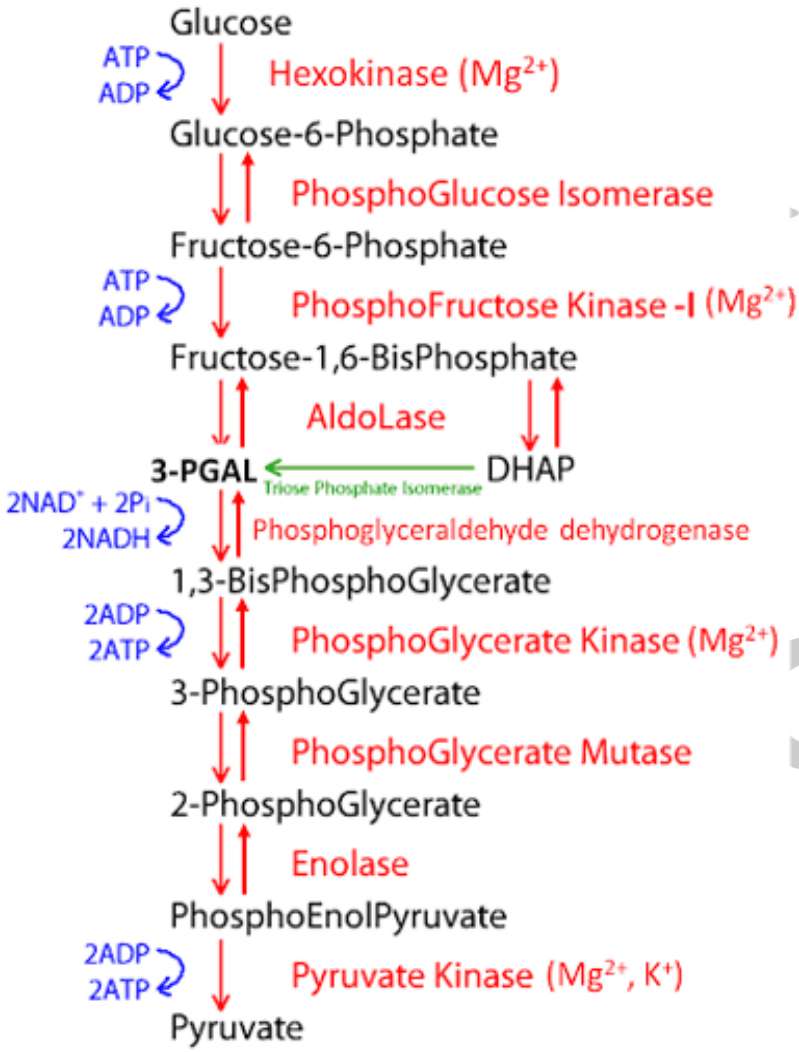
Metabolic Pathways:

Catabolism/breakdown of Glucose:

Glycolysis: Glycolysis occurs in the cytoplasm of all the living cells. It is also called the EMP (Embden, Mayerhoff, Parnas) pathway. Glycolysis is a common step between aerobic and anaerobic respiration. It is a 10 step (reactions) pathway in which glucose is partially oxidized into 2 molecules of pyruvic acid. The ten reactions could be divided into two phases: **(i) Activation phase** and **(ii) energy synthesis phase**, each phase has five reactions.



