

The Cellular Organization of a Living Organism

INTRODUCTION

Biology is a broad field of science focusing on the "study of life." It covers a wide-range of subjects from cell biology that explains the workings of the cells to the study of ecosystems that govern the survival of the living organisms. Technological advances have made it possible to examine the contents of the cells, the organelles, in minute details to unraveling the contents of these organelles especially, the deoxyribonucleic acid (DNA) inside the nucleus. As long as there is an urge to lead a life without diseases and live longer with better quality, it is important to study biology because it provides clues to solving many of these problems. Understanding the nature of the cellular organelles and its functions provides basic information about the cell that can help us to devise strategies to correct the problems seen in this cellular machinery in diseases.

Genetic information stored in the form of DNA in the chromosomes of the nucleus is not only important for propagation of species but also in the production of various proteins that is critical for the survival of an organism. Genes serve as blueprints for synthesis of proteins that have several functions in the body: provide structural support, regulate metabolism, and stimulate chemical reactions involved in anabolism and catabolism of biomolecules. Metabolism is a key process through which the living organism is able to generate energy for its sustenance. Plants get energy through photosynthesis using sunlight, water, and carbon dioxide while animals depend on external sources including plants. All the processes within the organism are carried out by maintaining equilibrium in order to adjust to the external environment. This process of homeostasis allows the organism to live under different climatic conditions and during healthy and diseased states. Reproduction is a key process for the propagation of living organisms and is done through both mitosis and meiosis involving cell division.

1.1 BIOLOGY AS ONE OF THE FIELDS OF SCIENCE

Science is an organized approach to a systematic study of the universe with the aim to increase our knowledge about the universe. Biology is one of the realms of science and its sole purpose is to understand the living organisms. A *living organism* is defined as a complex entity of physicochemical components that is capable of surviving through self-regulatory mechanisms such as metabolism, reproducing, and coping with the external environment. It also possesses the capabilities to move, respond to external and internal stimuli, grow and develop to adjust to the environment in which they live in.

Biologists believe in the concept of *evolution* which states that the present day living organisms have originated from ancestral forms of life which had undergone continuous modifications over a period of time. These concepts have been developed by Jean Baptiste Lamarck (1801) and later modified by Charles Darwin (1859). It also helped in the classification of living organisms into groups in such a manner that they are linked chronologically and morphologically. The branch of science dealing with classification organisms is called as taxonomy. A kingdom is the broadest classification in taxonomy and all living organisms belong to one of the 5 kingdoms (Table 1.1).

The five kingdoms are Monera, Protista, Fungi, Plantae, and Animalia. Living organisms are further classified into prokaryote and eukaryote based on the presence or absence of nucleus. Monera consists of unicellular organisms that lack a nucleus and many of the specialized cell parts, called organelles. Such organisms are said to be prokaryotic (pro “before”; karyotic “kernel,” “nucleus”) and consist of bacteria. All of the other kingdoms consist of eukaryotic (eu: “true”) organisms, which have cells that contain a nucleus and a number of specialized organelles.

Table 1.1 Classification of kingdoms with their characteristic features

S. No.	Kingdom	Characteristics	Examples
1	Monera	Single-celled, prokaryotic, cells do not have nucleus and specialized organelles	Bacteria
2	Protista	Single-celled, eukaryotic, cells possess nucleus and specialized organelles	Protozoa
3	Plantae	Multicellular, eukaryotic, produce their own food for survival and reproduction	Trees
4	Fungi	Single or multicellular, eukaryotic, acquire food from their surroundings	Yeasts and molds
5	Animalia	Multicellular, eukaryotic, obtain food from the environment and process it through metabolic pathways for survival and reproduction	Fishes, Birds, Reptiles, Cows, Human beings

Biologists have been able to classify the living organisms by investigating their characteristic features. This was accomplished by adopting rigorous *scientific methods* as a model of research developed by Francis Bacon (1561–1626). It has the following sequences:

1. Recognizing the problem
2. Gathering data through experiments (measurement, observations, etc)
3. Analyzing the data for meaningful connections between various parameters chosen for study and any deviations
4. Formulating a *hypothesis* (a generalization), which is an educated guess that explains the existing data and suggests further avenues of investigation
5. Testing the hypothesis rigorously by gathering new data
6. Confirming, modifying, or rejecting the hypothesis in light of the new findings

Scientists have strict guidelines of doing research as postulated by Francis Bacon. Any procedure or data that do not conform to the rigors of testing and go wrong are discarded and the whole process is repeated. However in some instances, errors have led to new discoveries.

- Wilhelm Röntgen observed a faint shimmering in the corner of the laboratory where he had kept a chemical that later led to the discovery of X-rays.
- Charles Goodyear accidentally dropped a mixture of rubber and sulfur on a hot stove and found the mixture to be flexible and tough leading to the discovery of vulcanization process
- Alexander Fleming found a contaminated mold growing in a bacterial culture on a petri dish. Any bacteriologist would have thrown away that petri dish because of contamination. But Fleming observed an area around the mold had no bacterial growth. He realized that this may have been due to the product produced by the mold. He isolated the chemical from the mold which happens to be penicillin, the first antibiotic that revolutionized the treatment options for various bacterial diseases.

1.2 CELL: BASIC UNIT OF LIFE

All living beings are made up of the basic unit of life- cells (Fig:1.1). It is the smallest unit of living matter and each cell is able to carry out the processes of life. Some structures transport materials, some make food and others

release energy for the cell to use. All the cells are involved in metabolic processes through cellular respiration, reproduction (meiosis), and growth (mitosis). They are also capable of transforming into different types of cells, a specialization called as cell differentiation. The cells have a few things in common such as having cell membrane, deoxyribonucleic acid (DNA), cytoplasm, and ribosome but they are different with regard to structure, shape, and functions.

The cells were first described by Robert Hooke in 1665. He examined thin slices of cork and found pores. But his examination did not indicate any nucleus, and other organelles. Later in 1674, Antony van Leeuwenhoek found moving organisms by observing them under lenses and microscopes. The observation of Hooke and others led to the development of cell theory.

The cell theory states

- All living things and organisms are made up of cells and their products. Multicellular organisms (example: humans) are composed of many cells while unicellular organisms (example: bacteria) are composed of only one cell.
- Cells are the basic building units of life.
They are the smallest structures capable of surviving on their own.
- New cells arise from the pre-existing cells by division.
For example, new cells arise from cell division and a zygote (the very first cell formed when an organism is produced) arises from the fusion of an egg cell and a sperm cell.

Evidence for the cell theory

When scientists started to look at the structures of organisms under the microscope, they discovered that all living organisms were made up of these small units which they named them as cells. When these cells were taken from tissues they were able to survive for some period of time. Nothing smaller than the cell was able to live independently and so it was concluded that the cell was the smallest unit of life. For some time, scientists thought that cells must arise from non-living material but it was eventually proven that this was not the case, and instead proved to arise from pre-existing cells.

A simple experiment to prove this can be done as follows:

- Take two containers and put food in both of these
- Sterilize both of the containers so that all living organisms are killed
- Leave one of the containers open and seal the other closed

One will be able to observe that there will be growth of mold in the open container whereas there will be no such growth in the sealed container. The reason for this is because in the open container, cells are able to enter the container from the external environment and start to divide and grow. However, due to the sealing on the other container no cells could enter and hence, no mold growth was observed proving that cells cannot arise from non-living material.

Multicellular organisms possess developing properties

Multicellular organisms are the product of development from simpler to complex structures. For example: cells form tissues, tissues form organs, organs form organ systems and organ systems form multicellular organisms. The idea is that the whole is greater than the composition of its parts. For example your lungs are made of many cells. However, the cells by themselves aren't much use. It is the many cells working as a unit that allow the lungs to perform their function.

Every cell in multicellular organisms contains all the genes of that organism. However, the genes that are activated vary from cell to cell. The reason we have different types of cells in our body (the cells in your eyes are not the same as the ones that make up your hair) is because different genes are activated in different cells. For example, the gene that produces keratin will be active in hair and nail cells. Keratin is the protein which makes up hair and nails. Genes encode for proteins and the proteins affect the cell's structure and function so that the cell can specialize. This means cells develop in different ways. This is called differentiation. Differentiation depends on gene expression which is regulated mostly during transcription. It is an advantage for multicellular organisms as cells can differentiate to be more efficient unlike unicellular organisms that have to carry out all of the functions within that one cell.

Prokaryotes

These kinds of organisms do not have a nucleus, mitochondria or any other membrane-bound organelles. In other words, neither their DNA nor any other of their metabolic functions is collected together in a discrete membrane enclosed area. Instead everything is openly accessible within the cell; though some bacteria have internal membranes as sites of metabolic activity, these membranes do not enclose a separate area of the cytoplasm.

The prokaryote cell is simpler and therefore smaller than a eukaryote cell. The prokaryotes do not have a nucleus and most other organelles of

eukaryotes. There are two kinds of prokaryotes, bacteria and archaea. Nuclear material of prokaryotic cell consists of a single chromosome which is in direct contact with cytoplasm. Here the undefined nuclear region in the cytoplasm is called nucleiod. A prokaryotic cell has the following features:

- On the outside, flagella and pili project from the cell's surface. These are structures (not present in all prokaryotes) made of proteins that facilitate movement and communication between cells;
- Enclosing the cell is the cell envelope consisting of a cell wall covering a plasma membrane though some bacteria also have a further covering layer called a capsule. The envelope gives rigidity to the cell and separates the interior of the cell from its environment.
- Prokaryotes can carry extra chromosomal DNA elements called plasmids, which are usually circular. Plasmids enable additional functions, such as antibiotic resistance and therefore, survival.

Eukaryotes

Eukaryotic cells are about 15 times wider than a typical prokaryote and can be as much as 1000 times greater in volume. The major difference between prokaryotes and eukaryotes is that eukaryotic cells contain membrane-bound compartments in which specific metabolic activities take place. Most important among these is a cell nucleus, a membrane-delineated compartment that houses the eukaryotic cell's DNA. This nucleus gives the eukaryote its name, which means "true nucleus." Other differences include:

- The plasma membrane resembles that of prokaryotes in function, with minor differences in the setup. Cell wall may or may not be present.
- The eukaryotic DNA is organized in one or more linear molecules, called chromosomes, which are associated with histone proteins. All chromosomal DNA is stored in the cell nucleus, separated from the cytoplasm by a membrane. Some eukaryotic organelles such as mitochondria also contain some DNA.
- Many eukaryotic cells are ciliated with primary cilia. Primary cilia play important roles in chemo-sensation, mechano-sensation, and thermo-sensation.
- Eukaryotes can move using motile cilia. The flagella are more complex than those of prokaryotes.
- Plastids are a feature of most plant cells but are not found in the cells of animals. Vacuoles are quite prominent in plant cells, but are far less significant in or absent from animal cells.

1.3 CELL STRUCTURE AND FUNCTION

Earlier before the advent of electron microscope, cell was described as a unit possessing a limiting outer membrane and an inner central nucleus surrounded by large mass of cytoplasm (Fig. 1.1). Staining of cells facilitated to identification of subcellular features such as chromosome and nucleolus of the nucleus. Electron microscopic studies made it possible for the elucidation of the subcellular structures called as *organelles* that perform specialized functions. Most of the organelles are derived from membranes but some of them do not possess membrane structure such as ribosomes, microtubules, and microfilaments, flagella, cilia, and centrioles.

Cell/plasma membrane: The outermost layer of the living cell that gives structure and shape is the cell membrane. The chief function is to regulate the passage of materials into and out of the cell. Initial structural studies using electron microscope revealed that it consists of inner and outer dense protein layer enclosing a less dense phospholipid layer. Channels were also observed to traverse the through exterior surface of the membrane. Recent studies by Singer and Nicholson have demonstrated that the cell membrane has fluid

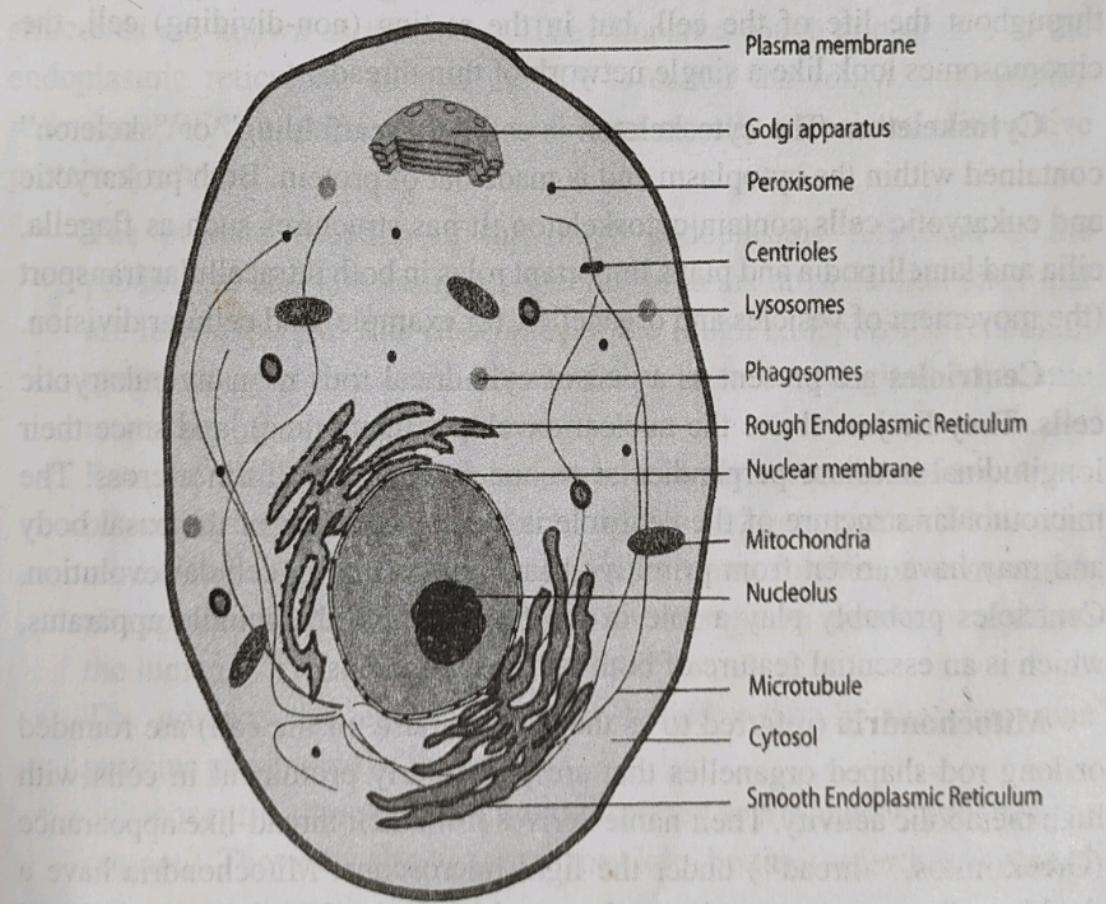


Fig. 1.1 Cell structure with outer plasma membrane and inner cytoplasm, organelles, and nucleus

mosaic model which better explains the dynamic nature of the proteins in the cell membrane. The only difference in the proposed model was the arrangement of phospholipids: their polar ends facing the inner and outer surfaces and the hydrophobic, non-polar ends opposed at the center of the bilayer.

