Metabolism & ATP

(Part 1 of 2)

Lecture 13

Objectives

- Define the term metabolism and describe its main two pathways
- Describe the structure of ATP and explain how it is used to carry and provide energy to the cell
- List the two main ways of ATP production in the body
- List the three main pathways of cellular respiration and know the site of each process
- List the electron acceptor and non-electron acceptor coenzymes and show their related vitamins
- Describe BRIEFLY the process of glycolysis
  - its main purpose
  - ATP accounting
  - its resulting products
- List the three possible fates of pyruvate after it is produced from glycolysis

Metabolism

etymology (Gr. "to change")

catabolism

biochemical reactions that liberate the energy and couple it to the synthesis of ATP

anabolism/biosynthesis

biochemical reactions that utilize cell energy in ATP in order to synthesize larger molecules

Anabolism

Anabolic pathways (Greek “ana” = “up”)

- Pathways synthesizing cellular components which often increase molecular size and require energy
- Polymer synthesis & biological reduction of CO_2 to sugar are examples of anabolic pathways

Catabolism

Catabolic pathways (Greek ”kata”= “down”)

- Pathways involving breakdown of cellular constituents which decrease molecule size and are energy-releasing
- Biochemical reactions are usually oxidations or hydrolysis
- Catabolic pathways play two roles:
  1. They release the free energy needed to drive cellular functions
  2. They give rise to small organic molecules (metabolites) that are the building blocks for biosynthesis

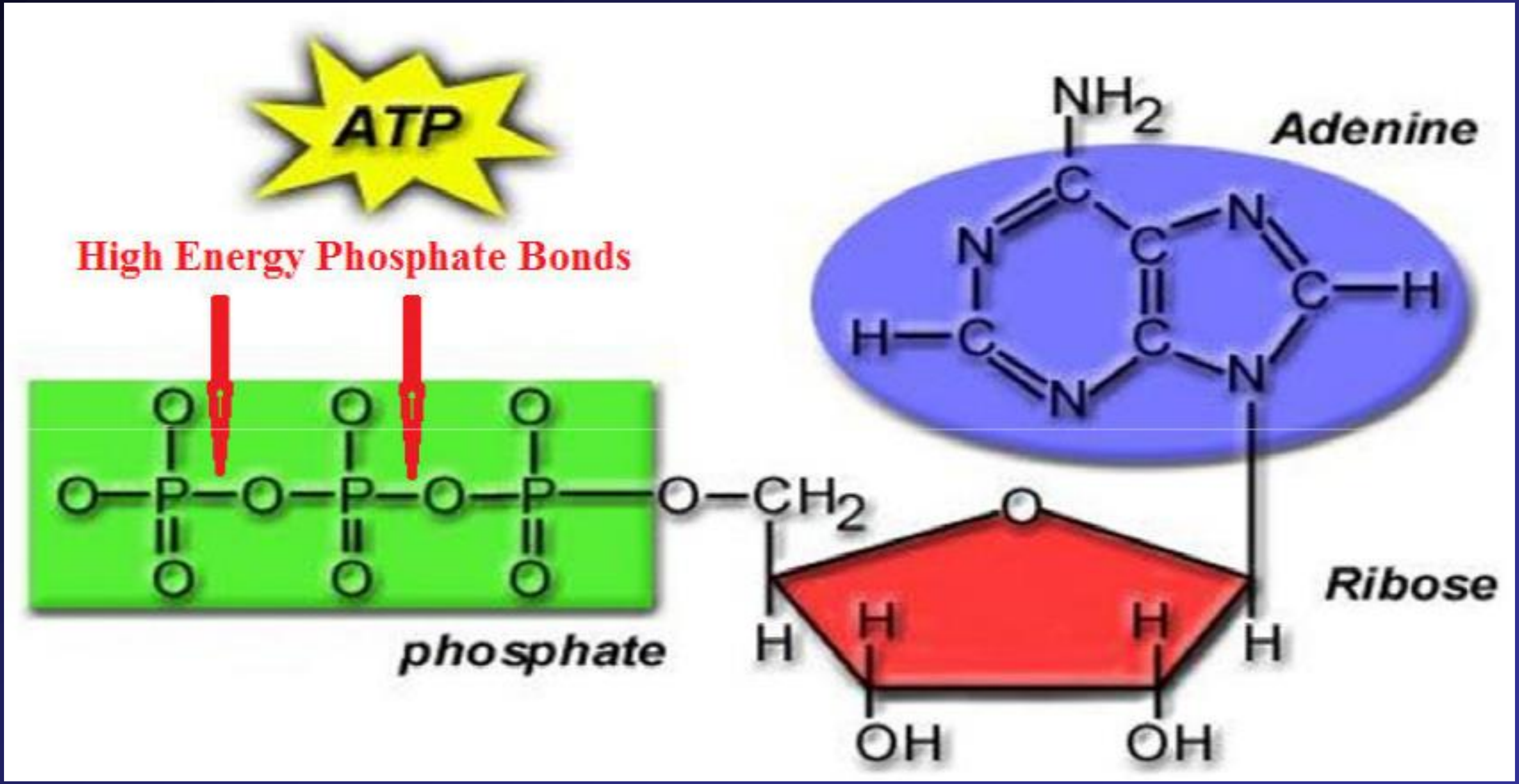
ATP As The Energy Go-Between

Primary "Energy Currency of the Biological World"

