Semester III

Paper MHG-301: Human Molecular Genetics and Human Genomics

Unit I
1. Genetic mapping of Mendelian and complex characters:
   1.1 Identifying recombinants and non-recombinants in pedigrees
   1.2 Genetic and physical map distances
   1.3 Genetic markers
2. Mapping of genetic traits:
   2.1 Two-point mapping- LOD score analysis
   2.2 Multipoint mapping
   2.3 Homozygosity mapping
3. Genetic mapping of complex traits; Difficulties in mapping
   3.1 Allele sharing methods- affected sib pair analysis
   3.2 Allelic association, Linkage disequilibrium mapping, Transmission disequilibrium test
4. Physical mapping of the human genome: Low resolution mapping- Cell hybrids, mini- and microcells, synteny of genes, Radiation hybrid mapping.

Unit II
5. Integration of cytogenetic, genetic and physical maps
6. Human genome mapping: Assembly of clone contigs and identifying genes in cloned DNA
7. History, HGP organization and goals of human genome project
8. The Genome projects:
   8.1 Mapping strategies, current status of various maps; DNA segment nomenclature
   8.2 ELSI
   8.3 Benefits & patenting of genetic materials

Unit III
9. Human genome diversity project (HGDP): Concept and goals
10. Bioethics: Definition, history, principles & Theories
11. Comparative genomics - Characteristics of genomes of human and other model organisms (yeast, Caenorhabditis elegans, Drosophila, Fungus and mouse)
12. Organization of human genome:
   12.1 Mitochondrial genome
   12.2 Nuclear genome - Gross base composition, gene density, CpG islands

Unit IV
13. Human genome structure:
   13.1 RNA-encoding genes, functionally identical/similar genes
   13.2 Diversity in size and organization of genes
   13.2 Pseudogenes
14. Functional genomics - ESTs, Transcriptosome, Proteome, Multiplex and DNA microarray
    (chip) based analysis
15. Gene families in human genome
   15.1 Multigene families - Classical gene families, families with large conserved domains,
    families with small conserved domains
   15.2 Gene super families
   15.3 Gene families in clusters
16. DNA testing
   16.1 Direct and indirect testing (gene tracking) in individuals
   16.2 DNA tests for identity and relationships including forensic applications
   16.3 Population screening- ethics, organization and advantages
Paper MHG-302: Clinical Genetics and Genetic Counseling

Unit I
1. An overview of the genetic basis of syndromes and disorders
2. Monogenic diseases with well known molecular pathology
   2.1. Cystic fibrosis
   2.2. Tay-Sachs Syndrome
   2.3. Marfan syndrome
3. Inborn errors of metabolism and their genetic bases
   3.1 Phenylketonuria
   3.2 Mucopolysaccharidosis
   3.3 Galactosemia
4. Neurogenetic disorders
   4.1 Major regions of human brain and nerve conduction
   4.2 Charcot-Marie tooth syndrome. Spino-muscular atrophy
   4.3 Alzheimer’s disease

Unit II
5. Syndromes due to triplet nucleotide expansion
6. Muscle genetic disorders
   6.1 Dystrophies (Duchenne Muscular dystrophy and Becker Muscular Dystrophy)
   6.2 Myotonias
   6.3 Myopathies
7. Genetic disorders of Haemopoetic systems
   7.1 Overview of Blood cell types and haemoglobin
   7.2 Sickle cell anemia
   7.3 Thalassemias
   7.4 Hemophilias
8. Genetic disorders of eye
   8.1 Colour Blindness
   8.2 Retinitis pigmentosa
   8.3 Glaucoma
   8.4 Cataracts

Unit III
9. Genetic disorders of skeleton
10. Genetic disorders of skin
11. Syndromes:
   11.1 Genomic syndromes: Neurofibromatosis I syndrome
   11.2 Genome imprinting: Prader-Willi and Angelman syndromes, Beckwith-Wiedeman syndrome
12. Cancers and cancer-prone syndromes
   12.1 Haematological malignancies
   12.2 Retinoblastoma, Wilm’s tumour, Colorectal cancer
   12.3 DNA-repair deficiency syndromes
   12.4 Breast cancer

Unit IV
13. Complex polygenic syndromes
   13.1 Hyperlipidemia
   13.2 Atherosclerosis
   13.3 Diabetes mellitus
14. Mitochondrial syndromes
15. Management of genetic disorders
16. Historical overview (philosophy & ethos) and Components of genetic counseling I:
   16.1 Indications for and purpose
   16.2 Information gathering and construction of pedigrees
16.3 Medical Genetic evaluation
16.3.1 Basic components of Medical History
16.3.2 Past medical history, social & family history

