



Course work for PhD in Medical Biotechnology (with specialization in Medical Genetics)

Department of Endocrinology, Diabetes and Metabolism,

Christian Medical College, Vellore.

(Ph.D. programme affiliated to Regional Centre for Biotechnology)

Each student is required to complete the coursework with minimum eight credits as a part of requirement of the PhD programme. The compulsory courses are mandatory. All other requirements for the PhD programme are as per RCB ordinances and regulations.

COURSE DETAILS

S. No.	Course	Code	Credits	Comp/Optional
1	Stem Cell Biology	CMC 405	1	Optional
2	Biostatistics	CMC 406	2	Compulsory
3	Research Methodology	CMC 407	2	Compulsory
4	Science Communication	CMC 409	2	Compulsory
5	Genetics & Molecular Endocrinology	CMC 410	2	Optional
6	Cell Biology	CMC 411	1	Optional
7	Molecular Methods	CMC 412	1	Optional

STEM CELL BIOLOGY

CMC 405 (1 Credit)

This course is designed to give students exposure to basic and clinical aspects of stem cell biology, scientific interactions, and research. Students develop an in-depth understanding of the field while working in a highly interactive and collaborative research environment.

COURSE CONTENT

The Science of Stem Cells -Basic overview of stem cells, the history of stem cell research, what makes a stem cell a stem cell?– Transcription factors, Chromatin structure, unique properties

Types of stem cells - Embryonic Stem cells, Mesenchymal Stem Cells (MSCs), Haematopoietic stem cells, functions, similarities and differences, proliferation and self- renewal

Induced Pluripotent stem cells (iPSCs)-Introduction, methods of making iPSCs, Direct Reprogramming, tests for pluripotency, applications

Stem Cell Niche- hypothesis and evidence for the stem cell niche, how a niche can regulate stem cell renewal and differentiation, cell-cell signaling in stem cells and differentiation of specialized cells, types of niche, human haematopoietic stem cell niche, The Epithelial Stem Cell Niche in Skin, The Intestinal Stem Cell Niche, The Neural Stem Cell Niche, Common Features, Structures, Functions of the Stem Cell Niche, Cellular and Molecular Components of the Stem Cell Niche, Role of niche in malignancy

Cancer stem cells- origin of cancer stem cells, methods of identification of cancer stem cells, signalling pathways involved in maintaining cancer stem cells, cancer stem cells in disease progression and metastasis, therapeutic implications

Nano Technology and stem cells - Nanomaterials for molecular and cellular imaging, nanoparticle based application for regenerative medicine, Gene manipulation using nanomaterials

Epigenetics & Reprogramming in stem cell biology – epigenetics and cell differentiation, chromatin remodelling, pluripotency gene networks, DNA and Histone modifications

Stem cell therapy -Regenerative Therapy, Applications of Regenerative Medicine in the nervous system, eye, heart, lung, liver, kidney, pancreas and kidney, Large scale manufacturing of cells, tissues and organs, Artificial organs, Gene therapy applications, Engineered Tissues and Regenerative Medicine, Molecular therapy for regeneration, Personalized therapies in Regenerative Medicine, Policy, Regulations and Ethics in stem cell research

Suggested Readings:

1. R. Lanza, J. Gearhart et al (Eds), Essential of Stem Cell Biology. (2014), Elsevier Academic press.
- 2 J. J. Mao, G. Vunjak-Novakovic et al (Ed): Translational Approaches in Tissue Engineering & Regenerative Medicine 2008, Artech House, INC Publications.
3. Stein et al. Human Stem Cell Technology and Biology: A Research Guide and Laboratory Manual. Wiley-Blackwell; 1 edition (January 4, 2011)
4. Lanza et al. Handbook of Stem Cells, Two-Volume Set: Volume 1-Embryonic Stem Cells; Volume 2-Adult & Fetal Stem Cells (v. 1). Academic Press (September 28, 2004)
5. Hossein Baharvand (Editor), Nasser Aghdami (Editor). Regenerative Medicine and Cell Therapy (Stem Cell Biology and Regenerative Medicine). Humana Press; 2013 edition (August 8, 2012)

BIOSTATISTICS
CMC 406 (2 Credits)

The course will provide information regarding basic concepts and common practices for the analysis of biological data using statistical tools and provide opportunity to students to apply these methods on available data sets.

