RV - MERCK

Skill development certification program by RV Institutions in collaboration with Merck in life sciences

R V Institutions

MERCK

June - November 2023

RVCE, NMKRV, RVDC & MERCK

RV-MERCK CERTIFICATION PROGRAM

CONTENTS

RV-MERCK COLLABORATION

1. ABOUT THE PROGRAM- AN INITIATIVE BY RSST, RVCE, NMKRV, RVDC & MERCK

Collaboration between academia and industry is crucial for the inception of growth and innovation. Academia often focuses on fostering new knowledge through education and research, while industry values delivering solutions of near-term commercial values. With these two combined, breakthroughs in the field of technology will move at an accelerated pace. However, there is still a gap between academia and industry, which is a major dearth for the students' prospects. The RV group of institutions (inclusive of RVCE, RVDC and NMKRV, falling under the RSST umbrella) offer an education system that aid students realize their aspirations and go beyond their textbooks. With increasing demand and admissions to all RV institutions each year, the students require a higher skill-set that equal the global IT-BT market. This dream of bridging the gap between industry and academia is now being met with a collaboration with MERCK-life Sciences, a leading pharmaceutical industry.

With this initiative by RV and MERCK, giants in academics and industry, combined efforts to set up training and certification programs is being put in place that can offer students a chance to upskill and be ready for the IT-BT market with improved employment prospects. Various domains will be explored individually, with laboratories being conducted at different RV institutions, with curriculum for the same formulated after considering the current research and market trends. Prospects for publication and patenting will augment for all participating students, thereby creating a benchmark through this collaboration.

This dream collaborative initiative hopes to fulfill the primary objective: offering better prospects for students and adding value to their current skill-set in Biotechnology.

- The hands on-training will be at MERCK, with bridge course and basics being taught at RVCE, NMKRV and RVDC.
- This certification course will be sponsored by MERCK under the CSR initiatives for 20 women students from RVCE, NMKRV and RVDC.

2. RV-MERCK ENTRANCE EXAMINATION

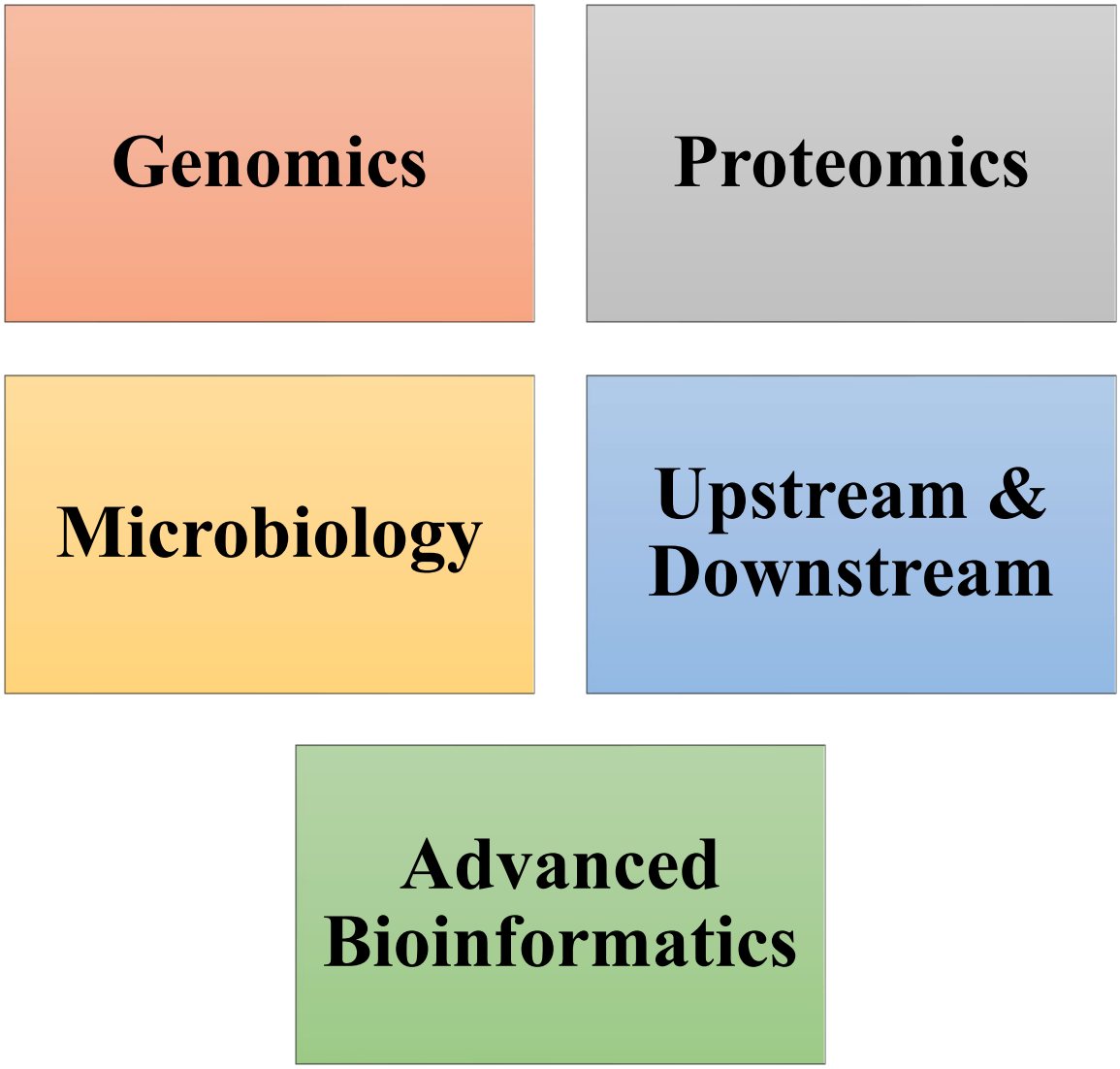
In view of the RV-MERCK certification program, the entrance exam for the RV-MERCK collaboration will be conducted on 13th May, 2023 10 am onwards at NMKRV campus.

