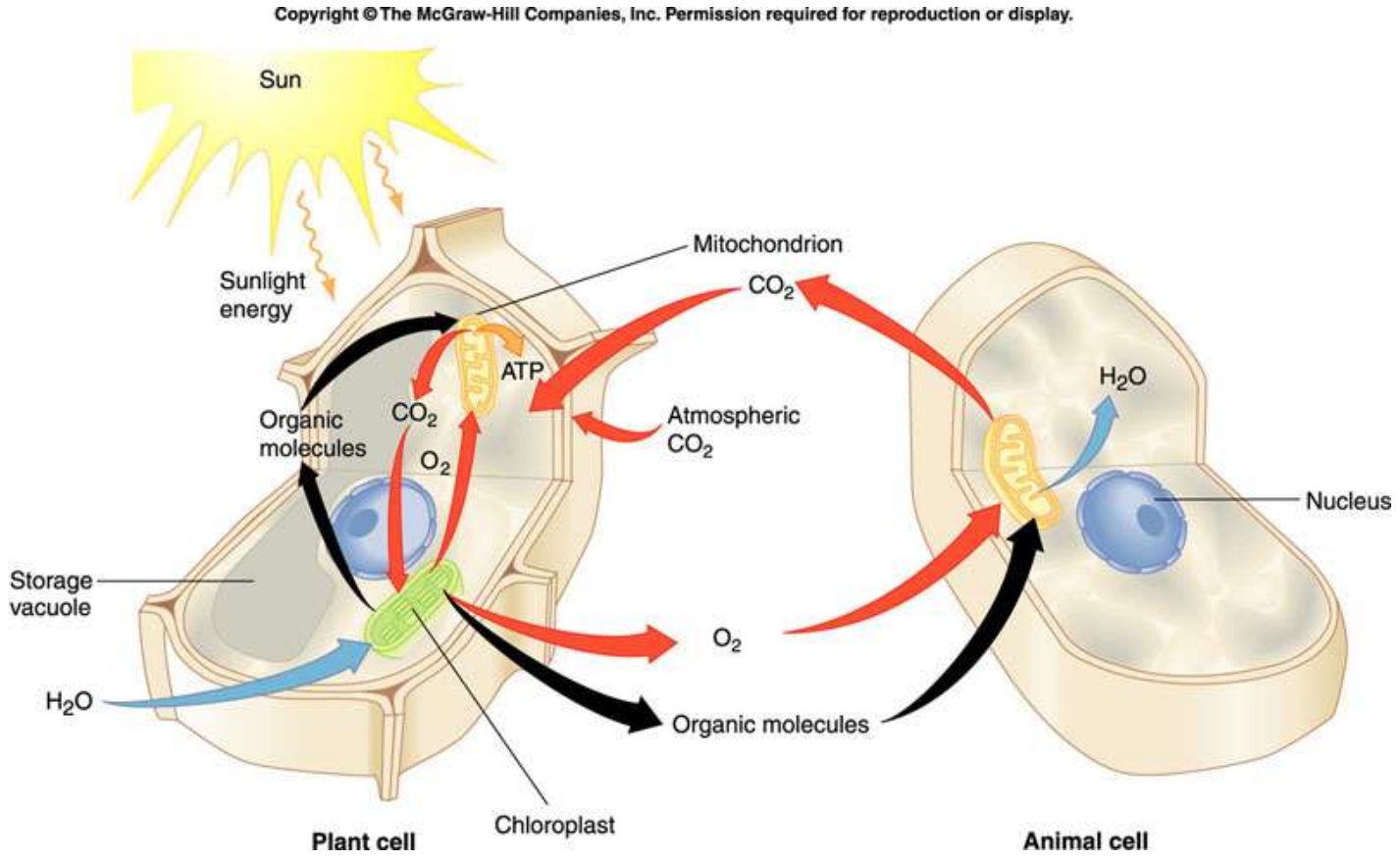
Energy Transformation



Photosynthesis and respiration are complementary.

- **Photosynthesis: Converts light energy into chemical energy (glucose) and produces oxygen.**
- **Respiration**: Breaks down glucose to release chemical energy (ATP) and produces carbon dioxide.
- Together, these processes form a **biochemical cycle** that sustains life by recycling carbon and energy between organisms and the environment.
-

Energy Classification of Organisms

Autotrophs:

- **- Energy Source: Sunlight**
- **- Process: Photosynthesis**
- **- Converts light energy to organic molecules (sugar)**
- **- Uses these organic molecules to produce ATP through Cellular Respiration**
- **Heterotrophs:**
- **- Energy Source:Organic molecules from Autotrophs**
- **- Process: Cellular Respiration**
- **- Uses the energy from organic molecules to generate ATP**
- Commonality:
- -All organisms rely on Cellular Respiration to generate ATP from organic molecules.

Aerobic Respiration: A Series of Enzyme-Controlled Reactions

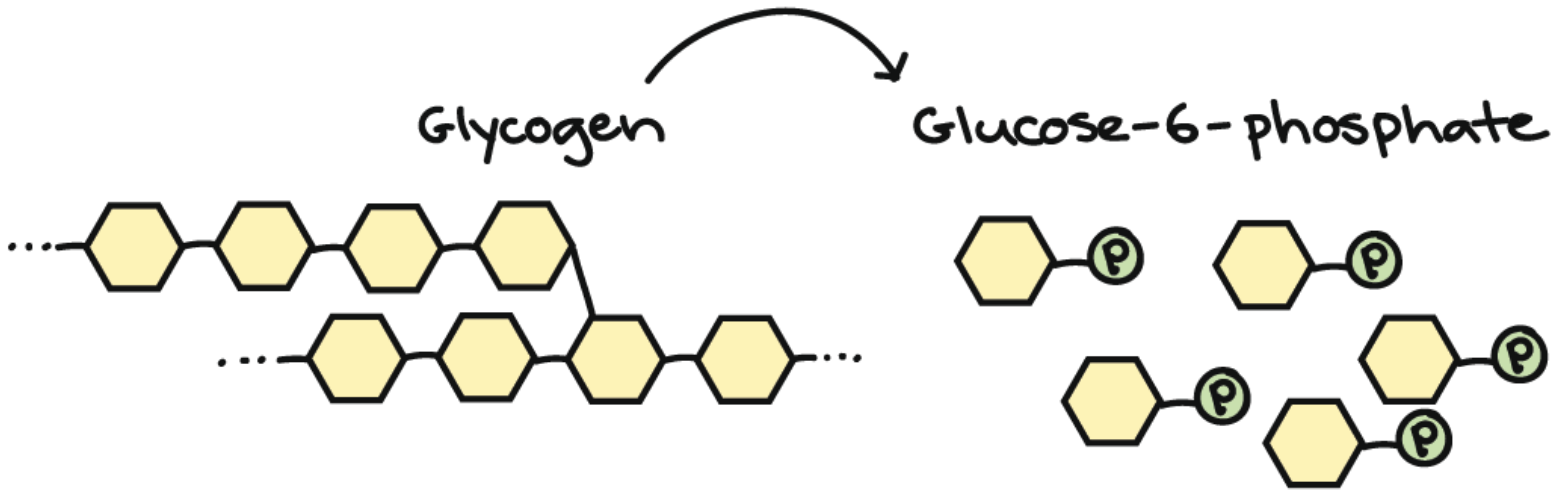
- **Overview**
  - Oxygen is used to oxidize glucose.
  - Glucose is oxidized to form carbon dioxide.
  - Released energy is used to form ATP.
  - Oxygen is reduced to form water.

Drowning AND Death

- In drowning, a person is submerged in water and **cannot breathe**. This cuts off the supply of oxygen to the body.
- When there is no oxygen, the cells in the body **cannot perform aerobic respiration**. This means the ETC in mitochondria shuts down because there is no **final electron acceptor**.
- Without oxygen, the cell **cannot produce sufficient ATP** via the ETC.
- While cells can switch to **anaerobic respiration** (glycolysis) for a short time, this produces much less ATP and leads to the accumulation of **lactic acid**, which can cause **acidosis**.
- the brain relies heavily on oxygen for energy production. Without oxygen, brain cells begin to die in just a few minutes, leading to brain damage and eventual death.

How carbohydrates enter the pathway

- **Carbohydrates in Cellular Respiration:**
- **Glycolysis**
  - **Entry Point for Carbohydrates:**
    - **Most carbohydrates enter cellular respiration through glycolysis.**
    - **Glycolysis breaks down glucose into pyruvate.**
- **Glycogen Metabolism**
  - **Glycogen Storage:**
    - **Glycogen is a glucose polymer stored in liver and muscle cells.**
  - **Glycogen Breakdown:**
    - **When blood sugar levels drop, glycogen is broken down into glucose-6-phosphate.**
    - **Glucose-6-phosphate easily enters glycolysis for energy production.**

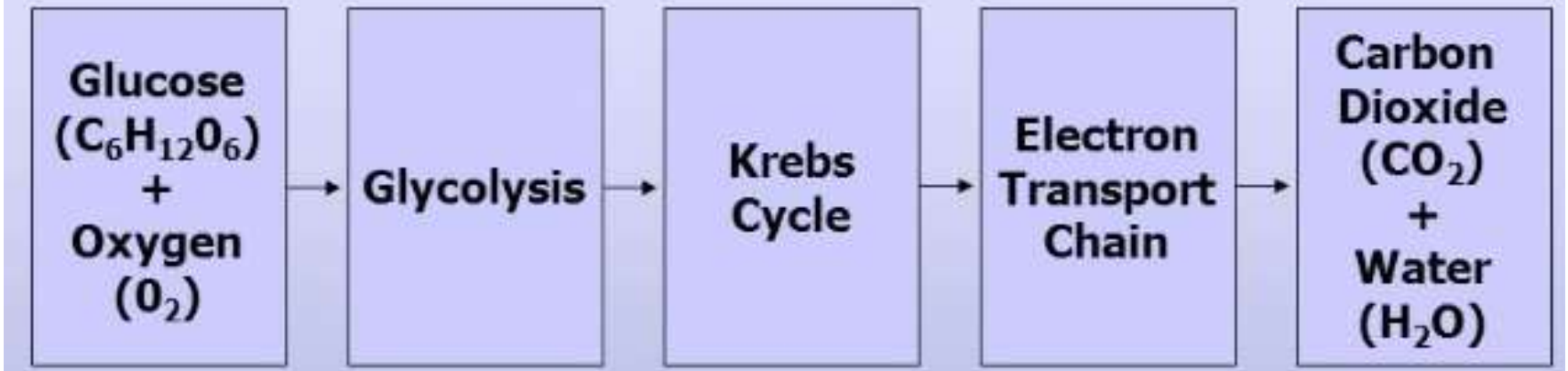


- Involves 3 stages:
- Glycolysis: 1 Glucose +2ATP +2NAD+ ⟶ 2 Pyruvic Acid +4ATP +2NADH(2 high energy electrons)
- Citric Acid Cycle: Pyruvic Acid ⟶ CO_2 +ATP+NADH+$FADH_2$

- Electron Transport Chain: High energy electrons are used to pump H+ and supply them to

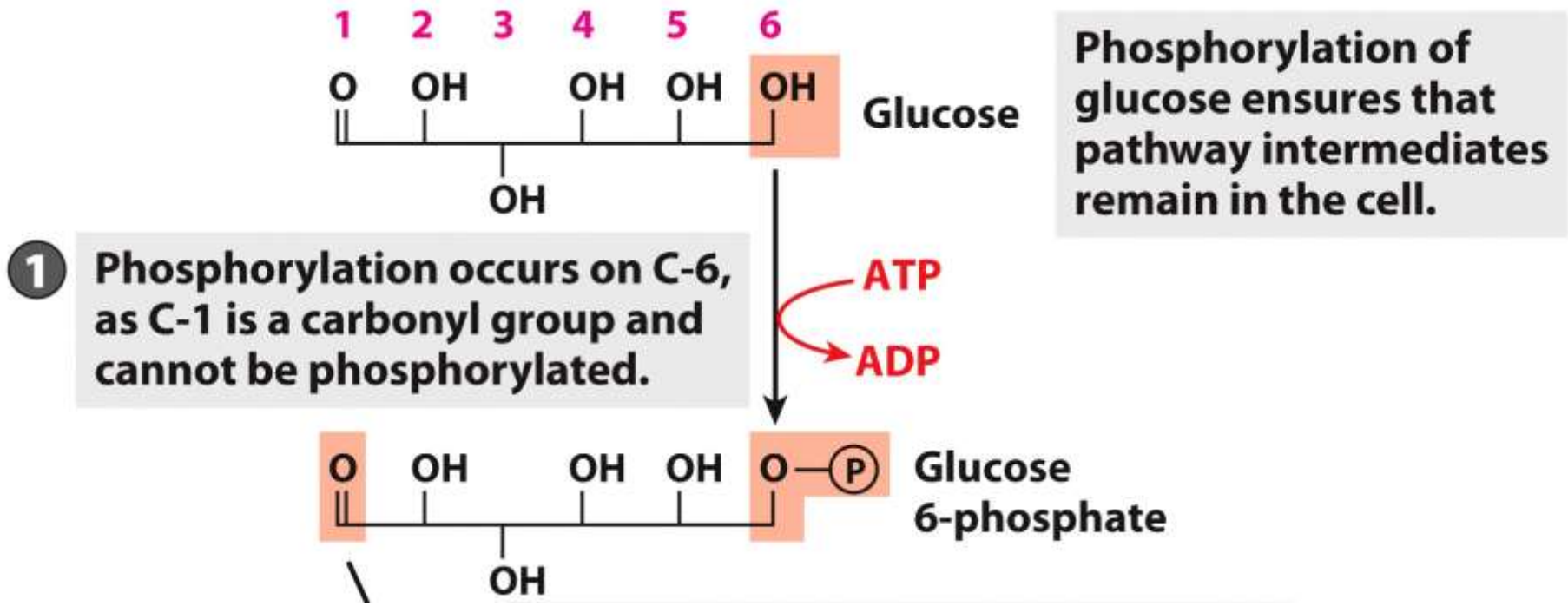
$$O_2 \longrightarrow H_2O$$

Cellular Respiration Flowchart



GLYCOLYSIS

Reaction 1: *phosphorylation*



Reaction 1: *phosphorylation- WHY??????????????*

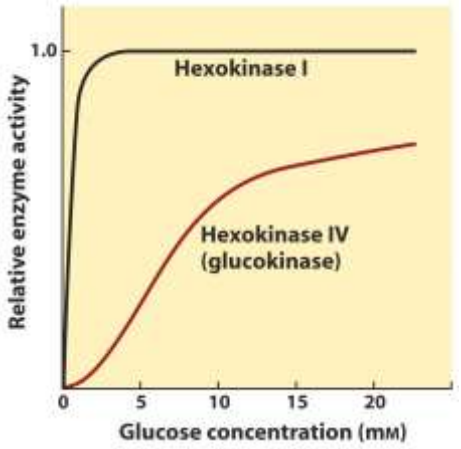
1. Trapping Glucose Inside the Cell:

•When glucose enters the cell through membrane channels (such as GLUT transporters), it is quickly phosphorylated by **hexokinase** or **glucokinase** to form **glucose-6-phosphate (G6P)**.

