REVISED CURRICULUM

M. Sc.

MOLECULAR & HUMAN GENETICS

Department of Biotechnology
Ministry of Science & Technology,
Government of India
REVISED CURRICULUM

M. Sc.

MOLECULAR & HUMAN GENETICS

Department of Biotechnology
Ministry of Science & Technology,
Government of India
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**LIST OF ELECTIVES**

1. Diagnostics ................................................................. 3
2. Cancer Genetics ............................................................. 3
3. Neurogenetics ............................................................... 3
4. Evolutionary Genetics ..................................................... 1.5
5. Model Genetic Systems .................................................... 1.5
6. Reproductive Genetics ................................................... 1.5
7. Pharmacogenomics .......................................................... 1.5
8. Stem Cell Biology ......................................................... 1.5
9. Nanobiotechnology ........................................................ 1.5

^Any two 1.5 credit courses can be taken up to make one 3 credit course.

Contents for electives are given separately.
SEMESTER - I

Cell Biology & Cytogenetics - 3 Credits

Unit I
Plasma Membrane: Organization and dynamics of transport across membrane; Mechanism of endocytosis and exocytosis; Cytoskeleton; Microfilaments: Structural organization, cell motility and cell shape; Microtubule: Structural and functional organization; Cilia, flagella, centriole; Intermediate filaments; Mitochondria: Ultrastructure; Chemiosmotic theory and respiratory chain complexes; Structure and function of peroxisome; Nucleolus and biosynthesis of ribosome

Unit II
Cell-Cell Interactions: Cell adhesion molecules; Cellular junctions; Extracellular matrix; Signal transduction: Intracellular receptor and cell surface receptors; Signaling via G-protein linked receptors (PKA, PKC, CaM kinase); Enzyme linked receptor signaling pathways; Network and cross-talk between different signal mechanisms; Programmed cell death

Unit III
Chromatin structure: Histones, DNA, Nucleosome and higher level organization; Chromosome organization: Metaphase chromosome: centromere, kinetochore, telomere and its maintenance; Holocentric chromosomes and supernumerary chromosomes; Chromosomal domains (matrix, loop domains) and their functional significance; Heterochromatin and euchromatin; Position effect; Variegation; Boundary elements; Chromosome bandings; Functional states of chromatin and alterations in chromatin organization; Structural and functional organization of interphase nucleus

Unit IV
Giant chromosomes: Polytene chromosomes, Lampbrush chromosomes; Mitosis: Mitotic spindle and arrangement of chromosomes on equator; Regulation of exit from metaphase; Chromosome movement at anaphase; Meiosis: Overview of the process; Meiosis specific cellular changes; Genetic control of meiosis (example: yeast)

Unit V
Chromosomal anomalies: Numerical, Structural, Meiosis in inversion and translocation heterozygotes; Breakage; Fusion-bridge cycles; Induced chromosomal aberrations in somatic cells; Sister chromatid exchanges and somatic crossing over; Dosage compensation in Caenorhabditis, Drosophila and mammals

Texts/References
Principles of Genetics - 3 Credits

Unit I

*Mendelism and its extensions*

Law of segregation; Law of independent assortment; Chromosomal basis of segregation and independent assortment; Linkage; Crossing over; Multiple allelism; Pleiotropy; Cytoplasmic inheritance

Unit II

*Cytogenetics*

International System for Human Chromosome Nomenclature; Mechanisms of numerical and structural chromosomal aberrations; Chromosomal basis of sex determination; Non-chromosomal basis of sex determination; Cytoplasmic inheritance

Unit III

*Molecular Genetics*

Nature of genetic material and flow of genetic information; Organization of Prokaryotic and Eukaryotic genomes; Gene clusters: Identity and variation in tandem gene clusters; Organization of the organelle genomes; Recombination, deletion and complementation mapping in T4 (rII locus); Gene mapping in bacteria: Transformation, conjugation, transduction and sexduction; Transposable elements

Unit IV

*Human Molecular Genetics*

Organization of human genome; Pedigree analysis; Monogenic and polygenic traits; Gene mapping and linkage analysis; Genetic counseling; Prenatal diagnosis; Cancer Genetics; Molecular mechanisms of carcinogenesis; Multistage evolution of cancer; Apoptosis and cancer

Unit V

*Genetic disorders*

Inborn errors of metabolism: Phenylketonuria; Neurogenetic disorders: Alzheimer’s disease; Muscle genetic disorders: Duchenne Muscular Dystrophy; Genetic disorders of Haematopoietic systems: Sickle cell anemia; Multifactorial disorders: Diabetes mellitus; Mitochondrial syndromes; Management of genetic disorders

Texts/References

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; Kreb’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

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

Eukaryotic 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

Laboratory Tools & 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 based 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 MALDI-TOF; Mass spectrometry; Enzyme and cell immobilization techniques; DNA & Peptide Synthesis.

