

## Ph.D. Biochemistry/Biotechnology Coursework

### Paper I – Research Methodology

#### Unit–I Scientific Research and Scientific Writing

Importance and need for research ethics and scientific research. Formulation of hypothesis- Types and characteristics. Designing a research work. Scientific Writing:Characteristics. Logical format for writing thesis and papers. Essential features of abstract, introduction, review of literature, materials and methods, and discussion. Effective illustration:tables and figures. Reference styles:Harvard and Vancouver Systems.

#### Unit–II Biostatistics

Collection and classification of data- diagrammatic and graphic representation of data. Measurement of central tendency-standard deviation-normal distribution-test of significance based on large samples-small samples. Student *t* test. Correlation and regression.Chi square test for independence of attributes. ANOVA.

#### Unit–III Basic Concepts of Computers

History of Computers, Concept

of Computer hardware, Concept of Computer languages, Concept of Computer Software. Computer applications in Biology.

Spreadsheet tools: Introduction to spreadsheet applications, features, Using formulae and functions, Data storing, Features for Statistical data analysis, Generating charts/graph, and other features, Tools–Microsoft Excel or similar presentation tools: Introduction, features and functions, Power Point Presentation, Customizing and showing presentation. Use of Internet and WWW, Use of search engines.

#### Unit–IV Bioethics and Patenting

Declaration of Bologna.Ethics in animal experimentation. CPCSEA guidelines:Animal care and technical personnel environment, animal husbandry, feed, bedding, water, sanitation and cleanliness, water disposal, anesthesia and euthanasia.

Composition of Human Institutional Ethical Committee.General ethical issues. Specific principles for clinical evaluation of drugs and human genetics research. Ethics in food and drug safety. Environmental release of microorganisms and genetically engineered organisms. Ethical issues in human gene therapy and human cloning. Patenting- definition of patent. Product and process patents. Patenting multicellular organisms.Patenting and fundamental research.

#### Unit–V Bioinformatics

Introduction. Biological databases: primary and secondary sequence databases, organism-specific databases, miscellaneous databases. Data submission.Information retrieval from databases- *Entrez* and SRS. Sequence alignment- sequence homology versus sequence similarity. Database similarity searching- FASTA, BLAST. Multiple sequencing alignments (CLUSTAL) Amino acid substitution matrices. Molecular phylogenetics: phylogenetic tree construction methods, software programs and analysis. Protein structure database- protein structure visualization, comparison and classification. Protein motifs and domain prediction.

#### Books recommended

1. R.A. Day. How to write a scientific paper. Cambridge University Press.
2. Lesk A.M. Introduction to Bioinformatics Oxford 2002.
3. Xiong J. Essential Bioinformatics. Cambridge University Press. 2006.
4. Krane et al. Fundamental concepts of bioinformatics. Benjamin Cummings.
5. S.P. Gupta. Fundamentals of Statistics, Sultan Chand.
6. Ethics and the use of alternatives to animals in research and education. Shiranee Pereira, CPCSEA.
7. Ethical guidelines for biomedical research on human subjects. ICMR, New Delhi, 2000.

## Ph.D. Biochemistry / Biotechnology Coursework

### Paper II- Analytical Techniques

#### Unit-I Chromatography Techniques

Performance parameters (retention time, elution volume, capacity factor, plate height, and resolution). Low pressure liquid chromatography (LPLC):principle, columns, matrix materials, procedure. HPLC- columns, matrix, mobile and stationary phases, sample application, pumps, detectors.HPTLC- principle, procedure, applications. Fast protein liquid chromatography. Reversed phase chromatography.

#### Unit-II Microscopy and Cell culture techniques

Light microscopy- components, specimen preparation. Optical contrast, specimen stains. Fluorescence microscopy, fluorophores. Optical sectioning:confocal microscopes, multiple photon microscopes. Imaging living cells and tissues. Stereomicroscope. Electron microscopy:principle, specimen preparation for TEM &SEM.

Cell culture techniques: Equipment- hoods, CO<sub>2</sub> incubator. Safety considerations, aseptic techniques, eradication of infections. Animal cell cultures:primary cultures, cell lines, media and growth requirement, subcultures, cell quantification, cryopreservation, cell viability. Elementary details of bacterial and plant cell cultures.

#### Unit-III Immunochemical techniques

Antibody labeling: radiolabeling, labeling with fluorochromes and enzymes, biotinylation. Immunoassays: competitive binding, immunometric, solid-phase immunobinding, enhanced, peptide-based, fluorescence and photoluminescence-based. Immunohisto/cytochemistry. Immunofluorescence techniques. Immunoelectron microscopy. Flow cytometry.

