LIFE SCIENCES

Programme Code: LIFE04

Programme Outcome:

- At the end of the course work pursued, the Ph.D. student will be well versed in the recent advances in crucial areas of Life Sciences such as Immunology, Cell Biology, Plant Sciences, Microbiology and Cancer biology.
- The students will receive hands on experience in several techniques related to the above fields as well as those structural Biology and Bioinformatics.
- The design course works will help the students to have a broader outlook of their research work and be able to judge and use techniques for a superior outcome and higher impact publications.

DETAILED COURSE STRUCTURE

S. No	Course Code	Subject Title	Hours	Credits
Compulsory Core Courses (2 credits)				
1	09-LIFE04-601-C	Research Methodology & Ethics	15	1
2	09-LIFE04-601-C	Biostatistics	16	1
Elective Courses (Total 10 out of 15 Credits to be opted from the following)				
1	10-LIFE04-602-E	Structural and Functional Bioinformatics and Macromolecules	30	2
2	10-LIFE04-602-E	Deregulation of Cell Growth in Cancer	30	2
3	10-LIFE24-603-E	Molecular Basis of Cancer Therapeutics	30	2
4	10-LIFE24-603-E	Biogenesis of Macromolecules and their deregulation in Cancer	30	2
5	10-LIFE24-603-E	Experimental Biophysics and its Application in Cancer Research	15	1
6	10-LIFE24-603-E	Cancer Metabolism	18	1
7	10-LIFE24-603-E	Stem Cells in Development and Disease	15	1
8	10-LIFE24-603-E	Metastasis	19	1
9	10-LIFE24-603-E	Animal Models in Cancer Research	16	1
10	10-LIFE24-603-E	Biology of Tumor Microenvironment	15	1
11	10-LIFE24-603-E	Basics of Immunology and Implications in Cancer	15	1
		TOTAL		**12**

S. No	Course Code	Subject Title	Hours	Credits
12		Scientific writing and Laboratory Marks		2
13		Seminar Presentation		2
14		Oral General Comprehensive Examination (OGCE)		2
		TOTAL	**6**	**6**

Course	Hours	Credits
Courses		12
Scientific Writing and Laboratory Marks		6
Seminar Presentation		
Oral General Comprehensive Examination (OGCE)		
Total	18	

COORDINATORS

Program Coordinators:

Dr. Sorab N. Dalal (E-mail: sdalal@actrec.gov.in)
Mrs Sadhana Kannan (E-mail: skannan@actrec.gov.in)
Dr. Manoj Mahimkar (E-mail: mmahimkar@actrec.gov.in)

Course Co-ordinators

Course	Coordinators	E-mail
Research Methodology & Ethics	Dr. Sorab N. Dalal	sdalal@actrec.gov.in
Biostatistics	Mrs. Sadhna Kannnan Dr. Manoh Mahimkar	skannan@actrec.gov.in mmahimkar@actrec.gov.in
Structural and Functional Bioinformatics and Macromolecules	Dr. Ashok Varma Dr. Kakoli Bose Dr. Prasanna Venkatraman Dr. Gourab Das	avarma@actrec.gov.in kbose@actrec.gov.in vprasanna@actrec.gov.in gdas@actrec.gov.in
Deregulation of Cell Growth in Cancer	Dr. Sorab N. Dalal	sdalal@actrec.gov.in
Molecular Basis of Cancer Therapeutics	Dr. Abhijit De	ade@actrec.gov.in
Biogenesis of Macromolecules and their deregulation in Cancer	Dr. Sunil Shetty Dr. Sanjay Gupta	sunil.shetty@actrec.gov.in sgupta.dob812@gmail.com
Experimental Biophysics and its Application in Cancer Research	Dr. Kakoli Bose	kbose@actrec.gov.in
Cancer Metabolism	Dr. Sanjeev Waghmare Dr. Sanjay Gupta	swaghmare@actrec.gov.in sgupta.dob812@gmail.com
Stem Cells in Development and Disease	Dr. Sanjeev Waghmare	swaghmare@actrec.gov.in
Metastasis	Dr. Pritha Ray	pray@actrec.gov.in
Animal Models in Cancer Research	Dr. Arviund Ingle Dr. Pradip Choudhari	aingle@actrec.gov.in pradip.r.chaudhari@gmail.com
Biology of Tumor Microenvironment	Dr. Sharath Chandra Arandkar	sarandkar@actrec.gov.in
Basics of Immunology and Implications in Cancer	Dr. Rohan Khadilkar Dr. Subir Biswas	rkhadilkar@actrec.gov.in sbiswas@actrec.gov.in

COMPULSORY CORE COURSES

09-LIFE04-601-C: Research Methodology & Ethics (15 Lecture Hrs)

Coordinators: Dr. Sorab N. Dalal
(sdalal@actrec.gov.in)

Course Details:

The course will teach them the basics of writing scientific documents and making presentations. Finally, the course will give them a firm grounding in the ethical practices of science, including plagiarism, the ethics of working with animals and human samples and data manipulation.

- **Good research practice. Laboratory notebook maintenance - Do's and don'ts**
- **Literature review - where to get material, the quality and quantity of content. Establishing a background for a research project**
- **How to write manuscripts and grants.**
- **The fine art of PowerPoint presentation**
- **Preparing figures for manuscripts and grants**
- **Other software (E.g. Graphpad, plagiarism check, proofing for images)**
- **Content for Publication Ethics Workshop**

- **I. Plagiarism:**

- Introduction and definition of Plagiarism.
- Case studies indicating incidents of Plagiarism and their impact.
- Types of Plagiarism
- Ways to avoid plagiarism, including ideas about "Common Scientific Knowledge", process of citing sources.
- Class Quiz and game on Plagiarism

- **II. Authorship, Open Access, Journal Selection and peer review**

A. Authorship

- The significance of authorship/ role of different authors (1st author vs corresponding author)
- Introduction to authorship criteria.
- Various scenarios of authorship.
- Acknowledging contribution to the manuscript.
- Appropriateness of discussing authorship at start of a project.
- Inappropriate authorship practices.
- Case studies on Authorship criteria/ Scenarios

B. Open Access, predatory journals and peer review process

- Open access publications and various types of open access.
- Criteria to identify journals to publish.
- Introduction to Sherpa Romeo and another online resource to know publisher policy and self-

archiving practices.

