Glycolysis

Imports

Glycolysis

Glycolysis is a metabolic pathway involving the stepwise degradation of glucose

Background

Glycolysis is a very ancient process, which arose relatively early on in evolutionary history. As a result of its age, today almost all living organisms undergo some form of glycolysis. Glycolysis is an anaerobic process, as it arose before oxygen formed a large substituent of the earths atmosphere. Even in aerobic organism glycolysis still remains anaerobic, although the products of glycolysis are then fed into other aerobic pathways.

Process

Glycolysis involves the break down of glucose molecule into pyruvate through ten enzyme catalysed steps. These ten steps can be generally grouped into two phases, the initially priming phase in which glucose is transformed into a less stable form, a process which requires energy provided by coupling with ATP hydrolysis, and the second energy release phase in which new ATP is generated. For each one molecule of glucose metabolised, two molecules of pyruvate are produced. The balanced equation for the overall reaction is as follows:
$Glucose_2Pi + 4NAD^+ + 2ADP \rightarrow 4NADN + 2H_2O + 2ATP + 4H^+ + 2Acetyl - CoA + 2CO_2 + 2CoASH$

Phase #1 (Priming)

Phase one includes the first 4 reactions of glycolysis, in which, overall, Glyceraldehyde-3-phosphate is produced by the splitting of glucose. The balanced equation for this phase is as follows:

Energy requirements

2 ATP molecules are used up in this phase.

Reactions

Reaction #1

Glucose is phosphorylated by hexokinase or glucokinase to form glucose-6-phosphate, coupled with the hydrolysis of one ATP molecule. The balanced equation for this reaction is as follows.

$\text{Glucose} + ATP \rightarrow \text{glucose-6-phosphate} + ADP + H^+ \qquad \Delta G^\circ = -16.7kJ \cdot ml^{-1}$

> NOTE: Extracellular glucose will move into the cell as glucose is converted from glucose to glucose 6 phosphate, by the law of mass action.
>
> NOTE: Reaction one is often referred to as the first priming reaction.

Energetics

The reaction itself is not thermodynamically favorable, and hence must be coupled with ATP hydrolysis to achieve spontaneity.

Enzymes

The reaction can be catalysed by glucokinase, or hexokinase. Both glucokinase and hexokinase require magnesium ions to function. Glucokinase only functions at high glucose levels whereas hexokinase binds glucose at low glucose concentrations, hence glucokinase is only active after consumption of a high glucose meal.

Regulation.

Hexokinase is one of the regulated enzymes in glycolysis, the reaction is targeted as a regulation point due to its large negative free energy change.

Reaction #2

Glucose-6 Phosphate is converted into fructose 6 phosphate by phosphoglucoisomerase.

Enzyme

Phosphoglucoisomerase is used for the reaction. This enzyme requires magnesium ions to function.

Reaction #3

Fructose-6-phosphate is phosphorylated into fructose-1,6-bisphosphate by phosphofructokinase. The reaction is natively endothermic so must coupled with ATP Hydrolysis to occur. The balanced reaction is given as:

Fructose-6-phosphate $+ ATP \rightarrow$ fructose-1,6,-bisphosphate $+ ATP \qquad \Delta G^{\circ}\prime = 14.2kJ \cdot mol^{-1}$

NOTE: Reaction 3 is often referred to as the second primary reaction.

Enzyme

The reaction is catalysed by phosphofructokinase.

Regulation

The phosphofructokinase reaction controls the rate of glycolysis. Intermediates of the citric acid cycle form allosteric inhibitor's which act on phosphofructokinase.

Reaction #4

Fructose biphosphate aldose, producs two 3 carbo intermediate.

Phase #2

Phase two includes the last 6 reactions of glycolysis in which, overall,glyceraldehyde 3 phosphate is converted to pyruvate.

Reaction #5

Triose phosphare isomerase compelets the first phase of glycolysis by catalysing an ismoerisation reaction.

Phase 2

Reaction #6

Glyceraldehyde-3-phosphate dehydrogenase produces a high energy intermediate in an oxidation reaction.

In the absence of oxygen reaction 6 cannot occur if there is no NAD^+ the recycling of NAD^+ via the reduction of pyruvate. ### reaction #7

Spontaneity

Very spontaneous coupling with reaction six, drives reaction six

Reaction

$1,3-BPG + ADP \rightarrow 3phosphoglycerate + ATP$ $\Delta G°\prime - 18.9kJ.mol^{-1}$

Enzyme

Phosphoglycerate Kinase

Cofactors

ATP Production

regenerates ATP used earlier in Glycolysis.

Phosphoglycerate kinase (Mg^{2+}) as in the back reaction the phosphoglycerate is phosphorylated. or it could be called 1,3-Bisphosphate phosphatase.

this reaction has a large negative ΔG and hence is a site of regulation.

first substrate level phosphrylation occurs, ie the phosphate group derrives dirrectly from the phosphate, in the ETC ATP is formed from ATP by substrate level phosphorylation.

Break even reaction, energy lost is equal to energy gained

Reaction #7

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Reaction #8

Phosphoglycerate mutase (mutases move only one functional group). this reaction prepares the substrate for the following reaction involving the synthesis of ATP, ie priming the phosphate group for removal.

Reaction #9

Enzyme

Enolase.

Reaction

Dehydration reaction

$2 phosphoglycerate \rightarrow phosphoenolpyruvate$

As much more instable in the enol form so it is a muich higher energy molecule (it has not gained energy, only instability). enols tautomerise to ketones.

produces PEP via dehydrogenase (?)

Reaction #10

Enzyme

pyruvate kinase (phosphoenolpyruvate phosphatase)

transfer of a phosphoryl group from PEP to ADP to generate ATP and Pyruvate, enol tautomer converted to more favourable keto tautomer,

tautomers are isomers which can readily intraconvert between each other.

Reaction

$Phosphoenolpyruvate \rightarrow pyruvate$ pyruvate Kinase produces pyruvate and mro ATP

Kinase enzymes.

transfer a phosphate group.

phosphatase

a dephosphorylating enzyme.

Location

Glycolysis occurs in the cytoplasm.

Biological significance

Glycolysis is a particularly important process as in many cases glucose is the only source of metabolic energy. Cells of the brain kidney contractual skeletal muscles, erythrocytes, and sperm cell, are all solely reliant on glycolysis for energy.

Products

Pyruvate is a versatile metabolite, depending on the availability of oxygen, pyruvate can undergo further oxidation to form acetyl-CoA and carbon dioxide. If oxygen is not present then in animal cells the pyruvate will be converted to lactic acid (lactate), and in yeast cells it will undergo alcoholic fermentation to form ethanol.

Stage 2

amino acids to alpha keto acids, and then pyruvate or acetylp co A glycerol and glucose to pyruvate. and fatty acids to acetyl CoA. pyruvate can be further brocked down into acetyl-coA (the common end product of metabolism

final waste products are carbon dioxide and water.

regulation of glycolysis COPY IMAGE. no significant trend in free energyies released, however under physiological conditions all most run close to eqilibrium,

Appendix