#### Unit-IV Electrophoretic and Spectroscopy techniques

Electrophoresis of proteins. SDS-PAGE, isoelectric focusing, 2D-PAGE.Detection, estimation and recovery of proteins in gels. Electrophoresis of nucleic acids: agarose gel electrophoresis, DNA sequencing gels, pulsed field gel electrophoresis. Electrophoretic mobility shift assay. Southern, Northern, Western, and Southwestern blotting. Elementary details of mass spectrometry:principle, instrumentation, ionization, mass analyzers, MALDI-TOF, tandem mass spectrometry, PMF. Basic principle and biological applications of IR, NMR and ESR.

#### Unit-V Molecular Biology Techniques

Probe preparation: end labeling, random primer labeling, nick translation, molecular beacon-based probes. RFLP, DNA fingerprinting, FISH. PCR-principle and applications. RT-PCR. Real-time quantitative PCR, differential display PCR. DNA sequencing: automated fluorescence method, pyrosequencing, cycle sequencing. Whole-genome sequencing (shotgun and clone-by-clone approach). Microarrays: DNA and protein arrays.

#### Books recommended

1. Wilson and Walker.Principles and techniques of Biochemistry and Molecular biology.7th ed. Cambridge University Press 2012.
2. Boyer, R. Modern Experimental Biochemistry.3rd ed. Addison Wesley Longman, 2000.
3. Sambrook.Molecular Cloning.Cold Spring Harbor Laboratory, 2001.
4. Friefelder and Friefelder.Physical Biochemistry - Applications to Biochemistry and Molecular Biology.WH Freeman & Co. 1994.
5. Upadhyay, Upadhyay and Nath. Biophysical Chemistry Principles and Techniques. Himalaya Publ. 1997.

## Ph.D. Biochemistry / Biotechnology Coursework

### Paper III– Cell and Molecular Biology

#### Unit–I Intercellular communication, Cell cycle, and Cell death

Cell junctions- anchoring, tight and gap junctions. Cell adhesion molecules (CAMs): cadherins and integrins (elementary details). The cell cycle: phases and regulation by cyclins and cyclin-dependent kinases. Basic principles of cell death, apoptosis and necrosis. Death receptors and mitochondrial pathways.

#### Unit–II Cell Signaling

Fundamental concepts and general features of cell signalling. Endocrine, paracrine, autocrine signaling and juxtacrine signalling. Types of receptors. Nuclear and cytosolic receptors. G-protein-coupled receptors. Second messengers: c-AMP, cGMP, diacylglycerol, inositol triphosphate and  $Ca^{2+}$ . Receptor tyrosine kinases- insulin signalling, ras-raf-MAP kinase and JAK-STAT pathways. Crosstalk between signalling pathways.

#### Unit–III Genome Complexity

Eukaryotic chromatin: nucleosomes, higher order chromatin structure. DNA sequence elements: unique sequence DNA, repetitive DNA- SINEs, LINEs, satellite, minisatellite and microsatellite DNA. C-value paradox. Gene families, pseudogenes (brief account).

#### Unit–IV Regulation of Gene Expression

Regulation of gene expression in eukaryotes: Euchromatin, heterochromatin, DNase I sensitivity. Epigenetics. DNA methylation, Histone acetylation and deacetylation. Gene regulation by steroid hormone receptors, phosphorylation (STAT proteins). RNA interference (siRNA and miRNA).

#### Unit–V Nucleic acid-Protein Interactions and Protein folding

Nucleic acid recognition by proteins. Nucleic acid-binding motifs in proteins: helix-turn-helix, zinc finger, leucine zipper, and helix-loop-helix. Techniques characterizing nucleic acid-protein interactions: gel retardation assay, DNase I footprinting. Protein folding: models, molecular chaperones, chromatin immunoprecipitation, yeast monohybrid system.

#### Text Books

1. Karp. Cell & Mol Biol 7<sup>th</sup> ed 2013. Wiley.
2. Nelson & Cox. Lehninger Principles of Biochemistry. Freeman, 6<sup>th</sup> ed. 2012.
3. Krebs JE et al. Lewin's. Genes XI. Jones & Bartlett Publ, 2012.
4. Alberts et al Molecular biology of the cell. 5<sup>th</sup> ed. Garland Sci. 2007.
5. Watson. Molecular Biology of the Gene. 7<sup>th</sup> ed. Pearson Edu, 2013.
6. Twyman. Advanced Molecular Biology. BIOS Sci Publ. 2000.

