UNIVERSITÀ
DEGLI STUDI DI MILANO-BICOCCA

COURSE SYLLABUS

Functional Genomics

2526-1-H4103D157

Aims

The course aims to provide and deepen the biological tools and fundamental genetic bases necessary for understanding human genetic diseases, within the framework of genomic medicine.

Contents

The cellular and molecular bases of human genetics will be explored in detail, and the organization of genes and the human genome, its modifications, and the DNA repair mechanisms implemented by cells will be thoroughly analyzed.
Significant emphasis will also be placed on the epigenome, its modifications, and the complex mechanisms regulating gene expression.
To complete the course, and for illustrative purposes, a series of diseases related to different branches of medicine—now increasingly managed by geneticists—will be discussed.
To support and enhance overall understanding, technologies for the analysis and modification of nucleic acids, next-generation sequencing (NGS), and the bioinformatic approaches required to interpret the results obtained using these methodologies will also be examined.

Detailed program

Organization of the Human Genome and Genome Projects
• From genetics to genomics: the Human Genome Project
• Organization and evolution of the human genome
o Protein-coding genes
o Non-coding RNA genes and regulatory elements

o Organization of gene families
o Importance of gene duplication
o Highly repetitive non-coding DNA in the human genome
• Distribution of genes within the human genome
• Origin of sequence variability
• DNA repair mechanisms
• Population genomics and the extent of human genetic variability
• Evolution of the concept of the gene
Technologies for the Study and Analysis of DNA
• Principles of DNA analysis technologies
• PCR and quantitative PCR
• Sanger sequencing
• Arrays
• Next-generation sequencing (NGS): second- and third-generation sequencing techniques (long-read sequencing)
• NGS data analysis
Genetic and Epigenetic Regulation of Gene Expression (RM) (8 hours)
• Promoters, enhancers, and silencers
• Transcription factors: binding and specificity
• Gene regulation during RNA maturation: splicing and editing
• Gene silencing mediated by microRNAs
• Chromatin modifications and epigenetic factors in gene regulation
o Writers, erasers, and readers
o DNA methylation
• Role of long non-coding RNAs in epigenetic regulation
• Genomic imprinting
• X chromosome inactivation
• Organization of the interphase nucleus
Omics and New Technologies in Biomedicine
• Examples of applications of NGS technologies
• DNA-based approaches: whole genome sequencing (WGS), exome sequencing, deep sequencing
• ChIP-Seq
• DNA methylation analysis
• Metagenomics
• RNA-based approaches: transcriptomics
• Introduction to multi-omics approaches
Genetic Variability and Its Consequences
• Pathogenic nucleotide substitutions and small insertions and deletions
• Copy number variation of short tandem repeat sequences
• Pathogenesis induced by long tandem repeat expansions and interspersed repetitive sequences
• Molecular bases of mitochondrial diseases
• Genotype–phenotype correlations and complexity of monogenic diseases (gain of function, loss of function, haploinsufficiency, dominant-negative effects)
Genetic Variability of the Immune System
• Concepts of innate and adaptive immunity
• Structure and function of antibodies and T-cell receptors
• Somatic recombination: molecular mechanisms
• Modifications following antigen encounter
Genetic Approaches to the Study of Multifactorial Diseases
• Definition of multifactorial diseases and assessment of the genetic component
• Parametric and non-parametric linkage studies
• Genome-wide association studies (GWAS)
• Examples of multifactorial diseases: celiac disease, inflammatory bowel diseases (IBDs), diabetes
Stem Cells and Differentiation
• Cellular differentiation
• Molecular mechanisms underlying embryonic development

• Stem cells and induced pluripotent stem cells (iPSCs)
• Model organisms: advantages and limitations
• Transgenic mice
• Examples of differentiation and development: nervous system, intestinal epithelium, connective tissues, muscle cells, hematopoietic system
Gene Therapy
• In vivo and ex vivo gene therapy
• Viral and non-viral vectors for gene therapy: advantages and disadvantages
• Gene therapy for ADA-SCID and sickle cell disease/thalassemia as success stories
• Gene therapy in cancer: the example of CAR-T therapy
• Gene therapy in genodermatoses
• Gene and cell therapy in degenerative diseases: approaches to the treatment of muscular dystrophies
• Gene therapy in the treatment of HIV
• CRISPR-Cas9 and applications in clinical trials
Cytogenomics
• Banding techniques and advanced methods for the study of cytogenetic abnormalities and the genome
• Fluorescence in situ hybridization (FISH) and its developments
• Array comparative genomic hybridization (array CGH)
• Optical Genome Mapping
Mechanisms Underlying Chromosomal Aberrations
• Chromosomal syndromes and genomic disorders
• Segmental duplications
• Microdeletion and microduplication syndromes
Prenatal Diagnosis: Non-Invasive and Invasive Tests
• Non-invasive prenatal testing (NIPT)
• Chorionic villus sampling
• Amniocentesis
• Mosaicism
UPD and Its Implications in Imprinting Disorders
Cancer Cytogenetics
Molecular Diagnostic Techniques in Medical Genetics
• Simulation of exome analysis and interpretation of genetic variants
• Precision medicine: genetics in support of clinical protocols
• Cancer predisposition, with a focus on acute lymphoblastic leukemia
• Medical genetics: genetic counseling and diagnostic testing
• Non-Mendelian inherited diseases: trinucleotide repeat expansions
Clinical Cases

Prerequisites

Strong foundations in general and molecular biology, as well as general genetics

Teaching form

6 CFU of lectures
1 CFU of classroom practical sessions

Textbook and teaching resource

Recommended textbooks:
Human and Medical Genetics by Neri and Genuardi, Edra, 5th edition
Genetics and Genomics in Medical Sciences by T. Strachan and A. Lucassen, Zanichelli, 2nd edition
Lecture presentations
Scientific articles

Semester

2° semester

Assessment method

The exam is designed to assess the knowledge and skills acquired across the different modules that make up the course and consists of a WRITTEN EXAM.
The exam covers all topics addressed during lectures and consists of a test with 28 multiple-choice questions and 2 short open-ended questions. For the quizzes, each correct answer is worth 1 point, an unanswered question 0 points, and an incorrect answer –0.2 points. For the short open-ended questions, each correct answer is worth 2 points.

Any oral examination will be held only at the student’s request or if clarification is deemed necessary by the instructors.

The final evaluation takes into account:
the knowledge demonstrated in answering the questions
the ability to express oneself clearly and using appropriate terminology
any active participation in classroom practical sessions

Office hours

By appointment

Sustainable Development Goals

GOOD HEALTH AND WELL-BEING | GENDER EQUALITY | REDUCED INEQUALITIES