

# Molecular Medicine

**Learning objectives for candidates preparing for the Wits Additional Placement Test (WAPT) – 2024**

**REFERENCES Textbooks**

Marieb EN, Hoehn K. Human anatomy & physiology (10th ed.) San Francisco: Pearson/Benjamin Cummings  
 Marieb EN. Essentials of human anatomy & physiology (11th ed.) San Francisco: Pearson/ Benjamin Cummings

**Online**

As provided below next to the objectives.

Please note that the use of Wikipedia is deliberate as it is freely available and it is better than many of the other potential resources that have been checked for use. The lecturers responsible for Molecular Medicine have satisfied themselves with the quality and reliability of content presented in the Wikipedia sites referenced below. Each article has been confirmed as suitable for the current WAPT.

**THE DETAILED OBJECTIVES**

NOTE: There may be some overlap/ duplication between sections within Physiology and Molecular Medicine

**Part 1: Basic Biology & Immunology**

Topic	Objectives	Possible resources – One can consult other resources
<b>The cell nucleus</b>	Define the term ‘chromosome’	
	Describe the packaging of DNA from the double helix through to a condensed (mitotic) chromosome	
	List the steps in the process of DNA replication and synthesis	
	List and briefly describe the functions of the different types of RNA	
	Define transcription and briefly describe the steps of the transcription process	
	Define a ‘gene’	
	Explain how the sequence of nucleotide bases in a gene translates into instructions for amino acid sequences in polypeptides	
	Briefly explain the difference between exons and introns	
	Briefly explain how genes are controlled	
<b>Techniques using DNA and RNA hybridisation</b>	Define PCR and briefly outline the technique	<b>Wikipedia PCR:</b> read to the end of Infectious diseases applications
	Briefly describe the simple techniques used for DNA sequencing	<b>Wikipedia:</b> Sanger sequencing. Only read the method as far as automation
	Briefly describe the techniques and use of Restriction Digests	<b>Wikipedia:</b> Restriction digest
	Define a karyotype and describe how this is obtained	Any basic genetic textbook will have information on how karyotypes are made

	Briefly describe how FISH (fluorescent in situ hybridization) is performed and what this technique can be used for.	<a href="https://www.nature.com/scitable/topic_page/fluorescence-in-situ-hybridizationfish-327/">https://www.nature.com/scitable/topic_page/fluorescence-in-situ-hybridizationfish-327/</a>
<b>The cytosol and proteins</b>	Describe the steps of protein synthesis in the cytosol	
	Briefly describe protein structure (primary to quaternary)	
	List the differences between fibrous (structural) and globular (functional) proteins	
	List the general functions of proteins and give examples of each function in the body	
	Describe the process and effects of protein denaturation	
	Explain the nature and role of recombinant proteins	<b>Wikipedia:</b> Recombinant DNA. Read to the end of Expression
	Describe how damaged or unnecessary proteins are degraded/ destroyed in the cytosol	
<b>Protein techniques</b>	Briefly describe the process of gel electrophoresis, including SDS-PAGE	<b>Wikipedia:</b> Gel electrophoresis
	Briefly describe the principles of a Western blot	<b>Wikipedia:</b> Western Blot
<b>The cell membrane</b>	Describe the chemical composition of the plasma membrane and explain how the composition relates to the functions of the membrane	
	Describe the nature and functioning of membrane receptors responding to contact signalling, chemical signalling and electrical signalling	
	List the types of chemical signal receptors	
	Briefly describe the functioning of G protein-linked receptors including the role of second messengers and protein (phosphate) kinase enzymes	
	Briefly describe the 3 types of membrane junctions	
	List the roles of cell adhesion molecules	
<b>Laboratory techniques to identify cell markers</b>		<b>Note:</b> It may be easier to complete this section after the immunology section
	Briefly describe flow cytometry	<a href="https://www.iitk.ac.in/che/pdf/re-source/s/Flow-Cytometry-reading-material.pdf">https://www.iitk.ac.in/che/pdf/re-source/s/Flow-Cytometry-reading-material.pdf</a>
	Briefly describe the process of immunohistochemistry	Briefly describe the process of immunohistochemistry
<b>Extracellular matrix</b>	List and briefly describe the types of extracellular materials and their functions	
<b>Basis of Immunology</b>		The strength of the immune system lies in the integration of all its facets so that is how you should study this section.
<b>Functions of the lymphatic system</b>	List the functions of lymphatic vessels lymphocytes, lymphoid tissues and organs	Study the whole chapter related to immunology and the immune system in 'Human anatomy & physiology' (Marieb EN, Hoehn K)

