Cori Cycle and Entner-Doudoroff Pathway

Entner- Doudoroff Pathway

It was for the first time reported by Michael Doudoroff and Nathan Entner in 1952. It is described as an alternative reaction sequence of glucose catabolizing to pyruvate with a completely different set of enzymes than the Glycolysis or Pentose Phosphate Pathway. Entner- Doudoroff Pathway is distinctive in that it occurs only in prokaryotes. It uses 2- keto 3-deoxyphosphogluconate aldolase and 6- phosphogluconate dehydratase to convert glucose to pyruvate. In this process, every glucose molecule yields 1 ATP, 1 NADH and 1 NADPH, whereas, with glycolysis, there are two ATP and two NADH for each Glucose molecule. This pathway is mainly found in *Agrobacterium, Rhizobium, Pseudomonas, Azatobacter* and other Gram-negative bacteria that lack enzymes like phosphofructokinase-1 essential for glycolysis. Few exceptions like Enterococcus faecalis, a Gram Positive bacteria, follow this pathway.

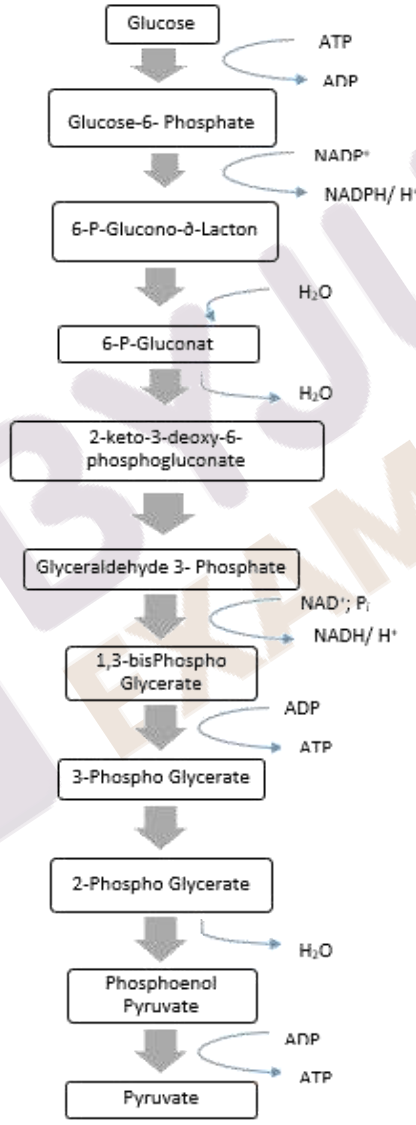


Figure 1. Entner- Doudoroff Pathway

Cori Cycle of fermentation

It was for the first time studied by Carl and Gerty Cori in the 1930s and 1940s, who then clarified its pathway and role. The cycle of reactions involves glucose conversion to lactate in muscle and lactate converting to glucose in the liver. Aerobic organisms convert glucose to pyruvate by glycolysis, and they then use the molecular oxygen to oxidize pyruvate wholly into CO2 and H2O. However, even in aerobic organisms,

anaerobic catabolism of glucose occurs during short spurts of extreme muscular activity because it is difficult for muscles to carry oxygen fast enough to oxidize at that particular point of time pyruvate, for example, in a 100 m sprint race. In its place, the muscles, via the fermentation process, use glycogen (stored glucose) as fuel to generate ATP, with lactate as the end product. The lactate built up to high concentrations in the blood is gradually converted back to glucose by gluconeogenesis in the liver during the recovery period or subsequent rest. Oxygen intake diminishes until the breathing rate returns to normal. The excess oxygen intake during the recovery period signifies repayment of oxygen debt. The amount of oxygen required to source ATP for gluconeogenesis during recovery to regenerate the glycogen "rented" from liver and muscle to carry out an intense muscular activity or during fast emergency movements.