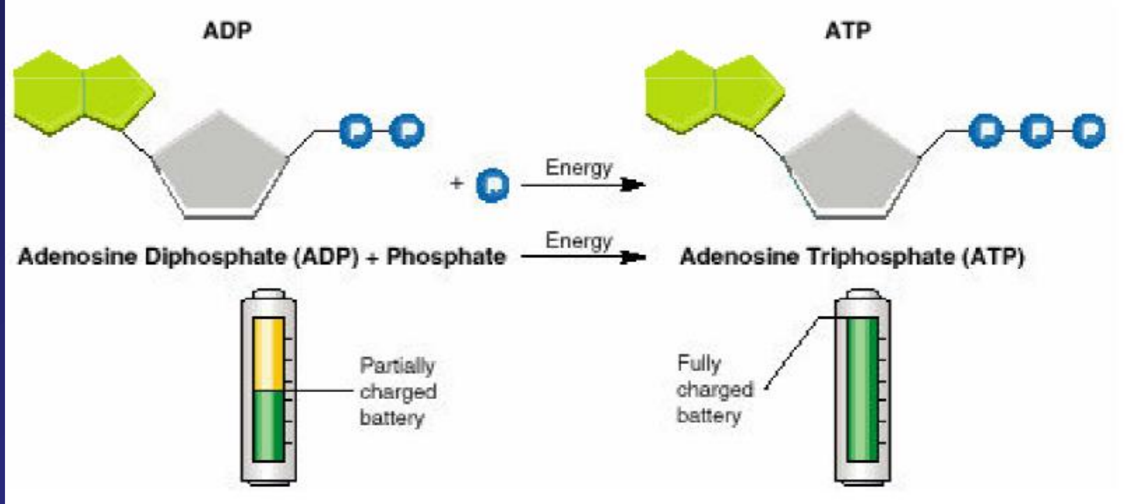
- Food fuels cannot be used to energize body activities directly
- Energy from food (glucose catabolism) is stored in the bonds of adenosine triphosphate (ATP)
- Energy for cellular processes of all kinds is then coupled to the break-and-transfer of ATP phosphate anhydride bond energy
- Many metabolic (catabolic and anabolic) utilize ATP or create ATP
- ATP can be regenerated in metabolic processes fundamental to photosynthesis in the plant chloroplast and respiration in mitochondria

ATP Structure

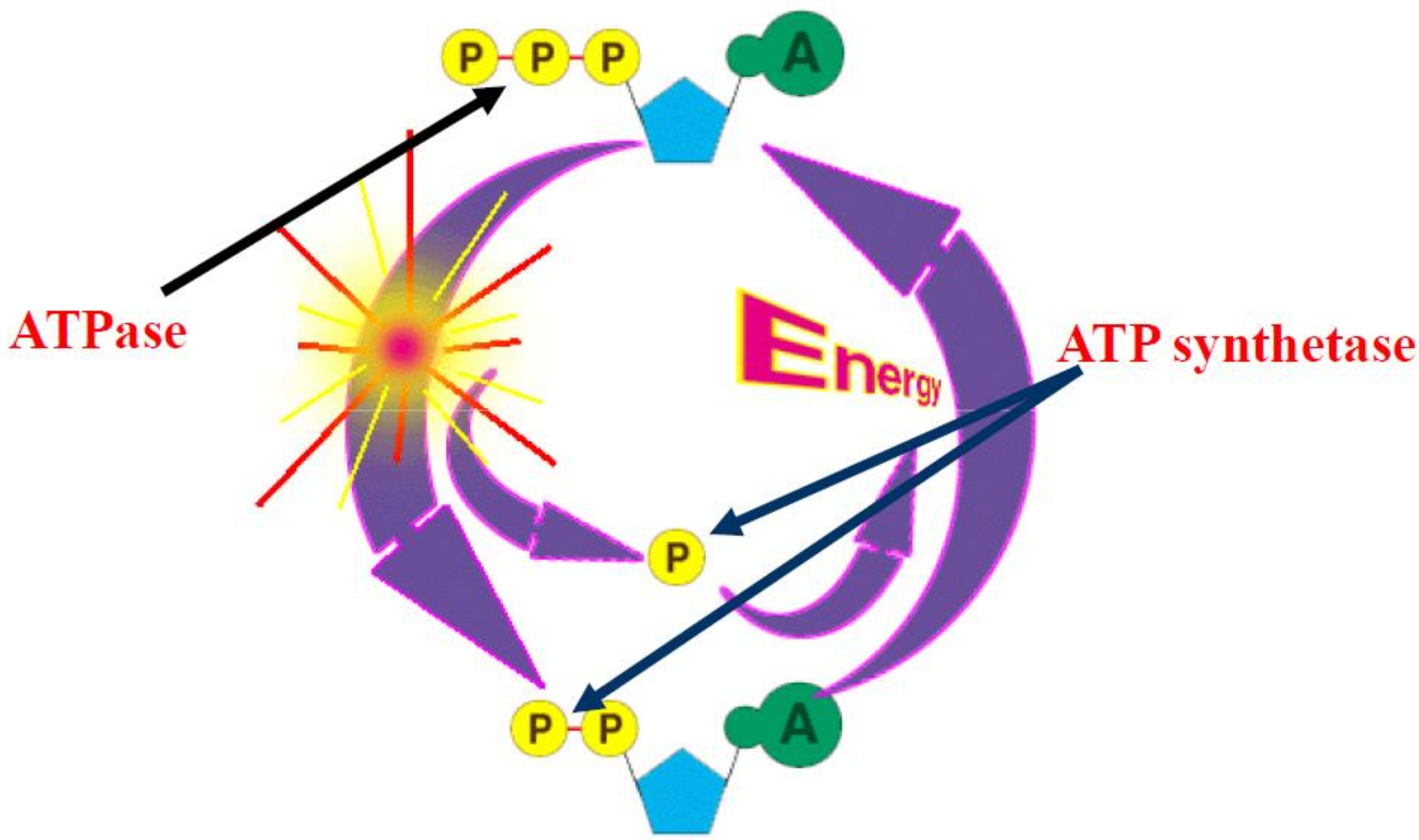
- ATP consists of adenine + ribose + three phosphates
- Adenine + ribose = adenosine
- AMP = adenosine monophosphate: this phosphate is attached by an ester bond without high energy
- ADP = adenosine diphosphate: the second phosphate is attached by a high energy phosphate bond
- In ATP: the third phosphate is attached by an even higher energy phosphate bond
- High energy phosphate bonds in ATP are NOT highest energy phosphate bonds possible in the cell: they are intermediate on the energy scale of phosphate bonds
- This makes ATP a useful because the 3rd phosphate bond is of sufficiently high energy to enable metabolism, but not so high that it is difficult for cell to make


