

Cellular and Molecular Diagnostics
Syllabus of the theory papers

BiSEP1: Cell biology and genetics in diagnostics

Total Hours: 52

Unit – I

(2 hours)

Introduction to Molecular Diagnostics: History of diagnostics, Age of molecular diagnostics, Significance, Scope, Rise of diagnostic industry in Indian and global scenario.

Unit – II

(16 hours)

Cellular Complexity: Cell components, Cell Differentiation, Cellular communication – endocrine signalling, paracrine signalling and autocrine signalling, contact dependent and synaptic communications

Intracellular networks – transport pathways, signalling pathways and metabolic networks.

Eukaryotic Cell Control System and their Components, Intracellular cell cycle control system, Extracellular Cell Cycle Control System, Regulation of Cell Growth and Apoptosis.

Genetic and epigenetic factors that regulate these pathways, their abnormalities that alter the pathways and cellular functions, Normal Vs diseased cells.

Principle, types and application of different microscopes.

Unit – III

(16 hours)

Molecular Oncology Mitochondrial disorders: Cancer – Benign and Malignant neoplasms, multifactorial disposition, Cancer pathogenesis, positive and negative mediators of neoplastic development, Proto-oncogenes, Oncogenes and Tumor suppressors. Allele loss and loss of Heterozygosity. Mitochondrial inheritance, Mitochondrial myopathy, lactic acidosis, MELAS, LHONs, identity testing.

Unit – IV

(6 hours)

Biomarkers in disease diagnostics: FDA definition of disease markers, Role of markers in Disease diagnosis. Approaches and methods in the identification of disease markers, predictive value, diagnostic value, emerging blood markers for sepsis, tumour & cancer markers, markers in inflammation and diagnosis of cytoskeletal disorders.

Unit – V

(12 hours)

Chromosomes, Human disorders, and Cytogenetic analysis : Structure, types and organization; Chromosome organization, Euchromatin and heterochromatin and Histone modifications. Chromosome banding and nomenclature; Nomenclature and functional

significances of chromosome bands. GC and AT rich isochores. Structural and Numerical aberrations and its consequences. X-chromosome dosage compensation and inactivation mechanism. Sex determination and Y chromosome; function, and diseases. Uniparental disomy, Genomic Imprinting and disorders. FISH, CGH, Flow cytometry techniques and clinical diagnostics.

Unit – VI

(10 hours)

Genomic instability, Chromosome mapping & Genome plasticity: Common fragile sites and methods of induction, Heritable fragile sites and FXS. Genomic Instability, mechanism and diseases. Trinucleotide Repeats; Mechanism of expansion and triplet repeats and related disorders. Genetic linkage maps, Relation to the probability of recombination, Pedigree analysis with genetic markers and overview of human genome project.

References and text books:

1. Molecular biology of the cell. Bruce Alberts, 6th Edition
2. Principles of tissue engineering. Robert Lanza. Elsevier Publications.
3. Introduction to Tissue engineering, applications and challenges. Ravi Birla. Wiley Publications.
4. Molecular Cell Biology: Darnell J, Lodish H and Baltimore D
5. Cell and Molecular Biology: De Robertis EDP and De Robertis EMF
6. Animal cell culture: Ian Freshney
7. An introduction to Human Molecular Genetics by Pasternak et al., John Wiley & Sons
8. Human Chromosomes by Miller & Tharman, Springer Publishing Company,
9. Molecular Biology of the cell by Alberts et al., Garland Press
10. Genes IX, by Lewin B, Pearson India
11. Cell and Molecular Biology by De Robertis and De Robertis, Lipincott & Wilkins
12. Genome III by Brown TA, Garland Press
13. Elements of medical Genetics by Turnpenny and Ellard, Churchill Livingstone

BiSEP2: Immunodiagnostics

Total Hours: 52

Unit – I

(12hours)

Infectious diseases and diagnosis: Microbial pathogenesis, diagnostic pathology, immune pathology, and immunohistopathology. Detection & differentiation of pathogens – bacterial, viral, fungal, zoonotic, protozoan, Drug susceptibility testing, drug resistance testing, Point of care testing, Cellular and functional genomics in diagnostics.

