Biochemistry IN PERSPECTIVE

The Nucleotides: IMP Biosynthesis

How is inosine-5'-monophosphate (IMP), the precursor for the purine nucleotides AMP and GMP, synthesized? The biosynthetic pathway by which PRPP (5-phospho-α-D-ribosyl-1-pyrophosphate) is converted to IMP, the first purine nucleotide, is outlined in Figure 14E. The process begins with the displacement of the pyrophosphate group of PRPP by the amide nitrogen of glutamine in a reaction catalyzed by glutamine PRPP amidotransferase. This reaction is the committed step in purine synthesis. The product formed is 5-phospho-β-D-ribosylamine.

Once 5-phospho-β-D-ribosylamine has formed, the building of the purine ring structure begins. Phosphoribosylglycinamide synthase catalyzes the formation of an amide bond between the carboxyl group of glycine and the amino group of 5-phospho-β-D-ribosylamine. In eight subsequent reactions, the first purine nucleotide IMP is formed. Other precursors of the base component of IMP (hypoxanthine) include CO_2, aspartate, and N^{10}-formyl THF. This pathway requires the hydrolysis of four ATP molecules.

SUMMARY: IMP is synthesized in an ATP-requiring pathway with ten reactions. In addition to PRPP, glutamine, glycine, carbon dioxide, aspartate, and N10-formyl THF are also substates in IMP biosynthesis.

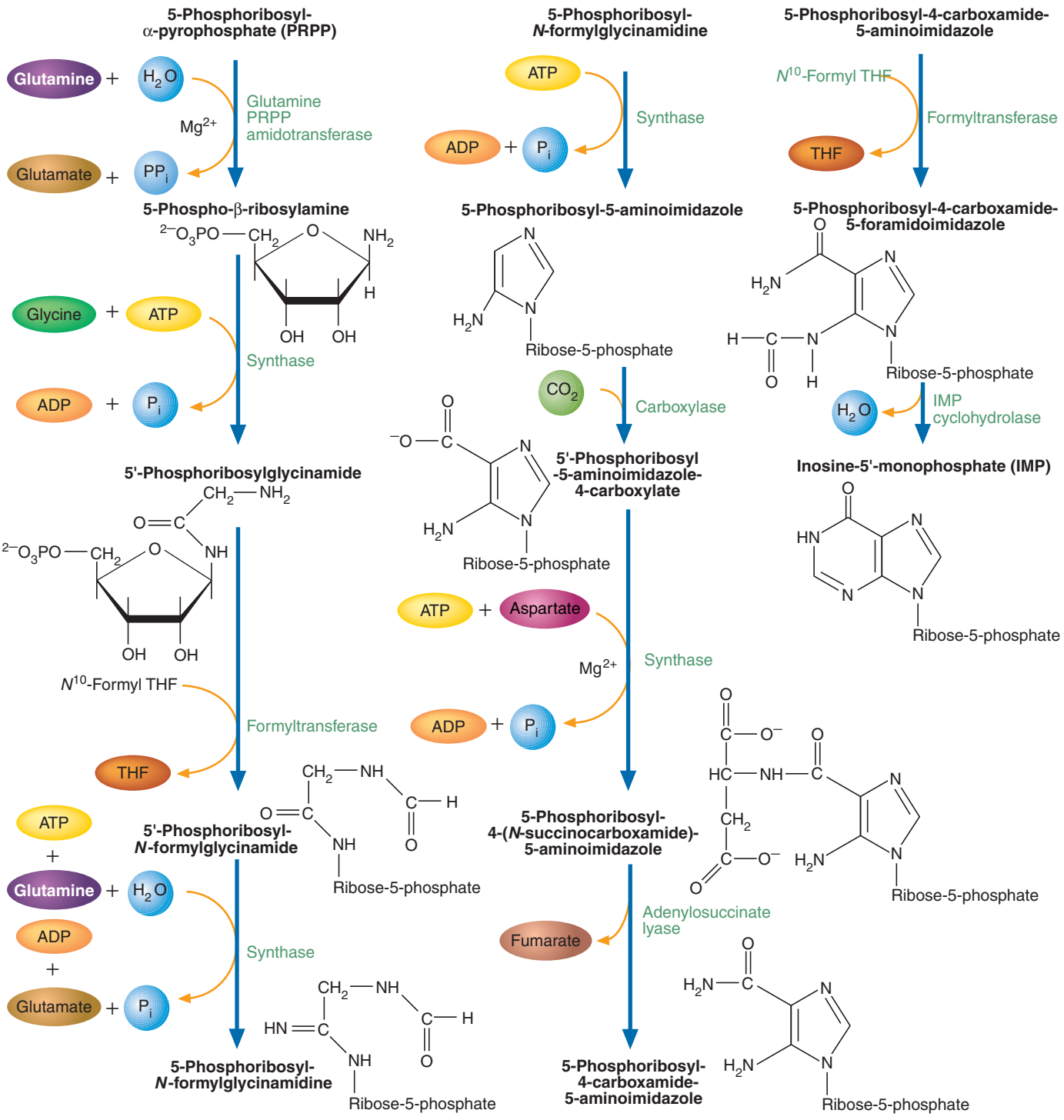

FIGURE 14E

Synthesis of Inosine-5′-Monophosphate

The biosynthesis of IMP begins with the reaction between an amino group of glutamine with C-1 of PRPP. The product, 5-phospho-*β*-ribosylamine, subsequently undergoes a series of reactions in which the purine ring is constructed using carbon atoms from formate (via N^{10}-formyl THF) and CO_2, and nitrogen atoms from glycine, glutamine, and aspartate.