ATP
High Energy Phosphate Bonds
NH2
Adenine
Ribose
phosphate
O—CH2
OH
OH

- All energy is stored in the bonds of ATP: breaking the bond releases the energy
- When the cell has energy available it can store this energy by adding a phosphate group to ADP, producing ATP



ADP vs. ATP ATP can be compared to a fully charged battery because both contain stored energy, whereas ADP resembles a partially charged battery. **Predicting** ***What happens when a phosphate group is removed from ATP?***



The ADP-ATP Cycle

Energy Source for Producing ATP

- ATP is produced during a process called cellular respiration
- The energy comes ultimately sunlight, which was used to drive glucose formation by photosynthesis, which is utilized by the cell, and creates again the materials for photosynthesis:

$$6CO_2 + 6H_2O + \text{Energy} \underset{\text{Respiration}}{\overset{\text{Photosynthesis}}{\rightleftharpoons}} C_6H_{12}O_6 + 6O_2$$

- The energy which is stored in the whole glucose molecule is approximately 100-fold the amount of energy which is stored in a high-energy phosphate bond in 1 ATP molecule
- Therefore, we release the energy from glucose step-wise, releasing tiny packets of energy so that ATP can be synthesized one molecule at a time, where possible.

Cellular Pathways for Producing ATP

ATP may be made in 2 ways:

1. Substrate-level phosphorylation utilizes the energy of a single exergonic substrate conversion to directly power the phosphorylation of ADP to make ATP
   - This is ATP that is formed by biochemical reactions within metabolic pathways like glycolysis & TCA (Krebs) cycle
2. Oxidative phosphorylation utilizes the energy of alternating oxidation and reduction of coenzymes in the electron transport system (ETS) to make ATP

Glucose → ATP Metabolic Pathways

Three pathways in fundamental cellular metabolism:

