Curriculum

for

Post-Doctoral Certificate Course (PDCC)

in

Molecular and Biochemical Genetics

All India Institute of Medical Sciences, Kalyani

(Nadia, West Bengal)

CONTENTS

INTRODUCTION

The All India Institute of Medical Sciences Kalyani was established by an Act of Parliament as an Institute of National Importance. The Institute has started its Medical UG and PG degree programs from 2019 and 2023 respectively.

Genetics is the specialty of medicine that involves the diagnosis and management of genetic disorders. With the recent dramatic advances in genomics and genetics, Medical Genetics has emerged as an important clinical specialty worldwide. It is true to say that all diseases have a genetic component, which varies with the disorder. All families with genetic disorders can be helped by making a precise diagnosis, appropriate management and proper counseling. In a resource poor country like India, there is a paramount need for preventing the birth of affected children, and reduce the socio-economic burden of genetic disorders through community control programs comprising genetic screening and prenatal diagnosis. To achieve these objectives a cadre of physicians and scientists trained in genetic medicine is required. This is especially important as Human Genome Project has generated lot of new information that can be applied to help patients and be the basis of personalized medicine.

In India there are several DM and DNB Superspeciality programs available in Medical Genetics catering to the Clinical Disciplines. Till date there is no NMC recognized program catering to the need of Laboratory Geneticists. This Post-Doctoral Certificate Course in Molecular and Biochemical Genetics, therefore, aims to fulfill the pressing need totrain Clinicians/ Laboratorians in Molecular and Biochemical medical genetics, so that they can bring the benefits of modern biology and genomics to the people of India.

PROGRAMME GOAL

This Post-Doctoral Certificate Course in Molecular and Biochemical Genetics will be designed to give Clinicians/ Laboratorians a thorough knowledge of the principles and practice of medical genetics, and prepare themfor a leadership role in training other medical geneticists for Laboratory service and research.

The candidates will be provided hands-on training in modern genetic technologies such as PCR, Sanger sequencing, Next Generation Sequencing, micro-arrays, enzyme assays, FISH and Luminex multiplexing etc. They will be imparted knowledge of the principles of epidemiology and statistics as applied to genetic and genomic research. They will be given the opportunity to carry out research on a chosen topic. They will learn ethical principles as applied to genetic services and practice.

The main goals of This Post-Doctoral Certificate Course in Molecular and Biochemical Genetics are:

- *Impart* training that will enable the trainees to evaluate patients with genetic disease, order appropriate tests, perform these tests independently, interpret them for the patient, make a precise diagnosis and provide genetic counselling.
- *Inform* about screening pregnant women for genetic disease and take appropriate action to prevent birth of children with malformationsand genetic disorders.
- *Provide* skills in laboratory genetics to enable them to establish genetic tests using chromosomal studies, biochemical assays and molecular techniques.
- *Acquaint* candidates with the principles of ethics as applied to genetic services and research.

PROGRAMME OBJECTIVES

In this course main emphasis is laid on practical training in genetic counseling of diverse conditions like mental retardation, metabolic disorders, neurological disorders etc.; as well as basic and advanced genetic and genomic techniques through rotation in different institutions.

The core objective is to inspire in the students a curiosity that prompts them to explore the new world of genetics; to instill in them intellectual and technical tools for a career in clinical genetics; and to emphasize learning of genetics is a lifelong process.

The objectives of the course are summarized below divided into three domains:

(I) Specific knowledge,
(II) Specific skills, and
(III) Attitudes

I. SPECIFIC KNOWLEDGE

At the end of the course the students should have a basic understanding of the following:

1.1) Biology of the cell
1.2) Structure, Function and Behaviour of Genes, and Chromosomes
1.3) Anatomy of the human genome – Gene mapping, linkage and positional Cloning
1.4) Genetic variation - its origin and detection
1.5) Family history and type of inheritance: Mendelian (autosomal dominant, autosomal recessive, x-linked)
1.6) Non-Traditional inheritance – mitochondrial, uniparental disomy, genomic imprinting

1.7) Consanguinity and its Consequences

1.8) Biochemical genetics and inborn errors of metabolism

1.9) Molecular genetics of human diseases - Hemoglobinopathies, Duchenne Muscular Dystrophy (DMD), Spinal Muscular Atrophy, Triplet repeat expansion etc.

