		Semester – VI
17MBU603A	**CELL BIOLOGY**	**(3H –3C)**

Instruction Hours / week: L: 3 T: 0 P: 0 **Marks:** Internal: **40** External: **60** Total: **100**

End Semester Exam: 3 Hours

SCOPE

To describe the basic concept of cell structure, membrane, cellular functions of different types of cell, modes of cellular signaling and signal amplification.

OBJECTIVES

- To explain the cell structure and functions of organelle.
- To determine the transportations through cell membrane.
- To categorize the different receptors and model of signaling.
- To analyze the concept of cell signaling.

Course out come:

- By end of this paper students can able to interpret about the cell and its functions.

Unit I

Cell Organization – Eukaryotic (Plant and animal cells) and prokaryotic. Plasma membrane: Structure and transport of small molecules. Cell Wall: Eukaryotic cell wall, Extra cellular matrix and cell matrix interactions, Cell-Cell Interactions - adhesion junctions, tight junctions, gap junctions, and plasmodesmata (only structural aspects).Mitochondria, chloroplasts and peroxisomes. Cytoskeleton: Structure and organization of actin filaments, association of actin filaments with plasma membrane, cell surface protrusions, intermediate filaments, microtubules.

Unit II

Nuclear envelope, nuclear pore complex and nuclear lamina. Chromatin – Molecular organization. Nucleolus.

Unit III

Ribosomes, Endoplasmic Reticulum – Structure, targeting and insertion of proteins in the ER, protein folding, processing and quality control in ER, smooth ER and lipid synthesis, export of proteins and lipids. Golgi Apparatus – Organization, protein glycosylation, protein sorting and export from Golgi Apparatus Lysosomes.

Unit IV

Signalling molecules and their receptors. Function of cell surface receptors. Pathways of intra-cellular receptors – Cyclic AMP pathway, cyclic GMP and MAP kinase pathway.

Unit V

Eukaryotic cell cycle and its regulation, Mitosis and Meiosis, Development of cancer, causes and types, Programmed cell death, Stem cells, Embryonic stem cell, induced pleuripotent stem cells.

SUGGESTED READING

1. Hardin J, Bertoni G and Kleinsmith LJ. (2010). Becker's World of the Cell. 8th edition. Pearson.
2. Karp G. (2010) Cell and Molecular Biology: Concepts and Experiments. 6th edition. John Wiley & Sons. Inc.
3. De Robertis, EDP and De Robertis EMF. (2006). Cell and Molecular Biology. 8th edition. Lipincott Williams and Wilkins, Philadelphia.
4. Cooper, G.M. and Hausman, R.E. (2009). The Cell: A Molecular Approach. 5th Edition. ASM Press & Sunderland, Washington, D.C.; Sinauer Associates, MA.

KARPAGAM ACADEMY OF HIGHER EDUCATION

CLASS: III BSC Microbiology COURSE NAME: CELL BIOLOGY

COURSE CODE: 17MBU603ALECTURE PLAN BATCH: 2017-2020

UNIT I

Duration	Topic	Reference
1h	Cell Organization – Eukaryotic (Plant and animal cells) and prokaryotic	T1:R1:7-27 W1
2h	Plasma membrane: Structure and transport of small molecules	R1:384-400 W2
2h	Cell Wall: Eukaryotic cell wall, Extra cellular matrix and cell matrix interactions	R1:384-400 W3
1h	Cell-Cell Interactions - adhesion junctions, tight junctions, gap junctions	J1 W3
1h	plasmodesmata (only structural aspects).Mitochondria, chloroplasts and peroxisomes.	R1:3-27 J1
1h	Cytoskeleton: Structure and organization of actin filaments, association of actin filaments with plasma membrane	R1:390-392 J1
1h	cell surface protrusions, intermediate filaments, microtubules	R1 J1
1h	Unit Revisions	
	Total hours: 10 h	

UNIT II

Duration	Topic	Reference
1h	Nuclear envelope	R1:356-397 W1
1h	nuclear pore complex	R1:356-397 W1
1h	nuclear lamina	R1:356-397 W2
1h	Chromatin- Molecular organization	R1:356-397 W2
1h	Nucleolus	R1:356-397 W2
1h	Unit Revisions	
	Total hours: 6 h	

UNIT III

Duration	Topic	Reference
1h	Ribosomes	R1 W1
1h	Endoplasmic Reticulum	R1 W2
1h	Structure, targeting and insertion of proteins in the ER	R1 :275-405,W2
2h	protein folding, processing and quality control in ER	R1: 275-405,W2
2h	Smooth ER and lipid synthesis, export of proteins and lipids	R1: 275-405 ,W2
1h	Golgi Apparatus – Organization,	R1: 275-405 ,W3
1h	protein glycosylation	R1: 275-405 ,W3
1h	protein sorting and export from Golgi Apparatus	R1: 275-405 ,W3
1h	Lysosomes.	R1 : 275-405,W3
1h	Unit Revisions	
	Total hours:12h	

UNIT IV

Duration	Topic	Reference
1h	Signalling molecules and their receptors	R1:110-125,W1
1h	Function of cell surface receptors	R:1110-125,W1
1h	Pathways of intra-cellular receptors	R1: 110-125,W1
1h	Cyclic AMP pathway	R1: 110-125,W2
1h	Cyclic GMP	R1: 110-125,W2
1h	MAP kinase pathway	R1: 110-125,W2
1h	Unit Revisions	
	Total hours: 7 h	

UNIT V

Duration	Topic	Reference
1h	Eukaryotic cell cycle and its regulation	R1:664-685,W1
1h	Mitosis	R1: 664-685,W1
1h	Meiosis	R1: 664-685,W2
1h	Development of cancer, causes and types	W3
1h	Programmed cell death	W4
1h	Stem cells	W4
1h	Embryonic stem cell	
1h	Induced pleuripotent stem cells.	
1h	Unit Revisions	
	Total hours: 8 h	

TEXTBOOKS

T1: Cell biology organelle structure and Functions by David.E Sadava 5thedition, 2004. New Delhi, India.

REFERENCES

R1: Fundamentalis of Microbiology by Edward Alicamo,Cell Biology by Gerald Karp.

WEBSITES

W1: www.shomusbiology/cell biology /index.conjugationandtransduction %crp/html.

Unit I
Syllabus

Cell organization-Eukaryotic (plant and animal cell)and prokaryotic. Plasma membrane :Structure and transport of small molecules.Cell Wall: Eukaryotic cell wall, extra cellular matrix and cell matrix interaction, CELL-CELL interaction- adhesion junction, tight junction ,gap junctionand plasmadesmata(structureal aspect only). Mitochondria chloroplast, peroxisomes.Cytoskeleton: Structure and organization of actin filaments, associationof actin filaments with plasma membrane ,cell surface protrusions, intermediate filaments, microtubules

Cell Structure

Plants are unique among the eukaryotes, organisms whose cells have membrane-enclosed nuclei and organelles, because they can manufacture their own food. Chlorophyll, which gives plants their green color, enables them to use sunlight to convert water and carbon dioxide into sugars and carbohydrates, chemicals the cell uses for fuel.

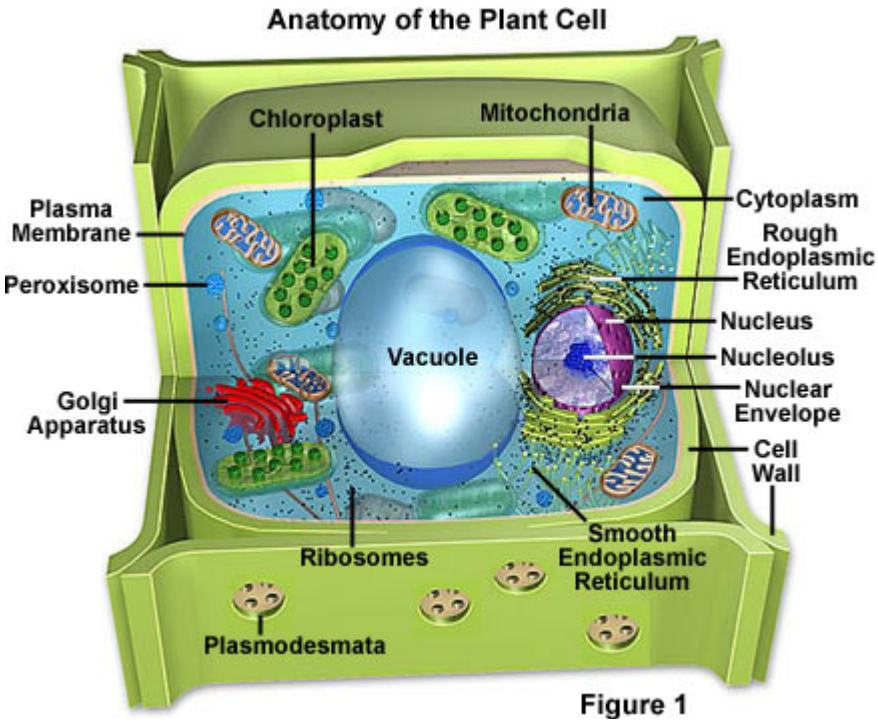


Figure 1

Like the fungi, another kingdom of eukaryotes, plant cells have retained the protective cell wall structure of their prokaryotic ancestors. The basic plant cell shares a similar construction motif with the typical eukaryote cell, but does not have centrioles, lysosomes, intermediate filaments, cilia, or flagella, as does the animal cell. Plant cells do, however, have a number of other specialized structures, including a rigid cell wall, central vacuole,

plasmodesmata, and chloroplasts. Although plants (and their typical cells) are non-motile, some species produce gametes that do exhibit flagella and are, therefore, able to move about.
Plants can be broadly categorized into two basic types: vascular and nonvascular. Vascular plants are considered to be more advanced than nonvascular plants because they have evolved specialized tissues, namely xylem, which is involved in structural support and water conduction, and phloem, which functions in food conduction. Consequently, they also possess roots, stems, and leaves, representing a higher form of organization that is characteristically absent in plants lacking vascular tissues. The nonvascular plants, members of the division Bryophyta, are usually no more than an inch or two in height because they do not have adequate support, which is provided by vascular tissues to other plants, to grow bigger. They also are more dependent on the environment that surrounds them to maintain appropriate amounts of moisture and, therefore, tend to inhabit damp, shady areas.

It is estimated that there are at least 260,000 species of plants in the world today. They range in size and complexity from small, nonvascular mosses to giant sequoia trees, the largest living organisms, growing as tall as 330 feet (100 meters). Only a tiny percentage of those species are directly used by people for food, shelter, fiber, and medicine. Nonetheless, plants are the basis for the Earth's ecosystem and food web, and without them complex animal life forms (such as humans) could never have evolved. Indeed, all living organisms are dependent either directly or indirectly on the energy produced by photosynthesis, and the byproduct of this process, oxygen, is essential to animals. Plants also reduce the amount of carbon dioxide present in the atmosphere, hinder soil erosion, and influence water levels and quality.

Plants exhibit life cycles that involve alternating generations of diploid forms, which contain paired chromosome sets in their cell nuclei, and haploid forms, which only possess a single set. Generally these two forms of a plant are very dissimilar in appearance. In higher plants, the diploid generation, the members of which are known as sporophytes due to their ability to produce spores, is usually dominant and more recognizable than the haploid gametophyte generation. In Bryophytes, however, the gametophyte form is dominant and physiologically necessary to the sporophyte form.
Animals are required to consume protein in order to obtain nitrogen, but plants are able to utilize inorganic forms of the element and, therefore, do not need an outside source of protein. Plants do, however, usually require significant amounts of water, which is needed for the photosynthetic process, to maintain cell structure and facilitate growth, and as a means of bringing nutrients to plant cells. The amount of nutrients needed by plant species varies significantly, but nine elements are generally considered to be necessary in relatively large amounts. Termed macroelements, these nutrients include calcium, carbon, hydrogen, magnesium, nitrogen, oxygen, phosphorus, potassium, and sulfur. Seven microelements, which are required by plants in smaller quantities, have also been identified: boron, chlorine, copper, iron, manganese, molybdenum, and zinc.

Thought to have evolved from the green algae, plants have been around since the early Paleozoic era, more than 500 million years ago. The earliest fossil evidence of land plants dates to the Ordovician Period (505 to 438 million years ago). By the Carboniferous Period,

about 355 million years ago, most of the Earth was covered by forests of primitive vascular plants, such as lycopods (scale trees) and gymnosperms (pine trees, ginkgos). Angiosperms, the flowering plants, didn't develop until the end of the Cretaceous Period, about 65 million years ago—just as the dinosaurs became extinct.

- Cell Wall - Like their prokaryotic ancestors, plant cells have a rigid wall surrounding the plasma membrane. It is a far more complex structure, however, and serves a variety of functions, from protecting the cell to regulating the life cycle of the plant organism.

- Chloroplasts - The most important characteristic of plants is their ability to photosynthesize, in effect, to make their own food by converting light energy into chemical energy. This process is carried out in specialized organelles called chloroplasts.

- Endoplasmic Reticulum - The endoplasmic reticulum is a network of sacs that manufactures, processes, and transports chemical compounds for use inside and outside of the cell. It is connected to the double-layered nuclear envelope, providing a pipeline between the nucleus and the cytoplasm. In plants, the endoplasmic reticulum also connects between cells via the plasmodesmata.

- Golgi Apparatus - The Golgi apparatus is the distribution and shipping department for the cell's chemical products. It modifies proteins and fats built in the endoplasmic reticulum and prepares them for export as outside of the cell.

- Microfilaments - Microfilaments are solid rods made of globular proteins called actin. These filaments are primarily structural in function and are an important component of the cytoskeleton.

- Microtubules - These straight, hollow cylinders are found throughout the cytoplasm of all eukaryotic cells (prokaryotes don't have them) and carry out a variety of functions, ranging from transport to structural support.

- Mitochondria - Mitochondria are oblong shaped organelles found in the cytoplasm of all eukaryotic cells. In plant cells, they break down carbohydrate and sugar molecules to provide energy, particularly when light isn't available for the chloroplasts to produce energy.

- Nucleus - The nucleus is a highly specialized organelle that serves as the information processing and administrative center of the cell. This organelle has two major functions: it stores the cell's hereditary material, or DNA, and it coordinates the cell's activities, which include growth, intermediary metabolism, protein synthesis, and reproduction (cell division).

- Peroxisomes - Microbodies are a diverse group of organelles that are found in the cytoplasm, roughly spherical and bound by a single membrane. There are several types of microbodies but peroxisomes are the most common.

- Plasmodesmata - Plasmodesmata are small tubes that connect plant cells to each other, providing living bridges between cells.

- Plasma Membrane - All living cells have a plasma membrane that encloses their contents. In prokaryotes and plants, the membrane is the inner layer of protection surrounded by a rigid cell wall. These membranes also regulate the passage of molecules in and out of the cells.

- Ribosomes - All living cells contain ribosomes, tiny organelles composed of approximately 60 percent RNA and 40 percent protein. In eukaryotes, ribosomes are made of four strands of RNA. In prokaryotes, they consist of three strands of RNA.

- Vacuole - Each plant cell has a large, single vacuole that stores compounds, helps in plant growth, and plays an important structural role for the plant.

Animal Cell Structure:

Animal cells are typical of the eukaryotic cell, enclosed by a plasma membrane and containing a membrane-bound nucleus and organelles. Unlike the eukaryotic cells of plants and fungi, animal cells do not have a cell wall. This feature was lost in the distant past by the single-celled organisms that gave rise to the kingdom Animalia. Most cells, both animal and plant, range in size between 1 and 100 micrometers and are thus visible only with the aid of a microscope.

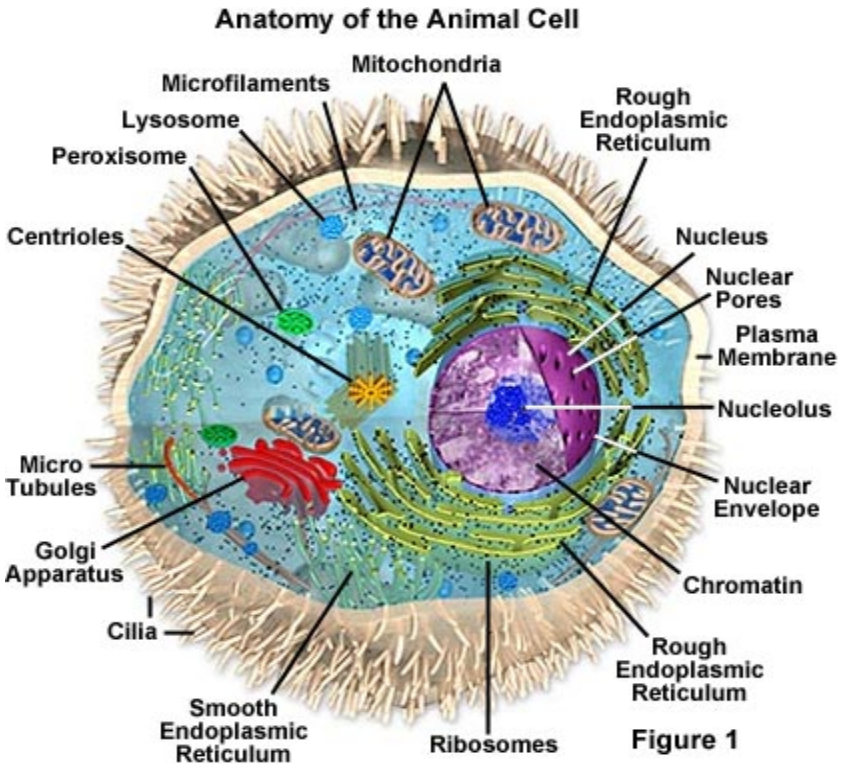


Figure 1

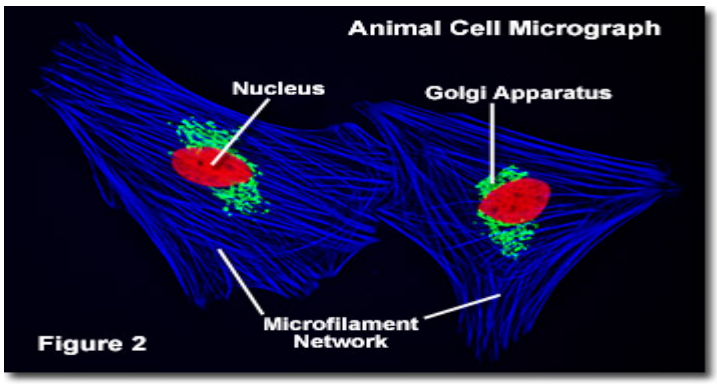
The lack of a rigid cell wall allowed animals to develop a greater diversity of cell types, tissues, and organs. Specialized cells that formed nerves and muscles—tissues impossible for plants to evolve—gave these organisms mobility. The ability to move about by the use of specialized muscle tissues is a hallmark of the animal world, though a few animals, primarily sponges, do not possess differentiated tissues. Notably, protozoans locomote, but it is only via nonmuscular means, in effect, using cilia, flagella, and pseudopodia.

The animal kingdom is unique among eukaryotic organisms because most animal tissues are bound together in an extracellular matrix by a triple helix of protein known as collagen. Plant and fungal cells are bound together in tissues or aggregations by other molecules, such as pectin. The fact that no other organisms utilize collagen in this manner is one of the indications that all animals arose from a common unicellular ancestor. Bones, shells, spicules, and other hardened structures are formed when the collagen-containing extracellular matrix between animal cells becomes calcified.

Animals are a large and incredibly diverse group of organisms. Making up about three-quarters of the species on Earth, they run the gamut from corals and jellyfish to ants, whales, elephants, and, of course, humans. Being mobile has given animals, which are capable of sensing and responding to their environment, the flexibility to adopt many different modes of feeding, defense, and reproduction. Unlike plants, however, animals are unable to manufacture their own food, and therefore, are always directly or indirectly dependent on plant life.

Most animal cells are diploid, meaning that their chromosomes exist in homologous pairs. Different chromosomal ploidies are also, however, known to occasionally occur. The proliferation of animal cells occurs in a variety of ways. In instances of sexual reproduction, the cellular process of meiosis is first necessary so that haploid daughter cells, or gametes, can be produced. Two haploid cells then fuse to form a diploid zygote, which develops into a new organism as its cells divide and multiply.

The earliest fossil evidence of animals dates from the Vendian Period (650 to 544 million years ago), with coelenterate-type creatures that left traces of their soft bodies in shallow-water sediments. The first mass extinction ended that period, but during the Cambrian Period which followed, an explosion of new forms began the evolutionary radiation that produced most of the major groups, or phyla, known today. Vertebrates (animals with backbones) are not known to have occurred until the early Ordovician Period (505 to 438 million years ago).



Cells were discovered in 1665 by British scientist Robert Hooke who first observed them in his crude (by today's standards) seventeenth century optical microscope. In fact, Hooke coined the term "cell", in a biological context, when he described the microscopic structure of cork like a tiny, bare room or monk's cell. Illustrated in Figure 2 are a pair of fibroblast deer skin cells that have been labeled with fluorescent probes and photographed in the microscope to reveal their internal structure. The nuclei are stained with a red probe, while the Golgi apparatus and microfilament actin network are stained green and blue, respectively. The microscope has been a fundamental tool in the field of cell biology and is often used to observe living cells in culture. Use the links below to obtain more detailed information about the various components that are found in animal cells.

- Centrioles - Centrioles are self-replicating organelles made up of nine bundles of microtubules and are found only in animal cells. They appear to help in organizing cell division, but aren't essential to the process.

- Cilia and Flagella - For single-celled eukaryotes, cilia and flagella are essential for the locomotion of individual organisms. In multicellular organisms, cilia function to move fluid or materials past an immobile cell as well as moving a cell or group of cells.

- Endoplasmic Reticulum - The endoplasmic reticulum is a network of sacs that manufactures, processes, and transports chemical compounds for use inside and outside of the cell. It is connected to the double-layered nuclear envelope, providing a pipeline between the nucleus and the cytoplasm.

- Endosomes and Endocytosis - Endosomes are membrane-bound vesicles, formed via a complex family of processes collectively known as endocytosis, and found in the cytoplasm of virtually every animal cell. The basic mechanism of endocytosis is the reverse of what occurs during exocytosis or cellular secretion. It involves the invagination (folding inward) of a cell's plasma membrane to surround macromolecules or other matter diffusing through the extracellular fluid.

- Golgi Apparatus - The Golgi apparatus is the distribution and shipping department for the cell's chemical products. It modifies proteins and fats built in the endoplasmic reticulum and prepares them for export to the outside of the cell.

- Intermediate Filaments - Intermediate filaments are a very broad class of fibrous proteins that play an important role as both structural and functional elements of the cytoskeleton. Ranging in size from 8 to 12 nanometers, intermediate filaments function as tension-bearing elements to help maintain cell shape and rigidity.

- Lysosomes - The main function of these microbodies is digestion. Lysosomes break down cellular waste products and debris from outside the cell into simple compounds, which are transferred to the cytoplasm as new cell-building materials.

- Microfilaments - Microfilaments are solid rods made of globular proteins called actin. These filaments are primarily structural in function and are an important component of the cytoskeleton.

- Microtubules - These straight, hollow cylinders are found throughout the cytoplasm of all eukaryotic cells (prokaryotes don't have them) and carry out a variety of functions, ranging from transport to structural support.

- Mitochondria - Mitochondria are oblong shaped organelles that are found in the cytoplasm of every eukaryotic cell. In the animal cell, they are the main power generators, converting oxygen and nutrients into energy.

- Nucleus - The nucleus is a highly specialized organelle that serves as the information processing and administrative center of the cell. This organelle has two major functions: it stores the cell's hereditary material, or DNA, and it coordinates the cell's activities, which include growth, intermediary metabolism, protein synthesis, and reproduction (cell division).

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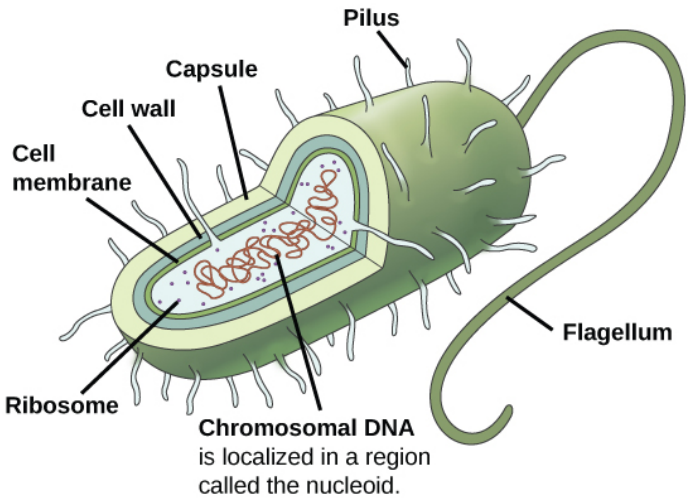
- Plasma Membrane - All living cells have a plasma membrane that encloses their contents. In prokaryotes, the membrane is the inner layer of protection surrounded by a rigid cell wall. Eukaryotic animal cells have only the membrane to contain and protect their contents. These membranes also regulate the passage of molecules in and out of the cells.

- Ribosomes - All living cells contain ribosomes, tiny organelles composed of approximately 60 percent RNA and 40 percent protein. In eukaryotes, ribosomes are made of four strands of RNA. In prokaryotes, they consist of three strands of RNA.

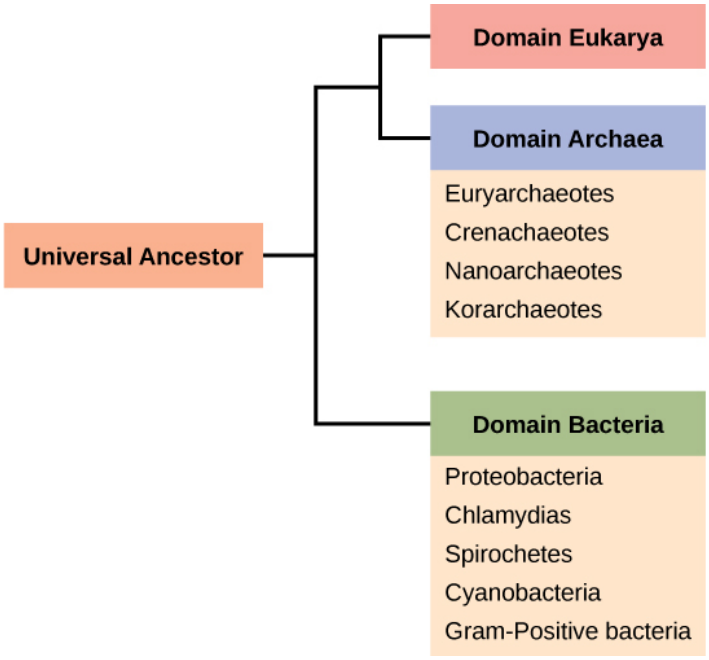
Prokaryotic Cell Structure

Prokaryotes are unicellular organisms that lack organelles or other internal membrane-bound structures. Therefore, they do not have a nucleus, but, instead, generally have a single chromosome: a piece of circular, double-stranded DNA located in an area of the cell called the nucleoid. Most prokaryotes have a cell wall outside the plasma membrane.



Prokaryotic cell structure:

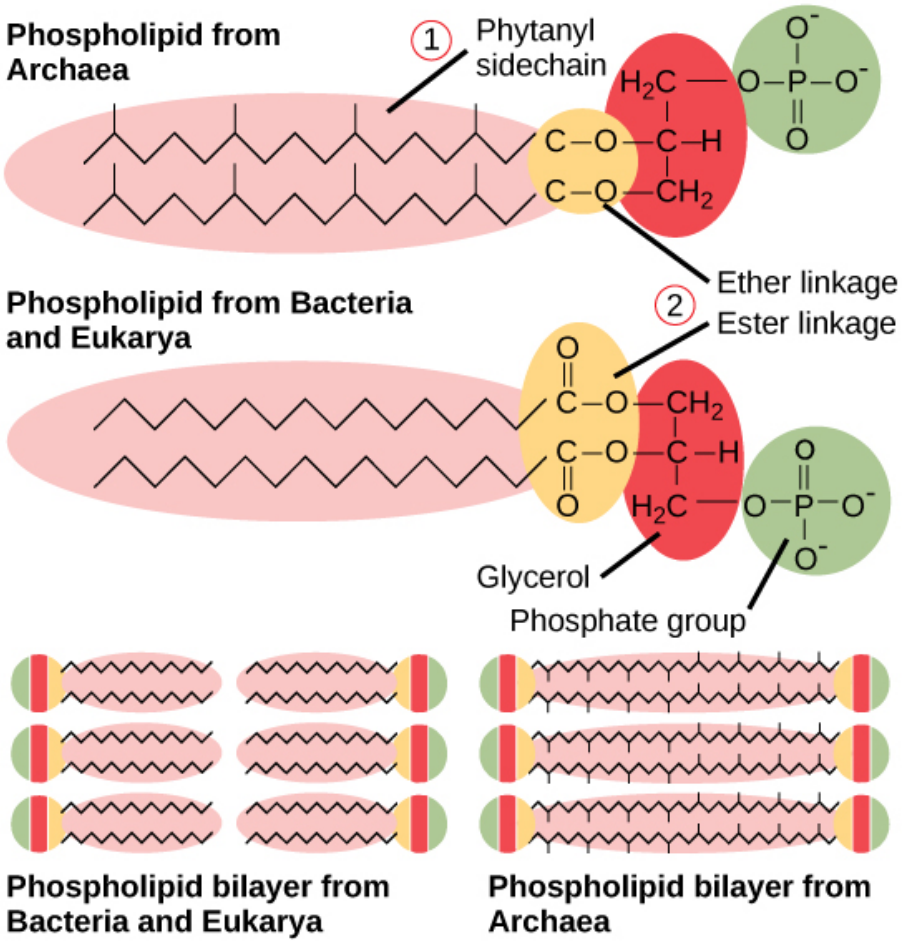
The composition of the cell wall differs significantly between the domains Bacteria and Archaea, the two domains of life into which prokaryotes are divided. The composition of their cell walls also differs from the eukaryotic cell walls found in plants (cellulose) or fungi and insects (chitin). The cell wall functions as a protective layer and is responsible for the organism's shape. Some bacteria have a capsule outside the cell wall. Other structures are present in some prokaryotic species, but not in others. For example, the capsule found in some species enables the organism to attach to surfaces, protects it from dehydration and attack by phagocytic cells, and increases its resistance to our immune responses. Some species also have flagella used for locomotion and pili used for attachment to surfaces. Plasmids, which consist of extra-chromosomal DNA, are also present in many species of bacteria and archaea.



Domains of life: Bacteria and Archaea are both prokaryotes, but differ enough to be placed in separate domains. An ancestor of modern Archaea is believed to have given rise to Eukarya, the third domain of life. Archaeal and bacterial phyla are shown; the evolutionary relationship between these phyla is still open to debate.

The Plasma Membrane

The plasma membrane is a thin lipid bilayer (6 to 8 nanometers) that completely surrounds the cell and separates the inside from the outside. Its selectively-permeable nature keeps ions, proteins, and other molecules within the cell, preventing them from diffusing into the extracellular environment, while other molecules may move through the membrane. The general structure of a cell membrane is a phospholipid bilayer composed of two layers of lipid molecules. In archaeal cell membranes, isoprene (phytanyl) chains linked to glycerol replace the fatty acids linked to glycerol in bacterial membranes. Some archaeal membranes are lipid monolayers instead of bilayers.



Plasma membrane structure: Archaeal phospholipids differ from those found in Bacteria and Eukarya in two ways. First, they have branched phytanyl sidechains instead of linear ones. Second, an ether bond instead of an ester bond connects the lipid to the glycerol.

The Cell Wall

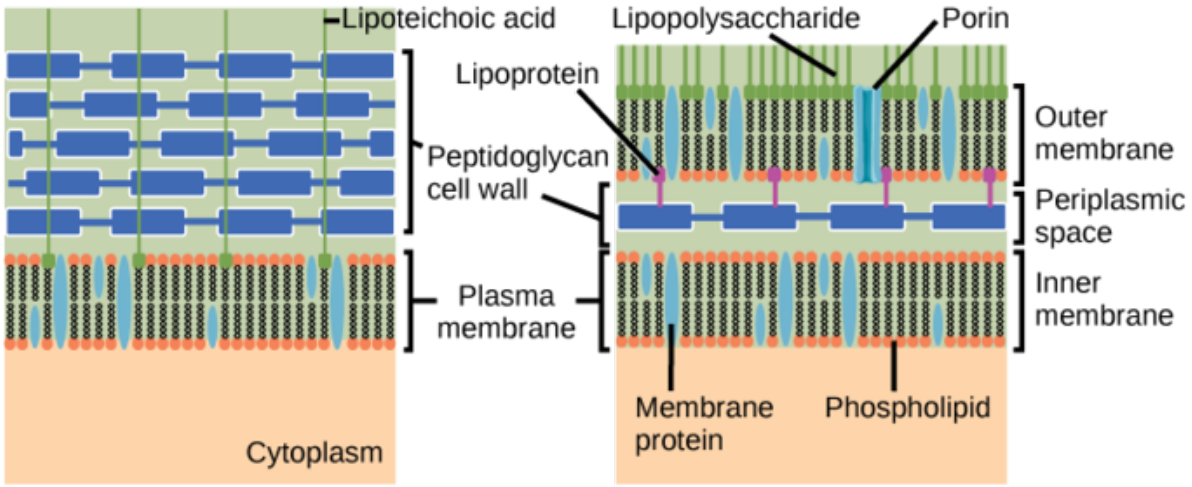
The cytoplasm of prokaryotic cells has a high concentration of dissolved solutes. Therefore, the osmotic pressure within the cell is relatively high. The cell wall is a protective layer that surrounds some cells and gives them shape and rigidity. It is located outside the cell membrane and prevents osmotic lysis (bursting due to increasing volume). The chemical composition of the cell walls varies between archaea and bacteria. It also varies between bacterial species.

Bacterial cell walls contain peptidoglycan composed of polysaccharide chains that are cross-linked by unusual peptides containing both L- and D-amino acids, including D-glutamic acid and D-alanine. Proteins normally have only L-amino acids; as a consequence, many of our antibiotics work by mimicking D-amino acids and, therefore, have specific effects on bacterial

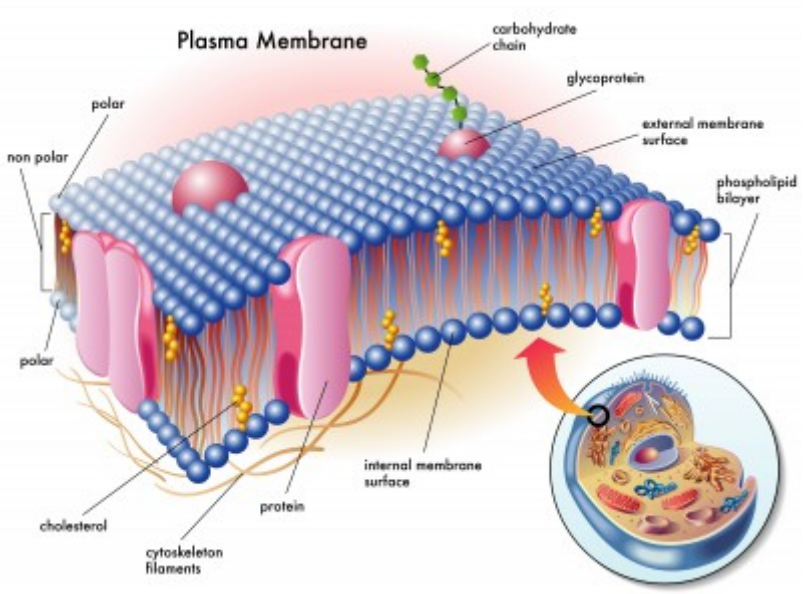
cell wall development. There are more than 100 different forms of peptidoglycan. S-layer (surface layer) proteins are also present on the outside of cell walls of both archaea and bacteria.

Bacteria are divided into two major groups: gram-positive and gram-negative, based on their reaction to gram staining. Note that all gram-positive bacteria belong to one phylum; bacteria in the other phyla (Proteobacteria, Chlamydias, Spirochetes, Cyanobacteria, and others) are gram-negative. The gram-staining method is named after its inventor, Danish scientist Hans Christian Gram (1853–1938). The different bacterial responses to the staining procedure are ultimately due to cell wall structure. Gram-positive organisms typically lack the outer membrane found in gram-negative organisms. Up to 90 percent of the cell wall in gram-positive bacteria is composed of peptidoglycan, with most of the rest composed of acidic substances called teichoic acids.

Teichoic acids may be covalently linked to lipids in the plasma membrane to form lipoteichoic acids. Lipoteichoic acids anchor the cell wall to the cell membrane. Gram-negative bacteria have a relatively thin cell wall composed of a few layers of peptidoglycan (only 10 percent of the total cell wall), surrounded by an outer envelope containing lipopolysaccharides (LPS) and lipoproteins. This outer envelope is sometimes referred to as a second lipid bilayer. The chemistry of this outer envelope is very different, however, from that of the typical lipid bilayer that forms plasma membranes.



Gram-positive and gram-negative bacteria: Bacteria are divided into two major groups: gram-positive and gram-negative. Both groups have a cell wall composed of peptidoglycan: in gram-positive bacteria, the wall is thick, whereas in gram-negative bacteria, the wall is thin. In gram-negative bacteria, the cell wall is surrounded by an outer membrane that contains lipopolysaccharides and lipoproteins. Porins, proteins in this cell membrane, allow substances to pass through the outer membrane of gram-negative bacteria. In gram-positive bacteria, lipoteichoic acid anchors the cell wall to the cell membrane.



plasma membrane structure:

Cell membrane, also called plasma membrane, thin membrane that surrounds every living cell, delimiting the cell from the environment around it. Enclosed by this cell membrane (also known as the plasma membrane) are the cell's constituents, often large, water-soluble, highly charged molecules such as proteins, nucleic acids, carbohydrates, and substances involved in cellular metabolism. Outside the cell, in the surrounding water-based environment, are ions, acids, and alkalis that are toxic to the cell, as well as nutrients that the cell must absorb in order to live and grow. The cell membrane, therefore, has two functions: first, to be a barrier keeping the constituents of the cell in and unwanted substances out and, second, to be a gate allowing transport into the cell of essential nutrients and movement from the cell of waste products.

Models of Plasma Membrane:

The models are: 1. Lipid and Lipid Bilayer Models 2. Unit Membrane Model (Protein-Lipid Bilayer-Protein) 3. Fluid Mosaic Model 4. Dannelli Model

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1. Lipid and Lipid Bilayer Model:

This model to explain the structure of plasma membrane was given by Overton, Gorion and Grendel. Previously only indirect information was available to explain the structure of plasma membrane. In 1902, Overton observed that substances soluble in lipid could selectively pass through the membranes. On this basis he stated that plasma membrane is composed of a thin layer of lipid.

Subsequently, Gorter and Grendel in 1926 observed that the extracted from erythrocyte membranes was twice the amount expected if a single layer was present throughout the surface area of these cells. On this basis they stated that plasma membrane is made up of double layer of lipid molecules. These models of Gorter and Grendel could not explain the proper structure of plasma membrane but they put the foundation of future models of membrane structure.

2. Unit Membrane Model (Protein-Lipid Bilayer-Protein):

This is also known as unit membrane model. This model was proposed by Davson Daniell and Robertson. When surface tension measurements made on the membranes, it suggests the presence of proteins. After the existence of proteins the initial lipid bilayer model proposed by Gorter and Grendel was modified. It was suggested that surface tension of cells is much lower than what one would expect if only lipids were involved.

It may also be observed that if protein is added to model lipid water system, surface tension is lowered. This suggested indirectly the presence of proteins. On this basis Davson and Danielli proposed that plasma membrane contained a lipid bilayer with protein on both surfaces. Initially they supposed that proteins existed as covalently bonded globular structures bound to the polar ends of lipids. Subsequently they developed the model in which the protein appears to be smeared over the hydrophilic ends of the lipid bilayer. This model makes its popularity for a long time.

With the availability of electron microscope later, fine structure of plasma membrane could be studied. Definite plasma membrane of 6 nm to 10 nm (10nm = 100 Å; 1 nm = 10^{-6}mm) thickness was observed on surface of all cells, and plasma membranes of two adjacent cells were found to be separated by a space, 1-15nm wide.

