



डा. बी. आर. अम्बेडकर जैव चिकित्सा अनुसंधान केन्द्र (एसीबीआर)  
Dr. B.R. Ambedkar Center for Biomedical Research (ACBR)  
दिल्ली विश्वविद्यालय (उत्तरी परिसर) दिल्ली- ११०००७, भारत  
University of Delhi (North Campus), Delhi-110 007, INDIA

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Dr B R Ambedkar Center For Biomedical Research  
University of Delhi  
Delhi-110007, INDIA

01.06.2018

The document below is the proposed revised Syllabus for **M.Sc. Biomedical sciences** and **B.Sc. Biomedical sciences** for introduction with effect from the next academic year, 2018-2019. This was prepared after intense minuted discussions in the Committee of Courses, amongst meetings of UG and PG teachers from the different streams of specialization in the Center of Biomedical Sciences and in several meetings of the subcommittees. Before sending it for a final review by the Committee of Courses and Faculty of Science the Center wanted to place it in the public realm for the valuable feedback of different stakeholders.

Please go through the enclosed documents and let us have your feedback at [directoracbr@gmail.com](mailto:directoracbr@gmail.com) and comments at with the subject heading: "*Feedback on proposed Program for B.Sc Biomedical Sciences 2018*" and "*Feedback on proposed Program for M.Sc. Biomedical Sciences 2018*". Your opinions in the framing of our curriculum will be invaluable. Please let us have your comments by 6<sup>th</sup> June, 2018.

Sincerely yours,

Prof. Daman Saluja  
Director, ACBR  
University of Delhi



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## COURSE STRUCTURE FOR M.Sc. Biomedical Science

### SEMESTER I

**TOTAL CREDITS/SEMESTER**                      **24**

<b>PAPER</b>	<b>L</b>	<b>T</b>	<b>P</b>	<b>Credits</b>
Biochemistry	3	0	2	5
Concepts of Genetics	3	0	2	5
Biologic chemistry I	3	1	2	6
Cell Biology	3	1	0	4
Medical Microbiology	3	0	1	4
<b>TOTAL</b>	<b>15</b>	<b>2</b>	<b>7</b>	<b>24</b>

### SEMESTER II

**TOTAL CREDITS/SEMESTER**                      **24**

<b>PAPER</b>	<b>L</b>	<b>T</b>	<b>P</b>	<b>Credits</b>
Human Physiology I	4	0	2	6
Recombinant DNA	3	0	2	5
Technology & Biotechnology				
Immunology	3	1	2	6
Biological Chemistry II	3	1	0	4
Molecular biology	3	0	0	3
<b>TOTAL</b>	<b>16</b>	<b>2</b>	<b>6</b>	<b>24</b>

### SEMESTER III

**TOTAL CREDITS/SEMESTER**                      **24**

<b>PAPER</b>	<b>L</b>	<b>T</b>	<b>P</b>	<b>Credits</b>
Human Physiology II	3	1	0	4
Principles of Medicinal chemistry	4	0	0	4
Pharmacology & Toxicology	4	0	2	6
Techniques & Instrumentation	3	1	2	6
Elective I	4	0	0	4
Or take two open electives				
Open electives I	2	0	0	2
Open Elective II	2	0	0	2
<b>TOTAL</b>	<b>18</b>	<b>2</b>	<b>4</b>	<b>24</b>

Although they have five papers, they have practicals only on two days so they will get time to do project work or self study.

**SEMESTER IV**

**TOTAL CREDITS/SEMESTER                      20**

<b>PAPER</b>	<b>L</b>	<b>T</b>	<b>P</b>	<b>Credits</b>
Elective II	4	0	0	4
Elective III	4	0	0	4
Elective IV	4	0	0	4
PROJECT*	8	0	0	8

If a student wish not to do the research project, he/she can take two more electives (electives V and Elective VI).

**AT THE END OF TWO YEARS, STUDENT MUST TAKE ATLEAST 92 CREDITS.**

### **ELECTIVE Papers (Choice based papers) for III semester**

- 1. Molecular Oncology**
- 2. Stem cell Biology for developmental and translational research**
- 3. Advance Immunology**
- 4. Medical Virology & Mycology**
- 5. New methods in Organic synthesis**

### **ELECTIVES (Choice based papers) for IV semester**

- 1. Advance Toxicology**
- 2. Genome Biology**
- 3. Neurobiology**
- 4. Pathophysiology**
- 5. Advances in protein science**
- 6. Advance concepts in medicinal chemistry**
- 7. Drug discovery and process development.**
- 8. Bioinformatics, computational biology and drug design**
- 9. Medical Bacteriology and Parasitology**

### **OPEN ELECTIVES To be offered by ACBR**

**Bioethics & Biosafety**

**Application of statistics for Biology**

# **BIOCHEMISTRY**

## **Core paper**

### **I<sup>st</sup> Semester**

**Credits: (3 + 0 + 2 = 5)**

#### **Preamble**

*Understanding about protein structure, function and their relations has been key toward understanding almost all biological processes as proteins and enzymes are machineries in the cells. Moreover, contemporary biochemistry needs the thorough understanding of the basic processes like transcription, translation and replication and how different protein complexes and domains interact to perform these processes.*

#### **Protein Structure**

**L1-L2.** Protein folding, Secondary and tertiary structure of protein: a helix,  $\beta$  sheets, examples of proteins, Ramachandran plot

**L3.** Factors effecting secondary and tertiary structure (disulphide bonds, heat, organic solvents, detergents).

**L4.** Concept of Motiff and examples of some common structural motifs in proteins.

**L5-L6.** Domains, structural diversity of different domains with appropriate examples, domain swapping with examples, Protein Dynamics: concept of macro states & ensembles, how dynamics affects protein function

**L7.** Intrinsically disordered proteins, structure and function of alpha, beta and kappa casein, functional and evolutionary significances, role in different multi-protein complexes

**L8.** Structure and function of hemoglobin: conformational studies, binding of oxygen and it's release, oxygen saturation curves.

**L9.** Structural proteins: structure of collagen, keratin and other fibrous proteins.

**L10.** Disorder of amino acid and protein metabolism.

#### **Tutorial & Class Test**

#### **Enzymology**

**L11.** Introduction: General characteristics of enzymes, definition of coenzyme, holo-enzyme, prosthetic groups, classification.

**L12-L14.** Enzyme Kinetics: Substrate, active site, transition state, activation energy, equilibrium constant  $K_m$ ,  $V_{max}$ , specificity, Michaelis-Menten equation.

**L15.** Reaction Mechanism: Acid-base catalysis and covalent catalysis (giving examples).

**L16-L17.** Regulation of enzyme activity: Reversible and irreversible inhibition (non-competitive, uncompetitive) and their effects on  $K_m$  and  $V_{max}$ , effect of pH, heat, PMSF and other inhibitors.

**L18.** Models to explain their kinetic behavior. Problems on enzyme kinetics:

**L19.** Determination of active sites and turnover number, factors affecting enzyme functions

**L20.** Bi- substrate enzyme kinetics: ping-pong and sequential mechanism

### **Tutorial & Class Test**

#### **Protein purification, physical separation & Analysis**

**L21.** Methods of protein production, isolation, purification strategies, concept of inclusion body

**L22.** Chromatography (ion exchange, affinity, size exclusion),

**L23.** Dialysis, molecular sieving, PAGE, electrofocussing, FPLC

**L24.** Methods of protein sequencing: N and C-terminal analysis, Edman degradation

#### **Regulation of protein function**

**L25.** Concept of Structural allostery, examples of self-inhibited proteins, limited proteolysis,

**L26-L27.** Post-translational modifications: enzymatic and non-enzymatic,

**L28.** Protein quality control system: ubiquitination, proteosomal and lysosomal-mediated degradation,

**L29.** Molecular chaperones (structure and functional mechanisms of Hsp90, Hsp70, Hsp60 & Hsp40)

**L30.** Chaperonin (structure of GroEL & GroES).

### **Tutorial & Class Test**

#### **DNA REPLICATION IN PROKARYOTES AND EUKARYOTES**

**L31:** Concept of origin of replication, experimental evidence for bidirectional and semiconservative replication

**L32:** Mechanism of DNA Replication: Structure and function of DNA polymerases. Experimental approach to differentiate and identify replication proteins

**L33:** Role of helicase, primase, gyrase, topoisomerase and other proteins in DNA replication in E.coli.

**L34:** Replication mechanism in viruses, mitochondrial DNA replication (D loop)

### **Tutorial & Class Test**

**L35:** Replication in eukaryotes, differences from prokaryotes, experiments to prove the model of replication.

**L36:** Initiation of replication, proteins involved, their functions, Inhibitors of replication

**L37:** Elongation and termination of DNA synthesis in prokaryotes and eukaryotes.,

**L38-39:** Replication at telomeres, Diseases associated with defective DNA replication.

### **Tutorial & Class Test**

#### **Translation**

**L40:** Translation in Prokaryotes-initiation:

**L41:** activation of amino acid, role of 30s and 50s ribosomal subunits

**L42:** role of 30s and 50s ribosomal subunits, initiation factors

**L43-44:** Shine-dalgarno sequences, Kozak sequences, selection of first AUG in eukaryotic mRNA with experimental evidence.

**L45:** Elongation factors, peptidyl transferase termination signal, release factors.

**L46-47:** Inhibition of protein synthesis - by antibiotics and inhibitors of eukaryotic translation

**L48:** Methods to determine Half-life of protein.

### **Tutorial & Class Test**

#### **Practicals**

1. Preparation of buffers and other solutions
2. Salting in and salting out of proteins.
3. Void Volume estimation
4. Desalting of proteins by dialysis
5. Desalting of proteins by Sephadex G-25
6. Protein estimation by Lowrys & Bradford methods.
7. Protein estimation by Lamberts & beer law
8. Ion-exchange chromatography.

9. Affinity chromatography for protein: **(i)** protein induction & binding to affinity column **(ii)** running gel & analysis
10. To check purity of protein & subunit structure by SDS page silver staining **(i)** reducing Gel **(ii)** non reducing Gel
11. (i) Running Western blot of a specific protein: **(i)** SDS, transfer & blocking and **(ii)** probing with antibodies & analysis of result
12. To run Native Gel of a protein/Far western blot.
13. Protein & Nucleic Acid blasts, Clustal W and sequence alignment etc.
14. Measurement of Enzyme activity parameters
15. Measurement of Enzyme inhibition mechanisms

### **Suggested Readings**

1. Proteins: Structure and Function; David Whitford; 1<sup>st</sup> Ed; Wiley, 2005.
2. Biochemistry by Donald Voet and Judith G. Voet; Ed. 4<sup>th</sup> ; Wiley; 2010.
3. Lehninger principles of biochemistry by David L. Nelson and Michael M. Cox; Ed. 6<sup>th</sup> ; W.H. Freeman, 2012.
4. Biochemistry by Christopher K. Mathews and Kensal E. van Holde and Kevin G. Ahern; Ed. 3<sup>rd</sup> ; Prentice Hall, 1999.
5. Biochemistry by Jeremy M. Berg and John L. Tymoczko and Lubert-Stryer; Ed. 6<sup>th</sup> ; W.H. Freeman, 2008.
6. Fundamentals of Protein structure and function, Buxbaum Engelberg; Springer, 2015.

### **Course Outcome**

Students will be able to have a comprehensive understanding of the diversities of protein structure, mechanisms how enzymes work and also the structure function relation. Students will also develop ideas of how important the fidelity of protein folding in the cells and its connectivity to the development of human diseases. The basic concepts of the protein biosynthesis, DNA replication and transcription are revised. The students are taught the various experimental techniques which led to the development of these concepts. This initiates the analytical and experimental approach of solving any problem.

Practical part of the paper will help to develop skills on protein purification, analysis, quantitation and checking purity by various techniques.

**M.Sc. Biomedical Sciences  
MBS-105 Concepts in Genetics**

**Core Course Credits 3 +2 Practicals**

*Sub-committee: Dr. Richa Arya, Dr. Ankita Narang, Prof. Vani Brahmachari.*

*Feedback from: Dr. Gautam Kshatriya.*

**Preamble:** *This course would be offered as compulsory course in the second semester for M.Sc.-Ph.D. combined course in Biomedical Sciences. Most of the undergraduate courses have introduction to Mendelian Genetics as a topic under their syllabus. But it is necessary in our experience to refurbish this in the context of the molecular biology that has changed the implication and meaning of genetic terminologies. Though Mendel's work had a strong mathematical basis and hence analytical, genetics often has the negative reputation of being loaded with terminology. But the interface of molecular biology with genetics has changed this scenario thus making it even more logical. This course is meant to highlight the basis of inheritance, the deviations from Mendelian genetics and reflect the immense contribution of model systems to understand the genetic basis of biological processes /systems.*

**Course outcome:** *At the end of the course the students are expected to recognise the insight of Mendel, and his successors, T.H.Morgan and his illustrious academic lineage, the intuition of Barabara McLintock and the amazing superimposition of epigenetics over genetics. They should be able to understand how the ratio of segregation and patterns of inheritance reflect the underlying molecular logic and why it is unreasonable to expect a purely Mendelian pattern of inheritance in any system given the molecular basis. The introduction to development as route to cellular asymmetry in prokaryotes and yeast mating type.*

- 1. The students will be able to understand genetic interaction in terms of molecular basis.*
- 2. They will know the genetic basis of several chromosomal anomalies and syndromes.*
- 3. The nature of novel mutational processes.*
- 4. They will get an idea of mapping genes using model organisms like, Drosophila, yeast and Neurospora.*
- 5. The original experiments that led to the concepts of mutation occurrence and genetic analysis of bacteria and their virus.*
- 6. They will know the current concepts of epigenetics, dynamic mutations and sex determination in humans and Drosophila.*
- 7. They will be introduced to network and novel molecular processes in the regulation of gene function in Yeast mating type switching and the phage lamda; as an evolutionarily maintained theme of differential expression and its cascading effect on functional specialization during development.*

## Section A;

**L1-4:** Introduction to the Science of Genetics: Genetic terminology Impact of Genetics on other disciplines. Mendelian Genetics: Mendelian Laws of inheritance, its application in animal Genetics, analysis of results of Genetic crosses by various methods.

**L5-7:** Chromosomal basis of inheritance and data analysis: Sex chromosomes in grasshopper, Development of the concept of co-linearity of genes on chromosomes, Non-disjunction in *Drosophila* and its role in deciphering chromosomal basis of inheritance. Analysis of patterns of inheritance, Punnett square, statistical methods.

**L 8 & 9:** Deviations from Mendelian Genetics I: Codominance, incomplete dominance, RFLP markers, gene interactions, multiple alleles, Understanding possible Molecular basis/biochemical basis of gene-interaction.

**L 10- 13 :** Mutation and mutational analysis: Spontaneous occurrence of mutations in bacteria Lederberg and Lederberg experiment, Types of mutations i.e. point mutations, deletions, rearrangements, insertions, dynamic mutations (repeat expansions) with appropriate examples, Chromosomal anomalies and related syndromes.

**L 14 &15:** Mutation mapping using balancers, Clb technique in *Drosophila*.

**L16 &17:** Linkage as a deviation from Mendelian Genetics: Recombination, Gene mapping using *Drosophila* as an example, experiments demonstrating physical basis of recombination, crossing over. Gene mapping using special systems, yeast and Neurospora.

**L18 &19:** Bacterial and Phage genetics: Transformation, transduction , Conjugation, genetic map construction in *E.coli*. Phage genetics, fine structure of rII region, work of Seymour Benzer., highlighting the design of experiment and choice of the experimental model.

**L20 & 21:** Genetic Variation; transposition and its application in genetic studies. Extra chromosomal inheritance, chloroplast and mitochondrial inheritance, mitochondrial mutations in yeast, human genetic disorders related to mitochondrial inheritance.

**L22-24:** Deviations from Mendelian Genetics II: Genomic imprinting in insects, mice and man, understanding molecular basis of epigenetic inheritance, human disorders related to imprinting, Prader Willi and Angelmen syndrome, Molecular basis of Epigenetic regulation in H19 and Igf2 region, histone modification marks, Position effect variegation.

**L25 & 26:** Genetic control mechanisms and generation of cellular asymmetry: The lambda phage control of lytic and lysogenic phase, molecular basis of regulatory mechanisms in phage lambda.

**L 27& 28:** Mating type switching in *Saccharomyces cerevisiae* as a primer for generating asymmetry during development

**L 29 & 30** : Sex determination in *Drosophila* and humans: Chromosomal basis to genetic basis, Linking sex determination and dosage compensation in *Drosophila*, genetic and molecular basis. X inactivation in mammals and its molecular basis, role of non-coding RNA.

**L 31**: Introduction to human Genetics: Pedigree analysis and basic inheritance patterns in humans.

**L32 & 33**: Discussion of any 2 classical papers in Genetics.

### **Section B: Population Genetics:**

**L34 & L35**: Definition, aim and scope of population genetics, population structure, factors maintaining population boundaries, effective breeding size, gene pool.

**L36 & L37**: The Hardy–Weinberg Law and its application, factors affecting the Hardy- Weinberg equilibrium.

**L38-41**: Human polymorphism (transient and balanced), relationship between sickle cell polymorphism and malaria, other polymorphisms that may be an adaptation to malaria eg. G6PD deficiency. Duffy blood groups, thalassemia and haptoglobins. X linked polymorphism (G6PD and colour blindness).

**L42- L45**: Natural Selection in Human Population. Non-random mating, inbreeding and its consequences. Migration and Genetics, types of migration, models to study genetic effects of migration, gene flow, effects of gene flow, admixture and natural selection, calculation of admixture.

**Tutorials and assessment: 3 hours.**

Text and reference books:

1. Principles of Genetics by D. Peter Snustad and Michael J. Simmons.
2. Gardner Principles of Genetics. Eldon J. Gardner and D. Peter Snustad
3. Principles of Genetics by Eldon J. Gardner
4. Introduction to Genetic Analysis by Anthony J.F. Griffiths, Susan Wessler, Sean B.Carroll, John Doebley. Tenth edition
5. Introduction to Genetic Analysis by Anthony J.F. Griffiths; Susan R. Wessler; Richard C. Lewontin, Sean B.Carroll. 9th Edition
6. Original papers and review articles for Genomic Imprinting and epigenetics (To be shared with the students).
7. Genes (Current edition) Benjamin Lewin (For molecular cascade in yeast mating type)

8. Original papers and reviews for mating type switch in yeast, (To be shared with the students).
9. Cavalli-Sforza, LL and Bodmer, WF (1971 Ed.) The genetics of human population. San Francisco- Freeman.
10. Relethford, J.H. (2012 Ed) Human Population Genetics. Wiley-Blackwell

**(Practicals on the next page)**

**Practicals for Genetics Course; I Semester 2017-19 Batch**

<b>Semester I : Genetics Practicals</b>		
<b>Expt. No.</b>	<b>Experiment</b>	<b>Exercise</b>
I	Selection based on Phenotype: Yeast mutants based on auxotrophy	Preparation of media for selection and plating
II	Selection (Contd)	Observation & Interpretation
III	Drosophila Genetics	Fly media preparation, stages of life cycle, Observation of mutant phenotypes and recognition of mutants
IV	C.elegans as a model organism	Media preparation and observation of developmental stages
V	Sex determination in C.elegans	Induction of male development: molecular players to be explained.
VI	Metaphase chromosome preparation	Demonstration of cell culture, Chromosome preparation, staining & observation. Metaphase arrested cells to be provided to students.
VII	Development in Drosophila Immunostaining of imaginal discs using primary Antibody against homeotic protein	Isolation of Imaginal disc from wild type Drosophila General staining and staining for homeotic gene expression
VIII	Immunostaining (Contd)	Secondary Ab. Treatment and observation under florescent microscope.
IX	Nucleosome Analysis	Isolation of nuclei from Zebrafish using sucrose cushion
X	Nucleosome analysis (Contd)	Micrococcal Nuclease digestion & DNA extraction Analysis by Agarose gel electrophoresis
XI	Analysis of VNTR-Variable Number of Tandem Repeats in human DNA (IHEC cleared experiment)	Prior consent of the individuals (Students) is obtained by IHEC cleared Consent form. 50-100 microL of blood is taken by sterile pin prick. Genomic DNA extraction and estimation of concentration.
XII	VNTR expt.(Contd)	Setting of PCR with VNTR primers and analysis by Agarose electrophoresis.

## **NAME OF PAPER : BIOLOGICAL CHEMISTRY 1**

**CREDITS 4+0+2=6**

### **Core Course Semester 1**

#### Preamble

This course aims to bring together the various facets of introductory organic chemistry with a small overview of its applications in medicinal chemistry and biology. The course outcomes are to train students in the understanding of chemical entities which can and those which cannot be isolated such as carbocations, carbanions and free radicals. In addition to this reactions in organic chemistry are studied with a concomitant understanding of their stereochemistry which is also discussed. Heterocyclic chemistry is discussed with a view to understanding molecules which make modern day medicines.

#### Reactive Intermediates in Organic Reactions

L1-2 Carbocation stability, formation and reactions with examples

L3-4 carbanions, pKa values, methods of formation, stability, shapes and reactions

L5-6 Free radicals their stability, methods of synthesis and reactions

L7-8 Examples of reactive intermediates with applications to biological systems,

L9-10 benzyne, carbenes, radical cations and radical anions,

#### Stereochemistry of Organic compounds

The definition of the following terms with suitable examples:

L-11 Elementary treatment of symmetric elements,

L-12 chirality, polarimetry

L-13 prochirality (enantiomer, epimer, diastereomer),

L-14 Absolute and relative configuration, R & S notation,

L-15-16 enantiotopic and diastereotopic faces, endo and exo faces.

L-17-18 Regioselective, enantioselective stereoselective and stereospecific reactions

L-19 conformation of 2,3-dibromobutane, E & Z notations,

L-20 cyclohexane diols

#### Mechanism and stereochemistry of following reactions

L-20-21 Substitution reactions

L-22 addition reactions,

L-23 oxidation and reduction,

L-24 Elimination reactions

L-25 ester formation and hydrolysis,

L-26 Aromaticity,

L-27 -28 aromatic and Nucleophilic substitution,  
L-29 -30 Woodward Hoffmann rules, photocyclization ,  
L-31-32 concept of suprafacial and antarafacial

#### Asymmetric synthesis

L-33 Examples of Asymmetric synthesis involving active substrate  
L-34-35 Cram and Prelog rule,  
L-36 Examples of asymmetric synthesis involving active reagents  
L-37 Examples of asymmetric synthesis involving active catalysts  
L-38-39 Chiral synthesis (with suitable examples)  
L-40 asymmetric epoxidation  
L-41 Sharpless asymmetric epoxidation

#### Heterocyclic chemistry

structure, synthesis and reactivity of the following heterocycles and their significance in biology and the synthesis of medicines

L-42 furan and pyrrole  
L-43 thiophene and imidazole  
L-44 oxazole and thiazole  
L-45 carbazole and indole  
L-46 pyridine, quinoline and isoquinoline  
L-47 purines and pyrimidines  
L-48-53 synthesis of medicines involving some of the above molecules

### **Practicals for Organic Chemistry**

**Semester 1**

**Credits 2**

1. Recrystallization and Melting Determination
2. Thin Layer Chromatography (mixture of 2 compounds)
3. Thin Layer chromatography (mixture of 3 compounds)
4. Claisen Schmidt reactions
5. Infrared spectroscopy (instrumentation and spectra analysis)
6. Cannizarro reaction
- 7&8. Optical activity by polarimetry of known optically active compound of known concentration and hence to determine concentration of unknown sample
9. Column chromatography
10. Aldol condensation
11. Schotten Baumann reaction

#### **Suggested reading:**

1. Quantitative organic chemistry by Vogel
2. Quantitative experimental organic chemistry by Vogel

# **CELL BIOLOGY**

## **Ist Semester**

### **Core paper**

**Credits: 3+1+0 = 4**

#### **Biomembranes:**

L1-L2. Basic structure, lipid and protein composition and their basic functions Transport of molecules across membranes.

