GUIDELINES FOR COMPETENCY BASED TRAINING PROGRAMME FOR D.M. IN MEDICAL GENETICS

I. Preamble

There have been significant advances in the field of Medical Genetics in recent years, which are of direct relevance to patient care. Following the completion of the Human Genome Project and the development of advanced molecular genetic testing technologies such as microarray and next generation sequencing, the genetic basis of a large number of chromosomal, monogenic as well as multifactorial disorders has been identified and many novel genetic disorders are being continuously discovered. This will include not only the genes causing monogenic disorders, but also those which predispose to complex multifactorial disorders and those which may be responsible for causing cancer, autoimmunity & aging.

Antenatal diagnosis is currently being offered for chromosomal, monogenic and copy number variations (CNVs) disorders. With wider availability of carrier screening in coming years, primary prevention of genetic disorders will be possible and thus will prevent the birth of a first affected child with genetic disorder. Other important clinical application is pre-symptomatic diagnosis of late onset diseases including cancers.

Advances of genetic technologies have already led to radical changes in the practice of Medical Genetics as well as concepts of genetic counselling. Access to these benefits that aim at birth of healthy children could be of immense importance to our National Family Welfare Program. Besides prevention, better understanding of pathophysiology of genetic diseases shall open new avenues of pharmaco-therapy, and even cure by gene therapy, of these disorders. Availability of treatments using many novel strategies like enzyme replacement therapy, drugs acting on molecular pathways, gene therapy, antisense oligo-therapy and drugs for read-through stop codon mutations has caused paradigm change in the management of many monogenic disorders. This calls for trained specialized medical professionals to deal with genetic disorders with expertise in diagnosis, treatment and genetic counseling. The proposed course aims to train internists, pediatricians and obstetrician &

gynecologists in this super-specialty and provide state of art medical genetics services to the patients and families with genetic disorders.

II. Eligibility for D.M. Medical Genetics Course

Postgraduate degree in Medicine, Pediatrics or Obstetrics & Gynecology

III. Introduction:

The DM program in medical genetics offered at SGPGI, Lucknow is organised under 4 courses which will be counted as paper I, II, III & IV in the final exit exam.

Course I: Basic Genetics

Course II: Clinical Genetics

Course III: Applied and Laboratory Genetics

Course IV: Recent advances in Medical Genetics

III(A) Program objectives: Competency based training for DM in Medical Genetics aims to produce a postgraduate student who after undergoing the required training should be able to deal effectively with the needs of the patients, community and should be competent to handle medical problems related to genetic disorders. These include clinical evaluation, investigations, genetic work ups requiring pre-test and post-test counseling, up to-date information and abilities to carry out novel treatments and skills for planning and implementation of population-based prevention programs. Last but not least, be ready for carrying out clinical practice of personalized medicine in the 21st century molecular medicine era. The post graduate student should also acquire skills to teach Medical Genetics to undergraduates and paramedical students as well.

The objectives of D.M. in Medical Genetics Program are to produce a competent Medical Geneticist who:

1. is a medical doctor who can evaluate a patient with possible genetic disorder, ascertain the risk of a genetic disorders, make a clinical diagnosis, able to decide appropriate test to confirm the diagnosis and provide latest form of treatment. The

other goal is genetic counseling to the patient, family and extended family about management, carrier screening, prenatal diagnosis and prevention.

2. is aware of contemporary advances and developments in Medical Genetics, and ways for continued learning for keeping updated about diagnostic investigations, technological developments and treatment.
3. is trained in use of novel clinical ways of phenotyping, use of software for phenotyping and correlation with genotypes, interpretation of genetic variants and CNVs regarding their pathogenicity and causal nature and comfortable with the use of databases of genetic disorders, CNVs and genetic variants.
4. acquires the competencies pertaining to Medical Genetics that are required for practice in the community and at all levels of health system, especially population-based prevention program, screening for late onset disorder and susceptibility to cancer.
5. recognizes the health needs of patients and families with genetic disorders and carries out professional obligations in keeping with principles of the National Health Policy and professional ethics.
6. identify the disorders which are prevalent in Indian populations (identifying pockets)
7. is oriented to principles of research methodology.
8. has acquired skills in educating lay persons, medical and paramedical professional
9. has acquired skills in effectively communicating with the person, family and the community.
10. has acquired skills in DNA diagnostic tests including those for screening of carriers and antenatal diagnosis, as well as pre-morbid diagnosis for primary prevention (predictive/preventive medicine), being aware of the PCPNDT 2003 Act and related guidelines as well as processes.
11. has acquired knowledge and skills in genetic counseling and have developed confidence in psychological & social issues involved.

III (B) Subject specific competencies:

During the course, the student should acquire the following knowledge/skills/expertise:

A. Theoretical Knowledge:

The post graduate student in Medical Genetics must acquire knowledge in all aspects relevant to the practice of medical genetics. This includes clinical presentations of genetic disorders, organ specific genetic disorders, principles of basic genetics, genetic counseling, and knowledge of genes, chromosomes, genome and epigenome including molecular techniques. In whole, this is described as genomic medicine.

B. Clinical/Practical Skills:

The post graduate student must undergo training in all aspects relevant to the practice of Medical Genetics, be able to clinically evaluate, interpret genetic laboratory data and diagnose, investigate and manage patients with gene related conditions. This is similar to any other organ based clinical super-specialty. Here, the disorders for which the expertise is needed are not specific to any organ or system; but are those where genetic etiology is known. The steps and principles are similar to any clinical situation and involves [1] history taking and examination of a patient to draw up a differential diagnosis, [2] advise the relevant non-genetic and genetic investigations, and [3] treatment of the patient. However, genetic disorder has other implications for the patient and the family due to genetic nature of the etiology and medical geneticist has two more responsibilities, namely counseling the family for prevention and recurrence risks and prenatal diagnosis in appropriate conditions.

C. **Teaching Skills**:

Should be able to teach relevant aspects of genetic diseases to junior colleagues, nursing and para-medical staff. Population based screening programs like antenatal, neonatal screening and screening for susceptibility to late onset disorders are important components of medical genetics and advocacy, communication with lay persons and educating lay persons, society leaders, policy makers are the responsibilities of medical genetics community and require appropriate skills for teaching in informal ways.

D. Research Methodology:

Should be able to identify and investigate a research problem in Medical Genetics using appropriate methodology and molecular techniques. Most of the genetic disorders being rare, many cases even in clinical settings need research approach. This needs in depth understanding of deep phenotyping, genomic techniques, principles of ethics and

guidelines for ethics of research. This needs access to and understanding of rules and regulations of Ethics Committee.

E. Group Approach:

There are some overlap of patients seen by medical geneticists with other organ-based specialists. The organ-based specialists may need expert opinion from medical geneticists about genetic disorders and medical geneticists may need clinical opinion and guidance / support for management from the specialist like neurologist, ophthalmologist, etc. Hence ability to organize /participate in multi-disciplinary meetings with clinicians, laboratory colleagues and experts from allied clinical disciplines is necessary in the interest of the patients. The medical geneticist when counseling or acting as a consultant, must know the impact of genetic heterogeneity, pleiotropy, variable expression and lack of penetrance, so that the validity and accuracy of the diagnosis is assured. Therefore, the medical geneticist requires a broad exposure to genetic disease as it occurs in the area of many specialties/subspecialties so as to be competent to question, validate, or consider a new diagnosis. This knowledge will include the ability to appropriately use consultations with other specialists who may not be aware of these intricacies of genetic approaches.

The most important related specialties in which the student should gain exposure include: Internal Medicine, Pediatrics, Obstetrics and Gynecology, Cardiology, Radiology (skeletal) including prenatal ultrasound, Endocrinology, Hematology, Oncology, Nephrology, Neurology, Physical Medicine & Rehabilitation, Psychiatry, Ophthalmology, Clinical Immunology, Clinical Pharmacology, and Orthopedics. Combined case wise interaction/ discussion should be carried out for better understanding and management.

F. Attitudes including Communication Skills:

Should be able to communicate effectively with patients, colleagues and the community about genetic diseases as well as counsel patients and relatives about various decisions taken during management. The compassion, empathy, communication skills are intrinsic but vary in texture and amount amongst different persons. Though all physicians need these skills, their contribution is high for becoming a successful medical geneticist. These attitudes need to be developed and polished by observation, training and practice.

