Manipal Institute of Regenerative Medicine, Bengaluru

M.Sc. Stem Cell Technology and Regenerative Biology

Revised Syllabus 2017 onwards

Preface

The Manipal Institute of Regenerative Medicine, Manipal Academy of Higher Education (MAHE) has offered a post graduate M.Sc. course in Regenerative Medicine since 2007. The syllabus was last modified in 2009. In the intervening years this area has developed rapidly and several new concepts have emerged in the field. Therefore we are proposing to revise the syllabus of this course from the academic year 2017-18 onwards.

The guiding principle of this course revision is to make the syllabus more project oriented and vocational without compromising on the academic and theoretical content of the existing syllabus. Over all the revised course would devote 420 hours to theory classes and 1078 hours to practicals in comparison to 716 hours for theory classes and 630 hours for practicals in the existing course. The Practical module shall include a 15 day exercise at the end of Semester II to give training in scientific project writing to the students. In addition the revised course shall offer elective topics and the students to do two in house projects- one of short (3 month) and one long duration (6 months)

Some salient features of the revised syllabus are as follows:

- The course structure would be modular and each module shall be handled by an assigned faculty member and Guest Speakers.
- The theory classes would be of 90 minutes duration comprising 1 hour of formal lecture followed by 30 minute discussion/tutorial session that shall comprise clarifications and questions from the students and evaluation of the students by faculty through short tests quizzes and group discussions.
- Student's performance in the discussion/tutorial sessions shall be used for their internal assessments and grading.
- The afternoon practical sessions, in each module would be in line with the topics covered during the theory classes in the morning sessions.

- All key fundamental concepts and practicals, related to regenerative medicine, shall be covered during Semester I and II.
- At the end of Semester II students would be given exercises to write and assess scientific projects and critique scientific publications in the form of journal club presentations
- Lectures in Semester III would be on advanced elective topics. Students shall opt for their elective subject and their allotment would be done based upon their performance in the previous semesters.
- During Semester III students would have only 10 lectures on advanced topics in the field and would do practicals related to those topics. They would also do a short project with their assigned PIs.
- Projects for Semester IV shall be formulated under the supervision of the PIs selected/ allotted for their elective subjects in Semester III.

REGULATIONS

These regulations shall come into effect from the academic year 2017-18. These regulations are subject to modifications from time to time by authorities of Manipal University.

1. **Minimum Qualification for Admission:**

   Admission is open to candidates who possess a MBBS, BDS, BE (Biotechnology) B.Sc, B Pharm or equivalent level of education from a recognized University.

2. **Duration of Program:**

   It is a 2 year program with 4 semesters.

3. **Attendance Requirement:**

   Each course of the semester will be treated as a separate unit to determine the attendance. Every student must have not less than 80% attendance in each unit to be eligible to appear for examination.

   If a student for any reason discontinues the course after 1^{st} / 3^{rd} semester may be permitted for 2^{nd} / 4^{th} semester respectively after 1 year in the following academic year, subject to the condition the entire academic program is completed by the student with 2 years of original admission to the course.

PROGRAM STRUCTURE

M.Sc. Stem Cell Technology and Regenerative Biology

Semester 1

Code	Course Title	Hours Per Week			C	Maximum Marks		
		L	T	P		IA	*UNI EXAM	TOTAL
RM 401	Biomolecules	3	1	-	4	30	70	100
RM 403	Laboratory Methodologies, Biostatistics, Bioinformatics and Ethics	3	1	-	4	30	70	100
RM 405	Architecture of Cells, Tissues and Organs	3	1	-	4	30	70	100
RM 407	Embryonic Development and Cell Differentiation	3	1	-	4	30	70	100
RM 409	Biomolecules Lab	-	-	4	2	40	60	100
RM 411	Laboratory Practices	-	-	6	3	40	60	100
RM 413	Architecture of Cells, Tissues and Organs Lab	-	-	4	2	40	60	100
RM 415	Embryonic Development and Cell Differentiation Lab	-	-	4	2	40	60	100
	TOTAL	**12**	**4**	**18**	**25**	**-**	**-**	**800**

***Minimum marks for all University Examinations for a pass credit = 50%**

Semester 2

Code	Course Title	Hours per week (Lectures per week)			C	Maximum Marks		
		L	T	P		IA	*UNI EXAM	TOTAL
RM 402	Intercellular Communication in Stem Cell Niches	2	1	-	3	30	70	100
RM 404	Biomaterials and Tissue Engineering	2	1	-	3	30	70	100
RM 406	Clinical Applications of Stem Cells	2	1	-	3	30	70	100
RM 408	Non Clinical Applications of Stem Cells	2	1	-	3	30	70	100
RM 410	Intercellular Communication in Stem Cell Niches Lab	-	-	6	3	40	60	100
RM 412	Biomaterials and Tissue Engineering Lab	-	-	2	1	40	60	100
RM 414	Clinical Applications of Stem Cells Lab	-	-	4	2	40	60	100
RM 416	Non Clinical Application of Stem Cells Lab	-	-	4	2	40	60	100
RM 418	Research Methodologies and Scientific Project Management – (Mandatory Learning Course-MLC)	-	-	-	2	-	-	-
	TOTAL	**8**	**4**	**16**	**22**	**-**	**-**	**800**

*Minimum marks for all University Examinations for a pass credit = 50%

Grades for Mandatory Learning Course (Code RM 418) will be Audit Pass/ Satisfactory / Not Satisfactory

Overall grade for second semester will not include the grade for Mandatory Learning Course (Code RM 418).