L3. Passive and active transport across membranes.

L4-L5. Factors regulating them, ion channels, ABC pumps of bacteria.

#### **Tutorial and Class test**

#### **Organelles of eukaryotic cells**

L6-L12. Introduction basic structure and function of various organelles, ER, golgi bodies, chloroplasts, mitochondria endosomes, lysosomes etc.

L13-L14. separation and visualization methods of various cell organelles. Muscle & Nerve Cells.

#### **Tutorial and Class test**

#### **Nucleus and Chromosome Structure**

L15-L17. Introduction: Prokaryotic and Eukaryotic genome and its organization, eukaryotic chromosome.

L18-L19. Basic structure of DNA; hairpins and cruciform, Z-DNA, triple helix.

L20-L22. DNA Supercoiling: Histones, nonhistone proteins, topoisomerases and telomerase and their functions in chromatin structure. Yeast artificial chromosome.

#### **Tutorial and Class test**

#### **The Cytoskeleton**

L23. Cytoskeleton proteins, and Cell motility and shape,

L24. protein sorting, Transport of proteins.

L25. Microfilaments and actin filaments

#### **Tutorial and Class test**

#### **ECM Proteins and Cell Adhesion**

L26. Cell-cell interaction, Cell junctions,

L27-L29. Adhesion proteins, Cell matrix interaction, Integrins, Functional role of adhesion proteins.

#### **Eukaryotic Cell Cycle**

L30-L31. Cell cycle and its control: Loss of cell regulation by viral infection,

L32. checkpoints in cell cycle regulation.

## **Tutorial and Class test**

### **Cell to Cell Signaling**

L33. Introduction to cell surface receptors, and concept of receptors.

L34-L35. G-protein mediated signaling, camp, receptors tyrosine kinases, second messengers.

### **Cell death**

L36. Apoptosis, Necrosis, Proapoptotic and Antiapoptotic proteins

L37. mechanism of action Autophagy,

L38-L40. Senescence, Cell death mechanisms in health and diseases.

**L41-42.** Cell Differentiation

## **Tutorial and Class test**

### **Cellular Stress Response**

L43. Stress response proteins and pathways,

L44-L45. Post translational modifications in stress response,

L46-L47. General responses to hyperthermia nutritional deprivation and other stressors.

## **Tutorial and Class test**

### **Reading List**

1. Molecular biology of the cell by Bruce, Alberts and Alexander Johnson and Julian Lewis, and Martin Raff; Ed. 5<sup>th</sup>; Garland Science; 2008.
2. Molecular biology of the cell: the problem book by John Wilson and Tim Hunt; Ed. 5<sup>th</sup>; Garland Science; 2008.
3. Molecular cell biology by Harvey Lodish and Arnold Berk, Chris A. Kaiser, and Monty Krieger; Ed. 6<sup>th</sup>; W H Freeman and Company; New York; 2008.
4. Cell: molecular approach by Geoffrey M. Cooper and Robert E. Hausman; Ed. 4<sup>th</sup>; ASM Press; 2007.
5. Cell biology by Thomas D. Pollard and William C. Earnshaw; Ed. 2<sup>nd</sup>; Saunders; 2008.

### **Course Outcome:**

a) Study more about human cells, and organelle structure and functions

b) Elaborate study on types of human cells and the communication of signalling messages between cells, will develop understanding the concept of tissues and organ

c) Study the mode of cell to cell communication and response can also be interpreted under genotoxic stresses, which help students to study more in building the concept in disease dignosis and therapeutics



# MEDICAL MICROBIOLOGY

## Core paper

## I Semester

Credits: 3+0+1 (practical)

48 lectures

### Preamble

*Medical Microbiology course has been formulated to impart basic and medically relevant information on the microbes (Bacteria, fungi, viruses and parasites). The microbial structure, growth and development, methods and sterilization techniques in the context of study of microbes are included. The pathogenic microbes and the diseases caused by them are included to broaden the perspective of the subject. Lastly the course deals with the problem of emerging antimicrobial resistance with reference to known pathogens. The course has been designed to get integrated practical based knowledge about medically important bacteria, fungi, viruses and parasites. The students will be able to understand the structure and function of medically important bacteria, fungi, viruses and parasites. In addition they will also understand pathogenesis, diagnosis, clinical features, virulence factors and treatment strategies of medically important bacteria, fungi, viruses and parasites.*

### Detailed Contents

- L1-5.** History and scope of medical microbiology; How bacteria are different in terms of colony morphology and pattern of arrangement. Bacterial morphology: detailed structural features of gram positive and gram negative bacteria, Staining techniques for identification of bacteria. Detailed structure and functions of various bacterial organelles, cell wall, cell membrane, ribosomes, flagella, spores, capsules, storage components, quorum sensing.
- L6. Tutorial**
- L7-9.** Techniques to study morphology of bacteria, Nutrition and condition requirements of bacteria: Macro and micronutrients, growth of bacteria , temperature, moisture and dessication, oxygen and carbon dioxide requirements of bacteria.
- L10-12.** Multiplication and bacterial growth and methods to study growth patterns in bacteria. Aseptic techniques, methods for pure culture isolation. Cultivation methods for bacteria. Types of Nutrient media for bacteria. Aerobic and anaerobic culture methods
- L13-14.** Identification of bacteria using biochemical methods.

**L15. Tutorial**

**L16-17.** Microscopy: History, basic principles of microscopy. Bright field microscopy and phase contrast microscopy. Florescence microscopy, Confocal microscopy, SEM and TEM.

**L18-19.** Disinfection and sterilization: definition, importance, Physical agents: autoclave, hot air sterilization, incinerators, pasteurisation, tyndallisation, methods of quality check. Disinfection and sterilization: Radiation and filtration techniques, Laminar flow hoods. Disinfection and sterilization: chemical disinfectants, uses of halogen compounds, alcohol based compounds, aldehydes, detergents, heavy metals. Methods for developments and quality check of disinfectants, phenol coefficient test.

**L20-21.** Normal flora of human body and their significance. Nosocomial infections.

**L22-24.** GI tract infections: Salmonella, Shigella, Staphylococcus, E. coli, Helicobacter pylori

**L25. Tutorial/Test**

**L26-27.** Microbial pathogenicity, virulence factors and their effect on pathogenesis. Chemotherapy: structure and mechanism of action of Cell wall inhibitors, antimetabolites. Antimicrobial chemotherapy, protein synthesis inhibitors, Nucleic acid inhibitors.

**L28.** Methods for estimation of antimicrobial activity. Mechanisms of Antibiotic resistance. Literature for new emerging antibiotics. Urinary tract infections.

**L29. Tutorial**

**L30-31.** New and re-emerging diseases. infections of the respiratory system: commensals vs infectious organisms, Diagnosis and prevalence of *Corynebacterium diphtheriae* in India and the world. Virulence factors of *Corynebacterium diphtheriae*, Treatment and management of *Corynebacterium diphtheriae*.

**L32-33.** Spore formation in fungi, Economic importance of fungi. Mycoses, *Tenia Versicolor*, White Piedra, Black Piedra. Dermatophytes, Dermatophytiditis, Candidiasis, Cryptococcosis. Opportunistic Fungi, Ostomycosis. Fungal Contaminants.

**L34.** Medical parasitology overview and classification of medically important parasites. Nematodes: *Ascaris sp.*, *Necator americanus*.

**L35. Tutorial**

**L36-37.** Lymphatic filariasis : *Wuchereria bancrofti*, *Brugia malayi*, *Mansonina ozzardi*

**L38-39.** Cestodes: *Taenia solium*, *Taenia saginata*, *Diphyllobothrium latum*

**L40.** Trematode: *Faciola hepatica*, *Faciolopsis buskii*

- L41.** Medically important protozoans: Malaria,
- L42.** Medically important protozoans: Trypanosoma , Leishmania
- L43-44.** Medically important protozoans: Giardia, Entamoeba , Toxoplasma , Trichomonas, Cryptosporidium.
- L45-46.** Shapes and structure of viruses, classification of viruses. Life cycle of various viruses as per Baltimore system of classification.
- L47-48.** Arboviruses, their genetics, pathogenesis, epidemiology, diagnosis and clinical features with emphasis on hepatitis, Dengue, Zika and Chikungunya viruses.

### ***Course outcome***

*Medical Microbiology is one of the foundation courses for the biomedical sciences students. Students will gain insights on the nature of various infectious agents and diseases pathologies caused by common bacteria, fungi and viruses (for eg. urogenital infections, Blood and CNS infections, fungi such as Candidiasis, aspergillosis and viruses such as hepatitis, Dengue, Zika)*

### **Reading list:**

1. Topley and Wilson's Microbiology and Microbial Infections by Leslie Collier and Albert Balows and Max Sussman; Ed. 9th; 6-Volume Set; A Hodder Arnold Publication, 2000.
2. Medical Microbiology by Geo. Brooks and Karen C. Carroll and Janet Butel and Stephen Morse; Ed. 24th; McGraw-Hill Medical, 2007.
3. Microbiology by Lansing M. Prescott and John P. Harley and Donald Klein; Ed. 6th; McGraw-Hill Science, 2004.
4. Medical microbiology: a guide to microbial infections: pathogenesis, immunity, laboratory diagnosis and control by David Greenwood and Richard C. B. Slack and John F. Peutherer, ed. 17th Ed. Churchill Livingstone; 2007.
5. Fundamental Virology: Fields and Knipe, ed. Raven Press, 1991.
6. Strauss, E. G. and Strauss, J. H., "Viruses and Human Disease", Academic Press, 2002.
7. Flint, S.J., Enquist, L.W., Krug, R. M., Racaniello, V. R., and Skalka, A. M., "Principles of Virology: Molecular Biology, Pathogenesis and Control", ASM Press. 2000.

# **MEDICAL MICROBIOLOGY PRACTICALS**

**I Semester**

**Credits: 1**

## **Detailed practicals**

- 1-3. Demonstration of sterilization techniques related equipments and use of aseptic techniques for preparation of pure cultures. Plating methods and identification of colony morphology of key bacteria.
- 4-6. Demonstration of differential staining techniques like Gram's staining, AFB staining, spore staining etc. Differentiation of flagellate vs nonflagellate bacteria.
- 7-8. Differential diagnosis of bacteria based on biochemical tests.
- 9-10. Spread plate technique and antibiotic sensitivity assay.
- 11-12. Identification of medically important fungi.

# HUMAN PHYSIOLOGY-I

Core paper

II Semester

Credits: (3+1) + 2 credit practicals

## **PREAMBLE:**

*The goal of physiology is to explain the physical and chemical factors that are responsible for the origin and sustainability of life. Each type of life, from the simple virus to the largest tree or the complicated human being, has its own functional characteristics. Therefore, the vast field of physiology can be divided into many divisions. In human physiology-I course, we attempt to explain the various features and mechanisms of the human body that make it a living being. The very fact that we remain alive is almost beyond our control, for hunger makes us seek food and fear makes us seek refuge. Sensations of cold make us look for warmth. Thus, the human being is actually an automaton, and the fact that we are sensing, feeling, and knowledgeable beings is a part of this automatic sequence of life and these attributes of our being living propel us to understand the various biological phenomenon and its alteration in the diseased state. This course starts with the basic understanding of being living from the cell itself and in the process, course through various organ systems and their functioning.*

**UNIT 1: Membrane and muscle physiology:** *cell membranes are ubiquitous from cell organelle to organ system so its imperative to understand the basic structure and function of membranes and how they can modulate the function of an organ system as whole starting with the emphasis on the nerve and skeletal muscle cell.*

**L1:** Organization and functional systems of the cell with reference to nerve and muscle cells: Fluid mosaic model of the membrane, Fluidity, Transport of ions and molecules through cell membrane: diffusion and active transport.

**L2: Concept of Membrane potentials:** types of membrane potential, resting membrane potential, graded and action potentials, methods to record and observe membrane potential.

**L3-6:** Physiologic anatomy of skeletal muscle, neuromuscular transmission and excitation-contraction coupling, Molecular mechanisms of muscle contraction, Energetics of muscle contraction, muscle fatigue, motor unit recruitment, size principle, muscle mechanics, and Electromyogram.

**Tutorial:** Group discussion, Student seminar and test

## **UNIT 2: Respiratory system**

**L7-8:** Anatomy and Functions of respiratory passageways, pulmonary circulation, pulmonary edema and pleural fluid.

**L8-9: Pulmonary ventilation:** mechanisms of pulmonary ventilation, pulmonary volumes and capacities, alveolar ventilation.

**L10-11:** Physical principles of gas exchange, Diffusion of gases through respiratory membrane, Transport of oxygen and carbon dioxide in blood and body fluids.

**L12: Regulation of respiration:** respiratory center, peripheral chemoreceptor system, central chemoreceptor system and their regulatory function.

**L13-14: Respiratory Adjustments in Health & Disease:** Effects of Exercise, Other Forms

of Hypoxia, Oxygen Treatment, Hypercapnia & Hypocapnia, Effects of Increased Barometric Pressure, Artificial Respiration, Respiratory acidosis and alkalosis, Regulation of acid-base balance.

**Tutorial:** Group discussion, Student seminar and test

### **UNIT 3: Body fluid and excretory system**

**L15: *Body fluid compartments:*** Basic principles of osmosis and osmotic pressure: Extracellular and intracellular fluids, Interstitial fluid and edema with its etiology.

**L16-18: Urine formation by kidneys:** renal blood flow and their control, Glomerular filtration, Determinants of glomerular filtration rate, Tubular processing of glomerular filtrate, Reabsorption and secretion along different parts of nephron,

**L19-21:** Regulation of tubular reabsorption, Functions of kidneys in homeostasis, Diuretics, Micturition and disorders of Non-excretory function of kidney

**L22:** Integration of renal mechanisms for control of blood volume and extracellular fluid volume.

**L23-24:** Regulation of extracellular fluid osmolarity and sodium concentration, Role of thirst in controlling extracellular fluid osmolarity and sodium concentration, Renal regulation of potassium, calcium, phosphate and magnesium.

**Tutorial:** Group discussion, Student seminar and test

### **UNIT 4: Gastrointestinal system**

**L25-26:** Histology of Gut with Characteristic features and functioning of smooth muscle lining the gastrointestinal tract.

**L27-28:** General principles of gastrointestinal function - motility, nervous control, and blood circulation, Transport and mixing of food in the entire alimentary tract, sphincters of gastrointestinal tract.

**L29:** Ingestion of food, vomiting, motor functions of stomach, Defecation and its control.

**L30-32:** Secretory functions of alimentary tract: Secretion of saliva, Gastric secretion, pancreatic secretion, Secretion of bile by liver, Secretions of small and large intestine.

**L33-34:** Digestion and absorption in gastrointestinal tract, Digestion of various foods, Neuronal regulation of feeding, obesity and starvation.

**Tutorial:** Group discussion, Student seminar and test

### **UNIT 5: Reproductive system**

#### **Anatomical and functional aspects of human genital system**

**L35-36:** Sex Differentiation & Development, Aberrant Sexual Differentiation, Embryology of the Human Reproductive System, defects of reproductive system, Puberty: Precocious & Delayed Puberty, Menopause

**L37-38: Male:** Gametogenesis, Development structure and function of testis with Ejaculation, Control of Testicular Function, Abnormalities of Testicular Function,

**L39-40: Female:** Gametogenesis Development structure and function of ovary The Menstrual Cycle, Control of Ovarian Function, Abnormalities of Ovarian Function

**L41-42:** Pregnancy: conception, fetal development, placenta, parturition, Lactation, fertility and infertility, Physiological concepts for a planned family

**Tutorial:** Group discussion, Student seminar and test

## **UNIT 6: Endocrine system**

**L43-44:** Anatomy and structure, formation, secretion and regulation of hormones, hypo- and hyper secretions.

**L45-46:** Diseases of the following glands Thyroid, Adrenal, Parathyroid, Pituitary Thyroid Anatomic Considerations, Formation & Secretion of Thyroid Hormones, Transport of Thyroid Hormones, Effects of Thyroid Hormones, Regulation of Thyroid Secretion, Clinical Correlates.

**L47-48:** Adrenal Medulla, Structure & Function of Medullary Hormones: Regulation of Adrenal Medullary Secretion, Adrenal Cortex Structure & Biosynthesis of Adrenocortical Hormones

**L49-50:** Effects of Adrenal Androgens & Estrogens, Physiologic, Pharmacologic & Pathologic considerations

**L51-52:** Effects of Glucocorticoids, Regulation of Glucocorticoid Secretion,

**L53-54:** Effects of Mineralocorticoids, Regulation of Aldosterone Secretion, Summary of the effects of Adrenocortical Hyper & Hypofunction in Humans.

**L55-56:** The Parathyroid Glands, Calcitonin, Effects of Other Hormones & Humoral Agents on Calcium Metabolism, Posterior pituitary hormones Growth Hormone

**Tutorial:** Group discussion, Student seminar and test

## ***COURSE OUTCOME***

**Human physiology I:** This course is a part of core course offered in second semester. On satisfying the requirements of this course, students will have the knowledge and skills to:

1. Describe the anatomy and histology of major organ systems.
2. Explain the functioning of these organ system in maintenance of normal and healthy individuals
3. Narrate the contribution of each organ system to the maintenance of homeostasis.
4. Interpret and analyze the human physiological data, and responses to experimental conditions
5. Understand the physiological processes accurately with relevant scientific terminology and nomenclature leading to develop more consciousness towards a healthy body.
6. List the physiological principles underlying pathogenesis and treatment of disease.

## **Reading list:**

1. Textbook of medical physiology by Arthur C. Guyton and John E. Hall; Ed.13<sup>th</sup> & 14<sup>th</sup>.
2. Review of medical physiology by William F. Ganong; Ed. 23<sup>rd</sup>; McGraw Hill; 2010.
3. Essential medical physiology by Leonard R. Johnson and Ed. 3<sup>rd</sup>; ELSEVIER; 2003.
4. Principles of anatomy and physiology by Gerard J. Tortora and Bryan Derrickson; Ed.15<sup>th</sup>; John Wiley; 2016.
5. Hole's Human Anatomy & Physiology, McGraw-Hill Education; 14<sup>th</sup> edition, 2015
6. Medical Physiology: A cellular and molecular approach by Walter F. Boron and Emile L. Boulpaep; Saunders; Ed. 3<sup>rd</sup>, 2017.
7. Physiology by Robert M. Berne and Matthew N. Levy; Mosby; ELSEVIER, Ed.7<sup>th</sup> 2018.
8. Essentials of Anatomy & Physiology Plus Mastering A&P with Pearson (7th Edition) 2016

# **HUMAN PHYSIOLOGY PRACTICALS**

## **II Semester**

**Credits: 2**

### **Detailed practicals**

#### **Histopathology**

1. Demonstration of biological sample retrieval, sectioning (cryotome/microtome), fixation and staining of various tissue types from rodent tissue sample.
2. Study of various types of human tissues in normal and diseased condition from permanent slides.

#### **Blood physiology**

1. Preparation and staining of blood smear with Leishman's stain and Identification of the various types of blood cells.
2. To record the Bleeding time, clotting time and determine the blood group from own blood sample.
3. To determine the total count of RBC and WBC from own blood sample.

#### **Electrophysiology (using appropriate hardware and software)**

1. To observe, record, and correlate motor unit recruitment and muscle fatigue with increased power of skeletal muscle contraction through Electromyogram (EMG).
2. Measurement of forced expiratory volume (FEV) and Forced vital capacity (FVC).
3. To observe rate and rhythm changes in the ECG associated with body position and estimate the mean electrical axis of the QRS complex
4. To measure reflex time of different nerves in the body under different conditions using the reflex hammer.
5. To record the Reaction time for various Short term memory test.
6. To record an EEG of different areas of brain from an awake, resting subject.
7. Record EOG on the horizontal plane and compare eye movements under the following conditions: pendulum tracking, pendulum simulation, reading silently, reading aloud, and reading challenging material or material written in an unfamiliar language.
8. Assessment of cranial nerves functioning by the battery of non-invasive tests.

#### **Reading list**

1. Exploring Anatomy & Physiology in the Laboratory, Morton Publishing Company; 3 edition (2017)
2. [http://physiology.elte.hu/gyakorlat/jegyzet/Physiology\\_Pactical\\_\(2013\).pdf](http://physiology.elte.hu/gyakorlat/jegyzet/Physiology_Pactical_(2013).pdf)

## **Semester II: Recombinant DNA technology and Biotechnology**

### **CORE Subject (Credit 3+2(p))**

*Preamble: The unique preposition of this subject paper is that the students learn the advancement in basic molecular techniques and different methodologies used in the diagnosis and for the various human diseases therapeutics. The concepts of gene cloning and its expression leading to desired gene product is explored.*

*Aims in the paper is to train students towards the advancement*

#### **Total 50 Lectures**

**L (1-5):** Prokaryotic Restriction Modification system, Types of Restriction endonucleases & restriction maps, Endonucleases produces 3' Overhang and 5' Overhang, Producing new restriction endonuclease sites.