- Identifying predatory journals and understanding consequences of publishing in a predatory journal.
- Basic idea about the need for peer review and various modes of peer review
- Peer review and conflict of interest
- Qualities of good peer review assessment
- Responding to review comments

- **III. Research Data management**

- Basic idea about data and information
- Various types of data [primary, secondary and metadata)
- Various stages of Data management cycle including naming of file, storage and version control.
- Dealing with specific data such as images
- Options for data sharing

Course Outcomes:

- Students who take this course will have learned how to catalog their data in a logical manner, learn how to write and present their work and have a firm grounding in the ethical practice of science.
- The objective of the course is to introduce the students to good laboratory practices, including maintenance of records.

References:

1. G. D. Gopen and J.A. Swain. The Science of Scientific Writing. American Scientist Vol 78.
2. Guidelines on style for scientific writing. Will G Hopkins. Sportscience 3(1)

09-LIFE04-601-C: Biostatistics (16 Lecture Hrs)

Coordinators: Mrs. Sadhna Kannnan, Dr. Manoh Mahimkar (skannan@actrec.gov.in, mmahimkar@actrec.gov.in)

Course Details:

Course will provide an insight on statistical methods used in biomedical research.

- An Overview of Biostatistics-
- Why apply statistics to biological data? Data Management
- Basic data management using Excel and SPSS Probability distribution (Normal, Poisson, t, F, Chi-square)
- Problem-solving- 1
- Sample size determination and justification of power estimates in biological research protocol - Observational studies Clinical trials (superiority, non-inferiority/ equivalence) Animal studies.
- Problem-solving- 2
- Hypothesis testing: analysis of categorical data
- Problem-solving- 3
- Hypothesis testing: analysis of continuous data - Parametric & Non-parametric tests (t-test, ANOVA, repeated measures ANOVA, correlation, regression -logistic)
- Problem-solving- 4
- Overview survival analysis
- Hypothesis testing: analysis of time to event (survival data - Kaplan Meier analysis. log-rank test and Cox regression analvsis
- Problem-solving- 5

Course Outcomes:

- This course will provide an insight into the statistical methods used in research settings which are important for all students who will be pursuing the research.

References:

Problem-solving questions for hands-on session lectures, presentations for theory lectures, online tools and statistical software

ELECTIVE COURSES

10-LIFE04-602-E: Structural And Functional Bioinformatics And Macromolecules (30 Lecture Hrs)

Coordinators: Dr. Ashok Varma,
Dr. Kakoli Bose,
Dr. Prasanna Venkatraman,
Dr. Gourab Das
(avarma@actrec.gov.in,
kbose@actrec.gov.in,
vprasanna@actrec.gov.in,
gdas@actrec.gov.in)

Section A: Bioinformatics

Course Details:

Structural Bioinformatics, basic computer languages, applications in biomedicine.

- **Fundamentals of computational biology (part 1) computing concepts for biologists**
  Introduction to computer hardware and software, scalable computing (workstations, HPC, cloud computing), linux command line access, Hands on demo of ACTREC-HPC
- Structural Bioinformatics: tools to study physicochemical properties of macromolecules (ExPASy), secondary structural properties in details-types of helices, turns, sheets, super secondary structures, motifs, and domains, families/ superfamilies and their functions Ramachandran Plot
- Sequence alignments (MSA, pairwise alignment), BLAST search, retrieving structure from pdb, Relationship between structure and· Function-Sequence and structural alignment of proteins; Example workflow for assigning functional annotation from primary sequence and structures
- Structural Bioinformatics: Molecular modeling (homology, threading, ab initio); Small molecule/ peptide design
- Molecular docking (protein-protein, protein-ligand/small molecules); Drug design - challenges, in silica drug design - advantages, steps and tools (QSAR, 30-QSAR etc); Application - How drug designing leads to clinical trial - with examples
- Molecular dynamics simulation: Different tools for these studies. Hands-on-session on Structural Bioinformatics, Molecular docking and MDS
- Introduction to R Programming
  - Overview and key components of programming

- Data types, objects, operators
- Control statements, loops and functions
- Using special functions in Data mining and analysis
- Data representation through plotting

- Biological Data Analysis using R
  - Differential protein expression analysis
  -

- NGS-The journey from raw data to pathway analysis AND enrichment- (Gene Expression Data)

- **Fundamentals of computational biology (part 2) - artificial intelligence in biomedical research**

Fundamental of artificial intelligence for biologists, data sources in bioinformatics, application of Al in biomedical sciences

Course Outcomes:

- Understanding the role of Bioinformatics and computational methods in biological research

References:

Reviews/textbooks/research papers and online tools

Section B: BIOPHYSICS AND STRUCTURAL BIOLOGY

Course Outcomes:

- Understand concepts of biophysics and structural biology in the field of biomedicine

Course Details:

Basic Concepts of biophysics, quantitative analysis of enzymatic reactions/protein-ligand interactions using different probes to determine macromolecular structure and dynamics

- **Proteins-Structure**

Overview including domains and motifs; Classes of proteins with examples. Protein Folding: Forces that determine the structure; thermodynamic and kinetic concepts of folding; tools to study protein folding