COURSE CONTENT

Data Presentation

Primary and Secondary source data; Significance of Diagrams and graphs (Bar, Pie, Line); Frequency Distribution; Characteristics of frequency distribution; Class intervals: A method of grouping data; Graphical representation of frequency distribution; percentile scales; Types of data, summarizing data; Basic Concepts, type of data, various data collection methods, Measures of central tendency (Mean/Median/Mode); Measures of dispersion (Standard Deviation, Variance, Standard Error, Inter quartile range, Mean Deviation, Coefficient of Variation), Skewness, Moments, Kurtosis.

Basic of SPSS and data manipulation

What is SPSS? Import/Export data, coding, compute, recode, Select cases, If condition,

Basic probability concepts

Introduction to probability; The Probability scale; Measurement of Probability; Laws of Probability for independent events, Conditional Probability; Random variables (Discrete and Continuous, Mean and Standard deviation) and probability distribution; Bayes Theorem; Application of Bayes Theorem; Other applications of Probability.

Distribution Theory

Introduction; Types of distribution; Binomial Distribution (properties, mean and standard deviation); Poisson Distribution (assumptions and mean and standard deviation of Poisson); Normal distribution (properties of Normal Distribution, Area under the normal distribution curve, standard scores; standard normal distribution), t-distribution, Exponential Distribution ; F-distribution; Chi-square distribution.

Sampling techniques and sample size

Introduction; Definition, Types of Population; types of sampling, Sample, Sampling frame sampling variation and bias, Principles of Sampling, Methods of Sampling; probability & Nonprobability sampling techniques; Listing of population, Sample Size, Sampling and Non sampling error

Estimation theory and Statistical Inference

Introduction; Sampling Distribution; Statistical Inference; Type 1 and Type 2 Errors
Test of Significance and Hypothesis (basic principles and test of means and proportions).
Introduction; Procedure; For Large Samples with examples; for small samples with examples;
Estimation: for large samples with examples; Estimation: small samples with examples; reading computer output; confidence intervals.

Linear Regression and Correlation

Introduction; Scatter diagram; Correlation (types of correlation; Linear and Non-linear Correlation; Simple, Partial and Multiple correlation, Rank Correlation, Misuse of correlation coefficient, Correlation and causality) and Regression (Regression Equation; Regression equation of X on Y); Regression Coefficients; Correlation coefficient; Regression Equation, Percentage of variance; Restrictions; Non-linear Regression; Multiple Regression; Other Extensions

Tests of Association

Introduction; Chi-square formula; Distribution of Chi-square and Degrees of freedom; Application of chi-square; Misuse of chi-square test; Goodness of fit statistics; McNemar test for paired samples; Fisher's exact test for small samples.

ANOVA

Introduction; The F-test; One-way ANOVA; Two models of analysis; Assumptions of ANOVA; Two-way ANOVA; Methods of comparing means in the Two-way ANOVA.

Non-parametric tests

Introduction; Advantages of non-parametric test; Disadvantages of Non-parametric test (Mann Whitney U test, Wilcoxon sign rank test, Kruskal Wallis test) t; Some Non-parametric test; some illustrations

Suggested Readings:

1. Altman DG. Practical Statistics for Medical Research, Chapman and Hall.
2. P.S.S. Sundar Rao & J. Richard. Introduction to Biostatistics and Research Methods. PHI Learning Pvt.Ltd.
3. S.P. Gupta, University of Delhi. Elementary Statistical Methods
4. Richard J Shavelson. Statistical Reasoning for the Behavioural Sciences. University of California
5. David S Moore. The Basic Practice of Statistics

RESEARCH METHODOLOGY

CMC 407 (2 Credits)

This course is designed to enable the student to understand the basic principles and practices of common methods used for research in Life Science & Biotechnology. The course deals with contemporary research methodologies, experimental design, data analysis and presentation.