**L(6-9):** Various RDT enzymes such as S1 nuclease, Alkaline phosphatases, polynucleotide kinase, mung bean nuclease their mechanism and application

**L(10-13):** Vectors-Origin of cloning vectors and various modified versions of vectors, Bacterial, yeast expression vectors, mammalian expression vector

#### **L14: Tutorial Class**

**L(15-18):** Cloning vectors, Tetracycline regulated vectors, shuttle vectors, YAC &BAC.

**L(19-22):** Principles of selection of gene cloning, preparation of probes, Blue white selection, insertional inactivation, LacZ application, luciferase reporter system

**L(23-25):** Detection and identification of cloned DNA sequencing, methods of DNA sequencing, pyrosequencing, nanopore sequencing, Next generation sequencing

**L(26-30):** Application and principles of Polymerase Chain Reaction, RFLP analysis, real time PCR, Disease diagnostics eg: genetic diseases (cystic fibrosis, sickle cell anemia, hemophilia etc), detection of pathogenic strain, single nucleotide polymorphism in disease diagnosis

#### **L31: Tutorial Class**

**L(32-35):** Gene Mutagenesis-Different methods used to generate recombinant mutants (deletion and point mutations), exonucleases, S1 nuclease, Genome editing system using ZFN, CRISPR, TALEN

**L(36-37):** Application of recombinant DNA technology, DNA fingerprinting in forensic sciences

**L(38-41):** Biotechnology towards therapeutics, Gene therapy (Viral on non-Viral), Adenoviral vectors or retroviral based gene therapy, stem cell based disease diagnosis and therapies

#### **L42: Tutorial Class**

**L(43-45):** Introduction to the concept of Regenerative Medicine, Advance Pleuripotent stem cell derived therapies, Induced pleuripotent stem cell, mesenchymal stem cell

**L(46-48):** Exosomes: Biomarkers, Cancer diagnosis, Tissue repair

**L(49-50):** Bio-safety and ethics for recombinant DNA technology

**L51: Tutorial Class**

### **Text Books:**

- a) **Principles of Gene manipulation (Primrose), 7<sup>th</sup> Edition**
- b) **Molecular Cloning (A laboratory manual), Vol 1, Vol 2, Vol 3**
- c) **Molecular Cell Biology (Lodish), 7<sup>th</sup> Edition**
- d) **Review articles from: Nature Reviews (Journals)**

# **Recombinant DNA technology and Biotechnology**

## **Practicals:**

- 1) Primer designing for gene amplification using PCR, and other types of primers for real time PCR based detection or analysis
- 2) Preparation of Various solutions and Buffers, cell culture LB (Luria-Bertani) media preparation, LB-Agar Plates, Ampicillin Antibiotics preparation, autoclaving, sterilized surface, laminar flow operation.
- 3) Adopting calcium chloride methodology for Competent cells preparation
- 4) Polymerase Chain Reaction based gene amplification and recombinant formation using cloning vector
- 5) Recombinant plasmid isolation and preparation
- 6) Recombinant restriction digestion of DNA and excision of DNA from Agarose gel
- 7) Heat shock methodology based recombinant transformation, competent efficiency calculation and Blue white colony screening
- 8) Application of Polymerase Chain Reaction based infectious or non-infectious disease diagnosis
- 9) Loop mediated isothermal amplification assay
- 10) Concept of cell culture (Demonstration)

## **Subject Outcome:**

### **Theory & Practical Outcome:**

- 1) M.Sc. student after attaining recombinant DNA technology course work, they are then well versed with the knowledge and practical approach to pick out any gene from cell or tissues using some potential technique using PCR technology, where student can amplify the interested gene, and to clone in any expression vector to produce more protein, for functional studies.
- 2) Cloning any gene of interest can help students to analyze the isolated gene and complete sequencing, will help in disease manifestation.
- 3) Applications of subject knowledge has commercial values
- 4) Developing a diagnosis technique for the disease treatment, at low cost values
- 5) Developing a efficient therapies against various diseases to work

# IMMUNOLOGY

## Core paper

## II Semester

**Credits: 4+0+2 (practical)**

### 56 lectures

*Preamble: Immunology course has been formulated to understand the basics of vertebrate Immune system at the molecular, cellular and organ system level and to know how our body defends to the “Danger/foreign” entities . The students will understand primary and secondary lymphoid system in mouse and human system . The practical and theoretical illustration of functions of cells of innate immune responses: macrophages dendritic cells through estimation of reactive oxygen species, reactive nitrogen species, malondialdehyde, protein- carbonyl adducts, process of phagocytosis and activation of immune cells etc. Understand the mechanisms of cell mediated and humoral immune responses at organ system , cellular and molecular level.*

L1: History and scope of Immunology

L2: Introduction to Immune System , concepts of Innate and acquired Immune responses , Active and passive Immunity , Natural and artificial immunity, primary and secondary immune responses

L3: Lymphoid System- overview . Lymphatic system and lymphocyte traffic .Lymphoid Tissue: Primary and Secondary Lymphoid organs. Anatomy and functional significance of Thymus, Bone marrow

L4: Anatomy and functional significance of spleen ,various lymph nodes, MALT,GALT, NALT,ILT

L5: Cells involved in the Immune Response : Structural and functional features of cells involved in immune responses and their relative significance. Lymphocytes (B& T lymphocytes), NK Cells

L6: Mononuclear Phagocytes, Antigen- presenting cells, Polymorphonuclear cells, eosinophils, basophils and mast cells, Cluster designation Ag specific receptors (comparison of Human and Mouse Lineages)

**L7 is Tutorial**

L8: What is an immune response. Evolution of cells and molecules of the immune system with associated functions. Dendritic cells: discovery types and functions: DC 1 vs DC2 vs Follicular DC.

L9: Antigen recognition processing, presentation and cross-presentation of antigens by DC subsets

L10: DC priming of T independent antigens, DCs as immunotherapeutics

L11: Innate immune system: overview. Cells and receptors of the innate immune system. Diversity in Antigen recognition receptors of innate immunity

L12: Signaling from Toll Like Receptors

L13: Cell surface and intracellular antigen/pathogen recognition systems: NOD/NLR/TLR9

L14: Secretory receptors of innate immune system and their functions

L15: Innate memory and danger hypothesis. Macrophages: types, location and function. Neutrophils and NK cells: mode of action and neutralization of pathogens

### **L16 is Tutorial/Test**

L17: Antibody Generation, structure and Function : Over View of Humoral immunity, Clonal Selection Theory, Immunoglobulins classes and their functions , Antibody Structure and Function

L18-19 : Antibody Effector Mechanisms, Antibody Receptors, Basis of Antibody Diversity, Mechanisms of Immunoglobulin Gene Recombination, and B cell development

L20: Mechanism and Effect of Somatic Mutations on the Antibody Diversity, Mechanism of Ab Class switching.

L21 : Antibody Responses in vivo, Enhanced Secondary Responses , significance Isotype switching, Affinity Maturation and development of Memory responses.

L22-23 : Major Histocompatibility Complex overview and significance. Structure of MHC Class I Molecules, Structure of MHC Class II Molecules,

L24: Genomic Organisation of the MHC locus in Mice and Humans, Diversity of MHC molecules and their effect of immune response modulation.

L25 : Gene polymorphism and polygeny on MHC locus and their effect on the disease pattern with respect to resistance and susceptibility to diseases.

L26-27 : Antigen Recognition and Presentation overview: Structure and assembly of MHC molecules/Peptide complexes. Mechanisms of Antigen Processing (exogenous and endogenous antigens) and Presentation to T-lymphocytes (CD4<sup>+</sup> and CD8<sup>+</sup>).

L28-29: Complement System. Nomenclature of complement system, Classical, Lectin and Alternative Activation of complement pathway, assays for complement activation. Biological Effects of complement system , Regulation of complement system. Complement system related diseases

### **L30 is Tutorial**

L31-33 : Cell Mediated Immune Response Overview, T lymphocyte classification, lineage and Mechanisms of development of T cells in thymus. Structure of T cell receptors , Mechanisms of recombination and diversity of TCR genes, self tolerance mechanisms. Regulation of innate and humoral responses by T cells. T cell APC interactions and modulation of Immune responses.

L 34 : T independent and T dependent Defense Mechanisms, Cell Mediated Cytotoxicity. Idiotypic modulation of immune responses

L35-36 : Regulation of Immune Response: Antigens, classification of antigens based on their interaction and functions. Superantigens, interaction of Antigens with Antigen Presenting Cells, Antibody, Lymphocytes. Idiotypic Modulation of Response, Neuroendocrine Modulation of Responses, Genetic control of Immune Response.

L37 : Cell Migration and Adhesion. Patterns of Cell Migration, Structure and function of various adhesion Molecules, Mechanism of Cell Migration and their involvement in disease

L38-39 : Immunopathology: overview Rh- blood groupings, Autoimmune Diseases, Basis of breach of central and peripheral tolerance.

L 40 : Immuno-deficiencies, Genetic disorders congenital and acquired.

L 41-42 : Hypersensitivity Reactions (type I and type IV), Role of IgE, Mast cells, Genetic basis of Allergic Response and pathogenesis.

L 43 : Immune Tolerance overview: Self Tolerance, Transplantation and Rejection mechanisms

### **L44 is Tutorial**

L 45-46 : Mechanism of Antigen-Antibody Interaction, Experiment based evidence to calculate antigen binding sites, avidity, affinity. Immunological Techniques: Principles, significance and methods; Agglutination( Direct/Indirect), Precipitation(Radial and double immunodiffusion) and Radioimmunoassays.

L 47 : Immunological techniques : Immunoflorescence ( direct/ indirect) , Enzyme linked Immunosorbent assay ( principles of various types of ELISA) and its variants.

L48 : Magnetic cell sorting, Flowcytometry, western blotting

L49 : Techniques for generation of polyclonal and monoclonal antibodies. Hybridoma Technology for Mab Production.

L 50 : Techniques for isolation of specific antibodies.

L 51 : Gene Targeting: Knock out and Transgenic animals

L 52 : Basis of Tumor Immunology

L 53 : Vaccines : History and overview , adjuvants, Immune responses following vaccination

L 54 : Various types of vaccines and methods of their development with examples

**L 55 is Tutorial**

**L 56 is Test**

### ***Course outcome***

*Immunology is one of the foundation courses for the biomedical sciences students. Students will gain insights on the immune system and the immune responses at the molecular , cellular and organ system level. The students will be prepared to take further advanced courses/ research in immunology , immunodiagnostics , immunopathogenesis and immunotherapeutics .*

### **Suggested Readings**

1. Fundamental Immunology William Paul (Ed) 2017. Lippincott Williams & Wilkins.
2. Kuby Immunology by Thomas Kindt and Richard A. Goldsby and Barbara A. Osborne; Ed. 6<sup>th</sup> edition. W.H. Freeman and Company, New York; 2007
3. Cellular and molecular immunology by Abul K. Abbas and Andrew H. Lichtman and Shiv Pillai; Ed. 6<sup>th</sup>; Saunders, 2007.
4. Immunology; Ed.7<sup>th</sup> by David Male and Jonathan Brastoff and David B. Both and Ivan Roitt; Mosby Elsevier; 2006.

5. Immunobiology: the immune system in health and disease by Charles A. Janeway and Paul Travers and Mark Walport and Mark J. Shlomchik; 7<sup>th</sup> Ed; Garland Science; 2008.
6. Immunology of infection diseases by Stefan H. E. Kaufmann and Alan Sher and Rafi Ahmed; ASM Press, Washington; 2002.
7. Essentials of immunology & serology by Jacqueline H. Stanley; DELMAR; Australia; 2002.

**Practicals:**

1-3. To demonstrate that activation of peritoneal macrophages/ myeloid lineage cells by lipopolysaccharides results in reactive oxygen production (RNS) and reactive nitrogen species production. Estimation will be done by flowcytometry, Colorimetry and microscopy assays.

3-6. The antigen antibody interaction mechanisms will be demonstrated by precipitation and agglutination assays (octerlony, mancini methods and indirect agglutination tests)

6-9. The T cell and B cell separation and their proliferation will be done using MACS and FACS

10. Proinflammatory cytokine expression will be demonstrated in activated cells by ELISA or immunofluorescence.

**NAME OF PAPER : BIOLOGICAL CHEMISTRY 2**  
**CORE PAPER ;**  
**Semester II, Credits 4**

Preamble

The course aims to impart to the students a thorough understanding of chemical macromolecules found in biological systems. Synthetic macromolecules and their self assembly is also discussed as is the important area of nanotechnology. Carbohydrate chemistry forms an essential part of this course. Enzyme and coenzyme catalysis is thoroughly discussed

Molecules and macromolecules in biological systems

- L-1 Amino acids, peptides and proteins,
- L-2 Structure and Functions of proteins
- L-3 Formation of peptide bonds,
- L-4-5 Protecting groups and peptide bond formation,
- L-6-7 protein degradation and sequencing of amino acids,
- L-8 DNA and RNA bases,
- L-9-10 nucleosides and nucleotides, phosphodiester
- L-11-12 formation of N- and C- glycosides,
- L-13-14 conformation and configuration of 5 carbon and 6-carbon sugars,
- L-15-16 maltose, sucrose and lactose,

Synthetic macromolecules and polymers in biology

- L-17-18 Building of macromolecules and molecular frameworks and their biomedical applications.
- L-19 Synthetic strategies for artificial systems that mimic biological entities,
- L-20-23 applications of supramolecular principles to molecular diagnosis, therapeutic applications of supramolecular chemistry.
- L24-26 Nanotechnology and its applications in drug delivery and other biomedical applications

Mechanisms in Biological Chemistry

- L-27 Active methylene groups,
- L-28-29 aldol and retroaldol reactions,
- L-30 schiff bases and enamine reactions,
- L31-32 nitrogen, phosphorus and sulfur ylides.
- L-33 Umpolung reaction,
- L-34 Michael addition,
- L-35 Polymer supported organic reactions,
- L-36 -37 phase transfer catalysis, Equivalence of these reactions in biological system

## Enzyme and Coenzyme systems

L-38 Enzyme classifications, Inhibitors,  
L-39-40 Mechanisms of Enzymes.

Mechanism of coenzyme catalysis,

L-41 Coenzyme A,

L-42 NAD<sup>+</sup> and NADPH,

L-43 FMN and FAD,

L-44 biotin ,

L-45 PLP,

L-46 TPP,

L-47 lipoic acid, tetrahydrofolate, ascorbic acid,

L-48 cyanocobalamine and

L-49 cytochrome P-450

## Hammett and Taft equation

L-50 Steric and solvent effects,

L-51 role of pH,

L-52 role of reaction media on certain reactions

## **MBS 202: MOLECULAR BIOLOGY (CORE PAPER)**

**Credits :3 (3+0+0)**

**Preamble:** Molecular Biology is a core course where in students will be explained the various basic processes of the prokaryotic and eukaryotic cell. Several essential techniques used in understanding its gene expression, DNA synthesis and translation will also be discussed.

### **TRANSCRIPTION IN PROKARYOTES & EUKARYOTES**

L1: Basic concepts of transcription in prokaryotes using E-coli as an example

L2: Structure & function of RNA polymerases.

L3: Transcription initiation, proteins involved in initiation,

L4: Experimental evidence to check their function.

L5: Transcription elongation and termination.

#### **L6: TUTORIAL**

L7: Transcription in eukaryotes- differences and similarities, inhibitors of transcription

L8 : Structure of TFIID, and other general transcription factors.

L9: Methods to identify the subunits of complexes.

L10: Post transcriptional regulation of transcription (polyadenylation, capping), mechanism and their role in transcription

L11: Transcription regulation by methylation, acetylation of histones.

#### **L12: TUTORIAL**

L13: Inhibitors of transcription in prokaryotes and eukaryotes

L14: Determining the mRNA half life of mRNA.

L15: Promoter structure and Transcription by RNA polymerase I,

L16: Structure of Promoter and Transcription by RNA polymerase III

#### **L17: TUTORIAL**

#### **L18: TEST (10 MARKS)**

**Regulation of gene expression in Prokaryotes**

**L19:** Coordinated control of clustered genes-operon model, with example of inducible systems like Lac– Operon.

**L20:** Experimental proof for the operon, use of mutants of I gene, O<sup>c</sup> mutants in understanding operon function

**L21:** Role of cyclic AMP, catabolite repression and regulation by glucose.

**L22:** Repressible systems like Trp operon. Concept of attenuation

**L23:** Trp operon cond.

**L24:** Arabinose operon concepts of dual role of regulatory protein

**L25:** Arabinose operon contd

**L26:** Identification and understanding the role of sRNA in gene regulation in prokaryotes.

**L27:** Other regulatory pathways in prokaryotes

**L28 Tutorial**

**L29: Test**

### **Regulation of Gene expression in Eukaryotes**

**L30:** Introduction-Organization of genes in eukaryotic DNA Repetitive DNA sequences, multiple regulatory sequences, activators, coactivators, repressors

**L31:** Activators contd, enhancers. Modular structure of transactivators (Zn fingers, HLH, HTH etc).

**L32:** Repressor complexes, mechanism of their function in gene regulation.

**L33:** Regulation of gene expression by hormone receptors. Concept of half-site.

**L34:** Methods used to study protein-DNA interactions EMSA controls, supershift etc.

**L35:** DNA foot printing, reporter assays to prove binding.

### **L36: TUTORIAL**

**L37:** Homodimers and heterodimers in differential gene regulation with examples. Diseases linked with altered gene expression

**L38:** Methods used to study protein-protein interactions (i) yeast two hybrid, controls, library screening to identify new interacting partners.

**L39:** (ii) Concept of co-Immunoprecipitation, uses, advantages and disadvantages of two techniques

**L40:** Alternate splicing in gene regulation, mechanism.

**L41:** Alternate splicing contd. splicing factors etc, gene editing

**L42:** Ribozymes–Structure and mechanism of action.

**L 43:** microRNA and its role in gene regulation (in brief).

**L44:** TEST (MARKS 10)

### **Chromatin remodeling**

**L45:** Introduction to chromatin remodeling concepts and factors involved. Role of various remodeling proteins such as NURF, ACF

**L46:** Role of DNA and histone methylation and histone acetylation in chromatin remodeling and gene regulation.

**L 47:** Concept of insulators, nuclear matrix in gene regulation

**L48:** Methods to understand chromatin remodeling.

**Course outcome:** Student should be able to understand the differences and similarities in prokaryotic and eukaryotic gene expression and its regulation. Student will be able to analyze the data on protein DNA interaction. He/She should be able to design experiments for testing whether a new protein is a transactivator and how to identify the binding site on a promoter.

## **HUMAN PHYSIOLOGY-II**

**Core paper**

**III Semester**

**Credits: (3+1+ 0)**

### ***PREAMBLE:***

*In continuity to understand the physiology of various organ systems in Human physiology-II, we ought to understand two of the vital organ system i.e. cardiovascular and nervous system. These system are vital as cessation in the functioning of any of these system straight away leads to death, therefore these system are dealt in detail along with their inter-relationship with other organ systems.*

### **UNIT 1: Cardiovascular system**

**L1-4:** Physiology of cardiac muscle (contractile and auto-rhythmic myocytes), Cardiac Cycle Control and Regulation of excitation, contraction and conduction of heart pumping, Heart sounds

**L5-10:** Characteristics of normal electrocardiogram, analysis of ECG for various myopathies, Cardiac arrhythmias

**L11-14:** Physical characteristics and basic theory of circulation, Vascular dispensability and functions of arterial and venous systems, Microcirculation and lymphatic system, Capillary fluid exchange, interstitial fluid and lymph flow, Local control of blood flow by tissues and humoral regulation, Nervous regulation of circulation, Cardiac output, venous return and their regulation, coronary circulation.

**L15-18:** Blood and circulation: blood corpuscles, haemotopoiesis and formed elements, plasma function, Hemostasis and blood coagulation, Blood banking, blood groups, and Transfusion.

**Tutorial:** Group discussion, Student seminar and test

### **UNIT 2: Overview of the Nervous System**

**L19-22:** Neuron and classification of nerve cell, nerve fibers, nerve, intracellular trafficking of neuron, Resting membrane potential of nerves, Nerve action potential, neurotransmitters: synthesis, models of exocytosis of synaptic vesicles and its inhibitors, synapse: types, pre and post synaptic regulation.

**L23-25:** Anatomical and functional division of nervous system, Spinal cord and cranial nerve, Blood-Brain barrier, Cerebral Blood Flow, Regulation of Cerebral Circulation.

**Tutorial:** Group discussion, Student seminar and test

### **UNIT 3: Motor System**

**L26:** Motor Units, Motor neurons types and characteristic of upper and lower motor neuron, lesions of upper and lower motor neuron. Muscle Receptors,

**L27-29:** Posture: Neural Systems Controlling Postural Orientation and Stability, Automatic Postural Reactions, Postural Reflexes: Infant to Adult, Spinal Reflexes. Grouping of Motor pathways: direct and indirect pathways, Cortical and brain stem control of motor function.

**Tutorial:** Group discussion, Student seminar and test

#### **UNIT 4: Cognitive System**

**L30: Neural Basis of Instinctual Behavior & Emotions:** Limbic Functions: behavior, Sexual Behavior, Fear & Rage, Motivation

**Tutorial:** Group discussion, Student seminar and test

#### **UNIT 4: Learning and Memory**

**L31-33:** Cerebral Cortex: Intellectual functions of brain, learning and memory, Physiologic anatomy of cerebral cortex, Functions of specific cortical areas, Association areas, Function of brain in communication - language input and output, Function of corpus callosum and anterior commissure.

**L34-35:** Thoughts, consciousness and memory: Memory formation, types of memory, molecular pathway of memory formation, Activating-driving systems of brain, Functional anatomy and functions of limbic system and hypothalamus, States of brain activity, Brain waves, Origin in brain of brain waves (EEG).

**L36-37:** Sleep: Slow-wave sleep, REM sleep, Basic theories of sleep and awake, Physiological Mechanisms of Sleep and Waking, dreams sleep deprivation, Epilepsy, Psychotic behavior and dementia - roles of specific neurotransmitter systems.

**Tutorial:** Group discussion, Student seminar and test

#### **UNIT 5: Sensory Physiology**

**L38-39:** Neuronal circuits for processing information, “Coding” of Sensory Information, Electrical & Ionic Events in Receptors.

**L40-41:** Somatic sensations: Tactile and position senses, Sensory pathways for transmission of somatic signals into the central nervous system, Sensory receptors, Transmission in dorsal column – medial lemniscal system.

**L42-43:** Pain and thermal sensations: Pain receptors and their stimulation, Dual transmission of pain signals into the central nervous system, Types of pain.

**Tutorial:** Group discussion, Student seminar and test

#### **Special Senses**

**L44-45: Eye:** The Image-Forming Mechanism (accommodation and visual acuity), Receptor and Photochemistry of vision, Neural function of retina. Visual Pathways and effects of lesions of these pathways

**L46-47: Hearing and equilibrium:** Tympanic membrane and ossicular system, Cochlea, Central auditory mechanisms, directionality of sound, Vestibular sensations and maintenance of equilibrium, auditory and vestibular reflexes, oculo-vestibular system

**L48: Taste and smell:** Anatomical aspects of olfaction and gustation, Receptors and sensory transduction of olfaction and gustation & Neuronal Pathways of olfaction and gestation

**Tutorial:** Group discussion, Student seminar and test

#### **UNIT 6: The Autonomic Nervous**

**L49:** System Introduction Anatomic Organization of Autonomic Outflow Chemical Transmission at autonomic Junctions Responses of Effector Organs to Autonomic Nerve Impulses Cholinergic and Adrenergic Discharge.

