CURRICULUM

FOR

PHD MOLECULAR BIOLOGY

SHAHEED ZULFIQAR ALI BHUTTO MEDICAL UNIVERSITY, ISLAMABAD,

PAKISTAN

LIST OF PhD COURSES

No.	Course Code	Course Title	Cr. Hrs
1.	SZABMUMB701	Human Molecular Genetics	4(4-0)
2.	SZABMUMB702	Identification of Human Disease Genes	4(3-1)
3.	SZABMUMB703	Molecular Medicine	3(3-0)
4.	SZABMUMB704	Biomedical Ethics	3(3-0)
5.	SZABMUMB705	Techniques in Molecular Biology	4(2-2)
6.	SZABMUMB706	Bioinformatics: A Molecular Evolution	4(2-2)
7.	SZABMUMB707	Genetics and Physiology of Brain development	3(3-0)
8.	SZABMUMB708	Genetics and patho-physiology of sensory systems	2(2-0)
9.	SZABMUMB709	Scientific Paper/Proposal Writing Skills	2(2-0)
10.	SZABMUMB710	Research Paper Review and Presentation	2(1-1)

DESCRIPTION OF PhD COURSES

1. SZABMUMB701 HUMAN MOLECULAR GENETICS

COURSE DESCRIPTION

- Molecular Genetics is a course that explores how information contained in genomic DNA is (i) propagated, and manipulated and (ii) functionally expressed by regulated transcription into RNA - the core molecular properties and processes of genetic systems that underlie all further investigations of organism, clinical, and population genetics.
- The course will focus on developing advanced understanding of these molecules and reactions. It will explore what experimental research in model organisms and humans has taught us about the encoding of genetic information while simultaneously exposing gaps in our understanding.

LEARNING OBJECTIVES

Students will:

1. Learn the mechanistic details of transcription and mRNA translation.
2. Learn the mechanistic details of RNA processing and transport from nucleus to cytoplasm.
3. Describe main modes of Mendelian and non-Mendelian inheritance.
4. Describe the chromosomal basis of inheritance and how alterations in chromosome number or structure may arise during mitosis and meiosis.
5. Learn techniques for analyzing gene expression at the mRNA and protein levels.
6. Demonstrate ability to design experiments to measure mRNA and protein levels and study interaction between RNA/DNA and protein and between different proteins.
7. Demonstrate an ability to use bioinformatics approaches and gain clues about gene/protein function

COURSE CONTENTS:

Human Genome Structure, function and its organization. The cellular and molecular basis of inheritance, , Regulation of gene expression, Large structural variants, copy number variants, How mutations arise, Different types of mutations, SNVs/SNPs, Human migration and genetic diversity, Human Genome Project, Hap Map Project, Haplotypes, Linkage disequilibrium, Family Studies and Significance of Mendelian inheritance, characteristics of Mendelian disorders, Single gene disorders, Inheritance Patterns, Pedigree analysis, Multiple Alleles and complex Traits, segregation analysis, Anticipation, Mosaicism, Uniparental Disomy, Genetic

Polymorphisms, Genomic imprinting, Mitochondrial Inheritance, Genetic Susceptibility to common disease, Types and Mechanisms of Genetic Susceptibility, Disease Models for Multifactorial inheritance, Type 1 and Type 2 Diabetes, Hypertension, Schizophrenia, Alzheimer Disease, Age related macular Degeneration, Cancer Genetics.

COURSE MATERIAL:

1. Human Molecular Genetics 4th Edition, T. Strachan and A.P. Read, Garland Science Press, April 2010
2. Advanced Genetic Analysis: Genes, Genomes and Networks in Eukaryotes. Philip Meneely, ISBN-13: 978-0199219827 , Oxford University Press. 2009
3. Molecular Biology of the Cell, (2008) 5th Editon .B. Alberts, A. Johnson, J. Lewis, M. Raff, K. Roberts & P. Walter 5th Edition Garland Sciences, Taylor and Francis.