Semester 3

Code	Course Title	Hours per week			C	Maximum Marks		
		L	T	P		IA	UNI EXAM	TOTAL
RM 501	Elective Theory*	1	-	-	1	100	-	100
RM 503	Elective Lab**	-	-	8	4	100	-	100
RM 505	Mini Project***	-	-	-	8	100	-	100
RM 600	Preparation for Main Project	-	-	-	-	-	-	-
	TOTAL	**-**	**-**	**-**	**13**	**-**	**-**	**300**

***Elective Theory**

RM 501.01- Engineering Substrates and Scaffolds for the Growth and Differentiation of Lineage Specific Cells
RM 501.02- Effect of AGEs on Mesenchymal Stem Cell Differentiation
RM 501.03- Drug Screens for Cancer Stem Cells and Degenerative Disease Models
RM 501.04- Understanding the Role of Transcription Factors during Early Neural Development using Gene Editing Approach
RM 501.05- Assessment of Neuroprotective Potential of Mesenchymal Stem Cells in Vitro Model of Hippocampal Excitotoxicity

****Elective Lab**

RM 503.01- Engineering Substrates and Scaffolds for the Growth and Differentiation of Lineage Specific Cells
RM 503.02- Effect of AGEs on Mesenchymal Stem Cell Differentiation
RM 503.03- Drug Screens for Cancer Stem Cells and Degenerative Disease Models
RM 503.04- Understanding the Role of Transcription Factors during Early Neural Development using Gene Editing Approach
RM 503.05- Assessment of Neuroprotective Potential of Mesenchymal Stem Cells in Vitro Model of Hippocampal Excitotoxicity

*****Mini Project**

RM 505.01- Engineering Substrates and Scaffolds for the Growth and Differentiation of Lineage Specific Cells
RM 505.02- Effect of AGEs on Mesenchymal Stem Cell Differentiation
RM 505.03- Drug Screens for Cancer Stem Cells and Degenerative Disease Models
RM 505.04- Understanding the Role of Transcription Factors during Early Neural Development using Gene Editing Approach
RM 505.05- Assessment of Neuroprotective Potential of Mesenchymal Stem Cells in Vitro Model of Hippocampal Excitotoxicity

Evaluation of Mini Project: Evaluated by a panel with external member.

Semester 4

Code	Course Title	Hours per week			C	Maximum Marks
		L	T	P		
RM 600	Project Work and Dissertation*	-	-	-	20	300

L= Lecture, T= Tutorial, P= Practicals, C= Credit, IA= Internal assessment, UNI Exam= University examination

*** Project Work and Dissertation**

RM 600.01- Engineering Substrates and Scaffolds for the Growth and Differentiation of Lineage Specific Cells
RM 600.02- Effect of AGEs on Mesenchymal Stem Cell Differentiation
RM 600.03- Drug Screens for Cancer Stem Cells and Degenerative Disease Models
RM 600.04- Understanding the Role of Transcription Factors during Early Neural Development using Gene Editing Approach
RM 600.05- Assessment of Neuroprotective Potential of Mesenchymal Stem Cells in Vitro Model of Hippocampal Excitotoxicity

Evaluation of Project Work and Dissertation: Evaluated by a panel with external member.

Rules regarding the Sessional Examination are as follows:

No. of Sessionals for each Semester : 4 Sessionals per Semester (1 sessional one module)

Pass Marks for Sessional Examination : 50% for both theory and practical

Carry Over rules:

Theory Examination :

M.Sc. students can carry all theory subjects from semester 1 to semester 2. From semester 2 to semester 3 only 2 theory subjects from any previous semester can be carried over. No more than four attempts will be permitted (including regular examination) to pass any subject. All chances must be completed within two years from the date of first scheduled examination for that subject.

Practical Examination :

M.Sc. students can carry all practical subjects from semester 1 to semester 2. From semester 2 to semester 3 only 2 practical subjects from any previous semester can be carried over. No more than four attempts will be permitted (including regular examination) to pass any subject. All chances must be completed within two years from the date of first scheduled examination for that practical subject.

SYLLABUS

M.Sc. Stem Cell Technology and Regenerative Biology

SEMESTER I

- Biomolecules
- Laboratory Methodologies, Biostatistics, Bioinformatics and Ethics
- Architecture of Cells, Tissues and Organs
- Embryonic Development and Cell Differentiation

There would be 140 lectures each of 90 min. duration on all working days between August-November. THERE WILL BE **FOUR** MAIN MODULES AND **FIFTEEN** SUBMODULES IN THE THEORY LECTURES

MODULE NUMBER	**MODULE**		**NUMBER OF LECTURES**
1	**BIOMOLECULES**		**35 Lectures**
	SUB MODULE		
	a	Proteins	12 Lectures
	b	Carbohydrates	6 Lectures
	c	Lipids	8 Lectures
	d	Nucleic Acids	9 Lectures
2	**LABORATORY METHODOLOGIES, BIOSTATISTICS, BIOINFORMATICS AND ETHICS**		**35 Lectures**
	SUB MODULE		
	a	Physico-Chemical Principles of Lab Techniques	10 Lectures
	b	Statistical Principles in Biology	8 Lectures
	c	Bioinformatics	7 Lectures
	d	Clinical Research, Bioethics and Regulatory Guidance	5 Lectures
3	**ARCHITECTURE OF CELLS TISSUES AND ORGANS**		**35 Lectures**
	SUB MODULE		
	a	Basic Cell Structure and Functions	10 Lectures
	b	Tissue organization and functions	10 Lectures
	c	Organ Structure and Functions	10 Lectures
	d	Integrated Cell Biology	5 Lectures
4	**EMBRYONIC DEVELOPMENT AND CELL DIFFERENTIATION**		**35 Lectures**
	SUB MODULE		
	a	Early Embryonic Development	11 Lectures
	b	Mid to Late Embryonic Development	12 Lectures
	c	Tissue specific Stem Cells	12 Lectures

MODULE I

TOPIC: BIOMOLECULES

THEORY CLASSES (53 HOURS)

SUB-MODULES:

(a) Proteins 12 Lectures

(b) Carbohydrates 6 Lectures

(c) Lipids 8 Lectures

(d) Nucleic acids 9 Lectures

SUB-MODULE: (a) PROTEINS (12 Lectures)

Lecture 1: Primary Secondary and Tertiary structures of Proteins: (a) amino acids-names etc. (b) peptide bond and modifications (c) acetylation (d) secondary structures S-S bonds (e) tertiary structure

Lecture 2: Proteins as Enzymes, categories, nomenclature etc.