1. Glycolysis

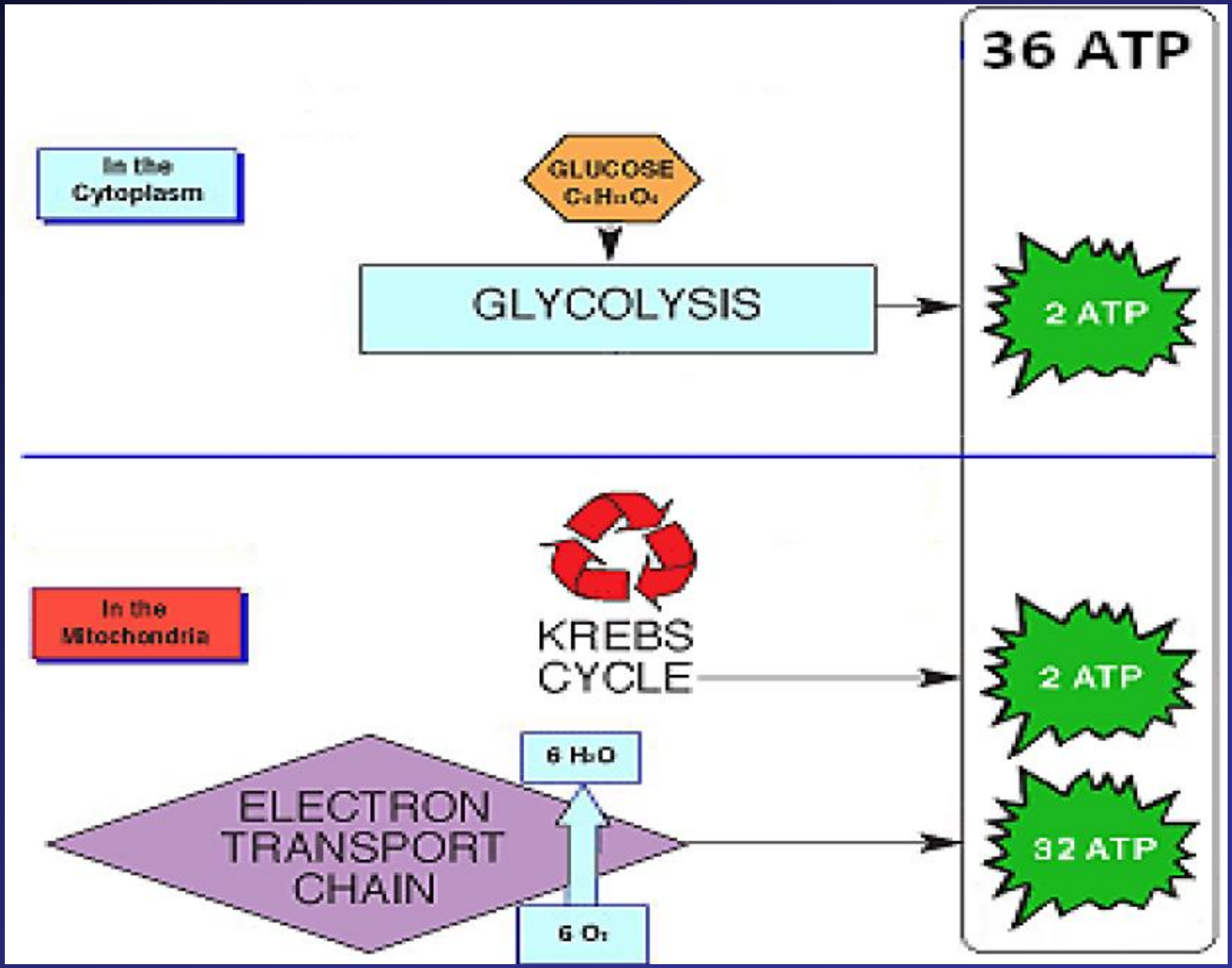
   occurs in cytosol

2. Tricarboxylic acid (TCA) cycle
   - also called Krebs cycle after its discoverer
   - occurs in the mitochondria matrix

3. Electron Transport Chain or System (ETS/ETC)

   occurs in the mitochondria inner membrane

- These three pathways will produce a net total of 36 ATP molecules: 2 from glycolysis, 2 from Krebs cycle, and 32 from ETS, all from one glucose molecule
- These metabolic pathways occur in a definite order, and we will consider them in that order


36 ATP
In the Cytoplasm
GLUCOSE
$C_6H_{12}O_6$
GLYCOLYSIS
2 ATP
In the Mitochondria
KREBS CYCLE
2 ATP
6 H_2O
ELECTRON TRANSPORT CHAIN
6 O_2
32 ATP

Cofactors / Coenzymes

It should be noted that many components in these pathways rely on molecules that are derived from vitamins

- Nicotinamide adenine dinucleotide (NAD^+) is involved in redox reaction and is made from nicotinamide or niacin, vitamin B_3
- Flavin adenine dinucleotide (FAD) is made from riboflavin, or vitamin B_2 and involved in redox reactions
- Flavin mononucleotide (FMN) is a derivative of riboflavin
- Coenzyme Q is not derived from a vitamin, but an important redox component
- Cytochromes are redox proteins with iron- and copper-containing heme components
- Thiamine pyrophosphate (TPP) is made from thiamine, vitamin B_1 and is involved in the pyruvate dehydrogenase reaction
- Coenzyme A is made from pantothenate, vitamin B_5.

Glycolysis Overview

- 10 enzymatic reactions all in the cytosol
- Starts with one 6-carbon glucose and finishes with two 3-carbon pyruvate molecules
- Two ATP are used at first
  - one by enzyme hexokinase to phosphorylate glucose (Glc) to glucose-6-phosphate (G6P) as it enter cells through the glucose transporter

    this traps Glc, since it can actually diffuse out of the cell
  - the other is by phosphofructokinase (PFK), which phosphorylates fructose-6-phosphate (F6P)–isomerized from G6P to fructose-1,6-bisphosphate (FBP)

Glycolysis Overview

- Later, four ATP molecules will be produced from one Glc
- Thus a net gain of two ATP is produced from the one metabolic pathway that is glycolysis
- This ATP produced is called substrate level phosphorylation, because all the ATP produced are from reactions with metabolic pathway substrates (carbohydrate molecules)

  Later, far more ATP molecules will be generated by oxidative phosphorylation
- Another important energy-producing step is the generation of two NADH molecules from NAD^+ + H^+

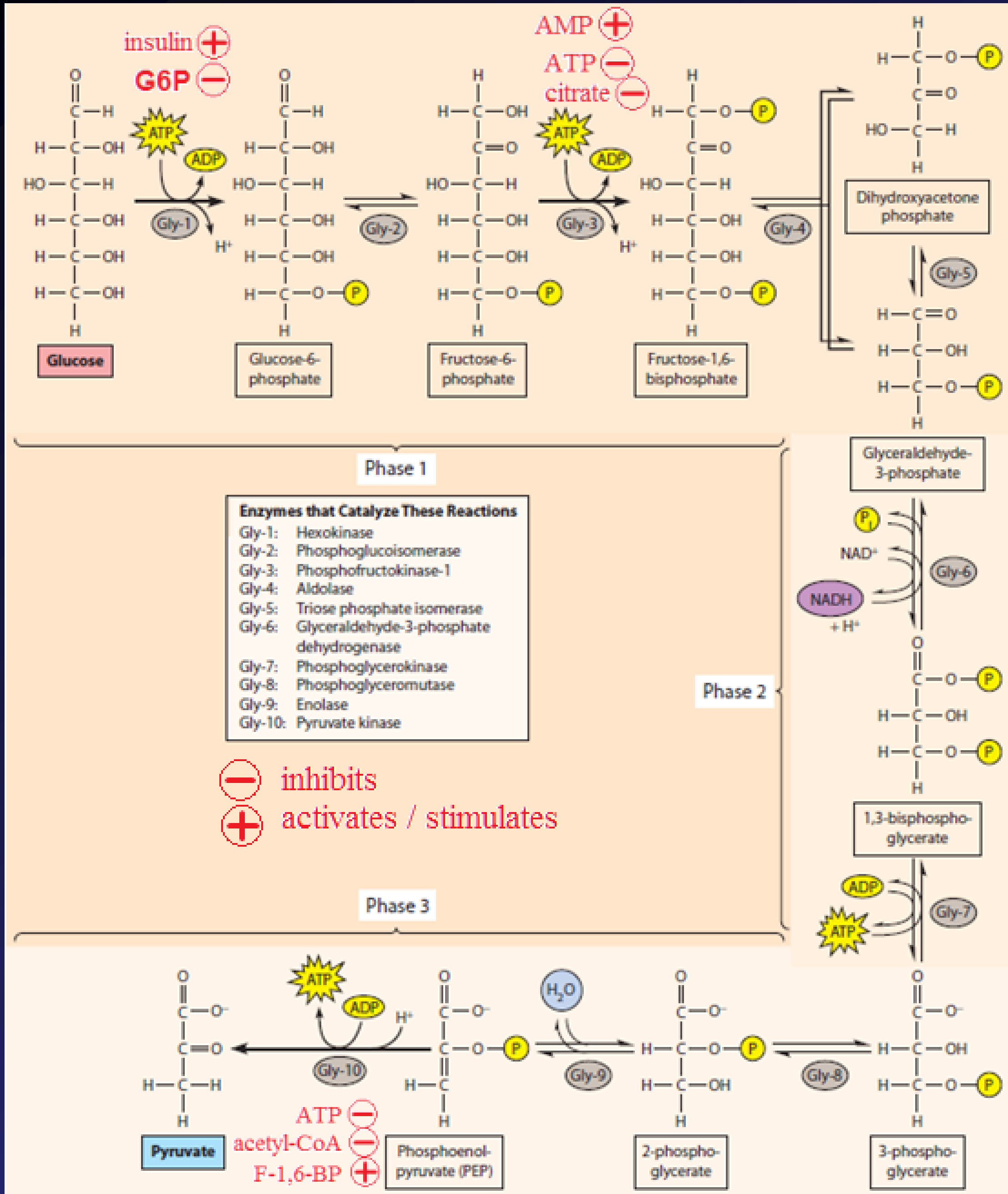


FIGURE 9-7 The Glycolytic Pathway from Glucose to Pyruvate. Glycolysis is a sequence of ten reactions in which glucose is catabolized to pyruvate, with a single oxidative reaction (Gly-6) and two ATP-generating steps (Gly-7 and Gly-10). The enzymes that catalyze these reactions are identified in the center box.

- 10 enzymatic steps from glucose to pyruvate

Summarizing the Detail

Reactions 1-3: preparation

Glucose is phosphorylated to make fructose 1,6-bisphosphate. Two molecules of ATP are used up in this process.

Reactions 4-5: cleavage

Fructose 1,6-bisphosphate is split into two molecules, which at first are slightly different from each other. One of them undergoes an isomerization to make them the same, so we end up with two identical molecules of glyceraldehyde-3-phosphate. From this point, the process is in duplicate if we think on a "per glucose" basis.

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Summarizing the Detail

Reactions 6-7: oxidation & ATP production

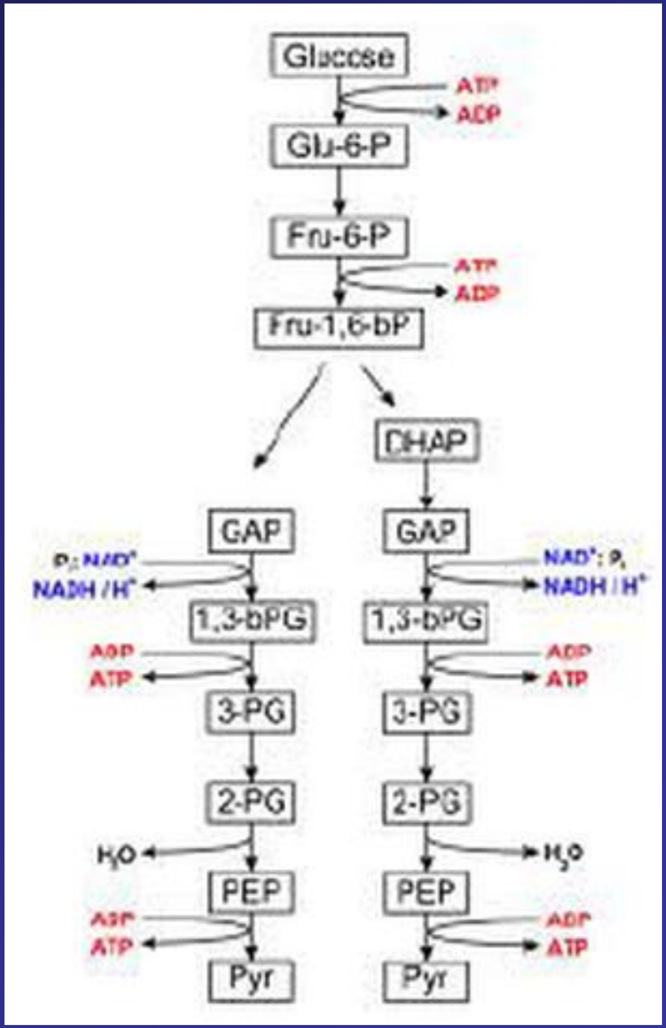
Glyceraldehyde-3-phosphate is oxidized to 3-phosphoglycerate. (Note that this reaction oxidizes an aldehyde to a carboxylic acid). This is an oxidation, so it requires an electron acceptor, which is $NAD^+ \rightarrow NADH + H^+$. ATP is produced through substrate-level phosphorylation.

Reactions 8-10: molecular rearrangement & ATP production

3-phosphoglycerate undergoes three rearrangements, and then its energy is in the right place for it to be used for substrate-level phosphrylation to make more ATP. The final product is pyruvate.

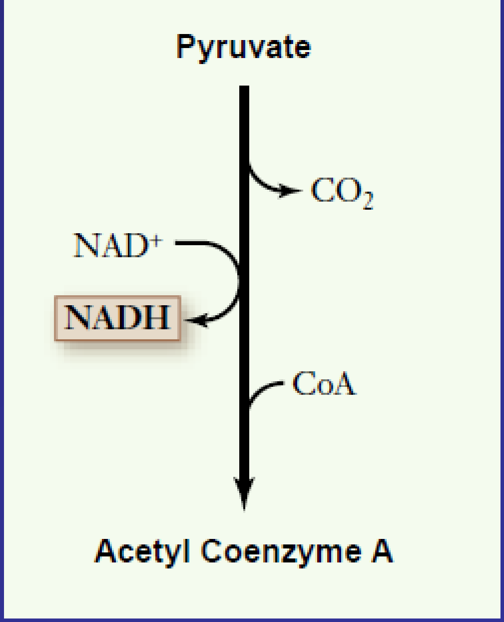
Taken from a previous lecture, this shows

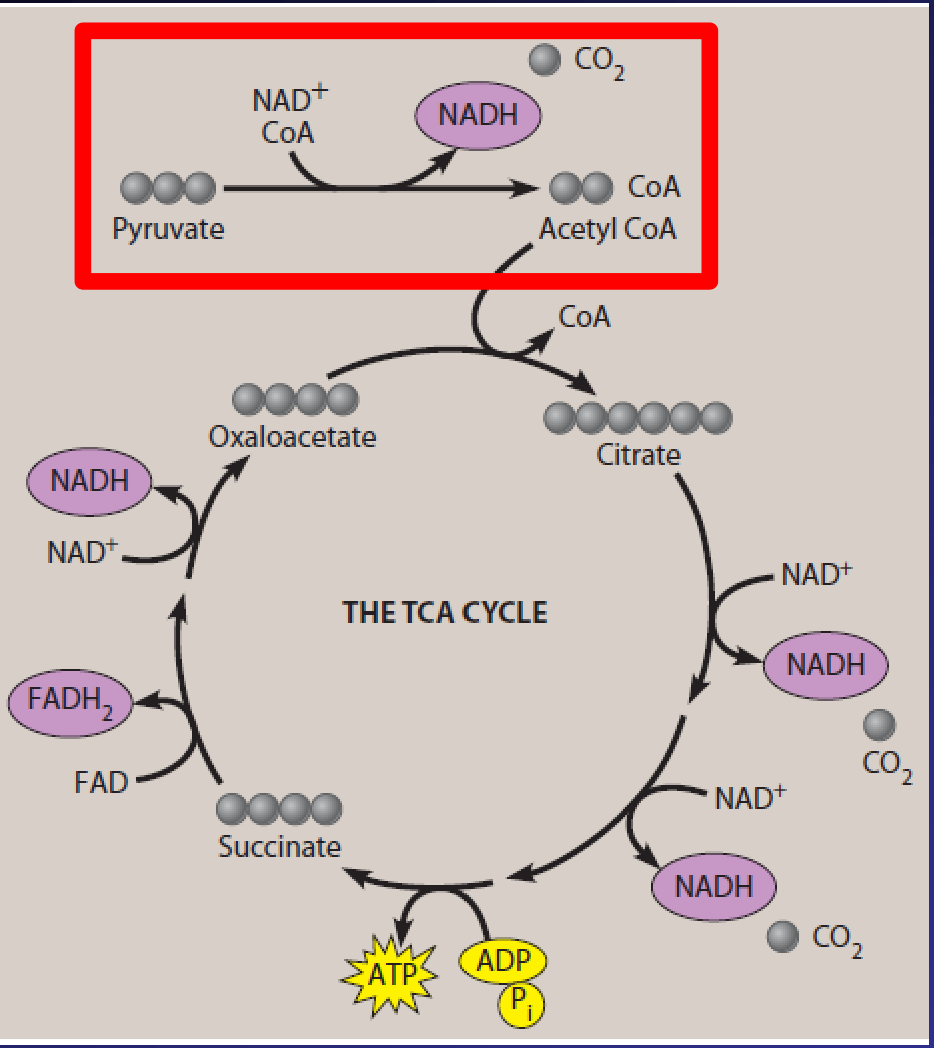
- the energy-using and –producing steps
- the metabolic pathway from GAP → pyruvate is duplicated because 6C molecules split to two 3C molecules



Pyruvate → Acetyl-CoA

- After forming in glycolysis, pyruvate enters into the mitochondrial matrix: it must be transported across inner membrane
- Pyruvate dehydrogenase is a protein complex with multiple enzymatic activities and intermediate metabolites
- It will produce one NADH and one CO_2 molecule
- It will use Coenzyme A to store a high energy bond in the 2-carbon acetyl product: acetyl-CoA, which then enter the TCA (Krebs) cycle





- The pyruvate dehydrogenase reaction is shown in the reaction outlined in red
- It joins glycolysis with the TCA (Krebs) cycle

Fermentation (Anaerobic Metabolism)

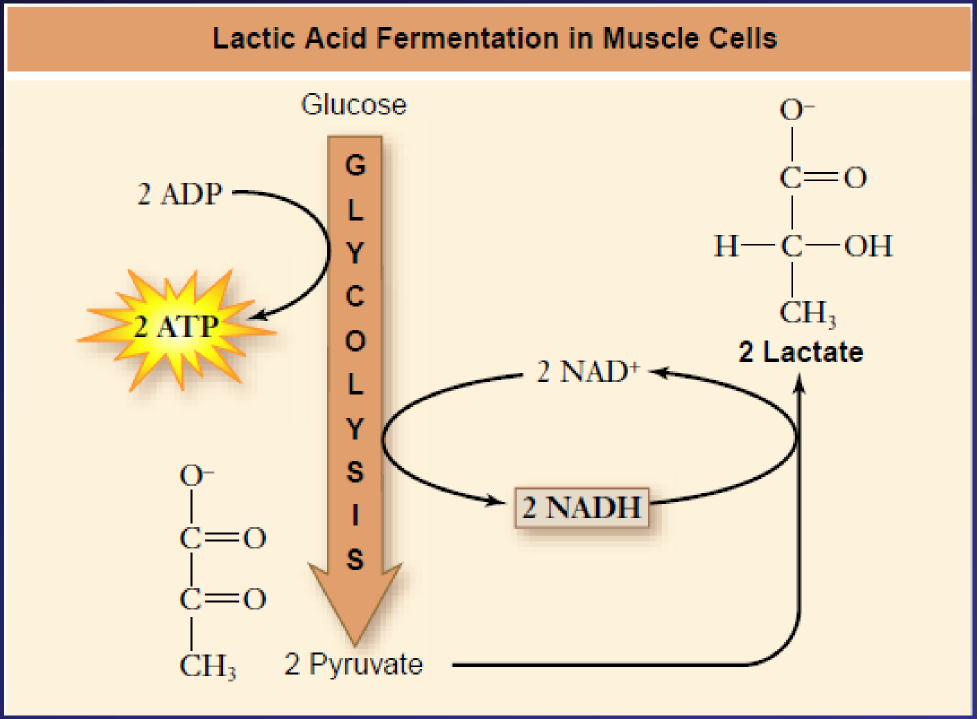
- When oxygen is not available for production of ATP by respiration, NAD^+ used by the reaction of glyceraldehyde-3-phosphate dehydrogenase is depleted
- Cells have an "escape" pathway to regenerate NAD+ so that glycolysis can at least continue
- This is called fermentation

There are two types of fermentation pathways

1. Lactate
2. Ethanol + carbon dioxide

Lactate Fermentation

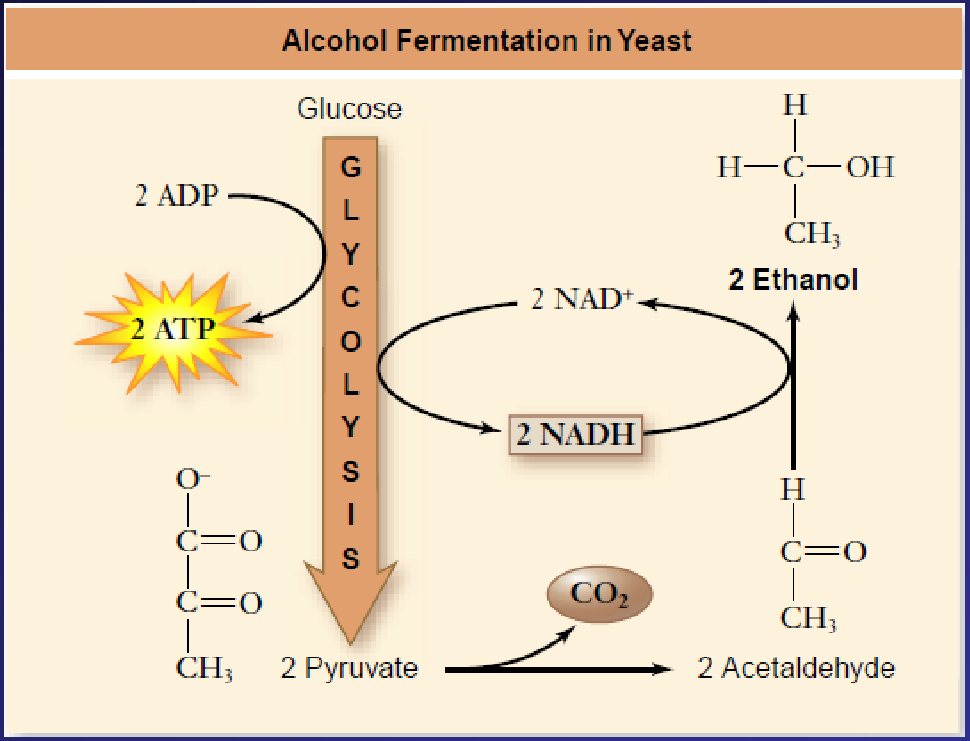
- This happens when skeletal muscle cannot get oxygen to make it work
- Pyruvate builds up as glycolysis occurs rapidly in muscle movement



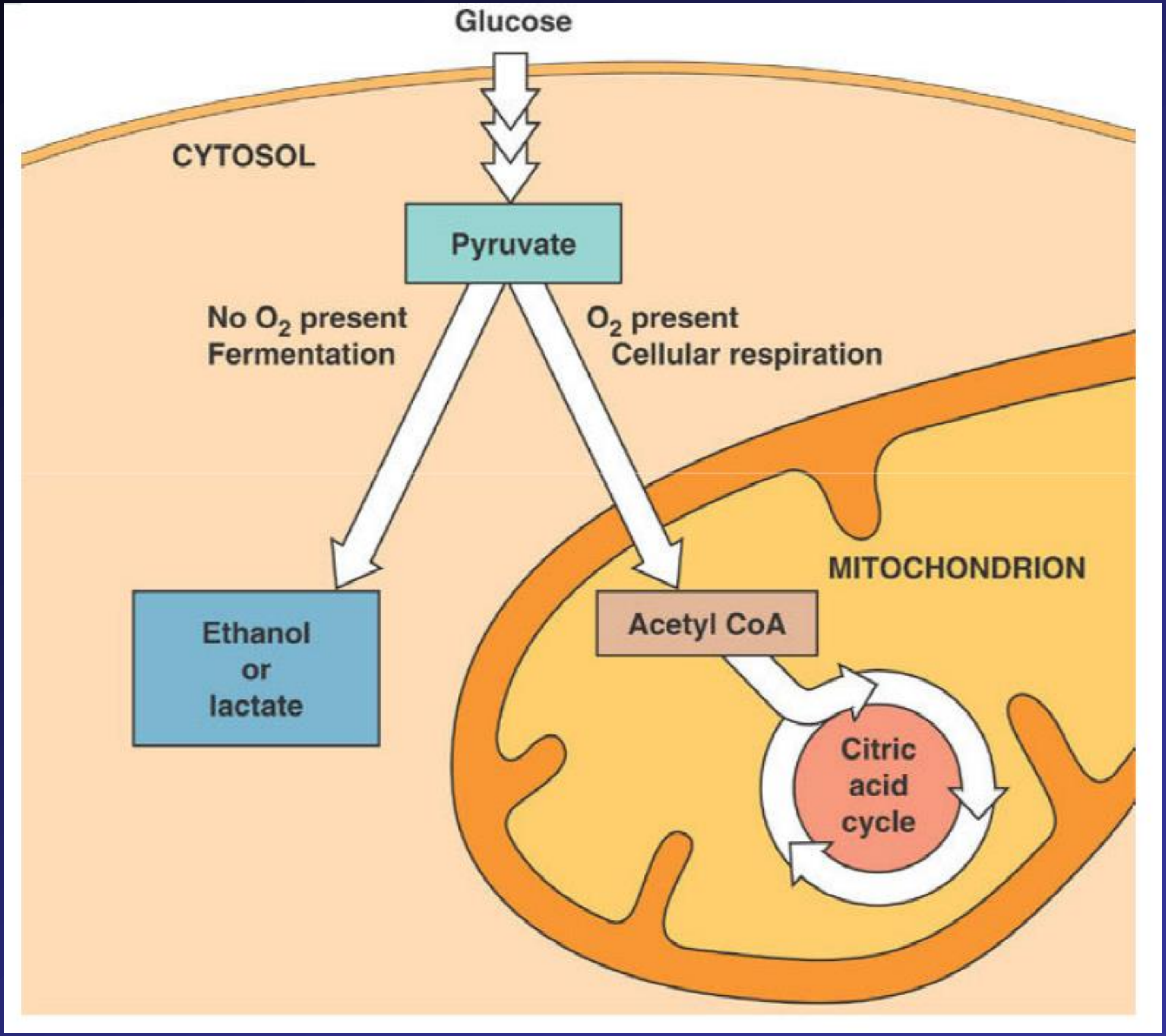
- The pyruvate is converted to lactate by the enzyme lactate dehydrogenase, which uses NADH to reduce pyruvate to lactate: this restores NAD^+ concentrations so glycolysis can continue

Alcoholic Fermentation

- This metabolic pathway occurs in yeast and is the basis for wine, beer, and distilled spirits production
- Instead of one enzyme (LDH) for the lactate pathway, this pathway uses two enzymes:



1. pyruvate decarboxylase catalyzes the loss of CO_2 from pyruvate to form acetaldehyde
2. alcohol dehydrogenase converts acetaldehyde to ethanol, and is the enzymatic step restoring NAD^+ from NADH



Glucose
CYTOSOL
Pyruvate
No O_2 present
Fermentation
O_2 present
Cellular respiration
MITOCHONDRION
Ethanol
or
lactate
Acetyl CoA
Citric
acid
cycle

Reading

- Becker's WotC: 224-236, 252-263, 267-272, 274-288
- Raven: pp 108-110, 112-113, 117-119, 123-138