It was also observed that the plasma membrane of most of the cells appeared to be three layered. Two outer dense layers were about 2.0nm thick and the middle layer about 3.5nm. The early ideas of Gorter and Grendel and those of Davson and Danielli were first formalized by Robertson in 1959 in the form of his unit membrane concept.

This concept of unit membrane with three layers (two protein layers and one lipid bilayer) only supported the concept proposed earlier by Davson and Danielli. In this unit membrane the less dense middle layer corresponded to hydrocarbon chains of lipids. Thickness of unit membrane

(10nm) was found to be greater in plasma membrane than in intracellular membranes of endoplasmic reticulum or golgi complex.

3. Fluid Mosaic Model:

To explain the structure plasma membrane various models have been put forward from time to time. But none was universally accepted. In this relation Gorter and Grendel, Davson and Danielli, etc. proposed model for plasma membrane after that Fluid Mosaic Model for plasma membrane was proposed which was universally accepted.

It was proposed by Singer and Nicholson (1912). This model postulates that lipid and integrated proteins are disposed in a sort of mosaic pattern and all the biological membranes have a quasi-fluid structure where both lipid and protein components are able to perform transitional movement within lipid bilayer.

In this model, lipid molecules may exhibit intra-molecular movement or may rotate about their axis or may display flip-flop movement including transfer from one side of bilayer to the other. Thus this concept implies that main components of the membrane, i.e., lipids, proteins and oligosaccharides are held together by means of non-covalent interactions as suggested by Gitler (1972). A term amphipathy was coined by Hartley (1936) to the molecules having both hydrophilic and hydrophobic groups. Thus lipids and integrated proteins are amphipatic in nature of plasma membrane is based on integration of data from chemical analysis Our present knowledge and those from the study of biophysical properties with the help of various types of techniques. These have provided the main components which are integrated in plasma membrane. In this relation, following four major techniques as discoveries have given support.
These are as follows:
(i) Freeze fracture technique was used to study membrane. Freeze fractured electron microscope, revealed the presence of bums and depressions which are 7- 8 nm in diameter. These remains randomly distributed. These were later shown to be intra-membrane protein particles which transverse the bilayer.

(ii) Frye and Edidin (1970) labeled selectively the species specific proteins of human and mouse cells and then fused these cells of the two species to make a heterokaryon. After incubating the heterokaryons for 30-35 minutes at 37°C, human and mouse proteins in these heterokaryons were seen intermixing (as demonstrated by using specific antibodies), so that human and mouse proteins became randomly distributed suggesting that membrane proteins are mobile in the plane of the membrane.

(iii) The process named patching and capping also provide evidence about the mobility of proteins within the lipid bilayer. This process suggested that when ligands like antibodies have more than one sites for binding the specific proteins on the cell surface, the proteins tend to aggregate into clusters through cross-linking. This indicates that proteins diffuse laterally in the bilayer.

(iv) Fluorescence recovery after photo-bleaching (FRAP) has also been used for measuring rates of lateral diffusion of proteins. A cell surface protein of interest is marked with a fluorescent ligand (e.g., antibody). The ligand is bleached in a small area by a laser beam and the time taken for bleached and unbleached fluorescent ligands to diffuse and mix is measured. The rate of diffusion of protein is not constant.

The evidences as above suggested that lipid bilayer has fluid properties enabling membrane proteins to diffuse rapidly. Rotational diffusion of proteins is possible. However no evidence of flip-flop mechanism as suggested for lipids has been available for proteins. Later on it was suggested that not only proteins, but individual lipid molecules are also able to diffuse freely within the lipid bilayers.

And it was found true in synthetic as well as isolated biological membranes which were obtained from mycoplasmas, bacteria and red blood cells. Initially, this was demonstrated in the following two types of synthetic lipid bilayers i.e., liposomes and black membranes, liposomes are spherical vesicles.

These measures from 25nm to 1/nm (1000nm) in diameter Black membranes extend across a hole in a partition between two aqueous compartments. The motion of individual lipid molecules could be measured by ‘spin labeling’.

(The spin of unpaired electron creates a paramagnetic signal that can be detected by electron spin resonance (E.S.R) spectroscopy). The motion and orientation of a spin labelled lipid can be deduced from the ESR spectrum. The lipid molecules can also rotate or readily exchange places within the same monolayer (10^7 times in a second) with a diffusion coefficient (D) of about 10^{-8} cm^2/sec, so that a lipid molecule could diffuse the length of a large bacterial cell (–2µm) in about one second.

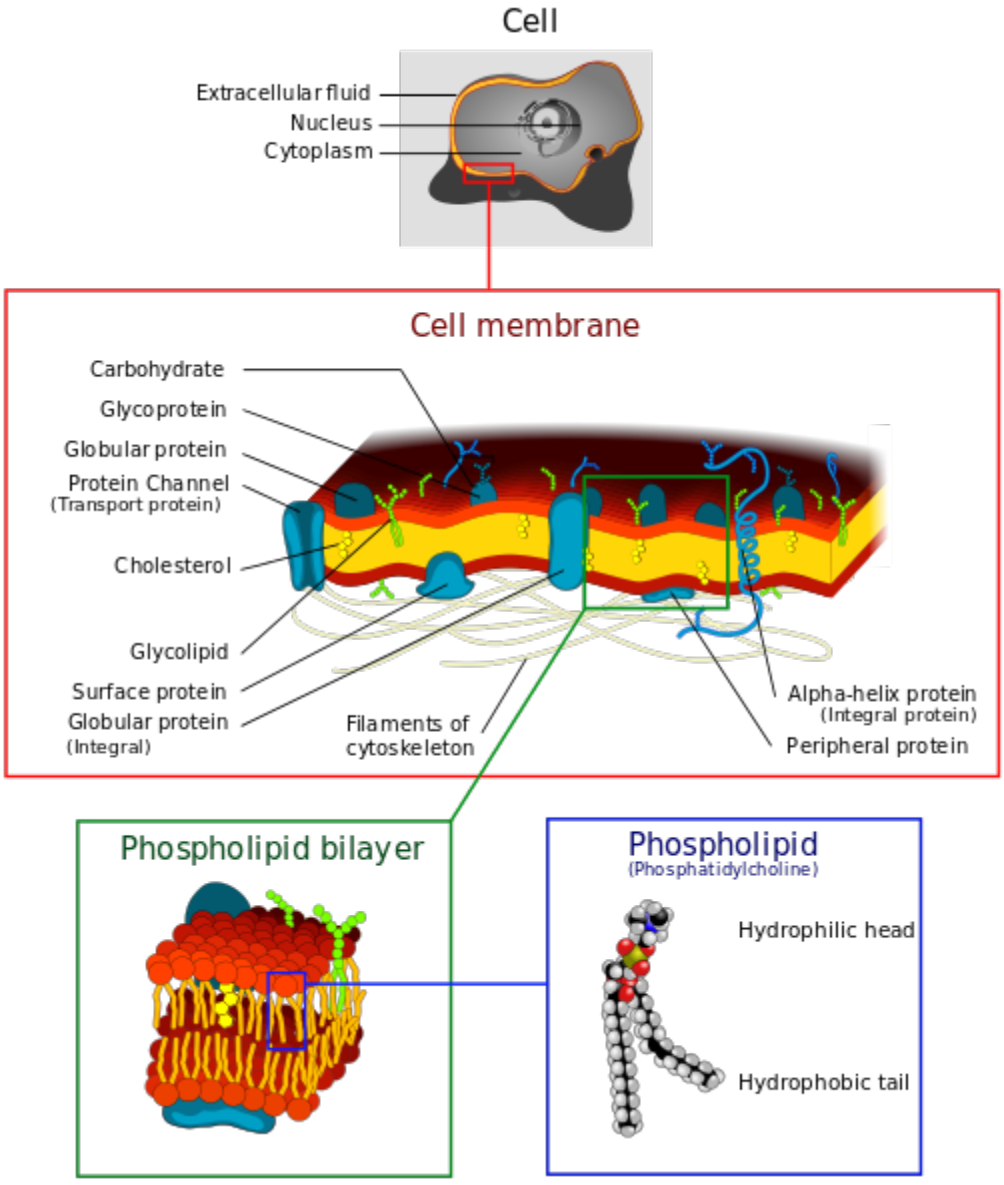
Even when the lipid molecule is static, the hydrocarbon chains are flexible. Similar results were obtained from isolated biological membranes, except that in the natural. On the basis of these facts, Singer and Nicolson proposed a hypothesis to explain the structure of plasma membrane. This is known as fluid mosaic model. Basically this model was modification of Robertson and Davson.

Transport through Cellular Membrane:

The 'cell membrane' (also known as the plasma membrane or cytoplasmic membrane) is a biological membrane that separates the interior of all cells from the outside environment. The cell membrane is selectively permeable to ions and organic molecules and controls the movement of substances in and out of cells. The basic function of the cell membrane is to protect the cell from its surroundings. It consists of the phospholipid bilayer with embedded proteins.

The cell membrane is selectively permeable and able to regulate what enters and exits the cell, thus facilitating the transport of materials needed for survival. The movement of substances

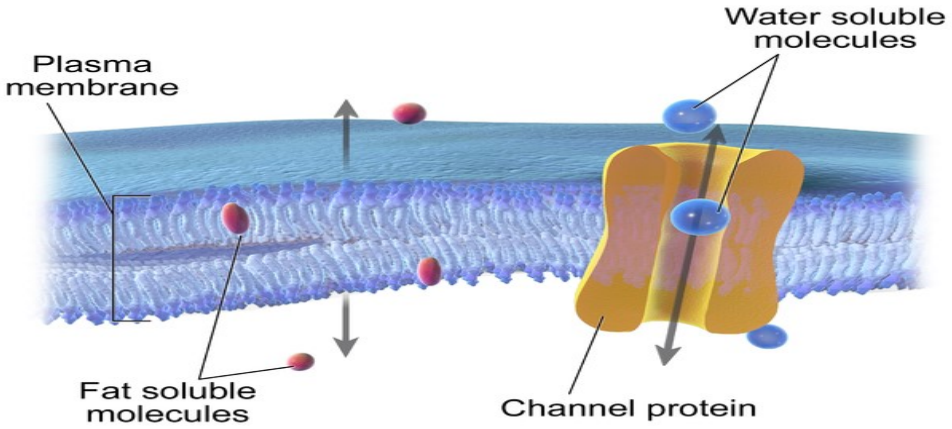
across the membrane can be either "passive", occurring without the input of cellular energy, or "active", requiring the cell to expend energy in transporting it. The membrane also maintains the cell potential. The cell membrane thus works as a selective filter that allows only certain things to come inside or go outside the cell. The cell employs a number of transport mechanisms that involve biological membranes:



Types of cellular transport:

Passive osmosis and diffusion

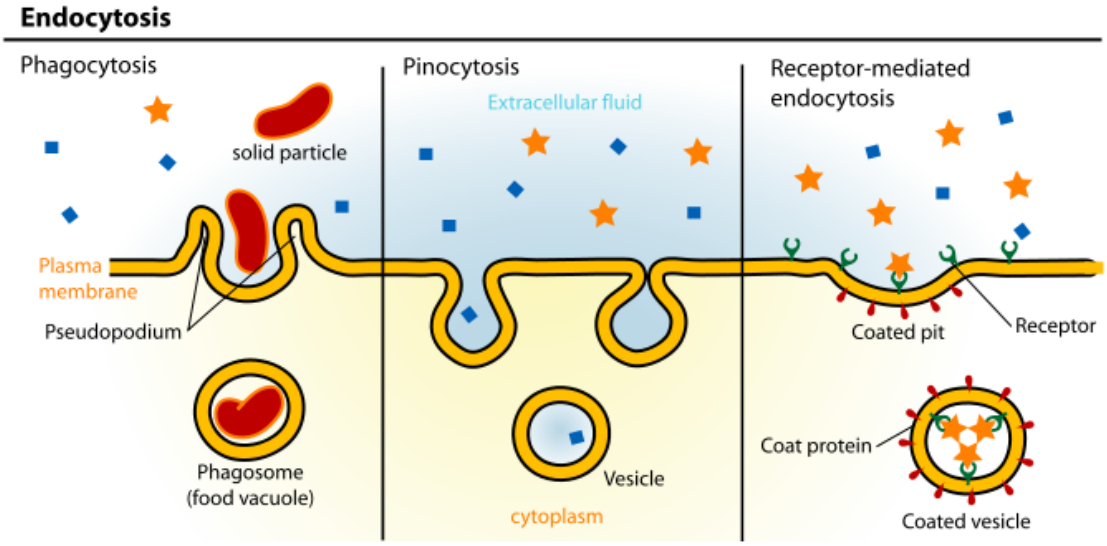
Some substances (small molecules, ions) such as carbon dioxide (CO2) and oxygen (O2), can move across the plasma membrane by diffusion, which is a passive transport process. Because the membrane acts as a barrier for certain molecules and ions, they can occur in different concentrations on the two sides of the membrane. Such a concentration gradient across a semipermeable membrane sets up an osmotic flow for the water.



Diffusion Across the Plasma Membrane

Transmembrane protein channels and transporters

Nutrients, such as sugars or amino acids, must enter the cell, and certain products of metabolism must leave the cell. Such molecules diffuse passively through protein channels in facilitated diffusion or are pumped across the membrane by transmembrane transporters. Protein channel proteins, also called permeases, are usually quite specific, recognizing and transporting only a limited food group of chemical substances, often even only a single substance.

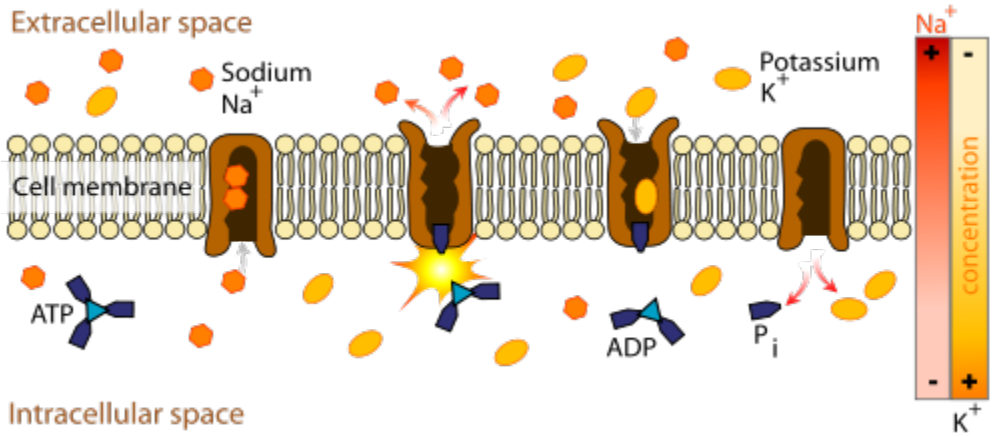


Endocytosis

Endocytosis is the process in which cells absorb molecules by engulfing them. The plasma membrane creates a small deformation inward, called an invagination, in which the substance to be transported is captured. The deformation then pinches off from the membrane on the inside of the cell, creating a vesicle containing the captured substance. Endocytosis is a pathway for internalizing solid particles ("cell eating" or phagocytosis), small molecules and ions ("cell drinking" or pinocytosis), and macromolecules. Endocytosis requires energy and is thus a form of active transport.Receptor-mediated endocytosis is a process by which cells internalize molecules (endocytosis) by the inward budding of plasma membrane vesicles containing proteins with receptor sites specific to the molecules being internalized. Coat proteins of the vesicle signals proteins of specific organelles in the cell, which allow the direct transmission of specific internal molecules be delivered directly to the organelles that require them.

Exocytosis

Just as material can be brought into the cell by invagination and formation of a vesicle, the membrane of a vesicle can be fused with the plasma membrane, extruding its contents to the surrounding medium. This is the process of exocytosis. Exocytosis occurs in various cells to remove undigested residues of substances brought in by endocytosis, to secrete substances such as hormones and enzymes, and to transport a substance completely across a cellular barrier. In the process of exocytosis, the undigested waste-containing food vacuole or the secretory vesicle budded from Golgi apparatus, is first moved by cytoskeleton from the interior of the cell to the surface. The vesicle membrane comes in contact with the plasma membrane. The lipid molecules of the two bilayers rearrange themselves and the two membranes are, thus, fused. A passage is formed in the fused membrane and the vesicles discharges its contents outside the cell.



Active transport: the sodium-potassium pump

Active Transport

Active transport is the movement of molecules across a cell membrane in the direction against their concentration gradient, going from a low concentration to a high concentration. Active transport is usually associated with accumulating high concentrations of molecules that the cell needs, such as ions, glucose and amino acids. If the process uses chemical energy, such as from adenosine triphosphate (ATP), it is termed primary active transport. Secondary active transport involves the use of an electrochemical gradient. Active transport uses cellular energy, unlike passive transport, which does not use cellular energy. Active transport is a good example of a process for which cells require energy.

Cell Wall of Eukaryotic Cells: Structure and Function

Robert Hooke (1665) discovered cell wall when he observed dead empty cells in a very thin slice of cork under his microscope.

Definition:

Cell wall is the thick, rigid, non-living, semi-elastic, transparent, specialized form of protective extra-cellular matrix that present outside the plasma lemma of cells.

Occurrence:

Found in plant cells, fungal cells, some protists and prokaryotes except a few lower plants, gametes and in animal cells.

Thickness:

The thickness varies from 0.1 to 10/µm and xylem vessels have thickest cell wall, while thinnest cell wall found in meristematic and parenchymatous cells.

Chemical composition:

In plants, cell wall composed of cellulose micro-fibrils embedded in the matrix. Matrix is the gel-like ground substance which consists of water, hemicellulose, pectin, glycoproteins and lipids. The cell wall may have lignin for hardness, silica for stillness and protection, cut in to prevent water loss and suberin for impermeability. In fungi, cell wall composed of chitin or fungal cellulose, a polymer of NAG. In bacteria, cell wall composed of peptidoglycan which consists of polymers of NAG (N-acetyl glucosamine) and NAM (N-acetyl muramic acid) cross-linked by short peptides.

Structure:

The structure of cell wall determines the architecture and function of plant cell.

A typical cell wall composed of 3-4 layers that are formed sequentially from outside to inwards are as follows: Middle lamella, Primary wall, Secondary wall & occasionally tertiary wall is

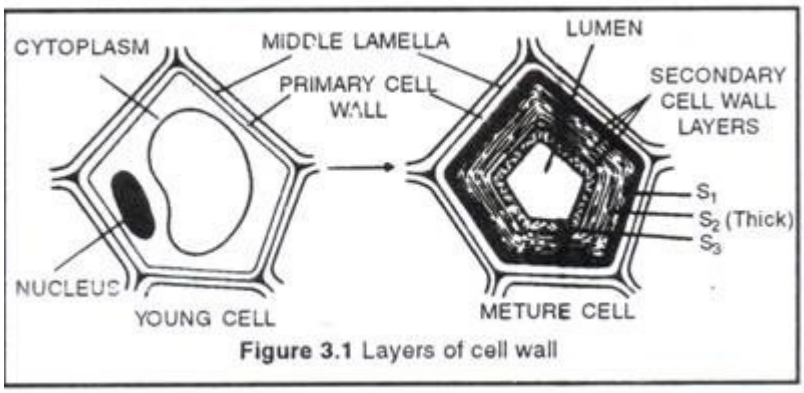


Figure 3.1 Layers of cell wall

(a) Middle Lamella.

It is a cementing layer present between adjacent cells but absent on the free surface of plant cells and in plasmadesmata region. Chemically it is composed of pectin (calcium and magnesium-pectate). Softening of fruits and fiber retting involves the dissolution of middle lamella.

(b) Primary Wall:

It is the first formed wall of the cell which is deposited inner to the middle lamella. Primary wall is usually thin (0.1-3.0/µm) and capable of extension. Its thickness increases with the growth of the plant cell. It grows by intussusceptions (internal growth) i.e. wall materials deposited into the existing primary wall. Cells engaged active division, photosynthesis, respiration and secretion have only primary walls.

(c) Secondary wall:

It is deposited inner to primary wall only in mature and non-dividing cells. It is generally seen in parenchyma, collenchyma, sclerenchyma, tracheids and vessels. The secondary wall grows by accretion i.e. deposited in layers. It is about 3 –l0/µm thick and consists of usually three layers, designated as S_1, S_2 (thickest) and S_3, sometimes even more as in latex tube of Euphorbia milli. During the formation of secondary cell wall in tracheids and vessels of xylem, its constituents are deposited unevenly inner to primary wall. As a result, various patterns of secondary thickening develop such as annular, spiral, scalariform, reticulate and pitted.

(d) Tertiary wall:

It is a xylan-rich layer deposited inner to the secondary wall of some plant cells, e.g., tension wood of gymnosperms.

Pits:

These are the depressions in the secondary wall of plant cells.

A pit consists of:
(i) Pit chamber, the actual hole within the secondary wall;
(ii) Pit membrane, composed of middle lamella and primary walls between two adjacent pits; and
(iii) Pit aperture, an opening that communicate pit chamber with the interior of the cell. Pit membrane is permeable like primary wall. Pits of adjacent cells usually occur opposite and form a pit pair. A pit present on the free surface of cell without its corresponding partner is called blind pit

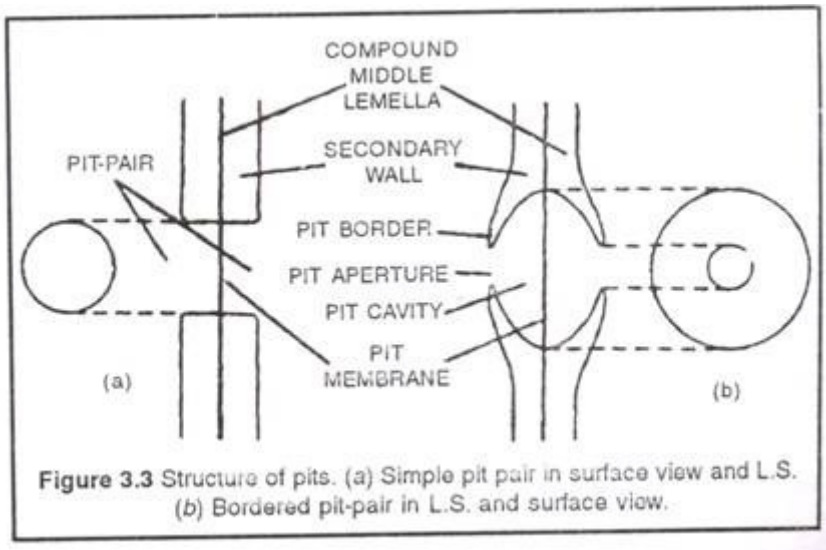


Figure 3.3 Structure of pits. (a) Simple pit pair in surface view and L.S. (*b*) Bordered pit-pair in L.S. and surface view.

Plasmodesmata (Singl. Plasmodesma):

These are the fine protoplasmic channels (20-40 nm in diameter) that connect the protoplasts of adjacent plant cells (Fig. 3.4). Plasmodesmata were discovered by Tangle (1879)

and studied in details by Strasburger (1901). It is roughly cylindrical and contains a fine simple or branched desmotubule which connect ER of 2 adjacent cells. Around desmotubule a cytosolic annulus is present. It is formed around SER that become trapped during cytokinesis within the cell plate. Their number is abundant in the cell walls leading towards site of intense secretion.

Function:

(i) Help in transfer of nutrients, stimuli and other material between adjacent cells,
(ii) Produce a protoplasmic continuum called symplast.
(iii) Plant virus like TMV synthesize a protein P_{30} that nullifies the normal regulatory mechanism of plasmodesmata.
(iv) TMV enlarges plasmodesmata in order to use this route to pass from cell to cell.

Extracellular Matrix – What is it?

A general form is found widely distributed in animals. The two main groups of biochemicals that make up the basic ECM are complex chains of sugar molecules (polysaccharides) and polysaccharides joined to protein (glycoproteins such as fibronectin, laminin and thrombospondin) and include the very viscous substance proteoglycans. Embedded in this can be various types and amounts of structural and insoluble collagen fibres and flexible elastic fibres that give resilience to tissues.

Modified forms appear in the form of bone, the exoskeleton of an insect, animal shells and the cell wall of plants.

ECM – where does it come from?

All cells can make extracellular matrix but certain specialist cells produce a specific type of ECM:

Fibroblast cells secrete connective tissue ECM
Osteoblast cells secrete bone-forming ECM and
Chondroblast cells secrete cartlilage-forming ECM.
Fibroblasts and epitheal cells together make basement membrane ECM

ECM – what does it do?

This depends on where it is and how specialised the ECM is. Different forms in different locations have different properties.

Specialised types of ECM in animals

ECM can be modified, mainly by calcification to produce bones, teeth and shells or chitinisation to form the chitin exoskeleton of insects. These types of ECM clearly provide mechanical facility and protection.

A less rigid type of ECM forms tendons and cartilage and a soft transparent gel form is found for example in the cornea of the eye where it provides hydraulic protection.

Specialised ECM in plants:

The ECM in plants is mainly cellulose and surrounds each cell. Along with water it contributes to the total rigidity of the plant. The ability of a tree to grow to a great height and retain its rigidity is partly due to the cellulose ECM of the cell walls together with other biochemicals including lignin and extensins.

A less easily observed form of ECM is found in vertebrates in three main forms

1. Connective tissue – This contains lots of ECM and only a few cells.
2. Basal lamina – This can be considered as the ECM of epithelial cells but formed into a tough layer containing a great many collagen fibres and laminin and upon which the cells of the epithelia 'sit'. Very little ECM surrounds each individual cell and they are joined to each other in different ways.
3. Pericellular matrix – With a few exceptions all cells are surrounded by cell extracellular matrix to some degree. It is this material that not only gives mechanical support by binding cells together but with the glycocalyx provides a biochemical barrier around the cell, a docking facility for imports and exports to and from the cell, and a medium through which chemical signalling can take place. Recent work indicates that ECM sugar molecules may have an important role to play in cancer biology.

Cell–cell interaction

Cell–cell interaction refers to the direct interactions between cell surfaces that play a crucial role in the development and function of multicellular organisms. These interactions allow cells to communicate with each other in response to changes in their microenvironment. This ability to send and receive signals is essential for the survival of the cell. Interactions between cells can be stable such as those made through cell junctions. These junctions are involved in the communication and organization of cells within a particular tissue. Others are transient or temporary such as those between cells of the immune system or the interactions involved in tissue inflammation. These types of intercellular interactions are distinguished from other types such as those between cells and the extracellular matrix. The loss of communication between cells can result in uncontrollable cell growth and cancer.

Stable interactions

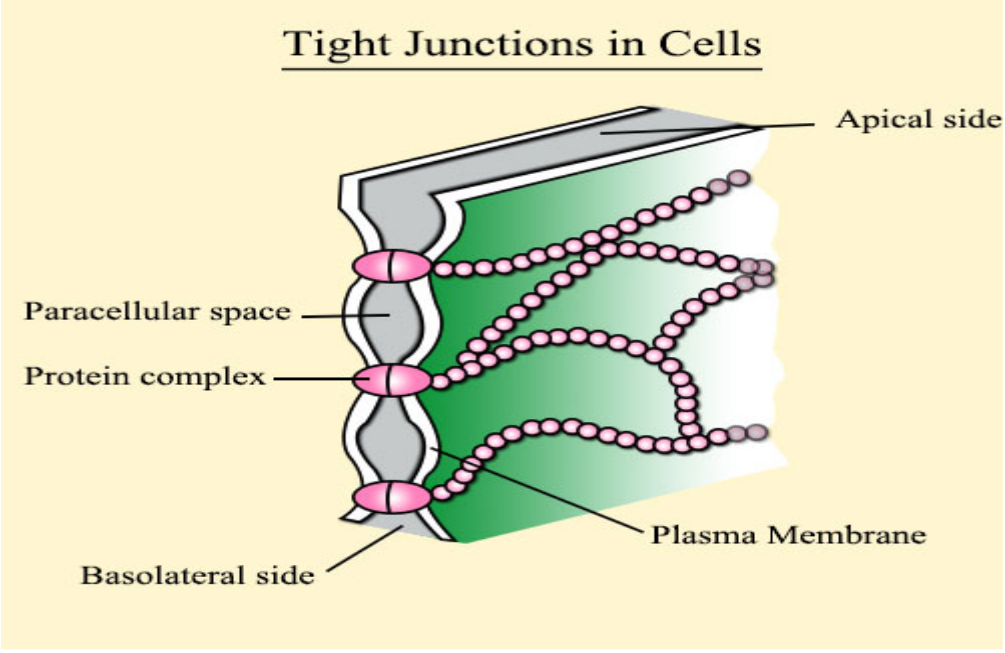
Stable cell-cell interactions are required for cell adhesion within a tissue and controlling the shape and function of cells. These stable interactions involve cell junctions which are multiprotein complexes that provide contact between neighboring cells. Cell junctions allow for the preservation and proper functioning of epithelial cell sheets. These junctions are also important in the

organization of tissues where cells of one type can only adhere to cells of the same tissue rather than to a different tissue.

Tight junctions

Tight junctions are multi-protein complexes that hold cells of a same tissue together and prevent movement of water and water-soluble molecules between cells. In epithelial cells, they function also to separate the extracellular fluid surrounding their apical and basolateral membranes. These junctions exist as a continuous band located just below the apical surface between the membranes of neighboring epithelial cells. The tight junctions on adjacent cells line up so as to produce a seal between different tissues and body cavities. For example, the apical surface of gastrointestinal epithelial cells serve as a selective permeable barrier that separates the external environment from the body. The permeability of these junctions is dependent on a variety of factors including protein makeup of that junction, tissue type and signaling from the cells.

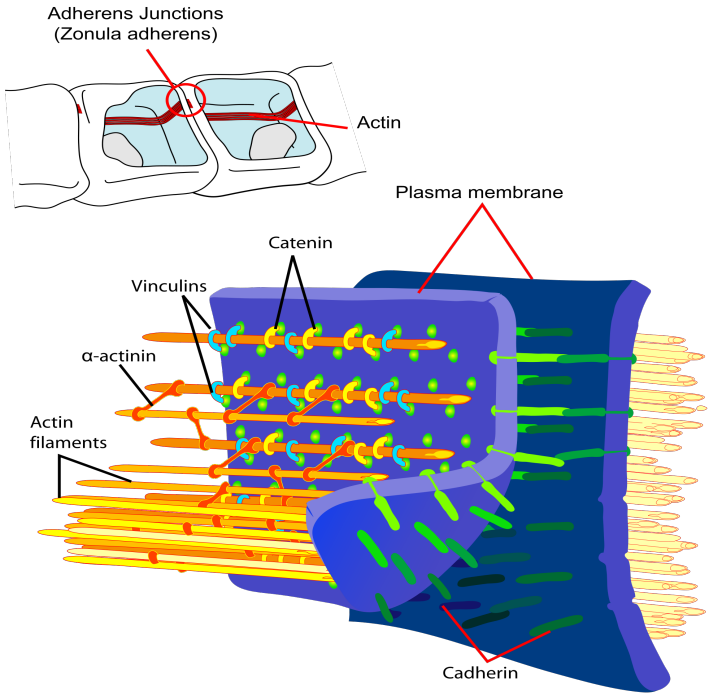
Tight junctions are made up of many different proteins. The four main transmembrane proteins are occludin, claudin, junctional adhesion molecules (JAMs) and tricellulins. The extracellular domains of these proteins form the tight junction barrier by making homophilic (between proteins of the same kind) and heterophilic interactions (between different types of proteins) with the protein domains on adjacent cells. Their cytoplasmic domains interact with the cell cytoskeleton to anchor them.



Anchoring junctions:

The three types of anchoring junctions, only two are involved in cell-cell interactions: adherens junctions and desmosomes. Both are found in many types of cells. Adjacent epithelial cells are connected by adherens junctions on their lateral membranes. They are located just below tight junctions. Their function is to give shape and tension to cells and tissues and they are also the site of cell-cell signaling. Adherens junctions are made of cell adhesion molecules from the cadherin family. There are over 100 types of cadherins, corresponding to the many different types of cells and tissues with varying anchoring needs. The most common are E-, N- and P-cadherins. In the adherens junctions of epithelial cells, E-cadherin is the most abundant.

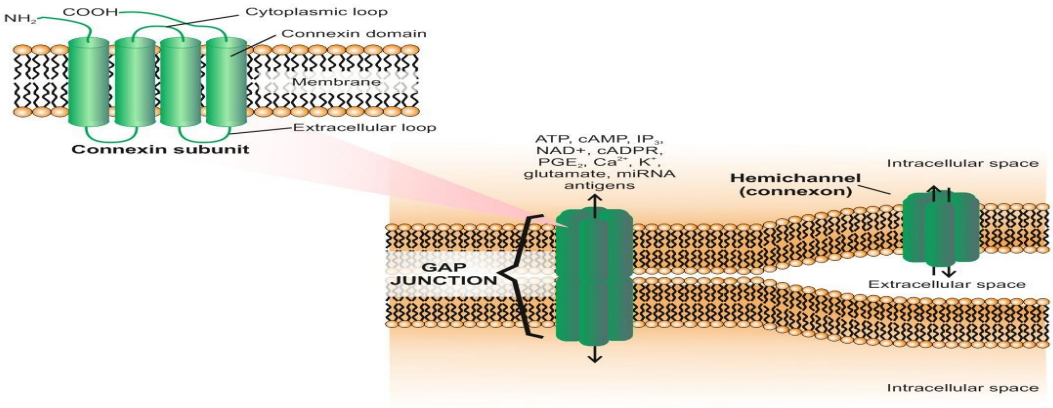
Desmosomes also provide strength and durability to cells and tissues and are located just below adherens junctions. They are sites of adhesion and do not encircle the cell. They are made of two specialized cadherins, desmoglein and desmocollin. These proteins have extracellular domains that interact with each other on adjacent cells. On the cytoplasmic side, plakins form plaques which anchor the desmosomes to intermediate filaments composed of keratin proteins. Desmosomes also play a role in cell-cell signaling.



Gap junctions:

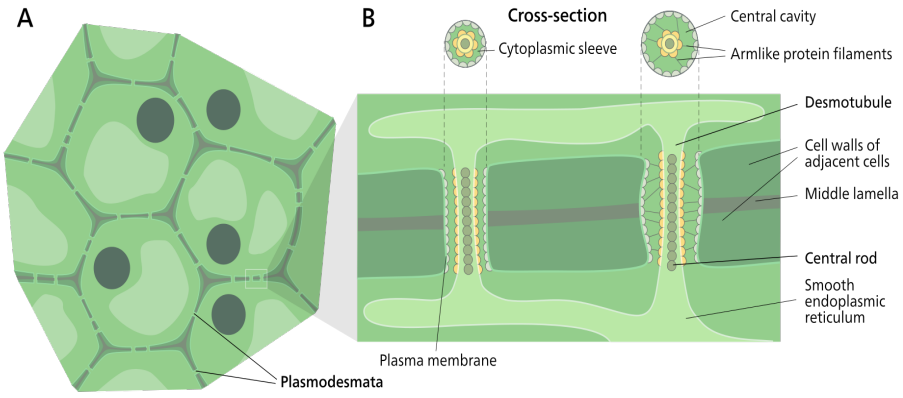
Gap junctions are the main site of cell-cell signaling or communication that allow small molecules to diffuse between adjacent cells. In vertebrates, gap junctions are composed of transmembrane proteins called connexins. They form hexagonal pores or channels through which

ions, sugars, and other small molecules can pass. Each pore is made of 12 connexin molecules; 6 form a hemichannel on one cell membrane and interact with a hemichannel on an adjacent cell membrane. The permeability of these junctions is regulated by many factors including pH and Ca^{2+} concentration.



Plasmodesmata structure:

Plasmodesmata (singular: plasmodesma) are microscopic channels which traverse the cell walls of plant cells[2] and some algal cells, enabling transport and communication between them. Plasmodesmata evolved independently in several lineages,[3] and species that have these structures include members of the Charophyceae, Charales, Coleochaetales and Phaeophyceae (which are all algae), as well as all embryophytes, better known as land plants.[4] Unlike animal cells, almost every plant cell is surrounded by a polysaccharide cell wall. Neighbouring plant cells are therefore separated by a pair of cell walls and the intervening middle lamella, forming an extracellular domain known as the apoplast. Although cell walls are permeable to small soluble proteins and other solutes, plasmodesmata enable direct, regulated, symplastic transport of substances between cells. There are two forms of plasmodesmata: primary plasmodesmata, which are formed during cell division, and secondary plasmodesmata, which can form between mature cells.



Primary plasmodesmata:

The formation of primary plasmodesmata occurs during the part of the cellular division process where the endoplasmic reticulum and the new plate are fused together, this process results in the formation of a cytoplasmic pore (or cytoplasmic sleeve). The desmotubule, also known as the appressed ER, forms alongside the cortical ER. Both the appressed ER and the cortical ER are packed tightly together, thus leaving no room for any luminal space. It is proposed that the appressed ER acts as a membrane transportation route in the plasmodesmata. When filaments of the cortical ER are entangled in the formation of a new cell plate, plasmodesmata formation occurs in land plants. It is hypothesized that the appressed ER forms due to a combination of pressure from a growing cell wall and interaction from ER and PM proteins. Primary plasmodesmata are often present in areas where the cell walls appear to be thinner. This is due to the fact that as a cell wall expands, the abundance of the primary plasmodesmata decreases. In order to further expand plasmodesmal density during cell wall growth secondary plasmodesmata are produced. The process of secondary plasmodesmata formation is still to be fully understood, however various degrading enzymes and ER proteins are said to stimulate the process.

Plasmodesmatal plasma membrane:

A typical plant cell may have between 10^3 and 10^5 plasmodesmata connecting it with adjacent cells equating to between 1 and 10 per µm Plasmodesmata are approximately 50–60 nm in diameter at the midpoint and are constructed of three main layers, the plasma membrane, the cytoplasmic sleeve, and the desmotubule.They can transverse cell walls that are up to 90 nm thick.

The plasma membrane portion of the plasmodesma is a continuous extension of the cell membrane or plasmalemma and has a similar phospholipid bilayer structure.

The cytoplasmic sleeve is a fluid-filled space enclosed by the plasmalemma and is a continuous extension of the cytosol. Trafficking of molecules and ions through plasmodesmata occurs through this space. Smaller molecules (e.g. sugars and amino acids) and ions can easily pass through plasmodesmata by diffusion without the need for additional chemical energy. Larger molecules, including proteins (for example green fluorescent protein) and RNA, can also pass through the cytoplasmic sleeve diffusively. Plasmodesmatal transport of some larger molecules is facilitated by mechanisms that are currently unknown. One mechanism of regulation of the permeability of plasmodesmata is the accumulation of the polysaccharide callose around the neck region to form a collar, thereby reducing the diameter of the pore available for transport of substances.Through dilation, active gating or structural remodeling the permeability of the plasmodesmata is increased. This increase in plasmodesmata pore permeability allows for larger molecules, or ((macromolecules)), such as signaling molecules, transcription factors and RNA-protein complexes to be transported to various cellular compartments.

Mitochondria

Mitochondria Definition

Mitochondria (singular: mitochondrion) are organelles within eukaryotic cells that produce adenosine triphosphate (ATP), the main energy molecule used by the cell. For this reason, the mitochondrion is sometimes referred to as "the powerhouse of the cell". Mitochondria are found in all eukaryotes, which are all living things that are not bacteria or archaea. It is thought that mitochondria arose from once free-living bacteria that were incorporated into cells.

Function of Mitochondria

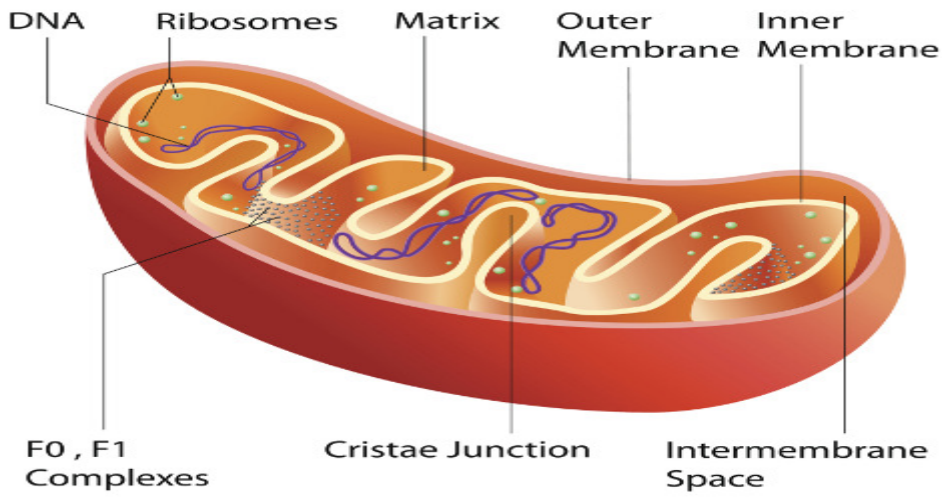
Mitochondria produce ATP through process of cellular respiration—specifically, aerobic respiration, which requires oxygen. The citric acid cycle, or Krebs cycle, takes place in the mitochondria. This cycle involves the oxidation of pyruvate, which comes from glucose, to form the molecule acetyl-CoA. Acetyl-CoA is in turn oxidized and ATP is produced.

