

M.Sc. Medical Biotechnology expanded syllabus

Part-I (1st year)

Theory

Paper-I: Biochemistry

Paper-II: Cell Biology

Paper-III: Molecular Biology & Microbial Genetics

Practical

Biochemistry

Cell biology

Molecular Biology & Microbial Genetics

Part-II (2nd year)

Theory

Paper-IV: Immunology and Immunogenetics

Paper-V: Human genetics and Gene based Diagnosis and Therapy

Paper-VI: Bioinformatics

Practical

Immunology and Immunogenetics

Human genetics and Gene based Diagnosis and Therapy

Bioinformatics

Project work

Paper-I: Biochemistry

Biomolecules

Chemical basis of life; Composition of living matter; Water –properties, pH, ionization and hydrophobicity; Emergent properties of biomolecules in water; Biomolecular hierarchy; Macromolecules; Molecular assemblies; Structure-function relationships.

Hormone receptor interaction

Mechanism of steroid, thyroid hormones to regulate gene expression, Steroid hormones and nuclear receptor superfamily, estrogen action, Hormone activated Phospholipase C, Hormonal signals that use cAMP, Eicosanoids –synthesis, function, non-steroidal anti-inflammatory drugs, Nitric Oxide induced relaxation of cardiac and smooth muscle.

G-Protein coupled receptors and their effectors

Structure, activation, Sensory transduction of Olfaction, Vision, Disease relevance of stimulatory and inhibitory G-protein, Cholera, Pertussis.

Receptor Tyrosine kinases and Ras

Structure, Dimerization, Autophosphorylation, Src protein tyrosine kinase, SH2 domain binding, Insulin receptor is a tyrosine specific protein kinase, Signaling proteins that act via receptor tyrosine kinases, Dominant negative inhibition by mutant receptor, PTK inhibitors, JAK-STAT pathway. Ras activation by GEFs, Membrane localization and activation of Ras, Regulation of Ras activity by GAPs, Grb-2, Sos, Oncogenic property and function of Ras.

MAP kinase pathways

Pathway and function significance, ERK, P38, JNK and disease relevance, Induction of immediate early genes by ERK.

Second Messengers

cAMP: cAMP and gene expression, transduction of epinephrine signal and beta adrenergic pathway, PKA, Desensitization by Arrestin. **cGMP:** NO synthase. **PIP₂:** activation of glycogen synthase by insulin, DAG, IP-3, PLC, mimicking of IP-3 and DAG by ionomycin and phorbol ester. **Ca:** Calcium Calmodulin dependent protein kinases, Vasopressin induced Calcium Oscillation, mammalian proteins triggered by calcium, calcium induced calcium release.

Interaction and regulation of Signaling Pathways

Six general types of Signal transducers, Five parallel intracellular signaling Pathways, Signals from plasma membrane to nucleus.

Protein conformation

Structure of protein, Protein conformation, Primary, Secondary, Tertiary, Quaternary structure of proteins, Fibrous proteins- Keratin and Collagen (associated diseases),

Structure and function of hemoglobin and myoglobin (associated diseases),
Chaperons and Chaperonins

Protein purification and Protein/ Enzyme engineering

Factors stabilizing proteins, Purification procedures, Visualization of proteins,
Protein sequencing methods, Objectives, Principles, Different steps used to engineer
proteins, Site directed mutagenesis technique

Protein sorting, modification and degradation

Protein translocation - Secretory pathway, Protein modification- glycosylation and
lipid addition, Protein sorting to Golgi bodies, Endoplasmic reticulum, Lysosomes,
Mitochondria, Chloroplasts, peroxisomes, Nucleus, plasma membranes, Diseases
associated with misfolding of proteins, Lysosomal degradation, Ubiquitinylation,
Proteosome degradation

Enzymes

General properties and characteristics of enzymes, Transition state of an enzyme-
substrate reaction, Key features of active site of enzymes, Michelis-Menton kinetics-
 k_m , V_{max} , k_{cat} , Competitive, Uncompetitive, Mixed (non-competitive), Allosteric
regulation Enzyme catalysis- Acid –Base catalysis, Covalent catalysis, Metal ion
catalysis, Proximity and concentration effect on catalysis, Preferential binding of
Transition State complex on catalysis, Enzyme immobilization, Advantages and
Disadvantages of enzyme immobilization, Uses in Medicine

Metabolism

Anabolism and catabolism of carbohydrates, lipids, amino acids and nucleic acids.

