__/__/__

Cell (Sreevidya Ma'am)

→ Cell is the structural and functional unit of life

→ Sub cellular organelles:

Nucleus, ER, golgi apparatus, Mitochondria, Lysosome, peroxisome

→ Organelles have specific fn. Specific enzyme activities serve as MARKERS of the organelle during isolation.

• tween-20 + lipid solvent

• lysis carried out in 0.25M sucrose at pH 7.4

★ Albert Claude got Nobel Prize in 1974 for fractionating subcellular organelles

MARKER ENZYMES OF ORGANELLES

Mitochondria	ATP Synthase
Golgi complex	Galactosyl transferase
ER	Glucose-6-phosphatase
Lysosome	Acid phosphatase

• NUCLEUS

→ Absent in RBC (uppermost layer of skin also may not posess readily identifiable nucleus)

• small lymphocytes & spermatozoa → nucleus occupies most of the space

→ Nuclear membrane contains numerous pores of abt 90nm in diameter

→ Major sub compartment Nucleolus

★ Gabriel Valentine in 1836 described the nucleolus

→ Fn: • Replication, Repair of DNA

• Synthesis and processing of RNA's

• ENDOPLASMIC RETICULUM

→ A network of interconnecting membrane that are continuous from the nuclear envelope to plasma membrane

→ It has role in protein synthesis and many synthetic pathways

• SER → Synthesis of lipids and steroids

→ site of drug metabolism

• RER → protein synthesis

• GOLGI APPARATUS

→ Is a network of flattened smooth membrane sacs → cisternae

→ fns: • Involved in secretion, modification and sorting of proteins
• Glycosylation of proteins
• Major site of new membrane synthesis

• MITOCHONDRIA

→ Spherical, oval or rod like bodies

→ Size : 0.2 - 0.8 μm

→ Absent in RBC, intestine, centriole

→ Bilayered

→ Outer mitochondrial membrane (OMM) → smooth IMM → convalutes into folds → crystae

→ 2 compartments : Intermembrane space, matrix

→ Supplies most of the cell's need for ATP

→ IMM contains the ETC (e^- transport chain)

→ Matrix : • Enzyme of TCA cycle
• Beta oxdn of fatty acid

→ Extracellular DNA is found in the matrix of mitochondria

→ fns: • Production of ATP
• Cellular respiration
• Oxdn of carbohydrates and lipids
• Urea and heme synthesis

Clinical Significance:

→ Luft's disease - Defective energy transduction

→ Mt. Myopathies - Oxphos diseases due to mutation in Mt. DNA

→ Parkinson's, cardiomyopathies - age related degenerative diseases

• LYSOSOMES

→ Vesicular str

→ Size : 0.4 μm

→ Surrounded by lipoprotein membrane

→ Acidic pH (~5)

→ contains a grp of hydrolytic enzymes

★ Lysosomes are the cell's garbage disposal system

→ It recycle materials by breaking down worn-out parts of a cell into smaller units

→ They deliver these materials to the cytoplasm for use in constructing new proteins

→ If the membrane of lysosome breaks, the enzyme released may also destroy the cell itself, giving lysosomes the name suicide bags

→ Fns: • Cellular digestion

• Hydrolysis of carbohydrates, protein, lipids and nucleic acids

Clinical aspects:

→ Lysosomal storage disorders

→ Inclusion cell disease - a protein targeting defect – accumulation of undergraded molecules - inclusion bodies

→ Gout - Urate crystals are phagocytosed and cause physical damage of lysosomes releasing enzymes producing inflammation and arthritis

• PEROXISOMES

→ Diverse grp of organelles found in eukaryotic cell

→ they are named so because they play unique role in Hydrogen Peroxide metabolism

→ Contains enzymes that use molecular oxygen to remove H_2 atoms from specific substrates

$$RH_2 + O_2 \longrightarrow R + H_2O_2$$

→ Hydrogen peroxide is used up or detoxified
→ Catalases in peroxisome convert this H_2 peroxide to water

$$2H_2O_2 \longrightarrow 2H_2O + O_2$$

→ fns: • Imp role in lipid metabolism
• Metabolism of free O_2 radicals
• Synthesis of cholestrol and ether lipids
• Bile acid formation
• Catabolism of purines, prostaglandins
• Alcohol detoxification in liver
• Metabolism of estradiol

Clinical Significance:
• Peroxisomes indirectly linked to human conditions such as obesity, heart disease, diabetes and certain cancers
• Peroxisomal disorders
→ The Zellweger syndrome
→ Refsum's disease
→ Hyperoxaluria