Nucleus and Nucleolus: The nucleus is a round or oval body lying in the center of the cell enclosed by a double membrane that is called as nuclear membrane or envelope. In certain regions of the nuclear envelope, these membranes join together and there may be pores in these areas. The pores serve as a direct passage route for the substances to leave the nucleus. The outer membrane of the nuclear envelope is continuous with the endoplasmic reticulum and thus, may facilitate passage of materials from the nucleus directly into the channels of endoplasmic reticulum. Within the nucleus, one or more *nucleoli* may be seen. These are dense bodies containing the subunits for the ribosomes, the cytoplasmic organelles involved in the synthesis of protein. The nucleolus is involved in the assembly and synthesis of ribosomes.

The nucleus is the storehouse of the genetic material called as *chromosomes*. Each chromosome exists as a tiny individual rod or string throughout the life of the cell, but in the resting (non-dividing) cell, the chromosomes look like a single network of thin threads.

Cytoskeleton: The cytoskeleton is cellular "scaffolding" or "skeleton" contained within the cytoplasm and is made out of protein. Both prokaryotic and eukaryotic cells contain cytoskeleton. It has structures such as flagella, cilia and lamellipodia and plays important roles in both intracellular transport (the movement of vesicles and organelles, for example) and cellular division.

Centrioles are present as a pair of cylindrical rods in many eukaryotic cells. They lie just above the nuclear envelope (membrane), and since their longitudinal axes are perpendicular to one another, they form a cross. The microtubular structure of the centriole is the same as that of the basal body and may have arisen from primitive basal bodies during cellular evolution. Centrioles probably play a role in the formation of the spindle apparatus, which is an essential feature of both mitosis and meiosis.

Mitochondria (referred to as the 'Powerhouse' of the cell) are rounded or long rod-shaped organelles that are particularly prominent in cells with high metabolic activity. Their name derives from their thread-like appearance (Greek *mitos*, "thread") under the light microscope. Mitochondria have a double wall: an outer smooth membrane which forms the outer boundary and an inner membrane which is extensively folded. The folds, or cristae, project into the interior of the organelle and have a variety of enzymes embedded in

them. These enzymes are involved in the systematic degradation of organic molecules to yield energy for the cell. They are responsible for the breakdown of sugar molecules to release ATP (adenosine triphosphate), which is used to transport energy within the cell for metabolism. (through citric acid cycle and electron transport chain as explained in chapter 3). Like the chloroplasts of plants, the mitochondria contain their own DNA and ribosomes; they replicate independently of the rest of the cell and appear to control the synthesis of their membranes.

Endoplasmic reticulum (ER) is a series of membranous channels that traverse the cytoplasm of most eukaryotic cells. It forms a continuous network extending from the cell membrane to the nuclear membrane. In some regions of the cell, it may appear as a series of flattened disks or sacs. The endoplasmic reticulum serves many general functions, including the facilitation of protein folding and the transport of synthesized proteins in sacs called cisternae. Only properly-folded proteins are transported from the rough ER to the Golgi complex.

In many parts of the cell, the endoplasmic reticulum is associated with small dense granules lying along the outer border of its membrane. These structures are known as *ribosomes*. They impart a rough appearance to the endoplasmic reticulum, so that the ER is called the *rough endoplasmic reticulum (RER)* in these regions, which are usually associated with active protein synthesis.

- The primary function of the rough endoplasmic reticulum is the production and processing of specific proteins at ribosomal sites that are later exported. The ribosomes in the rough endoplasmic reticulum synthesize proteins which are then sent in to the rough endoplasmic reticulum for advanced processing.
- Rough endoplasmic reticulum function involves creation of two types of proteins. One is the type which fortifies and gets embedded into the reticulum membrane. The other types are water-soluble proteins which after production at ribosomal sites, pass through the membrane and into the lumen.
- The proteins that enter are further folded inside by the chaperone proteins present in the lumen.
- Subsequently, these proteins are transported to the sites where they are required. They may also be sent to the Golgi bodies for further advanced processing, through vesicles.

The *smooth endoplasmic reticulum (SER)* does not contain any ribosomes and is associated with cellular regions which are involved in the synthesis and

transport of lipids or the detoxification of a variety of poisons. Smooth endoplasmic reticulum is found in a variety of cell types and it serves different functions in each. It consists of tubules and vesicles that branch forming a network. The network of smooth endoplasmic reticulum allows increased surface area for the action or storage of key enzymes and the products of these enzymes.

Ribosomes are the components of cells that make proteins from the amino acids. Ribosomes are the workhorses of protein biosynthesis, the process of translating messenger ribonucleic acid (mRNA) into protein. The “central dogma” of biology is that DNA is used to make RNA, which, in turn, is used to make protein (discussed in detail in Chapter 2). The DNA sequence in genes is copied (transcription) into an mRNA. Ribosomes then read the information in this RNA and use it to create proteins. This process is known as translation; i.e., the ribosome “translates” the genetic information from RNA into proteins. Ribosomes do this by binding to an mRNA and using it as a template for the correct sequence of amino acids in a particular protein. The amino acids are attached to transfer RNA (tRNA) molecules, which enter one part of the ribosome and bind to the messenger RNA sequence. The attached amino acids are then joined together by another part of the ribosome. The ribosome moves along the mRNA, “reading” its sequence and producing a chain of amino acids.

Ribosomes are made from complexes of RNAs and proteins. Ribosomes are divided into two subunits, one larger and another smaller subunit. The smaller subunit binds to the mRNA, while the larger subunit binds to the tRNA and the amino acids. When a ribosome finishes reading an mRNA, these two subunits split apart. Ribosomes have been classified as ribozymes, since the ribosomal RNA seems to be most important for the peptidyl transferase activity that links amino acids together.

Golgi apparatus/bodies: They exist as stacks of flattened sacs, or vesicles that are continuous with the channels of the smooth endoplasmic reticulum. Their major function is the storage, modification, and packing of materials for release outside the cell membrane. These organelles are particularly prominent in secretory cells such as those of the pancreas. The outer portion of the Golgi apparatus releases its secretory material within membrane-enclosed globules (secretory vesicles) that migrate to the surface of the cell. The Golgi apparatus may actually be part of a dynamic system of membranous channels within the cell in which all elements such as the nuclear envelope, the endoplasmic reticulum, the Golgi apparatus, and the cell membrane are connected to each other without sharp boundaries. This interconnected network facilitates transport of materials across the cell.

Lysosomes are similar in shape to mitochondria but are smaller and consist of a single membrane covering the structure. They contain powerful enzymes that would digest the cellular contents if they were not contained within the impermeable lysosomal membrane. Rupture of this membrane releases these enzymes. The lysosome plays a role in intracellular digestion and may also be important in the destruction of certain structures during the process of development.

Vacuoles are discrete, clear regions within the cell that contain water and dissolved materials. The vacuole may act as a reservoir for fluids and salts that might otherwise interfere with metabolic processes occurring in the cytoplasm. The membrane enclosing the vacuole is called a tonoplast. Many protozoans have a contractile vacuole, which periodically contracts and forces fluid and salts out of the cell. The structure serves to prevent an accumulation of fluids in organisms that live in fresh water. Vacuoles containing digestive enzymes may also be formed around ingested food particles in a variety of cells. In the cells of many plants, a large central vacuole is a prominent feature; this vacuole may swell, press against the rigid cell wall, and give the cell a high degree of rigidity or turgor.

●**Organelles in plant cell**

Plant and animal cells differ in the number and structure of the above organelles, but the most fundamental difference in plant cell organelles is the presence of the chloroplast and cell wall. Plants differ integrally from animals in their ability to prepare food within their cells by the process of photosynthesis.

Chloroplasts are organelles found in plant cells and other eukaryotic organisms that conduct photosynthesis. The material within the chloroplast is called the stroma containing the stacks of thylakoids, the sub-organelles, which are the site of photosynthesis (described in detail in chapter 3).

Cell Wall is a structure made out of polysaccharide, peptidoglycan or glycoprotein that provides structural support and protection to the cell. In combination with the vacuole, which is large in plant cells, the other cell wall function includes controlling the turgidity of the cell.

All cells, whether prokaryotic or eukaryotic, have a membrane that envelops the cell, separates its interior from its environment, regulates what moves in and out (selectively permeable), and maintains the electric potential of the cell. Inside the membrane, a salty cytoplasm takes up most of the cell volume. All cells possess DNA, the hereditary material of genes, and RNA, containing the information necessary to build various proteins such as

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enzymes, the cell's primary machinery. There are also other kinds of biomolecules in cells.

Electron microscope uses a beam of electrons to illuminate the specimen and produce a magnified image of the specimen under study. It can magnify an object million times whereas light microscopes can do it only thousand times the original image. It was invented by a Hungarian physicist, Leo Szilárd but was developed into a prototype in 1930s by German physicist, Ernst Ruska and electrical engineer Max Knoll. Subsequently, several engineers worked on the prototype to increase its magnification power and practical utility that resulted in the development of two types of electron microscopes: scanning electron microscope and transmission electron microscope. These microscopes are not only of use in biology and life sciences field but also in other fields such as semiconductor and data storage, nanotechnology, mining, chemical and petrochemical, and high-resolution imaging.

support ATP production via ATP synthase provided a coupling mechanism, such as a common intermediate, is available. Proton translocation and the development of a transmembrane proton gradient provide the required coupling mechanism.

These topics are further discussed in detail in Chapter 3 under photosynthesis, metabolism and bioenergetics.

1.7 HOMEOSTASIS

Human beings have trillions of cells all working together for the maintenance of the entire body. While certain cells may perform very different functions, all the cells are quite similar in their metabolic requirements and perform certain basic functions essential for their own survival such as -

- Obtaining nutrients and oxygen from the environment surrounding the cell.
- Nutrients and oxygen to provide energy.
- Eliminating CO_2 and other wastes produced during chemical reactions by the cells into the surrounding environment.
- Synthesizing proteins and other components needed for cell structure.
- Controlling the exchange of materials between the cell and its surrounding environment.

Maintaining a constant internal environment with all that the cells need to survive (O_2 , glucose, minerals, ions, and waste removal) is necessary for individual cells. The processes by which the body regulates its internal environment are referred to as *homeostasis*.

The concept of homeostasis was first articulated by the French scientist Claude Bernard. He said "all the vital mechanisms, varied as they are have only one object that of preserving constant the conditions of life in the internal environment". The term, homeostasis, was coined by American physiologist Walter Cannon, author of the "Wisdom of the Body" (1932). The word comes from the Greek *homoios* (same) and *stasis* (to stand). For e.g., after cut or abrasion, blood comes out of the wound site. In order to prevent further loss of blood and promote survival of the organism, following process need to take place:

- Primary homeostasis: This is defined as the formation of the platelet plug.
- Secondary homeostasis: This is defined as the formation of fibrin through the coagulation cascade.

- **Tertiary homeostasis:** This is defined as the formation of plasma for breakdown of the clot.

Homeostatic regulation: The adjusting of physiological systems within the body in order to maintain a stable internal environment and which requires constant monitoring and adjustments as conditions change is called *homeostatic regulation*. Homeostatic regulation involves three parts (or) mechanisms:

Receptor: The receptor receives information that something changes in the environment.

Control center: It receives and processes information from the receptor.

Effectors: It responds to the commands of the control center by either opposing (or) enhancing the stimulus.