1.10) Genetic testing and Genetic screening

1.11) Sequencing, Deep sequencing, Exome sequencing

II. SPECIFIC SKILLS

a) Laboratory techniques

1. Molecular

- ✓ DNA isolation and quantification
- ✓ Probe and primer designing
- ✓ PCR - standard and various modifications
- ✓ Real time PCR
- ✓ MLPA analysis
- ✓ Southern blotting – isotopic and nonisotopic methods
- ✓ Western blotting
- ✓ DNA Sequencing, including massively parallel sequencing
- ✓ Use of microarrays
- ✓ Bioinformatics as applied to sequencing and microarrays

2. Biochemical Genetics

- ✓ Enzyme analysis for storage disorders and neurodegenerative disorders
- ✓ Assays for various metabolites in blood and urine: e.g. succinylacetone, alpha 1 antitrypsin, ceruloplasmin

- ✓ Metabolic tests in urine, thin layer chromatography and High performance Liquid Chromatography for analysis of amino acids

III. ATTITUDES

At the end of the course, the students should learn to:

- *Appreciate* the importance of confidentiality and the difficulties that confidentiality poses when relatives are found to be at risk for a serious and potentially preventable disease.
- *Apply* appropriate techniques for conveying difficult genetic information.
- *Recognize* the importance of imparting information to patients who are anxious or unfamiliar with the concepts being presented
- *Cope* emotionally with patient responses.
- *Recognize* the limitations of their own skills and seek consultation when necessary

ELIGIBILITY CRITERIA FOR ADMISSIONS TO THE PROGRAMME

(A) Post-Doctoral Certificate Course in Molecular and Biochemical Genetics Course:

1. Any medical graduate with DNB/MD/MS in Biochemistry/ Pathology/ Pediatrics/ General Medicine/ OBG qualification, who has qualified the ***Entrance Examination*** conducted by AIIMS are eligible to participate in the Centralized counseling for allocation of Post-Doctoral Certificate Course in Molecular and Biochemical Genetics seats purely on merit cum choice basis.

Duration of Course: 1 Year

Every candidate admitted to the training programme shall pursue a regular course of study (on whole time basis) in the concerned recognized institution under the guidance of recognized post graduate teacher for assigned period of the course.

sTEACHING AND TRAINING ACTIVITIES

The fundamental components of the teaching programme should include:

1. Seminar – Once a week
2. Journal club- Once a week
3. Laboratory/ Clinical Grand round presentation (by rotation departments and subspecialties)-once a week
4. Faculty lecture teaching- once a month
5. A poster and have one oral presentation at least once during their training period in a recognized conference.

The rounds should include bedside sessions, file rounds & documentation of case history and examination, progress notes, round discussions, investigations and management plan) interesting and difficult case unit discussions.

The training program would focus on knowledge, skills and attitudes (behavior), all essential components of education. It is being divided into theoretical, clinical andpractical in all aspects of the delivery of the rehabilitative care, including methodology of research and teaching.

Theoretical: The theoretical knowledge would be imparted to the candidates through discussions, journal clubs, symposia and seminars. The students are exposed to recent advances through discussions in journal clubs. These are considered necessary in view of an inadequate exposure to the subject in the undergraduate curriculum.

Practical Laboratory Training: Trainees would be required to participate in the diagnostic testing services of AIIMS Kalyani so as to attain independent skills in designing and carrying out diagnostic assays.

Symposia: Trainees would be required to present a minimum of 20 topics based on the curriculum in a period of three years to the combined class of teachers and students. A free discussion would be encouraged in these symposia. The topics of the symposia would be given to the trainees with the dates for presentation.

Journal Clubs: This would be a weekly academic exercise. A list of suggested Journals is given towards the end of this document. The candidate would summarize and discuss the scientific article critically. A faculty member will suggest the article and moderate the discussion, with participation by other faculty members and resident doctors. The contributions made by the article in furtherance of the scientific knowledge and limitations, if any, will be highlighted.

SYLLABUS

A. PRINCIPLES OF HUMAN GENETICS

1 Basic Cell Biology: Structure and Function of genes

- DNA, RNA and Protein:
- DNA replication, Transcription, Translation,
- Regulation of gene expression
- Mutations and Mutagenesis- Types of mutations, Structural and Functional effects of mutation on the protein, Different mutagens

2 Patterns of Inheritance

- Family Studies
- Mendelian Inheritance- Autosomal dominant, Autosomal recessive, Sex-linked recessive and dominant inheritance
- Multiple Alleles and Complex Traits
- Genetic heterogeneity
- Variable expressivity
- Genetic instability and Anticipation
- Mosaicism
- Uniparental Disomy
- Genomic Imprinting
- Mitochondrial Inheritance