• CYTOSOL
→ Organelle free sap
→ No specific str
→ Rich in proteins
→ Supports synthesis of proteins on ribosome which are free or bound to ER by supplying the cofactor and energy.
★ Enzymes of hydrolysis, fatty acid synthesis

• STR OF MEMBRANE
→ Trilaminar appearance
→ width: 50-80A°

- LIPIDS → Phospholipids, Glycospingolipids and cholesterol
- PROTEINS → Peripheral proteins and integral membrane proteins
- CARBOHYDRATES → Glycoproteins or glycolipids

__/__/____

→ Dynamic nature
→ Amphipathetic
→ membranes are asymmetrical
→ Irregular distribution of proteins
→ The carbohydrates are located exclusively on the outside (ectoenzyme) and inside the membrane
→ Composed of lipids, proteins and carbohydrates

Lipids (Swedha mabm)

→ heterogenous grp of compd which are relatively insoluble in water, but soluble in non-polar organic solvents such as benzene, ether, acetone, chloroform etc

→ Fns:
- Sources of energy (9 Kcal/g) - storage form of energy is Triacyl glycerol
- Structural components of biomembrane (phospholipids & cholestrol)
- Metabolic regulators (steroid hormones & prostaglandin)
- Act as electric insulators in neurons
- Act as surfactants, detergents and emulsifying agent

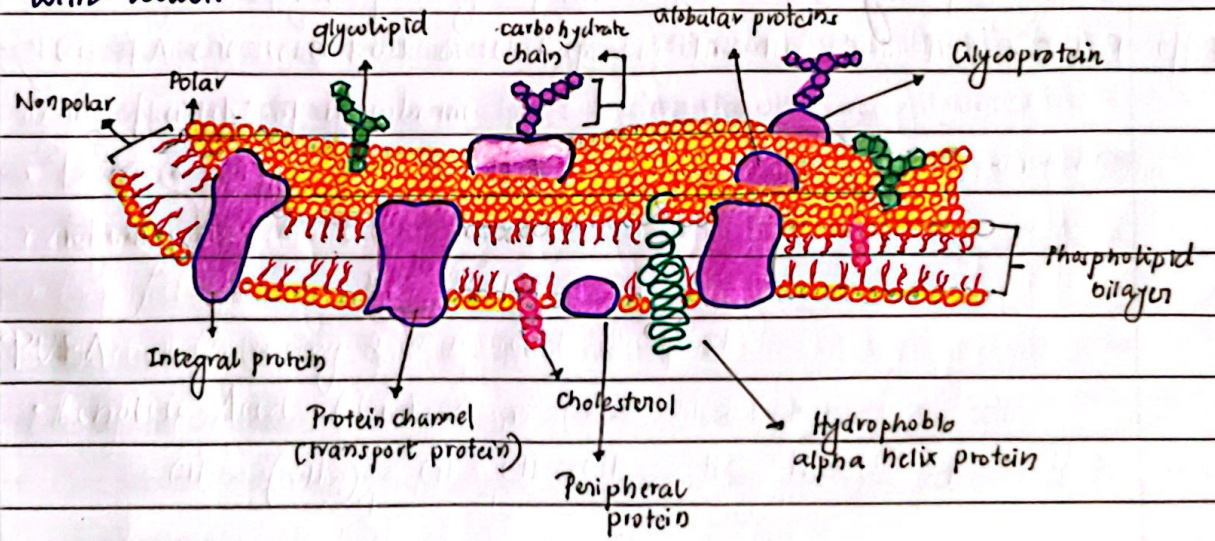
- Hypercholesterolemia

Str of Membrane

- Davson and Danielle (1935)
  ↓
  Lipid bilayer

FLUID MOSAIC MODEL (By Singer & Nicolson in 1972)

→ The phospholipids are arranged in bilayer with polar head grps oriented towards the outside and the hydrophobic tails towards b/w the bilayer
→ The proteins are either on the surface or span the lipid bilayer
→ The hydrophobic lipids and protein are arranged to minimise the interaction with water.