In regulating body temperature there are temperature receptors in the skin which communicate information to the brain, which is the control center, and the effectors are our blood vessels and sweat glands in our skin. Following factors homeostatically regulated:

1. Concentration of nutrients: Cells need a constant supply of nutrients molecules for energy production. Energy is needed to support life sustaining and specialized cell activities.
2. Concentrations of O_2 and CO_2 : Oxygen used to carry out the energy yielding chemical reactions and the CO_2 produced during these reactions must be removed so that acid forming CO_2 does not increase the acidity of the internal environment.
3. Concentrations of waste products: Some of the chemical reaction produce that may have a toxic effect on the cells if these wastes are accumulate.
4. Concentrations of water, salt and other electrolytes: The concentration of salt ($NaCl$) and water in extracellular fluid influence how much water enters or leaves the cells, these concentrations are carefully regulated to maintain the proper volume of cells.
5. Volume and pressure: The circulating component of the internal environment, the plasma, is maintained by volume and pressure.

Pathways that alter homeostasis

A variety of homeostatic mechanisms maintain the internal environment within tolerable limits. Homeostasis is maintained through a series of control mechanisms or the body suffers various illness or disease. When the cells in the body begin to malfunction, the homeostatic balance becomes disrupted. Disease and cellular malfunction can be caused in two basic ways, either

deficiency (cells not getting all they need) or toxicity (cells being poisoned by things they do not need).

Extrinsic homeostatic system: Most homeostatic systems are extrinsic and regulated by nervous system and endocrine system in higher animals.

1. The nervous system depends on sensors in the skin or sensory organs to receive stimuli and transmit a message to the spinal cord or brain. Sensory input is processed and a signal is sent to an effector system, such as muscles or glands that affects the response to the stimulus.
2. The endocrine system is the second type of extrinsic control, and involves a chemical component to the reflex. Sensors detect a change within the body and send a message to an endocrine effector (parathyroid), which makes parathyroid hormone(PTH). PTH is released into the blood when blood calcium levels are low. PTH causes bone to release calcium into the bloodstream, raising the blood calcium levels and ultimately, shutting down further production of PTH.

Some reflexes have a combination of nervous and endocrine responses.

The thyroid gland secretes thyroxine (which controls the metabolic rate) into the bloodstream. Falling levels of thyroxine stimulate receptors in the brain to signal the hypothalamus to release a hormone that acts on the pituitary gland to release thyroid-stimulating hormone (TSH) into the blood. TSH acts on the thyroid, causing it to increase production of thyroxine.

Intrinsic homeostatic system: The control systems usually involve only one organ or tissue. When muscles use more oxygen, and also produce more carbon dioxide, intrinsic controls cause dilation of the blood vessels allowing more blood into those active areas of the muscles. Eventually the vessels will return to "normal".

Each organ system contributes to the homeostasis of other systems and of the entire organism. No system of the body works in isolation, and the well-being of the person depends upon the well-being of all the interacting body systems. A disruption within one system generally has consequences for several other body systems. Nervous system and endocrine system (discussed in detail in Chapter 5) are critical to the maintenance of homeostasis (Fig. 1.4).

Nervous System: The nervous system receives a continuous supply of nutrients from the blood. Any interruption to the flow of blood may bring brain damage or death. The nervous system maintains homeostasis by controlling and regulating the other parts of the body. A deviation from a normal set point acts as a stimulus to a receptor, which sends nerve impulses to a regulating center in the brain. The brain directs an effector to act in such

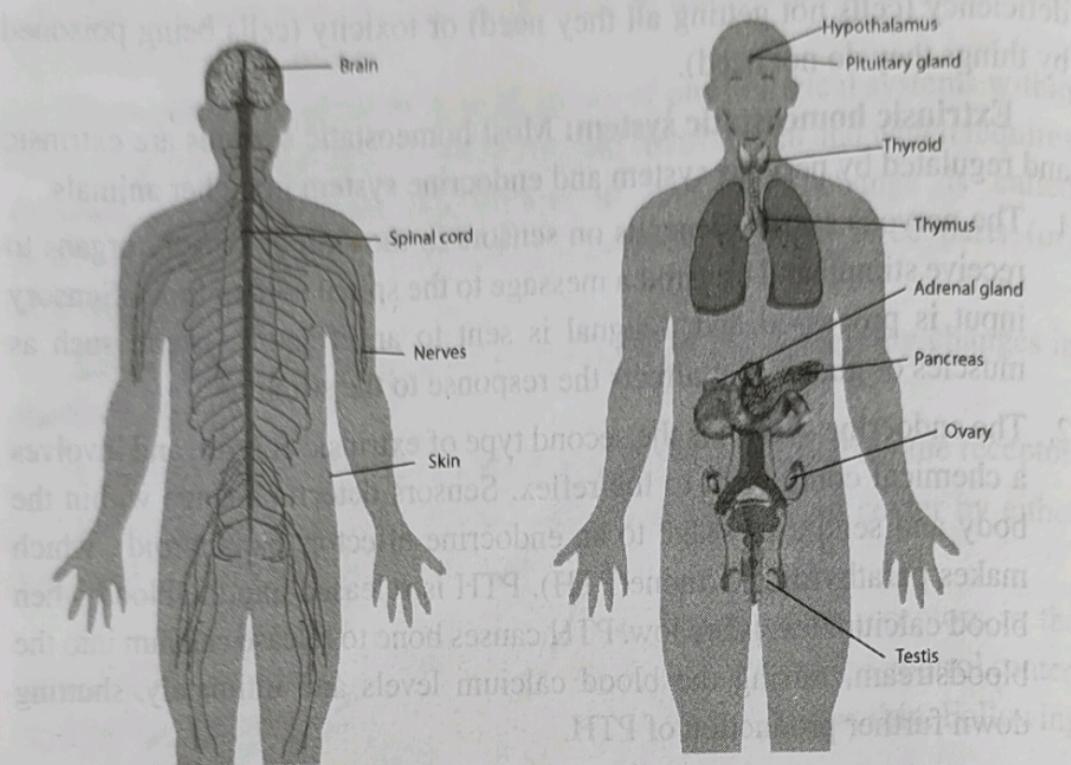


Fig. 1.4 Nervous system (brain, spinal cord and nerves) and endocrine system (endocrine glands) maintain homeostasis

a way that an adaptive response takes place. For e.g., if there is abnormal lowering of body temperature, the effector acts to increase body temperature. The adaptive response returns the body to a state of normalcy and the receptor, the regulating center, and the effector temporarily cease their activities.

The nervous system has two major portions: the central nervous system and the peripheral nervous system. The peripheral nervous system consists of the spinal nerves. The autonomic nervous system is a part of peripheral nervous system and contains motor neurons that control internal organs. It operates at the subconscious level and has two divisions, the sympathetic and parasympathetic systems. In general, the sympathetic system brings about those results we associate with emergency situations, often called fight or flight reactions, and the parasympathetic system produces those effects necessary to our everyday existence.

Regulating centers are located in the central nervous system, consisting of the brain and spinal cord. The hypothalamus is a portion of the brain particularly concerned with homeostasis; it influences the action of the medulla oblongata, a lower part of the brain, the autonomic nervous system, and the pituitary gland.

Endocrine System: The endocrine system consists of glands which secrete special compounds called hormones into the bloodstream. Each

hormone has an effect on one or more target tissues. In this way the endocrine system regulates the metabolism and development of most body cells and body systems. For e.g. the endocrine system has sex hormones that can activate sebaceous glands, development of mammary glands, alter dermal blood flow, and release lipids from adipocytes etc besides governing reproduction.

Bone growth is regulated by several hormones, and the endocrine system helps with the mobilization of minerals like calcium by the hormone, calcitonin. In the muscular system, hormones adjust muscle metabolism, energy production, and growth. In the nervous system, hormones affect neural metabolism, regulate fluid/electrolyte balance and help with reproductive hormones that influence CNS (central nervous system), development and behaviours. In the cardiovascular system, hormones regulate heart rate and blood pressure. Hormones also have anti-inflammatory effects and control the lymphatic system.

1.8 CELL GROWTH AND REPRODUCTION

Cells, like an organism, have the ability to grow, reproduce, communicate, and carryout a multitude of reactions and are regarded as the basic units of life. In order to have an optimum functionality, a cell must maintain a higher surface area to volume ratio. As an object grows larger, its volume increases more rapidly than its surface area. Similarly as a living cell grows larger, its rate of waste production and its need for resources increases faster than its surface area creating an unhealthy condition. So a cell must divide to have a small volume in order to maintain a larger surface area to volume ratio.

Growth and reproduction are the major characteristics of life without which life would come to an end. Reproduction continues life and provides the basis for evolution. Cells reproduce by duplicating their contents and then dividing into two. In case of unicellular organisms, such as bacteria, each cell division produces a whole new organism. This controlled cycle of duplication and division is termed *cell-cycle*. An ordered series of events must occur for a cell to divide uniformly which can be summed up as follows: -

- a) A reproductive signal that activates the cellular reproductive machinery.
- b) Duplication of the genetic material and other vital components so that each cell after division becomes complete and identical to each other.
- c) Segregation of the genetic material.
- d) Cytokinesis.

Cell division in eukaryotes, like that in prokaryotes, involves reproductive signals, DNA replication, segregation, and cytokinesis, but are much more complicated (Fig. 1.5). First, cell division does not depend upon the environment cues of a single cell rather than on the needs of the whole cell.

Eukaryotic Cell Division

Cytokinesis: The division of cytoplasm starts once the cell has successfully replicated its genetic material. The process starts with the pinching in of the cell membrane. As the membrane pinches in the materials required for cell wall synthesis are produced and ultimately the cells are separated.

Replication of DNA: DNA replication is followed by the segregation of bacterial cell. There are two chromosomes, one at either end of the lengthened replication, the two are replicated, one at either end of the lengthened membrane forms between them as the cell grows longer. By the end of the two orientations separate as the new chromosome forms and new plasma membrane is attached to the plasma membrane. After replication, the replicated DNA molecules are distributed to the two new cells. The first replication to be replicated DNA molecules to the two new cells. The first replication to be replicated DNA molecules to the two new cells. The first replication to be replicated DNA molecules to the two new cells.

Segregation of DNA: DNA replication is followed by the segregation of bacterial cell. There are two chromosomes, one at either end of the lengthened replication, the two are replicated, one at either end of the lengthened membrane forms between them as the cell grows longer. By the end of the two orientations separate as the new chromosome forms and new plasma membrane is attached to the plasma membrane. After replication, the replicated DNA molecules are distributed to the two new cells. The first replication to be replicated DNA molecules to the two new cells.

Termination of replication: The site where replication ends: the terminus of replication, "ter".

Origin of replication: The site where replication starts: the origin of replication, designated as "ori".

Replication of genetic material: Most of the prokaryotes contain a single circular DNA, which is packaged tightly to fit into a tiny cell that is a hundred times smaller than it. Functionally, the prokaryotic chromosome has two regions that are important for cell reproduction:

Reproductive signal: The reproductive mechanism of many prokaryotes depends upon the environmental stimuli. The cell division in case of bacteria, *Escherichia coli*, takes 40 minutes at 37°C where as in presence of adequate carbohydrates and salts, the cycle time gets reduced to 20 minutes. So this suggests that materials in the environment act as signals to control the division of a cell.

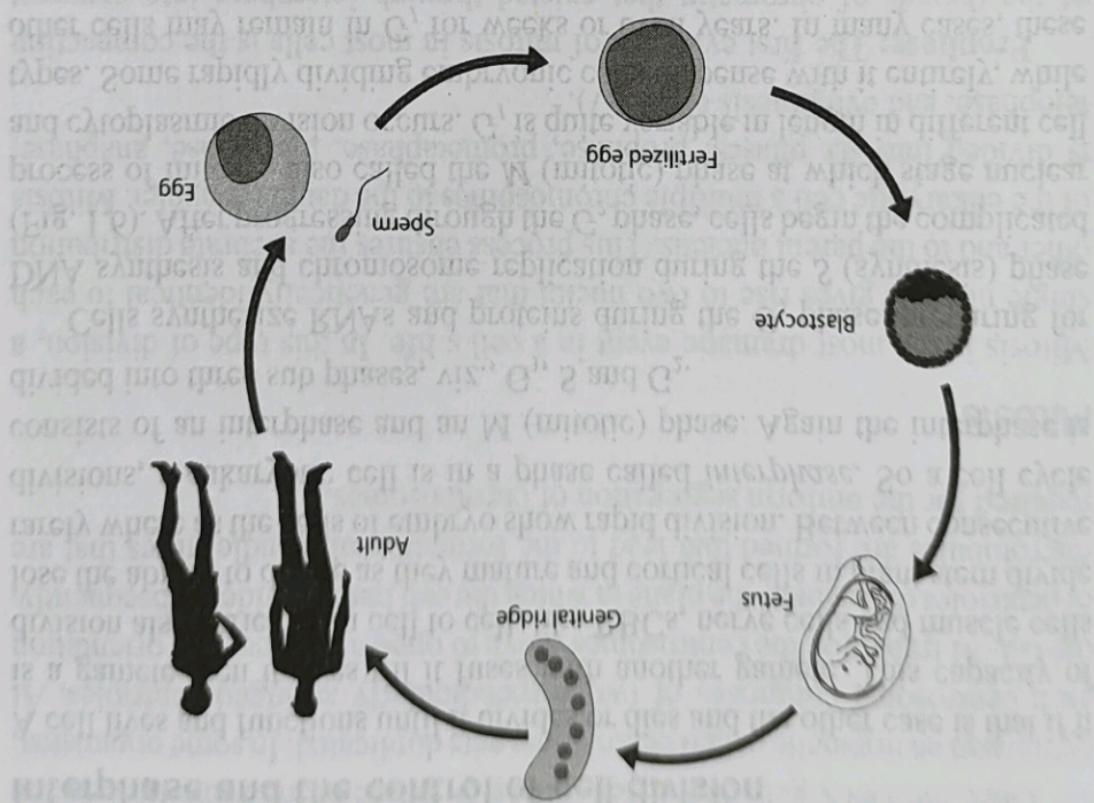
In prokaryotes, there is neither mitosis nor meiosis but rather a different type of cell division. The type of cell division is termed *fission* wherein the cell grows, replicates its genetic material and then divides into two single-cell complete entities.

