COURSE OF STUDIES

for

Doctor of Philosophy

in

Human Genetics & Molecular Biology

UNIVERSITY OF HEALTH SCIENCES, LAHORE PAKISTAN

Program Rationale:

The rationale behind a PhD program in Human Genetics & Molecular Biology is to explore the fundamental biological questions related to genetics and molecular biology. It seeks to unravel the complex systems of human body by exploring how genes, proteins, and other molecules interact to regulate physiological, developmental, and health related processes. It also highlights the latest medical innovations to enhance the quality of life of individuals worldwide. With the high standard of quality teaching and research in various areas of basic and clinical Genetics & Molecular Biology, the program aims to train students/manpower in modern principles of genetic research and provide an encouraging and stimulating environment to foster learning in the discipline of Human Genetics & Molecular Biology. The program also disseminates up-to-date knowledge of Human Genetics & Molecular Biology by organizing journal clubs, seminars and symposia.

Mission Statement:

To provide students with in-depth knowledge of genetics and molecular biology, to familiarize students with recent trends in treatment of genetic disorders and equip them with necessary skills, knowledge and practical training for their research requirements. With a curriculum featuring an interdisciplinary and clinically oriented approach to education and research training, students learn how to perform innovative research as independent scientific investigators**.**

Program Educational Objectives:

1. To flourish and facilitate the continued academic growth and development of basic science education at all academic levels by provision of qualified and competent educators which can successfully streamline and implement the operations of degree awarding institutions.
2. To develop skilled human resources for addressing the indigenous clinical genetic problems (more prevalent in our population) in a better way through focused education, training and research in genetic disorders and genetic counselling.

3. To acquire and execute the research and development projects efficiently and to promote healthy research culture by creating collaborative research opportunities and development of linkages, at national and international frontiers, with top universities and research bodies.
4. To ensure and implement the academic integrity policy of the university through scholarly endeavors requiring original research, thus ensuring that the program challenges students to think logically and creatively and to express themselves independently.

Program Learning Outcomes:

The entire doctoral program in Human Genetics and Molecular Biology typically spans a period of three years. The first year of the study will comprise of two semesters, each of 6 months duration. During the first and second semesters, students will take an intensive set of core courses, which will include modules for research methodology, advanced laboratory techniques and advanced biostatics to develop and implement essential theoretical concepts in research and publications. The subject specific courses in the first and second semester will deepen understanding of the students about genetics, hereditary diseases, innovative treatment options and biological mechanisms at the cell and molecule level. Both the “course work” and “practical lab” sessions are designed to allow students a chance to experience the "big picture" in the field of Human Genetics and Molecular Biology, as well as supplying the facts needed to make an informed decision for the choice of thesis research advisor in view of the research opportunities available in the department. After completion of course work, the students will select a thesis research supervisor, prepare and submit a synopsis of their doctoral research project for subsequent consideration and approval by research/thesis advisory committee. Also the students will sharpen their scientific and grant writing skills by undergoing through a research/review article writing, submission and research grant application procedure. Beginning in the second year, students will focus almost entirely on research and will strive towards achieving a significant scientific accomplishment.

Scheme of Studies(3-Years)

PhD: Human Genetics & Molecular Biology

Semester #	Course code	Course title	Credit hours		
			Theory	Practical	Total
1	ARM-801	Research Methodology	2	0	02
	ABS-802	Advance Biostatistics	2	0	02
	HGMB-804	Fundamentals of Human Genetics and Molecular Biology	2	1	03
	HGMB-805	Molecular basis of genetic diseases	2	0	02
2	ALT-803	Advanced Laboratory Techniques	2	0	02
	HGMB-806	Stem Cells and Gene Therapy	2	1	03
	HGMB-807	Genome Editing Technologies	2	0	02
	HGMB-808	Advanced Cell Biology	02	0	02
3	Research (thesis)		30		30
(Total: 48)					

Course Title: Fundamentals of Human Genetics and Molecular Biology

Contact Hours:	**Credit Hours:**
Theory = 32 hours	**Theory =** 2.0
Practical = 48 hours	**Practical =** 01
Total = 80 hours	**Total =** 3.0

Course Objectives

Through completion of this course, students will gain

1. An extensive knowledge of molecular biology, basic principles of genetics, genetic variation and hereditary mechanisms.
2. Gain knowledge of molecular biology essential for understanding the genetic mechanisms such as DNA replication, transcription, translation and regulation.
3. Explore the relationship between genotype and phenotype, including the inheritance patterns of Mendelian and non-Mendelian traits.
4. Exposure to techniques used in classical as well as modern-day molecular biology and human genetics research, and an appreciation for how they have been used to create the current knowledge in the aforementioned research fields.
5. Practice in experimental design and proposal presentation, using problems addressing contemporary research questions from molecular biology.

