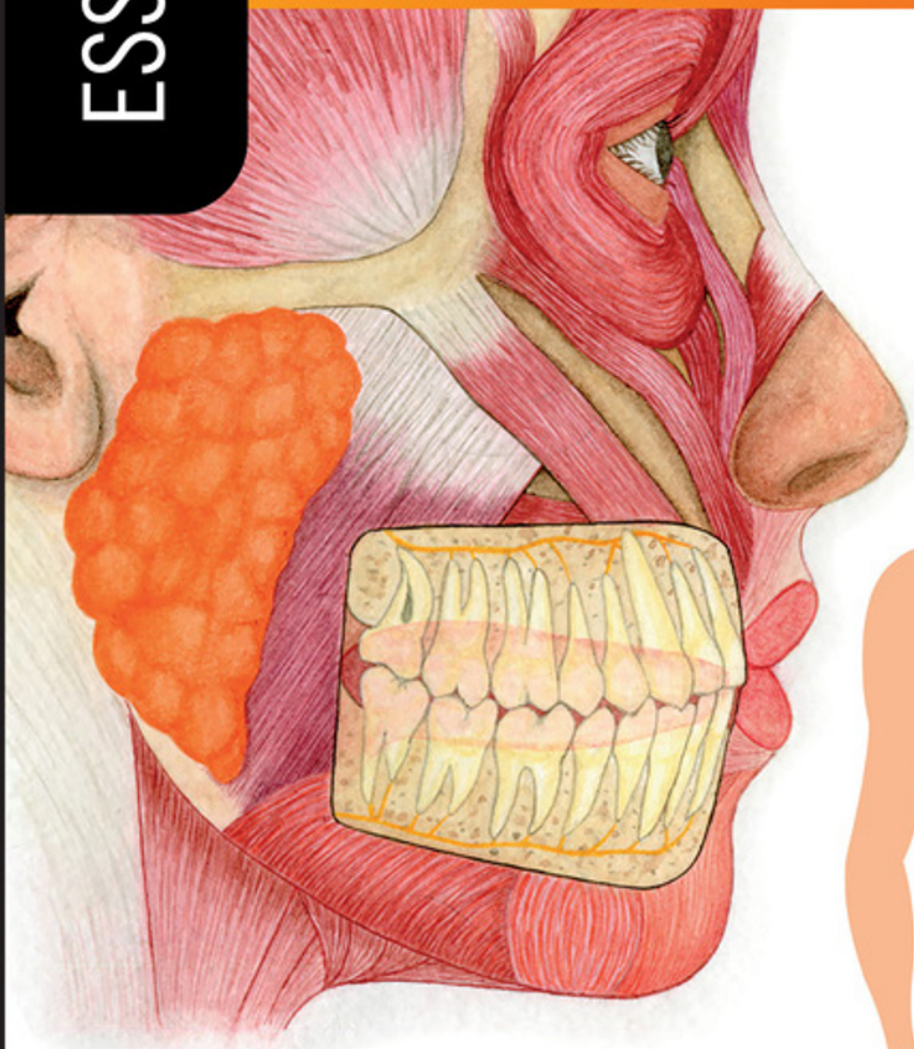
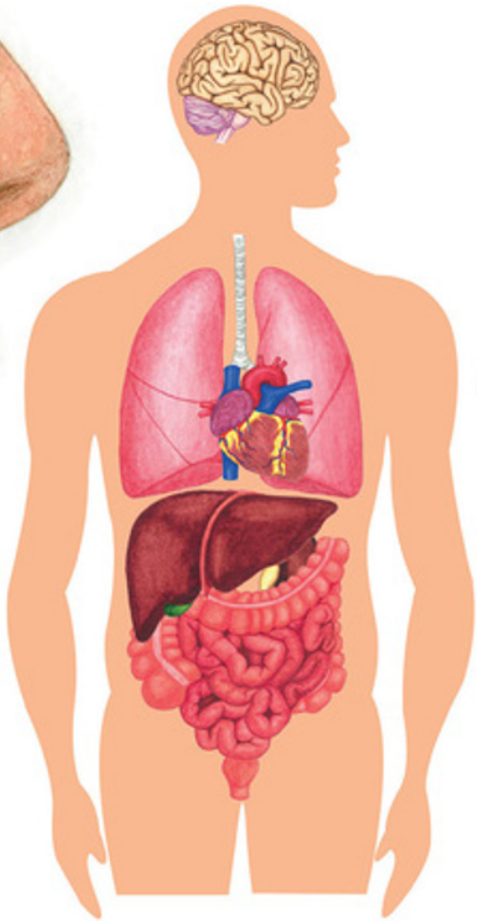
ESSENTIALS

ESSENTIAL PHYSIOLOGY FOR DENTAL STUDENTS

EDITED BY KAMRAN ALI
AND ELIZABETH PRABHAKAR





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Essential Physiology for Dental Students

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To my mother and father, who are my role models and taught me the core human values.

