Annamalai University

Faculty of Science

Department of Biochemistry & Biotechnology

Ph.D. Biochemistry

Programme Code: SBIO81

Ph.D. Biotechnology

Programme Code: SBIO82

Syllabi - 2019

Department of Biochemistry and Biotechnology

SBIO81 Ph.D. Biochemistry
SBIO82 Ph.D. Biotechnology

Syllabus

Course I – Research Methodology

Learning Objectives (LO):

To learn in detail about the ethics in scientific research and elements in scientific writing as well as to understand the applications of computers and tools in statistics and bioinformatics essential for biological research.

Unit–1 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–2 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–3 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–4 Bioethics and Patenting

Ethics in animal experimentation. CPCSEA guidelines : Animal care and technical personnel environment, animal husbandry, feed, bedding, water, sanitation and cleanliness, water disposal, anaesthesia 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–5 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. Molecular phylogenetics: phylogenetic tree construction methods, software programs and analysis. Protein structure database - protein structure visualization, comparison and classification. Protein motifs and domain prediction.

Text Books

1. R. A. Day. How to Write a Scientific Paper. Cambridge University Press. 6th ed. 2006.
2. C. R. Kothari. Research Methodology: Methods and Techniques. New Age International Publishers. 2004
3. N. Gurumani. Research Methodology: For Biological Sciences. M.J.P publisher. 1st ed. 2013
4. Lesk A.M. Introduction to Bioinformatics. Oxford University press. 4th ed. 2014.
5. S. C. Gupta. Fundamentals of Statistics. Himalaya Publishing House. 7th. 2018

Course Outcomes

At the end of the course, the student will be able to

CO1: Understand and apply the ethical principles in scientific research. Formulate an hypothesis and design an experiments.

CO2: Demonstrate skill in literature analysis, compile and prepare dissertation/thesis in a logical format.

CO3: Communicate biological concepts through written and oral presentation.

CO4: Understand the basic concepts of computer, the various databases and their applications in other branches of bioinformatics.

CO5: Comprehend the rules of bioethics and patenting.

Ph.D. Biochemistry / Biotechnology Course Work
Course II - Analytical Techniques

Learning Objective (LO): To gain knowledge about the chromatography, microscopy, cell culture, electrophoretic, spectroscopy, immunochemical and molecular biology techniques.

Unit–1 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.

Unit–2 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_2 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–3 Immunochemical Techniques

Antibody labelling : 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–4 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–5 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. Whole-genome sequencing (shotgun and clone-by-clone approach). Microarrays: DNA and protein arrays.

Text Books

1. Andreas Hofmann and Samuel Clokie. Wilson and Walker's Principles and techniques of Biochemistry and Molecular Biology. Cambridge University Press. 8th ed. 2018.
2. Rodney. F. Boyer. Modern Experimental Biochemistry. Pearson education, Inc. 3rd ed. 2000.
3. Sambrook. Molecular Cloning.Cold Spring Harbor Laboratory. 4th ed. 2012.
4. Friefelder and Friefelder. Physical Biochemistry - Applications to Biochemistry and Molecular Biology.WH Freeman & Co. 1983.
5. Upadhyay, Upadhyay and Nath. Biophysical Chemistry Principles and Techniques. Himalaya Publ. 2010.

Course Outcomes

At the end of the course, the student will be able to

CO1: Understand the principle, instrumentation, methodology and troubleshooting of chromatographic techniques.

CO2: Grasp the principle, instrumentation and specimen preparation of diverse types of microscopy and familiarize the salient features of cell biology techniques.

CO3: Comprehend the principle, methodology and troubleshooting of immunochemical techniques.

CO4: Be aware of the principle, instrumentation, methodology and troubleshooting of electrophoretic and spectroscopy techniques.

CO5: Appreciate the principle, instrumentation, method and troubleshooting of requisite molecular biology techniques

Ph.D. Biochemistry / Biotechnology Course Work

Course III – Cell and Molecular Biology

Learning Objective (LO): To recapitulate the various aspects of cell biology and molecular biology for research applications.

Unit–1 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–2 Cell Signaling

Fundamental concepts and general features of cell signalling. Endocrine, paracrine, autocrine 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–3 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–4 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–5 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 foot printing. Protein folding: models, molecular chaperones.