Prokaryotic Cell Division

The major difference between prokaryotes and eukaryotes in terms of cell reproduction is that the chromosomes get segregated once they are duplicated in case of prokaryotes whereas they remain associated as sister chromatids in case of eukaryotes, cell division is of two types, viz., mitosis and meiosis. Mitosis is basically a process of duplication that generates two identical daughter cells from a single parent cell. Multicellular organisms grow from a single embryonic cell by the process of mitosis, even after they are fully grown it helps them to replenish the lost cells by everyday's wear and tear. It takes place in all parts of the body to keep the tissues and organs in good working condition. Meiosis occurs in germ cells. It shuffles the genetic deck to generate daughter cells that are distinct from each other and even from the parent cell. So mitosis is for growth and maintenance while meiosis is for sexual reproduction.

In plants, cytokinesis is different from animals as it involves a cell wall which clear nucleus whose division is essential prior to cell division. Finally in case of animals whose division is simple as that of prokaryotes. Third, they have a second, these cells have many chromosomes, so the process of replication and segregation are not that simple as that of prokaryotes. Third, they have a third difference that multicellular organisms produce a multicellular organism. Eukaryotic cells are mostly parts of multicellular organisms. So in case of eukaryotes cell division is of two types, viz., mitosis and meiosis. Mitosis is basically a process of duplication that generates two identical daughter cells from a single parent cell. Multicellular organisms grow from a single embryonic cell by the process of mitosis, even after they are fully grown it helps them to replenish the lost cells by everyday's wear and tear. It takes place in all parts of the body to keep the tissues and organs in good working condition. Meiosis occurs in germ cells. It shuffles the genetic deck to generate daughter cells that are distinct from each other and even from the parent cell. So mitosis is for growth and maintenance while meiosis is for sexual reproduction.

Fig. 1.5 Cell division in eukaryotes involves multiple processes to produce a multicellular organism.



Interphase and the control of cell division

A cell lives and functions until it divides or dies and the other case is that if it is a gamete then it lives till it fuses with another gamete. This capacity of division also varies from cell to cell, like RBCs, nerve cells and muscle cells lose the ability to divide as they mature and cortical cells in plant stem divide rarely whereas the cells of embryo show rapid division. Between consecutive divisions, a eukaryotic cell is in a phase called *interphase*. So a cell cycle consists of an interphase and an M (mitotic) phase. Again the interphase is divided into three sub phases, viz., G₁, S and G₂.

Cells synthesize RNAs and proteins during the G₁ phase, preparing for DNA synthesis and chromosome replication during the S (synthesis) phase (Fig. 1.6). After progressing through the G₂ phase, cells begin the complicated process of mitosis, also called the M (mitotic) phase at which stage nuclear and cytoplasmic division occurs. G₁ is quite variable in length in different cell types. Some rapidly dividing embryonic cells dispense with it entirely, while other cells may remain in G₁ for weeks or even years. In many cases, these cells enter a resting phase called G₀. Special internal and external signals are needed to prompt a cell to leave G₀ and re-enter the cell cycle at G₁. It is the preparing stage for S phase. During G₂ phase, the cell makes preparations for mitosis like for example by synthesizing microtubules that will help in segregation of chromosomes.

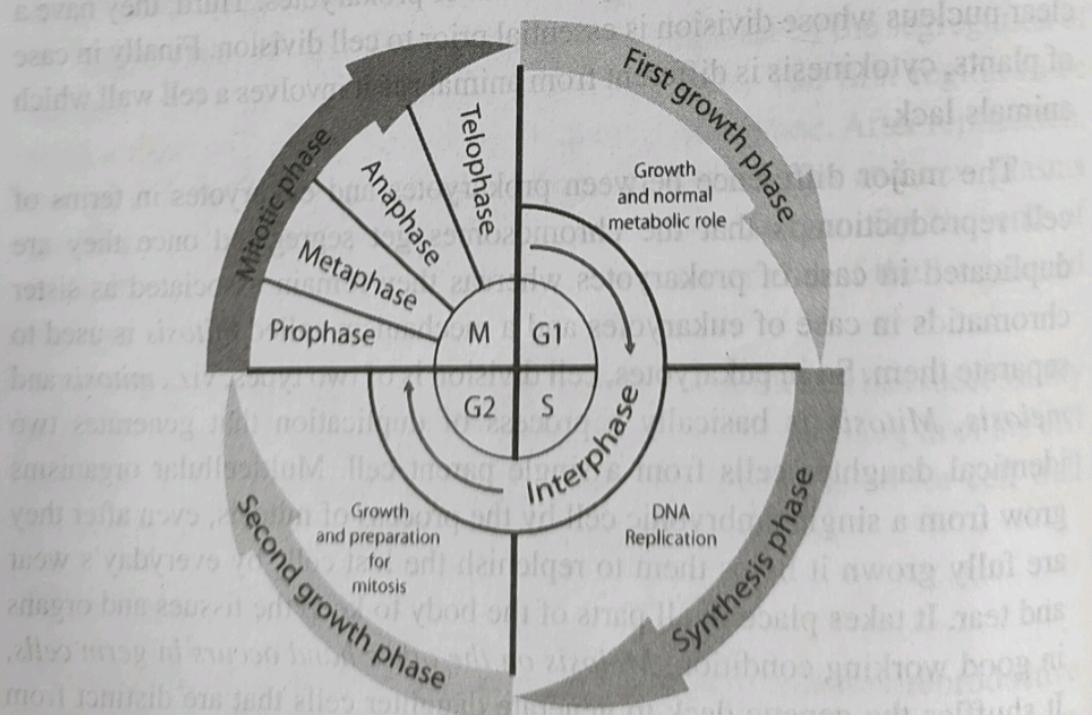


Fig. 1.6 Major events in a cell cycle that consists of growth phases (1 and 2), DNA synthesis phase, and mitotic phase.

Once the DNA gets duplicated during S- phase at the same time in the cytoplasm an organelle called centrosome gets duplicated. In some organisms, each centrosome comprises of two perpendicularly arranged centrioles. At the G2- M transition the centrosomes move to opposite poles. The orientation of centrioles determines the plane in which the cell has to divide. Subsequently, microtubules are formed that lead to the formation of spindle fibres that are required for the uniform segregation of chromosomes.

Mitosis

Mitosis is the most dramatic event in a cell's life. In this type of division, a single nucleus gives rise to two nuclei that are genetically identical to each other and to the parent nucleus. This process ensures the accurate distribution of the eukaryotic cell's multiple chromosomes to the daughter nuclei. Mitosis is divided into six phases: prophase, prometaphase, metaphase, anaphase, telophase, and cytokinesis (Fig. 1.7).

Prophase: The first evidence of mitosis in most cells is the compaction of the threads of chromatin that existed through interphase into compact chromosomes that are visible in the light microscope. As the chromosomes compact, each can be seen to be paired structures composed of two chromatids. This is the visible effect of the DNA molecules having been replicated in interphase. Chromosome condensation reduces the chance of long DNA molecules becoming tangled and broken. Each chromosome has a constriction

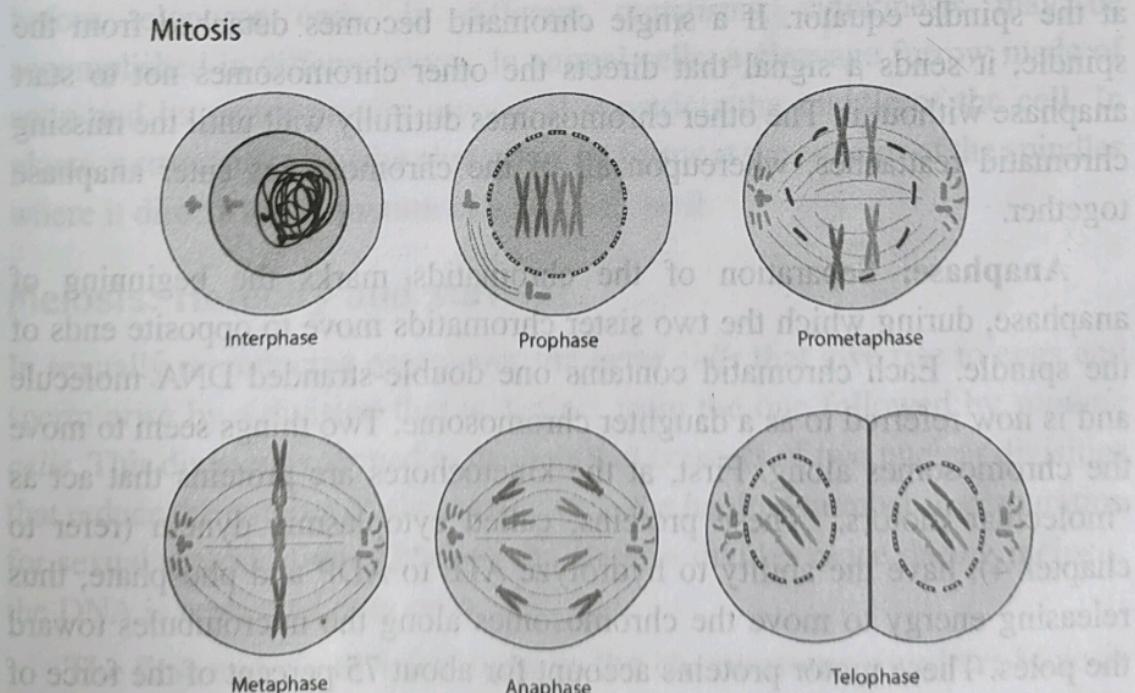


Fig. 1.7 Various phases of mitotic cell division where a single cell yields two cells that are identical to the parent cell.

called the kinetochore, a structure that forms around a region rich in satellite DNA called the centromere. The kinetochore is the point of attachment of the chromosome to the spindle. At the same time as the chromosomes are condensing within the nucleus, the centrosomes, which lie on the cytoplasmic side of the nuclear envelope, begin to separate to establish the mitotic spindle.

Prometaphase: At the breakdown of the nuclear envelope, the chromosomes become free to interact with the forming spindle. Microtubule assembly from the centrosomes is random and dynamic. The growing ends of individual microtubules make chance contact with and are captured by the kinetochores. Because of the random nature of these events, the kinetochores of chromatid pairs are initially associated with different numbers of microtubules, and the forces acting upon each chromosome are unbalanced. Initially, therefore, the spindle is highly unstable and chromosomes make frequent excursions toward and away from the poles. Gradually, a balance of forces is established and the chromosomes become aligned at the equator, with the kinetochores of each member of a chromatid pair oriented toward opposite poles.

Metaphase: Metaphase is the most stable period of mitosis. The system can be regarded as being at steady-state with the chromosomes lined up at the equatorial plate. The metaphase spindle consists of two major groups of microtubules: those connecting the chromatids to the poles and a second group extending from each pole toward the other. The second group overlap at the spindle equator. If a single chromatid becomes detached from the spindle, it sends a signal that directs the other chromosomes not to start anaphase without it. The other chromosomes dutifully wait until the missing chromatid reattaches, whereupon all of the chromosomes enter anaphase together.

Anaphase: Separation of the chromatids marks the beginning of anaphase, during which the two sister chromatids move to opposite ends of the spindle. Each chromatid contains one double-stranded DNA molecule and is now referred to as a daughter chromosome. Two things seem to move the chromosomes along. First, at the kinetochores are proteins that act as “molecular motors.” These proteins, called cytoplasmic dynein (refer to chapter 4), have the ability to hydrolyze ATP to ADP and phosphate, thus releasing energy to move the chromosomes along the microtubules toward the poles. These motor proteins account for about 75 percent of the force of motion. Second, the kinetochores microtubules shorten from the poles, drawing the chromosomes towards them. This shortening accounts for about 25 percent of the motion.

During anaphase the poles of the spindle are pushed farther apart, doubling the distance between them. The distance between poles increases because the overlapping polar microtubules extending from opposite ends of the spindle contain motor proteins that cause them to slide past each other, in much the same way that microtubules slide in cilia and flagella. This polar separation further separates one set of daughter chromosomes from the other. During this segregation process the chromosomes move very slowly at about 1 μ m per minute ensuring their proper segregation.

Telophase: This stage sees the reversal of many of the events of prophase; the chromosomes decondense, the spindle disassembles, the nuclear envelope reforms, Golgi apparatus and endoplasmic reticulum reform, and the nucleolus reappears. Each progeny nucleus now contains one complete copy of the genome from the father and one copy from the mother. When these and other changes are complete, telophase—and mitosis—is at an end, and each of the daughter nuclei enters another interphase.

Mitosis is beautifully precise. It result in two nuclei that are identical to each other and to the parent nucleus in chromosomal makeup, and hence in genetic constitution. Next, the two nuclei must be isolated in separate cells, which require the division of the cytoplasm.