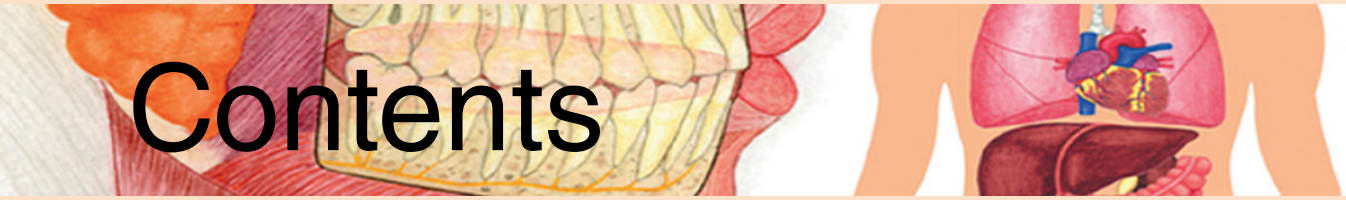
To my wife and children, for their extraordinary love and support.

Kamran Ali

Dedicated to the memory of my late father, who was an unending source of inspiration, strength, and wisdom and for shaping my intellect.

To my mother and the rest of my family, for their encouragement, love, and support.

Elizabeth Prabhakar



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Preface

We are delighted to present a book on medical physiology written exclusively for a dental audience. It is envisaged that the book will be used not only in the early years of dental courses but also for preparation of postgraduate examinations in dentistry. Moreover, dentists and dental care professionals may also benefit from it to refresh and update their knowledge of physiology.

Physiology is a complex and challenging subject, and traditionally the dental students have learnt it from standard medical textbooks with limited reference to dentistry. A concerted effort has been made to provide the relevance of each topic area to dentistry so that dental students are able to relate the subject to their own clinical practice. We have not only focused on physiology but also tried to assimilate relevant concepts of allied subjects to achieve integration with other basic and clinical subjects.

A wide selection of online self-assessment questions accompany this text, and readers can use this resource not only to prepare for relevant examinations but also as a drive for their learning. While every effort has been made to discuss core topic areas in physiology comprehensively, it is suggested that readers explore additional resources to further enhance their understanding of the subject. Recommendations for additional online and text resources are listed at the end of each chapter.

Finally, we hope this book will be a useful addition to existing resources for dental students. We would like to express our utmost gratitude to all the contributors for sharing their knowledge and expertise in the subject.

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- EMQs
- Glossary
- List of abbreviations
- PowerPoint slides of figures