Text Books

1. Karp. Cell & Mol Biol. Wiley. 8th ed. 2016.
2. Nelson & Cox. Lehninger Principles of Biochemistry. Freeman. 7th ed. 2017.
3. Krebs JE et al. Lewin's. Genes XII. Jones & Bartlett Publ. 2017.
4. Watson. Molecular Biology of the Gene. Pearson Edu. 7th ed. 2013.
5. Twyman. Advanced Molecular Biology. Garland Science. 2018.

Course Outcomes

At the end of the course, the student will be able to

CO1: Understand cell-cell communication, cell junction, cell cycle and apoptosis.

CO2: Understand the fundamental concepts of cell signaling, mechanism of signal transduction and the crosstalk between the various signaling pathways

CO3: Understand the organization of the genome and the sequence elements in DNA

CO4: Gain an understanding on the regulation of gene expression at transcriptional, translational and epigenetic levels.

CO5: Demonstrate nucleic acid - protein interaction and the concepts of protein folding.

Special Course

Ph.D. Biochemistry / Biotechnology Course Work

Course IV Diabetes Mellitus

Learning Objective (LO): To understand glucose homeostasis mechanisms, pathogenesis of diabetes mellitus, insulin action and the biochemistry of diabetic complications and therapeutic approaches to 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, GSK3β), 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 -TNFα, 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 β-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, α 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).

Text Books

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

Course Outcomes

At the end of the course, the student will be able to

CO1: Understand the role of hormones and tissues in blood glucose homeostasis, etiology, classification and complications of diabetes mellitus

CO2: Comprehend the insulin action and identify its downstream targets, insulin resistance and the role of adipokines

CO3: Sketch the pathogenesis of diabetes mellitus

CO4: Understand the mechanisms of diabetic complications

CO5: Appraise glycemic index of foods and their nutritive values, summarize antidiabetic agents and their mode of action, learn the modern therapeutic strategies, develop and improve therapeutics to diabetes mellitus.

Ph.D. Biochemistry / Biotechnology Course Work

Course IV – Cancer Biology

Learning Objective (LO): To acquire knowledge on basic principles of oncology, carcinogens, genetics and epigenetic basis of cancer, cancer hallmarks and tumour diagnosis and therapeutics.

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.

Text Books

1. M. R. Alison. The Cancer Handbook. Nature Publ. Group. Vol I. 2007
2. De Vita V.T. Jr., Hellman, S. and Rosenberg, S.A., J.B. Lippincott, Co., Philadelphia. Cancer Principles and Practice of Oncology. 8th ed. 2008.
3. Tannock, I. and Hill, R.P. Basic Science of Oncology. Mc Graw Hill Publication. 5th ed. 2013.
4. Fundamentals of Oncology. H.C. Pitot. 4th ed. 2002
5. Journal articles.

Course Outcomes

At the end of the course, the student will be able to

- **CO1:** Understand the types of growth, cancer epidemiology and tumour assessment.
- **CO2:** Evaluate the principles underlying neoplastic transformation and the mechanism of carcinogenesis.
- **CO3:** Analyse the mechanisms of oncogene activation and epigenetic alterations in cancer.
- **CO4:** Appreciate the intricate signaling networks that enable acquisition of cancer hallmarks.
- **CO5:** Gain an interest into the various methods of diagnosis and therapeutic interventions for cancer.

Ph.D. Biochemistry / Biotechnology Course Work

Course IV – Cardiovascular Biology

Learning Objective (LO): To learn the normal physiology and the pathological mechanisms of cardiovascular system and cardiovascular disease management.

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, β-adrenergic blockers, α-adrenergic blockers, central sympatholytics, vasodilators. Cardiac glycosides, Antiarrhythmic drugs, nitrates, anticoagulants, antiplatelets, fibrinolytics.

Text Books

1. Cortran, Kumar, Collins. Pathologic basis of disease. 9th ed. 2015.
2. Guyton. Text book of Medical Physiology. 12th ed. 2012
3. Harrison's. Principles of Internal Medicine. Vol-1. 19th ed. 2015
4. Tripathi. K. D. Essentials of Medical Pharmacology. 8th ed. 2018
5. David E. Mohrman and Lois Jane Heller, Cardiovascular Physiology. McGraw-Hill. 8th ed. 2013.