IV. Course objectives:

By the end of each course, the student should have acquired knowledge (cognitive domain), professionalism (affective domain) and skills (psychomotor domain) as given below:

IV (A): Course 1: Basic Genetics

a) KNOWLEDGE/COGNITIVE DOMAIN

By the end of the course, the post graduate student should have acquired knowledge in Core Discipline: Competencies unique to Medical Genetics

1. The history of use and misuse of human genetics
2. What genes are, how they are organized and controlled, what they do, and how they segregate, what is the structure and configuration of genome
3. The nature of mutations and pre-mutations and how they contribute to human variability and to disease
4. The patterns of inheritance characteristic of autosomal dominant, autosomal recessive, X-linked dominant and X-linked recessive traits
5. Factors that affect development of the phenotype in single-gene disorders, including variable expressivity and incomplete penetrance
6. The basis of mitochondrial diseases and the expected pattern for mitochondrial (maternal) inheritance and other non-Mendelian form of inheritances like genomic imprinting, isodisomy, unstable/dynamic mutations, copy number variation, etc.
7. Organization of genes, chromosomes, how chromosomes replicate in mitosis and meiosis, and mode of their transmission from parent to child.
8. Epigenetics
9. Clinical manifestations of common numeric, structural and mosaic chromosomal anomalies
10. Concepts and clinical importance of genetic imprinting and uniparental disomy
11. Principles of population genetics and the public health implications of genetic epidemiology
12. The basic principles of inborn errors of metabolism and of pharmaco-genetic variations and their general clinical manifestations
13. The multi-factorial nature of human traits, both normal and abnormal, and the principles of multi-factorial inheritance
14. The mechanisms of teratogenesis and the effects of major human teratogens

15. Methods to recognize and classify congenital anomalies and the approach to diagnosis of multiple congenital anomaly syndrome
16. Take history including collecting complete family history in the form of a pedigree
17. Interpret family history data
18. Examine the patient for general findings, dysmorphism, systemic findings, evaluation of growth and development in a systematic way and with great sensitivity (examination of parents, relatives for subtle findings, dysmorphism is a part of clinical evaluation of the patient.
19. Evaluation of patient for dysmorphism and examination of relatives should be done with an extra sensitivity as this may psychological touchy points/ areas)
20. Ability to recognize variations in human form taking into account the features of the parents)
21. Understand principle of cytogenetic, biochemical, and molecular laboratory methods.
22. Effectively use information systems, including library and electronic resources, in the evaluation and management of patients with genetic diseases, including diagnosis of multiple congenital anomaly syndromes, and the recognition of teratogenic exposures.
23. Ensure that the testing is done in an Accredited Lab Only (Authenticity and legal protection for the referring clinician). Interpretation of the results is an art and science and hence should be included empathetically.
24. The procedures available for prenatal & pre-implantation genetic diagnosis and the type of disease that can be detected prenatally/before implantation
25. Familiarity with basic research methodology, epidemiology, basic information technology skills, knowledge to access data and information systems, electronic health records
26. Take informed written consent from the patient in the language they understand (English and vernacular)
27. Ability to maintain records as per PCPNDT guidelines
28. Writing a proposal for submission to Ethics Committee

b) AFFECTIVE DOMAIN

The postgraduate student should:

1. Be able to function as a part of a team, develop an attitude of cooperation with colleagues, and interact with the patient and the clinician or other colleagues to provide the best possible diagnosis or opinion

2. Always adopt ethical principles and maintain proper etiquette in dealings with patients, relatives and other health personnel and to respect the rights of the patient including the right to information and second opinion.
3. Appreciate the importance of disease prediction and prevention
4. Respect patients' religious, moral, and ethical beliefs and biases, even if they differ from the student's own beliefs
5. Communicate genetic information in a manner that is suitable for each particular patient and family.
6. Provide patients with access to diagnostic and predictive tests that are appropriate for the condition in their family and advise patients of the benefits, limitations, and risks of such tests.
7. Present all available options accurately and non-directively

c) PSYCHOMOTOR DOMAIN

The post graduate student must acquire the following practice–based competencies/skills:

1. Acquire ability to elicit medical history of the patient, including developmental and reproductive history
2. Ability to elicit the family history, including drawing of detailed pedigree chart
3. Ability to conduct physical examination of affected and related individuals (including examination of the affected fetus where required), with special emphasis on morphological features (with sensitivity and subtly, without offending the patient or parents' sensitivity about body image and dysmorphism) and anthropometric measurements and proper documentation of the findings, including photographs
4. Integrate the clinical & genetic information to exclude the non-genetic causes of the clinical presentation (phenocopy) and formulate an appropriate differential diagnosis of genetic causes related to the case
5. Obtain samples for genetic studies e.g. skin biopsy (after obtaining the informed consent), requisition/conduct tests, medical consultations
6. Understand principle of cytogenetic, biochemical, and molecular laboratory methods.
    - Cytogenetics- karyotyping
    - Molecular Cytogenetics - MLPA

- Molecular Techniques- Polymerase Chain Reaction (PCR), Gel Electrophoresis (DNA/RNA i.e., ribonucleic acid, Protein, etc), Southern blotting, ARMS-PCR

IV (B): Course 2: Clinical Genetics

a) KNOWLEDGE/ COGNITIVE DOMAIN

1. Clinical presentations of organ specific genetic disorders and approaches to clinical phenotypes of genetic disorders
2. Role of genetics in the pathogenesis of neoplasms and in the predisposition to malignancies
3. Use of evolutionary principles to understand human biology and disease
4. Disease frequency variations in different ethnic groups
5. Conventional as well as advanced molecular genetics, cytogenetics and metabolic genetic diagnostic techniques, and their application to genetic disorders
6. Various databases of genes, genetic variations, genetic disorders and tools / software for studying effects of genetic variations, genotype phenotype correlations
7. Understand prenatal diagnostic procedures both invasive (amniocentesis, chorionic villous sampling, cordocentesis, etc) and non-invasive (fetal ultrasonography).
8. Perform fetal autopsy.
9. Perform specialized tests through biochemical, cytogenetic, and molecular genetic laboratories.
10. Learn interpretation of cytogenetic, biochemical, and molecular laboratory reports. On the basis of results, formulate an appropriate diagnosis
11. The advantages, limitations, and dangers of predictive testing for genetic disease
12. The existence of and justification for screening programs to prevent genetic disease
13. Approaches to screening for genetic diseases and concepts of personalized medicine
14. Identify and find information relevant to a clinical problem, using consultation, texts, and the archival literature and electronic media
15. Generate an initial list of differential diagnoses (including appropriate non-genetic disorders) given a specific complaint and patient characteristics
16. Plan investigations and provide information about the need and utility of the genetic investigations along with the information about the diagnostic yield and limitations (also described as pretest counseling)

17. Re-rank the differential diagnoses based on information gathered from the history, physical, and auxiliary studies
18. Determine the mode of inheritance and risk of occurrence and recurrence of the genetic condition/birth defect, and give appropriate information on the same to the patient and family, including availability of antenatal diagnosis and other reproductive options
19. Write case summary and electronic health records for comprehensive data collection
20. Demonstrates ability to engage the patient family in diagnosis and therapeutic treatment planning
21. Demonstrates understanding of the roles and competencies of other health care providers
22. Preparing Case Report for various presentations
23. Planning the protocol of a thesis, its execution and final report

b) AFFECTIVE DOMAIN

The postgraduate student should:

1. Demonstrates appropriate truthfulness and honesty with colleagues
2. Respect patient confidentiality at all times in verbal and written communication
3. Accurately assess a patient's assumptions in accessing the health care system
4. Be aware of both 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
5. Demonstrate use and correct interpretation of diagnostic procedures and their results

c) PSYCHOMOTOR DOMAIN

The post graduate student must acquire the following practice–based competencies/skills:

1. Follow a logical approach in syndrome identification including the use of diagnostic aids e.g. computer assisted diagnosis, literature search, image analysis software, etc
2. Use the diagnostic support of the software logically using subjective interpretations and review of latest literature
3. Recognize psycho-social and economic implications of the genetic problem in the family
4. Understand the uses, limitations, interpretation and significance of specialized laboratory procedures and formulate an appropriate plan for medical consultations and investigations, and conduct pre-test counseling with the family

