

REVISED CURRICULUM

M. Sc.

MEDICAL
BIOTECHNOLOGY



सत्यमेव जयते

Department of Biotechnology

Ministry of Science & Technology,
Government of India

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LIST OF ELECTIVES

1. Cancer Genetics
2. Clinical Genetics & Counseling
3. Nanobiotechnology
4. Clinical Trials & Bioethics
5. Pharmacogenomics
6. Vaccines

**^Any two 1.5 credit courses can be taken up to make one 3 credit course.
Contents for electives are given separately.**

SEMESTER - I

Biochemistry - 3 Credits

Unit I

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

Amino acids – structure and functional group properties; Peptides and covalent structure of proteins; Elucidation of primary and higher order structures; Evolution of protein structure; Structure-function relationships in model proteins like ribonuclease A, myoglobin, hemoglobin, chymotrypsin etc.; Tools to characterize expressed proteins.

Unit II

Enzyme catalysis – general principles of catalysis; Quantitation of enzyme activity and efficiency; Enzyme characterization and Michaelis-Menten kinetics; Relevance of enzymes in metabolic regulation, activation, inhibition and covalent modification; Single substrate enzymes

Unit III

Sugars - mono, di, and polysaccharides; Suitability in the context of their different functions- cellular structure, energy storage, signaling; Glycosylation of other biomolecules - glycoproteins and glycolipids

Lipids - structure and properties of important members of storage and membrane lipids; lipoproteins

Unit IV

Biomembrane organization - sidedness and function; Membrane bound proteins - structure, properties and function; Transport phenomena;

Nucleosides, nucleotides, nucleic acids - structure, diversity and function; sequencing; Brief overview of central dogma

Unit V

Bioenergetics-basic principles; Equilibria and concept of free energy; Coupled processes; Glycolytic pathway; Krebs's cycle; Oxidative phosphorylation; Photosynthesis; Elucidation of metabolic pathways; Logic and integration of central metabolism; entry/ exit of various biomolecules from central pathways; Principles of metabolic regulation; Regulatory steps; Signals and second messengers.

Texts/References

1. V.Voet and J.G.Voet, Biochemistry, 3rd edition, John Wiley, New York, 2004.
2. A.L. Lehninger, Principles of Biochemistry, 4th edition, W.H Freeman and Company, 2004.
3. L. Stryer, Biochemistry, 5th edition, W.H. Freeman and Company, 2002.

Cell & Developmental Biology - 3 Credits

Unit I

Cell Theory & Methods of Study

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

Membrane Structure and Function

Structural models; Composition and dynamics; Transport of ions and macromolecules; Pumps, carriers and channels; Endo- and Exocytosis; Membrane carbohydrates and their significance in cellular recognition; Cellular junctions and adhesions; Structure and functional significance of plasmodesmata.

Unit II

Organelles

Nucleus – Structure and function of nuclear envelope, lamina and nucleolus; Macromolecular trafficking; Chromatin organization and packaging; Cell cycle and control mechanisms; Mitochondria – structure, organization of respiratory chain complexes, ATP synthase, Structure-function relationship; Mitochondrial DNA and male sterility; Origin and evolution; Chloroplast– Structure-function relationship; Chloroplast DNA and its significance; Chloroplast biogenesis; Origin and evolution.

Unit III

Endo-membrane System and Cellular Motility

Structure and function of microbodies, Golgi apparatus, Lysosomes and Endoplasmic Reticulum; Organization and role of microtubules and microfilaments; Cell shape and motility; Actin-binding proteins and their significance; Muscle organization and function; Molecular motors; Intermediate filaments; Extracellular matrix in plants and animals.

Unit IV

Cellular Movements and Pattern Formation

Laying of body axis planes; Differentiation of germ layers; Cellular polarity; Model plants like Fucus and Volvox; Maternal gene effects; Zygotic gene effects; Homeotic gene effects in Drosophila; Embryogenesis and early pattern formation in plants; Cell lineages and developmental control genes in Caenorhabditis.

Unit V

Differentiation of Specialized Cells

Stem cell differentiation; Blood cell formation; Fibroblasts and their differentiation; Cellular basis of immunity; Differentiation of cancerous cells and role of proto-oncogenes; Phase changes in Salmonella; Mating cell types in yeast; Surface antigen changes in Trypanosomes; Heterocyst differentiation in Anabaena; Sex determination in Drosophila.

Plant Meristem Organization and Differentiation

Organization of Shoot Apical Meristem(SAM); Organization of Root Apical Meristem(RAM); Pollen germination and pollen tube guidance; Phloem differentiation; Self-incompatibility and its genetic control; Embryo and endosperm development; Heterosis and apomixis.

Texts/References

1. Lodish *et al.*, Molecular cell Biology, 4th Edition, W.H. Freeman & Company, 2000.
2. Smith & Wood, Cell Biology, 2nd Edition, Chapman & Hall, London, 1996.
3. Watson *et al.*, Molecular Biology of the gene, 5th Edition, Pearson Prentice Hall. USA, 2003.
4. B. M. Turner, Chromatin & Gene regulation, 1st Edition, Wiley-Blackwell, 2002.
5. Benjamin Lewin, Gene IX, 9th Edition, Jones and Barlett Publishers, 2007.