B. MOLECULAR GENETICS

1 DNA Technology and Applications

- Structure of a gene
- DNA Cloning and The PCR
- Techniques of DNA Analysis- Nucleic acid probes, Nucleic acid hybridization assays
- DNA Sequencing – Sanger, and massively parallel
- Application of DNA sequence polymorphisms- SNPs, VNTRs, Minisatellites, Microsatellites

C. GENETICS IN MEDICINE

1 Hemoglobin and the Hemoglobinopathies

- Structure and Developmental Expression of Hemoglobin
- Synthesis and Control of Hemoglobin Expression
- Disorders of Hemoglobin – alpha , beta and gamma
- Clinical Variation of the Hemoglobinopathies
- Antenatal and Newborn Hemoglobinopathy Screening

2 Biochemical Genetics

- Introduction of Inborn Errors of Metabolism
- Disorders of Amino Acid and Branched-Chain Amino Acid Metabolism
- Urea Cycle Disorders
- Disorders of Carbohydrate Metabolism
- Disorders of Steroid Metabolism
- Disorders of Lipid Metabolism,
- LDL receptor defects
- Lysosomal Storage Disorders
- Disorders of Purine/Pyrimidine Metabolism
- Disorders of Porphyrin Metabolism
- Organic-Acid Disorders
- Disorders of Copper Metabolism
- Peroxisomal Disorders
- Disorders Affecting Mitochondrial Function

- Prenatal Diagnosis of Inborn Errors of Metabolism

3 Pharmacogenetics

- Definition
- Drug Metabolism
- Genetic Variations Revealed by the Effects of Drugs
- Pharmacogenetics

4 Cancer Genetics

- Differentiation between Genetic and Environmental
- Factors in Cancer
- Oncogenes
- Tumor Suppressor Genes
- Epigenetics and Cancer
- Genetics of Common Cancers
- Genetic Counseling in Familial Cancer
- Tumor profiling in cancer and identifying targets for drug therapy

8a. Semester Based Teaching

The 1-year course will be divided into two semesters. Each semester will consist of Laboratory teaching by practice in a continuous way. The postings for the various topics, including clinical and laboratory, are shown in theprogram. In each semester there will be a one-week course on different advanced topics in genetics, organized in, nearby centers like NIBMG Kalyani and IPGMER Kolkata for the candidates. After each module of posting, the candidates will have to assessment as outlined below.

Details of Semester Teaching:

Semester	Activity
1	Metabolic genetics, includes lysosomal disorders & newborn screening **– 12 wk**
	Prenatal genetics – 4 **weeks**
	Cancer genetics **– 4 weeks**
	Clinical Cytogenetics – 4weeks
2	Introduction to Laboratory Medicine in Genetics and it Clinical Application
	Molecular genetics – **6 weeks**
	Cytogenetics – **6 weeks**

	Biochemical genetics **– 6 weeks**
	Immuno-hematology + HLA **– 4 wks,**
	Prenatal procedures - 2 weeks

LOG BOOK

A candidate shall maintain a log book of operations (assisted / performed) during the training period, certified by the concerned post graduate teacher / Head of the department / senior consultant.

This log book shall be made available to the board of examiners for their perusal at the time of the final examination.

The log book should show evidence that the before mentioned subjects were covered (with dates and the name of teacher(s) The candidate will maintain the record of all academic activities undertaken by him/her in log book .

1. Personal profile of the candidate
2. Educational qualification/Professional data
3. Record of case histories
4. Procedures learnt
5. Record of case Demonstration/Presentations
6. Every candidate, at the time of practical examination, will be required to produce performance record (log book) containing details of the work done by him/her during the entire period of training as per requirements of the log book. It should be duly certified by the supervisor as work done by thecandidate and countersigned by the administrative Head of the Institution.
7. In the absence of production of log book, the result will not be declared.

EXAMINATION

FORMATIVE ASSESSMENT

Formative assessment includes various formal and informal assessment procedures by which evaluation of student's learning, comprehension, and academic progress is done by the teachers/ faculty to improve student attainment. Formative assessment test (FAT) is called as "Formative "as it informs the in process teaching and learning modifications. FAT is an integral part of the effective teaching .The goal of the FAT is to collect information which can be used to improve the student learning process.

Formative assessment is essentially positive in intent, directed towardspromoting learning; it is therefore part of teaching. Validity and usefulness are paramount in formative assessment and should take precedence over concerns for reliability. The assessment scheme consists of Three Parts which has to be essentially completed by the candidates.