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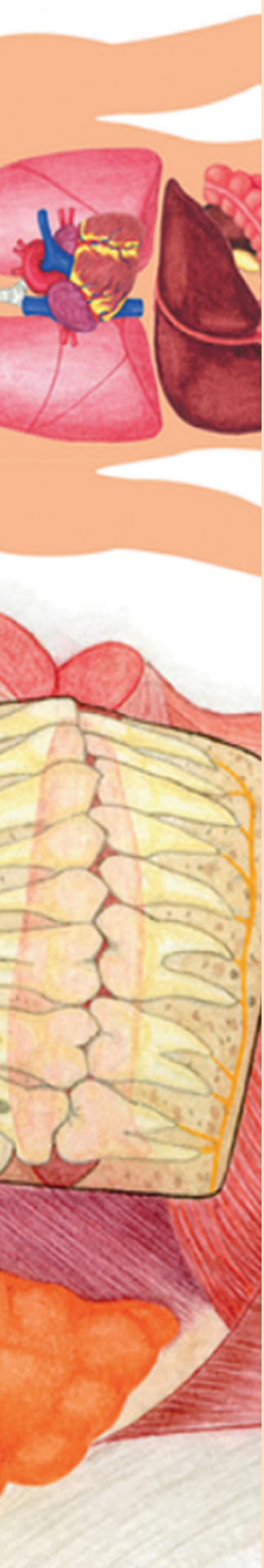
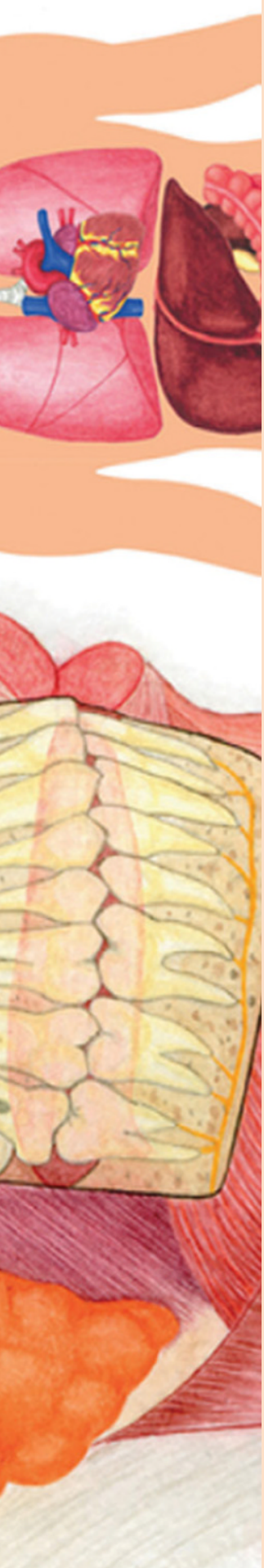


PART I

Introduction



CHAPTER 1

The Cell: Structure and Function

Vehid Salih and Kamran Ali

Key Topics

- Overview of different types of living organisms
- Organisation of the human body
- Components of human cells
- Regeneration and repair

Learning Objectives

To demonstrate an understanding of the:

- Differences between prokaryotes and eukaryotes
- Structure and functions of the cell organelles
- Relevance of regeneration and repair to oral and dental tissues
- Potential applications of stem cells

Introduction

A cell is the fundamental structural, functional, and biological unit of all known living organisms (except viruses). Individual cells range from 1 to 100 µm and are visible only under a microscope as the human eye is unable to see anything smaller than 100 µm. Living organisms are described as unicellular (microorganisms) or multicellular (e.g. plants and animals). Unicellular organisms are also classified as *prokaryotes* and multicellular organisms as *eukaryotes*. Prokaryotes lack a nucleus and cytoplasmic organelles and are represented by bacteria. Eukaryotes have a nucleus as well as cytoplasmic organelles and include microorganisms such as fungi, protozoa, algae as well as animals and humans. Nevertheless, both types possess a cell membrane and contain deoxyribonucleic acid (DNA). Viruses are neither prokaryotes nor eukaryotes as they lack characteristics of living organisms,

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apart from the ability to replicate. They are best regarded as obligate parasites as they can only replicate in living cells.

An adult human body comprises approximately 75–100 trillion cells, and more than 200 varieties of specialised cells have already been identified. The cells in the human body join to form tissues. Four basic human tissues include epithelium, connective tissue, nervous tissue, and muscle. Different tissues are grouped to form organs which in turn join to form various systems of the human body. The function of the human body is maintained by thousands of control systems at the level of cells, tissues, organs as well as systems allowing the body to maintain a constant internal environment, or *homeostasis*. Nevertheless, all physiological processes as well as disease mechanisms can be described at, and ascribed to, the cellular level. Cells are diverse and vary tremendously in their morphology and function. Figure 1.1 shows the main features of a typical human cell.

Components of the Human Cell

Cell Membrane

The cell membrane (plasmalemma) forms the outer boundary of the cell. The selective permeability of the cell membrane allows the cell to interact with its environment in a controlled way. The cell membrane is composed of a fluid combination of lipids (phospholipids and cholesterol), proteins and a small amount of carbohydrates. The basic structure of the cell membrane is formed by a phospholipid bilayer (Figure 1.2). The hydrophilic head region of the phospholipids faces the exterior (extracellular fluid or interstitial or tissue fluid) or aqueous interior (intracellular fluid or cytoplasmic face) of the cell, while the hydrophobic tails remain isolated. A variety of proteins attach to the surface of the phospholipid bilayer, while others traverse it partly or completely. The membrane proteins perform a variety of roles including: *channel proteins*, which facilitate passive transport across the cell membrane;

