Lecture 27: Introduction to Metabolism

Key Points

- Catabolism
- Anabolism
- Glycolysis
- Fatty acid metabolism
- Citric acid (TCA, Krebs) cycle
- ATP energy content
- Electron transport
- Enzyme nomenclature
- Redox reactions.

Metabolic pathways are:

1. Conserved in different organisms.
2. Overall irreversible (but most of the individual steps are not)
3. Consist of a number of small changes.
4. Usually committed after the initial steps
5. Regulated (usually at initial step(s))
6. Compartmentalized in eukaryotes

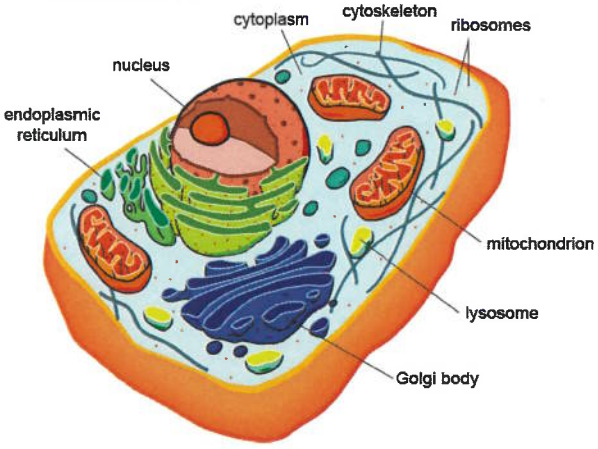
Catabolism [degradative] – conversion of a diverse set of compounds to a small number of simple compounds for energy production.

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

Central Pathways of Energy Production:

Intracellular locations:

- Glycolysis - cytosol
- Fatty Acid Oxidation: Inner matrix of mitochondria
- Citric Acid Cycle (TCA): Inner matrix of mitochondria
- Oxidative Phosphorylation: Inner membrane of mitochondria



Energy Transactions: Organic compounds (e.g. glucose) → Electron Carriers→Proton Gradient → ATP

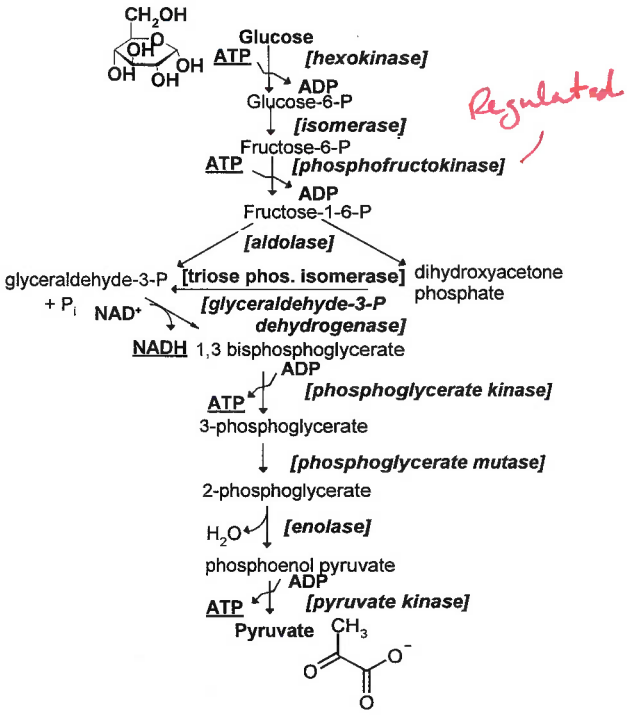
Energy Utilization:

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

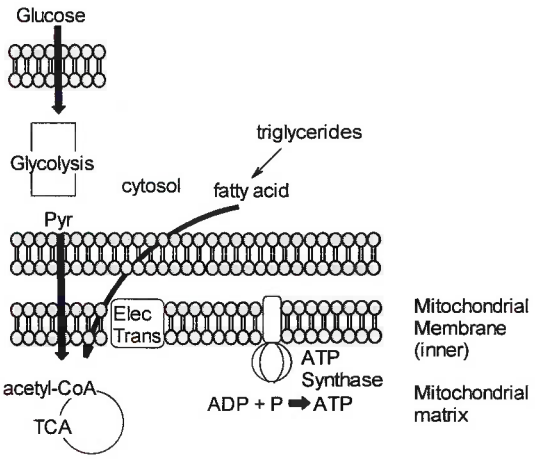
What you need to know:

1. Input and output metabolites
2. Steps that control flux
3. How flux through pathway is controlled
4. Cellular location of metabolic steps
5. Selected enzyme mechanisms
6. Selected substrates/products

What you should not do: Memorize pathways.