Cytokinesis: division of the Cytoplasm: Mitosis refers only to the division of the nucleus. The division of the cell's cytoplasm, which follows mitosis, is accomplished by cytokinesis. This process may actually begin before telophase ends. In different organisms, cytokinesis may be accomplished in different ways. In animal cells, a cleavage furrow made of actin and its motor protein myosin II constricts the middle of the cell. In plants, a structure called the phragmoplast forms at the equator of the spindles where it directs the formation of a new cell wall.

Meiosis: Heredity and survival

In sexually reproducing organisms, the *germ cells* that give rise to eggs and sperm arise by a division that is distinct from the one followed by *somatic cells*. This division is termed as meiosis that consists of two nuclear divisions that reduce the number of chromosomes to the haploid number in preparation for sexual reproduction. Although the nucleus divides twice during meiosis, the DNA is replicated only once.

The first meiotic division reduces the chromosome number: Meiosis I is characterised by two unique features (Fig. 1.8). First, the homologous chromosomes pair along their entire length, a feature distinct from mitosis. Second, the homologous chromosomes separate after metaphase I. The

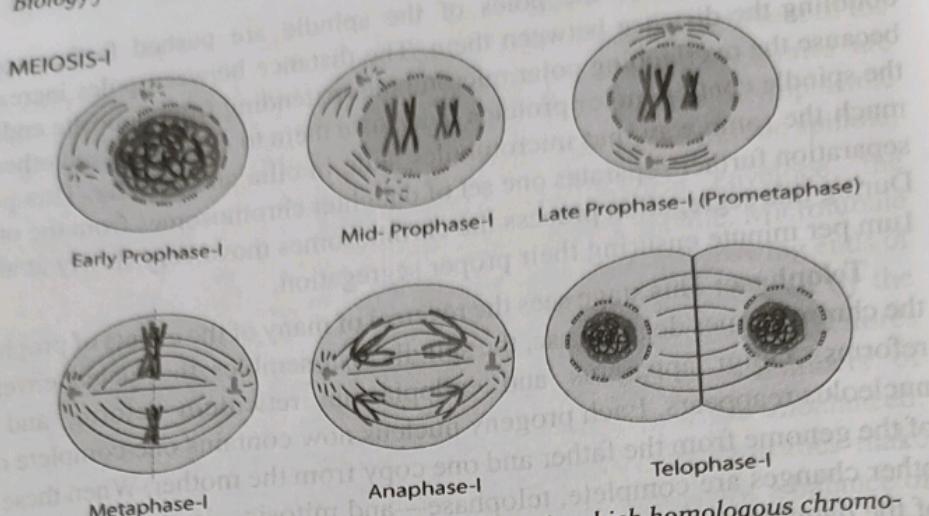


Fig. 1.8 Different phases of meiotic cell division I in which homologous chromosome pairs align along their entire length and remain until metaphase II of meiotic division II.

individual chromosomes, each consisting of two sister chromatids, remain intact until the end of metaphase II in the second meiotic division.

Like mitosis, meiosis I is preceded by an interphase with an S phase during which each chromosome is replicated. As a result, each chromosome consists of two sister chromatids, held together by cohesin proteins. Meiosis I begins with a long prophase I during which the chromosomes change markedly. The homologous chromosomes pair by adhering along their lengths, a process called synapsis. This process lasts from prophase I to the end of metaphase I. By the time chromosomes can be clearly seen under light microscope, the two homologs are already tightly joined. This joining begins at the centromeres and is mediated by recognition of homologous DNA sequences on homologous chromosomes. In addition, a special group of proteins may form a scaffold called the synaptonemal complex, which runs lengthwise along the homologous chromosomes and appears to join them together.

The four chromatids of each pair of homologous chromosomes form what is called a tetrad, or bivalent. In other words, a tetrad consists of four chromatids, two each from two homologous chromosomes. For example, there are 46 chromosomes in a human diploid cell at the beginning of meiosis, so there are 23 homologous pairs of chromosomes, each with two chromatids (that is, 23 tetrads), for a total of 92 chromatids during prophase I. Throughout prophase I and metaphase I, the chromatin continues to coil and compact, so

that the chromosomes they are held together. Cohesins are and are calle

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that the chromosomes appear ever thicker. At a certain point, the homologous chromosomes seem to repel each other, especially near the centromeres, but they are held together by physical attachments mediated by cohesins. These cohesins are different from the ones holding the two sister chromatids together. Regions having these attachments take on an X-shaped appearance and are called chiasmata.

A chiasma reflects an exchange of genetic material between nonsister chromatids on homologous chromosomes—what geneticists call crossing over. The chromosomes begin exchanging material shortly after synapsis begins, but chiasmata do not become visible until later, when the homologs are repelling each other. Crossing over increases genetic variation among the products of meiosis by reshuffling genetic information among the homologous pairs. There seems to be plenty of time for the complicated events of prophase I to occur. Whereas mitotic prophase is usually measured in minutes, and all of mitosis seldom takes more than an hour or two, meiosis can take much longer. In human males, the cells in the testes that undergo meiosis take about a week for prophase I and about a month for the entire meiotic cycle. In the cells that will become eggs, prophase I begins long before a woman's birth, during her early fetal development, and ends as much as decades later, during the monthly ovarian cycle. Prophase I is followed by prometaphase I, during which the nuclear envelope and the nucleoli disaggregate.

A spindle forms, and microtubules become attached to the kinetochores of the chromosomes. In meiosis I, the kinetochores of both chromatids in each chromosome become attached to the same half-spindle. Thus the entire chromosome, consisting of two chromatids, will migrate to one pole. There is a randomness in the pairing of homologous chromosome pair to each half-spindle, and the migration to the pole. By metaphase I, all the chromosomes have moved to the equatorial plate. Up to this point, homologous pairs are held together by chiasmata. The homologous chromosomes separate in anaphase I, when the individual chromosomes, each still consisting of two chromatids, are pulled to the poles, with one homolog of a pair going to one pole and the other homolog going to the opposite pole. Each of the two daughter nuclei from this division thus contains only one set of chromosomes, not the two sets that were present in the original diploid nucleus. However, because they consist of two chromatids rather than just one, each of these chromosomes has twice the mass that a chromosome at the end of a mitotic division.

In some organisms, there is a telophase I, with the reappearance of the nuclear envelopes. When there is a telophase I, it is followed by an interphase,

called interkinesis, similar to the mitotic interphase. During interkinesis the chromatin is partially uncoiled; however, there is no replication of the genetic material, because each chromosome already consists of two chromatids. Furthermore, the sister chromatids in interkinesis are generally not genetically identical, because crossing over in prophase I has reshuffled genetic material between the maternal and paternal chromosomes. In other organisms, the chromosomes move directly into the second meiotic division.

The second meiotic division separates the chromatids: Meiosis II is similar to mitosis in many ways (Fig. 1.9). In each nucleus produced by meiosis I, the chromosomes line up at equatorial plate at metaphase II. The centromeres of the sister chromatids separate because of cohesin breakdown and the daughter chromosomes move to the poles in anaphase II.

The result of meiosis is four nuclei; each nucleus is haploid and has a single set of unreplicated chromosomes that differs from other such sets in its exact genetic composition. The differences among the haploid nuclei result from crossing over during prophase I and from the random segregation of homologous chromosomes during anaphase I.

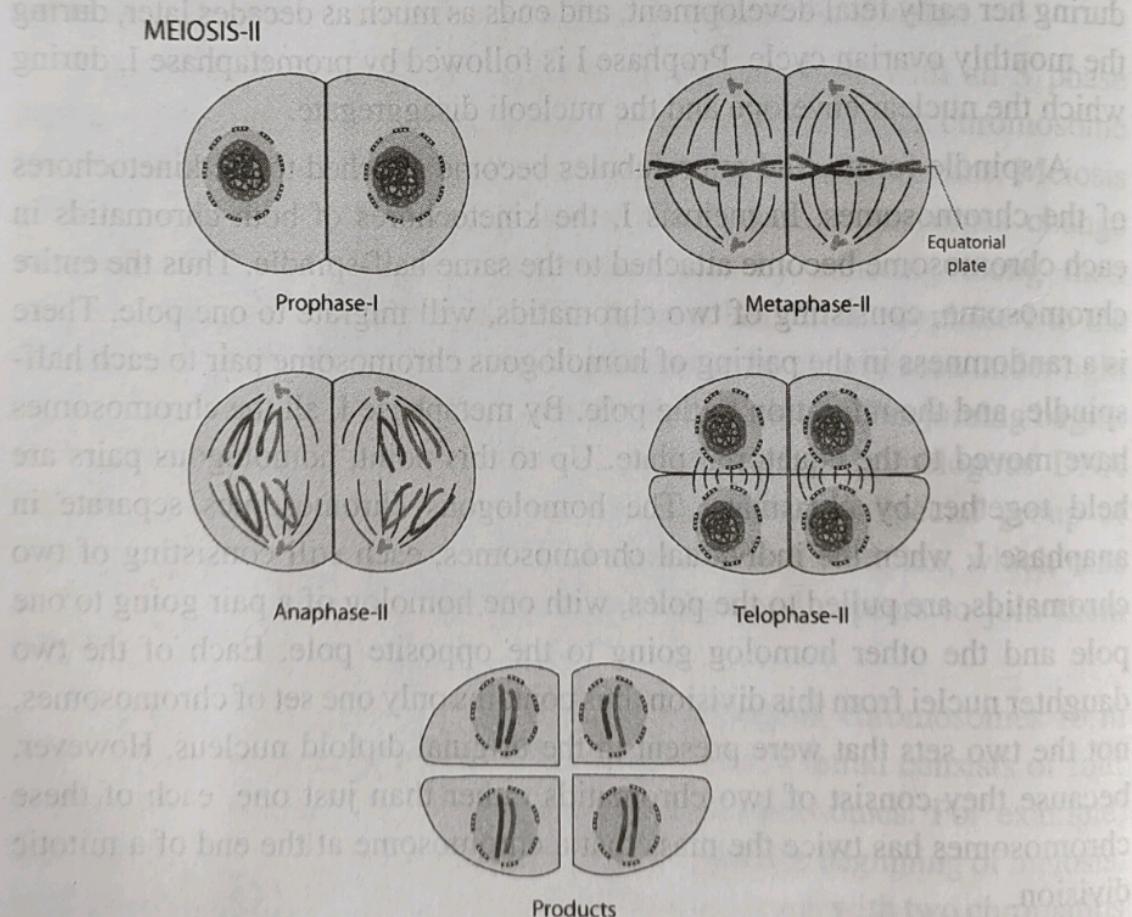


Fig. 1.9 Meiotic division II yields four cells consisting of haploid number of chromosomes.

1.9 CELL DIFFERENTIATION

Differentiation is the biological process whereby an unspecialized cell acquires the properties of a specialized cell (e.g., stem cells as described in chapter 2). It defines the specific structures and functions of a cell (Fig. 1.10). Mitosis produces daughter cells that are genetically identical but still the cells of multicellular organism are obviously not all identical in structures or functions. This is because of the regulation of the gene expression of various parts of the genome. The regulation of gene expression starts from the embryo level. When the embryo consists of only a few cells, each cell has the potential to develop in many different ways. As development proceeds, the possibilities available to individual cells gradually narrow, until each cell's fate is fully determined and the cell has differentiated.

Differentiated cells are different from one another starting from their protein products to morphology. So the main cause is differential gene expression for the cellular differentiation process to happen. The fertilized egg or zygote has the ability to give rise to every type of cell in the adult body and hence, referred to as *totipotent*. The genomes of these cells carry instructions for all of the structures and the functions that will arise throughout

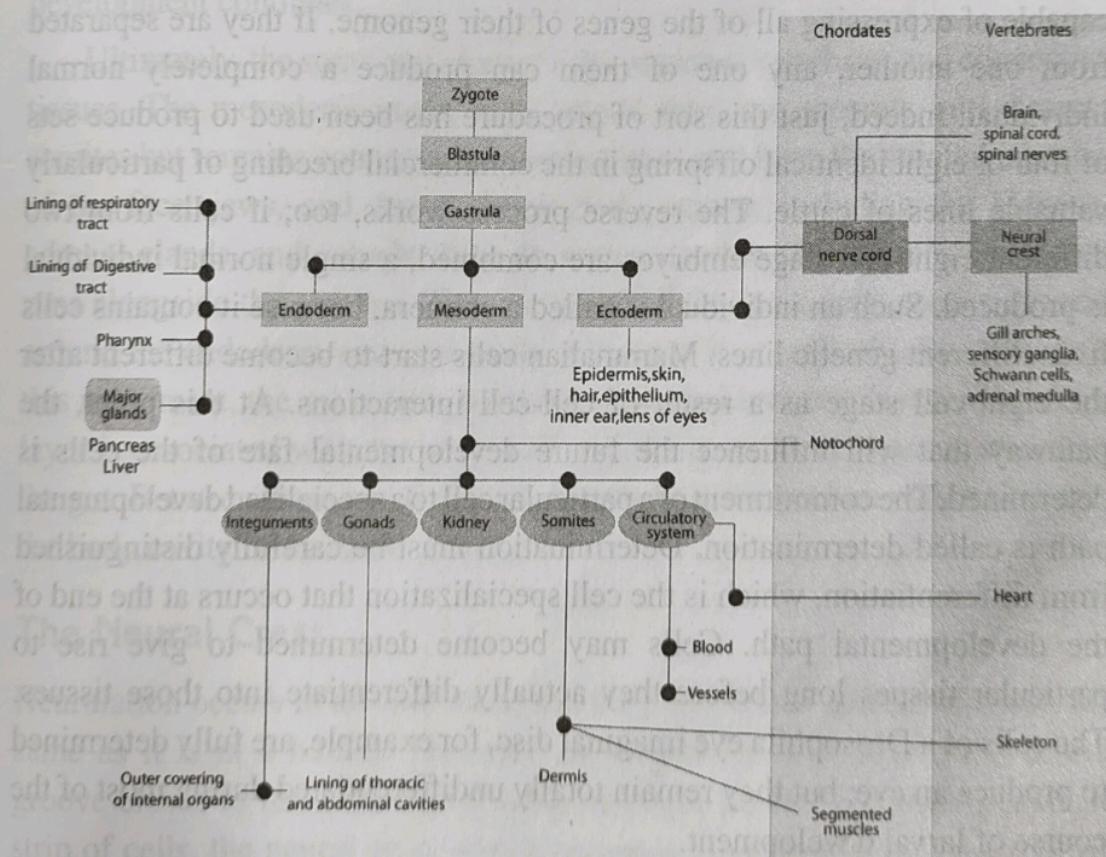


Fig. 1.10 Development of various cellular and organ structures of the body from cellular differentiation during the fetal maturation.

the life cycle. Later in the development of animals, the cellular descendants of the zygote lose their totipotency and become determined cells, then differentiate into specific types of cells.