Texts/References

Lab on Biochemistry & Laboratory Techniques - 4 Credits

1. To prepare an Acetic - Na Acetate 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) 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: Km, Vmax and Kcat.
5. Biophysical methods (Circular dichroism spectroscopy, fluorescence spectroscopy).
6. Determination of mass of small molecules and fragmentation patterns by Mass Spectrometry

Lab on Cytogenetics & Molecular Biology - 4 Credits

Isolation of Genomic DNA from Chicken blood or mouse tissues
1. Genomic DNA isolation and purification from the nuclei and quantitation of DNA by spectrophotometer.
2. EcoRI digestion of total DNA
3. Transfer of digested DNA and probing with a labeled gene probe

**Analysis of RNA**
1. Isolation of total RNA from mouse liver using guanidine isothiocyanate method
2. Quantitation of RNA by spectrophotometer
3. Size fractionation of total RNA on MOPS agarose gel
4. Visualization of 18S and 28S rRNA bands and transfer of RNA onto membrane
5. Northern blot using rRNA specific PCR amplified DNA probe

**Polymerase chain reaction and its applications**
1. cDNA synthesis from the total RNA using oligo dT primers
2. Amplification of actin gene segment using actin specific primers
3. qPCR using real time PCR machine
4. Detection of known/unknown mutation by SSCP analysis (appropriate primers from a normal and a mutant cell lines or from known patient samples)
5. PCR detection of known mutation using Allele specific primers of a known gene, e.g. globin gene in Thalassemia patient
6. RFLP analysis of PCR amplified DNA, DNA finger printing, using a PCR method (using Bangalore-Genei teaching kits)

**Conditional expression of genes**
1. In *Drosophila* using the Gal4-UAS system (e.g. crossing Dpp-Gal4 and UAS-eyeless flies for induction of ectopic eyes in legs and wings in progeny or crossing HS-Gal4 and UAS-GFP flies and examining GFP expression in progeny following heat shock)

**Cytogenetics laboratory**
1. Identification of normal and mutant flies (*Drosophila melanogaster*)
2. Preparation of Drosophila polytene Chromosomes (temporary and permanent preparations)
3. *Drosophila* genetic crosses
4. In situ hybridization using DIG labeled Hsp gene probe on polytene chromosomes
5. Separation and short term culture of lymphocytes using Ficoll-Hypaque
6. Chromosome preparation from mouse bone marrow and human blood lymphocytes
7. G-banding and karyotyping
8. Identification of inactivated X chromosome as Barr body and drumstick

**Introductory Biology**

**Unit I**

*Introduction to Macromolecules*
Introduction to Biology; Macromolecules; Carbon chemistry; Proteins: Structure, folding, catalysis; Nucleic acids: storage and transfer of genetic information; Lipids: membranes, energy storage; Carbohydrates: energy storage, building blocks
Unit II  
**Molecular genetics**  
Genes; Basics of DNA replication, transcription, translation, Genome organization; Mutations; Gene technology

Unit III  
**Cell biology and energetics**  
Cell structure; Membranes; Function of cell organelles; Energetics; ATP and glycolysis; Respiration; Photosynthesis

Unit IV  
**Reproduction, Heredity, Evolution**  
Reproduction and Heredity; Cell division: mitosis, meiosis, gamete formation, pollination; Mendelian genetics; Evolution; Gene variation (Hardy-Weinberg principle); Darwin's theory of evolution.

