

Glycolysis II/III

1. Other sugars than glucose can be metabolized by glycolysis, if they are converted to intermediates of glycolysis.
2. Galactose can enter glycolysis by being converted to galactose-1-phosphate followed by conversion (ultimately) to glucose-1-phosphate and subsequently to glucose-6-phosphate, which is a glycolysis intermediate.
3. Deficiency of galactose conversion enzymes results in accumulation of galactose (from breakdown of lactose). Excess galactose is converted to galactitol (a sugar alcohol). Galactitol in the human eye lens causes it to absorb water and this may be a factor in formation of cataracts.
4. Deficiency of the enzyme lactase leads to lactose intolerance
5. Regulation of glycolysis is controlled by three enzymes - hexokinase, PFK, and pyruvate kinase. Hexokinase's regulation is a bit complicated and is controlled partly by availability of substrate.
6. PFK is very unusual in being negatively regulated by a molecule (ATP) that is also a substrate. This is possible because the enzyme has an allosteric binding site for ATP in addition to the substrate binding site and the K_m for the allosteric site is higher than the substrate binding site.
7. Pyruvate kinase is regulated both allosterically and by covalent modification (phosphorylation/dephosphorylation). Phosphorylation of the enzyme by a protein kinase turns the enzyme activity down, whereas F1,6BP acts as an allosteric activator. This activation is known as feedforward activation.
8. Feed forward activation is rare in metabolism. It is a term used to describe a metabolic product (such as F1,6BP above) that **ACTIVATES** an enzyme that catalyzes a reaction further ahead of it in a metabolic pathway. In glycolysis, feedforward activation acts to start the pyruvate kinase reaction and **PULLS** the reactions forward to get over the energy "hump" of the aldolase reaction.
9. Hypoxia refers to the condition where cells are short of oxygen. Since oxygen is necessary for maximum energy production from glucose, they must respond to this condition. One way they respond is by making a transcription factor known as Hypoxia Induction Factor 1 (HIF-1). HIF-1 activates transcription of genes involved in glucose transport and glycolysis. Cancer cells are frequently hypoxic and induce HIF-1, as well. Another way cancer cells battle hypoxia is to stimulate the growth of blood vessels to them by making another factor known as angiogenin. Blocking HIF-1 and angiogenin are anti-cancer therapies.