The citric acid cycle reduces nicotinamide adenine dinucleotide (NAD^+) to NADH. NADH is then used in the process of oxidative phosphorylation, which also takes place in the mitochondria. Electrons from NADH travel through protein complexes that are embedded in the inner membrane of the mitochondria. This set of proteins is called an electron transport chain. Energy from the electron transport chain is then used to transport proteins back across the membrane, which power ATP synthase to form ATP.

The amount of mitochondria in a cell depends on how much energy that cell needs to produce. Muscle cells, for example, have many mitochondria because they need to produce energy to move the body. Red blood cells, which carry oxygen to other cells, have none; they do not need to produce energy. Mitochondria are analogous to a furnace or a powerhouse in the cell because, like furnaces and powerhouses, mitochondria produce energy from basic components (in this case, molecules that have been broken down so that they can be used).
Mitochondria have many other functions as well. They can store calcium, which maintains homeostasis of calcium levels in the cell. They also regulate the cell's metabolism and have roles in apoptosis (controlled cell death), cell signaling, and thermogenesis (heat production).

Structure of Mitochondria

Mitochondria have two membranes, an outer membrane and an inner membrane. These membranes are made of phospholipid layers, just like the cell's outer membrane. The outer membrane covers the surface of the mitochondrion, while the inner membrane is located within and has many folds called cristae. The folds increase surface area of the membrane, which is important because the inner membrane holds the proteins involved in the electron transport chain. It is also where many other chemical reactions take place to carry out the mitochondria's many functions. An increased surface area creates more space for more reactions to occur, and increases the mitochondria's output. The space between the outer and inner membranes is called the intermembrane space, and the space inside the inner membrane is called the matrix.



Evolution of Mitochondria

Mitochondria are thought to have evolved from free-living bacteria that developed into a symbiotic relationship with a prokaryotic cell, providing it energy in return for a safe place to live. It eventually became an organelle, a specialized structure within the cell, the presence of which are used to distinguish eukaryotic cells from prokaryotic cells. This occurred over a long process of millions of years, and now the mitochondria inside the cell cannot live separately from it. The idea that mitochondria evolved this way is called endosymbiotic theory.

Endosymbiotic theory has multiple forms of evidence. For example, mitochondria have their own DNA that is separate from the DNA in the cell's nucleus. It is called mitochondrial DNA or mtDNA, and it is only passed down through females because sperm do not have mitochondria. You received your mtDNA from your mother, and you can only pass it on if you are a female who has a child. It is also circular, like bacterial DNA. Another form of evidence is the way new mitochondria are created in the cell. New mitochondria only arise from binary fission, or splitting, which is the same way that bacteria asexually reproduce. If all of the mitochondria are removed from a cell, it can't make new ones because there are no existing mitochondria there to split. Also, the genome of mitochondria and Rickettsia bacteria (bacteria that can cause spotted fever and typhus) have been compared, and the sequence is so similar that it suggests that mitochondria are closely related to Rickettsia.

Chloroplasts:

Chloroplasts, the organelles in plants where photosynthesis occurs, are also thought to have evolved from endosymbiotic bacteria for similar reasons: they have separate, circular DNA, a double membrane structure, and split through binary fission.

Chloroplasts are the site of photosynthesis in eukaryotic cells. They are only present in photosynthetic cells like plant cells and algae. There are no chloroplasts in animal or bacterial cells.

Structure of Chloroplasts

- Chloroplasts found in higher plants are generally biconvex or planoconvex shaped.
- Chloroplasts can be found in the cells of the mesophyll in plant leaves.
- In different plants chloroplasts have different shapes, they vary from spheroid, filamentous saucer-shaped, discoid or ovoid shaped.
- They are vesicular and have a colorless center.
- Some chloroplasts are in shape of club, they have a thin middle zone and the ends are filled with chlorophyll.
- In algae a single huge chloroplast is seen that appears as a network, a spiral band or a stellate plate.
- The size of the chloroplast also varies from species to species and it is constant for a given cell type.
- In higher plants, the average size of chloroplast is 4-6 Âµ in diameter and 1-3 Âµ in thickness.

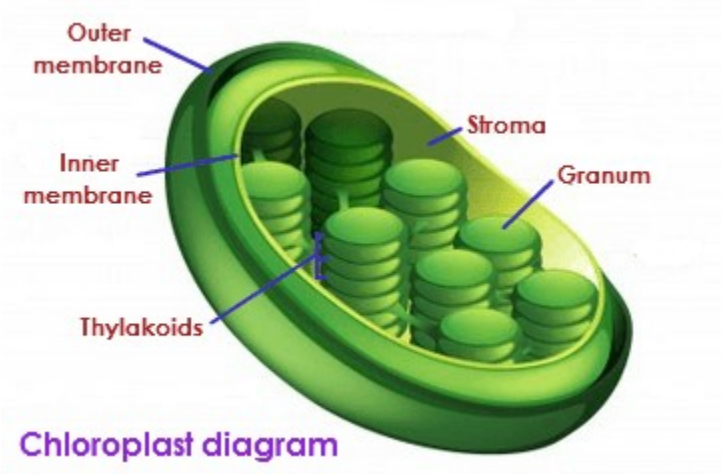
Parts of Chloroplasts

- Outer membrane – It is a semi-porous membrane and is permeable to small molecules and ions, which diffuses easily. The outer membrane is not permeable to larger proteins.
- Intermembrane Space – It is usually a thin intermembrane space about 10-20 nanometers and it is present between the outer and the inner membrane of the chloroplast.
- Inner membrane – The inner membrane of the chloroplast forms a border to the stroma. It regulates passage of materials in and out of the chloroplast. In addition of regulation activity, the fatty acids, lipids and carotenoids are synthesized in the inner chloroplast membrane.
- Stroma- Stroma is a alkaline, aqueous fluid which is protein rich and is present within the inner membrane of the chloroplast. The space outside the thylakoid space is called the stroma. The chloroplast DNA chlroplast ribosomes and the thylakoid sytem, starch granules and many proteins are found floating around the stroma.
- Thylakoid System- The thylakoid system is suspended in the stroma. The thylakoid system is a collection of membranous sacks called thylakoids. The chlorophyll is found in the thylakoids and is the sight for the process of light reactions of photosynthesis to happen. The thylakoids are arranged in stacks known as grana. Each granum contains around 10-20 thylakoids.

Functions of Chloroplast

- Absorption of light energy and conversion of it into biological energy.
- Production of NAPDH2 and evolution of oxygen through the process of photosys of water.

- Production of ATP by photophosphorylation. NADPH2 and ATP are the assimilatory powers of photosynthesis. Transfer of CO2 obtained from the air to 5 carbon sugar in the stream during dark reaction.
- Breaking of 6-carbon atom compound into two molecules of phosphoglyceric acid by the utilization of assimilatory powers.
- Conversion of PGA into different sugars and store as stratch. The chloroplast is very important as it is the cooking place for all the green plants. All heterotrophs also depend on plasts for this food.
- In plants all the cells participate in plant immune response as they lack specialized immune cells.
- The chloroplasts with the nucleus and cell membrane and ER are the key organelles of pathogen defense.
- The most important function of chloroplast is to make food by the process of photosynthesis.
- Food is prepared in the form of sugars. During the process of photosynthesis sugar and oxygen are made using light energy, water, and carbon dioxide.
- Light reactions takes place on the membranes of the thylakoids.
- Chloroplasts, like the mitochondria use the potential energy of the H+ ions or the hydrogen ion gradient to generate energy in the form of ATP.
- The dark reactions also known as the Calvin cycle takes place in the stroma of chloroplast.
- Production of NADPH2 molecules and oxygen as a result of photolysis of water.
- By the utilization of assimilatory powers the 6-carbon atom is broken into two molecules of phosphoglyceric acid.



Peroxisomes:

Peroxisomes are small vesicles, single membrane-bound organelles found around the eukaryotic cells. They contain digestive enzymes for breaking down toxic materials in the cell and oxidative enzymes for metabolic activity. They are a heterogeneous group of organelles and the presence of the marker enzymes distinguished them from other cell organelles.

Peroxisomes play an important role in lipid production and are also involved in the conversion of reactive oxygen species such as hydrogen peroxide into safer molecules like water and oxygen.

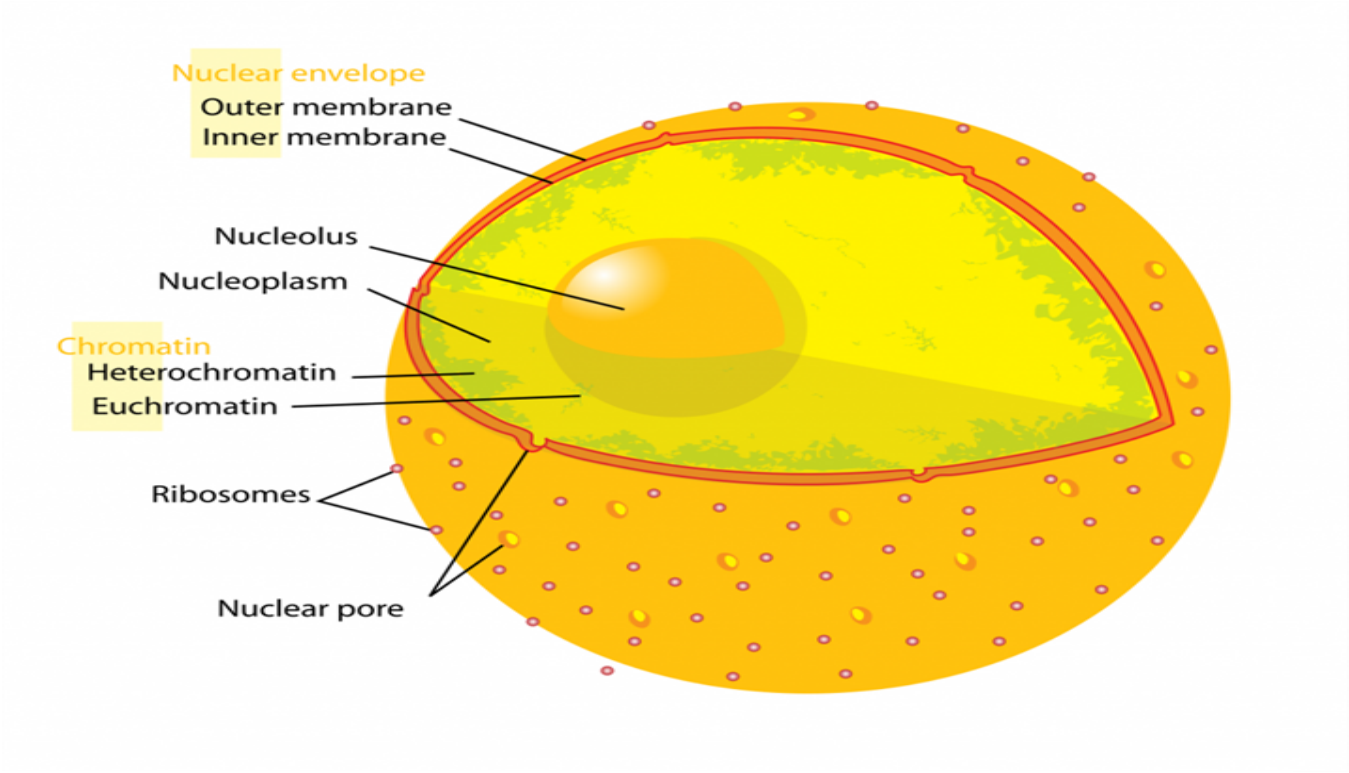
The peroxisome derives its name from the fact that many metabolic enzymes that generate hydrogen peroxide as a by-product are sequestered here because peroxides are toxic to cells. Within peroxisomes, hydrogen peroxide is degraded by the enzyme catalase to water and oxygen.

Peroxisomes are surrounded by a single membrane and they range in the diameter from 0.1 to 1 mm. They exist either in the form of a network of interconnected tubules (peroxisome reticulum) as in liver cells or as individual micro peroxisomes in other cells such as tissue culture fibroblasts.

Peroxisome Structure

Peroxisomes vary in shape, size and number depending upon the energy requirements of the cell. These are made of a phospholipid bilayer with many membrane-bound proteins.
The enzymes involved in lipid metabolism are synthesised on free ribosomes and selectively imported to peroxisomes. These enzymes include one of the two signalling sequences- Peroxisome Target Sequence 1 being the most common one.

The phospholipids of peroxisomes are usually synthesised in smooth Endoplasmic reticulum. Due to the ingress of proteins and lipids, the peroxisome grows in size and divides into two organelles.



Peroxisome Function

The main function of peroxisome is the lipid metabolism and the processing of reactive oxygen species. Other peroxisome functions include:

- The synthesis of ether glycerolipids of plasmalogens.
- The formation of bile acids, dolichol, and cholesterol.
- The catabolism of purines, polyamines, and amino acids, and the detoxification of reactive oxygen species
- In methylotrophic yeasts, peroxisomes are also involved in the metabolism of methanol and methylamines.

In plants, peroxisomes facilitate photosynthesis and seed germination. They prevent loss of energy during photosynthesis carbon fixation.

Metabolism of Peroxisomes

Isolated peroxisomes are permeable to small molecules such as sucrose. During the isolation process, they often lose proteins that are normally confined to the peroxisomal matrix. In all living cells, peroxisomes are the sealed vesicles surrounded by a single membrane.

Biogenesis of Peroxisomes

As peroxisomes have no DNA, all their proteins must be imported from genes encoded in the nucleus. Most of the proteins that reside in the peroxisome matrix and membrane are synthesized in the cytosol and then imported posttranslationally to the organelle.
About 25 PEX genes, encoding proteins called peroxins are necessary for the biogenesis of the organelle. Most of these genes are found in multiple organisms and 13 are conserved in humans.

Cytoskeleton
Cytoskeleton Definition

The cytoskeleton is a network of filaments and tubules that extends throughout a cell, through the cytoplasm, which is all of the material within a cell except for the nucleus. It is found in all cells, though the proteins that it is made of vary between organisms. The cytoskeleton supports the cell, gives it shape, organizes and tethers the organelles, and has roles in molecule transport, cell division and cell signaling.

Structure of the Cytoskeleton:

All cells have a cytoskeleton, but usually the cytoskeleton of eukaryotic cells is what is meant when discussing the cytoskeleton. Eukaryotic cells are complex cells that have a nucleus and organelles. Plants, animals, fungi, and protists have eukaryotic cells. Prokaryotic cells are less complex, with no true nucleus or organelles except ribosomes, and they are found in the single-celled organisms bacteria and archaea. The cytoskeleton of prokaryotic cells was originally thought not to exist; it was not discovered until the early 1990s.
The eukaryotic cytoskeleton consists of three types of filaments, which are elongated chains of proteins: microfilaments, intermediate filaments, and microtubules.

Microfilaments
Microfilaments are also called actin filaments because they are mostly composed of the protein actin; their structure is two strands of actin wound in a spiral. They are about 7 nanometers thick, making them the thinnest filaments in the cytoskeleton. Microfilaments have many functions. They aid in cytokinesis, which is the division of a cytoplasm of a cell when it is dividing into two daughter cells. They aid in cell motility and allow single-celled organisms like amoebas to move. They are also involved in cytoplasmic streaming, which is the flowing of cytosol (the liquid part of the cytoplasm) throughout the cell. Cytoplasmic streaming transports nutrients and cell organelles. Microfilaments are also part of muscle cells and allow these cells to contract, along with myosin. Actin and myosin are the two main components of muscle contractile elements.

Intermediate Filaments

Intermediate filaments are about 8-12 nm wide; they are called intermediate because they are in-between the size of microfilaments and microtubules. Intermediate filaments are made of different proteins such as keratin (found in hair and nails, and also in animals with scales, horns, or hooves), vimentin, desmin, and lamin. All intermediate filaments are found in the cytoplasm except for lamins, which are found in the nucleus and help support the nuclear envelope that surrounds the nucleus. The intermediate filaments in the cytoplasm maintain the cell's shape, bear tension, and provide structural support to the cell.

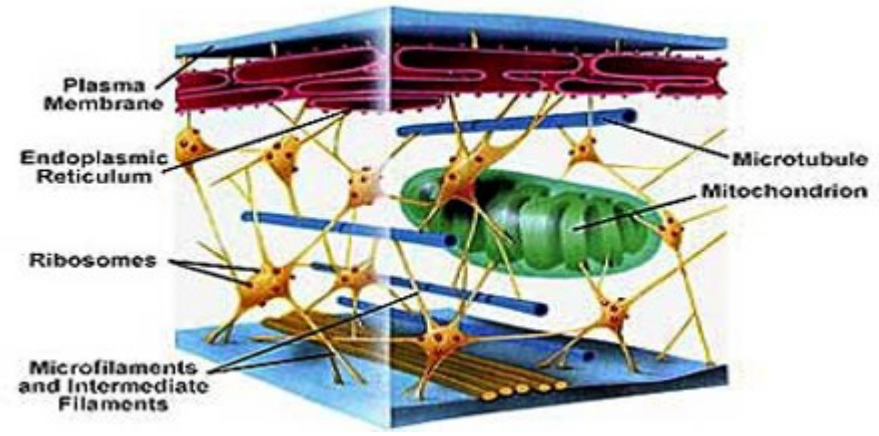
Microtubules

Microtubules are the largest of the cytoskeleton's fibers at about 23 nm. They are hollow tubes made of alpha and beta tubulin. Microtubules form structures like flagella, which are "tails" that propel a cell forward. They are also found in structures like cilia, which are appendages that increase a cell's surface area and in some cases allow the cell to move. Most of the microtubules in an animal cell come from a cell organelle called the centrosome, which is a microtubule organizing center (MTOC). The centrosome is found near the middle of the cell, and microtubules radiate outward from it. Microtubules are important in forming the spindle apparatus (or mitotic spindle), which separates sister chromatids so that one copy can go to each daughter cell during cell division. They are also involved in transporting molecules within the cell and in the formation of the cell wall in plant cells.

Function of the Cytoskeleton

As described above, the cytoskeleton has several functions. First, it gives the cell shape. This is especially important in cells without cell walls, such as animal cells, that do not get their shape from a thick outer layer. It can also give the cell movement. The microfilaments and microtubules can disassemble, reassemble, and contract, allowing cells to crawl and migrate, and microtubules help form structures like cilia and flagella that allow for cell movement.
The cytoskeleton organizes the cell and keeps the cell's organelles in place, but it also aids in the movement of organelles throughout the cell. For example, during endocytosis when a cell engulfs a molecule, microfilaments pull the vesicle containing the engulfed particles into the cell. Similarly, the cytoskeleton helps move chromosomes during cell division.

One analogy for the cytoskeleton is the frame of a building. Like a building's frame, the cytoskeleton is the "frame" of the cell, keeping structures in place, providing support, and giving the cell a definite shape.



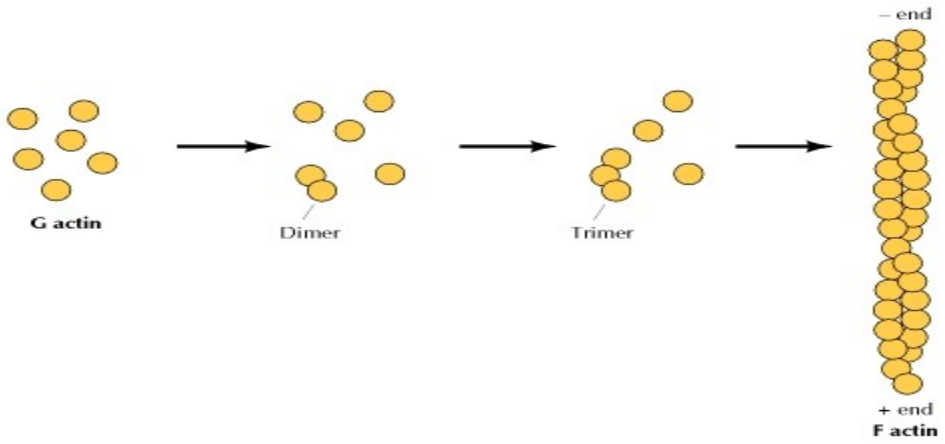
Cytoskeleton & Actin Filaments

Without our skeleton, we would just be a big sloppy lump of organs, muscles and skin. Our skeleton gives us our shape, and with it the structure required to move around and do things. The same thing is true for cells. Without the cytoskeleton, cells would not be able to maintain and change their shapes as needed, to resist physical stresses, to transport vesicles through the cytosol, or to move around autonomously, just to name a few. The cytoskeleton is clearly a very important part of the cell. Here, we will learn about one of type of cytoskeletal filament, actin filaments, and some of their functions in cells.

Actin Filament Structure

Actin filaments are the smallest cytoskeletal filaments, with a diameter of 7 nm. They are thin, relatively flexible threads that can be crosslinked together in different ways to form very different structures.

Actin monomers are called globular actin or G-actin. As their name suggests, they are fairly globe-shaped in structure. At the right concentration of monomers, they can polymerize head to tail to form filamentous actin or F-actin. F-actin threads associate with each other in a thin double-helical structure, as shown in this diagram.



G-actin monomers polymerize into F-actin filaments.

Because the G-actin monomers are arranged in the same orientation, actin filaments have two distinct ends. The ends are called plus (+) and minus (-). The plus end grows about 5-10 times faster than the minus end. The plus and minus ends are also important because motor proteins such as myosin move along the actin filament only in one direction. This is important in muscle contraction.

Actin Crosslinking

There are many proteins in the cell that can link actin filaments to each other in various three-dimensional structures. Some, like alpha actinin, villin and fimbrin, link individual filaments together in actin bundles where the filaments are all lined up parallel to one another. Others, like spectrin and filamin, cross-link actin filaments at angles to each other, forming actin networks, which are web or cushion-like structures. In addition, actin bundles and actin networks change the cell's shape and structure in different ways.

Functions of Actin: Muscle Contraction

Actin filaments have many functions within the cell. For example, our muscle cells are packed with actin filaments arranged in bundles by alpha actinin. As you can see in the diagram, the motor protein myosin is located in between the parallel actin filaments. By 'walking' toward the plus ends of the actin filaments, myosin slides the filaments inwards so that the whole structure gets shorter. This is what makes our muscles contract.

Possible Questions

Part-A (1 mark)

Part-B (2 marks)

1.describe plasma membrane?
2.give a notes on eukaryotic cell wall structure?
3. what is gap junction?
4. Notes on Actin filaments?
5. What is microtubule and it function?

Part-C (8 marks)

1. Explain model and structure of plasma membrane
2. Describe the Extra cellular matrix and cell matrix interacrions
3.brief about cell – cell interactions
4. Explain structure and function of Mitochondria.
5, Give a account on Chloroplaste structure and functions
6. Explain the structure of cytoskeleton.

KARPAGAM ACADEMY OF HIGHER EDUCATION

CLASS: III BSC Microbiology COURSE NAME: CELL BIOLOGY

COURSE CODE: 17MBU603A UNIT: `I BATCH: 2017-2020

S.NO	QUESTIONS	POSSIBILITY A	POSSIBILITY B	POSSIBILITY C	POSSIBILITY D	ANSWER
1	The Plasma membrane made up of	A protein layer between two lipid layers	A lipid layer between two protein layers	A protein, a lipid and a cellulose layer	Bimolecular lipid layer surrounded by protein layers	Bimolecular lipid layer surrounded by protein layers
2	The cell membrane name,plasmalemma" was given by	Porter	Nageli	Cramer	J. Q. Plowe	J. Q. Plowe
3	Which pair of structures are usually found in both plant and animal cells	Cell membrane and nucleolus	Cell membrane and cell wall	Nucleolus and chloroplast	Nucleus and cell wall	Cell membrane and nucleolus
4	Beet root if kept in cold water anthocyanin does not come out due to plasma membrane	Differentially permeable	Impermeable to anthocyanins	Permeable to anthocyanins	Dead	Impermeable to anthocyanins
5	Which of the following layer is present nearest to plasma membrane in plant cell	Secondary wall	Middle lamella	Primary wall	Tonoplast	Secondary wall
6	According to Robertson, thickness of lipid zone in the cell membrane ranges from	10-20Å	25-35Å	50-60Å	35-50Å	25-35Å
7	Lipid molecule in plasma membrane are arranged in	Scattered	Series	Alternate	Head parallel	Head parallel
8	Phospholipids are	Amphipathic	Amphibolic	Hydrophobic	None of these	Amphipathic

9	Ion carriers are located in	Nucleus	Cell wall	Cellular space	Plasma membranes	Plasma membranes
10	The plasma membrane is composed of	Proteins	Lipids	Carbohydrates	Both proteins and lipids	Both proteins and lipids
11	Desmosomes are concerned with	Cell division	Cell division	Cytolysis	Cell adherence	Cell adherence
12	The secretory material is discharged by the golgi vesicles, from the surface of cell membrane by	Pinocytosis	Endocytosis	Reverse pinocytosis	Dissolving the cell membrane	Reverse pinocytosis
13	According to the 'Unit membrane model' the thickness of the cell membrane is about	200 nm	7.5 nm	150 nm	1.0 nm	150 nm
14	Which of the following does not require carrier molecules during transport through cell membranes	Simple diffusion	Facilitated diffusion	Na+ -K+ transport	Active transport of sugars and amino acids	Simple diffusion
15	Which of the following structures controls the transport of the material into and out of living cells	Centrosome	Cell membrane	Cell wall	Ribosome	Cell membrane
16	Every living cell has a	Membrane	Food vacuole	Chloroplast	Cell wall	Membrane

17	When a cell engulfs or surrounds a particle and forms a vesicle around it, the phenomenon is known as	Exocytosis	Phagocytosis	Endocytosis	Endocytosis	Phagocytosis
18	Cell was discovered by	Leeuwenhoek	Robert Hooke	Robert Swanson	Robert Brown	Robert Hooke
19	The spherical structured organelle that contains the genetic material is	Cell walls	Ribosomes	Nucleus	Mitochondria	Nucleus
20	Prokaryotic genetic system has	DNA but no histone	Both DNA and histones	Neither DNA nor histones	Either DNA or histone	DNA but no histone
21	Which of the following statements are true about Eukaryotes? (a) They are cells with a nucleus. (b) They are found both in humans and multicellular organisms. (c) Endoplasmic reticulum is present in Eukaryotes. (d) They have chemically complexed cell wall.	(a), (b) and (c)	(a), (c) and (d)	(a), (b) and (d)	all are correct	(a), (b) and (c)
22	Cell sap is a	Living content of the cell	Non living content of the vacuole	Non-living content of the protoplasm	Living content of the cytoplasm	Non living content of the vacuole
23	Animal cell differs from plant cells in possessing	Plastid	Golgi body	Vacuole	Centrosome	Centrosome

24	Who observed the "mitochondria" first	Kolliker	Robert Brown	Robert Hooke	Altmann	Kolliker
25	The mitochondrial DNA differs from the nuclear DNA because of	Being linear	Having A = T and C - G	Lacking binding histones	Being highly twisted	Lacking binding histones
26	ATP is formed in	Mitochondria	Nucleus	Nucleolus	Ribosomes	Mitochondria
27	The Power House of the cell is	Mitochondria	Nucleus	Nucleolus	Ribosomes	Mitochondria
28	F1 particles are also called	Electron transport particles	Elementary particles	Cytochromes	Cristae	Elementary particles
29	Prokaryotic origin of mitochondria was proposed by	Rabinowitch	Altmann and Schimper	Salton	Morrison	Altmann and Schimper
30	Mitochondria are related to	Prokaryotes	Plasmids	Plastids	Viruses	Plastids
31	f1particles / oxysome/ elementary particles are present in	Endoplasmic reticulum	Chloroplast	Mitochondria	Golgi complex	Mitochondria

32	The number of mitochondria increases in cells of	Dormant seeds	Germinating seeds	Dry seeds	Dead seeds	Germinating seeds
33	In prokaryotes, the mitochondria are absent. Even then Krebs cycle takes place. What is the site of Krebs cycle in bacteria	Ribosomes	Nucleoid	Cytoplasm	Mesosomes	Mesosomes
34	Chondriospheres are formed due to	Fusion of mitochondria	Division of mitochondria	DNA replication	Transcription	Fusion of mitochondria
35	Green pigment (Chlorophyll) presents in plants is	Chromoplast	Chloroplast	Ribosome	Lysosome	Chloroplast
36	The bright colours of ripe fruits are due to	Leucoplasts	Chloroplasts	Amyloplasts	Chromoplasts	Chromoplasts
37	In which plastids are not found	Blue green algae	Bacteria	Fungi	All of the above	All of the above
38	A flattened disc-like sac in a chloroplast is called a	Loculus	Thylakoid	Stroma	Margin	Thylakoid
39	Extracellular fluids are LEAST likely to move through the space between cells that are joined by which type of intercellular junction?	Desmosome	Tight Junction	Macula adherens	Gap junction	Tight Junction

40	Network of microtubules and microfilaments is classified as	endoplasmic skeleton	vertebral skeleton	active skeleton	cytoskeleton	active skeleton
41	Tubulin protein is used by cells to	to perform glycolysis	hold their shape	function properly	change their shape	hold their shape
42	Microfilaments are composed of	actin protein	chitin protein	tubulin protein	mosaic protein	actin protein
43	In cardiac muscle tissue, what is the primary purpose of intercalated discs	Depolarization and repolarization of cell	Generating electrical impulses in cell	permitting the passage of ions between cell	preventing separation of muscle cells	permitting the passage of ions between cell
44	Who proposed the "Cell theory"	Schleiden and Schwann	Watson and Crick	Mendel and Morgan	Robert Hooke	Schleiden and Schwann
45	Which of the following is the exception of cell theory	Bacteria	Fungi	Lichen	Virus	Virus
46	Who proposed the concept of unit membrane for tripartite structure	Davson and Deniell	Robertson	Sanger and Singer	Scifriz	Robertson
47	Which one of the following is present outside the plasma membrane but inside the cell wall	Sphaerosome	Peroxisome	Lomasome	Golgi body	Lomasome

48	Which one enzyme of plasma membrane gets inactivated in the absence of lipids	ATPase	Alkaline phosphatase	Acid phosphomonoesterase	RNAase	ATPase
49	Which one of the following is not present in plasma membrane	Phospholipids	Albumins	Oligosaccharides	Spectrins	Albumins
50	Longest cell of plants is found in	Victoria amazonica	Eucalyptus	Boehmeria nivea	Sequoia	Boehmeria nivea
51	The chloroplasts of algae usually lack	Grana	Pigments	Quantasomes	Lamellae	Grana
52	"Quantasomes" were discovered by	Garner and Allard	Muller and Morgan	Lederberg and Tatum	Park and Biggins	Park and Biggins
53	The smallest living cells with cell wall are	Viroids	Algae	Bacteria	Mycoplasma	Bacteria
54	The branch which deals with the study of cell structure and function is known as	Histology	Ecology	Morphology	Cytology	Cytology
55	Distribution of intrinsic proteins in the plasma membrane is	Random	Symmetrical	Asymmetrical	None	Asymmetrical

56	Which cell organelle is involved in apoptosis?	Lysosome	ER	Golgi	Mitochondria	Mitochondria
57	Glycolipids in the plasma membrane are located at	Inner leaflet of the plasma membrane	The outer leaflet of the plasma membrane	Evenly distributed in the inner and outer leaflets	It varies according to cell types	The outer leaflet of the plasma membrane
58	A cell without a cell wall is termed as	Tonoplast	Protoplast	Symplast	Apoplast	Protoplast
59	Lysosomes are known as “suicidal bags” because	Parasitic activity	Presence of food vacuole	Hydrolytic activity	1. Catalytic activity	Hydrolytic activity
60	Bulk drinking of fluid by cells is termed as	Phagocytosis	Pinocytosis	Cyclosis	Osmosis	Pinocytosis

Unit II
Syllabus

Nuclear envelope, nuclear pore complex, and nuclear lamina.Chromatin-molecular organization of nucleolus

Nuclear Membrane

Nuclear Membrane Definition:

The nuclear membrane, also called the nuclear envelope, is a double membrane layer that separates the contents of the nucleus from the rest of the cell. It is found in both animal and plant cells. A cell has many jobs, such as building proteins, converting molecules into energy, and removing waste products. The nuclear envelope protects the cell's genetic material from the chemical reactions that take place outside the nucleus. It also contains many proteins that are used in organizing DNA and regulating genes.

Function of the Nuclear Membrane

The nuclear membrane is a barrier that physically protects the cell's DNA from the chemical reactions that are occurring elsewhere in the cell. If molecules that stay in the cytoplasm were to enter the nucleus, they could destroy part of the cell's DNA, which would stop it from functioning properly and could even lead to cell death. The envelope also contains a network of proteins that keep the genetic material in place inside the nucleus.

It also manages what materials can enter and exit the nucleus. It does so by being selectively permeable. Only certain proteins can physically pass through the double layer. This protects genetic information from mixing with other parts of the cell, and allows different cellular activities to occur inside the nucleus and outside the nucleus in the cytoplasm, where all other cellular structures are located.

Parts of the Nuclear Membrane

The nuclear membrane surrounds the nucleus of the cell.

Outer Membrane

Like the cell membrane, the nuclear membrane is a lipid bilayer, meaning that it consists of two layers of lipid molecules. The outer layer of lipids has ribosomes, structures that make proteins, on its surface. It is connected to the endoplasmic reticulum, a cell structure that packages and transports proteins.

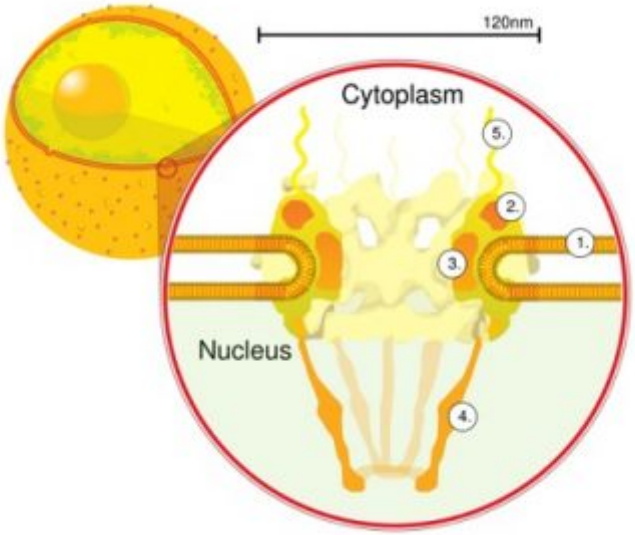
Inner Membrane

The inner membrane contains proteins that help organize the nucleus and tether genetic material in place. This network of fibers and proteins attached to the inner membrane is called the nuclear lamina. It structurally supports the nucleus, plays a role in repairing DNA, and regulates events in the cell cycle such as cell division and the replication of DNA. The nuclear lamina is only found in animal cells, although plant cells may have some similar proteins on the inner membrane.

Nuclear Pores

Nuclear pores pass through both the outer and inner membranes of the nuclear membrane. They are made up of large complexes of proteins and allow certain molecules to pass through the nuclear membrane. Each nuclear pore is made up of about 30 different proteins that work together to transport materials. They also connect the outer and inner membranes.
During cell division, more nuclear pores are formed in the nuclear membrane in preparation for cell division. The nuclear membrane eventually breaks down and is reformed around the nuclei of each of the two daughter cells.

The figure below shows a nuclear pore close-up:



Differences Between Nuclear Membranes in Plant and Animal Cells

Much more is known about animal and yeast cell nuclear membranes than those of plant cells, but the knowledge gap is decreasing thanks to recent research. Plant nuclear membranes lack many of the proteins that are found on the nuclear membranes of animal cells, but they have other pore membrane proteins that are unique to plants. Animal cells have centrosomes, structures that help organize DNA when the cell is preparing to divide; plants lack these structures and appear to

rely entirely on the nuclear membrane for organization during cell division. With further research, scientists may better understand the uniqueness of plant cell nuclear membranes.

Molecular organization of nucleolus:

The nucleolus is a round body located inside the nucleus of a eukaryotic cell. It is not surrounded by a membrane but sits in the nucleus. The nucleolus makes ribosomal subunits from proteins and ribosomal RNA, also known as rRNA. It then sends the subunits out to the rest of the cell where they combine into complete ribosomes. Ribosomes make proteins; therefore, the nucleolus plays a vital role in making proteins in the cell.

Three major components of the nucleolus are recognized: the fibrillar center (FC), the dense fibrillar component (DFC), and the granular component (GC). Transcription of the rDNA occurs in the FC.The DFC contains the protein fibrillarin . which is important in rRNA processing. The GC contains the protein nucleophosmin, (B23 in the external image) which is also involved in ribosome biogenesis.

However, it has been proposed that this particular organization is only observed in higher eukaryotes and that it evolved from a bipartite organization with the transition from anamniotes to amniotes. Reflecting the substantial increase in the DNA intergenic region, an original fibrillar component would have separated into the FC and the DFC. Another structure identified within many nucleoli (particularly in plants) is a clear area in the center of the structure referred to as a nucleolar vacuole. Nucleoli of various plant species have been shown to have very high concentrations of iron in contrast to human and animal cell nucleoli.

The nucleolus ultrastructure can be seen through an electron microscope, while the organization and dynamics can be studied through fluorescent protein tagging and fluorescent recovery after photobleaching (FRAP). Antibodies against the PAF49 protein can also be used as a marker for the nucleolus in immunofluorescence experiments.

Although usually only one or two nucleoli can be seen, a diploid human cell has ten nucleolus organizer regions (NORs) and could have more nucleoli. Most often multiple NORs participate in each nucleolus.

Function and Ribosomes Assemble:

In ribosome biogenesis, two of the three eukaryotic RNA polymerases (pol I and III) are required, and these function in a coordinated manner. In an initial stage, the rRNA genes are transcribed as a single unit within the nucleolus by RNA polymerase I. In order for this transcription to occur, several pol I-associated factors and DNA-specific trans-acting factors are required. In yeast, the most important are: UAF (upstream activating factor), TBP (TATA-box binding protein), and core binding factor (CBF)) which bind promoter elements and form the preinitiation complex (PIC), which is in turn recognized by RNA pol. In humans, a similar PIC is assembled with SL1, the promoter selectivity factor (composed of TBP and TBP-associated factors, or TAFs),

transcription initiation factors, and UBF (upstream binding factor). RNA polymerase I transcribes most rRNA transcripts 28S, 18S, and 5.8S) but the 5S rRNA subunit (component of the 60S ribosomal subunit) is transcribed by RNA polymerase III.

Transcription of rRNA yields a long precursor molecule (45S pre-rRNA) which still contains the ITS and ETS. Further processing is needed to generate the 18S RNA, 5.8S and 28S RNA molecules. In eukaryotes, the RNA-modifying enzymes are brought to their respective recognition sites by interaction with guide RNAs, which bind these specific sequences. These guide RNAs belong to the class of small nucleolar RNAs (snoRNAs) which are complexed with proteins and exist as small-nucleolar-ribonucleoproteins (snoRNPs). Once the rRNA subunits are processed, they are ready to be assembled into larger ribosomal subunits. However, an additional rRNA molecule, the 5S rRNA, is also necessary. In yeast, the 5S rDNA sequence is localized in the intergenic spacer and is transcribed in the nucleolus by RNA pol.