Molecular Biology - 3 Credits

Unit I

Genome organization

Organization of bacterial genome; Structure of eukaryotic chromosomes; Role of nuclear matrix in chromosome organization and function; Matrix binding proteins; Heterochromatin and Euchromatin; DNA reassociation kinetics(Cot curve analysis); Repetitive and unique sequences; Satellite DNA; DNA melting and buoyant density; Nucleosome phasing; DNase I hypersensitive regions; DNA methylation & Imprinting

Unit II

DNA Structure; Replication; Repair & Recombination

Structure of DNA - A-,B-, Z- and triplex DNA; Measurement of properties-Spectrophotometric, CD, AFM and Electron microscope analysis of DNA structure; Replication initiation, elongation and termination in prokaryotes and eukaryotes; Enzymes and accessory proteins; Fidelity; Replication of single stranded circular DNA; Gene stability and DNA repair- enzymes; Photoreactivation; Nucleotide excision repair; Mismatch correction; SOS repair; Recombination: Homologous and non-homologous; Site specific recombination; Chi sequences in prokaryotes; Gene targeting; Gene disruption; FLP/FRT and Cre/Lox recombination.

Unit III

Prokaryotic & Eukaryotic Transcription

Prokaryotic Transcription; Transcription unit; Promoters- Constitutive and Inducible; Operators; Regulatory elements; Initiation; Attenuation; Termination-Rho-dependent and independent; Anti-termination; Transcriptional regulation-Positive and negative; Operon concept-lac, trp, ara, his, and gal operons; Transcriptional control in lambda phage; Transcript processing; Processing of tRNA and rRNA

Eucaryotic transcription and regulation; RNA polymerase structure and assembly; RNA polymerase I, II, III; Eukaryotic promoters and enhancers; General Transcription factors; TATA binding proteins (TBP) and TBP associated factors (TAF); Activators and repressors; Transcriptional and post-transcriptional gene silencing

Unit IV

Post Transcriptional Modifications

Processing of hnRNA, tRNA, rRNA; 5'-Cap formation; 3'-end processing and polyadenylation; Splicing; RNA editing; Nuclear export of mRNA; mRNA stability; Catalytic RNA.

Translation & Transport

Translation machinery; Ribosomes; Composition and assembly; Universal genetic code; Degeneracy of codons; Termination codons; Isoaccepting tRNA; Wobble hypothesis; Mechanism of initiation, elongation and termination; Co- and post-translational modifications; Genetic code in mitochondria; Transport of proteins and molecular chaperones; Protein stability; Protein turnover and degradation

Unit V

Mutations; Oncogenes and Tumor suppressor genes

Nonsense, missense and point mutations; Intragenic and Intergenic suppression; Frameshift mutations; Physical, chemical and biological mutagens; Transposition - Transposable genetic elements in prokaryotes and eukaryotes; Mechanisms of transposition; Role of transposons in mutation; Viral and cellular oncogenes; Tumor suppressor genes from humans; Structure, function and mechanism of action of pRB and p53 tumor suppressor proteins; Activation of oncogenes and dominant negative effect; Suppression of tumor suppressor genes; Oncogenes as transcriptional activators.

Text/References

1. Benjamin Lewin, Gene IX, 9th Edition, Jones and Barlett Publishers, 2007.
2. J.D. Watson, N.H. Hopkins, J.W Roberts, J. A. Seitz & A.M. Weiner; Molecular Biology of the Gene, 6th Edition, Benjamin Cummings Publishing Company Inc, 2007.
3. Alberts et al; Molecular Biology of the Cell, 4th edition, Garland, 2002.

Analytical Techniques - 3 Credits

Unit I

Basic Techniques

Buffers; Methods of cell disintegration; Enzyme assays and controls; Detergents and membrane proteins; Dialysis, Ultrafiltration and other membrane techniques

Spectroscopy Techniques

UV, Visible and Raman Spectroscopy; Theory and application of Circular Dichroism; Fluorescence; MS, NMR, PMR, ESR and Plasma Emission spectroscopy

Unit II

Chromatography Techniques

TLC and Paper chromatography; Chromatographic methods for macromolecule separation - Gel permeation, Ion exchange, Hydrophobic, Reverse-phase and Affinity chromatography; HPLC and FPLC; Criteria of protein purity

Electrophoretic techniques

Theory and application of Polyacrylamide and Agarose gel electrophoresis; Capillary electrophoresis; 2D Electrophoresis; Disc gel electrophoresis; Gradient electrophoresis; Pulsed field gel electrophoresis

Unit III

Centrifugation

Basic principles; Mathematics & theory (RCF, Sedimentation coefficient etc); Types of centrifuge - Microcentrifuge, High speed & Ultracentrifuges; Preparative centrifugation; Differential & density gradient centrifugation; Applications (Isolation of cell components); Analytical centrifugation; Determination of molecular weight by sedimentation velocity & sedimentation equilibrium methods

Unit IV

Radioactivity

Radioactive & stable isotopes; Pattern and rate of radioactive decay; Units of radioactivity; Measurement of radioactivity; Geiger-Muller counter; Solid & Liquid scintillation counters (Basic principle, instrumentation & technique); Brief idea of radiation dosimetry; Cerenkov radiation; Autoradiography; Measurement of stable isotopes; Falling drop method; Applications of isotopes in biochemistry; Radiotracer techniques; Distribution studies; Isotope dilution technique; Metabolic studies; Clinical application; Radioimmunoassay

Unit V

Advanced Techniques:

Protein crystallization; Theory and methods; API-electrospray and MADI-TOF; Mass spectrometry; Enzyme and cell immobilization techniques; DNA & Peptide Synthesis.

Texts/References

1. Freifelder D., Physical Biochemistry, Application to Biochemistry and Molecular Biology, 2nd Edition, W.H. Freeman & Company, San Fransisco, 1982.
2. Keith Wilson and John Walker, Principles and Techniques of Practical Biochemistry, 5th Edition, Cambridge University Press, 2000.
3. D. Holme & H. Peck, Analytical Biochemistry, 3rd Edition, Longman, 1998.
4. R. Scopes, Protein Purification - Principles & Practices, 3rd Edition, Springer Verlag, 1994.
5. Selected readings from Methods in Enzymology, Academic Press.