✦Tissue-specific isozymes.

Hexokinase vs. Glucokinase

- **Hexokinase:**
  - **Function:** Catalyzes the conversion of glucose to glucose-6-phosphate.
  - **Location:** Found in most tissues (excluding liver and beta cells of the pancreas).
  - **Substrate Specificity:** Acts on hexoses such as glucose, fructose, and galactose.
  - **Mechanism:** Adds a phosphate group to the substrate, utilizing ATP for energy.
- **Glucokinase:**
  - **Function:** Isozyme of hexokinase, specifically found in the liver and beta cells of the pancreas.
  - **Role:** Works effectively under high glucose concentrations.
  - **Regulation:** Functions optimally when glucose levels are high, playing a key role in regulating blood sugar levels.
- **Key Differences:**
  - **Hexokinase:** Present in most tissues, operates efficiently even at low glucose concentrations.
  - **Glucokinase:** Specific to liver and pancreas, adapted to handle high glucose concentrations and regulate glucose uptake.



UTILITY OF GLUCOKINASE

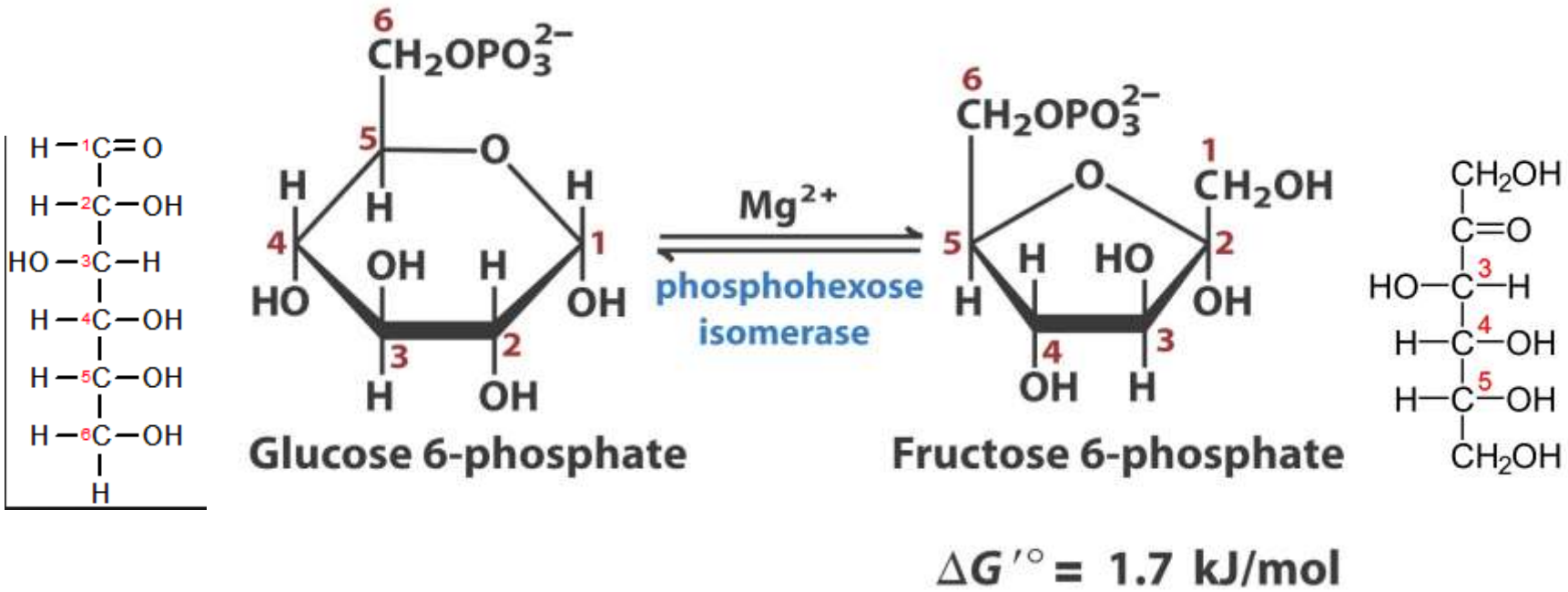
•**Glucokinase has a low affinity for glucose**, meaning it only becomes active when glucose levels are **high** (such as after a meal).

•**Prevention of Hypoglycemia**:

A scientist is studying a cell line that shows increased glycogen synthesis despite low blood glucose levels. Which of the following would most likely explain this phenomenon?

- A) Overactive glucokinase
- B) Inhibited glucose-6-phosphatase
- C) Overactive hexokinase
- D) Excessive glucose transport into the cell

Reaction 2: *isomerization*



Moves the carbonyl to C2 position; a prerequisite for further steps

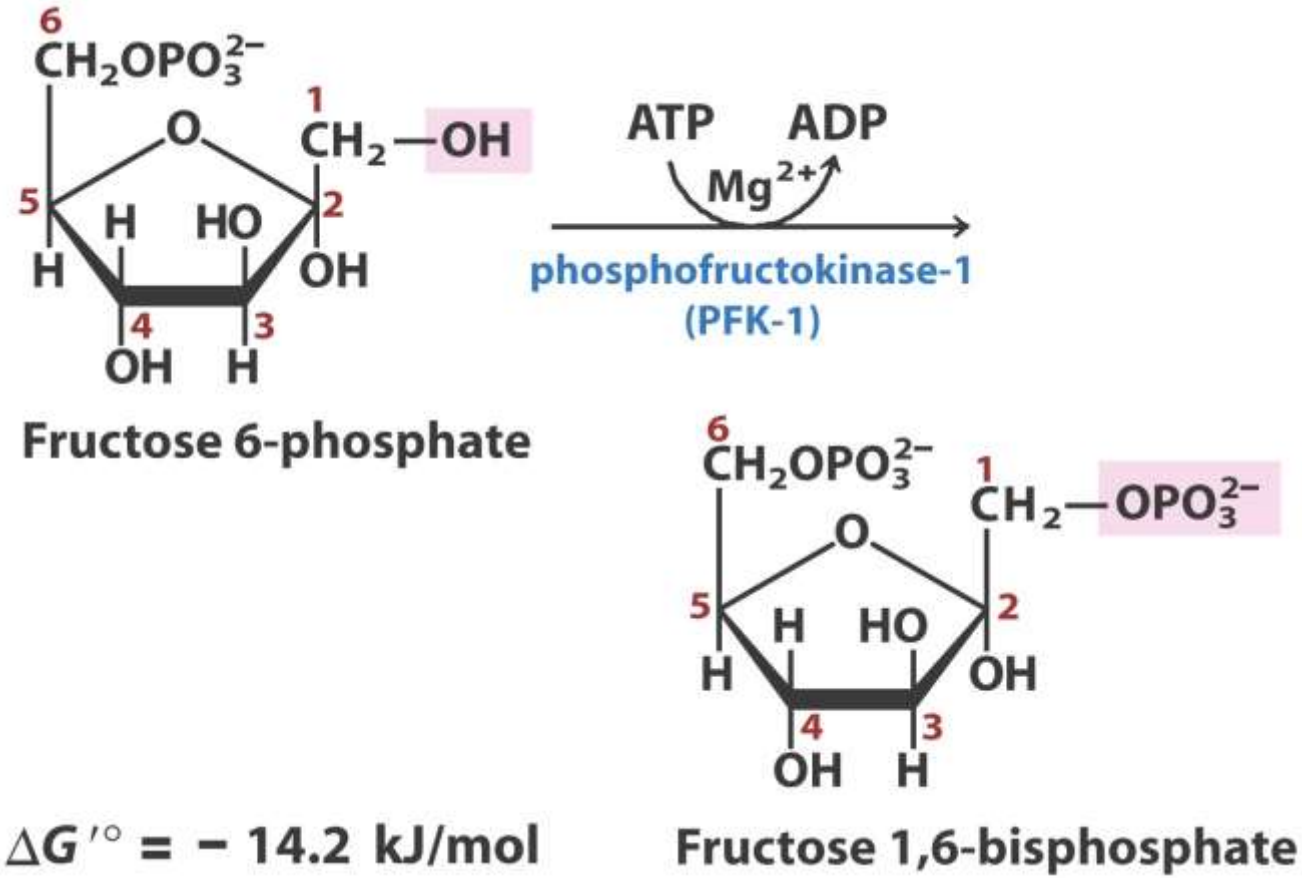
Reason for isomerization step

- The conversion of G6P to F6P facilitates the eventual splitting of the six-carbon sugar into two three-carbon molecules.
- Specifically, this rearrangement makes it easier for the subsequent steps in glycolysis to cleave the sugar symmetrically in the next reactions.

A scientist studies a mutant plant that has an altered phosphoglucose isomerase enzyme with reduced catalytic efficiency. This results in a significantly slower conversion of G6P to F6P. Which metabolic consequence is most likely to occur in this strain?

- A) Elevated levels of G6P and decreased levels of ATP
- C) Enhanced conversion of pyruvate to acetyl-CoA
- D) Increased lactate production due to elevated G6P levels

Reaction 3: *phosphorylation*



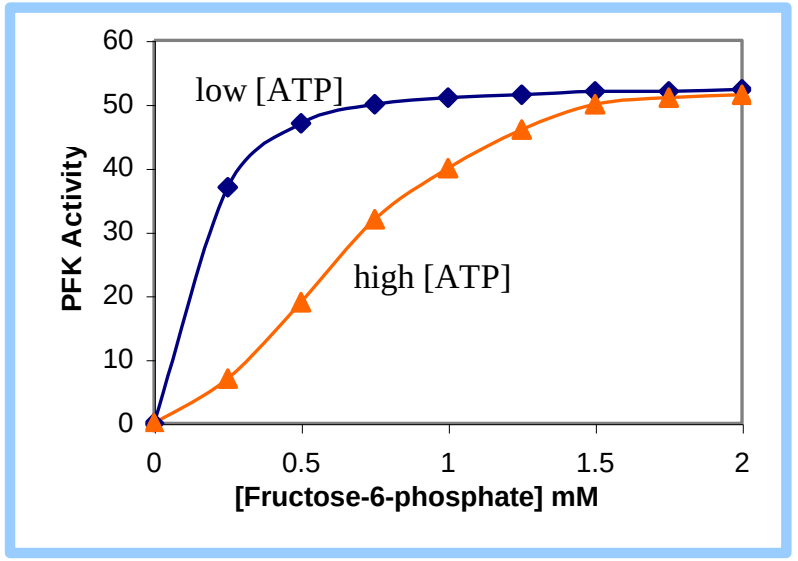
The Phosphofructokinase reaction is the **rate-limiting step** of Glycolysis.

Phosphorylation to Fructose-1,6-Bisphosphate
Purpose of Phosphorylation:

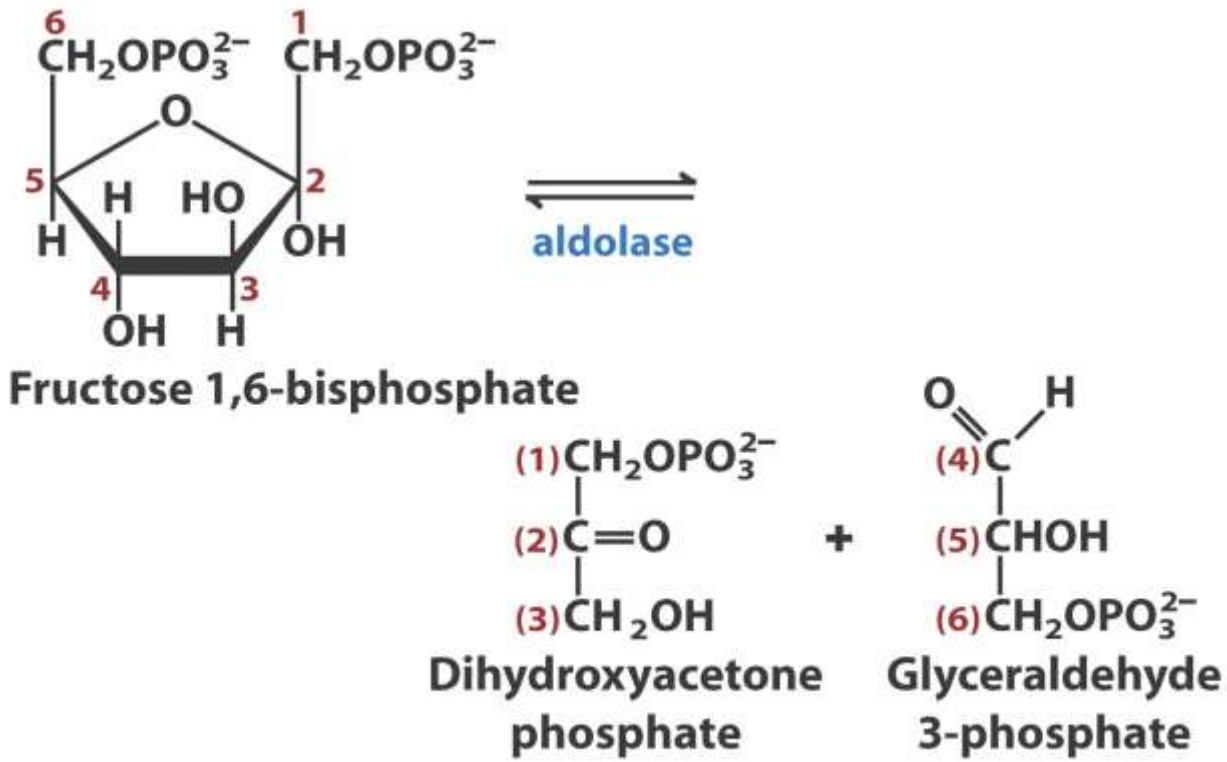
- **Energy Investment:**
  - **Phosphorylation to fructose-1,6-bisphosphate consumes 2 ATP molecules (one in each phosphorylation step).**
  - **This energy investment is essential for the subsequent steps of glycolysis.**