## Special Paper

### Ph.D. Biochemistry/ Biotechnology course work Paper IV DIABETES MELLITUS

#### Unit 1: Insulin-Blood glucose homeostasis and diabetes

Blood glucose homeostasis: role of tissues and hormones. Insulin: structure, metabolic functions of insulin. Metabolic abnormalities in insulin deficiency. Diabetes-Definition and diagnostic criteria by ADA; WHO classification of diabetes; Etiology of type 1 and 2 diabetes. Complications of diabetes — acute complications: Hypoglycemia – causes, symptoms and prevention of hypoglycemia, Treatment of hypoglycemia; Diabetic ketoacidosis; HONK coma.

#### Unit 2: Molecular mechanism of insulin action and regulation of metabolism

Insulin signaling pathways; Insulin receptor and its substrates, PI3K, Akt and downstream targets (GLUT, FOXO, GSK3 $\beta$ ), Cbl pathway, Ras – Mitogen – activated protein kinase cascade; Turning off the insulin signal by PTP1B and serine kinases.

**Insulin resistance (IR)** — definition; tissue sites of IR; defects in insulin signaling; genetic and acquired forms of IR; role of FFA and intracellular TG in IR, Role of cytokines secreted by adipose tissue — TNF- $\alpha$ , adiponectin, resistin, leptin, interleukin 6.

#### Unit 3: Pathogenesis of Diabetes

**Type 1 Diabetes Mellitus:** Genetic factors — HLA genes and molecules; Environmental agents — autoantigens, chemicals, viruses, bacteria, vaccination, perinatal factors, food components, stress; gut dysfunction and diabetes; Islet histology in type 1 diabetes, immune mechanisms of beta - cell destruction; Animal models for type 1 diabetes —alloxan, streptozotocin, other  $\beta$ -cell toxins, spontaneous type 1 diabetes – BB rats.

**Type 2 Diabetes Mellitus:** Obesity and Nutritional factors — epidemiology, body mass index, sympathetic nervous system activation- role of hypothalamus, insulin resistance, beta cell defects; Animal syndromes resembling type 2 diabetes — diabetic mice (db/db), desert rodents, sand rats and spiny mice, obese (ob/ob) mice – Diet induced type 2 diabetes.

#### Unit 4: Biochemistry and molecular cell biology of diabetic complications

Mechanisms of Diabetic complications: Hyperglycemia induced damage — Polyol pathway, advanced glycation end products (AGE) formation, protein kinase C pathway, hexosamine pathway; Oxidative stress — Glucose induced production of free radicals, Free radicals and AGE, Nitric oxide.

**Diabetic vascular disease:** Risk factors for diabetic vasculopathy — hyperglycemia, dyslipidemia, hypertension and the renin angiotensin system. Micro and macrovascular damage, organ complications-molecular changes in nephropathy, neuropathy and retinopathy, diabetic foot disease.

#### Unit 5: Therapeutics

**Medical nutrition therapy:** Glycemic index of common foods; Recommended nutrient composition of diet in diabetes; Macronutrients and Micronutrients. Nutritive and non nutritive sweeteners.

**Pharmacotherapy:** Antidiabetic agents, hypoglycemic agents, antihyperglycemic agents, Mode of action – Inhibitors of intestinal carbohydrate digestion and absorption (dietary fibre supplements,  $\alpha$  glucosidase inhibitors), Rapid acting and long acting insulin analogues, Insulin secretagogues, Potentiators of insulin secretion (sulphonyl ureas, meglitinides, GLP-1, exendin 4 and DPP4 inhibitors), insulin mimetics (vanadium), insulin sensitizers (thiazolidinediones, metformin), lipid lowering agents, fatty acid oxidation inhibitors, soluble amylin analogues.

Pancreas and islet transplantation. Stem cell therapy and gene therapy for diabetes (Elementary details).

#### References:

1. Joslin's Diabetes Mellitus, 14<sup>th</sup> Ed., C. Ronald Kahn, Gordon C. Weir, George I. King, Aln M. Jacobson, Alan C. Moses, Robert J. Smith, Lippincott Williams and Wilkins Publ., 2006.
2. Diabetes Mellitus – A Fundamental and Clinical text, 3<sup>rd</sup> Ed., Derek Lerooith, Siemon I. Taylor, Jerrold M. Olefsky, Lippincott Williams and Wilkins Publ., 2004.
3. Textbook of Diabetes 1 & 2, 3<sup>rd</sup> Ed., John C. Pickup & Gareth Williams, Blackwell Science Publ., 2003.
4. International Textbook of Diabetes Mellitus Vol.1 & 2, 3<sup>rd</sup> Ed., R. A. Defronzo, E. Ferrannini, H. Keen, P. Zimmet, Wiley Publ., 2004.