The results will be announced on the 20th of May, 2023.

A 4-day bridge course will be held between 24-27th May, 2023.
24th and 25th May: at RVCE
26th and 27th May: at NMKRV

3. MODULES FOR THE CERTIFICATION COURSE

The certification course will be conducted for five modules:



Consolidated Training Modules

Module 1: Proteomics Module

Sl. No.	Experiments /Lab	Theory	Instruments	HR
1.	Cloning	Concepts of primer design, restriction digestion, Ligation, Cloning and sequencing	PCR (RVCE)	1 instructor+1foreman
2.	Sequencing	Concepts of sequencing, Plasmid prep for sequencing, analysis of sequencing	Sequencer	1 instructor+1foreman
3.	Expression and purification of protein	Concept of protein purification, Specific activity, Protein purification table, SDS PAGE, LC-MS/MS analysis for protein identification.	Orbital shaker (RVCE) Low pressure liquid chromatography system (with peristaltic pump, fraction collector and UV detector attached to a computer) – 1 unit if it is an automated system. (MERCK) If peristaltic pumps and fraction collectors	

			are only used, then ¾ of each may be needed for all the students to undergo hands on training. (provided we take 10 students in a batch) SDS – PAGE -1 (MERCK) Enzyme /protein assay kit (depending on the protein to be purified)	

Module 2: Genomics Module

Sl. No.	Experiments/Lab	Theory	Instruments	HR
1.	Identification of problem statement	Literature studies		1 instructor + 1 foreman
2.	Extraction of DNA/gene	1. Fundamental concepts of	Kits available	

3.	Sequencing and analysis	genomics, functional genomics and techniques used in the real world 2. Structure of nucleic acid and types of DNA and RNA 3. Transcription in Eukaryotes 4. Methods of understanding gene regulation and expression 5. Related papers on genomic studies	Nanopore (Genotypic)	
4.	NGS analysis . Introduction to Galaxy · Data pre-processing · SAM and BAM files · VCF analysis · SNP analysis and visualization · Plots using R visualization		High computing GPUs, servers, systems	
5.	Gene of interest identification with respect to drug targets			

Module 3: Microbiology

Sl. No.	Course title	Lab	Hours
1	Isolation of food pathogens (Differential/Selective media)	**Lab 6** Microbial Food Analysis NMKRV	2
2	Determination of Mycotoxins by Thin layer chromatography		2
3	Methods of Food Preservation (Physical/Chemical/Biological)		4
4	Microbial Identification (Biochemical profiling by API identification system)		3