2. SZABMUMB702_IDENTIFICATION OF HUMAN DISEASE GENES

COURSE DESCRIPTION

- This course will cover the basic concepts of mapping disease genes using pedigrees.
- This includes the modes of Mendelian inheritance, mapping a Mendelian disease using linkage analysis, the type of mutations that can be found, and the predicted effect of mutation on gene function.
- This course will also cover a number of factors that complicate these studies, and approaches that can be used to circumvent them.
- Finally, this course will cover experimental approaches for identifying disease-associated variants in the absence of protein-coding sequence differences.
- Experimental approaches to discern between haplo-insufficiency and dominant-negative effects will also be discussed.

LEARNING OBJECTIVES

1. Student will be able to take family history and construct and interpret a pedigree. Understand why population ancestry may affect the frequency of Mendelian disease and susceptibility disease
2. Be able to calculate LOD scores
3. Explain how haplotypes are inherited and identify individual haplotypes when given parent and offspring alleles

4. Design an experiment to calculate map distance between two genes.
5. Gain an understanding of methods that are presently in the field and under development to increase the speed and decrease the cost of sequencing

COURSE CONTENTS:

DNA: The hereditary material, Chromosome structure, Types of DNA sequences, Nuclear genes, Multigenes, Transcription, Translation, The Genetic code, Methods of chromosomes analysis, Molecular cytogenetics, chromosome abnormalities, Methods of DNA analysis, Position-independent identification of Human Disease genes, Functional Cloning, Use of Animal Models, Mapping Trinucleotide Repeat disorders, Next Generation Clonal Sequencing, Positional Cloning, Linkage Analysis, Contig Analysis, Candidate Genes, Confirmatory Testing of Candidate Genes, The Human Gene Map, Human Gene maps and mapping of Human Inherited Diseases, Development of New DNA technologies, Sequencing of the Human Genome, Development of Bioinformatics, Comparative Genomics, Functional Genomics, Multifactorial Inheritance-The Liability/Threshold Model, Heritability, Identifying genes that cause Multifactorial disorders.

COURSE MATERIAL:

- Human Molecular Genetics 4th Edition, T. Strachan and A.P. Read, Garland Science Press, April 2010
- Thompson and Thompson Genetics in Medicine. 7th Edition.
- Molecular Cell Biology (2007) 6th Edition. H. Lodish; C.A. Kaiser; M.Krieger. M.P. Scott; A. Bretscher; H. Ploegh; & P. Matsudaira; W.H. Freeman.
- Emery's Elements of Medical Genetics (2012) 14th Edition. Peter D. Turnpenny and Sian Ellard.

3. SZABMUMB703_MOLECULAR MEDICINE

COURSE DESCRIPTION

- This course is designed for Identification of fundamental **molecular** and genetic errors of disease, and development of molecular interventions to correct them.
- Many genetic disorders are characterized by progressive disability or chronic ill health for which there is, at present, no effective treatment.

- Consequently, one of the most exciting aspects of the development of molecular and genomic technologies is the prospect of new treatments mediated through gene transfer, RNA modification and stem cell therapy.
- Limitations of these approaches for the immediate future are also discussed along with conventional approaches to the treatment of genetic disease.
- Until recently, couples at high risk of having a child with a genetic disorder had to choose among contraception, sterilization, termination of pregnancy, adoption, long term fostering and donor insemination. This course describes the development in past three decades about prenatal diagnosis- the ability to detect abnormality in an unborn child.

LEARNING OBJECTIVES

- Student will learn that treatment of genetic disease by conventional means require identification of gene product and understanding the pathophysiology of the disease process and will find out that Therapeutic Options may include dietary restriction or supplementation, drug therapy, replacement of abnormal or deficient protein or enzyme, and replacement or removal of an abnormal tissue.
- How modern DNA technologies have enabled human derived biosynthetic gene products such as human insulin and human growth hormone to be produced for the treatment of human disease.
- The safety and effectiveness of the particular modality of gene therapy has to demonstrated in an animal model
- Acceptability of Stem Cell Therapy against Germline Gene Therapy.
- Use of Embryonic Stem Cells as delivery vehicles for gene transfer technology.
- Prenatal diagnosis can be carried out by non-invasive procedures such as maternal serum, Alpha fetoprotein screening for neural tube defects, the triplet test and nuchal pad screening for Down's syndrome, ultrasonography for structural abnormalities and in the future analysis of free fetal DNA in the maternal circulation.