COURSE CONTENT

Objectives and types of research: Motivation and objectives – Research methods vs Methodology. Types of research – Descriptive vs. Analytical, Applied vs. Fundamental, Quantitative vs. Qualitative, Conceptual vs. Empirical.

Research Formulation – Defining and formulating the research problem - Selecting the problem - Necessity of defining the problem - Importance of literature review in defining a problem – Literature review – Primary and secondary sources – reviews, treatise, monographs- patents – web as a source – searching the web - Critical literature review – Identifying gap areas from literature review - Development of working hypothesis.

Research design and methods – Research design – Basic Principles- Need of research design
— Features of good design – Important concepts relating to research design – Observation and Facts, Laws and Theories, Prediction and explanation, Induction, Deduction, Development of Models. Developing a research plan - Exploration, Description, Diagnosis, Experimentation
Determining experimental and sample designs.

Data Collection and analysis: Execution of the research - Observation and Collection of data - Methods of data collection – Sampling Methods- Data Processing and Analysis strategies - Data Analysis with Statistical Packages - Hypothesis-testing - Generalization and Interpretation.

Reporting and thesis writing – Structure and components of scientific reports - Types of report – Technical reports and thesis – Significance – Different steps in the preparation – Layout, structure and Language of typical reports – Illustrations and tables - Bibliography, referencing and footnotes - Oral presentation – Planning – Preparation – Practice – Making presentation – Use of visual aids - Importance of effective communication –.

Ethics in Science -- Copyright, Royalty, Intellectual property rights and Patent laws, Reproduction of published material, Plagiarism, Citation and acknowledgements, Reproducibility and accountability, Conflict of Interest, related topics.

Suggested Readings:

1. Garg, B.L., Karadia, R., Agarwal, F. and Agarwal, U.K., 2002. An introduction to Research Methodology, RBSA Publishers.
2. Kothari, C.R., 1990. Research Methodology: Methods and Techniques. New Age International. 418p
3. Sinha, S.C. and Dhiman, A.K., 2002. Research Methodology, Ess Ess Publications. 2 volumes.
4. Trochim, W.M.K., 2005. Research Methods: the concise knowledge base, Atomic Dog Publishing. 270p.
5. Wadehra, B.L. 2000. Law relating to patents, trade marks, copyright designs and geographical indications. Universal Law Publishing.
6. Katz MJ. From Research to Manuscript, Springer.
7. Kumar A. Mathematics for Biologists, Alpha Science.

SCIENCE COMMUNICATION

CMC 409 (2 Credits)

For a successful scientist, it is very important to effectively convey his work to both the technical and non-technical audience. This may be in the form of verbal and visual communication in the form of seminars and presentations, and written communication in the form of reports, manuscripts, and grant proposals. This course aims to encourage the students to inculcate these attributes by making presentations and writing reports.

Each student will be required to choose a recent high-quality primary research publication and make a power point presentation to the class. The presentation should cover all the background literature of the chosen research area. Stress should be given to the objectives of the paper, logic of each experiment and the data analyses. In addition, they will be expected to highlight shortcomings and alternate approaches as appropriate. This endeavour would give them the exposure of what it takes to defend a scientific concept in an open audience. Additionally, students of this course will mandatorily attend all seminars conducted at the Centre.

For developing the writing skills, the student will choose an area related to his research interest and write a 10-page review of the field providing a critique of the research opportunities. The area may be chosen in consultation with the guide who should help the student with the preparation of the report.

GENETICS AND MOLECULAR ENDOCRINOLOGY

CMC 410 (2 credits)

This course is structured to familiarize students with the fundamental and applied concepts of Human genetics and Genomics that would enable them to apply the theoretical knowledge in formulating research questions and conceptualizing research experiments. This contents on molecular endocrinology aims to impart comprehensive knowledge to the basic science students on molecular and genetic aspects of various endocrine disorders and its clinical relevance.