5. Acquire skills to conduct all required cytogenetic, biochemical and laboratory tests, and discuss the results with clinician-in-charge of the patient to arrive at a logical conclusion on the disease and its management
6. Promote informed decision-making about further testing and management of the risk of occurrence/recurrence, including provision of antenatal diagnosis, if possible
7. Provide written documentation of medical, genetic and counseling information for families and other health professionals
8. Understand principle of cytogenetic, biochemical, and molecular laboratory methods e.g. Real Time PCR, Quantitative Fluorescent PCR (QF PCR), DNA Sequencing, cytogenetic microarray, next generation sequencing (NGS), epigenetics techniques,

IV (C): Course 3: Applied and Laboratory Genetics

a) KNOWLEDGE/ COGNITIVE DOMAIN

1. Traditional and novel approaches to the treatments of genetic disorders
2. Techniques to study in vitro functional effects of genetic variations
3. Appropriate methods of genetic counselling
4. Legal and ethical issues involved in the practice of medical genetics
5. Organizational and economic aspects of the health care system with regard to genetics
6. Relevance of polymorphisms, gene linkage, and human gene mapping in medicine
7. Explain a mechanism for each aspect of a patient's problem, including biological, behavioural, and social aspects
8. Providing appropriate information about phenotype of the patient in the form of Human Phenotype Ontology (HPO) terms to the laboratory while sending samples for genomic tests like cytogenetic microarray (CMA) and next generation sequencing (NGS)
9. Interpret the results of CMA, NGS. Revaluate them based on various databases of variants, using software for pathogenicity testing and using guidelines and review of latest literature
10. Demonstrates competency in use of genetic databases, software and bioinformatic tools
11. Write referral notes to other specialists and primary care physician for continued management, surveillance for complications and sick day management
12. Demonstrates practical, efficient and cost-effective approach to screening, diagnosis and treatment planning and recognizes its social and economic impact
13. Demonstrates ability to engage with other health care professionals

14. Review of literature
15. Conducting clinical sessions for undergraduate medical students, nurses and paramedical workers
16. Participate in treating genetic diseases where applicable; for e.g. Lysosomal Storage Diseases (enzyme replacement, substrate reduction & Pharmacologic Chaperone Therapy), hypophosphatemia (burosumab), Multiple Exostoses (palovarotene), Metaphyseal Chondrodysplasia Schmid type (carbamazepine), Osteoporosis Pseudoglioma (lithium carbonate).

b) AFFECTIVE DOMAIN

The postgraduate student should:

1. Accepts personal responsibility for care of patients with genetic disorder, consistent with good work ethics and empathy
2. Recognize personal beliefs, prejudices, and limitations, which should not come in the way of providing service
3. Effectively engage the patient and/or family in communications
    a. Non-judgmental and non-coercive
    b. Non-directive in genetic counselling
4. Be aware of the advantages and potential hazards of referring patients and families to community or national resources
5. Recognize the limitations of their own skills and seek consultation when necessary
6. Explain the diagnosis, etiology, natural history, and management of the condition to the patient and the family in a way that is comprehensible to the patient and family
7. Provide general, supportive and specific medical care to the patient including appropriate interventions where necessary
8. Advise appropriate treatments, including dietary, pharmacological, enzyme-replacement, transplantation, and gene therapy.

c) PSYCHOMOTOR DOMAIN

The post graduate student must acquire the following practice–based competencies/skills:

1. Communicate to the patient / relatives at a level appropriate to the consultant, information concerning the medical implications and prognosis, the risks that apply, the options

available, and to help the individual/ family choose an appropriate course of action for themselves

2. Identify psychosocial issues in the family and if need arises refer to a psychiatrist for evaluation and assistance
3. Apply appropriate communication techniques for conveying bad news.
4. Recognize patients' defense mechanisms and be able to determine when it is better to leave them intact and when they may need to be breached.
5. Cope emotionally with responses of patients.
6. Interpret their own attitudes toward ethical, social, cultural, religious, and ethnic issues and develop an ability to individualize each patient or family member
7. Resolve varying cultural, social, and religious attitudes in relation to issues such as contraception, abortion, parenting, and gender roles.
8. Utilize community support services and agencies appropriately.
9. Plan and give an appropriate surveillance/ follow-up monitoring plan for anticipated complications and issues

IV (D): Course 4: Recent Advances in Medical Genetics

i. KNOWLEDGE/ COGNITIVE DOMAIN

1. Knowledge in the area of bioinformatics for DNA/ RNA interrogation
2. The results of the tests need clinical correlation and deep / reverse phenotyping after the results are available.
3. Emphasis on genetic results, as they are irreversible and heritable transmissions are known and are socially stigmatizing (important aspect in marriage counseling)
4. Evaluate scientific/clinical information and critically analyze conflicting data and hypothesis
5. Keep themselves updated with latest developments in the field of human and medical genetics with respect to new genes, diseases and technology
6. Appreciate the principles and advantages and disadvantages of new techniques
7. Critically discuss latest studies in international and national journals
8. Develop an aptitude to look for and think about new treatment for common genetic disorder and new techniques for diagnosis of genetic disorder

9. Availability of treatments using many novel strategies like enzyme replacement therapy, drugs acting on molecular pathways, gene therapy, antisense oligo-therapy and drugs for read-through stop codon mutations
10. Develop skills to carry out clinical practice of personalized medicine in molecular medicine era.
11. Treat the patients with available modalities of treatment, look for latest drug developments
12. Communicate the diagnosis and uncertainties/limitations in diagnosis
13. Demonstrates ability to analyze the quality and implications of medical literature and apply new knowledge in the delivery of health care
14. Demonstrates interest and ability to identify future areas of inquiry in medical genetics research
15. Demonstrates enthusiasm and positive attitude in the educational process and participates fully in educational activities
16. Demonstrates ability to recognize and outline initial treatment for patient with life threatening emergencies regardless of etiology
17. Demonstrates knowledge of health-care financing and applies it in assisting patient to access the best possible care
18. Utilizes knowledge of population based and evidence-based medicine in making patient management decisions
19. Works with patient support groups in the area of advocacy and as a communicator with the policy makers
20. Utilizes knowledge of managed care systems in making patient treatment plans and health care maintenance plans
21. Demonstrates training, allotment of work and supervision of paramedical workers like genetic counselor, social worker, genetic nurse, medical photographer
22. Demonstrates ability to follow and lead in a team approach to health care delivery
23. Writing patient information brochures in local languages
24. Writing and presenting a paper
25. Appreciate the role of biomedical research and develop techniques for critical analysis of current scientific developments.

ii. AFFECTIVE DOMAIN

The postgraduate student should:

1. Develop communication skills to word reports and professional opinion as well as to interact with patients, relatives, peers and paramedical staff, and for effective teaching
2. Demonstrate an effective system for identifying and addressing ethical, cultural, and spiritual issues associated with health care delivery
3. Demonstrate knowledge or applies an understanding of psychological, social, and economic factors which are pertinent to the delivery of health care
4. Able to coordinate information from multiple sources into a coherent and rational plan of management of genetic disorders.
5. Able to communicate and counsel patients and families who sometimes may be disturbed and psychologically upset.
6. Understand all the associated and anticipated multisystem manifestations in order to refer for appropriate multidisciplinary management.

iii. PSYCHOMOTOR DOMAIN

The post graduate student must acquire the following practice–based competencies/skills:

1. Provide client-centered counseling and anticipatory guidance
2. Understand human behavior, maturation, and intelligence, in order to facilitate counseling of varying individuals.
3. Tolerate and encourage reiteration of information because of patient anxiety or unfamiliarity with the concepts being presented.
4. Provide psychosocial support including (a) areas of difficulty and conflict, (b) help families and individuals recognize and cope with their emotional and psychological needs, and (c) recognize situations requiring psychiatric referral
5. Identify and use community resources that provide medical, educational, financial and psychosocial support and advocacy
6. Acquire necessary management skills to coordinate the care of individuals affected with complex genetic conditions that will require a long-term multidisciplinary approach
7. Demonstrate mastery of adequate medical record keeping.