Course Outcomes

At the end of the course, the student will be able to

CO1: Explain the structure and function of the circulatory system and describe neural, endothelial and pharmacological mediation of excitation-contraction coupling in vascular smooth muscle.
CO2: Understand the process of new blood vessel formation and how new blood vessels take shape from existing blood vessels.
CO3: Describe the structure and functions of the heart and to describe the electrical events of a normal electrocardiogram and identify and list a number of risk factors that contribute to the development of cardiovascular diseases.
CO4: Discuss the pathological processes leading to disorders such as hypertension and atherosclerosis.
CO5: Acquire knowledge on the drugs in the management of cardiovascular diseases.

Ph.D. Biochemistry / Biotechnology Course Work

Course IV Chronobiology

Learning Objective (LO): To learn in detail about the basics of chronobiology, anatomy and physiology of circadian clocks, chronoendocrinology, salient features of chronopharmacology, chronotherapy and molecular basis of biological clocks.

Unit-1 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-2 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-3 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 ultadian variations of glucose tolerance and insulin secretion, Abnormal circadian rhythms of adrenal hormones in Addison's disease and Cushing's syndrome.

Unit-4 Chronopharmacology and Chronotherapy

Basics of chronopharmacology-clinicial chronopharmacology-circadian dependence of drug pharmacokinetics-chronoefficacy of doxorubicin, oxaliplatin and cisplatin - chronopharmacokinetics of antineoplatic 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-5 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.

Text Books

1. F.H. Columbus. Trends in Chronobiology Nova Sci Pub Inc. 2006
2. R. Refinetti Circadian Physiology. CRC Press, Boca Raton, FL, USA. 2nd ed. 2005
3. A. Sehgal. Molecular Biology of Circadian Rhythms Wiley - Liss, USA. 2004
4. J. C. Hall. Genetics and Molecular Biology of Rhythms in Drosophila and other Insects. Elsevier Science, USA. 2003
5. Wilson and Foster. Williams Text book of Endocrinology. 9th ed.

Course Outcomes

At the end of the course, the student will be able to

- CO1: Understand the ubiquity of circadian rhythms, measurement and analysis of rhythm data.
- CO2: Comprehend the anatomy and physiology of circadian clocks in mammals
- CO3: Appreciate the circadian rhythms of hormones, and the importance of circadian rhythms of hormones in health and disease
- CO4: Gain knowledge on salient featurs and importance of chronopharmacology and chronotherapy in disease
- CO5: Understand the molecular bases of circadian rhythms

Ph.D. Biochemistry / Biotechnology Course Work

Course IV Radiation Biology

Learning Objective (LO)*:* To learn in detail about the markers of radiation exposure, radiation response elements, natural radiation countermeasures, methods and techniques in radiobiological research.

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 - Fluoroscence 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: Aamifostine. Free radical scavengers as radioprotectors. Natural products and dietry phytochemicals in radiation protection. Radioresistance. Radioresistant organisms: *Deinococcol 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.

Text Books

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

Course Outcomes

At the end of the course, the student will be able to

CO1: Understand basic of radiation biology, acute radiation effects on mammalian cellular system and heritable radiation effects.

CO2: Understand biomarkers of radiation exposure and techniques involved in understanding radiation effects in cellular system.

CO3: Understand radiation - induced signal transduction pathways, radiation response elements and critical regulators of radiation response elements.

CO4: Understand criteria of radiation protection and possible applications of radiation protectors and radio resistance organisms in clinics and in biotechnology.

CO5: Understand methods in radiobiological research and suitable experimental models for radiobiological research.

Ph.D. Biochemistry / Biotechnology Course Work

Course IV- Neurobiology

Learning Objective (LO): To understand the structure and functions of the nervous system and the associated disorders.

Unit–1

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–2 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–3 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–4 Bipolar Disorder, Schizophrenia, Substance abuse disorders, Major affective disorders, Anxiety disorders, antipsychotic drugs and mood stabilizers.