Unit – II

(8 hours)

Inflammatory diseases: Inflammatory disorders, Diagnosis of inflammatory diseases - Inflammatory bowel disease, ankylosing spondylitis, Crohn's disease, allergies.

Unit – III

(6 hours)

Autoimmune disorders: Autoimmune diseases, types of autoimmune disorders, diagnosis of rheumatoid arthritis, systemic lupus erythromatosis, psoriasis, Type I Diabetes.

Unit – IV

(8 hours)

Antibody production techniques: Polyclonal sera, monoclonal antibody production, purification, enzyme conjugation, labelling and immobilization

Unit – V

(12hours)

Immunodiagnostic techniques: Introduction, Radioactive isotopes, DNA reporters, fluorogenic reporters, electro-chemiluminescent tags & label free immunoassays.

Immunoassays – precipitation, agglutination hemagglutination, RIA,ELISA, RIA, MELISAand specific applications. Quantum dots. Immunohistochemistry – principle and techniques.

Unit – VI

(6 hours)

Quality, Ethical and Legal Implications: International standards, Quality accreditation and certification – NABH standards, Elements of quality management, Quality control, Quality assessment and validation.

Privacy and confidentiality, Psychological impact, Counselling, Standards and commercialization. FDA regulations for clinical use of DNA tests.

References and text books:

1. Immunology and Immunobiotechnology Ashim K Chakravarty, Oxford University Press, 2006
2. Immunology, C Vaman Rao, Narosa Publishing House, New Delhi.
3. Kuby Immunology (6th edition) Thomas J Kindt, Richard A Goldsby WH Freeman & Co.
4. Topley and Wilson's Immunology (10th edition) S H E Kaufmann, M W Steward, Hodder Arnold 2005.
5. Principles of Immunology and Immunodiagnostics, Ralph Michael Aloisi. Lippincott Williams and Wilkins

BiSEP 3: Biochemistry and molecular biology in diagnostics

Total Hours: 52

Unit – I

(16 hours)

Metabolism and disorders: Carbohydrates – structure, function, metabolism, regulation and disorders.

Protein and amino acids – structure, function, metabolism, deficiencies and disorders.

Lipids - structure, function, metabolism, cholesterol biosynthesis, regulation and disorders.

Vitamins - Classification, Sources, daily allowance, activation, absorption, transport, storage, biochemical function, their coenzyme activity. Deficiencies and diagnosis.

Minerals: Calcium, Phosphorous, Sodium, Potassium, Chloride, Iron, Copper, Iodine. RDA, sources, biochemical function, deficiency manifestations and diagnosis.

Unit – II

(10 hours)

Clinical Biochemistry in Diagnostics: Laboratory diagnostics – routine blood & urine analysis, enzyme assays - liver function tests, cell free biopsies, non-invasive testing, HPLC.

Unit – III

(6 hours)

Nucleic acids: Principle and methods, Genomic DNA isolation, Plasmid isolation, Restriction digestion, DNA ligation, and agarose gel electrophoresis, quantification, RNA isolation and purification methods

Unit – IV

(12 hours)

Nucleic acid analysis technologies: PCR Principle, procedure, types and applications. cDNA synthesis and cloning, DNA primers, linkers, adapters, cDNA library construction and screening. DNA finger printing, chromosome walking and chromosome jumping. RFLP maps, RAPD, Micro satellites, SCAR (Sequence characterized amplified region), DNA sequencing methods – principle, types, automated process, Next-generation sequencing (NGS).

Unit – V

(4 hours)

Hybridisation techniques: Principle of hybridization. Southern, Northern, in-situ Hybridization. Whole Genome analysis, DNA microarray. Gene mapping and applications. Transcriptome and Proteome analysis. Protein microarrays. Advantages and disadvantages of DNA and protein microarrays.

Unit – VI

(4 hours)

Omics in Diagnostics: Role of transcriptomic, proteomic and metabolomic profiles as diagnostic markers.