V. Course Curriculum

V (A) Course I: Basic Genetics

History of Medical Genetics

Foundations of Medical Genetics Before 1956

Growth and Development of Medical Genetics: 1956 to the Present

The Future

Genetics in Medicine

The Principles of Disease, Defining Disease, Prevention and Treatment

Nature and Frequency of Genetic Disease

Frequency of Genetic Disease

Single-Gene Disorders

Multifactorial Disorders

Somatic Cell Genetic Disorders

Genomics and Proteomics

Genes and Human Disease

Genomics

Mapping the Human Genome

Sequencing the Human Genome

Current Approaches to Sequence Human Genome

Cloning Human Disease Genes

Sequence-Based Methods for Detecting Chromosomal Abnormalities

Proteomics

Genome and Gene Structure

Double Helix Structure, DNA Replication, Transcription, and Meiotic Recombination

Organization of Genomic DNA

Gene Structure and the Molecular Pathway of Gene Expression

Epigenetics

- Epigenetic Mechanisms: Chromatin, DNA Methylation and Long Noncoding RNAs
- Epigenetic Reprogramming
- Epigenetic Regulation of X Inactivation
- Genomic Imprinting
- Genetic Disorders Due to Genes Affecting Chromatin Structure
- Methods for Studying Epigenetic Marks
- Cancer Epigenetics
- Environmental Influences on Epigenetic Traits
- Abnormalities in Epigenetic Programming Linked to Infertility and ART
- In Utero Epigenetic Programming of Adult Traits and Disease
- Genetic–Epigenetic Interactions

Clinical Teratology

- Recognized Teratogenic Exposures
- Paternal Exposures and Maternal Exposures

Human Gene Mutation in Inherited Disease: Molecular Mechanisms and Clinical Consequences

- Molecular Mechanisms of Mutation Causing Human Inherited Disease
- Disease-Causing Mutations, Consequences of Mutations
- General Principles of Genotype–Phenotype Correlation

Genes in Families

- Pedigree Construction
- Unifactorial Inheritance/Single-Gene Disorders
- Dominance and Recessiveness
- Autosomal-Dominant Inheritance

Genome-Wide Association Studies

Association Methods/Statistical Analysis

Analysis of Rare Variants Using New Technologies

Integration of Genetic, Genomic, and Functional Data for Multifactorial Diseases

Population Genetics

Hardy–Weinberg Law, Factors that affect Hardy–Weinberg Equilibrium

Applications in Population Genetics

Pathogenetics of Disease

The Scope of Abnormal Phenotypes: Disease and Malformation

Multivariate Normal Distributions and the Threshold Model

Pathogenetics of Refined Traits

Molecular Pathogenetics

Human Developmental Genetics

The Concept of Developmental Fields and Field Defects

Cellular Signaling in Development

Steps and Concepts in Embryonic Development

Regulation of Gene Expression in Development

Organogenesis

Twins and Twinning

Determining Zygosity

Incidence of Twins, Vanishing Twin, Structural Defects in Twins

Twins in Genetic Studies

Dizygotic Twins, Monozygotic Twins

Pharmacogenetics and Pharmacogenomics

Classical Genetics and Pharmacogenetics

Ethnic Differences in Gene–Drug Interactions

Pharmacogenomics

Autosomal Abnormalities

Genetic Counseling in the Trisomies: Trisomy 21, Trisomy 18, Trisomy 13

Translocations

Uniparental Disomy

Deletion, Duplication

Sex-Chromosome Abnormalities

Turner Syndrome, Klinefelter Syndrome, 47,XXX Syndrome, 47,XYY Karyotype

Sex Chromosome Mosaicism

Sex Chromosome Tetrasomy and Pentasomy (Polysomy)

Structural Abnormalities of the Y Chromosome

Prenatal Diagnosis of Sex Chromosome Abnormalities

Cytogenetic Analysis

Milestones in Human Cytogenetics

The Indications for Cytogenetic Analysis

Tissue Samples and Cell Culture, Chromosome Banding

The Normal Human Karyotype

Chromosome Abnormalities

Molecular cytogenetics

Diagnostic Molecular Genetics

Indications for Molecular Genetic Testing

Technical Approaches to Molecular Genetic Testing

Molecular Genetic Diagnosis of Disease– Sanger sequencing & Next generation sequencing

Mitochondrial DNA Disorders

Quality Assurance, and Regulatory Issues

Internet Resources for Molecular Genetic Testing

Bioinformatics

V (B) Course II: Clinical Genetics

Genetic Evaluation for Common Diseases of Adulthood

The Process of Genetic Evaluation for Common Diseases

Integrating Genetic Information into Routine Clinical Practice

The Molecular Biology of Cancer

Genetic Basis of Cancer

Tumor Suppressor Genes and Viral Oncogenes

Oncogenic Alleles in Human Cancers

The Role of DNA Damage Repair Genes in Inherited Cancer Syndromes

Genetic Counseling and Clinical Risk Assessment

Process of Genetic Counseling

Adult-Onset Disorders

Genetic Risk Assessment and Calculation in the Clinical Setting

Heterozygote Testing and Carrier Screening

Carrier Screening in Clinical Practice

Carrier Screening in Individuals of Defined Subpopulation Groups

Therapeutic Implications for Heterozygotes

Methods and Tissues used in Carrier Identification

Diagnostic Genetic Testing, Predictive Genetic Testing

Confidentiality

Genetic Testing in Childhood, Population Genetic Screening, Newborn Screening, Antenatal Screening, Carrier Screening

Genetics, Geneticization and Society

Reproductive Technologies and Cloning: “Reproductive genetics”

Legal Issues in Medical Genetics

Genetic Malpractice

Genetic Counseling, Abortion, Adoption, Surrogacy, Embryo cryopreservation

Newborn Screening

Prenatal and Carrier Screening

Genetic Discrimination

Regulation of Genetic Diagnostic Tests

Direct to Consumer Genetic Testing

Regulation of Human Genetic Research

Regulation of Research with Stem Cells Derived from Human Embryos

Genetics of Male & Female Infertility

The Hypothalamic – Pituitary - Gonadal Axis

Hypogonadism: Hypogonadotropic & Hypergonadotropic Hypogonadism

Eugonadal Infertility

Chromosome Anomalies and Gene defects

Fetal Loss

Early Pregnancy Loss, Late Pregnancy Loss

Evaluation and Management of Recurrent Abortion

Clinical Approach to the Dysmorphic Child

Disorders of Nucleotide Excision Repair: Xeroderma Pigmentosum and Cockayne Syndrome

Disorders of Base Excision Repair: MUTYH and Colon Cancer Risk

Disorders of Mismatch Repair: Lynch Syndrome and Turcot Syndrome

Disorders Associated with Double Strand Break Recognition and Repair: Ataxia-Telangiectasia and Related Conditions

Crosslink Repair and Homologous Recombination Defects: Breast–Ovarian Cancer and Fanconi Anemia

Disorders Associated with RECQ Helicase Deficiency: Bloom, Werner, and Rothmund–Thomson Syndromes

Gene - Environment Interactions: Gorlin - Goltz Syndrome

The Biological Basis of Aging: Implications for Medical Genetics

Progeroid Syndromes of Humans

Human Allelic Variants Homologous to Pro-Longevity Genes

V (C) Course III: Applied and Laboratory Genetics

Cardio-vascular system: Congenital Heart Defects and Inherited Cardiomyopathies

Specific Syndromes with Congenital Heart Defect

Chromosomal Disorders

Microdeletions/Microduplication Syndromes

Single-Gene Disorders

Holt–Oram syndrome

CHARGE Syndrome

Maternal Diabetes, Drug Ingestion

Folic Acid Supplementation

Risks for Sibs and Offspring of Children with Isolated Heart Defects

Hypertrophic, Dilated and Atypical Cardiomyopathy

Hereditary Hemorrhagic Telangiectasia (Osler–Weber–Rendu Syndrome)

Hereditary Disorders of the Lymphatic System and Venous System (varicose vein)

Capillary Malformation/Arteriovenous Malformation (Capillary Malformation, Sturge–Weber Syndrome, Capillary Malformation–arteriovenous Malformation, Cerebral Cavernous Malformation)

The Genetics of Cardiac Electrophysiology in Humans

Genetics of Blood Pressure Regulation

Preeclampsia

Common Genetic Determinants of Coagulation and Fibrinolysis (Genetic Variants Influencing Components of the Coagulation Cascade, Genetic Variants Influencing Natural Anticoagulants, Genetic Variants Influencing Components of the Fibrinolytic Cascade, Genetic Variants Influencing Platelet Function, Genome-Wide Association Analysis for Thrombosis)