The scheme includes:-

Part I:- Conduction of theory examination
Part-II :- Feedback session on the theory performance
Part-III :- Work place based clinical assessment

Scheme of Formative assessment

PART – I	**CONDUCT OF THEORY EXAMINATION**	Candidate has to appear for Theory Exam and it will be held for One day.
PART – II	**FEEDBACK SESSION ON THE THEORY PERFORMANCE**	Candidate has to appear for his/her Theory Exam Assessment Workshop.
PART – III	**WORK PLACE BASED CLINICAL ASSESSMENT**	After Theory Examination, Candidate has to appear for Clinical Assessment.

FINAL EXAMINATION

Theory Examination

Paper I: Basic Sciences as applied to Genetics

Paper II: Applied/Laboratory Genetics

(e.g., genetics of various organ systems disorders, pre-implantation genetic screening/diagnosis, non-invasive prenatal screening, prenatal diagnosis,chromosomal microarray in dysmorphology, next generation sequencing, gene panel test, diagnosis of triplet repeat disorder, common and rare genetic disorders in India)

a) Practical Examination:

Laboratory tests/other skills (10 tests/skills): (including OSCE / OSPE stations)

- Cytogenetics: slide reporting
- Molecular Cytogenetics: slide reporting
- DNA electrophoresis
- Primer designing
- Hemoglobin A2 Estimation
- Hemoglobin Electrophoresis
- Other Biochemical Genetics Tests
- Syndrome/disease/findings identification
- (slide/spot/photograph/specimen/radiologic/gel/electrophorogram/etc)
- Syndrome diagnosis using the databases and software
- Pedigree Construction (5 generation)

- Analysis of Sanger sequence chromatograms
- Analysis of MLPA electropherogram
- Analysis of TP-PCR and QF-PCR electropherograms
- Analysis of chromosomal microarray results
- Analysis of NGS data
- In silico analysis of sequence variants and CNVs including use of populationdatabases, mutation databases, & mutation prediction software
- Analysis and interpretation of TMS, urine GCMS and plasma amino acid HPLCresults

3. Oral/viva voce examination

Oral examination shall be comprehensive enough to test the post graduate student's overallknowledge on the subject

Books (latest edition)

1. Emery and Rimoin's Principles and Practice of Medical Genetics and Genomics. Editors: Reed Pyeritz, Bruce Korf, Wayne Grody. Publisher: Elsevier. 6th Edn. 2013. (ISBN:9780123838353).
2. Practical Genetic Counseling. Editors: Peter Harper, Buterworth Heinmann. Publisher: Edward Arnold Ltd. 3rd Edn. 2013. (ISBN: 9781483183664).
3. Smith's Recognizable Pattern of Human malformations. Editor: Kennethlyon Nenes. Publisher: WB Saunders Company. 7th Edn. 2013. (ISBN: 1455738115).
4. Mendelian Inheritance in Man. Editor: Victor A Mckusick. Publisher: The Johns Hopkins University Press. 2014. (ISBN: 9780801820878).
5. Metabolic and Molecular Basis of Inherited Disease. Editors: Charles R. Scriver, Arthur
   L. Beaudet, William S. Sly, David Valle, Mc Graw-Hill. Publisher: McGraw-Hill. 8th Edn.2001. (ISBN10 0079130356).
6. The Principles of Clinical Cytogenetics. Editors: SL Gersen, M B Keagle, Publisher: Humana Press. 3rd Edn. 2013. (ISBN 978-1-4419-1688-4).
7. Textbook of Fetal and Perinatal Pathology, Vol. I & II. Editors: Jonathan S Wigglesworth, Don B Singh. Publisher: Wiley–Blackwell. 2nd Edn. 1998. (ISBN-10:0865421188).
8. Catalog of Teratogenic Agents. Editors: TS Shepard. Publisher: John Hopkins UniversityPress. 13th Edn. 2011. (ISBN-13:978-0801897849).
9. Emery's Elements of Medical Genetics. Editors: Peter Turnpenny, Sian Ellard. Publisher: Elsevier Churchill Livingston. 15th Edn. 2017. (ISBN: 9780702066856).
10. The Practical Guide to the Genetic Family History. Editors: Bennett Robin. Publisher: Wiley-Liss. 1st Edn. 2010. (ISBN: 0471251542).
11. Chromosomal abnormalities and genetic counseling. Editors: RjJM Gardner, GRSutherland. Publisher: Oxford university press. 5th Edn. 2018. (ISBN: 9780199329007).
12. Medical Cytogenetics. Editors: Mark Hon Fong L. Publisher: Marcel Dek. CRC Press. 1stEdn. 2000. (ISBN: 0824719999).
13. Congenital malformation evidence-based evaluation and management. Editors: PravinKumar, Barbara K Burton. Publisher: McGraw Hill. 1st Edn. 2007 (ISBN:0071471898).
14. Human Molecular Genetics. Editors: Tom Strachan, Andrew Read. Publisher: GarlandScience. 5th Edn. 2018. (ISBN 978-0815345893).
15. Genetic disorders and the foetus: diagnosis, prevention and treatment. Editors: AubreyMilunsky Publisher: Wiley. 7th Edn. 2015. (ISBN: 978-1-1189-8152-8).
16. Management of genetic syndromes. Editors: Cassidy SB, Allanson JE. Publisher: Wileyliss. 4th Edn. 2020. (ISBN: 978-1-119-43267-8).
17. Essentials of Medical Genomics. Editors: Brown Stuart M. Publisher: Wiley-Liss. 1st Edn.2008. (ISBN: 047121003X)
18. New Clinical Genetics. Editors: Andrew Read and Dian Donnai. Publisher: Scionpublishing. 4th Edn. 2020. (ISBN 9781911510703).
19. Human malformations and related anomalies. Editors: Stevenson RE, Hall JG. Publisher: Oxford university press. 3rd Edn. 2015. (ISBN-13: 9780199386031).