In higher eukaryotes and plants, the situation is more complex, for the 5S DNA sequence lies outside the Nucleolus Organiser Region (NOR) and is transcribed by RNA pol III in the nucleoplasm, after which it finds its way into the nucleolus to participate in the ribosome assembly. This assembly not only involves the rRNA, but ribosomal proteins as well. The genes encoding these r-proteins are transcribed by pol II in the nucleoplasm by a "conventional" pathway of protein synthesis (transcription, pre-mRNA processing, nuclear export of mature mRNA and translation on cytoplasmic ribosomes). The mature r-proteins are then "imported" back into the nucleus and finally the nucleolus. Association and maturation of rRNA and r-proteins result in the formation of the 40S (small) and 60S (large) subunits of the complete ribosome. These are exported through the nuclear pore complexes to the cytoplasm, where they remain free or become associated with the endoplasmic reticulum, forming rough endoplasmic reticulum (RER).

In human endometrial cells, a network of nucleolar channels is sometimes formed. The origin and function of this network has not yet been clearly identified.

Chromatin:

In eukaryotic cells the genetic material is organized into a complex structure composed of DNA and proteins and localized in a specialized compartment, the nucleus. This structure was called chromatin (from the Greek "khroma" meaning coloured and "soma" meaning body). Close to two meters of DNA in each cell must be assembled into a small nucleus of some □m in diameter. Despite this enormous degree of compaction, DNA must be rapidly accessible to permit its interaction with protein machineries that regulate the functions of chromatin:

1. Replication,
2. Repair and
3. Recombination.

The dynamic organization of chromatin structure thereby influences, potentially, all functions of the genome.

The fundamental unit of chromatin, termed the nucleosome, is composed of DNA and histone proteins. This structure provides the first level of compaction of DNA into the nucleus. Nucleosomes are regularly spaced along the genome to form a nucleofilament which can adopt higher levels of compaction (Fig 1 and 3), ultimately resulting in the highly condensed metaphase chromosome. Within an interphase nucleus chromatin is organized into functional territories.
Chromatin has been divided into:

- euchromatin and
- heterochromatin.

Heterochromatin was defined as a structure that does not alter in its condensation throughout the cell cycle whereas euchromatin is decondensed during interphase. Heterochromatin is localized principally on the periphery of the nucleus and euchromatin in the interior of the nucleoplasm. We can distinguish:

- constitutive heterochromatin, containing few genes and formed principally of repetitive sequences located in large regions coincident with centromeres and telomeres, from
- facultative heterochromatin composed of transcriptionally active regions that can adopt the structural and functional characteristics of heterochromatin, such as the inactive X chromosome of mammals.
- In this review we will define the components of chromatin and outline the different levels of its organization from the nucleosome to domains in the nucleus.
- We will discuss how variation in the basic constituents of chromatin can impact on its activity and how stimulatory factors play a critical role in imparting diversity to this dynamic structure.
- Finally we will summarize how chromatin influences the organization of the genome at the level of the nucleus.

II- The nucleosome

The partial digestion of DNA assembled into chromatin, generated fragments of 180-200 base pairs in length which were resolved by electrophoretic migration. This regularity of chromatin structure was later confirmed by electron microscope analysis that revealed chromatin as regularly spaced particles or "beads on a string". The stoichiometry of DNA and histones in the nucleosome was found to be 1/1 based on their mass.
The nucleosome is the fundamental unit of chromatin. It is composed of:

- a core particle and
- a linker region (or internucleosomal region) that joins adjacent core particles.

The core particle is highly conserved between species and is composed of 146 base pairs of DNA wrapped 1.7 turns around a protein octamer of two each of the core histones H3, H4, H2A and H2B. The length of the linker region, however, varies between species and cell type. It is within this region that the variable linker histones are incorporated. Therefore, the total length of DNA in the nucleosome can vary with species from 160 to 241 base pairs.

Analyses revealed, firstly, the distortion of the DNA wound around the histone octamer and, secondly, that the histone/DNA and histone/histone interactions through their "histone fold domain" formed a configuration remniscent of a hand shake.

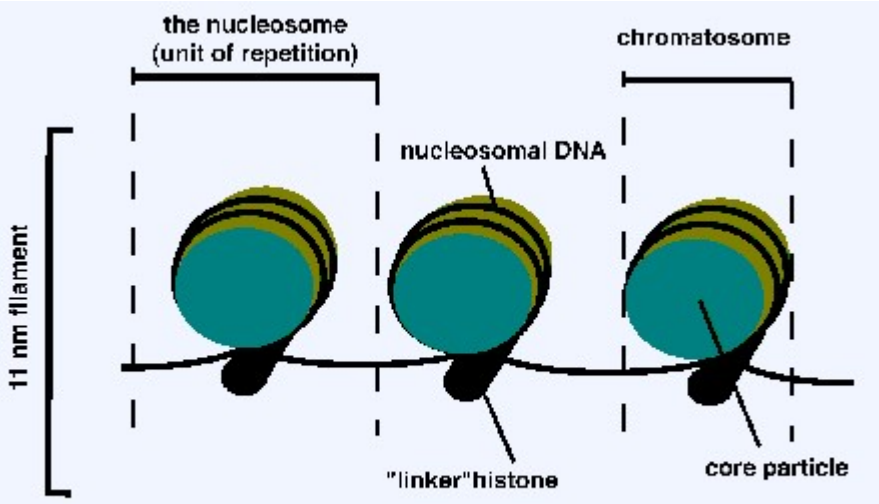


Figure 1. Defining elements of nucleosomes and chromatosome

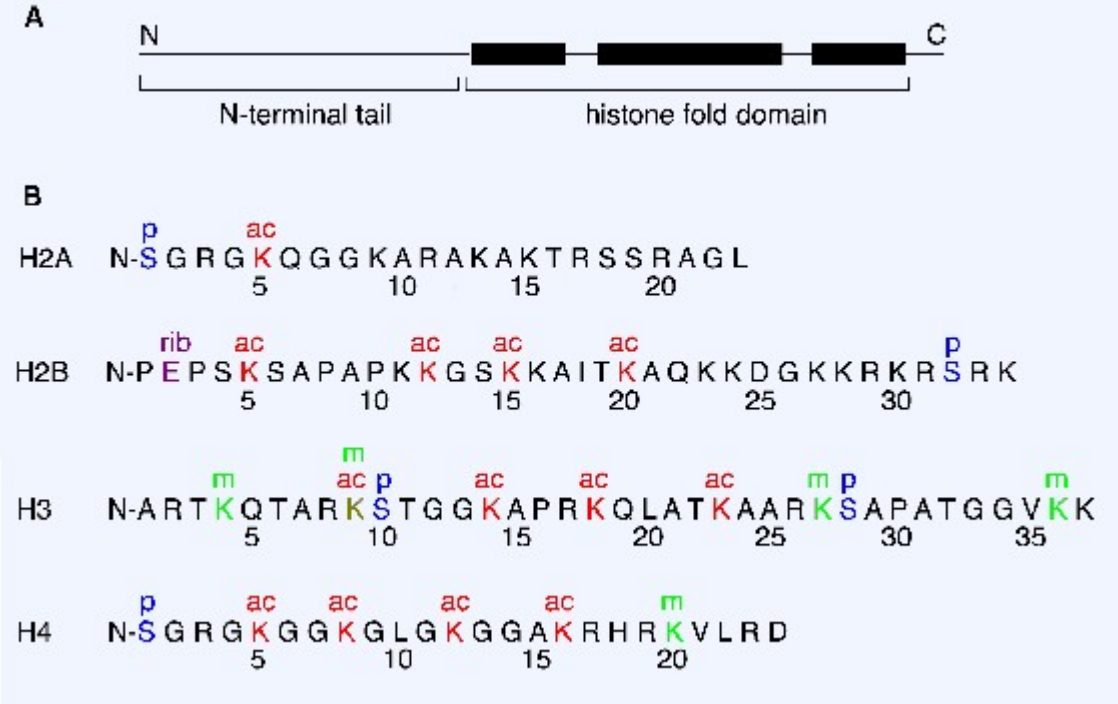
Defining elements of nucleosomes and chromatosome

III- Histone proteins
III-1. Core histones

The core histones, H3, H4, H2A and H2B, are small, basic proteins highly conserved in evolution (Figure 2). The most conserved region of these histones is their central domain structurally composed of the "histone fold domain" consisting of three a-helicies separated by two loop regions. In contrast, the N-terminal tails of each core histone is more variable and unstructured. The tails are particularily rich in lysine and arginine residues making them extremely basic. This region is the site of numerous post-translational modifications that are proposed to modify its charge and thereby alter DNA accessibility and protein/protein interactions with the nucleosome.

It is significant to note that other proteins that interact with DNA also contain the "histone fold domain"

The core histones.
A. Structure of nucleosomal histones.
B. Amino-terminal tails of core histones. The numbers indicate amino acid position. The post-translational modifications are indicated (red ac = acetylation sites ; blue p = phosphorylation sites ; green m = methylation sites ; purple rib = ADP ribosylation).



III-2. Linker histones

Linker histones associate with the linker region of DNA between two nucleosome cores and, unlike the core histones, they are not well conserved between species. In higher eukaryotes, they are composed of three domains: a globular, non-polar central domain essential for interactions with DNA and two non-structured N- and C- terminal tails that are highly basic and proposed to be the site of post translational modifications. The linker histones have a role in spacing nucleosomes and can modulate higher order compaction by providing an interaction region between adjacent nucleosomes.

IV- General steps in chromatin assembly

The assembly of DNA into chromatin involves a range of events, beginning with the formation of the basic unit, the nucleosome, and ultimately giving rise to a complex organization of specific domains within the nucleus. This step-wise assembly is described schematically in Fig 3.

The first step is the deposition onto the DNA of a tetramer of newly synthesized (H3-H4)2 to form a sub-nucleosomal particle, which is followed by the addition of two H2A-H2B dimers. This produces a nucleosomal core particle consisting of 146 base pairs of DNA wound around the histoneoctamer.

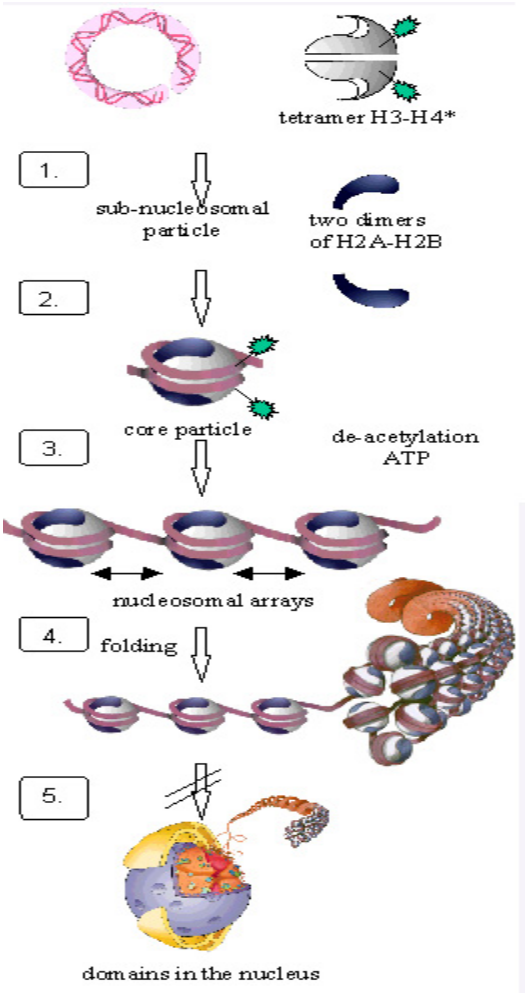
This core particle and the linker DNA together form the nucleosome. Newly synthesized histones are specifically modified (e.g.the acetylation of histone H4).

The next step is the maturation step that requires ATP to establish regular spacing of the nucleosome cores to form the nucleofilament. During this step the newly incorporated histones are de-acetylated.

Next the incorporation of linker histones is accompanied by folding of the nucleofilament into the 30nm fibre, the structure of which remains to be elucidated. Two principal models exist : the solenoid model and the zig zag.

Finally, further successive folding events lead to a high level of organization and specific domains in the nucleus.

At each of the steps described above, variation in the composition and activity of chromatin can be obtained by modifying its basic constituents and the activity of stimulatory factors implicated in the processes of its assembly and disassembly.



General steps in chromatin assembly.

Assembly begins with the incorporation of the H3/H4 tetramer (1), followed by the addition of two H2A-H2B dimers (2) to form a core particle. The newly synthesized histones utilized are specifically modified; typically, histone H4 is acetylated at Lys5 and Lys12 (H3-H4*). Maturation requires ATP to establish a regular spacing, and histones are de-acetylated (3). The incorporation of linker histones is accompanied by folding of the nucleofilament. Here the model presents a solenoid structure in which there are six nucleosomes per gyre (4). Further folding events lead ultimately to a defined domain organization within the nucleus (5).

V- Variation in basic constituents

In the first steps of chromatin assembly, the elementary particle can assume variations:

- at the level of DNA (for example by methylation) or
- at the histone level by differential post-translational modification and the incorporation of variant forms (for example CENP-A, a variant of H3).

All of these variations are capable of introducing differences in the structure and activity of chromatin. The vast array of post-translational modifications of the histone tails summarized in Fig 2 (such as acetylation, phosphorylation, methylation, ubiquitination, polyADP-ribosylation), and their association with specific biological processes has led to a proposed hypothesis of a language, refered to as the "histone code", that marks genomic regions (It must be emphasized that this code is a working hypothesis)). The code is "read"by other proteins or protein complexes that are capable of understanding and interpreting the profiles of specific modifications. The incorporation of histone variants may be important at specific domains of the genome: in this context, CENP-A, a variant of histone H3 is associated with silent centromeric regions and macro H2A on the inactive X chromosome of female mammals. H2A-X is implicated in the formation of foci containing DNA repair factors in the regions of DNA double-strand breaks. Growing evidence exists that H2A.Z has a role in modifying chromatin structure to regulate transcription.

During the maturation step, incorporation of linker histones, non-histone chromatin associated proteins, called HMG (High Mobility Group), and other specific DNA-binding factors help to space and fold the nucleofilament. Therefore the early steps in assembly can have a great impact on the final characteristics of chromatin in specific nuclear domains.

VI- Stimulatory Assembly Factors

VI-1. Histone interacting factors

Acidic factors can form complexes with histones and enhance the process of histone deposition. They act as histone chaperones by facilitating the formation of nucleosome cores without being part of the final reaction product. These histone-interacting factors, also called chromatin-assembly factors, can bind preferentially to a subset of histone proteins.

For instance, Chromatin Assembly Factor-1 (CAF-1) interacts with newly synthesized acetylated histones H3 and H4 to preferentialy assemble chromatin during DNA replication. CAF-1 is also capable of promoting the assembly of chromatin specifically coupled to the repair of DNA. The recent demonstration of the interaction of CAF-1 with the protein PCNA (Proliferating Cell Nuclear Antigen) established a molecular link between the assembly of chromatin and the processes of replication and repair of DNA. The assembly of specialized structures in centromeric regions, by deposition of variant histones such as CENP-A, or telomeres may be a result of the specificity and the diversity of as yet uncharacterised histone chaperones.

VI-2. Remodelling machines and histone-modifying enzymes:

Stimulatory factors also act during the chromatin maturation stage to organize and maintain a defined chromatin state. Their effects on chromatin can induce changes in conformation at the level of the nucleosome or more globally over large chromatin domains. These factors are of two types; one requiring energy in the form of ATP, generally refered to as chromatin remodelling machines, and the other that act as enzymes to post-translationally modify histones.

Chromatin remodelling machines are multi-protein complexes (SWI/SNF, ISWI, Mi2/NuRD families).The activity of the ATPase permits the complex to modify nucleosomal structure, driven by the liberation of energy during the hydrolysis of ATP. The study of factors that stimulate the regular arrangement of nucleosomes during the assembly of chromatin led to the identification of several multi-protein complexes, capable in vitro of "sliding" nucleosomes along DNA. The common feature of these chromatin remodelling factors is their large size and multiple protein subunits including the ATPase, however, they display differences in abundance and activity.

post-translational modifications: the "histone code" hypothesis has been proposed to explain the diversity of chromatin activity in the nucleus. The unstructured N-terminal histone tails extend outside the nucleosome core and are the sites of action for enzymes that catalyze with high specificity their post-translational modification. The most well characterized of these modifications is the acetylation of lysine residues. Acetylation is the result of an equilibrium between two opposing activities: histone acetyl transferase (HAT) and histone deacetylation (HDAC) (e.g. HAT A, with a histone acetyltransferase activity and HDAC1, a histone deacetylase). Numerous proteins that play a role in the regulation of transcription have intrinsic histone acetyltransferase activity. Similarly, histone deacetylases have been described as components of multi-protein complexes associated with repressive chromatin. Also within these complexes are the Mi-2 family of remodeling factors providing a link between remodelling of nucleosomes and histone deacetylation during chromatin-mediated repression.

Methylation of histones plays a functionally important role. A histone-methyltransferase specifically methylates histone H3 on lysine residue 9 and this methylation modifies the interaction of H3 with heterochromatin associated proteins.

The two possible modifications (acetylation and methylation) on the same residue (lysine 9) of the N-terminal tail of H3 is a perfect illustration of the "histone code" hypothesis in action.

Indeed, acetylated lysine in H3 and H4 N-terminal tail selectively interact with chromodomain present in numerous proteins having intrinsic histone acetyltransferase activity. However, H3 methylated on lysine residue 9 interact specifically with the chromodomain of an heterochromatin associated protein HP1.

Therefore, in addition to producing alterations in the overall charge of the histone tails, proposed to physically destabilize the nucleosome, modifications appear to impart specificity to protein:protein interactions with the histones. They are associated with different regions of the genome and are correlated with precise nuclear functions.

VII- Organization of the genome in the nucleus:

The higher level of compaction of chromatin is not as well characterized. The nucleofilament is compacted to form the 30nm fibre that is organized into folds of 150 to 200 Kbp (250nm during interphase) to obtain a maximum level of compaction in the metaphase chromosome (850nm).

At interphase the organization of the genome relies on the structure of chromosomes that have been characterized into different regions based on a specific banding pattern.

The principle bands are:

- G and C bands that are late replicating in S phase and correspond to heterochromatin and the
- R bands that replicate earlier in S-phase and represent euchromatin. The R bands are enriched in acetylated histones and this modification is conserved through mitosis suggesting that histone acetylation may serve as a marker for the memory of domain organization through the cell cycle.
- The localization of chromosomes in the interphase nucleus reveals that each chromosome occupies a defined space. In mammals, the organization of the chromosomes in the nucleus varies as a function of cell type. During interphase, regions that correspond to the bands of metaphase chromosomes are located in the nucleus based on the timing of their replication:
- on the nuclear periphery are the later replicating regions, corresponding to G and C bands and the transcriptionally silent telomeres, while gene rich regions are preferentially localized more internally.
- Therefore, although each chromosome occupies a different territory, distinct parts of chromosomes can unite to form functional domains. The localization of coincident and non-coincident regions by FISH suggests that genes tend to be localized at the surface of chromosome territories. In the model based on the localization of some genes, transcripts are released into interchromosomal channels, transferred to sites for processing, then exported to the cytoplasm after maturation.

Possible Questions

Part-A (1 mark)

Part-B (2 marks)

1.what is Nucleus?
2.what are Chromatins?
3.what is the fuction of Nuclear pore?
4.describe nuclear lamina.
5.describe structure of nuclear envelope?

Part-C (8 marks)

1.briefly explain about stureture of nucleus
2.describe and explain about nuclear pore and its functions
3. Explain about nuclear Lamina structure and functions
4.Explain the Molecular organization of Nucleolus
5.Explain the structure of Chromatin.

S.NO	QUESTIONS	POSSIBILITY A	POSSIBILITY B	POSSIBILITY C	POSSIBILITY D	ANSWER
1	Controlling centre of cell is	Nucleus	Nucleolus	Mitochondria	Ribosome	Nucleolus
2	The role of nucleus in regulating the morphology of plant was discovered in	Maize	Garden pea	Neurospora	Acetabularia	Acetabularia
3	Nucleolus is found in	Protoplasm	Nucleus	Cytoplasm	None of these	Nucleus
4	The function of nucleolus is the synthesis of	DNA	m-RNA	r-RNA	t-RNA	r-RNA
5	Nuclear material without nuclear membrane is observed in	Bacteria and green algae	Cyanobacteria and red algae	Bacteria and cyanobacteria	Mycoplasmas and green algae	Bacteria and cyanobacteria
6	The nucleoplasm is continuous with the cytoplasm of a cell through	Centriole	Endoplasmic reticulum	Nuclear pores	Golgi apparatus	Nuclear pores
7	The term 'nucleolus' was coined by	R. Brown	H. Hooks	Bowman	Hanstein	Bowman

8	Karyolymph is a	Nuclear sap	SPM membrane	Nuclear pore	None of these	Nuclear sap
9	The nuclear spindle consists of	One type of fibre	Two types of fibres	Three types of fibres	Four types of fibres	Three types of fibres
10	Watson has calculated the nuclear pores of the mammalian cells to be ..... of the total surface area of the nucleus	5 percent	50 percent	25 percent	10 percent	50 percent
11	The "master mind" of the cell is	Protoplast	Nucleolus	Nucleus	Plastid	Nucleus
12	Pars amorpha is associated with	Nucleus	Chloroplast	Mitochondria	Nucleolus	Nucleolus
13	Nucleoli are rich in	DNA and RNA	DNA, RNA and proteins	DNA	RNA	DNA, RNA and proteins
14	Histone proteins found in nuclei of eukaryotes are	Acidic	Basic	Neutral	Amphoteric	Basic
15	The structure of nuclear membrane facilitates	Synapsis of homologous chromosomes at meiosis	Nucleo-cytoplasmic exchange of materials	Anaphasic separation of daughter chromosomes	Organization of spindles	Nucleo-cytoplasmic exchange of materials

16	The nucleus has	One membrane with pores	Two membranes with pores	Two membranes with pores through which substances do not pass	Two membranes with pores through which macromolecules may pass	Two membranes with pores through which macromolecules may pass
17	Nucleus is absent in	Sieve tubes	Companion cells	Chlorenchyma	All the above	Sieve tubes
18	True nucleus is absent in	Green algae	Fungi	Lichens	Bacteria	Bacteria
19	Cell which does not contain nuclear membrane	Bacteria	Fungi	Lichens	Algae	Bacteria
20	What will happen if nucleus is removed	The metabolism will increase	The cell will die	The metabolism will decrease	None of the above	The cell will die
21	Amount of which one of the following is more in the nucleus but less in the chromosome	DNA	RNA	Histone proteins	Non-histone proteins	Non-histone proteins
22	In nucleoplasm, a conspicuous body of spherical shape attached to a particular chromosome on a definite position is called	Plasmid	Karyolymph	Nucleolus	Nuclear reticulumg	Nucleolus
23	Who showed that the nuclear membrane has many pores or circular structures or annuli	Fawcell	Strasburger	Butchen	Callan and Tomlin	Callan and Tomlin

24	Nucleolemma is a part of	Nuclear membrane	Nuclear reticulum	Nucleolus	Nucleoplasm	Nucleoplasm
25	Pore size of nuclear membrane is	100Å	200Å	300Å	400Å	**400**Å
26	Study of nuclear cytology is called	Neurology	Karyology	Mycology	Rhinology	Karyology
27	In which of the following places messenger RNA is formed in a living cell	Inside mitochondria	Inside nucleolus	Inside nucleus but outside nucleolus	Inside endoplasmic reticulum	Inside nucleus but outside nucleolus
28	An undefined or undifferentiated fibrillar nucleus is seen in	Eukaryotic cells	Prokaryotic cells	Cells of higher organisms	Cells of higher plants	Prokaryotic cells
29	Nucleoproteins in a cell are synthesized in	Outside the nucleolus	Nucleoplasm	Nuclear membrane	Nucleolus	Nucleoplasm
30	The condition when a large number of nucleus are found due to the absence of cytpolasmic division (which happens after telophase stage). This condition are called	Polyploidy	Syncytium	Heterokaryon	None of these	Syncytium
31	Which type of protein is found in nucleus	Simple protein	Structural protein	Conjugated protein	Derived protein	Conjugated protein

32	Which of the following regulates and governs the physiological processes of the cell	Protoplast	Nucleolus	Mitochondria	Nucleus	Nucleus
33	Nucleus is enclosed in	Double and non-porous layer	Double and non-porous layer	Single and non-porous layer	Single and porous layer	Double and non-porous layer
34	DNA is mainly found in	Nucleus only	Nucleus and cytoplasm	Cytoplasm only	All of these	Nucleus only
35	Which of the following is not contained in a eukaryotic nucleus	Nucleosome	Nucleolus	Chromatin	Circular DNA molecules	Circular DNA molecules
36	Nucleolus in eukaryotic cells is	Visible in metaphase	The site for synthesis of RNA polymerase	Bounded by a memebrane	The side of packaging of rRNAs with ribosomal proteins	The side of packaging of rRNAs with ribosomal proteins
37	The nucleus is separated from surrounding cytoplasm by a nuclear membrane, which is	Single layered with pores	Single layered without pores	Double layered with pores	Double layered without pores	Double layered with pores
38	Pars granulosa of nucleoplasm is made up of	DNA	RNA	Protein	Protein and carbohydrate	Protein
39	The sex chromosomes of plants were first discovered in	Algae	Fungi	Pteridophyta	Flowering plants	Flowering plants

40	In which kind of study is banding done	Creation of new species	Production of disease resistant variety	Mapping of chromosomes	Artificial pollination	Mapping of chromosomes
41	Minimum haploid numbers of chromosomes in plant kingdom	3	2	1	4	2
42	A chromosome in which the centromere is situated near one end is known as	Telocentric	Acrocentric	Submetacentric	Metacentric	Acrocentric
43	L-shaped chromosomes are called	Sex chromosome	Acrocentric	Telocentric	Sub-metacentric	Sub-metacentric
44	Spindle chromosomes have	Centriole	Kinetochore	Chromocentre	Chromomere	Kinetochore
45	Supercoiled structure of eucaryotic chromosome is explained by	Taylor model	Freese-Taylor model	Nucleosome model	Nebel model	Nucleosome model
46	Kinetochore is present in	Mitochondria	Chromosomes	Lysosomes	Sphaerosomes	Chromosomes
47	A chromosome having sub-terminal centromere is called	Telocentric	Acrocentric	Metacentric	Sub-metacentric	Acrocentric

48	Four different types of chromosomes but of the same size are serialized as	Telocentric, metacentric, acrocentric, submetacentric	Metacentric, acrocentric, submetacentric, telocentric	Metacentric, submetacentric, acrocentric, telocentric	Metacentric, telocentric, acrocentric, submetacentric	Metacentric, submetacentric, acrocentric, telocentric
49	The beaded appearance of chromosome is known as	Centromere	Chromomere	Centriole	Centrosphere	Chromomere
50	Chromosomes always exist	In pairs	In association with mitochondria	Singly	None of these	Singly
51	Spindle fibres attach to chromosomes at their	Telomeres	Chromomeres	Kinetochores	Centromeres	Kinetochores
52	In a cell that is not dividing, the chromosomes are visible as a tangle of fine threads called	Microtubules	Chromatin	Microfilaments	Nucleotin	Chromatin
53	A tetrad consists of	Four non-homologous chromatids	Four non-homologous chromosomes	Two sets of homologous chromosomes, each with two chromatids	Four homologous pairs of chromosomes	Two sets of homologous chromosomes, each with two chromatids
54	Centromere is concerned with	Splitting of chromosomes	Formation of spindle fibres	Movement of chromosomes to poles	Duplication of DNA	Movement of chromosomes to poles
55	Basic structure of chromatin is composed of	Non-histone proteins wrapped around DNA	Histone proteins wrapped around DNA	RNA wrapped around histones	DNA wrapped around histones	Histone proteins wrapped around DNA

56	Heterosome is called	Somatic chromosome	B chromosome	Sex chromosome	Giant chromosome	Sex chromosome
57	Tips of chromosome are called	Centromere	Chromomere	Telomere	Metamere	Telomere
58	Polytene chromosomes in salivary glands of Drosophila are formed as a result of	Endoduplication	Duplication without separation	Replication of DNA without cell division	All the above	All the above
59	Minimum number of chromosomes are present in	Haplopappus	Helianthus	Tagetus	Lotus	Haplopappus
60	The arrangement of genes on chromosomes is	Linear	Ovoid	Diffused	Spiral	Linear

Unit III

Syllabus

Ribosomes, Endoplasmic Reticulum – Structure, targeting and insertion of proteins in the ER, protein folding, processing and quality control in ER, smooth ER and lipid synthesis, export of proteins and lipids. Golgi Apparatus – Organization, glycosylation, protein sorting and export from Golgi Apparatus Lysosomes

STRUCTURE OF RIBOSOMES:

Ribosomes are made of proteins and ribonucleic acid (abbreviated as RNA), in almost equal amounts. It comprises of two sections, known as subunits. The tinier subunit is the place the mRNA binds and it decodes, whereas the bigger subunit is the place the amino acids are included.

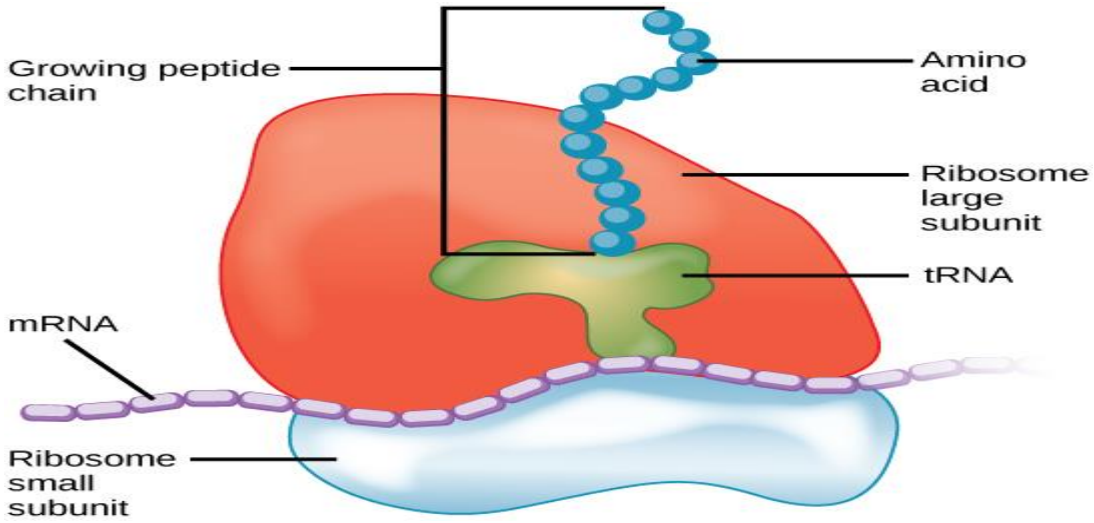
Both subunits comprise of both ribonucleic acid and protein components and are linked to each other by interactions between the proteins in one subunit and the rRNAs in the other subunit. The ribonucleic acid is obtained from the nucleolus, at the point where ribosomes are arranged in a cell.

The structures of ribosomes include:

Situated in two areas of the cytoplasm.

They are seen scattered in the cytoplasm and a few are connected to the endoplasmic reticulum.

- Whenever joined to the ER they are called the rough endoplasmic reticulum.
- The free and the bound ribosomes are very much alike in structure and are associated with protein synthesis.
- Around 37 to 62% of RNA is comprised of RNA and the rest is proteins.
- Prokaryotes have 70S ribosomes respectively subunits comprising the little subunit of 30S and the bigger subunit of 50S. Eukaryotes have 80S ribosomes respectively comprising of little (40S) and substantial (60S) subunits.
- The ribosomes seen in the chloroplasts of mitochondria of eukaryotes are comprised of big and little subunits composed of proteins inside a 70S particle.
- Share a center structure which is very much alike to all ribosomes in spite of changes in its size.
- The RNA is arranged in different tertiary structures. The RNA in the bigger ribosomes is into numerous continuous infusions as they create loops out of the center of the structure without disturbing or altering it.
- The contrast between those of eukaryotic and bacteria are utilized to make antibiotics that can crush bacterial disease without damaging human cells.



Ribosomes comprise of two subunits that are suitably composed and function as one to translate the mRNA into a polypeptide chain amid protein synthesis. Due to the fact that they are made from two subunits of differing size, they are a little longer in the hinge than in diameter. They vary in size between prokaryotic cells and eukaryotic cells.

The prokaryotic is comprised of a 30s (Svedberg) subunit and a 50s (Svedberg) subunit meaning 70s for the entire organelle equal to the molecular weight of 2.7×106 Daltons. Prokaryotic ribosomes are about 20 nm (200 Å) in diameter and are made of 35% ribosomal proteins and 65% rRNA.

Notwithstanding, the eukaryotic are amidst 25 and 30 nm (250–300 Å) in diameter. They comprise of a 40s (Svedberg) subunit and a 60s (Svedberg) subunit which means 80s (Svedberg) for the entire organelle which is equal to the molecular weight of 4×106 Dalton.

Ribosomes are organelles located inside the animal, human cell, and plant cells. They are situated in the cytosol, some bound and free-floating to the membrane of the coarse endoplasmic reticulum.

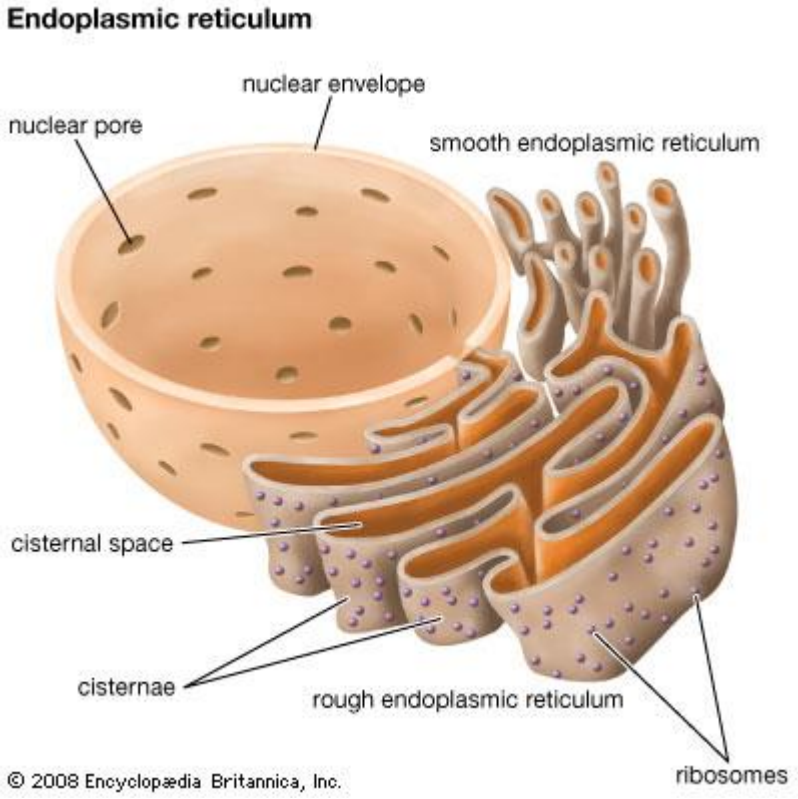
They are utilized in decoding DNA (deoxyribonucleic acid) to proteins and no rRNA is forever bound to the RER, they release or bind as directed by the kind of protein they proceed to combine. In an animal or human cell, there could be up to 10 million ribosomes and numerous ribosomes can be connected to the equivalent mRNA strand, this structure is known as a POLYSOME.

Function

When it comes to the main functions of ribosomes, they assume the role of bringing together amino acids to form particular proteins, which are important for completing the cell's activities. Protein is required for numerous cell functions, for example, directing chemical processes or fixing the damage. Ribosomes can yet be discovered floating inside the cytoplasm or joined to the endoplasmic reticulum.

Endoplasmic reticulum (ER) structure :

The endoplasmic reticulum (ER) is an important organelle in eukaryotic cells. It plays a major role in the production, processing, and transport of proteins and lipids. The ER produces transmembrane proteins and lipids for its membrane and for many other cell components including lysosomes, secretory vesicles, the Golgi appatatus, the cell membrane, and plant cell vacuoles.



Structure of Endoplasmic Reticulum (ER)

- The endoplasmic reticulum membrane system can be morphologically divided into two structures–cisternae and sheets.
- Cisternae are tubular in structure, and form a three-dimensional polygonal network.

- They are about 50 nm in diameter in mammals and 30 nm in diameter in yeast.
- ER sheets, on the other hand, are membrane-enclosed, two-dimensional flattened sacs that extend across the cytoplasm.
- They are frequently associated with ribosomes and special proteins called translocons that are necessary for protein translation within the RER.
- Endoplasmic reticulum is an extensive membrane network of cisternae (sac-like structures), which are held together by the cytoskeleton.
- The phospholipid membrane encloses a space, the lumen from the cytosol, which is continuous with the perinuclear space.
- The surface of the rough endoplasmic reticulum is studded with the protein manufacturing ribosome, which gives it a rough appearance. Hence it is referred as a rough endoplasmic reticulum.
- The smooth endoplasmic reticulum consists of tubules, which are located near the cell periphery. This network increases the surface area for the storage of key enzymes and the products of these enzymes.
- Rough endoplasmic reticulum synthesizes proteins, while smooth endoplasmic reticulum synthesizes lipids and steroids. It also metabolizes carbohydrates and regulates calcium concentration, drug detoxification, and attachment of receptors on cell membrane proteins.
- Endoplasmic reticulum varies extensive extending from the cell membrane through the cytoplasm and forming a continuous connection with the nuclear envelope.

Functions of Endoplasmic Reticulum (ER)

1. It is mainly responsible for the transportation of proteins and other carbohydrates to another organelle, which includes lysosomes, Golgi apparatus, plasma membrane, etc.
2. They provide the increased surface area for cellular reactions.
3. They help in the formation of nuclear membrane during cell division.
4. They play a vital role in the formation of the skeletal framework.
5. They play a vital role in the synthesis of proteins, lipids, glycogen and other steroids like cholesterol, progesterone, testosterone, etc.

Protein targeting & Insertion to the Endoplasmic Reticulum:

Targeting of Proteins to the Endoplasmic Reticulum.

Synopsis. Synthesis of proteins entering the endoplasmic reticulum is initiated on free ribosomes. A targeting sequence of hydrophobic amino acids near the amino terminal end of the growing polypeptide results in the binding of the ribosome to ER membrane and in insertion of the polypeptide into the endoplasmic reticuluum.

Proteins secretory or lysosomal pathways enter the ER and don't come out again. The proteins entering either of these pathways may be of either of two types:

- Proteins that are completely translocated into the endoplasmic reticuluum. These proteins are soluble (not membrane proteins) and are destined for secretion, or for transfer to lysosomes. In all of these cases the proteins are never part of membranes.
- Proteins that are inserted into membranes, and hence are only partially translocated into the endoplasmic reticuluum. These proteins may be destined for ER, membranes of another organelle (Golgi, lysosomes or endosomes), or the plasma membrane. In all of these cases the proteins stay within the membrane once they are inserted into the ER membrane (e.g. cellulose synthase).

Translation of all proteins begins on free ribosomes. Those ribosomes that produce proteins for export through the endoplasmic reticulum become attached to the endoplasmic reticulum as ribosomes of the rough ER. The signal for ER entry is 8 or more hydrophobic amino acid residues. which rivets the polypeptide to the ER membrane and is also involved in translocation.

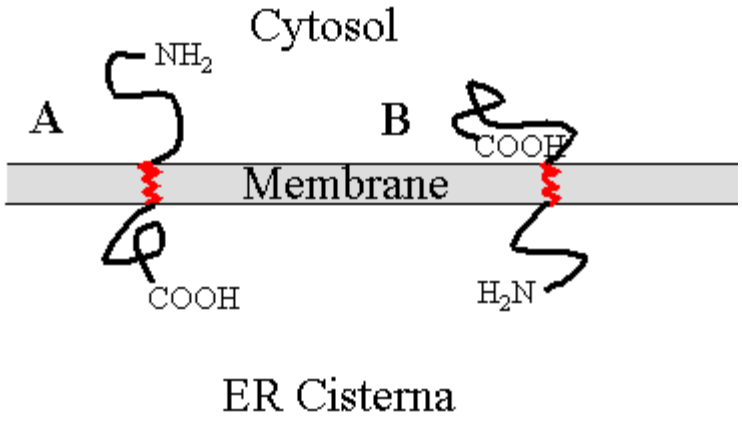
Whether or not a ribosome becomes attached to the endoplasmic reticulum depends on the nature of the message being translated, the protein being made, and is not an intrinsic property of the ribosome itself. The ribosome and its attached nascent peptide become targeted to the endoplasmic reticulum.