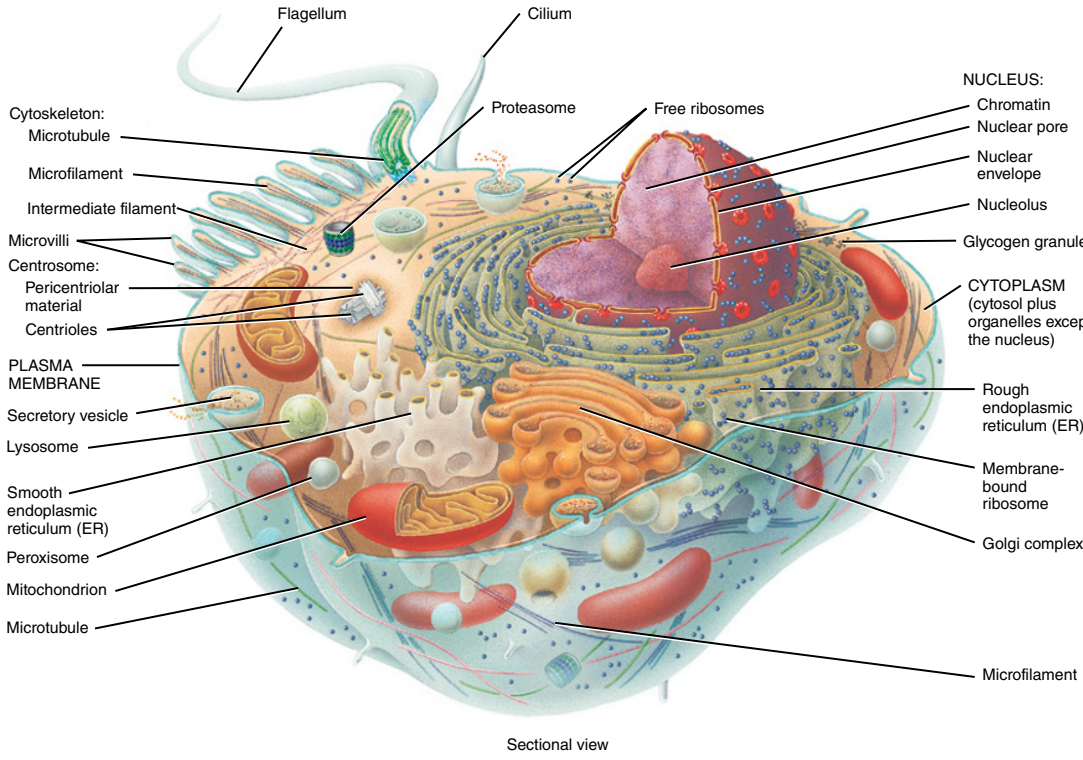

Figure 1.1 Components of a cell. *Source:* Tortora and Derrickson (2013).