Regulation of Phosphofructokinase (PFK) in Glycolysis

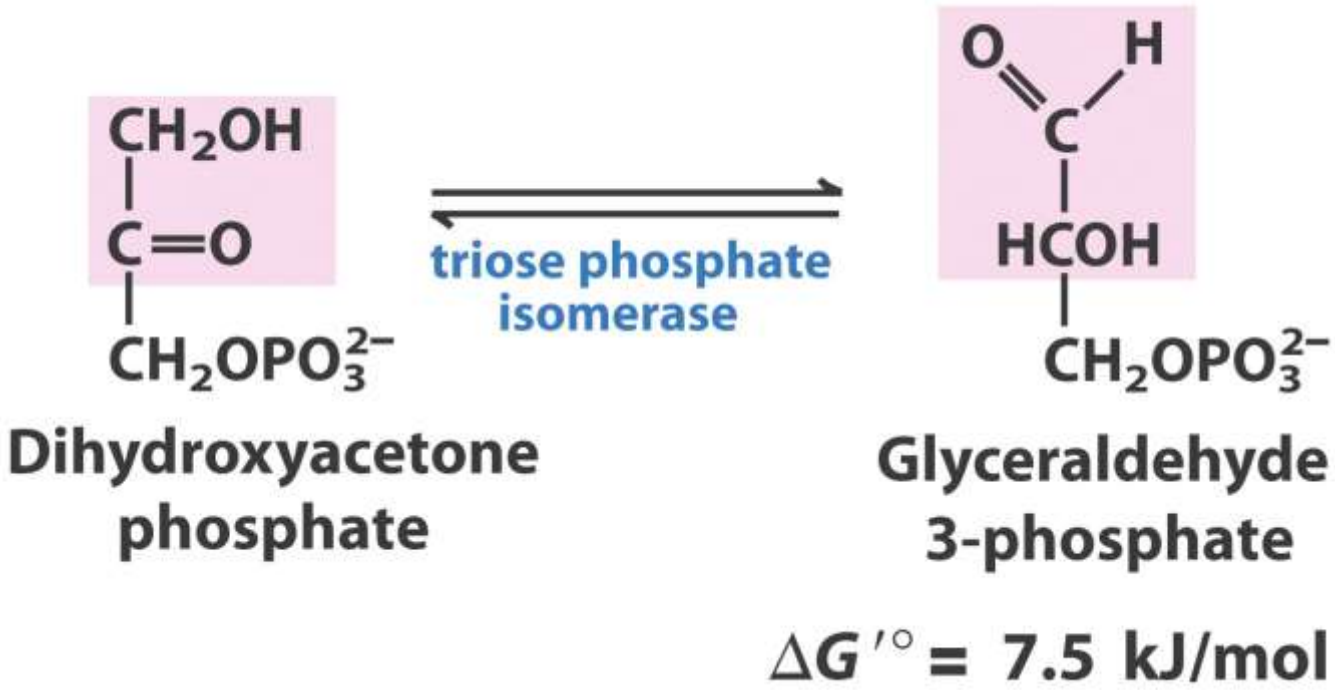
- **PFK Function:**
  - Catalyzes the conversion of fructose-6-phosphate to fructose-1,6-bisphosphate.
  - A key regulatory step in glycolysis.
- **Effect of High ATP Concentration:**
  - **Lower Affinity:** At high ATP concentrations, PFK has a reduced affinity for its substrate, fructose-6-phosphate.
  - **Inhibition:** High ATP levels inhibit PFK activity.
    - **Reason:** Prevents excessive glucose breakdown in glycolysis when ATP is already abundant.



Reaction 4: *cleavage*

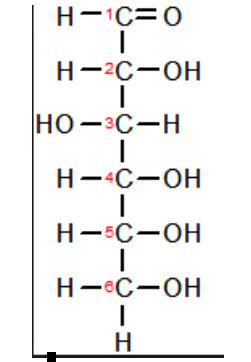


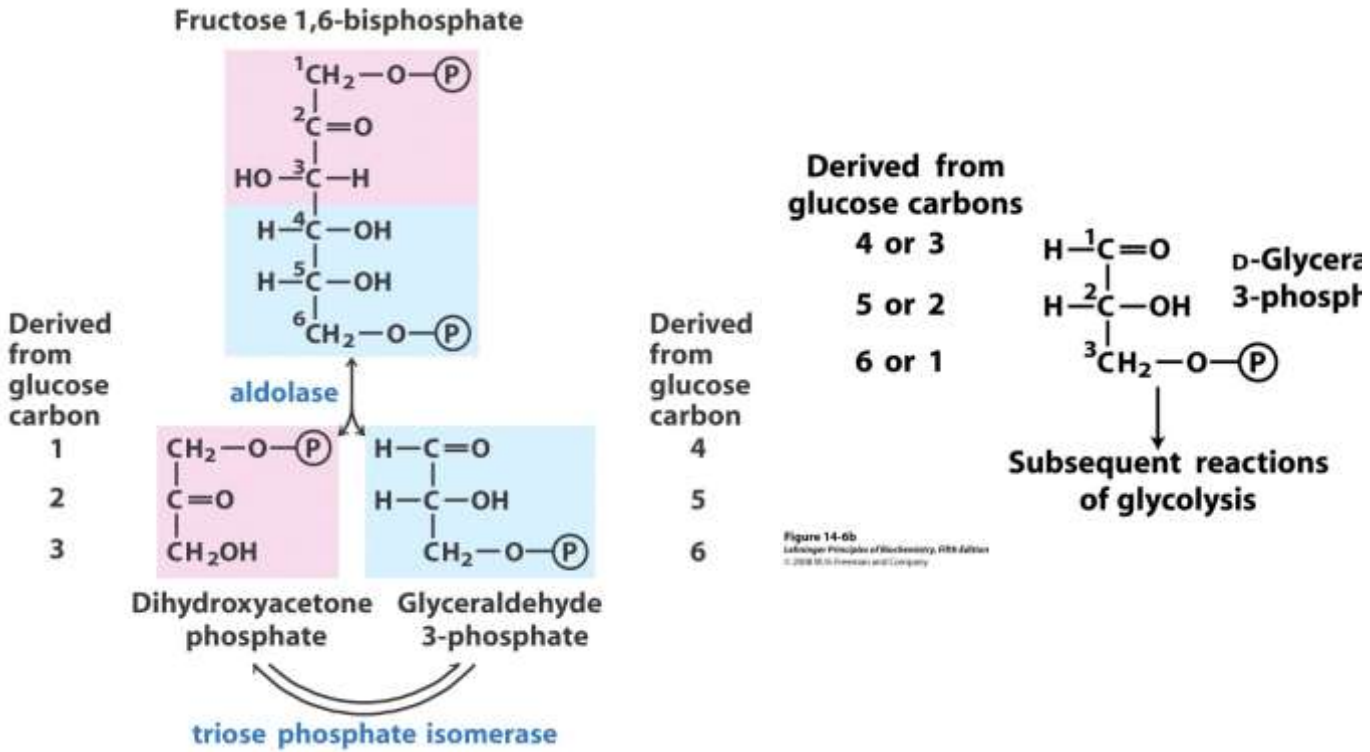
Reaction 5: *isomerization*



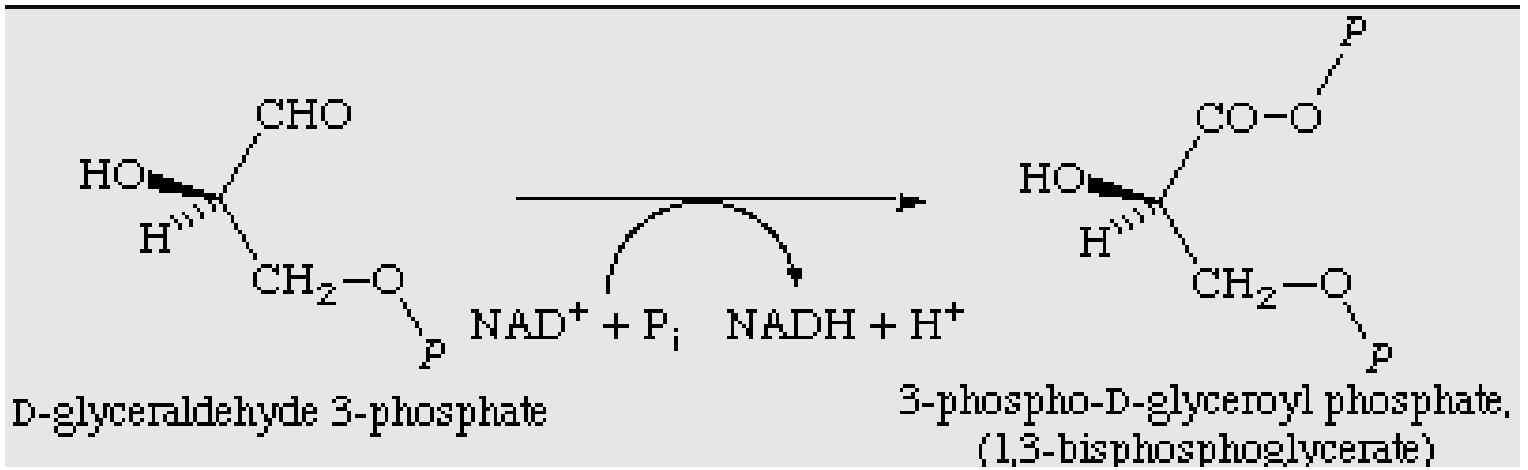
- The isomerization of DHAP to G3P is essential because it ensures that **both molecules produced from the cleavage of fructose-1,6-bisphosphate** can continue through glycolysis

Keeping Track of Carbons

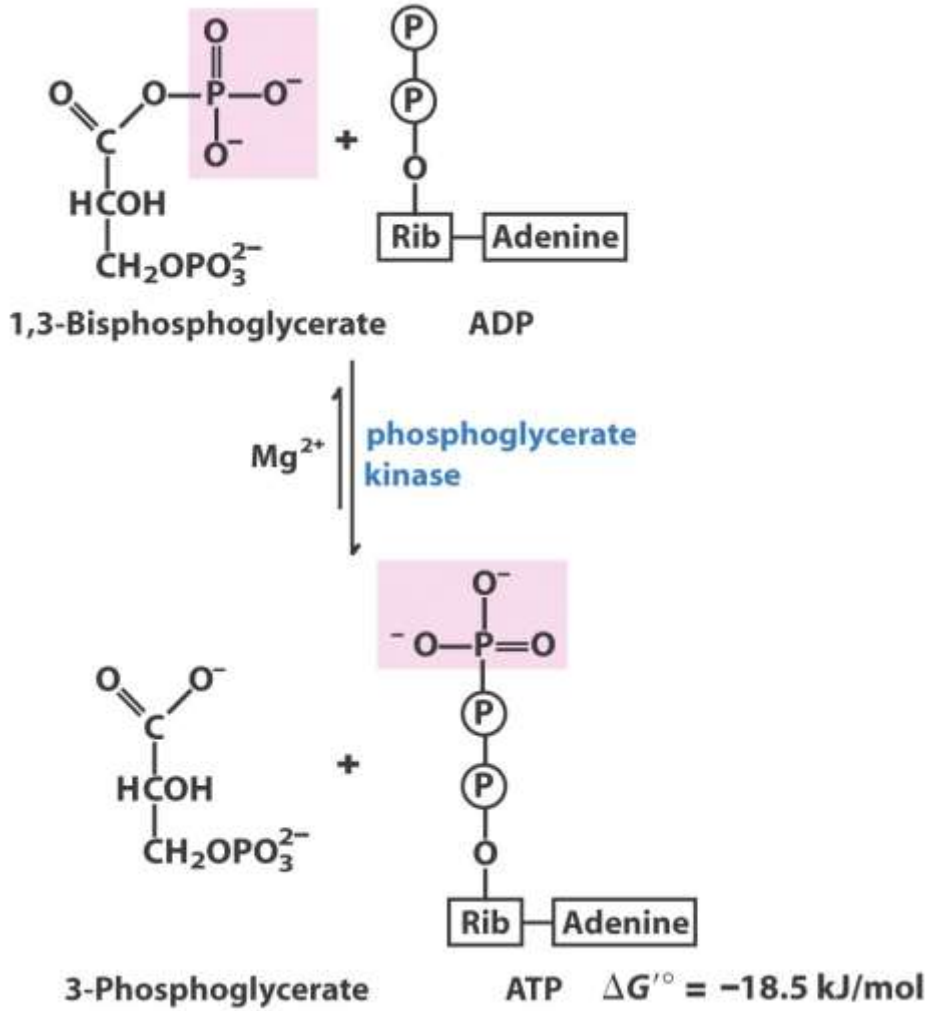




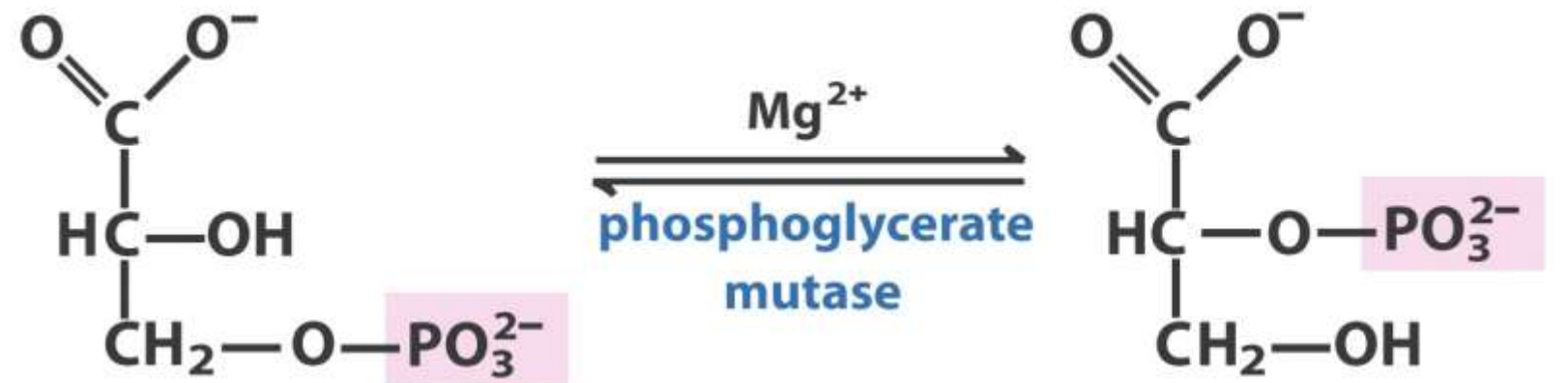
Reaction 6: *PRODUCTION OF* 1,3-bisphosphoglycerate