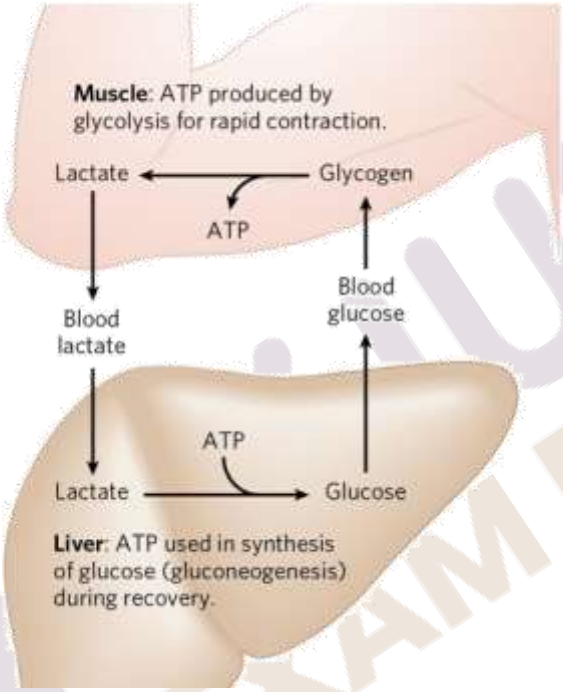
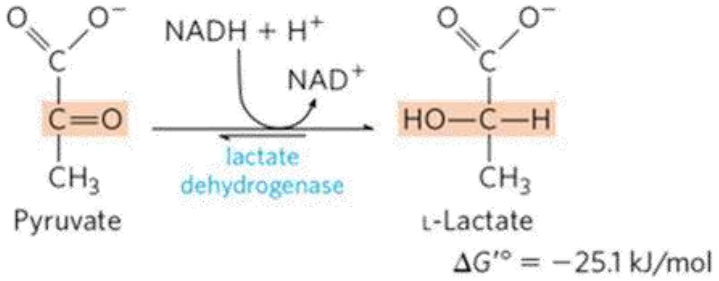


Figure 2. Cori cycle: metabolic cooperation between liver and the skeletal muscles. This overall pathway: Glucose to Lactate to Glucose, constitute Cori Cycle.

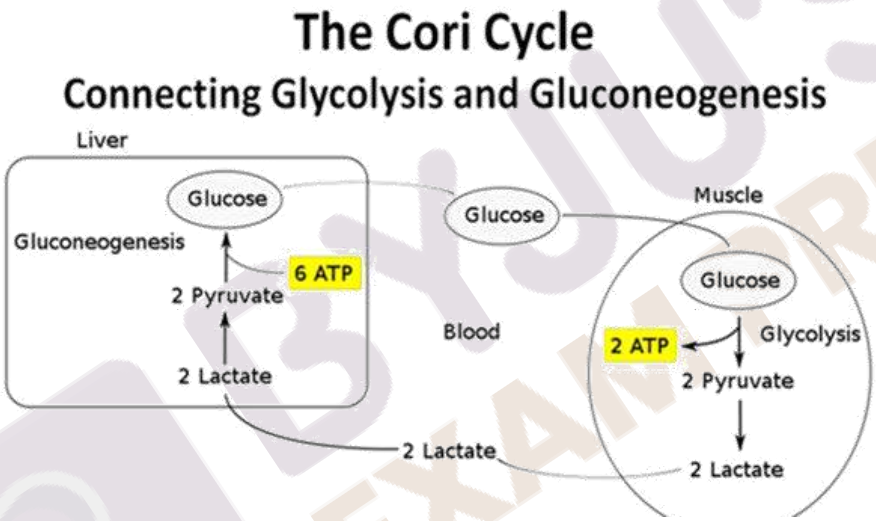
Conversion of glucose to lactate comprises two oxidation-reduction steps, but there is no net change in the oxidation state of carbon; the H: C ratio in glucose ($C_6H_{12}O_6$) and lactic acid ($C_3H_6O_3$) remains the same. However, some of the energy of glucose molecules is extracted by its conversion to lactate, giving a net yield of two ATP molecules for each glucose molecule consumed. This process, in general terms, is called fermentation, which extracts energy as ATP without consuming oxygen or changing the concentrations of NADH or NAD+.

Under hypoxic (low-oxygen) conditions such as solid skeletal muscles, solid tumours, submerged plant tissues, or lactic acid bacteria, NADH (generated by glycolysis) cannot be reoxidized by O_2. Since NAD^+ regeneration fails, the cell lacks an electron acceptor for oxidation of glyceraldehyde 3- phosphate, which stops the energy-yielding reactions of glycolysis. To avoid this, NAD+ must hence be regenerated in some other ways. Taking a cue from the earliest cells that lived in an anaerobic environment, strategies are developed to derive energy from fuel molecules under the anaerobic environment. Most present-day organisms have retained the capability to constantly regenerate NAD+ during anaerobic glycolysis by transferring NADH electrons to form a reduced end product like lactate or ethanol.

Some tissues and cells like erythrocytes have no mitochondria and therefore cannot oxidize pyruvate to CO_2, even under aerobic conditions. They produce lactate from glucose. In this pathway, pyruvate reduction to lactate is catalyzed by lactate dehydrogenase, forming the L isomer of lactate (at pH 7):



The reaction equilibrium strongly favours lactate formation, quite evident from the significant negative standard of Gibb's free energy change. The figure given below depicts the cyclic relationship between glycolysis in muscles and gluconeogenesis in the liver:



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