Lecture 3: Proteins as structural complexes Supra Molecular Organization

Lecture 4: Secretory Proteins: synthesis, protein transport, functions

Lecture 5: Proteins as hormones

Lecture 6: Proteins as Neurotransmitters

Lecture 7: Proteins and immune regulation-cytokines

Lectures 8-10: Membrane Proteins

Lecture 11: Protein folding and diseases

Lecture 12: Protein Engineering

SUB-MODULE: (b) CARBOHYDRATE (6 Lectures)

Lecture 13: Classification of Carbohydrates; Primary and secondary structure, Monosaccharides, Glycosidic bond - Reducing & Non reducing sugars; Composition & linkage Polysaccharides,

Lecture 14: Conjugated Carbohydrate: Glycoproteins; proteoglycans and glycolipids

Lecture 15-16: Carbohydrate metabolism-synthesis and breakdown

Lectures 17-18: Metabolic Disorders

SUB-MODULE: (c) LIPIDS (8 Lectures)

Lecture 19:	Fatty acids and Triacylglycerols: Nomenclature, Classification and structures
Lecture 20:	Phospholipids and Sphingolipids: structure and biological roles
Lecture 21:	Sterols: Structural aspects in different membranes, lipid rafts
Lecture 22-23:	Metabolism of Lipids: Biogenesis of fatty acids and Cholesterol, ketone biosynthesis, degradation of lipids, beta oxidation and association with diseases.
Lecture 24-25:	Lipids in mitochondrial and chloroplast membranes
Lecture 26-27:	Steroids and prostaglandins as signalling molecules

SUB-MODULE: (d) NUCLEIC ACIDS (9 Lectures)

Lecture 27:	Primary, secondary and tertiary structural organization and modification of DNA
Lecture 28:	Primary, secondary and tertiary structural organization and modification of RNA
Lecture 29:	Nucleotide Metabolism: Synthesis and degradation of Nucleotides
Lecture 30-32:	Gene regulation through DNA modifications and RNA molecules
Lecture 33-35:	Genome organization and whole genome analysis

MODULE 1

PRACTICALS (56 HOURS)

Practical 1:	Electrophoresis (1 day)
Practical 2:	Nucleic Acids isolation solution prep (2 days)
Practical 3:	DNA Amplification-PCR (1 day)
Practical 4:	Protein Solution Preparation, Standards (1 day)
Practical 5:	Isolation and estimation of Proteins, (1 day)
Practical 6:	SDS PAGE (2 days)
Practical 7:	Western Blotting (3 days)
Practical 8:	Membrane isolation (2 days)
Practical 9:	Cholesterol Analysis (1 day)
Practical 10:	GEM (Glycolipid enriched membrane) analysis (2 days)

MODULE II

TOPIC: LABORATORY METHODOLOGIES, BIOSTATISTICS, BIOINFORMATICS AND ETHICS

THEORY CLASSES (53 HOURS)

SUB-MODULES:

(a) Physico-Chemical Principles of Lab Techniques (15 Lectures)

(b) Biostatistics (8 Lectures)

(c) Bioinformatics (7 Lectures)

(d) Clinical Research, Bioethics and Regulatory Guidance (5 Lectures)

SUB-MODULES: (a) PHYSICO-CHEMICAL PRINCIPLES OF LAB TECHNIQUES (15 Lectures)

Lecture 1: Chromatography: Gel Filtration chromatography, TLC/Gas chromatography, Ion exchange and Affinity chromatography.

Lecture 2: Spectroscopy**:** Principles and Methods of UV visible spectroscopy (Nanodrop), Fluorescence spectroscopy, Mass Spectrophotometry, Circular dichroism, Nuclear magnetic resonance

Lecture 3: Electrophoresis: Brief Introduction to types of electrophoresis Paper, Starch and Gel

Lecture 4-6: Nucleic Acid Analysis**:** Principles for Gel Electrophoresis- Agarose and Polyacrylamide. Brief Introduction to Northern, Southern and Western Blotting, PCR- Types of PCR: Hot-Start PCR, Touch Down, Long and Accurate PCR (LA), Inverse PCR; Nested PCR; Real Time PCR. RNA Analysis: RNA Sequencing, *In situ* RNA hybridization; Karyotyping, FISH. Genome Analysis: Microarrays; NGS; DNA methylation Studies; Chromatin immuoprecipitation.

Lecture 7: Bimolecular Interaction Studies**:** Protein-Protein- Yeast two hybrid system systems. Protein DNA: DNA foot printing/ EMSA.

Lecture 8: Microscopy**:** Types of Microscopy Light, Phase Contrast, Fluorescence, FRET (fluorescent anisotropy); FRAP and FLIP; Confocal, Electron Microscopy-Transmission and Scanning; Differential Interference Contrast Microscopy

Lecture 9: Flow Cytometry: Principles, methods and applications of flow Cytometry, Fluorescence activated Cell sorting, BrdU Incorporation, Immuno phenotyping, Cells cycle analysis, Cell Sorting.

Lecture 10: Immunological analysis**:** Immunofluorescence, ELISA, Magnetic sorting.

Lecture 11: Embedding and Sectioning and Staining - Paraffin Sectioning, Cryosectioning, Histological Staining; IHC.

Lecture 12: Cell Culture Techniques**:** Isolation of Primary Cultures; Embryonic Stem Cell Derivation; Generation of IPSCs, Organoid Cultures, Hybridoma Technology

Lecture13-14: Genetic Manipulation**:** Cloning (Nuclear Transfer; SCNT). Generation of Cell Lines (Transformation of primary cells to cell lines, Report Constructs; Selectable Markers). Gene Editing (Homologous Recombination –Cre/loxP system; CRISPR Cas9 system, RNA Interference using siRNA, miRNA, Selection of Recombinants).

Lecture 15: Animal Models - Types of Models (Spontaneous, Experimental, Humanized) Breeding Systems (Inbreed/outbreed). Transgenic Models: (Knock in, Knock Out). Mouse Handling Techniques.

SUB-MODULE: (b) BIOSTATISTICS (8 LECTURES)

Lecture 16: Introduction and basic concepts: Definition – Biostatistics, Examples of applications of statistics in Biology, Variable – Qualitative & Quantitative: Nominal, Ordinal, Discrete, and Continuous

Lecture 17: Sampling: Definitions: Population Sample, Advantages of Sample Studies, Types of Sampling (Probability & Non Probability Sampling), Methods of Sampling (Procedure, merits, demerits and applications only- Simple random sampling, stratified random sampling, systematic sampling, cluster sampling), Sampling error

Lecture 18-19: Descriptive statistics**:** Averages (Calculations, merits, demerits and uses), Arithmetic mean, Geometric mean, Median and Mode; Measures of dispersion (Computation, merits, demerits and application). Range, Inter Quartile Range, Variance, Standard deviation, Coefficient of Variation; Graphical Presentation of data (Pie chart, Bar diagram, Line graph, Histogram, Frequency polygon, Frequency Curve)

Lecture 20: Probability and Probability distributions**:** Sample space, Events. Definition of probability (Classical, Relative Frequency, Axiomatic). Properties of probability (only statements), Conditional probability, Addition theorem, Multiplication theorem and Baye's theorem (only statements). Discrete probability distributions - Binomial and Poisson (concept and list of applications). Continuous probability distribution - Normal distribution (concept, properties and applications).