Reaction 7: *substrate level phosphorylation*



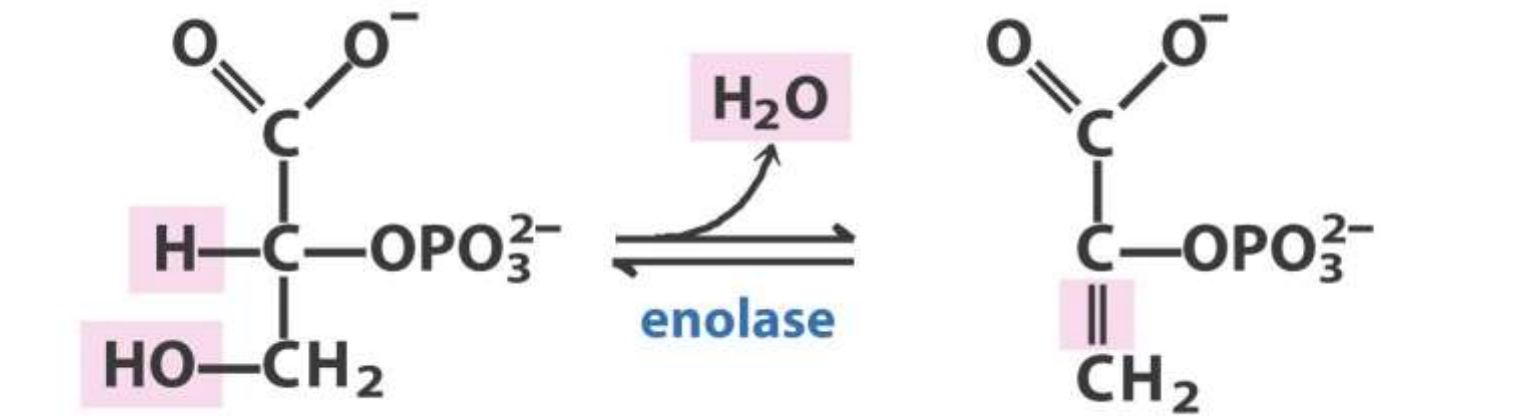
Reaction 8: *shift of phosphoryl group*



3-Phosphoglycerate **2-Phosphoglycerate**

$\Delta G'^{\circ} = 4.4$ kJ/mol

Reaction 9: *dehydration*

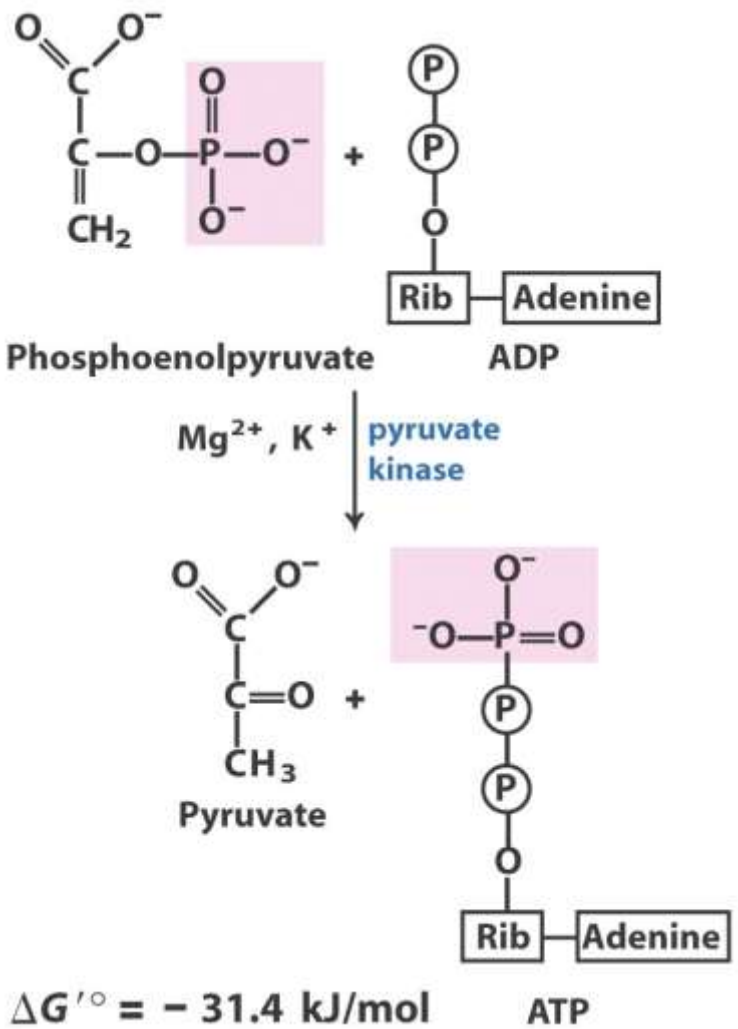


2-Phosphoglycerate

Phosphoenolpyruvate

$\Delta G'^{\circ} = 7.5$ kJ/mol

Reaction 10: *substrate level phosphorylation*

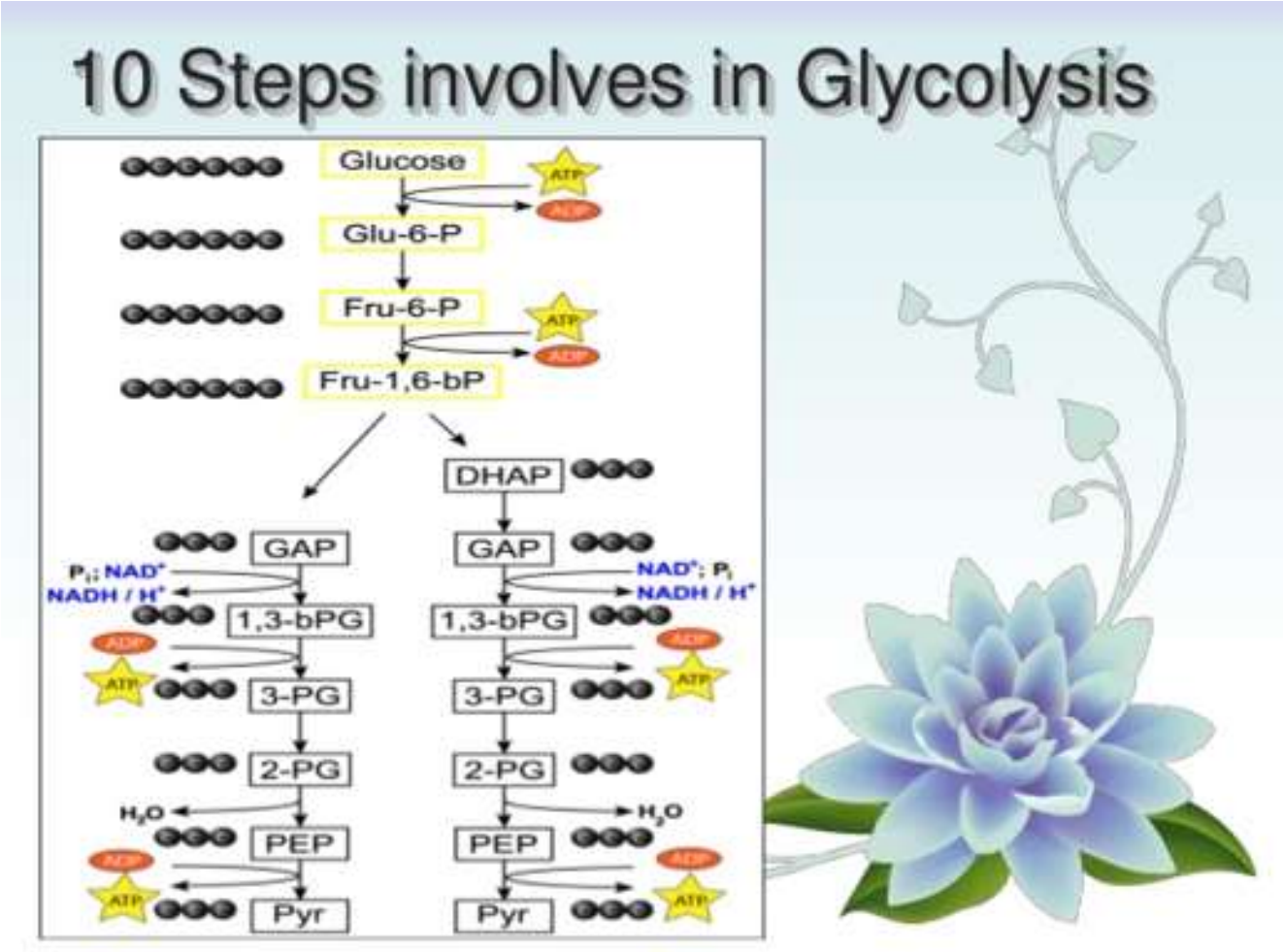


Summary

Energy investment

Cleavage

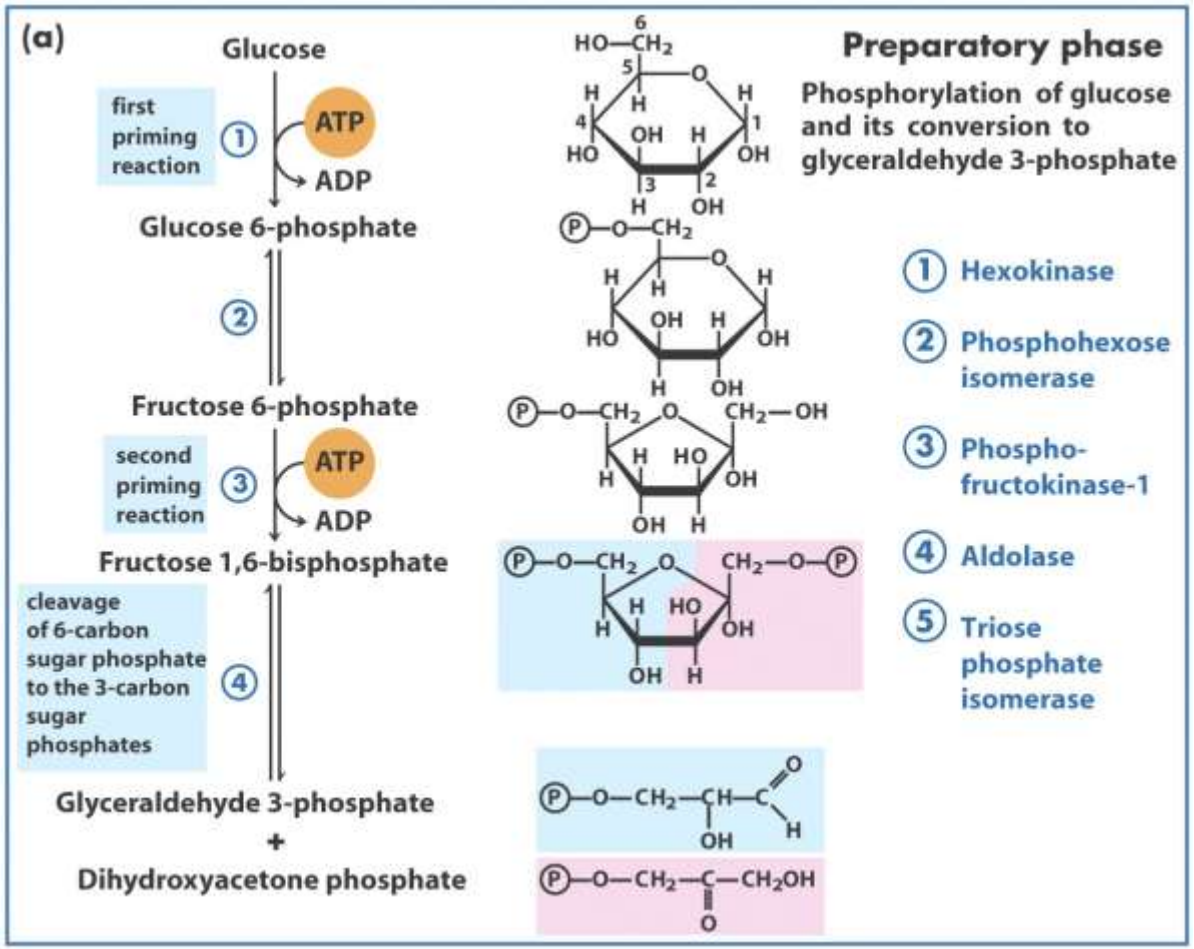
Energy Harvest



Roles of Glycolysis in Cellular Respiration

- **1. ATP Production:**
  - **Glycolysis directly generates 2 ATPs per glucose molecule.**
  - **It provides substrates for the citric acid cycle and oxidative phosphorylation.**
  - **Most ATP is produced in the citric acid cycle and oxidative phosphorylation.**
- **2. Biosynthetic Pathway Intermediates:**
  - **Glycolysis produces intermediates used in various biosynthetic pathways.**
  - **Example: Acetyl CoA, derived from glycolysis, serves as a precursor for fatty acid synthesis.**

Glycolysis (WHY ANAEROBIC)



