Chapter

3

eSmartQuiz

Cell and Tissue

Chapter Outline

- Plasma membrane
  - Modified fluid-mosaic model
  - Functions
- Transport across plasma membrane
- Endoplasmic reticulum (ER)
- Golgi complex
- Mitochondria
- Ribosomes
- Lysosomes
- Lysosomal storage diseases
- Peroxisomes
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  - Nucleoplasm
  - Chromatin
  - Nucleolus
- Tissue
  - Definition
  - Classification

CELL

Introduction

- Cell is basic structural and functional unit of all organisms.
- Human tissue consists of *eukaryotic cells* that have nucleus, cell organelles, and cytoplasm (Note: prokaryotic cells/unicellular organisms do not have membranous nucleus and membranous cell organelles).
- Each cell is bounded by a cell/plasma membrane that encloses *protoplasm.*
- Protoplasm consists of a nucleus and cytoplasm.
- Cytoplasm consists of gel-like matrix called *cytosol/hyaloplasm,* cell organelles, cytoskeleton, and inclusions. Cytoskeleton consists of microtubules, intermediate, and actin filaments.
- Cell organelles are grouped as membranous (membrane-limited) and nonmembranous-bound (Fig. 3.1).
- *Membranous-bound organelles* include plasma/cell membrane, rough endoplasmic reticulum (rER), smooth-surfaced endoplasmic reticulum (sER), Golgi apparatus, endosomes, lysosomes, pinocytic vesicles, endocytic vesicles, mitochondria, and peroxisomes.
- Membranes of intracellular organelles increase intracellular surface area and create intracellular microcompartments for proper physiological functions.
- *Nonmembranous organelles* include microtubules, filaments (actin and intermediate filaments), centrioles, ribosomes, and proteasomes.
- Various cell organelles and their functions are listed in Table 3.1.

PLASMA MEMBRANE (CELL MEMBRANE)

- Plasma membrane is also called cell membrane or *plasmalemma.*
- It separates intracellular compartment from extracellular compartment of the tissue.
- Plasma membrane is a dynamic structure. It consists of an amphipathic lipid bilayer, integral membrane proteins, and peripheral proteins (Fig. 3.2).

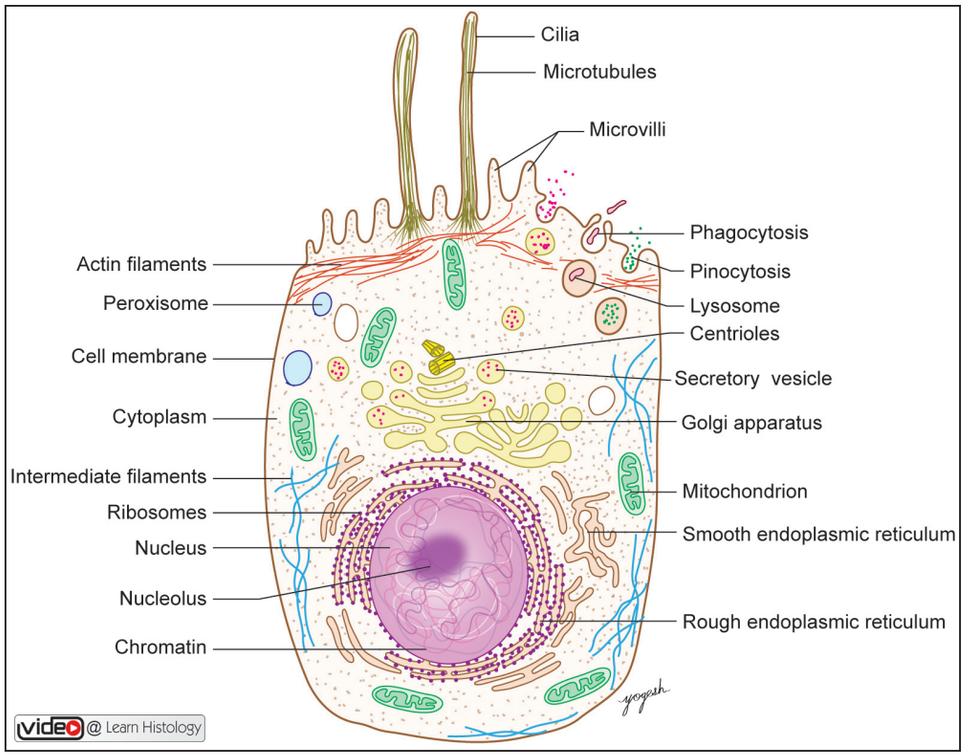

Fig. 3.1: Cell and cell organelles (practice figure).

Table 3.1: Cell organelles and functions *viva*

Cell organelles	Functions	Remarks/characteristics
Plasma membrane	Selective barrier, cell adhesion	Bilipid layer
rER	Synthesis and transfer of proteins to Golgi complex	Flattened sheets with attached ribosomes
sER	Lipid and steroid metabolism	Flattened sheets without ribosomes
Golgi apparatus	Posttranslational modification of proteins	Flattened sheets
Secretory vesicles	Transport and storage of secretory proteins	Small membrane-bound vesicles
Mitochondria	Power house of cell	Outer and inner membranes
		Inner membrane shows cristae (folds)
Lysosomes	Disintegration of phagocytosed material	Membrane-bound vesicles
Peroxisomes	Oxidation of fatty acids, detoxification	Membrane-bound vesicles
Ribosomes	Protein synthesis	Have 40S and 60S subunits

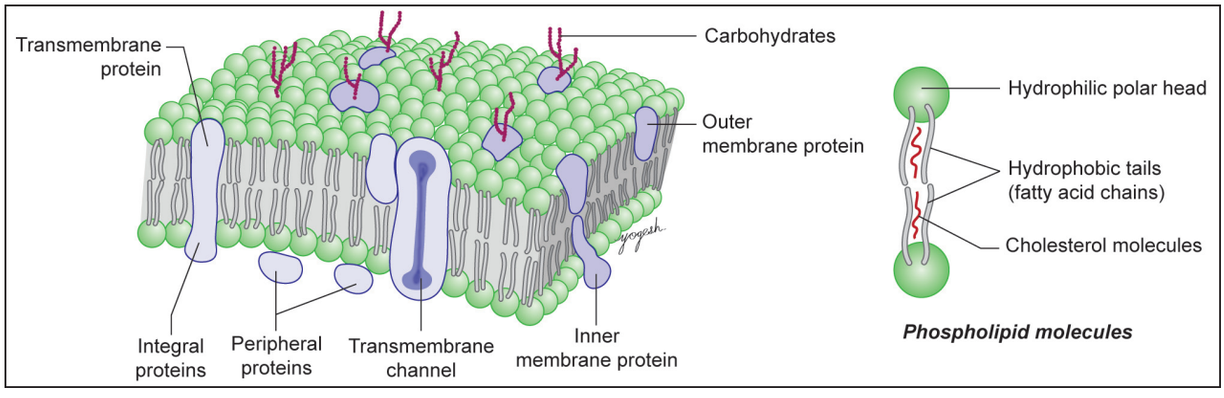

Fig. 3.2: Structure of cell membrane.

