M.Sc. Medical Biotechnology syllabus 2018

Part-I (1st year)

Theory

Paper-I: Biochemistry
Paper-II: Cell Biology
Paper-III: Molecular Biology and Microbial Genetics

Practical

Biochemistry
Cell biology
Molecular Biology and Microbial Genetics

Part-II (2nd year)

Theory

Paper-IV: Immunology and Immunogenetics
Paper-V: Bioinformatics
Paper-VI: Gene based Diagnosis and Therapy

Practical

Immunology and Immunogenetics
Bioinformatics
Gene based Diagnosis and Therapy

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.

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-km, Vmax, kcat, 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 engineering- *in vitro* mutagenesis

Metabolism

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

Hormone receptor interaction

Mechanism of steroid, thyroid hormones to regulate gene expression, Steroid hormones and nuclear receptor superfamily, estrogen action, Hormone activated Phospholipase C, 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.

Second Messengers

cAMP and gene expression , signal transduction of insulin, epinephrine and beta adrenergic pathway , PKA, Desensitization by Arrestin. **cGMP:** NO synthase. **PIP_2:** activation of glycogen synthase by insulin, DAG, 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.

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: Concepts and Experiments- Gerald Karp
6. The Cell – Bruce Alberts
7. The Cell – Geoffrey M. Cooper and Robert E. Hausman

Paper-II: Cell Biology

Structural organization and basic functions of Biomembranes and Extracellular matrix

The phospholipids bilayer, Membrane proteins, RBC membrane, Mobility of membrane proteins, Fluorescence recovery after photobleaching (FRAP), the Glycocalyx. Singer & Nicholson's Fluid mosaic model. Matrix structural proteins, matrix Polysaccharides, Matrix adhesion proteins, Adhesion junction, Tight junctions, Gap junctions – disease relevance. Passive diffusion , Facilitated diffusion and Carrier proteins , Passive and active transport, Inter-cellular transport of glucose, Ion 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), Nicotinic acetylcholine receptor. Action potential and propagation of nerve impulse, patch clamp recording technique, Transmitter gated ion channels- excitatory, inhibitory.

Mitochondria and Nucleus

Structure , Biochemical functions of mitochondria, Electron Transport chain , Chemiosmotic coupling , Transport of metabolites, Protein import (TIM, TOM, OXA complexes) mitochondrial assembly, Brown fat. 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. Importance of telomere and telomerase

Receptor Tyrosine kinases , Ras and MAP kinase pathways

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

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.

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), Atomic Force Microscopy, Immunofluorescence microscopy.

Cytochemical methods

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

Books:

1. Cell and Molecular Biology: 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

DNA Replication, Mutations and Repair

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. Replication errors and their repair – DNA damages – DNA damage repair pathways

Chromatin Modeling

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

Transcription and Post transcriptional modification

Transcription in prokaryotes and eukaryotes, types of RNA polymerase – RNA splicing and processing- Spliceosome machinery – Alternate splicing – Regulators of alternate splicing – Exon Shuffling – RNA editing – rRNA processing – tRNA processing in Prokaryotes and Eukaryote, RNA interference.

Genetic code and translocation

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

DNA Recombination

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

Bacterial Genetics and Transcriptional regulation in prokaryotes

History; Transduction – generalized and specialized; Conjugation –F, F', Hfr; F transfer; Hfr-mediated chromosome transfer; Transformation – natural and artificial transformation; Transcription cycle and RNA polymerase in bacteria – Principles of transcriptional regulation – Regulation of transcript initiation – lac operon, ara and BAD operon – Regulation of transcription after initiation- trp operon.

Recombinant DNA and Genetic Engineering

Restriction endonucleases and gene cloning – Cloning vectors and their characteristics – Construction of genomic and cDNA Libraries – Screening of Libraries – Genetic mapping and analysis – DNA sequencing, PCR, Real time PCR – Engineered genes and their use – Transgenic and knockout animal models

Transposons

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

Bacteriophages and 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 Friefelder

Biochemistry Practical

1. Preparation of buffers at desired pH - Henderson-Hasselbalch equation.
2. To determine an unknown protein concentration using Bradford and Lowry's methods by plotting a standard graph of BSA using UV-Vis Spectrophotometer and validating the Beer- Lambert's Law.
3. Separation of aliphatic, aromatic and polar amino acids by Thin layer chromatography.
4. Determination of the activity of SGOT and SGPT in serum.
5. Estimation of Glucose in Blood by GOD – POD Method
6. Estimation of Urea and cholesterol in serum

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 exclusion)
11. Cytochemistry: Myeloperoxidase staining
12. Cell Proliferation assay

Molecular Biology and Microbial Genetics Practical

1. Preparation of liquid media for growth of microorganisms & determination of bacterial growth curve
2. Isolation and maintenance of organisms by plating, streaking and serial dilution methods
3. Isolation and characterization of pure cultures from soil, water or patients samples
4. Determination of Minimal inhibitory concentration against different antibiotics.
5. Preparation of competent cells & transfer of selected genetic marker by transformation. Demonstration of episome transfer using "F" plasmid.
6. Demonstration of plaque assay of bacteriophages.
7. Isolation of genomic DNA from bacteria.
8. Restriction digestion of λ DNA & analysis of the restriction pattern by agarose gel electrophoresis.
9. Isolation of antibiotic resistant mutants & preparation of plasmid DNA & molecular weight determination.