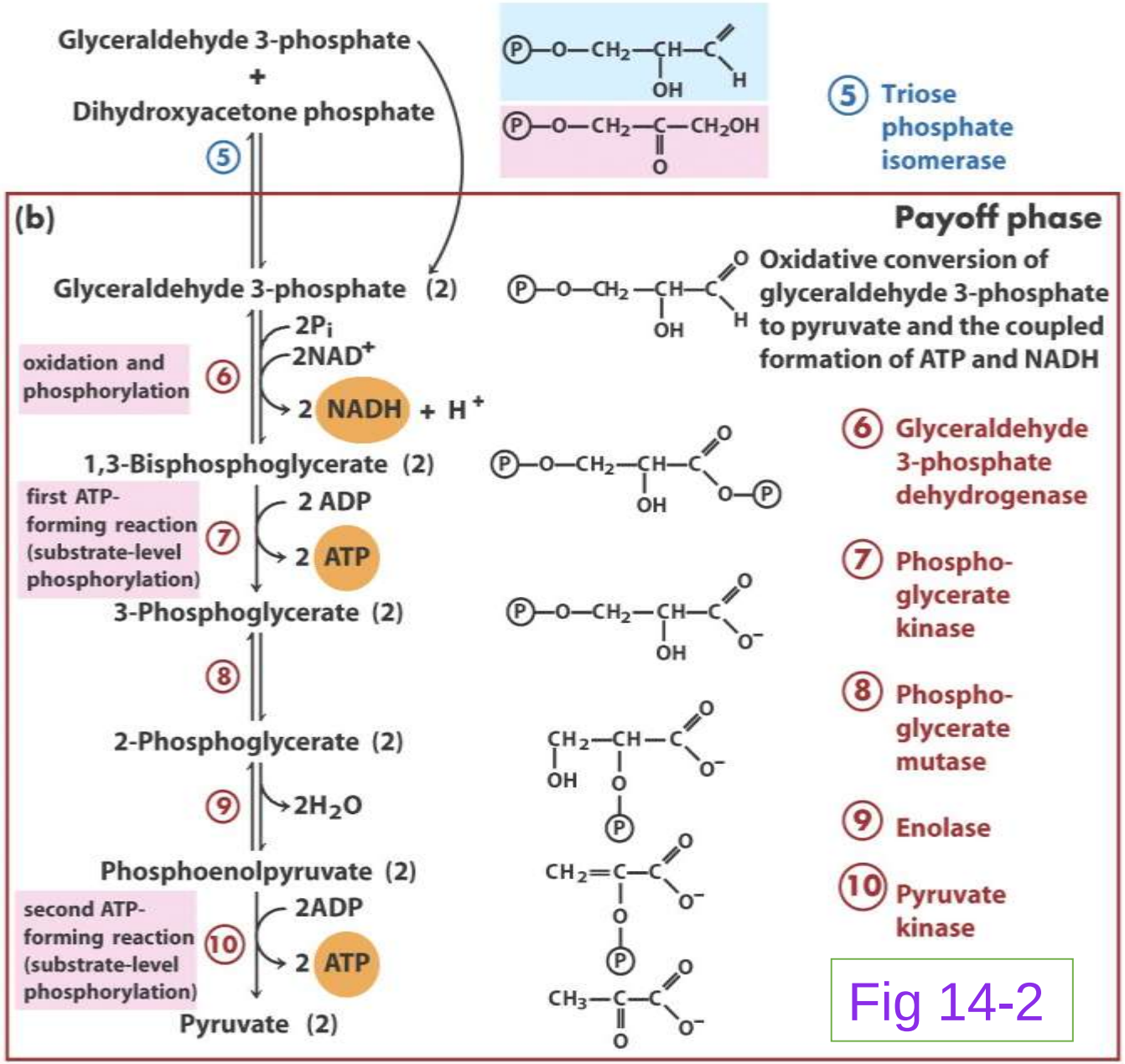
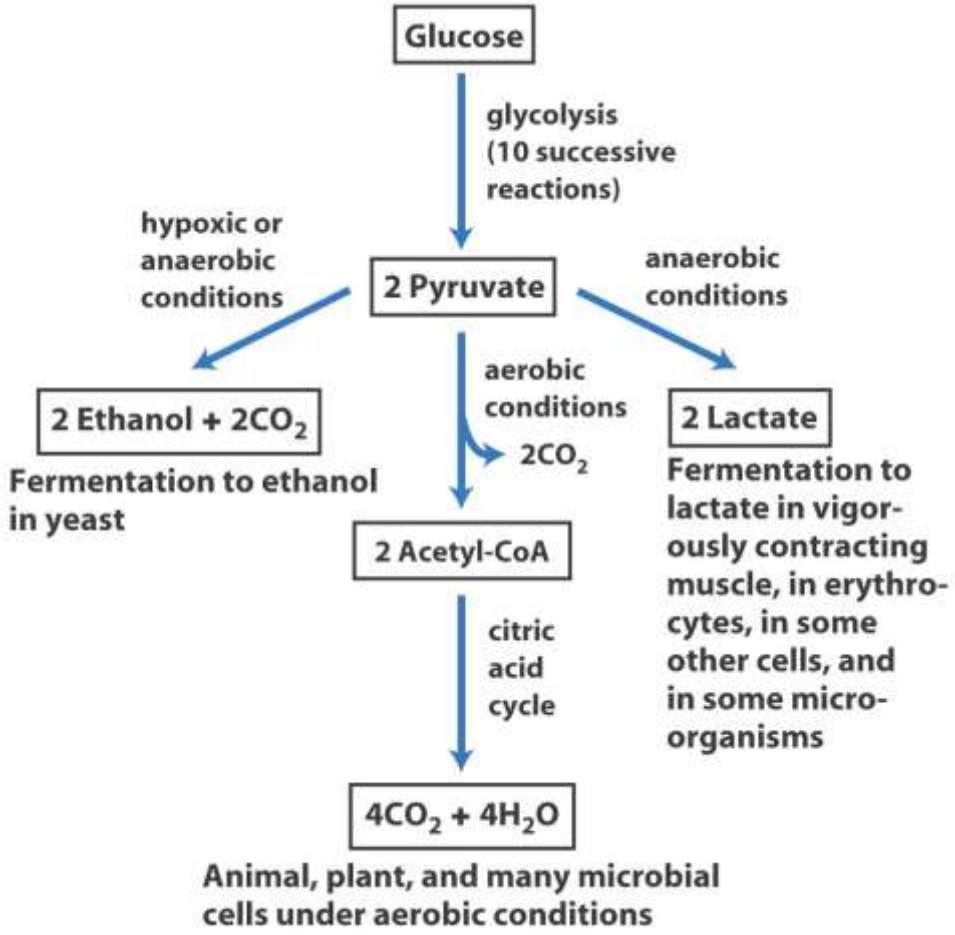

Glyceraldehyde 3-phosphate
+
Dihydroxyacetone phosphate
5
5 Triose phosphate isomerase
(b)
Payoff phase
Glyceraldehyde 3-phosphate (2)
Oxidative conversion of glyceraldehyde 3-phosphate to pyruvate and the coupled formation of ATP and NADH
oxidation and phosphorylation
6
2Pi
2NAD+
2 NADH + H+
6 Glyceraldehyde 3-phosphate dehydrogenase
1,3-Bisphosphoglycerate (2)
first ATP-forming reaction (substrate-level phosphorylation)
7
2 ADP
2 ATP
7 Phospho-glycerate kinase
3-Phosphoglycerate (2)
8
8 Phospho-glycerate mutase
2-Phosphoglycerate (2)
9
2H2O
9 Enolase
Phosphoenolpyruvate (2)
second ATP-forming reaction (substrate-level phosphorylation)
10
2ADP
2 ATP
10 Pyruvate kinase
Pyruvate (2)

Fig 14-2

Why Glycolysis is Anaerobic?

- **No Oxygen Needed**:
  - **The entire glycolytic pathway involves converting one molecule of glucose ($C_6H_{12}O_6$) into two molecules of pyruvate ($C_3H_4O_3$) without the involvement of oxygen.**
  - **The reactions in glycolysis rely on enzymes that catalyze these steps, and oxygen does not play a role at this stage.**
- **Energy Production via Substrate-Level Phosphorylation**:
  - Glycolysis produces a small amount of ATP through **substrate-level phosphorylation**, where a phosphate group is directly transferred from a high-energy substrate to ADP to form ATP.
  - This is different from oxidative phosphorylation in the electron transport chain, which requires oxygen.

Fate of the products, pyruvate and NADH



Fructose Metabolism in Different Tissues

- **Muscle and Adipose Tissue:**
  - **Enzyme:** Hexokinase
  - **Function:** Phosphorylates both glucose and fructose.
  - **Pathway:**
    - Fructose is phosphorylated to fructose-6-phosphate.
    - Enters glycolysis for energy production.
- **Liver:**
  - **Enzyme:** Glucokinase (predominant, phosphorylates only glucose)
  - **Alternative Pathway for Fructose:**
    - **Fructose 1-Phosphate Pathway:**
      - Fructose is phosphorylated to fructose-1-phosphate by fructokinase.
      - Pathway: fructose 1-phosphate pathway yields the glyceraldehyde 3-phosphate
      - **Result:** Glyceraldehyde-3-phosphate enters glycolysis or gluconeogenesis.

- **Muscle/Adipose Tissue:** Utilizes hexokinase for direct entry into glycolysis.
- **Liver:** Uses a different pathway for fructose metabolism due to the presence of glucokinase.

- Depending on the oxidation state of the cell:
  - **Aerobic** – converted to acetyl-CoA via TCA cycle
  - **Anaerobic** – converted to lactate (lactate dehydrogenase reaction)
- **Pyruvate also is converted to :**
  - Alanine
  - oxaloacetate
  - Glucose [Gluco-neogenesis]
  - to alcohol (yeasts)

If 8 glucose molecules enter glycolysis, the net products will be ____ pyruvate molecules and ____ ATP molecules.

16 ... 16

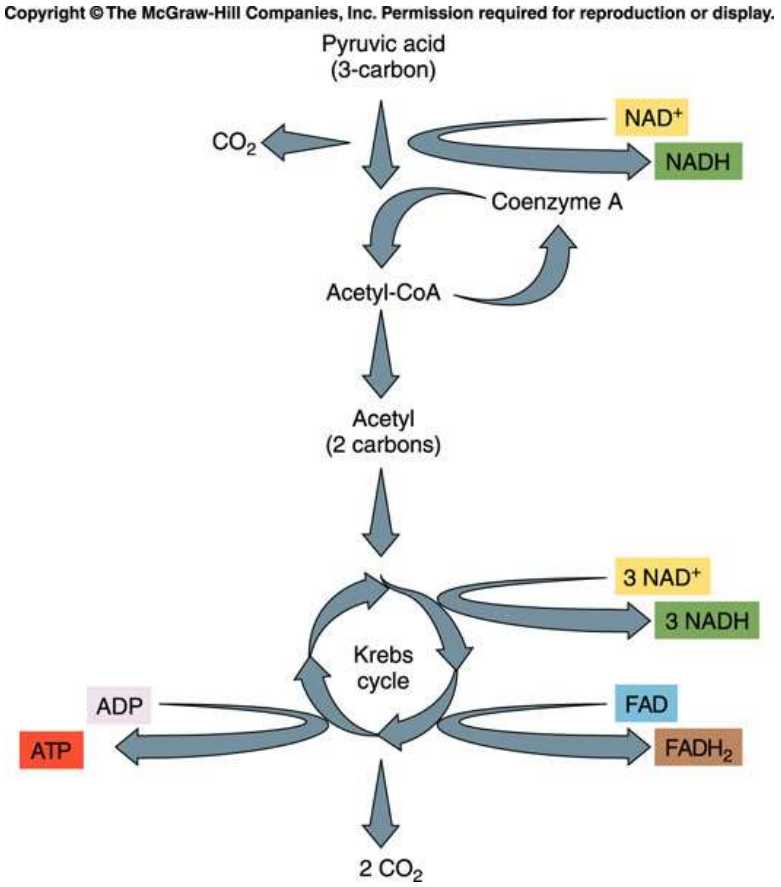
TCA or Tricarboxylic Acid Cycle

[also known Kreb's or Citric Acid cycle]

- **Definition:**
  - TCA cycle is defined as the metabolic pathway in which Acetyl-coA A is oxidized to carbon dioxide and water and leads to formation of ATP, NADH and $FADH_2$.
  - TCA cycle is a common pathway for oxidation of all nutrients (carbohydrate, lipids and proteins).
- **Location :**
  - The cycle operates in mitochondrial matrix in close proximity to electron transport chain which is present in the inner mitochondrial membrane.

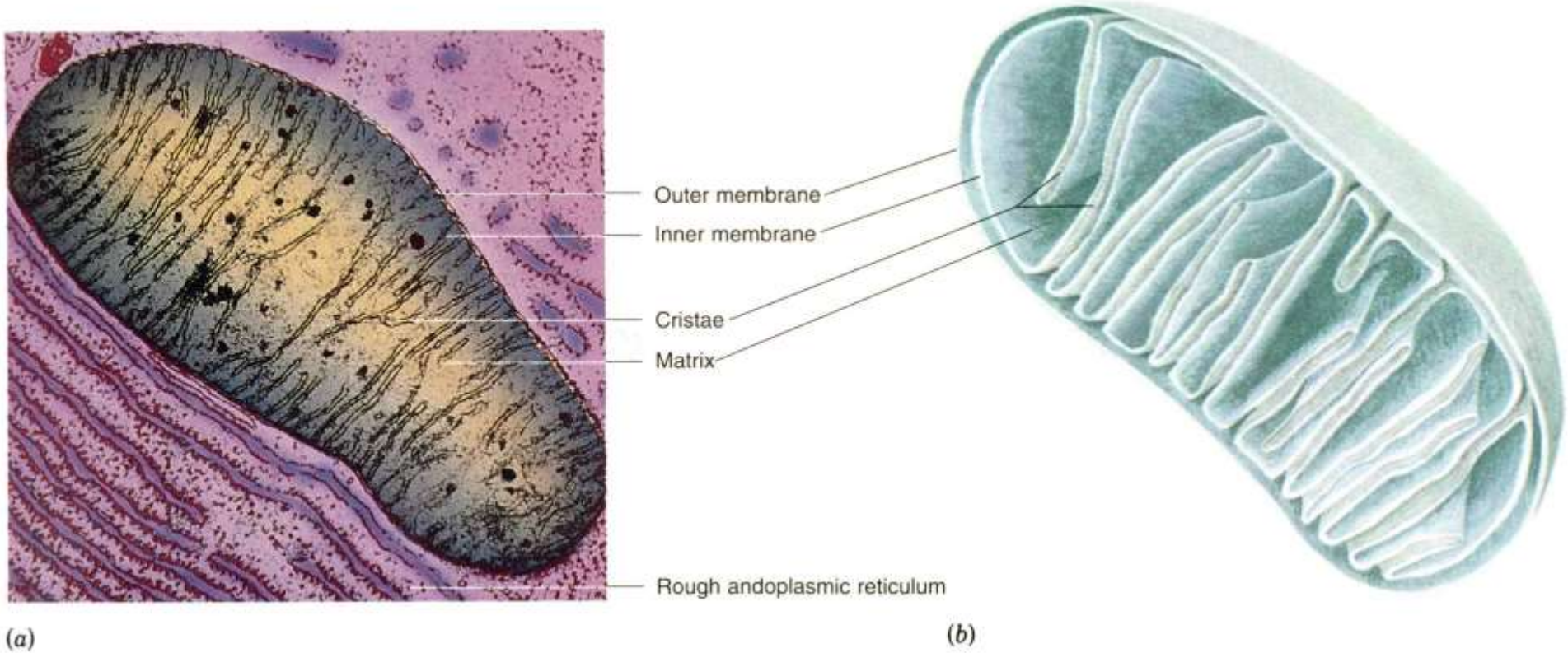
Kreb's Cycle

- The breakdown of pyruvic acid
  - Released as carbon dioxide
- Enough energy is released as one pyruvic acid molecule is metabolized to
  - Make 1 ATP
  - Reduce 4 NAD+ to form 4 NADH
  - Reduce 1 FAD to form 1 $FADH_2$.



The citric acid cycle enzymes are found in the matrix of the mitochondria

Substrates have to flow across the outer and inner parts of the mitochondria



Oxidative decarboxylation of pyruvate

- The **oxidative decarboxylation of pyruvate** is a key metabolic reaction that occurs in the mitochondria during cellular respiration.
- It links **glycolysis** (which takes place in the cytoplasm) with the **Krebs cycle** (also called the citric acid cycle), which occurs in the mitochondrial matrix.
- This reaction transforms pyruvate, the end product of glycolysis, into **acetyl-CoA**, which enters the Krebs cycle for further energy extraction.

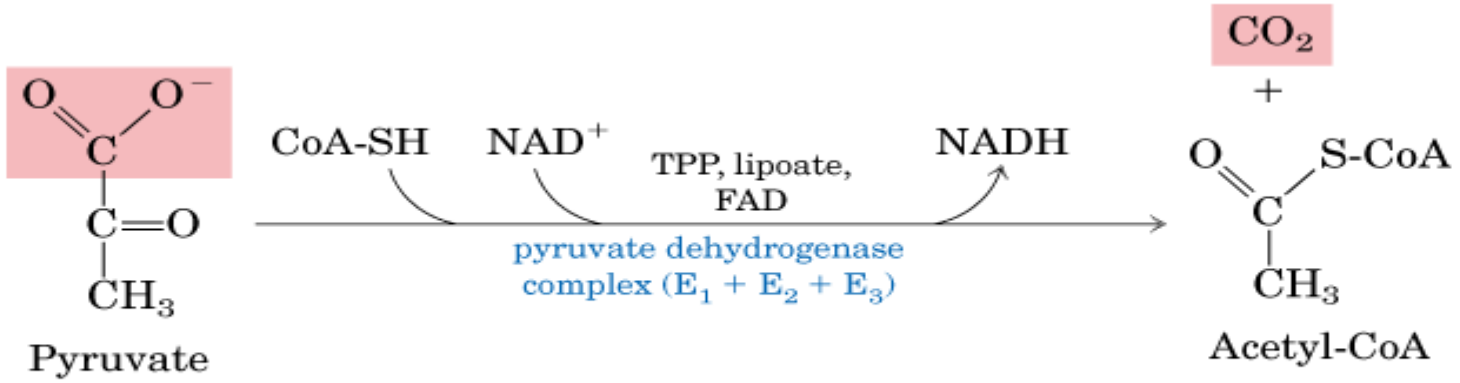
Pyruvate dehydrogenase converts pyruvate to acetyl-CoA and CO_2

CoA acts as a carrier of acetyl groups

Oxidative decarboxylation

Enzyme Complex: This reaction is catalyzed by the **pyruvate dehydrogenase complex (PDC)**, a large multienzyme complex consisting of three core enzymes and several cofactors and coenzymes.