5	Microbiological assay of Antibiotics (Antibiotic assay)	**Lab 7** Pharmaceutical Microbiology **NMKRV**	3
		Lab Assistant	15,000/ batch of 10 students
		Other Lab requirements (Micropipette, Glassware, Centifuge tubes, etc)	30,000
			TOTAL
6	Introduction to industrial microbiology	Lab 8 - Microbiology Application and Training (MAT) Lab MERCK	1
7	Microbial risk assessment - Pharma & Biopharma and Food & beverages		1
8	Environmental monitoring - Air (Active and Passive Sampling), Surface (Contact plate swab method), Personnel / Hygiene monitoring, Rapid Hygiene		1
9	Bioburden testing concept and methodology (Plating method, MPN & Membrane filtration)		2
10	Non-sterile products and microbial limits testing		1
11	Innovative solutions for culture media and its application	Lab 8 - Microbiology Application and Training (MAT) Lab	1
12	Detection of Food pathogens by traditional and Rapid method		1
13	Sterility indicators - Chemical (Melting or colour changes Biological (Bacterial spores)		1
14	Sterility testing - Direct inoculation, Membrane filtration (Open & Closed method), Bacteriostasis/Fungistasis Testing		2
15	Pyrogen testing – In-vitro method		1
16	Gene search and BLAST		1

17	Reactome database	Lab 13 Bioinformatics component RVCE	1
18	Metabolic pathways and interaction		1
19	Pathway comparison		2
20	Understanding regulatory mechanism via KEGG		

Module 4: Upstream and Downstream

Sl. No.	Course title	RV/MERCK	Hours
1	Importance of Cell line development Media and feeds Types of the upstream process – Fed-batch & perfusion Mammalian culture – Bioreactor design and concept Clarification Basics and Optimization Clarification Practical/Hands-on Demo (Lab session) Basics of TFF and its Operation TFF Process Flow Hands-on demo: Operations, NWP, and Integrity/ Excursion Curve Practical (Lab session)	**Lab 9**: Upstream processing	5 hours
2	Virus clearance by filtration & Validation Filter Selection and Sizing Sterile Filtration & Regulatory Requirements Integrity Testing Introduction to Single use Formulation and fill Finish Sterile sampling in Biopharmaceutical Manufacturing Single use - Lab session (1 hour)	**Lab 10:** Downstreaming processing M lab Merck	16 hours

3	Mining microbial strains	**Lab 14**: Bioinformatics component RVCE	5
4	Analyzing metabolic pathways		
5	Phenotypic effect of strains metabolism		
6	Enzyme search using databases		
7	Analyzing Mass spec data		
8	De-novo Sequencing and data analysis		

Module 5: Advanced Bioinformatics

Sl. No.	Experiments/Lab	Theory	Instruments	HR
1.	Drug discovery from identified proteins- problem statement identification	Introduction to drug discovery, literature study	High computing GPUs, servers, systems	1 senior instructor + 1 foreman
2.	Understanding protein-ligand concepts+ MS based bioinformatic studies	Concepts of chemogenomics + related papers on recent studies		
3.	Selection of ligands			
4.	Molecular docking (Protein and lig prep)	Working of various tools and related softwares		
5.	Analysis of docking results			
6.	MD simulations			
7.	Using various tools for MDS			

Advanced Hands-on Training Module

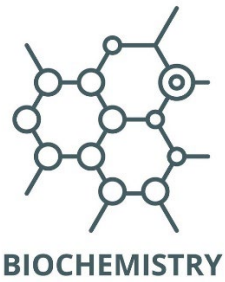
S.No	Topics	RVCE/MERCK	Hours
1	Mass spectrometry data analysis	Lab 15: Advanced Bioinformatics - RVCE	3
2	De-novo protein sequencing		
3	Expression data analysis		
4	Pathway mapping and clustering		
5	Protein networks		
6	Protein-protein interaction analysis		
7	Introduction to galaxy	Lab 15: Advanced Bioinformatics -RVCE	3.5
8	Data pre-processing		
9	SAM and BAM files		
10	VCF analysis		
11	SNP analysis and visualization		
12	Plots using R visualization		
13	Introduction to MATLAB	Lab 15- Advanced Bioinformatics RVCE	1
14	Scripting and model development		
15	Bioreactor model and growth kinetics		
16	Reconstruction of metabolic pathways		
17	Metabolic networks		
18	Metagenomic analysis		
19	Reactome search and metabolic pathway	Lab 15- Advanced Bioinformatics -RVCE	2
20	Introduction to MATLAB on reactor engineering		
21	Reaction engineering and growth kinetics		
22	Understanding and reconstruction of metabolic pathways via KEGG database		
23	Protein networks and interaction pattern analysis		

