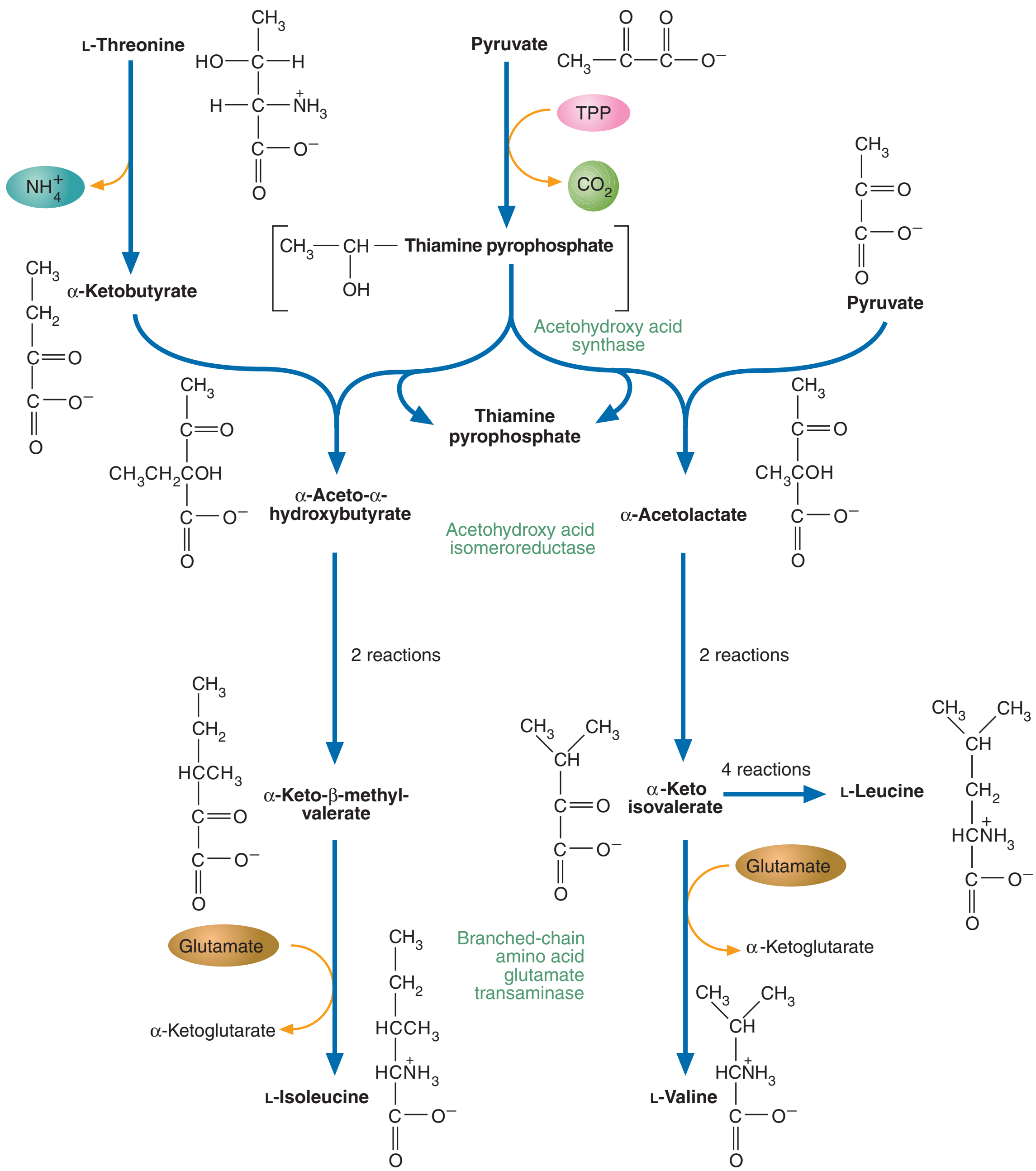


FIGURE 14B

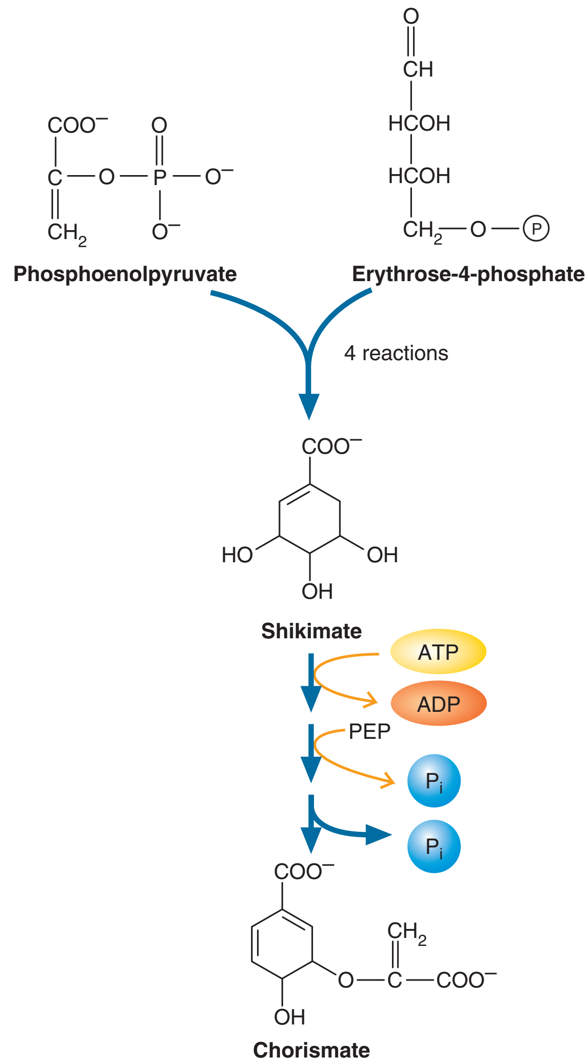
Biosynthesis of Valine, Leucine, and Isoleucine

