Recent Advances in Stem Cells and Regenerative Medicine

Core course for Pre-PhD: 4 credits

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Course Name: Recent Advances in Stem Cells and Regenerative Medicine

1. Course Type : Core
2. Level : Ph.D. (Pre-PhD course work)
3. Credit Value: : 4 Credits
4. Total Hours : 60 (L:P:S: 10:25:25)
5. Total Marks: : 100 (IA= 40 + Final exam= 60)

6. Course Objectives

- To develop understanding on the basics of stem cell biology, evolution of regenerative and cancer stem cells, different analytical techniques at the molecular level.
- To train to understand the differences and similarities between regenerative adult, embryonic and cancer stem cells.
- To familiarize with marker expressions in stem cells using various molecular biology techniques
- Equip with basic theory and lab skills needed for research applications.

7. Learning Outcome

This course will enable the students to gain necessary knowledge and skills to perform research in Stem Cells or Regenerative medicine

8. Competencies.

1. Describe the use of the important analytical experimental tools and equipments for stem cell research.
2. Describe important cellular processes relevant to stem cell maintenance and differentiation.
3. Demonstrate physical and chemical methods of sterilization techniques and its importance in stem cell culturing.
4. Perform stem cell culture and characterization experiments using suitable molecular biology tools.
5. Perform cell cycle and sequential marker expressing profiling of embryonic, adult and cancer stem cells and experiments on stem cell energetics.
6. Demonstrate different *in vitro* and *in vivo* models used to describe the mechanisms of stem cell based therapeutics.
7. Practice of safety procedures and appropriate waste disposal protocol in stem cell research.
8. Practice research ethics and adhere to regulatory guidelines while performing stem cell research using biological samples.

9. Content of the Course

Module 1: Bio-Analytical Methods

1.1 Microscopy- Types (Light, Fluorescence, Confocal, SEM and TEM) techniques and applications

1.2 Spectroscopy-Different types of spectroscopies, e.g., UV-Vis, Fluorescence, NMR and their applications

1.3 Separation Methods: Centrifugation-Sedimentation principle, differential centrifugation, different types of centrifuges. Chromatography: types (adsorption, partition, affinity, ion exchange and size exclusion) and applications

1.4 Biological techniques-PCR, qRT-PCR, Electrophoresis, Blotting techniques, ELISA

1.5 Physical and chemical methods of sterilization, Media and buffers, Mammalian and Microbial culture techniques

Module 2: Cell and Molecular Biology

2.1 Biological macromolecules –Carbohydrates, lipids, proteins and nucleic acids– structure and function, Central Dogma, membranes and cell architecture

2.2 Cell cycle regulation- cellular differentiation, proliferation, apoptosis

2.3 Basic principles of Pharmacology/toxicology–Agonist, Antagonist, Receptors, Dose response relationships, Cellular communication

2.4 Enzymes- DNA polymerase, restriction endonucleases, reverse transcriptase, kinase, cloning vector, Plasmids Vectors, Gene cloning, Cloning Strategies

Module 3: Fundamentals of Regenerative and Cancer Stem Cells

3.1 Early development and origin of stem cells; Evolution of stem cells; Stemness basics; Types of stem cells; Embryonic and adult stem cells

3.2 Potency, Stem cell markers, stem cell differentiation, adult stem cells: skeletal muscle, ocular, Wharton's jelly, Bone-marrow, Adipose tissue stem cells

3.3 Cancer stem cells colon and breast. Molecular mechanism of self-renewal; Genetic regulation of stem cell fate; Telomerase and its regulation; Transcriptional regulation, Oncogenes and Tumor suppressor genes

3.4 Stem cell niches; Differentiation, Trans-differentiation; De-differentiation, Changing of phenotypes; Isolation techniques: Explant and enzymatic (primary cultures)

3.5 Characterization techniques - Flow cytometry, Immunofluorescence, Cells cycle analysis, Cell Sorting.

Module 4: Developmental biology, cellular and molecular basis of regenerative and cancer stem cells

4.1 Human and mouse embryonic early development and origin of stem cells; Transcriptional regulation; Symmetric and asymmetric divisions; Regulation of hypoxic genes; Regulation of gap junctions; Cell cycle control; Stem Cell niche under *in vivo* milieu and its significance

4.2 History of embryonic stem cells; Isolation, characterization, differentiation and expansion of human embryonic stem cells; Commercially available human embryonic cell lines; Fetal stem cells – stem cells from umbilical cord; Stem cell niches; Signaling pathways governing stem cell behavior.

4.3 Mesenchymal Stem Cells - Isolation, Characterization and Expansion; Multipotent adult progenitor cells; Differentiation. Wharton's jelly mesenchymal stem cells; isolation, expansion and characterization; Multi-lineage differentiation. Derivation of Adipose, bone marrow, dental pulp and ocular stem cells and their respective developmental origin.

4.4 Autophagy; Autophagy in regenerative and cancer stem cells, Telomere and telomerase dynamics in regenerative and cancer stem cells; Epithelial Mesenchymal Transition (EMT); Altered metabolism in cancer cells; Murine models, carcinogen-induced models, transgenic models, xenograft models, Knock-out and transgenic mice in diabetes research.