24	Gene expression analysis for Co-expression vs co-regulation	Lab 15: Advanced Bioinformatics RVCE	3
25	Comparative genomics with relationship between genes and protein-protein interactions		
26	Conceptual introduction to machine learning		
27	Training data and overfitting		
28	Introduction and basics of AutoML		
29	Test case of SNP prediction using Random Forest		

4. ENTRANCE EXAM SYLLABUS AND SCHEME

BTH- 104 BIOCHEMISTRY

(Total Hours: 52)



Unit-1 (6 Hours)

Principles of Bioenergetics:

Introduction, Laws of thermodynamics, Gibbs free energy, Relationship of Standard free energy to enthalpy, entropy and equilibrium constant, High energy compounds, ATP as universal currency of free energy, Oxidation-Reduction Reactions, Electromotive force, Half reactions, Redox potentials, Relationship of standard redox potential and standard free energy change. Standard redox potentials of some biologically important Half reactions.

Unit-2 (8 Hours)

Oxidative phosphorylation:

Electron transport chain, Electron transfer reactions in mitochondria, Electron carriers, Ubiquinone, Cytochromes, Iron sulfur centers, Methods to determine sequence of electron carriers, Fractionation of Multi enzyme complexes I, II, III, IV of Mitochondria and their inhibitors, Oxidative phosphorylation, ATP synthesis, Chemiosmotic model, Proton gradient, Structure of ATP synthetase, Mechanism of ATP synthesis, Brown fat, Regulation of Oxidative phosphorylation.

Unit-3 (12 Hours)

Carbohydrates:

Classification, structure and Properties of mono, oligo and polysacharides. Chirality and optical activity, stereoisomerism, cyclic structure of monosaccharide, (pyranoses and furanoses), structures of glucose. absolute and relative configuration (D & L and R & S nomenclature).

Derived sugars- Sugar acids (Aldonic, Aldaric and Saccharic acids), Amino sugars.

Disaccharides-structures of Maltose, Lactose, Sucrose, Trehalose, Raffinose. Polysaccharides-structure and properties of homo and hetero polysaccharides. Storage polysaccharides. (Starch, Glycogen, cellulose, chitin) Glycosamino glycans and glycoproteins.

Carbohydrate metabolism: Glycogenolysis, Glycogenesis, Coordinated regulation of Glycogen metabolism. Glycolysis-Energetics and Regulation, Fermentation reactions (Lactic acid and alcoholic fermentation), Gluconeogenesis, Reciprocal regulation of Glycolysis and Gluconeogenesis, Citric acid cycle-Energetics and regulation, Glyoxylate cycle. Pentose-phosphate pathway.

Unit-4 (10 Hours)

Amino acids and Proteins:

Classification, structure and properties of amino acids, reactions of amino acids, peptide bond.

Classification of proteins- Structural organisations of proteins (primary, secondary, tertiary and quaternary), conformational analysis, Ramachandran's plot. Thermodynamic aspects of protein folding.

General aspects of amino acid metabolism: Transamination, Deamination, Decarboxylation, basic glutamine and glutamic acid pathways, urea cycle and its regulation, formation of uric acid.

Unit-5 (10 Hours)

Lipids:

Classification- Structure, properties, reactions and biological functions of lipids. Phospholipids, Sphingo and Glyco lipids, Steroids-cholesterol-bile salts, steroid hormones.

Metabolism of Lipids: Beta oxidation of Fatty acids-activation, transport to mitochondria, Beta oxidation reactions. Oxidation of unsaturated fatty acids. Alpha and omega oxidation.

Biosynthesis of saturated and unsaturated fatty acids and cholesterol. Biological functions of eicosanoids (prostaglandin, leucotrienes and thromboxane).

Unit-6 (6 Hours)

Nucleic acids:

Structure and properties- Bases, Nucleosides, Nucleotides, Polynucleotides.

Nucleic acid metabolism: Biosynthesis of purines and pyrimidines, Denovo and Salvage pathways, biodegradation of purines and pyrimidines.