**PH.D. BIOCHEMISTRY / BIOTECHNOLOGY SYLLABUS**  
**Paper IV – CANCER BIOLOGY**

**UNIT 1: Introduction to Cancer**

Types of growth– hyperplasia, metaplasia, dysplasia, anaplasia and neoplasia. Nomenclature of neoplasms. Differences between benign and malignant tumours. Epidemiology of cancer- types of epidemiological research. Methods of epidemiological investigation- cohort studies, case-control studies (elementary details only). Tumour assessment– grading and staging (elementary details only).

**UNIT 2: Carcinogenesis**

Growth characteristics of cancer cells. Morphological and ultrastructural properties of cancer cells. Metabolic alterations in neoplastic transformation. Tumour markers. Radiation and viral carcinogenesis. Chemical carcinogenesis– Activation of procarcinogens (benzo(a)pyrene only). Stages in chemical carcinogenesis– Initiation, Promotion and Progression. Tumour promoters. Screening for chemical carcinogens– Ames test and whole animal bioassay.

**UNIT 3: Genetic and Epigenetic Basis of Cancer**

Oncogenes and Proto-oncogenes. Mechanisms of oncogene activation. Oncogenic proteins involved in signaling pathways- growth factors and their receptors, Ras oncogenes, nonreceptor cytoplasmic kinases, nuclear transcription factors, anti-apoptotic proteins. Tumour suppressor genes– loss of heterozygosity. *p53*, *Rb*, *PTEN*, *BRCA1* and *BRCA2*. The genetic model for colorectal cancer. Epigenetic alterations in cancer- DNA methylation, histone acetylation and deacetylation. HDAC inhibitors. MicroRNA and cancer.

**UNIT 4: Hallmarks of Cancer**

Overview of hallmarks of cancer. Cell proliferation- overview of cell cycle, role of Myc and Ras in cell cycle control, deregulation of cell cycle in cancer. Apoptosis- overview, dysregulation of apoptosis in cancer. Cellular and molecular mechanisms of invasion and metastasis. Tumour angiogenesis. VEGF signaling. Brief account of role of inflammation in cancer.

**UNIT 5: Tumour analysis and therapeutics**

Identification of tumours by imaging and histological techniques (brief account only). Molecular methods of analysis: genomic methods- *FISH*, comparative genomic hybridization, Microarrays and laser capture microdissection. Cancer chemotherapy– antimetabolites, antibiotics, platinum compounds, hormones. Multidrug resistance. Basic concepts of radiotherapy, ADEPT, genetic prodrug activation therapy, biological therapy- brief account of gene therapy and immunotherapy for cancer. Multidrug resistance.

**REFERENCES**

1. The Cancer Handbook- M. R. Alison., Nature Publ. Group (2007)
2. Cancer Principles and Practice of Oncology – De Vita V.T. Jr., Hellman, S. and Rosenberg, S.A., J.B. Lippincott, Co., Philadelphia (2008) 8th edition.
3. Basic Science of Oncology. Tannock, I. and Hill, R.P., Mc Graw Hill Publication (2004).
4. Fundamentals of Oncology. H.C.Pitot (2002) 4th edition.
5. Journal articles.

**PH.D. BIOCHEMISTRY / BIOTECHNOLOGY SYLLABUS**  
**Paper IV – Cardiovascular Biology**

**Unit 1 Blood flow and Vasculature**

Circulatory System. Macro versus microvasculature, structure of blood vessels, pressure and peripheral vascular resistance, conducting versus resistant vessels, blood flow and endothelial function, endothelial heterogeneity, neuronal, endocrine and autocrine regulation of vessel tone, autocoid production by haemodynamic forces, cardiovascular response to exercise, vascular permeability and diapedesis.

**Unit 2 Vasculogenesis and Angiogenesis**

Vascular progenitors, concepts of sprouting and intussusceptive angiogenesis, vascular endothelial growth factors, pericytes and vessel maturation, integrins and extracellular matrices in angiogenesis, concepts in lymphangiogenesis, angiogenic and angiostatic factors, matrix metalloproteases in angiogenesis, hypoxia and angiogenesis.