References and text books:

1. Biochemistry (7th edition) JM Berg, JLT Tymoczko and L. Stryer, 2012, WH Freeman and Co., New York.
2. Biochemistry (4th edition): D Voet and JE Voet, 2011 John Wiley and Sons. Principles of Biochemistry (Lehninger) (5th edition), MM Cox and DL Nelson, CBS Publishers.
3. Scientific Foundations of Clinical Biochemistry: Ed, D.L. Williams, R.F. Nun, V. Marks; William Heinemann Medical Books Ltd.
4. Harper's Review of Biochemistry (29th edition) RK Murray, DA Benderer, PJ Kennelly, VW Rodwell and PA Weil. 2012, McGraw Hill Co.
5. Textbook of Biochemistry for Medical Students (6th edition) DM Vasudevan, S Sreekumari and K Vaidyanathan 2011, Jaypee Medical Publishers, New Delhi.
6. Practical Biochemistry, Principles and Techniques (4th edition) edited by Keith Wilson and John Walker, 1994, Cambridge University Press.
7. Biochemistry "Lippincott's Illustrated Reviews" (5th edition) RA Harvey (series editor), 2011, Lippincott Williams & Wilkins, Wolters Kluwer.
8. Genomes (3rd edition) TA Brown, Wiley-Liss Publications.
9. Cell and Molecular Biology (5th edition) Gerald Karp, John Wiley and Sons Ltd.
10. Molecular Biology of the Cell (5th edition) Bruce Alberts, Alexander Johnson, Julian Lewis, Martin Raff, Keith Roberts, Peter Walter. Garland Science Publications
11. Molecular Cell Biology, (6th edition) Harvey Lodish, Arnold Berk, Paul Matsudaira, Chris A. Kaiser, Monty Krieger, Matthew P. Scott, Lawrence Zipursky, and James Darnell. WH Freeman Publications

BiSEP4: Syllabus of the Elective theory papers

(Choose from any one of the following)

BiSEP4a: Product development - biologist

Total Hours: 52

Unit – I (12 hours)

Essentials of product development :Company protocols for research, privacy policies, institutional and professional code of ethics and standards of practice, IPR guidelines, Knowledge of basic laboratory procedures, GLP and GMP, relevant EOPs, SOPs, process flows in manufacturing, product life cycle and product properties, competitor products. Stability studies – generate stability data & prepare stability reports for innovation products

Unit – II (10 hours)

Reporting and documentation: Reporting – different standard reference materials used like drugs, products, side effects, adverse reactions, process details, statistical analysis of test data. Documentation – methods and procedures of writing and maintaining lab, research records, research performance reports, schemes and guidelines, power point presentations, tables, charts, word documents, development of research objectives and proposal writing for funding and contractual purposes, publications and technical writing, Regulatory compliance of the final documents

Unit – III (8 hours)

Planning and communication :Research planning – resource, time, timeline & budget considerations, technical feasibility analysis on the NPD ideas by analyzing current development plans, plan day to day activities. Research communications - preparation of progress reports/ research outcomes for steering groups/ bodies, principal investigator, communication with upstream and downstream teams

Unit – IV (6 hours)

Problem solving and decision making : Research initiatives – use new areas of research, techniques and methods, extend research/ product portfolio, creative analysis & interpretation of research data. Decision making – collaborative, appropriate, optimum & best possible solution, Trouble- shoot & Resolve problems to avoid delays

Unit – V**(8 hours)**

Safety and Security at workplace: Different types of occupational health hazards, knowledge of chemical substances, characteristics & safety measures, use of safety gears, masks, gloves & accessories, evacuation procedures for workers & visitors. Health, safety & security issues – types (illness, fire accidents), company policies and procedures, When and how to report, summon medical assistance & emergency services.

Unit –VI**(8 hours)**

Interpersonal Skills :Understand work output requirements, company rules, guidelines & policies related to the process flow, identifying and reporting issues requiring intervention, delivery of quality work on time & report any anticipated reasons for the delay, effective interpersonal communication, conflict-resolution techniques, importance of collaborative working, multi-tasking, training the team members, knowledge of project management.

BiSEP4b : Quality control/Quality assurance biologist

Total Hours: 52

Unit – I

(16 hours)

Essentials of quality control : Preparations - buffer, solvents, solutions and microbial media for running bio-analytical quality tests, assays to carry out quality control procedures on biopharmaceutical products.