Changes in the genome during differentiation: Changes are of two types, either reversible or irreversible. Differentiation is irreversible in certain types of cells like mammalian RBC. It loses its nucleus during development and become specialized for oxygen uptake and transportation.

Genomic equivalence: No information is lost from the nucleus of cells as they pass through the early stages of embryonic developments.

The zygotic cells are regarded to be totipotent as they hold the ability to generate the whole organism. As the cell divides by responding to internal and external stimuli, its potency decreases. The cells at the blastula stage are then referred to as *pluripotent*, as they can generate all the cell types except the trophoectoderm. Further upon division, they become more restricted and give rise to *multipotent* stem cells like hematopoietic stem cell that can generate different blood cell types.

The mammalian egg is symmetrical in its contents as well as in shape, so that all of the cells of an early blastoderm are equivalent up to the eight-cell stage. The cells are said to be totipotent, meaning that they are potentially capable of expressing all of the genes of their genome. If they are separated from one another, any one of them can produce a completely normal individual. Indeed, just this sort of procedure has been used to produce sets of four or eight identical offspring in the commercial breeding of particularly valuable lines of cattle. The reverse process works, too; if cells from two different eight-cell-stage embryos are combined, a single normal individual is produced. Such an individual is called a chimera, because it contains cells from different genetic lines. Mammalian cells start to become different after the eight-cell stage as a result of cell-cell interactions. At this point, the pathway that will influence the future developmental fate of the cells is determined. The commitment of a particular cell to a specialized developmental path is called determination. Determination must be carefully distinguished from differentiation, which is the cell specialization that occurs at the end of the developmental path. Cells may become determined to give rise to particular tissues long before they actually differentiate into those tissues. The cells of a Drosophila eye imaginal disc, for example, are fully determined to produce an eye, but they remain totally undifferentiated during most of the course of larval development.

After the development of three primary cell layers from the zygote, their transformation into body's tissue and organs starts. The process of tissue

differentiation begins with the formation of two morphological features found only in chordates, the notochord and the hollow dorsal nerve cord. This development of the dorsal nerve cord is called neurulation.

The notochord is first visible soon after gastrulation is complete, forming from mesoderm along the dorsal midline of the embryo. It is a flexible rod located along the dorsal midline in the embryos of all chordates, although its function is replaced by the vertebral column when it develops from mesoderm in the vertebrates. After the notochord has been laid down, a layer of ectodermal cells situated above the notochord invaginates, forming a long crease, the neural groove, down the long axis of the embryo. The edges of the neural groove then move toward each other and fuse, creating a long hollow cylinder, the neural tube, which runs beneath the surface of the embryo's back. The neural tube later differentiates into the spinal cord and brain. The dorsal lip of the blastopore induces the formation of a notochord, and the presence of the notochord induces the overlying ectoderm to differentiate into the neural tube. While the neural tube is forming from ectoderm, the rest of the basic architecture of the body is being determined rapidly by changes in the mesoderm. On either side of the developing notochord, segmented blocks of mesoderm tissue called somites form; more somites are added as development continues.

Ultimately, the somites give rise to the muscles, vertebrae, and connective tissues. The mesoderm in the head region does not separate into discrete somites but remains connected as somitomeres and form the striated muscles of the face, jaws, and throat. Some body organs, including the kidneys, adrenal glands, and gonads, develop within another strip of mesoderm that runs alongside the somites. The remainder of the mesoderm moves out and around the endoderm and eventually surrounds it completely. As a result of this movement, the mesoderm becomes separated into two layers. The outer layer is associated with the body wall and the inner layer is associated with the gut. Between these two layers of mesoderm is the coelom which becomes the body cavity of the adult.

The Neural Crest

Neurulation occurs in all chordates, and the process in a lancelet is much the same as it is in a human. However, in vertebrates, just before the neural groove closes to form the neural tube, its edges pinch off, forming a small strip of cells, the neural crest, which becomes incorporated into the roof of the neural tube. The cells of the neural crest later move to the sides of the developing embryo. The appearance of the neural crest was a key event in the

evolution of the vertebrates because neural crest cells, after migrating to different parts of the embryo, ultimately develop into the structures characteristic of (though not necessarily unique to) the vertebrate body.

The differentiation of neural crest cells depends on their location. At the anterior end of the embryo, they merge with the anterior portion of the brain, the forebrain. Nearby clusters of ectodermal cells associated with the neural crest cells thicken into placodes, which are distinct from neural crest cells although they arise from similar cellular interactions. Placodes subsequently develop into parts of the sense organs in the head. The neural crest and associated placodes exist in two lateral strips, which is why the vertebrate sense organs that develop from them are paired. Neural crest cells located in more posterior positions have very different developmental fates. These cells migrate away from the neural tube to other locations in the head and trunk, where they form connections between the neural tube and the surrounding tissues. The migration of neural crest cells is unique in that it is not simply a change in the relative positions of cells, such as that seen in gastrulation. Instead, neural crest cells actually pass through other tissues.

Some neural crest cells migrate ventrally toward the notochord and form sensory neurons in the dorsal root ganglia. Others become specialized as Schwann cells, which insulate nerve fibres and permit the rapid conduction of nerve impulses. Still others form the autonomic ganglia and the adrenal medulla. Cells in the adrenal medulla secrete epinephrine when stimulated by the sympathetic division of the autonomic nervous system during the fight-or-flight reaction. The similarity in the chemical nature of the hormone epinephrine and the neurotransmitter norepinephrine, released by sympathetic neurons, is understandable— both adrenal medullary cells and sympathetic neurons are derived from the neural crest.

A variety of sense organs develop from the placodes. Included among them are the olfactory (smell) and lateral line (primitive hearing) organs. Neural crest cells contribute to tooth development and to some of the facial and cranial bones of the skull. Thus, differentiation of cells lead to the formation of the whole living organism.

Chapter highlights

- Living organisms are classified into 5 kingdoms, Monera, Protista, Fungi, Plantae, and Animalia. Prokaryotes do not have nucleus while eukaryotic cells have a proper nucleus.
- Cell theory states that all living organisms are made up of cells which are the fundamental units of life and the new cells arise by cell division.

- Cells have multiple organelles such as cell membrane, nucleus, mitochondria, endoplasmic reticulum, Golgi apparatus, cytoskeleton, centrioles, lysosomes and vacuoles performing multifarious functions such as metabolism, differentiation, and division. Plant cells have additional features including chloroplasts and cell wall.
- Proteins are synthesized with the input from DNA transcribed to mRNA and subsequent translation process. Proteins have several functions within the cell and the body of the living organism.
- The structure of proteins include primary, secondary, tertiary, and quaternary. Primary structure is the amino acid sequence of the protein. Secondary structures of the protein are alpha helix and beta strand. Tertiary structure is the three dimensional structure of the protein in which there is folding of alpha helix and beta strands. Quaternary structure is composed of several protein molecules or polypeptide chains of amino acids.
- Cell metabolism is the process within the cell where several chemical reactions involving carbohydrates, proteins, and fats occur to generate cellular energy.
- Homeostasis is the maintenance of equilibrium within the internal environment of the living organisms to adapt to changes in the external environment.
- Growth and reproduction are critical to propagation of life on Earth. Prokaryotic cells reproduce by binary fission whereas eukaryotic cells have evolved exquisite mechanisms such as mitosis and meiosis for cell division. Meiosis is exclusively for germ cells (sperms and ova) whereas mitosis is observed in somatic cells.
- Cell differentiation is a process by which unspecialized cells become specialized cells. Unspecialized stem cells differentiate into specific set of cells such as neuron, muscle fiber, liver cells etc through various stimuli.

to facilitate this process by developing technologies involving the expertise of biologists, chemists, engineers, and mathematicians. The high-throughput machine, DNA sequencer, was crucial to the success of the genome project. GRAIL (Gene Recognition and Assembly Internet Link) was one of the initial computer programs for identifying genes in DNA and DNA sequence analysis. The automation process of DNA sequencing led to cutting costs and hastening the DNA sequencing process.

2.5 STEM CELLS AND THEIR APPLICATIONS

Stem cells are unspecialized cells having the ability of self-renewal through cell division for long period. These stem cells have the potential to develop into specialized cells such as blood cells, muscle cells, neurons, myocytes, bone cells, hepatocytes etc.

Importance of stem cells

Stem cells can replicate indefinitely so they are serving as internal repair system for body to replace dead or damaged cells.

When a stem cell divides, one of the daughter cells has to remain unspecialized (like a parent stem cell) and the another daughter cell has become specialized cell type such as brain cell, blood cell under certain physiological condition (Fig. 2.9).

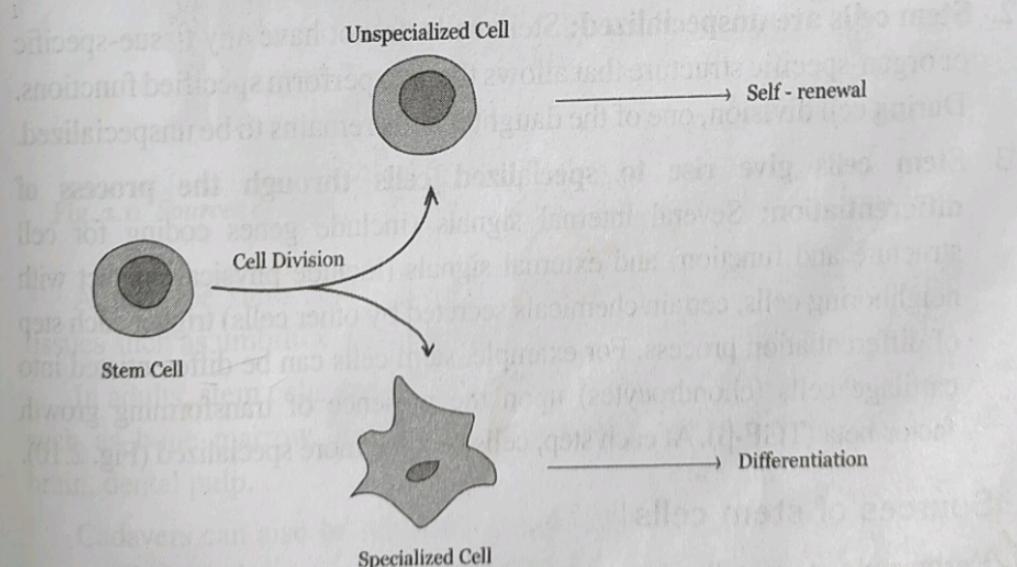


Fig. 2.9 Unique properties of stem cells

This is a promising area to know how an organism develops from a single cell with different types of potential properties. Since stem cells are having unique regenerative abilities, they offer new potentials for treatment of various diseases those results from dysfunction of a single type of cell.

Unique properties of stem cells

Stem cells are having three unique properties (Fig. 2.10). They are:

- Self-renewal:** Stem cells are immortal, unlimited in number and are capable of replicating/proliferating for a long period. They have potential to divide and maintain long term self-renewal.

