WEEK ONE

Enzymes

- ➢ Function as catalysts to speed up rxns
- ➢ Can catalyse the rxns of 1000s of substrate molecules every second
- ➢ Often require a cofactor for correct functioning
- ➢ Usually are involved with a series of complex rxns
- ➢ $E + S \rightleftharpoons ES \rightleftharpoons EP \rightleftharpoons E + P$
- ➢ Enzymes enhance reaction rates by lowering activation energies
- ➢ Enzymes do not affect the equilibrium of a reaction (and thus can be bidirectional)
- ➢ Factors affecting activity of enzymes:
  - Amount of enzyme > rate of transcription
  - Catalytic activities of enzyme > allosteric control, feedback inhibition, covalent modification or proteolytic cleavage
  - Accessibility of substrates > into cells or subcellular compartments

Allosteric control of enzymes

- ➢ Allosteric control is the regulation of an enzyme by a regulatory molecule that interacts at a site (allosteric site) other than the active site (at which catalytic activity occurs)
- ➢ Can be either +ve or -ve; that is stimulatory or inhibitory

Feedback inhibition of Enzymes

- ➢ = the inhibition of the first irreversible (committed) rxns in a linear pathway

Zymogens

- ➢ Inactive precursors that become active following cleavage
- ➢ Often involved in pathways mediating digestion, blood coagulation, immune responses and cell death

Energy for organisms

- ➢ Required for;
  - Mechanical work in muscle contractions and cellular movements
  - Active transport of molecules and ions
  - Synthesis of macromolecules and other molecules from single precursors
- ➢ Basic principles underlying energy flow
  - Fuels are degraded and large molecules are constructed in a series of rxns (metab path)
  - ATP links energy releasing pathways with energy requiring pathways
  - Oxidation of carbon fuels powers ATP formation
  - Metab path are highly regulated and compartmentalised
- ➢ Three forms of energy

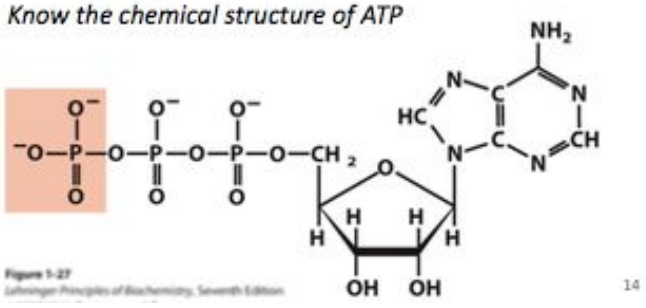
- 1. Energy carriers >> which contain one or more energy rich covalent bond
- 2. Macromolecules >> highly reduced molecules, large branched polysacc, fatty acids, sugars and fats both of which are degraded into acetyl-CoA in the mitochondria
- 3. Electrochemical gradients >> electrical force (membrane potentials) or chemical force (ion concentration)

Metabolism

- Highly coord cellular activity in which multi-enzyme systems cooperate to;
  - Obtain energy via the degradation of energy-rich nutrients
  - Convert nutrient molecules to cells own molecules
  - Polymerise monomers to polymers
  - Synthesis and degrade biomolecules
  - Maintain distinctive composition of different cell compartments
- Catabolic = breaking down into useful molecules
- Anabolic = building molecules which are useful to the body from the building blocks
- Flow of e'
  - Ultimately responsible for all work done in living organisms
  - Source of electrons is food or stored molecules (reduced compounds) in non-photosynthetic organisms
  - E' move from a range of metabolic intermediates to specialised e' carriers

Energy carriers

- Examples; ATP, NADPH, NADH, $FADH_2$, CoA and others
- ATP
  - Most abundant and widely used energy carrier
  - Its breakdown is EXERGONIC >> THEREFORE it is thermodynamically favourable
  - Cells maintain ATP concs far above its conc equilibrium
  - ATP participates in the enzyme catalysed rxn and supplies it with free energy
  - ATP provides energy by transfer of groups (P_i, PP_i or AMP)
  - ATP hydrolysis *per se* is not the source of energy
  - NOTE: learn the structure of ATP



- NADH and NADPH
  - Act as cofactors for many enzymes
  - Act to 'shuttle' electrons and H+ between anabolic and catabolic processes
  - The additional P group on NADPH > has no effect of the e' properties of molecule compared to NADH and allows NADPH to bind to different substrates compared to NADH
  - NADPH is mainly used in synthesis of organic molecules
  - NADH is mainly used in ATP generation
  - Both are derivatives of vitamin B_3 (niacin)

Compartmentation

- Different metabolic pathways occur in different cells and tissues in order to meet the requirements of living

WEEK TWO

Cellular Respiration

- ➢ Process = cells consume O_2 and produce CO_2 as a by-product
- ➢ Provides energy in form of ATP
- ➢ Occurs in three major stages
    - 1. Acetyl CoA production (occurs in cytoplasm)
    - 2. Acetyl CoA oxidation (occurs in the mitochondrial matrix)
    - 3. E' transfer and oxidative phosphorylation (occurs in the inner mitochondrial membrane)
- ➢ One source of acetyl CoA is pyruvate > generated from glycolysis (other sources = AAs and FAs)

Glycolysis

- ➢ Overall rxn = Glucose + $2NAD^+$ + 2ADP + $2PO_4^{-2}$ → 2 Pyruvate + 2NADH + $2H^+$ + 2ATP + $2H_2O$
- ➢ IMPORTANCE
    - For some tissues and cells (brain, kidney medulla and rapidly contracting skeletal muscles glucose is the only source of metabolic energy
    - Pyruvate is a v vertisitile metabolite (useful is several ways)
    - In microorganisms such as brewer's yeast (Saccharomyces cerevisiae) and in certain plant tissues, pyruvate can be reduced to ethanol, again with oxidation of NADH to NAD+. This is termed alcoholic fermentation.
    - Aerobic conditions;
        - pyruvate is oxidised (with loss of the carboxyl group as CO2), and the remaining two carbon unit becomes the acetyl group of acetyl-coenzyme A (acetyl CoA). This acetyl group is metabolised in the TCA cycle (aka citric acid cycle) and fully oxidised to yield CO2.
        - Produces 30-32 ATP molecules per glucose (called the *Pasteur Effect)*
    - Anaerobic conditions;
        - pyruvate can be reduced to lactate through oxidation of NADH to NAD+ - a process termed lactic acid fermentation
        - Produces 2 ATP molecules per glucose (called the *Pasteur Effect*)
- ➢ The flux of glucose through glycolysis is regulated to maintain:
    - Nearly constant ATP levels
    - Adequate supplies of glycolytic intermediates for biosynthesis
- ➢ Oxdia of glucose (started in glycolysis) ultimately leads to production of more ATP through the TCA cycle and oxidative phosphorylation
- ➢ Some tissues and cell types that have no mitochondria cannot oxidise pyruvate to CO_2 and produce lactate from glucose even under aerobic conditions.