Biostatistics & Computer Applications - 3 Credits

Unit I

Fundamental concepts in applied probability; Exploratory data analysis and statistical inference; Probability and analysis of one and two way samples; discrete and continuous probability models; Expectation and variance; Central limit theorem; Inference; Hypothesis; Critical region and error probabilities; Tests for proportion; Equality of proportions; equality of means of normal populations (variance known, variance unknown); Chi-square test for independence; P-value of the statistic; Confidence limits; Introduction to one way and two-way analysis of variance; Data transformations

Unit II

Elements of programming languages - C and PERL; Data base concept; Database management system; Database browsing and Data retrieval; Sequence database and genome database; Data Structures and Databases; Databases such as GenBank; EMBL; DDBJ; Swissprot; PIR; MIPS; TIGR; Hovergen; TAIR; PlasmODB; ECDC; Searching for sequence database like FASTA and BLAST algorithm.

Unit III

Cluster analysis; Phylogenetic clustering by simple matching coefficients; Sequence Comparison; Sequence pattern; Regular expression based pattern; Theory of profiles and their use in sequence analysis; Markov models; Concept of HMMS; Baum-Welch algorithm; Use of profile HMM for protein family classification; Pattern recognition methods

Unit IV

Goals of a Microarray experiment; Normalization of Microarray data; Detecting differential gene expression; Principle component analysis; Clustering of microarray data; Structure determination by X-ray crystallography; NMR spectroscopy; PDB (Protein Data Bank) and NDB (Nucleic Acid Data Bank); File formats for storage and dissemination of molecular structure.

Unit V

Methods for modeling; Homology modeling; Threading and protein structure prediction; Structure-structure comparison of macromolecules with reference to proteins; Force fields; Molecular energy minimization; Monte Carlo and molecular dynamics simulation

Practicals

Introduction to MS EXCEL-Use of worksheet to enter data, edit data, copy data, move data. Use of in-built statistical functions for computations of Mean, S.D., Correlation, regression coefficients etc. Use of bar diagram, histogram, scatter plots, etc. graphical tools in EXCEL for presentation of data. Introduction to SYSTAT package.

Searching PubMed, Introduction to NCBI, NCBI data bases, BLAST BLASTn, BLASTp, PSI-BLAST, Sequence manipulation Suite, Multiple sequence alignment, Primer designing, Phylogenetic Analysis. Protein Modeling, Protein structure Analysis, Docking, Ligplot interactions.

Texts/References

1. Wayne W. Daniel, Biostatistics : A foundation for Analysis in the Health Sciences, 8th Edition, Wiley, 2004.
2. Prem S. Mann, Introductory Statistics, 6th Edition, Wiley, 2006.
3. John A. Rice, Mathematical Statistics and Data Analysis, 3rd Edition, John A. Rice, Duxbury Press, 2006.
4. Campbell and Heyer, Discovering Genomics, Proteomics, & Bioinformatics, 2nd Edition, Benjamin Cummings, 2002.
5. Cynthia Gibas and Per Jambeck, Developing Bioinformatics Computer Skill, 1st Edition, O'Reilly Publication, 2001.

Lab on Biochemistry & Analytical Techniques - 4 Credits

Lab Courses

1. To prepare an Acetic-Na Acetate Buffer system and validate the Henderson-Hasselbalch 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) Ammonium Sulfate precipitation
 - (c) Ion-exchange Chromatography
 - (d) Gel Filtration
 - (e) Affinity Chromatography
 - (f) Generating a Purification Table
 - (g) Assessing purity by SDS-PAGE Gel Electrophoresis
 - (h) Assessing purity by 2-D gel Electrophoresis
 - (i) Enzyme Kinetic Parameters: K_m , V_{max} and K_{cat} .
5. Biophysical methods (Circular dichroism spectroscopy, fluorescence spectroscopy).
 6. Determination of mass of small molecules and fragmentation patterns by Mass Spectrometry

Lab on Molecular Biology - 4 Credits

1. Plasmid DNA isolation and DNA quantitation: Plasmid minipreps
2. Restriction digestion
3. Preparation of competent cells.
4. Agarose gel electrophoresis
3. Restriction Enzyme digestion of DNA
4. Purification of DNA from an agarose gel
5. DNA Ligation
6. Transformation of E.coli with standard plasmids, Calculation of transformation efficiency
7. Cloning of genomic DNA in standard plasmid vectors
8. Confirmation of the insert, Miniprep of recombinant plasmid DNA Restriction mapping
9. Polymerase Chain reaction, using standard 16srRNA eubacterial primers
10. RFLP analysis of the PCR product
11. Transformation of yeast *Saccharomyces cerevisiae*

Communication Skills

Process of communication

Concept of effective communication- Setting clear goals for communication; Determining outcomes and results; Initiating communication; Avoiding breakdowns while communicating; Creating value in conversation; Barriers to effective communication; Non verbal communication- Interpreting non verbal cues; Importance of body language, Power of effective listening; recognizing cultural differences

Presentation skills

Formal presentation skills; Preparing and presenting using Over Head Projector, Power Point; Defending Interrogation; Scientific poster preparation & presentation; Participating in group discussions

Technical Writing Skills

Types of reports; Layout of a formal report; Scientific writing skills: Importance of communicating Science; Problems while writing a scientific document; Plagiarism; Scientific Publication Writing: Elements of a Scientific paper including Abstract, Introduction, Materials & Methods, Results, Discussion, References; Drafting titles and framing abstracts

Computing Skills for Scientific Research

Web browsing for information search; search engines and their mechanism of searching; Hidden Web and its importance in Scientific research; Internet as a medium of interaction between scientists; Effective email strategy using the right tone and conciseness