<b>Nonspecific immune defences</b>	Define the terms antigen, hapten and antigenic determinant	
	Describe the general role of the following in host defences: <ul style="list-style-type: none"> <li>• physical barriers</li> <li>• phagocytes – neutrophils and macrophages</li> <li>• natural killer cells</li> <li>• chemicals</li> </ul>	
	With respect to the complement system: List the proteins which make up the system and their functions Describe the activation of the system in the context of the classical and alternate pathways	
	Describe the processes that make up the inflammatory response with reference to: <ul style="list-style-type: none"> <li>• the cells involved</li> <li>• the mediators involved</li> <li>• the consequences</li> <li>• termination of the response</li> </ul>	
<b>Specific immune defences</b>	Define ‘adaptive immune response’ and list its main features	
	List the antigen-presenting cells	
	Describe the functions of antigen-presenting cells	
	Briefly describe the role of the humoral response (i.e. B-cells and antibody-mediated immunity)	
	Describe the structure of an antibody	
	Compare the structures of the 5 classes of antibody and relate these to their specific functions	
	Describe the molecular process by which antibody diversity is generated	
	Briefly outline the cell-mediated immune response	
	Identify and describe the roles of MHC class I and MHC class II molecules	
	Describe the role of CD4 T-cells	
	Describe the role of CD8 T-cells	
	Describe the molecular process by which T-cell receptor diversity is generated	
<b>Cell and tissue development &amp; death</b>	Define a stem cell in terms of the fundamental properties of this cell	
	Briefly describe the factors that lead to differentiation of cells	
	Define apoptosis, briefly describe its causes, and briefly describe the process of cell death up to phagocytosis	
	List and briefly describe the phases of the cell life cycle	
	Describe the process of cell division: DNA reduplication, mitosis (with its 4 phases) and cytokinesis	
	Name the factors which control cell division	
	Name the enzymes that enable cells to enter the different phases of mitosis, or inhibit the process	

## Part 2: Molecular Basis of Genetics

Topic	Objectives	Possible resources – One can consult other resources
<b>Basics of genetics</b>	Define allele, genotype, phenotype	
	Define autosomal chromosomes, sex chromosomes and homologous chromosomes	
	Compare mitosis and meiosis with respect to phases, number of divisions, synapses of homologous chromosomes, number of daughter cells and genetic composition of daughter cells	
	Briefly describe the following sources of genetic variation: <ul style="list-style-type: none"> <li>• chromosome segregation and independent assortment</li> <li>• crossover of homologues and gene recombination - random fertilization</li> </ul>	
<b>Patterns of Mendelian inheritance</b>	Define ‘dominant allele/ trait’ and ‘recessive allele/ trait’, and give common examples of each	
	Define ‘homozygous’ and ‘heterozygous’	
	Explain how dominant and recessive inheritance takes place at a genetic level	
	Explain the chances that two siblings of heterozygous parents will have the same dominant trait and the same recessive trait	
	Define ‘incomplete dominance’ and give an example	
	Define ‘codominance’ and give an example	
	Explain how sex-linked inheritance takes place at a genetic level, and give examples of common traits inherited in this way	
	Explain how polygenetic/ multifactorial inheritance takes place at a genetic level, and give examples of common traits inherited in this way	
<b>Epigenetic inheritance</b>	Briefly explain how epigenetic marks such as methyl or acetyl groups affect the activation of transcription and functioning of DNA	
<b>Chromosome abnormalities</b>	Define ‘structural chromosome abnormalities’ and give examples of the clinical conditions and effects they produce	<b>Wikipedia:</b> Chromosome abnormality
	Define ‘numerical chromosome abnormalities’ and give examples of the clinical conditions and effects they produce	