The valine and isoleucine biosynthetic pathways share four enzymes. Isoleucine synthesis begins with the reaction of α-ketobutyrate (a derivative of threonine) with pyruvate. In valine synthesis the condensation of two pyruvate molecules is the first step. Leucine is produced by a series of reactions that begins with α-ketoisovalerate, an intermediate in valine synthesis.

FIGURE 14C

Chorismate Biosynthesis

Chorismate is an intermediate in the shikimate pathway. The formation of chorismate involves the ring closure of an intermediate (not shown) and the subsequent creation of two double bonds. The side chain of chorismate is derived from phosphoenolpyruvate (PEP).



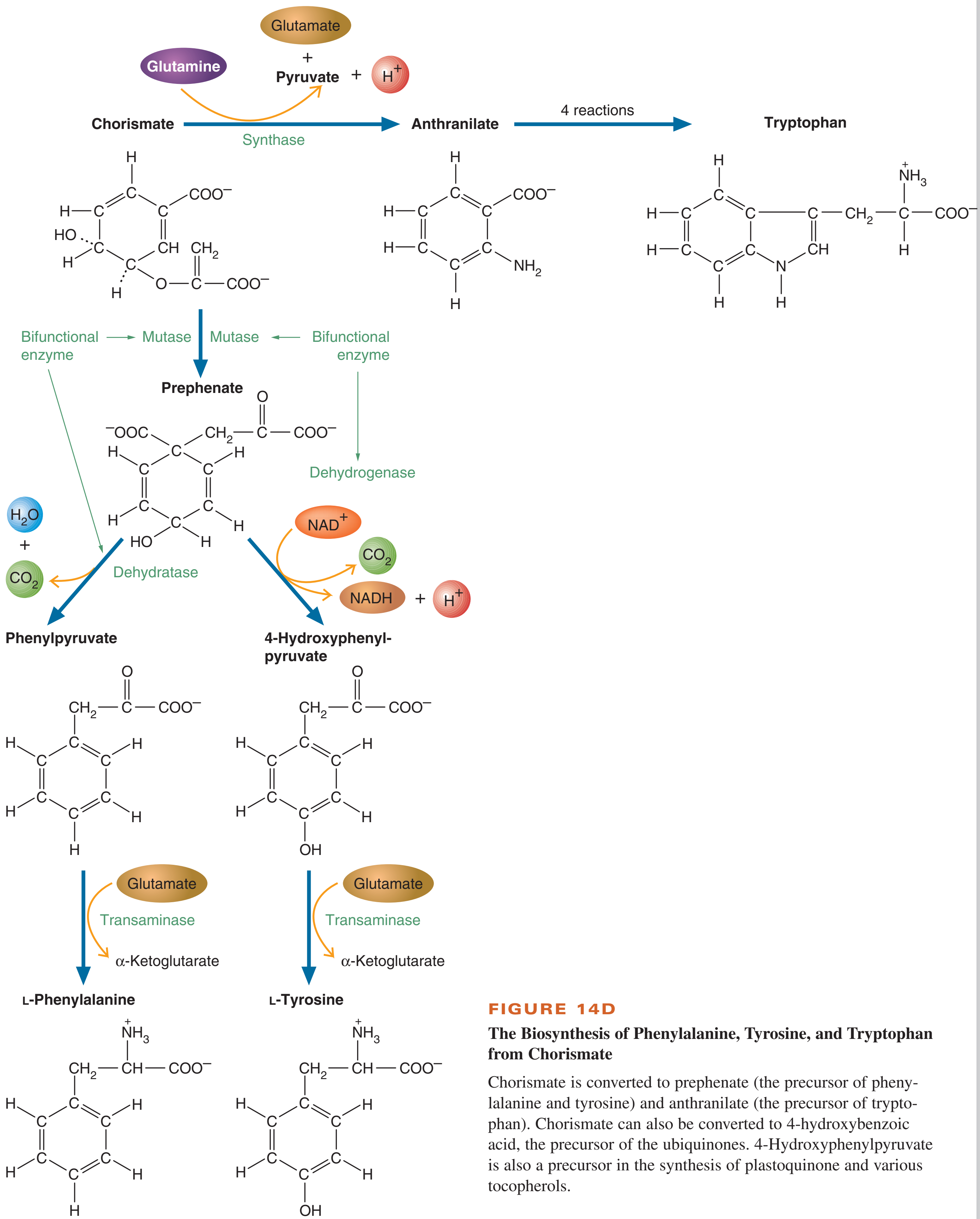


FIGURE 14D

The Biosynthesis of Phenylalanine, Tyrosine, and Tryptophan from Chorismate

Chorismate is converted to prephenate (the precursor of phenylalanine and tyrosine) and anthranilate (the precursor of tryptophan). Chorismate can also be converted to 4-hydroxybenzoic acid, the precursor of the ubiquinones. 4-Hydroxyphenylpyruvate is also a precursor in the synthesis of plastoquinone and various tocopherols.