Texts/References

1. Mohan Krishna and N.P. Singh, Speaking English effectively, Macmillan, 2003.

Immunology - 3 Credits

Unit I

Immunology- fundamental concepts and anatomy of the immune system

Components of innate and acquired immunity; Phagocytosis; Complement and Inflammatory responses; Haematopoiesis; Organs and cells of the immune system- primary and secondary lymphoid organs; Lymphatic system; Lymphocyte circulation; Lymphocyte homing; Mucosal and Cutaneous associated Lymphoid tissue (MALT & CALT); Mucosal Immunity; Antigens - immunogens, haptens; Major Histocompatibility Complex - MHC genes, MHC and immune responsiveness and disease susceptibility, HLA typing

Unit II

Immune responses generated by B and T lymphocytes

Immunoglobulins-basic structure, classes and subclasses of immunoglobulins, antigenic determinants; Multigene organization of immunoglobulin genes; B-cell receptor; Immunoglobulin superfamily; Principles of cell signaling; Immunological basis of self –non-self discrimination; Kinetics of immune response, memory; B cell maturation, activation and differentiation; Generation of antibody diversity; T-cell maturation, activation and differentiation and T-cell receptors; Functional T Cell Subsets; Cell-mediated immune responses, ADCC; Cytokines-properties, receptors and therapeutic uses; Antigen processing and presentation- endogenous antigens, exogenous antigens, non-peptide bacterial antigens and super-antigens; Cell-cell co-operation, Hapten-carrier system

Unit III

Antigen-antibody interactions

Precipitation, agglutination and complement mediated immune reactions; Advanced immunological techniques - RIA, ELISA, Western blotting, ELISPOT assay, immunofluorescence, flow cytometry and immunoelectron microscopy; Surface plasmon resonance, Biosensor assays for assessing ligand –receptor interaction, CMI techniques- lymphoproliferation assay, Mixed lymphocyte reaction, Cell Cytotoxicity assays, Apoptosis, Microarrays, Transgenic mice, Gene knock outs

Unit IV

Vaccinology

Active and passive immunization; Live, killed, attenuated, sub unit vaccines; Vaccine technology- Role and properties of adjuvants, recombinant DNA and protein based vaccines, plant-based vaccines, reverse vaccinology; Peptide vaccines, conjugate vaccines; Antibody genes and antibody engineering- chimeric and hybrid monoclonal antibodies; Catalytic antibodies and generation of immunoglobulin gene libraries.

Unit V

Clinical Immunology

Immunity to Infection : Bacteria, viral, fungal and parasitic infections (with examples from each group); Hypersensitivity – Type I-IV; Autoimmunity; Types of autoimmune diseases; Mechanism and role of CD4+ T cells; MHC and TCR in autoimmunity; Treatment of autoimmune diseases; Transplantation – Immunological basis of graft rejection; Clinical transplantation and immunosuppressive therapy; Tumor immunology – Tumor antigens; Immune response to tumors and tumor evasion of the immune system, Cancer immunotherapy; Immunodeficiency-Primary immunodeficiencies, Acquired or secondary immunodeficiencies.

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.

Medical Microbiology - 3 Credits

Unit I

Infections of the Gastrointestinal Tract

Amoebiasis; Giardiasis and cryptosporidiosis; Intestinal infection by nematodes; Intestinal infection by cestodes (taeniasis and H.nana infection); Trematodes; Bacterial food poisoning(toxic and infective); *E.coli* Diarrhoea; Cholera; Bacillary dysentery; Hepatitis

Unit II

Infections of the Respiratory system

Streptococcal infections; Viral infections; Diphtheria; Whooping cough; Bacterial pneumonias (Haemophilus and GNB, Pneumococcus/Legionella/ etc); Tuberculosis

Unit III

Pyrexial Illness

Malaria; Kala-azar; Leishmaniasis; Filaria; Enteric fever; Brucellosis; Rickettsial diseases; Leptospirosis and relapsing fever; Viral Hemorrhagic fever

Unit IV

Infections of the Nervous System

Viral encephalitis and Aseptic meningitis; Rabies; Cysticercosis and other CNS parasitic infections; Tetanus

Unit V

Sexually Transmitted Diseases and Congenital Infections

Herpes Simplex virus infections; HIV infection and AIDS; Chlamydial infection; Syphilis; Mycoplasma and Ureaplasma infection; Gonorrhoea and other bacterial STD; Congenital viral infections; Toxoplasmosis

Texts/References

1. Betty Forbes, Daniel Sahn, Alice Weinfield, Bailey-Scott's Diagnostic Microbiology, 12th Edition, Mosby. 2007.
2. Gerald Collee J, Andrew G Fraser, Barrie P Marmion, Mackie and McCartney's Practical Medical Microbiology, Elsevier. 2006.
3. Elmer W Koneman et al., Koneman's, Color Atlas and Text Book of Diagnostic Microbiology, 6th Edition, Lippincott Williams and Wilkins, 2005.

Genetic Engineering - 3 Credits

Unit I

Basics Concepts

DNA Structure and properties; Restriction Enzymes; DNA ligase, Klenow enzyme, T4 DNA polymerase, Polynucleotide kinase, Alkaline phosphatase; Cohesive and blunt end ligation; Linkers; Adaptors; Homopolymeric tailing; Labeling of DNA: Nick translation, Random priming, Radioactive and non-radioactive probes, Hybridization techniques: Northern, Southern and Colony hybridization, Fluorescence in situ hybridization; Chromatin Immunoprecipitation; DNA-Protein Interactions-Electromobility shift assay; DNaseI footprinting; Methyl interference assay