References:

1. Nelson, D.L., Cox, M.M. Lehninger. (2004). Principles of Biochemistry 4th edition Pub WH Freeman Co.

2. Elliott, W.H., Elliott, D.C. Biochemistry and Molecular Biology 3rd Indian edition, Pub. Oxford.

3. Mathews, Van Holde and Ahern, Biochemistry by 3rd edition, Pub Pearson education

4. Stryer, L. Biochemistry 4th Edn. W.H. Freeman and Co. NY.

5. Kuchel, P.W., Ralston Schaums, G.B. Outlines of Biochemistry 2nd edition Pub: Tata.

6. Voet, D., Voet J.G. (2004). Biochemistry 2nd Edn.

7. Devlin, T.M. (1997). Biochemistry with clinical correlations, Wiley-Liss Inc. NY

8. Zubey, G.L. Parson, W.W., Vance, D.E. (1994). Principles of Biochemistry WmC Brown publishers. Oxford.

9. Edwards and Hassall. Biochemistry and Physiology of the cell 2nd Edn. McGraw Hill Co. UK. Ltd.

BTH-103: GENERAL MICROBIOLOGY

(Total Hours: 52**)**

Unit 1 (12 Hours)

Microbial classification:

Three domain system of classification, Phylogenetic Relationships, Code for bacterial nomenclature and taxonomy, Criteria for microbial classification- morphological, staining techniques, biochemical methods, serological techniques, phage typing, fatty acid profiles, Flow cytometry, DNA base composition, DNA fingerprinting, rRNA sequence, Nucleic acid hybridization, Numerical Taxonomy, Chemotaxonomy, Classification of bacteria according to Bergey‟s Manual of systematic Bacteriology, Dichotomous keys, Cladograms, dendrograms, universal phylogenetic tree.

Unit 2 (10 Hours)

Prokaryotic Microorganism- General properties, Structure, and Reproduction:

Domain Bacteria: Proteobacteria (Alpha, Beta, Gamma, Delta and Epsilon Proteobacteria), Cyanobacteria, Chlorobium, Firmicutes, Actinobacteria, Chlamydiae, Spirochaetes, Bacteroidetes, Fusobacteria. Domain Archea: Crenarchaeota, Euryarchaeota.

Unit 3 (8 Hours)

Eukaryotic Microorganisms- General characters, Structure and Reproduction:

Fungi (Saccharomyces), Algae (Spirulina), Protozoa (Plasmodium), Slime molds (Physarum)

Unit 4 (10 Hours)

Viruses, Virioids and Prions (Acellular entities)

General characters, Structure, Criteria for classification of Viruses, Viruses that affect humans, animals and plants, Isolation, cultivation and identification of Viruses (Growing in Bacteria, Living Animals, embryonated eggs, Cell Cultures). Viral Multiplication (Lytic and lysogenic life cycle), Virioids and Prions - General properties and diseases caused by virioids and prions.

Unit 5 (6 Hours)

Microbial Growth and Control

Physical parameters (Temperature, pH, Osmotic Pressure), Chemical parameters (Carbon, Nitrogen, Phosphorous, Sulphur, Trace elements, oxygen), Growth factors, Culture Media, Phases of Growth, Growth Measurements, Microbial growth control - Physical methods (Heat, Pasteurization, Filtration, Radiation, Desiccation, Low

Temperature, High Pressure, Osmotic Pressure) and Chemical Methods (Phenols, Halogens, Alcohols, quaternary ammonium compounds).

Unit 6 (6 Hours)

Microbiological methods:

Isolation and cultivation of microorganisms from Water, Soil, Air, Rhizosphere, Phyllosphere and Mycorrhiza, Biogeochemical cycle.