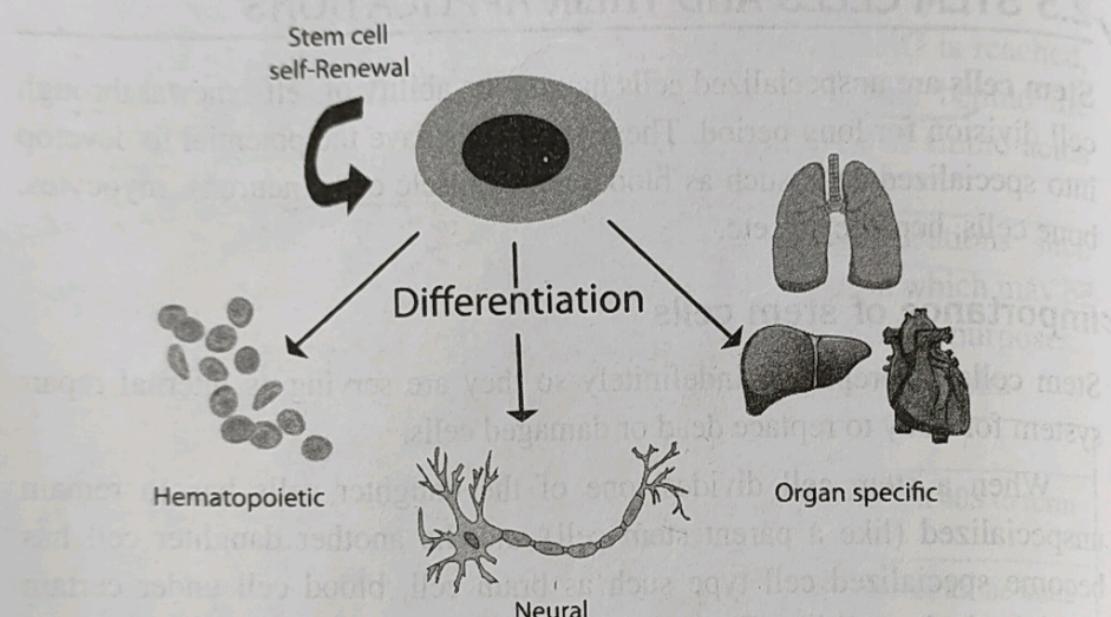


Fig. 2.10 Differentiation of stem cells into other types of cells

- Stem cells are unspecialized:** Stem cells do not have any tissue-specific or organ-specific structure that allows them to perform specified functions. During cell division, one of the daughter cells remains to be unspecialized.
- Stem cells give rise to specialized cells through the process of differentiation:** Several internal signals (include genes coding for cell structure and function) and external signals (include physical contact with neighboring cells, certain chemicals secreted by other cells) trigger each step of differentiation process. For example, stem cells can be differentiated into cartilage cells (chondrocytes) upon the presence of transforming growth factor-beta (TGF- β). At each step, cells become more specialized (Fig. 2.10).

Sources of stem cells

Embryonic stem cells: In embryogenesis, eggs are fertilized by sperm *in vitro* which is known as *in vitro* fertilization. As a result, zygote is developed

which undergoes series of cell division, and produces blastocyst. In early blastocyst stage (5 - 7 days), a group of approximately 30 cells called inner cell mass (ICM) is surrounded by an outer layer. The outer layer is called as trophoblast which provides nutrient to the embryo and develops into a large part of the placenta. ICM can give rise to all types of cells or tissues except trophoblast.

Adult stem cells: Adult stem cells are tissue-specific, undifferentiated cells found in differentiated tissues or organs including brain, bone marrow, peripheral blood, blood vessels, skeletal muscle, skin, teeth, heart, gut, liver, ovarian epithelium, and testes (Fig. 2.11). Their main role is to play in tissue repair and tissue maintenance.

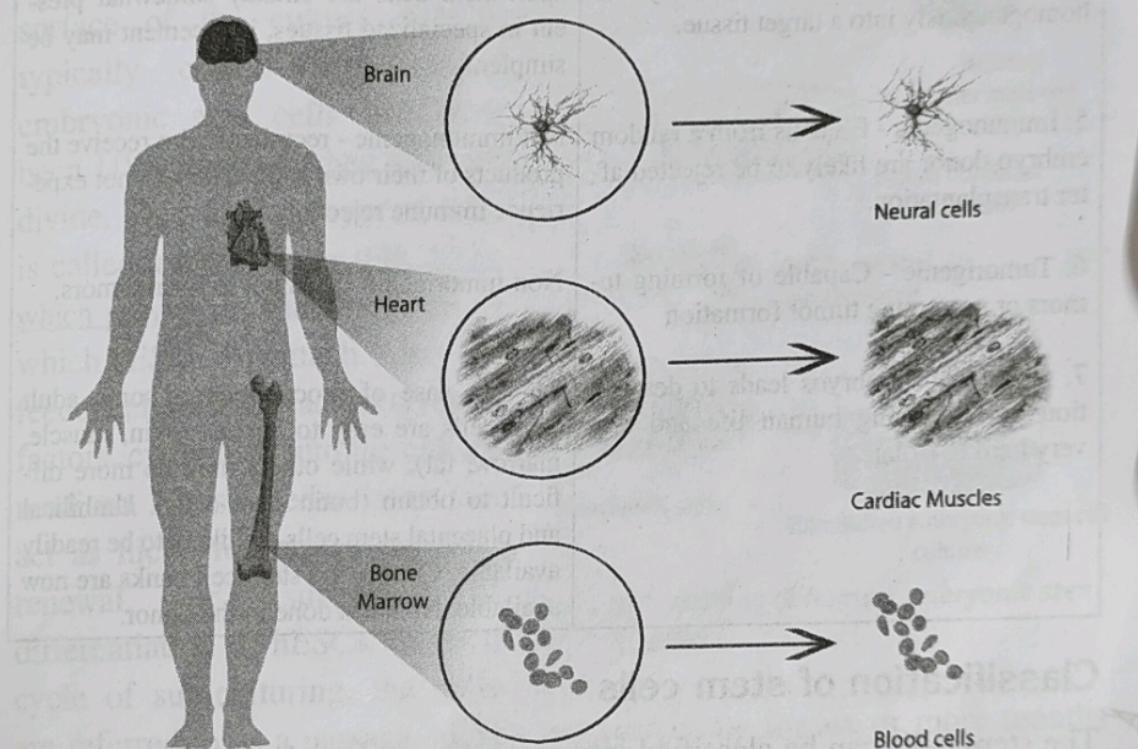


Fig. 2.11 Sources of adult stem cells

Adult type stem cells can be derived from various pregnancy-related tissues such as umbilical cords, placentas, and amniotic fluids.

In adults, stem cells are present within various tissues and organ systems such as bone marrow, liver, epidermis, retina, skeletal muscle, intestine, brain, dental pulp.

Cadavers can also be a source of adult stem cells. For example, neural stem cells have been removed from specific areas in post-mortem human brains as late as 20 hours following death.

Differentiation between embryonic and adult stem cells

Embryonic stem (ES) cells	Adult stem cells
1. Flexible- i.e., ES cells appear to have the potential to make almost all types of cells except trophoblast.	Less flexible- i.e., difficult to reprogram to form other tissue types.
2. Immortal- one ES cell line can potentially provide an endless supply of cells with defined characteristics.	Mortal with finite life time when cultured.
3. Availability - embryos can be obtained from in vitro fertilization and nuclear transplantation source.	Limited quantity - can sometimes be difficult to purify and obtain in large numbers.
4. Difficult to differentiate uniformly and homogeneously into a target tissue.	adult stem cells are already somewhat present in specialized tissues, inducement may be simpler.
5. Immunogenic - ES cells from a random embryo donor are likely to be rejected after transplantation.	Not immunogenic - recipients who receive the products of their own stem cells will not experience immune rejection.
6. Tumorigenic - Capable of forming tumors or promoting tumor formation	Non-tumorigenic - tend not to form tumors.
7. Isolation of embryos leads to destruction of developing human life and also very hard to isolate	Relative ease of procurement - some adult stem cells are easy to harvest (skin, muscle, marrow, fat), while others may be more difficult to obtain (brain stem cells). Umbilical and placental stem cells are likely to be readily available. Cord blood stem cell banks are now available. No harm done to the donor.

Classification of stem cells

The stem cells can be classified into several types based on their potency or plasticity. Potency or plasticity can be defined as the ability of the stem cell from one tissue to generate the specialized cell type(s) of another tissue.

Unipotent stem cells can form only one type of specialized cell type. For example, brain stem cells differentiate into only brain cells.

Multipotent stem cells can form multiple types of cells. For example, mesenchymal stem cells derived from bone marrow can differentiate into osteoblasts, adipocytes, chondrocytes, myocytes, and neuron-like cells.

Pluripotent stem cells can differentiate into almost all types of cell lineages. For example, cells (ICM) from blastocyst can differentiate into three germ cell layers (ectoderm, mesoderm and endoderm) but do not contribute for trophoblast.

Totipotent stem cells can differentiate into all cell types including cells of the trophoectoderm lineage. For example, fertilized egg and early cleavage stage of blastomeres.

Human embryonic stem cell isolation and culturing

Cell culture is a process of growing cells in the laboratory conditions. For generating human embryonic stem cells (hESCs), cells (ICM) from blastocyst are transferred into a culture dish containing a nutrient broth known as culture medium. The cells attach, proliferate and spread on the surface of the dish. The inner surface of the culture dish is typically coated with mouse embryonic skin cells that have been UV treated so they will not divide. This coating layer of cells is called a feeder layer (Fig. 2.12), which provides a sticky surface to which hESCs can attach. Also, the feeder cells release factors (growth factors, cytokines) into the culture medium. Thus, feeder layer can act as niche for promoting self-renewal or suppress of differentiation of hESCs. In each cycle of sub-culturing, the cells are referred to as a passage. hESCs can proliferate for six or more months without differentiation but can also maintain their pluripotent properties.

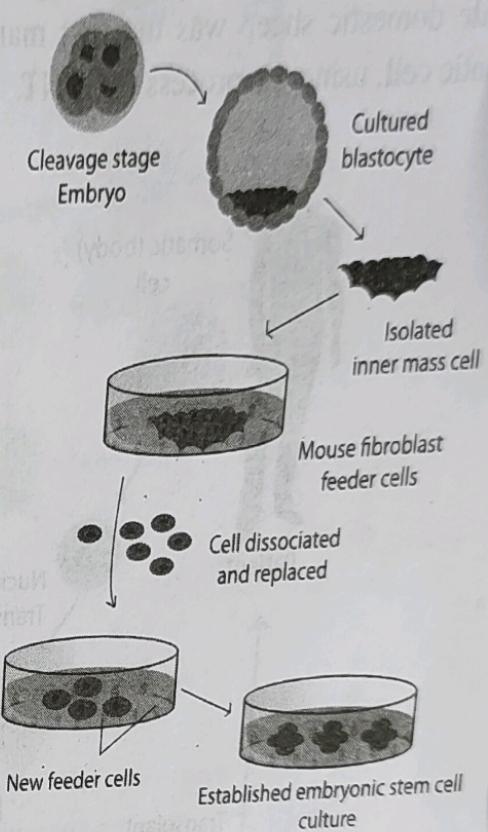
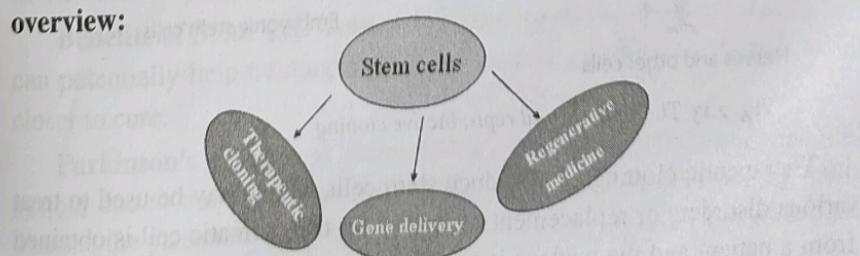


Fig. 2.12 Culturing of human embryonic stem cells

Applications:

Stem cell technology has a broad range of applications; here is an overview:



Therapeutic cloning

Somatic cell nuclear transfer (SCNT) involves extracting the nucleus of a cell and putting the nucleus into an egg which has been enucleated. Then, the egg is allowed to divide and grow. In therapeutic cloning, the growing egg is used as a source of stem cells, which are undifferentiated cells that can grow into a wide variety of different types of cells. In reproductive cloning, the egg is implanted into surrogate mother to grow a baby (Fig. 2.13). Dolly, a first female domestic sheep was the first mammal to be cloned from an adult somatic cell, using the process of SCNT.

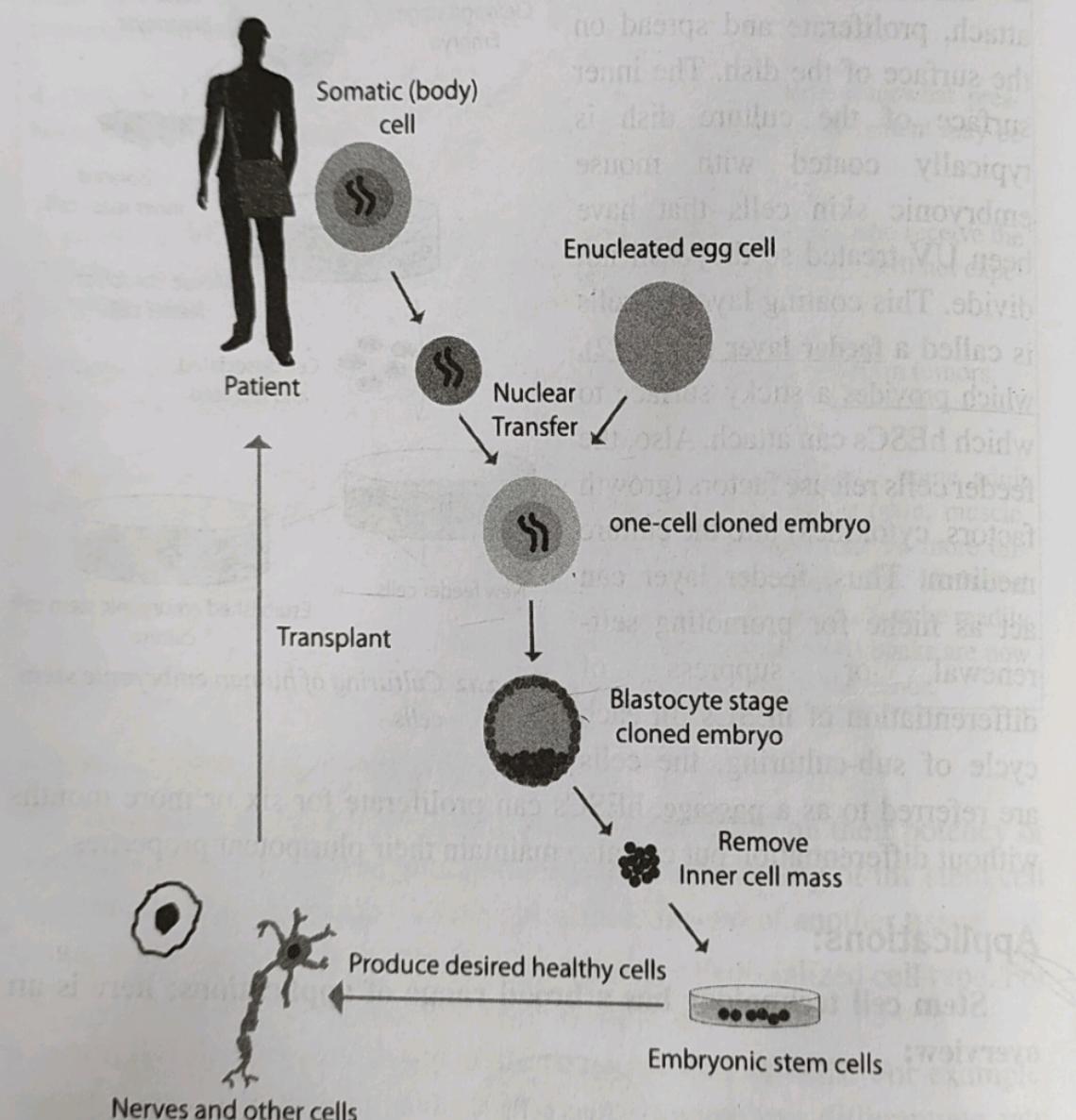


Fig. 2.13 Therapeutic and reproductive cloning

Therapeutic cloning can produce stem cells which may be used to treat various disorders or replacement of organs. In this, somatic cell is obtained from a patient and the nucleus is transferred into enucleated egg cell which