Modified Fluid-Mosaic Model
(Singer and Nicolson, 1972):

- Transmission electron microscopy (TEM): On TEM examination, plasma membrane consists of two electron-dense layers separated by middle electron lucent layer (Fig. 3.2).
- Thickness is ~8–10 nm.

Lipids of Plasma Membrane

- Plasma membrane has three types of lipids: phospholipids, cholesterol, and glycolipids.
- *Phospholipid* molecules have polar hydrophilic end/head and nonpolar hydrophobic end/tail. The head consists of choline, phosphate, and glycerol. Nonpolar end consists of two fatty acid chains.
- Hydrophilic ends face toward extracellular and intracellular surfaces.
- *Lipid rafts* are microdomains of the plasma membrane. It consists of high concentration of cholesterol and glycolipids.*Viva*
- Lipid rafts also contain integral and peripheral membrane proteins that are involved in cell signaling.
- *Freeze fracture:* It is a method of tissue processing for electron microscopy. On freeze-fracture, cell membrane shows *E-face* (backed by extracellular compartment) and *P-face* (backed by protoplasm/cytoplasm). This method is useful for identification of integral proteins of cell membrane.

Proteins of Plasma Membrane

- Plasma membrane has two types of proteins: integral membrane proteins and peripheral membrane proteins.
- *Integral proteins* are confined within the plasma membrane and cross the entire or partial thickness of the cell membrane, whereas *peripheral proteins* are confined only on the surfaces of plasma membrane.
- Integral proteins form pumps (Na^+ pump), channels (gap junctions), receptor proteins, linker proteins (anchor cytoskeleton), enzymes (ATPase), and structural proteins.
- Integral proteins can move within the lipid bilayer.

Carbohydrates of Plasma Membrane

- Carbohydrates of plasma membrane form glycoproteins and glycolipids.
- They form *glycocalyx coat* on the outer surface of the plasma membrane.
- They help cell to interact with extracellular environment, cell recognition, cell adhesion, and metabolism.*Functional Correlation*
- Glycocalyx also forms major histocompatibility complexes (MHC) and blood group antigens on RBCs.*Neet*

Functional Correlation of Plasma Membrane

- *Selective barrier*: Plasma membrane limits the mobility of the substances across it.
- *Protection*: Plasma membrane isolates the intracellular environment from extracellular environment.
- *Cell shape/adhesion*: Plasma membrane anchors the cytoskeleton and provides attachment with adjacent cells and basement membrane to provide a particular shape to the cell.
- *Polarity*: Plasma membrane maintains ionic polarization and respond to stimuli by depolarizing.
- *Receptors*: Plasma membrane has receptors for specific molecules (hormones).
- *Transport*: Plasma membrane help in transport across it by endocytosis, exocytosis, pinocytosis, and so on.

TRANSPORT ACROSS PLASMA MEMBRANE

Selective substances can enter or leave the cell through the plasma membrane. These substances follow one of the following modalities of transport (Fig. 3.3).

1. Passive transport
2. Active transport
3. Vesicular transport.

Passive Transport

- For passive transport, energy is not required for transport of substances across plasma membrane. It can take place by simple diffusion or facilitated diffusion (Fig. 3.3).
- *Simple diffusion*
  By simple diffusion, lipid-soluble and uncharged molecules cross plasma membrane from higher to lower concentration.
  For example, oxygen, carbon dioxide, glycerol, and so on.
- *Facilitated diffusion*
  In facilitated diffusion, *channel/carrier proteins* or channels of the plasma membrane help in transport of certain small and water-soluble molecules.
  Carrier proteins move across the plasma membrane and help in the transport of small, water-soluble molecules.
  Channel proteins are transmembrane (integral) proteins. They have pore domain that regulates entry or exit of substances.

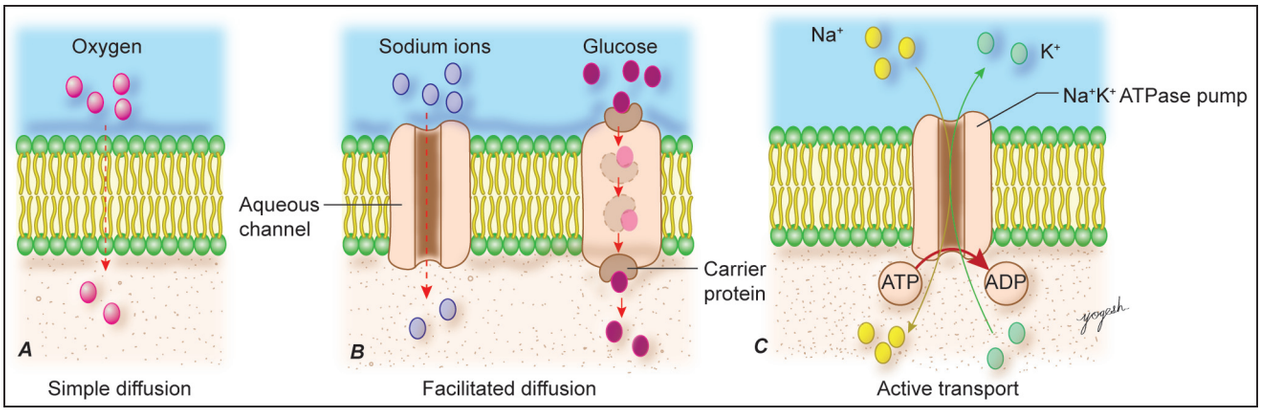

Fig. 3.3: Transport across the cell membrane. (A) Simple diffusion, (B) Facilitated diffusion, (C) Active transport.

Channel proteins are:

- *Voltage-gated ion channels* regulated by membrane potentials
- *Ligand-gated ion channels* regulated by neurotransmitters
- *Mechanical-gated ion channels* regulated by stress (hair cells in internal ear).

Active Transport

- The transport of molecules across the plasma membrane against the concentration gradient requires energy (ATPs). Such transport of molecules is called active transport.
  For example, sodium pump for Na^+ ion transport.