Unit V  
**Principles of Classification**  
Viruses, bacteria, protists, fungi; Physiology aspects of Plants & Animals; Regulatory systems (nervous, endocrine, immune systems); Ecology; Populations and communities; Biosphere; Conservation

Texts/References  
   http://www.whfreeman.com/thelifewirebridge2/  
   http://www.ravenbiology.com

**Introductory Mathematics**

**Notation, error analysis, and probability**  
Scientific notation: significant digits, rounding off, scientific notation; Error analysis; Counting and Probability; Addition rules; Permutations; Combinations; Inclusion-exclusion rule; Sampling with and without replacement; Conditional probability: Bayes’ theorem; Independence

**Descriptive statistics and Random variables**  
Measures of central tendency: mean, median, mode; Expectation; Measures of spread: range, percentile, standard deviation; Higher moments: kurtosis, skew; Displaying data: Histograms, stem-and-leaf plots, box plots, frequency distributions; Discrete random variables: Bernoulli, Binomial, Poisson, Geometric distributions, Continuous random variables: Normal, Exponential distributions, Standard normal distribution

**Inferential statistics and one sample hypothesis testing**  
Samples and populations: Random, stratified and cluster sampling. Single- and Double-blind experiments. Point and interval estimates, Sampling distributions: $t$, chi-square, $F$ distributions, Hypothesis testing: null and alternative hypotheses, decision criteria, critical values, type I and type II errors, the meaning of statistical significance, power of a test, One sample hypothesis testing: Normally distributed data: $z$, $t$ and chi-square tests. Binomial proportion testing.
Multi-sample and nonparametric hypothesis testing
Two sample hypothesis testing; Nonparametric methods: signed rank test, rank sum test, Kruskal-Wallis test, Analysis of variance: One-way ANOVA. Curve fitting, Regression and correlation: simple linear regression, the least squares method, Analysis of enzyme kinetic data. Michaelis-Menten, Lineweaver-Burk and the direct linear plot, Polynomial curve fitting.

Texts/References

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
Immunology & Immunogenetics - 3 Credits

Unit I

Introduction to immune system
Innate and adaptive immunity; Cells and organs of the immune system; Primary and secondary immune responses; Antigens; Antibodies and T cell receptors: Antigens, Structure and function of immunoglobulins, Monoclonal antibodies, B and T cell receptors and coreceptors, Antigen-antibody interactions

Unit II

Immunoglobulin and T-cell receptor genes
Organization of Ig gene loci; Molecular mechanisms of generation of antibody diversity; Expression of Ig genes; Regulation of Ig gene transcription; Antibody engineering; Organization of TCR gene loci; Generation of TCR diversity

The HLA complex
Organization of HLA complex; Structure of class I and II HLA molecules; Expression of HLA genes; HLA polymorphism

Unit III

Generation and regulation of immune responses
Antigen processing and presentation; MHC-restriction; Cytokines; T Cell Maturation, activation and differentiation; B Cell Generation, activation and differentiation; Clonal selection and immunological memory; Complement system; Leukocyte activation and migration; Cell mediated cytotoxic responses; Regulation of immune responses; Immunological tolerance

Unit IV

Disorders of Human Immune System
Primary and secondary immunodeficiencies; Autoimmune disorders; Hypersensitive reactions; Cytokine-related diseases

Unit V

Immune system in human health
Immune response to infectious diseases and malignancy; Concept of immunotherapy; Vaccines; Transplantation immunology

Texts/References

**Biostatistics & Population Genetics - 3 Credits**

**Unit I**

*Biostatistics*
Overview; Measures of central tendency: Mean, Median, Mode; Measures of dispersion: Standard deviation, standard error, Variance, Coefficient of variation; Various methods of presentation and interpretation of data

Hypothesis testing: Definition; Statistical & Scientific hypothesis; The null and alternative hypothesis; Procedure (steps) for Hypothesis testing; Brief idea about various softwares used in biostatistics; Population genetics and clinical data analysis (SPSS, Analyse IT, POGENE, Sigma Plot, Phylip, Popstar, Arlequin, BLAST search & FASTA)

**Unit II**

ANOVA: General idea of one way & two way analysis; General idea of Correlation Analysis; General idea of Regression Analysis; Test of significance: Student’s t-test, Chi-square tests, F-tests, Test of proportion; Methods of statistical inference: Parametric and Non Parametric Methods; Methods of Sampling and Cluster Analysis; Sample size calculation.

**Unit III**

*Population Genetics*
Mendelian Genetics in Population-I: The Hardy- Weinberg Equilibrium for more than two alleles; A simulation; A numerical calculation: Genotype and allele frequencies; Use of HW principle; Odds ratio and Relative risk.

Mendelian Genetics in Population-II: Migration; Genetic Drift; Nonrandom Mating; General analysis of inbreeding; coefficient of inbreeding; Inbreeding depression.