- Pyruvate ⟶ Acetic Acid +CO2
- Acetic Acid +CoA +NAD^+ ⟶ Acetyl Coa +NADH
- Enzyme: **Pyruvate dehydrogenase**



$\Delta G'^{\circ} = -33.4$ kJ/mol

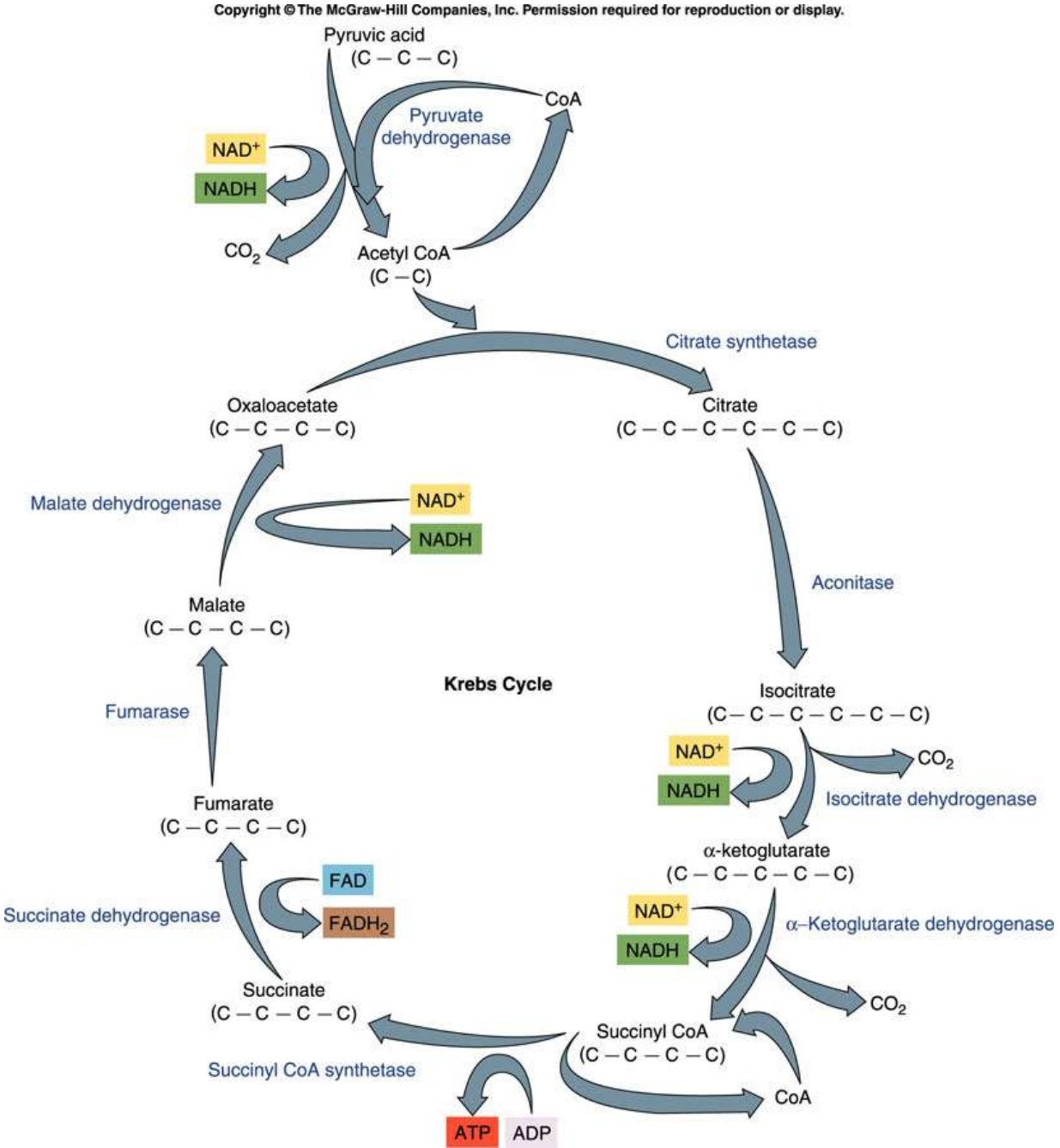
The enzyme requires five coenzymes and five reactions

Pyruvate + CoA + NAD^+ ⟶ acetyl-CoA + CO_2 + NADH

Pyruvate dehydrogenase is a multi-enzyme complex containing three enzymes associated together non-covalently and five coenzymes

Since the reaction involves both an oxidation and a loss of CO2, the process is called **oxidative decarboxylation.**

The Details of the Kreb's Cycle



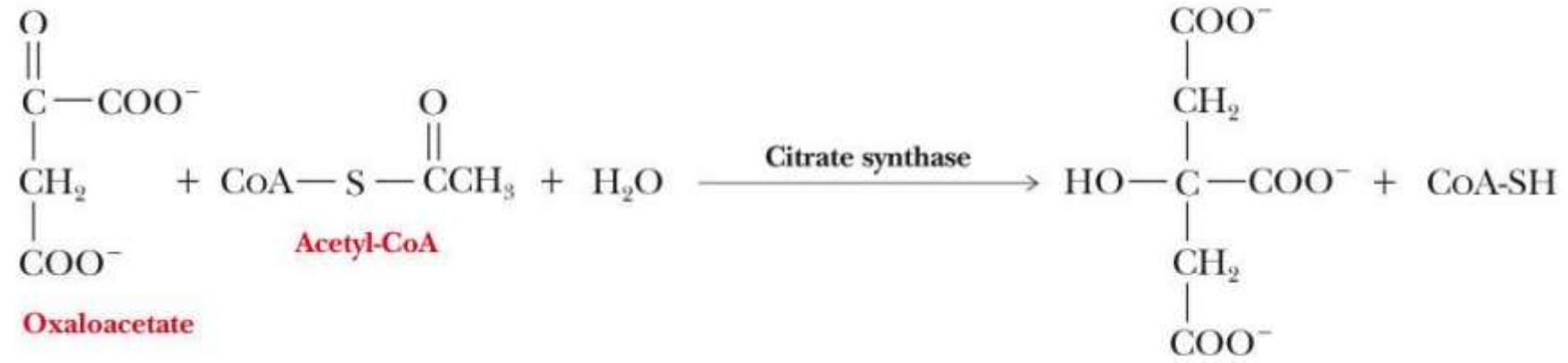
Citric Acid or TCA Cycle

- occurs in the inner mitochondrial matrix
- the acetyl group detaches from the co-enzyme A and enters the reaction cycle
- an aerobic process; will proceed only in the presence of O_2
- net yield of 2 ATP per glucose molecule (per 2 acetyl CoA)
- net yield of 6 NADH and 2 $FADH_2$ (**FAD** serves the same purpose as NAD)
- in this stage of cellular respiration, the oxidation of glucose to CO_2 is completed

step 1

The condensation of acetyl-CoA and oxaloacetate to form citrate

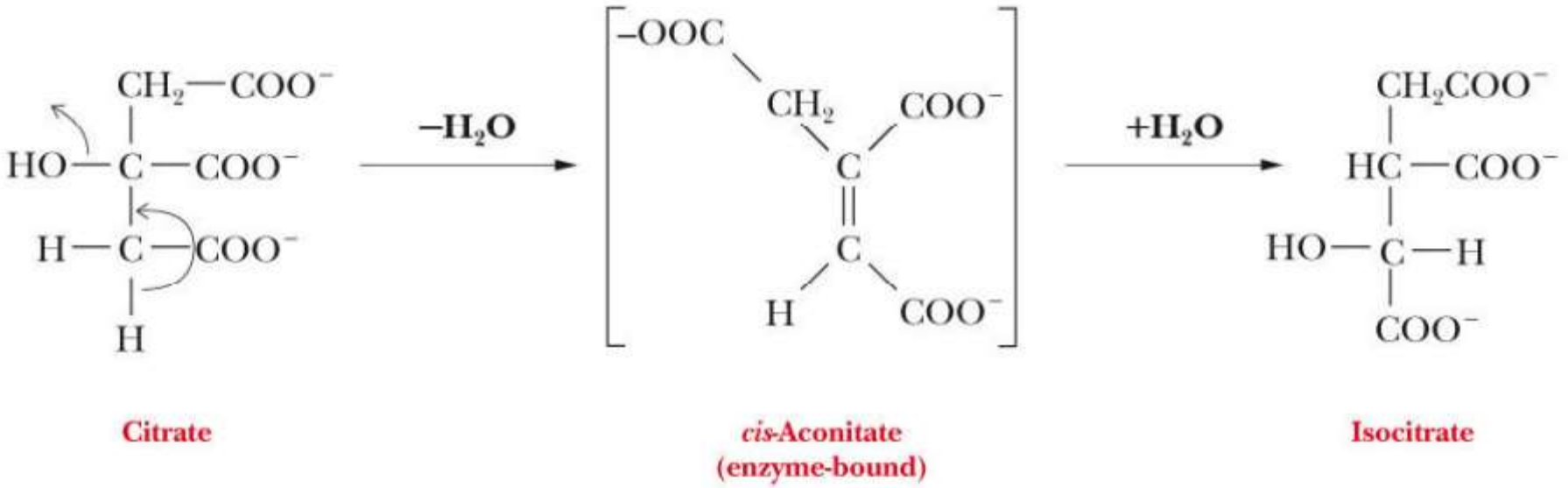
Overall reaction



isomerization

step 2

***cis*-Aconitate as an intermediate in the conversion of citrate to isocitrate**

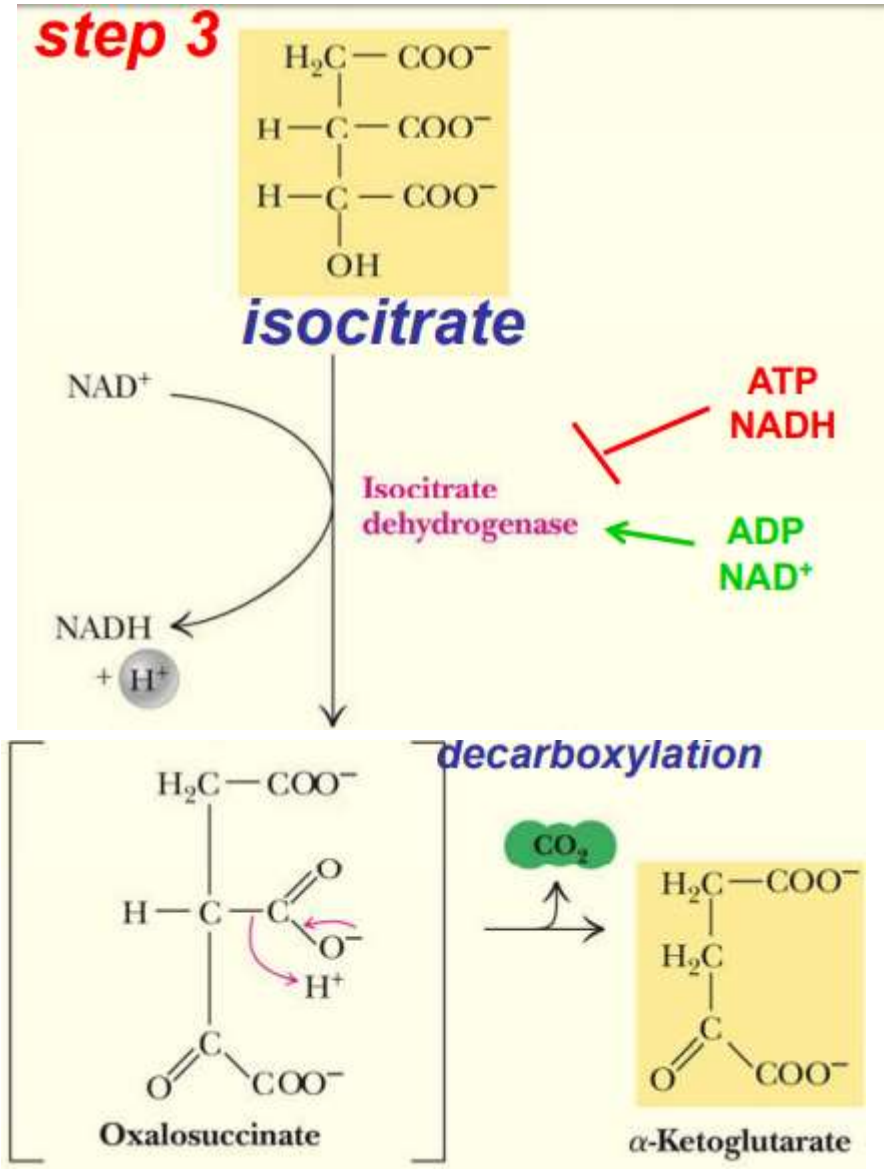


Citrate

***cis*-Aconitate (enzyme-bound)**

Isocitrate

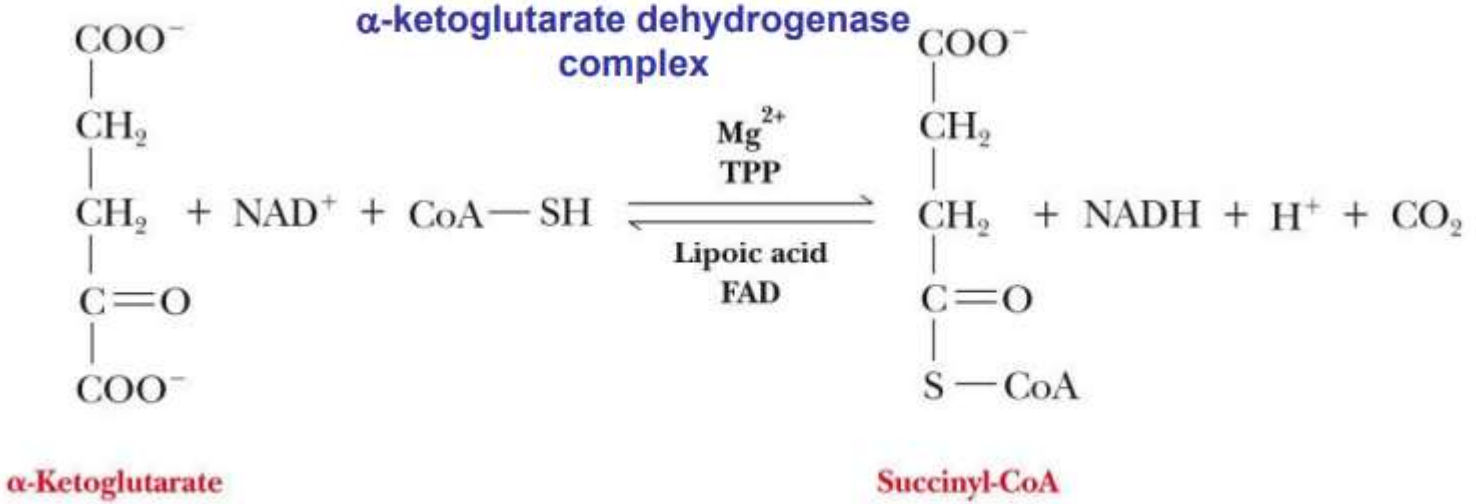
- In step 3, there is an oxidation of isocitrate followed by decarboxylation to form α-ketoglutarate and CO_2
- The reaction is catalyzed by isocitrate dehydrogenase,