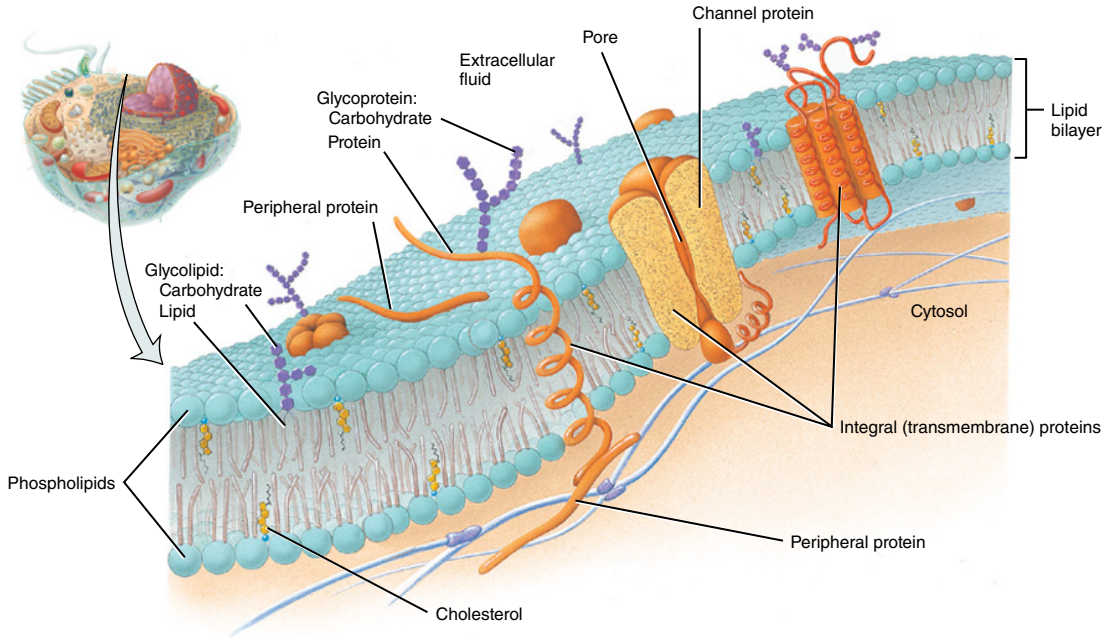

Figure 1.2 Fluid mosaic model of plasma membrane. *Source:* Tortora and Derrickson (2013).

protein pumps for active transport (Chapter 2); and *receptor proteins* for hormones and other endogenous as well as exogenous chemicals. Carbohydrates are either found in combination with proteins (glycoproteins) or lipids (glycolipids) and function as recognition markers, allowing the immune system to differentiate 'self' from foreign cells.

Nucleus

The nucleus is a double membrane-bound structure and measures approximately 3–14 µm in most cells. It stores the DNA and associated proteins (= chromatin) in the form of chromosomes. The nuclear membrane (nucleolemma) isolates the DNA from the cytoplasm and is continuous with the endoplasmic reticulum (Figure 1.1). The nucleolemma contains pores to allow passage of messenger RNA (mRNA) units of nucleic acid. The gel-like portion of the nucleus is known as nucleoplasm. Within the nucleus, proteins, DNA, and ribonucleic acid (RNA) are concentrated around specific chromosomal regions to form the *nucleolus* (plural: nucleoli). The nucleolus itself is not bound by a membrane and is responsible for synthesis of ribosomes.

The functions of the cell are coded in the genes. The genetic code or nucleotide sequence of DNA in the genes is used to direct protein synthesis, a process known as gene expression. First, the DNA is used as a template to link nucleotides, forming a strand of an mRNA molecule. This process is referred to as *transcription* and is facilitated by the enzyme RNA polymerase. The mRNA is then transferred across the nucleolemma into the cytoplasm and is used as a template by ribosomes to synthesise proteins, a process referred to as *translation*. Further processing of the proteins such as addition of phosphate (phosphorylation) or carbohydrates (glycosylation) takes place through a process known as *post-translation modification*.

The nucleus is present in all cells of the body, excluding red blood cells and platelets. Liver cells (hepatocytes) can have one or two nuclei, while the osteoclasts and skeletal muscle cells are multinucleated.

Cytoplasm

The cytoplasm refers to the contents of the cell bounded by the cell membrane on the outer aspect and the nucleus in the inner part of the cell

(Figure 1.1). The liquid portion of the cytoplasm is termed cytosol, and contains mainly water (70–85%), proteins (10–20%), lipids (2%), carbohydrates (1%), and electrolytes. Two distinct components of the cytoplasm include:

- *Organelles*, which are membrane-bound structures with a specific metabolic function. The membrane around different organelles serves to isolate the chemical reactions in the cytoplasm from each other.
- *Inclusions*, which are non-membrane-bound particulate matter in the cytoplasm and do not have any specific metabolic function.

Cytoplasmic Organelles

- *Ribosomes*

Ribosomes are small spherical structures (15 nm in diameter) which may exist as free-floating particles or can be found in clusters lining the outer membrane of the rough endoplasmic reticulum. Ribosomes are the site of protein synthesis and translate the message obtained from the nucleus via transcription and effectively function as the working template or conveyor belt for assembling proteins.

- *Endoplasmic Reticulum*

ER consists of a complex and multi-folded system of parallel membranes and tubules which is contiguous with the nuclear membrane and Golgi apparatus.

The rough endoplasmic reticulum (rER) is studded with ribosomes. rER works with the ribosomes to synthesise proteins which are collected in spaces (cisternae) within the rER. A limited amount of packaging of proteins also takes place in the rER (pancreas).

The smooth endoplasmic reticulum (sER) contributes to lipid metabolism, including synthesis of steroid hormones, the lipid portion of lipoprotein in the liver, and lipid absorption and resynthesis of triglycerides in the intestinal mucosa. sER in skeletal and cardiac muscle, known as the sarcoplasmic reticulum, sequesters calcium for the cytosol. Finally, ER inactivates harmful by-products of metabolism and drugs (liver).