Learning Outcome:

1. Demonstrate a thorough understanding of the basic principles of human genetics, including inheritance patterns, genetic variation, and molecular mechanisms underlying gene expression and regulation.
2. Describe the structure and function of DNA, RNA, and proteins, and explain how genetic information is encoded, transmitted, and translated within the cells.
3. Evaluate the relationship between genotype and phenotype, and understand how genetic mutations contribute to human traits, diseases, and genetic disorders.

4. Collaborate effectively in laboratory settings to design and conduct experiments, analyze data, and draw meaningful conclusions related to human genetics and molecular biology.

Course outline:

Module I: Fundamentals of Genetics and Molecular Biology: An introduction to genetics and molecular biology, nucleic acids as the hereditary material**,** DNA structure, DNA replication in eukaryotes and prokaryotes, Gene action: Transcription, Translation, Gene mutation, DNA repair.

Module II: Mendelian Genetics: Single-gene inheritance, Mendel's Laws, Probability, pedigrees

Module III: Non-Mendelian inheritance

Beyond Mendel's laws: incomplete dominance, codominance, multiple alleles, pleiotropy, epistasis, environmental effects, sex-linked inheritance

Practical:

1. Isolation and quantification of DNA & RNA from different tissues

2. Reverse transcriptase PCR

3. Nested PCR

4. Real time PCR

5. Sanger Sequencing

Recommended Books and Literature

1. LEWIS, R. 12th edition *Human Genetics: Concepts and Applications*, McGraw-Hill Companies,Incorporated
2. WATSON & D, W. J. 2004. *Molecular Biology of the Gene*, Pearson Education India.
3. ALBERTS, B., JOHNSON, A., LEWIS, J., RAFF, M., ROBERTS, K. & WALTER, P. 2002. *Molecular Biology of the Cell*, Garland Science.
4. Robert J Brooker. Genetics Analysis and Principles (4th edition). McGraw Hill·

Course Title: Molecular Basis of Genetic Diseases

Contact Hours:	**Credit Hours:**
Theory = 32	**Theory =** 2.0
Practical = 0	**Practical =** 0
Total = 32	**Total =** 2.0

Course Objective:

This course will introduce the historical core of molecular genetics of human diseases and the latest breakthroughs in this rapidly developing discipline and different techniques to find causative elements.

Learning Outcome:

Students will be able to:

1. Distinguish different modes of inheritance for genetic diseases.
2. Gain knowlegede of different molecular biology techniques to find the causative factors of genetic diseases.
3. Distinguish selected inherited diseases based on the molecular mechanisms.

Course Outline:

Single gene, olygenic and Multifactorial disorders, Pedigree analysis, Inheritance patterns, Homozygosity Mapping, Repeat expansion, Chromosomal aberrations and karyotypes, Cancer a genetic disease, Optimizing PCR for clinical diagnosis, Current and emerging techniques for diagnostic mutation detection, Sanger sequencing, Mutations scanning for the clinical laboratory: DHPLC, Mutations scanning for the clinical laboratory: protein truncation test, Comparative sequence analysis, Genes doses analysis by multiplex amplifiable probe hybridization, Prenatal detection of chromosome aneuploidy by quantitative flourescence PCR, Huntington's disease, Hematological applications: Hemoglobinopathies, Cystic fibrosis, Neurofibrometosis, Duchenne and Becker muscular dystrophy, Genetic testing.