Mendelian Genetics in Population III: Factors affecting changes in allele and genotype frequencies; Selection; Statistical analysis of allele and genotype frequencies using Chi-square test; Mutation, rate of mutation; Mutation and Selection.

**Unit IV**

Multiple Loci: Linkage equilibrium and Linkage disequilibrium (LD); Sexual Reproduction, random mating and LD; Quantitative Traits and QTLs; Identifying QTLs: Mapping; Heritability: Measurement, Narrow sense and Broad Sense heritability; Monogenic traits: Bayesian calculations

**Unit V**

Genetic variability in natural populations: Chromosomal and allozyme polymorphism; Adaptive genetic polymorphism; DNA polymorphism; Genetic co-adaptation & Linkage disequilibrium

Balanced genetic polymorphism; Heterosis & heterozygous superiority
Texts/References
3. Hartl and Jones, Genetics - Principles and Analysis, 5th edition Jones and Barlet.[2001]
4. SK Gupta, Statistical Methods, S Chand Company.

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; Cosmids; Artificial chromosome vectors (YACs; BACs); Animal Virus derived vectors-SV-40; vaccinia/baculco & 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
4. Selected papers from scientific journals.
5. Technical Literature from Stratagene, Promega, Novagen, New England Biolab etc.

Developmental Genetics- 3 Credits

Unit I
Fertilization-vertebrates (including human): Germ cell determination and differentiation: spermatogenesis, oogenesis, maturation of germ cells, ovulation and implantation; External fertilization, e.g., Sea Urchin.; Internal Fertilization in mammals; Polyspermy.

Elements of Early Development in vertebrates (including human): Fertilization to Cleavage; Pattern of Cleavage; Gastrulation; Cell specification and axis formation.

Drosophila early development: Fertilization, cleavage and gastrulation; Pattern Formation; Primary axis formation during oogenesis; Dorsal ventral patterning; Segmentation and anterior and posterior patterning; Segmentation genes; Homeotic selector genes; Homeobox and its evolutionary significance.

Unit II
Central Nervous System in vertebrates: Neural tube formation; Tissue architecture of CNS; Limb development in vertebrates: Formation of Limb Bud; Proximal Distal axis of the limb; Cell death and formation of digits and joints; Regeneration and Senescence: Epimorphic, morphallactic and compensatory regeneration; Ageing: causes and regulation; Pleuropotency of Stem cells: Embryonic and adult stem cells, organization, characteristics and therapeutic applications.

Unit III
Understanding Human Birth defects through Model Organism: Developmental malformation; Teratogen Induced Reproductive Problems; Gene-Teratogen Interaction; Environmental Factors and Genetic Susceptibility; Genomic imprinting: Parent-of-origin effect; Gene silencing; Prader-Willi syndrome, Angelman syndromes and Beckwith-Wiedemann Syndrome; Human embryonic development: Brief account of embryonic development: Blastulation, Gastrulation, formation of notochord and establishment of body axis; Organogenesis: Formation of embryonic germ layers and their derivatives; Fetal development and placentation (development, structure and function); Fetal membrane in twins.
Unit IV
Molecular regulations of human development and defects I: Human Hox genes and genetic defects due to mutation in Hox genes; Somite differentiation and homeobox genes (anterior-posterior patterning); Limb development & limb defects; Molecular regulations of human development and defect II: Eye development and eye defects; Development of spinal cord and neural tube defects; Brain development and cranial defects; Molecular regulations of human development and defect II: Cardiac development and heart defects; Facial development and facial cleft defects; Muscle development; Kidney development and kidney defects

Unit V
Genetic defects due to abnormalities in human developmental processes –I: Abnormal gametes and infertility; Abnormal implantation: contribution of maternal and paternal genes; Teratogenesis and tumors associated with gastrulation; Birth defects: erythroblastosis fetalis, fetal hydrops and twin defects; Genetic defects due to abnormalities in human developmental processes –II: Craniofacial and skeletal dysplasias; Defects in sex differentiation; Neural crest and craniofacial defects; Vertebral defects: spina bifida and scoliosis; Spontaneous abortions and still birth (etiology, pathogenesis, genetic and other causes like immunological basis of pregnancy, clinical notes, diagnosis and management), Reproductive failure: Infertility and Assisted reproduction (ART)

Texts/References

Genomics & 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 maps – 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; 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 diseases; 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 pharamacogenetics and drug development; Toxicogenomics; metagenomics