- *Golgi Apparatus*

The Golgi apparatus (GA) like the ER, is also a stacked series of folded membranous sacs. Its main function is to process and package both proteins and non-proteins. The GA is the central delivery system from the cell and 'packages' cellular products into secretory vesicles which bud off from main Golgi membranes to enable them to migrate to and merge with the plasma membrane, releasing their contents outside the cell by a process known as exocytosis. The GA additionally produces lysosomes and digestion-related organelles.

- *Lysosomes*

Lysosomes are small membranous compartments (25–50 nm in diameter) which emanate from the GA. Lysosomes contain several degradative enzymes and assist in the degradation of toxic and waste cell products, including cell debris as well as microbial organisms (e.g. bacteria). Although found in all cells (except erythrocytes), lysosomes are particularly prominent in macrophages and neutrophils. Lysosomes also play a key role in programmed cell death, or *apoptosis*.

- *Peroxisomes*

Peroxisomes are membrane-bound structures, somewhat larger than lysosomes (0.3–1.5 µm in diameter), which arise from ER. They contain specific enzymes (oxidases and catalases) which help the breakdown of long-chain lipids and are involved in the detoxification of certain chemicals (e.g. converting hydrogen peroxide to water). Apart from macrophages, peroxisomes are prominent in liver cells where they are involved in the degradation of alcohol.

- *Secretory Vesicles*

These have a predominantly storage and transport role in cells and originate from the GA. These typically are transported by non-constitutive secretion, which means that the secretions are released continuously regardless of any external factors. This is the standard mechanism and ensures proteins and other important molecules are continuously maintained at the plasma membrane. Non-constitutive transport is very much regulated and requires specific signalling pathways to get the proteins delivered to the cell membrane.

- *Mitochondria*

Mitochondria (singular: mitochondrion) are 0.75–3 µm in diameter and produce energy required for cell functions, effectively functioning as the powerhouse of the cell. They consist of a double-layered membrane. Their inner membrane is highly folded into *cristae*, which markedly increase its surface area. Mitochondria have their own DNA, which allows independent replication of mitochondria and synthesis of enzymes and proteins involved

in cellular respiration. They are studded with enzyme-rich proteins responsible for production of energy molecules known as adenosine triphosphate (ATP). Mitochondria use oxygen (cellular respiration) to liberate energy stored in the sugars through a process known as *oxidative phosphorylation*. The energy is stored in the ATP molecules and is used for various cell functions such as protein synthesis and transport. Mitochondria are most numerous in cells with high energy requirements such as the cells in muscle and liver. In addition, mitochondria also store intracellular calcium.

- *Cytoskeletal Components*

The cells are supported by a cytoskeletal network of extensive microtubules and microfilaments and intermediate filaments, which act as a scaffold for cell integrity, provide cell shape as well as being an additional means of transport of substances throughout the cell.

- *Microtubules*

Microtubules are hollow cylindrical structures (25 nm in diameter) and are predominantly made up of α-tubulin and β-tubulin proteins. They have a role in the cellular transport of organelles such as mitochondria and vesicles. They also contribute to the *axoneme*, a cytoskeletal core in cellular appendages like cilia (respiratory tract, fallopian tubes) and flagella (sperms). Finally, microtubules also contribute to centrioles which help in cell division.

- *Intermediate Filaments*

Intermediate filaments are made of fibrous proteins (8–10 nm in diameter) and contribute to the structural integrity and shape of the cell. Examples include: cytokeratin (epithelia, hair, nails); vimentin (connective tissue, blood cells); desmin and synemin (muscle, Z-line proteins); and neurofilaments (neurons).

- *Microfilaments*

Microfilaments are narrow (7 nm) filamentous structures made of the globular protein actin – a very common cell filament (Figure 1.3). They are located near to the inner surface of the cell membrane and help the cell to maintain its shape, and are involved in contraction (muscle) and movement (white blood cells).