Unit V
17. Components of genetic counseling II:
   17.1 Physical examination, General and dysmorphology examination
   17.2 Documentation, Legal and ethical considerations
18. Patterns of inheritance, risk assessment and counseling in common Mendelian and Multifactor syndromes
19. Genetic testing: biochemical & molecular tests
   19.1 In children
   19.2 Presymptomatic testing for late onset diseases (predictive medicine)
20. Prenatal and Preimplantation diagnosis
   20.1 Indications for prenatal diagnosis
   20.2 Indications for chromosomal testing
   20.3 Noninvasive methods
   20.4 Invasive methods

Recommended Books
1. Thompson & Thompson, Genetics in Medicine, 7th Ed., Nuusbaum et al, Elsevier, 2007
3. New Clinical Genetics, Read & Donnai, Scion, 2007
5. Genetics for Healthcare Professionals, Skirton & Patch, Bios, 2002
8. Prenatal Medicine, Vugt & Shulman, Informa Healthcare, 2006
10. Neural tube defects, Oppenheimer, Informa, 2007
14. Introduction to Risk Calculation in Genetic Counselling, Young Oxford 1999
Paper MHG-303: Recombinant DNA Technology and Molecular Diagnostics in Human Diseases

Unit I
1. Enzymes used in DNA technology
   1.1 Restriction and modification enzymes
   1.2 Other nucleases
   1.3 Polymerases
   1.4 Ligase, kinases and phosphatases
2. Cloning vectors
   2.1 Plasmids
   2.2 Phages
   2.3 Cosmids
   2.4 Artificial chromosomes
   2.5 Shuttle vectors
   2.6 Expression vectors
3. Cloning Techniques
   3.1 Isolation & purification of genomic & plasmid DNA & RNA
   3.2 Gel electrophoresis of nucleic acids (RNA & DNA); Pulse field gel electrophoresis
   3.3 Construction of genomic libraries
   3.4 Construction of cDNA libraries
4. Microcloning and Positional cloning: RFLP mapping, chromosome walking and jumping

Unit II
5. Screening of clones from libraries
   5.1 Expression based screening
   5.2 Interaction based screening: yeast two-hybrid system
   5.3 Preparation of probes
   5.4 Restriction mapping
6. Principles of hybridizations and hybridization based techniques:
   6.1 Colony, plaque, Southern, Northern and in situ hybridizations
   6.2 ELISA, western and southwestern blotting
   6.3 Microarray based detections
7. Characterization of clones
   7.1 DNA sequencing methods
   7.2 S1 nuclease and RNase mapping of nascent RNAs

Unit III
9. Oligonucleotide synthesis
10. Principles & applications of Polymerase Chain Reaction (Types)
11 DNA fingerprinting
12 Mutagenesis
   12.1 Site directed mutagenesis
   12.2 Transposon mutagenesis
   12.3 Construction of knockout mutants

Unit IV
13. Gene transfer techniques
   13.1 Microinjection
   13.2 Transfection of cells: Principles and methods
14. Germ line transformation in Drosophila, transgenic and knock out mice: Strategies and methods
15. Applications of Recombinant DNA Technology
   15.1 Monitoring of gene expression in live cells
   15.2 Molecular genetic analysis of human diseases
   15.3 Biosafety & ethical considerations
16. Gene therapy & Stem cells:
   17.1 Somatic and germ line gene therapy
   17.2 DNA drugs and vaccines
   17.3 Stem Cells: Type, sources, culture and applications in therapy

Unit V Molecular Diagnostics (General ideas)
17. Testing DNA variation for diseases association
   17.1 SNPs; SNPs & Diseases
   17.2 Methods of SNP Typing: Brief idea of Traditional approach, Microchip (Affymetrix) & Taqman
18. Microarray approach to gene expression analysis (Brief idea)
   18.1 DNA microarray platforms
   18.2 cDNA array
   18.3 oligonucleotide arrays
   18.4 Concept of genome-wide association studies (GWAS)
   18.5 SAGE, CGH, Array CGH, SNP arrays
19. HLA Typing using molecular methods (Brief idea)
   19.1 PCR with sequence-specific primer
   19.2 Sequence-specific oligonucleotide probe hybridization
   19.3 Sequence-based HLA typing
   19.4 Methods based on determination of conformation: SSC polymorphism, Heteroduplex analysis
20. Methods for analysis of DNA Methylation (Brief idea)
   20.1 Bisulphite modification
   20.2 Methylation-specific PCR
   20.3 Real time PCR methods
   20.4 Methylation-sensitive SSC analysis
   20.5 Profiling and arrays