Concepts of pharmacopeia like BP, USP, EP and other applicable guidelines such as WHO, ICH and EMEA, etc., statistical tools and software like combistats, safe handling of infectious materials like cultures, strains and seed strains, procedures for handling infectious spillage control, GLP/GMP, biochemical analysis of proteins, bio analytical and microbiological methods, working of instruments/apparatus/equipment, biological assays, application of various analytical techniques such as HPLC, capillary electrophoresis including icIEF, FTIR, Circular Dichroism, UV and Fluorescence spectroscopy, ELISAs, enzyme assays and other applicable methods for the testing of biopharmaceuticals, application of microbiological techniques such as air monitoring, water testing, surface monitoring, microbial monitoring, biosafety levels and biosafety hazards

Unit – II

(10 hours)

Quality Assurance:Quality checks - quality assurance samples, master sample, internal controls, statistical analysis of test data, techniques and concepts of statistical quality control and statistical process control, non-conformities. Operational aspects – calibration, accuracy checks of quality control equipments like stability chambers and BOD incubators, HPLC, gas chromatography, photofluorometer, etc., application softwares used in quality analysis

Unit – III

(6 hours)

Safety and Security at workplace : Different types of occupational health hazards, knowledge of chemical substances, characteristics & safety measures, use of safety gears, masks, gloves & accessories, evacuation procedures for workers & visitors. Health, safety & security issues – types (illness, fire accidents), company policies and procedures, When and how to report, summon medical assistance & emergency services

Unit – IV

(6 hours)

Interpersonal Skills :Understand work output requirements, company rules, guidelines & policies related to the process flow, identifying and reporting issues requiring intervention, delivery of quality work on time &report any anticipated reasons for the delay, importance of team work, resolution of conflicts, multi-tasking, training the team members, knowledge of project management

Unit – V**(6 hours)**

Clean work station: Cleaning the work area and equipments, materials and equipments required for cleaning, adequate ventilation for the work area, personal protective equipments, dealing with accidental damage, procuring and storing housekeeping equipment and supplies, disposal of wastes, maintain schedules and records for housekeeping

Unit – VI**(8 hours)**

Reporting and documentation in quality : Reporting – company procedures, escalation matrix for reporting identified issues - defects, problem, incidents, quality issues and test results, feedback to production manager and R&D staff. Documentation – procedures and good documentation practices, offline and online mode, accuracy, details, controlled document files and test records, regulatory and compliance requirements, inspection - procedures, protocols and checklists, inspection reports.

Syllabus of the practical papers

BiSEP 5: Lab-1: Cellular and molecular diagnostics:

1. Basics of reagents/chemical preparation (Buffer, Molar, Normal, percent solution)
2. Basics of Lab instrumentation—pH meter, Centrifuge, spectrophotometer
3. Sample preparation - Specimen collection, handling, preparation, processing, containment, barcoding, and tracking.
4. Microscopy – light, fluorescent and confocal microscopy
5. Isolation of genomic DNA from peripheral blood and agarose gel electrophoresis
6. DNA - qualitative and quantitative analysis by spectrophotometry
7. Plasmid preparation – alkaline lysis method
8. RNA isolation (from rat liver)
9. Northern/Southern blotting
10. Polymerase chain reaction (PCR)
11. RT-PCR/RFLP/RAPD
12. Automated DNA Sequencing/Nextgen Sequencing
13. Protein Estimation Techniques
14. SDS-PAGE and Western blotting
15. Mass Spectrometry
16. HPLC - Applications

BiSEP6: Lab-2: Genetics and immunodiagnostics

1. Animal Cell Media Preparation
2. Culture of Human Lymphocytes
3. Cell Viability Assays
4. Karyotype using Human lymphocyte culture and banding techniques: GTG, CBG, QFQ, RHG and NOR, and High-resolutionbanding.
5. Chromosome breakages and Sister chromatid exchanges analysis for Fanconi anemia and Fragile X syndrome
6. Mouse sperm – morphology and other characteristics
7. Pedigree Analysis
8. Microbial Cell culture techniques
9. Flowcytometry
10. Fluorescence *in situ* hybridization
11. Spectral karyotyping
12. Immunotechniques: Agglutination and Precipitation Techniques
13. Diagnostic enzymology
14. Sandwich ELISA
15. Dot ELISA
16. Immunohistochemistry