- **CD and Fluorescence**

Theory, basic principle and application in biological studies

- **Macromolecular crystallography**

Crystal systems, crystal lattice, symmetry operations and point group, space group determination. Weak inter and intramolecular interactions, protein-DNA, Protein-RNA structure

- **Protein crystallization, structure solution and refinement**

Different methods of protein crystallization including sitting- drop and hanging -drop vapor diffusion methods. Methods for x-ray diffraction data collection, structure solution methods; Molecular

replacement methods, Multiwavelength anomalous diffraction (MAD); isomorphous replacement method, Different Methods for structure refinement; examples from literature

- NMR - Theory, basic principle and application in biological studies
- cryo-EM- Theory, basic principle and application in biological studies
- **Protein-protein/ligand interactions**

- Biochemical tools and some spectroscopic tools (tagging with other proteins such as MBP, GST, Fluorescence etc.) -basic principles; applications with eg (reading material)
- Biophysical-FRET, ITC, OCTET, FP, nanoDSF - basic principles, applications with eg-
- Applications of mass spectrometry for protein structure determination and protein interaction-Mass spectrometry has come of age to determine protein structure, conformation and stoichiometry, Interactions can now be deduced at residue levels. Protein-protein interactions and protein-ligand interactions can also be studied in situ. (The classes will take the student through the basics of mass spectrometry and then through the concept and application of these new advances).

- **Enzymes**

Classes of enzymes; Active site and Catalysis; Kinetics; Concept of initial rate, Vmax, Km and kcat; Enzyme Inhibition; Different type of inhibitions; some examples from biological systems and applications

References:

Review articles, recent advanced literature and textbooks

10-LIFE04-602-E: Deregulation Of Cell Growth In Cancer (30 Lecture Hrs)

Coordinators: Dr. Sorab N. Dalal (sdalal@actrec.gov.in)

Course Details:

The purpose of this course is to cover various aspects of how cell growth and proliferation are altered in tumors with an emphasis on how we know what we know and more importantly how these different pathways crosstalk with each other.
The list of topics to be covered in the course and the number of lectures for each topic are listed below. The lecturers for each topic are also listed.
Each lecture will run for one and a half hour with a total of 20 lectures.
This will be followed by two paper presentations and two assignments that will be handed out to students.

- **Cell cycle control - 1**
  - Cell cycle phases. How do you define G0?
  - Why a cyclin is called a cyclin?
  - Post-translational regulation of cdks.
- **Cell cycle control - 2**
  - Regulation of cellular localization of cyclins
  - Regulation of cyclin turnover
  - The Spindle Assembly Checkpoint
- **Cell cycle control - 3**
  - How do cyclin - cdk complexes recognize substrates?
  - Phenotypes of cyclin / cdk knockout mice: what do they teach us about cell cycle regulation?
- **Rb family of proteins in the regulation of cell growth -1**
  - Identification of Rb as a tumor suppressor - Knudsens hypothesis.
  - Rb family members
  - The E2F and DP family.
- **Rb family of proteins in the regulation of cell growth -2**
  - Regulation of Rb family members and bow this impacts cell cycle and tumor progression.
  - Analysis of K0 mice for the family members - lessons for tumor progression and cell cycle control.
- **The Src Y-kinase**
  - Discovery and domain structure.
  - Activation of Src and downstream pathways.
  - Role in tumor progression
- **Receptor Y-kinase signaling**
  - Domain structure
  - Activation and Inactivation
  - Downstream signalling
- **Role of Ras family in regulating cell growth**

- How do small G proteins work? How is activity measured?
- Ras family members, differences in expression and activation of different family members in tumor types.
- Regulation of Ras activity.
- Ras effectors and how the effectors affect different aspects of tumor formation

- **Myc**
  - Discovery
  - Regulation of Myc activity
  - Role in tumor progression

- **Role of the P13K-AKT-mTOR pathway in cancer**
  - How is the activation of PI3K and AKT regulated?
  - How does this impact mTOR signaling?
  - What are the downstream consequences of activation of this pathway
    a. Metabolism1
    b. Cell survival
    c. Control of translation

- **Cell cycle checkpoints and cancer -1**
  - What is a checkpoint pathway?
  - How does one study checkpoint signaling.
  - Role of ATM/ATR in regulating checkpoint control and tumor progression

- **Cell cycle checkpoints and cancer -2**
  - The downstream kinases – Chk1 and Chk2. How do the checkpoint kinases regulate:
    a. Cell cycle progression
    b. DNA repair
    c. Tumor progression

- **The p53 family-1**
  - Identification of p53 - oncogene or tumor suppressor? Domain structure and mutation profile.
  - Regulation of p53 function

- **The p53 family - 2**
  - p63 and p73
  - Domain structure and cross talk with p53 pathways.
  - Developmental phenotypes of KO mice of all three family members.
  - What do they teach us about tumor progression?

- **DNA tumor viruses**
  - SV40
  - Polyoma
  - HPV

- **Telomerase and cancer**
  - What is telomerase and the end replication problem.
  - How is telomerase activity regulated and measured?
  - Telomere structure
  - Telomerase and immortalization.

- Telomerase knockout mice and their contribution to understanding tumor progression

- **The BRCA1 tumor suppressor**
  - Identification of BRCA1 and later BRCA2
  - Functions of these proteins in regulating checkpoint control, DNA repair, tumor progression and development.
  - Phenotypes of knockout animals.

- **DNA damage and repair in cancer**
  - Types of DNA damage
  - Base excision repair
  - Mismatch repair
  - DSB repair
  - How alterations of these pathways affect tumor progression

- **Wnt pathway in cancer**
  - The Wnt β-catenin pathway.
  - Regulation of β -catenin by degradation and by cell-cell adhesion.
  - APC mutations and the phenotypes of KO mice.