Genetics of Atherosclerotic Cardiovascular Disease (Genetic Studies of CHD, Candidate Gene Studies in Humans, Genome Wide Association Studies, GWAS Findings for CVD Risk Factors, Genetic Risk Scores and Prediction Algorithms for Personalized Medicine)

Respiratory tract disorders

Cystic Fibrosis

Genetic Underpinnings of Asthma and Related Traits

Disorders of ciliary function

Hereditary Pulmonary Emphysema

Interstitial and Restrictive Pulmonary Disorders

Congenital Anomalies of the Kidney and Urinary Tract

Cystic Diseases of the Kidney

Nephrotic Disorders

Renal Tubular Disorders

Cancer of the Kidney and Urogenital Tract

Gastrointestinal Tract and Hepatobiliary Duct System

Inflammatory Bowel Disease

Bile Pigment Metabolism and its Disorders including cholestasis

Cancer of the Colon and Gastrointestinal Tract

Blood

Hemoglobinopathies and Thalassemia

Other Hereditary Red Blood Cell Disorders

Hemophilia and Other Disorders of Hemostasis

Rhesus and Other Fetomaternal Incompatibilities

Disorders of bone marrow aplasia and dyserythropoesis

Immunologic Disorders: Autoimmunity: Genetics and Immunologic Mechanisms

Immunodeficiency Disorders

Inherited Complement Deficiencies

Disorders of Leukocyte Function

Genetic Basis of Autoimmune Thyroid Disease

Endocrine

Abnormalities of growth hormone- pituitary axis

Monogenic diabetes mellitus

Susceptibility to type I and type II diabetes

Genetic Basis of Thyroid Carcinoma

Familial Hypocalciuric Hypercalcemia

CASR Mutations in Familial Hypocalciuric Hypercalcemia and Neonatal Severe Hyperparathyroidism

Neonatal Hyperparathyroidism

Multiple Endocrine Neoplasia

Familial Isolated Hypoparathyroidism

NHERF1 Mutations and Renal Responsiveness to Parathyroid Hormone

Adrenal Gland

Congenital Adrenal Hyperplasia (21, 11β, 3β, 17α-Hydroxylase Deficiency, 17,20-Lyase Deficiency, Congenital Lipoid Adrenal Hyperplasia, etc): Prenatal Diagnosis and Treatment

Congenital adrenal hypoplasia

Reproductive system

Disorders of the Gonads, Genital Tract, and Genitalia

Disorders of Sexual Development and differentiation

Hereditary Cancers

Familial Breast Cancers (BRCA1, BRCA2)

Familial Breast or Ovarian Cancer

Familial Ovarian Cancer

Familial Endometrial Cancer

Hereditary Nonpolyposis Colorectal Cancer Syndrome (or Lynch Syndrome)

Li Fraumeni syndrome

IEM Amino Acid Metabolism

Disorders of Phenylalanine Metabolism

Disorders of Tyrosine Metabolism

Disorders of Glycine Metabolism

Disorders of Proline and Hydroxyproline

Disorders of the Urea Cycle and Ornithine

Disorders of Serine Metabolism

IEM Disorders of Carbohydrate Metabolism

Disorders of Galactose Metabolism

Disorders of Fructose Metabolism

Disorders of Pentose Metabolism

Glycogen Storage Diseases

Gluconeogenic Disorders Associated with Lactic Acidosis

Congenital Disorders of Protein Glycosylation

Congenital Disorders of Protein N-Glycosylation

Congenital Disorders of Protein O-Glycosylation

Congenital Disorders of Protein N- and O-Glycosylation

Purine and Pyrimidine Metabolism

Lipoprotein and Lipid Metabolism

Monogenic Disorders of Lipoprotein Metabolism

Disorders with Primarily Elevated LDL Cholesterol

Disorders with Primarily Depressed LDL Cholesterol

Disorders with Primarily Elevated HDL Cholesterol

Disorders with Primarily Depressed HDL Cholesterol

Disorders with Primarily Elevated Triglycerides

Disorders with Multiple Lipoprotein Disturbances

Organic Acidemias and Disorders of Fatty Acid Oxidation

Vitamin D Metabolism or Action

Hereditary Vitamin D Dependency Type 1 (VDDR-1)-1-α-Hydroxylase Deficiency

Hereditary Vitamin D-Dependent Rickets Type 2 (VDDR-2)

States Resembling Hereditary Generalized Resistance to 1,25(OH)2D

Inherited Porphyrias

Regulation of Heme Biosynthesis

Classification and Diagnosis of the Porphyrias

Inherited Disorders of Human Copper Metabolism

Menkes Disease

Wilson Disease

Iron Metabolism and Related Disorders

Syndromes of Iron Overload

Other Disorders Resulting in Derangements of Iron Handling

Mucopolysaccharidoses

Mucopolysaccharidosis I (IH Hurler, IS Scheie and IH/S Hurler–Scheie Disease)

Mucopolysaccharidosis II (Hunter Syndrome)

Mucopolysaccharidosis IIIA (Sanfilippo Syndrome, MPS IIIA)

Mucopolysaccharidosis IIIB (Sanfilippo Syndrome, MPS IIIB)

Mucopolysaccharidosis IIIC (Sanfilippo Syndrome, MPS IIIC)

Mucopolysaccharidosis IIID (Sanfilippo Syndrome, MPS IIID)

Mucopolysaccharidosis IVA and IVB (Morquio Syndrome, MPS IVA, MPS IVB)

Mucopolysaccharidosis V (Scheie Syndrome, MPS V)

Mucopolysaccharidosis VI (Maroteaux–Lamy Syndrome, MPS VI)

Mucopolysaccharidosis VII (Sly Syndrome, MPS VII)

Mucopolysaccharidosis VIII

Mucopolysaccharidosis IX (Natowicz Syndrome, MPS IX)

Oligosaccharidoses: Disorders Allied to the Oligosaccharidoses

Sphingolipid Disorders and the Neuronal Ceroid Lipofuscinoses or Batten Disease (Wolman Disease, Cholesteryl Ester Storage Disease, and Cerebrotendinous Xanthomatosis)

GM1-Gangliosidosis (β-Galactosidosis)

GM2-Gangliosidosis

Loss-of-Function Mutation of GM3-Synthase

Niemann–Pick Disease

Niemann–Pick Disease, Types A and B

Niemann–Pick Disease, Types C and D

Farber's Disease

Acid Lipase Deficiency (Wolman Disease and Cholesteryl Ester Storage Disease)

Gaucher Disease

Galactosylceramide Lipidosis, Globoid Cell Leukodystrophy, or Krabbe Disease

Metachromatic Leukodystrophy

Fabry Disease

Neuronal Ceroid Lipofuscinosis or Batten Disease

Kufs Disease or Adult NCL

Congenital NCL/CNCL-CLN10/Cathepsin D or CTSD Deficiency

Peroxisomal Disorders

Nervous System (CNS & PNS)

Fragile X Syndrome and X-linked Intellectual Disability

Dyslexia and Related Communication Disorders

Attention-Deficit/Hyperactivity Disorder

Autism Spectrum Disorders

Genetics of Alzheimer Disease

Schizophrenia and Affective Disorders

Addictive Disorders

Neural Tube Defects

Genetic Disorders of Cerebral Cortical Development

Genetic Aspects of Human Epilepsy

Basal Ganglia Disorders (Parkinson Disease, Dystonias, Choreic Disorders)

Hereditary Ataxias (Autosomal-Dominant, Recessive, X-linked ataxias, Intermittent Ataxias, Episodic Ataxias, Progressive Ataxias, Mitochondrial Ataxias)

Hereditary Spastic Paraplegia (Autosomal Dominant, Autosomal Recessive, X-Linked)

Autonomic and Sensory Disorders (Familial Dysautonomia, Congenital Sensory Neuropathy with Anhidrosis)

The Phakomatoses (The Neurofibromatoses)

Tuberous sclerosis

Demyelinating Disorders (Krabbe Disease, Metachromatic & X-Linked Adrenoleukodystrophy)

Hereditary Motor and Sensory Neuropathies (Charcot–Marie–Tooth)