Texts/References

Lab on Immunology & Immunogenetics - 3 Credits

1. To prepare single cell suspension of splenocytes and report the yield of viable cells by performing trypan blue dye exclusion test.
2. Isolation of Peritoneal cavity macrophages from mouse and preparation of monolayer.
3. Immunization of rabbit with BSA and collection of serum from immunized rabbit.
4. To detect the presence of antigen/antibody using Enzyme Linked ImmunoSorbent Assay (ELISA).
5. To detect a specific antigen in a cell homogenate using Western blot/hybridization.
7. To test the pattern of antigen-antibody interaction through Ouchterlony double diffusion assay.
8. Blood group typing using haemagglutination tests.
9. Latex agglutination test for detection of antigen in a sample using antibody bound to a bead.
10. Precipitin test for detecting specific soluble antigens for an antibody.
11. Immunostaining of B cells to show proliferating germinal centers.
12. T cell rosette assay to check for the presence of pre-activated T cells.

Lab on Developmental & Population Genetics - 3 Credits

Developmental Genetics
1. Life cycle studies of Yeast, Dictyostelium, C. elegans, Drosophila
2. Study of expression of segmentation genes in Drosophila
3. Observation of homeotic mutants of Drosophila
4. Study of Development of Frog/ Toad
5. Study of Chick embryo development (preparation of whole mounts & permanent slides)
6. Maintenance of mouse colony (observation of vaginal plug)
7. Study of mouse embryonic development (observation of embryos)
8. Study of various stages of human fetuses (Observation of fixed specimens)
9. Study of museum specimens of abnormal fetuses in local medical colleges
10. Study of permanent slides of endometrium in different stages of menstrual cycles in rat/mice
11. Study of permanent slides on development in vertebrates.

Population Genetics
1. Genetic variance and positive assortative mating for height
2. Calculation of allelic identity by descent (IBD) in inbred families
3. Hardy-Weinberg Genetic equilibrium: Study of gene & genotype; frequencies. (PTC Tasters & non-tasters)
4. Hardy-Weinberg Genetic equilibrium and Enzyme polymorphism
5. Phylogeny based on Amino acid sequences
6. Correlation of amino acid sequence data with nucleotide sequence data (BLAST and FASTA)
7. Microsatellite based detection of molecular polymorphism in populations
8. Development of molecular markers (DNA- RAPD, RFLP)
9. Phylogenetic analysis: DNA sequence analysis of conserved genes like mitochondrial (cytochromeb, ND4 etc.) and rDNA genes
10. Application of various software packages in population genetics: Statistical Package for Social Sciences (SPSS), ANALYSE- IT, POPGENE
11. Genetic polymorphism: natural(different structural/ morphological traits) and artificial model based studies
Lab on Genetic Engineering - 2 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 DH5α* and gel analysis.
4. Restriction digestion of vector (gel analysis) and insert with Ncol and XhoI.
5. a. Vector and Insert ligation
   b. Transformation in *E.coli DH5α*.
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.*
Human Molecular Genetics - 3 Credits

Unit I
History of Human Genetics: Pedigrees- gathering family history; Pedigree symbols; Construction of pedigrees; Presentation of molecular genetic data in pedigrees; Pedigree analysis of monogenic traits: Autosomal inheritance-dominant, recessive; Sex-linked inheritance- X-linked recessive, dominant; Y–linked; Sex-limited and sex-influenced traits; Mitochondrial inheritance; MIM number; Complications to the basic pedigree patterns I: Non-penetrance, variable expressivity, pleiotropy, onset, dominance problem; Anticipation; Compound heterozygosity

Unit II
Complications to the basic pedigree patterns II: Genomic imprinting and uniparental disomy; Spontaneous mutations; Mosaicism and chimerism; Male lethality; X-inactivation; Consanguinity and its effects in the pedigree pattern; Allele frequency in population; Complex traits-polygenic and multifactorial: Approaches to analysis of complex traits- ‘Nature vs nurture’; Role of family and shared environment; Monozygotic and dizygotic twins and adoption studies; Polygenic inheritance of continuous (quantitative) traits, normal growth charts, Dysmorphology; Polygenic inheritance of discontinuous (dichotomous) traits - threshold model, liability and recurrence risk; Genetic susceptibility in complex traits; Alcoholism, cardiovascular disease, diabetes mellitus, obesity & epilepsy; Estimation of genetic components of multifactorial traits: emperic risk; Heritability; Coefficient of relationship; Application of Bayes’ theorem.