Unit–5 Neurodegenerative diseases- types. Parkinson's diseases: epidemiology, signs and symptoms, causes, pathophysiology - α-syuclein and Lewy bodies, experimental models and treatment stratergies. Alzheimer's disease- epidemiology, signs and symptoms, risk factors, pathology - amyloidogenesis and nonamyloidogenesis, neurofibrillary tangles, experimental models and treatment strategies.

Text Books

1. Guyton and Hall. Textbook of Medical Physiology. 12th ed. 2010.
2. Michele Tagliati. et al. Parkinson's Disease For Dummies. 1st ed. 2011
3. Alzheimer Disease: From Clinical Description to a Theory of Disease and Treatment, Armenian Medical Network. 2011.
4. Lakshmi N. Yatham and Mario Maj. Bipolar Disorder: Clinical and Neurobiological Foundations. Wiley-Blackwell. 2010.
5. Clete A.Kushida. Sleep Deprivation: Basic Science, Physiology and Behavior. Taylor & Francis. 2004.

Course Outcomes

At the end of the course, the student will be able to

CO1: Describe the anatomy, cytoartichecture and molecular organization of brain.
CO2: Understand the features of the structure and fucntions of the nervous system and the spinal cord.
CO3: Understand the stucture and fucntions of neurons, role of neurotransmitters in nerve conduction and sleep biology.
CO4: Comprehend the biological and clinical aspects of anxiety and psychiatry disorders and their treatment.
CO5: Acquire knowledge on pathological mechanisms and treatment of neurodegenerative disorders.

Ph.D. Biochemistry / Biotechnology Course Work

Course IV- Toxicology

Learning Objective (LO): To learn in detail about the nature of toxicants, their distribution, toxicity and toxicity testing.

Unit-1 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-2 Absorption and Distribution of Toxicants

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-3 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 (LC_{50}), Median lethal dose (LD_{50}), Median lethal time (LT_{50}), Absolute lethal concentration (LC_{100}) and Absolute lethal dose (LD_{100}).
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-4 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-5 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.

Text Books

1. Ernest Hodgson - A Textbook of Modern Toxicology. John Wiley & Sons. 4th ed. 2010.
2. V.V. Pillay - Modern Medical Toxicology. Jaypee Kindle. 4th ed. 2013
3. Ramesh Gupta - Biomarkers in Toxicology. Academic press. 1st ed.2014.

Course Outcomes

At the end of the course, the student will be able to

CO1: Gain a fundamental understanding in the different types of toxicants.
CO2: Acquire knowledge on the mechanisms of absorption, distribution and elimination of toxicants.
CO3: Understand the effects of toxicants and toxicity testing.
CO4: Understand the tissue or organs specific toxicity.
CO5: Understand the effect of toxicants on endocrine secretion and immune system.

Ph.D. Biochemistry/ Biotechnology Course Work

Course IV- Plant Molecular Biology and Abiotic stress

Learning Objectives (LO): To recapitulate the fundamentals of molecular biology and the principles of genetic engineering as well as to know the adaptive mechanisms in plants to cope up with stress conditions.

Unit- 1 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–2 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 -3 Abiotic Stress: Drought, Salinity, Temperature are major abiotic stresses- effects on plant cellular and physiological processes, Plant growth and development.

Unit–4 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-5 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. H. S. Chawla. Introduction to Plant Biotechnology. Science publisher. 3rd ed. 2009
2. Lincoln Taiz, Eduardo Zeiger, Ian M. Møller, and Angus Murphy. Plant Physiology and Development, Sinauer Associates. 6th ed. 2018
3. P. K. Gupta. Plant Biotechnology. Rastogi Publications. 2010
4. Twyman. Advanced Molecular Biology. Garland Science. 2018
5. H. John Newbury. Plant Molecular Breeding. Sci. publications. 2009.

Course Outcomes

At the end of the course, the student will be able to

CO1: Understand the genome organisation and the central dogma of molecular biology
CO2: Understand the mechanisms of gene regulation at transcriptional, translational and epigenetic levels
CO3: Learn and apply molecular techniques used in gene transfer, expression of cloned gene and methods used in rDNA technology
CO4: To perform plant tissue culture
CO5: To learn the impact of major abiotic stress and the tolerance mechanisms at cellular and molecular levels
CO6: Identify stress responsive genes and develop transgenic plants with improved tolerance and resistance to abiotic stress