Module 1: Introduction and Cell Biology

Different types of microscopes:

1) **Light Microscope (LM):** Uses white light of the Visible Light spectrum to magnify and resolve images
2) **Electron Microscope (EM) – Transmission EM, Scanning EM:** Uses electron to magnify and resolve images. Greater resolution and higher magnification because electron is smaller than the wavelength of white light

Basic terminology:

- Cell is the smallest thing which is alive (virus = smaller but not alive as it can't reproduce without a cell)
- **Cytology** = Study of Cells. Cells are organised into complex arrays of cells called tissues
- **Histology** = Study of Tissues (Histopathology = Study of diseased/ abnormal cell/tissue). Cells are usually 5~20 μm (10-6m). RBC = 7μm = Internal scale on slide

Basic tissue types:

- functionally the most important part of organs
- **Parenchyma** = Functional parts of an organ e.g. epithelial
- **Stroma** = Structural tissue of organs e.g. connective

1) **Epithelial:** Separates the body from the outside world. Structure is characterised by cells tightly packed together. e.g. skin
2) **Connective:** Structure: cells are much widely dispersed and filled with non-living material. e.g. tendon, ligament, bone
3) **Muscle:** Consist of cells specialised for contraction. Types of muscle tissue: cardiac, smooth and skeletal
4) **Nervous:** Consist of cells, neurons which are specialised to conduct electrical impulses. Structure: generally tightly packed together
5) **Adipose (fat):** Consist of molecules called lipids which accumulate under skin and act as energy storage. Not tightly packed. Adipose is another form of connective tissue: embryologically same but structurally different. In large multicellular organisms, different combinations of basic tissue types form the structural and functional units of organs. Organs form the organ systems which form the general structure of the body.

Cell theory

- All living things are composed of cells and products of cells.
- Cells consist of one or more nuclei surrounded by watery cytoplasm containing organelles surrounded by plasma membrane.
- All cells arise from pre-existing cells by cell division.

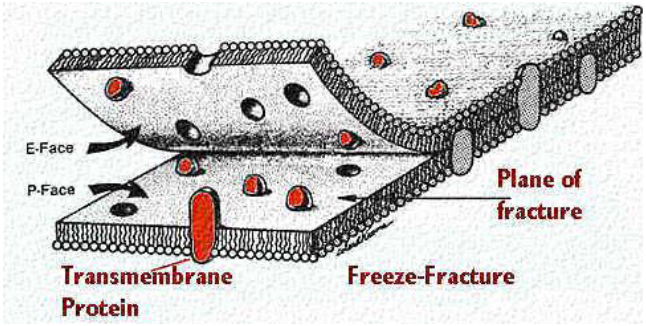
2 types of cells

- Eukaryotic cell contains a defined nucleus where genetic material is stored surrounded by nuclear membrane/ envelope.
- Prokaryotic cell contains no nucleus and the genetic material is not collected together, moving around the cytoplasm.

Cellular organelles

Major functions and their relation to structures:

- **Plasma membrane:** Selectively/ Semi-permeable barrier around cell. Regulates and selects what gets in and out of the cell. 10nm across; tramline appearance = absolutely characteristic of any plasma membrane in eukaryotes. Made up of 3 different class of molecules: protein, lipid, carbohydrate
  - **Functions:** Limits and regulates what gets in and out. Ion transport – Passive & Active. Receptor sites e.g. blood type ABO in glycocacyx of RBC. 'Bulk' movement – Exocytosis & Endocytosis. Cohesion – fusion of cells to form tissue. Communication between cells
- **Fluid mosaic model of membrane organisation:** Lipid bilayer – backbone of membrane (head facing outward and tail filling the core). Proteins – Integral (proteins integrated into the bilayer) and Peripheral (edge of the membrane). Carbohydrates – exclusively on the outer surface of membrane, covalently bound to lipid & protein. Glycocacyx = Layer of carbohydrate (sugar coat) on the external surface of plasma membrane
- **Freeze-fracture technique** (direct visual confirmation for fluid mosaic model). A cell is frozen then hit with a knife, splitting the plasma membrane along the hydrophobic plane (between the two lipid layers) to expose two interior faces of the membrane. The numerous bumps on the image represent the integral proteins of the membrane that disrupt the layer.