- **The VHL tumor suppressor**
  - Function and Biochemistry of the VHL tumor suppressor
  - How does VHL regulate hypoxia inducible factor (HIF).
  - Other functions of VHL

Course Outcomes:

- The goal of this course is to provide enough information about the basic biology of these different programs so that after going through the course, the student should be able to critically read and review a paper in the field.
- It will prepare them to analyze the data in these publications and hopefully to be able to use the published literature as the basis for a scientific proposal.

References:

The study material for these courses will be review articles in the relevant fields that will cover the topics listed above. The reviews will cover older more basic material and the latest information in the field

10-LIFE24-603-E: Molecular Basis Of Cancer Therapeutics (30 Lecture Hrs)

Coordinators: Dr. Abhijit De (ade@actrec.gov.in)

Course Details:

This course will provide the required foundation of the principles of all major cancer therapy approaches. Biological targets, pharmacologic rationales and mechanistic approaches will be explained.
Agents that damage DNA, and the response of tumor cells to such insults will be emphasized.
In-depth presentations will consider all classes of chemotherapeutic agents, their metabolism, mechanisms of action, as well as the resistance mechanisms of tumor cells.
Mechanistic rationales for other therapeutic modalities used for cancer treatment such as radiotherapy, gene therapy, immunotherapy and nanomedicines will also be covered.
Students will have the opportunity to learn about novel and upcoming therapeutic targets, and the combinatorial procedures used to develop new agents for clinical evaluation.

- **Introduction to Cancer Therapeutics**
  Historical journey in developing cancer treatment; physical and molecular basis; Understanding disease stages; common terminologies and principles followed.
- **Surgical intervention**
  Deciding factors governing surgical interventions; operating procedures and advanced methods like image guidance, robotic surgery; current difficulties and problems associated with surgical intervention.
- **Cancer drug development**
  General pipeline for drug development; in silico, in vitro and in vivo screening; understanding steps of clinical trials; toxicological assessments
- **Common chemotherapy**
  Principle of common chemotherapeutic drug development and mechanisms of action for various generic chemo drugs used in cancer clinics, e.g. Alkylating agents, Platinum derivatives, Topoisomerase Inhibitors, SFU and Nucleoside analogs.
- **Concept of personalized cancer medicines**
  Molecular targets leading to personalized drugs; small molecule inhibitors, antibody drug and antibody-drug conjugates
- **Phytochemicals and Natural products as cancer medicines**
  Plant Derived cancer medicines; tumor-related protein targeting with phytomedicines and natural products; compounds progressed in preclinical and clinical pipelines
- **Radiation therapy I**
  Basic principle of radiation therapy; various forms of radiation source used in radiation therapy; external beam RT and IMRT, brachytherapy, proton beam therapy; cancer conditions treated; risk factors; bystander effect.
- **Radiation therapy II**
  Use of Radioisotopes and Radiotracers; Radiopharmaceutical therapies; concept of radiosensitizer and radioprotector; hyperthermia.
- **Therapy resistance I**
  Basic mechanisms of Chemoresistance against common and personalized medicines; Hallmarks of chemoresistance
- **Therapy resistance II**

Understanding mechanisms of Radiation resistance; Susceptible genes

- **Therapy resistance III**
  Emerging Strategies to overcome therapy resistance against targeted medicine
- **Targeting Cell Cycle Regulation for cancer therapy**
  Molecular basis; progress in drug development targeting cell cycle regulatory molecules.
- **Targeting Epigenome in Cancer Therapeutics**
  Therapy approaches targeting epigenetic signatures in cancer; mechanisms involved in cancer epigenomic drug development; targeting non-coding RNA
- **Targeting Proteasome**
  Ubiquitination; concept of degrons; PROTACs and proteasome Inhibitors under development
- **Targeting Tumor Angiogenesis**
  Angiogenesis; molecular targets of angiogenesis for cancer therapy; challenges and success of anti-angiogenic therapy
- **Targeting Reactive Oxygen Species (ROS)**
  Generation, cytotoxicity and drug target; use as sensitizers for radiation and chemotherapy interventions
- **Cancer Gene Therapy**
  Concept of gene transfer and oncolytic virotherapy; research methodologies; progress in clinical translation
- **Immune cell therapy**
  Concepts and principles; advances in immunotherapy: tumor-infiltrating lymphocytes (or TIL) therapy, NK cell therapy
- **CAR-T cell therapy- principle of CAR**
  T cell therapy for cancer treatment; preclinical and clinical experience of CAR-T therapy in blood cancer
- **Nanomedicines**
  Basic concept of nano-drug development; physical characterization parameters; drug formulation principles; practicing and novel nanomedicines under development; concept of theranostics.

Course Outcomes:

Upon successful completion of this course, you will -

- Learn the basis and core mechanisms of actions for cancer intervention methods, i.e. chemotherapy and radiation therapy. This course will take reference of the core molecular mechanisms such as DNA replication, transcription, splicing, translation, epigenetic targets, cell division & cell cycle, DNA damage and repair, ROS generation, metabolism.
- Learn mechanisms and drug targets towards protein-protein, protein-DNA interactions in tumor cells.
- Learn how cancer-associated signaling pathways can be targeted and how cells adapt and generate resistance mechanisms.
- Learn different ways in which immunologic components can be used for the treatment and prevention of malignancy.

References:

The study material for these courses will be review articles/textbooks/research papers in the relevant fields that will cover the topics listed above

10-LIFE24-603-E: Biogenesis Of Macromolecules And Their Deregulation In Cancer (30 Lecture Hrs)

Coordinators: Dr. Sunil Shetty,

Dr. Sanjay Gupta
(sunil.shetty@actrec.gov.in,
sgupta.dob812@gmail.com)

Course Details:

This course will provide basic knowledge of central dogma and how they are deregulated in cancer.
Also, it will cover the latest techniques and genetic engineering approaches that are useful to the students.