**Tutorial:** Group discussion, Student seminar and test

**Central Regulation of Visceral Function**

**L50:** Hypothalamic Function: Autonomic Function, Cyclic Phenomena and circadian rhythm, Hunger Thirst Control of Posterior Pituitary Secretion Control of Anterior pituitary Secretion Temperature Regulation, fever.

**Tutorial:** Group discussion, Student seminar and test

***COURSE OUTCOME***

**Human physiology II:** This course is a core course and continuation of Human physiology I to be offered in third semester. On satisfying the requirements of this course, students will have the knowledge and skills to:

1. Describe the anatomy and histology of nervous system and cardiovascular system.
2. Understand the indications for, interpretation of, and risks of the common cardiovascular testing modalities for normal and diseased state
3. Become familiar with the emergency sign and symptoms in case of cardiac/ nervous system dysfunction.
4. Be aware of the i) symptom and approach knowledge, ii) disease based knowledge for nervous system dysfunction
5. Create awareness for the importance of healthy mind and heart.

**Reading list:**

1. Textbook of medical physiology by Arthur C. Guyton and John E. Hall; Ed.13<sup>th</sup> & 14<sup>th</sup>.
2. Review of medical physiology by William F. Ganong; Ed. 23<sup>nd</sup> ; McGraw Hill; 2010.
3. Essential medical physiology by Leonard R. Johnson and Ed. 3<sup>rd</sup>; ELSEVIER; 2003.
4. Principles of anatomy and physiology by Gerard J. Tortora and Bryan Derrickson; Ed.15<sup>th</sup>; John Wiley; 2016.
5. Hole's Human Anatomy & Physiology , McGraw-Hill Education; 14 edition, 2015
6. Medical Physiology: A cellular and molecular approach by Walter F. Boron and Emile L. Boulpaep; Saunders; Ed. 3<sup>rd</sup> , 2017.
7. Physiology by Robert M. Berne and Matthew N. Levy; Mosby; ELSEVIER, Ed.7<sup>th</sup> 2018.
8. Principles of Neural Science, (Kandel) 5th Edition, 2013.
9. Fundamental Neuroscience, ELSEVIER 4th Edition, 2012
10. Neuroscience Online, an Open-Access Neuroscience Electronic Textbook  
<https://nba.uth.tmc.edu/neuroscience/>

**CORE COURSE**

**CREDITS 3+1**

**Preamble**

The course includes theoretical studies in the field of Medicinal Chemistry. This encompasses the de-novo approach to design of drug candidates, the potential physico-chemical interaction between low molecular-weight compounds and biomolecules such as proteins and DNA, plausible biochemical transformations for elimination of small molecules. In addition, few examples of rational drug design to target specific protein/ receptor for the human pathologies such as peptic ulcers, hypertension, atherosclerosis, cancer, neuronal pathologies etc. will be studied. Thus, the course includes theoretical elements concerning the identification, design, synthesis and evaluation of low molecular organic substances for specific pathological state from the perspective of medicinal chemistry.

**Expected outcomes**

After completing the course, students shall be able to:

- describe the various steps involved in the design of a drug,
- describe the "interaction between ligand and receptor" concept
- identify and describe the connection between chemical structure and physical-chemical properties,
- describe the design of organic compounds, for example, statistical or structure-based design,
- in groups, plan and conduct a medicinal chemistry project,
- independently acquire and critically assess biological and medicinal information from databases,
- actively participate in discussions during seminars and group exercises,
- present results verbally and in writing, and
- communicate principles, problems and research results with specialists and non-specialists on issues within the scope of the content of the course.

**COURSE CONTENTS**

**1. Role of Medicinal Chemistry in discovery of drugs**

**L1- L2** Introduction to medicinal chemistry as a strategy to the design of new drug candidates for the human pathologies.

**2. Drug Design**

(a) **Discovery of lead compound-**

**L3- L4** Serendipous, Random and Non-random screening, drug metabolism studies, clinical observations

**L5- L6** Rational approaches to lead discovery- Homologation, chain branching, ring-chain transformations, bioisosterism.

**(b) Lead modifications**

**L7- L8** Conventional drug screening and structural modifications, concept of isosteres and bioisosteres, structure activity relationship,

**L9-10** Quantitative structure activity relationships- Electronic effects: Hammett equation, lipophilicity effects. Hansch equation, steric effects.

**L 11-12** Taft equation, mathematical method for de novo design, Manual stepwise scheme 2D QSAR; 3D-QSAR examples, CoMFA

**c. Introduction to molecular modeling and molecular graphics, pharmacophore descriptors**

**L 13** The classical mechanics model (e.g., MM1, MM2), Quantum chemical methods semi-empirical and ab initio methods.

**L 14** Molecular graphics: View and manipulate molecular structures

**L 15-16** Pharmacophore descriptors: Based on Genetic Algorithms--Partial Least Squares (GA-PLS) and K-Nearest Neighbors (KNN) to achieve a robust QSAR model characterized by the highest value of cross-validated R<sup>2</sup> (q<sup>2</sup>).

**3. Receptors**

**Chemical nature of receptors**

**L17-18** Covalent, ion-ion, ion-dipole, Hydrogen bonding, C-H hydrogen bonding, dihydrogen bonding, Van der Waals interactions and the associated energies, Chirality and receptor binding.

**Drug receptor interactions**

**L19-20** Occupancy Theory, Rate Theory, Induced Fit Theory, Macromolecular perturbation theory, Activation-Aggregation theory.

**L21-22** Classification of receptors and receptor subtypes, Neurotransmitters and their receptors, Receptor modulation and mimics, Receptor sites.

**L23-24** Chirality and receptor binding, Signal transduction and second messenger systems.

**L25-28** Active transport, affinity and efficacy, antagonism, partial antagonism, inverse agonism, allosteric binding sites.

**4. Introduction of various classes of drugs based on their interaction with target site.**

**With suitable examples, the drugs interacting with**

**L 29-30 (i) Receptors**-Rational design of agonist/antagonist

**L 31-32 (ii) Enzymes** Mechanisms of enzyme catalysis, Electrostatic catalysis and desolvation. Covalent catalysis, Acid-base catalysis, Strain / distortion in enzyme catalysis. Coenzyme catalysis.

**L 33-36 (iii) Enzyme Inhibition**-Reversible and irreversible, rational design of various enzyme inhibitors, Adverse drug reactions, Drugs acting on cell wall, Fungal membrane and Nuclear membrane, Drugs inhibiting protein synthesis.

**L 37-40 (iii) DNA**- NA as targets for drug action. NA-interactive agents. Classes of drugs that interact with nucleic acids. Intercalation, NA-alkylation, NA-strand breaking and their importance in drug action,

**L 41-42 (iv) Carbohydrates**- development of glyco-conjugates in cancer models

**5. Structure activity relationship illustrated with examples from**

**L 43-44 Sulphonamides, b-lactams, Quinolones, Nucleosides and Alkaloids.**

## **6. Drug Metabolism**

**L 45 (i)**Biotransformations and their Mechanisms

**L 46-48 (ii)**Phase I and Phase II metabolism, Oxidation, Reduction, Hydrolysis, Deamination and Conjugation (GSH, Sulfate, Glucuronide and Amino acids)

**L 48-50 (iii)** Role of non-specific enzymes: Oxidases, Mono-oxygenases, Di-oxygenases and Peroxidases,

**L 51-52 (iv)** Biotransformations illustrated by suitable examples of commonly used drugs, Chirality and drug metabolism.

**L 53-60           Tutorials/ discussions**

## **Reading List**

1. Organic chemistry of drug design and drug action by Richard B. Silverman; Ed. 2<sup>nd</sup>; ELSEVIER; 2004.
2. Foye's Principles of Medicinal Chemistry by Thomas L Lemke and David A Williams; Ed. 6<sup>th</sup>; Lippincott Williams & Wilkins; 2007.
3. Medicinal chemistry: principles and practice by Frank D. King; Ed. 2<sup>nd</sup>; The Royal Society of Chemistry; 2002.
4. Introduction to Medicinal chemistry by Graham L. Patrick; Ed. 3<sup>rd</sup>; Oxford; 2006.



# **Pharmacology and Toxicology**

**Core paper**

**III<sup>rd</sup> Semester**

**Credits: (3+1+2=6)**

## **Preamble**

*The course develops the understanding of theoretical and practical studies in the field of Pharmacology and Toxicology. The course involves the building up the knowledge of pharmacokinetic and pharmacodynamic profile of drug, pharmacological classification and principle of drug action and the types of toxicity assessments of various type toxicants of chemical and biological origin and environmental pollutants on organ system and drug disposition.*

## **Introduction to pharmacology**

**L1.** Scope of pharmacology: Introductory class to define pharmacology, historical background and limitations

## **Pharmacokinetics**

**L2-L3.** Absorption- Routes of administration of drugs, their advantages and disadvantages. Various processes of absorption of drugs and the factors affecting them

**L4-L5.** Metabolism i) Microsomal and non-microsomal mechanisms ii) Effect of Enzyme induction and inhibition on drug metabolism and the factors influencing them.

**L6-L9.** Distribution - i) distribution of drugs and the factors affecting them ii) Loading and maintenance doses Excretion of drugs- i) zero order, first order and steady state kinetics and half life of drugs, Numerical problems Pharmacodynamics: General mechanism of drug action and the factors, which modify drug action. : i) Dose response relationship curves and different types of antagonisms.

## **Pharmacodynamics**

**L10-L12.** i) General mechanism of drug action and the factors, which modify drug action (signal transduction mechanisms in general. Dose-response relationship curves and different types of antagonisms. ii) Drug receptor interaction and Theories.

## **Pharmacological classification of drugs; the brief introduction of drugs should emphasize the ADME profile of following systems**

**L13-L14.** Drugs acting on the central nervous system: Anesthetics- History, theory, mechanism and stages of anesthesia, Drug classification based on mechanism of action of anesthesia, Inhalation and general anesthesia; Local anaesthetics-classification and mechanism of local anesthesia, adverse reactions of Anesthesia

**L15-L16.** Psycho-pharmacological agents: Sedatives, Hypnotics, anxiolytics, anti-manic, antidepressants

**L17-L19.** Drugs acting on the autonomic nervous system: Cholinergic drugs, anticholinergic drugs, anticholinesterase drugs, dopaminergic drugs, Adrenergic drugs and adrenergic receptor blockers, Neuron blockers and ganglion blockers, Neuromuscular blockers, drugs used in myasthenia gravis.

**L20-L21.** Cardiovascular drugs, cardiotonics, antianginal agents, antihypertensive agents, peripheral vasodilators and drugs used in atherosclerosis, coagulants and anticoagulants.

**L22-L26.** Drugs acting on the respiratory system, Expectorants and antitussive agents, Drugs acting on the digestive system, Drug acting on Renal system, Coagulants and anticoagulants, Analgesics- Opioid analgesics (Morphine) and NSAIDs (Brufen)

**L28.** Hormones and hormone antagonists (Classification of hormones based on their pharmacological and physiological action), Mechanism of hormonal action (Hypothalamopituitary adrenal / thyroid axis).

### **L29-L30. TUTORIALS & CLASS TEST**

## **Principles of Toxicology**

**L31-L34.** Definition, scope and different branches of toxicology. A brief review of toxic substances: Synthetic organic compounds: Chemical additives in food, Chemicals in the work place, Solvents, Pesticides, Cosmetics, Drugs of abuse. Inorganic chemicals: Industrial and chemical environmental inorganic toxicants polluting air/ water/ food. Naturally occurring poisons: Mycotoxins, Bacterial toxins, Plant toxins and Animal toxins.

## **Types of toxicity and its measurement**

**L35-L39** Acute, Sub-acute or Chronic and its manifestations. Acute toxicity: Mode of application/ administration/ exposure, in-vitro tests, Dose response relationship, Measurement of TD 50/ TC 50 and LD 50/ LC 50. Sub-acute and chronic toxicity. Risk and safety analysis: Margin of safety, Therapeutic index, Ideal therapeutic index. Inter-species extrapolation of dose-response data, NOEL, ADI, TLV, WHO standards. Special toxicity studies: Carcinogenicity, \ teratogenicity, in-vitro mutagenicity tests.

## **Epidemiology of toxicity**

**L40-L42.** Cohort study, Retrospect study, Case-control study, Cross-sectional study, Confounding.

## **Pharmacokinetic aspects of toxicants**

**L43-L44.** Site of metabolism, Metabolizing enzymes of liver, kidney, lung, GI tract, skin and their role in activation and detoxification of drugs and chemicals. Physiological (route of exposure, species, sex and age), Nutritional and environmental (temperature, altitude and circadian rhythms related) factors affecting metabolism, detoxification and toxic responses of drugs and chemicals.

## **Organ toxicities**

**L45- L48.** Hepatotoxicity: A brief description of morphological and functional aspects of liver with special reference to hepatotoxicity, various hepatotoxic agents, types of liver injuries- Fatty liver formation, Necrosis, Cholestasis, Hepatitis, Fibrosis, Cirrhosis, Carcinogenesis.

**L49-L50.** Nephrotoxicity: A brief description of morphological and functional aspects of kidney in relation of nephrotoxicity, nephrotoxic agents, detailed mechanisms of chemical induced nephrotoxicity.

**L51-L52.** Cardiovascular toxicity: A brief description of mechanisms of cardiovascular toxicity and cardiotoxic agents- subcellular and biochemical mechanisms.

**L53-L54.** Neurotoxicity: A brief description neurotoxic agents and types of neurotoxic effects- Axonopathy, Nerveopathy, Neuronopathy, Myelinopathy. Broncho-pulmonary (inhalation) toxicity.

**L55.** Gastro-intestinal toxicity.

**L56.** Skin toxicity/ photosensitivity.

## **Tests for evaluation of toxicities in different organs**

**L57-L58.** Therapeutic aspects: General measures and treatment of poisoning cases, Specific antidotes, Agents of first choice, Contraindications.

## **L59-L60. TUTORIALS & CLASS TEST**

## **PHARMACOLOGY & TOXICOLOGY (Practicals)**

1. CPCSEA guidelines for animal experiments, Animal handling and precautions.
2. To study the different routes of administration in different animal models.
3. Preparation of buffers and reagents require for the forthcoming experiments.
4. Topical application of Atropine and Pilocarpine on rabbit eye
5. Analgesic effect of diclofenac on mice/rat.
6. Study the effects of acetylcholine (Ach) and plot the dose-response curve.
7. Study the effect of general anaesthesia with ketamine in rat.
8. Study the haloperidol induced PD-like symptoms in mice.
9. To determine the effect of promethazine on phenobarbitone induced sleeping time in mice.
10. To determine the acute toxicity of a given drug and calculate the LD50 value.
11. Detection of organophosphorous pesticides in biological sample.
12. To test the presence of paracetamol in the given biological sample.
13. To determine the lethal concentration of Arsenic in Zebra fish according to OECD guidelines.
14. To determine the lethal concentration of Copper in Zebra fish according to OECD guidelines.
15. To identify plants which are toxic to human and animals in a given set up of garden or farm field.

## **READING LIST**

1. Essential of medical pharmacology; 6thEd. By K.D. Tripathi; Jaypee Brothers; New Delhi; 2008.
2. Goodman & Gilman's the pharmacological basisof therapeutics by Laurence Brunton and John Lazo and Keith Parker; Ed. 11th; McGraw-Hill Professional; 2005.
3. Pharmacology H. P. Rang and M.M. Dale and J.M. Ritter and P.K. Moore; Ed. 5th; Churchill Livingstone, 2003.

4. Integrated Pharmacology: With Student Consult Access by Clive P. Page and M.J. Curtis and M.C. Sutter and M.J. Walker and B.B. Hoffman; Ed. 3rd; Mosby; 2006.
5. Principles of toxicology by Karen E. Stine and Thomas M. Brown; Ed. 2nd; CRC Press; 2006.
6. Lu's basic toxicology: fundamentals, target organs and risk assessment by Frank C. Lu and Sam Kacew; Ed. 5th; Informa Healthcare; 2009.
7. Casarett and Dull's toxicology: the basic science of poisons by Curties D. Klaassen; Ed. 7th; McGraw Hill; New York; 2007.
8. Toxicology by Hans Marquardt and S.G. Schafer and R.D. McClellah and Academic Press; 1999.
9. Principles and practice of toxicology in public health by Ira R. Richards; Jones and Bartlett Publishers; 2007.
10. Handbook of human toxicology by E.J. Massaro; CRC Press; 1997.

## **Course outcome**

After completing the course, students shall be able to:

- describe the various steps involved in the interaction of a drug to its target,
- Administer the drug through various routes to the rats or mice and do toxicity assays.
- describe the pharmacokinetic and toxicokinetic profile of the drugs and chemicals respectively,
- Describe the design of treatment strategy - in animal group,
- plan and conduct a pharmacology project and toxicological assays,
- Independently acquire and critically assess Pharmacological and Toxicological information from databases

# **ANALYTICAL & BIOMEDICAL TECHNIQUES AND INSTRUMENTATION**

## **CORE COURSE**

**IIIrd Semester**

**Credits (3 + 1 = 4)**

**60 lectures**

**Preamble:** The course on Analytical and Biomedical Techniques and Instrumentation will be offered as CORE course in the 3<sup>rd</sup> Semester and covers various techniques used in analytical and Biomedical analysis. The course will be able to make students understand theoretical basis of these techniques as well as train them in handling various instruments and analysing the data. The students will be given hands on training to learn these techniques and apply the knowledge in developing skills which are essentially needed to work in clinical diagnostic and research laboratories in the field of biology and analytical biochemistry. The course has been designed to make them gain theoretical knowledge, practical handling of instruments and analysing the results obtained from these techniques for biomedical research.

**Introduction** **1**  
**Lecture**

**L1** Principles of Instrumental Analysis, Types of Instrumental Methods to be covered in the course. Selecting an analytical method and developing a new Analytical Technique.

**Optical Methods and their applications in Biomedical Sciences** **11**  
**Lectures**

**L2-3.** Ultraviolet / Visible molecular absorption spectroscopy, Theoretical basis, transitions, Lambert's Beers Law, factors affecting Absorption,

**L4-5.** Fluorescence and Phosphorescence (principle Jablonski diagram), Fluorescence quenching (dynamic, static, Stern volmer constant, FRET with examples from Biomedical field.

**L6-7.** Biomolecular interactions using spectroscopic methods

**L8-9.** Infrared – vibrational spectroscopy introduction, Functional group identification, Effects of various factors on IR frequencies and biomedical application.

**L10.** Concept of circularly polarized light and principles of CD

**L11.** CD instrumentation, concepts of band width, slit width, scan speed, and other factors in getting proper resolution of bands

**L12.** Application of CD in macromolecular structure determination, binding studies and other applications

**Separation Methods** **4**  
**lectures**

**L13–16.** An introduction to chromatographic separation, Gas Chromatography, Pressure Liquid Chromatography and FPLC, Supercritical fluid chromatography

**Nuclear Magnetic Resonance Spectroscopy** **10**  
**Lectures**

- L17-19.** Theory of NMR: Quantum description, Classical description – Precessional motion, Larmour frequency, Relaxation processes, T1 and T2 and their measurement. Fourier Transform NMR: Pulsed excitation, FID, Types of NMR Spectra – Wild line and high - resolution spectra.
- L20-21.** NMR Spectrometers: Instrumentation. Environmental Effects: Types, Chemical shift theory, Magnetic anisotropy,
- L22-24.** Spin–spin splitting, first order and second order spectra, Double Resonance Techniques, Proton on heteroatom. Application of proton NMR: Identification of compounds.
- L25-26.** Introduction to <sup>13</sup>C NMR: Proton decoupling: Broad band, off-resonance, Pulsed decoupling, NOE, application to structure determination.

**Magnetic Resonance Imaging: 6**  
**Lectures**

- L27-28.** The concept of MRI, BOLD imaging, fMRI,  
**L29- 30.** Application in Muscle Physiology, functional mapping of brain.  
**L31-32.** Other nuclei : <sup>31</sup>P, <sup>19</sup>F, <sup>23</sup>Na, <sup>15</sup>N, metabolomics studies using NMR

**Mass Spectrometry 6**  
**lectures**

- L33-35.** Introduction to mass Spectrometry. Forming charged particles: Electron impact (EI) and Chemical Ionization(CI), Fast Atom Bombardment (FAB), Field Desorption (FD), Electrospray Ionization, Matrix Assisted Laser Desorption Ionization (MALDI).
- L36-37.** Mass Analyzers: Magnetic sector mass spectrometers, Double focusing mass spectrometers, Quadrupole pole mass spectrometers, ion cyclotron resonance, Time of Flight mass analyzers. Combine the mass spectrometer with Gas Chromatography (GC/MS) and with liquid chromatography (LC/MS).
- L38.** Applications of mass spectrometry in Biomedical field- Peptide mass fingerprinting, protein sequencing using MASS spectrometry.

**Flow Cytometry, Magnetic Assisted Cell Sorting: 4**  
**lectures**

- L39.** Introduction to flow cytometer: Need and versatility of FACS. Fluidics and Optics in FACS
- L40& 41.** Filters and detectors in FACS: choosing the right fluorochromes, compensation of overlapping emissions
- L42.** Plotting of data in various formats (Histograms/dot plots/ contour plots) Gating, Principles of cell Sorting by FACS and MACS

**Miscellaneous TECHNIQUES 5**  
**Lectures**

- L43.** Confocal Microscopy: Applications in Cell Biology, Electron Microscopy,  
**L44-46.** Tracer Techniques in Biology: tumor diagnosis and imaging, infectious diseases

such as tuberculosis.

**L47-48.** Biomolecular Structure determination techniques: X-Ray crystallography.

**Tutorial classes/class tests/ discussion periods  
lectures**

**12**

### **Course Learning Outcomes**

- The students of the course will be able to learn theoretical basis of various analytical and biomedical techniques. They will be trained in spectroscopic techniques such as UV-Visible, Infrared, Fluorescence, Circular Dichroism and their applications in the field of Biomedical Analysis.
- Students will learn analytical separation techniques such as Gas Chromatography, High Performance Liquid Chromatography, Supercritical Fluid Chromatography.
- Students will understand theoretical basis of Magnetic Resonance Spectroscopy (MRS) as well as Imaging (MRI). They will be able to understand the application of NMR in the field of drug analysis and diagnosis using MRI etc.
- Students will also learn about MASS spectroscopy and its application in the field of analytical and biomedical research. Students will be able to solve structures of small drug molecules based on analytical data based on IR, NMR and MASS spectroscopic techniques.
- Students will be able to analyse and interpret results obtained from fluorescence assisted flow cytometry (FACS), confocal microscopy and tracer techniques in this field.

