IIII PDCC in Clinical Molecular Genetics & Genomics

1. **Program Name**

   PDCC in Clinical Molecular Genetics & Genomics

2. **Motivation**

   The field of medical genetics has evolved as an important subspecialty of medicine worldwide, translating the research in the field of medical genetics into patient care. With the completion of Human Genome Project, the advances in clinical approach, laboratory diagnosis, genetic counseling, prenatal diagnosis and treatment of genetic

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SGPGIMS,Lucknow

diseases and birth defects have had tremendous impact on human health care. Most of the universities in the USA and Europe have departments and programs for training in laboratory medical genetics. India is yet to catch up with teaching and training of medical professionals in clinical molecular genetics with the developed world. At present only Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, offers a DM course in medical genetics which includes laboratory and clinical training. However training programs focused on clinical molecular genetics & genomics are still not available in our country. There is an urgent need for trained professionals in this field as there is a requirement for large number of genetic tests to be done for vast population of our country. Hence it is pertinent to start a fellowship program in clinical molecular genetics.

3. **Program duration**

   Twelve months, full time

4. **Eligibility**

   The candidate must have a postgraduate degree (MD/MS/DNB) in Pathology/Microbiology/Biochemistry/Anatomy/Physiology or any similar laboratory speciality.

5. **Intake (Number of students)**

   Two per calendar year

6. **Mode of selection**

   As per SGPGIMS rules

7. **Goals and Objectives**

   The program will provide the trainee with competence in the application of clinical molecular genetics to modern medical practice and relevant research experience. Competence implies that the individual possesses the knowledge, skills and attitudes necessary to 1) identify and interpret molecular abnormalities, 2)) supervise and direct the operations of a clinical molecular genetics diagnostic laboratory; and 3) assume the day-today responsibilities for the operation and standards of a molecular genetics laboratory.

   Knowledge

   Trainees must demonstrate:

   - general knowledge of molecular biology;

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Needs: Local : Pink, National : Orange, Regional: light blue, International : green

- advanced knowledge of molecular genetics, particularly as it is applied to the investigation of human disease;
- general knowledge of the pathophysiology of inherited disorders, particularly those amenable to molecular diagnosis;
- advanced knowledge of human genome, structure of genes, the nature of mutation at well recognized human loci and the correlation between genotype and phenotype at these loci;
- advanced knowledge of methods for direct analysis of mutations;
- advanced understanding of the estimation of genetic risk by inferential methods including linkage analysis and LOD scores, Bayesian probability, pedigree analysis and risk calculation in familial or potential new mutation situations using linked polymorphisms. Candidates will be expected to be familiar with a broad spectrum of disorders representing all modes of inheritance, as well as an understanding of the relationship between physical and genetic maps of chromosomes;
- advanced knowledge of the human genome project
- advanced knowledge of next generation sequencing approaches

Colour Coding
Global GREEN
Regional BLUE
National ORANGE
Local (State) PINK

Skills

The trainee must demonstrate competence in the theory and practice of techniques used in the molecular analysis of genetic disease, including an awareness of the variables that contribute to the quality of results and an ability to "trouble-shoot" successfully. These should include (but are not limited to) the following:

- tissue culture - sterile technique, and the specific culture of relevant cell types (ie. amniocytes, chorionic villi, fibroblasts, lymphoblasts);
- DNA and RNA isolation in full scale from sources such as blood, tissue, cultured cells; in small scale, from sources such as archival materials or blood spots;
- propagation analysis and manipulation of organisms used as tools in molecular analysis;
- labeling techniques including isotopic and non-isotopic methods;
- Southern and Northern blotting including dot blots or equivalent;
- Polymerase Chain Reaction, including familiarity both with basic methods and with special applications in current use for molecular analysis;
- DNA sequencing;

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Global	GREEN
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- direct mutation screening techniques - such as chemical cleavage, single strand confirmation polymorphisms etc.;
- ability to recognize and interpret artefacts or unusual results and to conduct appropriate checks and balances in procedural matters;
- ability to plan and interpret indirect molecular analyses based on linked markers. This includes assessment of a priori risks, determination of appropriate tests to be conducted, interpretation of raw data from genotyping etc. Expertise should include a variety of genetic diseases representing the spectrum that may be encountered in a diagnostic laboratory;
- ability to plan and interpret direct mutation analysis by a variety of methods to screen for known common point mutations (alteration of restriction sites polymorphisms, allele specific oligonucleotides, reverse dot blots, heteroduplexes, allele specific amplification etc.);
- ability to plan and interpret results of analyses for "dynamic mutations", including their technical limitations and genetic implications;
- understanding of physical gene mapping technique including pulse field gel electrophoresis, yeast artificial chromosomes, development of ordered arrays of overlapping clones (contigs), theory of radiation fragmentation techniques, cytogenetic clues to gene location (deletions, translocations, in situ hybridization) somatic cell hybrids, and chromosome specific deletion panels;
- understanding of mathematical gene mapping techniques including the estimation of linkage by the LOD score method and estimation of linkage by radiation fragmentation;
- understanding the approaches to determining required sample sizes for linkage analysis;
- understanding of the implications of imprinting in genetic analysis;
- computer literacy with respect to the calculation of LOD scores and genetic risks, laboratory management, maintenance of laboratory data bases, and accessing information stored in national and international data bases;
- ability to recognize and interpret artefacts or unusual results and to conduct appropriate checks and balances in procedural matters;
- understanding of the principles of quality assurance (management) and the ability to implement and document adherence to a QA program;