References:

1. Microbiology by MJ Pelczar Jr, ECS Chan, NR Krieg 5th Edition, Pub: Tata Mcgra-Hill Publishing Co Ltd.

2. Introductory Microbiology by Heritage Pub Heritage

3. General Microbiology by Stainer Pub; Ingraham and Wheeler (McMillan)

4. Alexander M (1977) Introduction to soil microbiology, John Wiley and Sons Inc.N.Y.

5. Atlas R.M. (1998) Microbiology, Fundamentals and applications 2nd Edition, Milan Publishing Co.

6. Brock T.D. and Madigan M.T (1992) Biology of Microorganisms 6th Edn. Prentice Hall, Eagle wood cliffs N.j.

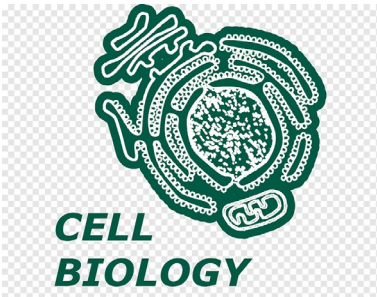
7. Holt J.S. Kreig N.R., Sneath P.H.A and Williams S.T (1994) Bergey‟s Manual of Systemic Bacteriology 9th Edn. William and Wilkins, Baltimore.

8. Prescott L.M, Harley T.P and Klein D.A. (1996) Microbiology WMC. Brown publishers

I SEMESTER (THEORY)

BTH- 101: CELL BIOLOGY

Total Hours: 52



Unit 1 (8 Hours)

Basic Characteristics of the Cell:

Structure, organization and composition of prokaryotic and eukaryotic cell. Plasma membrane-structure and functions, membrane models. Components of Blood & their functions (Plasma, RBC, WBC, Platelets). Extracellular matrix (collagen, proteoglycans, fibronectin, lamins).

Unit 2 (8 Hours)

Cytoskeleton:

Nature of cytoskeleton, Actin filaments, actin binding proteins, Intermediate filaments, Microtubules, MAPs, Structure and functions of cilia and flagella.

Unit 3 (8 Hours)

Membrane Transport:

Transport across membrane- passive diffusion, osmosis, active transport, Ion Channels, A B C transporters, Na+ and K+ pump, Ca2+ ATPase pump, co-transport, symport, antiport, endocytosis and exocytosis. Membrane vesicular traffic.

Unit 4 (8 Hours)

Cell Signalling:

Cell to cell interactions, Cell adhesion- integrins, selectins, cadherins. Cell Junction- Tight and gap junctions, Desmosomes, plasmodesmata. General

principles of cell signaling, signaling via G-protein coupled receptors, kinase receptors, role of secondary messengers.

Unit 5 (6 Hours)

Cell Cycle:

Molecular events of cell division and cell cycle, regulation of cell cycle events- Cyclins, Cyclin dependent kinases, inhibitors. Apoptosis, necrosis.

Unit 6 (8 Hours)

Specialized Cells (Muscle & Nerve cells):

Structure & functions of muscles (Straited, non-straited and cardiac). Molecular basis of muscle contraction. Structure of neuron, neuroglia. Mechanism of nerve transmission- Resting and action potential, electrical and chemical transmission, Neurotransmitters and their receptors.

Unit 7 (6 Hours)

Antioxidant defence system and Senescence:

Free radicals- ROS, RNS. Effect of free radicals on Proteins, Lipids and Nucleic acids. Mechanism of antioxidant defence system- enzymatic and non-enzymatic. Senescence-theories and concepts of aging.

References:

1. Matthews, C.A. (2003). Cellular physiology of nerve and muscle. 4th Edn. Blackwell publishers.

2. Alberts, B., Bray, D., Lewis, J., Raf, M., Roberts, K., Watson, J.D. (1994). Molecular Biology of the Cell.

3. Cooper, G.M. (1997).The Cell: A molecular approach, ASM Press, USA.

4. Darnell, J., Lodish, H., Baltimore, D. (1990). Molecular Cell Biology. Scientific American Books Inc. NY.

5. Edwards and Hassall (1980). Biochemistry and Physiology of cell, 2nd Edn. McGraw Hill Company.

6. Garrett, R.H., Gresham, C.M. (1995). Molecular aspects of Cell Biology, International edition, Saunders College Pub.

7. Holy Ahern (1992). Introduction to Experimental Cell Biology, Wm. C. Brown Publishers.

8. Karp, G. (1996). Cell and Molecular Biology concepts and experiments, John Wiley and Sons Inc. NY.

9. Lodish, H., Baltimore, D., Berk, A., Zipursky, B.L., Mastsydaira, P., Darnell, J. (2004). Molecular Cell Biology, Scientific American Books Inc. NY.