### **Reading List**

- 1 Spectrometric identification of organic compounds by Robert M. Silverstein and Francis X. Webster; Ed. 6<sup>th</sup>; John Wiley; 1997.
- 2 Principles of instrumental analysis by Douglas Skoog and F. James Holler and Timothy A. Nieman; Ed. 5<sup>th</sup>; Saunders; 1998.
- 3 Contemporary instrumental analysis by Kenneth A. Rubinson and Judith F. Rubinson; Prentice Hall 2000.
- 4 Organic spectroscopy by William Kemp; Ed. 3<sup>rd</sup>; Palgrave; 1991.
- 5 Basic one and two dimensional NMR spectroscopy by Horst Friebolin; Ed.3<sup>rd</sup>; Wiley-VCH; 1998.
- 6 Principles of Fluorescence Spectroscopy by Lacowicz, 3<sup>rd</sup> Ed. 2006, Springer US.
- 7 NMR and its applications to living systems by David G. Gadian; Ed. 2<sup>nd</sup>; Oxford; 1995.
- 8 Structure determination of organic compounds: tables of spectral data by E. Pretsch and P. Buhlmann and C. Affolter; Springer; 2005.
- 9 MRI principles by Donald G. Mitchell; W S Saunders; 1999.
- 10 HPLC: a practical user's guide; Ed.2<sup>nd</sup> by Marvin C. McMaster; Wiley-Interscience; 2007.

### **Practicals**

**Course: ANALYTICAL & BIOMEDICAL TECHNIQUES AND INSTRUMENTATION  
Semester IIIrd**

## Credits 2

1. To verify Lambert Beer's law and calculating concentration of unknown analyte
  - a. using UV-VIS spectroscopy.
  - b. Fluorescence spectroscopy
2. To study interaction of intercalating agents like ethidium bromide with DNA using:
  - a. UV –visible spectroscopy.
  - b. Fluorescence spectroscopy.
3. Studying and analysing CD spectrum of a protein
4. To study the Conformation change of Biomolecule using CD spectroscopy.
5. Infra-red Spectroscopy. Recording and interpretation of IR of a metabolite.
6. HPLC- introduction to the working of the instrument and analysis of a sample. Calculating concentration of unknow sample from standard surve
7. Separation of two samples using HPLC using isocratic and gradient mobile system.
8. Mass Spectroscopy: Identification of a biopolymer using MALDI/ LC-MS.
9. NMR: <sup>1</sup>H and <sup>31</sup>P spectroscopy of muscle physiology during exercise and calculation of pH change from spectra.
10. Spectral Identification of a simple organic compound/metabolite/drug. (two examples)
11. Flow Cytometry:
  - a. Cell cycle analysis
  - b. To monitor real time influx in intercellular calcium levels

## Course specific learning outcome (Practicals)

- At the end of this course student will be able to able to instruments such as UV-VIS, Fluorescence and CD spectrophotometer.
- They will be able to analyse samples using HPLC and flow cytometer.
- The students will also learn how to analyse characterization data of given unknown compound and interpret its structure from the data.
- They will also learn to study the biomolecular interactions using the spectroscopic techniques, analysing secondary structure of a biomolecule etc.

# MOLECULAR ONCOLOGY

ELECTIVE paper in III semester

Credits 4 (4+0+0)

*Preamble: With increase in incidence of cancer in our country, it is considered important to have a basic background of molecular basis of cancer. The students will be taught various risk factors and types of cancer. Basic concept of mechanism of carcinogenesis will be taught wherein important proteins and pathways will be taught. At the end of the course some of the research papers related to these topics will be presented and discussed in the class.*

## **The Cancer Problem**

**L1:** Introduction to Cancer, Global and Indian incidence, various types of cancers, Epidemiology,

**L2:** Environmental carcinogens, chemical and physical carcinogens types with examples.

**L3:** Various risk factors, life style, changing patterns, the Indian scenario.

## **Mechanisms of Carcinogenesis**

**L4:** Various theories, multi-step and multistage processes, concept of transformation

**L5:** Initiation, Promotion and Progression of cancer.

**L6:** Role of DNA damage, repair and mutations by physicochemical agents and viruses,

**L7:** Interaction of various agents in cancer

**L8:** Differentiation: hyperplasia and precancerous lesions. Strategies of chemoprevention.

## **L 9: TUTORIAL CLASS**

**L10: TEST (10marks)**

## **Tumor types and leukemia**

**L11:** Benign and malignant tumors, localized and metastatic disease

**L12:** Schemes of classification, WHO classification, staging and grading, degree of malignancy.

**L13:** Introduction to leukemia, Classification of leukemia, types of chromosomal translocations. Examples of common types based on prevalence.

**L14:** Diagnosis of leukemia (Flow cytometric method, qPCR).

## **Modulation of the Eukaryotic Cell Cycle and cell death in cancer**

**L15:** Cell cycle and check points, role of kinases,

**L16:** Mechanism of deregulation of cell cycle during cancer. Various proteins involved and their mechanism

**L17:** Apoptosis, **and** Necrosis regulation in normal cell and dysregulation in cancer

**L18:** Proapoptotic and Antiapoptotic proteins and mechanism of action in controlling apoptosis.

**L19:** Methods used to study apoptosis (western, Flow cytometry, tunnel assay)

**L20:** methods contd, Cellular senescence

**L21: TUTORIAL CLASS**

**L22: CLASS TEST 2 (Marks 10)**

### **Cell-cell Interactions in Development of cancer**

**L23:** Cell-cell interaction, integrins, and other proteins involved in cellular adhesion.

**L24:** Concept of invasion, changes in cellular proteins.

**L25:** Mechanism of invasion by cancerous cells.

**L26:** Metalloproteases and their role in cancer metastasis

**L27:** Methods to study invasion in vitro.

**L28:** Tumor microenvironment, interaction between malignant and normal cells

**L 29:** Research papers presentation

**L30** Research Papers presentations and Discussion

**L31:** Test based (Marks 10)

### **ANGIOGENESIS:**

**L32:** Angiogenesis and various factors involved in angiogenesis

**L33:** Molecular mechanism of angiogenesis

**L34:** Concepts and molecular mechanism of Neoangiogenesis in cancer

**L35:** Methods to study angiogenesis.

**L 36: Tutorial Research papers discussion on angiogenesis**

### **Tumor suppressor genes and Viral oncogenes**

**L37:** Concept of tumour suppressor proteins and oncoproteins. transformed cells and immortal cells.

**L38:** Mechanisms of action of P53 in cancer

**L39:** Mechanisms of action of P53 in cancer contd

**L40:** Role of other members of p53 protein in cancer

**L 41:** Tutorial on Research papers discussion related to P53 isoforms.

**L42:** Role of RB proteins in cancer

**L43:** Altered mechanisms of action of Rb protein in cancer cells

**L44:** Other tumour suppressor proteins, BRCA1, BRCA2, APC and WT1, Mismatch repair proteins

**L45:** Oncoproteins and their examples, Basic concept of proto-oncogene, discovery, gain of function mutations etc. methods to identify.

**L46:** Role and mechanism of viral oncogenes with 1-2 examples.

L47: understanding the role of large T antigen, HPV in cervical cancer.  
L48: Role of cellular oncogenes in altered gene regulation (basic mechanisms of action)  
L49: Mechanism of action of oncogenes contd using specific examples: jun-fos, Ras  
L50: condn. AML-ETO etc in gene regulation.

**L51: Research paper presentations and discussion**  
**L 52: Research paper presentations and discussion**  
**L 53 Research paper presentations and discussion**  
**L54: Test (Marks 10)**

#### **Growth factor-signalling pathways in cancer**

L55: Relationship between oncogene products and growth factors,  
L56: Understanding altered pathways using example of receptor kinases, Src, Wnt signalling  
L57: Abl, cKit, Rho and Ras factors  
L58: GAP and growth factors.  
L59: Effect of viral infection on signal transduction.  
L60: Tyrosine kinases and inhibitors

L 61: **Research paper presentations and discussion**  
L62: **Research paper presentations and discussion**  
L63: **Research paper presentations and discussion**

#### ***COURSE OUTCOME:***

***By the end of the course students will be familiar with common carcinogens and how life style can contribute to increase in cancer incident. They will also be aware of various steps and different mechanisms that form the basis of differences in cancer progression and drug response. A basic understanding of various techniques that can be used so as to decipher these pathways and to identify the proteins involved in cancer will help them in pursuing research in this important area.***

**Stem Cell Biology for developmental and translational research  
(III Semester Elective Course, Credits 3+1)**

*Members of the sub-committee: Dr. Manisha Yadav, Dr. Richa Arya, Prof. Vani Brahmachari.*

*Feedback received from: Dr. Maneesha Inamder, JNCASR, Dr. Jyotsna, InStem, Prof. B.C. Das*

*Preamble: This course is conceived in the light of relevance of stem cells to biomedical research. The natural process of development is the journey of living organisms from totipotency to pluripotency and further to differentiation towards functional specialization to make a complex and self-propagating system. Therefore the course begins with the concepts of developmental biology, the unification of molecular mechanisms across phyla is emphasised. The course tries to bring out how this knowledge also gives us the ability to reverse the process to address important aspects of human health.*

*Course outcome:*

- The students will gain an understanding of common theme and the varied strategies of development that nature has evolved by the comparison between different systems*
- The students will be aware of the characteristics of stem cells and the limitations in the use of stem cells.*
- They will appreciate how nature has preserved the mechanisms invented at various stages of evolution.*
- They will be aware of the tools used in stem research, the ethical issues involved in the application of stem cell usage in medical research.*
- Throughout the course the students will be exposed to original papers that led to the various discoveries that have kindled the enthusiasm and hope of use of stem cells in health sciences.*

**L1 - 3: Introduction:** what are stem cells ( embryonic stem cells, adult stem cells, iPS), History of stem cell research, Differentiated cell vs stem cells, What determines stemness, scope of stem cells to cure disease, Early experiments on stem cell and regeneration. Cloning and aging issues (Dolly, etc..), what we do not know about stemness (discussion to introduce importance of learning developmental biology).

**Journey from stemness to differentiation I;**

**L4- 5: Insights from Drosophila model:** Early embryonic development, Maternal inheritance, **L6-8:** Genetic basis of axis determination, pattern formation, regulatory cascade in development in Drosophila,

**L 9 & 10:** Homeotic genes and their regulation.

**L11-12-Student Seminar**

**Journey from stemness to differentiation II;**

**L13-14: Amphibian development:** Xenopus development as a model, Salient feature of amphibian development

**L15:** Positional information in development- the 'Organizer ' concept, cell-cell interaction in development,

**L16-17:** Concept of morphogen gradients, their generation and effect on development.

**Journey from stemness to differentiation III;**

**L18-19; Mammalian development:** Salient features of Mouse and Human embryonic development as examples of regulated development, generation of mosaic embryos.

**L20:** Pattern formation example of limb development.

**L21-22: Conservation of pathways of development and differentiation** across phyla with example; Notch, Wnt, Hippo, discovery and evolutionary conservation (the teacher may choose one of the examples to illustrate the concept)

**L23-25: Molecular basis of stem cell** renewal and differentiation, Metaplasia and trans-differentiation. Molecular basis of pluripotency and stem cell niche and reprogramming.

**L26-27- Student Seminar**

**L28-31: Reversing differentiation by reprogramming:** (i) Developmental reprogramming, regeneration "Young all the Time!"; Planaria, Hydra, earthworm. Induced pluripotent Stem cells (iPSCs).

**L32-35: Overview of tools for stem cell research:** Isolation & characterizations, markers & their identification, growth factor requirements and their maintenance in culture. Cell cycle regulators in stem cells

**L36-38: Ethical issues** related to stem cell research; Ethics in use of stem cell, regulatory bodies for use of material for human need, commercial developments and stem cell based products, bio-vigilance, Stem cell regulatory aspects in international and Indian context.

**L39- 42: Bench to Bedside using naturally occurring stem cells and induced pluripotent stem cells** – Discuss research papers on the advancements in the field

**L43- 46:** Group discussion on Topics discussed and Paper presentation by students

2 hours for tests.

**Books:**

1. David Warburton, Stem Cells, Tissue Engineering and Regenerative Medicine, 2015, World Scientific.
2. Sell Stewart, Stem Cell Handbook, 2013, Humana Press.
3. R. Lanza, I. Weissman, J. Thomson, and R. Pedersen, Handbook of Stem Cells, Volume 1-2: 2012, Academic Press.
4. R. Lanza, J. Gearhart et al (Ed), Essential of Stem Cell Biology, 2009, Elsevier Academic press.
5. A. Naggy, N. Habib, M.Y. Levicar, L.G. Jiao and N. Fisk: Stem Cell Repair and Regeneration. Volume-2, 2007, Imperial College Press.

6. R. Lanza and I. Klimanskaya, Essential Stem Cells Methods. (2009), Academic Press.
7. Developmental biology by Scott F. Gilbert; Ed.8th; Sinauer Associates; 2006

## **NEW PAPER: NEW METHODS IN ORGANIC SYNTHESIS**

### **Elective Paper:**

**Credits 3**

The course aims at understanding the methods by which chemically and biologically important molecules and macromolecules are synthesized and characterized. This course includes an overview of nucleotide synthesis, peptide synthesis alkene metathesis, green chemistry and total synthesis of pharmaceutically beneficial compounds.

#### Methods in nucleotide synthesis

- L1 - Advantage of chemical synthesis
- L-2- Protecting groups
- L-3 nucleoside3-phosphoramidates
- L-4 solid phase synthesis
- L-5 Oligonucleotide synthesis cycle
- L-6 Automated oligonucleotide synthesizer
- L-7 DNA microarrays
- L-8 Light directed chemical synthesis
- L-9 Microarray synthesis using micro mirrors
- L-10 Structure validation

#### Methods in peptide synthesis

- L11 solid phase synthesis
- L12 Protecting groups/deprotection
- L-13 structure validation

#### Alkene metathesis

- L-14 Mechanism
- L-15 Metal carbenes
- L-16 Schrock's catalyst
- L-17 Grubb's catalyst
- L-18 Ruthenium catalysts
- L-19 Ring closing metathesis
- L-20 Cross metathesis
- L-21 Polymerization
- L-22 Ring closing metathesis of small rings
- L-23 Ring closing metathesis of medium rings
- L-24 Macrocyclization

#### Green chemistry

- L-25 Introduction
- L-26 Atom economy

- L-27 Less Hazardous synthesis
- L-28 Designing safer chemicals
- L-29 Design for energy efficiency
- L-30 Design for degradation
- L-31-32 Relevant examples
- L-33-38 Relevant examples of total synthesis
  
- L-38-48 Tutorials/tests/student seminar

# **ADVANCED IMMUNOLOGY**

**Semester: III**

**Elective Paper**

**Credits: 3+1**

**Credits: 60 Lectures**

## **Preamble**

The course on Advanced Immunology is offered as an Elective paper in the IV semester that builds on the basics taught in the Immunology (MBS204) paper in the II semester. The course begins with a recap on the basics of immunology and immune responses. Emphasis is laid on the recent advances in each aspect of immunology by constant references to peer reviewed papers published in high impact factor journals. Further, eminent scientists working in leading institutes like NII, ICGEB and AIIMS are invited to give lectures on certain topics that have been already covered by teachers.

## **Course Outcome**

At the end of the course the student will have:

1. A detailed knowledge of T cell differentiation, activation and regulation.
2. Appreciated the difference between systemic and mucosal immune responses.
3. The ability to design experiments critically following the experience they have gained via presenting papers in seminars.
4. Knowledge of the nuances of immune responses to various infections and the qualitative and quantum roles of inter-cellular and intracellular molecules.
5. Understanding on the reasons of weaker immunity displayed by aged individuals compared with young individuals to newer and older infections.

6. Thus, after finishing the course a student is well trained in all the aspects of immunology and how the body reacts and responds to invading pathogens and other antigenic stimulations.

## **Detailed Contents**

### ***Introduction and Recap of Basic Immunology***

L1: Introduction to the Immune system

L2: Adaptive and innate immunity: regulation by Immunoglobulin gene expression, Immunoglobulin loci, TLRs, complement, diversity via gene translocation at Ig loci

L3: Factors regulating immune effector functions

L4: Structure, Function & Antigen processing on MHC class I and MHC class II, factors governing peptide binding, loading and presentation to T cells

L5: Pathogen Interface with Antigen Presentation

### ***T Cell Differentiation, Activation and Functions***

L6: Differentiation of T cells: TCR gene recombination, regulation and function therein. Positive and Negative selection of T cells

L7: Factors regulating T cell diversity and cross-reactivity

L8: T cell migration and turnover

L9: Role of costimulatory molecules in T cell selection

L10: T cell functions during various immune responses

L11: Signaling from innate, B cell and T cell receptors: avidity vs affinity of the interactions

L12: T cell response generation and magnitude of the immune response

L13: Heterogeneity in CD4 and CD8 T cell population. CD4 T cell subsets and functions. TH1/TH2/TH9/TH17/Tfh subsets and functions in immunity and disease

L14: Hybridoma vs T cell clones vs transgenic vs Knockout mice: applications thereof

L15: Regulatory T cells and fine-tuning of immune response

L16: Solutions and compromises of studying T cells response

L17: T cell memory and short-term and long-term immunity

### ***B Lymphocyte Differentiation, Activation and Functions***

L18: Differentiation of B lymphocytes

L19: Activation of B cells by Antigens and modulations by costimulations

L20: Memory B cell responses, turnover and regulation

### ***APC-T Cell Interactions via Costimulation and Immune Synapse***

L21: Costimulatory networks in immune response building and maintenance

L22: Positive and negative costimulation by various molecules during building up, maintenance and termination of immune response

L23: Immune synapse and regulation of immune response to pathogens

### ***Mucosal Immunity and Allergy***

L24: Introduction to Mucosal immunity vis-à-vis systemic immunity

L25: Intrinsic and extrinsic factors affecting immunity at mucosal surfaces

L26: Exploitation of gaps and weaknesses in the mucosal immunity by pathogens

L27: Mucosal vaccines and diseases

L28: Allergy and hypersensitivity reactions during an immune response

L29: Striking a balance between immunity to infections and allergy

### ***Immunity to pathogens***

L30: Immunity to Mycobacteria

L31: Immunity to *Streptococcus pneumoniae* and pneumonia vaccines

L32: Immunity to HIV: Pitfalls of immune-deficiency

L33: Immunity to *Salmonella*: Current trends and future perspectives

### ***Regulation and Deregulation of Immune Responses***

L34: Systemic and organ specific Autoimmunity

L35: microRNAs in regulating immune responses and protozoan immunity

L36: Aging and Immunity and Immune-senescence

L37: Role of Autophagy in mediating immune responses

### ***Transplantation and Tumor Immunology***

L38: Transplantation immunology and MHC restriction

L39: Immunity to cancers/tumors vs long-term persistent infections: similarities and differences

### ***Immuno-Therapeutics and Vaccines***

L40: Alternative approaches to chemotherapy via immune-therapeutics and tweaking of the immune system

L41: Vaccines: short-term and long-term protection: inbuilt mechanisms of innate and adaptive memory.

### ***Organogenesis and Lymphoid Development***

L42: Organogenesis of secondary lymphoid organs: Overview of the immune system, localization of the lymphoid organs in the body, mouse and human.

L43: The gross anatomy and functional relevance of lymphoid organs.

L44: Review of Timeline based experiments (literature) of development of Peyer's patches

L45: Review of Timeline based experiments(literature) of development of lymph nodes

L46: Literature review of Early and late patterning of lymphoid genes

L47: Lymphotoxin signalling and secondary lymphoid organ development analysis of NALT, MALT, Peyer's patches and lymphnode.

### **L48-L60: Seminars/Tests/Discussions**

#### **Suggested Readings**

##### **Books**

1. *Fundamental Immunology* William Paul (Ed) 2017. Lippincott Williams & Wilkins.

##### **Journals (Latest volumes)**

1. Nature Reviews Immunology
2. Nature Medicine
3. Nature Immunology
4. Immunity
5. Cell Host and Microbe
6. PLoS Pathogens
7. Journal of Experimental Medicine
8. Journal of Immunology
9. PLOS Pathogens
10. Infection and Immunity
11. Journal of Infectious Diseases
12. Journal of Infection

# MEDICAL VIROLOGY AND MYCOLOGY

**Elective paper**

**III Semester**

**Credits: (4+0)**

**60 lectures**

## **Preamble**

*Medical Virology and Mycology is one of the elective courses for the biomedical sciences students. Students will gain insights on the nature of various infectious agents and diseases pathologies caused by common fungi and viruses. In addition, they will also understand pathogenesis, diagnosis, clinical features, virulence factors and treatment strategies of medically important fungi and viruses. The structure and function of medically important viruses such as Dengue and Chikungunya viruses will also be studied. In addition the detail study of human fungal infections such as fungal Eye, Nail and Skin Infections will de studied in detail.*

## **Detailed Contents**

### **MEDICAL VIROLOGY**

- L1-2.** Concept of viroids, virusoids, satellite viruses and prions. Theories of viral origin.
- L3-10.** Detail study of DNA Viruses: for eg. Small pox, Herpes viruses, Human Papilloma viruses, Parvoviruses, adenoviruses, chickenpox, Papova viruses, Hepatitis virus
- L11-17.** Detail study of RNA viruses: for eg. HIV, Influenza virus, poliovirus, Reoviruses, Rhinovirus, Ebola virus, Enterovirus.
- L18-20.** Zika virus, Dengue and Chikungunya viruses and emerging viruses will be studied.

### **Reproduction and Growth**

- L21-22.** DNA virus transcription and replication, Positive-strand RNA virus replication, Negative-strand RNA virus replication.
- L23.** Regulation of retrovirus replication.
- L24.** Virulence factors and evasive strategies of viruses.
- L25-26.** Use of viral vectors in cloning and expression, current uses of viruses in gene therapy and vaccine applications.

## **Epidemiology and Pathogenicity**

- L27-28.** The prevalence and distribution of various viral infections in the world will be covered. Tools to study epidemiological data and their analyses will be discussed.
- L29.** Pathogenesis caused by structural, nonstructural and envelop proteins will be discussed.

## **Diagnosis, Treatment and Prevention**

- L30.** The conventional and current methods of diagnosis of the infections will be discussed along with the limitations. Alternative strategies towards developing newer tools and technologies in developing diagnostic platforms will be covered.
- L31.** The current modes of treatment and alternative strategies to combat viral infections in lieu of increased reports of resistance will be covered in detail.
- L32-34.** Antiviral compounds, interferons, designing and screening for antivirals, mechanisms of action, antiviral libraries, antiretrovirals-mechanism of action and drug resistance.

## **Immunity to viral infections**

- L35-36.** The immune responses, both innate and adaptive will be extensively covered. As a prelude the intricacies involved in host-pathogen interactions at the cellular and molecular levels will be discussed in detail. This will include the involvement of cell surface receptors on the pathogen and the host cell and their interactions.
- L37-38.** Signal transduction from the pathogen receptors and the immune evasion strategies evolved by different viruses will be discussed.

## **MEDICAL MYCOLOGY**

### **Introduction**

- L39.** Fungi and their significance, Relationship of fungi with plants and animals, Milestones in mycological and pathological studies.
- L40-41.** Fungal cell-structure and composition, Physiology of fungal growth, Ecological groups of Fungi, Fungal spores, Molecular method of fungal taxonomy, Fungi as model organism for genetic studies.