Targeting to the endoplasmic reticulum takes place through the interaction of the signal peptide sequence (a sequence of at least eight hydrophobic amino acids at the amino terminal end of the polypeptide. The emerging signal sequence combines with a 'signal recognition particle' (SRP). This greatly reduces the rate of translocation and allows the ribosome to attach to the endoplasm reticulum by means of a special SRP receptor in the ER membrane.

The ribosome becomes attached to a ribosome receptor that also functions as the translocation channel for the newly synthesized polypeptide. As the ribosome becomes attached, the SRP is removed and translation resumes.

1. There is a Signal Recognition Particle (SRP) in the cytosol. This binds to the ER Signal sequence when it is exposed on the ribosome and slows protein synthesis long enough to allow the SRP to find the second part, the SRP Receptor.

2. The Signal Recognition Particle Receptor (SRPR) which is embedded in the ER membrane. We now have the new polypeptide synthesizing system in place and protein synthesis speeds up. It seems that the Signal Sequence opens the translocation channel.



PROTEIN FOLDING PROCESS:

Protein Folding and Processing

Translation completes the flow of genetic information within the cell. The sequence of nucleotides in DNA has now been converted to the sequence of amino acids in a polypeptide chain. The synthesis of a polypeptide, however, is not equivalent to the production of a functional protein. To be useful, polypeptides must fold into distinct three-dimensional conformations, and in many cases multiple polypeptide chains must assemble into a functional complex. In addition, many proteins undergo further modifications, including cleavage and the covalent attachment of carbohydrates and lipids, that are critical for the function and correct localization of proteins within the cell.

Chaperones and Protein Folding:

The three-dimensional conformations of proteins result from interactions between the side chains of their constituent amino acids, as reviewed in Chapter 2. The classic principle of protein folding is that all the information required for a protein to adopt the correct three-dimensional conformation is provided by its amino acid sequence. This was initially established by Christian Anfinsen's experiments demonstrating that denatured RNase can spontaneously refold in vitro to its active conformation . Protein folding thus appeared to be a self-assembly process that did not require additional cellular factors. More recent studies, however, have shown that this is not an adequate description of protein folding within the cell. The proper folding of proteins within cells is mediated by the activities of other proteins.

Proteins that facilitate the folding of other proteins are called molecular chaperones. The term "chaperone" was first used by Ron Laskey and his colleagues to describe a protein (nucleoplasmin) that is required for the assembly of nucleosomes from histones and DNA. Nucleoplasmin binds to histones and mediates their assembly into nucleosomes, but nucleoplasmin itself is not incorporated into the final nucleosome structure. Chaperones thus act as catalysts that facilitate assembly without being part of the assembled complex. Subsequent studies have extended

the concept to include proteins that mediate a variety of other assembly processes, particularly protein folding.

It is important to note that chaperones do not convey additional information required for the folding of polypeptides into their correct three-dimensional conformations; the folded conformation of a protein is determined solely by its amino acid sequence. Rather, chaperones catalyze protein folding by assisting the self-assembly process. They appear to function by binding to and stabilizing unfolded or partially folded polypeptides that are intermediates along the pathway leading to the final correctly folded state. In the absence of chaperones, unfolded or partially folded polypeptide chains would be unstable within the cell, frequently folding incorrectly or aggregating into insoluble complexes. The binding of chaperones stabilizes these unfolded polypeptides, thereby preventing incorrect folding or aggregation and allowing the polypeptide chain to fold into its correct conformation.

A good example is provided by chaperones that bind to nascent polypeptide chains that are still being translated on ribosomes, thereby preventing incorrect folding or aggregation of the amino-terminal portion of the polypeptide before synthesis of the chain is finished . Presumably, this interaction is particularly important for proteins in which the carboxy terminus (the last to be synthesized) is required for correct folding of the amino terminus. In such cases, chaperone binding stabilizes the amino-terminal portion in an unfolded conformation until the rest of the polypeptide chain is synthesized and the completed protein can fold correctly.

Chaperones also stabilize unfolded polypeptide chains during their transport into subcellular organelles—for example, during the transfer of proteins into mitochondria from the cytosol . Proteins are transported across the mitochondrial membrane in partially unfolded conformations that are stabilized by chaperones in the cytosol. Chaperones within the mitochondrion then facilitate transfer of the polypeptide chain across the membrane and its subsequent folding within the organelle. In addition, chaperones are involved in the assembly of proteins that consist of multiple polypeptide chains, in the assembly of macromolecular structures (e.g., nucleoplasmin), and (as discussed later in this chapter) in the regulation of protein degradation.

Many of the proteins now known to function as molecular chaperones were initially identified as heat-shock proteins, a group of proteins expressed in cells that have been subjected to elevated temperatures or other forms of environmental stress. The heat-shock proteins (abbreviated Hsp), which are highly conserved in both prokaryotic and eukaryotic cells, are thought to stabilize and facilitate the refolding of proteins that have been partially denatured as a result of exposure to elevated temperature. However, many members of the heat-shock protein family are expressed and have essential cellular functions under normal growth conditions. These proteins serve as molecular chaperones, which are needed for polypeptide folding and transport under normal conditions as well as in cells subjected to environmental stress.

A Role for the Ubiquitin Proteasome Pathway in ER Quality Control:

The discovery that lactacystia fungal metabolite that specifically binds to and inhibits multiple proteolytic activities of the mammalian proteasome .this an effective inhibitor of "ER degradation," pointed a long-awaited finger at the proteasome as the culprit in this process. Proteasomes are cylindrical ring-like assemblies with a central chamber into which the proteolytic active site is segregated from the bulk solution. Efficient targeting to the proteasome requires that substrates be tagged with covalently attached multiubiquitin chains. The proteasome cooperates with a 19S "cap" structure that recognizes and removes the ubiquitin and possesses ATPase activity that probably helps to unfold and to "feed" the unfolded substrate into the active site. Proteasomes are abundant in the cytoplasm and nucleus, but are apparently absent from the ER lumen.

Mutations in the cystic fibrosis transmembrane conductance regulator (CFTR), a polytopic integral membrane protein, cause the human genetic disease cystic fibrosis by interfering with the biosynthetic folding of nascent CFTR polypeptides in the ER and targeting them for rapid destruction via a process bearing all of the hallmarks of classical "ER degradation" .Evidence of a role for the proteasome in CFTR degradation, suggested by its sensitivity to inhibition by lactacystin, was strengthened by the discovery that undegraded CFTR molecules that accumulate in the presence of lactacystin are modified by covalently attached multiubiquitin chains.

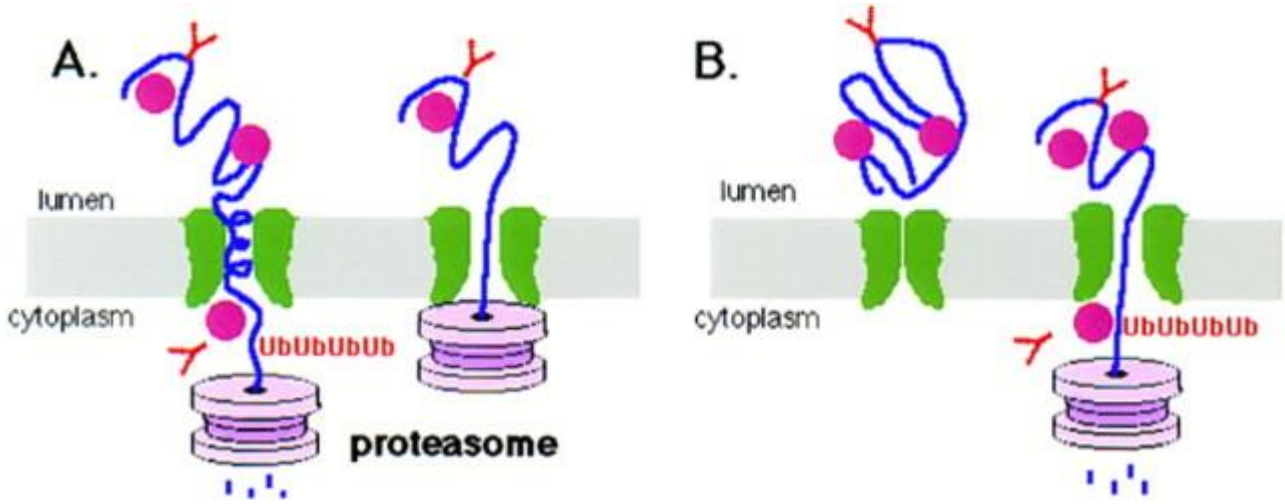
Moreover, mutant CFTR molecules are stabilized by coexpression of UbK48R, a dominant negative form of ubiquitin that is unable to form multiubiquitin chains, and by conditional inactivation of the ubiquitin-activating enzyme, E1.

Additional evidence supporting a role for the ubiquitin pathway in ER degradation was suggested by the genetic interaction between UBC6, a ubiquitin-conjugating enzyme that is associated with the cytoplasmic face of the ER membrane and SEC61, which encodes an ER-resident polytopic integral membrane protein .

Mutant, unassembled forms of Sec61p are rapidly degraded by a process requiring the function of two cytoplasmic ubiquitin-conjugating enzymes, UBC6 and UBC7. The degradation of mutant unassembled forms of Sec61p is also blocked by overexpression of UbK48R and by mutations in PRE1, which encodes a subunit of the proteasome, further implicating the ubiquitin–proteasome pathway in the process of ER degradation .

The apparent absence of proteasomes from the ER lumen poses a topological problem for degradation of proteins in the ER, since some or all of these substrates are segregated from the proteasome by a phospholipid bilayer membrane. However, nearly half of CFTR's amino acids are predicted to be exposed to the cytoplasm and could thus be substrates for ubiquitin-dependent proteasomal degradation. What is the fate of the other half of the protein, which dips into and out of the membrane in a serpentine fashion? Does the proteasome work like a razor, shaving off only the cytoplasmically exposed residues and leaving the membrane and lumenal portions to another, unidentified protease? Can the proteasome, known to be a highly processive enzyme, initiate and

terminate degradation in the middle of a polypeptide chain? Recent data suggest an alternative model in which ER degradation substrates must be reverse translocated or "dislocated" from the ER membrane prior to presentation to the cytoplasmic degradation apparatus.



Structure of the Smooth Endoplasmic Reticulum

The smooth endoplasmic reticulum is primarily composed of three-dimensional polygonal networks of tubules called cisternae. They are about 50 nm in diameter in mammals and 30 nm in diameter in yeast. The high curvature of these structures needs to be stabilized by many proteins, including reticulons, DP1 and receptor expression enhancing proteins (REEPs). These proteins either bend the membrane through structural elements that wedge themselves into the lipid bilayer or shape the membrane through oligomerization. The presence of these proteins seems crucial for the existence of tubular cisternae since their suppression or deletion leads to an excess of flattened sac-like structures in the ER and a near complete absence of tubules.

The smooth ER is also a dynamic structure, with new tubules budding off from the sides of existing structures. With the aid of GTP hydrolysis, some tubule branches can also fuse with one another. The extent of the smooth ER network depends on the actin and microtubule cytoskeleton of the cell. ER tubules can slide along the cytoskeletal framework using motor proteins, or grow along with a microtubule at its plus end.

The structure of the smooth ER is of particular significance in two types of cells in the human body – muscle cells and neurons. The presence of an extensive ER network along the neuron is closely associated with its interaction with actin and microtubules and the organelle forms a continuous network across the entire cell. It is present in small dendritic spines, all along the narrow axon, and is spread across the synapse. At the synapse, the smooth ER is often associated with mitochondria. Even when the cytoskeleton depolymerizes, and the ER network of tubules undergoes major morphological changes, the association between mitochondria and smooth ER

remains intact. In muscle cells, the smooth endoplasmic reticulum is called the sarcoplasmic reticulum and is an important locus for the storage of calcium ions.

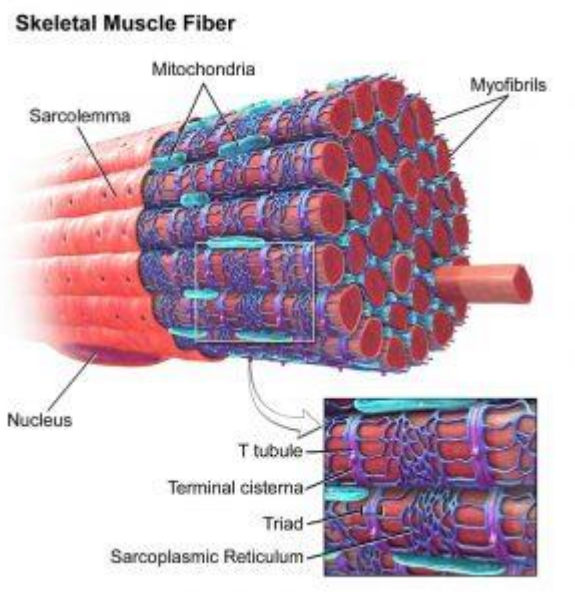


Image shows a skeletal muscle, with the sarcoplasmic reticulum colored blue. Along with special structures in the plasma membrane of the muscle cell (T-tubules), the sarcoplasmic reticulum plays an important role in the contraction of muscle fibers.

Functions of the Smooth Endoplasmic Reticulum

The smooth ER is important in the synthesis of lipids, such as cholesterol and phospholipids, which form all the membranes of the organism. In addition it is important for the synthesis and secretion of steroid hormones from cholesterol and other lipid precursors. In addition, it is involved in carbohydrate metabolism. For instance, the final reaction of gluconeogenesis occurs in the lumen of the smooth ER since it contains the enzyme glucose-6-phosphatase. This enzyme catalyzes the production of glucose from glucose-6-phosphate.

The dynamic nature of the smooth endoplasmic reticulum is particularly important in the liver that detoxifies a number of substances and makes them easy to remove from the body. For instance, when there is a sudden and drastic increase in the amount of some lipid soluble drugs in the body, the smooth ER of hepatocytes in the liver metabolize them into water-soluble compounds, so that they can be excreted in the urine. In order to do this, the smooth ER network of a hepatocyte can nearly double in size and then revert to its original shape and size after the chemical assault has been neutralized.

Lipid Synthesis

Steroid-secreting cells are characterized by abundant smooth endoplasmic reticulum whose membranes contain the enzymes involved in sterol and steroid synthesis.

The adrenal cortex is an important organ for the synthesis and secretion of steroid hormones. Cells involved in this process contain an extensive ER network. While there is a wide range of hormones produced by the cells of the adrenal glands, they can be classified broadly as glucocorticoids, mineralocorticoids, and sex hormones. Sex hormones are produced in much larger quantities in the gonads, but glucocorticoids and mineralocorticoids are produced largely in the adrenal glands and are synthesized from cholesterol. Cholesterol is converted into a number of different steroid molecules, with the reactions being catalyzed by the enzymes of the cytochrome p450 family of proteins. Some parts of this pathway reside in the ER and others occur in mitochondria.

There has been some evidence to suggest that cells that are heavily involved in lipid metabolism contain relatively little rough endoplasmic reticulum, in spite of the obvious need for a variety of enzymes. In such cells, researchers have identified smooth ER subfractions that contain proteins normally seen in the rough endoplasmic reticulum, such as the translocon complex and chaperone proteins. This suggests that the smooth ER can also be involved in protein synthesis, cotranslational import of polypeptides and quality control for newly synthesized proteins.

Organization of ER exit sites

Another layer of potential regulation of ER export revolves around the clear sub-division of the ER into discrete domains. COPII vesicles appear to arise from distinct regions of the ER known as transitional ER (tER) or ERES. These structures, marked by COPII proteins, are relatively stable, largely immobile structures of approximately 0.5 μm that form at small ribosome-free regions within the rough ER . In mammalian cells, ERES are not evenly distributed along the ER membrane but are found in discrete sites that face towards small structures, known as vesicular tubular clusters (VTCs) or the ER-Golgi intermediate compartment (ERGIC) . The budding yeast, Pichia pastoris, similarly has discrete ERES that are relatively few in number and are apposed to the Golgi, whereas Saccharomyces cerevisiae appears to lack this higher layer of organization with COPII vesicles budding across the entire ER membrane . Two proposed functions of ERES are (i) to enable cargo destined for export to be efficiently packaged and (ii) to ensure that ER resident proteins and other non-cargo substrates remain in the ER.

The molecular makeup and structure of ERES is an emerging area that seeks to expand our understanding of the mechanisms by which unique subdomains are maintained in such a fluid membrane environment. The lipid composition of the membrane has long been proposed to play a role in ER trafficking, however only relatively recently has concrete evidence emerged that suggests phosphatidylinositol (4)-phosphate (PtdIns4P) is specifically enriched in ER subdomains, potentially acting to regulate the recruitment of Sar1 . ERES themselves may also come in distinct

flavors: Castillon and colleagues identified that yeast maintain three distinct ERES populations that differ by cargo they concentrate for export.

The three different populations carry either soluble cargoes like pro-α-factor, transmembrane cargoes like amino acid permeases, or GPI-anchored proteins . Such segregation of ERES is consistent with previous findings that suggest there also at least two distinct COPII vesicle populations incorporating either GPI-anchored proteins or non-GPI-anchored proteins . How these different identities are established and maintained is unclear, but the requirement of different lipids in the ERES as well as the recruitment of specific COPII components (Sec24, Lst1, Iss1) could also define specific characteristics for distinct ERES.

The only known player in ERES organization is the relatively large (~240 kDa) peripheral membrane protein, Sec16. First identified in a genetic screen in S. cerevisiae as a secretion mutant, this essential protein is conserved across species, marks ERES and could provide a scaffold to support coat assembly through its interactions with each of the COPII coat proteins. Although the precise molecular function of Sec16 has not been established, the current view is that it is recruited to ERES upstream of the COPII subunits and is required for maintenance of these structures. Depletion of Sec16 from mammalian cells disperses ERES on the membrane . Regulation of Sec16 and these early secretory pathway steps were recently reported to be, in part, controlled by two kinases, the Mitotic-Associated Protein Kinase (MAPK) Extracellularly regulated kinases (ERKs) ERK2 and ERK7 . ERK2 directly phosphorylates human Sec16 at threonine 415 resulting in the recruitment of Sec16 to ERES, leading to up-regulation of ERES and in turn, up-regulation of ER-to-Golgi transport . Conversely, upon nutrient starvation, ERK7 induces Sec16 phosphorylation releasing Sec16 from the tER sites, ERES disassembly and hence diminished ER-to-Golgi transport.

2. ER export of protein cargo:

The process of accurate and selective recruitment of cargo proteins into nascent COPII vesicles is an integral part of the fidelity of ER export and transport through the secretory pathway. Indeed, the sheer volume and diversity of molecules that traffic through the ER is testament to the flexibility of this process: it is estimated up to one-third of all proteins in yeast, ~70% of hepatocyte proteins and ~6000 proteins in human cells traffic through the ER for secretion or delivery to other organelles of the endomembrane system . Upon translation/translocation into the ER, chaperones and folding enzymes recognize the newly synthesized proteins to complete protein assembly prior to ER egress via concentrated, signal-mediated export or bulk-flow . To ensure the effective onward transport of correctly folded proteins and the removal of aberrant proteins, protein biogenesis and trafficking is highly regulated, and is intertwined with the COPII functionality, to ensure that only acceptable cargo are released from the quality control system of the ER.

Golgi Apparatus Definition

The Golgi apparatus is an organelle in eukaryotic organisms that moves molecules from the endoplasmic reticulum to their destination. The organelle also modifies products of the

endoplasmic reticulum to their final form. The Golgi apparatus is comprised of a series of flattened sacs that extend from the endoplasmic reticulum.

Golgi Apparatus Overview

The main function of the Golgi apparatus is the ability to deliver vesicles, or packets of various cell products, to different locations throughout the cell. The Golgi also has important functions in tagging vesicles with proteins and sugar molecules, which serve as identifiers for the vesicles so they can be delivered to the proper target. The organelle is also called the Golgi complex or Golgi body.

Typically, proteins and cellular products are manufactured in the endoplasmic reticulum. The rough endoplasmic reticulum has a number of ribosomes, which assemble proteins from instructions contained in messenger RNA. Throughout the rest of the endoplasmic reticulum, these protein products are folded and modified. As they reach the Golgi apparatus, more modifications are made. Finally, the products are packaged within vesicles which are "labeled" by other proteins and molecules. The vesicles are released and based on their tags or labels they are carried to the appropriate location within the cell by the cytoskeleton.

Golgi Apparatus Functions

The Golgi apparatus has many discrete functions. But, all functions are associated with moving molecules from the endoplasmic reticulum to their final destination and modifying certain products along the way. The multiple sacs of the Golgi serve as different chambers for chemical reactions. As the products of the endoplasmic reticulum move through the Golgi apparatus, they are continuously transferred into new environments, and the reactions that can take place are different. In this way, a product can be given modifications, or multiple products can be combined to form large macromolecules. The many sacs and folds of the Golgi apparatus allow for many reactions to take place at the same time, increasing the speed at which an organism can produce products.

Tagging Cellular Products

Regardless of the product, the vesicles containing the product move from the endoplasmic reticulum and into the cis face of the Golgi apparatus. In layman's terms, this is the side facing the endoplasmic reticulum. The side furthest from the endoplasmic reticulum is known as the trans face of the Golgi apparatus, and this is where products are headed.

After having any modifications or additions to their structure, the products are packaged in vesicles and tagged with markers that indicate where the vesicle needs to end up. These tags can be molecules, such as phosphate groups, or special proteins on the surface of the vesicle. Once tagged, the vesicle is excreted from the Golgi apparatus, on its way to its final destination.

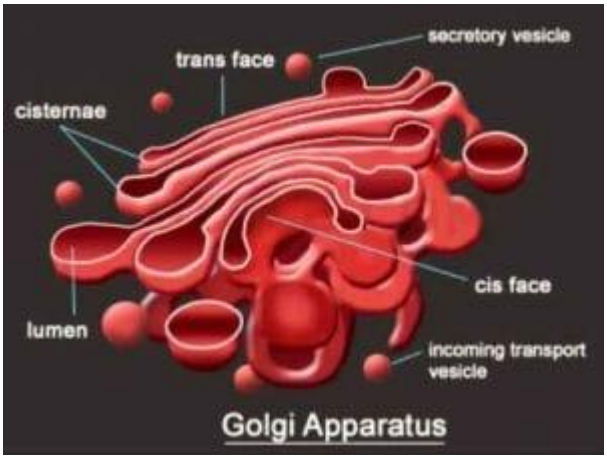
Finalizing Cellular Products

There are many products that are produced by eukaryotes, from proteins that can carry out chemical reactions to lipid molecules that can build new cell membranes. Some products are meant for the endoplasmic reticulum or the Golgi apparatus itself and travel in the opposite direction of most vesicles. While the endoplasmic reticulum produces most of the products and bases used, it is the Golgi apparatus that is responsible for the final presentation and assembly of products. Often, the environment must be slightly different from that present in the endoplasmic reticulum to obtain certain end products. The many sacs of the Golgi apparatus function to provide many different areas in which reactions can take place in the most favorable of conditions.

In secretory cells, or cells which produce large amounts of a substance that your body needs, the Golgi apparatus will be very large. Consider the cells in your stomach that secrete acid. The acid is produced by reactions in the endoplasmic reticulum and is modified as is goes through the Golgi apparatus. Once to the trans side of the Golgi apparatus, the acid is packaged in a vesicle and sent towards the cell's surface. As the vesicle joins with the plasma membrane, the acid is released into the stomach, so it can digest your food.

Golgi Apparatus Structure

The image below shows the structure of the Golgi apparatus. The cis face of the organelle is closest to the endoplasmic reticulum. The trans face is the side furthest from the nucleus, which secretes vesicles to various parts of the cell. Further, there are a number of lumens and cisternae through which products flow. These appear as a series of flattened sacs stack on each other, much like the endoplasmic reticulum.



Golgi Apparatus Location

The Golgi apparatus is situated in between the endoplasmic reticulum and the cell membrane. Most often, the Golgi appears to be an extension of the endoplasmic reticulum which is slightly smaller and smoother in appearance. However, the Golgi apparatus can be easily mistaken for smooth endoplasmic reticulum. Although they look similar, the Golgi is an independent organelle which has different functions.

Theory of Golgi Apparatus Function

The most prevalent theory of how the Golgi apparatus forms is the cisternal maturation model. This model suggests that the sacs themselves tend to move from the cis face to the trans face of the Golgi apparatus over time. New sacs are formed closest to the endoplasmic reticulum. These sacs "age" as they move towards the trans face of the Golgi apparatus and their product becomes fully mature.

Specific Products

It may seem like there could never be enough lipids to produce the continual flow of cell membrane needed to continually make transport vesicles between the endoplasmic reticulum and the Golgi apparatus. However, there are constantly segments of cell membrane being produced and recycled by the endoplasmic reticulum, Golgi apparatus, lysosomes, and other organelles in the cell, as well as the outer cell membrane itself. The Golgi apparatus and endoplasmic reticulum work together to produce new cell membrane, as well as recycle the cell membranes of vesicles by merging two membranes when vesicles are absorbed.

The Golgi also creates lysosomes. These sacs contain digestive materials. The sacs are pinched off from the Golgi apparatus, and they are used to process materials which have been phagocytized or to digest organelles which no longer function. The lysosome delivers raw ingredients to the endoplasmic reticulum.

Golgi Apparatus in Plant Cells

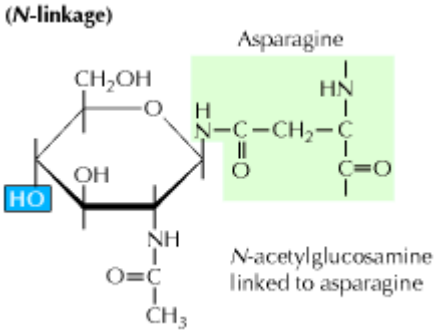
While this article primarily discusses the operation of the Golgi apparatus within animal cells, plant cells also have a Golgi apparatus. In fact, plant cells may contain hundreds of these organelles.

Within plant cells, the Golgi apparatus serves the additional function of synthesizing the major polysaccharide molecules which help form the cell wall. To do this, plants often have many more Golgi bodies than an animal cell. Further, plant cells do not contain lysosomes. These digestive organelles are replaced in the plant with the central vacuole, which serves as a large lysosome as well as an organelle to store water. Thus, many vesicles from the Golgi bodies of plants move to the vacuole and fuse their contents with this large organelle.

Protein Glycosylation

The addition of a carbohydrate moiety to a protein molecule is referred to as protein glycosylation. It is a common post translational modification for protein molecules involved in cell membrane formation. During this process,the linking of monosaccharide units to the amino acid chains sets up the stage for a series of enzymatic reactions that lead to the formation of glycoproteins (n and o linked oligosaccharides that are found to a protein entity). In all 16 known enzymes are supposed to mediate this reaction. A typical glycoprotein has at least 41 bonds which involve 8 amino acids and 13 different monosaccharide units and includes the glycophosphatidylinositol (GPI) and phosphoglycosyl linkages. Protein glycosylation helps in proper folding of proteins, stability and in cell to cell adhesion commonly needed by cells of the immune system. The major sites of protein glycosylation in the body are ER, Golgi body, nucleus and the cell fluid.

Protein glycosylation can be categorized in two main types:



a) N-linked glycosylation: It begins with the addition of a 14-sugar precursor to an asparagine amino acid. It contains glucose, mannose and n-acetylglucosamine molecules. This entity is then transferred to the ER lumen. The oligosaccharyl transferase enzyme attaches the oligosaccharide chain to asparagine that occurs in the tripeptide sequence, Asn-X-Ser or Asn-X-Thr. X can be any amino acid other than Proline. The oligosaccharide attached protein sequence now folds correctly and is now translocated to the Golgi body where the mannose residue is removed.

b) O-linked glycosylation: Glycosylation begins with an enzyme mediated addition of N-acetyl-galactosamine followed by other carbohydrates to serine or threonine residues. Studies reveal that O linked glycosylation occurs at a later stage in protein processing.

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Lysosome

Lysosome Definition

Lysosomes are specialized vesicles within cells that digest large molecules through the use of hydrolytic enzymes. Vesicles are small spheres of fluid surrounded by a lipid bilayer membrane, and they have roles in transporting molecules within the cell. Lysosomes are only found in animal cells; a human cell contains around 300 of them. Not only do they digest large molecules, they are also responsible for breaking down and getting rid of waste products of the cell. Lysosomes contain over 60 different enzymes that allow them to carry out these processes.

Functions of the Lysosome

Lysosomes digest many complex molecules such as carbohydrates, lipids, proteins, and nucleic acids, which the cell then recycles for other uses. The pH of lysosomes is acidic (around pH 5) because their hydrolytic enzymes function best at this pH instead of at the neutral pH of the rest of the cell. Hydrolytic enzymes specifically break down large molecules through hydrolysis. During the process of hydrolysis, a molecule of water is added to a substance, causing it to cleave. Like the digestive system of the human body, which breaks down food using enzymes, the lysosome can be thought of as the "digestive system" of the cell because it breaks down molecules using enzymes.

Lysosomes digest several different kinds of molecules. They can digest food molecules that enter the cell into smaller pieces if an endocytic vesicle (a vesicle that brings particles into the cell) fuses with them. They can also perform autophagy, which is the destruction of improperly functioning organelles. In addition, lysosomes have a role in phagocytosis, which is when a cell engulfs a molecule in order to break it down; it is also known as "cell eating". For example, the white blood cells called phagocytes ingest invading bacteria in order to break it down and destroy it, and the bacteria is enclosed by a vesicle that lysosomes fuse with. These lysosomes then break down the bacteria.

Lysosome Structure

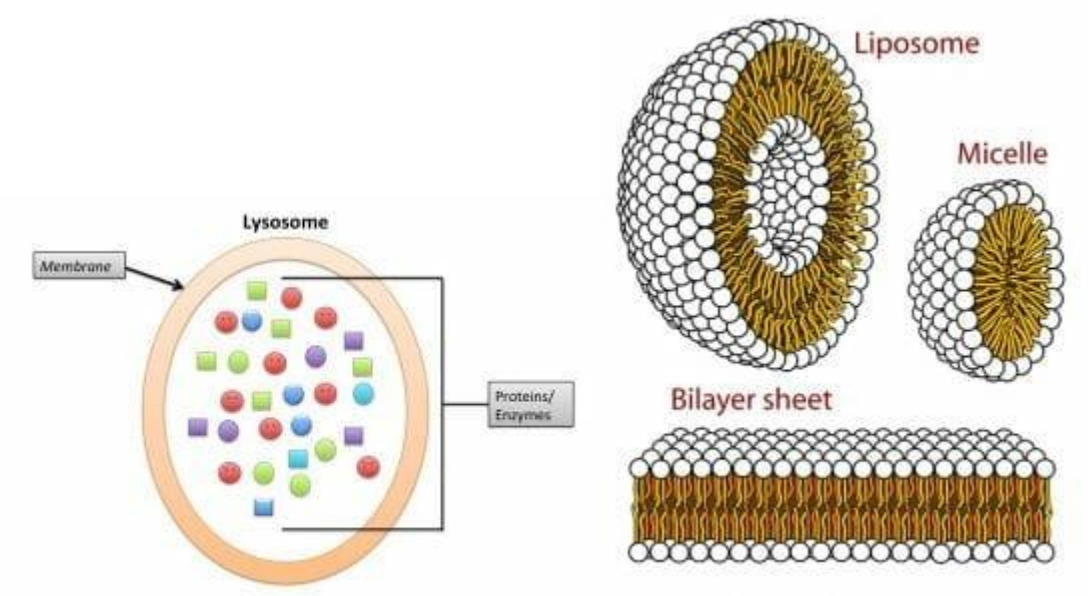
Lysosomes are generally very small, ranging in size from 0.1-0.5 µm, though they can reach up to 1.2 µm. They have a simple structure; they are spheres made up of a lipid bilayer that encloses fluid that contains a variety of hydrolytic enzymes. The lipids that make up the bilayer are phospholipids, which are molecules that have hydrophilic phosphate group heads, a glycerol molecule, and hydrophobic fatty acid tails. Due to these differences in properties, phospholipids naturally form double-layered membranes when placed in a solution containing water. The phosphate group heads move to the outside of the layer, while the fatty acid tails move to the inside of the layer to be away from water. Phospholipids make up many other membranes in the cell, such as the cell membrane which surrounds the entire cell, the nuclear membrane (or nuclear envelope) that surrounds the nucleus, the Golgi apparatus, and the endoplasmic reticulum.

Lysosomes are formed by budding off of the Golgi apparatus, and the hydrolytic enzymes within them are formed in the endoplasmic reticulum. The enzymes are tagged with the molecule

mannose-6-phosphate, transported to the Golgi apparatus in vesicles, and then packaged into the lysosomes.

There are many different types of enzymes in lysosomes including proteases, amylases, nucleases, lipases, and acid phosphatases, among many others. Enzymes are usually named for the molecules that they break down; for example, proteases break down proteins, and nucleases break down nucleic acids. Amylases break down starches into sugars.

The following images are a simplified structure of the lysosome and a more detailed depiction of the phospholipid bilayer structure.



Lysosome Phospholipids bilayer structure

Liposomes, not to be confused with lysosomes, are artificially created vesicles that, like all vesicles including lysosomes, have phospholipid bilayers. They are sometimes used to deliver nutrients and pharmaceutical drugs.

Possible Questions

Part-A (1 mark)

Part-B (2 marks)

1.what is polysome?

2.define translation process.

3.define suicidal bages

4.what is protein folding.

5.what is protein glycosylation.

Part-C (8 marks)

1.explain structure and function of Ribosomes

2.explain about the protein folding process in golgi comples.

3.describe structure and function of ER.

4.Brief about lipid synthesis in SER.

5.Explain function and structure of Lysosomes.

S.NO	QUESTIONS	POSSIBILITY A	POSSIBILITY B	POSSIBILITY C	POSSIBILIY D	ANSWER
1	SER produces	Protein	Carbohydrate	Lipid	Nucleic acid	Lipid
2	The main organelle involved in modification and routing of newly synthesized proteins to their destinations is	Chloroplast	Mitochondria	Lysosome	Endoplasmic reticulum	Endoplasmic reticulum
3	The transfer vesicle from RER fuse with which region of golgi complex	Cis	Medial	Trans	Protein arms	Cis
4	Which of the following is related to glycosylation of protein	ER	Peroxisome	Lysosome	Mitochondria	ER
5	Endoplasmic reticulum is more developed in	Green cells	Young cells	Mature cells	Bacteriophage	Young cells
6	GERL system was proposed by	Aschoff	Metchnikoff	Novikoff	None of these	Novikoff
7	Sarcoplasmic reticulum is related with	Protein synthesis	Hormone synthesis	Release of Ca++ ions and contraction of muscles	None of these	Release of Ca++ ions and contraction of muscles

8	During ultracentrifugation the ER and bodies associated with it are separated as a fraction known as	Microsome	Polysome	Quantosome	Episome	Microsome
9	The most important function of endoplasmic reticulum is	Protein synthesis	Nourishing the nucleus	Secretion of materials	To give shape to the cell	Protein synthesis
10	In rapidly dividing cells, endoplasmic reticulum is	Highly developed	Poorly developed	Absent	Non-functional	Poorly developed
11	Which one of the following pairs is correctly matched	Microsomes Participate in the process of photosynthesis	Lysosomes Involved in synthesizing amino acids	ER Plays role in the formation of a new nuclear membrane during cell division	Centrosomes Provide enzymes required in the digestive process	ER Plays role in the formation of a new nuclear membrane during cell division
12	In endoplasmic reticulum the following process take place	Lipid synthesis	Channeling of biosynthetic processes	Steroid synthesis	All of the above	All of the above
13	Single unit membrane structure present in the cytoplasm in the form of a net is	Golgi complex	Microtubules	Microsomes	Endoplasmic reticulum	Endoplasmic reticulum
14	The endoplasmic reticulum often bears	Lysosomes	Centrioles	Peroxisomes	Ribosomes	Ribosomes
15	When the region of endoplasmic reticulum are studded by ribosome on their outer surface of the cisternae, it is called	Sarcoplasmic reticulum	Smooth endoplasmic reticulum	Granular endoplasmic reticulum	None of the above	Granular endoplasmic reticulum

16	The fine network of single unit membrane distributed extensively throughout the cytoplasm in a cell is referred to as	Golgi bodies	Peroxisome	Lysosome	Endoplasmic reticulum	Endoplasmic reticulum
17	The endoskeleton of cell is made up of	Cell wall	Endoplasmic reticulum	Cytoplasm	Mitochondria	Endoplasmic reticulum
18	"Endoplasmic reticulum" was discovered by	Porter	Altmann	Golgi	Benda	Porter
19	RER is mainly concerned with	Proteolysis	Fatty acids synthesis	Peptide bond formation	Cholesterol synthesis	Peptide bond formation
20	Which of the following is responsible for mechanical support, enzyme transport and protein synthesis	Dictyosomes	Cell membrane	Mitochondria	Endoplasmic reticulum	Endoplasmic reticulum
21	Least stable endoplasmic reticulum is	Rough E.R.	Smooth E.R.	Cisternae	Tubules	Smooth E.R.
22	Golgi body originated from	Lysosome	Endoplasmic reticulum	Mitochondria	Cell membrane	Endoplasmic reticulum
23	Which is not function of golgibody	Secretion	Formation of plasmamembrane	Fat synthesis	Cell wall formation	Fat synthesis

24	Flattened sacs of golgi bodies are separated from each other by a space which is	13Å	130Å	113Å	123Å	130Å
25	In plant cells the number of golgi bodies increases during	Cell division	Food synthesis	Translocation	Respiration	Food synthesis
26	The golgi apparatus contains	DNA	RNA	Phospholipids, proteins, enzymes and vitamin C	Protein-lipid-protein.	Phospholipids, proteins, enzymes and vitamin C
27	In plants cells, the dictysomes are derived from	ER	Plasma membrane	Mitochondria	Tonoplast	ER
28	Golgi bodies are absent in	Plants	Bacteria	Animals	Eukaryotic cells	Bacteria
29	The golgi apparatus is bounded by	Cellulose	Hemicellulose	Pectin	None of the above	None of the above
30	Secretory and membrane proteins are processed in	Peroxisomes	Glyoxysomes	Golgi complex	Sphaerosomes	Golgi complex
31	Main function of dictyosomes is	Respiration	Storage	Secretion	Breakdwon of fats	Storage

32	The scattered sacs of golgi in plants are called as	Dictyosome	Ribosome	Cisternae	Microsome	Dictyosome
33	Zone of exclusion is associated with	Golgi complex	Endoplasmic reticulum	Mitochondria	Chloroplast	Golgi complex
34	Cell wall materials are synthesized by	Dictyosomes	Ribosomes	Lysosomes	Centrosomes	Dictyosome
35	Which of the following structure is the functional unit in a golgi complex	Cristae	Cisternae	Thylakoid	None of the above	Cisternae
36	Dictyosomes are	Class of ribosomes	Place of flagellar organelles	Respiratory particles	Golgi bodies (of plant cells)	Golgi bodies (of plant cells)
37	Golgi bodies are maximum in	Calyptrogen	Root tip	Root cap	None of these	Root cap
38	The enzyme present in golgi bodies is	PEP carboxylase	Peptidyl transferase	Thymine ligase	Glycosyl transferase	Glycosyl transferase
39	The major role of golgi bodies is	Fermentation	Phosphorylation	Glycosidation	Translocation	Glycosidation

40	Endoplasmic reticulum is in continuation with	Golgibody	Nuclear wall	Mitochondria	cell wall	Nuclear wall
41	"Lysosomes" were discovered by	Haekel	De Duve	De Vries	Purkinje	Haekel
42	Which of the following statements is incorrect with reference to lysosomes	They are filled acid hydrolase and other enzymes	They are monomorphic and uniform in structure and function	They may be autophagic	They can digest proteins, nuclei acids, lipids and polysaccharides	They are monomorphic and uniform in structure and function
43	The main function of lysosomes is	Digestion	Replication	Translation	Translocation	Digestion
44	Scavenging of worn out cell parts and denatured proteins in the cells is done by	Vacuoles	Golgi bodies	Lysosomes	Endoplasmic reticulum	Lysosomes
45	What would happen if lysosomes get ruptured inside the cells in which they are present	Cells will swell	Cells will shrink	Cells will die	Nothing would happen	Cells will die
46	Microbodies differ from lysosomes in that	Microbodies are surrounded by a single unit membrane while lysosome membrane is double	Microbodies are surrounded by double membrane while lysosomes membrane is single unit	Microbodies contain lytic enzymes while lysosomes do not	Lysosome contain lytic enzymes while microbodies do not	Lysosome contain lytic enzymes while microbodies do not
47	Lysosomes are so called because these contain	Carboxylating enzymes	Respiratory enzymes	Oxidizing enzymes	Digestive enzymes	Digestive enzymes

48	The organelles whose major function is storage of hydrolytic enzymes are	Centrioles	Chromoplasts	Lysosomes	Chloroplasts	Lysosomes
49	The cellular role for lysosome is not	Ingestion of foreign bodies	Digestion of aged organelles	Cell destruction during development	Osmoregulation	Osmoregulation
50	Which is concerned with autolysis	Ribosome	Golgi bodies	Lysosome	Oxysome	Lysosome
51	Lysosome along with the food content is called	Primary lysosome	Secondary lysosome	Residual bodies	Cytosome	Secondary lysosome
52	The cell organelle showing extensive polymorphism is	Dictyosomes	Chloroplasts	Lysosomes	Ribosomes	Lysosomes
53	Lysosomes are known as suicidal bags because of	Catalytic enzymes	Hydrolytic enzymes	Parasitic on nucleus	Proteolytic enzymes	Hydrolytic enzymes
54	Secondary lysosomes are also called	Autophagic vacuoles	Lipofuscin granules	Residual body	Heterophagosomes	Heterophagosomes
55	The "marker" enzyme of lysosome is	Lysozyme (muramidase)	Acid protease	Acid phosphatase	Beta-galactosidase	Acid phosphatase

56	Lysosomes are generally found in	Animal cells	Plant cells	Both (a) and (b)	Bacterial cells	Animal cells
57	A lysosome in which intracellular organells is digested is called	Primary lysosome	Secondary lysosome	Autophagosome	None of the above	Autophagosome
58	Which of the following cell organelles is having single layered unit membrane	Centrosome	Lysosome	Mesosome	Nucleus	Lysosome
59	Who discovered "ribosomes" in animal cells	Watson	Talvim	Cowdry	Palade	Palade
60	Ribosomes, similar to those of bacteria, are found in	Plant nuclei	Pancreatic mitochondria	Liver endoplasmic reticulum	Cardiac muscle cytoplasm	Pancreatic mitochondria

Unit IV

Syllabus

Signalling molecules and their receptor-function of the cell surface receptors.Pathway of intra cellular receptors-cyclic AMP,cyclic GMP, and MAP Kinase pathway.