Unit III
Genetic mapping of Mendelian and complex characters: Identifying recombinants and non-recombinants in pedigrees; Genetic and physical map distances; Genetic markers; Mapping of genetic traits: Two-point mapping- LOD score analysis; Multipoint mapping; Homozygosity mapping; Genetic mapping of complex traits; Difficulties in mapping; Allele sharing methods- affected sib pair analysis; Allelic association, Linkage disequilibrium mapping, Transmission disequilibrium test; Human Genome Mapping: Physical mapping of the human genome: Low resolution mapping- Cell hybrids, mini- and microcells, synteny of genes, Radiation hybrid mapping; Human genome mapping: Assembly of clone contigs and identifying genes in cloned DNA. Integration of cytogenetic, genetic and physical maps; DNA testing; Direct and indirect testing (gene tracking) in individuals; DNA tests for identity and relationships including forensic applications; Population screening: ethics, organization and advantages

Unit IV
Identifying human disease genes: Principles and strategies; Position-independent and positional cloning; Candidate gene approaches; Confirming a candidate gene, mutation screening, testing in animal models; Molecular pathology: Nomenclature of mutations and their databases; Loss of function and gain of function mutations in diseases; Molecular pathology: Instability of the human genome and diseases- pathogenicity associated with repeated sequences; Slipped strand mispairing; Unequal crossover and unequal sister chromatid exchange; Gene conversion; Retrotransposition; Illegitimate recombination; Approaches to treat genetic diseases: Pharmacogenetics, cell based treatment, recombinant protein and vaccines; Gene Therapy: Strategies, role of Viral Vectors, non viral vectors; Repairing and inactivating pathogenic gene; RNAi: General idea and applications.
Texts/References

Clinical Genetics & Genetic Counseling - 3 Credits

Unit I
Genetics in Medical Practice: Genetic Principles and their application in medical practice; Case studies (Interacting with patients, learning family history and drawing pedigree chart); Syndromes and disorders: Definition and their genetic basis; Molecular pathology of monogenic diseases: Cystic fibrosis, Tay Sach’s Syndrome & Marfan Syndrome; Genetics of diseases due to Inborn errors of metabolism: Phenylketonuria, Galactosemia & Mucopolysaccharidosis.

Unit II
Genetics of Neurogenetic disorders: Charcot-Marie tooth syndrome, Spino-muscular atrophy, Alzheimer’s disease & Syndromes due to triplet nucleotide expansion; Genetic basis of muscle disorders: Dystrophies (Duchenne Muscular dystrophy and Becker Muscular Dystrophy), Myotonias & Myopathies; Genetic disorders of Haemopoietic systems: Overview of hematopoisis, Blood cell types and haemoglobin, Sickle cell anemia, Thalassemias & Hemophilias.

Unit III
Genetic basis of eye disorders: Colour Blindness, Retinitis pigmentosa, Glaucosa & Cataracts; Genetics of skeleton & skin disorders; Genetics of Syndromes & Genomic Imprinting: Neurofibromatosis I, Prader-Willi & Angelman syndromes, Beckwith-Wiedeman syndrome; Genetics of Cancers and cancer-prone syndromes: Haematological malignancies, Retinoblastoma, Wilm’s tumour, Colorectal cancer, DNA-repair deficiency syndromes, Breast cancer.

Unit IV
Complex polygenic syndromes: Hyperlipidemia, Atherosclerosis, Diabetes mellitus ; Mitochondrial syndromes; Management of genetic disorders; Genetic counseling: Historical overview (philosophy & ethos) and Components of genetic counseling: Indications for and purpose; Information gathering and construction of pedigrees; Medical Genetic evaluation (Basic components of Medical History, Past medical history, social & family history).

Unit V
Components of genetic counseling: Physical examination (General and dysmorphology examination, Documentation), Legal and ethical considerations; Patterns of inheritance, risk assessment and counseling in common Mendelian and multifactor syndromes; Genetic testing: biochemical & molecular tests: in children, Presymptomatic testing for late onset diseases (predictive medicine); Prenatal and Preimplantation screening
and diagnosis: Indications for prenatal diagnosis, Indications for chromosomal testing, Noninvasive methods (Ultrasound, Embryoscopy, MRI, etc.); Invasive methods; Prenatal screening for Down's syndrome (maternal serum) & Neural tube defect; Pre-implantation genetic diagnosis; Ethical issues in pre-natal screening & diagnosis.