Spinal Muscular Atrophies

Motor Neuron Disease: Familial Amyotrophic Lateral Sclerosis

Muscles

Muscular Dystrophies (Dystrophinopathies, Facioscapulohumeral Muscular

Dystrophy

Emery–Dreifuss Muscular Dystrophies and Other Contractural Phenotypes, Limb-Girdle Muscular Dystrophies, Myofibrillar Myopathies and Other Distal Phenotypes, Congenital Muscular Dystrophies)

Congenital (Structural) Myopathies

Hereditary Muscle Channelopathies

Myotonic Dystrophies

Hereditary and Autoimmune Myasthenias

Eye

Color Vision Defects (Molecular Basis of Variation in Normal Color Vision, Genetics of Red–green Color Vision in Women, Blue–Yellow (Tritan) Color Vision Defects, etc)

The Achromatopsias

Optic Atrophy

Glaucoma

Congenital Defects of the Cornea

Congenital Cataracts and Genetic Anomalies of the Lens

Hereditary Retinal and Choroidal Dystrophies: Pigmentary Retinopathies/Retinitis Pigmentosa, Leber's Congenital Amaurosis, The Primary Cone Degenerations

Strabismus

Retinoblastoma and the RB1 Cancer Syndrome

Anophthalmia, Microphthalmia, and Uveal Coloboma

Ear: Hereditary Hearing Impairment

Clefting, Dental, and Craniofacial Syndromes

Craniosynostosis

Skin and Hair

Abnormalities of Pigmentation: Disorders of Melanosome Biogenesis/Transport—Hermansky–Pudlak Syndrome, Chédiak–Higashi Syndrome, and Griscelli Syndrome; Disorders of Melanocyte Survival—Vitiligo

Ichthyosiform Dermatoses

Epidermolysis Bullosa

Ectodermal Dysplasias

Xeroderma Pigmentosum

Epidermodysplasia Verruciformis

Porokeratoses

Muir–Torre Syndrome

Melanoma

Cutaneous Hamartoneoplastic Disorders: Hereditary Leiomyomatosis and Renal-Cell Cancer, Birt–Hogg–Dubé Syndrome

Inherited Disorders of the Hair: Hypotrichosis, Hypertrichosis

Marfan Syndrome and Related Disorders

Ehlers–Danlos Syndrome

Heritable Diseases Affecting the Elastic Fibers: Cutis Laxa, Pseudoxanthoma Elasticum, and Related Disorders

Bone

Osteogenesis Imperfecta (and Other Disorders of Bone Matrix)

Disorders of Bone Density, Volume, and Mineralization: Osteopetrosis Group of Disorders, Raine Dysplasia, Pyknodysostosis, Dysosteosclerosis, Osteopoikilosis, Craniotubular Remodeling Disorders, Hyperphosphatasemia with Osteoectasia, etc

Chondrodysplasias

Abnormalities of Bone Structure (Dysplasia Epiphysealis Hemimelica, Hereditary Multiple Exostoses, Langer–Giedion Syndrome, Enchondromatosis, Maffucci Syndrome, Metachondromatosis, Fibrous Dysplasia of Bone, etc)

Dysostoses

Arthrogryposes (Multiple Congenital Contractures)

Common Skeletal Deformities

Hereditary Non-inflammatory Arthropathies

Cohesinopathies

Ciliopathies

V (D) Course IV: Recent Advances in Medical Genetics

Gene Therapy: From Theoretical Potential to Clinical Implementation

- Genes as Medicines -The Origins of Gene Therapy
- The Basic Science: Gene Transfer
- Developing Cell-Type-Specific and Regulatable Gene Delivery Vectors
- The Clinical Science: Toward Gene Therapy of Human Disease

Antisense oligonucleotide

Artificial intelligence in genetics

Biobanks

Updates on novel phenotypes and causative genes identified

Complete human genome sequencing

Long read sequencing

COVID 19 genetics

CRISPR in cancer and functional genomics

Direct to consumer testing

Recent treatment strategies: DMD, SMA, hemophilia, thalassemia, cystic fibrosis, IEM, LSD

Cloning, Genome editing

Personalised medicine

National policy of rare disease

Proteomics

RNA interference

Single cell genomics

Prenatal exome sequencing

Expanded carrier screening

Therapeutic recombinant proteins

Transgene expression

NIPS

VI. Outcomes

(A) Program Outcomes

The program is to create experts in the field of medical genetics who are astute clinicians with excellent understanding of principles and knowledge of basic genetics and diagnosis and management of genetic disorders. These trained superspecialists will have expertise and experience in analysing family history and clinical presentations of genetic disorders, use sophisticated and latest genomic diagnostic tools to make accurate diagnosis. They will be able to order the appropriate genetic investigations, analyse and interpret the results, communicate the diagnosis and its implications to the patient and family. The training will also provide the expertise to understand the laboratory work so that the medical geneticist will be able to supervise the lab and create the reports. The clinicians of this speciality will be able to take up the responsibilities of carrying out novel treatments like gene therapies, latest drugs, RNA based strategies as well.

The program also provides specialised skills necessary for this novel speciality including genetic counselling, fetal autopsy, prenatal diagnosis and / or collaborate and contribute to these processes in liaison with appropriate specialists. The program training is expected to provide basic skills in research and high level of research in the area of genomics including clinical skills, laboratory and computations genetics, databases, etc for understanding pathogenesis of diseases, document new phenotypes and contribute to the development of new drugs and novel management strategies.

(B) Course Outcomes:

Each course is expected to teach and train a part of the course curriculum as described. The outcomes of each course are described below and will contribute equally to the super specialized training in medical genetics.

Course I: Basic Genetics

This course will provide knowledge of cell, cell division, anatomy and physiology of cell and chromosomes. The structure of genome, function of gene, their complex control and interactions and their role in health and disease. The outcome of this course will be to provide basic understanding of human genetics in health and disease and various ways to study gene and genome and their functions at RNA, protein and cellular levels.

Course II: Clinical Genetics

This course will make the superspecialist in medical genetics able to deal with various clinical presentations of genetic disorders, clinical and laboratory diagnostic approaches, appropriate usage of appropriate genetic tests. The outcome will also include ability to plan and run population based screening programs, working with patient support groups and efficiency in supportive skills like prenatal diagnosis, genetic counselling and fetal autopsy. The use of genetic and disease databases, softwares for clinical diagnosis and computational tools, analysing next generation sequencing data, interpretation of genetic variants, etc. are the abilities expected from the trainee at the end of the course. The trainee will be able to design research project, write case reports and review articles.

Course III: Applied and Laboratory Genetics

This course will provide vast experience of dealing with patients and logical diagnosis approach using the laboratory as well as computerised databases and softwares. The trainee will be equipped with theoretical knowledge and experience of evaluation and taking care of patients with genetic disorders of all systems. The trainee will be able to review the latest literature and make decisions about diagnosis and management of patients and families including pre-symptomatic diagnosis and pre-test and post-test counselling. The trainee will be able to handle cases with multiple malformations, syndromic diagnosis and carry out interdisciplinary consultations and run speciality clinics for specific disorders. With more than 6000 genetic disorders the challenging task of dealing with disorders of other systems will be expertly handled by medical geneticists.

Course IV: Recent developments in Medical Genetics

The speed of development in medicine, especially in genomic medicine is tremendous. Continuous [2 yearly] update of curriculum of this course will be done but the most important outcome of this course will be to learn how to keep oneself up-to date in the speciality of

genomic medicine and see that the patients get state of art diagnostics, management and advice.

In the recent era, this course outcomes will be updates about stem cell research, therapies like RNA based therapies, CRISPR-Cas, gene therapy, NGS based screening of newborns, polygenic scores, etc. This course will be interesting and introduce the trainee to the fascinating world of research in two ways; i.e. enjoying the latest developments in the field, applying to the patient care and contributing by way of conducting research in select niche areas.

VII. TEACHING AND LEARNING METHODS

VII (A) Clinical Training

Clinical training must provide students with opportunities to have first-hand experience with individuals and families affected by a broad range of genetic disorders. These clinical experiences must expose post graduate students to the natural history and management of common genetic conditions and birth defects and to relevant psychosocial issues. Students must have the opportunity to develop counseling and psychomotor skills in a variety of clinical settings where genetic services are provided. Such settings must include those where patients are seen for prenatal diagnosis; clinical and laboratory diagnosis of genetic syndromes and mental retardation; multidisciplinary management of chronic genetic disorders and birth defects; newborn, carrier or predisposition screening and evaluation of mutagenic, teratogenic or other risk factors. These clinical experiences must help students to observe and practice skills relating to obtaining medical and family histories; determining risks; performing psychosocial assessments; communicating information about disease characteristics, inheritance and natural history; providing anticipatory guidance and supportive counseling; identifying and using medical and community resources; communicating information to other health-care professionals, case management and follow-up. The students should become proficient in communicating the genetic burden and reproductive options including antenatal diagnosis to the patient and relatives.

