GENETICS OF HUMAN DISEASES

Introduction to disease genetics

OUTLINE

- Genetics and genomics in medicine
- Perspectives

LEARNING OBJECTIVES

The student becomes familiar with the concepts of genetic and genomics in medicine and the field of clinical research, diagnosis and treatment of diseases based on their genetic basis and / or predisposition through a series of clinical cases. In addition, he/she acquires basic knowledge about the categories of genetic diseases (chromosomal abnormalities, monogenic disorders, and diseases with multifactorial inheritance).

The human genome and the chromosomal basis of heredity

OUTLINE

- The human genome and its chromosomes
- Cell division
- Gametogenesis and fertilization in humans
- The relationship between mitigation and reduction in medicine

LEARNING OBJECTIVES

The student understands the organization and structure of the human genome, and the chromosomal basis of heredity, and the importance of assessing the role of genetics in medicine, as well as the emerging principles of genomics and personalized medicine. He/she learns the basic principles of the transmission of genetic information and through an overview of the cell cycle, cell division and gametogenesis and fertilization, he/she understands the relationship between mitosis and meiosis in medicine to ensure the stability of the number of chromosomes - and therefore of the integrity of the genome - from one cell to its offspring and from one generation to the next.

The Human Genome: Gene Structure and Function

OUTLINE

- The information content of the human genome

- The central dogma: DNA → RNA → Protein
- The structure and organization of genes
- Fundamental principles of gene expression
- An example of a gene expression: The β-globin gene
- Gene regulation and changes in gene activity
- The diversity of gene regulation and its importance in medicine

LEARNING OBJECTIVES

The student understands the structure and function of human genes and chromosomes and how the information content of the genome determines the phenotype. He learns the central doctrine of Molecular Biology, the organization of genes and their structural features, and the importance of non-coding RNAs. He/she becomes aware of the fundamental principles of gene expression as well as its epigenetic and epigenetic aspects through DNA methylation, histone modification, and chromatin architecture. He/she understands the importance of regulated gene expression through a set of complex interactions and different levels of control, and the modern approaches that are followed and are critical in medical practice.

Tools for human molecular genetics

OUTLINE

- Isolation and analysis of DNA and RNA sequences
- Nucleic acid analysis methods
- The polymerase chain reaction
- Determination of DNA sequence
- Advanced technologies for fluorescence imaging
- Western blot analysis

LEARNING OBJECTIVES

The student familiarizes with the modern methods and tools of advanced technology used to isolate and sequence nucleic acids. He learns about the polymerase chain reaction (PCR) for the amplification of specific DNA (or RNA) regions through primers, the methods of determining this sequence and the computational methods of processing and analyzing sequences and the identification of polymorphisms and mutations.

Principles of clinical cytogenetics

OUTLINE

- Introduction to cytogenetics
- Chromosomal abnormalities

- Parent-of-origin effect
- Study of human chromosomes during meiosis
- Mendelian disorders with cytogenetic effects
- Cancer genetics

LEARNING OBJECTIVES

The student learns the basic principles of clinical cytogenetics, the study of chromosomes, their structure and their heredity, as applied in clinical medicine. He/she is able to recognize the types of chromosomal abnormalities (in structure or number, autosomal and / or sex), the parent-of-origin effect and Mendelian disorders with cytogenetic effects, as well as to explain the association of cancer with cytogenetics.

Clinical cytogenetics: Disorders of the autosomes and sex chromosomes

OUTLINE

- Disorders of autosomal chromosomes
- Sex chromosomes and their abnormalities
- Disorders in sex development and sex determination

LEARNING OBJECTIVES

The student learns some of the most common chromosomal and genomic disorders through a set of clinical cases and understands the clinical approach based on the general principles of clinical cytogenetics and genome analysis. He/she familiarizes with the wide range of phenotypes observed in clinical medicine including chromosomal and hypochromosomal mutations, and disorders characterized by mental disability and abnormal or ambiguous sexual development.

Patterns of single-gene inheritance

OUTLINE

- Overview and basic concepts
- Mendelian inheritance
- Factors affecting hereditary patterns in genealogical trees
- Genotype-phenotype correlation
- Autosomal patterns of Mendelian inheritance
- X-linked inheritance
- Pseudoautosomal inheritance
- Mosaicism

- Genomic imprinting in genealogical trees
- Disorders due to unstable repeat expansions
- Conditions that mimic the Mendelian pattern of inheritance of single-gene disorders
- Maternal inheritance of disorders due to mutations in the mitochondrial genome
- Family history in personalized medicine

LEARNING OBJECTIVES

The student learns in detail and through a series of examples the mechanisms and patterns of single-gene inheritance. Specifically, he/she learns about Mendelian inheritance, factors that affect the patterns of inheritance in genealogical trees, the genotype-phenotype correlation, the autosomal patterns of Mendelian inheritance, the X-linked inheritance, pseudoautosomal inheritance, mosaicism, genomic imprinting in genealogical trees, disorders due to unstable repeat expansion, conditions that mimic the Mendelian pattern of inheritance of single-gene disorders, the maternal inheritance of disorders caused by mutations in the mitochondrial genome, and the importance of family history in the context of personalized medicine.