COURSE CONTENTS:

Genetic diseases and genetic treatment of diseases, Gene therapy, RNA modification, Targeted Gene Correction, stem cells and therapeutic cloning. Assisted Reproductive Technologies and implications for Genetic Disease, Multistep nature of cancer, Genetic Screening, Population Carrier Screening, Neonatal Screening, Prenatal testing and

Reproductive Genetics, Techniques used in Prenatal Diagnosis, Utility of Genetic Testing, Non-invasive prenatal diagnosis, Whole Genome Analysis, Molecular understanding of the immune system, Pharmaco-genomic Testing, Genetic counseling, Establishing the Diagnosis, calculating and presenting the Risk, Ethical Considerations in Carrier detection and predictive testing, Prenatal treatment

COURSE MATERIAL:

- Emery's Elements of Medical Genetics (2012) 14th Edition. Peter D. Turnpenny and Sian Ellard.

- Principles of Molecular Medicine (2006)Editors: Marschall S. Runge MD, PhD, Cam Patterson MD ISBN: 978-1-58829-202-5 (Print) 978-1-59259-963-9 (Online)

4. SZABMUMB704_BIOMEDICAL ETHICS

COURSE DESCRIPTION

- New developments in biotechnology and biomedical sciences that has created the need to address ethical, legal and policy issues that result as a consequence of scientific advancement. The use of human biological material, patents for biological material, cloning and use of stem cells, genetic engineering, onset of human life and death, and the use of vertebrate bio-models.
- This course will cover these issues and develop solutions of such problems. A solution may be found within the socio-cultural problems. Intensive discussion will be accomplished to clarify ethical rules. Thus, essential cell biology seems to be the important part of education for life sciences students and medical students would touch the social and ethical implications of recent biotechnologies in each knowledge-based economy.
- The course outline mainly comprises of the use of human biological material, embryonic stem cells, animal models, biomedicine patenting, education for ethical responsibility

LEARNING OBJECTIVES

In this course student will:

- learn about major ethical questions related to healthcare and bio-medical sciences

- develop an ability to produce and consume moral arguments about those questions(and other real-world issues)
- hone writing skills, learning to write clear and persuasive philosophical arguments
- hone critical thinking skills, learning to engage charitably in discussion aboutmoral issues and how to critically consume moral arguments

COURSE CONTENTS:

Biomedical Ethics, Healthier Humans, Exploration of ethical issues, Ethical legal and social implications of Genomic research, role of Empirical research in Ethical world, Ethics of Assisted Reproductive Technologies, Impact of Genomic technologies on People, Recognition, Uses and limitations of technology in Human Life.the sanctity of human life, Our power to end life, Our power to enhance life ,Our power to interfere with life processes, Power relationships between ourselves and the public and between ourselves and our fellow-researchers, Ethics of Synthetic Genomics, Ethics involved in Stem Cell research, use of cell cultures as alternatives to use of animals, Organ Transplantation in Human beings, Ethics in Xenotransplantation, The need for Ethical review in Biomedical research, Intellectual property rights and patenting in Pakistan.

COURSE MATERIAL:

- Bioethics and Biosafety in Biotechnology (2007) V.Sree Krishna ISBN(10):81-224-2248-9 ISBN (13): 978-81-224-2248-1 New Age International (P) Limited, Publishers, New Delhi- India.
- A collection of relevant review and research articles will also be distributed in class as required reading.