Signaling Molecules and Cellular Receptors

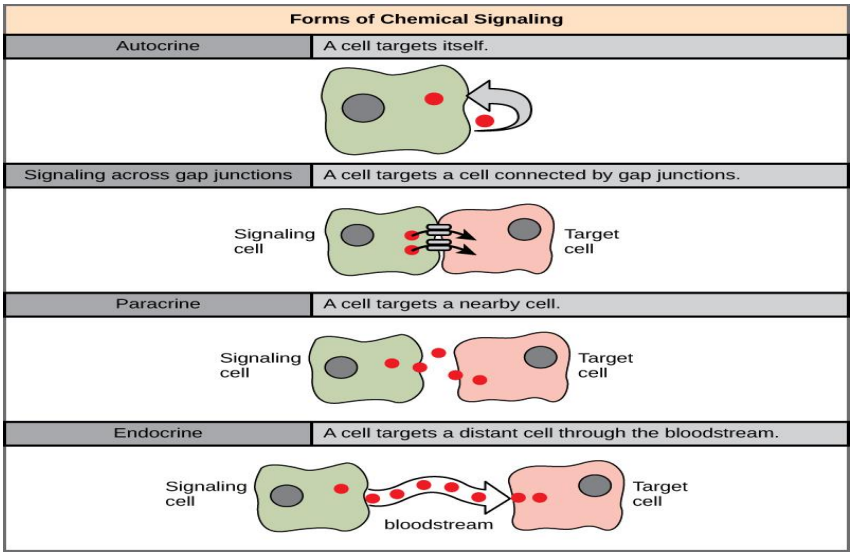
Differentiate between different types of signals:

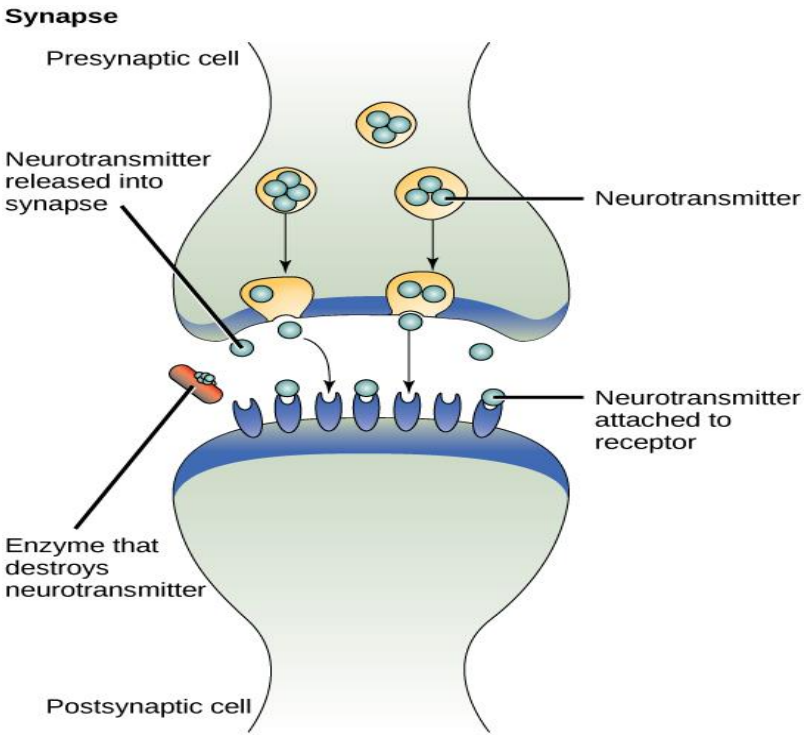
There are two kinds of communication in the world of living cells. Communication between cells is called intercellular signaling, and communication within a cell is called intracellular signaling. An easy way to remember the distinction is by understanding the Latin origin of the prefixes: inter– means "between" (for example, intersecting lines are those that cross each other) and intra– means "inside" (like intravenous).

Chemical signals are released by signaling cells in the form of small, usually volatile or soluble molecules called ligands. A ligand is a molecule that binds another specific molecule, in some cases, delivering a signal in the process. Ligands can thus be thought of as signaling molecules. Ligands interact with proteins in target cells, which are cells that are affected by chemical signals; these proteins are also called receptors. Ligands and receptors exist in several varieties; however, a specific ligand will have a specific receptor that typically binds only that ligand.

Types of Signals

There are four categories of chemical signaling found in multicellular organisms: paracrine signaling, endocrine signaling, autocrine signaling, and direct signaling across gap junctions (Figure 1). The main difference between the different categories of signaling is the distance that the signal travels through the organism to reach the target cell. Not all cells are affected by the same signals.





The distance between the presynaptic cell and the postsynaptic cell—called the synaptic gap—is very small and allows for rapid diffusion of the neurotransmitter. Enzymes in the synaptic cleft degrade some types of neurotransmitters to terminate the signal.

Signals that act locally between cells that are close together are called paracrine signals. Paracrine signals move by diffusion through the extracellular matrix. These types of signals usually elicit quick responses that last only a short amount of time. In order to keep the response localized, paracrine ligand molecules are normally quickly degraded by enzymes or removed by neighboring cells. Removing the signals will reestablish the concentration gradient for the signal, allowing them to quickly diffuse through the intracellular space if released again.

One example of paracrine signaling is the transfer of signals across synapses between nerve cells. A nerve cell consists of a cell body, several short, branched extensions called dendrites that receive stimuli, and a long extension called an axon, which transmits signals to other nerve cells or muscle cells. The junction between nerve cells where signal transmission occurs is called a synapse. A synaptic signal is a chemical signal that travels between nerve cells. Signals within the nerve cells are propagated by fast-moving electrical impulses. When these impulses reach the end of the axon, the signal continues on to a dendrite of the next cell by the release of chemical ligands called neurotransmitters by the presynaptic cell (the cell emitting the signal). The neurotransmitters are transported across the very small distances between nerve cells, which are called chemical synapses (Figure 2). The small distance between nerve cells allows the signal to travel quickly; this enables an immediate response.

When the neurotransmitter binds the receptor on the surface of the postsynaptic cell, the electrochemical potential of the target cell changes, and the next electrical impulse is launched. The neurotransmitters that are released into the chemical synapse are degraded quickly or get reabsorbed by the presynaptic cell so that the recipient nerve cell can recover quickly and be prepared to respond rapidly to the next synaptic signal.

Endocrine Signaling

Signals from distant cells are called endocrine signals, and they originate from endocrine cells. (In the body, many endocrine cells are located in endocrine glands, such as the thyroid gland, the hypothalamus, and the pituitary gland.) These types of signals usually produce a slower response but have a longer-lasting effect. The ligands released in endocrine signaling are called hormones, signaling molecules that are produced in one part of the body but affect other body regions some distance away.

Hormones travel the large distances between endocrine cells and their target cells via the bloodstream, which is a relatively slow way to move throughout the body. Because of their form of transport, hormones get diluted and are present in low concentrations when they act on their target cells. This is different from paracrine signaling, in which local concentrations of ligands can be very high.

Autocrine Signaling

Autocrine signals are produced by signaling cells that can also bind to the ligand that is released. This means the signaling cell and the target cell can be the same or a similar cell (the

prefix auto- means self, a reminder that the signaling cell sends a signal to itself). This type of signaling often occurs during the early development of an organism to ensure that cells develop into the correct tissues and take on the proper function.

Autocrine signaling also regulates pain sensation and inflammatory responses. Further, if a cell is infected with a virus, the cell can signal itself to undergo programmed cell death, killing the virus in the process. In some cases, neighboring cells of the same type are also influenced by the released ligand. In embryological development, this process of stimulating a group of neighboring cells may help to direct the differentiation of identical cells into the same cell type, thus ensuring the proper developmental outcome.

Direct Signaling Across Gap Junctions

Gap junctions in animals and plasmodesmata in plants are connections between the plasma membranes of neighboring cells. These water-filled channels allow small signaling molecules, called intracellular mediators, to diffuse between the two cells. Small molecules, such as calcium ions (Ca^{2+}), are able to move between cells, but large molecules like proteins and DNA cannot fit through the channels. The specificity of the channels ensures that the cells remain independent but can quickly and easily transmit signals. The transfer of signaling molecules communicates the current state of the cell that is directly next to the target cell; this allows a group of cells to coordinate their response to a signal that only one of them may have received. In plants, plasmodesmata are ubiquitous, making the entire plant into a giant, communication network.

Signaling Molecules

Produced by signaling cells and the subsequent binding to receptors in target cells, ligands act as chemical signals that travel to the target cells to coordinate responses. The types of molecules that serve as ligands are incredibly varied and range from small proteins to small ions like calcium (Ca^{2+}).

Small Hydrophobic Ligands

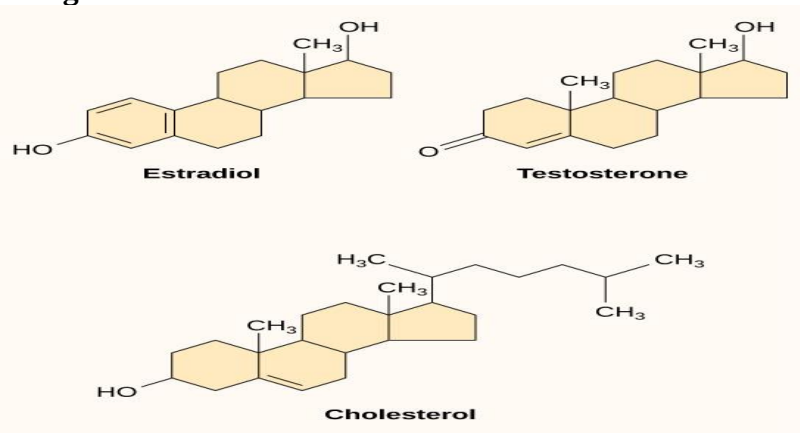


Figure 3. Steroid hormones have similar chemical structures to their precursor, cholesterol. Because these molecules are small and hydrophobic, they can diffuse directly across the plasma membrane into the cell, where they interact with internal receptors.

Small hydrophobic ligands can directly diffuse through the plasma membrane and interact with internal receptors. Important members of this class of ligands are the steroid hormones. Steroids are lipids that have a hydrocarbon skeleton with four fused rings; different steroids have different functional groups attached to the carbon skeleton. Steroid hormones include the female sex hormone, estradiol, which is a type of estrogen; the male sex hormone, testosterone; and cholesterol, which is an important structural component of biological membranes and a precursor of steroid hormones (Figure 3). Other hydrophobic hormones include thyroid hormones and vitamin D. In order to be soluble in blood, hydrophobic ligands must bind to carrier proteins while they are being transported through the bloodstream.

Water-Soluble Ligands

Water-soluble ligands are polar and therefore cannot pass through the plasma membrane unaided; sometimes, they are too large to pass through the membrane at all. Instead, most water-soluble ligands bind to the extracellular domain of cell-surface receptors. This group of ligands is quite diverse and includes small molecules, peptides, and proteins.

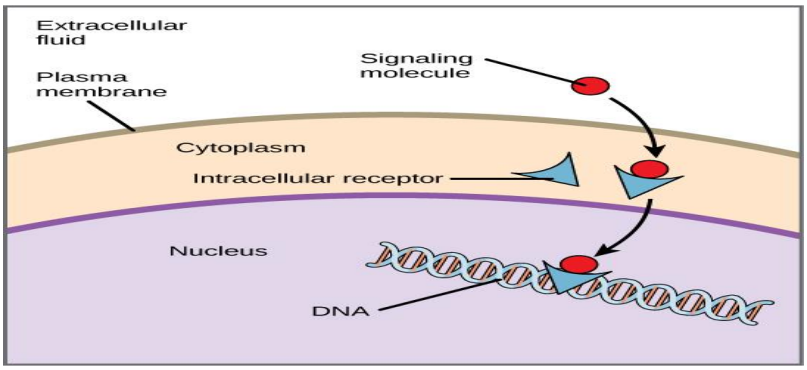
Other Ligands

Nitric oxide (NO) is a gas that also acts as a ligand. It is able to diffuse directly across the plasma membrane, and one of its roles is to interact with receptors in smooth muscle and induce relaxation of the tissue. NO has a very short half-life and therefore only functions over short distances. Nitroglycerin, a treatment for heart disease, acts by triggering the release of NO, which causes blood vessels to dilate (expand), thus restoring blood flow to the heart. NO has become better known recently because the pathway that it affects is targeted by prescription medications for erectile dysfunction, such as Viagra (erection involves dilated blood vessels).

Signaling Receptors

Receptors are protein molecules in the target cell or on its surface that bind ligand. There are two types of receptors, internal receptors and cell-surface receptors.

Internal receptors



Hydrophobic signaling molecules typically diffuse across the plasma membrane and interact with intracellular receptors in the cytoplasm. Many intracellular receptors are transcription factors that interact with DNA in the nucleus and regulate gene expression.

Internal receptors, also known as intracellular or cytoplasmic receptors, are found in the cytoplasm of the cell and respond to hydrophobic ligand molecules that are able to travel across the plasma membrane. Once inside the cell, many of these molecules bind to proteins that act as regulators of mRNA synthesis (transcription) to mediate gene expression. Gene expression is the cellular process of transforming the information in a cell's DNA into a sequence of amino acids, which ultimately forms a protein. When the ligand binds to the internal receptor, a conformational change is triggered that exposes a DNA-binding site on the protein. The ligand-receptor complex moves into the nucleus, then binds to specific regulatory regions of the chromosomal DNA and promotes the initiation of transcription (Figure 4). Transcription is the process of copying the information in a cell's DNA into a special form of RNA called messenger RNA (mRNA); the cell uses information in the mRNA (which moves out into the cytoplasm and associates with ribosomes) to link specific amino acids in the correct order, producing a protein. Internal receptors can directly influence gene expression without having to pass the signal on to other receptors or messengers.

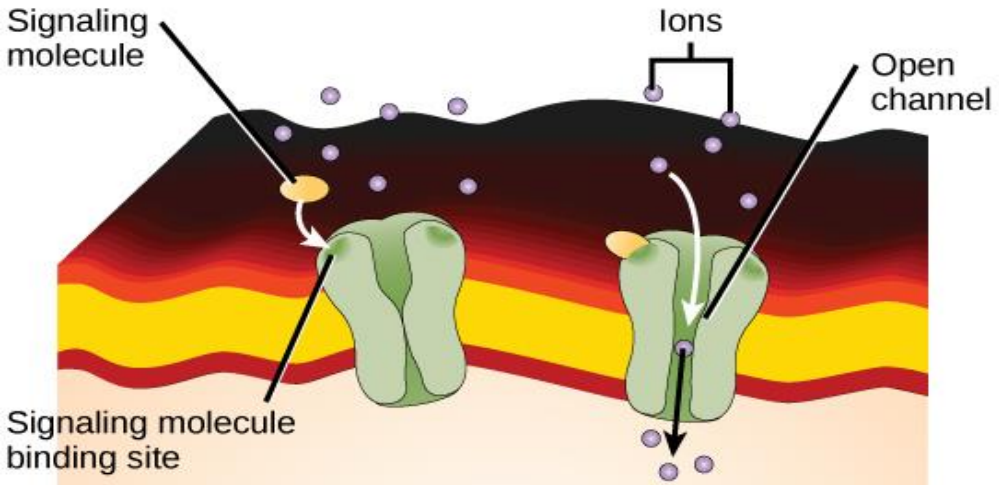
Cell-Surface Receptors

Cell-surface receptors, also known as transmembrane receptors, are cell surface, membrane-anchored (integral) proteins that bind to external ligand molecules. This type of receptor spans the plasma membrane and performs signal transduction, in which an extracellular signal is converted into an intercellular signal. Ligands that interact with cell-surface receptors do not have to enter the cell that they affect. Cell-surface receptors are also called cell-specific proteins or markers because they are specific to individual cell types.

Each cell-surface receptor has three main components: an external ligand-binding domain, a hydrophobic membrane-spanning region, and an intracellular domain inside the cell. The ligand-binding domain is also called the extracellular domain. The size and extent of each of these domains vary widely, depending on the type of receptor.

Because cell-surface receptor proteins are fundamental to normal cell functioning, it should come as no surprise that a malfunction in any one of these proteins could have severe consequences. Errors in the protein structures of certain receptor molecules have been shown to play a role in hypertension (high blood pressure), asthma, heart disease, and cancer.

Cell-surface receptors are involved in most of the signaling in multicellular organisms. There are three general categories of cell-surface receptors: ion channel-linked receptors, G-protein-linked receptors, and enzyme-linked receptors.



Ion channel-linked receptors bind a ligand and open a channel through the membrane that allows specific ions to pass through. To form a channel, this type of cell-surface receptor has an extensive membrane-spanning region. In order to interact with the phospholipid fatty acid tails that form the center of the plasma membrane, many of the amino acids in the membrane-spanning region are hydrophobic in nature. Conversely, the amino acids that line the inside of the channel are hydrophilic to allow for the passage of water or ions. When a ligand binds to the extracellular region of the channel, there is a conformational change in the proteins structure that allows ions such as sodium, calcium, magnesium, and hydrogen to pass through.

G-protein-linked receptors bind a ligand and activate a membrane protein called a G-protein. The activated G-protein then interacts with either an ion channel or an enzyme in the membrane (Figure 6). All G-protein-linked receptors have seven transmembrane domains, but each receptor has its own specific extracellular domain and G-protein-binding site.

Cell signaling using G-protein-linked receptors occurs as a cyclic series of events. Before the ligand binds, the inactive G-protein can bind to a newly revealed site on the receptor specific for its binding. Once the G-protein binds to the receptor, the resultant shape change activates the G-protein, which releases GDP and picks up GTP. The subunits of the G-protein then split into the α subunit and the βγ subunit. One or both of these G-protein fragments may be able to activate other proteins as a result. After awhile, the GTP on the active α subunit of the G-protein is hydrolyzed to GDP and the βγ subunit is deactivated. The subunits reassociate to form the inactive G-protein and the cycle begins anew.

cAMP-dependent pathway

In the field of molecular biology, the cAMP-dependent pathway, also known as the adenylyl cyclase pathway, is a G protein-coupled receptor-triggered signaling cascade used in cell communication.

Mechanism

G protein-coupled receptors (GPCRs) are a large family of integral membrane proteins that respond to a variety of extracellular stimuli. Each GPCR binds to and is activated by a specific ligand stimulus that ranges in size from small molecule catecholamines, lipids, or neurotransmitters to large protein hormones. When a GPCR is activated by its extracellular ligand, a conformational change is induced in the receptor that is transmitted to an attached intracellular heterotrimeric G protein complex. The G_s alpha subunit of the stimulated G protein complex exchanges GDP for GTP and is released from the complex.

In a cAMP-dependent pathway, the activated G_s alpha subunit binds to and activates an enzyme called adenylyl cyclase, which, in turn, catalyzes the conversion of ATP into cyclic adenosine monophosphate (cAMP). Increases in concentration of the second messenger cAMP may lead to the activation of

- cyclic nucleotide-gated ion channels
- exchange proteins activated by cAMP (EPAC) such as RAPGEF3
- popeye domain containing proteins (Popdc)
- an enzyme called protein kinase A (PKA).

The PKA enzyme is also known as cAMP-dependent enzyme because it gets activated only if cAMP is present. Once PKA is activated, it phosphorylates a number of other proteins including: enzymes that convert glycogen into glucose enzymes that promote muscle contraction in the heart leading to an increase in heart rate transcription factors, which regulate gene expression

Also phosphorylate AMP

Specificity of signaling between a GPCR and its ultimate molecular target through a cAMP-dependent pathway may be achieved through formation of a multiprotein complex that includes the GPCR, adenylyl cyclase, and the effector protein.

Importance:

In humans, cAMP works by activating protein kinase A (PKA, cAMP-dependent protein kinase), one of the first few kinases discovered. It has four sub-units two catalytic and two regulatory. cAMP binds to the regulatory sub-units. It causes them to break apart from the catalytic sub-units. The Catalytic sub-units make their way in to the nucleus to influence

transcription.Further effects mainly depend on cAMP-dependent protein kinase, which vary based on the type of cell.

cAMP-dependent pathway is necessary for many living organisms and life processes. Many different cell responses are mediated by cAMP; these include increase in heart rate, cortisol secretion, and breakdown of glycogen and fat. cAMP is essential for the maintenance of memory in the brain, relaxation in the heart, and water absorbed in the kidney. This pathway can activate enzymes and regulate gene expression. The activation of preexisting enzymes is a much faster process, whereas regulation of gene expression is much longer and can take up to hours. The cAMP pathway is studied through loss of function (inhibition) and gain of function (increase) of cAMP.
If cAMP-dependent pathway is not controlled, it can ultimately lead to hyper-proliferation, which may contribute to the development and/or progression of cancer.

Activation

Activated GPCRs cause a conformational change in the attached G protein complex, which results in the G_s alpha subunit's exchanging GDP for GTP and separation from the beta and gamma subunits. The G_s alpha subunit, in turn, activates adenylyl cyclase, which quickly converts ATP into cAMP. This leads to the activation of the cAMP-dependent pathway. This pathway can also be activated downstream by directly activating adenylyl cyclase or PKA. bucladesine (dibutyryl cAMP, db cAMP) - also a phosphodiesterase inhibitor pertussis toxin, which increases cAMP levels by inhibiting Gi to its GDP (inactive) form. This leads to an increase in adenylyl cyclase activity, thereby increasing cAMP levels, which can lead to an increase in insulin and therefore hypoglycemia.

Cyclic GMP (cGMP)

This chapter is related to the aims of Section C(iv) from the 2017 CICM Primary Syllabus, which expects the exam candidate to "explain receptor activity with regard to... second messengers and G proteins". Whereas cyclic AMP is probably the stereotypic secondary messenger molecule with importance primarily to catecholamine inotropes, cyclic GMP is the critical molecule required for smooth muscle relaxation.

If your home institution gives you access to archive copies of Pharmacological Reviews, the 1987 article by Waldman and Murad is an excellent and highly detailed introduction to this topic. It is of course well in excess of what is required for the CICM primary exam, in which this topic has never appeared. A more pragmatic article, which happens to be available for free is Tsai & Kass (2009) - this probably has more exam relevance because the focus is on the role of cGMP in regulating cardiovascular phenomena.

Synthesis and characteristics of cGMP

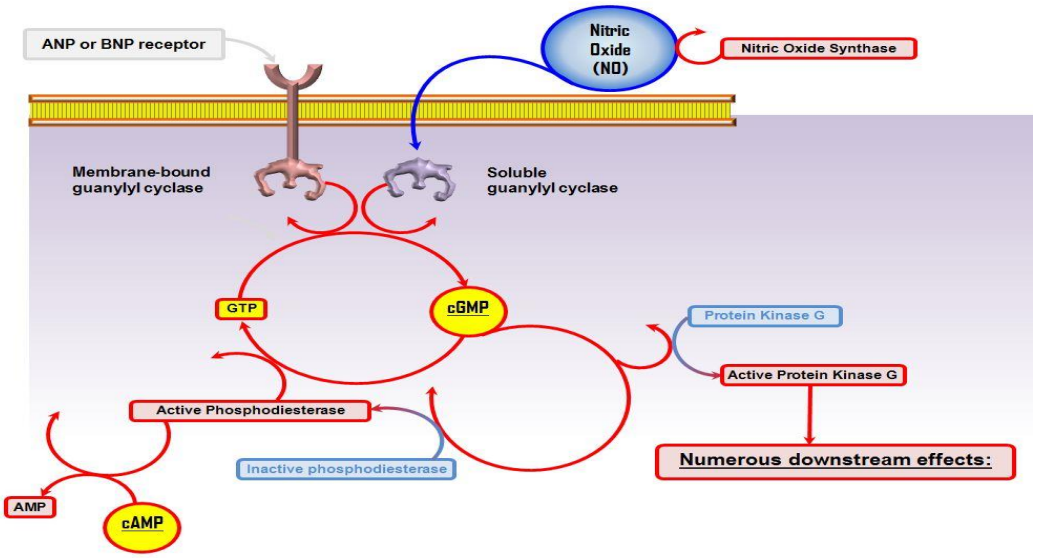
Cyclic guanosine monophosphate is similar to cyclic AMP, with the exception that instead of adenine cGMP has a guanine nucleobase. It is derived from GTP (guanosine triphosphate). There are two major pathways of its synthesis, one via a membrane-bound guanylyl cyclase bound to a natriuretic peptide receptor, and the other a soluble guanylyl cyclase which is activated by nitric oxide. Like cyclic AMP, cGMP is degraded by phosphodiesterases. Some phosphodiesterases only affect cGMP (eg. PDE-5A, the target of sildenafil) whereas others (PDE-2 and PDE-3) can hydrolyse both cAMP and cGMP.

cGMP has numerous downstream effects, listed nicely in Tsai & Kass (2009):
From Protein Kinase G activation

- Smooth muscle relaxation by decreased intracellular calcium availability
- Negative inotropic effect, by reduction of myofilament calcium responsiveness
- Promotion of angiogenesis

From cGNP-gated ion channels mainly unselective cation channels, relevant to the movement of sodium and calcium ions (Kaupp et al, 2002) - these are mainly expressed in retinal and olfactory neuroepithelium and in nephrons (i.e. these channels have no relevance to the cardiovascular system).

From cGMP-modulated phosphodiesterase :cGMP can bind to phosphodiesterases which increases their activity against both cGMP and cAMP, resulting in the inhibition of both secondary messenger systems.



Clinically relevant effects of cGMP signalling pathways

In short, the relevance of cGMP to cardiovascular physiology and pharmacology is mainly related to its activation by nitric oxide, and the relevance of this is mainly to vascular smooth muscle. The steps of this activity are as follows:

- Something (anything) activates nitric oxide synthase
- Nitric oxide (NO) is synthesized
- NO activates the soluble form of guanylyl cyclase at nanomolar concentrations
- Guanylyl cyclase produces cGMP
- cGMP activates Protein Kinase G (PKG)
- The 1β isoform of PKG phosphorylates the IP3 receptor, inhibiting IP3-mediated release of calcium
- PKG also phosphorylates and thus inactivates voltage-gated calcium channels.
- PKG also phosphorylates phospholamban, leading to increased calcium ion uptake into sarcoplasmic reticulum

The net effect of these changes is a decrease in the availability of intracellular calcium, and therefore smooth muscle relaxation.

MPK KINASE PATHWAY:

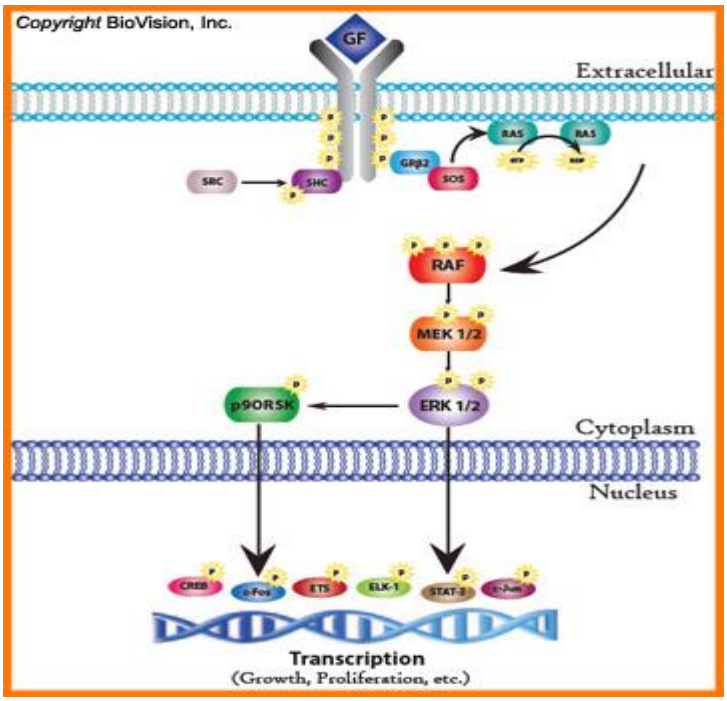
Mitogen-activated protein kinases (MAPK) are proteins that are serine/ threonine specific kinases which are activated by a wide range of stimuli including proinflammatory cytokines, growth factors, mitogens, osmotic stress, heat shock etc. These proteins function in a signaling cascade are activated upon ligand binding to a cell surface receptor activating several MAP/ER kinases, which in turn phosphorylate their respective substrates. These events thereby regulate various cellular activities, such as gene expression, mitosis, differentiation, proliferation, and cell survival/apoptosis.

Upon the extracellular mitogen binding to the ligand, Ras a GTPase exchanges GDP for GTP. This in turn initializes a cascade activating MAP3K (Raf) which in turn activates MAP2K which activates MAPK. This MAPK can activate a number of transcription factors which control key processes in the cell.For example epidermal growth factor (EGF) binds the EGFR which activates the tyrosine kinase activity of the EGFR (receptor). Grb2 and SH2 domain containing proteins recognize phosphorylated residues along with a guanine nucleotide exchange factor SOS, and binds to the EGFR. GDP is then swapped for GTP which binds Ras to make it active. Ras activates Raf which can phosphorylate and activate MEK1 and MEK2 which in turn activate

MAPK.

MAPK regulates a number of transcription factors including c-myc, CREB, C-Fos etc. All these regulate expression of a number of genes involved in apoptosis, differentiation, cancer etc.

Defects in the regulation of this pathway can lead to uncontrolled growth in cells,leading to cancer. Over the last decade, important advances have been made in developing novel agents that modulate key proteins in this pathway culminating in the approval by the FDA of Sorafenib (Nexavar®) for the treatment of advanced renal carcinoma. Therapeutic advances in this area should continue for many years to come.



Possible Questions

Part-A (1 mark)

Part-B (2 marks)

1.What is paracrine signals?
2. define legind molecules?
3.write about the types of signal?
4.wht is autocrine signal?
5.What is the function of Cyclic AMP in lac operon.?

Part-C (8 marks)

1.explain about signaling molecules and their Receptors
2.explain the types of signals in human immune system
3.describe about cyclic AMP pathway
4.Brief about cyclic GMP
5.Give a account on MPK kinase pathway.

S.NO	QUESTIONS	POSSIBILITY A	POSSIBILITY B	POSSIBILITY C	POSSIBILITY D	ANSWERS
1	Which of the following signal molecule is NOT used for extracellular signaling	Autocrine	Endocrine	Paracrine	Cyclic AMP	Cyclic AMP
2	In endocrine signaling, the signal molecule act on target cell only in close proximity	TRUE	FALSE	GMP signal	AMP signal	FALSE
3	Which of the following signaling pathway is followed by T-lymphocytes in response to antigenic stimulation?	Autocrine signaling	Juxtacrine signaling	Paracrine signaling	Endocrine signaling	Autocrine signaling
4	Name the signaling which requires physical contacts between the cells involved.	Paracrine signaling	Intracellular signaling	Autocrine signaling	Juxtacrine signaling	Juxtacrine signaling
5	Mark the signal molecule which does not interact with cell surface receptor.	Insulin	Glucagon	Testosterone	Gastrin	Testosterone
6	Name the largest family of cell surface receptor?	GPCR	Ion-channel receptor	Enzyme-linked receptor	Nuclear receptor	GPCR
7	Which of the following G-protein takes part in the regulation of vision?	Gs family	Gi family	Gq family	Golf	Gi family

8	Name the family of monomeric G-protein which regulates the growth of the cell?	Ras	Rab	Ran	Rho	Ras
9	Chemical messengers secreted by ductless glands are called	Lymph	Platelets	Plasma	Hormones	Hormones
10	Endocrine glands secret products into the ducts and transfer it into body cavities.	TRUE	FALSE	GMP signal	AMP signal	FALSE
11	Which of the following is NOT an endocrine gland?	Hypothalamus	Pituitary	Parathyroid	Pancreas	Hypothalamus
12	Which of this statement is INCORRECT regarding the function of hormones	Reproduction and sexual differentiation	Maintenance of internal environment	Maintain body temperature	Development and growth	Maintain body temperature
13	Mark the one, which is NOT the precursor of the hormone	Amino acids	Cholesterol	Phospholipids	Proteins	Proteins
14	What is the precursor of steroid hormone	Protein	Cholesterol	Carbohydrate	Lipid	Cholesterol
15	Which of the is a fat soluble hormone	Amine hormone	Peptide hormone	Thyroid hormone	Protein hormone	Thyroid hormone

16	Name the hormone which is synthesized from histidine amino acid	Histamine	Epinephrine	Norepinephrine	Dopamine	Histamine
17	Which of the following is protein hormone	Oxytocin	Insulin	TSH	Antidiuretic hormone	Insulin
18	Name the gland, which releases Neurohormone	Hypothalamus	Pituitary	Thyroid	Pancreas	Hypothalamus
19	Name the hormone which takes part in the release of FSH and LH from the anterior pituitary.	Growth hormone	GnRH	Somatostatin	TRH	GnRH
20	Which of the following is Growth hormone inhibiting hormone	FSH	TRH	GHRH	Somatostatin	Somatostatin
21	Which neurotransmitter is involved in muscle movements?	Acetylcholine	Endorphins	Serotonin	GABA	Acetylcholine
22	Which neurotransmitter is released in to relieve pain?	Acetylcholine	Endorphins	Serotonin	GABA	Endorphins
23	Which neurotransmitter is involved in the "Fight of Flight" response?	Acetylcholine	Endorphins	Norepinephrine	Serotonin	Norepinephrine

24	Which neurotransmitter inhibits brain activity	Acetylcholine	GABA	Endorphins	Dopamine	GABA
25	Serotonin is a neurotransmitter that helps regulate	learning and memory	pain and pleasure	muscle movements	mood, sleep, emotions	mood, sleep, emotions
26	Too much of this neurotransmitter can cause severe muscle spasms and even death	Serotonin	Endorphins	Acetylcholine	GABA	Acetylcholine
27	Prozac works to combat depression by keeping this neurotransmitter in the synapse longer:	Serotonin	Endorphins	Acetylcholine	GABA	Serotonin
28	This neurotransmitter is most often associated with motivation and pleasure/reward	Acetylcholine	GABA	Dopamine	Serotonin	Dopamine
29	What is a neurotransmitter	fatty covering of the axon	nerve cell	chemical messenger	gap between neurons	chemical messenger
30	The junction between 2 neurons is called the	dendrite	axon	node of Ranvier	synapse	synapse
31	If a neuron responds at all, it responds completely. This is known as the	threshold	all-or-none response	neuronal pool	withdrawal reflex	all-or-none response

32	These receive messages and conduct impulses to the Cell Body	Axon	End Bulbs	Dendrites	Myelin Sheath	Dendrites
33	This is a fatty layer that prevents interference and increases the speed of impulses going down the axon	Dendrites	Nodes of Ranvier	Myelin Sheath	End Bulbs	Myelin Sheath
34	This is the electrical charge that travels down an axon when a neuron is firing	Resting Potential	Action Potential	Threshold	Refractory Period	Action Potential
35	Which brain structure is labelled by 1d?	Frontal	Parietal	Temporal	Occipital	Occipital
36	The part of the neuron that takes in and receives messages is called the _____	dendrite	nucleus	axon	synapse	dendrite
37	Neurons that only travel from the body to the brain are called _____	sensory neurons	interneurons	motor neurons	Non sensory neurons	sensory neurons
38	Which of the following is not a type of cell surface receptor	Ion Channel Receptors	G-Protein Coupled Receptors	Signal Coupled Receptors	Enzyme Coupled Receptors	Signal Coupled Receptors
39	Which of the following receptors responds to an electrical gradient accross a membrane	Ion Channel Receptors	G-Protein Coupled Receptors	Signal Coupled Receptors	Enzyme Coupled Receptors	Ion Channel Receptors

40	Which of the following is not a classification of signaling molecules?	Autocrine	Paracrine	Endocrine	Lyoncrine	Lyoncrine
41	Signaling molecules work only though signaling cascades.	TRUE	FALSE	Endocrine	Autocrine	FALSE
42	Which of the following is true regarding G-protein coupled receptors?	It contains three transmembrane sections	The G protein binds the intracellular side of the G protein coupled receptors	There are four intracellular and extracellular loops	G proteins respond only to calcium.	The G protein binds the intracellular side of the G protein coupled receptors
43	cAMP levels are kept at high levels in the cell.	During lacoperon	TRUE	During trpoperon	FALSE	FALSE
44	Calmodulin is an important signaling molecule because it does what?	Cleaves PIP2 into IP3 and DAG	Creates cAMP	Mediates the animal cell response to calcium	Blocks GPCR activation	Mediates the animal cell response to calcium
45	Which of the following is not a common example of protein kinase signaling cascades?	TGF(beta)	Inositol Phospholipid pathway	MAP Kinase pathway	GTP signaling	GTP signaling
46	Ligand binding to a receptor kinase causes what to happen?	Immediate activation of the single receptor kinase	Dimerization and inactivation of two receptor kinases	Dimerization and activation of two receptor kinases	Binding of the kinase to the receptor	Dimerization and activation of two receptor kinases
47	Which pathway can activate the MAP kinase pathway?	TGF(beta)	Inositol Phospholipid pathway	Ras signaling	JAK/STAT	Ras signaling

48	Steroid hormones signaling through binding....	GTPases	Nuclear receptors	Kinases	Phosphatases	Nuclear receptors
49	Nitric Oxide signals by binding to which of the following molecules?	GTPases	Nuclear receptors	Adenyl cyclase	Guanyl cyclase	Guanyl cyclase
50	The inositol signaling pathway can be activated by both GPCRs and RTKs.	True	Activate cycic amp	Activate map pathway	FALSE	True
51	Which of the following molecules removes phosphates from PI-3 kinase?	Phospholipase C	Phosphatidylinositol-3 kinae	PTEN Phosphatase	Protein Kinase C	PTEN Phosphatase
52	A signaling network is usually linear, with little interaction with other signaling pathways.	True	Interact with cell receptors	FALSE	Interact with plasma membrane	True
53	When insulin binds to insulin receptors what happens to glucose	Glucose is brought into the cell	Glucose is created by the cell	Glucose is exported into the bloodstream	Glucose is degraded	Glucose is brought into the cell
54	Apoptosis can only be stimulated through intracellular signals.	TRUE	False	50% by signal molecules	Ribosomes	FALSE
55	In the intrinsic pathway of regulating apoptosis, Bcl2 controls what?	It releases cytochrome C from the mitochondria	It binds to cytochrome C and prevents its release	It binds to Bad and Bax and prevents cytochrome C release	It binds to Bad and Bax and triggers cytochrome release	It binds to Bad and Bax and prevents cytochrome C release

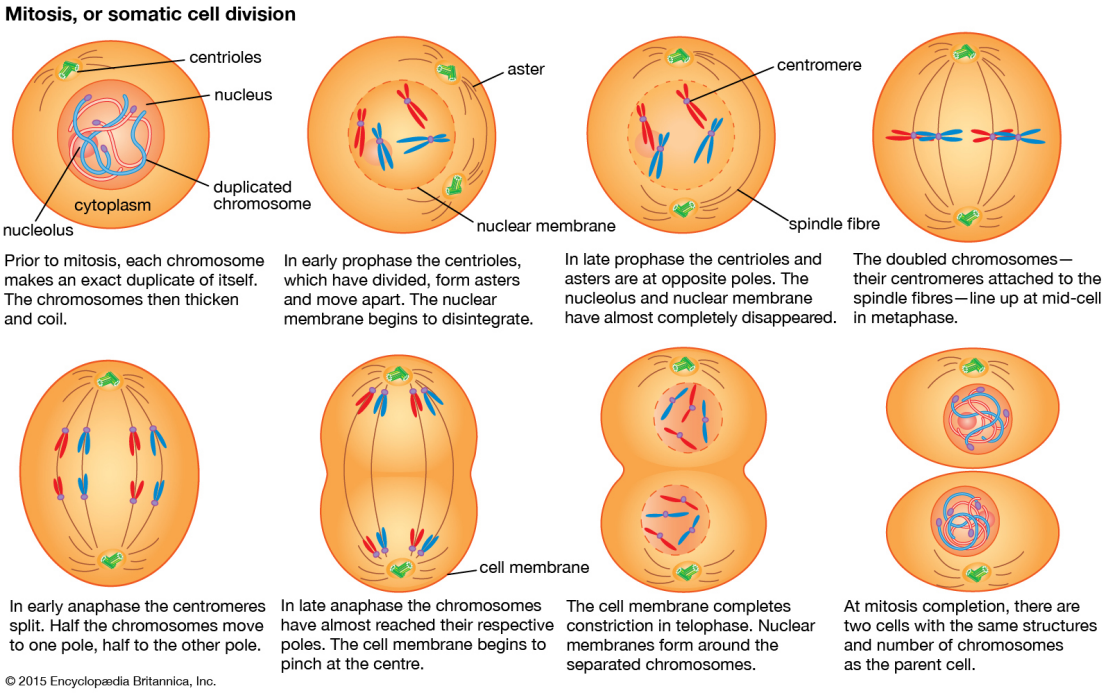
56	Which signaling molecule stimulates fruit ripening?	Auxins	Ethylene	Phytochromes	Gibberelins	Ethylene
57	The enzyme activated by cyclic AMP, passing on the hormonal signal is	Protein kinase B	Protein kinase A	Protein kinase C	G protein receptor kinase	Protein kinase A
58	cGMP-dependent protein kinase is also called	Protein kinase B	Protein kinase A	Protein kinase C	Protein kinase G	Protein kinase G
59	Ras protein is a	G-protein switch	Small monomeric GTPase switch protein	Serine-threonine kinase	Tyrosine kinase	Small monomeric GTPase switch protein
60	Which of the following is a short-lived messenger that acts by stimulating a soluble guanylyl cyclase, raising [cGMP] and stimulating PKG?	NO	NO2	NO3	N2O	No.