Students must be supervised by qualified genetics professionals and given the opportunity for involvement in a variety of cases. Throughout clinical posting, student should maintain clinical/case management records in logbook.

VII (B) Rotation Postings:

- 24 months of training in a clinical genetic unit where the post graduate student should participate in the care of at least 100 patients with various genetic disorders besides three months posting in fetal medicine, obstetrics &neonatology/pediatrics
- 12 months of posting in Genetics laboratory

VII (C) Laboratory Training

The students must attain proficiency in carrying out prescribed list of laboratory tests themselves and attain overall ability to organize, supervise and report on results of various specialized genetic laboratory investigations employed in workup of patients with genetic disorders (this posting may run concurrently with clinical training). For this purpose, laboratory posting should be scheduled as given below:

a) 2 months of training in Cytogenetics including molecular cytogenetic techniques namely FISH (fluorescence *in situ* hybridization), microarray, QF PCR, MLPA
b) 2 months of training in biochemical genetics including Newborn Screening
c) 2 months of training in molecular genetics including PCR, Sanger sequencing, analysis of Next Generation Sequencing data, reverse transcription PCR (RT PCR), Real Time PCR
d) 6 months Research Project work

These rotations shall focus not only on developing consultative/interpretive skills, but also will provide adequate opportunity for hands-on training. The time spent in the laboratory towards research project should be entered in Log book. During postings, students should be exposed to the following laboratory techniques:

- Cytogenetics including Prenatal Cytogenetic Diagnosis
- Molecular Cytogenetics including Prenatal, Preimplantation and Cancer
- Microarray including molecular karyotyping
- Molecular Techniques including Polymerase Chain Reaction (PCR), Gel Electrophoresis (DNA/RNA i.e., ribonucleic acid, Protein, etc), Southern blotting,

Arms technique, Real Time PCR, Quantitative Fluorescent PCR (QF PCR), DNA Sequencing, next generation sequencing (NGS), epigenetics techniques,

VII (D) Teaching methodology

1. This should include regular case presentations, didactic lectures, seminars, journal clubs, clinical meetings, and combined conferences with allied departments. Hours of lecture must be 6-8 hours a week as doctors undergoing this training are not exposed to basic genetics in their basic graduation.
2. The post graduate student should be given the responsibility of managing and caring for patients in a gradual manner under supervision.
3. Department should encourage e-learning activities.
4. Formal teaching sessions

   In addition to bedside teaching rounds, at least 5-hr of formal teaching per week are necessary. The departments may select a mix of activities as given under formative assessment. The students should also attend:

   - Attend accredited scientific meetings (CME, symposia, and conferences).
   - Additional sessions on basic sciences, biostatistics, research methodology, teaching methodology, hospital waste management, health economics, medical ethics and legal issues related to medical practice.

4. There should be a training program on Research methodology for existing faculty to build capacity to guide research.
5. The postgraduate students shall be required to participate in the teaching and training program of undergraduate students and interns.
6. A postgraduate student of a postgraduate degree course in broad specialties/super specialties would be required to present one poster presentation/ to read one paper at a national/state conference and to present one research paper which should be published/accepted for publication/sent for publication during the period of his postgraduate studies so as to make him eligible to appear at the postgraduate degree examination.
7. **Log book:** During the training period, the post graduate student should maintain a Log Book indicating the duration of the postings/work done. This should indicate the procedures assisted and performed, and the teaching sessions attended. The Log book shall be checked and assessed periodically by the faculty members imparting the training.

During the training programme, patient safety is of paramount importance; therefore, skills are to be learnt initially on the models, later to be performed under supervision followed by performing independently; for this purpose, provision of skills laboratories in medical colleges is mandatory. Various basic courses organized by the Institute for all round development of the clinician should be attended for increasing knowledge.

VIII. Methods of computing attainment of course outcomes based on course curriculum

VIII (A) FORMATIVE ASSESSMENT (during the training program)

Formative assessment should be continual and should assess medical knowledge, patient care, procedural & academic skills, interpersonal skills, professionalism, self-directed learning and ability to practice in the system.

General Principles

Internal Assessment should be frequent, cover all domains of learning and used to provide feedback to improve learning; it should also cover professionalism and communication skills. The Internal Assessment should be conducted in theory and clinical examination.

Quarterly assessment during the DM training should be based on:

1. Journal based / recent advances learning
2. Patient based /Laboratory or Skill based learning
3. Self-directed learning and teaching
4. Departmental and interdepartmental learning activity
5. External and Outreach Activities / CMEs

Internal assessment to be carried out every 6 months with theory paper and practical assessment(Viva Voice, Clinical case and Laboratory skill)

The student to be assessed periodically as per categories listed in postgraduate student appraisal form.

VIII (B) SUMMATIVE ASSESSMENT, i.e., assessment at the end of training

The summative examination would be carried out as per the Rules given in POSTGRADUATE MEDICAL EDUCATION REGULATIONS, 2000.

The final examination will be in three parts:

1. Thesis

Every post graduate student shall carry out work on an assigned research project under the guidance of a recognized Post Graduate Teacher, the result of which shall be written up and submitted in the form of a Thesis. Work for writing the Thesis is aimed at contributing to the development of a spirit of enquiry, besides exposing the post graduate student to the techniques of research, critical analysis, acquaintance with the latest advances in medical science and the manner of identifying and consulting available literature.

Thesis shall be submitted at least six months before the Theory and Clinical / Practical examination. The thesis shall be examined by a minimum of three examiners; one internal and two external examiners, who shall not be the examiners for Theory and Clinical examination. A post graduate student shall be allowed to appear for the Theory and Practical/Clinical examination only after the acceptance of the Thesis by the examiners.

The research work should be published/ publishable (as accepted by the examiners) in an indexed journal. Every postgraduate student would be required to present one poster/ read one paper at national/ state conference.

2. Theory Examination:

The examinations shall be organized on the basis of 'Grading' or 'Marking system' to evaluate and to certify post graduate student's level of knowledge, skill and competence at the end of the training. The examination for DM shall be held at the end of third academic year.

There shall be four Theory papers based on courses I, II, III and IV each of 100 marks (10 long answer based questions)

Paper I: Basic Genetics

Paper II: Clinical Genetics

Paper III: Applied and Laboratory Genetics

Paper IV: Recent Advances in Medical Genetics

3. Clinical/Practical Examination

Clinical Case Presentation:

Long Case: 1

Short Cases: 3

Genetic Counseling

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 population databases, mutation databases, & mutation prediction software
- Analysis and interpretation of TMS, urine GCMS and plasma amino acid HPLC results

3. Oral/viva voce examination

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

IX. Choices available to the students for selecting the courses within their programs

The institute offers a multitude of 01 and 02 courses based upon a credit score system. 01 course consisting of foundation and bioethics course is compulsory. A number of 02 courses are available throughout the year lasting for 12 hours or 24 hours spread over 1-2 weeks and consisting of a score. A student is expected to obtain at least 8 points over the 3 years to secure eligibility for the final exam.

Representative courses held during last 4 years are listed here. The objectives of these course are lateral growth in the knowledge and interactive applications in various other fields. The objectives and outcomes are self -explanatory. In general the objective is for gain of knowledge in other specialities of medicine, science, computers, research, humanities and art, so that the clinician becomes a better doctor, human being, researcher and develops fruitful interactions with patients and colleagues.