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, function and Cells of the immune system:

The classification of human immune response: Humoral and cellular immunity, Innate and Adaptive immune response, Cellular components of the adaptive immune system, Phases of adaptive immune responses, Clonal expression, Toll like receptors, ABO blood Group. Lymphoid cells, clinical focus on the stem cells. Clinical uses and potential.B-lymphocytes and T-lymphocytes. Primary and Secondary lymphoid organs.

Antigens and Antigen presentation

Super antigens. Immunogenicity versus Antigencity. Haptens. Autoimmunity, Epitopes and paratopes, Properties of antigens recognized by T lymphocytes. Cell biology of antigen processing.Monoclonal and polyclonal antibodies.

The HLA major histocompatibility 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.

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.

Immunoglobin function

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

Regulatory and Cytotoxic T cell, macrophages and NK cell function

T cell maturation and the thymus.T cell activation.T cell differentiation. 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.

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. αβ and γδ T cell receptors. Organization and rearrangement of TCR genes. T-cell receptor complex : TCR-CD3.

Tolerance

Establishment and Maintenance of Tolerance. Central tolerance, 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.

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 ?mmune suppressive therapy. Specific ?mmune suppressive therapy. Immune tolerance to allograft. Clinical transplantation.

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.

Immune response to microbes: Function of phagocytes, mast cells, basophils and eosinophils.

Viral infections. Bacterial infections. Parasitic diseases.Fungal diseases. Emerging infection diseases. Clinical manifestations.

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.

Primary and Secondary Immunodeficiencies

Immunodeficiencies- lymphoid system, Myeloid systems, complement defects, Experimental model of immunodeficiency, AIDS and other acquired or secondary immunodeficiencies.

Allergic responses in host defense

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

Clinical manifestations.

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: Bioinformatics

Bioinformatics in Biotechnology:

PERL programming language and its application in Bioinformatics.

Basic commands of UNIX, Concept of DBMS and SQL. Commands of SQL for database management using MySQL.

Biological Databases: Nucleotide and protein. Primary, Secondary and Tertiary database.

Definition and significance of Pairwise and Multiple Sequence Alignment. Gap penalties: Opening and extension. Calculation of alignment score. Methods and algorithms used in Pairwise alignment for Local and Global: Dot Matrix, Dynammic Programming algorithm and k-tuple Methods for doing MSA: CLUSTALW, ClustalX and PILEUP, Scoring MSA.Details of Scoring matrices: PAM and BLOSUM series.

Algorithms used in Database similarity searching: BLAST and FASTA. Definition of Profile and Pattern. PSI-BLAST and PHI-BLAST.

Phylogenetic analysis: Concept and method: Distance based (Fitch and Margoliash & UPGMA) and character based methods (Parsimony).

Introduction of protein structure prediction and gene prediction.

Biostatistics and Computer Applications:

Brief description and tabulation of different type data and it's graphical representation.
Measurement of central tendency: Mean Median, Mode, Range, Standard Deviation, and Variance, Idea of two types of error and its level of significance, Chi-Square Test, Simple linear regression and correlation, Probability Distribution (Binomial, Poisson, Gaussian).

Introduction of digital computer: Low level and high-level language, the binary system.
Programming in C: Data Types, Condition checking and looping, Function, Array, Pointer, String Handling.

Introduction of R language and Bioconductor and their application in Bioinformatics.
Computer oriented statistical techniques employing C language: Bubble Sorting, Computation of Median, Variance, Standard Deviation, and Correlation Coefficient.

Texts/References:

1. David W. Mount, Bioinformatics : Sequence and Genome Analysis
2. S.C.Rastogi, Namita Mendiratta and Parag Rastogi, Bioinformatics Concepts, Skills & Application.
3. Essential Bioinformatics. Jin Xiong
4. Bioinformatics and Functional Genomics. Jonathan Pevsner

Paper-VI: 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, Physical and Cytogenetic mapping, SNP, RFLP, TRE, PCR-OLA, SSCP, RAPD

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 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 and Environmental factors Amyotrophic lateral sclerosis pathogenesis, Role of environment on epigenetics of neurodegenerative diseases, Teratology, Molecular genetics of coronary heart disease, Schizophrenia,Diabetes mellitus.

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 sex determination, 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

Immunology and Immunogenetics Practical

1. Identification of lymphoid cells in blood smears and tissue sections.
2. Separation of PBMC from blood
3. Spleen cell preparation from mouse
4. Identification of lymphocyte populations by FACS
5. Ouchterlony immunodiffusion
6. Immuno-electrophoresis of rabbit serum proteins
7. Agglutination of erythrocytes by lectin
8. Enzyme linked immunosorbent assay for cytokines
9. ABO blood grouping
10. Immuno dot blot.

Bioinformatics Practical

1. Searching for a particular literature through PubMed.
2. Use of Public Domain Interfacees 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 MySOL
7. Computer Application: Programming for Solving

a) Statistical problems (eg. Median, Std. Deviation, Correlation Coefficient) through C programming

b) Sequence analysis.

8. Solving the problems of Biostatistics (Average, Median, Mode, Chi square, correlation coefficient, Normal/Poisson Distribution) through MS- Excel.

Gene based diagnosis and Therapy Practical

1. Total RNA extraction & quantification.
2. Southern hybridization of bacterial genome with non-radioactive probe.
3. DNA fingerprinting using RFLP method
4. Single Nucleotide polymorphism analysis
5. Amplification of human gene with specific primer by PCR technique and analysis by agarose gel electrophoresis.
6. Demonstration of cloning of genomic DNA in standard plasmid vectors & measurement of gene expression using reporter assay

Project work