Books:

1. Biochemistry – Lubert Stryer
2. Biochemistry- Donald Voet & Judith Voet
3. Harper's Biochemistry- Murray, Robert K., Granner, Darryl K., Mayes, Peter A., and
Rodwell, Victor W.
4. Lehninger's Principles of Biochemistry- David L Nelson & Michael M Cox
5. Cell and molecular Biology, take note!: Concepts and Experiments- Gerald Karp
6. The cell - Bruce Alberts
7. The Cell - Geoffrey M. Cooper and Robert E. Hausman

Paper-II: Cell Biology

The architecture of Cells

Endoplasmic reticulum: structure, protein Folding and processing, detoxification by Smooth ER, Autophagocytosis, Rough and smooth regions of ER separation by centrifugation, Mitochondria: Structure , Biochemical fractionation of mitochondria, Electron Transport chain , Chemiosmotic coupling , Transport of metabolites, Protein import (TIM, TOM, OXA complexes) mitochondrial assembly , Brown fat, Lebers Hereditary Optic Neuropathy (LHON).

Integration of cells into tissues

Stem Cell : three major sources of stem cell , types of Stem cells, Division, Epidermis and it's renewal by stem cell , Blood cell formation from Bone marrow stem cell, Embryonic stem cell and therapeutic cloning , Bone marrow transplantation versus Stem cell transplantation and GVHD.

Cell cloning: Somatic cell Nuclear transfer for Cloning (Reproductive Cloning), Cloning and Transgenic animal product (Hybrid cloning), Nuclear reprogramming and factors affecting it.

Cell Culture: General considerations of cell culture: Sterilization , Media , Carbon dioxide incubator, Feeder layer, Substrates on which cells grow , Contamination , Types of Culture (organ, Organotypic , single cell , Histotypic / 3D) etc.

The Nucleus

Structure of the Nuclear envelope, The Nuclear pore complex, Selective transport of proteins to and from the nucleus, Regulation of Nuclear protein import, Transport of RNAs, Internal organization of the nucleus, Chromosomes, Nuclear lamina diseases.

Cell Junction , Cell Adhesion and Extracellular matrix

Matrix structural proteins, matrix Polysaccharides, Matrix adhesion proteins , Cell matrix interactions, Adhesion junction , Tight junctions, Gap junctions – disease relevance.

Bioenergetics

Nature of chemical bonding, Free energy, enthalpy and entropy, Generation of ATP and Energy utilization

Structural organization and basic functions of Biomembranes

The phospholipids bilayer, Gorter and Grendel Experiment, Membrane proteins, RBC membrane, Mobility of membrane proteins, Fluorescence recovery after photobleaching(FRAP), Frye and Edidin experiment, the Glycocalyx. Fluid mosaic model.

Membrane Transport

Passive diffusion , Facilitated diffusion and Carrier proteins , Passive and active transport, Transcellular transport of glucose, Ion Channels (ligand gated channel, voltage gated channel), Nicotinic acetylcholine receptor, Active transport driven by ATP hydrolysis, Active transport driven by Ion gradients.

Pumps and channels

Plasma membrane Na^+ and K^+ pump ATPase, Na^+ and K^+ channel , Ca^{++} pump and three main types of Ca^{++} channels , H^+ pump, ABC transporter, Multidrug resistant protein (MDR), Cystic fibrosis.

Neurotransmission

Action potential and propagation of nerve impulse, patch clamp recording technique, Transmitter gated ion channels- excitatory, inhibitory.

Cell Function

Cell cycle-Different phases, Maturation promoting factor, Families of cyclins and cyclin dependent kinases, Regulation and cell cycle checkpoints, Inhibitors of cell cycle progression, M phase- Mitosis and Meiosis, Cytokinesis, Fertilization.

Microscopy

Microscope and its modifications – Light, phase contrast and interference, Fluorescence, Confocal, Electron (TEM and SEM), etc.

Cytochemical methods

Myeloperoxidase, Acid Schiff, Pearls Prussian Blue, Sudan Black.