20. Radiology of syndromes, metabolic disorders and skeletal dysplasias. Editors: Taybi H,Lachman RS. Publisher: Elsevier. 5th Edn. 2006. (ISBN-13: 978-0815187097).

Journals

10-15 international Journals and 02-05 national (all indexed) journals

Miscellaneous Resources (including web resources)

1. OMIM - Online Mendelian Inheritance in Man, Catalog of all known human genesand genetic phenotypes (The Johns Hopkins University School of Medicine)
2. LMD (London Medical Databases), POSSUM, etc dysmorphology database
3. DECIPHER, ISCA, DGV, UPD, ICCG, etc database
4. GeneClinics: Medical Genetics Knowledge Base, formerly (Genline), diagnosis,management and counseling for individuals and families with inherited conditions
5. GeneTests (formerly Helix) - DNA diagnostic testing and research information
6. ClinGen: The Clinical Genome Resource
7. The Hereditary Cancer Working Group (centralize and curate genetic knowledge in order todevelop guidance for molecular diagnostic germline cancer testing)
8. TERIS (teratogen information system), University of Washington
9. Gene/Disease Specific Information (locus specific databases)
10. GeneCards, database of human genes, products and involvement in diseases
11. Merck Manual (professional version): General Genetics, Inheritance of Single-Gene Defects, Multifactorial Inheritance, Nontraditional Inheritance, Chromosomal Disorders,Mitochondrial DNA Abnormalities, Immunogenetics, Forensic Genetics, Genetic Therapy, Congenital Anomalies, Pedigree symbols, Pharmacogenetics, Cancer Genetics, PrenatalGenetic Evaluation and Counseling, etc
12. World Wide Web Biochemical Genetics Test List, University of California, San Diego, Biochemical Genetics
13. EuroGenTest, includes unites on genetic testing: quality management, information databases,public health, new technologies and education, new 5/07
14. Genetics and Cancer (https://www.cancer.org/cancer/cancer-causes/genetics.html)
15. Cytogenetic images and animations, Tokyo Medical College, Hironao Numabe, M.D.
16. Before You are Pregnant, March of Dimes

(https://www.marchofdimes.org/pregnancy/getting-ready-for-pregnancy-preconception-health.aspx)
17. European Teratology Society (ETS)
18. Folic Acid and Prevention of NTD Educational Materials, by CORN education committee
19. Illinois Teratogen Information Service, Chicago
20. Preconception Screening and Counseling Checklist, March of Dimes
21. Policy statements, American College of Medical Genetics
22. Policy statements, American Academy of Pediatrics
23. Policy statements, American Society of Human Genetics
24. Genetic Screening, American Society for Reproductive Medicine
25. Drugs in Pregnancy and Lactation, Perinatology.com
26. Ethics and genetics in medicine. In: Bioethics for clinicians. Burgess MM, et al. CMAJ.1998. 158:1309-13.
27. AAFP Core Educational Guidelines in Medical Genetics