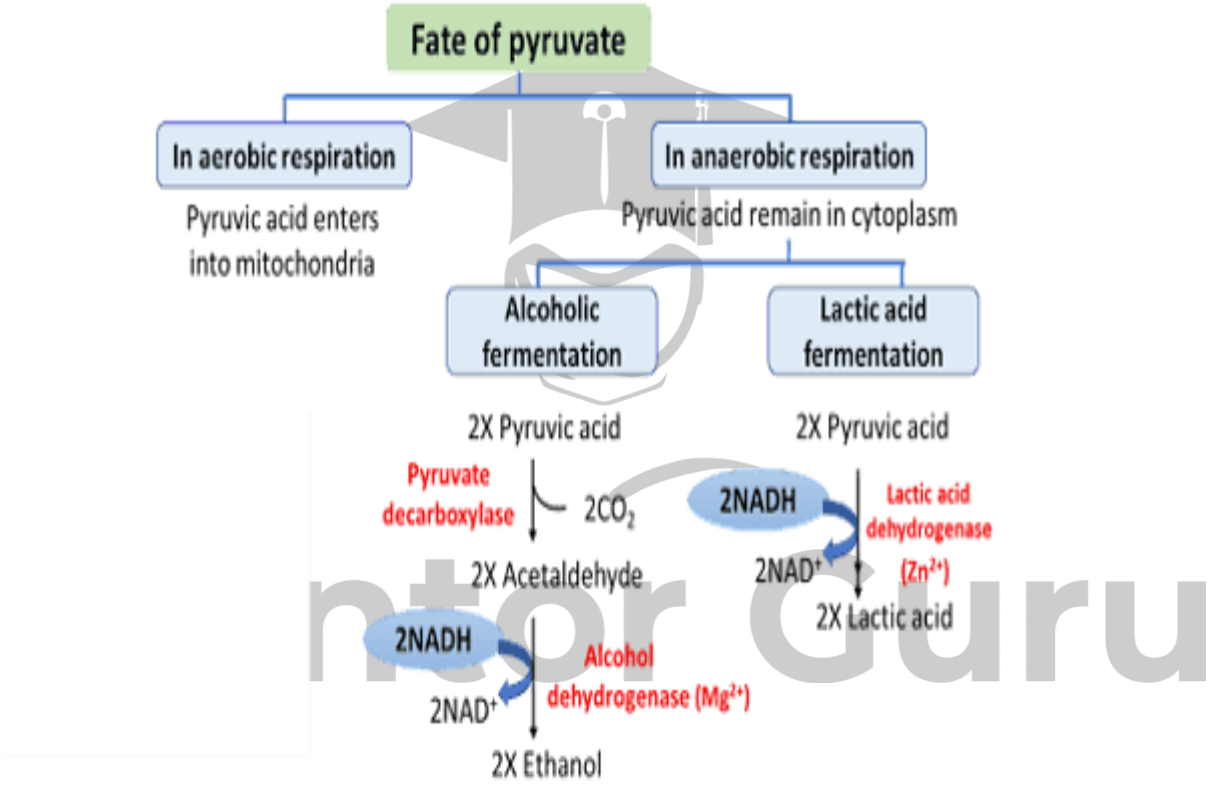
Few Important Points About Glycolysis:

- Steps catalysed by **hexokinase, phosphofructokinase-I (PFK-I)** and **pyruvate kinase** (1st, 3rd and 10th steps) are three irreversible steps of glycolysis, rest all are reversible.
- Step catalysed by PFK-I is the slowest and rate-limiting step of glycolysis.

- Fructose-2,6-bisphosphate and AMP molecules are allosteric activators of PFK-I enzyme, while ATP is the allosteric inhibitor of PFK-I enzyme.
- In last five reactions, a total of **4 ATP** molecules (**in two different steps**) are synthesised via **substrate level phosphorylation i.e., ATP synthesis directly without any electron transport process**.
- Net gain from glycolysis is 2 ATP, 2 NADH and 2 pyruvate molecules.

Fate of Pyruvate Molecules Synthesized in Glycolysis:

Pyruvate Molecules Synthesized in Glycolysis, Can Either Enter in **mitochondria for aerobic respiration** or those pyruvate molecules can **remain in cytoplasm to undergo fermentation or anaerobic respiration**.