5. SZABMUMB705_TECHNIQUES IN MOLECULAR BIOLOGY

COURSE DESCRIPTION

- An introduction to the theory and laboratory techniques in molecular biology with an emphasis on DNA replication, transcription, gene expression and regulation, DNA sequencing and bioinformatics tools.
- There is both a laboratory and lecture component to this course, which must be taken together. There will be required readings from the textbooks, as well as occasional

additional reading assignments from the literature. Both the lecture and laboratory components will require the use of the Internet which is made available to the student

- Students will learn principles and practice of agarose gel electrophoresis, nucleic acid purification (genomic DNA) nucleic acid quantification, polymerase chain reaction (PCR), and basics of computer based DNA sequence analysis and data acquisition over the internet.
- We will examine aspects of newer/advanced molecular technologies such as next-generation sequencing and microarrays that are especially important in genomics, and discuss the burgeoning 'Genomics and Proteomics' fields.
- We will apply our newly learned molecular techniques toward solving real biological research questions, and presenting results on a poster at International conferences.

LEARNING OBJECTIVES

- Practice basic laboratory techniques and safety in DNA extraction
- Gel electrophoresis to analyze DNA
- Be able to perform and analyze a PCR
- Genotyping and homozygosity mapping by using STR markers
- Be familiar with modern DNA sequencing methods and microarrays and genome determination
- Be able to use readily available computer methods for the modern molecular biology lab
- Know how to work cooperatively in a molecular biology lab

COURSE CONTENTS:

Preparation of genomic DNA from Mammalian tissue , Principles and application of visible UV, Mass spectroscopy, Flame Photometry, Atomic Absorption, Fluorescence Spectroscopy, Chromatographic Techniques, Polymerase Chain Reaction, Sds-Page, 2d gel Electrophoresis, Silver Staining, Isoelectric Focusing, Agarose Gel Electrophoresis, Blotting Techniques (southern, western & northern), Culturing Of Mammalian Cells, DNA Microarrays, Size analysis of PCR products, Restriction Fragment Length Polymorphism, Amplification-Refractory mutation system (ARMS) PCR, Oligonucleotide Ligation Assay,

Confirmation sensitive capillary Electrophoresis, High Resolution Melt Curve Analysis, Sanger Sequencing, Pyro-Sequencing, Next Generation Clonal Sequencing, Dosage Analysis.

PRACTICALS:

Sterilization and Autoclaving, DNA Isolation, RNA Isolation, DNA Isolation from Bacteria, Polymerase Chain Reaction (PCR) Genotyping and Sequencing PCR. Measuring Nucleic Acid and Protein Concentration SDS (Sodium Dodecyl Sulphate) Polyacrylamide Gel Electrophoresis

COURSE MATERIAL:

- Gene Cloning & DNA Analysis by Brown, 6th Edition, ©2001, Blackwell Publishing
- ***Lewin's Genes XI ,*** Jones and Bartlett Publishers,11th Revised edition
- Robert, F. W., 2005. Molecular Biology. McGraw-Hill.

6. SZABMUMB706_BIOINFORMATICS: A MOLECULAR EVOLUTION

COURSE DESCRIPTION

- This course introduces fundamental concepts and methods for bioinformatics and the advanced applications. Topics covered include bioinformatics database, sequence and structure alignments, protein folding and protein structure prediction, protein-protein interaction. Emphasis is on the understanding of the concepts taught and their practical utilization, with the objective of helping student use cutting-edge bioinformatics tools/methods to solve problems in their own research.
- This is a hands-on, project-oriented class. Most weeks will include one classroom lecture and one period of computer lab time. There will be several homework projects assigned throughout the term.
- Additional time in the lab will be offered for students who want more help with the online portion of their work. Lab work may also be completed on students' own PC at any time.

LEARNING OBJECTIVES

- Learn about bioinformatics and gain understanding of lab and research techniques using molecular biology methods.

- Understand the error, limitations, and costs/sample for each technology.
- Understand methods for producing and using SNP arrays , Compare and contrast exome sequencing to whole genome and SNP sequencing, including their limitations
- Gain familiarity with computational methods in order to address problems in molecular biology.
- Become knowledgeable about the storage, retrieval, sharing and use of biological data, information, and tools

COURSE CONTENTS:

