UNIVERSITÀ
DEGLI STUDI DI MILANO-BICOCCA

SYLLABUS DEL CORSO

Genetica II

2122-2-E1301Q072-E1301Q076M

Aims

To provide the essential bases to the understanding of Genetics, from the point of view of basic notions, concepts and methodology1. Knowledge and understanding
to know the basic concepts of Genetics
2. Applying knowledge and understanding
to use the acquired knowledge in the courses of advanced Genetics
3. Making judgements
to apply the basic principles of Genetics in order to solve Genetics problems
5. Learning skills
to acquire the methodological and scientific skills required in the advanced courses
.

Contents

Part 1 (Prof. Silvia Nicolis): conceptual bases for the understanding of gene structure and function, and their relation with the laws and mechanisms of inheritance, gene evolution, and the factors that determine gene frequencies in populations.
Part 2 (Prof. Antonella Ronchi) methodological approaches for the studies of the different genome components. miRNAs: impact on phenotypes (examples). Transposons. Quantitative trait loci. DNA end RNA tumor viruses. Basic principles of cancer genetics. Genetic control of development in D. melanogaster. Genetics of the immune system.

Detailed program

PART1 Genes and DNA. DNA structure and replication, transcription, transduction.

Cell reproduction and chromosomes: mitosis, meiosis. Gametogenesis in diploid organisms.
Transmission of traits and inheritance from the Mendelian point of view. Alleles. Dominant and recessive inheritance from the formal point of view (to be later compared to the molecular point of view).
F1, F2, test-cross. Indipendent assortment of hereditary “factors”. Monohybrids, dihybrids, trihybrids. Chi-square test.
Extensions of Mendelian analysis. Gene interactions. Epistasis. Duplicated genes with similar functions.
Gene function: congenital errors in human metabolism. Complementation; complementation tests. Modifier genes. Penetrance.
Multiple alleles. Codominance. Blood groups, AB0 system.
Linkage, crossing-over and genetic maps. Parental and recombinant (as compared to independent segregation). Recombination frequency and map distance. Three-point test-cross. Gene order: determination by the three-point test-cross. Estimate of map distance from the phenotypic class frequencies in a three-point testcross. Haldane map function. Restriction fragment length polymorphisms, other polymorphic DNA markers and mapping of disease genes (briefly).
Genealogical trees and mendelian inheritance in man. Dominant, recessive, X-linked inheritance. Estimating genetic disease probability in the conceptus from genealogical tree analysis.
Linkage disequilibrium. Aplotypes in linkage disequilibrium and their origin.
Linkage of thalassemic mutations to their haplotype of origin. Polymorphic DNA markers and mapping of disease genes.
Molecular nature of the gene. DNA: replication and transcription. “Gene” from a molecular point of view. Exons and introns. Splicing. Alternative splicing: physiological regulation of splicing (in brief). Translation. Genetic code. mRNA translation, miRNAs, nonsense-mediated decay (in brief).
Mutation. Point mutations. Mutations and the genetic code: missense, nonsense, frameshift mutations. Mutations that cause slicing abnormalities; pathological splicing.
How to analyze a genomic DNA sequence. ORF, intron-exon junctions, evolutionary conserved sequences.
DNA sequences encoding a product (protein, or noncoding RNA), and regulatory sequences (recognized by transcription factors). Combinatory regulation of transcription by transcription factors. Evolution of regulatory elements (in brief).
Principles of gene regulation. Regulatory mutations. Transcriptional programs. Development and transcriptional programs. Transcription factors and reprogramming.
Molecular nature of the gene and molecular genetic pathology. Organization of genes on the chromosome: a modern view. Overlapping genes. Gene and locus, a molecular definition: coding + regulatory elements. Mutation of regulatory elements and pathology.
Molecular mechanisms of recessive and dominant inheritance. Dominance by haploinsufficiency; gain of function; negative dominance. Examples from human genetic pathology. Levels of gene activity and genetic disease.
Cytogenetics. Kariotype, chromosome banding, molecular probes and FISH.
Chromosomal mutations. Duplications, deletions, translocations. Examples. Lepore hemoglobin. Bar. Translocations which activate oncogenes: chronic myelogenous leukemia, Philadelphia chromosome and BCR/ABL fusion; Burkitt Lymphoma and myc translocations. Aneuploidies. Down syndrome; translocation Down syndrome. Functional study of genes in the Down syndrome critical region in mouse. Non-disjunction and aneuploidies. Imprinting. Position effect variegation. Synthenic regions in different species (and possible implications for genome evolution-in brief). Consequences of chromosome rearrangements on molecular gene structure and function. Rearrangements and gene expression: the human globin genes.
X chromosome inactivation. Dosage compensation. X chromosome counting, random choice for inactivation, inactivation. X-inactivation center (XIC). XIST. Translocations and X-inactivation. X-autosome translocations. Mechanisms of X-linked disease (dystrophy; fragile X; hemophilia).
Population genetics. Mendelian populations. Genetic structure of populations: genotypic and allelic frequencies. Hardy-Weinberg law and equilibrium. Test of HW equilibrium and random breeding. Factors that change gene frequencies: Natural selection (against homozygous recessives, against dominant, against heterozygotes, in favour of heterozygotes). Fitness. Evolution by natural selection. Mutation. Migration. Genetic drift. Inbreeding.
PART 2
Basic techniques for the study of genetic material: cloning and sequencing of genomes. DNA and cDNA libraries. Functional analysis (overexpression, downregulation and knock out) of genes. How to study regulatory sequences. Functional analysis of microRNAs. Phenotypic consequences of miRNA deregulation (examples).
Transposable elements: genetic evidences at the basis of their discovery. Examples of different classes of

transposons. Consequences of their transposition for the host organism. Their evolutionary role.
Quantitative trait loci: genetic basis and examples.
DNA and RNA tumor viruses
Cancer cell genetics. oncogenes, oncosuppressor genes, genes controlling genome stability.
Developmental genetics. Basic concepts. The model of D. melanogaster.
Molecular genetics of the immune system

Prerequisites

A basic understanding of cell biology and biochemistry; basic knowledge of zoology and botany is also useful.

Teaching form

class lessons

Textbook and teaching resource

Semester

I Modulo: first semester

II Modulo : II semester

Assessment method

Written exam. The exam consists of two parts (in two successive days). The first part consists of five problems to solve, on different and complementary aspects of Genetics (such as genetic maps; genealogical trees; the genetic code; epistasis and gene interactions; population genetics), for which specific examples have been given in class. The second part consists of guided open questions (a general theme, with suggested subthemes) relative to different aspects of Genetics. Students have the possibility to ask for an oral discussion of their written exams.
The oral exam consists of three questions. The first topic of discussion will be chosen by the Student.

Office hours

By appointment,
please write to silvia.nicolis@unimib.it or antonella.ronchi@unimib.it