Books:

1. Cell and molecular Biology, take note!: Concepts and Experiments- Gerald Karp
2. The cell - Bruce Alberts
3. The Cell - Geoffrey M. Cooper and Robert E. Hausman
4. Molecular Cell Biology- Harvey Lodish, Arnold Berk, S. Lawrence Zipursky, Paul Matsudaira, David Baltimore, and James Darnell
5. Lehninger's Principles of Biochemistry- David L Nelson & Michael M Cox

Paper III: Molecular Biology and Microbial Genetics

Origins of life

DNA the Genetic information - The central dogma - DNA structure - DNA topology - RNA structure

Genomic Characteristics

DNA Replication

The chemistry of DNA synthesis - Mechanism of DNA polymerase - Specialization of DNA polymerase - Initiation of DNA replication - Replication fork and DNA synthesis at replication fork - Termination of replication

DNA Recombination

Models of homologous recombination - Homologous recombination protein machinery - Homologous recombination in eukaryotes

Mutations and DNA Repair

Replication errors and their repair - DNA damages - DNA damage repair pathways

Transposons

DNA transposon organization and mechanism of its transposition - Viral-like retrotransposons organization and mechanisms of its transposition. - Poly A retrotransposons organization and mechanism of its transposition - Transposable elements and their regulation.

Chromatin Modeling

The nucleosome - Higher order chromatin structure - Regulation of chromatin structure - Nucleosome assembly

Transcription and its Regulation

Transcription cycle and RNA polymerase - Transcription cycle in bacteria - Transcription cycle in eukaryotes - Principles of transcriptional regulation - Regulation of transcript initiation – lac operon and ara BAD operon - Regulation of transcription after initiation- trp operon.

RNA Splicing and processing

Spliceosome machinery - Splicing mechanisms - Alternative slicing - Regulators of alternative splicing - Exon Shuffling - RNA editing - rRNA processing - tRNA processing

Genetic code and translation

Genetic code - tRNA structure - Aminoacyl tRNA synthetase - Ribosomes- prokaryotic and eukaryotic - Translation- Initiation, Elongation, Termination - Antibiotics in the translation process

Recombinant DNA and Genetic Engineering

Restriction endonucleases and gene cloning - Cloning vectors and their characteristics - Construction of DNA and RNA libraries - Screening of Libraries - Genetic mapping and analysis - PCR cloning of selected DNA segments - Engineered genes and their use - Transgenic and knockout animal models

Bacterial Genetics

History; Transduction – generalized and specialized; Conjugation –F, F', Hfr; F transfer; Hfr-mediated chromosome transfer; Transformation – natural and artificial transformation;

Eukaryotic viruses

Basic structure and life cycle - RNA and DNA viruses - Retroviruses and hepatitis B virus - Bacteriophage – structure; assay; Lambda phage – genetic map, lysogenic and lytic cycles; Gene regulation; - Interferon multigene family

Molecular Basis of cancer

Types of Cancer - Stages of cancer development - Properties of cancer cells - Cell transformation - Tumor viruses - Genetic basis of cancer – Oncogenes - Tumor suppressor genes - Care taker genes

Books:

1. Molecular Biology of the Gene- James Watson
2. The Cell - Geoffrey M. Cooper and Robert E. Hausman
3. Fundamentals of Molecular Biology- David Friefilder

Biochemistry Practical

1. To prepare an Acetic-NaAcetate Buffer system and validate the Henderson-Hasselbach equation.
2. To determine an unknown protein concentration by plotting a standard graph of BSA using UV-Vis Spectrophotometer and validating the Beer- Lambert's Law.
3. Titration of Amino Acids and separation of aliphatic, aromatic and polar amino acids by TLC.
4. AN ENZYME PURIFICATION THEME (such as E.coli Alkaline phosphatase or any enzyme of the institutions choice).
 - (a) Preparation of cell-free lysates
 - (b) Assessing purity by SDS-PAGE Gel Electrophoresis
 - (c) Separation of the isoenzyme by agarose gel electrophoresis
5. Colorimetric determination of the activity of SGOT and SGPT .
6. Estimation of Glucose in Blood by GOD – POD Method