01 Courses: Representative list {New courses are developed and started regularly}

1. History of medicine
2. Communication skills
3. Presentation skills
4. Biostatistics
5. Ethics and law in medicine
6. Laboratory instrumentations
7. Photography and documentations
8. Importance of Communication in medicine
9. Scientific communication
10. Fluid and electrolyte
11. Ethics and law in medicine
12. Laboratory instrumentations
13. Photography and videos in medicine
14. Immunology for clinicians
15. Patient safety
16. Introduction to Lab animal science practices
17. CPCR and life support
18. Radiation biology

19. Therapeutic nutrition
20. Artificial intelligence
21. Innovation and IPR issues
22. Industry-Academia relationship: A delicate balance
23. Social Media in medicine
24. Outreach community program
25. Telemedicine: Opportunities and Issues

X. Define the horizontal flexibility offered to the students for the courses within their program

1 week compulsory posting for every student in the following departments of the institute

i. Neonatology
ii. Pediatric gastroenterology and endocrinology
iii. Neurology

XI. Added courses:

Student is expected to participate in department activities of patient and family interaction on Down syndrome day, thalassemia day, hemophilia day, rare disease day and involved in advocacy activities.

XII. RECOMMENDED READING

XII (A) Books (latest edition)

1. Emery and Rimoin's Principles and Practice of Medical Genetics and Genomics; Reed Pyeritz, Bruce Korf, Wayne Grody.**ISBN:**9780123838353.
2. Human Genetics Problems and Approaches; F Vogel, AG Motulsky, Springer. ISBN: 978-3-540-37654-5.
3. Practical Genetic Counseling; Peter Harper, ButerworthHeinmann. ISBN:9781483183664, 1483183661.
4. Birth Defects Encylopedia; Mary Louise Buyse, Blackwell Scientific Publication. ISBN: 13: 978-0865422285.
5. Smith's Recognizable Pattern of Human malformations; KennethlyonNenes, WB Saunders Company. ISBN:1455738115.
6. Mendelian Inheritance in Man; Victor A Mckusick, The Johns Hopkins University Press. ISBN: 9780801820878.
7. Metabolic and Molecular Basis of Inherited Disease; Charles R. Scriver, Arthur L. Beaudet, William S. Sly, David Valle, McGraw-Hill. ISBN: 10 0079130356.
8. The Principles of Clinical Cytogenetics; SL Gersen, M B Keagle, Humana Press. ISBN: 978-1-4419-1688-4.

9. Human Cytogenetic Techniques and Clinical Applications; HemaPurandare, Amit Chakrravarty. Bhalani Publishing House. ISBN:8185578419.
10. Textbook of Fetal and Perinatal Pathology, Vol. I & II, Jonathan S. Wigglesworth, Don B Singh. ISBN-10: 0865421188.
11. Catalog of Teratogenic Agents; T S Shepard, John Hopkins University Press.ISBN-13: 978-0801897849.
12. Emery's Elements of Medical Genetics; Peter Turnpenny, Sian Ellard. Elsevier Churchill Livingston. **ISBN:** 9780702066856.
13. Essential of Human Genetics; HemaPurandarey.Jaypee Publishers.ISBN-10:9788184485356.
14. Genetics for clinicians;Shubha R Phadke. Prism Books, Bangalore. ISBN: 8172865015.
15. Practical Genetic Counseling; Peter Harper. Oxford University Press. ISBN:978-1138445659.
16. The Practical Guide to the Genetic Family History; Bennett Robin. Wiley-Liss. ISBN: 0471251542.
17. All God's mistakes:Genetic Counseling in a Pediatric Hospital;Bosk Charles L. University of Chicago Press, Chicago. ISBN: 0226066819.
18. Chromosomal abnormalities and genetic counseling;RJM Gardner, GR Sutherland, Lsa G. Shaffer.Oxford University Press. ISBN:9780199329007.
19. Medical cytogenetics; Mark Hon Fong L. CRC Press. ISBN: 0824719999
20. Congenital malformation evidence-based evaluation and management; Pravin Kumar, Barbara K Burton. McGraw Hill. ISBN:0071471898.
21. Human Molecular Genetics;Tom Strachan, Andrew Read.Garland Science. ISBN 978-0815345893.
22. Genetic disorders and the foetus: diagnosis, prevention and treatment; Aubrey Milunsky Baltimore, John Hopkins. ISBN: 978-1-1189-8152-8.
23. Atlas of Human Chromosomal Disorders;HemaPurandarey.JaypeePublishers, ISBN:9789351522386.
24. Genetic Disorders and Pregnancy Outcome; Platt Lawrence D. Taylor and F. ISBN: 1850707219
25. Management of genetic syndromes; Cassidy S B, AllansonJE. Wiley Liss. ISBN: 978-1-119-43267-8.
26. Principles and practice of fetal medicine;RajuSahetya,Jaideep Malhotra and HemaPurandarey.Jaypee Brothers. ISBN:9385999699.
27. Essentials of Medical Genomics; Brown Stuart M. Wiley-Liss.ISBN: 047121003X
28. Genetic Polymorphisms and Susceptibility to Disease; Miller Mark Steven. CRC Press.ISBN: 0748408223.
29. Common Heteromorphism in Human Chromosomes: Applications and Implications;HemaPurandarey. LAP Lambert Academic Publishing. ISBN: 3659103373.
30. Current Perspectives in Genetics: Insights and Applications in Molecular, Classical, and Human Genetics, Shelly Cummings. Brooks Cole. ISBN-13: 978-0534252809.
31. The Origins of Genome Architecture, Michael Lynch. Sunderland MA. ISBN 978-0-87893-484-3.
32. Genetics: Analysis and Principles, Robert Booker. ISBN10: 1260240851.
33. Genetics in Medicine, Thompson & Thompson. ISBN: 9781437706963
34. Human Molecular Genetics, Tom Strachan and Andrew Read. ISBN 9780815345893.
35. New Clinical Genetics, Andrew Read and Dian Donnai. ISBN 9781911510703.
36. Human malformations and related anomalies. Stevenson RE, Hall JG. ISBN-13:

9780199386031.
37. Radiology of syndromes, metabolic disorders and skeletal dysplasias. Taybi H, Lachman RS. ISBN-13: 978-0815187097.
38. Ultrasonography in Obstetrics and Gynecology. Callen PW. **ISBN:** 9780323328340.
39. The AGT Cytogenetics Laboratory Manual. Marilyn S Arsham, Margaret J Barch, Helen J Lawce. ISBN:9781119061229.
40. Oxford Desk Reference Clinical Genetics. Jane A Hurst,Helen V Firth, Judith G Hall.ISBN-13: 978-0192628961.
41. Physician's Guide to the diagnosis, treatment, and follow-up of inherited metabolic diseases**.** **Blau**N, **Dionisi-Vici**C, **Ferreira**CR, **Vianey-Saban C, van Karnebeek**CDM. ISBN: 978-3642403361.
42. Handbook of Medical Genetics and Genetic Counseling,Panigrahi I, Halder A. Noble Vision Publishers, New Delhi. ISBN:978-81-906227-4-5.
43. A Clinical Guide to Inherited Metabolic Diseases, Joe TR Clarke. Cambridge University Press. ISBN:9780521890762, 0521890764.

XII (B) Journals

03-05 international Journals and 02 national (all indexed) journals

XII (C) Miscellaneous Resources (including web resources)

1. **OMIM**- *Online Mendelian Inheritance in Man,* Catalog of all known human genes and 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. Gene Clinics*:* 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 to develop 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, Non-traditional Inheritance, Chromosomal Disorders, Mitochondrial DNA Abnormalities, Immunogenetics, Forensic Genetics, Genetic

Therapy, Congenital Anomalies, Pedigree symbols, Pharmacogenetics, Cancer Genetics, Prenatal Genetic 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

Annexure I

Postgraduate Students Appraisal Form

Pre / Para /Clinical Disciplines

Name of the Department/Unit:

Name of the PG Student :

Period of Training : FROM……TO……

Sr. No.	PARTICULARS	Not Satisfactory	Satisfactory	More Than Satisfactory	Remarks
		1 2 3	4 5 6	7 8 9	
1.	Journal based / recent advances learning				
2.	Patient based /Laboratory or Skill based learning				
3.	Self-directed learning and teaching				
4.	Departmental and interdepartmental learning activity				
5.	External and Outreach Activities / CMEs				
6.	Thesis / Research work				
7.	Log Book Maintenance				

Publications Yes/ No

Remarks*_____

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*REMARKS: Any significant positive or negative attributes of a postgraduate student to be mentioned. For score less than 4 in any category, remediation must be suggested. Individual feedback to postgraduate student is strongly recommended.

SIGNATURE OF ASSESSEE SIGNATURE OF CONSULTANT SIGNATURE OF HOD