5.3. GLUCOSE METABOLISM: GLYCOLYSIS AND THE TCA CYCLE

Glucose is a major carbon and energy source for many organisms. Several different metabolic pathways are used by different organisms for the catabolism of glucose. The catabolism of glucose by *glycolysis*, or the *Embden–Meyerhof–Parnas* (EMP) pathway, is the primary pathway in many organisms. Other pathways, such as the *hexose monophosphate* (HMP) and *Entner–Doudoroff* (ED) pathways, will be covered later.

Aerobic catabolism of organic compounds such as glucose may be considered in three different phases:

1. EMP pathway for fermentation of glucose to pyruvate.
2. *Krebs*, *tricarboxylic acid (TCA)*, or *citric acid cycle* for conversion of pyruvate to CO_2 and NADH.
3. Respiratory or *electron transport chain* for formation of ATP by transferring electrons from NADH to an electron acceptor.

The final phase, respiration, changes reducing power into a biologically useful energy form (ATP). *Respiration* may be aerobic or anaerobic, depending on the final electron acceptor. If oxygen is used as final electron acceptor, the respiration is called *aerobic respiration*. When other electron acceptors, such as NO_3^-, SO_4^{3-}, Fe^{3+}, Cu^{2+}, and S^0, are used, the respiration is termed *anaerobic respiration*.

Glycolysis or the EMP pathway results in the breakdown of glucose to two pyruvate molecules. The enzymatic reaction sequence involved in glycolysis is presented in Fig. 5.4. The first step in glycolysis is phosphorylation of glucose to glucose-6-phosphate (G-6P) by hexokinase. Phosphorylated glucose can be kept inside the cell. Glucose-6-phosphate is converted to fructose-6-phosphate (F-6P) by phosphoglucose isomerase, which is converted to fructose 1,6-diphosphate by phosphofructokinase. The first and the third reactions are the only two ATP-consuming reactions in glycolysis. They are irreversible. The breakdown of fructose-1,6-diphosphate into dihydroxyacetone phosphate (DHAP) and glyceraldehyde-3-phosphate (GA-3P) by aldolase is one of the key steps in glycolysis (e.g., C_6 to 2 C_3). DHAP and GA-3P are in equilibrium. As GA-3P is utilized in glycolysis, DHAP is continuously converted to GA-3P. Glyceraldehyde-3-phosphate is first oxidized with the addition of inorganic phosphate (Pi) to 1,3-diphosphoglycerate (1,3-dP-GA) by glyceraldehyde-3-phosphate dehydrogenase. 1,3-dP-GA releases one phosphate group to form ATP from ADP and is converted to 3-phosphoglycerate (3P-GA) by 3-phosphoglycerate kinase. 3P-GA is further converted to 2-phosphoglycerate (2P-GA) by phosphoglyceromutase. Dehydration of 2P-GA to phosphenol pyruvate (PEP) by enolase is the next step. PEP is further dephosphorylated to pyruvate (Pyr) by pyruvate kinase, with the formation of an ATP. Reactions after DHAP and GA-3P formation repeat twice during glycolysis.

The end-product pyruvate is a key metabolite in metabolism. Under anaerobic conditions, pyruvate may be converted to lactic acid, ethanol, or other products, such as acetone, butanol, and acetic acid. Anaerobic conversion of glucose to the aforementioned compounds used to be known as *fermentation*. However, that term today covers a whole