Practicals:

NA

Recommended Books:

1. Robert F.W., 2005. Molecular Biology. McGraw-Hill.

2. Lewis, R. 12th edition Human Genetics: Concepts and Applications, McGraw-Hill Companies,

3. Bert,V., and Kinzler, K.W., 2002. The Genetic Basis of Human Cancer. McGraw-Hill.

4. Hanley, M.E., and Welsh, C.H., 2004. Current Diagnosis & Treatment in Pulmonary Medicine. McGraw-Hill Medical.

Course Title: Stem Cells and Gene Therapy

Contact Hours:	**Credit Hours:**
Theory = 32	**Theory =** 02
Practical = 48	**Practical =** 01
Total = 80	**Total =** 03

Course Objectives:

Through completion of this course, students will gain

1. Basic concepts behind the use of stem cells for regenerative medicine applications.
2. Understanding of the basic characteristics, various types and potential capabilities of stem cells.
3. Knowledge about the isolation and characteristics of various types of stem cells as candidates for regenerative medicine, including embryonic stem cells, induced pluripotent stem cells, adult stem cells, neonatal stem cells and tissue resident stem cells.
4. Understanding of the basic concepts, types and strategies of gene therapy
5. Information of the molecular mechanisms of various genome editing techniques and their applications in treating genetic diseases, such as cancer.
6. Knowledge about the gene delivery systems used in gene therapy, and understand their advantages, limitations, and safety considerations.
7. Practical experience through laboratory training used in stem cell culture, gene editing, and gene therapy.

Learning outcomes:

After the completion of this course, students will be able to

1. Demonstrate the fundamental concepts related to the regenerative potential of stem cells and applications of gene therapy.
2. Describe an insightful knowledge of the principles of stem cell based and gene therapy-based treatment options.
3. Know the use and applications of various important techniques such as microscopy, flow cytometry, immunocytochemistry and cell counting.
4. Describe methods and protocols for the isolation and culturing of stem cells from various sources.
5. Develop a deep understanding of the applications of stem cells and gene therapy as treatment modalities for genetic diseases.
6. Know the ethical considerations and challenges associated with stem cell research and gene therapy.

Course Contents

Module I: Stem cell Biology: Introduction of stem cells, Basic characteristics of stem cells, types of stem cells based on their potential (totipotent, pluripotent, multipotent, oligopotent, unipotent), classification of stem cells based on sources (embryonic, adult, neonatal, induced pluripotent), Stem cell niche, 2D culturing vs 3D culturing, current stem cell-based therapies.

Module II: Important techniques: Microscopy, use of microscopy in visualizing stem cells, flow cytometry for analyzing cell populations based on specific markers, cell sorting technique for isolating specific cell populations, immunocytochemistry for visualizing and identifying specific proteins within cells, stem cell counting methods for quantifying the number of viable stem cells.

Module III: Introduction to gene therapy: definition and basic concepts, historical perspective on the development of gene therapy. Types of gene therapy: gene augmentation therapy, targeted killing of specific cells, targeted inhibition of gene

expression, targeted gene mutation correction, Gene Therapy Strategies: Gene therapy approaches, including classical and non-classical methods, methods of gene therapy, such as ex vivo and in vivo gene therapy, methods of gene delivery; applications in Cancer, Genetic diseases and infectious diseases, Adverse effects, limitations

Practicals:

1. Isolation and culturing of stem cells from adipose tissue
2. Isolation and culturing of stem cells from cord blood/cord tissue
3. Microscopy and counting of stem cells
4. Percentage viability of stem cells
5. Population doublings, doubling time, CFUs, plating efficiency
6. Characterization of stem cells using CD markers

Recommended Books and Literature

1. LEWIS, R. 12th edition. *Human Genetics: Concepts and Applications*, McGraw-Hill Companies,Incorporated
2. Updated internet sources
3. https://www.mayoclinic.org/tests-procedures/gene-therapy/about/pac-20384619
4. https://www.news-medical.net/health/What-is-Gene-Therapy.aspx
5. https://www.britannica.com/science/gene-therapy

Course Title: Genome Editing Technologies

Contact Hours:	Credit Hours:
Theory = 32	**Theory =** 02
Practical = 0	**Practical =** 0
Total = 32	**Total =** 02

Course Objective:

Through completion of this course, students will gain

1. Understanding of the basic molecular biology techniques such as PCR, DNA sequencing and cloning.
2. Knowledge of the basic concepts of genome editing techniques such as CRISPR-Cas9 and the molecular mechanisms underlying their genome editing potential at a molecular level.
3. To discover ways by which genome editing can be used for genetic research and treatment of human diseases.

Learning Outcome:

After the completion of this course, students will be able to

1. Explain the principle and the mechanism of various genome editing techniques such as CRISPR-Cas9.
2. Demonstrate genome editing as a treatment option for genetic diseases
3. Knowledge about the diverse applications of genome editing in various fields including medicine and biotechnology.
4. Acquire practical skills in designing and conducting genome editing experiments, analyzing data, and interpreting results.