Cell Biology Practical

1. Tail Vein puncture and complete Hemogram of Swiss Albino mouse
2. Microscopy : Simple, Dissecting, Compound
3. Preparation of blood smear and staining of human blood sample (Leishman)
4. Whole and differential blood count (TLC & RBC total count)[Human sample]
5. Hb estimation (Drabkin Method)
6. Reticulocyte Count (Brilliant Cresyl Blue)
7. Measurement of Cell size by micrometry
8. Study of Squamous epithelium by Methylene blue
9. Methods of sterilization and preparation of culture media.
10. Animal cell culture:
 - i) General Concept
 - ii) Tumor cell isolation and counting
 - iii) Determination of cell viability (Trypan Blue
11. Cytochemistry: Myeloperoxidase staining
12. Cell Proliferation assay

Molecular Biology and Microbial Genetics Practical

Preparation of liquid media for growth of microorganisms & determination of growth curve, Isolation and maintenance of organisms by plating, streaking and serial dilution

methods, Isolation and characterization of pure cultures from soil, water or patients samples, Determination of MIC, Preparation of competent cells & transfer of selected genetic marker by transformation, Demonstration of episome transfer using “F” plasmid, Demonstration of plaque assay of bacteriophages.

Isolation of genomic DNA from bacteria, Restriction digestion of λ DNA & analysis of the restriction pattern by agarose gel electrophoresis, Isolation of antibiotic resistant mutants & preparation of plasmid DNA & molecular weight determination, Isolation of genomic DNA from human blood samples, PCR amplification & analysis by agarose gel electrophoresis, Total RNA extraction & quantification.

Books:

1. J. Sambrook & D. W. Russell; Molecular Cloning A laboratory manual, 3rd ED. Cold Spring Harbor Laboratory Press- New York.
2. F. M. Ausubel, R. Brent, R. E. Kingston, D. D. Moore, J. G. Seidman, J. A. Smith, K. Struhl; Short Protocols in Molecular Biology, 4th Ed., Wiley.
3. R. C. Dubey & D. K. Maheshwari; Practical Microbiology, S. Chand & Company Ltd., New Delhi.

Paper-IV: Immunology and Immunogenetics

Structure and function of the immune system:

The classification of human immune response: Early studies of humoral and cellular immunity, Innate and Adaptive immune response, Cellular components of the adaptive immune system, Phase of adaptive immune responses, Clonal expression, Toll like receptors, ABO Group.

Cells of the immune system:

Lymphoid cells, clinical focus on the stem cells. Clinical uses and potential. B-lymphocytes and T-lymphocytes. Natural killer cells. Mononuclear phagocytes. Phagocytosis is followed by digestion and presentation of antigen. Granulocytic cells, Mast cells, Dendritic cells. Follicular dendritic cells. Primary lymphoid organs. Secondary lymphoid organs.

Antigens and Antigen presentation: Super antigens. Immunogenicity versus Antigenicity. Haptens are valuable research and diagnostic tool. Epitopes
Properties of antigens recognized by T lymphocytes. Cell biology of antigen processing.

Cytokine, cellular adhesion and interactions: Properties of cytokines .Cytokine receptor. Cytokine antagonists. Cytokine secretion by $T_H 1$ and $T_H 2$ subsets . Cytokine related diseases-Septic shock, Chagas's diseases.Cell adhesion molecule.Chemokines. Leukocyte Extravasation – the multistep paradigm. Lymphocyte Extravasation. Immune regulation.

Tolerance: Establishment and Maintenance of Tolerance. Central tolerance units development of auto reactive T and B cells. Peripheral tolerance regulates Auto reactive cells in circulation. Peripheral tolerance- regulatory T-cell . Failure of tolerance leads to autoimmunity.

Host defense and inflammation:

Immunoglobulin function: Basic structure of antibodies. Antibody binding site.Antibody-mediated effector function.Antibody classes and biological activity. Antigenic . determinants on immunoglobulins.Immunoglobulin super family .Monoclonal antibodies.

Regulatory and effector of CD4+ T lymphocyte:T cell maturation and the thymus.T cell activation.T cell differentiation.

Cytotoxic T cell function, cytotoxic function of macrophages, NK cell function: Cell death and T population.Effector responses. General principles of effector T cells. Cytotoxic T cell. NK cell . Antibody dependent cell mediated cytotoxicity (ADCC). Experimental assessment of cell mediated cytotoxicity.