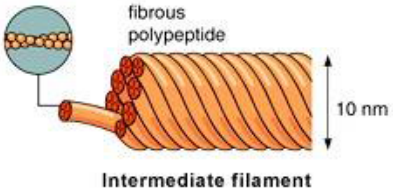


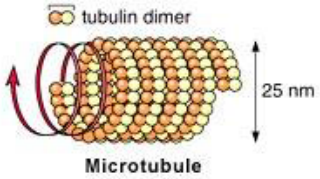
- **Cytoplasm:** Organelle. Cytosol (Cytoplasmic matrix) = Watery component. Featureless in electro micrographs. Highly organised into complex network array of fibres = Cytoskeleton

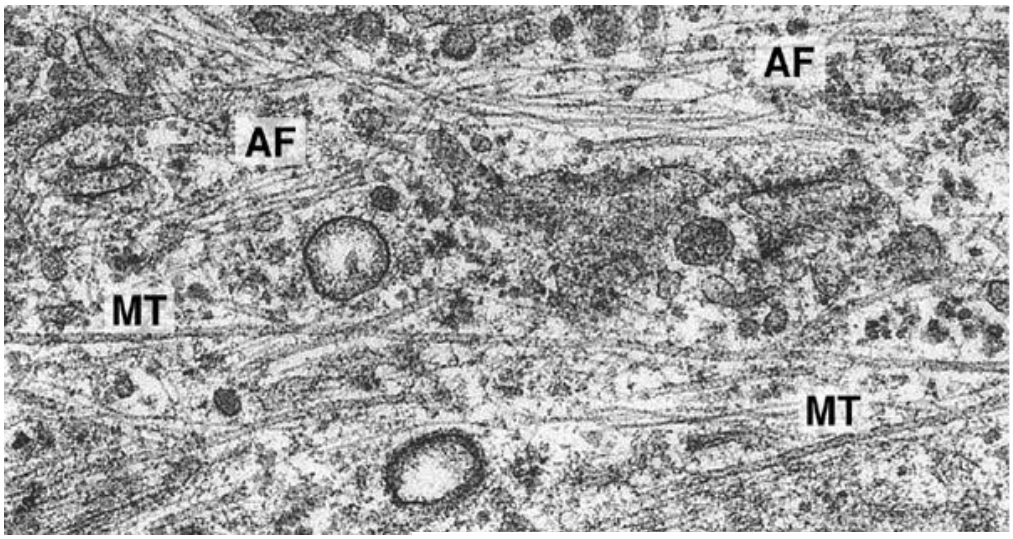
- **Cytoskeleton**
  - **Functions:** Involved in maintaining cell shape (MT). Moving molecules into and out of cell. Transport material inside the cell (MT, MF). Allows movement of cells e.g. WBC move by major reorganisations of cytoskeleton. Sensory receptors e.g. sound cells in ears filled with MT, MF which wiggle and transmit impulse to brain

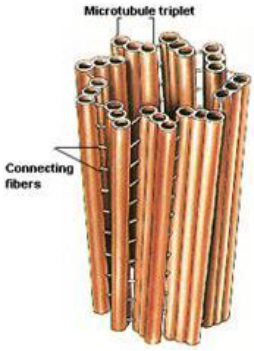
  - **Structures:**

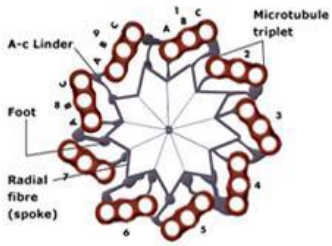
Structure	Size	Description
Microtubules	24nm	• Tubular structure. Protein Tubulin (60000MW) connecting end-on-end and forming a tube. Cells can change length/number by adding/ subtracting tubulin blocks
Microfilaments	Actin = 6nm Myosin = 15nm	• Densely packed in muscle cells. Found in ALL eukaryotic cells. Contractile – They can contract
Intermediate filaments	7-10nm	• All cells have intermediate filaments – They are different in different cells. Can be used as a diagnostic tool. Usually associated with maintaining structure/shape
Centriole	0.5 x 0.2µm	• All eukaryotic cells have a pair of centrioles that are perpendicular to each other and located close to the nucleus. The wall of centriole is made up of 9 groups of 3 microtubules. Protein pericentriolar material surrounds the centriole. Critical in cell division mechanism. Critical in formation of basal body (in turn of cilia). Master organizer of cell shape



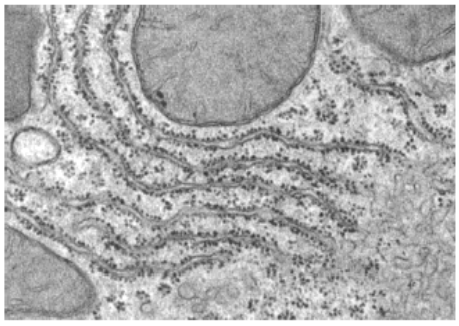




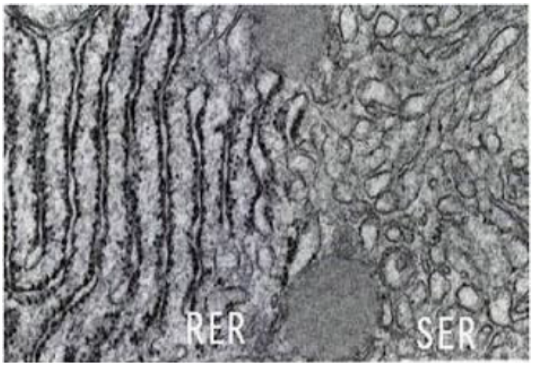


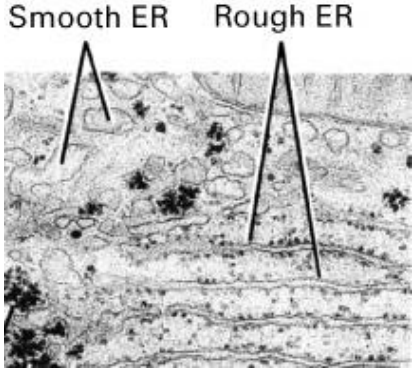


- **Ribosomes**
  - **Structure:** Smallest of all organelles with fixed size and shape. 25 x 12 nm in size. Composed of roughly equal proportion of protein and rRNA. Freely floating in cytoplasm OR bound to membranes of endoplasmic reticulum. Occur singly (mostly inactive) OR in groups called polyribosomes/ polysomes.
  - **Functions:** Active unit for protein synthesis – Cells which need protein synthesis are filled with ribosomes
- **Endomembrane system** = system of membranes inside the cell in the cytoplasm.
  - (1) Nuclear envelope.
  - (2) Endoplasmic Reticulum:
    - **2 Structural types**
      - a. Cisternal = sheet-like (Regular/ Irregular)
      - b. Tubular = tubes
  - **Functional types**

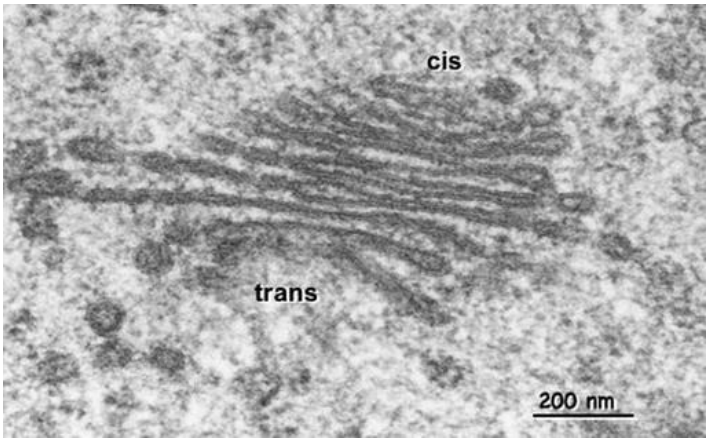


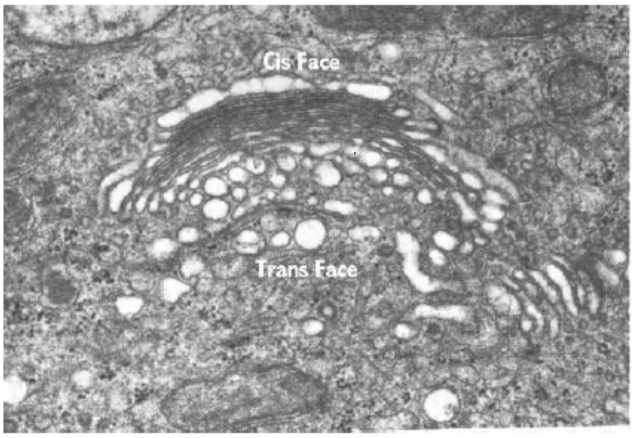
Rough ER	Smooth ER
• Mostly regular cisternal shape	Mostly tubular shape
• In cross section, you can see ribosomes studded in black dots • The ribosomes on the surface giving it a rough appearance	• In cross section, you can see the tubes (tramlines) and tubules cut in cross section (circular shape) • No ribosome on the surface giving it a smooth appearance
• Synthesis of proteins destined for secretion from the cell e.g. stomach lining cell • Transport of new protein around cell • Modification of protein • Lipid metabolism	• Synthesis of steroids (by the enzymes in the membrane of the sER) • Synthesis of glycogen • Ion transport • Breakdown of carbohydrates • Drug detoxification – liver cells are full of sER





- **Golgi apparatus (body/complex)**
  - **Structure:** Membranes consist of series of flattened, curved, membranous sacs. 1µm across. Convex surface has a large number of small membrane-bound vesicles. Concave surface has a small number of larger vesicles
  - **Functions:** Package the newly synthesised protein for secretion in vesicles. Modification of the protein (sulfation, glycosylation). Transport inside the cell to the plasma membrane. Protein is transported to the sacs, travels through golgi apparatus, emerges from concave surface in secretory vesicles, fuse together to form secretory granules which fuse with plasma membrane to release the protein. Processing factory for membranes