COURSE CONTENT

Essentials of Genetics and Genomics

Structure and composition of DNA; Mechanisms of Replication, Transcription and translation. Modes of inheritance; Gene regulation mechanisms; Chromatin structure and remodeling; DNA methylation and Histone modifications.

Gene Mapping

Introduction to gene mapping; Gene Mapping in Humans; Gene Mapping and Disease; Idiograms; Rare Genetic Disorders: Learning about Genetic Disease through Gene Mapping, SNPs, and Microarray Data.

Genetic Testing

Genetic Counseling: Genetic Testing, Family History and Psychosocial Evaluation; Cytogenetic Methods in Diagnosing Genetic Disorders; Prenatal Screening; Direct-to-Consumer Genetic Tests; Protecting Your Genetic Information; Ethics of Genetic Testing: Medical Insurance and Genetic Discrimination; Protecting Your Genetic Identity: GINA and HIPAA.

Genomes and Diseases

DNA Sequencing Technologies; Variation in Genomes; Using SNP Data to Examine Human Phenotypic Differences; Copy Number Variation; Sequence Variation & Disease; Genome-Wide Association Studies (GWAS) and Human Disease Networks; Applications: Personalized Medicine.

Population and Quantitative Genetics

Genetic Drift: Bottleneck Effect and the Case of the Bearded Vulture; Genetic Drift and Effective Population Size; Adaptation and Phenotypic Variance; Estimating Trait Heritability.

Molecular Endocrinology with emphasis on clinical relevance and management

1. Syndromes of Resistance to Thyroid Hormone
2. Glucocorticoid Resistance
3. Hereditary Diseases Predisposing to Endocrine Tumors
4. Overview of Genetically Determined Diseases/Multiple Endocrine Neoplasia Syndromes
5. Hereditary Diseases Predisposing to Pheochromocytoma
6. Diseases Predisposing to Adrenocortical Malignancy
7. Genetics of Pituitary Tumours
8. Timeline of Advances in Genetics of Primary Aldosteronism
9. Congenital Adrenal Hyperplasia
10. Diabetes – WHO classification, Monogenic Forms of Diabetes Mellitus
11. Monogenic Diseases Predisposing to Hormone Deficiency, Infertility
12. Pituitary Transcription Factor Mutations Leading to Hypopituitarism
13. Hereditary Neurohypophyseal Diabetes Insipidus
14. Nephrogenic Diabetes Insipidus
15. Monogenic Forms of Male and Female Infertility
16. Genetics of Obesity
17. Chromosomal Aberrations in Endocrine related syndromes (Turner Syndrome, Klinefelter Syndrome, Prader-Willi Syndrome).
18. Overview of Inborn errors of Metabolism.
19. Basics of Neurogenetics including SMA, muscular dystrophy, and other common disorders

Suggested Reading:

1. Gardner EJ, Simmons MJ, Snustad DP. Principles of Genetics. 8th Edition, Wiley.
2. Pierce BA. Genetics: A Conceptual Approach, 6th Edition, W. H. Freeman Publishers.
3. Wolpert L, Tickle C, Arias AM. Principles of Development, 5th Edition, Oxford University Press.
4. <https://www.nature.com/scitable/topic/genetics-5/>
5. Melmed, Shlomo, et al. Williams textbook of endocrinology. Elsevier Health Sciences, 2015.
6. Jameson, J. Harrison's Endocrinology, 3E. McGraw-Hill Education, 2013.
7. Molecular Endocrinology by Franklyn Bolander (Author), Franklyn F. Bolander (Editor)

CELL BIOLOGY

CMC 411 (1 credit)

This course is designed to introduce the basic concepts of eukaryotic cell biology to students. The topics covered include the organization of a typical eukaryotic cell, its compartments and its cytoskeleton, cell division and specialized cell types and the communication between cells.