**Unit 3 Cardiac Physiology, Myocardial Infarction and Ischemia-reperfusion Injury**

Anatomy of the heart, valves, physiology and functions. Cardiac cycle. Electrocardiogram, ion channels in cardiac function, gap junctions and conductivity.

Myocardial infarction-risk factors, etiology, metabolic abnormalities, animal models of MI.

Introduction to Ischemia-reperfusion injury. Cellular and molecular mechanisms, clinical implications, Langendorff Heart: a model system to study ischemia-reperfusion injury.

**Unit 4 Atherosclerosis and Hypertension**

Atherosclerosis, causes, risk factors, atherosclerotic plaque, consequences, biochemical findings and treatment. Inflammation and atherosclerosis.

Hypertension, classification, etiology, clinical features and pathogenesis. The Renin-Angiotensin system. Animal models of atherosclerosis and hypertension.

**Unit 5 Drugs in the management of cardiovascular diseases**

Antihypertensive drugs- Diuretics, ACE inhibitors, angiotensin receptor blockers, calcium channel blockers,  $\beta$ -adrenergic blockers,  $\alpha$ -adrenergic blockers, central sympatholytics, vasodilators. Cardiac glycosides, Antiarrhythmic drugs, nitrates, anticoagulants, antiplatelets, fibrinolytics.

**References**

1. Pathologic basis of disease-Cortran, Kumar, Collins (2009), 8<sup>th</sup> edition.
2. Text book of Medical Physiology-Guyton (2010) 12<sup>th</sup> edition.
3. Harper's Biochemistry-Murray, Granner, Mayes, Roadwell (2012), 29<sup>th</sup> Edition
4. Harrison's Principles of Internal Medicine, Vol-1,2001, 15<sup>th</sup> edition.
5. Lehninger Principles of Biochemistry, David L. Nelson and Micheal M.Cox, 2008. 5<sup>th</sup> edition
6. Essentials of Medical Pharmacology-Tripathi.K.D.-7<sup>th</sup> edition.
7. Cardiovascular Physiology- David E. Mohrman and Lois Jane Heller, McGraw-Hill, 8<sup>th</sup> Ed., 2013.

## PH.D. BIOCHEMISTRY / BIOTECHNOLOGY SYLLABUS

### Paper IV Chronobiology

#### Unit-I: Introduction

History of chronobiology, ubiquity of biological rhythms, types of biological rhythms, glossary of terms used in biological rhythm studies, fundamental properties of biological rhythms, selective advantages of biological rhythms in organisms, ultradian, infradian and circannual rhythms, measurement and analysis of rhythm data, cosinor analysis

#### Unit-II: Anatomy and physiology of circadian clocks

Anatomy and physiology of biological clocks, circadian pacemakers in various organisms, suprachiasmatic nuclei (SCN) – neuroanatomy and neurochemistry, pineal gland, afferent and efferent pathways of central biological clock, peripheral clocks, functional organization of circadian systems in eukaryotes

#### Unit-III: Chronoendocrinology

Endocrine rhythms in mammals, ultradian rhythms of hormones, normal rhythms of ACTH and alterations in disease states, 24h GH profile in men and women – alterations in disease states, 24h profile of prolactin in normal subjects – alterations in disease states. Diurnal and ultradian variations of leptin in normal subjects – alterations in obesity and weight loss, temporal pattern of release of prolactin and oxytocin, pineal gland and melatonin rhythm, diurnal and ultradian variations of glucose tolerance and insulin secretion, Abnormal circadian rhythms of adrenal hormones in Addison's disease and Cushing's syndrome

#### Unit-IV: Chronopharmacology and chronotherapy

Basics of chronopharmacology – clinical chronopharmacology – circadian dependence of drug pharmacokinetics – chronoefficacy of doxorubicin, oxaliplatin and cisplatin – chronopharmacokinetics of antineoplastic drugs, chronotolerance, circadian rhythms and cancer chemotherapy, cancer chronotherapy, chronobiological concepts underlying the chronotherapy of cancer, chronotherapy of metastatic colorectal cancer, the relevance of circadian rhythms in human health, jet lag, shift work, chronobiology of asthma, human blood pressure and sleep disorders

#### Unit-V: Molecular chronobiology

Circadian clock genes in *Drosophila* (*per*, *tim*, *dbt*, *dclock* and *cycle*), regulation of expression of clock genes, autoregulatory transcriptional feedback loops, basic actions and interactions among clock gene products, circadian clock controlled genes, circadian clock genes in mammals, autoregulatory transcriptional feedback loops of clock genes in mammals, autonomous functions of clock genes in peripheral tissues, circadian clock genes in humans.