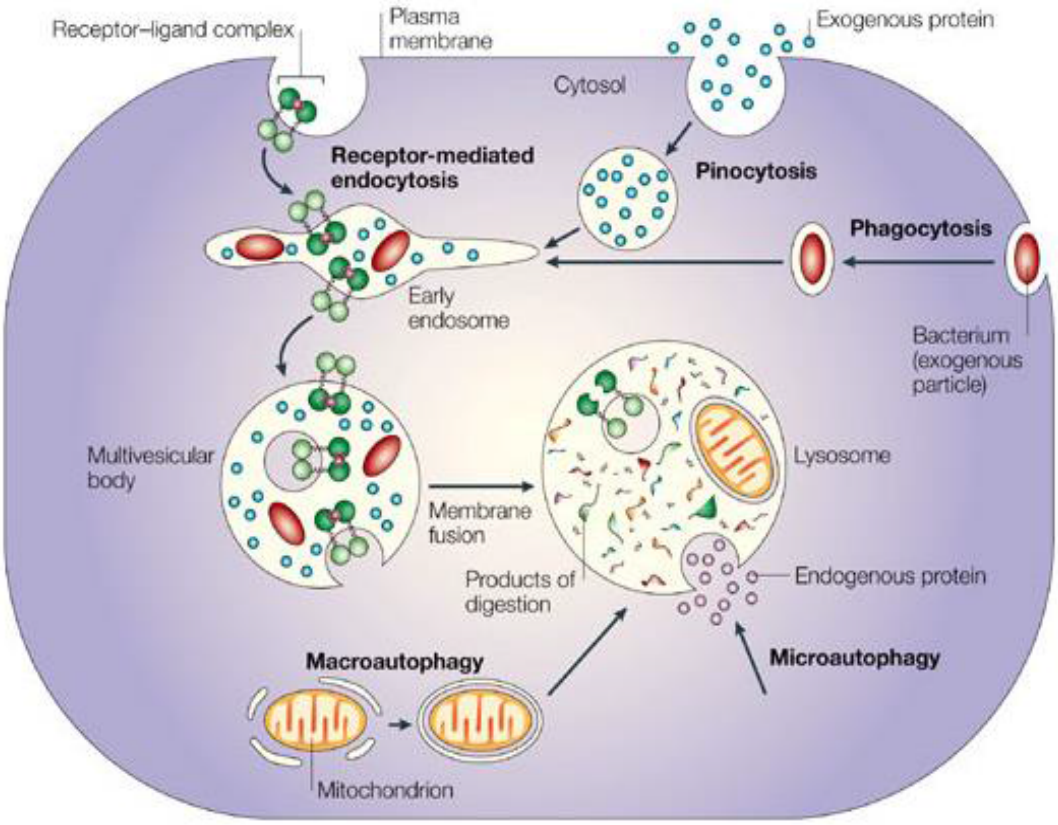




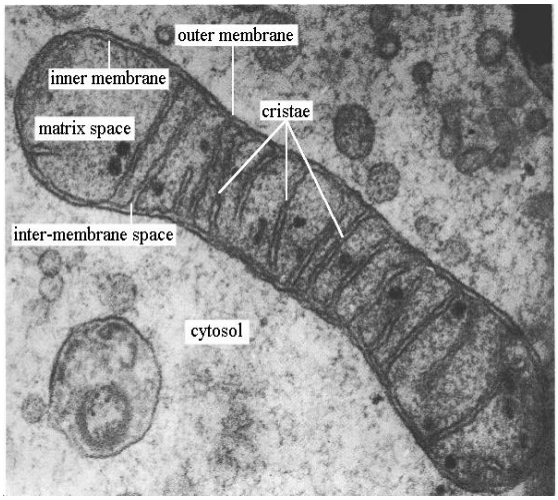
- **Lysosomes:** membrane-bound cellular organelles which contain hydrolytic enzymes. Lysosome is synthesised in Trans Golgi Network and carries out intracellular digestion (digestion of material inside the cell brought back in through the Golgi apparatus). In it, it has a family of 40-50 enzymes – typically, acid phosphatase – functioning at pH 5 (acid) – hydrolytic enzymes are synthesized in the rER, pass in transport vesicles to the Golgi and through the Golgi and are then added to endosomes to form the lysosomes. It has a dark coloured core and a membrane. The addition of all the enzymes from early endosome, late endosome to maturing into lysosome – very variable. Lysosomes are involved in heterophagy = digestion, within a cell, of the cell of different material that has been ingested. In lysosome, enzymes break down the material into molecular level (fat to lipid, protein to amino acid, complex to simple carbohydrates).
  - **Intracellular digestion:** The materials which is digested by lysosomes can reach them in different ways.
    - **Endocytosis:**
      - **(1) Phagocytosis:** "eating" by cell – ingestion of insoluble material
      - **(2) Pinocytosis:** "drinking" by cell – ingestion of soluble material. The endocytotic and phagocytotic vesicles fuse with the lysosome
      - **(3) Receptor mediated endocytosis:** Taking material into cell selectively by the use of receptor. Coated vesicles (not smoother vesicles like endocytotic and phagocytotic vesicles) have coat on the inside and outside of the membrane. They end up in lysosomal system. They prevent familial hypercholesterolemia by regulating the level of cholesterol – genetic damage in receptors inhibits removal of cholesterol and lead to death by cardiac attack
      - **(4) Autophagy:** self-eating. Cells break down their own damaged or unwanted components. These components become surrounded by a membrane and vesicle and form an autophagosome. This fuses with lysosome and the material is broken down to molecular level. All these various components end up in endosomes which mature into lysosomes. The digestion takes place inside the lysosomes. The materials digested pass through the membrane of the lysosome into the cytoplasm where they may be used by the cell for its own metabolism. Some material is left undigested and a residual body is formed which contains the remaining material.

- **Peroxisomes:**Class of vesicles containing enzymes = catalase. Catalase breaks down hydrogen peroxide (H_2O_2 = powerful oxidizing agent and by-product of many intracellular reactions) as its

accumulation can lead to death. Catalase regulates the content of H2O2 in cells. They aren't usually darkly stained



- **Mitochondria**
  - **Structure:** Vary In size and number -In general, 0.5-2.0 µm. 2 membranes surrounding the structure: outer and inner mitochondrial membrane:
    - **Outer:** smooth in outline and define the course of mitochondria
    - **Inner:** highly folded in series = Cristae = flat, shelf-like structure (except cristae in cells that secrete steroids – tubular in shape) – vary in number and shape. **Matrix space:** mitochondrial matrix.
  - **Function:** Powerhouse of the cell = produce energy in the form of ATP (universal energy molecule). More cristae, more ATP is being produced – in cristae membranes are the components of electron transfer chain and the matrix has components of the Krebs cycle – the two processes are principles of ATP production -Concentration of Ca2+ ions - Involved in aspects of fatty acid metabolism.



