Human Genetic and Epigenetic Disorders: molecular mechanisms, diagnosis and therapy

Course Code: JAL 303
Credits: 3-1-0

Instructors: Prof. Tapas Kundu, Prof. Ravi Manjithaya, Dr. Kushagra Bansal,
Dr. Lavanya Sivashanmugam (Coordinator)

Unit 1: The human genome and disease genes (5 hrs)

Chromosomal distribution of disease genes in human genome, genetic variations among individual genome, SNPs and small scale length variations, deletions and duplication of DNA regions, positional cloning, Genome-Wide Association Studies (GWAS), Non-coding genetic variants in human disease

Unit 2: Molecular Basis of Human Disorders (5 hrs)

Numerical and structural chromosomal disorders, inherited disorders due to defective metabolic pathways, Single gene disorders, Complex genetic diseases, Inborn errors of metabolism, Multifactorial disorders and their study, Etiology - genetic and non-genetic determinants, Epigenetics and disease: Mechanisms (Imprinting/methylation; chromatin remodelling), mitochondrial abnormalities

Unit 3: Genetic factors in common diseases (5 hrs)

Congenital defects: Coronary heart disease; Late onset disease: diabetes, mental diseases, Defects in membrane Transport, Defects in structural proteins, collagen disorders, Locus Heterogeneity; Inter-allelic and intra-allelic heterogeneity; phenotypic heterogeneity, Genetics of triplet repeat disorders

Unit 4: Rare genetic disorders (5 hrs)

Mitochondrial diseases (mitochondrial myopathies, mitochondrial DNA depletion, MERRF syndrome, mitochondrial dysfunction in acquired conditions), neurological disorders (Cerebral palsy, Spinocerebellar ataxia, Huntington's disease), lysosomal storage disorders (Lipid storage disorders, Mucopolysaccharidoses), Actinopathy, Cardiomyopathy.

Unit 5: Genetic and epigenetic diagnosis of human disorders (4 hrs)

Cytogenetic, biochemical and molecular testing, DNA microarray, genome-wide DNA methylation analysis, Screening for mutation/ chromosomal anomaly - Adult/Prenatal/Newborn screening.

Unit 6: Advances in gene therapy (5 hrs)

CAR T cell therapy (or chimeric antigen receptor T cell therapy), RNA therapy, genome editing, Sickle cell disease gene therapy (Casgevy™, Lyfgenia™), retinal gene therapy, gene therapies for beta thalassemia.

Unit 7: Advances in epigenetic therapy (5 hrs)

Epigenetic anticancer therapeutics: DNA methyltransferase inhibitor, drugs regulating histone modification, epigenetic biomarker development.

Suggested reading:

- Genetics: From Genes to Genomes – Hartwell et al.
- Human Molecular Genetics, 3rd edition by Peter & Ian Sudbery.
- How the Human Genome Works by Edwin H. McConkey,
- Epigenetics at the epicenter of modern medicine, Feinberg, JAMA, 2008, 299:1345-1350.
- Crow, James F. "The Origins, Patterns and Implications of Human Spontaneous Mutation." Nature Reviews Genetics 1 (2000): 40-47.
- Human Genetics: One gene, twenty years, Nature, 2009, 460:165-169
- Puccio, Helene, and Michel Koenig. "Friedreich Ataxia: A Paradigm for Mitochondrial Diseases." Current Opinion in Genetics and Development 12 (2202): 272-277.
- Butler, Rachel, and Gillian P. Bates. "Histone Deacetylase Inhibitors as Therapeutics for Polyglutamine Disorders." Nature Reviews Neuroscience 7 (2006): 784-796.

Invited speakers: