Lecture 28 – Introduction to Metabolism

Goals

- Understand differences between anabolic and catabolic pathways.
- Identify common themes in pathways
- Describe the cellular location and inter-pathway connections.
- Explain why ATP is an energy source for the cell.
- Identify kinases, phosphatases based on reaction they catalyze.
- Identify oxidation/reduction reactions.

Metabolic pathways are:

1. Consist of a number of steps, each catalyzed by an enzyme causing a small change to the chemical structure, i.e. A→B→C→D→E
2. Many are conserved in different organisms.
3. Overall irreversible (but most of the individual steps are not)
4. Usually committed after the initial steps
5. Regulated.
6. Compartmentalized in eukaryotes

Catabolism [degradative] – conversion of a diverse set of compounds to a small number of simple compounds, usually for energy production.

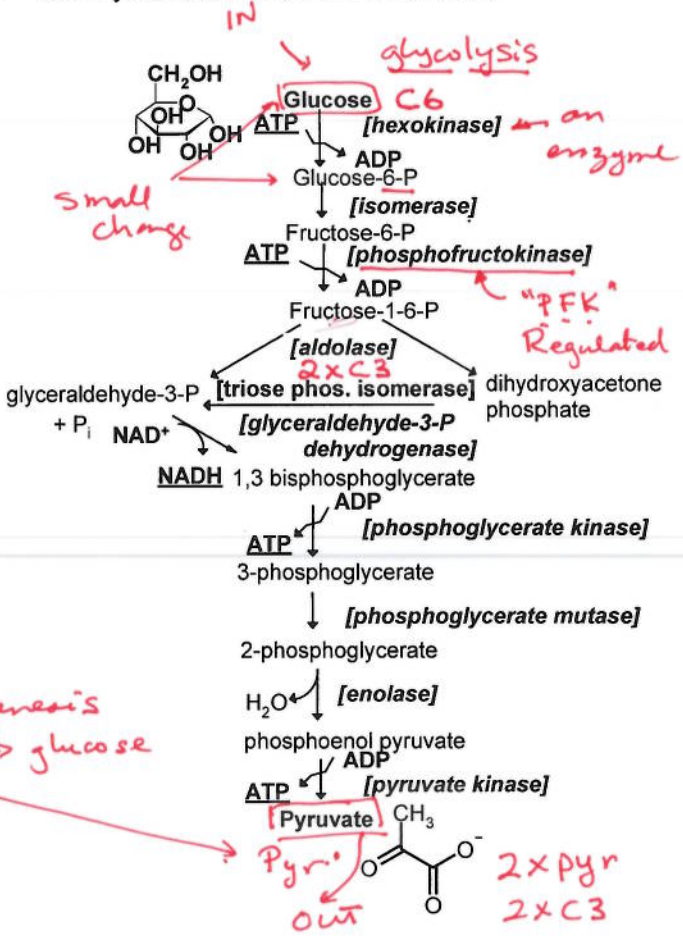
Complex → simple + energy

Anabolism [synthetic] – conversion of a small number of simple compounds to complex organic molecules, usually requiring energy.

Simple + energy → complex.

Expectations:

- Input and output of each pathway
- Overall energy and carbon flow
- Regulation.

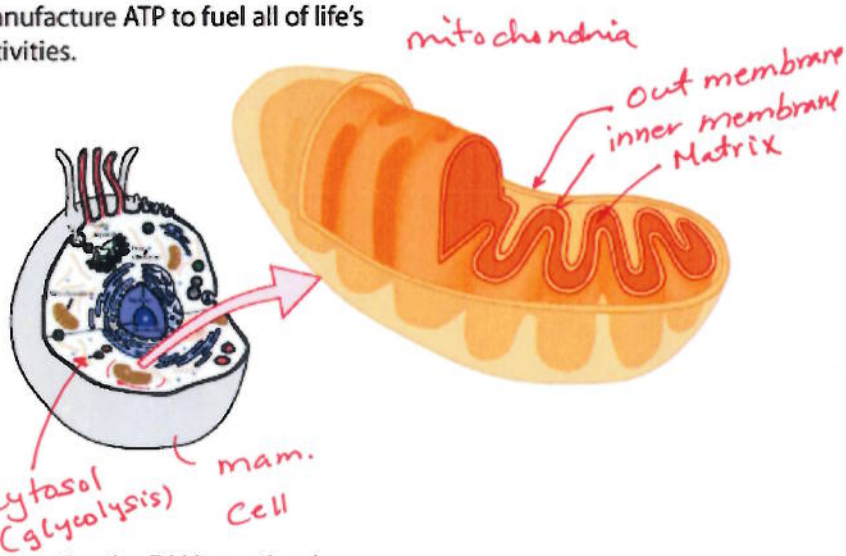


Central Pathways of Energy Production:

Intracellular locations:

- **Glycolysis** - cytosol
- **Citric Acid Cycle**: Inner matrix of mitochondria (also called the Krebs cycle or the TCA cycle.
- **Electron transport**: Inner membrane of mitochondria.
- **ATP synthesis**: Inner membrane of mitochondria

The cell's energy factories, the mitochondria manufacture ATP to fuel all of life's activities.



Energy Currency:

Stored in the following ways:

- Redox compounds (NADH, $FADH_2$)
- Membrane potentials (concentration gradient and voltage difference across a membrane)
- "High energy" chemical species (ATP, and sometimes GTP):

Energy Utilization:

- Chemical synthesis reactions (e.g. protein synthesis, DNA synthesis
- Mechanical work (e.g. transport, muscle function, kinesins in mitosis)
- Electrical work (e.g. nerve conduction)

$ATP \longrightarrow ADP + P_i + energy$

high levels of ADP ⇒ need to make more ATP

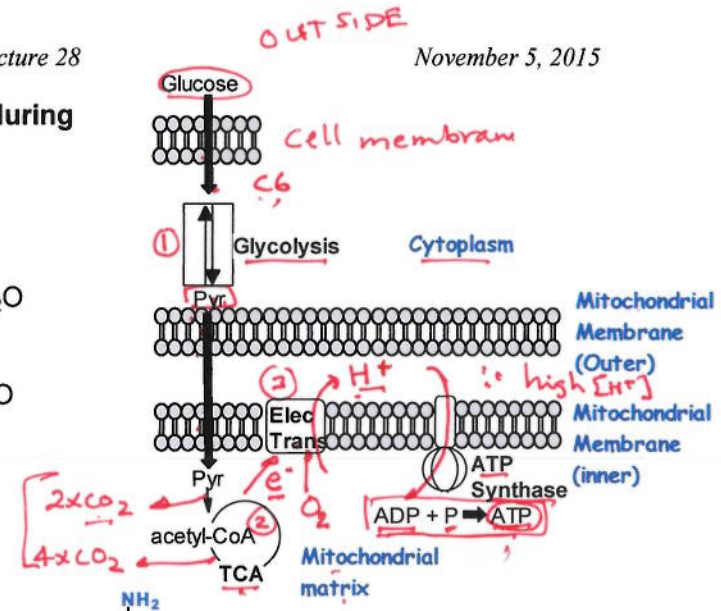
Overall Carbon & Energy Interconversion during metabolism of glucose:

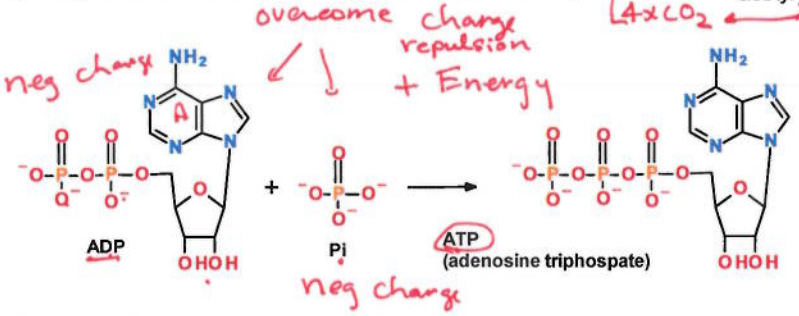
Overall Reaction: $C_6H_{12}O_6 + 6\ O_2 \rightarrow 6CO_2 + 6\ H_2O$ + Energy (ATP) $\Delta G^\circ = -2823$ kJ/mol

Glycolysis + Citric Acid Cycle: $C_6H_{12}O_6 + 6H_2O \rightarrow 6CO_2 + 24H^+ + 24\ e^- + 4ATP$

Electron Transport: $6O_2 + 24\ H^+ + 24\ e^- \rightarrow 12\ H_2O$

ATP synthesis (oxidative phosphorylation):
Proton gradient + ADP & $P_i \rightarrow$ ATP
(Enzyme is called ATPase, or ATP synthase)





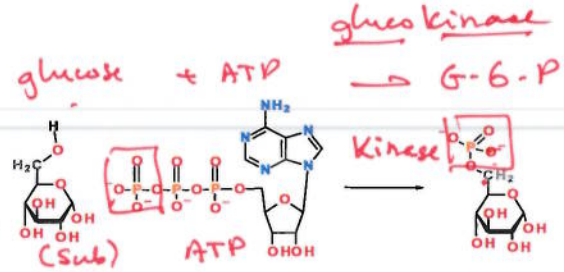
General Enzyme Nomenclature:

Name - usually consists of three parts:

i) the substrate is usually used to name the enzyme. e.g. glucose kinase

ii) the nature of the chemical reaction.

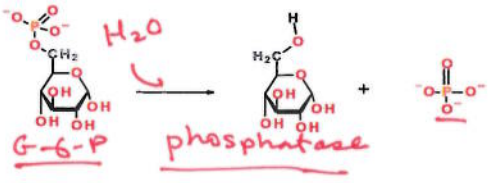
iii) most names end in *"-ase"*



Common Enzymes Involved in Metabolism:

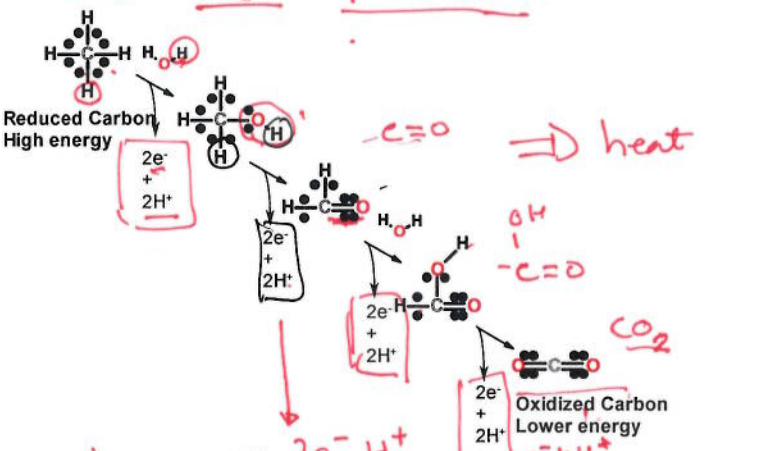
Kinase: transfers a phosphate group from ATP to another compound (e.g. glucose kinase).

Phosphatase: Removes a phosphate group from a substrate, no ATP/ADP required (e.g. phosphoglucose phosphatase).



Dehydrogenase (redox reactions):

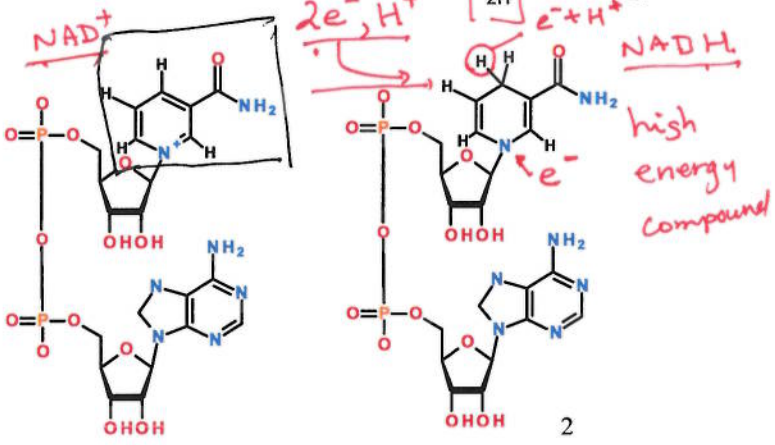
- Oxidizes or reduces compounds by removal or addition of electrons.
- Usually two electrons are removed/add at a time, often transferred with a proton (e.g. $H^+ + e^-$)
- Oxidation is usually accompanied by the addition of oxygen to the compound (but there are exceptions)
- **Oxidation generally releases energy as electrons are pulled towards the more electronegative oxygen.**



OILRIG:

- oxidation involves loss
- reduction involves gain.

- Electrons (and energy) are captured by organic electron carriers:
  - **NAD^+ converted to NADH**
  - FAD converted to $FADH_2$



electron acceptors

high energy

C → oxidized → stored energy as NADH $FADH_2$