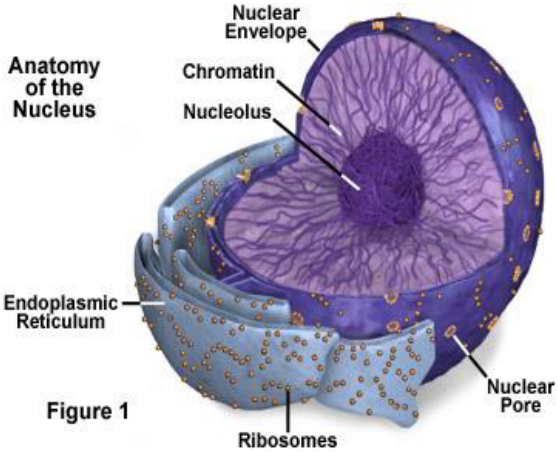


Figure 1

- **Nucleus:** Rounded/ elongated structure close to the centre of the cell (shape of the cell = shape of the nucleus)
  - **(1) Nuclear envelope**
    - **Structure:** Double membrane: inner and outer membranes parallel with each other around the circumference of the nucleus. Perinuclear space = small space between the two membranes (10-15nm). In some proportions, membranes run into each other and form small pores. Nuclear pores = not holes but an elaborate structure consisting of ring of protein in the centre of pore (70nm in diameter).

In some cells, the nucleus is continuous with rough ER with ribosomes.
    - **Function:** Second permeability barrier in the cell. Separate genetic material from the cytoplasm of the cell. Regulates what gets in and out of the nucleus through the nuclear pore complex. mRNA leaves the nucleus through the pores, receptors to switch genetic material on and off
- **(2) Nucleoplasm:** Featureless in electron micrographs (not much to see). 30% dry weight protein. Potent influence on how the genetic material functions -No membranes in the nucleoplasm - continuous and not separated from one another 3) Nucleolus (nucleoli). It is dense, generally round structure**.**
- **(3) Nucleolus (nucleoli):** Dense, generally round structure. Darkly stained – often possible to see alternating dark and light structure (dark stain = DNA loops of chromosomes that contain rRNA genes, RNA pol I and TFs/ light stain = ribosomal genes actively undergoing transcription, rRNAs). Region involved in the synthesis and assembly of ribosomal RNA (exported out the cell and join with the protein in cytoplasm) -Active cell has more nucleoli as it synthesizes more rRNA. Each chromosome in the interphase nucleus consists of a single chromatin filament which is tightly coiled and of considerable length. A filament of chromatin consists of a very long DNA molecule in subunits called nucleosomes. Nucleosomes have a central region consisting of 2 molecules of each of the four histone proteins and the DNA helix is wound around this central**.**
- **(4) Chromatin:** Genetic material – Microscopical view of DNA -Nucleosome = basic unit of chromatin (10nm in diameter) – chromatin is packed in the form of nucleosomes. DNA is wound around a core of protein as the amount of DNA is too long to be fitted into the nucleus without being tightly packed -In nucleosomes, DNA is packed 10x more tightly than completely unravelled state -In chromosomes, DNA is packed 10000x more tightly packed than the completely unravelled state. 2 principle kinds of chromatin:
    - Heterochromatin: darkly staining material. Represents inactive DNA. DNA is tightly packaged in the form of chromosomes – the intense tight packing stains it deeply, it takes up more and hence darker stain. Small, dark nucleus = inactive cell (too tightly packed to synthesise**.**
    - Euchromatin: pale staining material. Represents active DNA – DNA that is actively transcribed into RNA to go into cytoplasm for protein synthesis. DNA is mostly in the unravelled nucleosome form – it doesn't take up stain so it stains more palely. More pale region = more euchromatin = more active DNA. Large, pale nucleus = active cell (loose enough to give rise to RNA