Course Outline:

An introduction to genetics, DNA structure and gene expression, An overview of molecular biology techniques such as PCR, DNA sequencing, and gene cloning. An introduction to genome editing: Historical perspective of genome editing research. Types of genome editing techniques such as Zinc finger nucleases (ZFNs), Transcription activator-like effector nucleases (TALENs), CRISPR-Cas9, and other emerging technologies. CRISPR-Cas9 System: Molecular components of CRISPR-Cas9. Designing guide RNAs for target specificity. Applications of CRISPR-Cas9 in gene knockout and knock-in. Challenges and strategies for minimizing off-target effects. Therapeutic applications in gene therapy and personalized medicine. Ethical implications of genome editing

Practicals:

NA

Recommended Books:

1. CRISPR-Cas: A Laboratory Manual" by Jennifer Doudna and Prashant Mali. Cold Spring Harbor Laboratory Press
2. Genome Editing: A Practical Guide to Research and Clinical Applications. 1st Edition" edited by Debmalya Barh and Santosh Kumar.
3. CRISPR Gene Editing: Methods and Protocols" edited by Rodolphe Barrangou – Springer Nature.
4. Updated information from internet resources
5. Genome Editing: The Next Step in Gene Therapy" edited by Daniel Scherman and Christophe Benoist. Springer Nature.

Course Title: Advance Cell Biology

Contact Hours:	**Credit Hours:**
Theory = 32	**Theory =** 2
Practical = 0	**Practical =** 0
Total = 32	**Total =** 2

Course Objectives

Through completion of this course, students will gain

1. Understanding of advanced concepts related to membrane structure, cellular transport mechanisms, and intracellular trafficking.
2. Insight about the compartmentalization in eukaryotic cells and its significance, general principles of cell signaling, and structure and function cytoskeleton.
3. Understanding the role of cell-cell junctions in tissue organization and communication, how cells respond to various stresses.

Learning Outcome:

After the completion of this course, students will be able to

1. Demonstrate a comprehensive understanding of the complex structure of biological membranes, and evaluate the intricate mechanisms involved in cellular transport, intracellular trafficking pathways, including protein sorting, vesicle formation, and targeting to specific organelles.
2. Evaluate the importance of compartmentalization in eukaryotic cells for cellular organization, function, and regulation of biochemical processes.
3. Apply general principles of cell signaling to understand the mechanisms of signal reception, transduction, and cellular responses to extracellular stimuli.
4. Explain the structure and function of the cytoskeleton, and evaluate the significance of cell-cell junctions in tissue architecture, integrity, and communication.

5. Analyze cellular responses to various stresses and the mechanisms underlying stress-induced responses such as DNA repair, apoptosis, and cellular adaptation.

Course Contents:

Module I: Internal Organization of the Cell: Membrane structure, Membrane proteins, Membrane transport of small molecules and the ionic basis of membrane excitability, Principles of membrane transport, Carrier proteins and active membrane transport

Module II. Intracellular compartments and protein sorting: The compartmentalization of higher cells, transport of molecules into and out of the nucleus, transport of proteins into mitochondria, peroxisomes, endoplasmic reticulum, **v**esicular traffic in the secretory and endocytic pathways

Module III. Cell Signaling: general principles of cell signaling, signaling via G-protein-linked cell-surface receptors, signaling via enzyme-linked cell-surface receptors

Module IV. The Cytoskeleton: Intermediate filaments, microtubules, actin filaments. Cells in their social context, Stem cells and their role in development. Cellular responses to stress and environmental signals, cellular responses to DNA damage, apoptosis and programmed cell death, Cellular responses to various environmental stresses.

Practicals:

NA

Recommended Books and Literature

1. Molecular Biology of the Cell, 4th edition. Bruce Alberts, Alexander Johnson, Julian Lewis, Martin Raff, Keith Roberts, and Peter Walter. New York: Garland Science; 2002. ISBN-10: 0-8153-3218-1ISBN-10: 0-8153-4072-9
2. Essential Cell Biology, 3rd Edition. Alberts Bray Hopkin Johnson Lewis Raff Roberts Walter. ISBN 978-0-8153-4129-1 (hardcover) -- ISBN 978-0-8153-4130-7 (pbk.).
3. Campbell Biology in Focus. **Lisa A. Urry et al.,** ISBN-10: 0-321-81380-4.
4. Cell and Molecular Biology (Concepts and Experiments). Gerald Karp 7th Edition