- **DNA Replication and its deregulation in cancer**
  Basics of DNA replication, DNA polymerases, regulation, checkpoint kinases
- **DNA repair and its contribution to cancer**
  Base excision, nucleotide excision, mismatch repair, and their deregulation in cancer
- **DNA repair and DNA damage response**
  Homologous and non-homologous recombination, deregulation in cancer, ATM, ATR pathways, p53
- **Basics of transcription and transcription factors**
  RNA polymerases; composition and role played by promoters, enhancer, repressor elements; transcription factors; transcriptional activation mechanism
- **Deregulation of Transcription in cancer**
  Oncogenic transcription factors, applications of transcriptional modulators in cancer
- **Post-transcriptional regulation**
  Splicing, poly-adenylation, mRNA modification
- **mRNA degradation pathways**
  P-bodies, Stress granules, decapping, exosomes
- **Regulation of transcription by signaling pathways**
  In brief, JAK-STAT, myc signaling, MAPK pathway, steroid signaling
- **Epigenetic regulation of transcription**
  DNA methylations, histone modifications, histone variants, and isoforms
- **Epigenetic regulation of transcription**
  RNA methylation, ATP-dependent chromatin remodelers
- **Noncoding RNAs and regulation in cancer**
  miRNAs, IncRNAs, circRNAs
- **Translation mechanism and its regulation**
  Basic translation, translation factors, mTOR, PI3K, MNK, GCN2, ISR pathways
- **Post-translation regulation and alternative translation**
  PTMs, ubiquitination, proteasome, autophagy, and translation reprogramming
- **Ribosome biogenesis and regulation**

Ribosome biogenesis, deregulation in cancer, ribosome modifications, ribosomopathies

- **Ribosome quality control**
  Ribosome stalling, NMD, No-Go Decay, Non-Stop Decay
- **Genetic engineering techniques**
  Recombinant DNA technology, Gibson cloning, etc.
- **Gene editing techniques**
  CRISPR-Cas9, Talens, Cre-Lox system, etc.
- **High throughput transcriptomic techniques**
  RT-PCR, RNA-seq, single-cell RNA seq,ATAC seq, Hi-Seq, CHIP-seq etc.
- **Proteomic techniques**
  mass spectrometry, Ribo-seq

Course Outcomes:

Providing molecular basis of posttranscriptional and posttranslational modifications and epigenetics and their contributions to cancer, and the latest techniques in this field of research

References:

Reviews/textbooks

10-LIFE24-603-E: Experimental Biophysics And Its Application In Cancer Research (15 Lecture Hrs)

Coordinators: Dr. Kakoli Bose
(kbose@actrec.gov.in)

Course Details:

The course will provide an in-depth understanding of quantitative biophysical methods in biomedical research.

- **Raman spectroscopy**
  Theory and applications with real time data analysis
- **A-CD**
  Theory including real-time data analysis tutorial and applications-secondary structure, tertiary structure, and thermal denaturation
- **B-Fluorescence Spectroscopy and its applications**
  Theory including real-time data analysis tutorial and applications -Fluorescence emission, fluorescence quenching, FRET
- **BRET**
  Theory and applications and real time experimental analyses
- Enzyme kinetics using fluorescence plate reader (theory will already be covered in the lecture)- so data reading applications, and analysis lecture
- Protein-protein/ligand interaction studies using OCTET, FP and any other tool(s)
- **ITC**
  Theory, data acquisition, understanding of the data, data analysis, and applications
- **EXTRA LECTURE**
  Application of biophysical principles in nanoscience

Course Outcomes:

- It will train students in performing advanced biophysical experiments and data analysis.

References:

Reviews/textbooks/research papers and online tools

10-LIFE24-603-E: Cancer Metabolism (18 Lecture Hrs)

Coordinators: Dr. Sanjeev Waghmare,

Dr. Sanjay Gupta
(swaghmare@actrec.gov.in,
sgupta.dob812@gmail.com)

Course Details:

Tumor cell metabolism involves various combinations of factors such as epigenetic changes, nutrient and metabolic interplay, cell signaling, tumor microenvironment, hypoxia cells thereby enabling cancer cells to proliferate, escape from primary site to secondary site followed by metastasis thereby leading to develop resistance to chemo-and radio-therapies.

This is due to the fact that cancer cells undergo metabolic reprogramming in glycolysis, amino acid, and lipid metabolism support the growth of therapy-resistant cancers.

This course encompasses the topics for in-depth understanding of the metabolic reprogramming, epigenetics, cell signaling and tumor microenvironment.

Finally, current applications such as spectroscopy to identify metabolic alterations biomarker identification, imaging, and treatments for the clinical management of cancer.

- Molecular carcinogenesis and metabolism in cancer
- Basic cancer and metabolic reprogramming-Glycolysis and Pentose phosphate pathway in cancer- Lactate and nucleoside metabolism
- Mitochondrial energy metabolism, TCA, glutamate - driver in cancer promotion
- Lipid metabolism involvement in cancer progression
- One carbon metabolism and cancer therapy resistance
- Cross talk of nuclear and mitochondrial genes in cancer metabolism
- Cell signaling and metabolism in cancer 'and therapy resistance
- Spectroscopy, metabolic changes in cancer and therapy resistance
- Metabolomics and therapeutic avenues in cancer
- Metabolic reprogramming, tumor microenvironment and immune suppression
- Metabolic rewiring of the innate immune cells during tumor progression Concept of selfish immunity, selfish immune factors, systemic insulin resistance, amino acid sensing and metabolism in innate immune cells in tumor scenario, metabolic factors in macrophage polarization, carbohydrate and lipid metabolism rewiring in innate immune cells
- Iron and copper metabolism in cancer cells and its role in cancer cell growth, metastasis and drug resistance

Course Outcomes:

- This course aims to cover the topics on basic cancer metabolism that includes glycolysis, pentose phosphate pathway, TCA.
- In addition, it covers the topic on lipid and mitochondrial metabolism involved in cancer including one carbon metabolism.
- Further, how the crosstalk of nuclear, signaling and mitochondrial genes regulate cancer.
- Importantly, the advanced technologies used in cancer.