Unit II

Cloning Vectors

Plasmids; Bacteriophages; M13 mp vectors; PUC19 and Bluescript vectors, Phagemids; Lambda vectors; Insertion and Replacement vectors; EMBL; Cosmids; Artificial chromosome vectors (YACs; BACs); Animal Virus derived vectors-SV-40; vaccinia/baculo & retroviral vectors; Expression vectors; pMal; GST; pET-based vectors; Protein purification; His-tag; GST-tag; MBP-tag etc.; Intein-based vectors; Inclusion bodies; Methodologies to reduce formation of inclusion bodies; Baculovirus and pichia vectors system, Plant based vectors, Ti and Ri as vectors, Yeast vectors, Shuttle vectors

Unit III

Cloning Methodologies

Insertion of Foreign DNA into Host Cells; Transformation; Construction of libraries; Isolation of mRNA and total RNA; cDNA and genomic libraries; cDNA and genomic cloning; Expression cloning; Jumping and hopping libraries; Southwestern and Far-western cloning; Protein-protein interactive cloning and Yeast two hybrid system; Phage display; Principles in maximizing gene expression

Unit IV

PCR and Its Applications

Primer design; Fidelity of thermostable enzymes; DNA polymerases; Types of PCR – multiplex, nested, reverse transcriptase, real time PCR, touchdown PCR, hot start PCR, colony PCR, cloning of PCR products; T-vectors; Proof reading enzymes; PCR in gene recombination; Deletion; addition; Overlap extension; and SOEing; Site specific mutagenesis; PCR in molecular diagnostics; Viral and bacterial detection; PCR based mutagenesis, Mutation detection: SSCP, DGGE, RFLP, Oligo Ligation Assay (OLA), MCC (Mismatch Chemical Cleavage, ASA (Allele-Specific Amplification), PTT (Protein Truncation Test)

Unit V

Sequencing methods; Enzymatic DNA sequencing; Chemical sequencing of DNA; Automated DNA sequencing; RNA sequencing;

Chemical Synthesis of oligonucleotides; Introduction of DNA into mammalian cells; Transfection techniques; Gene silencing techniques; Introduction to siRNA; siRNA technology; Micro RNA; Construction of siRNA vectors; Principle and application of gene silencing; Gene knockouts and Gene Therapy; Creation of knock out mice; Disease model; Somatic and germ-line therapy- in vivo and ex-vivo; Suicide gene therapy; Gene replacement; Gene targeting; Transgenics; cDNA and intragenic arrays; Differential gene expression and protein array.

Text/References

1. S.B. Primrose, R.M. Twyman and R.W.Old; Principles of Gene Manipulation. 6th Edition, S.B.University Press, 2001.
2. J. Sambrook and D.W. Russel; Molecular Cloning: A Laboratory Manual, Vols 1-3, CSHL, 2001.
3. Brown TA, Genomes, 3rd ed. Garland Science 2006
4. Selected papers from scientific journals.
5. Technical Literature from Stratagene, Promega, Novagen, New England Biolab etc.

Microbial & Human Genetics - 3 Credits

Unit I

Bacterial mutants and mutations

Isolation; useful phenotypes (auxotrophic; conditional lethal; resistant); Mutation rate; Types of mutations (base pair changes; frameshift; insertions; deletions; tandem duplication); Reversion vs. suppression; Mutagenic agents; Mechanisms of mutagenesis; Assay of mutagenic agents (Ames test)

Gene transfer in bacteria

History; Transduction – generalized and specialized; Conjugation – F, F', Hfr; F transfer; Hfr-mediated chromosome transfer; Transformation – natural and artificial transformation; Merodiploid generation; Gene mapping; Transposable genetic elements; Insertion sequences; Composite and Complex transposons; Replicative and non-replicative transposition; Genetic analysis using transposons.

Unit II

Bacteriophages and Plasmids

Bacteriophage – structure; assay; Lambda phage – genetic map, lysogenic and lytic cycles; Gene regulation; Filamentous phages such as M13; Plasmids – natural plasmids; their properties and phenotypes; Plasmid biology - copy number and its control; Incompatibility; Plasmid survival strategies; Antibiotic resistance markers on plasmids (mechanism of action and resistance); Genetic analysis using phage and plasmid

Restriction-modification systems

History; types of systems and their characteristics; Methylation-dependent restriction systems; applications.

Unit III

Mendelian Genetics

Introduction to human genetics; Background and history; Types of genetic diseases; Role of genetics in medicine; Human pedigrees; Patterns of single gene inheritance - autosomal recessive; autosomal dominant; X linked inheritance; Complicating factors - incomplete penetrance; variable expression; Multiple alleles; Co dominance; Sex influenced expression; Hemoglobinopathies - Genetic disorders of hemoglobin and their diseases.

Non Mendelian inheritance patterns

Mitochondrial inheritance; genomic imprinting; Lyon hypothesis; isodisomy. Complex inheritance - genetic and environmental variation; Heritability; Twin studies; Behavioral traits; Analysis of quantitative and qualitative traits

Unit IV

Cytogenetics

Cell division and errors in cell division; Non disjunction; Structural and numerical chromosomal abnormalities – deletion; duplication; translocation; Sex determination; Role of Y chromosome; Genetic recombination; Disorders of sex chromosomes and autosomes; Molecular cytogenetics – Fluorescence In Situ Hybridization (FISH); Comparative Genomic Hybridization (CGH).

Developmental genetics

Genes in early development; Maternal effect genes; Pattern formation genes; Homeotic genes; and Signaling and adhesion molecules.

Immunogenetics

Major histocompatibility complex; Immunoglobulin genes - tissue antigen and organ transplantation; Single gene disorders of immune system.

Unit V

Genetic variation

Mutations; kinds of mutation; agents of mutation; genome polymorphism; uses of polymorphism.

Gene mapping and human genome project

Physical mapping; linkage and association

Population genetics and evolution

Phenotype; genotype; gene frequency; Hardy-Weinberg law; Factors distinguishing Hardy-Weinberg equilibrium; Mutation selection; Migration; Gene flow; Genetic drift. Human genetic diversity; Origin of major human groups.

