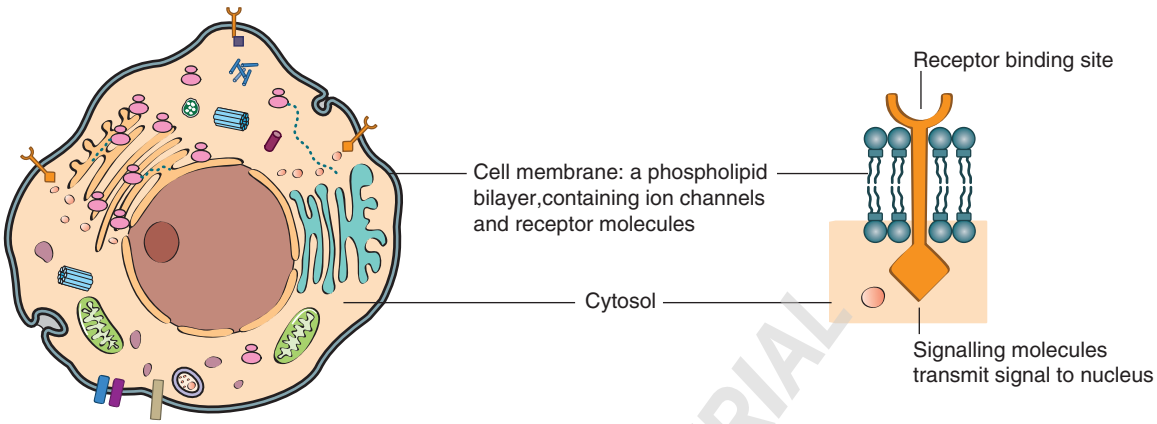
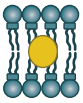
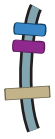
1 The normal human cell

Overview of the structure of normal human cells



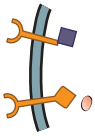
Controlling the intracellular environment: cell membrane and ion pumps


Phospholipid bilayer: hydrophilic ends on outer and inner aspects. Hydrophobic ends inside membrane, stabilised by cholesterol


Na/Cl pump

Calcium channel

Receiving signals


Cell surface receptors and second messengers

Intracellular transport, cell movement and mitosis


Centriole: spindle formation (cell division)

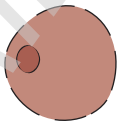

Cytoskeletal components: microtubules and filaments

Degradation/destruction


Lysosome


Peroxisome

Protein production and secretion


Nucleus


Ribosome and newly producedpeptide

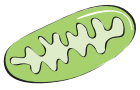

Rough (with ribosomes) and smooth endoplasmic reticulum


Golgi apparatus: protein modification (folding and addition of carbohydrate)


Secretory vesicle containing protein/glycoprotein product


Proteosome: degrades defective protein

Energy production


Mitochondrion

 Pathology at a Glance, Second Edition. Barry Newell, Asma Z. Faruqi and Caroline Finlayson. © 2022 John Wiley & Sons Ltd. Published 2022 by John Wiley & Sons Ltd.

The important functions of the cell are: manufacture of proteins for local or distant use, energy generation, functions appropriate to tissue type and replication.

The main elements are the nucleus, the cytoplasm (cytosol), the cytoskeleton and the subcellular organelles, all bound by membranes.

Nucleus

The nuclear membrane contains pores to permit metabolites, RNA and ribosomal subunits in or out. It contains:

- DNA, the nuclear chromatin, which only forms about 20% of the nuclear mass.
- Nucleoli – ribosomal RNA synthesis and ribosome subunit assembly.
- Nucleoprotein, e.g. synthetic enzymes for DNA, RNA and regulatory proteins, all made in the cytoplasm and imported into the nucleus.
- Messenger, transfer and ribosomal RNA en route for the cytoplasm.

Cytosol

The nutritious fluid medium that bathes and supports the organelles, through which the cytoskeleton ramifies. Many reactions take place here.