References

The study material for these courses will be review articles/textbooks/research papers in the relevant fields that will cover the topics listed above

10-LIFE24-603-E: Stem Cells in Development And Disease (15 Lecture Hrs)

Coordinators: Dr. Sanjeev Waghmare
(swaghmare@actrec.gov.in)

Course Details:

The development of the embryo initiates from a fertilized egg that divides and undergo differentiation to give rise to germ layers-ectoderm, endoderm and mesoderm, that further forms into a multicellular organism.
Embryonic stem cells are pluripotent as they are able to produce multiple lineages of all the tissues.
Adult Stem cells reside in niches that possess self-renewal property that maintain tissue homeostasis and repair the injured tissue.
Thus it is important to understand the molecular mechanisms such signalling, epigenetics and metabolic regulation.
Further, within tumor there exists specialized cell that are as termed cancer stem cells that escape chemo-radio-therapy.
It warrants exploring the molecular mechanism that imparts therapy resistance in cancer.
The topics would be covered on Stem cells, Induced pluripotent stem cells and its therapeutic potential in
regenerative medicine.

- Embryonic development in drosophila - fundamental principles in development
- Embryonic stem cells, Adult Stem cells and their niches, Differentiation, mechanisms regulating stem cells and tissue homestasis, SCNT and xenotransplantation
- Ipsc reprogramming & pluripotency, disease modelling, cell therapy and therapeutic implications
- Mechanobiology and Its Effect on Stem Cells
- Origin of cancer, environmental - intrinsic and extrinsic factors
- History and origin of cancer stem cells, cancer stem cells niches, hybrid-EMT, signaling regulating cancer stem cell, challenges to target CSCs
- Epigenetic and metabolic regulation in normal and cancer stem cells regulation
- Chemo-resistance, radioresistance mechanisms involved in CSCs therapy resistance
- Tumor microenvironment in CSCs regulation and therapy resistance
- Molecular imaging in stem cells and cancer stem cells research

Course Outcomes:

- The course aims to cover the topics on·the embryonic development, fundamental steps indevelopment.
- It includes self-renewal and differentiation of adult stem cells.
- JPS reprogramming and pluripotency in regenerative medicine.
- Further, it includes the course on cancer stem cells (CSCs), epigenetic & metabolic regulation of CSCs and therapy resistance, tumor-microenvironment and molecular imaging.

References:

The study material for these courses will be review articles/textbooks/research papers in the relevant fields that will cover the topics listed above

10-LIFE24-603-E: Metastasis (19 Lecture Hrs)

Coordinators: Dr. Pritha Ray (pray@actrec.gov.in)

Course Details:

Majority of the cancer death occurs due to wide spread metastasis to distant organs.
Till now it is difficult to predict which cell will successfully complete their migration from primary tumor to eventual recolonization in a far-flung region of the body. Interestingly, only 0.01% of all metastatic tumor cells can complete their journey to faraway organs exerting the fatal outcome.
Therefore, it is important to understand the molecular and structural alterations, the role of various signalling pathways and biological processes, the underlying molecular cues and ability to survive the toughest conditions, the capability for successful colonization and growth in an unfamiliar territory and finally the therapeutic intervention strategies for blocking metastatic spread.

- **Introduction to cancer cell plasticity and initiation of metastasis**
  - Regulation of cell-cell and cell-matrix adhesion
  - Regulation of cellular plasticity and cell polarity
  - Dissolution of cell matrix and cell migration through tissue layer
- **Neoangiogenesis in primary tumor**
  - Molecular basis of neoangiogenesis
  - Contribution of Notch and other Signaling in neoangiogenesis
  - Role of hypoxia in neoangiogenesisand metastatic initiation
- **EMT, Anoikis & MET during metastasis**
  - EMT-MET in phenotypic plasticity
  - Mechanisms that link oncogenic EMT and suppression of anoikis
  - MET and anoikis
  - MET in colonisation of tumor cells
- **Molecular basis of Intravasation**
  - Haematogenous, Lymphatic spread of metastatic tumor cells
  - Mechanism of Intravasation in blood and body fluid
  - Molecular regulation of intravasation in blood and body fluid
- **Molecular basis survival in bloodstream & extravasion**
  - Survival in vascular environment through biophysical and biochemical alteration
  - Role of immune cells in survival of tumor cells in bloodstream
  - Extravasation to secondary site
- **Molecular basis of metastatic colonisation**
  - Seed & soil hypothesis
  - Adaptive cellular processes in metastatic colonisation
- **Dormancy and secondary tumor growth and disease relapse**
  - Factors controlling dormancy/quiescence of tumor cells at secondary site
  - Microenvironment in re-initiating proliferation of dormant tumor cells
  - Implication of tumor dormancy in relapse of various cancers