Lecture 21: Concepts of tests of significance: Null hypothesis, Alternate hypothesis**.** Type I error, Type II error**.** level of significance**.** p-value**.** Power of the test. Tests of significance (Chi-square test, Z test (for proportions), Student's t-test (paired and unpaired), One-way analysis of variance (only introduction))**.** Confidence interval for mean and proportion.

Lecture 22: Correlation and regression : Dependent Variable, Independent Variable. Definition and properties of simple Pearson's correlation co-efficient. Test of significance of correlation co-efficient. Concept of simple linear regression. Scatter graph with regression line

Lecture 23: Sample size determination: Importance of sample size determination in Biological Sciences Research. Sample Size for -estimating mean, comparing two means, estimation proportion, comparing two proportions.

SUB-MODULE: (c) BIOINFORMATICS (7 LECTURES)

Lecture 24: Introduction to biological databases.

Lecture 25: Literature and sequence databases.

Lecture 26: Concepts of sequence alignment programs.

Lecture 27: High-throughput genomics.

Lecture 28: Protein-protein interactions.

Lecture 29: Systems biology and pathway databases.

Lecture 30: Biocomputing for informatics.

SUB-MODULE: (d) CLINICAL RESEARCH, BIOETHICS AND REGULATORY GUIDANCE (5 Lectures)

Lecture 31:	Fundamental Ethical Principles
Lecture 32:	Laboratory-based Human Embryonic Stem Cell Research, Embryo Research, and Related Research Activities:Review Processes,Procurement of Biomaterials, Derivation, Banking and Distribution of Human Pluripotent Stem Cell Lines and Mechanisms for Enforcement
Lecture 33-34:	Clinical Translation of Stem Cells: Cell Processing and Manufacture, Preclinical Studies, Clinical Research, Stem Cell-based Medical Innovation and Clinical Application
Lecture 35:	Communications and Standards in Stem Cell Research

MODULE II

PRACTICALS (70 HOURS)

Practical 1:	Spectrophotometery general concepts (1 Day)
Practical 2:	Chromatography general concepts (1 Day)
Practical 3:	Restriction Digestion (1 Day)
Practical 4:	Ligation (1 Day)
Practical 5:	Transformation (1 Day)
Practical 6:	PAS Staining/Starch Staining (1 Day)
Practical 7:	Enzyme action and Analysis (1 Day)
Practical 8:	Introduction to phase Contrast/Fluorescent/Time Lapse Microscope (1 Day)
Practical 9:	Introduction to Flow Cytometry (1 Day)
Practical 10:	Descriptive statistics (2 Days)
Practical 11:	Probability and probability distributions (2 Days)
Practical 12:	Concepts of tests of significance (2 Days)
Practical 13:	Search strategies for biological databases (1 Day)
Practical 14:	Assessment of homologous sequences using phylogenetic analysis (1 Day)
Practical 15:	Visualization of genomic data using genome browsers (1 Day)
Practical 16:	Online tools for bioinformatics analysis (gene expression, ontology and pathway) (1 Day)
Practical 17:	Protein databases and visualization (1 Day)

MODULE III

TOPIC: ARCHITECTURE OF CELLS TISSUES AND ORGANS

THEORY CLASSES (53 HOURS)

SUB-MODULES

(a) Basic cell structure and functions 10 Lectures

(b) Tissue organization and functions 10 lectures

(c) Organ structure and functions 10 lectures

(d) Integrated cell biology 5 Lectures

SUB-MODULE: (a) BASIC CELL STRUCTURE AND FUNCTIONS (10 Lectures)

Lecture 1: Bio-membranes: composition and structural organization

Lecture 2-5: Cellular organelles: Structure, function and biogenesis of (a) Mitochondria (b) Nucleus (c) Other Vesicular structures (Golgi/lysosomes/ER) (d) Relevance of chaperons and unfolded protein response. Abnormal biogenesis and metabolic diseases. Organelle fractionation and techniques to study vesicular traffic in live cells

Lecture 6-8: Cytoskeleton: Basic components (Microfilaments, Microtubules, and Intermediate filaments), Cytoskeletal reorganization during cell migration, cell division, chemotaxis, vesicular traffic, EMT

Lecture 9-10: Eukaryotic cell cycle and its regulation

SUB-MODULE: (b) TISSUE ORGANIZATION AND FUNCTIONS (10 lectures)

Lecture 11: Tissue types: Key features of Epithelial, connective, Muscular, Nervous tissues

Lecture 12-14: Integrating cells into tissues: Cell-cell junctions, cell-ECM interactions adhesion molecules, maintaining cell polarity

Lecture 15-17: Maintenance of tissue architecture**:** Outside-in and inside-out signaling (Integrin signaling), adhesive interactions in motile and non-motile cells

Lecture 18-20: Intercellular communication in tissues: Gap junction mediated cell-cell communication (during apoptosis, in electrically active cells/tissues, during development)

SUB-MODULE: (c) ORGAN STRUCTURE AND FUNCTIONS (10 LECTURES)

Lecture 21: Cardiovascular system

Lecture 22-24: GI (Liver, pancreas, intestine, gall bladder)

Lecture 25-26: Nervous System (CNS, PNS, structure of Neurons & Glia, Action potential, neural transmission)

Lecture 27: Respiratory System

Lecture 28-30: Connective Tissues (bone, cartilage, adipose)

SUB-MODULE: (d) INTEGRATED CELL BIOLOGY (5 LECTURES)

Lecture 31-33: Organ homeostasis, Tissue repair, remodeling and regeneration (in homeostasis and disease)

Lectures 34-35: Model organisms and organ systems to study repair and regeneration (examples from Hydra, Drosophila, Zebrafish, C. elegans models)