In step 4, there is an oxidative decarboxylation of α-ketoglutarate to succinyl-CoA

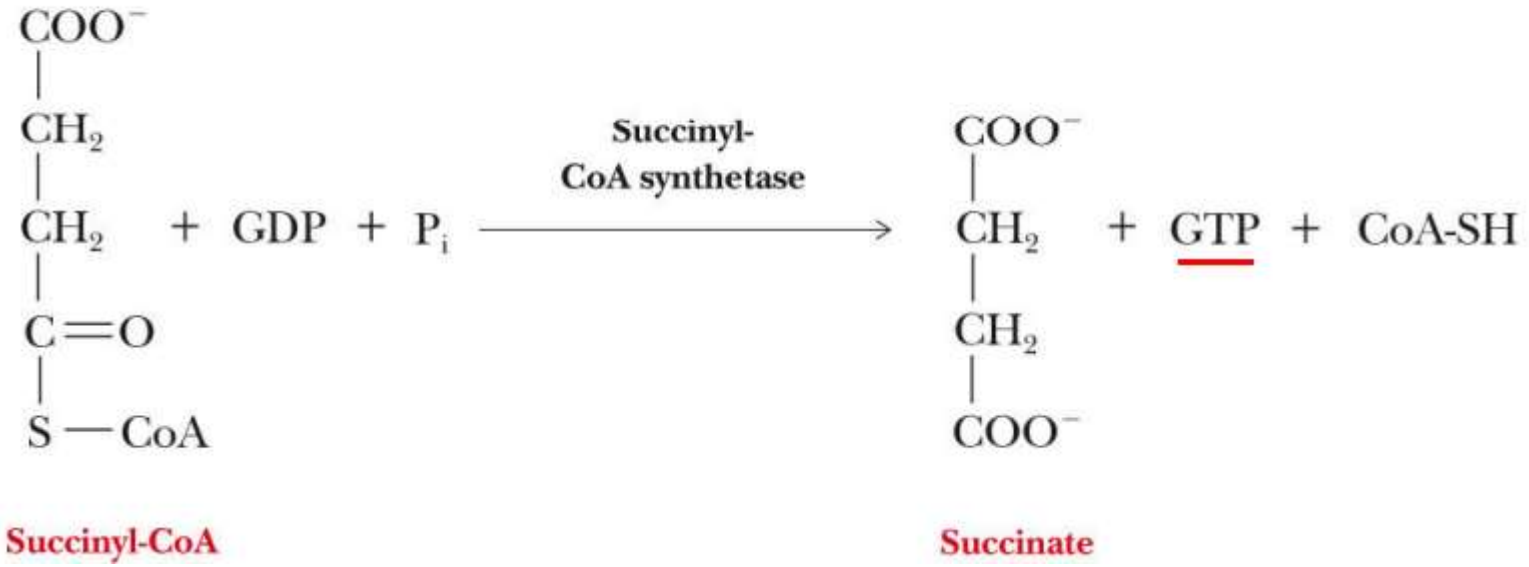
step 4

The conversion of α-ketoglutarate to succinyl-CoA



Next, the thioester bond of succinyl-CoA if hydrolyzed in the formation of succinate

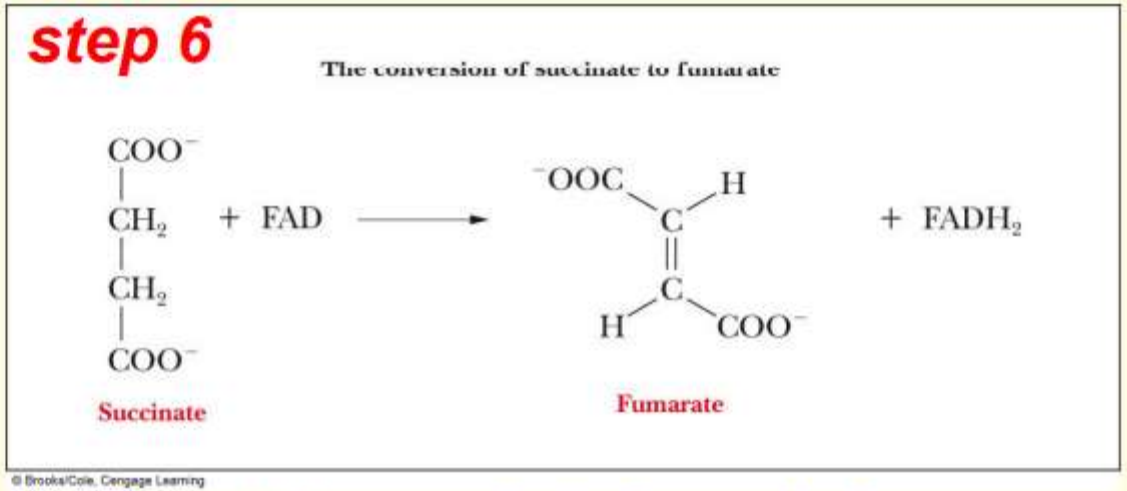
step 5 The conversion of succinyl-CoA to succinate



Succinyl-CoA Succinate

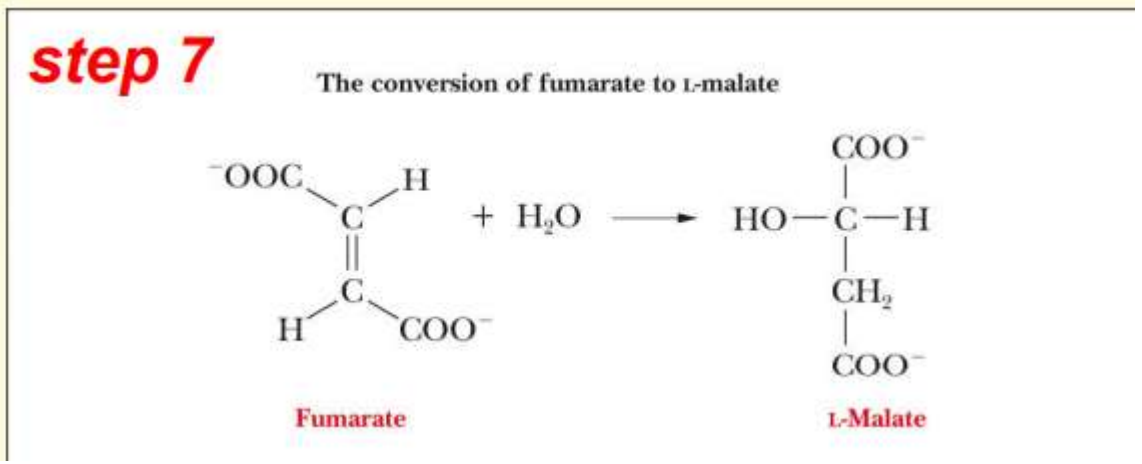
Next, there is an oxidation of succinate to **fumarate**

step 6



Then, the hydration of fumarate to **L-malate** occurs

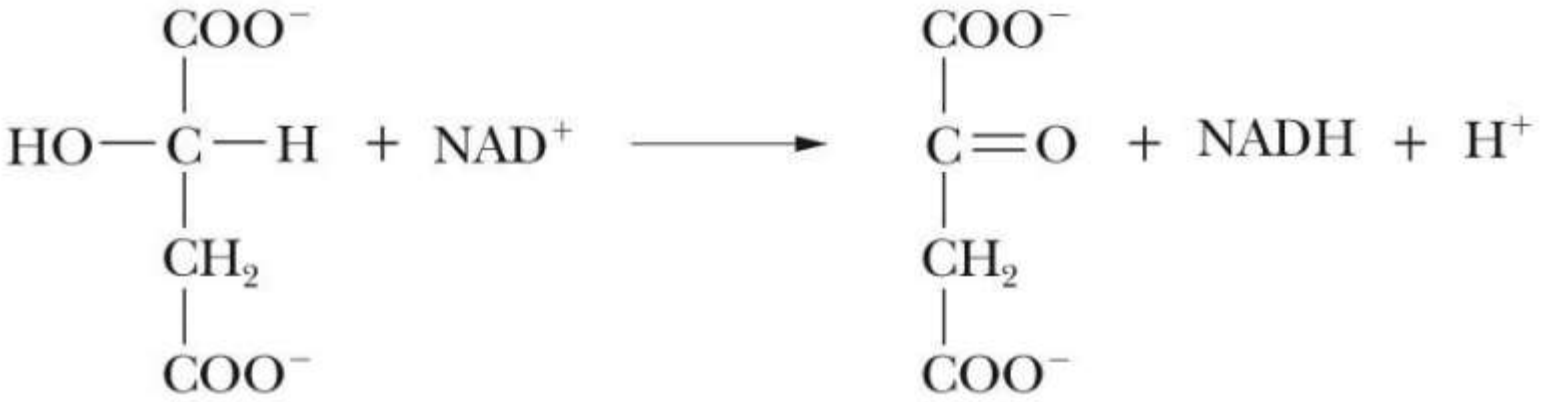
step 7



- Then, malate is oxidized to **Oxaloacetate**

step 8

The conversion of L-malate to oxaloacetate



Oxidation of Pyruvate Forms CO_2 and ATP

Pyruvate dehydrogenase complex:

$$\text{Pyruvate} + \text{CoA-SH} + \text{NAD}^+ \rightarrow \text{Acetyl-CoA} + \text{NADH} + \text{CO}_2 + \text{H}^+$$

Citric acid cycle:

$$\text{Acetyl-CoA} + 3\text{NAD}^+ + \text{FAD} + \text{GDP} + \text{P}_i + 2\text{H}_2\text{O} \rightarrow$$

$$2\text{CO}_2 + \text{CoA-SH} + 3\text{NADH} + 3\text{H}^+ + \text{FADH}_2 + \text{GTP}$$

Overall reaction:

$$\text{Pyruvate} + 4\text{NAD}^+ + \text{FAD} + \text{GDP} + \text{P}_i + 2\text{H}_2\text{O} \rightarrow$$

$$3\text{CO}_2 + 4\text{NADH} + \text{FADH}_2 + \text{GTP} + 4\text{H}^+$$

Electron Transport Chain (ETC): Coupling Oxidation to ATP Synthesis

- **Oxidation:** Loss of electrons (OIL - Oxidation Is Loss).
- **Reduction:** Gain of electrons (RIG - Reduction Is Gain).

•ETC :

- **Function:** Coupling the oxidation of food molecules to the synthesis of ATP.
- **Process:**
  - Electrons from food molecules enter the ETC.
  - The electrons travel through a series of molecules in the ETC.
  - Each transfer of electrons releases energy.
  - This energy is used to pump protons across the mitochondrial membrane.

•ETC Structure:

- **Components:** A series of protein complexes and mobile carriers.
- **Energy Conversion:**
  - Electrons lose energy at each step of the cascade.
  - The energy is utilized to create a proton gradient across the membrane.

•ATP Synthesis:

- The proton gradient drives ATP synthesis through ATP synthase.
- **Process:** Protons flow back through ATP synthase, driving the conversion of ADP and inorganic phosphate into ATP.

Natural Electron ACCEPTORS

Pyridine nucleotides

Nicotinamide Adenine Dinucleotide (**NAD**)

Flavine Adenine Dinucleotide (**FAD**)

$$NAD^+ + 2H^+ + 2e^- \underset{\text{Oxidation}}{\overset{\text{Reduction}}{\rightleftharpoons}} NADH + H^+$$

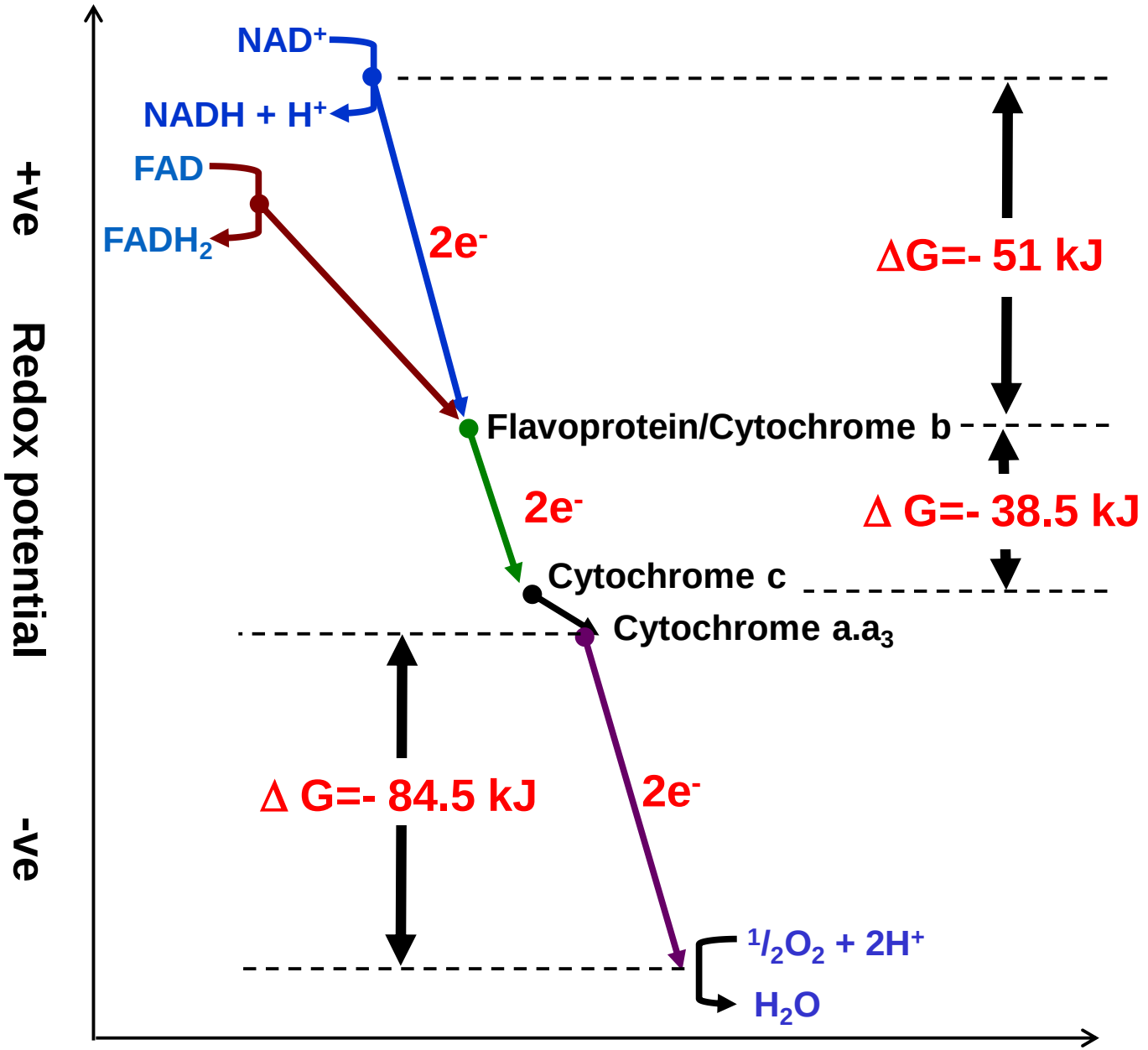
Cytochromes Conjugate proteins which contain a haem group.