Gene ontology and gene annotations, ontology and identification of molecular pathways, Databases of human genes, Mouse Genes, Gene Expression Patterns, Profiling of micro RNA mRNA Proteins and disease genes by various Browsers, Statistical correlations between Entities in a Database, Statistical correlations between Entities in different Databases, Network models and Pathways, cAMP Pathway, G Protein receptors coupled Pathways, Introduction to Data Mining and its Application, Utilization and exploitation of NCBI, UCSC, ENSEMBL and BioGPS genomic browsers in Genomics and Proteomics research. Primer designing. Repeatmasker, PHRED, PHRAP, BLAST, Prosite/BLOCKS/PFAM, CLUSTALW, Emotif, RasMol, Oligo, Primer3, Molscript, Treeview, Alscript,

COURSE MATERIAL:

- Evolutionary Computation in Bioinformatics Fogel, G.B. and Corne, D.W.
- Pierre Baldi and Soren Brunak, Bioinformatics: The Machine Learning Approach.
- Introduction to Bioinformatics. (A Theoretical and Practical Approach). A. Krawetz and D. Womble. 2002.
- Introduction to Bioinformatics. Lesk, A.M. 2002 Oxford University Press.

A collection of relevant review and research articles will also be distributed in class as required reading.

7. SZABMUMB707_GENETICS AND PHYSIOLOGY OF BRAIN DEVELOPEMENT

COURSE DESCRIPTION

- Brain is the Body's most complex organ.
- Identify each of the major subdivisions of the adult nervous system, and relate them to their embryological precursors and associated ventricular spaces
- Mechanisms of neural development.
- Intelligence arises as the brain reasons, plans, and solves problems.
- Understanding The Power of Human Brain which endows us with a natural curiosity to understand how the world works.
- Brain Excitement in the 21st Century.
- Blue Brain Project.

LEARNING OBJECTIVES

- Characterize the events that occur during gastrulation and neurulation.
- State the significance of induction for the initial development of the CNS.
- Discuss the factors the guide migrating neuroblasts to their final destinations in the developing gray matter structures of the CNS
- Characterize the cellular mechanisms that influence the differentiation of neurons and glia in the CNS.
- Characterize the behaviors and corresponding neural processes that contribute to cognition.
- Discuss the major similarities and differences in the organization of primary cortex and associational cortex
- Discuss the major functions that are localized to the associational cortex of the parietal lobe, frontal and temporal lobe.
- Understanding the mechanisms and actions of various neurotransmitters and their receptors.

COURSE CONTENTS:

Embryological subdivisions of the Human CNS, Early brain development, construction of neural circuits, Overview of the entire nervous system, Structure and function of neurons, memory and learning, Introduction to the neuroscience of cognition, Optogenetics, Brainbow technology, cognition Associational cortex of parietal, frontal and temporal lobe. Anatomical Location and function of Brain Lobes. Neural signaling, Ionic Basis of the Resting Membrane Potential and Action potential. Molecular mechanisms of action potential generation and propagation. Neurotransmitters receptors, Known Genetic Architecture of Brain Patho-physiological mechanisms.

COURSE MATERIAL:

- Medical Physiology Principles for clinical medicine (2012) 4th Edition, Rodney A. Rhoades, David R. Bell. ISBN 978-1-60913-427-3
- Oxford Text book of Medicine (2003) Oxford University Press.
- Pathophysiology- Concepts of altered health states 2007 7th edition Carol mattson Porth.
- Sherwood-Principles of Human Physiology 7th Edition.

8. SZABMUMB708_GENETICS AND PATHO-PHYSIOLOGY OF SENSORY SYSTEMS

COURSE DESCRIPTION

- This course enhances the understanding of Physicians for underlying pathophysiological molecular mechanisms of disease.
- Genetic and molecular components of Vision impairment, Hearing Impairment and vestibular dysfunctions are addressed.
- Neurons communicate using both electrical and chemical signals.

LEARNING OBJECTIVES

- Understanding the neuronal processing mechanisms for Sensation, Perception and action.
- Understanding the genetic and molecular basis of sound transduction.

- Understanding the genetic and molecular basis of vision impairment.
- Identify the neural mechanisms for localizing sounds in space.
- Discuss the organization of the auditory cortex.
- Describe the biomechanics of sensory transduction in the vestibular labyrinth, including the biophysics of hair cell sensory transduction.
- Early processing of sensory information
- Higher-order processing of sensory information
- Life experiences change the nervous system.