### **Detail study of human fungal infections**

- L42-50.** Cryptococcosis, Candidiasis, Blastomycosis, Aspergillosis, Blastomycosis, Histoplasmosis, Coccidiomycosis, Mucormycosis. Pneumocystis pneumonia
- L51-52:** Fungal Eye, Nail and Skin Infections, Central nervous system.

## **Prevention and control of fungal diseases**

**L53-55.** Antifungal Therapeutic Agents. Fungal allergies and types of Mushroom Poisoning and other Mycotoxins. Prognosis and Treatment.

## **L56-60. Student seminar/Discussions/Tests**

### ***Course outcome***

*Students will gain insights on the nature of various infectious agents and diseases pathologies caused by common fungi and viruses (for eg. Candidiasis, aspergillosis small pox, HPV etc.) The students will be able to understand the structure and function of medically important viruses such as Zika, Dengue and Chikungunya viruses. They will also understand pathogenesis, diagnosis, clinical features, virulence factors and treatment strategies of medically important fungi and viruses.*

### **Reading list:**

1. Fundamental Virology: Fields and Knipe, ed. Raven Press, 1991
2. Strauss, E. G. and Strauss, J. H., "Viruses and Human Disease", Academic Press, 2002
3. Antiviral Drug Discovery for Emerging Diseases and Bioterrorism Threats. Paul F. Torrence (Editor), Wiley, John & Sons, Incorporated. 2005
4. Vaccines. Stanley A. Plotkin, Walter A. Orenstein. Elsevier Health Sciences 2003
5. Flint, S.J., Enquist, L.W., Krug, R. M., Racaniello, V. R., and Skalka, A. M., "Principles of Virology: Molecular Biology, Pathogenesis and Control", ASM Press. 2000
6. Microbiology by Lansing M. Prescott and John P. Harley and Donald Klein; Ed. 6th; McGraw-Hill Science, 2004.
7. Medical microbiology: a guide to microbial infections: pathogenesis, immunity, laboratory diagnosis and control by David Greenwood and Richard C. B. Slack and John F. Peuthere, ed. 17th Ed. Churchill Livingstone; 2007.
8. Essentials of diagnostic microbiology by Lisa Anne Shimeld and Anne T. Rodgers; Delmar Publishers, 1999.
9. Medical Microbiology by Geo. Brooks and Karen C. Carroll and Janet Butel and Stephen Morse; Ed. 24th; McGraw-Hill Medical, 2007.
10. Topley and Wilson's Microbiology and Microbial Infections by Leslie Collier and Albert Balows and Max Sussman; Ed. 9th; 6-Volume Set; A Hodder Arnold Publication, 2000.

## **ADVANCE TOXICOLOGY**

**Elective Paper**

**IV<sup>th</sup> semester**

**Credits (3+1=4)**

**Preamble:**

*Understanding about the basic toxicological principles, adverse drug reaction and therapeutic drug monitoring, risk assessment/safety assessment, metabolism for inducing toxicity and different mechanisms for drug, toxicological substances, heavy metal and pesticide. The student is expected to own such knowledge and skills on completion of the course that she/he in an independent way can process and present different problems within the subject area.*

### **ADVERSE DRUG REACTION AND THERAPEUTIC DRUG MONITORING**

**L1-L4:** Classifications, adverse interactions, and pharmacokinetic drug interactions, spontaneous case reports, and Adverse drug reaction reporting and management; human risk assessment, Toxicological database. Need for Therapeutic Drug Monitoring, factors to be considered during the Therapeutic Drug Monitoring. Adverse drug reactions and therapeutic drug monitoring.

**L5:** General concepts of Toxicovigilance, National poison information centres and poisoning management.

**L6:** Concepts of Toxicogenomics and personalized medicine

**L7-8: TUTORIALS**

### **TOXICOLOGY OF HEAVY METALS**

**L9-L13:** Source, exposure, absorption, target site interactions and health hazards of Metallic Pollutants Mercury, lead, arsenic, cadmium, Chromium.

**L14-L15:** Mechanisms of heavy metal toxicity- Induction of metallothionein, heat shock proteins, cytoskeletal effects, lipid peroxidation, Metal protein interaction, metal nucleic acid interactions.

**L16:** Source, exposure, absorption, target site interactions and health hazards of Fluoride.

**L17-L18:** Source, exposure, absorption, target site interactions and health hazards of trace elements- Iodine, iron, zinc, copper, manganese, selenium, molybdenum, and cobalt.

**L19:** Eco-toxicology of heavy metals- Case studies of Lead, arsenic, mercury and cadmium.

**L20-L21: TUTORIALS**

## **TOXICOLOGY OF PESTICIDES**

**L22-L23:** Pesticides: Brief classification with examples, residual and non-residual pesticides. Mode of entry and mode of action of pesticides in target and non-target organisms.

**L24-L25:** Ecotoxicology: Impact of pesticides residues on ecosystems, non-target organisms; Pesticide bioaccumulation, biomagnification through food chain

**L26-L27:** Environmental alteration of pesticides - microbial and solar, fate and dissipation of pesticides residue under tropical and temperature conditions.

**L28-L29:** Pesticide hazards to man Accidental and occupational exposure, entry through air, food and water, Residue levels in man: Indian experience Vs developed countries; Residues in tissues and organs – distribution and redistribution; Pregnancy and transfer to fetus.

**L30:** Environmental problems by organochlorine pesticides- Case studies of DDT, endosulphan, benzene hexachloride (Lindane).

**L31:** Environmental problems by organophosphate pesticides- Case studies of parathion, and malathion.

**L32:** Toxicity of pesticides in man- Case studies, Handigodu syndrome, Benzene Hexachloride poisoning in Turkey, and endosulphan toxicity in Kerala.

**L33-L34: TUTORIAL**

## **APPLIED TOXICOLOGY**

**L35-L36:** Cosmetic toxicology (General overview): Toxicity of shampoos, conditioners, bleachers, dyes, allergic and respiratory disorders.

**L37-L38:** Forensic toxicology (General overview): Specimen sample collection, types of testing, detection of poisons, applications of forensic toxicology

**L39-L40:** Toxicology of chemical warfare agents-(General overview): Chemical weapons, mustard gas, lewisite, nerve agents, hydrogen cyanide, management of chemical warfare agents.

**L41:** A brief review of Radioactive hazard

**LL42: TUTORIAL**

## **OCCUPATIONAL AND INDUSTRIAL TOXICOLOGY**

**L43-L44:** Brief review of Occupational hazards and diseases- Pneumoconiosis, silicosis, asbestosis, anthracosis, byssinosis, bagassosis, Farmers' lung, Skin cancer, Lung cancer, Bladder cancer, Leukemia.

**L45:** Industrial toxicology- History and basic features, Industrial hygiene, Risk assessment – Risk assessment for industrial chemicals in EU, OECD and USA.

**L46:** Concepts of Industrial hygiene, Threshold Limit Value and Occupational Safety Health Administration etc.

**L47:** Preventive toxicology- Bioremediation and Toxic site reclamation

**L48: TUTORIALS**

## **TOXICOKINETICS AND MOLECULAR MECHANISMS OF TOXICITY**

**L49-L50:** Toxicokinetics: Absorption, Distribution, and Excretion of xenobiotics; metabolism of pesticides, phase I and phase II reaction, elimination.

**L51-L53:** Molecular Mechanisms of toxicity– Reaction of toxicants with target molecules, Toxicological consequences of oxidative stress, Oxidative stress and protein, DNA and lipid damage, Disturbances in calcium homeostasis , Toxicological consequences of increased intracellular calcium concentrations; Disruption of cellular energy production – Mitochondrial targets, Inhibition of NADH production, Inhibition of electron transport change; Brief description of Necrotic and apoptotic cell death.

**L54: TUTORIAL**

## **DRUG SAFETY**

**L55-L56:** Principles of risk assessment and the role of safety pharmacology in the drug development process and the methodology associated with drug evaluation.

**L57-L58:** Regulatory toxicology: Regulatory agencies, Regulation of pesticides, pharmaceuticals, and food additives; Narcotic Drugs and Psychotropic substances Act-1985 and Rules. Drugs and cosmetic acts; Food and Drug Administration, Organization of Economic Corporation Development, International conference on harmonization, Schedule Y: Design non-clinical toxicity studies and clinical development. Clinical risk/benefit analysis.

**L59-L60:** Concept of Good Laboratories Practices, Good Manufacturing Practices, good Clinical Practices.

**L61: TUTORIAL**

## **READING LIST**

1. Casarett and Dull's toxicology: the basic science of poisons by Curties D. Klaassen; Ed. 7th; McGraw Hill; New York; 2007.
2. Toxicology by Hans Marquardt and S.G. Schafer and R.D. McClellah and Academic Press; 1999.
3. Principles and practice of toxicology in public health by Ira R. Richards; Jones and Bartlett Publishers; 2007.
4. Handbook of human toxicology by E.J. Massaro; CRC Press; 1997.
5. Schedule Y, ICMR guidelines
6. OECD Guidelines.

## **Course outcome**

*After completion of the course students will be able to develop the awareness of general principles of environmental, occupational toxicology including toxicovigilance; demonstrate in-depth knowledge of the interaction between exposure to exogenous chemicals and toxic effects in humans. Students are able to demonstrate a good ability to independently find, summarize and assess scientific information within the field of toxicology, and to be able to use this information in other problems and in assessing the health risks of chemical substances. Students develop awareness about adverse drug reactions, therapeutic drug monitoring and Forensic Toxicology.*

## Genome Biology

(Elective course: Credits 3+1)

*Revised course*

*Members of sub-committee: Dr. Richa Arya, Dr. Ankita Narang, Prof. Vani Brahmachari.*

*Feedback from: Dr. Mitali Mukheri and Current batch Student's feedback taken*

**Preamble:** *This course would be offered as an optional course in the IV semester for M.Sc. Biomedical Sciences. Students have a background in basic genetics and molecular biology. The course is meant to communicate the excitement in modern biology attributable principally to the tools for whole genome analysis and the genome sequencing that has come about over the last ten years or so. It is well known from the beginning that biological systems are amazing network of interacting molecules, macro and micro, but till recently it did not appear tractable for experimentation and analysis. But there are a faint signs of this comprehensive understanding due to the various technological advances, including the birth of "Systems Biology". But so far the science of Genome biology is in a phase of amassing large body of data using high-through-put techniques at DNA, RNA and protein level. Along with high end computing this knowledge should logically pave way to integration and hence to understand biological systems comprehensively. The Genome Biology course is an attempt to induce the curiosity of the students to venture in to these areas in their future research endeavours.*

**Course outcome:** *At the end of the course the students are expected to develop an appreciation for the groundwork carried out in genome research so far, relate to how it has been built on the numerous genetic studies carried out over decades on several model organisms that continue to contribute to the understanding of relationship between genotype and phenotype. The time is poised for understanding human as a model organism.*

- *The students will be able to understand the complexity of genetic inheritance in humans, beyond Mendelian genetics.*
- *The dependence of human genetics on statistical analysis. They will be familiar with the statistical tools used in genomic data analysis, linkage analysis by LOD score, association studies.*
- *They will know the methods used for whole genome analysis and their applications*
- *They will be able to use various databases containing annotation, experimental data from NGS, RNA seq and microarray and ENCODE.*
- *The students will be trained to read and critically evaluate research papers from journals.*

### **L1: Introduction:**

Overview of genomics. To highlight how biology is a network of interactions direct and indirect. What is the difference between genetics and genome biology? The transition from reductionist to comprehensive approach in understanding biological systems.

**L2-L4: Human genetics in pre-genomic era: Pedigree Analysis and deviations from basic pedigree patterns:**

1. Pedigree analysis and its relevance;
2. Deviations from the basic pedigree patterns- non-penetrance, variable expressivity, pleiotropy, late onset, dominance problems, anticipation, genetic heterogeneity,
3. Recapitulation of Genomic imprinting and Uniparental disomy and its implication on genetic diseases, X-inactivation and its consequence on genetic disease inheritance.
4. Introduction to OMIM and its utilization.

**L5 & L6: Human Genome Project:**

5. History, organization and goals of human genome project; Genetic and Physical map
6. Overview of outcomes of the project and ethical issues.

**L7-L10: Whole genome mapping strategies I: Constructing Genetic maps at whole genome level.**

7. Markers for genetic maps/meiotic maps
8. Linkage analysis in humans: LOD score based
9. Genotypic and Allelic frequencies.
10. Polymorphism screening (Genotyping of SNPs and Microsatellite markers)
11. Haplotype construction (two loci using SNPs and/or microsatellites)
12. Genetic maps; Marshfield and DeCode maps.

**L11-12: Web based data analysis**

**L13-16: Whole genome mapping strategies I: Constructing Physical maps at whole genome level.**

13. Different types of Physical mapping: Restriction maps and cytogenetic maps
14. Radiation Hybrids in mapping.
15. Tools (Vectors- BAC, PAC, YAC and sequencing techniques) and approaches (Hierarchical and Shotgun sequencing)
16. Visualizing genome maps using databases: UCSC and related browsers
17. Population polymorphism: 1000 genome project and its outcome

**L17-19: Organisation of the Human Genome:**

18. General features: Gene density, CpG islands, RNA-encoding genes,
19. Gene clusters, Diversity in size and organization of genes
20. Pseudogenes, repetitive DNA.

**L20-23: Functional Genomics I:**

21. Identification of the genetic basis of diseases.
22. Top-down and Bottom- up approaches

23. Positional and Candidate Gene approaches, Positional- cloning approach  
Examples- HD, CFTR.
24. Methods for whole genome expression analysis and proteome analysis.
25. Exome sequencing: methodology and one example of its application.

**L 24-28: Functional Genomics II:**

26. Manipulation of the unborn: Generation of transgenic animals: random integration, Knock-outs, Cre-lox for tissue specific and stage specific knock outs and knock-in models
27. Genome editing techniques: Zinc finger nuclease, TALENS and CRISPR-Cas system.
28. Generating disease models using different tools.

**L29- 31: Student seminar: Research paper presentation**

**L32-33: The ENCODE project and Epigenome analysis:**

29. Phase I and Phase II ENCODE project: Theme, Tools and outcome.
30. Epigenome analysis in health and disease
31. Long-range interaction in genome architecture and their significance.

**L 32-34: Student seminar**

**L35- 37: Genomics of model organisms and comparative genome analysis.**

32. *C.elegans*
33. *Drosophila melanogaster*
34. Zebrafish
35. Mouse.

**L37-39: Student Seminar** (One disease model/fundamental discovery from each model system)

**L 40- 41: Introduction to microbiomics:**

36. Microbiome analysis
37. Microbiome as a modifier of disease phenotype, with one example.

**L42- 44: Ayurgenomics:**

38. Introduction to endophenotyping methods of individuals based on Ayurvedic principles and exploring correlation of such classification with genomics. [This does not deal with Ayurvedic medicines/mechanism of their action].

**L45- 48; Implications of Genome Research:**

39. Pharmacogenomics (Genetic polymorphism in drug metabolism genes e.g. CytP450 and GST and their effect on drug metabolism and drug response)
40. Diagnosis and screening of Genetic Disorders.
41. Implication of genomics on prenatal diagnosis of genetic diseases.

**Recommended Books:**

Authors	Title	Publisher
Strachan & Read	Human Molecular Genetics	John Wiley & Sons
Cantor and Smith	Genomics	John Wiley & Sons
Hartwell et. al.	Genetics: From genes to genomes	McGraw Hill
Mange & Mange	Basic Human Genetics	Sinauer Associates
Maroni	Molecular and Genetic Analysis of Human Traits	Blackwell Publishers
McConkey	Human Genetics: The Molecular Revolution	Jones and Bartlett
Nussbaum <i>et al</i>	Genetics in Medicine	W.B.Saunders Company
Reference book		
Speicher, Antonarakis Motulsky	Vogel & Motulsky's Human Genetics: Problems and Approaches	4th Edition Springer Verlag
Original research papers and reviews		

# NEUROBIOLOGY

**Elective paper**

**IV Semester**

**Credits: (3+1+0)**

## ***Preamble:***

*Brain is the window of a person's physical existence with surroundings and other people, it is the medium through which a person is able to communicate and express oneself. Moreover, the brain is the organ an organ which not only defines our physical identity but also makes each of us unique human being, therefore it is imperative to understand the function of the brain and it is a very complicated organ system about which we only have a superficial knowledge. This course has been designed to provide the basic knowledge at both molecular and cellular level about the human brain and it's functioning and simultaneously laying the foundation in the young minds to explore and solve the mysteries of the human brain.*

## **UNIT 1: Neural signaling at molecular level**

L1: Wnt signaling, Notch pathway: Lateral inhibition

L2: Helix-loop-helix (bHLH) proteins: proneural

L3: Sox gene expression, Transcriptional networks and silencing

**Tutorial:** Group discussion, Student seminar and test

## **UNIT 2: Neural Induction, Pattern Formation, and Cell Specification**

L4-5: Neurulation, Neural induction in chicks and humans

L6-8: Morphogens, Sonic Hedgehog and neural patterning, Floor Plate patterning of ventral cell types: Ventral Patterning, Wnt pathway and neural patterning,

L9-10: Bone morphogenetic protein (BMP) signaling in the neuroectoderm, Retinoic Acid Signaling

L11-12: forebrain development, Midrain development, hindbrain development (spinal cord)

L13-16: neural patterning, Motor neuron specification in vertebrates, Axon Guidance and Synaptogenesis

**Tutorial:** Group discussion, Student seminar and test

## **UNIT 3: Cellular differentiation**

L17-18: From Stem Cell to Unique Neuron (drosophila and human)

L19-21: macroglial lineage, dopaminergic retinal, haircell, olfactory, oligodendrocytes, Schwann cell differentiation

L22-25: Neuronal plasticity

L26-27: Synaptogenesis, plasticity for motor cortex, sensory system and higher brain functions,

L28-29: Autonomic Neuroplasticity

**Tutorial:** Group discussion, Student seminar and test

#### **UNIT 4: Neurogenesis, Neurotrophism, and Regeneration**

L30-31: Neural cell division, CNS aging, neuronal programmed cell death, autophagy, Neurotrophic factors

L-32-33: Neuronogenesis and stem cells in normal brain aging, Axonal regeneration and sprouting with emphasis on spinal cord injuries and brain trauma

**Tutorial:** Group discussion, Student seminar and test

#### **UNIT 5: Methods in neuroscience research**

L-34-36: Brain tissue isolation and preparation for Immunohistochemistry, “Multi-omic” Research

L37-39: “Multi-omic” approach for biomarker studies

L40-42: Neuro-optogenetics, single-cell neuronal dissection and brain slice preparation for electrophysiological studies, stereotaxic injections in various parts of the brain

L43-44: Animal models for neurological disorders

L45-46: Isolation and culture of neural cell types from various model organisms

L47-48: In-vitro models for neuroscience

L49-50: Non-invasive neurophysiological imaging

**Tutorial:** Group discussion, Student seminar, and test

#### **COURSE OUTCOME**

This course is an elective course offered in the fourth semester which prerequisite human physiology I & II. After completing this course the students will be able to:

1. Demonstrate knowledge of, and recognize the relationships between, the structure and function of molecules and tissues involved in neurobiological systems at all levels: molecular, cellular, and organism.
2. Perform basic laboratory techniques used in neuroscience research and understand and apply principles of laboratory safety.
3. Apply and integrate their knowledge of neuroscience to other areas of their studies and to their everyday life

#### **Readings List**

1. Developmental Neurobiology - 1st Edition - Elsevier
2. Principles of Neural Science, (Kandel) 5th Edition, 2013.
3. Fundamental Neuroscience, ELSEVIER 4th Edition, 2012
4. Neuroscience Online, an Open-Access Neuroscience Electronic Textbook  
<https://nba.uth.tmc.edu/neuroscience/>
5. Neural plasticity: the effects of environment on the development of the cerebral cortex. Peter Huttenlocher - Harvard University Press – 2002

6. Current Laboratory Methods in Neuroscience Research. 10.1007/978-1-4614-8794-4.
7. Guide to Research Techniques in Neuroscience, Second Edition 2nd Edition by Matt Carter, Jennifer C. Shieh

**M.Sc. Biomedical Sciences**  
**PATHOPHYSIOLOGY (3+1+0)**

ELECTIVE COURSE

***Preamble:** Throughout the evolution of life almost all the living organism have succumbed to myriads of illness but with the advancement in science and technology human have come to understand and treat many of such dreadful diseases. This course is designed for the postgraduate students with foundation knowledge of human physiology to appreciate and understand the various aspects of the disease and enabling them to correlate with the normal physiology.*

**Unit 1: General patient assessment**

**L1:** General principles of history taking, General patient examination and differential diagnosis

**L2:** Assessment in Women, Children and adolescents, Older people, Psychiatric assessment, Patients presenting as emergencies, Patients in pain.

**Tutorial:** Group discussion, Student seminar and test

**Unit 2: Methods for patient assessment**

**L3-4:** Body temperature, pulse, blood pressure, blood profiles, disease specific blood test, urine test sputum, stool test, precaution for the retrieval of various biological samples from the patients,

**L5-6:** Radiology Test, their Application and Precautions to use (X-ray, CT-scan, PET scan, MRI)

**Tutorial:** Group discussion, Student seminar and test

**All the system specific diseases should cover following aspects: prevalence, significance, pathology/etiology, clinical manifestation, disease management/ treatment strategy**

**Unit 3: Genetic Diseases**

**L7:** Pathophysiological aspects of Genetic Disease, Mutation Rate & the Prevalence of Genetic Disease,

**L8-9:** Pathophysiology of Selected Genetic Diseases

**Tutorial:** Group discussion, Student seminar and test

**Unit 4: Pulmonary disorder**

**L10-11: Obstructive Lung Diseases:** Asthma, Chronic Bronchitis & Emphysema

**L12-13-: Restrictive Lung Disease:** Idiopathic Pulmonary Fibrosis, Pulmonary Edema, pulmonary embolism,

**Tutorial:** Group discussion, Student seminar and test

## **Unit 5: Cardiovascular Disorders**

**L14-16: Heart Disease:** Heart failure, Arrhythmias, Valvular Heart Disease, Coronary Artery Disease, Pericardial Disease

**L17-19: Vascular Disease:** Atherosclerosis, Hypertension, Shock,

**L20-22: Blood Disorders:** Blood cell disorders: red and white blood cell disorder, platelets disorders, coagulation disorder.