### Part 3: Molecular Basis of Cancer

The information for this section must be obtained from different sources as there is no freely available resource that has been found to cover all the objectives and the textbook you have been advised to use for anatomy and physiology (Marieb) has only one short section on cancer. It is, however, advisable to read the latter first to set the scene for this section. The main resources that it is suggested that you use are:

**1. Molecular Biology of the Cell. Alberts et al**

To access the book online, go to this site: <http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=search&db=pubmed>.

This brings you to the **PubMed** search page. Scroll down to the bottom of the page to find "Bookshelf" and

click on it. Go to "Browse". Type 'Molecular biology of the cell' into the search box and click on "Search".

The book by **Alberts et al** will be shown. Click on the icon. This brings you to the homepage for the book. You

now want to get access to the whole of Chapter 23 'Cancer' in the book. There are 5 sections in this chapter.

They are:

- Cancer as a Micro-evolutionary Process
- The Preventable Causes of Cancer
- Finding the Cancer-Critical Genes
- The Molecular Basis of Cancer-Cell Behavior
- Cancer Treatment: Present and Future

To find each of these sections, type its name into the search box on the book's homepage and click on 'Go'.

This brings you to that section.

**2. Wikipedia.** There is an entry on Cancer and it has numerous links to the various subsections/objectives. Use these as necessary to cover the objectives below. Where possible, there is an indication of which extra link to use next to the objectives.

**3. YouTube: Oncology for Medical Students** This is an excellent series of videos:

- Neoplasia part 1: definition, how it relates to cancer
- Neoplasia part 2: Differences between benign and malignant neoplasms
- Molecular basis of cancer part 1: changes in DNA underlie cancer
- Hallmarks of Cancer (part 1)
- Hallmarks of cancer (part 2)
- Tumour Suppressor Genes (Retinoblastoma and the two hit hypothesis, p53)
- Proto-oncogenes and Oncogenes
- Clonal Selection
- Clinical features of cancer: how cancers cause clinical symptoms

**4. General pathology textbooks.** If you have access to any general pathology textbooks, they usually have a chapter on cancer which should have much of the information you require. No particular textbook has been identified as not all candidates have access to such a resource.

Topic	Objectives	Possible resources – One can consult other resources
<b>Introduction to cancer</b>	<p>The student should:</p> <p>Recognise that cancer is a significant cause of morbidity and mortality (disease and death)</p> <p>Describe the differences between benign and malignant tumours</p> <p>Describe the gross patterns of cancer growth</p> <p>Describe the 2 pathways of carcinoma growth and progression</p> <p>Explain the concept of “differentiation” and “dedifferentiation” as applied to cancer</p> <p>Explain why cancer takes time to develop</p> <p>Explain why cancer is a disease of the genome</p> <p>Explain the development of cancer in terms of increasing numbers of mutations and epigenetic changes, and define “genetic instability”</p> <p>Outline the major “hallmarks” of cancer and describe the 2 “enabling characteristics” of cancer as defined by Hanahan &amp; Weinberg</p>	<p>Molecular Biology of the Cell</p> <p><b>Wikipedia:</b> The hallmarks of cancer</p> <p>Oncology for Medical Students: Hallmarks:  <a href="https://www.youtube.com/watch?v=ea-CALtn7hA">https://www.youtube.com/watch?v=ea-CALtn7hA</a>  <a href="https://www.youtube.com/watch?v=zSD0ZwfZ2BU">https://www.youtube.com/watch?v=zSD0ZwfZ2BU</a></p> <p>Hanahan &amp; Weinberg (Cell, 2011, 144:5 p646 -674)  Note: you do not need to read the original paper but you must know that there are 8 of them</p>
<b>Oncogenes and Tumour Suppressor Genes</b>	<p>Define proto oncogene and oncogene List the classes of proto-oncogenes.</p> <p>Explain the functions of proto-oncogenic proteins and give an example of each.</p> <p>Describe how proto-oncogenes are converted to oncogenes</p> <p>Explain how this conversion leads to over-activation or overexpression of the encoded protein</p> <p>Define tumour suppressor gene</p> <p>Describe the recessive nature of tumour suppressor genes Explain why germline mutations of tumour suppressor genes are possible and how they lead to increased cancer susceptibility</p> <p>Explain the Knudson two hit hypothesis</p> <p>Explain how anti-apoptotic protein (e.g. BCL2) up-regulation prevents apoptosis</p>	<p>Oncology for Medical Students  Molecular Biology of the Cell</p>
<b>Cell Cycle: Tumour Suppressor Genes and Oncogenes</b>	<p>Name two oncoproteins in the cell cycle</p> <p>Name two tumour suppressors which play an important role in regulating the cell cycle</p> <p>Describe how progression from G1 to S is regulated with particular reference to Rb</p> <p>Describe the functions of p53 in regulating the cell cycle, apoptosis, DNA repair and angiogenesis.</p>	<p>Oncology for Medical Students  Molecular Biology of the Cell</p>
<b>Immortalisation of tumour cells</b>	<p>Define cell senescence and immortality.</p> <p>Explain why telomere shortening leads to replicative senescence</p> <p>Describe how cells become immortal</p>	<p>Oncology for Medical Students  Molecular Biology of the Cell</p>