Recommended Books
2. Genes and Genome, Singer & Berg, USB, 1991
3. PCR, Hughes & Moody, Scion, 2007
11. DNA Science Micklos and Freyer Cold Spring Harbor 1990
Paper MHG-304: Immunogenetics and Molecular Genetics of Human Pathogens

Unit I
1. General introduction to immune system
   1.1 Innate and adaptive immunity
   1.2 Immune responses
   1.3 Antigens & antibodies
   1.4 cells and organs of the immune system
2. Antigens & antibodies
   2.1 Immunogenicity vs antigenicity
   2.2 Factors influencing immunogenicity
   2.3 Structure and function of antibody: Ig G, Ig M, Ig A, Ig E & Ig D
   2.4 Antigen-antibody interactions
3. Immunoglobulin -I
   3.1 The immunoglobulin super family
   3.2 Organization of Ig genes
4. Immunoglobulin -II
   4.2 Expression of Ig genes
   4.3 Regulation of Ig gene transcription

Unit II
5. Generation of antibody diversity and Antibody engineering
6. T-Cell receptor
   6.1 The T-cell receptor
   6.2 Organization of TCR gene loci
   6.3 Generation of TCR diversity
7. Major Histocompatibility Complex molecules (MHC)
   7.1 General organization & inheritance
   7.2 MHC molecules & genes
   7.3 Regulation of MHC Expression
8. The HLA complex I:
   8.1 Organization of HLA complex
   8.2 Structure of class I and II HLA molecules

Unit III
9. The HLA Complex II:
   9.1 Expression of HLA genes
   9.2 HLA polymorphism
10. Antigen processing and presentation
11. Generation and regulation of immune responses
   11.1 Cytokines and activation of T & B cells
   11.2 Clonal selection
   11.3 Complement system
   11.4 Regulation of immune responses
   11.5 Immunological tolerance
12. Transplantation immunology: general idea of
   12.1 Allograft
   12.2 Xenograft
   12.3 Syngraft
   12.4 Graft versus host and host versus graft rejections.
Unit IV
13. Immune disorders – I
   13.1 HLA associated diseases
   13.2 Immunodeficiencies: HIV
   13.3 Auto immunity & auto immune disorders (e.g., RA/SLE/MS)
14. Immune disorders – II
   14.1 Hypersensitive reactions
   14.2 Cytokine-related diseases
   14.3 Role of MHC in disease susceptibility
15. Immune system in human health
   15.1 Immune response to infectious diseases and malignancy
   15.2 Concept of immunotherapy
   15.3 Vaccines
16. Hybridoma Technology: Production and applications of monoclonal and polyclonal antibodies

Unit V
17. Basics of Host-Pathogen interaction, evolution of pathogenicity and regulation of virulence;
   Mechanism of drug resistance in pathogens: Viruses & Bacteria
18. Molecular pathology of following pathogens: HIV, Hepatitis virus Mycobacterium tuberculosis,
19. Molecular pathology of Plasmodium, Leishmania, & Trypanosoma
20. Development and application of molecular methods in diagnosis of infectious diseases and
    pathogen detection
   20.1 Immunoproteomics
   20.2 Immunoprecipitation, Immunoblotting and Immunofluorescence.
   20.3 Expression cloning
   20.4 PCR-based detection methods, etc.

Recommended Books
2. Immunology, 6th Ed Roitt, Mosby, 2002
3. Immunology, 5th Ed., Kuby, Freeman, 2002
7. Immunology, Janeway & Travers, Garland Publishing Inc, 1994
8. Essential Immunology, Roitt Blackwell 1994
9. Immunology, Roitt et al Mosley 1993
10. Immunology -A Short Course, Benjamin Wiley-Liss 2000
11. Text Book of Immunology, Barrett Mosley 1988
13. Introductory Microbiology, Heritage et al Cambridge Univ. 1996
14. Microbiology, Pel czar et al Tata 1993
15. Molecular Diagnosis of Infectious Diseases, Reischel Humana 1998
16. Fundamentals of Immunology, William Paul, Freeman