#### Reference Books

- 1) F.H. Columbus 2006 *Trends in Chronobiology* Nova Sci Pub Inc.
- 2) R. Refinetti 2005 *Circadian Physiology 2<sup>nd</sup> ed.* CRC Press, Boca Raton, FL, USA
- 3) A. Sehgal 2004 *Molecular biology of circadian rhythms* Wiley-Liss, USA
- 4) J. C. Hall 2003 *Genetics and molecular biology of rhythms in Drosophila and other insects* Elsevier Science, USA
- 5) Wilson and Foster, *Williams Text book of Endocrinology, 9<sup>th</sup> ed.*
- 6) Touitou Y *et al.*, 2006 *Handbook of Medical Chronobiology* Taylor and Francis
- 7) M. Smolensky and L. Lamberg 2001 *The body clock guide to better health* Henry Halt & Co. New York

**PH.D. BIOCHEMISTRY / BIOTECHNOLOGY SYLLABUS**  
**Paper IV Radiation Biology**

**Unit-1**

Electromagnetic spectrum. Units of radiation and radiation absorbed dose (rad). Ionizing radiation- LET and non-LET radiation. Gamma radiation. Radiation effects on cellular system- direct and indirect action, Radiolysis of water and radical formation. Time scale of radiation effects - acute radiation syndrome and chronic health effects. Bystander effect. Heritable radiation effects. Radiosensitivity of tissues. UV radiation- types and cellular effects. Cyclobutane thymidine and 6-4 photoproducts formation.

**Unit-2:**

Biomarkers of radiation exposure. Radiation induced DNA damage- Base damage and strand breaks. Multiple damaged sites and oxidative DNA damage. Chromosomal aberrations- dicentric aberration, dose response curve and biodosimetry. Chromosome translocation- Fluorescence in situ hybridization. Effect of radiation on actively dividing cells. Radiation sensitivity in different phases of cell cycle. Manifestations of radiation-induced cell death (apoptosis, necrosis, mitotic catastrophe and senescence).

**Unit-3**

Pathways of radiation- Induced signal transduction processes. Mechanism of DNA repair- BER, NER and DSBs repair. Homologous recombination and non-homologous recombination. Radiation response elements- DrRRA, oxyR, recA, XRCC1, GAAD45a, ATM, P21 and TP53. Double strand breaks and histone H2AX phosphorylation. Critical regulators of the extracellular matrix- matrix metalloproteinases and MAPK/P13K pathway. Low-dose radiation on Wnt/beta-catenin signaling. Radiation induced inflammatory and immune suppression signaling.

**Unit-4**

Radioprotectors: Amifostine. Free radical scavengers as radioprotectors. Natural products and dietary phytochemicals in radiation protection. Radioresistance. Radioresistant organisms: *Deinococcus radiodurans* – Common features and culture characteristics, DNA damage resistance and DNA repair mechanisms, transcriptional regulators, factors and proteins involved in radiation resistance, antioxidants biology in radiodurans. Possible applications of radiodurans in biotechnology. Antioxidant enzymes - thioredoxin reductase-mechanism of action, inhibitors of TrxR.

**Unit-5**

Methods in radiobiological research. Biomonitoring. Circulating lymphocytes as an experimental model. Assessment of radiation induced DNA damage- alkaline single cell gel electrophoresis, Cytokinesis- blocked micronuclei cytome assay, gamma-H2AX foci assay. Cytotoxicity assays- bacterial cell survival assay and MTT assay. Fluorescent based cellular assays- intracellular ROS measurement, analysis of mitochondrial membrane potential, calcein-AM transport assay. Cell cycle analysis- BrdU label and Hoechst-propidium iodide staining.

**References**

1. Hall EJ, Giaccia AJ. Radiobiology for the Radiologist. 6<sup>th</sup> ed. Philadelphia: Lippincott Williams & Wilkins; 2006.
2. Von Sonntag C.. The Chemical Basis of Radiation Biology. London: Taylor & Francis; 1987.

## Ph.D. Biochemistry/Biotechnology Coursework

### Paper IV- Neurobiology

#### Unit-I

Anatomy of the brain, major anatomical subdivisions of the human brain; the surface anatomy and interior structures of cortical and subcortical regions; anatomical connectivity among the various regions; development of brain, blood supply to brain and the CSF system, Cytoarchitecture and modular organization in the brain.