<b>Angiogenesis</b>	<p>Outline the process of angiogenesis</p> <p>Explain how cancer cells induce angiogenesis</p> <p>Describe how tumour vasculature differs from normal vasculature at the macro and micro level</p> <p>Explain how tumour angiogenesis could be a target for treatment of cancer</p>	<p><a href="https://www.youtube.com/watch?v=f4SgXw2Gx00">https://www.youtube.com/watch?v=f4SgXw2Gx00</a></p>
<b>Invasion and metastasis</b>	<p>Define “invasion” and “metastasis”</p> <p>Give 4 routes of metastasis</p> <p>Describe the necessary steps tumours must undergo in each of these forms of metastasis</p> <p>List the multiple sequential steps of the metastatic cascade Define and describe the role of the epithelial to mesenchymal transition in metastasis</p> <p>List some clinical manifestations and consequences of local tumour invasion and distant metastases</p>	<p>Molecular Biology of the Cell Oncology for Medical Students</p> <p><b>Wikipedia:</b> epithelial to mesenchymal transition</p>
<b>Concepts of the microenvironment &amp; cancer stem cells</b>	<p>List the components of the tumour microenvironment Describe how the microenvironment affects tumour growth and metastasis</p> <p>Define the function of a cancer stem cell</p>	<p>Molecular Biology of the Cell</p>
<b>Tumour metabolism</b>	<p>Describe how cancer cell metabolism differs from that in normal cells – the Warburg effect. Hypothesise why this difference occurs</p> <p>Explain how this difference is utilized to detect cancers by PET scans</p>	<p><b>Wikipedia:</b> Warburg effect (oncology). Do not go to the other entries on the Warburg effect.</p> <p><b>Wikipedia:</b> PET scan - use the oncology section</p>
<b>Epigenetics in cancer</b>	<p>Define epigenetics.</p> <p>Describe the major epigenetic mechanisms.</p> <p>Briefly explain how the above epigenetic mechanisms modify gene transcription.</p> <p>Discuss ways in which epigenetic abnormalities may contribute to carcinogenesis</p>	<p><b>Wikipedia:</b> Cancer epigenetics. Note: only use the Mechanisms section</p>
<b>Inherited tumour syndromes</b>	<p>Distinguish between acquired (somatic) and inherited (familial) cancer at the genetic level</p> <p>Describe the association between <i>Rb</i> and retinoblastoma.</p> <p>Describe the association between BRCA mutations and cancer</p>	<p>Molecular Biology of the Cell</p>
<b>Aetiological agents in cancer - toxins</b>	<p>Explain the differences between tumour initiators and promoters</p> <p>Explain what is meant by a procarcinogen and why activation varies in different individuals</p>	<p>Molecular Biology of the Cell</p> <p><b>Wikipedia:</b> Carcinogen. Do not learn the classification section.</p>
<b>Aetiological agents in cancer - viruses</b>	<p>Explain DNA virus oncogenesis and the role of P53 and Rb inactivation, e.g. by HPV</p> <p>Outline oncogenesis by RNA viruses</p> <p>List the common viruses which cause cancer and the specific types of cancer they cause.</p>	<p><b>Wikipedia:</b> Oncovirus. Do not learn the history section</p> <p><b>Wikipedia:</b> Infectious causes of cancer</p> <p>Molecular Biology of the Cell</p>
<b>Aetiological agents in cancer - radiation</b>	<p>Describe the mechanism by which radiation causes cancer List the most important sources of radiation for humans</p>	<p><b>Wikipedia:</b> Carcinogen</p>