Unit V
Syllabus

Eukaryotic cell cycle and its regulation, Mitosis and Meiosis, Development of cancer, causes and type Programmed cell death, Stem cells, Embryonic stem cell, induced pleuripotent stem cells.

MITOSIS CELL DEVISION:

Mitosis is the phase of the cell cycle where chromosomes in the nucleus are evenly divided between two cells. When the cell division process is complete, two daughter cells with identical genetic material are produced.

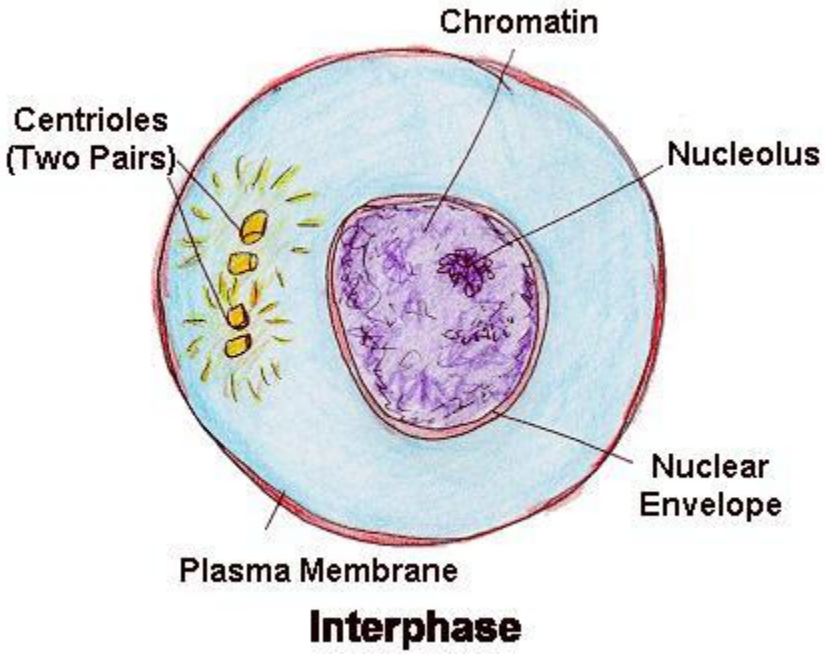


Interphase

Before a dividing cell enters mitosis, it undergoes a period of growth called interphase. About 90 percent of a cell's time in the normal cell cycle may be spent in interphase.

- G1 phase: The period prior to the synthesis of DNA. In this phase, the cell increases in mass in preparation for cell division. The G1 phase is the first gap phase.
- S phase: The period during which DNA is synthesized. In most cells, there is a narrow window of time during which DNA is synthesized. The S stands for synthesis.
- G2 phase: The period after DNA synthesis has occurred but prior to the start of prophase. The cell synthesizes proteins and continues to increase in size. The G2 phase is the second gap phase.
- In the latter part of interphase, the cell still has nucleoli present.

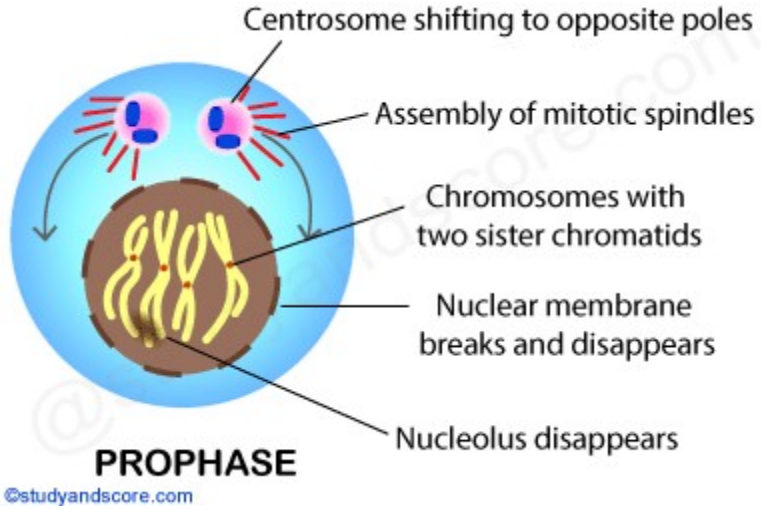
- The nucleus is bounded by a nuclear envelope and the cell's chromosomes have duplicated but are in the form of chromatin.



Prophase

In prophase, the chromatin condenses into discrete chromosomes. The nuclear envelope breaks down and spindles form at opposite poles of the cell. Prophase (versus interphase) is the first true step of the mitotic process. During prophase, a number of important changes occur:

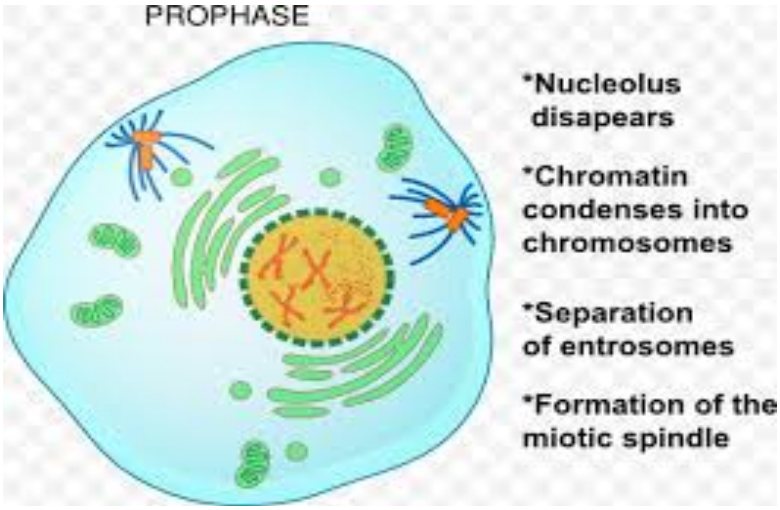
- Chromatin fibers become coiled into chromosomes, with each chromosome having two chromatids joined at a centromere.
- The mitotic spindle, composed of microtubules and proteins, forms in the cytoplasm.
- The two pairs of centrioles (formed from the replication of one pair in Interphase) move away from one another toward opposite ends of the cell due to the lengthening of the microtubules that form between them.
- Polar fibers, which are microtubules that make up the spindle fibers, reach from each cell pole to the cell's equator.
- Kinetochores, which are specialized regions in the centromeres of chromosomes, attach to a type of microtubule called kinetochore fibers.
- The kinetochore fibers "interact" with the spindle polar fibers connecting the kinetochores to the polar fibers.
- The chromosomes begin to migrate toward the cell center.



Metaphase

In metaphase, the spindle reaches maturity and the chromosomes align at the metaphase plate (a plane that is equally distant from the two spindle poles). During this phase, a number of changes occur:

- The nuclear membrane disappears completely.
- Polar fibers (microtubules that make up the spindle fibers) continue to extend from the poles to the center of the cell.
- Chromosomes move randomly until they attach (at their kinetochores) to polar fibers from both sides of their centromeres.
- Chromosomes align at the metaphase plate at right angles to the spindle poles.
- Chromosomes are held at the metaphase plate by the equal forces of the polar fibers pushing on the centromeres of the chromosomes.

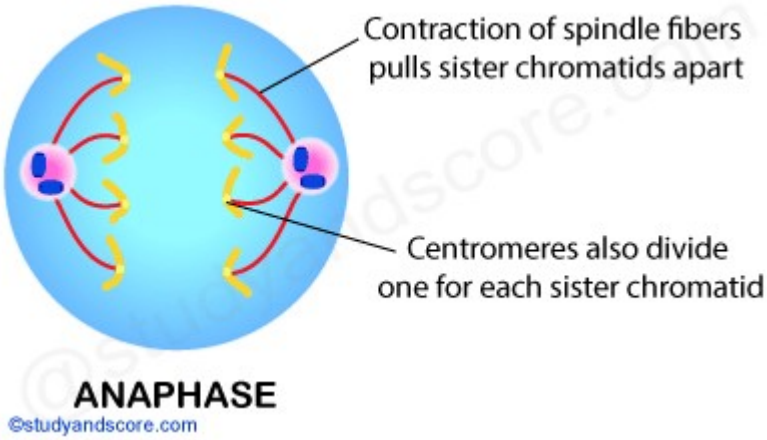


Anaphase

In anaphase, the paired chromosomes (sister chromatids) separate and begin moving to opposite ends (poles) of the cell. Spindle fibers not connected to chromatids lengthen and elongate the cell. At the end of anaphase, each pole contains a complete compilation of chromosomes.

During anaphase, the following key changes occur:

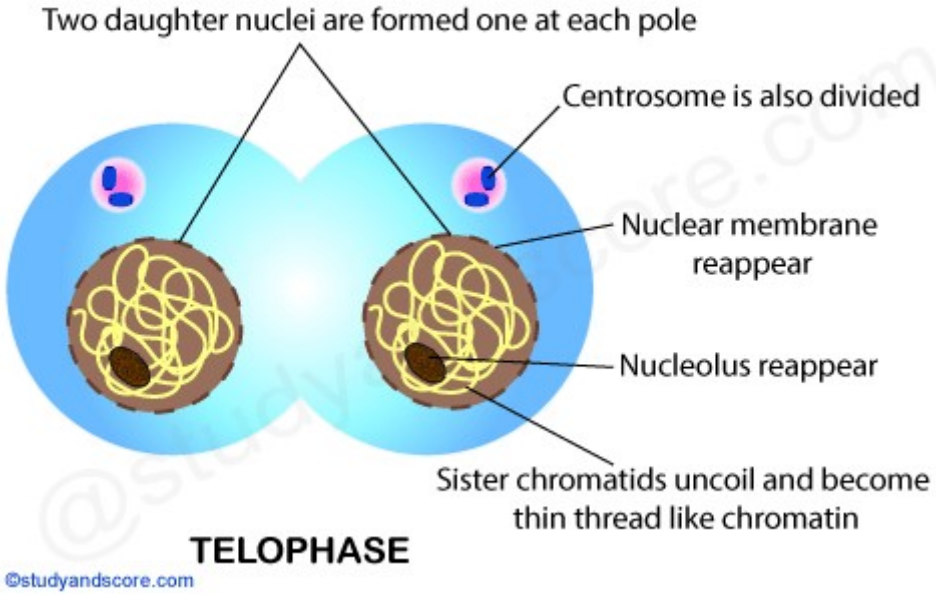
- The paired centromeres in each distinct chromosome begin to move apart.
- Once the paired sister chromatids separate from one another, each is considered a "full" chromosome. They are referred to as daughter chromosomes.
- Through the spindle apparatus, the daughter chromosomes move to the poles at opposite ends of the cell.
- The daughter chromosomes migrate centromere first and the kinetochore fibers become shorter as the chromosomes near a pole.
- In preparation for telophase, the two cell poles also move further apart during the course of anaphase. At the end of anaphase, each pole contains a complete compilation of chromosomes.



Telophase

In telophase, the chromosomes are cordoned off into distinct new nuclei in the emerging daughter cells. The following changes occur:

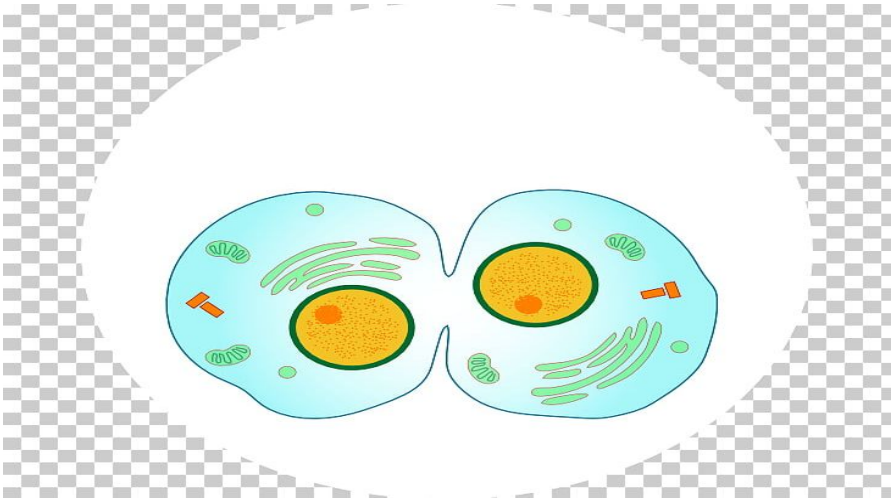
- The polar fibers continue to lengthen.
- Nuclei begin to form at opposite poles.
- The nuclear envelopes of these nuclei form from remnant pieces of the parent cell's nuclear envelope and from pieces of the endomembrane system.
- Nucleoli also reappear.
- Chromatin fibers of chromosomes uncoil.
- After these changes, telophase/mitosis is largely complete. The genetic contents of one cell have been divided equally into two.



Cytokinesis

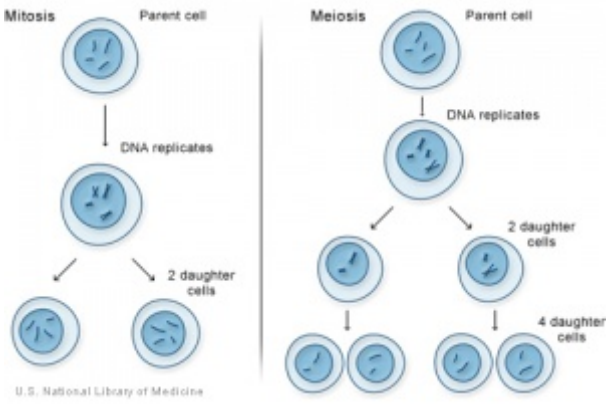
Cytokinesis is the division of the cell's cytoplasm. It begins prior to the end of mitosis in anaphase and completes shortly after telophase/mitosis. At the end of cytokinesis, two genetically identical daughter cells are produced. These are diploid cells, with each cell containing a full complement of chromosomes.

Cells produced through mitosis are different from those produced through meiosis. In meiosis, four daughter cells are produced. These cells are haploid cells, containing one-half the number of chromosomes as the original cell. Sex cells undergo meiosis. When sex cells unite during fertilization, these haploid cells become a diploid cell.



Meiosis cell division:

Introduction



Mitosis and Meiosis

Meiosis is the special type of recombinative and reductive cell division occurring only in the generation of the gametes or germ cells (oocyte and spermatozoa).
For recombination, meiosis requires that homologous chromosomes are properly paired and aligned by the induction of DNA double-strand breaks by the enzyme SPO11 during the prophase of the first meiotic division.

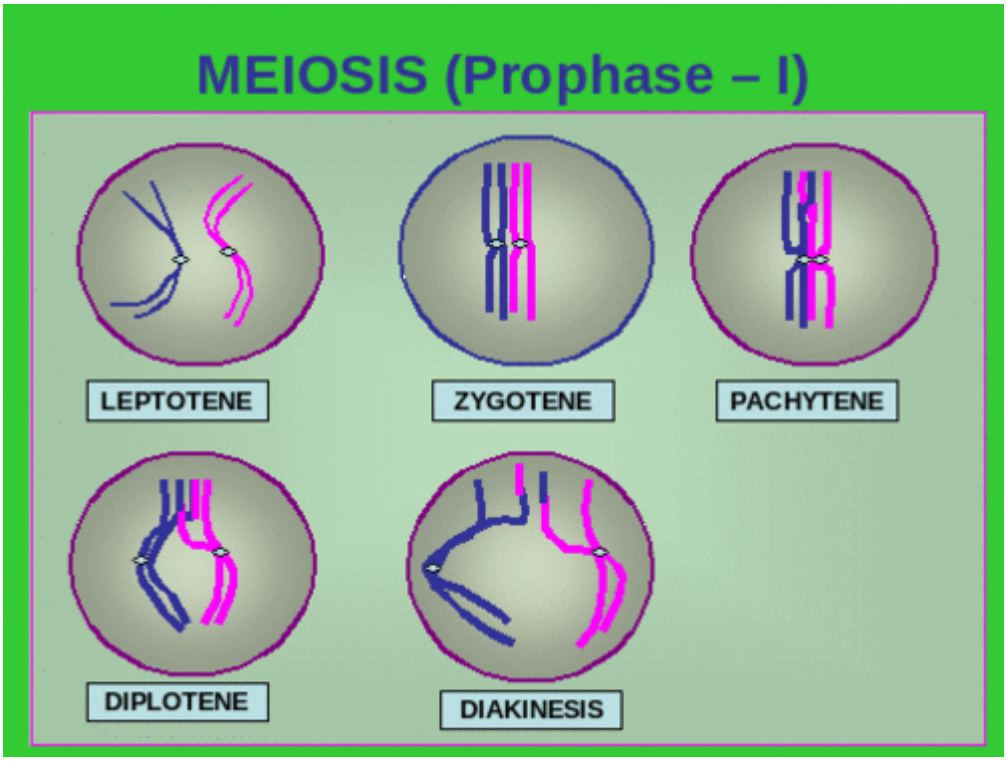
Meiotic cell division also reduces (halves) the chromosomal content. The overall process of germ cell development is called "gametogenesis" and includes not only meiosis but also the cellular morphological changes, that occur differently in male and female gametes.

Meiosis I and II

- Meiosis I separates the pairs of homologous chromosomes, reduces the cell from diploid to haploid.
- Meiosis II separates each chromosome into two chromatids (chromosome behavior in meiosis II is like that of mitosis).

Prophase I

- The homologous chromosomes pair and exchange DNA to form recombinant chromosomes.
- Note - in oocyte development, from birth until puberty oocytes are in "prophase I arrest" at diplotene stage. This is important for sustaining the ovarian oocyte pool and lutenizing hormone (LH) induces resumption of meiosis I.



Leptotene

- leptotene phase, leptonema; Greek, leptotene = "thin threads"
- the duplicated paired chromosome homologs condense.

Zygotene

- zygotene phase, zygonema, Greek, zygotene = "paired threads"
- homologous chromosomes become closely associated (synapsis) to form pairs of
- chromosomes consisting of four chromatids (tetrads).
- the synaptonemal complex begins to form between the two sets of sister chromatids in each bivalent (the duplicated chromosome paired with its homologous duplicated chromosome).

Pachytene

- pachytene phase, pachynema; Greek, pachytene = "thick threads"
- crossing over between pairs of homologous chromosomes (meiotic recombination or synapsis) to form chiasmata (form between two nonsister chromatids at points where they have crossed over)
- synaptonemal complex is complete and can be stable for some time.
- Autosomal non-sister chromatids of homologous chromosomes can now extensively exchange segments in regions of homology.
- Only small regions of non-paired sex chromosomes interact
- Mutations that compromise meiotic recombination in male spermatocytes result in arrest and apoptosis at this stage.

Diplotene

- diplotene phase, diplonema; Greek, diplonema = "two threads"
- homologous chromosomes begin to separate but remain attached by chiasmata.

- synaptonemal complex degrades and the chromosomes separate from one another a small amount giving this appearance.
- It is possible that some chromosome uncoiling may also occur allowing some gene transcription.
- In the developing human ovary, oocytes remain at the diplotene stage from fetal life through postnatal childhood, until puberty when the lutenizing hormone (LH) surges stimulate the resumption of meiosis.

Diakinesis

- diakinesis phase; Greek, diakinesis = "moving through"
- homologous chromosomes continue to separate, and chiasmata move to the ends of the chromosomes.
- prophase I ends and chromosomes now recondense, transcription stops and the transition to metaphase occurs.

Prometaphase I

- Spindle apparatus formed, and chromosomes attached to spindle fibres by kinetochores

Metaphase I

- Homologous pairs of chromosomes (bivalents) arranged as a double row along the metaphase plate. The arrangement of the paired chromosomes with respect to the poles of the spindle apparatus is random along the metaphase plate. (This is a source of genetic variation through random assortment, as the paternal and maternal chromosomes in a homologous pair are similar but not identical. The number of possible arrangements is 2n, where n is the number of chromosomes in a haploid set. Human beings have 23 different chromosomes, so the number of possible combinations is 223, which is over 8 million.)

Anaphase I

- The homologous chromosomes in each bivalent are separated and move to the opposite poles of the cell.

Telophase I

- The chromosomes become diffuse and the nuclear membrane reforms.

Cytokinesis I

- Cellular cytoplasmic division to form two new cells, followed by Meiosis II.
- Note - in oocyte meiosis, the extrusion of the first polar body (1 PB) indicates completion of the first meiotic division.

Prophase II

- Chromosomes begin to condense, nuclear membrane breaks down and spindle forms.

Metaphase II

- Spindle fibres attach to chromosomes, chromosomes align in cell centre.

Anaphase II

- Chromosomes separate and move to the opposite poles of the cell.

Telophase II

- Chromosomes reach spindle pole ends and the nuclear membrane reforms.

Cytokinesis

Cellular cytoplasmic division to form new cells.

Meiosis Sex Differences

Female (oogenesis)

- Meiosis initiated once in a finite population of cells
- 1 gamete produced / meiosis
- Completion of meiosis delayed for months or years
- Meiosis arrested at 1st meiotic prophase and reinitiated in a smaller population of cells
- Differentiation of gamete occurs while diploid in first meiotic prophase
- All chromosomes exhibit equivalent transcription and recombination during meiotic prophase

Male (spermatogenesis)

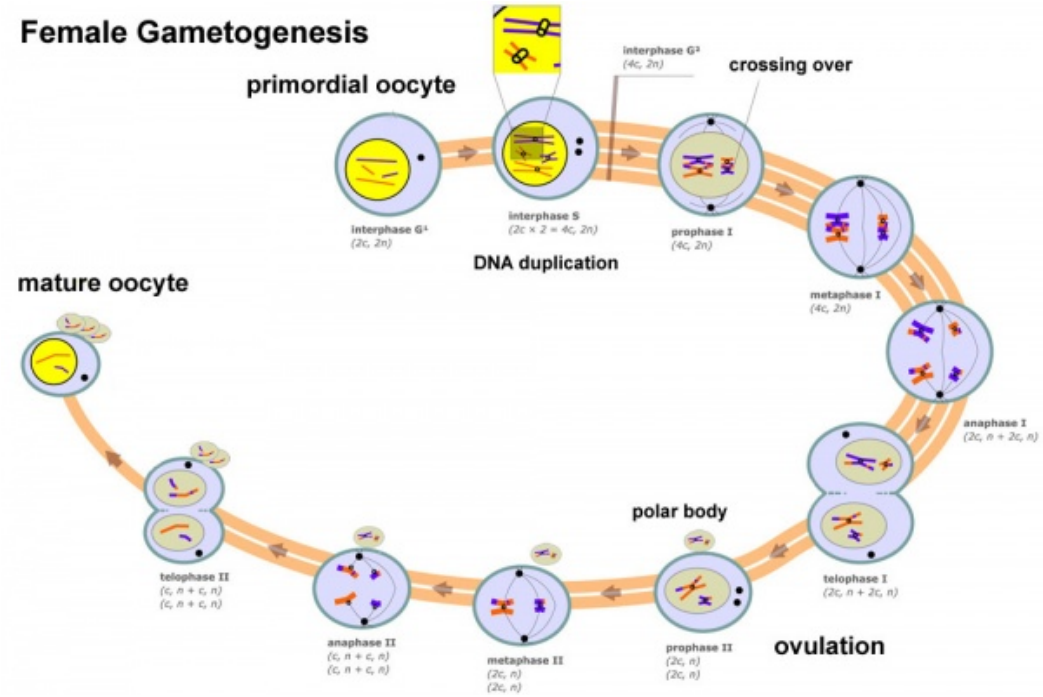
- Meiosis initiated continuously in a mitotically dividing stem cell population
- 4 gametes produced / meiosis
- Meiosis completed in days or weeks
- Meiosis and differentiation proceed continuously without cell cycle arrest
- Differentiation of gamete occurs while haploid after meiosis ends

Sex chromosomes excluded from recombination and transcription during first meiotic prophase

Female Gametogenesis

In females, the total number of eggs ever to be produced are present in the newborn female.

- All eggs are arrested at an early stage of the first meiotic division as a primary oocyte (primordial follicle). Following purberty, during each menstrual cycle, pituitary gonadotrophin stimulates completion of meiosis 1 the day before ovulation.
- In meiosis 1, a diploid cell becomes 2 haploid (23 chromosomes) daughter cells, each chromosome has two chromatids. One cell becomes the secondary oocyte the other cell forms the first polar body.
- The secondary oocyte then commences meiosis 2 which arrests at metaphase and will not continue without fertilization.
- At fertilization meiosis 2 completes, forming a second polar body. Note that the first polar body may also undergo this process forming a third polar body.



meiosis - divided into 3 temporally distinct phases.

1. Prophase - after DNA replication, homologous chromosomes (shown in red and blue) undergo pairi synapsis and recombination, and arrest at the diplotene (dictyate) stage.
2. Dictyate arrest - oocytes remain in meiotic arrest until the female reaches maturity and the oocyte l completed an extensive period of growth following follicle formation.
3. Divisions - luteinizing hormone (LH) surge that triggers ovulation also causes resumption and complet of the first meiotic division in the periovulatory oocyte. The ovulated egg is arrested at second meic metaphase, and anaphase onset and completion of meiosis II only occur if the egg is fertilized.

Oogenesis - complex involving 4 distinct phases.

1. Commitment to meiosis and meiotic initiation - occurs at GA 8–10 weeks in humans.
2. Follicle formation - occurs during the second trimester in humans.
3. Oocyte growth - occurs in the sexually mature female under the control of paracrine and endocrine signa Oocyte growth is thought to take approximately 85 days in humans and typically culminates in ovulation of a single egg.
4. Fertilization - of the ovulated egg results in the completion of the second meiotic division.

Development and Causes of Cancer.

The fundamental abnormality resulting in the development of cancer is the continual unregulated proliferation of cancer cells. Rather than responding appropriately to the signals that control normal cell behavior, cancer cells grow and divide in an uncontrolled manner, invading normal tissues and organs and eventually spreading throughout the body. The generalized loss of growth control exhibited by cancer cells is the net result o accumulated abnormalities in multiple cell regulatory systems and is reflected in several aspects of cell behavior that distinguish cancer cells from their normal counterparts.

Types of Cancer

Cancer can result from abnormal proliferation of any of the different kinds of cells in the body, so there more than a hundred distinct types of cancer, which can vary substantially in their behavior and response treatment. The most important issue in cancer pathology is the distinction between benign and malignant tum (Figure 15.1). A tumor is any abnormal proliferation of cells, which may be either benign or malignant. A ben tumor, such as a common skin wart, remains confined to its original location, neither invading surrounding norr tissue nor spreading to distant body sites. A malignant tumor, however, is capable of both invading surround normal tissue and spreading throughout the body via the circulatory or lymphatic systems (metastasis). O malignant tumors are properly referred to as cancers, and it is their ability to invade and metastasize that mal cancer so dangerous. Whereas benign tumors can usually be removed surgically, the spread of malignant tumors distant body sites frequently makes them resistant to such localized treatment.

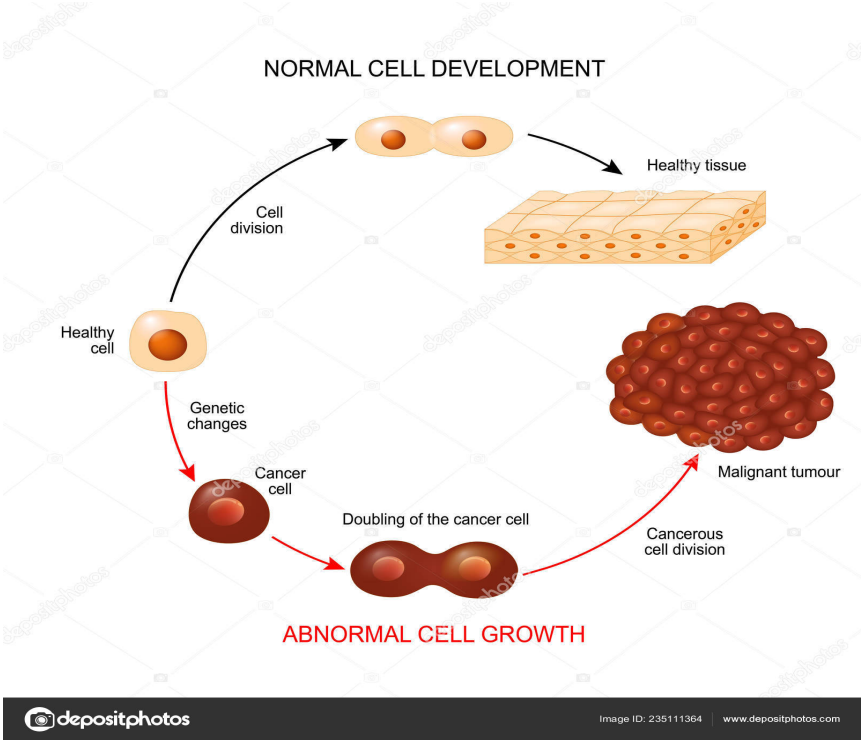
Both benign and malignant tumors are classified according to the type of cell from which they arise. M cancers fall into one of three main groups: carcinomas, sarcomas, and leukemias or lymphomas. Carcinomas, wh include approximately 90% of human cancers, are malignancies of epithelial cells. Sarcomas, which are rare humans, are solid tumors of connective tissues, such as muscle, bone, cartilage, and fibr tissue. Leukemias and lymphomas, which account for approximately 8% of human malignancies, arise from blood-forming cells and from cells of the immune system, respectively. Tumors are further classified according tissue of origin (e.g., lung or breast carcinomas) and the type of cell involved. For example, fibrosarcomas ar from fibroblasts, and erythroid leukemias from precursors of erythrocytes (red blood cells).

Although there are many kinds of cancer, only a few occur frequently (Table 15.1). More than a mill cases of cancer are diagnosed annually in the United States, and more than 500,000 Americans die of cancer ea year. Cancers of 10 different body sites account for more than 75% of this total cancer incidence. The four m common cancers, accounting for more than half of all cancer cases, are those of the breast, prostate, lung, a colon/rectum. Lung cancer, by far the most lethal, is responsible for nearly 30% of all cancer deaths.

The Development of Cancer:

One of the fundamental features of cancer is tumor clonality, the development of tumors from single c that begin to proliferate abnormally. The single-cell origin of many tumors has been demonstrated by analysis o chromosome inactivate . one member of the X chromosome pair is inactivated by being conver to heterochromatin in female cells. X inactivation occurs randomly during embryonic development, so one chromosome is inactivated in some cells, while the other X chromosome is inactivated in other cells. Thus, i female is heterozygous for an X chromosome gene, different alleles will be expressed in different cells. Norr tissues are composed of mixtures of cells with different inactive X chromosomes, so expression of both allele detected in normal tissues of heterozygous females. In contrast, tumor tissues generally express only one allele c heterozygous X chromosome gene. The implication is that all of the cells constituting such a tumor were deriv from a single cell of origin, in which the pattern of X inactivation was fixed before the tumor began to develop.
The clonal origin of tumors does not, however, imply that the original progenitor cell that gives rise to a tumor initially acquired all of the characteristics of a cancer cell. On the contrary, the development of cancer is a multis process in which cells gradually become malignant through a progressive series of alterations. One indication of multistep development of cancer is that most cancers develop late in life. The incidence of colon cancer, example, increases more than tenfold between the ages of 30 and 50, and another tenfold between 50 and 70. Suc dramatic increase of cancer incidence with age suggests that most cancers develop as a consequence of multi abnormalities, which accumulate over periods of many years.

At the cellular level, the development of cancer is viewed as a multistep process involving mutation a selection for cells with progressively increasing capacity for proliferation, survival, invasion, and metastasis . T first step in the process, tumor initiation, is thought to be the result of a genetic alteration leading to abnorr proliferation of a single cell. Cell proliferation then leads to the outgrowth of a population of clonally derived tun cells. Tumor progression continues as additional mutations occur within cells of the tumor population. Some these mutations confer a selective advantage to the cell, such as more rapid growth, and the descendants of a c bearing such a mutation will consequently become dominant within the tumor population. The process is cal clonal selection, since a new clone of tumor cells has evolved on the basis of its increased growth rate or ot properties (such as survival, invasion, or metastasis) that confer a selective advantage. Clonal selection contin throughout tumor development, so tumors continuously become more rapid-growing and increasingly malignant.



Causes of Cancer

Substances that cause cancer, called carcinogens, have been identified both by studies in experimer animals and by epidemiological analysis of cancer frequencies in human populations (e.g., the high incidence lung cancer among cigarette smokers). Since the development of malignancy is a complex multistep process, ma factors may affect the likelihood that cancer will develop, and it is overly simplistic to speak of single causes most cancers. Nonetheless, many agents, including radiation, chemicals, and viruses, have been found to indu cancer in both experimental animals and humans.

Radiation and many chemical carcinogent act by damaging DNA and inducing mutations. These carcinogens generally referred to as initiating agents, since the induction of mutations in key target genes is thought to be initial event leading to cancer development. Some of the initiating agents that contribute to human cancers inclu solar ultraviolet radiation (the major cause of skin cancer), carcinogenic chemicals in tobacco smoke, and aflato (a potent liver carcinogen produced by some molds that contaminate improperly stored supplies of peanuts a other grains). The carcinogens in tobacco smoke (including benzo(a)pyrene, dimethylnitrosamine, and nic

compounds) are the major identified causes of human cancer. Smoking is the undisputed cause of 80 to 90% of lu cancers, as well as being implicated in cancers of the oral cavity, pharynx, larynx, esophagus, and other sites. total, it is estimated that smoking is responsible for nearly one-third of all cancer deaths—an impressive toll fc single carcinogenic agent.

Treatments:

Innovative research has fueled the development of new medications and treatment technologies. Doctors usually prescribe treatments based on the type of cancer, its stage at diagnosis, and the person's ove health.

The side effects of chemotherapy include hair loss. However, advances in treatment are improving the outlook people with cancer.

Below are examples of approaches to cancer treatment:

- Chemotherapy aims to kill cancerous cells with medications that target rapidly dividing cells. The drugs also help shrink tumors, but the side effects can be severe.
- Hormone therapy involves taking medications that change how certain hormones work or interfere with body's ability to produce them. When hormones play a significant role, as with prostate and breast canc this is a common approach.
- Immunotherapy uses medications and other treatments to boost the immune system and encourage it to fi cancerous cells. Two examples of these treatments are checkpoint inhibitors and adoptive cell transfer.
- Precision medicine, or personalized medicine, is a newer, developing approach. It involves using gene testing to determine the best treatments for a person's particular presentation of cancer. Researchers ha yet to show that it can effectively treat all types of cancer, however.
- Radiation therapy uses high-dose radiation to kill cancerous cells. Also, a doctor may recommend us radiation to shrink a tumor before surgery or reduce tumor-related symptoms.
- Stem cell transplant can be especially beneficial for people with blood-related cancers, such as leuke or lymphoma. It involves removing cells, such as red or white blood cells, that chemotherapy or radiat has destroyed. Lab technicians then strengthen the cells and put them back into the body.
- Surgery is often a part of a treatment plan when a person has a cancerous tumor. Also, a surgeon m remove lymph nodes to reduce or prevent the disease's spread.
- Targeted therapies perform functions within cancerous cells to prevent them from multiplying. They also boost the immune system. Two examples of these therapies are small-molecule drugs and monoclo antibodies.

Doctors will often employ more than one type of treatment to maximize effectiveness.
Types

The most common typeTrusted Source of cancer in the U.S. is breast cancer, followed by lung and prostate canc according to the National Cancer Institute, which excluded nonmelanoma skin cancers from these findings.

Share on PinterestSmoking increases the risk of many different types of cancer.

Each year, more than 40,000 people in the country receive a diagnosis of one of the following types of cancer:

bladder
colon and rectal

endometrial
kidney
leukemia
liver
melanoma
non-Hodgkin's lymphoma
pancreatic
thyroid

Other forms are less common. According to the National Cancer Institute, there are over 100 typesTrusted Source cancer.
Cancer development and cell division

Doctors classify cancer by:

its location in the body
the tissues that it forms in

For example, sarcomas develop in bones or soft tissues, while carcinomas form in cells that cover internal external surfaces in the body. Basal cell carcinomas develop in the skin, while adenocarcinomas can form in breast.

When cancerous cells spread to other parts of the body, the medical term for this is metastasis.
A person can also have more than one type of cancer at a time.