Texts/References

1. S.R. Maloy, J.E. Cronan, D. Friefelder, Microbial Genetics, 2nd Edition, Jones and Bartlett Publishers, 1994.
2. N. Trun and J. Trempy, Fundamental Bacterial Genetics, Blackwell publishing, 2004.
3. Strachan T and Read A P, Human molecular genetics, 3rd Edition Wiley Bios, 2006.
4. Mange E J and Mange A. P., Human genetics, 2nd Edition, Sinauer Associates publications, 1999.
5. Hartl L D and Jones B, Analysis of genes and genomes, 3rd Edition, Jones and Bartlett Publishers, 1994.

Genomics and Proteomics - 3 Credits

Unit I

Introduction to Genomics

Structure and organization of prokaryotic and eukaryotic genomes - nuclear, mitochondrial and chloroplast genomes; Computational analysis of sequences- finding genes and regulatory regions; Gene annotation; Similarity searches; Pairwise and multiple alignments; Alignment statistics; Prediction of gene function using homology, context, structures, networks; Genetic variation-polymorphism, deleterious mutation; Phylogenetics; Tools for genome analysis- PCR, RFLP, DNA fingerprinting, RAPD, Automated DNA sequencing; Linkage and pedigree analysis; Construction of genetic maps; Physical maps, FISH to identify chromosome landmarks.

Unit II

Genome sequencing

Human genome project-landmarks on chromosomes generated by various mapping methods; BAC libraries and shotgun libraries preparation; Physical map-cytogenetic map, contig map, restriction map, DNA sequence; DNA sequencing and sequence assembly; Model organisms and other genome projects; Comparative genomics of relevant organisms such as pathogens and non-pathogens; Evolution of a pathogen e.g. Hepatitis C virus or a bacterial pathogen; Taxonomic classification of organisms using molecular markers- 16S rRNA typing/sequencing;

Unit III

DNA Microarray technology

Basic principles and design: cDNA and oligonucleotide arrays; Applications: Global gene expression analysis, Comparative transcriptomics, Differential gene expression; Genotyping/SNP detection; Detection technology; Computational analysis of microarray data.

Unit IV

Proteomics

Overview of protein structure-primary, secondary, tertiary and quaternary structure; Relationship between protein structure and function; Outline of a typical proteomics experiment; Identification and analysis of proteins by 2D analysis; Spot visualization and picking; Tryptic digestion of protein and peptide fingerprinting; Mass spectrometry : ion source (MALDI, spray sources); analyzer (ToF, quadrupole, quadrupole ion trap) and detector; clinical proteomics and disease biomarkers; Prions; proteins in disease; Protein-protein interactions: Solid phase ELISA, pull-down assays (using GST-tagged protein), far western analysis, by surface plasmon resonance technique, Yeast two hybrid system, Phage display; Protein interaction maps; Protein arrays-definition, applications- diagnostics, expression profiling.

Unit V

Human disease genes; DNA polymorphism including those involved in disease; Hemoglobin and the anemias; Phenylketonuria (monogenic) and diabetes (multigenic) genetic disorders; 'disease' gene vs. 'susceptibility' gene; SNP detection: hybridization based assays (allele specific probes); Polymerization based assays (allele

specific nucleotide incorporation, allele-specific PCR); Ligation based assays (allele specific oligonucleotide ligation); Polymorphism detection without sequence information: SSCP; Proteomics and drug discovery; High throughput screening for drug discovery; Identification of drug targets; Pharmacogenomics and pharmacogenetics and drug development; Toxicogenomics; Metagenomics.

Texts/References

1. Brown TA, Genomes, 3rd Edition, Garland Science, 2006.
2. Campbell AM & Heyer LJ, Discovering Genomics, Proteomics and
3. Bioinformatics, 2nd Edition, Benjamin Cummings, 2007.
4. Primrose S & Twyman R, Principles of Gene Manipulation and Genomics, 7th Edition, Blackwell, 2006.
5. Glick BR & Pasternak JJ, Molecular Biotechnology, 3rd Edition, ASM Press, 1998.
6. Ed. C. Cantor and C.L. Smith, Genomics: The Science and Technology behind the Human Genome Project, Wiley-Interscience, 2000.
7. G. Gibson, S. V. muse, A Primer of Genome Science, Sinauer Associates Inc. Publishers, 2002.
8. H. Rehm, Protein Biochemistry and Proteomics, 4th Edition, Academic Press, 2006.
9. E. de Hoffman and V. Stroobant, Mass Spectrometry, 2nd Edition, Wiley. 2002.

Lab on Immunology - 3 Credits

1. Isolation and purification of IgG from serum or IgY from chicken egg
2. Immunodiagnostics using commercial kits
3. Immunohistochemistry (direct and indirect peroxidase assay)
4. Complement fixation test
5. Hybridoma technology and monoclonal antibody production
6. Bio-assay for cytokines (Interleukin-2)
7. Cell cytotoxicity assay (Trypan blue indicator); (DNA ladder) – apoptosis of cells
8. Mixed lymphocyte reaction.

Lab on Genetic Engineering - 3 Credits

1. Isolation of genomic DNA from *Bacillus subtilis** genome.
2. PCR amplification of *scoC* gene and analysis by agarose gel electrophoresis
3. Preparation of plasmid, pET-28a from *E.coli* DH5 α and gel analysis.
4. Restriction digestion of vector (gel analysis) and insert with NcoI and XhoI
5. a. Vector and Insert ligation
b. Transformation in *E.coli* DH5 α
6. Plasmid isolation and confirming recombinant by PCR and RE digestion.