will develop into an embryo. At blastocyst stage of the embryo, the inner cell mass is isolated and cultured to differentiate into particular cell type which will be replaced into the patients as a transplant (Fig. 2.14).

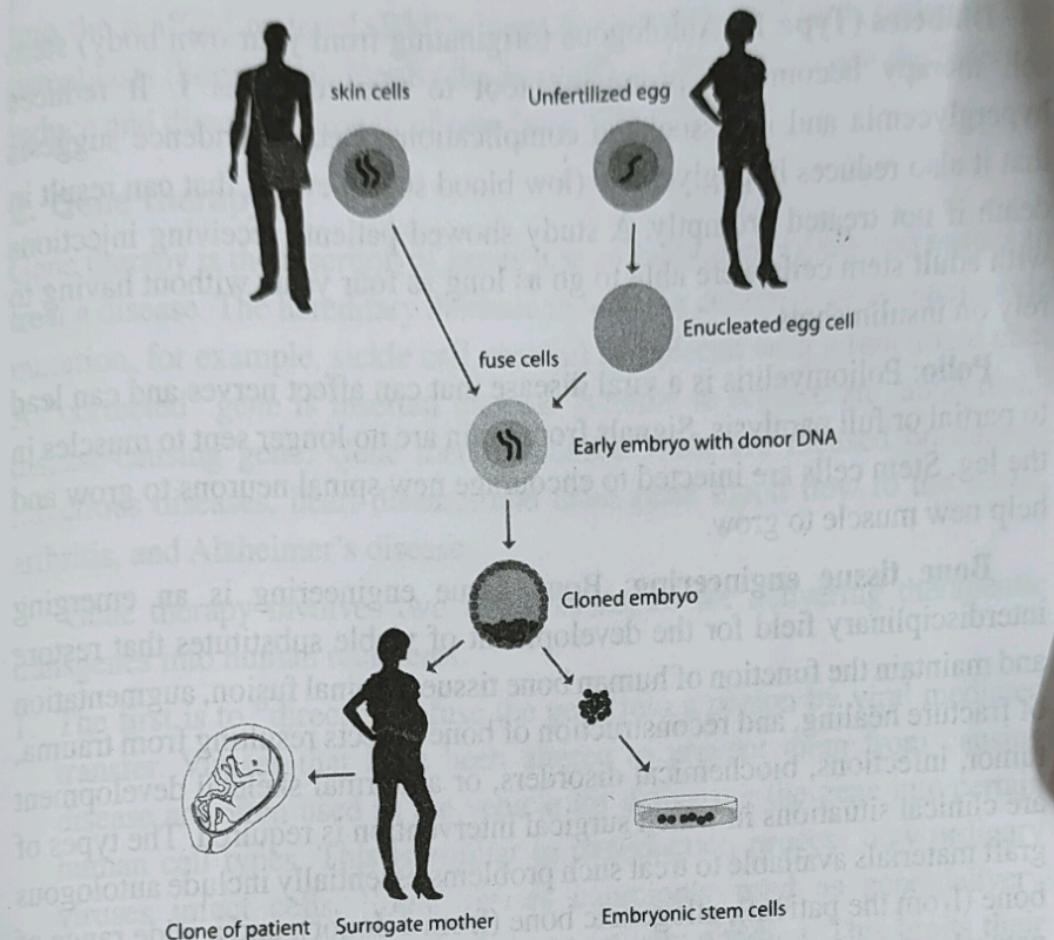


Fig. 2.14 Theoretical concept of therapeutic cloning

Regenerative medicine

Regenerative medicine is the process of creating functional tissues to repair or replace tissue or organ function lost due to damage, or congenital defects. This field holds the promise of regenerating damaged tissues and organs in the body by stimulating previously irreparable organs to heal themselves. Regenerative medicine also empowers scientists to grow tissues and organs in the laboratory and safely implant them when the body cannot heal itself.

Benefits of Stem Cell Research in curing diseases: Stem cell research can potentially help treating a range of medical problems. It could lead us closer to cure:

Parkinson's disease: A degenerative disorder of the central nervous system due to the lack of a brain chemical called dopamine. To cure this disease, the patients are injected with stem cells to multiply nerve cells that release dopamine.

Muscular dystrophy is a group of inherited disorders that involve muscle weakness and loss of muscle tissue, which get worse over time due to weakened heart and lung muscles. Patients are given injections of healthy stem cells and they are able to walk faster.

Diabetes (Type 1): Autologous (originating from your own body) stem cell therapy becomes a promising tool to treat diabetes I. It reduces hyperglycemia and its associated complications. Recent evidence suggests that it also reduces hypoglycemic (low blood sugar) events that can result in death if not treated promptly. A study showed patients receiving injections with adult stem cells were able to go as long as four years without having to rely on insulin shots.

Polio: Poliomyelitis is a viral disease that can affect nerves and can lead to partial or full paralysis. Signals from brain are no longer sent to muscles in the leg. Stem cells are injected to encourage new spinal neurons to grow and help new muscle to grow.

Bone tissue engineering: Bone tissue engineering is an emerging interdisciplinary field for the development of viable substitutes that restore and maintain the function of human bone tissues. Spinal fusion, augmentation of fracture healing, and reconstruction of bone defects resulting from trauma, tumor, infections, biochemical disorders, or abnormal skeletal development are clinical situations in which surgical intervention is required. The types of graft materials available to treat such problems essentially include autologous bone (from the patient), allogeneic bone (from a donor), and a wide range of natural or synthetic biomaterials such as metals, ceramics, polymers, and composites. In one approach, mesenchymal stem cells are seeded on scaffolds (that provide structure and shape) along with signaling molecules. The goal is for the cells to attach to the scaffold, and thus resulting proliferation and

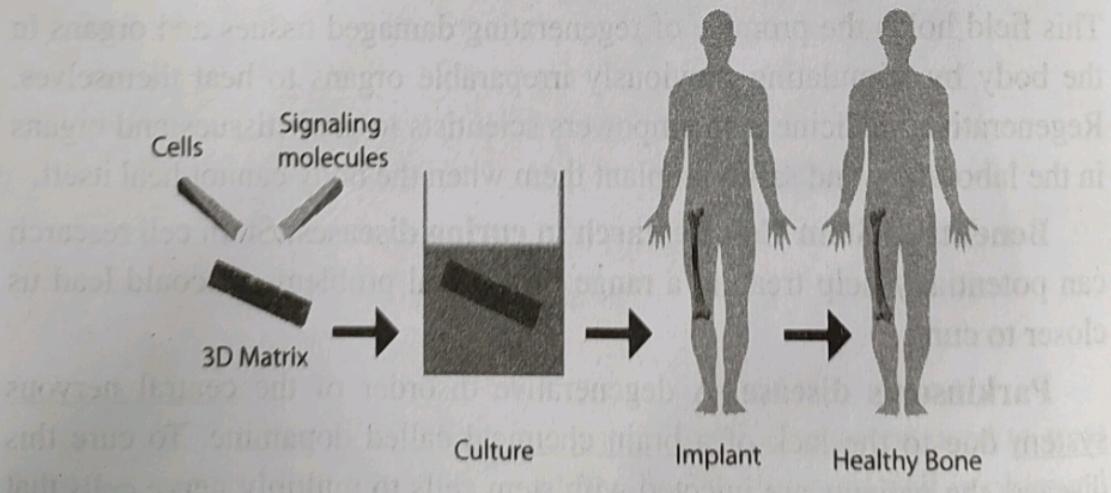


Fig. 2.15 Scaffolds-guided bone regeneration

differentiation of cells into normal, healthy bone. When bone grows, the scaffold degrades. At one stage there will be only bone and no more scaffold materials. The signaling molecules [for example, bone morphogenetic proteins (BMPs)] can also be adhered to the scaffold or incorporated directly into the scaffold material. BMPs promote mesenchymal stem cells towards osteoblasts (bone cells). Finally the scaffolds are implanted into the defect to induce and direct the growth of new bone (Fig. 2.15).

2. Gene therapy

Gene therapy is the insertion of genes into an individual's cells and tissues to treat a disease. The hereditary diseases in which a defective gene (nucleotide mutation, for example, sickle cell anemia) is replaced with a functional one. A "corrected" gene is inserted into the genome to replace an "abnormal," disease-causing gene. Gene therapy clinical trials are focused on cancer, infectious diseases, heart disease, and inadequate blood flow to the limbs, arthritis, and Alzheimer's disease.

Gene therapy involves two major strategies for delivering therapeutic transgenes into human recipients:

1. The first is to "directly" infuse the gene into a person by viral mediated transfer. Viruses that have been altered to prevent them from causing disease are often used as the vehicle for delivering the gene into certain human cell types. This is similar to transduction process how ordinary viruses infect cells. Some viruses commonly used as gene-delivery vehicles can only infect cells that are actively dividing. This limits their usefulness in treating diseases of the heart or brain, because these organs are largely composed of non-dividing cells.
2. The second strategy involves the use of living cells to deliver therapeutic transgenes into the body. In this method, the delivery cells often a type of stem cell, a lymphocyte, or a fibroblast, are removed from the body, and the therapeutic transgene is introduced into them via the vehicles. The genetically modified cells are tested and then allowed to grow and multiply and, finally, are infused back into the patient.

- A new computer vision technology has been developed to aid scientists investigating stem cells as to whether the dividing stem cell will further divide or become part of a future developing organ. It will be helpful in observing each and every stem cell and sort them into different categories.

- Cell density of stem cells in cell growth dishes determine further differentiation of these cells. To give a uniform density, electronic control of seeding density of stem cells have been achieved using thin electrode films of poly(3,4-ethylenedioxythiophene) (PEDOT); Tosylate.

Conclusions

Stem cells can now be artificially grown and transformed into specialized cell types with characteristics consistent with cells of various tissues. They can be taken from a variety of sources, including umbilical cord and bone marrow. Embryonic stem cell lines and autologous embryonic stem cells generated through therapeutic cloning have been proposed as promising candidates for future therapies. Adult stem cells are currently tested and used in medical therapies including tissue engineering. There are research and medical ethics associated with rules and regulations to be followed when stem cells are used for biomedical applications in human.

Chapter highlights

- The varieties of life on the Earth forming biodiversity are critical to sustenance of life on this planet. It can be genetic diversity, species diversity, and ecosystems diversity. Biodiversity is facing challenges and losses due to human population growth and their life style that may interfere and harm human way of life.
- All living and non-living beings are made up of atoms which then form molecules. The atoms within molecules are held by chemical bonds that are either weak or strong.
- In all living organisms, biochemical reactions called as metabolism occur that are essential for the survival of cells, structure, transport, cell signaling, cell division, etc.. Metabolism involves both anabolism and catabolism of biomacromolecules such as carbohydrates, lipids, proteins, and nucleic acids.
- Protein synthesis involves synthesis of proteins by the cells through the multi-step processes of transcription, post-transcriptional modification, translation and post-translational modifications.
- DNA replication is followed by messenger RNA (mRNA) production which carries the message of DNA from the nucleus to the cytoplasm. Transfer RNA (tRNA) carries the amino acids to ribosomal RNA (rRNA) to produce polypeptides according to the message on mRNA.

- Stem cells are unspecialized cells capable of developing into specialized cells such as neuron, liver cell, muscle fiber, etc. They can self-renew and differentiate into specialized cells. Embryonic and adult stem cells can be used for therapeutic cloning, gene therapy, and in regenerative medicine. Medical researchers believe that stem cells can be a source for curing a number of diseases afflicting human population.