**Tutorial:** Group discussion, Student seminar and test

## **Unit 6: Nervous System Disorders with case studies**

**L23-25: Mood Disorders:** bipolar disorder, depression, Seasonal affective disorder (SAD), obsessive compulsive disorder

**L26-28: Anxiety disorder:** Generalized anxiety disorder (GAD), panic disorder

**L29-31: Trauma Disorders:** Post-traumatic stress disorder (PTSD), Reactive Attachment Disorder, Disinhibited Social Engagement Disorder, Acute Stress Disorder, Adjustment Disorders, Dissociative identity disorder

**L32: Schizophrenia:** Signs and Symptoms, risk factor, therapies

**L33-34: Disorders of Impulse Control:** Pathological Gambling, Kleptomania, Pyromania, Trichotillomania, Intermittent Explosive Disorder, Compulsive Sexuality

**L35-37: Neurodegenerative disorder:** Parkinson's disease and Alzheimer's disease, Huntington disease, Multiple Sclerosis & Amyotrophic Lateral Sclerosis

**L38-39: Substance Abuse:** General Mechanisms, alcohol, nicotine and synthetic drugs

**Tutorial:** Group discussion, Student seminar and test

## **Unit 7: Endocrinal Disorders**

**L40-41:** Pheochromocytoma, Parathyroid, Thymus, Adrenal Gland

**L42-43:** Ovaries and Testis,

**L44-45:** Disorders of Thyroid

**L46-47:** Pituitary Gland,

**Tutorial:** Group discussion, Student seminar and test

## **Unit 8: Gastrointestinal Disease**

**L48-49: Disorders of Motility:** Esophageal Achalasia, Reflux Esophagitis, Gastric Ulcer, Gastroparesis,

**L50-51: Disorders of Secretion:** Cholelithiasis, Inflammatory Bowel Disease, Liver Diseases: Fatty Liver, Pancreatic Diseases, Diabetes

**L52-53: Disorders of Digestion & Absorption, GI Manifestations of Systemic Disease,**

**Tutorial:** Group discussion, Student seminar and test

### **Unit 9: Renal Diseases**

**L54:** Acute Kidney Injury, Chronic Kidney Disease,

**L55:** Glomerulonephritis & Nephrotic Syndrome, Renal Stones

**Tutorial:** Group discussion, Student seminar and test

### **Unit 10: Disorders of Reproductive Tract**

**L56-57: Female:** Disorders of the Ovary, Disorders of the Uterus, Fallopian Tubes, & Vagina, Disorders of Pregnancy, Disorders of the Breast, Disorders Of Sexual Development

**L58-59: Male:** Male Infertility, Penile Erectile Dysfunction, Prostate Gland Hyperplasia, Disorders of Sexual Development

**Tutorial:** Group discussion, Student seminar and test

## **LEARNING OUTCOME**

This course is an elective course offered in fourth semester which prerequisite human physiology I & II. After completing this course the students will be able to:

1. Effectively communicate case studies in pathophysiology through verbal, written and multimedia means.
2. Read, understand, and critically evaluate medical journals, health articles, and other forms of data related to pathophysiology.
3. Understand the basic laboratory tests and other diagnostic procedures.
4. Understand how the various organ systems are interrelated, and use this understanding to promote a holistic approach towards the identification of medical emergencies.
5. Create awareness about healthy practices and support the treatment regime of patients at home and community.

## **Readings**

1. Pathophysiology of Disease: An Introduction to Clinical Medicine 7/E (Lange Medical Books) by Gary D. Hammer
2. Understanding Pathophysiology, 6e by Sue E. Huether RN
3. Essential of Pathophysiology: Concepts of Altered State by Carol Mattson Porth, Glenn Matfin
4. Pathophysiology: The Biologic Basis for Disease in Adults and Children by Kathryn L. McCance

# **ADVANCES IN PROTEIN SCIENCE**

## **Elective Paper**

### **IV<sup>th</sup> Semester**

**Credits: 3 + 1 = 4**

#### **Preamble**

Nowadays growing number of human diseases are due to protein misfolding. Mutations and various unwanted post-translational modifications are known to cause aberrant protein folding. Protein amyloidosis additionally covers a large bulk of human diseases due to protein misfolding. Large spectrum of diseases again is due to defects in protein trafficking and translocation. Keeping in mind that subtle alteration in the protein folding environment is crucial toward the proper foldability of a protein, it is important to understand how protein folding, turnover and quality control system is finely tuned in the intracellular environment. Advances in Protein Science has been designed especially to cover all aspects of protein folding to protein quality control system and their interrelations to human diseases. Extensive knowledge on protein aggregates or amyloids and their managements by the cellular systems have been largely dealt.

#### **Unit 1. Basic Principles of protein folding in cell**

**L1.** Introduction to protein folding and its need, Levinthal paradox, protein folding problem, models of protein folding

**L2.** Protein folding in Endoplasmic reticulum: Mechanism and recent advances, few examples of proteins, folding in endoplasmic reticulum

**L3-L4.** Cytosolic protein folding, Co-translational protein folding: Mechanism and recent advances, few examples of proteins, folding in cytoplasm

**L5.** Protein sorting and transportation, addition of signal sequences, protein glycosylation

**L6.** Role of Protein disulfide isomerase (PDI) and Peptidyl proline isomerase (PPI) in protein folding, Structure and chaperoning mechanisms, examples of proteins that require PDI and PPI assistance

**L7.** Protein folding in prokaryotes.

#### **Tutorial and Class test**

#### **Unit 2. Chaperones**

**L8-L9.** Introduction to Chaperonin, structure of GroEL, GroES and their detail mechanism of assisting protein folding,

**L10.** Structure and function of other chaperones including Prefoldin, and tubulin-specific chaperones

**L11.** Introduction to inducible and house-keeping chaperones, examples of some house-keeping chaperones: mechanisms and mode of action, important chaperones in endoplasmic reticulum.

**L12-L13.** Introduction to small and large heat shock proteins, functional differences in terms of chaperoning mechanism, other additional biological functions to some of the small and large heat shock proteins, major chaperone systems in yeast and human.

**L14-16.** Small heat shock proteins (Hsp12, Hsp10, Hsp26, alpha-crystallin etc.): structure, function and interactions based on yeast and human systems

**L17-19.** Large heat shock protein: Hsp70, Hsp60, Hsp90, Hsp104 structure, function and interactions based on yeast and human system

**L20-21.** Role of chaperones in protein translocation, specific chaperones involved in protein degradation (e.g. CHIP, Hsp90, Hsp26)

**L22.** understanding chaperone cross-talks/networks

### **Tutorial and Class test**

## **Unit 3. Protein Quality control**

**L23-24.** Introduction to Protein degradation, Proteasomal-mediated protein degradation: Ubiquitin dependent and independent pathways with examples, and lysosomal-mediated protein degradation, introduction to some important proteases operating the the cells.

**L25.** structure and function of proteosome, recognition mechanism and mechanism of proteolysis

**L26-27.** Autophagy and its importance in many biological processes, advances in Autophagy research Concept of degrons, protein arginylation, Conditions that lead to arginylation with suitable examples

**L28-29.** Unfolded protein response and its role in stress response, protein quality control system in yeast, bacteria, and humans and their role in stress conditions

**L30.** Protein half-life and methods of determination, factors affecting protein half life.

### **Tutorial and Class test**

## **Unit 4. Protein misfolding and diseases**

**L31.** Introduction to protein unfolding, chaperones involved in protein unfolding, protein misfolding, Different causes of protein misfolding: mutation: how different mutation affects protein function,

**L32-33.** mechanism of oxidative stress-induced protein misfolding, protein misfolding by protein covalent modifications including homocystinylation, glycation, Understanding the pathological consequences of the misfolding processes

**L34.** Fates of different misfolded proteins, and strategy how cells takes care of malfolded proteins

**L35-38.** common human diseases associated with protein misfolding: Cystic fibrosis, Huntingtin's disease, Alzheimer's disease, Cardiac amyloidosis, Cataract, Diabetes, acute myloid leukemia and other cancers, cystic fibrosis, Pathophysiology and advances in treatment strategies

**L39-42.** Protein misfolding in ER and consequences, and pathologies, trafficking defects in various organelles, diseases associated with trafficking defects: tay sach disease, emphysema, Familial hypercholesterolaemia, I-cell disease, Zellweger syndrome, Primary hyperoxaluria.

**L43-45.** Common advances in protein misfolding rescue: pharmacological chaperones, Chemical chaperones, Immunotherapy, proteostatic modulators (at least with two-three examples each).

### **Tutorial and Class test**

### **Unit 5. Understanding Protein aggregation**

**46-47.** Pathways of protein aggregation, aggregation kinetics: nucleation phase, oligomerization and fibrillation phase, aggregate morphologies, structure of protein amyloids, different ways to induce protein aggregates or amyloids, co-aggregation

**48-49.** Concept that protein aggregation is for a good cause, oligomer versus fibril toxicity theory, Cellular mechanisms of aggregation mediated toxicity: Endoplasmic reticulum dysfunctioning, Mitochondria injury, Proteasomal dysfunctioning, oligome and annular ring

**50-52.** tools to analyse in-vivo protein fibrillation: Electron microscopy, Confocal and fluorescence Microscopy, NMR, different Fluorescent dyes and their properties, DLS.

### **Tutorial and Class test**

### **Suggested Readings**

1. Biochemistry by Donald Voet and Judith G. Voet; Ed. 4th Wiley; 2010.
2. Molecular cell biology by Harvey Lodish and Arnold Berk, Chris A. Kaiser, and Monty Krieger; Ed. 6th; W H Freeman and Company; New York; 2008.
3. Protein Folding in the Cell by Arthur Horwich, Ed. 1<sup>st</sup>, 2002
4. Protein folding in the cell. Mary-Jane Gething and Joseph Sambrook; Nature, 1992.
5. Protein targeting, transport and translocation by Ross Dalbey and Gunnar von Heijne; Ed. 1<sup>st</sup>; Elsevier; 2002.
6. Proteostasis and Chaperone Surveillance by Laishram Rajendrakumar Singh, Tanveer Ali Dar, and Parvaiz Ahmad; Ed. 1<sup>st</sup> Springer India; 2015.
7. Heat shock proteins: A review of the molecular chaperones by David Whitley, Steven P.Goldberg, and William D.Jordan; Journal of Vascular Surgery; Elsevier, 1999.
8. Protein folding and quality control in the endoplasmic reticulum by Bertrand Kleizen and Ineke Braakman; Current opinion in cell biology, 2004.

9. Molecular chaperones in protein folding and proteostasis by F. Ulrich Hartl, Andreas Bracher & Manajit Hayer-Hartl, *Nature*, 2011.
10. Protein Folding in the Cytoplasm and the Heat Shock Response by R. Martin Vabulas, Swasti Raychaudhuri, Manajit Hayer-Hartl, and F. Ulrich Hartl, Cold Spring Harbor Laboratory Press, 2018.
11. Protein quality control and elimination of protein waste: The role of the ubiquitin–proteasome system by Ingo Amma Thomas, Sommer b Dieter and H. Wolf; *Biochimica et Biophysica Acta (BBA) - Molecular Cell Research*, 2014.
12. Protein quality control in the cytosol and the endoplasmic reticulum: brothers in arms by Alexander Buchberger, Bernd Bukau, and Thomas Sommer; *Molecular cell*, 2010.
13. Chaperone-mediated autophagy in protein quality control. Esperanza Arias, and Ana Maria Cuervo. *Current opinion in cell biology*, 2011.
14. Aggresomes, inclusion bodies and protein aggregation by Ron R Kopito; *Trends in Cell biology*, 2000.

### **Course Outcome**

Students will have comprehensive understanding on cellular protein biochemistry especially, the importance of the fidelity of protein folding and quality control system and how they are linked with human diseases. Students will also develop skills on methods and treatment strategies of the large spectrum of human diseases caused due to protein misfolding.

# ADVANCED CONCEPTS IN MEDICINAL CHEMISTRY

**Elective Course**

**IV Semester**

**Credits 3 +1 = 4**

**60 Lectures**

**Preamble:** This course has been designed for students with background in basic principles in Medicinal Chemistry. The topics covered in the course starts with advanced topics in receptor chemistry and biology, Students will be taught drugs acting through novel targets in various diseases. The Biopharmaceutical agents and their mode of action will also be discussed with examples. Novel metal-based agents will be discussed and new methods of combinatorial synthesis with case studies are covered in detail. The course will cater to needs of students entering in the field of drug discovery and development.

## **Receptor Chemistry and Biology:**

**8 Lectures**

- L1. Chemistry of membrane and intracellular receptors;
- L2. Isolation and characterization of receptors;
- L3. Regulation of receptor number and affinity; Receptor cross-talk;
- L4. Organ Receptors; Non-liganded and constitutive receptor activation;
- L5. r -DNA receptor bioassays;
- L6. Desensitization of receptors;
- L7. Receptors as targets for vaccines and
- L8. Receptors for newer drug development.

## **Drugs acting on Novel Targets (examples from past one decade or so)**

**9 Lectures**

- L9.  $\beta$ -tubulin inhibitors and their mechanism.
- L10. Kinase inhibitors e.g. AKt inhibitors, discovery of gleevac etc.
- L11. HIV inhibitors: integrase inhibitors,
- L12. CCR5 inhibitors
- L13. New drugs developed for tuberculosis (e.g maraviroc) and other infectious diseases.
- L14. Continued
- L15. New drugs developed for cardiovascular disease Cholesterol, absorption inhibitors e. g. ezetimibe,
- L16. glycoprotein inhibitor e.g. abciximab,
- L17. Renin inhibitors e.g. aliskerin

## **Metal Complexes in Medicine**

**6 lectures**

- L18. Chemistry of Metal Species,
- L19. Biochemistry,
- L20. Structure Activity Relationship.
- L21. Complexes in Clinical Trial.
- L22. Metal containing imaging agents

## **Role of Biotechnology in Drug Discovery**

**7 Lectures**

- L23. The impact of biotechnology on small-molecular drug discovery and development.
- L24. Examples of approved biotechnology based drugs: Monoclonal antibodies,
- L25. Interferon alpha, Interferon beta, Interferon gamma, Inter leukins,
- L26. Growth hormones,
- L27. Antisense nucleotides,
- L28. Newer developments in the field of Biopharmaceuticals
- L29. Use of Transgenic animal models for drug evaluation

### **Combinatorial Drug Synthesis:**

**10 lectures**

- L30. Combinatorial Chemistry: Methods of solid Phase synthesis- tBoc, fMoc, orthogonal strategies
- L31. General Methods of combinatorial Synthesis, Premixed, mixed methods
- L32. Methods of synthesis continued , discuss examples from latest literature
- L33. Techniques used in Parallel synthesis (tea bag method)
- L34. Pin method, generation of a Combinatorial Library.
- L35. Photolithographic methods
- L36. Methods of deconvolution of synthetic libraries,
- L37. Methods of deconvolution of synthetic libraries continued
- L38. methods of identifications of chemical libraries.
- L39. Discuss application of combinatorial synthesis in drug development.

### **Personalised Drug Development-**

**6 Lectures**

- L40. Basics of Pharmacogenetics & Pharmacogenomics
- L41. Pharmacogenetics: Population variation in drug metabolism; genetic variability;
- L42. polymorphism relating to receptors and genes in drug metabolism;
- L43. molecular markers and Single nucleotide polymorphism as markers for emerging concepts in pharmacogenetics.
- L44. Ayurgenomics

### **Students' Seminar/tests/discussions**

**12-14 Lectures**

#### Course outcomes

- Students will be able to understand how receptors function, their chemistry and how understanding of the mechanism can be utilized for drug development.
- They will be able to learn novel drug targets emerging over last one decade in various diseases. They will learn discovery of drugs against these targets from bench to bedside.
- The students will also gain knowledge about the emerging metal complexes and Bio-pharmaceutical agents and their development.
- They will learn new methods of optimization of lead compounds through combinatorial library development
- They will also learn about the basic concepts of personalized drug development.
- Students will be encouraged to present latest research papers in the field of drug discovery and development.

## Reading List

- 1 Introduction to Medicinal Chemistry: How drugs act and why by Alex Gningauz and Bruce S. Burnham and Iris H. Hall; Ed. 2<sup>nd</sup>; Wiley-Interscience; 2007.
- 2 Organic chemistry of drug design and drug action by Richard B. Silverman; Ed. 2<sup>nd</sup>; ELSEVIER; 2004.
- 3 Textbook of drug design and discovery by Povl Krogsgaard-Larsen and Kristian Stromgaard and Ulf Madsen; Ed. 4<sup>th</sup>; CRC; 2009.
- 4 Biopharmaceuticals: Biochemistry and Biotechnology by Gary Walsh; Ed. 2<sup>nd</sup>; Wiley; 2003.
- 5 Combinatorial chemistry and molecular diversity in drug discovery by Eric M. Gordon and James F. Kerwin; Wiley-Liss; 1998.
- 6 Molecular diversity and combinatorial chemistry: principles and applications by Michael C. Pirrung; ELSEVIER; 2004.

## **M.Sc. IVth Semester**

### **Course Title: Drug discovery and Process development**

#### **Optional Paper**

**CREDITS 4+0 ( 60 LECTURES)**

#### **Preamble**

This course will explore the process of drug development, from target identification to drug development and registration. It will present the different stages of drug development such as target identification, selection of lead molecule using computer-aided drug design and combinatorial chemistry/ and synthesis and characterization of designed molecules and high-throughput screening. It also covers the safety evaluation, bioavailability, pharmacokinetics clinical trials, and the essence of patent law. The students will learn molecular recognition, computer aided drug design, and toxicology as applied to the development of new medicines. The course covers the drug development process from bench to bedside.

#### **Course outcome**

- Describe and justify the role and importance of the various disciplines involved in the different phases of drug discovery and development
- Account for decision points in the drug development process
- Explain how methods for predictions are used to make early decisions in the drug discovery and development
- Carry out searches to retrieve information relevant to the development of a new drug.
- Construct, review and evaluate preclinical and clinical pharmaceutical studies with a general understanding of aim, choice of procedures, results, conclusions and importance.
- Evaluate scientific, ethical and market-related considerations of importance in the drug development.

## **1. Introduction**

### **(i) Historical development of chemotherapeutics:**

**L 1** Drug discovery starting from dyes to sulphones/sulphonamides and antibiotics.

## **2. Drug Discovery as a Process**

**L 2-4** Target Identification and Validation: Genomics and chemoinformatics/bioinformatics approaches in target selection, analysis of nucleic acid sequence, protein sequence and structure, expression databases and functional pathway data in databases. Translational medicines and Biomarkers to expedite the discovery of new diagnostic tools and treatments leveraging new technology and data analysis tools.

## **3. Pre-Discovery Process**

**L 5-6** Understanding of pathophysiology of disease and molecular pathways (eg. Neuronal disorders, cancer, respiratory disease, diabetes, cardiovascular diseases, autoimmune diseases, anti-microbial infections).

## **4. Drug target identification**

**L 7-8** (i) the advantages and disadvantages of membrane proteins such as receptors, ion channels and transporters as drug targets, increased challenge due to the difficulty in obtaining pure, correctly-folded protein in sufficient quantity for functional or structural assays.

**L 9-10** (ii) the advantages and disadvantages of nucleic acids such as DNA, messenger RNA, and ribosomal RNA as molecular targets in the chemotherapy of cancer, viral, and microbial diseases.

**L 11-12** (iii) Rational approaches to the design of sequences specific DNA binding agents and the gene-specific inhibitors of transcription.

**L 13-16**(iv) Design of the drugs selectively blocking mRNA to inhibit gene expression at the level of translation through (a) the antisense oligonucleotides, (b) the ribozymes that selectively cleave designated mRNAs, and (3) the small inhibitory RNAs, known as siRNAs, in post-transcriptional gene silencing.

**L 17-18** (v) Stimulating or blocking of selected Proteins ( enzymes /receptors) as drug targets

## 5. Drug target Validation

**L 19-20** In silico methods and in vitro and vivo tools using radioligand binding, ELISA, Western blots etc. for validation of target.

## 6. Computer-Aided Drug Design

**L 21-24** Methods for geometry optimisation, molecular dynamics simulation, and conformational searching. Ligand-based Drug Design to improve the properties of a potential drug, quantitative structure-activity relationship (QSAR) and pharmacophore determination. Structure-based Drug Design: the 3-dimensional structure of the receptor, generally a protein, a nucleic acid, a protein-nucleic acid complex focusing on X-ray crystallography, NMR spectroscopy, and mass spectrometry.

## 7. Lead Identification

**L 25-30 (i)** Synthesis, characterization (IR, NMR, MS) of small molecules, and lead identification through virtual screening using in silico methods and High Throughput Screening. Advantages of High Throughput Screening. Types of assays and the advantages and disadvantages of each assay type, assay development and the screening assay.

**L 31 (ii)** Biologics or therapeutic proteins: antibodies, replacement or modulators of enzymes and of cell surface receptors.

**L 32 (iii)** Introduction of combinatorial methods of general organic synthesis, natural products and their analogues.

## 8. Drug Delivery

**L 33-38** Introduction to drug formulations and ADME (Absorption, Distribution, Metabolism and Excretion) processes, their impact on drug's bioavailability. Pro-drugs and Drug Delivery to enhance delivery and / or therapeutic effect

## 9. Pre-Clinical Toxicology and Clinical testing

**L 39-42 (i)** Pre-clinical Toxicology : In vivo toxicity tests required by the world's regulatory bodies; genotoxicity, acute and short-term toxicity tests, tests for carcinogenic potential, Q-T prolongation and others as required by chemical class - the theory and methodology underlying various in vivo toxicology tests - the ethics of in vivo toxicity testing and the potential for replacement by in vitro models.

**L 43-46 (ii)** Clinical Trials: The regulation of therapeutic products and the phases (I-IV) of clinical trial that a drug must pass through before registration, Clinical Trial Design- aims, design, controls and placebo, blinding, randomisation procedures, sample size, statistics, endpoints and ethics.

## **10. Ethics of Human and Animal Experimentation**

**L 47-50** Testing of drugs in animals and humans under strict regulation to limit any harm and distress to the research subject - the ethical conduct of biomedical research, including the policies governing biomedical and animal research in India. The role of institutional human ethics committees and what constitutes informed consent. The general principles for the care and use of animals for scientific purposes and the 3 R's, replacement, reduction and refinement and the role of institutional animal ethics committees.

## **11. Intellectual Property**

**L 51-56** The basic principles underlying the protection of intellectual property focusing on the legal issues relevant to the patenting of pharmaceutical agents according to the relevant sections of Indian Patent Law, the types of patents available and what can be protected, non-patentable inventions, the notions of invention disclosure and prior art, prior art searches, patentability assessment, challenges of pharmaceutical patenting, elements of a patent application and claim drafting.

## **12. Commercial Considerations in Drug Development**

**L 57-60** From target discovery to clinical trials and marketing (Lab to market), various steps from discovery to market including regulatory compliance, how and when to make Go/No-Go decisions, time-scales of various steps, program planning and the interactive perspectives of different groups involved in drug development in small and large pharmaceutical companies.