7. Transformation of recombinant plasmid in *E.coli* BL21 (DE3) strain
8. Induction of ScoC protein with IPTG and analysis on SDS-PAGE
9. Purification of protein on Ni-NTA column and analysis of purification by SDS-PAGE
10. a. Random Primer labeling of scoC with Dig-11-dUTP
b. Southern hybridization of *B. subtilis* genome with probe and non-radioactive detection.

*Any other bacterial strain can be used.

Lab on Microbial Genetics - 2 Credits

1. Pure culture techniques
2. Solid and liquid cultures enumeration
3. Growth curve using viable count; Total cell count
4. Determination of Antibiotic resistance
5. Isolation of auxotrophic and/or antibiotic resistant mutants
6. Behavior of mutants on indicator plates; Isolation of mutants using UV light
7. Reversion test (Ames Test)
8. Preparation and plaque assay of bacteriophages
9. Episome transfer using F' plasmid
10. Detection of restriction and modification enzyme activity
11. Gene complementation using gene transfer technique
12. Measurement of gene expression using reporter assay

Immunotechnology - 3 Credits

Unit 1

Introduction to Immunotechnology

Kinetics of immune response, memory; Principles of Immunization; Techniques for analysis of Immune response

Unit 2

Antibody Related Techniques

Immuno-chemistry of Antigens - Immunogenicity, Antigenicity, haptens, Toxins-Toxioids, Hapten-carrier system; Genetic bases of immune response – Heterogeneity; Role and properties of adjuvants, Immune modulators; B cell epitopes; Hybridoma Rabbit, human; Antigen – Antibody interaction, affinity, cross reactivity, specificity, epitope mapping; Immuno assays RIA, ELISA, Western blotting, ELISPOT assay, immunofluorescence, Surface plasmon resonance, Biosensor assays for assessing ligand – receptor interaction

Unit 3

New Generation Antibodies

Multigene organization of immunoglobulin genes, Ab diversity; Antibody engineering; Phage display libraries; Antibodies as in vitro and in vivo probes

Unit 4

CMI and Imaging techniques

CD nomenclature, Identification of immune Cells; Principle of Immunofluorescence Microscopy, Fluorochromes; Staining techniques for live cell imaging and fixed cells; Flow cytometry, Instrumentation, Applications; Cell Functional Assays – lymphoproliferation, Cell Cytotoxicity, mixed lymphocyte reaction, Apoptosis, Cytokine expression; Cell cloning, Reporter Assays, In-situ gene expression techniques; Cell imaging Techniques- *In vitro* and *In vivo*; Immuno-electron microscopy; *In vivo* cell tracking techniques; Microarrays; Transgenic mice, gene knock outs

Unit 5

Vaccine technology

Rationale vaccine design based on clinical requirements: Hypersensitivity, Immunity to Infection, Autoimmunity, Transplantation, Tumor immunology, immunodeficiency; Active immunization, live, killed, attenuated, Sub unit vaccines; Recombinant DNA and protein based vaccines, plant-based vaccines and reverse vaccinology; Peptide vaccines, conjugate vaccines; Passive Immunization; Antibody, Transfusion of immuno-competent cells, Stem cell therapy; Cell based vaccines

Texts/References

1. F.C. Hay, O.M.R. Westwood, Practical Immunology, 4th Edition-, Blackwell Publishing, 2002
2. S. Hockfield, S. Carlson, C. Evans, P. Levitt, J. Pintar, L. Silberstein, Selected Methods for Antibody and Nucleic Acid probes, Volume1, Cold Spring Harbor Laboratory Press,1993.
3. Ed Harlow, David Lane, Antibodies Laboratory Manual, Cold Spring Harbor, Laboratory Press, 1988.

Molecular Diagnostics - 3 Credits

Unit I

Host pathogen interactions in disease process; Protective immune response in Bacterial, Viral and Parasitic diseases; Cancer; Inappropriate Immune response; Disease pathology and clinical spectrum; Clinical diagnosis of diseases; Molecular Genetics of the host and the pathogen

Unit II

Biochemical disorders; Immune, Genetic and Neurological disorders; Molecular techniques for analysis of these disorders; Assays for the Diagnosis of inherited diseases; Bioinformatic tools for molecular diagnosis

Unit III

Antibody based diagnosis; Monoclonal antibodies as diagnostic reagents; Production of monoclonal antibodies with potential for diagnosis; Diagnosis of bacterial, viral and parasitic diseases by using; ELISA and Western blot.

Unit IV

Isolation of DNA; purification and analysis; DNA sequencing and diagnosis; PCR and Array based techniques in diagnosis; Single nucleotide polymorphism and disease association; Two dimensional gene scanning

Unit V

Isolation of proteins and other molecules associated with disease; Process and their profiling for diagnosis; 2D analysis of such proteins by sequencing individual spots by Mass Spectrometry; Protein Micro array; Present methods for diagnosis of Specific diseases like Tuberculosis, Malaria and AIDS; Ethics in Molecular Diagnosis

Texts/References

1. Campbell, M.A and Heyer L.J., Discovering Genomics, Proteomics and Bioinformatics, 2nd Edition, CSHL Press, Pearson/Benzamin Cummings San Francisco, USA, 2007.
2. Andrew Read and Dian Donnai, New Clinical Genetics, Scion Publishing Ltd, Oxfordshire, UK, 2007.
3. James W Goding, Monoclonal antibodies: Principles and Practice, 3rd Edition, Academic Press, 1996.
4. George Patrinos and Wilhelm Ansoarge, Molecular Diagnostics, 1st Edition, Academic Press, 2005.
5. Lela Buchingham and Maribeth L Flawsm, Molecular Diagnostics: Fundamentals, Methods and Clinical Applications, 1st Edition, F A Davis Company, Philadelphia, USA, 2007.