Texts/References
6. Rasko and Downes, Genes in Medicine, Chapman & Hall, 1996.

**Human Genome & Bioinformatics - 3 Credits**

**Unit I**

*Genome Analysis: Overview*
Organization and structure of genomes in higher organism; Genome size and sequence complexity and repeat sequences; Organization of mitochondrial and chloroplast genome

*DNA typing*
Significance of repeat sequences in genome mapping; DNA polymorphism: Basis of DNA typing; Assembling of physical map; RFLP and fingerprinting

**Unit II**

*Human Genome Project*
Goals of human genome project and its implications on research and society

*High throughput analysis of gene functions*
DNA microarray; Protein array; Mass spectrometry

**Unit III**

*Sequence Databases:* Introduction, Characteristics and implications of Database approach, Kinds of Databases e.g. PubMed and Medline

*Sequence formats:* Flat file, GenBank, FASTA

*Biological sequence databases:* ENTREZ with Boolean search terms and statements, SRS, GenBank, EMBL, PIR, SWISSPROT, UNIPROT

*Databases with reference to human genome:* EST, STS, GSS, HYG, SNP.

*Databases with reference to human genome:* OMIM and disease gene search

*Protein Structure Databases:* PDB, PDBsum
Unit IV

**Pairwise alignment**
Global alignment, Local alignment, Scoring functions. General and affine gap penalty; Scoring matrices PAM and BLOSUM; Statistical significance.

**Multiple sequence alignment**
SP (Sum of Pairs) measure; Tree Alignments; Alignment Representation and Applications: Consensus, motifs and Profiles

Unit V

**Methods for Database Searching**
BLAST and FASTA; BLAST algorithm, Significance of alignments. Statistical significance; BLAST versions: BLASTP, BLASTX, BLASTN, TBLASTN, TBLASTX. PSI-BLAST, PHI-BLAST.

**Phylogenetic analysis**
Evolutionary change in nucleotide sequences; Rates and patterns of nucleotide substitution; Terminology of phylogenetic trees– Branches, nodes, internal nodes, rooted and unrooted trees.

**Texts/References**

**IPR & Biosafety - 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
Unit III

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 IV

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 V

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.

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

Lab - VI Bioinformatics & Molecular Human Genetics - 3 Credits

Bioinformatics
Sequence information resource: Understanding and using on the web

1. EMBL
2. Genbank
3. Entrez
4. Swissprot/ TrEMBL
5. UniProt
6. Using BLAST and interpretation of results
7. On line Multiple sequence alignment using Clustal W
8. Phylogenetic analysis using Tree view or other software

**Molecular Human Genetics**
1. Preparation of Pedigree chart of some common phenotypic characters of human
2. Risk assessment in Pedigree
3. Facial landmarks and dermatoglyphia
4. Study of Sex-chromatin from buccal smear and hair root cells
5. C, G and Fluorescence banding of human/mice chromosomes
6. Extraction of DNA from human lymphocytes
7. Genomic DNA extraction from mouse/human/fly tissues
8. Calculation of the coefficient of relationship (r) in pedigree
9. Construction of Pedigree files in computer
10. PCR-based detection of allelic inheritance of a DNA marker
11. Experiment on DNA fingerprinting
12. Experiment on DNA sequencing
13. Single strand conformational polymorphism
14. Lymphocyte culture and chromosome preparations
15. Chromosome banding, karyotyping and making idiogram of the banded chromosomes
16. Detection of chromosome anomalies in cancer tissues
17. Chromosome preparations from aborted fetuses
18. Molecular detection of DMD/Thalassemia and other genetic diseases
19. Risk assessment (Binomial probability and Bayesian calculation)

**Lab on Clinical Assignments - 3 Credits**

Each student will visit a hospital (preferably a Medical College hospital). The hospital will assign different departments for each day (3 visits per week). Students will collect samples from the patients of some of the inherited diseases and from the patients of some of the diseases due to acquired genetic alterations (e.g., Leukemias, Lymphomas etc.) presented during these visits and undertake analysis. The analysis will include chromosomal analysis and/or mutation detection by PCR/RFLP. Each student will maintain a detailed record of the visits and the patients analyzed (including pedigrees and clinical information) and submit a Report on the same.