COURSE CONTENT

Essentials of cell biology

Cell structure and characteristics of cells; Decoding Genetic Information into Functional Proteins; Organization of Eukaryotic cells, Cell signaling and communication; Cell cycle.

Subcellular Compartments

Cell Membranes; Microtubules and Filaments; Endoplasmic Reticulum, Golgi apparatus, and Lysosomes; Mitochondria; Chloroplasts, and Cell Walls

Cell cycle and regulation

The cell cycle and its control system, Interphase, Mitosis, Cytokinesis and molecular regulation, cell transformation, cell death and apoptosis. Eukaryotes and Cell Cycle; CDK; Mitosis; Cell Differentiation and Tissue; Cell Division and Cancer

Intercellular communication

Transport mechanisms across membrane, Cell signaling, Cell junctions, Cell adhesion and the extracellular matrix, specialized cells, tissues, stem cells and tissue renewal.

Proteins and Gene Expression

Ribosomes, Transcription, and Translation, Chromosomes – structure and organization; Gene Expression and mechanisms of regulation; Protein Structure and function

Suggested Reading

1. Alberts B, Johnson A, Lewis J, Morgan D, Raff M, Roberts R, Walter P. Molecular Biology of the Cell, 6th Edition, Garland Science.
2. Lodish H, Berk A, Kaiser C, Krieger M, Scott M, Bretscher A, Ploegh H. Molecular Cell Biology, 6th Edition. WH Freeman.
3. <https://www.nature.com/scitable/topic/cell-biology-13906536/>

MOLECULAR METHODS

CMC 412 (1 credit)

The following module on molecular methods is intended to bring Ph. D students rapidly up to date with the current techniques widely used in molecular genetics and biotechnology – their principles, protocols and their application in clinical diagnosis and research.

COURSE CONTENT

1. Restriction Enzymes: Tools in Clinical Research
2. Southern Blotting as a Diagnostic Method
3. Western Blotting as a Diagnostic Method
4. Principles and Medical Applications of the Polymerase Chain Reaction
5. Introduction to Capillary Electrophoresis of DNA: Biomedical Applications
6. Single-Nucleotide Polymorphisms: Technology and Applications
7. cDNA Microarrays
8. MLPA
9. Oligonucleotide Ligation Assay
10. Quantitative TaqMan Real-Time PCR: Diagnostic and Scientific Applications
11. Use of Denaturing High-Performance Liquid Chromatography in Molecular Medicine
12. Liquid Chromatography-Mass Spectrometry of Nucleic Acids
13. Comparative Genomic Hybridization in Clinical and Medical Research
14. Bioinformatics Tools for Gene and Protein Sequence Analysis In Situ Hybridization
15. Protein Therapeutics: Mouse, Humanized, and Human Antibodies
16. Karyotyping
17. Microsatellite Analysis
18. Analysis of Chromosomal Translocations
19. Next-generation sequencing (2nd and 3rd generation)
20. Single Cell and single nuclei RNA sequencing
21. Methods in proteomics and phosphoproteomics
22. Techniques for Gene Expression
23. Capillary Electrophoresis in Clinical Analysis

24. Flow Cytometry in the Biomedical Arena
25. Immunocytochemistry
26. Ribotyping in Clinical Microbiology
27. The Human Genome Project
28. Prenatal Diagnosis of Inborn Errors of Metabolism
29. Gene Editing and Gene Therapy: Methods and Application
30. Electron Microscopy
31. Confocal Microscopy
32. Laser Microdissection

Suggested Readings:

1. Hofmann, Andreas, and Samuel Clokie, eds. *Wilson and Walker's principles and techniques of biochemistry and molecular biology*. Cambridge University Press, 2018.
2. Carson, Sue, et al. *Molecular biology techniques: a classroom laboratory manual*. Academic Press, 2019.
3. Schleif, Robert F., and Pieter C. Wensink. *Practical methods in molecular biology*. Springer Science & Business Media, 2012.