Molecular Therapeutics - 3 Credits

Unit I

Gene therapy; Intracellular barriers to gene delivery; Overview of inherited and acquired diseases for gene therapy; Retro and adeno virus mediated gene transfer; Liposome and nanoparticles mediated gene delivery

Unit II

Cellular therapy; Stem cells: definition, properties and potency of stem cells; Sources: embryonic and adult stem cells; Concept of tissue engineering; Role of scaffolds; Role of growth factors; Role of adult and embryonic stem cells; Clinical applications; Ethical issues

Unit III

Recombinant therapy; Clinical applications of recombinant technology; Erythropoietin; Insulin analogs and its role in diabetes; Recombinant human growth hormone; Streptokinase and urokinase in thrombosis; Recombinant coagulation factors

Unit IV

Immunotherapy; Monoclonal antibodies and their role in cancer; Role of recombinant interferons; Immunostimulants; Immunosuppressors in organ transplants; Role of cytokine therapy in cancers; Vaccines: types, recombinant vaccines and clinical applications

Unit V

Gene silencing technology; Antisense therapy; siRNA; Tissue and organ transplantation; Transgenics and their uses; Cloning; Ethical issues

Texts/References:

1. Bernhard Palsson and Sangeeta N Bhatia, Tissue Engineering, 2nd Edition, Prentice Hall, 2004.
2. Pamela Greenwell, Michelle McCulley, Molecular Therapeutics: 21st century medicine, 1st Edition, Springer, 2008.

IPR, Biosafety & Bioethics - 3 Credits

Unit I

Introduction to Intellectual Property

Types of IP: Patents, Trademarks, Copyright & Related Rights, Industrial Design, Traditional Knowledge, Geographical Indications, Protection of New GMOs; International framework for the protection of IP

IP as a factor in R&D; IPs of relevance to Biotechnology and few Case Studies; Introduction to History of GATT, WTO, WIPO and TRIPS

Unit II

Concept of 'prior art'

Invention in context of "prior art"; Patent databases; Searching International Databases; Country-wise patent searches (USPTO, EPO, India etc.); Analysis and report formation

Basics of Patents

Types of patents; Indian Patent Act 1970; Recent Amendments; Filing of a patent application; Precautions before patenting-disclosure/non-disclosure; WIPO Treaties; Budapest Treaty; PCT and Implications; Role of a Country Patent Office; Procedure for filing a PCT application

Unit III

Patent filing and Infringement

Patent application- forms and guidelines, fee structure, time frames; Types of patent applications: provisional and complete specifications; PCT and convention patent applications; International patenting-requirement, procedures and costs; Financial assistance for patenting-introduction to existing schemes; Publication of patents-gazette of India, status in Europe and US

Patenting by research students, lecturers and scientists-University/organizational rules in India and abroad, credit sharing by workers, financial incentives

Patent infringement- meaning, scope, litigation, case studies and examples

Unit IV

Biosafety

Introduction; Historical Background; Introduction to Biological Safety Cabinets; Primary Containment for Biohazards; Biosafety Levels; Biosafety Levels of Specific Microorganisms; Recommended Biosafety Levels for Infectious Agents and Infected Animals; Biosafety guidelines - Government of India; Definition of GMOs & LMOs; Roles of Institutional Biosafety Committee, RCGM, GEAC etc. for GMO applications in food and agriculture; Environmental release of GMOs; Risk Analysis; Risk Assessment; Risk management and communication; Overview of National Regulations and relevant International Agreements including Cartagena Protocol.

Unit V

Bioethics

Concepts; Philosophical considerations; Epistemology of Science; Ethical Terms; Principles & Theories; Relevance to Biotechnology; Ethics and the Law Issues: Genetic Engineering, Stem Cells, Cloning, Medical techniques, Transhumanism, Bioweapons; Research concerns - Animal Rights, Ethics of Human Cloning, Reproduction and Stem Cell Research; Emerging issues: Biotechnology's Impact on Society; DNA on the Witness Stand - Use of genetic evidence in civil and criminal court cases; Challenges to Public Policy - To Regulate or Not to Regulate; Improving public understanding of biotechnology products to correct misconceptions

Important Links

<http://www.w3.org/IPR/>

<http://www.wipo.int/portal/index.html.en>

http://www.ipr.co.uk/IP_conventions/patent_cooperation_treaty.html

www.patentoffice.nic.in

www.iprlawindia.org/ - 31k - Cached - Similar page

<http://www.cbd.int/biosafety/background.shtml>

<http://www.cdc.gov/OD/ohs/symp5/jyrtext.htm>

<http://web.princeton.edu/sites/ehs/biosafety/biosafetypage/section3.html>

Bioethics - by Ellen Frankel Paul , Fred D. Miller, Jeffrey Paul , Fred Dycus Miller

<http://www.accessexcellence.org/RC/AB/IE/#Anchor-Bioethics-6296> www.bioethics.net

Bioethics & Science

http://www.americanprogress.org/issues/domestic/science?_kk=bioethics&_kt=21a1e10d-48e4-44bc-8b39-21c695383746

The Stem cell debate

<http://www.billmuehlenberg.com/2005/09/02/the-stem-cell-debate/>

Lab on Immunotechnology - 3 Credits

Immunochemistry

1. Antibody assays
 - a. Immunodiffusion
 - b. Immunoelectrophoresis
 - c. Purification of Antibodies
2. Generation of antibodies – Rabbit or mice; Western Blot Analysis; ELISA.

Animal Cell Culture

1. Cell Culture lab practices
2. Cryopreservation, reviving frozen cultures
3. Hybridoma technology – Theory/demonstration
4. Macrophage cell line (eg. THP1) revival and *in vitro* phagocytosis assay
5. PBMC separation and analysis of monocytes
6. MTT assay to determine proliferation of T cells
7. T cell isolation–magnetic bead based
8. Flowcytometry–Theory/demonstration
9. HLA typing Theory/Demonstration.