Cytoskeleton

- Microtubules: organelles such as secretory vesicles or internalised receptors can be transported through the cell via the cytoskeleton.
- Microfilaments (actin, myosin): these stabilise cell shape and act as contractile proteins in muscle.
- Intermediate filaments, e.g. cytokeratin, desmin, neurofilament proteins and glial fibrillary acidic protein (the types differ between tissues and all are structural).

Organelles

Mitochondria

These are the main ATP/energy-generating organelles and house the Krebs cycle and oxidative phosphorylation. They have their own ssDNA (maternally derived) which codes a minority of their proteins. A porous outer membrane and folded inner membrane are present.

Ribosomes

Nucleolus-produced ribosomal subunits aggregate in the cytosol and attach to the endoplasmic reticulum or lie loose in the cytosol, depending on the destination of the protein to be made (free ribosomes make proteins for inside the cell itself). Ribosomes translate RNA strands into a correctly assembled amino acid sequence (peptide molecule).

Endoplasmic reticulum (ER)

The ER is an irregular maze of membrane-bound tubules, saccules and cisterns which ramifies through the cell.

- **Rough ER** is studded with ribosomes. Proteins made by the rough ER pass into the rough ER cisternae and undergo secondary folding and early glycosylation before being incorporated into membranes for export from the cell, receptor molecules on the cell, or components such as lysosomes within the cell.
- **Smooth ER**: there is a further addition of carbohydrate moieties to protein, folding to achieve tertiary structure.

Golgi apparatus – see diagram.

Secretory vesicles

These membrane-bound packets are moved via the cytoskeleton to fuse with the cell membrane to expel their contents outside.

Lysosomes

These are intracellular membrane-bound vesicles, containing destructive chemicals and enzymes, which fuse with phagosomes to release their contents into the phagolysosome and destroy pathogens. Lysosomes also degrade worn-out cell organelles (autophagy).

Peroxisomes

These small membrane-bound granules contain oxidative enzymes which make hydrogen peroxide plus its regulator catalase.

Proteasomes

These identify defective proteins and degrade them into their component peptides and amino acids for reuse by the cell. Portions of broken-down protein are bound by MHC class I molecules and displayed on the cell surface to Tc cells.

Centrosome

This contains the two linked centrioles, from which microtubules radiate into the cell. The centrioles duplicate and migrate to opposite ends of the cell during cell division, separating the duplicated chromosomes.

Membranes

Membranes are phospholipid barriers surrounding the cell itself and certain organelles. They isolate portions of the cell and permit several, often incompatible, metabolic processes to take place simultaneously.

The cell membrane

This phospholipid bilayer interacts with the extracellular world by assorted surface molecules. The centre is lipophilic and the surfaces hydrophilic, with cholesterol as a stabilising 'spacer' between them. The 'raft theory' suggests that intramembrane structures can float and be cross-linked around the perimeter of the cell.

Membrane proteins: proteins that project through the membrane outside the cell usually have attached carbohydrates. Glycolipids are carbohydrates attached to the lipid membrane and are important in cell recognition, cell–cell bonds and adsorbing molecules. Some tissues have a protective glycocalyx.

Transport through the cell membrane: the main mechanisms are as follows.

- Passive diffusion (needs only a concentration gradient), e.g. lipids and lipid-soluble agents like ethanol.
- Facilitated diffusion: the binding of a molecule triggers a conformational change which moves the molecule across the membrane.
- Active transport: against a concentration gradient to maintain ion concentrations within the cell, e.g. the Na^+/K^+-ATPase complex.
- Bulk transport: **endocytosis**, **transcytosis** and **exocytosis**. Endocytosis includes *receptor-mediated endocytosis* (ligands or viral

particles) and *phagocytosis* (engulfing of particles). *Pinocytosis*, the sampling of small quantities of extracellular fluid, is not receptor mediated.

Transmission of messages across the cell membrane

- Lipid-soluble agents (e.g. steroids) diffuse directly across cell membranes.
- Receptor binding and activation of secondary messengers: applies to protein messenger molecules, which bind to a specific cell surface receptor (*ligand*), resulting in active transport of the molecule through the membrane or the triggering of intracellular cascade reactions.

Neurotransmitters: these are chemical messengers for neurones or myocytes that cause an electrical response in the target by receptor-mediated opening of an ion channel.