<b>Aetiological agents in cancer - inflammation and infections</b>	Describe the role played by the immune system in the initiation and maintenance of cancer. Describe the role played by <i>H. pylori</i> in gastric cancer as an example of host-organism interaction. Outline some possible roles of infection in other cancers.	<b>Wikipedia:</b> Infectious causes of cancer
<b>Cancer therapy</b>	Outline the chemotherapy mechanisms which target dividing cells Define what is meant by “broad spectrum” therapy as opposed to “targeted” therapy Describe the types, cytotoxics, targeted therapies, & mechanisms of action Explain why and how angiogenesis can be a target for anticancer therapy	Molecular Biology of the Cell <b>Wikipedia:</b> Chemotherapy. Note: only use the following sections:
<b>Why cancer therapy fails</b>	Explain the <b>host</b> and <b>host-tumour</b> factors which lead to failure of chemotherapy Explain how individual tumour genetic variation contributes to resistance Explain the mechanism of drug efflux as a cause of resistance and the strategies used to counter this Explain why the cancer stem cell contributes to resistance	<b>Wikipedia:</b> Antineoplastic resistance. Do not learn the genetic markers section

#### Part 4: Molecular Basis of Genetics Molecular Basis of Infectious Diseases

The objectives for this section are covered in the following textbook, available online through the Pub Med bookshelf. The relevant chapter is given next to the headings. **Baron S (ed.) Medical Microbiology (4th edition).** University of Texas Medical Branch at Galveston, Galveston, Texas. Galveston (TX): University of Texas Medical Branch at Galveston; 1996. ISBN-10: 0-9631172-1-1

**NB: This textbook provides a very useful summary at the beginning of each chapter and it is strongly recommended that you begin with this summary.** It is also suggested that you follow the objectives closely as there is more information than required in some sections in this textbook.

Topic	Objectives	Possible resources – One can consult other resources
<b>Structure of bacteria</b>	Define what is meant by the terms “coccus” and “bacillus” Describe the different cell arrangements found in cocci Describe the different shapes of bacilli	<b>Chapter 2</b>
The nucleoid	Describe the general structure/shape of a bacterial chromosome Compare a bacterial nucleoid and chromosome structure with a mammalian cell nucleus and chromosome structure	
Surface appendages	Compare the structure and function of flagellae and pili	
Surface layers:	Explain what is meant by the terms “Gram positive” and “Gram negative” and how these different staining patterns arise Compare and contrast the surface layers of Gram positive and Gram negative bacteria Describe the structure and basic steps in the synthesis of peptidoglycan. Describe the basic structure of lipopolysaccharide/endotoxin (detail for different bacteria not required)	