Complex inheritance of common multifactorial disorders

OUTLINE

- Qualitative and quantitative traits
- Genetic and environmental contribution of single-gene disorders
- Examples of multifactorial traits for which genetic and environmental factors are known

LEARNING OBJECTIVES

The student is able to understand the difference in the inheritance of single-gene and multifactorial disorders. He/she learns the concepts of qualitative and quantitative traits of diseases and can identify the expected normal distribution in populations and the genetic and environmental factors that affect the multifactorial diseases inheritance.

Genetic variation in populations: mutations and polymorphism

OUTLINE

- Mutation
- Types of mutations and their effects
- Human genetic variation
- Hereditary variation and DNA polymorphism
- Inherited variation and polymorphism at the protein level

- Genotypes and phenotypes in populations
- Factors that alter Hardy-Weinberg equilibrium
- Population differences in the frequency of various genetic diseases

LEARNING OBJECTIVES

The nature of genetically determined differences between individuals is examined. The student understands the ways in which genetic variation is expressed, as differences in the organization of the genome, as nucleotide changes in the genome sequence, as change in the number of copies of large parts of the genome, as changes in their structure or quantity located in various tissues, or as any one of them in the context of clinical disease. He/she learns the concepts of mutation and their different types, single nucleotide polymorphisms and inherited variation. In addition, it learns about the distribution of alleles in populations and factors that affect the expected frequency of phenotypes in populations and about population differences in the frequency of specific genetic diseases.

Mapping and identifying human genes related to diseases

OUTLINE

- The genetic structure of human genome
- Mapping human gene based on linkage analysis
- Mapping multifactorial traits
- From gene mapping to gene identification

LEARNING OBJECTIVES

The student is able to understand the genetic structure of the human genome and to recognize the concepts of haplotypes, linkage analysis and genetic association. In addition, he/she learns the mapping of human genes based on genetic linkage analysis and understands the phenomenon of linkage disequilibrium in a population. He/she is familiar with the modern approaches of mapping multifactorial traits with genome wide association studies and the identification of genes and alleles associated with single-gene and complex disorders.

Hemoglobinopathy as standards of molecular disease

OUTLINE

- The effects of mutations on protein function
- The way mutations disrupt the formation of biologically normal proteins
- Hemoglobins
- Hemoglobinopathies

LEARNING OBJECTIVES

The effects of mutations on proteins are examined and the student is able, through the example of hemoglobin and hemoglobinopathies, to understand and explain the result of a mutation in the function of a protein but also the way in which the structure of biologically normal proteins is disturbed.

Molecular, Biochemical, and Cellular Basis of Genetic Disease

OUTLINE

- Diseases due to mutations in different classes of protein
- Enzymopathies
- Defects in receptors proteins
- Transport defects
- Disorders of structural protein
- Neurodegenerative disorders

LEARNING OBJECTIVES

The student is able to understand the effects of mutations in various classes of proteins. He/she has gained a detailed view and can cite examples of the mechanisms that lead to pathogenesis when mutations affect enzymes, protein receptors and transmembrane transporters. In addition, he/she learns the complexity and genetic basis of neurodegenerative disorders.

The treatment of genetic diseases

OUTLINE

- The treatment of genetic diseases - The current situation
- Specific issues related to the treatment of genetic diseases
- Therapeutic strategies
- Molecular treatment of the disease

LEARNING OBJECTIVES

The student becomes acquainted with modern approaches to the treatment of genetic diseases and the concept and methods of personalized medicine. He/she learns about the therapeutics strategies in single-gene diseases, the use of gene therapy and gene editing, and the development of new treatments with small molecules to restore the function of mutated proteins and prevent clinical manifestations that could cause premature death. He/she is able to scientifically approach specific issues arising from the treatment of genetic diseases.

Developmental genetics and birth defects

OUTLINE

- Developmental biology in medicine
- Introduction to developmental biology
- Genes and environment in development
- Basic principles of developmental biology
- Cellular and molecular mechanisms in development
- Interactions of developmental mechanisms in embryogenesis

LEARNING OBJECTIVES

The student becomes familiar with the principles and concepts of developmental biology, including the cellular and molecular mechanisms responsible for normal human development in utero. He/she learns, through an overview of clinical cases with genetic defects in embryological development, the importance of accuracy in the screening and evaluation by the clinical physician and the genetic approach that leads to prenatal diagnosis and appropriate management strategies.