- **Role of Hippo, Notch and Wnt signalling**
  - Cross talk between signalling pathways in cancer metastasis
  - Role of Hippo, Notch and Wnt signalling in various steps of metastasis
  - Therapeutic potential of Hippo signalling and other signalling pathways in cancer
- **CSCs, CTCs in metastasis**
  - Role of Cancer stem cell in metastatic spreading
  - Circulating tumor cells and their relation to metastatic progression
- **Role of tumor microenvironment on metastasis**
  - Role of tumor microenvironment on metastasis Subtopics:
  - Role of CAF, immune cells in neoangiogenesis of primary tumor
  - Role of biophysical properties of tumor bed on metastasis
  - Role of TME upon intravasation and extravasation of metastatic tumor cells
  - Role of TME on secondary metastasis
- **Targeted therapy in metastasis**
  - Biological effects of genetic alterations in cancer metastasis
  - Targeting metastasis through inhibition of angiogenesis
  - Targeting micro and macrometastasis
  - Clinical applications and future development
- **Immunotherapy in metastasis**
  - Therapeutic targets and biomarkers for tumor immunotherapy
  - Immunotherapy for metastasis: Timing and cancer type to benefit
  - Challenges treating metastatic cancer with Immunotherapy
- **Models of metastasis & Imaging metastasis**
  - In vivo metastatic models - chemically induced, transplantable and genetically modified model
  - Applications of imaging guidance in monitoring and quantitation of metastatic loads
  - Challenges in in vivo metastasis experiments

Course Outcomes:

- This course includes 13 lectures which will explain all the steps required for a tumor cell to adapt for successful metastasis into secondary organs.
- The course will also elucidate the molecular mechanism of EMT, Anoikis resistance and MET of tumor cells required for metastasis.
- Contribution of Cancer stem cells and Circulating tumor cells in metastatic load and various model systems and approaches to study metastasis will be taught in detail.
- Finally, various therapeutic strategies to comprehend metastasis will be taught in detail.
- The course will build the knowledge about Metastasis in depth and allow the students to come up with provocative ideas for future therapeutic approaches.

References:

The study material for these courses will be review articles/textbooks/research papers in the relevant fields that will cover the topics listed above

10-LIFE24-603-E: Animal Models in Cancer Research (16 Lecture Hrs)

Coordinators: Dr. Arviund Ingle,
Dr. Pradip Choudhari
(aingle@actrec.gov.in,
pradip.r.chaudhari@gmail.com)

Course Details:

This course covers anima various aspects of most common and relevant animal models used in cancer research.
The in-silico designing of anticancer drugs, their in-vitro evaluation in various cancer cell lines and finally in-vivo evaluation related topics are covered in this course.
The spontaneous, induced (chemically and using cell lines) models, basics of common surgical procedures involved in developing animal models are included in the syllabus.
The list of topics and individuals undertaking these topic heads are mentioned below.
There are total 16 lectures and each lecture has been assigned an hour.
This will be followed by two assignments that will be handed out to students.

- Introduction to Laboratory Animals
- Basics of rodents and no-rodent species, their usefulness in bio-medical research.
- Understanding Rodent Anatomy for Basic Experimental Techniques
- Common experimental procedures and relevant anatomy
- Biology of Commonly Used Laboratory Animals
- Physiological aspects, breeding, management and ethics and 3Rs
- Alternate Animal Models in Cancer Biology
- Overview of non-rodent models used in cancer research
- PK/PD Modelling in Preclinical Drug Development
- Understanding of PK/PD studies in drug development
- Animal Sampling Techniques for Research and Analysis of Laboratory Rodents
- Collection, preservation and transport of biological specimens.
- Carcinogenesis and Chemoprevention Modalities Using Animal Models
- Basics of cancer initiation and progression utilizing rodent models.
- Generation of Transgenic and Knock-Out Mice and Their Application in Cancer Research
- Understanding of GM animals, their development and application in cancer research.
- Principles of Anesthesia, Analgesia, and Aseptic Surgery in Animal Model Development for Cancer Research
- Basics of performing aseptic procedures and type of anaesthetics

- Development of Animal Models for Cancer Research by Different Surgical Approaches
- Common macro and micro surgical procedures, used to develop models.
- Rodent Survival Surgeries and Pain Assessment Strategies for Advancing Cancer Research
- Post surgery management of rodents
- CDX, PDX and Humanized Mice Models in Cancer Research
- Basics of development of common and advanced animal models used in cancer research
- Comparative Oncology: Canine Cancers in Advancing Cancer Research
- Large animals cancer models
- Radio-isotopic Techniques in Cancer Research
- Common applications of radioisotopes, basics of radiations and radiobiology
- Molecular Imaging Overview - Tools and Practices
- Basics and usefulness of molecular imaging of rodent'>
- In vivo model system - a roadmap to drug design
- Complete understanding of new drug discovery journey

Course Outcomes:

- The aim of this course to provide sufficient information about the laboratory animals, their anatomy, physiology, genetics, 3Rs, ethics and management relevant to animal model development.
- The students will learn various model development procedures, their advantages and disadvantages with respect to cancer biology and how to incorporate in their study plans.
- Students will have understanding of surgical procedures (minor and major) involved in developing these models, anaesthesia methods and post-surgical care/ management etc.
- The course will provide the complete understanding of drug discovery process utilizing various animal models.

References:

The study material for this courses will be review articles in the relevant fields covering all the topics listed above.
Reading material:

1. Animals 2023, 13(7), 1223; https://doi.org/10.3390/ani13071223
2. Cancer Res 2016 Oct 15;76(20):5921-5925.doi: 10.1158/0008-5472.CAN-16-1293.Epub 2016 Sep 30.
3. Exp Anim 2017 Oct 30;66(4):313-320.doi: 10.1538/expanim.17-0026. Epub 2017 Jun 7.
4. Anesthetic and analgesic considerations in the experimental animal. Soma LR.Ann N Y Acad Sci. 1983;406:32-47. doi: 10.1111/j.1749 6632.1983.tb53483.x.
5. J Transl Med. 2022 May 10;20(1):206.doi: 10.1186/s12967-022-03405-8.
6. Expert Opin Drug Discov. 2020 Jun;15(6):731-738.
7. Curr Drug Targets. 2020;21(1):3-17. doi: 0.2174/1389450120666190923162203.