Vesicular Transport

- Large molecules are transported with vesicular transport across the plasma membrane.
- It is of two types: Endocytosis and exocytosis.
- *Endocytosis*
  In endocytosis, the extracellular molecules are brought inside the cell as membranous vesicles.
  Endocytosis may be pinocytosis, phagocytosis, or receptor-mediated endocytosis (Fig. 3.4).
  Pinocytosis (*cell drinking*, in Greek): In pinocytosis, cell ingests liquid and forms pinocytic vesicles.
  Phagocytosis (*cell eating*, in Greek): In phagocytosis, cell ingests large substances such as cell debris, bacteria, and so on and forms large phagocytic vesicles (phagosomes).
  Receptor-mediated endocytosis: Specific molecules (ligand) enter cell with the help of receptor-mediated endocytosis. For example, peptide hormones.
- *Exocytosis*
  In exocytosis, molecules covered in a vesicle is expelled out of the cell through the plasma membrane (Fig. 3.5).

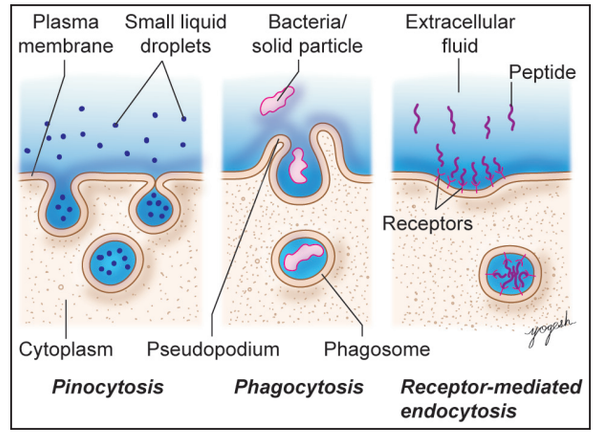

Fig. 3.4: Modalities of endocytosis.

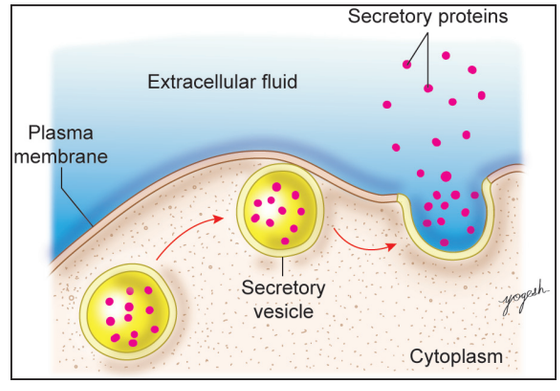

Fig. 3.5: Modalities of exocytosis.

There are two types of exocytosis:

1. Constitutive pathway: In this process, substance is exocytosed immediately after its synthesis. For example, secretion of immunoglobulins.
2. Regulated pathway: In this process, substance is stored temporarily in vesicle after its synthesis in cytoplasm and exocytosed on extracellular signaling. For example, zymogen granules secretion.

CELL ORGANELLES

- Cytoplasm contains numerous structures that perform various functions. These are called cell organelles.
- Cell organelles are grouped as follows:
  1. Membranous cell organelles: Endoplasmic reticulum, Golgi complex, mitochondria, phagosomes, lysosomes, peroxisomes, exocytic vesicles.
  2. Nonmembranous cell organelles: Cytoskeleton elements (microfilaments, microtubules, intermediate filaments).

Endoplasmic Reticulum (ER)

- Endoplasmic reticulum (ER) is a network of interconnecting membranes that form cisternae (Fig. 3.6).
- The cytoplasm enclosed within the cisternae of endoplasmic reticulum is *vaculoplasm*, whereas the rest of the cytoplasm is hyaloplasm/cytosol.
- There are two varieties of ER: Rough-surfaced ER (having coating of ribosomes) and smooth-surfaced ER (without ribosomes).

Rough-surfaced Endoplasmic Reticulum (rER)

- Ribosomes are present on the surface of rough endoplasmic reticulum (Fig. 3.6).
- As ribosomes contain RNA, they give basic (hematoxylin) staining to the cell.[Practical guide] *Ergastoplasm* is the portion of cytoplasm that stains with basic dyes.
- Ribosomes are attached on outer surface of rER by *ribosome docking proteins.*

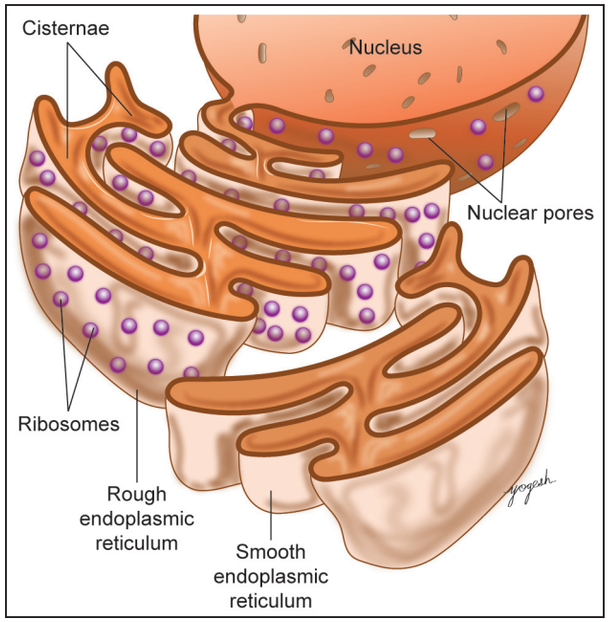

Fig. 3.6: Endoplasmic reticulum.

- Mostly, rER is continuous with outer nuclear membrane.
- The mRNA binds with many ribosomes to form polyribosome complex or *polysome*.
- Newly synthesized proteins have signal sequences/peptides that direct the protein to get transferred to its destination site within the cell.
- Newly synthesized protein enters the lumen/cisternae of rER and undergoes posttransitional modifications such as glycosylation, folding, and so on. Later, modified proteins are delivered to the Golgi apparatus.
- Clinical fact: In *emphysema*, there is an inability of rER to deliver the synthesized enzyme α-1 antitrypsin to Golgi apparatus that results in *α-1 antitrypsin deficiency.*[Neet]
- The rER is predominantly present in active protein secretory cells such as serous cells in the pancreas and salivary glands.
- Note: Free ribosomes synthesize cytoplasmic, structural and functional elements. For example, hemoglobin synthesis in precursor cells of RBCs, contractive protein synthesis in developing muscle.
- The rER and free ribosomes produce Nissl bodies in neurons and cytoplasmic basophilia in other secretory cells.[Practical guide]

Functional Correlation of rER

- *Protein synthesis*: Site for translation (mRNA → proteins)
- *Checkpoint*: rER destroys defective proteins.

Smooth-surfaced Endoplasmic Reticulum (sER)

- Smooth-surfaced endoplasmic reticulum consists of short anastomosing tubules (Fig. 3.6).
- The sER lacks ribosome docking proteins, hence they do not have ribosomes.[Viva]
- As sER is not associated with ribosomes, it gives eosinophilic (pink) color to cytoplasm.[Practical guide]

Functional Correlation of sER

- *Lipid metabolism*: sER is the main site for lipid synthesis. They are abundant in cells of liver, cells of adrenal cortex, and Leydig cells of testis.
- *Sarcoplasmic reticulum*: In smooth and cardiac muscles, sER forms sarcoplasmic reticulum that acts as Ca^{++} ion reservoir.
- *Detoxification*: sER is involved in detoxification of drugs and other chemicals.
- Glycogen metabolism.
- Membrane formation and recycling.

Golgi Complex (Camillo Golgi, 1843–1926)

- It is made up of 3–20 flattened curved membranous cisternae (sacs) that forms a shallow cup-like structure.
- It has convex/forming face (*cis-face*) and concave/maturing face (*trans-face*) (Fig. 3.7).
- Its *cis-face* faces toward rER and nucleus, whereas *trans-face* faces toward cell membrane.
- Middle part of Golgi apparatus is called media-*Golgi network.*

Note: *Glogi complex do not stain with H&E stain.* Practical guide

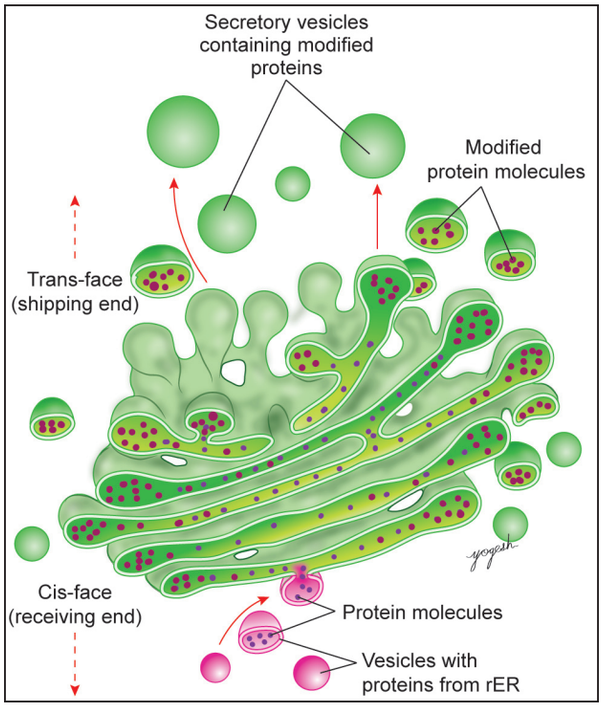

Fig. 3.7: Golgi apparatus.

Functional Correlation of Golgi Complex

- *Posttranslational modification of proteins*: Freshly synthesized proteins are transferred from rER to the Golgi apparatus. These proteins are modified by the Golgi apparatus.
- *Formation of secretory vesicles*: Modified proteins are wrapped around by the membrane of Golgi apparatus and get separated to form membrane-bound secretory vesicles or endosomes or lysosomes.

- Location: Usually, Golgi apparatus is located toward secretory portion (apical portion) of the cell membrane.

Mitochondria

- Mitochondria are *power houses* that generates energy (ATPs).
- Mitochondria are absent in RBCs and terminal keratinocytes of skin. MCQ
- Size: 0.5–2 µm, elliptical-shaped.
- It is bounded by bilaminar membrane (similar to plasma membrane) with intermembranous space and matrix (Fig. 3.8).
- *Outer mitochondrial membrane* is smooth and has voltage-dependent anion channels called *mitochondrial porins*.
- Inner mitochondrial membrane shows folding called *cristae* (for increasing surface area).
- Inner mitochondrial membrane is impermeable to ions due to its cardiolipin phospholipids. It is a site for oxidation reactions, respiratory electron transport chain, and ATP synthesis. It has tennis racket-shaped elementary (F1) particles. Heads of these particles carry out oxidative phosporylation to generate ATP.

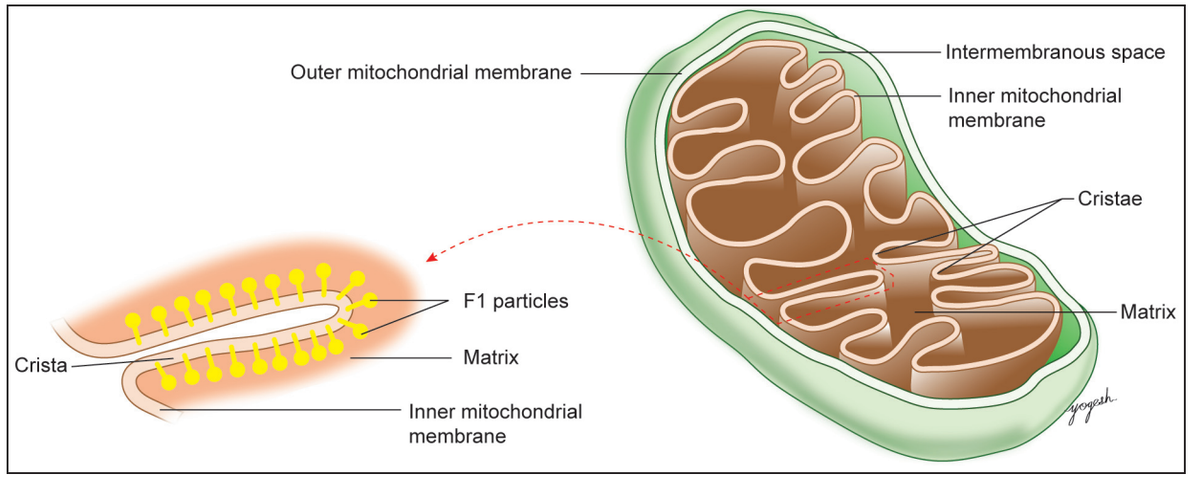

Fig. 3.8: Mitochondrion.

- *Mitochondrial matrix* contains enzymes of Krebs cycle and fatty acid β-oxidation, Ca^{++} storing matrix granules, mitochondrial DNA, and so on.
- *Mitochondrial DNA* is a small circular double helix DNA that contains 37 genes.[MCQ]
- Mitochondrial DNA is inherited from mother (ooplasm of ovum), as cytoplasm of sperm do not contribute to zygote.[Neet]
- Due to mitochondrial DNA, mitochondria are self-replicating.
- Life span: ~10 days.

Functional Correlation of Mitochondria

1. Powerhouse of cell: Mitochondria produces ATP by aerobic respiration.
2. Self-replication: Mitochondrial DNA helps in certain protein synthesis and replication of mitochondria.
3. Apoptosis (programmed cell death): Mitochondria sense cellular stress and release cytochrome C from intermembranous space into the cytoplasm. This cytochrome C initiates programmed cell death (apoptosis).

- *Mitochondrial cytopathy syndrome*: It is produced by defective mitochondrial DNA. It produces muscle weakness, neurological degenerative lesions, and lactic acidosis.[Neet]
- *Myoclonic epilepsy with ragged red fibers* (MERRF) is produced because of defective enzymes of ATP synthesis. It produces muscle weakness, ataxia, seizures, and cardiac and respiratory failures. Red muscle fibers show accumulation of abnormal mitochondria giving ragged-appearance on microscopic examination.

Ribosomes

[Discovered by *George Emil Palade, 1955*]

- Ribosomes are small cytoplasmic particles (15–20 nm)
- Ribosome consists of two subunits: Small (40S) and large (60S) (Fig. 3.9).

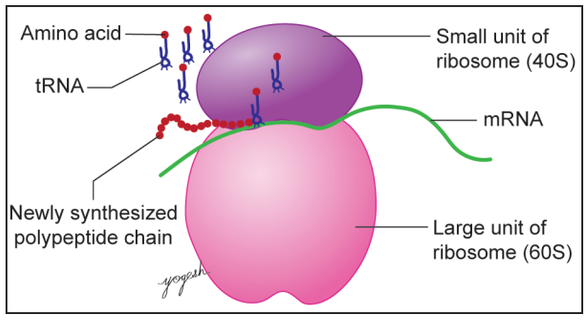

Fig. 3.9: Ribosome.

- Ribosomes lie in association with rER or in freeform in the cytoplasm.
- Polyribosome: It is a cluster of ribosomes bound to a single strand of messenger RNA.
- Ribosome synthesis is controlled by nucleolus (site of rRNA synthesis).
- Nissl bodies consists of both rER and free ribosomes.[MCQ]

Functional Correlation of Ribosomes

Ribosomes synthesize proteins as follows:

- Free ribosomes produce structural proteins of a cell
- Membranous ribosomes (rER) produce secretory proteins.

Lysosomes

- Christian de Duve, 1955 discovered lysosomes (He termed them as *suicide bags*).
- Lysosomes are membranous spherical cytoplasmic vesicles (0.2–0.8 μm in diameter).
- Electron microscopy: Lysosomes are electron-dense bodies.
- Formation: Lysosomes are derived from Golgi apparatus as primary lysosomes (Fig. 3.10).

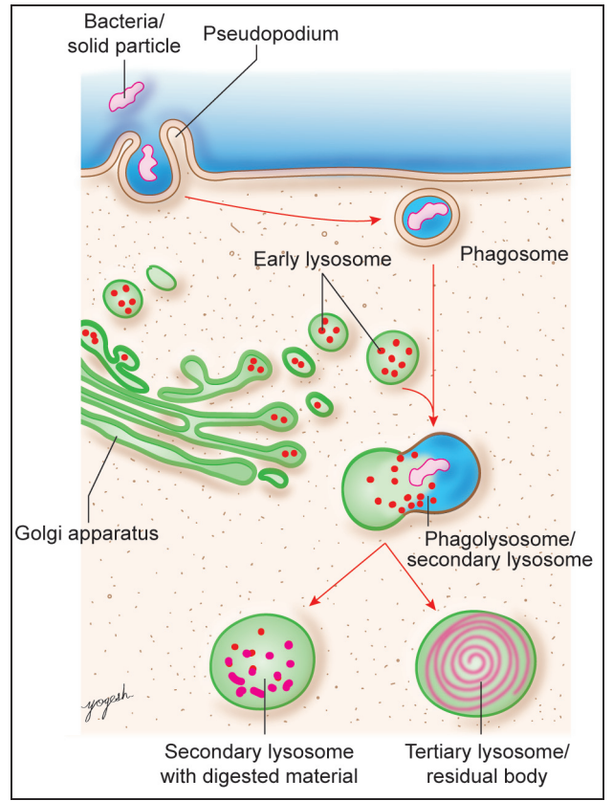

Fig. 3.10: Role of lysosome.

- Primary lysosome fuses with endocytic vesicle that contains material for digestion/destruction and forms secondary lysosome.
- Content: Lysosomes contain hydrolytic enzymes such as proteases, nucleases, glycosidases, lipases, and phospholipases.
- *New concept:* Endosomes receive hydrolytic enzymes from Golgi apparatus to form lysosomes.[Neet]
- Note: Proton (H^+ ion) pumps in lysosomal membrane make the content of lysosome highly acidic (<5 pH).
- Lysosomal membrane has unique lipid lysophosphatidic acid and other proteins. The inner surface of these lipids and proteins are covered by sugar molecules that protect lysosome from its own digestion by lysosomal enzymes.[Viva]
- Recognizable lysosomes in histology[Neet]
  1. Azurophilic granules in neutrophils.
  2. Lipofuscin granules (age pigment) are residual bodies in old cells. They are brown-pigmented granules developed due to lysosomal degradation.[Viva]

Functional Correlation of Lysosomes

- Digestion of foreign material (*Heterophagy*): Lysosomes digest material (bacteria) that entered in to the cell by endocytosis.
- *Autophagy* (removal of old cell organelles): Lysosome removes worn-out organelles of cytosol.
- *Autolysis:* In case of diseases/lack of oxygen supply to the cell, lysosomal enzymes destroy own cells (autolysis).
- Inflammation: Neutrophil releases lysosomal enzymes in extracellular space that digest extracellular matrix and initiates acute inflammation.

Box 3.1: Lysosomal storage diseases

- Many genetic disorders cause lysosomal storage disease because of deficiency of certain lysosomal enzymes.
- Table 3.2 includes some lysosomal storage diseases and responsible enzymes.
- *Tay–Sachs disease* is an inherited lysosomal disorder due to deficiency of *β-hexosaminidase*. It results in accumulation of gangliosides in neurons that cause seizures, muscle rigidity, and death (before 5 years of age).[Next]

Table 3.2: Lysosomal storage diseases[Neet]

Disease	Deficient enzyme
Gaucher disease	Glucocerebrosidase
Tay–Sachs disease	β-hexosaminidase
Krabbe disease	Galactosyl ceramidase
Niemann–Pick disease	Sphingomyelinase
Hurler syndrome	α-L-iduronidase
Hunter syndrome	L-iduronate sulfatase
Maroteaux–Lamy syndrome	Arylsulfatase B
Pompe disease	α-1, 4-glucosidase

Peroxisomes (Microbodies)

- Peroxisomes are membranous organelles.
- Peroxisomes contain oxidative enzymes that are required for the following:
  1. Amino acid oxidation
  2. β-oxidation of fatty acids
- Oxidation of these compounds generate hydrogen peroxide (H_2O_2) that is toxic for cell.
- H_2O_2 is broken down by enzyme *catalase* of peroxisomes and thus, the cell is protected.[MCQ, Functional Correlation]
- Peroxisomes help for detoxification in liver and kidney.[Functional Correlation]
- *Zellweger syndrome/cerebrohepatorenal syndrome:* It is an inherited nonfunctioning peroxisomal disorder and leads to early death. [Hans Ulrich Zellweger, 1909–1990, Swiss–American pediatrician].

Endosomes

- Endosomes are derived from *endocytosis*.
- *Early endosomes:* On endocytosis, the membrane-bound organelle called early endosome is formed.
- *Late endosomes/lysosomes:* Golgi apparatus transfers hydrolytic enzymes and convert early endosomes to late endosomes or lysosomes.
- Transfer of prohydrolase to endosome takes place with the help of mannose-6-phosphate (M-6-P) receptors that are present on endosome surface.
- Mannose-6-phosphate gets separated from prohydrolases by acidic environment to form active hydrolases.

CYTOSKELETON

- Cytoskeleton is a supporting network of protein filaments in cytoplasm.
- Cytoskeleton helps in the following:
  1. Maintaining cellular architecture
  2. Cellular mobility and migration
  3. Movement of cilia, microvilli, tail of sperms

4. Anchoring the cell on basal lamina
5. Form cell junctions
6. Intracellular vesicular transport.

- Components of cytoskeleton:
  1. Microtubules
  2. Microfilaments
  3. Intermediate filaments.

Microtubules

- Microtubules are nonbranching hollow tubules made up of tubulin proteins (α and β tubulin) (Fig. 3.11).
- Locations: Cilia, flagella, centrioles, mitotic spindle, elongating cell processes, and growing axons.
- **Structure**
  - Microtubules are 20–25 nm in diameter with 5 nm thick wall.
  - It consists of 13 protofilaments of dimeric tubulin molecules that have α-tubulin and β-tubulin subunits.
- Centriole has *microtubule organizing center* that gives rise to microtubules.
- Formation of microtubules requires guanosine triphosphate (GTP) and Mg^{++}.
- Microtubule-associated proteins stabilize the microtubules.

Functional Correlation of Microtubules

- Movement of cilia, flagella (tail of sperm)
- Intracellular transport of vesicles
- In cell division, formation of mitotic spindle
- Maintenance of cell shape.

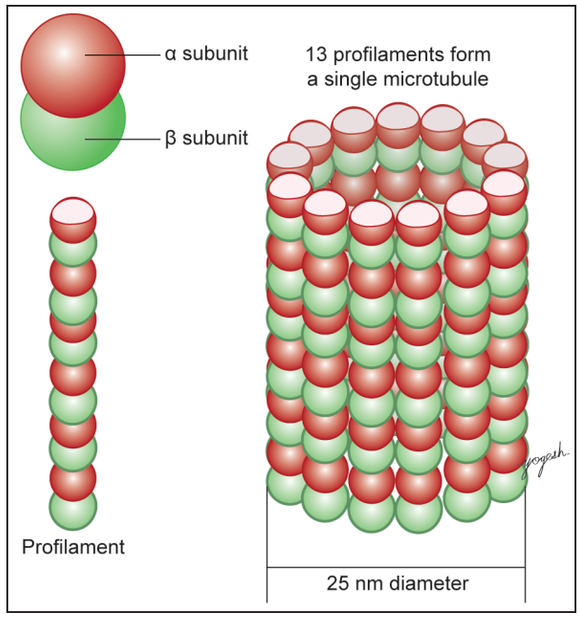

Fig. 3.11: Structure of microtubules.

- Molecular motor proteins help in the movement of cell organelles along the microtubules. For example, dynein (present in cilia and flagella), and kinesins.
- Dynein moves organelles toward the center of cell, whereas kinesins move organelles toward the periphery.

Actin Filaments/Microfilaments

- G-actin molecule assembles to form filamentous actin (F-actin) or microfilaments (Fig. 3.12).
- Microfilament is 6–8 nm in diameter.
- *Actin-binding proteins* (ABPs): They controls polymerization of G-actin, thus determining the length of actin filaments. They cross-link actin filaments to form bundles. For example, fascin, fimbrin in microvilli.
- Actin capping proteins (for example, tropomodulin) block further addition of actin molecules.

Functional Correlation of Actin Filaments

- Anchor the cell membrane by forming cell junctions
- Forms core of microvilli (Chapter 5)
- Forms terminal web (Chapter 5)
- Cell movement by forming extension of plasma membrane called *lamellipodia*.
- *Filopodia* are small spikes/processes on the surface of cell processes (lamellipodia). Filopodia contain actin filaments.

Intermediate Filaments

- The diameter of intermediate filament (8–10 nm) is intermediate between that of microtubules (20–25 nm) and actin filaments (6–8 nm). Hence, these are called intermediate filaments.
- Intermediate filaments are grouped into six major classes based on their protein composition and cellular distribution (Table 3.3).

Functional Correlation of Intermediate Filaments

- To link cells together with basal lamina.
- Keratins form superficial layers of stratified epithelium, core of hair and nails.
- Neurofilaments help maintain shape of nerve processes.
- Lamins maintains shape of nucleus, whereas beaded filaments maintain eye lens integrity.
- Intermediate filament-associated proteins: These include desmoplakins, desmoplakin-like proteins, and plakoglobins. These molecules help in cell to cell and cell to extracellular matrix junctions.

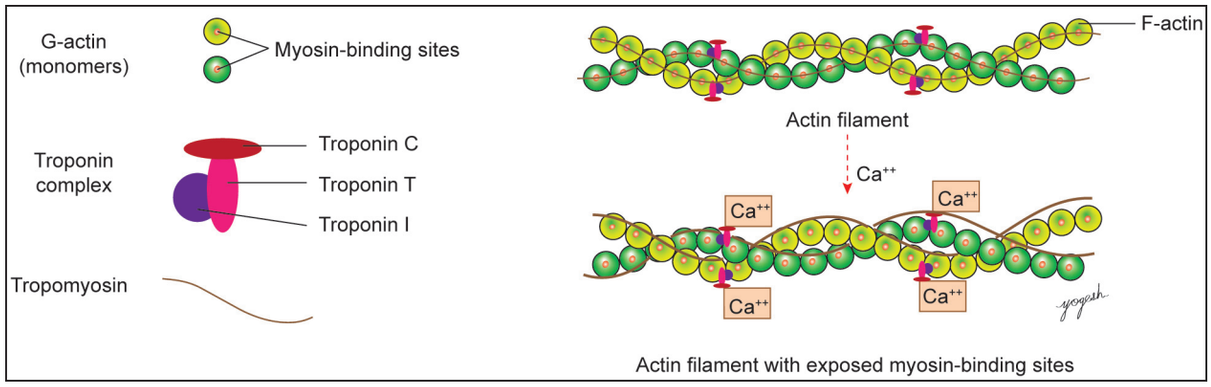

Fig. 3.12: Structure of thin filament. Actin consists of polypeptide chain of G-actin monomers. In relaxed stage, tropomyosin covers the active binding sites of F-actin for myosin. Ca^{++} ions bind with troponin C and results in release of tropomyosin from F-actin. Thus, Ca^{++} exposes myosin-binding sites of actin.

Table 3.3: Types of intermediate filaments

Type of protein	Examples	Location
Classes 1 and 2	Keratins	All epithelial cells
Class 3	Vimentin	Mesenchymal cells
	Desmin	Muscles
	Glial fibrillary acidic protein	Neuroglial cells, Schwann cells
	Peripherin	Peripheral neurons
Class 4	Neurofilaments	Neurons
Class 5	Lamins	Nucleus
Class 6	Phakinins, filensin	Lens (eyeball)

Centrioles

- Centrioles are small spherical area of cytoplasm situated near the nucleus.
- Centrioles are hollow cylindrical structures that are made up of nine microtubule triplets arranged in cylindrical pattern (Fig. 3.13).
- There are two centrioles in a cell. They are arranged at right angle to each other.
- Centrioles are surrounded by *pericentriolar area.*
- Centrioles and pericentriolar area together called as *centrosome or microtubule organizing region.*
- Centrioles are self-replicating organelles.

Functional Correlation of Centrioles

- Centrosome initiate formation of microtubules.
- Centrosome forms mitotic spindle.
- Centrosome provides basal bodies for cilia and flagella.
- Centrioles self-replicate just before cell division.

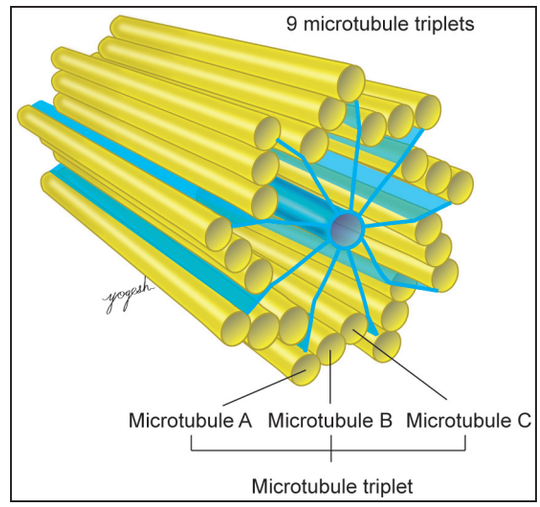

Fig. 3.13: Structure of centriole.

Clinical Correlation

- *Kartagener syndrome:* It is a defect in the organization of microtubules that results in *defective ciliary movement* in the respiratory tract, defective sperm movement, and defective ciliary movement of fallopian tubes. It results in repeated respiratory infections, and male and female infertility. *Next*
- Colchicine, vinblastine, and vincristine prevent mitotic spindle formation and arrest cell division in mitosis. Colchicine is useful for chromosomal studies in cytogenetics. *Next*
- *Alzheimer's disease:* Defective formation of neurofilaments (intermediate filaments) causes Alzheimer's disease. It results in accumulation of neurofibrillary tangles in neurons.
- In alcoholic liver cirrhosis, keratin filaments get accumulated in hepatocytes and form *Mallory bodies* (inclusions).

- *Duchenne muscular dystrophy* [Duchenne de Boulogne, 1806–1875, French Neurologist]: It is a X-linked recessive disorder that affects only boys. It involves a defective gene for dystrophin protein. Dystrophin is essential in binding contractile assembly to sarcolemma in skeletal muscles.[Next]

NUCLEUS

- Nucleus is an oval or spherical membranous structure.
- Most of the cell contain single nucleus except[MCQ]
  - RBCs and platelets do not have nuclei
  - Striated muscle cells, osteoclasts, and syncytiotrophoblast are multinucleated
  - Few hepatocytes and transitional epithelial cells are binucleated
- Nucleus is present during interphase of the cell.
- It consists of the following components: chromatin, nucleolus, nuclear membrane, and nucleoplasm (Fig. 3.14).

Nuclear Envelope

- Nuclear envelope is bilaminar membrane that separates nucleoplasm from the cytoplasm.
- *Perinuclear cisternal space* lies between two layers of nuclear envelope.
- *Nuclear pores* are intervals in nuclear membrane that transport RNAs and proteins between the nucleus and the cytoplasm.
- Outer membrane of nuclear envelope is continuous with rough endoplasmic reticulum.

Box 3.2: Inclusions

- Inclusions are cytoplasmic or nuclear structures that are products of metabolic activity of cell.
- Inclusions have characteristic staining property.
- Examples: lipofuscin, hemosiderin, glycogen, lipid inclusions, and so on.

Lipofuscin[Viva]

- These are brownish-gold pigments.
- It is visible on *H&E* staining.
- Locations: Neurons, skeletal, and cardiac muscles, macrophages.
- It is a wear and tear pigment.
- Mechanism of formation: Digested bacteria in macrophages, accumulated oxidized lipids in other cells.

Hemosiderin

- These are iron complexes formed by indigestible residues of hemoglobin in phagocytic cells.

Glycogen

- It is a glucose polymer found mostly in hepatocytes and muscle cells.
- Toluidine blue or periodic acid–Schiff staining is useful for detecting glycogen.

Lipid inclusions

- These are fat droplets found in intestinal absorptive cells and adipocytes. They are also found in hepatocytes in lipid storage disease.

