Glycolysis

GLYCOLYSIS

• 1 glucose (6-carbon sugar) breaks down to 2 pyruvates (3-carbon sugar).

• Net 2 ATP produced: 2 consumed (investment phase) and 4 generated (pay off)

• 2 NADH produced

REGULATED STEPS
Hexokinase

• Glucose + ATP Glucose-6-phosphate + ADP

Phosphofructokinase

• Fructose-6-phosphate + ATP ? fructose-1,6-biphosphate + ADP

Pyruvate kinase

• Phosphoenol pyruvate + ADP ? Pyruvate + ATP

ENZYMES OF GLYCOLYSIS Listed in chronological order (substrate/product in parentheses)

• Hexokinase (glucose/glucose-6P)

• Phosphoglucose isomerase (glucose-6P/fructose-6P)

• Phosphofructokinase (fructose-6P/fructose-1,6P)

• Aldolase (fructose-1,6P/G3P & DHAP)

• Triose phosphate isomerase (DHAP/G3P)

• Glyceraldehyde-3-phosphate dehydrogenase (G3P/1,3-bisphosphoglycerate)

• Phosphoglycerate kinase (1,3-bisphosphoglycerate /3-phosphoglycerate)

• Phosphoglycerate mutase (3-phosphoglycerate /2-phosphoglycerate)

• Enolase (2-phosphoglycerate /phosphoenol pyruvate)

• Pyruvate kinase (phosphoenol pyruvate /pyruvate)

FULL-LENGTH TEXT

• Here we'll learn about glycolysis, which involves the breakdown of glucose (a 6-carbon sugar) to pyruvate (a 3-carbon sugar) – a molecule that is used in many metabolic reactions.

• Start a table to note some key points about glycolysis.

• First, regarding glucose formation, denote that complex carbohydrates (like starch) breakdown to glucose.

• Denote that glycolysis is the metabolism of one molecule of glucose into two molecules of pyruvate.

• In our diagram, draw glucose in the upper left as six carbons linked together.

- We will use circles to keep track of the molecules in glycolysis

• Draw pyruvate in the lower right as 3 carbons linked together.

• Denote that glycolysis generates a net of two ATP molecules per molecule of glucose.

- Specifically, denote that 2 are consumed and 4 ATP are generated, which nets + 2 ATP.

- Because ATP is the energy currency of the cell, we can use an investment/payoff format in our accounting of ATP

• In our diagram, draw a line across the middle of the page.

- Indicate that reactions above the line require an investment, 2 ATP.

- Indicate that reactions below the line provide a payoff, 4 ATP.

- We'll keep track of the accounting throughout the reaction.

• In our diagram, insert three important enzymes:

- Hexokinase, just beneath glucose, insert.

- Phosphofructokinase, just above the line.

- Pyruvate kinase, at the end of the reaction.

• Denote that glycolysis has three regulated steps:

- Hexokinase catalyzes the phosphorylation of glucose.

- Phosphofructokinase catalyzes the phosphorylation of fructose-6-phosphate.

- Pyruvate kinase catalyzes the formation of pyruvate.

We learn more about glycolysis regulation, elsewhere.

Let's draw glucose now, in its ring form.

• Draw a hexagon with an oxygen atom inserted at the top right.

• Starting at the right of the oxygen atom, label carbons 1 through 5.

• Add a CH2OH group to carbon 5 and label its carbon 6.

Now let's draw the structure of pyruvate, in stick form.

• Draw a chain of three carbons.

• Add a double-bonded oxygen to the second carbon

• Add two oxygen atoms to the third carbon.

- Use dashed lines so show that the single carbon-oxygen bonds have double bond character.

• Add a negative charge.

Now we'll begin to fill in the various molecules made as glucose is metabolized to pyruvate.

• In the first reaction, glucose is phosphorylated to glucose-6-phosphate.

• Redraw our six circles, with a P attached to the sixth circle to represent the phosphate group.

• Use an arrow to show that this irreversible reaction is catalyzed by hexokinase, the first of the regulated enzymes.

• Use another arrow to show that in this step, ATP is converted to ADP, which is an energy-consuming reaction (show it in our accounting).

• The phosphorylation of glucose is an irreversible reaction that traps glucose inside the cell.

- To show this, dash a line between glucose and glucose-6-phospate to represent the cell membrane.

• Show that glucose-6-phosphate is then reversibly converted to fructose-6-phosphate.

• Indicate that the enzyme catalyzing this is phosphoglucose isomerase.

• Now, show that in the next step, fructose-6-phosphate is phosphorylated to fructose-1,6-bisphosphate, which has two phosphate groups: one on the first carbon and one on the sixth carbon.

• Indicate that it is an irreversible reaction, which phosphofructokinase catalyzes – it's the second regulated step of glycolysis.

• Since this is another energy consuming step, use an arrow to show that ATP is converted to ADP (show it in our accounting).

This is the end of the energy investment phase. The next reaction breaks the six-carbon sugar into two three-carbon sugars, and begins the energy payoff phase.

• Use a reversible arrow to show that aldolase cleaves fructose-1,6-bisphosphate into the 3-carbon sugars glyceraldehyde-3-phosphate (G3P) and dihydroxyacetone phosphate (DHAP).

• Also use a reversible arrow to show that G3P and DHAP can be interconverted by triose phosphate isomerase.

- Because of this, everything from this point is doubled.

• To remember this, draw a bracket next to the space between G3P and pyruvate and write times 2 next to it.

• Show that in the next step G3P is phosphorylated to 1,3-bisphosphoglycerate in a reversible reaction catalyzed by glyceraldehyde-3-phosphate dehydrogenase.

• Use an arrow to show that NAD+ and inorganic phosphate are input, and NADH is also formed.

• Next, show that 1,3-bisphosphoglycerate is reversibly converted to 3-phosphoglycerate by phosphoglycerate kinase.

• Use an arrow to show that this reaction generates ATP from ADP (show it in our accounting).

• Next show that 3-phosphoglycerate is isomerized to 2-phosphoglycerate by phosphoglycerate mutase.

• Then show that 2-phosphoglycerate is dehydrated to phosphoenol pyruvate by enolase.

The final step of glycolysis is the third regulated step.

• Show that phosphoenol pyruvate is converted to pyruvate in an irreversible reaction.

- The enzyme that catalyzes this reaction is pyruvate kinase.

• Use an arrow to show that ADP is converted to ATP in this step (show it in our accounting).

• Thus, indicate that although we've only shown a payoff of 2 ATP from the reaction, everything in the payoff phase is doubled, so we actually generate 4 ATP here!

In the next few tutorials, we will learn in greater detail how glycolysis is regulated, and what happens to pyruvate after glycolysis.

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