10-LIFE24-603-E: Biology of Tumor Microenvironment (15 Lecture Hrs)

Coordinators: Dr. Sharath Chandra Arandkar (sarandkar@actrec.gov.in)

Course Details:

This course covers the basics of the tumour microenvironment, which includes cellular and a cellular components and their impact on the outcome of the disease.
Also, this course gives information about different model systems for studying TME.

- Introduction to TME - Types of stromal cells (Immune cells, Endothelial cells, Pericytes, Fibroblasts and Immune Cells etc.)
- ECM remodelling in cancer. ECM structure, composition and function, ECM induced signaling, mechanosensing and mechanoadaptation, ECM remodelling in cancer and its impact on disease progression and metastasis, ECM targeting therapies
- Cancer secretome in TME: soluble factors and EVs. Growth factors, cytokines, chemokines, soluble receptors constituting the biochemical soup of TME; their spontaneous secretion vs regulated secretion, different types of EVs, their biogenesis and secretion and uptake pathways, applications in cancer therapy and diagnosis.
- Stromal cell heterogeneity and concepts CAF subtypes, Macrophages subtypes and other Immune cells subtypes.
- Different signaling pathways in TME Abundant TME signaling pathways, TGF beta, TNF alpha and other signaling pathways.
- Techniques to study Tumor-stromal cell interactions
- 2D, 3D cell culture, co-culture, Organoids, Xenograft, GEM mouse models to study the TME in different cancers.
- Role of TME in Metastasis and drug resistance, radio resistance
- Seed soil hypothesis, Stromal cell and ECM-mediated drug resistance (Pancreatic, Breast and Lung cancer)
- Complexity of Immune microenvironment, the impact of the stromal cells on immunotherapies Anti PD1and PDL1, anti CTLA4, CART, TIL therapies: influence of the stroma on these therapies and challenges.
- Crosstalk between Non-malignant cells and immune cells
- Cross talks between MSCs, Fibroblasts, Endothelial cells, and immune cells in TME.
- Hypoxia in TME: vasculature in normal tissue vs tumor, causes and types of hypoxia in TME, Hypoxia induced signaling, influence of hypoxia on metastasis, chemo and radiotherapy response; in vitro and in vivo methods to study hypoxia, clinical relevance.

Course Outcomes:

- This course includes 10 lectures which will give fundamentals of Tumor microenvironment
- The course will include different components of TME, like ECM, hypoxia and stromal cells.

- Also includes immune cells and their role in TME and the outcome of the disease.
- This course gives the idea of the relevant in vitro and in vivo models to study the importance of TME

References:

The study material for these courses will be review articles/textbooks/research papers in the relevant fields that will cover the topics listed above

10-LIFE24-603-E: Basics of Immunology and Implications in Cancer (15 Lecture Hrs)

Coordinators: Dr. Rohan Khadilkar, Dr. Subir Biswas (rkhadilkar@actrec.gov.in, sbiswas@actrec.gov.in)

Course Details:

This is a course that will touch upon the basics of immunology from a physiological perspective and in the tumor scenario.
This is a single credit course with 15 hours of lectures encompassing 10 lectures taught by 4 lecturers for 1.5 hours each.

- **Introduction, history, Organization of the immune system (lymphoid tissues and organs)**
  Jerne' Immune Network theory, MacFurlane Bumet's Clonal Selection theory 'Introduction to Types of immunity (Innate and Adaptive); Antigens and Patterns; Molecules of Immune System, Cells of Immune System, Immune recognition, Organs of Immune Sytem
- **Immune cell development (hematopoiesis, T and B cell development)**
  Detailed overview on hematopoietic development, waves of hematopoiesis, sites/organs of hematopoiesis, lymphoid and meyloid lineage differentiation and signalling regulating lineage differentiation
- **Innate immunity and Adaptive immunity, Antigens and Antibodies**
  Components and features, humoral and cell-mediated immunity, B cell development, maturation, activation and response, antigens recognition and processing, antibody structure, function and isotypes, T lymphocytes development, activation and effector functions.
- **Immune signaling**
  TLRs, inflammatory and cytokine responses, JAK-STAT, TCR BCR rearrangements, class switching, somatic hypermutation, TCR BCR signaling, activation and antibody production
- **Innate Immune cells, molecules and pathways**
  NK cells, Macrophages, Innate Lymphoid Cells, Pattern recorgnition receptos (PRRs), cell adhesion molecules, activation and inhibitory receptors, Interferons, Pathways viz. Natural cytotoxicity, Phagocytosis, NETosis, Pyroptosis, Inflammasome pathway, Acute and Physiological inflammation
- **Effector functions in tumor immunology**
  Effector function molecules involved in various immune cells of innate and adpative immunity, Target recognition and clearence process, immunoassays to study and assess function of immune cells.
- **Tumor Micro-environment**
  With a focus on tumor associated immune cells and their function (Tumor associated macrophages, NK cells, Dendritic Cell, T and B lymphocytes etc)
- **Immunotherapy**
  History, types, principles of monoclonal antibody production, mechanisms, clinical uses, future
- **CAR-T cell therapy**
  History, principles, design and engineering, manufacturing, mechanisms, clinical applications, and challenges.

- **Harnessing innate immunity for cancer immunotherapy**
  Using innate immune cells for targeting cancer cells with a specific focus on macrophages, NK cells and dendritic cell based therapies.

Course Outcomes:

- This course will provide students with the basics of immunology and its application in the field of tumor immunology with lectures dedicated towards understanding the basics as well as clinical aspects related to immunology.
- The course will also delve into newer innovations in the field of immunotherapy for cancer which is currently being employed in the clinics for treatment of cancer along with traditional chemo and radiation therapy.
- The lectures would thus cover a spectrum of topics in basic and tumor immunology.

References:

Research articles, review articles will be largely used for preparing the teaching material for this course.