MODULE III

PRACTICALS (53 HOURS)

Practical 1: Cell Culture Techniques, Media Preparation, Thawing cells (1 Day)

Practical 2: Sub culture, Freezing, Cell Counting by Trypan blue (1 Day)

Practical 3: Viable cell Counting (MTT) (1 Day)

Practical 4: Viable cell Counting (Flow Cytometry) (1 Day)

Practical 5: Cell culture techniques (2 Days)

Practical 6: Cytoskeletal Analysis by Immunocytochemistry (2 Days)

Practical 7: Cell cycle analysis (2 Days)

Practical 8: Sectioning and tissue specific staining (3 Days)

Practical 9: Karyotyping (3 Days)

MODULE IV

TOPIC: EMBRYONIC DEVELOPMENT AND CELL DIFFERENTIATION

THEORY CLASSES (53 HOURS)

SUB-MODULES

(a) Early embryonic development 11 Lectures

(b) Mid to late embryonic development 12 Lectures

(c) Tissue specific stem cells 12 Lectures

SUB-MODULE: (a) EARLY EMBRYONIC DEVELOPMENT (11 Lectures)

Lecture 1:	Fertilization- formation of the zygote
Lecture 2-3:	Cleavage and blastocyst formation
Lecture 4-6:	Implantation
Lecture 7-8:	Formation of germ layers- gastrulation
Lecture 9:	Medical implications - Infertility, *In Vitro* Fertilisation and Intra Cytoplasmic Sperm Injection
Lecture 10-11:	Embryonic stem cells

SUB-MODULE: (b) MID TO LATE EMBRYONIC DEVELOPMENT (12 Lectures)

Lecture 12-13:	Anterior/Posterior axis formation; left and right axis formation
Lecture 14-15:	Formation of heart and blood vessels
Lecture 16-17:	Formation of liver, pancreas and GI tract
Lecture 18:	Formation of bone and cartilage
Lecture 19-20:	Formation of CNS and PNS
Lecture 21:	Formation of hematopoietic system
Lecture 22:	Medical implications- Parturition and multiple pregnancies
Lecture 23:	Primordial tissue specific stem cells

SUB-MODULE: (c) TISSUE SPECIFIC STEM CELLS (12 Lectures)

Lecture 24-26:	Peri- and post-natal Mesenchymal stromal cells
Lecture 27-28:	Hematopoietic stem cells
Lecture 29-30:	Neural stem cells
Lecture 31-32:	Cardiac stem cells
Lecture 33:	Hepatic stem cells
Lecture 34-35:	Induced pluripotency

MODULE IV

PRACTICALS (53 HOURS)

Practical 1:	ESC culture and characterization (5 Days)
Practical 2:	Stages of Development- sectioning and tissue specific staining (4 Days)
Practical 3:	IVF clinic visit (1 Day)
Practical 4:	MSC culture and characterization (5 Days)

SEMESTER II

- Intercellular Communication in Stem Cell Niches
- Biomaterials and Tissue Engineering
- Clinical Applications of Stem Cells
- Non Clinical Applications of Stem Cells

Theory Classes: There would be 120 classes each of 90 min. duration on all working days. The theory classes would be followed by a 15 day program on Research Methodologies and Scientific Project Management during last two weeks of April. Study leave and examinations will be conducted from May 1 onwards.

THERE WILL BE **FOUR** MAIN MODULES AND **SIXTEEN** SUBMODULES IN THE THEORY LECTURES

MODULE NUMBER	**MODULE**		**NUMBER OF LECTURES**
1	**INTERCELLULAR COMMUNICATION IN STEM CELL NICHES**		**30 Lectures**
	SUB MODULE		
	a	Introduction to stem cell niches and niche regulation	10 Lectures
	b	Types of stem cell niches	10 Lectures
	c	Epithelial to Mesenchymal transition in stem cells	10 Lectures
2	**BIOMATERIALS AND TISSUE ENGINEERING**		**30 Lectures**
	SUB MODULE		
	a	Properties and fabrication of Biomaterials	10 Lectures
	b	Types of intercellular junctions	10 Lectures
	c	Tissue Printing Ex vivo Organogenesis	5 Lectures
	d	Current Challenges in Cell and Tissue Engineering	5 Lectures
3	**CLINICAL APPLICATIONS OF STEM CELLS**		**30 Lectures**
	SUB MODULE		
	a	Stem Cells Application in Ocular Diseases	5 Lectures
	b	Stem Cells Application in Endocrine Diseases	6 Lectures
	c	Stem Cells Application in Neurological Diseases	7 Lectures
	d	Stem Cells Application in Immunotherapy	6 Lectures
	e	Stem Cells Application in Hematological Disorders	6 Lectures
4	**NON CLINICAL APPLICATIONS OF STEM CELLS**		**30 Lectures**
	SUB MODULE		
	a	Stem Cells in Drug Screening and Toxicology	7 Lectures
	b	Disease Modeling with Stem Cells	7 Lectures
	c	Stem Cells in Tissue Remodeling	6 Lectures
	d	Stem Cells as Discovery Tools	6 Lectures

MODULE I

TOPIC: INTERCELLULAR COMMUNICATION IN STEM CELL NICHES

THEORY CLASSES (45 HOURS)

SUB-MODULES:

(a) Introduction to stem cell niches and niche regulation 10 Lectures

(b) Types of stem cell niches 10 Lectures

(c) Epithelial to Mesenchymal transition in stem cells 10 Lectures

SUB-MODULE: (a) JUNCTIONAL COMPLEXES AND THEIR SIGNALING FUNCTIONS (10 lectures)

Lecture 1-3: Types of Junctional complexes- Tight, Gap, Adherens

Lecture 4: Components of a stem cell niche- soluble, insoluble

Lecture 5: Extracellular matrix ECM regulated signaling

Lecture 6-8: Signaling in stem cells niches

Lecture 9: Dysregulation of stem cell niches

Lecture 10: *Ex vivo* generation of stem cell niches

SUB-MODULE: (b) TYPES OF STEM CELL NICHES (10 Lectures)