Few Important Points About Anaerobic Respiration or Fermentation:

- Alcoholic Fermentation Usually Takes Place in **yeast (*Saccharomyces cerevisiae*)** while lactic acid fermentation takes place in **muscle cells** & ***Lactobacillus* bacteria**.
- In fermentation, pyruvate molecules act as external electron acceptor molecules i.ePyruvate molecules undergo reduction.
- In the end of fermentation, along with the end products of incomplete oxidation (like **CO2 and ethanol in alcoholic fermentation** & **lactate in**

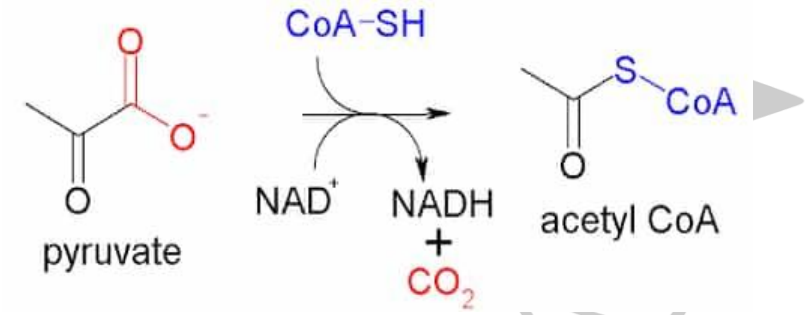
lactic acid fermentation) 2 ATP as the net gain are obtained, which were synthesized in the glycolysis.

Aerobic respiration of pyruvate molecules: After entering the mitochondria, pyruvate molecules undergo two steps for complete (aerobic) oxidation.

- Link reaction
- Krebs cycle (TCA or citric acid cycle)

Link Reaction:

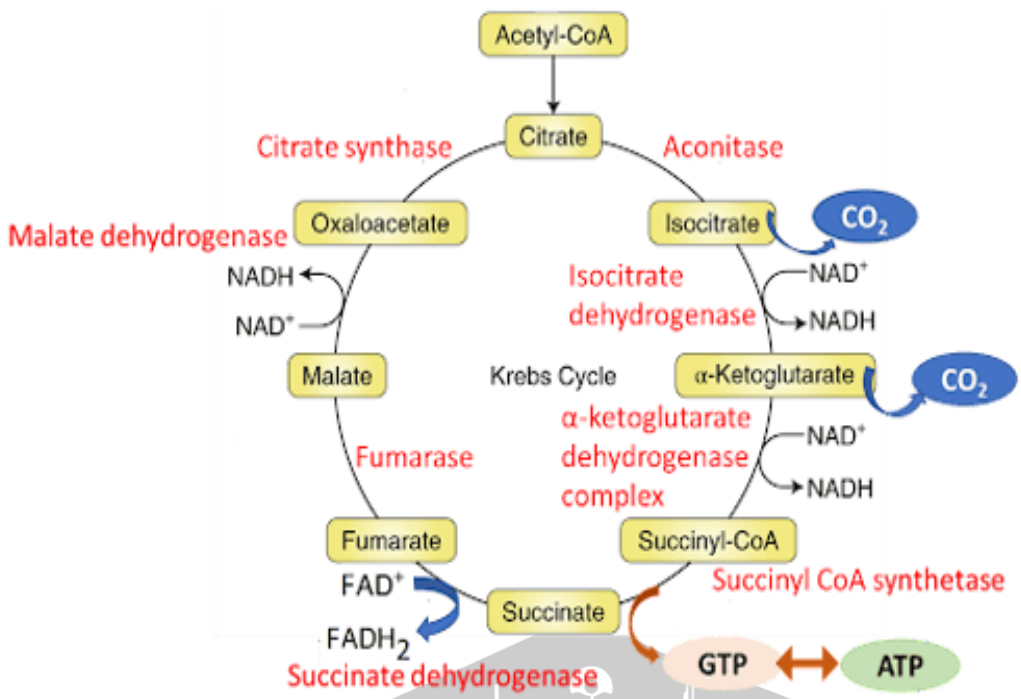
It is the **oxidative-decarboxylation** reaction, occurring in mitochondria, where each pyruvate molecule produces a **CO2** and an **acetyl CoA** molecule.