COURSE CONTENTS:

General Principles of Sensory systems, mechano-sensation and pathways, The Eye, Central visual Processing, Central and Peripheral Mechanisms of auditory and vestibular systems. Sensory Transduction, Higher order processing of sensory information. Key advances in understanding the molecular components of sensory pathways. Genetically determined circuits are the foundation of the nervous system.

COURSE MATERIAL:

- Medical Physiology Principles for clinical medicin (2012) 4th Edition, Rodney A. Rhoades, David R. Bell. ISBN 978-1-60913-427-3
- Oxford Text book of Medicine (2003) Oxford University Press.
- Pathophysiology- Concepts of altered health states 2007 7th edition Carol mattson Porth.
- Sherwood-Principles of Human Physiology 7th Edition.

9. SZABMUMB709_SCIENTIFIC PAPER/PROPOSAL WRITING SKILLS

COURSE DESCRIPTION

- A course designed to give graduate students the skills necessary to write a thesis, and to prepare other professional materials for presentation or publication. Topics covered in this course include: searching the scientific literature; scientific writing style; writing graduate level papers, proposals, projects, and thesis components; preparing scientific

presentations; presentation of data; using visual aids; and using word processing, spreadsheet, and presentation software.

- In this course, students will develop the scientific and technical reading and writing skills they need to understand and construct research articles. The course will be divided into two parts. In part one of the course, students will learn the principles of writing research papers. First, they will learn what research is, and how the process of research is revealed in the structure of research papers. Next, they will look at software tools that can assist them in the writing of research papers. At the end of the section, students will create their own corpus of research papers and will use throughout the remainder of the course. In part two of the course, students will write a full research paper in their field of specialization, working separately on the title, abstract, introduction, materials/methods, results, and discussion in each unit. For each part of the research paper, students will first analyze the sample texts in their corpus and then present their findings to other members of the class.

LEARNING OBJECTIVES

- Understand the importance of English in the fields of science.
- Understand common problems associated with using technical vocabulary in specialist fields.
- Use effective strategies to learn technical vocabulary in specialist fields.
- Use text analysis tools to identify differences in the audience, purpose, structure, style, and presentation of technical texts in different fields.
- Identify the structure of technical research papers in specialist fields.
- Understand research journal Call for Papers and Instructions for Authors.
- Write the title, abstract, introduction, materials/methods, results, discussion/conclusion sections of a research paper in a specialist field.
- Explain information in figures and tables.
- Know how to strengthen or weaken the interpretation of research findings.
- Understand the importance of references, citations, and avoidance of plagiarism.
- Follow common conventions for citing and referencing information in a research article.

COURSE MATERIAL:

- How to Write and Publish a Scientific Paper. 6th Edition, Robert A. Day and Barbara Gastel. ISBN: 0-313-33040-9

10. SZABMUMB710_RESEARCH PAPER REVIEW AND PRESENTATION

COURSE DESCRIPTION

- Articles types, parts of manuscript, the norms and standards in scientific writing, process of writing and submission, critical review of research articles
- Learning in the course will be facilitated by participation in different scientific workshops

LEARNING OBJECTIVES

This will enable students to

- Critically analyze the relative quality and merit of the research work
- Bring innovative research ideas
- Update on the latest development in the field of study

COURSE MATERIAL:

No textbook required for the class. A collection of relevant review and research articles will be distributed in class as required reading.

SUMMARY OF THE PLAN OF THE STUDY FOR PHD MOLECULAR BIOLOGY (SZABMU)

The Scheme of study is based on requirements in PhD Criteria after MPhil/MS CGPA3.0 (out of 4.0 in Semester system) or First Division (in the Annual System) by **Higher Education Commission of Pakistan.** All courses of Molecular Biology are designed in line with National needs and priority areas of research in this field.

PhD (Molecular Biology) Workload Guidance

Total Number of Credit Hours	18
Course Work Duration	1 year
Number of Regular Semesters	2
Semester Duration	16-18 weeks
Credit hours per semester	9