### **References:**

Basic Principles of Drug Discovery and Development by Benjamin E. Blass ELSEVIER 2015, ISBN: 978-0-12-411508-8

Practical Process Research and Development – A guide for Organic Chemists by Neal Anderson (2012).

Organic chemistry of drug design and drug action by Richard B. Silverman; Ed. 2<sup>nd</sup>; ELSEVIER; 2004.

2. Foye's Principles of Medicinal Chemistry by [Thomas L Lemke](#) and [David A Williams](#); Ed. 6<sup>th</sup>; Lippincott Williams & Wilkins; 2007.



# **BIOINFORMATICS, COMPUTATIONAL BIOLOGY AND DRUG DESIGN**

## **Elective Course**

## **IV Semester**

## **Credits (3 + 1)**

## **60 lectures**

### **Preamble**

This course has been designed for the students of Biomedical Sciences and related areas who are interested to study various technologies and tools in Bioinformatics, Computational Biology and Drug Design. The course has been designed to cater needs of students working in various laboratories in the field of Biomedical sciences and the students entering into this much demanding area of research. The aim of the course is to train the students in various tools available to aid research in the area of Bioinformatics, computational Biology and drug design. The students will be given training in the theoretical aspects of these methods and practical use of the computational tools available to carry out research in Biology and Drug Design.

### **Detailed Contents**

#### **Biological databases, Sequence Alignment and Phylogenetic Analysis** **6 Lectures**

- L1.** Introduction to various databases and their classification (primary and secondary databases).
- L2.** Local and global sequence alignments (Needleman-Wunsch and Smith-Waterman algorithms), pair-wise (BLAST and FASTA algorithms) and multiple sequence alignment (Clustal W) and its importance.
- L3.** BLAST score, amino acid substitution, matrices, s-value and e-value, calculating the alignment score and significance of e and p value.
- L4.** Basics and tools for phylogenetic analysis, cladistics, tree-building methods (character and distance - based methods),
- L5.** construction of phylogenetic trees (PHYLIP) and identifying homologs.
- L6.** Basics of Next Generation Sequencing and data analysis

#### **Structural Biology** **6 Lectures**

- L7.** Folding and flexibility, Prediction, engineering and design of protein structures.
- L8.** Methods to identify secondary structural elements,
- L9.** Structure visualization using PyMol and VMD, active site determination, Cavity analysis using CASTP or ACSITE or similar tools,
- L10.** Determination of protein structures by X-ray and NMR methods. Prediction of secondary structure- PHD and PSI-PRED methods.
- L11.** Tertiary Structure: homology modeling, fold recognition and ab-initio approaches.
- L12.** Structures of oligomeric proteins and study of interaction interfaces.

**Systems Biology:****8 lectures**

- L13.** Systems Biology Networks- basics of computer networks, Graph Theory, Biological uses and Integration.
- L14-17.** Topology of biological networks: Random vs Scale-Free networks. Metabolic networks, Signal transduction networks, Gene regulatory networks. Databases on metabolic & signaling pathways.
- L18.** Introduction to computational tools for analysis (Network analysis & clustering) of high throughput data from genomics (NGS), transcriptomics (Microarray/RNASeq), proteomics & metabolomics.
- L19 - 20.** Creating networks and analysis, Cytoscape and Pajek, STRING, KEGGS and other annotation tools.

**Molecular Modeling and Molecular Dynamics****15 lectures****L 21-24. Molecular Mechanics:****4 Lectures**

Introduction, The Morse Potential, The Harmonic Oscillator Model for Molecules, Comparison of Morse and Harmonic Potential, Types of Force Fields: AMBER, CHARMM, Merck Molecular Force Field, Consistent Force Field, MM2, MM3 and MM4 force fields.

**L 25- 28. Potential Energy Surface****4 Lectures**

Convergence Criteria, Characterizing Stationary Points, Search for Transition States. Optimization- multivariable Optimization Algorithms, level Sets, Level Curves, Gradients, Optimization Criteria, Unidirectional Search, Finding Minimum Point, Gradient based Methods-Steepest Descent and Conjugate Gradient Methods

**L 29 – 35 Molecular Dynamics Simulation:****7 lectures**

Introduction, Radial distribution functions, Pair Correlation function, Newtonian dynamics, Integrators- Leapfrog and Verlet algorithm, Potential truncation and shifted-force potentials, Implicit and explicit Solvation models, Periodic boundary conditions, Temperature and pressure control in molecular dynamics simulations

**Drug design using case studies****8 lectures**

- L 36.** Drug discovery process. Target identification and validation, lead optimization and validation.
- L37– 40.** Methods and Tools in Computer-aided molecular Design, Analog Based drug design- Pharmacophores (3D database searching, conformation searches, deriving and using 3D Pharmacophore, constrained systematic search, Genetic Algorithm, clique detection techniques, maximum likelihood method)
- L41 – 43** Structure based drug design- Docking, De Novo Drug Design (Fragment Placements, Connection Methods, Sequential Grow), Virtual screening.

**Structure Activity Relationship:****5 Lectures**

- L44.** Introduction to QSAR, QSPR, Various Descriptors used in QSARs: Electronics; Topology; Quantum Chemical based Descriptors.
- L45 - 47.** Regression Analysis, The Significance and Validity of QSAR Regression Equations, Partial Least Squares (PLS) Analysis, Multi Linear Regression Analysis.
- L48.** Use of Genetic Algorithms, Neural Networks and Principle Components Analysis in the QSAR equations.

**Students' Seminar/tests/discussions**

**12 Lectures**

### Course learning Outcomes

- **Biological databases, Sequence Alignment and Phylogenetic Analysis.** Student will be able to learn biological and bioinformatics databases, sequence alignments, scoring the alignment, phylogeny analysis and basics of Next Gen sequencing techniques.
- **Structural Biology:** Student will learn various aspects of Protein structure. Students will be familiarized with secondary structures elements, the visualization using various online softwares, cavity analysis, methods of protein structure determination, predicting protein secondary and tertiary structure, oligomeric proteins.
- **Systems Biology:** Student will learn basics of system biology networks, graph theory, uses etc. Topology of networks, different types of networks, computational tools for analysing networks, clustering etc,
- **Molecular modelling and molecular dynamics:** Student will learn how molecular modelling methods have evolved and integrate into modern, multidisciplinary structure-based design. Summarise the key concepts surrounding the potential energy surface, including methods of energy calculation and exploration, and appreciate the advantages and limitations of these methods, Describe various molecular dynamics methods.
- **Drug design using case studies** Describe computer-based 2D and 3D approaches to drug design and discovery, including functional group mapping, virtual screening, de novo design, quantitative-structure activity relationships and database analysis.
- **Structure Activity Relationships.** Compare and contrast 2D and 3D approaches QSAR and other computer-aided drug design, giving examples of their use in drug discovery projects.

### Text Books:

1. Protein structure, stability and folding Ed KP. Murphy, Humana press. 2001.
2. Bioinformatics: Sequence and Genome analysis, 2nd edition (2004), David W. Mount, Cold Spring Harbour Laboratory Press. ISBN-13: 978-0879697129.
3. Bioinformatics: A practical guide to the analysis of genes and proteins, 3rd edition (2004), Andreas D. Baxevanis and B.F. Francis Ouellette, John Wiley and Sons. ISBN-13: 978-0471478782.
4. Systems Biology: Definitions and perspectives by L.Alberghina H.V.westerhoff, Springer. 2005
5. Synthetic Biology, A New Paradigm for Biological Discovery, a report by Beachhead Consulting, 2006
6. The Process of New Drug Discovery and Development, 2nd edition (2006), C.G. Smith and J.T. O'Donnell, Informa Healthcare, ISBN-13: 978-0849327797.

7. Cheminformatics (2003), J. Gasteiger, Thomas Engel; Wiley-VCH. ISBN: 9783527618279.
8. Molecular modeling - Principles and Applications, 2nd edition (2003), A. R. Leach, Pearson Education Limited, UK. ISBN 13: 9780582382107.
9. Cheminformatics in Drug Discovery (2006), edited by. T.I. Opera; Wiley Publishers, ISBN: 9783527604203.
10. Molecular dynamics simulation: elementary methods (1992), J. M. Haile, Wiley-Interscience, New York. ISBN-13: 978-0471184393.
11. Molecular Modelling for Beginners, (2nd Edition) by Alan Hinchliffe, John Wiley & Sons Ltd. 2008

# **MEDICAL BACTERIOLOGY AND PARASITOLOGY**

**Semester: IV**

**Elective Paper**

**Credits: 3+1**

**Credits: 60 Lectures**

## **Preamble**

The course starts by recapitulating the various concepts of bacteriology and parasitology taught in Medical Microbiology in I semester. The course builds on the concepts learnt in the previous course and a detailed program on various aspects of bacterial and parasitic infections will be covered. Articles published in various peer-reviewed journals related to Bacteriology and Parasitology will be referred to. The course will be taught in an interactive manner with lectures, seminars debates on selected topics.

## **Course Outcome**

At the end of the course the students will have:

1. A detailed knowledge of various virulence determinants of different infections and the commonality and specificity pertaining to each infection.
2. Appreciated the regulation of expression of various virulence factors and their role in pathogenicity and establishment of successful infections
3. Knowledge on the global and Indian prevalence of each pathogen and seasonal patterns.
4. Knowledge of diagnosis of different infections by various tools and techniques.
5. Knowledge of the immune responses and current vaccines and those under development to various infections.

6. Knowledge on the mechanisms of drug resistance and methods to overcome these. Alternate approaches to treating drug resistant infections.
7. Thus, after finishing the course a student is well trained in all the aspects of Bacteriology and Parasitology.
8. In combination with Medical Microbiology in the I semester and Medical Virology and Mycology in the III semester, a student will have complete understanding of Microbiology as a whole

## **Detailed Contents**

### **Bacteriology**

#### ***Introduction***

L1 – L3: Overview of the history, nomenclature and classification based on morphology, scientific classification, Gram staining, 16s rRNA sequencing of Respiratory (Diphtheria, TB, Streptococcus, Staphylococcus, Bordetella, Klebsiella and Urino-Genital (E. coli sp) infections; Gastro-Intestinal Tract (Salmonella, Vibrio Cholera etc.) and blood (Sepsis) infections; Central Nervous System (Meningitis).

#### ***Virulence determinants and their regulation***

L4 – L5: Virulence factors: cell wall, exotoxins, endotoxins, toxin-anti-toxin systems, adhesions, invasion, intracellular and extracellular lifestyles.

L6 – L7: Regulation of virulence factors, sigma factors, two-component systems, quorum sensing of the virulence factors. Type I-IV secretion systems and their regulation.

#### ***Epidemiology and Modes of Infection and Diagnosis***

L8 – L9: Epidemiology; prevalence and distribution of various bacterial infections. Tools to study epidemiological data and their analyses.

L10 – L11: Modes of infection and sustenance of different bacterial and infections of the human body.

L12 – L13: The conventional and current methods of diagnosis of various infections along with the limitations. Alternative tools and technologies of diagnosis.

### ***Therapeutics, Immunity and Drug Resistance***

L14 – L16: The mechanisms of antibiotic resistance in Respiratory, Urinogenital and blood, GI-Tract and CNS infections.

L17 - L19: Role of innate and adaptive immunity in bacterial infections.

L20 - L21: Treatment of various infections. New therapeutic regimes and strategies to combat infections. Focus on host-mediated therapeutics and drug repurposing.

### **Parasitology**

L22: **Overview of apicomplexan parasites:** Babesia, Plasmodium sp. , Current drug and vaccine targets for malaria infections,

L23: Modern strategies to block malaria parasite escape and entry,

L24: Current trends in mosquito vector control

### **Pathophysiology of protozoan parasites:**

L25 Pathophysiology of plasmodium and its regulation

L26: Pathophysiology of Leishmania,

L27: Toxoplasma, Placental invasion and congenital transmission

L28: Trypanosoma , Placental invasion and congenital transmission.

### **Pathophysiology of Re-emerging protozoan infections:**

L29: Cryptosporidiosis,

L30: Pneumocystis carinii infections,

L31: Babesiosis, Amoebiasis,

L32: Trichomoniasis

L33 – L37: **Epidemiology, lifecycles**, Pathophysiology, diagnostics and therapeutics of Nematode infections : Intestinal, blood and tissue nematodes

L38 - L41: Epidemiology, lifecycles, Pathophysiology, diagnostics and therapeutics of key trematode infections

L42 - L45: Epidemiology, lifecycles, Pathophysiology , diagnostics and therapeutics of Cestode infections

L46: Gut protozoa: Friends or Foes to human gut microbiota: **debate topic**

The importance of gut microbiota on human health has sparked interest in study of factors that shape the composition and diversity. Despite the growing evidence suggesting that helminthes and protozoans interact with gut bacteria, microbiome studies still focus on prokaryotes.

L47: Human interventions: Driving force for insect vector evolution: **Debate topic**

Widespread use of insecticides provides an opportunity to examine the adaptive responses of the target species to human interventions. Rapid evolution of anopheles mosquito represents a potential threat to any vector based malaria control strategy. The genetic, behavioral and physiological mechanisms underlying insecticide resistance will yield potential knowledge for vector borne disease control. Trends in parasitology Vol: 34 issue 2, 2018

L48: Recent models and technologies to overcome Biological barriers to protozoan parasite control: **Debate topic**

The current strategies of malaria control program encompass the integrated vector management, new drug development and repurposing of drugs. The knowledge gained through system biology approaches for parasite, definitive (mosquito) and intermediate host (Human) as well as mechanisms involved in pathophysiology of malaria can serve the effective malaria control programs. Advances in Parasitology 2017; Trends in parasitology issue 4, 2014; Acta tropica 2017

L49: Current epidemiological evidence for predisposition to high or low intensity helminthic infections. **Debate topic**

## **L50-L60: Debates/Tests/Seminars/Discussions**

### **Suggested Readings:**

#### **Books**

1. Medical Microbiology Jawetz, Melnick and Adelberg (eds). 25<sup>th</sup> Edition. McGraw.
2. Microbiology, Prescott, Harley and Klein (eds). Seventh Edition. McGraw Hill.

#### **Journals (Latest volumes)**

1. Annual Reviews in Microbiology
2. Infection and Immunity
3. Journal of Infectious Diseases
4. Journal of Infection
5. PLoS pathogens
6. Cell Host and Microbe
7. Trends in Parasitology
8. Advances in Parasitology
9. Acta Tropica

# **BIOETHICS AND BIOSAFETY**

**OPEN ELECTIVE**

**CREDITS 2**

## ***Preamble:***

*Modern biotechnology and innovation-oriented scientific research have prompted formulation of new policies and regulatory guidelines which would have a direct impact on protection against the potential harms and/or exploitation of research participants. The establishment of a bioethics framework involving biomedical scientists, religious scholars, physicians, philosophers, legal experts, sociologists, and lay intellectuals would have a proactive directional impact on the inter-relation of medicine, ethics, law and religion vis-a-vis existent ethical standards and futuristic adaptability with the local/ state/ region/ international norms.*

## **L1-L3: INTRODUCTION TO BIOETHICS, CODES, COVENANTS, DECLARATIONS AND GUIDELINES**

Defining Bioethics in relation to Profession, Society, and Biomedicine, need of bioethics.  
Medical profession and biomedicine:

Prayers and Oaths in Bioethics and Covenants in Bioethics

Declarations: The Declaration of Geneva, WMA's Declaration of Helsinki (DOH, 1964) Universal Declaration on Bioethics and Human Rights and Guidelines

Codes of Bioethics

## **L4-L5: ISSUES CONCERNING GOOD LIFE AND HEALTHY LIFE**

Indian Philosophy of life, Various Philosophical systems, Issues in philosophy, Goals of life: *purusharthas*. *Dharma* and other moral concepts.

Indian traditional systems of medicine and their ethical principles: Introduction, Ayurveda, Siddha, Unani

## **L6-L11: JUSTICE, LAW AND SOCIETY & LEGAL AND ETHICAL ACCOUNTABILITY OF DOCTORS**

Justice Law and Society: Introduction, Constitution of India,  
Legal Framework: Substantive and Procedural, Legal System  
We, Healthcare and Our Society, Doctor-Patient Relationship

Right to Health and Health Care: Judicial perspective

Essential information about COPRA, Legal and Ethical Accountability of Doctors: Premise and Extent

Rights of patients who require critical care, Ethics, Triage, Futility (arguments in favour and against futile intervention, solutions to dilemmas), Case studies.

Euthanasia: End of life care decisions, Killing or letting die, Principle of double effect, Case studies.

Principle of ordinary vs. Extraordinary means: Withholding and withdrawal of treatment and life support

The Indian society of critical care medicine guidelines for limiting life- support interventions  
Policies in the ICU, Communication between the team and family, Handling the family,  
Resolving conflict in ICU, Consideration at the time of death.

Situation in India, Procedure to be adopted by the high court when such an application is filed.  
Case studies.

## **L12-L18. DOCTOR-PATIENT RELATIONSHIP**

Introduction, Qualities of the patient, Negative & Positive rights, Patient's Bill of rights (AHA), Qualities of the Doctor, Regulation, Types of doctor patient relationships

Qualities that patients expect from their doctors, Effects of an effective doctor-patient relationships

Bed Side Manner, Analysis of doctor – patient relations: The activity-passivity model or paternalistic model, the Guidance-Cooperation Model, the Mutual Participation Model - Shared Responsibility

Bargaining power of Patients and Physicians, Termination of relationship Some terms used in Doctor patient relationships (Veracity, Privacy, Professional fidelity, problems with fidelity).

Conflict of interest, Dual roles of clinician and investigator

Factors that influence Doctor patient relationships: Drug industry, Advertisements, Medical representatives, Gifts, Research, Case studies.

Doctor's relationship with other doctors and institutions: Physician Advertisements, Fee splitting Religious and political affiliations, Health Professional & Torture.

Boundary violations: Non sexual boundary violations and crossing, Sexual boundary violations Sexual impropriety, Sexual transgression, Sexual violations, the Physical Examination Prevention of Boundary Violations

## **L19-L26: MEDICAL ERRORS AND NEGLIGENCE**

Introduction, History of medical errors, Problem of medical errors

What is medical error? Types of medical errors, Person or system.

Type of action, Risk factors for medical errors, Prevention of medical errors, Ethical dilemmas

Disclosure to the patient: Ethical duties of the Physician, need for disclosure, Fiduciary obligations, Autonomy, Truth telling, Respect for the person, Justice & professional standards

Dealing with medical error, Patient and family attitudes to medical error, Potential advantages of disclosing medical error to Patient and health care personnel and Health care system

Barriers to disclosing error: Attitudinal barriers, Helplessness, Uncertainties, Fears/anxieties

How to disclose error, Effects of disclosure, Legal arguments against disclosure, Distress among physicians,

Medical negligence, Profession and occupational Negligence, Elements of Negligence, Duty of care, Standard of care.

Medical code and Negligence: Types of negligence, Relief for medical negligence

Legal positions: Medical council of India Civil courts, Approach High court (Constitutional law and PIL), Criminal law, Consumer protection act, Compensation

Defensive medicine: Protection against medical negligence, Effects of medical negligence litigation

### **L27-L29: CLINICAL RESEARCH AND ICMR GUIDELINES:**

The General Principles: What is Informed Consent? Concept and Process.

Informed Consent in different settings, Waiver of Consent, Gatekeeper's Consent/ permission, Children and Assent, Vulnerable population.

Guidelines for drug trials.

### **L30-L32: BIOSAFETY**

Use of recombinant DNA technology, manipulation of genes of bacteria, viruses and human cells.

Transport, storage and precautions in use and disposal of clinical samples and biological samples.

Biosafety levels: BSL1, BSL2 and BSL3 facilities.

### **COURSE OUT COME:**

- Define the term "Bioethics". Learn about gradation of moral and ethical norms from simpler to higher levels for initiating right actions to 'first do no harm'
- Learn about Prayers, Oaths, Covenants, Declarations, Guidelines and Codes which have relevance to bioethics.
- Recognize the key features of the Ayurveda, Unani and Siddha systems of medicine.
- Outline the ethical and moral values as described in the authentic texts of Ayurveda, Siddha and Unani systems of medicine.
- Clinical research and guidelines of ICMR for collecting clinical samples and drug trials.
- Rights of patients, responsibilities of doctors and legal justice.
- Understanding the biosafety rules in handling biological materials.

# **APPLICATION OF STATISTICS FOR BIOLOGY**

## **Open Elective**

## **IV<sup>th</sup> Semester**

**Credits: 2 + 0 = 2**

### **Preamble:**

Statistics plays a crucial role in data validation, analysis and interpretation, without which clinical, social science research and other researches involving huge number of samples would not be possible. The present course dealt with various common statistical methods involved in biological science research like tools for describing central tendency, correlation, and regression analysis, probability, hypothesis testing and methods of sampling of biological data.

### **Measures of central Tendency**

**L1-L3.** Concept, calculation and biological significances of Mean, mode, Median, Graphical representation of statistical data.

**L4.** Concept, calculation and biological significances of mean deviation, Standard deviation, Covariance, Standard error.

### **Tutorial and class test**

### **Correlation And Regression analysis**

**L5-L6.** Definition of correlations, Karl Pearson's Co-efficient of correlation, Co-efficient of variation,

**L7.** Rank correlation, Tied ranks, Relation between two variables, Scatter diagram.

**L8-L10.** Definition of regression analysis, curve fitting (linear and nonlinear), principles of least squares, two regression lines,

**L10-L11.** Definition of clustering, K-mean clustering, PCR analysis, Hierarchical clustering

### **Tutorial and class test**

### **Probability**

**L12-L14.** Theorems on probability, Random experiments, sample space, conditional probability, Bayes theorem

### **Probability Distribution**

**L15.** Exponential distribution, Gamma distribution, Beta distribution,

**L16-L18.** Binomial, Poisson distribution, Normal distributions. Standard normal distributions and Z score, applications.

### **Methods of Sampling of biological data and analysis using**

**L19-L22.** 't.' and 'Z.' and 'F.' tests of significance for small and large samples (with appropriate examples), Hypothetical tests, Parametric and Non-parametric tests, P-

value, Multiple testing.

### **Tutorial and class test**

#### **Suggested Reading**

1. Basic statistics by A. L. Nagar and R. K. Das; 2nd Ed.; Oxford; 2002.
2. Biostatistics: a manual of statistical methods for use in health, nutrition and anthropology by K. Visweswara Rao; Jaypee Borthers, 1996.
3. Introductory statistics by Prem S. Mann; 5th Ed.; John Wiley; 2003.
4. Biostatistics: a foundation for analysis in the health sciences by Wayne W. Daniel; 8th Ed.; John Wiley; 2005.
5. John E. Freund.'s mathematical statistics with application by Irwin Miller and Marylees Miller; Ed.7th; Pearson; 2006.

#### **Course Outcome**

Students will get skills on different ways of hypothesis testing and methods of sampling of biological data sets. Additionally, they will be able to interpret and analyze data containing large pool of biological samples to yield correlative insights.