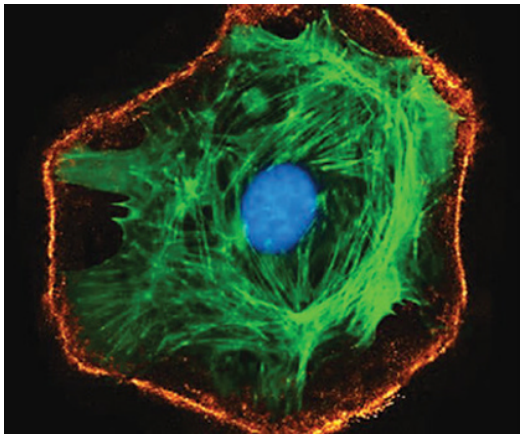

Figure 1.3 A human osteoblast cell stained for actin cytoskeletal filaments (green), plasma cell membrane (orange) and nucleus (blue). Figure courtesy Dr. Vehid Salih

Inclusions

Inclusions represent particulate regions in the cytoplasm which are not membrane-bound. These include stored food (e.g. glycogen particles, fat droplets); pigments (melanin, lipofuscin, haemosiderin). Pathological inclusions include bacteria, viruses, and exogenous particulate matter, such as carbon or asbestos in the lungs (not seen in Figure 1.1).

Cell Regeneration and Repair

Cells are said to be in a homeostatic state when they can perform their function normally. However, cells may get damaged from a variety of causes, such as lack of oxygen, physical or chemical agents, nutritional deficiencies, infection, genetic defects, and immunological reactions. Human cells vary in their ability to withstand injury as well as in their ability to regenerate. For example, the cells in the skin and lining mucosae continue to be replaced throughout life while brain and heart cells have limited regenerative ability. Irreversible cell injury results in cell death, which can translate into organ dysfunction, disease, and even death. The dental tissues possess limited capacity for regeneration and repair. The tooth enamel does not contain living cells and cannot regenerate. However, enamel can be remineralised in the early stages of tooth decay prior to cavitation. The dentin-pulp complex and the periodontium, on the other hand, contain living cells (including stem cells) and can undergo regeneration and/or repair to a limited extent, depending on the severity of the injury.

Stem Cells

Stem cells are undifferentiated cells of a multicellular organism which can divide indefinitely to give rise to more cells of the same type (totipotent), and from which certain other types of cell arise by differentiation (multipotent, pluripotent). Stem cells have the capacity therefore to self-renew and to differentiate into different cell types or tissues during embryonic development and typically throughout adulthood, too, although their differentiation potential declines with age. They are classified into two groups based on their origin: *embryonic* stem cells, which are pluripotent and can develop into *any* type of cell, and *adult* stem cells, which are deemed multipotent and these can develop into *many* cell types.

Embryonic stem cells offer immense promise but their clinical use and feasibility are limited, owing to ethical concerns. Adult stem cells may be harvested from different kind of tissues, like bone marrow, umbilical cord, amniotic fluid, brain tissue, liver, pancreas, cornea, various periodontal tissues, and even adipose tissue. Stem cells are currently used in a variety of research applications and for treating diseases of importance (e.g. dementia) as well as debilitating genetic conditions. The role of future stem cell therapy suggests that an adult's own (autologous) cells could be derived, differentiated, and utilised for cell therapy interventions.

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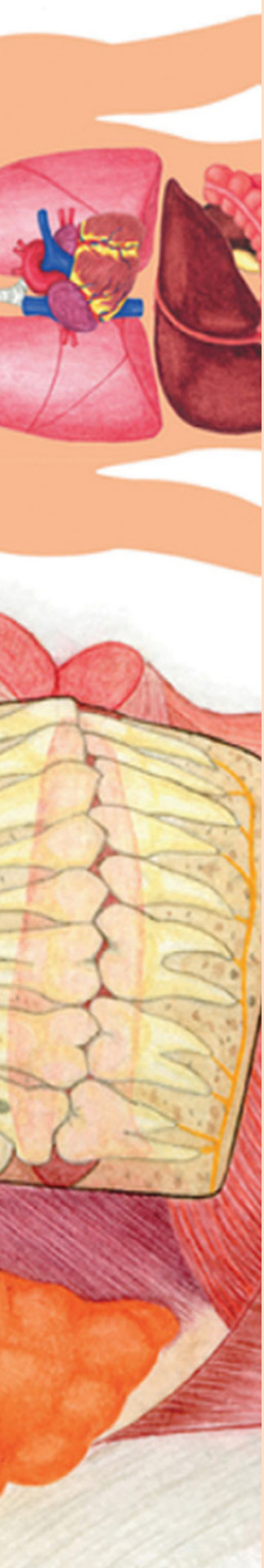

PART II

Nerve Muscle Physiology