Lecture 11: Embryonic stem cell niches

Lecture 12-13: Hematopoietic stem cell niche

Lecture 14: Limbal stem cell niche

Lecture 15: Intestinal stem cell niche

Lecture 16: Epidermal stem cell niches

Lecture 17: Neurogenic niche

Lecture 18: Muscle stem cell niche

Lecture 19: Germ stem cell niche

Lecture 20: Cancer stem cell niche

SUB-MODULE: (c) EPITHELIAL TO MESENCHYMAL TRANSITION (EMT) IN STEM CELLS (10 Lectures)

Lecture 21-22: EMT basic concepts-polarity to migration; MET

Lecture 23-24: Cellular events and Molecular mediators of EMT

Lecture 25: EMT during early embryo development (Type 1)

Lecture 26: EMT and MET in cellular reprogramming

Lecture 27: EMT in wound healing and regeneration [Type 2]

Lecture 28- 29: EMT in cancer progression and metastasis [Type 3]

Lecture 30: EMT in disease

MODULE 1

PRACTICALS (88 HOURS)

Practical 1: Analysis of Junctional proteins (3 Days)

Practical 2: Generation of acellular stroma (4 Days)

Practical 3: Staining of the acellular stroma (1 Day)

Practical 4: Magnetic cell sorting and analysis (2 Days)

Practical 5: Enumeration of CD34 cells (2 Days)

Practical 6: Growth of HSCs on acellular stroma (1 Day)

Practical 7: Plating of cells (1 Day)

Practical 8: Cell counts/calculation of HSC cell expansion (1 Day)

Practical 9: Mouse embryonic fibroblast isolation (2 Days)

Practical 10: Neural crest cell isolation from chick embryos (2 Days)

Practical 11: Stage profiling EMT markers from cancer cells (3 Days)

Practical 12: Nuclear and cytoplasmic beta catenin localization (3 Days)

Practical 13: Preparation of amniotic membrane as cell growth substrate (1 Day)

MODULE II

TOPIC: BIOMATERIALS AND TISSUE ENGINEERING

THEORY CLASSES (45 HOURS)

SUB-MODULES:

(a) Properties and fabrication of Biomaterials	10 Lectures
(b) Application of biomaterials in tissue and organ regeneration	10 Lectures
(c) Tissue Printing Ex vivo Organogenesis	5 Lectures
(d) Current Challenges in Cell and Tissue Engineering	5 Lectures

SUB-MODULE: (a) PROPERTIES AND FABRICATION OF BIOMATERIALS (10 lectures)

Lecture 1:	Introduction to Tissue Engineering
Lecture 2-3:	Natural and Synthetic Biomaterials
Lecture 4-5:	Surface and Biomechanical Properties of Scaffolds
Lecture 6-7:	Fabrication and modifications of Scaffolds
Lecture 8:	Extra Cellular Matrix as a Biomaterial
Lecture 9:	Bioreactors
Lecture 10:	Cellularized scaffolds with stem cells

SUB-MODULE: (b) APPLICATION OF BIOMATERIALS IN TISSUE AND ORGAN REGENERATION (10 Lectures)

Lecture 11-12:	Biomaterial Induced Osteognesis/Bone Regeneration
Lecture 13-14:	Biomaterial induced Chondrogenesis/Cartilage Regeneration
Lecture 15-16:	Biomaterial induced cardiovascular regeneration
Lecture 17-18:	Biomaterials induced repair/regeneration of pancreas and liver
Lecture 19:	Lineage specific hematopoiesis on scaffolds
Lecture 20:	Regeneration of corneal tissue on scaffolds

SUB-MODULE: (c) TISSUE PRINTING AND EX VIVO ORGANOGNESIS (5 lectures)

Lecture 21: 3D printing of scaffolds

Lecture 22: Bio Artificial Liver

Lecture 23: Regeneration of skin

Lecture 24: Mechanical and Biological heart valves

Lecture 25: Regeneration of the trachea

SUB-MODULE: (d) CURRENT CHALLENGES IN CELL AND TISSUE ENGINEERING (5 Lectures)

Lecture 26: Biomechanical incompatibility of scaffolds

Lecture 27: Cell-biomaterial interactions

Lecture 28: Immunosuppression and Immunomodulation

Lecture 29: Biomimetic Scaffolds

Lecture 30: 3D printing of Organs

MODULE II

PRACTICALS (18 HOURS)

Practical 1: Cell growth and toxicity analysis on biomaterials (5 Days)

MODULE III

TOPIC: CLINICAL APPLICATION OF STEM CELLS

THEORY CLASSES (45 HOURS)

SUB-MODULES

(a) Stem Cell Applications in Endocrine Diseases	6 Lectures
(b) Stem Cell Applications in Neurological Diseases	7 Lectures
(c) Stem Cell Applications in Ocular Diseases	5 Lectures
(d) Stem Cell Applications in Immunotherapy	6 Lectures
(e) Stem Cell Applications in Haematological Disorders	6 Lectures

SUB-MODULE: (a) STEM CELL APPLICATION IN ENDOCRINE DISEASES (6 Lectures)

Lecture 1-2: Disorders of endocrine system

Lecture 3-4: Generation of Gastro intestinal cells from stem cells

Lecture 5: Endodermal organoid culture system

Lecture 6: Modelling endodermal diseases using stem cells

SUB-MODULE: (b) STEM CELL APPLICATIONS IN NEUROLOGICAL DISEASES (7 Lectures)

Lecture 7: Sources of stem cells for brain repair

Lecture 8: Animal models of neurodegenerative disorders

Lecture 9-11: Treatment of Parkinson's disease, cerebral stroke, multiple sclerosis and ALS with stem cells

Lecture 12-13: Stem cells for the treatment of motor neuron disease and spinal cord injury

SUB-MODULE: (c) STEM CELL APPLICATIONS IN OCULAR DISEASES (5 Lectures)

Lecture 14-15: Ocular development and disorders

Lecture 16: Stem cells in corneal regeneration

Lecture 17: Stem cells in retinal regeneration

Lecture 18: Current status of Clinical trials

SUB-MODULE: (d) STEM CELL APPLICATIONS IN IMMUNOTHERAPY (6 Lectures)

Lecture 19: Introduction to immunotherapy, activation and suppression Immunotherapies

Lecture 20: Transplantation immunity

Lecture 21: Application of MSCs as an immunomodulator during transplantation

Lecture 22: Autoimmune disorder and application of stem cells

Lecture 23: Cancer immunotherapy

Lecture 24: Engineering stem cells for immunotherapy

SUB-MODULE: (e) STEM CELL APPLICATIONS IN HEMATOLOGICAL DISORDERS (6 Lectures)

Lecture 25: Hematopoietic stem cells: concepts, definitions

Lecture 26: Disorders of HSCs: Blood disorders, Anemia, Genetic disorders, Leukemia, Multiple myeloma.