- Link reaction is the link between glycolysis and Krabs cycle in aerobic respiration.
- In Link reaction, each pyruvate molecule produces one NADH molecule as the by-product of the redox reaction.
- Link reaction is catalysed by pyruvate dehydrogenase complex enzyme, which is a combination of three enzymes: **Dihydrolipoyl dehydrogenase** (NAD+ as the cofactor), **Dihydrolipoyl transacetylase** (lipoic acid and coenzyme A cofactors), **pyruvate dehydrogenase** (Mg2+ and thiamine pyrophosphate; TPP as cofactor).

Krebs cycle:

It is an enzymatic cyclic process, operating in the matrix of mitochondria. Krebs cycle was discovered by Hans Krebs as the major step in the aerobic respiration of glucose or other respiratory substrates (energy providing biomolecule).

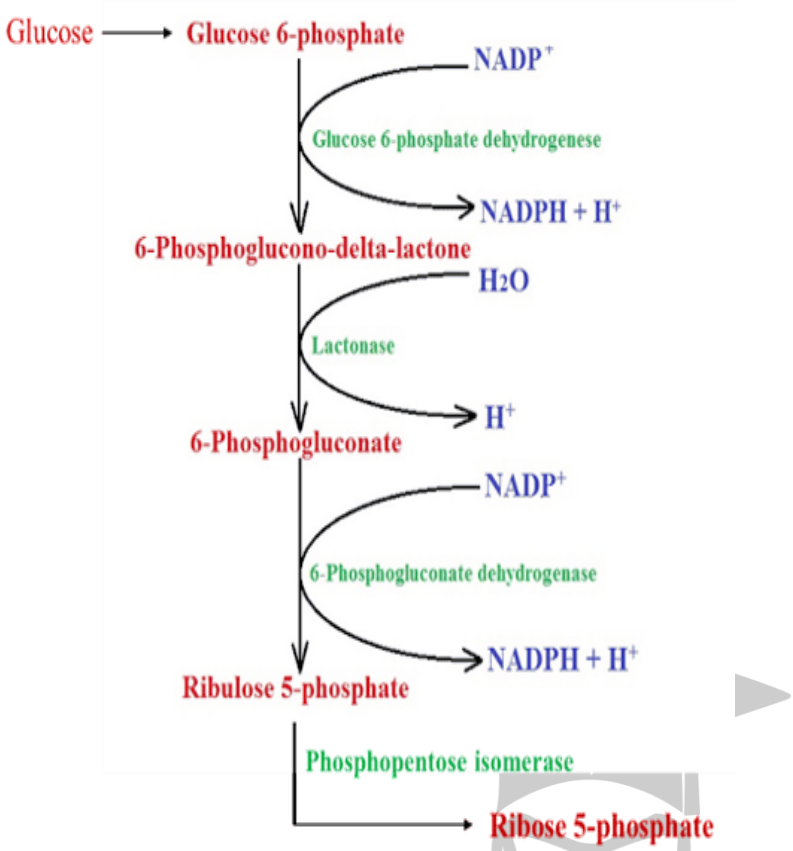


Few Important Points About Krebs Cycle:

- Krebs cycle is also called **TCA cycle** or **citric acid cycle**, because **citrate**, the first product of this cycle is a **tricarboxylic acid** (TCA; having three COOH groups).
- By the end of a Krebs cycle, from one pyruvate molecule, there is formation **3 NADH, 1 FADH2** and **1 GTP** molecule via substrate level phosphorylation. So, a total of **6 NADH, 2 FADH2** and **2 GTP** molecules will be produced in the TCA cycle from a single glucose molecule (i.e., from 2 pyruvate molecules).
- All the **NADH molecules (produced in glycolysis, link reaction and TCA cycle**) and **FADH2 molecules (produced in TCA cycle)**, enter into mitochondrial electron transport system **(ETS)** to produce ATP molecules. **Each NADH** produces **3 ATPs** via ETS, while each **FADH2** produces **2 ATPs** via ETS.