10. Tobin and Morel (1997). Asking about "Cells" Saunders College Publisher.

11. Wolfe, S.L. (1991). Molecular and Cellular Biology, Wordsworth Pub.Co.

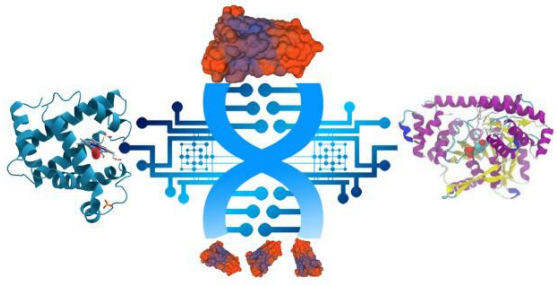
12. Hallwell, B., Gutteridge, J.M.C. (2002). Free Radicals Biology and Medicine. Oxford Press.UK.

13. Kanugo, M.S. (2002) Genes and aging. Cambridge University Press.

1. Genomics module

Introduction to genomics: historical overview, central dogma of molecular biology, and basic principles of genomics. DNA sequencing technologies: Sanger sequencing, next-generation sequencing (NGS), and third-generation sequencing technologies. Genome assembly: de novo assembly, reference-based assembly, and hybrid assembly. Genome annotation: gene prediction, functional annotation, and comparative genomics. Transcriptomics: gene expression analysis, RNA sequencing (RNA-seq), differential gene expression analysis, and functional annotation of transcripts. Epigenomics: DNA methylation, histone modifications, and chromatin accessibility. Metagenomics: analysis of microbial communities, metagenome assembly, taxonomic profiling, and functional analysis. Genomic data visualization: genome browsers, Circos plots, and heatmaps. Applications of genomics: personalized medicine, drug discovery, agriculture, and conservation biology. Ethics and social implications of genomics: privacy, genetic discrimination, and genetic counseling.

2. Proteomics module



Introduction to proteomics: historical overview, central dogma of molecular biology, and basic principles of proteomics. Protein separation techniques: gel electrophoresis, chromatography, and mass spectrometry. Mass spectrometry-based proteomics: ionization techniques, fragmentation methods, and data analysis. Protein identification: database searching, protein quantification, and post-translational modification analysis. Proteome profiling: shotgun proteomics, targeted proteomics, and label-free quantification. Structural proteomics: protein structure determination, X-ray crystallography, and NMR spectroscopy. Functional proteomics: protein-protein interactions, protein networks, and protein localization. Clinical proteomics: biomarker discovery, disease diagnosis, and drug discovery. Proteomics data analysis: statistical methods, bioinformatics tools, and databases. Ethics and social implications of proteomics: privacy, data sharing, and ethical considerations in human studies.

3. Bioinformatics

Introduction to bioinformatics: Overview of bioinformatics and its importance in modern biology, Introduction to biological databases and their use in bioinformatics, Basic programming concepts for bioinformatics. Sequence analysis: Sequence alignment algorithms and tools, Basic statistics of sequence data, Gene prediction and annotation. Structural bioinformatics: Protein structure prediction and modelling, Protein-ligand docking, Analysis of protein structures. Genomic

analysis: Genome assembly and annotation, Transcriptome analysis using RNA-seq data, Identification of genetic variations. Phylogenetic analysis: Introduction to phylogenetics and evolutionary biology, Construction of phylogenetic trees, Molecular evolution and selection analysis. Functional analysis: Gene ontology and functional annotation, Pathway and network analysis, Integration of multi-omics data. Applied bioinformatics: Bioinformatics in drug discovery and development, Clinical bioinformatics and personalized medicine, Bioinformatics in agriculture and biotechnology. Ethics and safety related to Bioinformatics.

REFERENCE TEXT BOOKS FOR MODULES: Genomics, Proteomics & Bioinformatics

1. Bioinformatics and Functional Genomics Jonathan Pevsner Wiley Blackwell 2nd Edition
2. Introduction to Proteomics Daniel C. Liebler Humana Press 2002.
3. Principles of Gene Manipulation and Genomics Primrose .S.B, Twayman .R.M, Blackwell 7th edition, Principles of Proteomics(Advanced 2006 text series), Twayman.R.M, Taylor and Francis 1st edition, 2004

5. CONTACT FOR QUERIES

Dr. Vidya Niranjan,

Professor and Head,

Dept. of Biotechnology, RVCE

Ph. No: +91-9945465657

Email: vidya.n@rvce.edu.in