#### Unit-II

Basic features of the nervous system, meninges, ventricular system, CSF, blood brain barrier, peripheral nervous system: cranial nerves, spinal nerves, autonomous nervous system; major structures and functions, spinal cord.

#### Unit-III

Cells of the nervous system, structure of neurons-types and functions, neural conduction, communication between neurons, Synaptic conduction, Neurotransmitters: acetylcholine, glutamate, GABA, serotonin, dopamine and histamine, neuromodulators, and hormones. Sleep: biological functions of sleep, rhythms of sleeping (ultradian, circadian, infradian), neural basis of biological clocks

#### Unit-IV

Bipolar Disorder, Schizophrenia, Substance abuse disorders, Major affective disorders, Anxiety disorders, antipsychotic drugs and mood stabilizers.

#### Unit-V

Neurodegenerative diseases- types. Parkinson's diseases: epidemiology, signs and symptoms, causes, pathophysiology-  $\alpha$ -synuclein and Lewy bodies, experimental models and treatment strategies. Alzheimer's disease- epidemiology, signs and symptoms, risk factors, pathology- amyloidogenesis and nonamyloidogenesis, neurofibrillary tangles, experimental models and treatment strategies.

#### References

1. Textbook of Medical Physiology. Guyton and Hall 12th ed. 2010.
2. Parkinson's Disease For Dummies. [Michele Tagliati](#) et al. 2011
3. Alzheimer Disease: From Clinical Description to a Theory of Disease and Treatment, Armenian Medical Network, 2011.
4. Bipolar Disorder: Clinical and Neurobiological Foundations, Wiley 2010.
5. Meyler's side effects of drugs -The international encyclopedia of adverse drug reaction and interactions. J.K Aronson, 2005.
6. Sleep Deprivation: Basic Science, Physiology and Behavior. Clete A. Kushida, Taylor & Francis, 2004.

**Ph.D. Biochemistry / Biotechnology Syllabus  
Paper IV- TOXICOLOGY**

**Unit-I, Classes of Toxicants:**

Metals, Agricultural chemicals (Pesticides), Food additives and Contaminants, Toxins, Solvents, Therapeutic drugs of Abuse, Combustion products, Cosmetics

**Toxicants:** Air, Water, Soil, Domestic and Occupational settings

**Unit-II, Absorption and Distribution of Toxicants**

Routes of absorption, Mechanisms of Transport, Physicochemical properties relevant to diffusion, Toxicant distribution, and Toxicokinetics.

**Metabolism of Toxicants:** Phase I Reactions and Phase II Reactions

**Reactive Metabolites:** Nature, Stability, Fate, Factors Affecting toxicity of reactive metabolites, Reactive Oxygen Species.

Elimination of Toxicants: Renal, Hepatic, and Respiratory system

**Unit-III, Acute and Chronic Toxicity**

Acute and chronic exposure and its effect

No-observed-adverse-effect level (NOAEL), Lowest-observed-adverse-effect level (LOAEL), Maximum tolerable concentration (MTC), Maximum tolerable dose (MTD), Median lethal concentration (LC50), Median lethal dose (LD50), Median lethal time (LT50), Absolute lethal concentration (LC100) and Absolute lethal dose (LD100).

**Toxicity Testing** Experimental Administration of Toxicants, Chemical and Physical Properties Exposure and Environmental Fate, In Vivo Tests, In Vitro and Other Short-Term Tests and Ecological Effects.

**Unit-IV, Organ Toxicity**

**Hepatotoxicity-** causes, mechanism of damage, diagnosis and treatment

**Nephrotoxicity-** types of toxicity, chronic interstitial nephritis and monitoring.

**Neurotoxicity-** neurotoxic agents, prognosis and treatment

**Unit-V, Reproductive and endocrine toxicology**

Developmental toxicology, endocrine disruptors, sites and mechanism of toxicity, adverse structural and functional changes of glands

**Respiratory toxicology-** Biochemical and molecular mechanisms of inhaled environmental and occupational chemicals-Pulmonary toxicity of metals and metal compound

**Immune system-** Immunosuppression or allergy, autoimmunity and inflammatory-based disease or pathologies

**Forensic and Clinical Toxicology-**Samples used detection and classification.

**Reference Books:**

1. Ernest Hodgson-A Textbook of Modern Toxicology, 4<sup>th</sup> Edition-2010-John Wiley & Sons.
2. V.V. Pillay –Modern Medical Toxicology-2013-Jaypee Kindle edition
3. Ramesh Gupta- Biomarkers in Toxicology, 1<sup>st</sup> Edition-2014-Academic press.