Prenatal diagnosis

OUTLINE

- Indications for prenatal diagnosis with invasive testing
- Methods of prenatal diagnosis
- Laboratory studies
- Emerging technologies of prenatal diagnosis
- Prenatal prevention and management of genetic diseases
- The role of genetic counseling in prenatal diagnosis

LEARNING OBJECTIVES

The student learns about the methods of prenatal testing and diagnosis with invasive and non-invasive methods, and the main indications that lead to the need for prenatal screening. In particular, he/she learns about amniocentesis and chorionic villus sampling (CVS), and the preimplantation genetic diagnosis for chromosomal abnormalities, as well as the use of ultrasonography to identify anomalies. In addition, he/she understands the importance of investigating family history as well as national background and genetic counseling in prenatal diagnosis.

Cancer genetics and genomics

OUTLINE

- The genetic basis of cancer
- Oncogenes
- Tumor suppression genes
- Tumor evolution
- Application of genomics to individualize cancer therapy
- Cancer and environment

LEARNING OBJECTIVES

The student understands the genetic basis of cancer through genetic and genomic studies. He/she learns about oncogenes and tumor suppressor genes, the profile of mutations and gene expression in cancer and their correlation with tumor progression. He/she recognizes the challenges of medical genetics and therapeutics for cancer treatment due to its high mutability. He/she learns the importance of early diagnosis and early treatment for people with a hereditary predisposition to cancer, and for the population, through whole genome sequencing and of gene expression analysis. The student also learns the environmental factors that act as carcinogens and the variation in cancer risk between different populations and within the same population in different environments.

Personalized medical genetics

OUTLINE

- Family history as part of personalized genetic medicine
- Genetic testing in populations
- Genetic predisposition testing for diseases

LEARNING OBJECTIVES

The student learns about genetic screening in populations and the detection of abnormalities in high-risk newborns for the prevention of the disease as one of the most established and extremely successful forms of genetic screening. He/she gains learns the importance of examining asymptomatic individuals for risk or susceptibility to disease in them or their family members and the use of these results for health care improvement. He/she is able to evaluate the screening methods for testing patients' genetic susceptibility by whole genome sequencing and the genetic epidemiology methods that are used to evaluate the genotypes under study.

Pharmacogenetics and Pharmacogenomics

OUTLINE

- Use of information on the risks of improving medical care: Pharmacogenetics
- Pharmacogenomics
- The role of nationality and population clusters in personalized medicine

LEARNING OBJECTIVES

The student learns the basic concepts and applications of pharmacogenetics and pharmacogenomics and how the knowledge of individualized variation that affects drug therapy is used to improve therapeutic efficacy and reduce adverse effects. He/she is able to understand the genetic diversity between individuals and the effect on drug response due to the gene variation that affect drug metabolism, efficacy and toxicity.

Genetic counseling and risk assessment

OUTLINE

- The process of genetic counseling
- Determining the recurrence risks of a disease
- Application of molecular genetics in determining the recurrence risk of a disease
- Empirical recurrence risks

LEARNING OBJECTIVES

The student understands how modern genomic approaches expand the possibilities and the efficacy of risk assessment and genetic counseling for patients and families with hereditary diseases. He/she is able to recognize different approaches to recurrence risks determination in single-gene and multifactorial diseases, and familiarizes with the principles on which geneticists evaluate empirical data to take decisions on recurrence risks and risk management.

Ethical issues and medical genetics

OUTLINE

- Ethical dilemmas in medical genetics
- Eugenic and dysgenic effects of medical genetics
- Genetics in medicine

LEARNING OBJECTIVES

The student is introduced to the basic principles considered in any ethical issue in medicine, i.e. respect for individual autonomy, ensuring an individual's rights to control his medical care and medical information, free of coercion, beneficence, avoidance of maleficence, and ensuring that all individuals are treated equally and fairly. In addition, he/she is able to understand the ethical issues arising by the eugenic and dysgenic effects of therapeutic genetics by selection of specific genotypes. Finally, he/she is able to weigh and evaluate conflicting views and moral dilemmas that arise in clinical practice of medical genetics.

Laboratory Exercises

OUTLINE

- Stress System, Mediators and Homeostasis
- Infantile Systemic Hyalinosis
- Sex disorders: Genetic and Endocrine Components
- Child Abuse and Stress. The role of Epigenetics
- Cancer Genetics. A clinical case of lung cancer – Genetic Panels
- Mapping and identifying human genes related to diseases
- Genetic counseling and risk assessment
- Cancer workshop
- Forensics workshop
- Final Assignment

LEARNING OBJECTIVES

The student is informed through examples of selected clinical cases about the applied genetic and medical approach that is followed in human genetic diseases. Typical cases of genetic diseases are analyzed and explained in terms of their genetic profile, molecular and medical diagnosis, and clinical treatment, therapy and outcome. He/she learns about the stress system and the generalized syndrome of resistance in glucocorticoids, infantile systemic hyalinosis, genetic and endocrine components in sex disorders, the role of epigenetics in childhood abuse and the genetics of cancer. In addition, through interactive workshops, he/she understands the genetic panels in cancer as well as STR analysis in forensics. Finally, in his/her final assignment he/she has the opportunity to sum up and present the acquired knowledge in human genetic diseases.