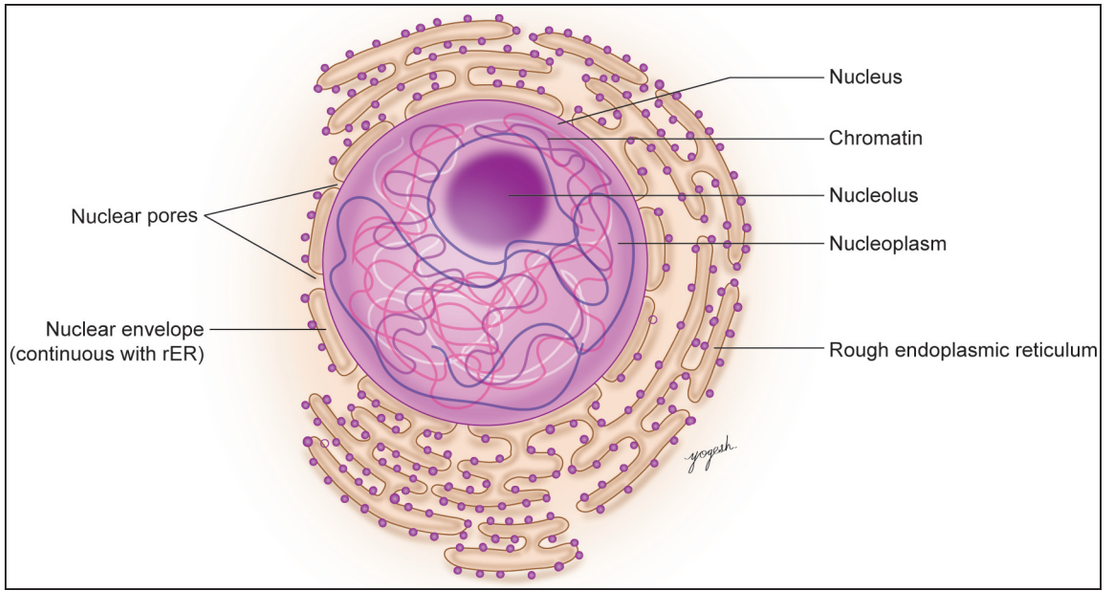

Fig. 3.14: Structure of nucleus.

- Inner nuclear membrane is supported by intermediate filaments (lamin).
- Abnormal lamin proteins are detected in Emery-Dreifuss muscular dystrophy (progressive muscle weakness, *contractures* of tendons and weakening of heart muscle).[Next]
- During cell division, nuclear envelope disappears to allow chromosomal separation. After cell division, nuclear envelope is reassembled.

Nucleoplasm

- Nucleoplasm is a material enclosed by nuclear envelope besides chromatin and nucleoli. It contains various proteins, ions, and inclusions.

Chromatin

- Genetic material of the cell located in the nucleus is in the form of a long thread called *chromatin.*
- Chromatin consists of (Human genome project–2003):
  - 1.8 m long DNA
  - 1000 times longer than the nucleus diameter
  - 46 chromosomes
  - 2.85 billion base pairs of nucleotides
  - 23,000 protein-coding genes
- Chromatin consists of DNA coiled around histone and nonhistone proteins (structural proteins). Presence of DNA and RNA (acids/negative charges) makes the chromatin basophilic (stained with hematoxylin).[Viva]
- Definition of gene: "*Gene is a union of genomic sequences encoding a coherent set of potentially overlapping functional products*" [Histology: A Text and Atlas, Pawlina W, 7th Ed].

Forms of Chromatin

- According to the functional activity, chromatin has coiled DNA and it produces two forms of chromatin as follows (Fig. 3.15):[Functional Correlation]

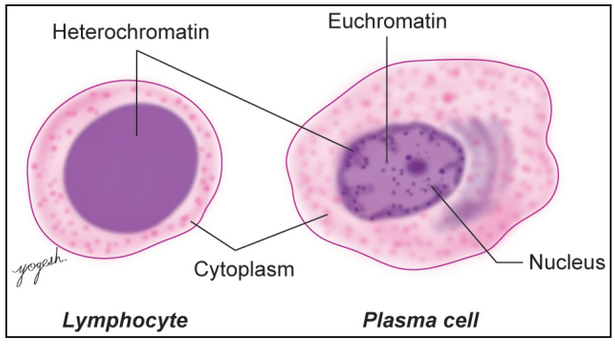

Fig. 3.15: Heterochromatic and euchromatic nuclei.

- *Euchromatin*[Viva]
  It is a partially condensed chromatin.
  It is more active and lightly stained.
  It is expressed during interphase.
- *Heterochromatin*[Viva]
  It is a condensed chromatin.
  It is inactive and darkly stained.
  It does not express during interphase.
  - *Constitutive heterochromatin* remains inactive throughout the cell cycle. For example, around centromere, telomeres, and C-band of chromosomes.
  - *Facultative heterochromatin* remains active in certain phase of the cell cycle. For example, both the X chromosomes remain active during embryogenesis and later one X chromosome becomes inactive. Inactive X chromosome in females form *Barr body* or *drumstick body* in neutrophils.[MCQ]
- Nucleosomes are the smallest units of chromatin. It consists of macromolecular complexes of DNA and histones.

Histone Proteins

- Histone proteins form an octamer having eight molecules of histone proteins. DNA wrapping around histone proteins produce *beads on a string* appearance.
- During cell division, chromatin condenses to form *chromosomes* (*color bodies* in Greek).

Nucleolus

- Nucleolus is a spherical mass of heterochromatin.
- It is a dark staining body, 1–3 µm in diameter.
- Each nucleus shows 1–2 nucleoli (maximum 5–6).[Viva]
- It contains a protein nucleostemin that binds p53 protein and regulates cell cycle and cell differentiation.

Some Interesting Facts

- In degenerative process, the nucleus loses its details and becomes shrunken, and darkly stained. Such nuclei are called *pyknotic nuclei.*[Viva]
- Apoptosis is programmed cell death. It is an active gene-directed process that requires energy.[Viva]
- Necrosis is not a programmed cell death. It may result from various factors such as mechanical chemical injury, infectious agents, toxins, and so on.[Viva]

Functional Correlation of Nucleolus

Ribosomal RNA synthesis and regulation of the cell cycle.

TISSUES

Definition

Tissue is an aggregation of group of cells organized to perform one or more specific functions.[Viva]

Classification

Four basic tissues of the body: The tissues of the body are grouped into four basic types as follows:[MCQ]

1. *Epithelial tissue (epithelium):* The surfaces of the body (inner and outer) and inner surface of tubular structures within the body are covered by a layer of cells that rests on the basement membrane. Such a covering layer is called epithelium. They also form secretory units of glands.
2. *Connective tissue:* It supports the other three basic tissues of the body. It consists of cells, connective tissue fibers and inter cellular matrix.

   Specialized connective tissue include bone (with mineralized matrix), cartilage (with hydrated matrix), and blood (flowing connective tissue).[Next]
3. *Muscle tissue:* It has contractile cells. It is further classified into skeletal, cardiac and smooth muscles.
4. *Nerve tissue:* It consists of cells that have the property of excitability and conduction. Nervous tissue receives information from external and internal environment, interpret the information, and convey it to other organs to control their functions. It consists of nerve cells and supporting neurological cells.