__/__/____

→ Fluid mosaic model shows free lateral movement
→ No flip-flop movement
** * Fluidity of plasma membrane is proportional to conc. of cholesterol and fatty acids

• Peripheral proteins
→ Exists on the surface of the membrane
→ Do not interact directly with the phospholipids
→ They r weakly bound to the hydrophilic region of integral proteins

• Integral membrane proteins
→ Commonest
→ Interact extensively with the phospholipids
→ Embedded or span the entire distance of membrane
→ Attached by hydrophobic bonds or vandrn walels force

Functions of Plasma membrane
→ Protective sheath
→ Selective transport of ions and molecules (selective permeability)
→ Recognition of various stimuli
→ Contain receptors for biomolecules like hormones, neurotransmitters etc
→ Maintenance of shape of cell
→ Cell motility

__/__/__

EXTRA CELLULAR MATRIX

(Sreevidhya Ma'am)

→ Constitutes the non-cellular component of all tissues and organs

→ Imp role in the development, differentiation and maintenance of the tissue and organ

GAGs → Glycosaminoglycan

→ Major components are water, proteins and polysaccharides

→ The two main components are proteoglycan (GAGs + Protein) and fibrous proteins (collagen, elastin, fibrillin and fibronectin, an adhesive protein)

COLLAGEN

→ Major structural protein in connective tissue

→ Very strong and tensile protein

→ Made up of 3 polypeptide chains

↳ These 3 polypeptide chains are wound into a right handed superhelix (triple helix) forming a rod like str.

→ Every 3rd amino a is glycine

→ contain proline, hydroxy proline and hydroxy lysine in good proportion

→ The repetitive amino acid sequence represented as $(Gly\text{-}X\text{-}Y)_n$.

Intracellular synthesis of collagen

→ The collagen is synthesised by fibroblasts as a large precursor intracellularly, called procollagen

→ Hydroxylation of proline and lysine residues (post-translation modification) by propyl hydroxylase and lysyl hydroxylase, required vit C & α-KG as cofactors

α-KG → α-Ketoglutarate

→ Glycosylation of hydroxy lysine occurs

Extracellular synthesis

→ After the synthesis, procollagen is then secreted outside the cell

→ The extra cellular procollagen is cleaved by specific peptidases to form tropocollagen

__/__/____

→ Multiple tropocollagen molecules assemble into collagen fibres.
→ Collagen fibres are arranged in a 'quarter staggered array'
→ The collagen fibres are strengthened by covalent cross-links b/w lysine and hydroxy lysine residues
→ The cross-links are formed by lysyl oxidase, a copper containing enzyme

→ Fn: - Type II is mainly seen in cartilage and vitreous humor
- Type III is in skin, lung and vascular tissues
- Type IV is seen in the basement membrane
- Give support to organs → Main fn
- Help in proliferation and differentiation of cell.

ELASTIN

→ Protein in connective tissue
→ Major component of elastic fibres
→ Allows many tissues in the body to resume their shape after stretching or contracting → fn
→ Composed of protein fibrillin and amino ā such as glycine, valine, alanine, lysine and proline
→ Cross-links are formed from 4 lysine residues (in presence of lysyl oxidase)
→ Found in ligaments and in the walls of blood vessels (Eg aorta)

1. Osteogenesis imperfecta
→ AKA 'brittle bone disease'
→ Abnormality in collagen str
→ Due to genetic mutation in single amino ā
→ Here glycine is replaced by cysteine in the polypeptide chain
→ Polypeptides excessively hydroxylated and glycosylated
→ Unfolding of the helix and result in brittle bones

2. Ehlers - Danlos Syndrome

→ The condition results from defective type III collagen formation due to defective lysyl oxidase or lysyl hydroxylase

→ Characterised by weakening of collagen, loose skin

3. Marfan Syndrome

→ The disease is produced by a defect in the gene, coding for connective tissue protein, fibrillin 1.

→ It is a component of microfibrils, which normally gives the substraction for deposition of elastin

→ If fibrillin and elastin are deposited at lower conc.

CONTRACTILE PROTEINS

→ The myofiber is the functional unit of skeletal muscle and is multinucleated

→ The cytoplasm (sarcoplasm) of a myofiber contains a regular array of contractile units - comprised of actin (thin filament) and myosin (thick filament)

MYOSIN

→ The myosin molecules are large, each with 6 polypeptide chains; 2 identical heavy chains and 4 light chains

→ Myosin molecule assemble into filaments

→ Myosine acts as the enzyme ATPase

→ Myosine binds to actin polymer

→ Sliding and shortening of actin and myosin is the basis of muscle contraction

→ During muscle contraction, myosin moves over actin filaments

ACTIN

→ It is the major protein of the thin filaments

→ It can polymerize into fibrous form, called F-actin, which is a helix of actin monomer

→ The muscle contraction results from the interaction of the actin and myosin, to form actomyosin with energy provided by ATP