**Ph.D. Biochemistry/ Biotechnology Course Work**  
**Paper IV- Plant molecular biology and Abiotic stress**

**Unit- I**

**Molecular Biology:** Basic concepts of Genome organization in Prokaryotic and Eukaryotic systems, Mitochondrial and chloroplast genome organization and regulation, Eukaryotic genome structure organization and replication, control of gene expression- transcription and post transcription mechanism, Epigenetics- DNA methylation, Histone acetylation and deacetylation, RNA Interference siRNA and miRNA.

**Unit - II**

**Genetic Engineering:** Plasmid cloning, Gene expression, Recombination mediated cloning, Infusion cloning, Golden gate assembly, Genome editing using CRISPR, Development of multi gene construct. Plant tissue culture, Genetic transformation, various types of gene transfer methods- Agrobacterium mediated gene transformation, Biolistics-mediated transformation, In-planta transformation, floral dip method; double haploid technology.

**Unit - III**

**Abiotic stress:** Drought, Salinity, Temperature are major abiotic stresses- effects on plant cellular and physiological processes, Plant growth and development.

**Unit - IV**

**Molecular mechanism for stress tolerance:** Stress signal perception and transduction and regulation of gene expression, ABA as a stress signaling molecule, cytokinin as a negative signal, Oxidative stress-Reactive Oxygen Species (ROS), Regulation of protein synthesis and turn over under stress.

**Unit - V**

**Plant adaptive mechanisms for improving stress tolerance:** Drought avoidance and tolerance mechanism, Water Use Efficiency (WUE), Phenotyping methods for drought, Identify of stress responsive genes to improve tolerance mechanism, molecular markers, QTLs, Transgenic and molecular breeding, Stress adaptive mechanism for temperature and salinity stresses

**TEXT BOOKS**

1. Primrose, R. Twyman, B. *Principles of Gene Manipulation*, Blackwell Science, 2005
2. H.S.Chawla. *Introduction to Plant Biotechnology*, 3<sup>rd</sup> Edition, Science publisher 2009
3. *Plant Physiology and Development*, Sixth Edition by Lincoln Taiz, Eduardo Zeiger, Ian M. Møller, and Angus Murphy, published by Sinauer Associates.
4. *Plant Biotechnology* by P.K. Gupta, Rastogi Publications, 2010
5. Nelson and Cox. *Lehninger Principle of Biochemistry*, Freeman, 6<sup>th</sup> edition 2012
6. Watson, *Molecular Biology of the gene*, 7<sup>th</sup> edition, Pearson education 2013
7. Twyman, *Advanced Molecular Biology*, BIOS Sci. Publications, 2000
8. *Plant Molecular Breeding*, H. John Newbury, Sci. publications 2009.

## **Ph.D. Biochemistry/ Biotechnology Course Work**

### **Paper IV- Plant molecular biology and Abiotic stress**

#### **UNIT- I**

**Molecular Biology:** Basic concepts of Genome organization in Prokaryotic and Eukaryotic systems, Mitochondrial and chloroplast genome organization and regulation, Eukaryotic genome structure organization and replication, control of gene expression- transcription and post transcription mechanism, Epigenetics- DNA methylation, Histone acetylation and deacetylation, RNA Interference siRNA and miRNA.

#### **Unit –II**

**Genetic Engineering:** Plasmid cloning, Gene expression, Recombination mediated cloning, Infusion cloning, Golden gate assembly, Genome editing using CRISPR, Development of multi gene construct. Plant tissue culture, Genetic transformation, various types of gene transfer methods- Agrobacterium mediated gene transformation, Biolistics mediated transformation, In-planta transformation, floral dip method; double haploid technology.

#### **Unit – III**

**Abiotic stress:** Drought, Salinity, Temperature are major abiotic stresses- effects on plant cellular and physiological processes, Plant growth and development.

#### **Unit- IV**

**Molecular mechanism for stress tolerance:** Stress signal perception and transduction and regulation of gene expression, ABA as a stress signaling molecule, cytokinin as a negative signal, Oxidative stress-Reactive Oxygen Species (ROS), Regulation of protein synthesis and turn over under stress.

#### **Unit- V**

**Plant adaptive mechanisms for improving stress tolerance:** Drought avoidance and tolerance mechanism, Water Use Efficiency (WUE), Phenotyping methods for drought, Identify of stress responsive genes to improve tolerance mechanism, molecular markers, QTLs, Transgenic and molecular breeding, Stress adaptive mechanism for temperature and salinity stresses