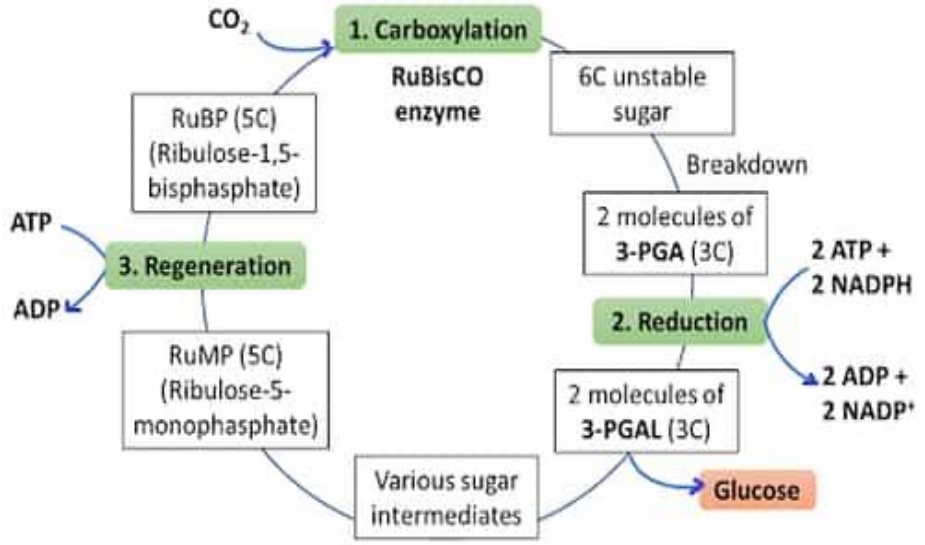
Pentose phosphate pathway (PPP) or Hexose Monophosphate (HMP) Shunt:

HMP shunt is a metabolic pathway parallel to glycolysis, which operates in the cytoplasm. It generates **12 NADPH** and **ribose 5-phosphate**, a precursor for the synthesis of nucleotides. While the pentose phosphate pathway does involve oxidation of glucose, its primary role is anabolic rather than catabolic. During catabolism of glucose HMP shunt operates usually when mitochondria are engaged or temporarily inhibited.



Calvin Cycle or C_3 cycle:

The Calvin cycle is the **light-independent** or **biosynthetic phase** of photosynthesis. This enzymatic cycle operates in the **stroma** of chloroplast, in which **CO2 molecules** via different intermediates eventually get **assimilated into glucose**. **Melvin Calvin** discovered C3 cycle in unicellular green alga, ***Chlorella*** using **14C** radioactive isotope.



Few Important Points About Calvin Cycle:

- Calvin Cycle Has **three important steps**: **(i) Carboxylation** of RUBP (a 5C-ketose sugar), **(ii) Reduction** of 3-Phosphoglyceric acid (3-PGA) and **(iii) Regeneration** of RUBP.
- The **first stable intermediate** of the Calvin cycle is a **3-carbon PGA** molecule; hence the cycle is also known as **C3 cycle**.
- The most important step of the Calvin cycle is carboxylation of RUBP, catalysed by **RuBisCO (RUBP carboxylase-oxygenase)** enzyme. RuBisCO is the most abundant protein/enzyme present on this planet.

Gluconeogenesis:

All glucogenic amino acids (except leucine and lysine) can form into TCA cycle intermediates or pyruvate. Pyruvate then via oxaloacetate, forms PEP (phosphoenol pyruvate), which in a series of reactions that are opposite to glycolysis in terms of direction, eventually can synthesize glucose molecules. This pathway is called gluconeogenesis. Gluconeogenesis can operate in the cytoplasm of liver or kidney cells.