Regulated



Enzyme Nomenclature (Enzyme Commission)

For example, the tripeptide aminopeptidases have the code "EC 3.4.11.4", whose components indicate the following groups of enzymes:

- *EC 3* enzymes are hydrolases (enzymes that use water to break up some other molecule)
- *EC 3.4* are hydrolases that act on peptide bonds
- *EC 3.4.11* are those hydrolases that cleave off the amino-terminal amino acid from a polypeptide
- *EC 3.4.11.4* are those that cleave off the amino-terminal end from a tripeptide

Common Names:

Name - usually consists of three parts:

i) the substrate is used to name the enzyme,
Keep in mind that many enzymatic reactions run in both directions in metabolism, consequently the "product" may be used to name the enzyme.

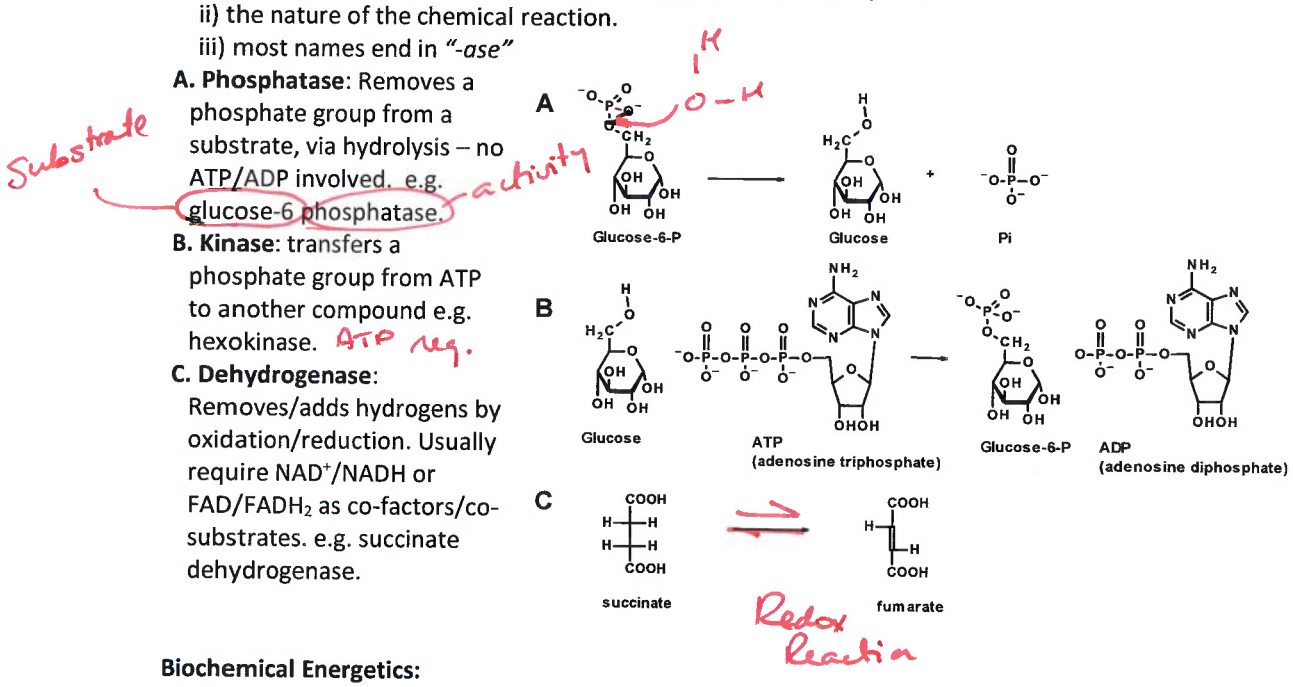
ii) the nature of the chemical reaction.

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

A. Phosphatase: Removes a phosphate group from a substrate, via hydrolysis – no ATP/ADP involved. e.g. glucose-6 phosphatase.

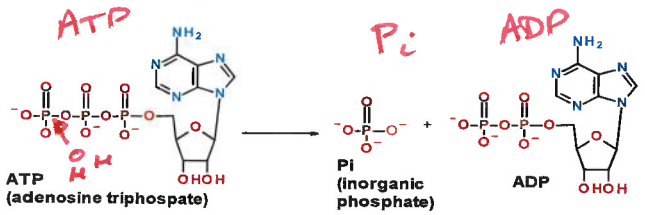
B. Kinase: transfers a phosphate group from ATP to another compound e.g. hexokinase.

C. Dehydrogenase: Removes/adds hydrogens by oxidation/reduction. Usually require NAD^+/NADH or $FAD/FADH_2$ as co-factors/co-substrates. e.g. succinate dehydrogenase.

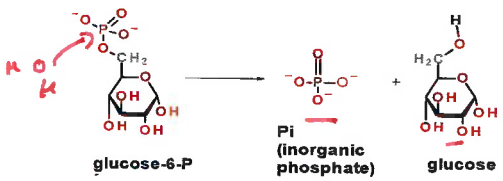


Biochemical Energetics:

1. Phosphate Hydrolysis: Consider the following two reactions:



$\Delta G^\circ = -30$ kJ/mol.



$\Delta G^\circ = -15$ kJ/mol.

Reflection: *Explain the difference between ΔG° of hydrolysis for ATP and G-6-P.*

most of the difference is electrostatic repulsion