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- ability to use online mutation databases and softwares for interpretation of results;
- ability to communicate effectively with other health professionals and to write clear and informative and complete reports based on the outcome of such analyses; and
- familiarity with bids and service contracts for laboratory equipment.

Attitudes

The trainee must:

- demonstrate a professional attitude to clinical and laboratory colleagues, to patients and to other laboratory staff;
- have a sense of responsibility in providing quality patient care. This will include a recognition of personal limitations and the necessity of seeking the opinions of colleagues or other professionals when necessary; and
- appreciate the importance of continuing professional education.

8. **Components of training**

A. Laboratory training:

The fellow will observe and conduct the following activities in cytogenetics laboratory to understand the indications for these tests and their interpretation.

- DNA and RNA isolation in full scale from sources such as blood, tissue, cultured cells;
- Polymerase Chain Reaction and its variations
- Direct and indirect mutation screening and detection techniques
- DNA Genotyping
- DNA Sequencing and interpretation
- NGS interpretation
- Preparation of reports using appropriate nomenclature and with appropriate review of literature
- Assessment of quality control and assurance measures

B. Project:

Each student will be assigned a project which needs to be completed during the last 6 months of the tenure and submit a project report at time of evaluation

C. Academic activities:

The student will be required to attend academic activities of the department and will be required to present at least 4 seminars, 2 journal clubs and

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5 case presentations (related to the lab tests done). The student will be required to attend various 03 courses held in the department.

D. Research activities

It is desirable that the fellow is actively involved in research activities of the department

9. **Prospects and placement**

With the huge population and demand for trained clinical molecular geneticists, our country is in need of large number of medical specialists in this field. With limited training facilities in India, it is expected that the demand for clinical molecular geneticists will be tremendous from medical colleges, corporate hospitals, and tertiary care centers across the country.

10. **Evaluation criteria**

- Performance of the candidate will be assessed by the teacher/guide throughout the tenure.
- Logbook: the fellow is expected to maintain a logbook of all activities and experiments/procedures carried out.
- Evaluation will be done based on the log books and performance during the period of training.

Recommended books and other resource material

a) **Books**

	Authors/Editors	Title	Publisher
1	Scriver CR, Beaudet AL, Sly WS, Valle D	The metabolic and molecular basis of inherited disease	McGraw Hill
2	Strachan T, Read AP	Human molecular genetics	BIOS Scientific Publishers Ltd, Oxford
3	Milunsky A	Genetic disorders and the fetus: Diagnosis, prevention and treatment	The Johns Hopkins University Press, London
4	Rimoin DL, Connor JM, Pyeritz RE	Emery and Rimoin's Principles and Practice of Medical Genetics	Churchill Livingstone
5	Harper PS	Practical Genetic Counseling	Butterworth-Heinemann
6	Aase JM	Diagnostic Dysmorphology	Plenum Medical Book Co.
7	Nussbaum RL, McInnes RR, Willard HF	Thompson & Thompson Genetics in Medicine	WB Saunders Company
8	Phadke SR	Genetics for Clinicians	Prism Books

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9	ISCN 2009	An International System for Human Cytogenetic Nomenclature (2009): Recommendations of the International Standing Committee on Human Cytogenetic Nomenclature	S. Karger AG

b) Journals

	Name of the journal	Publisher
1	Nature Genetics	Nature Publishing Group
2	Nature Reviews Genetics	Nature Publishing Group
3	American Journal of Human Genetics	University of Chicago Press (American Society of Human Genetics)
4	Clinical Genetics	Blackwell Publishing
5	Journal of Medical Genetics	BMJ Publishing Group
6	American Journal of Medical Genetics A and C	Wiley InterScience
7	Journal of Genetic Counseling	Springer
8	Clinical Dysmorphology	Lippin Williams & Wilkins
9	Prenatal Diagnosis	John Wiley & Sons, Ltd.

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