Tumor immunity: Malignant transformation of cells and immune responses. Tumor antigens, Tumor evasion of the immune system. Cancer immunotherapy. Proinflammatory and inhibitory cytokines. Other mediators of inflammation. The inflammatory process. Anti-inflammatory agents.

Complement: The function of complement. The components of complement. Complement activation. Regulation of the complement system. Biological consequences of complement activation. Complement deficiencies.

Function of phagocytes, mast cells, basophils and eosinophils.

Infection and immunity

Immune response to microbes: Viral infections. Bacterial infections. Parasitic diseases. Fungal diseases. Emerging infection diseases.

Infection in the immunocompromised host: Vaccines. Active and passive immunization. Designing vaccines for active immunization. Live, attenuated vaccines. Subunit vaccines. Conjugate vaccines. DNA vaccines. Recombinant vector vaccines.

Immunodeficiencies:

Primary immunodeficiency disorders:

Immunodeficiencies- lymphoid system, Myeloid systems, complement defects, Experimental model of immunodeficiency.

Aging and immune system.

Secondary Immunodeficiencies: AIDS and other acquired or secondary Immunodeficiencies.

Allergic diseases:

Allergic responses in host defence: Gell and Coombs Classification. IgE-Mediated (Type-I) hypersensitivity. Antibody-Mediated Cytotoxic (Type-II) hypersensitivity. Immune complex-Mediated (Type-III) Hypersensitivity. Type-IV or Delayed-type Hypersensitivity (DTH). Anaphylaxis.

Pathogenesis and management of allergic asthma and rhinitis

Systemic immune diseases:

Mechanism of auto immunity: Organ specific autoimmune diseases. Systemic autoimmune diseases Animal models for autoimmune diseases. Proposed mechanisms for induction of autoimmunity. Treatment of autoimmune diseases.

Transplantation immunology: Immunological basis of graft rejection. Clinical manifestation of graft rejection. General immuno suppressive therapy. Specific immuno suppressive therapy. Immune tolerance to allograft. Clinical transplantation.

Immunogenetics:

Immunoglobulin genes and proteins: Devising a genetic model compatible with Ig structure. Multigene organization of Ig genes. Generation of antibody diversity. Synthesis, Assembly and Secretion of immunoglobulins. Regulation of Ig gene transcription
Antibody genes and antibody engineering.

TCR genes, gene products and co-repressors: Early studies of T-cell receptor. $\alpha\beta$ and $\gamma\delta$ T cell receptors. Organization and rearrangement of TCR genes. T-cell receptor complex : TCR-CD3. Tcell accessory membrane molecules. Three dimensional structures of TCR-peptide.MHC complex

The HLA major histo compatibility complex: Discovery of the MHC its role in immune responses. Structure of MHC molecule (properties, binding of peptides to MHC molecules genomic organization of the MHC , expression of MHC molecules).

Texts/References:

1. Kuby, RA Goldsby, Thomas J. Kindt, Barbara, A. Osborne
Immunology, 6th Edition, Freeman, 2002.
2. Brostoff J, Seaddin JK, Male D, Roitt IM., Clinical Immunology, 6th
Edition, Gower Medical Publishing, 2002.
3. Janeway et al., Immunobiology, 4th Edition, Current Biology
publications., 1999.
4. Paul, Fundamental of Immunology, 4th edition, Lippencott Raven,
1999.
5. Goding, Monoclonal antibodies, Academic Press. 1985.

Paper-V: Human Genetics and Gene Based Diagnosis and Therapy

History of human genetics

Autosomal dominant inheritance (HD, MD, CDD etc), Autosomal recessive inheritance (SCA, CF, etc), Sex linked and mitochondrial (DMD, hemophilia, LHON), PKU, Alzheimer, Parkinsonism, Tay-Sachs, Mongolism, Cri-du-chat, Edwards, X and Y chromosomal, Prenatal and Postnatal studies, Chromosome analysis

Genetic mapping

Haplotype, Positional cloning, Somatic cell genetics, SNP, RFLP, TRE, PCR-OLA, ASO, SSCP, RAPD, Enzymatic diagnosis