Lecture 27: Differentiation of stem cells to hematopoietic cells

Lecture 28: Umbilical cord stem cells in Hematological disorders

Lecture 29: Therapeutic applications for hematopoietic stem cell gene transfer

Lecture 30: Stem cell model system to study Hematological disorders

MODULE III

PRACTICALS (56 HOURS)

Practical 1: Streptozotocin induced animal model for diabetes; isolation of islets from normal and diabetic mice (7 days)

Practical 2: Isolation of neural stem cells/neural progenitors from the Sub Ventricular Zone (SVZ) of mouse brain, their culture and characterization (9 days)

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MODULE IV

TOPIC: NON- CLINICAL APPLICATIONS OF STEM CELLS

THEORY CLASSES (45 HOURS)

SUB-MODULES

(a) Stem Cells in Drug Screening and Toxicology	9 lectures
(b) Disease Modelling with Stem Cells	8 lectures
(c) Stem Cells in Tissue Remodelling	8 lectures
(d) Stem Cells as Discovery Tools	5 lectures

SUB-MODULE: (a) STEM CELLS IN DRUG SCREENING AND TOXICOLOGY

(9 Lectures)

Lecture 1-3: Embryotoxic potential of chemicals and drugs by Embryonic Stem Cell Test (EST)

Lecture 4-6: Stem cell based drug screening platform for cardio toxicology testing

Lecture 7-8: Neurotoxicity testing using stem cell based screening assay

Lecture 9: Predictive hepato toxicological screen from stem cell derivatives

SUB-MODULE: (b) DISEASE MODELING WITH STEM CELLS (7 Lectures)

Lecture 10-11: Modelling of Haematological disorders

Lecture 12-13: *In vitro* models for cardiovascular diseases

Lecture 14-15: *In vitro* models for neurological diseases

Lecture 16: Stem cell models of genetic disorders

Lecture 17: Stem cell based diabetic models

SUB-MODULE: (c) STEM CELLS IN TISSUE REMODELLING (8 Lectures)

Lecture 18-21: Tissue remodelling in Cancer

Lecture 22-24: Tissue remodelling in Cardiovascular diseases

Lecture 25: Tissue remodelling in Neurological diseases

SUB-MODULE: (d) STEM CELLS AS DISCOVERY TOOLS (5 Lectures)

Lecture 26: High throughput drug screening using cancer stem cells

Lecture 27-28: Use of iPSC derived disease models for drug discovery- case studies (iPS cell repository)

Lecture 29: Discovery of potential small molecular compounds and repurposed drugs with a stem cell based assay platform

Lecture 30: Use of novel drug entities and investigational drugs with stem cell derived screens-case studies

MODULE IV

PRACTICALS (42 HOURS)

Practical 1: Drug Toxicity testing on primary cardiac and neuronal cells (5 days)

Practical 2: iPSC Induction protocols (3 days)

Practical 3: Cancer stem cell specific gene pathway analysis (4 days)

TOPIC: SCIENTIFIC PROJECT WRITING APTITUDE TEST (SP-WAT)

April 16-30.

Students shall be given the following exercises in this session:

1. Scientific paper review: Students will be asked to write a review of a selected research paper in 500 words highlighting the significant findings of that paper along with the critique.
2. Project proposal review: Students shall be given a project proposal as submitted to a funding agency and asked to write the salient features highlighting the strengths and weaknesses of the project proposal. The proposal format shall be selected from the web pages of national and international funding agencies.
3. Grant proposal preparation: Students shall be asked to prepare a short and structured proposal on a topic of their choice in the field of regenerative medicine. The proposal shall be prepared with the intention of request of funding and shall include the research plan and corresponding financial requirements.

N.B. The evaluation of the above exercises shall include the assessment of plagiarism on originality of writing.

SEMESTER III

ELECTIVES

- Neurological Disorders
- Genetic Engineering in Pluripotent Cells
- Stem Cells in Injury and Regeneration
- Organogenesis of Lung in a Dish
- 3D Cellular Models of Cancer Stem Cells

In Semester III the students shall be assigned a specific Principal Investigator (PI), among the SORM Faculty, based on their choice and their ranking in the previous semesters. Each PI will offer 10 Theory Classes, each of 90 min duration and General Practicals of about 170 hours. Following which the students will be offered a 'Mini Project' that shall be completed under the guidance of the respective PI. The performance of students shall be evaluated by internal and external examinations as detailed later.

The purpose of conducting Semester III in the above manner is to give the students hands-on-training in advanced techniques of Stem Cell Biology and train them to organize their experimental data as a scientific project report.

The details of the five representative elective courses are provided in the following pages. Elective topics would be added or revised in the following years.

ELECTIVE I

TOPIC: NEUROLOGICAL DISORDERS
THEORY CLASSES (15 HOURS)

Lecture 1: Neuron Doctorine

Lecture 2: Glial Physiology

Lecture 3: Neurotransmitters, Neuromodulators and receptors

Lecture 4: Sensory and Motor Functions

Lecture 5: Neurobiology of Learning and Memory

Lecture 6: Adult Neurogenesis and Its role in Brain Functions and Diseases

Lecture 7-8: Experimental Approaches to Study Neurodegenerative Diseases

Lecture 9-10: Stem Cell and Stem Cell Based Therapy for Neurodegenerative Disease: Current Status and Future Direction

ELECTIVE I

GENERAL PRACTICALS (170 HOURS)

Practical 1: Establishing Embryonic Chick Primary Cortical Culture

Practical 2: Culture Expansion and Maintenance of hippocampal and spinal cord neuronal cell lines

Practical 3: Immuno cytochemical Assessment of neurogenesis

Practical 4: Immunocytochemical Characterization of Neural and Glial Cells

Practical 5: Developing in vitro model of excitotoxicity using hippocampal/spinal cord neural cell lines

Practical 6: Assessment of neuronal death by lactate dehydrogenase and propidium iodide based flow cytometric method

ELECTIVE I

MINI-PROJECT (430 HOURS)

Assessment of neuroprotective potential of Mesenchymal stem cells in *in vitro* model of hippocampal excitotoxicity

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ELECTIVE II

TOPIC: GENETIC ENGINEERING IN PLURIPOTENT STEM CELLS

THEORY CLASSES (15 HOURS)

Lecture 1: Introduction to genetic engineering and different approaches in gene editing.