	<p>State which types of bacteria contain lipopolysaccharide Describe the outer membrane of Gram negative bacteria.</p> <p>Explain what is meant by the periplasmic space of Gram negative bacteria</p> <p>State which types of bacteria contain techoic acid Define what is meant by “mesosomes”.</p>	
<b>Bacterial genetics</b>	Compare binary fission in bacteria with mitosis in mammals	<b>Chapter 5</b>
The bacterial genome	<p>Describe a typical bacterial chromosome.</p> <p>Define the term “plasmid”</p> <p>Discuss the role of plasmids in human diseases caused by bacteria</p> <p>Define the term “bacteriophage”</p> <p>Describe the differences between virulent and temperate bacteriophages</p>	
Exchange of genetic information	<p>Describe the process of transformation in bacteria</p> <p>Describe the process of transduction with respect to bacteria</p> <p>Briefly outline the process of conjugation in bacteria</p> <p>Explain how the above processes contribute to genetic variation in bacteria.</p>	
<b>Bacterial pathogenesis</b>	<p>Define “host susceptibility” and “host resistance”</p> <p>Relate the above concepts to the immune system in humans Describe how the host response can cause disease.</p> <p>Describe the adaptations necessary for bacteria to live within mammalian cells</p> <p>Define “virulence”</p> <p>Define and describe each of the following factors involved in virulence:</p> <ol style="list-style-type: none"> <li>Adherence and colonisation factors</li> <li>Invasion factors</li> <li>Capsules</li> <li>Endotoxin</li> <li>Exotoxins</li> <li>Siderophores</li> </ol>	<b>Chapter 7</b>
<b>Antimicrobial chemotherapy</b>	<p>For each of the following different types of antimicrobial agent, list the major examples and describe the mechanism:</p> <ol style="list-style-type: none"> <li>Inhibition of bacterial wall synthesis</li> <li>Disruption of (a) bacterial membranes and (b) fungal membranes</li> <li>Inhibition of nucleic acid synthesis:</li> <li>Interference with nucleotide synthesis</li> <li>Impairment of template function of DNA</li> <li>Inhibition of DNA-directed DNA polymerase</li> <li>Inhibition of DNA replication</li> <li>Inhibition of ribosome function</li> <li>Inhibition of folate metabolism</li> </ol>	<b>Chapter 11</b>
	<p>For each of the following, describe the mechanism of resistance to antimicrobial chemotherapy:</p> <ol style="list-style-type: none"> <li>Resistance due to altered receptors (<math>\beta</math> Lactam, vancomycin, macrolide-lincomycin, rifampin, sulphonamide trimethoprim, quinolone)</li> </ol>	

	<p>b. Resistance due to decreased drug entry (tetracycline, aminoglycoside)</p> <p>c. Resistance due to destruction or inactivation (<math>\beta</math> Lactam)</p> <p>d. Synthesis of resistant metabolic pathways (concept only)</p>	
<b>Structure and classification of viruses</b>	<p>Define and describe what is meant by the term “virus”</p> <p>Describe the structure of a virus in terms of the nucleic acid, capsid and envelope</p> <p>Describe the morphological classification of viruses</p> <p>Describe the different arrangements of the genome in RNA viruses</p> <p>Describe the different arrangements of the genome in DNA viruses</p>	<b>Chapter 41</b>
<b>Human immunodeficiency virus</b>	<p>Relate the levels of virus and the function of the immune system in the different phases of disease caused by HIV</p> <p>Name the cells infected by HIV</p> <p>Define “opportunistic infection” and explain why this occurs in HIV infection Define “AIDS”</p> <p>Briefly describe the structure of HIV</p> <p>Explain the function of reverse transcriptase</p> <p>Describe the process of HIV replication from attachment of the virus to the budding of new virions</p> <p>Outline the pathogenesis of disease caused by HIV</p> <p>Describe how HIV infection is diagnosed by means of a) antibodies and b) PCR</p> <p>Describe the strategies used to control and prevent HIV infection</p>	<b>Chapter 62</b>
<b>Malaria</b>	<p>Describe the stages of the malaria paroxysm</p> <p>Describe and explain the periodicity of fever in malaria</p> <p>List the species of Plasmodium responsible for most cases of malaria in humans</p> <p>Name the vector of malaria</p> <p>Describe the lifecycle of malaria, highlighting the difference between Pl. falciparum and the other species Describe the pathogenesis of malaria</p> <p>Describe the host defences against malaria</p> <p>Outline the epidemiology of malaria</p>	Chapter 83