Gene environment interaction in complex diseases

Genetics of Alzheimer's disease- Causative genes for familial Alzheimer's disease (APP, PSEN1, PSEN2)-Alzheimer's disease susceptibility genes (APOE, BACE1, BACE2, NCSTN, PEN2, SORL1), Environmental factors in Alzheimer's disease pathogenesis, Genetics of Parkinson's disease-Causative genes for familial Parkinson's disease (Parkin genes)-Parkinson's disease susceptibility genes, Environmental factors in Parkinson's disease pathogenesis, Genetics of Amyotrophic lateral sclerosis-Causative genes for familial Amyotrophic lateral sclerosis- Amyotrophic lateral sclerosis susceptibility genes, Environmental factors in Amyotrophic lateral sclerosis pathogenesis, Role of environment on epigenetics of neurodegenerative diseases, Teratology, Molecular genetics of coronary heart disease, Schizophrenia

Identifying human disease genes

General gene therapy strategies, Targeted killing of specific cells, Targeted mutation correction, Targeted inhibition of gene expression. Gene replacement therapy by viral vectors: Oncovirus, Lentivirus, Adenovirus, Adenoassociated virus, Herpes Simplex virus, Naked DNA or direct injection or particle bombardment-gene gun, Liposome mediated DNA transfer, Receptor mediated endocytosis, Repair of mutations in situ through the cellular DNA repair machinery, Antisense induced exon splicing, In-utero fetal gene therapy

Gene blocking therapies

Gene Knockouts, Gene disruption-p53, prion diseases, immunological, short RNA, Gene therapy for non-inheritable diseases, stem cell therapy, somatic cell gene therapy and germ line gene therapy

Gene therapy: problem, solutions and future prospects

Controversial issues in medical genetics

In vitro fertilization, Prenatal sexing, Surrogate therapy, Genetic counseling, Germline gene therapy, ELSI, NBAC, IPR, Patenting, Human transgene

Books:

1. Human Molecular Genetics- Tom Strachan
2. Concepts of Genetics- William s. Klug
3. Emery's Elements of Medical Genetics- Robert F. Mueller & Ian D. Young

Paper VI: Bioinformatics

1. Role of Bioinformatics in Biotechnology.
2. PERL programming language and its application in Bioinformatics.
3. Some basic commands of UNIX, Concept of DBMS and SQL. Commands of SQL for database management using MySQL.
4. Biological Databases: Nucleotide and protein. Primary, Secondary and Tertiary database.
3. Definition and significance of Pairwise and Multiple Sequence Alignment. Gap penalties: Opening and extension. Calculation of alignment score.
4. Details of Scoring matrices: PAM and BLOSUM series.
5. Methods and algorithms used in Pairwise alignment for Local and Global: Dot Matrix, Dynamic Programming Algorithm and k-tuple Methods for doing MSA: CLUSTALW, ClustalX and PILEUP, Scoring MSA.
4. Algorithms used in Database similarity searching: BLAST and FASTA. Definition of Profile and Pattern. PSI-BLAST and PHI-BLAST.
5. Phylogenetic analysis: Concept and method: Distance based (Fitch and Margoliash & UPGMA) and character based methods (Parsimony).
6. Introduction of protein structure prediction and gene prediction.

Immunology and Immunogenetics Practical

- Identification of lymphoid cells in blood smears and tissue sections.
- Separation of PBMC from blood
- Spleen cell preparation from mouse
- Identification of lymphocyte populations by FACS
- Ouchterlony immunodiffusion
- Immuno-electrophoresis of rabbit serum proteins
- Agglutination of erythrocytes by lectin
- Enzyme linked immunosorbent assay for cytokines

Human Genetics and Gene based diagnosis and Therapy Practical

Southern hybridization of bacterial genome with probe & non-radioactive detection, Western blotting of GST protein from bacterial lysate, DNA fingerprinting using RFLP method, Single Nucleotide polymorphism, Amplification of human gene with specific primer by PCR technique, Demonstration of cloning of genomic DNA in standard plasmid vectors & measurement of gene expression using reporter assay.

Bioinformatics Practical:

1. Searching for a particular literature through PubMed.
2. Use of Public Domain Interfaces for downloading different DNA and Protein sequences from authenticated Databases (Using NCBI, SWISS-SPROT)
3. Performing BLAST and interpretation of the results.
4. Performing MSA by using CLUSTALW and presentation of the phylogenetic tree.
5. PERL programming.
6. Basics of MySQL

Project work