Programmed cell death :

Programmed cell death (or PCD) is the death of a cell in any form, mediated by an intracellular program, and also referred to as Cellular Suicide. PCD is carried out in a biological process, which usually confers advanta during an organism's life-cycle. For example, the differentiation of fingers and toes in a developing human emb occurs because cells between the fingers apoptose; the result is that the digits are separate. PCD serves fundamer functions during both plant and animal tissue development. Apoptosis and autophagy, both are the forms programmed cell death, but necrosis was long seen as a non-physiological process that occurs as a result of infect or injury.

Necrosis is the death of a cell caused by external factors such as trauma or infection and occurs in seve different forms. Recently a form of programmed necrosis, called necroptosis, has been recognized as an alternat form of programmed cell death. It is hypothesized that necroptosis can serve as a cell-death backup to apopto when the apoptosis signaling is blocked by endogenous or exogenous factors such as viruses or mutations. M recently, other types of regulated necrosis have been discovered as well, which share several signaling events w necroptosis and apoptosis.

Types
Overview of signal transduction pathways involved in apoptosis.

Apoptosis or Type I cell-death.
Autophagic or Type II cell-death. (Cytoplasmic: characterized by the formation of large vacuoles that away organelles in a specific sequence prior to the destruction of the nucleus.)

Apoptosis:

Apoptosis is the process of programmed cell death (PCD) that may occur in multicellu organisms.Biochemical events lead to characteristic cell changes (morphology) and death. These changes inclu blebbing, cell shrinkage, nuclear fragmentation, chromatin condensation, and chromosomal DNA fragmentation is now thought that- in a developmental context- cells are induced to positively commit suicide whilst ir homeostatic context; the absence of certain survival factors may provide the impetus for suicide. There appears be some variation in the morphology and indeed the biochemistry of these suicide pathways; some treading the p of "apoptosis", others following a more generalized pathway to deletion, but both usually being genetically a synthetically motivated. There is some evidence that certain symptoms of "apoptosis" such as endonucle activation can be spuriously induced without engaging a genetic cascade, however, presumably true apoptosis a programmed cell death must be genetically mediated. It is also becoming clear that mitosis and apoptosis toggled or linked in some way and that the balance achieved depends on signals received from appropriate grov or survival factors.

Autophagy:

Macroautophagy, often referred to as autophagy, is a catabolic process that results in the autophagosom lysosomal degradation of bulk cytoplasmic contents, abnormal protein aggregates, and excess or damag organelles.

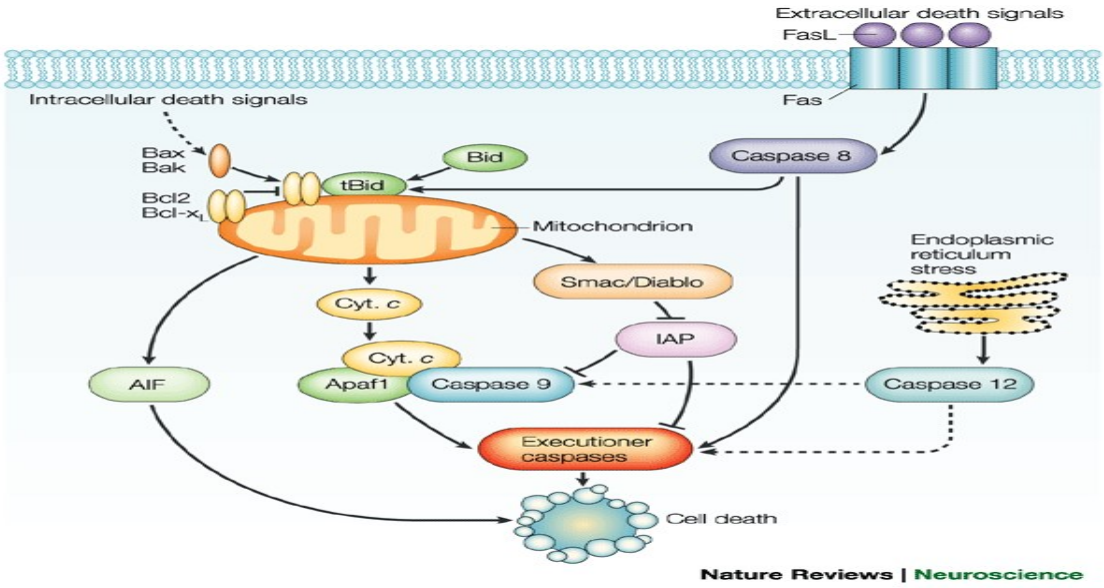
Autophagy is generally activated by conditions of nutrient deprivation but has also been associated w physiological as well as pathological processes such as development, differentiation, neurodegenerative diseas stress, infection and cancer.

Mechanism:

A critical regulator of autophagy induction is the kinase mTOR, which when activated, suppres autophagy and when not activated promotes it. Three related serine/threonine kinases, UNC-51-like kinase -1, and -3 (ULK1, ULK2, UKL3), which play a similar role as the yeast Atg1, act downstream of the mTOR compl ULK1 and ULK2 form a large complex with the mammalian homolog of an autophagy-related (Atg) gene prod (mAtg13) and the scaffold protein FIP200. Class III PI3K complex, containing hVps34, Beclin-1, p150 and Atg like protein or ultraviolet irradiation resistance-associated gene (UVRAG), is required for the induction autophagy.

The ATG genes control the autophagosome formation through ATG12-ATG5 and LC3-II (ATG8 complexes. ATG12 is conjugated to ATG5 in a ubiquitin-like reaction that requires ATG7 and ATG10. The Atg1 Atg5 conjugate then interacts non-covalently with ATG16 to form a large complex. LC3/ATG8 is cleaved at its terminus by ATG4 protease to generate the cytosolic LC3-I. LC3-I is conjugated to phosphatidylethanolamine (I also in a ubiquitin-like reaction that requires Atg7 and Atg3. The lipidated form of LC3, known as LC3-II, attached to the autophagosome membrane.

Autophagy and apoptosis are connected both positively and negatively, and extensive crosstalk exists between two. During nutrient deficiency, autophagy functions as a pro-survival mechanism, however, excessive autopha may lead to cell death, a process morphologically distinct from apoptosis. Several pro-apoptotic signals, such TNF, TRAIL, and FADD, also induce autophagy. Additionally, Bcl-2 inhibits Beclin-1-dependent autopha thereby functioning both as a pro-survival and as an anti-autophagic regulator.



Other types:

Besides the above two types of PCD, other pathways have been discovered. Called "non-apopto programmed cell-death" (or "caspase-independent programmed cell-death" or "necroptosis"), these alternat routes to death are as efficient as apoptosis and can function as either backup mechanisms or the main type of PC Other forms of programmed cell death include anoikis, almost identical to apoptosis except in induction; cornification, a form of cell death exclusive to the eyes; excitotoxicity; ferroptosis, an iron-depend form of cell death and Wallerian degeneration.

Necroptosis is a programmed form of necrosis, or inflammatory cell death. Conventionally, necrosis associated with unprogrammed cell death resulting from cellular damage or infiltration by pathogens, in contrast orderly, programmed cell death via apoptosis.

Eryptosis is a form of suicidal erythrocyte death.

Aponecrosis is a hybrid of apoptosis and necrosis and refers to an incomplete apoptotic process tha completed by necrosis.

NETosis is the process of cell-death generated by NETs

Paraptosis is another type of nonapoptotic cell death that is mediated by MAPK through the activat of IGF-1. It's characterized by the intracellular formation of vacuoles and swelling of mitochondria.

Pyroptosis, an inflammatory type of cell death, is uniquely mediated by caspase 1, an enzyme involved in apoptosis, in response to infection by certain microorganisms.

Plant cells undergo particular processes of PCD similar to autophagic cell death. However, so

common features of PCD are highly conserved in both plants and metazoa.

Atrophic factors:

An atrophic factor is a force that causes a cell to die. Only natural forces on the cell are considered to atrophic factors, whereas, for example, agents of mechanical or chemical abuse or lysis of the cell are conside not to be atrophic factors. Common types of atrophic factors are

Decreased workload
Loss of innervation
Diminished blood supply
Inadequate nutrition
Loss of endocrine stimulation
Senility
Compression.

Invertebrates and vertebrates:

Learning about PCD in various species is essential in understanding the evolutionary basis and reason apoptosis in development of the nervous system. During the development of the invertebrate nervous system, P plays different roles in different species. The similarity of the asymmetric cell death mechanism the nematode and the leech indicates that PCD may have an evolutionary significance in the development of nervous system. In the nematode, PCD occurs in the first hour of development leading to the elimination of 12% non-gonadal cells including neuronal lineages. Cell death in arthropods occurs first in the nervous syst when ectoderm cells differentiate and one daughter cell becomes a neuroblast and the other underg apoptosis. Furthermore, sex targeted cell death leads to different neuronal innervation of specific organs in ma and females. In Drosophila, PCD is essential in segmentation and specification during development.
In contrast to invertebrates, the mechanism of programmed cell death is found to be more conserved in vertebra Extensive studies performed on various vertebrates show that PCD of neurons and glia occurs in most parts of nervous system during development. It has been observed before and during synaptogenesis in the central nerv system as well as the peripheral nervous system. However, there are a few differences between vertebrate speci For example, mammals exhibit extensive arborization followed by PCD in the retina while birds do not. Althou synaptic refinement in vertebrate systems is largely dependent on PCD, other evolutionary mechanisms also pla role.

Stem cell:

Stem cell are undifferentiated cells that can turn into specific cells, as the body needs them.
Scientists and doctors are interested in stem cells as they help to explain how some functions of the body work, a how they sometimes go wrong.
Stem cells also show promise for treating some diseases that currently have no cure.
Sources of stem cells:
Stem cells originate from two main sources: adult body tissues and embryos. Scientists are also working on ways develop stem cells from other cells, using genetic "reprogramming" techniques.
Adult stem cells

Stem cells can turn into any type of cell before they become differentiated.
A person's body contains stem cells throughout their life. The body can use these stem cells whenever it needs the

Also called tissue-specific or somatic stem cells, adult stem cells exist throughout the body from the time an embı develops.

The cells are in a non-specific state, but they are more specialized than embryonic stem cells. They remain in t state until the body needs them for a specific purpose, say, as skin or muscle cells.
Day-to-day living means the body is constantly renewing its tissues. In some parts of the body, such as the and bone marrow, stem cells regularly divide to produce new body tissues for maintenance and repair.
Stem cells are present inside different types of tissue. Scientists have found stem cells in tissues, including:

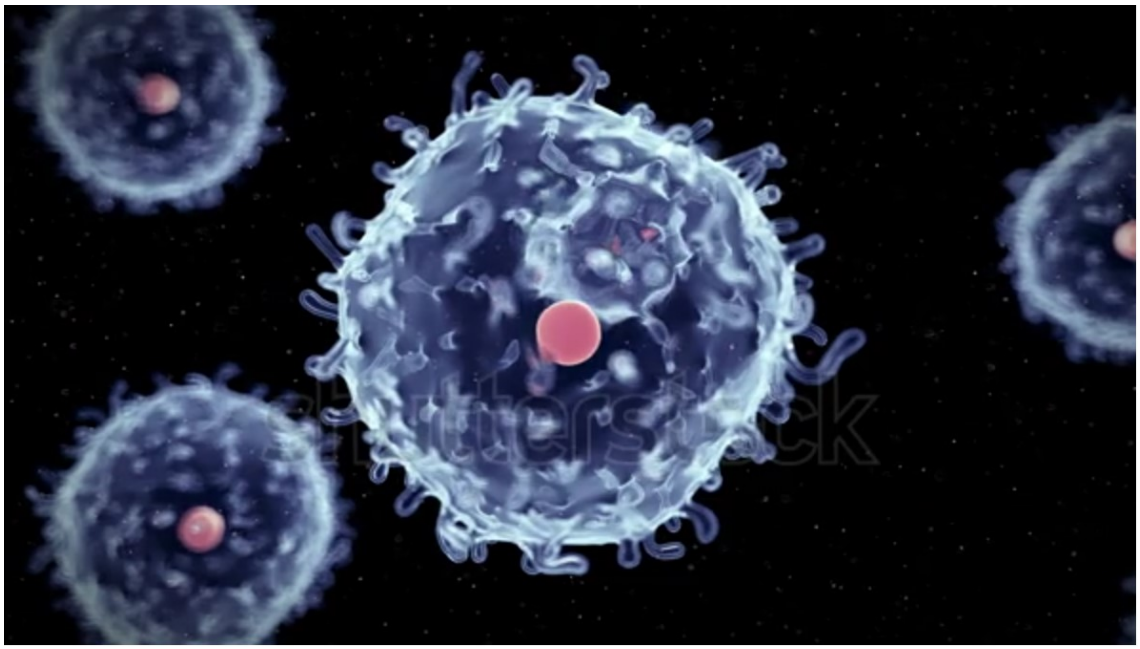
- the brain
- bone marrow
- blood and blood vessels
- skeletal muscles
- skin
- the liver

However, stem cells can be difficult to find. They can stay non-dividing and non-specific for years until the bc summons them to repair or grow new tissue.

Adult stem cells can divide or self-renew indefinitely. This means they can generate various cell types from originating organ or even regenerate the original organ, entirely.

This division and regeneration are how a skin wound heals, or how an organ such as the liver, for example, repair itself after damage.

In the past, scientists believed adult stem cells could only differentiate based on their tissue of origin. Howev some evidence now suggests that they can differentiate to become other cell types, as well.



Embryonic stem cells
From the very earliest stage of pregnancy, after the sperm fertilizes the egg, an embryo forms.

Around 3–5 days after a sperm fertilizes an egg, the embryo takes the form of a blastocyst or ball of cells.

The blastocyst contains stem cells and will later implant in the womb. Embryonic stem cells come from a blastoc that is 4–5 days old.

When scientists take stem cells from embryos, these are usually extra embryos that result from in vitro fertilizat (IVF).

In IVF clinics, the doctors fertilize several eggs in a test tube, to ensure that at least one survives. They will tl implant a limited number of eggs to start a pregnancy.

When a sperm fertilizes an egg, these cells combine to form a single cell called a zygote.

This single-celled zygote then starts to divide, forming 2, 4, 8, 16 cells, and so on. Now it is an embryo.
Soon, and before the embryo implants in the uterus, this mass of around 150–200 cells is the blastocyst. T blastocyst consists of two parts:

an outer cell mass that becomes part of the placenta
an inner cell mass that will develop into the human body

The inner cell mass is where embryonic stem cells are found. Scientists call these totipotent cells. The te totipotent refer to the fact that they have total potential to develop into any cell in the body.

With the right stimulation, the cells can become blood cells, skin cells, and all the other cell types that a body nee In early pregnancy, the blastocyst stage continues for about 5 days before the embryo implants in the uterus, womb. At this stage, stem cells begin to differentiate.

Embryonic stem cells can differentiate into more cell types than adult stem cells.

Mesenchymal stem cells (MSCs)

MSCs come from the connective tissue or stroma that surrounds the body's organs and other tissues.
Scientists have used MSCs to create new body tissues, such as bone, cartilage, and fat cells. They may one day p a role in solving a wide range of health problems.

Induced pluripotent stem cells (iPS)
Scientists create these in a lab, using skin cells and other tissue-specific cells. These cells behave in a similar way embryonic stem cells, so they could be useful for developing a range of therapies.

However, more research and development is necessary.

To grow stem cells, scientists first extract samples from adult tissue or an embryo. They then place these cells i controlled culture where they will divide and reproduce but not specialize further.

Stem cells that are dividing and reproducing in a controlled culture are called a stem-cell line.

Researchers manage and share stem-cell lines for different purposes. They can stimulate the stem cells to special

in a particular way. This process is known as directed differentiation.
Until now, it has been easier to grow large numbers of embryonic stem cells than adult stem cells. Howev scientists are making progress with both cell types.

Types of stem cells

Researchers categorize stem cells, according to their potential to differentiate into other types of cells.

Embryonic stem cells are the most potent, as their job is to become every type of cell in the body.

The full classification includes:
Totipotent: These stem cells can differentiate into all possible cell types. The first few cells that appear as zygote starts to divide are totipotent.

Pluripotent: These cells can turn into almost any cell. Cells from the early embryo are pluripotent.

Multipotent: These cells can differentiate into a closely related family of cells. Adult hematopoietic stem cells, example, can become red and white blood cells or platelets.

Oligopotent: These can differentiate into a few different cell types. Adult lymphoid or myeloid stem cells can this.

Unipotent: These can only produce cells of one kind, which is their own type. However, they are still stem c because they can renew themselves. Examples include adult muscle stem cells.

Embryonic stem cells are considered pluripotent instead of totipotent because they cannot become part of the ext embryonic membranes or the placenta.

Uses
Share on PinterestTransplants with stem cells are already helping people with diseases such as lymphoma.

Stem cells themselves do not serve any single purpose but are important for several reasons.

First, with the right stimulation, many stem cells can take on the role of any type of cell, and they can regener damaged tissue, under the right conditions.

This potential could save lives or repair wounds and tissue damage in people after an illness or injury. Scientists many possible uses for stem cells.

Tissue regeneration:
Tissue regeneration is probably the most important use of stem cells.

Until now, a person who needed a new kidney, for example, had to wait for a donor and then undergo a transplant There is a shortage of donor organs but, by instructing stem cells to differentiate in a certain way, scientists co use them to grow a specific tissue type or organ.

As an example, doctors have already used stem cells from just beneath the skin's surface to make new skin tiss They can then repair a severe burn or another injury by grafting this tissue onto the damaged skin, and new skin v

grow back.

Cardiovascular disease treatment:

In 2013, a team of researchers from Massachusetts General Hospital reported in PNAS Early Edition that they l created blood vessels in laboratory mice, using human stem cells.

Within 2 weeks of implanting the stem cells, networks of blood-perfused vessels had formed. The quality of th new blood vessels was as good as the nearby natural ones.

The authors hoped that this type of technique could eventually help to treat people with cardiovascular and vascu diseases.

Brain disease treatment:

In Parkinson's, for example, damage to brain cells leads to uncontrolled muscle movements. Scientists could stem cells to replenish the damaged brain tissue. This could bring back the specialized brain cells that stop uncontrolled muscle movements.

Cell deficiency therapy

Scientists hope one day to be able to develop healthy heart cells in a laboratory that they can transplant into peo with heart disease.

These new cells could repair heart damage by repopulating the heart with healthy tissue.

Similarly, people with type I diabetes could receive pancreatic cells to replace the insulin-producing cells that th own immune systems have lost or destroyed.

The only current therapy is a pancreatic transplant, and very few pancreases are available for transplant.

Blood disease treatments

Doctors now routinely use adult hematopoietic stem cells to treat diseases, such as leukemia, sickle cell anemia, a other immunodeficiency problems.

Hematopoietic stem cells occur in blood and bone marrow and can produce all blood cell types, including red blc cells that carry oxygen and white blood cells that fight disease.

Donating or harvesting stem cells

People can donate stem cells to help a loved one, or possibly for their own use in the future.

Donations can come from the following sources:

Bone marrow: These cells are taken under a general anesthetic, usually from the hip or pelvic bone. Technici then isolate the stem cells from the bone marrow for storage or donation.

Peripheral stem cells: A person receives several injections that cause their bone marrow to release stem cells into blood. Next, blood is removed from the body, a machine separates out the stem cells, and doctors return the blooc the body.

Umbilical cord blood: Stem cells can be harvested from the umbilical cord after delivery, with no harm to the ba

Some people donate the cord blood, and others store it.
This harvesting of stem cells can be expensive, but the advantages for future needs include:

the stem cells are easily accessible

less chance of transplanted tissue being rejected if it comes from the recipient's own body.

Embryonic stem cell

Embryonic stem cells (ESCs) are stem cells derived from the undifferentiated inner mass cells of a human embryo
Embryonic stem cells are pluripotent, meaning they are able to grow (i.e. differentiate) into all derivatives of three primary germ layers: ectoderm, endoderm and mesoderm.

In other words, they can develop into each of the more than 200 cell types of the adult body as long as they specified to do so.

Embryonic stem cells are distinguished by two distinctive properties: their pluripotency, and their ability to replic indefinitely.

ES cells are pluripotent, that is, they are able to differentiate into all derivatives of the three primary germ laye ectoderm, endoderm, and mesoderm.

These include each of the more than 220 cell types in the adult body.

Pluripotency distinguishes embryonic stem cells from adult stem cells found in adults; while embryonic stem ce can generate all cell types in the body, adult stem cells are multipotent and can produce only a limited number cell types.

Additionally, under defined conditions, embryonic stem cells are capable of propagating themselves indefinitely. This allows embryonic stem cells to be employed as useful tools for both research and regenerative medici because they can produce limitless numbers of themselves for continued research or clinical use.

Because of their plasticity and potentially unlimited capacity for self-renewal, ES cell therapies have been propos for regenerative medicine and tissue replacement after injury or disease.

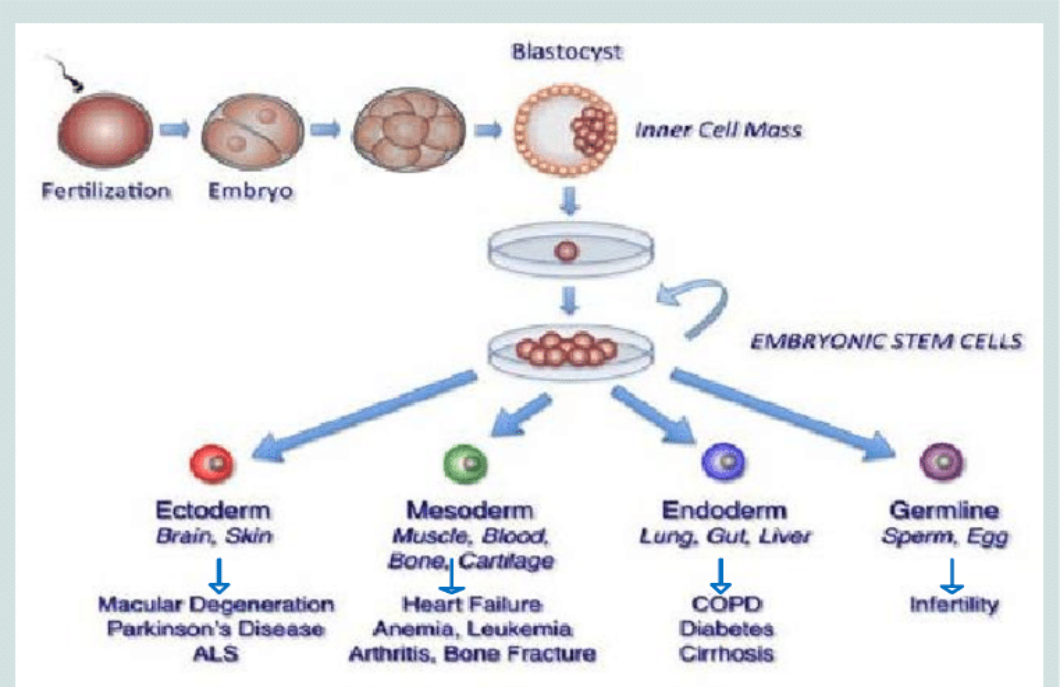
Diseases that could potentially be treated by pluripotent stem cells include a number of blood and immune-syst related genetic diseases, cancers, and disorders; juvenile diabetes;

Parkinson's; blindness and spinal cord injuries.

Besides the ethical concerns of stem cell therapy, there is a technical problem of graft-versus-host disease associa with allogeneic stem cell transplantation.

However, these problems associated with histocompatibility may be solved using autologous donor adult stem ce therapeutic cloning, stem cell banks or more recently by reprogramming of somatic cells with defined factors (e induced pluripotent stem cells).

Other potential uses of embryonic stem cells include investigation of early human development, study of gene disease and as in vitro systems for toxicology testing.



Pluripotent stem cells:

Pluripotent stem cells are master cells. They're able to make cells from all three basic body layers, so they potentially produce any cell or tissue the body needs to repair itself. This "master" property is called pluripoten Like all stem cells, pluripotent stem cells are also able to self-renew, meaning they can perpetually create m copies of themselves.

There are several types of pluripotent stem cells, including embryonic stem cells.

But all of them are able to differentiate, or mature, into the three primary groups of cells that form a human being

- ectoderm — giving rise to the skin and nervous system
- endoderm — forming the gastrointestinal and respiratory tracts, endocrine glands, liver, and pancreas
- mesoderm — forming bone, cartilage, most of the circulatory system, muscles, connective tissue, and mo

Right now, it's not clear which type or types of pluripotent stem cells will ultimately be used to create cells treatment, but all of them are valuable for research purposes, and each type has unique lessons to teach scienti Scientists are just beginning to understand the subtle differences between the different kinds of pluripotent st cells, and studying all of them offers the greatest chance of success in using them to help patients.

Types of pluripotent stem cells:

- Induced pluripotent cell (iPS cells)
- "True" embryonic stem cell (ES cells) derived from embryos
- Embryonic stem cells made by somatic cell nuclear transfer (ntES cells)
- Embryonic stem cells from unfertilized eggs (parthenogenesis embryonic stem cells, or pES cells)

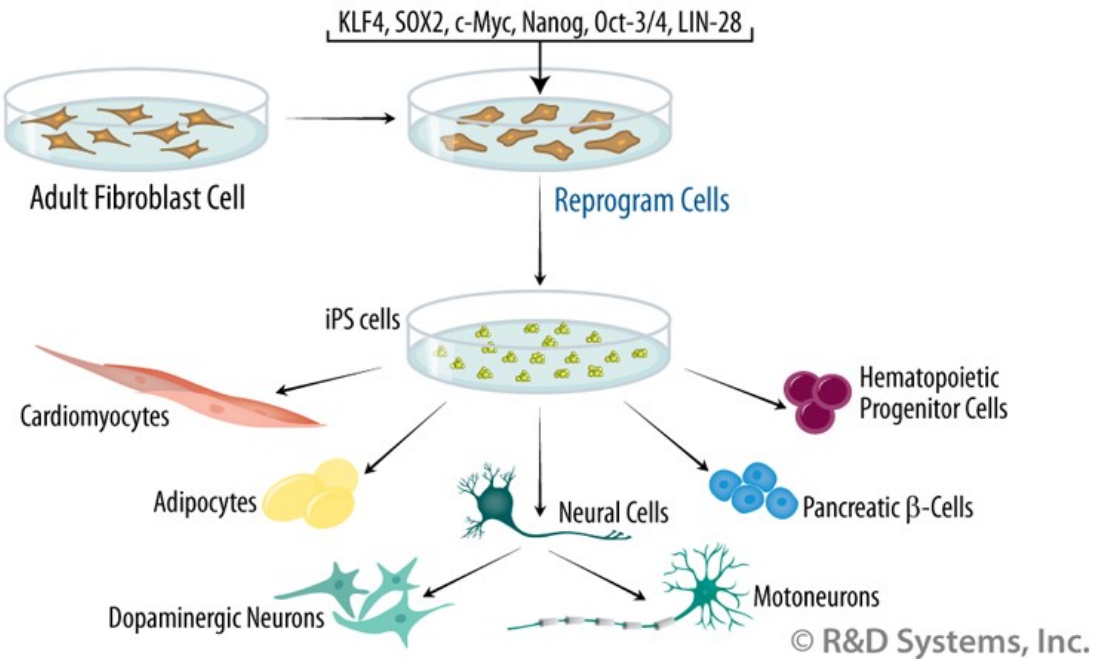
All four types of pluripotent stem cells are being actively studied at Children's.

Induced pluripotent cells (iPS cells):

Scientists have discovered ways to take an ordinary cell, such as a skin cell, and "reprogram" it by introduc several genes that convert it into a pluripotent cell. These genetically reprogrammed cells are known as induc pluripotent cells, or iPS cells. The Stem Cell Program at Children's Hospital Boston was one of the first three l to do this in human cells, an accomplishment cited as the Breakthrough of the Year in 2008 by the journal Scienc iPS cells offer great therapeutic potential. Because they come from a patient's own cells, they are genetica matched to that patient, so they can eliminate tissue matching and tissue rejection problems that currently hin successful cell and tissue transplantation. iPS cells are also a valuable research tool for understanding how differ diseases develop.

Because iPS cells are derived from skin or other body cells, some people feel that genetic reprogramming is m ethical than deriving embryonic stem cells from embryos or eggs. However, this process must be carefu controlled and tested for safety before it's used to create treatments. In animal studies, some of the genes and viruses used to introduce them have been observed to cause cancer. More research is also needed to make process of creating iPS cells more efficient.

iPS cells are of great interest at Children's, and the lab of George Q. Daley, MD, PhD, Director of Stem C Transplantation Program, reported creating 10 disease-specific iPS lines, the start of a growing repository of i cell lines.



Embryonic stem cells:

Scientists use "embryonic stem cell" as a general term for pluripotent stem cells that are made using embryos eggs, rather than for cells genetically reprogrammed from the body. There are several types of embryonic st cells:

1. **"True" embryonic stem cell (ES cells)**

These are perhaps the best-known type of pluripotent stem cell, made from unused embryos that are donated couples who have undergone in vitro fertilization (IVF). The IVF process, in which the egg and sperm are brou together in a lab dish, frequently generates more embryos than a couple needs to achieve a pregnancy.

These unused embryos are sometimes frozen for future use, sometimes made available to other couples undergo fertility treatment, and sometimes simply discarded, but some couples choose to donate them to science. For deta on how they're turned into stem cells, visit our page How do we get pluripotent stem cells?

Pluripotent stem cells made from embryos are "generic" and aren't genetically matched to a particular patient, are unlikely to be used to create cells for treatment. Instead, they are used to advance our knowledge of how st cells behave and differentiate.

2. **Stem cells made by somatic cell nuclear transfer (ntES cells)**

The term somatic cell nuclear transfer (SCNT) means, literally, transferring the nucleus (which contains all o cell's genetic instructions) from a somatic cell—any cell of the body—to another cell, in this case an egg cell. T type of pluripotent stem cell, sometimes called an ntES cell, has only been made successfully in lower animals. make ntES cells in human patients, an egg donor would be needed, as well as a cell from the patient (typicall skin cell).

The process of transferring a different nucleus into the egg "reprograms" it to a pluripotent state, reactivating full set of genes for making all the tissues of the body. The egg is then allowed to develop in the lab for seve days, and pluripotent stem cells are derived from it. (Read more in How do we get pluripotent stem cells?)
Like iPS cells, ntES cells match the patient genetically. If created successfully in humans, and if proven safe, nt cells could completely eliminate tissue matching and tissue rejection problems. For this reason, they are activ being researched at Children's.

3. **Stem cells from unfertilized eggs (parthenogenetic embryonic stem cells)**

Through chemical treatments, unfertilized eggs can be "tricked" into developing into embryos without be fertilized by sperm, a process called parthenogenesis. The embryos are allowed to develop in the lab for seve days, and then pluripotent stem cells can be derived from them (for more, see How do we get pluripotent st cells?)

If this technique is proven safe, a woman might be able to donate her own eggs to create pluripotent stem c matching her genetically that in turn could be used to make cells that wouldn't be rejected by her immune system. Through careful genetic typing, it might also be possible to use pES cells to create treatments for patients beyc the egg donor herself, by creating "master banks" of cells matched to different tissue types. In 2006, working w mice, Children's researchers were the first to demonstrate the potential feasibility of this approach. (For details, Turning pluripotent stem cells into treatment).

Because pES cells can be made more easily and more efficiently than ntES cells, they could potentially be ready clinical use sooner. However, more needs to be known about their safety. Concerns have been raised that tiss derived from them might not function normally

Possible Questions

Part-A (1 mark)

Part-B (2 marks)

1.what is pluripotent stem cell?
2. Embryonic stem cell describe.
3. what is Autophagy?
4.write about the difference between Mitosis and Meiosis.
5. explain telophase in mitosis cell division.

Part-C (8 marks)

1.describe various stages of Mitotic cell division
2. Explain about Meiosis cell Division.
3.Give a brief account on development of cancer ,types and treatments.
4. What is programmed cell Death –explain.
5. Explain Stem cell and its type.

S.NO	QUESTIONS	POSSIBILITY A	POSSIBILITY B	POSSIBILITY C	POSSIBILITY D	ANSWERS
1	The term "meiosis" was coined by	Hertwig and Van Bevedin	Sutton and Boveri	Hofmeister and Waldeyer	Farmer and Moore	Farmer and Moore
2	Coiling of chromatids in mitotic and meiotic division is	Paranemic in both	Plectonemic in both	Paranemic in mitosis and plectonemic in meiosis	Plectonemic in mitosis and paranemic in meiosis	Plectonemic in mitosis and paranemic in meiosis
3	As there occurs more and more condensation of chromatin during cell division, there occurs	Increase in heterochromatin	Increase in euchromatin	Differentiation of heterochromatin and euchromatin decreases	Differentiation of heterochromatin and euchromatin increases	Differentiation of heterochromatin and euchromatin decreases
4	Condensation of chromosomes occurs in	Prophase I	Prophase II	Anaphase	Metaphase	Prophase I
5	The replication of nuclear DNA occurs in	G1 phase	G2 phase	S phase	M phase	S phase
6	The role of meiosis	Formation of gametes	Bringing haplophase	Bringing diplophase	Completing life cycle	Bringing haplophase
7	The number of DNA in chromosome at G2 stage of cell	One	Two	Four	Eight	Two

8	Which stage connecting link between Meiosis I and Meiosis II	Interphase I	Interphase II	Interkinesis	Anaphase I	Interkinesis
9	Which of the following stage is affected by colchicum	Metaphase	Prophase	Interphase	Anaphase	Metaphase
10	G0 state of cells in eukaryotic cell cycle denotes	Check point before entering the next phase	Pausing in the middle of a cycle to cope with a temporary delay	Death of a cell	Exit of cells from cell cycle	Exit of cells from cell cycle
11	Synapsis is pairing of	Any two chromosomes	Non homologous chromosomes	Acentric chromosomes	Homologous chromosomes	Homologous chromosomes
12	Mitosis occurs in	Haploid individuals	Diploid individuals	Both (a) and (b)	In bacteria only	Both (a) and (b)
13	Spindle apparatus is formed during which stage of mitosis	Prophase	Metaphase	Anaphase	Telophase	Metaphase
14	Cyclin is associated with which one of the following	Glycolysis	Cyclosis	Haemolysis	Mitosis	Mitosis
15	For viewing diakinesis which one of the following would be a suitable material	Onion root tip	Leaf of Dichanthium	Rat tail	Flower bud	Flower bud

16	Which is not the character of mitosis	Leptotene	Zygotene	Pachytene	All of the above	All of the above
17	Synaptonemal complex is formed during	Meiosis	Amitosis	Mitosis	Cytokinesis	Meiosis
18	Synaptonemal complex was discovered in	1956	1950	1935	1980	1956
19	Recombinant nodules are found during which of the following	Anaphase	Prophase	Telophase	Metaphase	Prophase
20	Four daughter cells formed after meiosis are	Genetically similar	Genetically different	Anucleate	Multinucleate	Genetically different
21	Bivalents in meiosis are	Tetrad	Pairs of non-homologous chromosomes	Pairs of several chromatids	Pairs of homozygous chromosomes	Tetrad
22	Repulsion of homologous chromosomes takes place in	Zygotene	Leptotene	Diakinesis	Diplotene	Diplotene
23	Which cell division is found during cleavage	Amitosis	Mitosis	Closed mitosis	Meiosis	Closed mitosis

24	Which type of cell division occurs in the gonads	Mitosis only	Meiosis	Both (a) and (b)	Amitosis and meiosis	Both (a) and (b)
25	How many ATP is required during anaphase to move chromosomes from equator to the poles	38 ATP	5 ATP	30 ATP	76 ATP	30 ATP
26	Mitosis is the process by which eukaryotic cells	Expose the genes for protein synthesis	Become specialized in structure and function	Multiply	Grow	Multiply
27	In pachytene stage of meiosis the chromosomes appear	Single stranded	Double stranded	Three stranded	Four stranded	Four stranded
28	The spindle fibre contracts in	Metaphase I	Anaphase II	Prophase II	Telophase II	Anaphase II
29	Recombination of genes occur at	Prophase in mitosis	Prophase I in meiosis	Prophase II in meiosis	Metaphase II in meiosis	Prophase I in meiosis
30	The second division in meiosis is called	Equational division	Reduction division	Multiplied division	None of the above	Equational division
31	The meiotic process by which homologous chromosomes are paired during prophase I is called	Interkinesis	Crossing over	Chiasma	Synapsis	Synapsis

32	In which type of cell division spindle formation does not occur	Mitosis	Meiosis	Endomitosis	None of the above	Endomitosis
33	How may mitotic divisions must occur in a cell of root tip to form 256 cells	256	8	128	64	8
34	The best stage to count the number of chromosomes during mitosis is or structure of chromosomes can be best seen at	Prophase	Metaphase	Anaphase	Telophase	Metaphase
35	A repeated cycle of DNA replication without separation of daughter chromatids leads to the formation of	Pachytene chromosome	Leptotene chromosomes	Polytene chromosome	Zygotene chromosomes	Polytene chromosome
36	Cytokinesis in plants takes place by the formation of	Sphaeroblasts	Equatorial cell plate	Idioblasts	Cell budding	Equatorial cell plate
37	In meiosis, the centromere divides during	Prophase-I	Metaphase-I	Anaphase-I	Anaphase-II	Anaphase-II
38	Four chromatids and two centromeres which are homologous occurs in	Zygotene	Diplotene	Diakinesis	Pachytene	Zygotene
39	Mitosis results in	Reduction in chromosome number	Doubling of chromosome number	Constant chromosome number	Increase in cell volume	Constant chromosome number

40	Mitosis and meiosis take place respectively in	Meristem and gametangia	Gametangia and meristem	Permanent tissues and secretory tissues	Secretory tissues and permanent tissues	Meristem and gametangia
41	An anaphase chromosome contains	1 DNA molecule	2 DNA molecule	4 DNA molecule	3 DNA molecule	1 DNA molecule
42	Which of the following is an active cell death process?	Apoptosis	Necrosis	Senescence	Lysis	Apoptosis
43	Apoptosis can't kill which of the following	Cell infected with viruses	Cell with DNA damage	Cancer cells	Immune cells	Cancer cells
44	Epstein Barr virus can cause cancer by	Producing p53 binding protein	Inducing cytochrome release from mitochondria	Producing anti-apoptotic protein	Producing adaptor protein in excess	Producing anti-apoptotic protein
45	Downregulation of caspase 9 is seen in	Melanoma	Breast cancer	Colorectal cancer	Lung cancer	Colorectal cancer
46	Decoy molecules which binds to Fas L are seen in _	Lung cancer	Melanoma	Breast cancer	Ovarian cancer	Lung cancer
47	cancers that begin in the bones and in the soft (also called connective) tissues is	Melanoma	Breast cancer	Saracoma	Ovarian cancer	Saracoma

48	Medicine that deals with the prevention, diagnosis, and treatment of cancer is called	Anthology	Mycology	Oncology	Cytology	Oncology
49	Treatment that uses drugs to kill cancer cells is called	Chemotherapy	Immunotherapy	Hormone therapy	Stemcell therapy	Chemotherapy
50	cancer of plasma cells in the bone marrow is called	Melanoma	Saracoma	Plasmolysis	Myeloma	Myeloma
51	Differentiation potential of stem cells specifies	stochastic differentiation	asymmetric replication	potency	self-renewal	potency
52	Types of stem cells in mammals are	2	3	4	5	2
53	Stem cells are present in	unicellular organisms	multicellular organisms	non-living things	viruses	multicellular organisms
54	In a developing embryo, stem cells can differentiate into	ectoderm	endoderm	mesoderm	all of above	all of above
55	Stem cells can be obtained from	embryos	some adult tissues	umbilical cord blood	all of the above	all of the above

56	The cells are able to differentiate to generate primitive ectoderm is called	ectoderm	endoderm	stem cells	Pluripotent	Pluripotent
57	What does "pluripotent" mean?	able to divide and make many different types of cells	not able to divide	can only divide and make one cell type	if it divides, it will make a cancerous tumor	able to divide and make many different types of cells
58	What do stem cells have to do with clones?	Stem cells can divide and differentiate and grow into a clone	Clones can be grown from stem cells	Both (a) and (b)	None of these	Both (a) and (b)
59	iPS stem cells are derived from	Embryonic SC	IVF embryos	Blastocysts	Adult somatic cells	Adult somatic cells
60	Which of the following terms describes the potential of the inner mass cells from the blastocyst?	Totipotent	Pluripotent	Multipotent	Omnipotent	Pluripotent