Module 5: Translational and Regulatory aspects of stem research

5.1 Ethical issues of stem cell basic and translational research, Clinical trials pertaining to cell therapy products from embryonic, fetal, induced pluripotent and adult origins

5.2 Allogeneic/Autologous: Definitions; allogeneic stem cell transplantation for treating hematological malignancies, bone marrow failure syndromes, immune deficiencies, autologous CD34 cells for treating multiple myeloma.

5.3 Cell dose for transplantation: HLA-identical stem cell transplantation and increasing the cell dose by mobilizing the CD34+ cells into peripheral blood and approaches for the

same.

5.4 Drugs: Various drugs and water-soluble vitamins for targeting cancer stem cells.

Teaching-learning methods

Modules	**Teaching-learning**		
	Lecture	Practical/Hands on	Self study
Module 1: Bio-Analytical Methods	1.1		
			1.2 (Seminar)
	1.3	1.3 (Group discussion)	
	1.4	1.4	
		1.5	-
Module 2: Cell and Molecular Biology	2.1	2.1	2.1
		2.2	
	2.3	2.3 (Team work)	
	2.4	2.3 (Report generation)	2.4
Module 3: Fundamentals of Regenerative and Cancer Stem Cells	3.1	3.1	3.1
			3.2 (Seminar)
		3.3	3.3
		3.4 (Team work)	3.4
		3.5	3.5
Module 4: Developmental biology, cellular and molecular basis of regenerative and cancer stem cells	4.1		4.1 (Seminar)
			4.2 (Seminar)
	4.3	4.3	
	4.4	4.4	
Module 5: Translational and Regulatory aspects of stem research			5.1
	5.2		
	5.3		
		5.4 (Group discussion)	5.4

10. Assessments

Formative assessments: (40 Marks)

1	Internal Exams - 40 marks each (2)	20 M
2	Seminar (2)	8 M
3	Group discussion (2 Including ethical and regulatory issues)	6 M

4	Case studies (2)	6 M

Summative Assessment: (60 Marks)

Sl. No.	Details	Q X M
Two Questions to assess the knowledge and problem solving abilities in the given context		4X10 M=40 M
1	Knowledge on application of any of the major instruments used in used in stem cells for generating data (example; uses of different Microscopes for stem cell characterization)	
2	Problem solving ability: Designing experimental protocol for a given research problem and interpretation of data (Design of study methodology to determine e.g. Potency of embryonic and adult stem cells.)	
3 4	Two questions to assess the analytical skills to solve a given hypothetical research problem (E.g. Write the methodology for solving a given research problem such as organogenesis of pancreatic beta cells from embryonic stem cells.)	
5	Descriptive questions from module 3, 4 and 5 to assess the knowledge, ethics and attitude	4X5=20 M

Learning Resources

Text Books

1. Abul Abbas and Andrew H. Lichtman (2017). Cellular and Molecular Immunology, 9th edition. Elsevier.
2. Brown TA (2010). Gene cloning and DNA analysis: An introduction. Wiley-Blackwell.
3. Bruce Albert, Alexander Johnson, Julian Lewis, Martin Raff, Keith Roberts, Peter Walter (2007). Molecular Biology of the cell- 5th edition. Garland Science, New York.
4. Karp G (2009). Cell and molecular biology: Concepts and experiments. 7th edition. John Wiley& Sons.
5. Paul S. Levy, Stanley Lemeshow (2008) Sampling of Populations: Methods and Applications, Fourth Edition, John Wiley & Sons, Inc.
6. Primrose SB (1994) Molecular Biotechnology, 2nd edition, Blackwell Scientific Publications.
7. Slack JMW (2017). The Science of Stem Cells. John Wiley and Sons.

Reference Books

1. Abul Abbas, Andrew H. Lichtman and Shiv Pillai (2016). Basic Immunology 5th Edition. Elsevier.
2. David L. Nelson and Michael M. Cox (2017). Lehninger Principles of Biochemistry, 6th edition, W. H. Freeman.
3. Lodish H, et al. (2008). Molecular Cell Biology. W. H.Freeman.
4. Watson (1992). Recombinant DNA. Second edition. American Publishers.
5. Wilson K, Walker J (2010). Principles And Techniques of Biochemistry and Molecular Biology, 7th edition. Cambridge University Press.
6. National Ethical Guidelines for Biomedical and Health Research involving Human Participants, 2017, published by Indian Medical Research, 2017,
7. National Guidelines for Stem Cell Research, 2017, Indian Medical Research, New Delhi and Dept. of Biotechnology, 2017

Other Resources (Online Resources or others)

a) Student should also refer leading Journals in the subject category but not limited to specific titles.

b) Journals: e.g. URLs:

https://www.cell.com/cell-stem-cell/home

https://stemcellsjournals.onlinelibrary.wiley.com/journal/15494918

https://www.springer.com/journal/12015

https://www.ncbi.nlm.nih.gov/

https://www.ncbi.nlm.nih.gov/pmc/

https://shodhganga.inflibnet.ac.in/

http://www.ipindia.nic.in/

https://www.wipo.int/

https://www.biotech.co.in/en