Lecture 2: Gene targeting and transgenic animals

Lecture 3: Transgenic animals in complex disease modelling

Lecture 4-5: Zinc finger nuclease, TALEN and CRISPR-Cas9 methods of gene editing

Lecture 6: Application of gene editing in iPSC reprograming

Lecture 7-8: Application of Gene editing in understanding lineage development

Lecture 9-10: Application of gene editing in gene repair and disease modelling

ELECTIVE II

GENERAL PRACTICALS (170 HOURS)

Practical 1: PCR

Practical 2: Cloning

Practical 3: His Tag Protein Purification

Practical 4: SDS PAGE

Practical 5: Western Blotting

Practical 6: Culturing ESCs

ELECTIVE II

MINI-PROJECT (430 HOURS)

Understanding the role of transcription factors during early neural development using gene editing approach.

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ELECTIVE III

TOPIC: STEM CELLS IN INJURY AND REGENERATION

THEORY CLASSES: (15 HOURS)

Lecture1: Phases and components of cell/Tissue injury

Lecture 2: The wound healing response

Lecture 3: Macrophage in injury and regeneration

Lecture 4: Epigenetic regulation of wound healing

Lecture 5: Mesenchymal stem cells for regeneration: Mechanistic insights

Lecture 6: Matrix remodelling during injury and repair

Lecture 7: Chronic and acute injury (Examples from diseases, Diabetes, Ulcers etc

Lecture 8: Fibrosis and the scarring response

Lecture 9: Immune interactions in the tumorigenic niche

Lecture 10: Importance of vascular interactions during injury and regeneration

ELECTIVE III

GENERAL PRACTICAL (170 HOURS)

Practical 1: Differentiation of Mesenchymal stem cells to connective tissue lineages

Practical 2: Real time PCR analysis of differentiation related genes

Practical 3: Detection of intracellular ROS by fluorimetry/flow cytometry

Practical 4: Analysis of phosphorylated proteins by western blotting

Practical 5: ELISA based quantification of cytokines in cell culture supernatants

Practical 6: Immunocytochemistry based analysis of nuclear proteins

Practical 7: Transfection of cells with promoter-reporter constructs to evaluate specific gene promoter activity

ELECTIVE III : MINI-PROJECT (430 HOURS)

Effect of Advanced Glycation End (AGE) products on Mesenchymal stem cell differentiation.

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ELECTIVE IV

TOPIC: 3D CELLULAR MODELLING OF CANCER STEM CELLS AND NOVEL DRUG TARGETING

THEORY CLASSES: (15 HOURS)

Lecture 1: Introduction and fundamentals of the types of tissue engineering substrates

Lecture 2: Substrate and Scaffold Preparation and their surface modifications

Lecture 3: Physicochemical properties of substrates/scaffold - principles and techniques Part 1

Lecture 4: Physicochemical properties of substrates/scaffold - principles and techniques Part 2

Lecture 5: Biological Properties of substrates/scaffolds- Part 1

Lecture 6: Biological Properties of substrates/scaffolds- Part 2

Lecture 7: Scaffolds for maintenance and growth of stem cells

Lecture 8: Scaffolds for growth and differentiation of cardiomyocytes

Lecture 9: Scaffolds for growth and differentiation of osteochondral cells

Lecture 10: Scaffolds for growth and differentiation of neuronal cells

ELECTIVE IV

GENERAL PRACTICALS (170 HOURS)

Practical 1: Basic handling of adherent cell culture

Practical 2: Revival of frozen cell culture

Practical 3: Sub-culturing

Practical 4: Freezing

Practical 5: Establishing mouse embryonic fibroblast primary cell culture

Practical 6: Storage and record

Practical 7: Preparation of acellular matrices

Practical 8: Biochemical characterization of matrices

Practical 9: Microscopic characterization of matrices

ELECTIVE IV
MINI-PROJECT (430 HOURS)

Engineering Substrates and Scaffolds for the Growth and Differentiation of lineage specific cells.

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ELECTIVE V

TOPIC: 3D CELLULAR MODELLING OF CANCER STEM CELLS AND NOVEL DRUG TARGETING

THEORY CLASSES: (15 HOURS)

Lecture 1: Cancer stem cells- Therapeutic targets

Lecture 2: Tissue stem cells and cancer stem cells

Lecture 3: Organoid culture of cancers and tissue

Lecture 4: WNT signalling in cancers and cancer stem cells

Lecture 5: Myocardial ischemia

Lecture 6: Cardiomyopathy

Lecture 7: Stem cell based approach to cardiac disorders

Lecture 8: Signalling networks in neuro-regeneration

Lecture 9: WNT dysregulation neurodegenerative disorders- AD, PD

Lecture 10: Signalling regulation in ALS and MS

ELECTIVE V

GENERAL PRACTICALS (170 HOURS)

Practical 1: Culture of epithelial adherent glioma cell lines and compare with mammary adenocarcinoma lines

Practical 2: 3-D spheroid cultures

Practical 3: Sphere formation and secondary sphere formation assays

Practical 4: Cytotoxicity assay

Practical 5: Alamar blue assay

ELECTIVE V

MINI-PROJECT (430 HOURS)

Drug screens for cancer stem cells and degenerative disease models.

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SEMESTER IV

- DISSERTATION PROJECT

In this semester the students will do a detailed Project under the supervision of the respective Principal Investigators/Guides allocated in semester III. Students are free to choose to work in a laboratory outside SORM anywhere in India or overseas. However the allotted PIs/Guides shall be their immediate supervisors and over see their project progress. The students will submit a project report which will be evaluated as per the schedule given below. The evaluation shall be based upon the originality of the work, style of presentation, open defence and evaluation by an external examiner. The details are provided in the Examinations and Evaluation section.

The schedule for the semester shall be as follows:

1. Project work: January to May
2. Submission of Project Report: June 2nd week
3. Project Presentation: June last week