The iron atom undergoes redox reactions

$$Fe^{3+} + e^- \underset{\text{Oxidation}}{\overset{\text{Reduction}}{\rightleftharpoons}} Fe^{2+}$$

Down the chain

- If this energy release is > 30.5 kJ mol^{-1} a mole of ATP can be synthesised from ADP by a coupled reaction
- The first molecule in the series is **NAD** (or **FAD**), a COENZYME of various DEHYDROGENASE enzymes, which transports the e- from glucose and other fuels, to the top of the ETC
- [NAD (oxidised) $\leftrightarrow$ NADH + H^+ (reduced)]
- Next come a series of iron containing proteins called **CYTOCHROMES**
- **The last molecule of the ETC finally passes the e- to O2.**
- **½ O2+ 2H+ $\longrightarrow$ H2O**



The electron transport chain

Electrons are produced by splitting hydrogen atoms taken from the food molecules
($H \rightarrow H^+ + e^-$) by dehydrogenases

The last electron acceptor in the series is **OXYGEN**

Thus at the end of the ETC:

$$\mathbf{2H^+ + 2e^- + {}^1/_2O_2 \rightarrow H_2O}$$

Location and Structure of the Electron Transport Chain (ETC)

- **Location:**
  - **Eukaryotes:**
    - ETC is located in the **mitochondrial inner membrane**.
  - **Prokaryotes:**
    - ETC is found in the **plasma membrane**.
- **Structural Adaptations:**
  - **Cristae:**
    - **Function:** Increase the surface area of the inner mitochondrial membrane.
    - **Importance:** More surface area allows for more ETC complexes and ATP synthase, enhancing ATP production.
  - **Number of Cristae:**
    - Reflects the activity level of the cell.
    - **High Activity:** Cells with high energy demands have more cristae to accommodate increased ETC activity.

  - **The structure of the mitochondrial inner membrane and the presence of cristae are crucial for optimizing the efficiency of the ETC and ATP production.**

The Mechanism: THE CHEMIOSMOTIC PUMP

- The ETC creates a concentration gradient by pumping H^+ out of the mitochondrial inner matrix into the intermembrane space
- As the e- are transferred via the ETC , they release energy,which drives more H+ ions to the intermembrane space, leading to a proton gradient across the inner mito membrane.
- As soon as O2 takes up the e- , the huge proton gradient thus created causes H^+ to rush into the inner membrane via proton channel proteins called the ATP synthase.
- The energy derived from the movement of these H+ ions activates ATP synthase and phosphorylates ADP to give ATP
- Formation of ATP from ADP by this mechanism is called Oxidative phosphorylation.

Results of cellular respiration

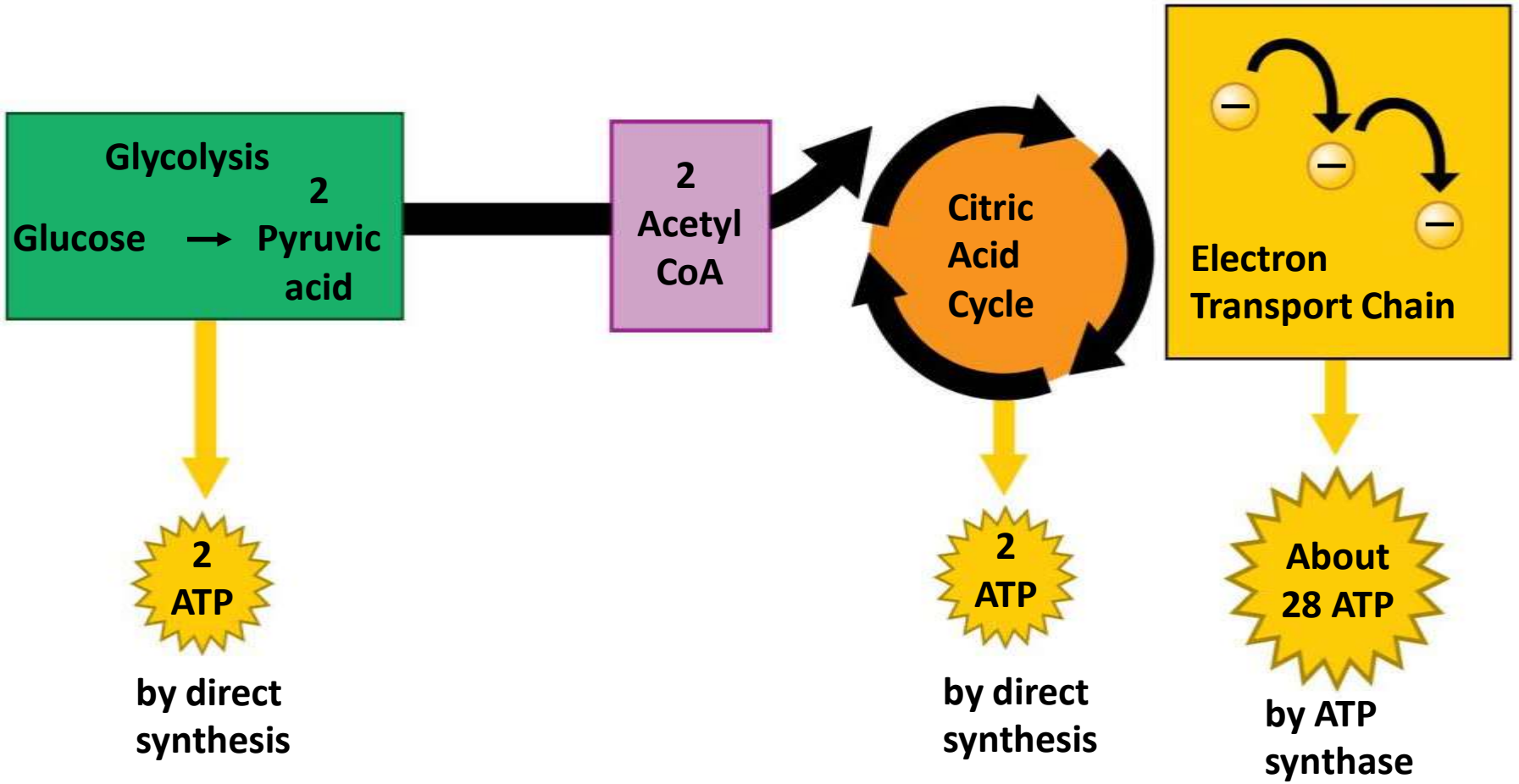
- **Glycolysis:**
- converts each molecule of glucose to two molecules of **pyruvic acid** (a 3-carbon molecule)
- an anaerobic process - proceeds whether or not O_2 is present ; O_2 is not required
- net yield of 2 ATP per glucose molecule
- net yield of 2 NADH per glucose

- The pyruvic acid diffuses into the inner compartment of the mitochondrion where
- (a) pyruvic acid ---- **acetic acid** + CO_2 (a waste product of cell metabolism) + $NADH^+$
- (b) acetic acid + co-enzyme A----- **acetyl CoA**

Electron Transport System:

- net yield of 34 ATP per glucose molecule
- 6 H_2O are formed when the electrons unite with O_2* at the end of electron transport chain.

Figure 6.11-1


Glycolysis
Glucose
2
Pyruvic acid
2
Acetyl CoA
Citric Acid Cycle
Electron Transport Chain
2
ATP
by direct synthesis
2
ATP
by direct synthesis
About 28 ATP
by ATP synthase

GLUCOSE AS AN ENERGY SOURCE

- When glucose is in adequate supply, such as shortly after consumption of a meal, the hormone **insulin** from the pancreas increases **glycogen** formation (**glycogenesis**) in the liver.
- When glucose levels drop between meals, the hormone **glucagon** is released from the pancreas and stimulates the conversion of glycogen into glucose (by the process of **glycogenolysis)**.
- If all glycogen supplies are depleted, then WHAT????

- Glugoneogenesis is the Answer
- The conversion of fatty acids (from lipids) or amino acids (from proteins) into glucose or intermediate products is called **gluconeogenesis**

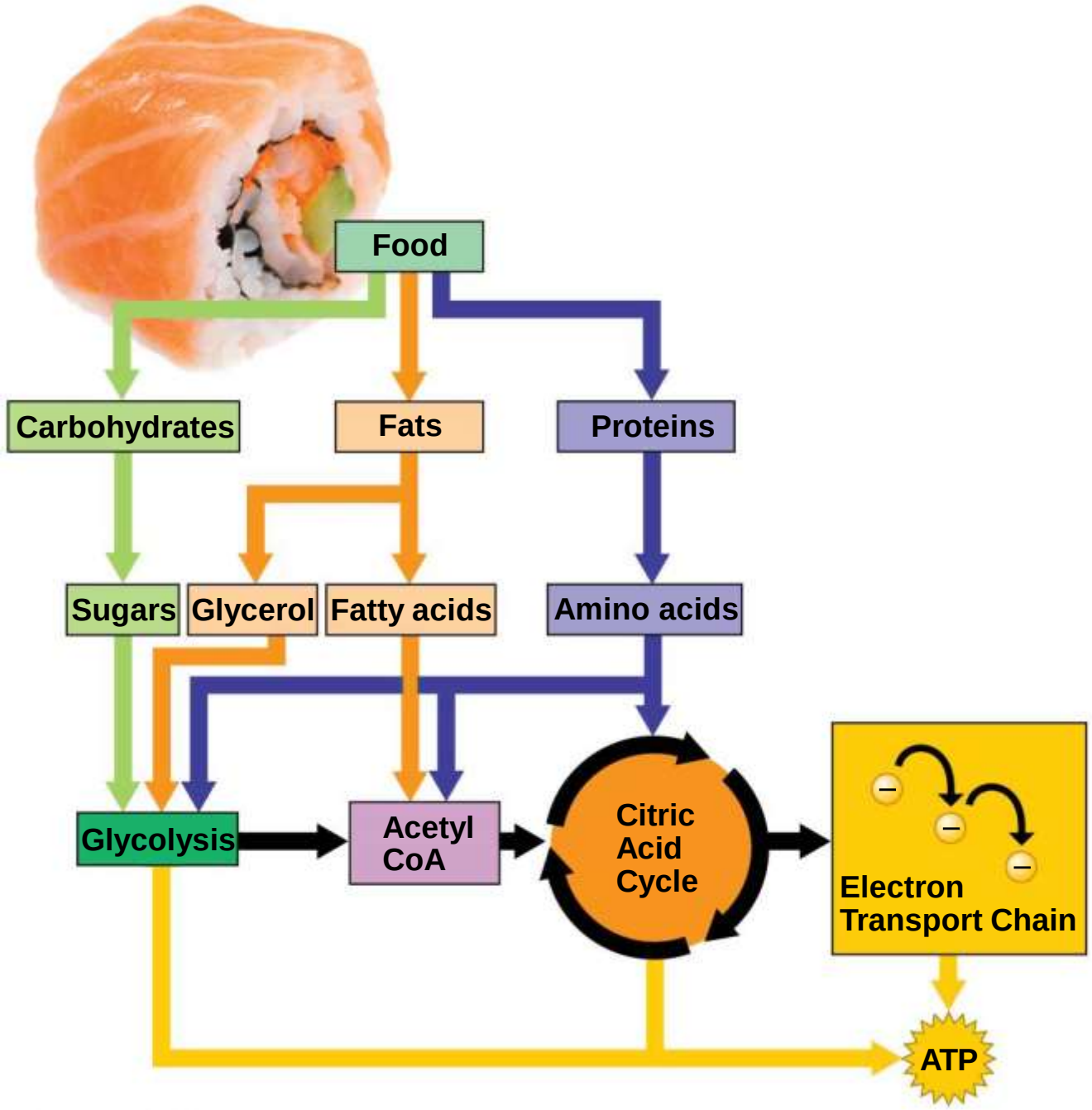
FAT AS AN ENERGY SOURCE

- Fats (lipids) are stored in adipose tissue.
- When needed as an energy source, the fat reserves are mobilized, moved out of adipose tissue, and broken down into glycerol and fatty acids in the liver by the process of **lipolysis.**
- Glycerol is changed into one of the intermediate products of glycolysis, so enters the cell respiration pathway.
- Fatty acids are changed in a series of reactions called **beta-oxidation** into acetyl CoA molecules, which enter cell metabolism at the Kreb's Cycle.

- When fats are being used as the primary energy source such as in starvation, fasting or untreated diabetes, an excess amount of acetyl CoA is produced, and is converted into acetone and **ketone bodies**. This produces the sweet smell of acetone on the breath, noticeable in a diabetic state.

PROTEIN AS AN ENERGY SOURCE

- Proteins are used as an energy source only if protein intake is high, or if glucose and fat sources are depleted
- Proteins are digested into amino acids.
- Then amino acids have the amino group removed.
  - Generates a keto acid (acetic acid, pyruvic acid, etc.)
  - Enter the Kreb's cycle at the appropriate place


Food
Carbohydrates
Fats
Proteins
Sugars
Glycerol
Fatty acids
Amino acids
Glycolysis
Acetyl CoA
Citric Acid Cycle
Electron Transport Chain
ATP

Total Yields for Aerobic Cellular Respiration per Glucose Molecule

- Glycolysis
  - 2 ATP
  - 2 NADH (converted to 2 $FADH_2$)
- Kreb's cycle
  - 2 ATP
  - 8 NADH
  - 2 $FADH_2$
- Electron transport chain
  - Each NADH fuels the formation of 3 ATP.
    - 8 NADH x 3 ATP = 24 ATP
  - Each $FADH_2$ fuels the formation of 2 ATP.
    - 4 FADH2 x 2 ATP = 8 ATP
- Total ATP=2+2+24+8=36 ATP made from the metabolism of one glucose molecule.