

Glycolysis and the Krebs cycle connect to many other metabolic pathways

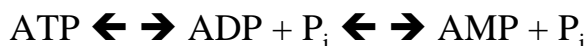
- Glycolysis can accept a wide range of carbohydrates.
 - Polysaccharides, like starch or glycogen, can be hydrolyzed to glucose monomers that enter glycolysis.
 - Other hexose sugars, like galactose and fructose, can also be modified to undergo glycolysis.
- The other two major fuels, proteins and fats, can also enter the respiratory pathways, including glycolysis and the Krebs cycle, used by carbohydrates.
- Proteins must first be digested into individual amino acids.
- Amino acids that will be catabolized must have their amino groups removed via deamination.
 - The nitrogenous waste is excreted as ammonia, urea, or another waste product.
- The carbon skeletons are modified by enzymes and enter as intermediaries into glycolysis or the Krebs cycle depending on their structure.
- The energy of fats can also be accessed via catabolic pathways.
- Fats must be digested to glycerol and fatty acids.
 - Glycerol can be converted to glyceraldehyde phosphate, an intermediate of glycolysis.
 - The rich energy of fatty acids is accessed as fatty acids are split into two-carbon fragments via **beta oxidation**.
 - These molecules enter the Krebs cycle as acetyl CoA.
- In fact, a gram of fat will generate twice as much ATP as a gram of carbohydrate via aerobic respiration.
- Carbohydrates, fats, and proteins can all be catabolized through the same pathways.

- The metabolic pathways of respiration also play a role in anabolic pathways of the cell.
- Not all the organic molecules of food are completely oxidized to make ATP.
- Intermediaries in glycolysis and the Krebs cycle can be diverted to anabolic pathways.
 - For example, a human cell can synthesize about half the 20 different amino acids by modifying compounds from the Krebs cycle.
 - Glucose can be synthesized from pyruvate and fatty acids from acetyl CoA.
- Glycolysis and the Krebs cycle function as metabolic interchanges that enable cells to convert one kind of molecule to another as needed.
 - For example, excess carbohydrates and proteins can be converted to fats through intermediaries of glycolysis and the Krebs cycle.
- Metabolism is remarkably versatile and adaptable.

Feedback mechanisms control cellular respiration

- Basic principles of supply and demand regulate the metabolic economy.
 - If a cell has an excess of a certain amino acid, it typically uses feedback inhibition to prevent the diversion of more intermediary molecules from the Krebs cycle to the synthesis pathway of that amino acid.
- The rate of catabolism is also regulated, typically by the level of ATP in the cell.
 - If ATP levels drop, catabolism speeds up to produce more ATP.
- Control of catabolism is based mainly on regulating the activity of enzymes at strategic points in the catabolic pathway.
- One strategic point occurs in the ***third*** step of glycolysis, catalyzed by ***phosphofructokinase***.

- Allosteric regulation of phosphofructokinase sets the pace of respiration.
 - This enzyme is inhibited by ATP and stimulated by AMP (derived from ADP).
 - It responds to shifts in balance between production and degradation of ATP:



- Thus, when ATP levels are high, inhibition of this enzyme slows glycolysis.
 - When ATP levels drop and ADP and AMP levels rise, the enzyme is active again and glycolysis speeds up.
- Citrate, the first product of the Krebs cycle, is also an inhibitor of phosphofructokinase.
 - This synchronizes the rate of glycolysis and the Krebs cycle.
 - Also, if intermediaries from the Krebs cycle are diverted to other uses (e.g., amino acid synthesis), glycolysis speeds up to replace these molecules.
- Metabolic balance is augmented by the control of other enzymes at other key locations in glycolysis and the Krebs cycle.
- Cells are thrifty, expedient, and responsive in their metabolism to meet the ever-changing needs of the organism.