COURSE DATA

Data Subject	
Code	43465
Name	Genetic pathology
Cycle	Master's degree
ECTS Credits	3.0
Academic year	2022 - 2023

Study (s)

Degree	Center	Acad. year	Period
2210 - M.D. in Research in Molecular, Cellular and Genetics Biology	Faculty of Biological Sciences	1	First term

Subject-matter

Degree	Subject-matter	Character
2210 - M.D. in Research in Molecular, Cellular and Genetics Biology	10 - Genetic pathology	Optional

Coordination

Name	Department
GARCIA PEREZ, MIGUEL ANGEL	194 - Genetics

SUMMARY

Increased awareness of the role of genetics in the etiology of the disease and its impact on individuals, families and society, has led to the Molecular Genetics at the head of biomedical research. Indeed, in recent years there have been major advances in the understanding of molecular and patho-physiological of many hereditary diseases, clearly genetic diseases, but also in the study of the genetic basis of susceptibility to common diseases such as osteoporosis, Alzheimer's disease, diabetes, cancer or heart disease, or multifactorial complex diseases called because they meet both genetic and environmental factors.

The main objective of this elective course in the Master of Research in Molecular and Cellular Biology and Genetics is to provide the basic knowledge necessary for understanding the genetic basis of both monogenic diseases and complex diseases as well as know current technology and methodology for genetic and molecular characterization of these genetically based diseases.

PREVIOUS KNOWLEDGE

Relationship to other subjects of the same degree

There are no specified enrollment restrictions with other subjects of the curriculum.

Other requirements

The subject "Genetic Pathology" is taught in the Master in Research in Molecular and Cell Biology, and Genetics as an elective. Students who enrol in it should have general knowledge in Molecular Biology and Molecular and Human Genetics.

OUTCOMES

2210 - M.D. in Research in Molecular, Cellular and Genetics Biology

- Students should apply acquired knowledge to solve problems in unfamiliar contexts within their field of study, including multidisciplinary scenarios.
- Students should be able to integrate knowledge and address the complexity of making informed judgments based on incomplete or limited information, including reflections on the social and ethical responsibilities associated with the application of their knowledge and judgments.
- Students should communicate conclusions and underlying knowledge clearly and unambiguously to both specialized and non-specialized audiences.
- Students should demonstrate self-directed learning skills for continued academic growth.
- Be able to access the information required (databases, scientific articles, etc.) and to interpret and use it sensibly.
- Students should possess and understand foundational knowledge that enables original thinking and research in the field.
- Be able to access to information tools in other areas of knowledge and use them properly.
- To be able to assess the need to complete the scientific, historical, language, informatics, literature, ethics, social and human background in general, attending conferences, courses or doing complementary activities, self-assessing the contribution of these activities towards a comprehensive development.

LEARNING OUTCOMES

Knowing the different types of mutations, such as chromosomal and point mutations, and other, causing human genetic diseases.

Differentiate between the concepts of monogenic Mendelian diseases and complex diseases. Know the pathophysiology of different examples of each of them.

Knowing the methodological differences that allow the study of complex diseases.

Know and identify genetic diseases caused by mutations in mitochondrial DNA, by mismatches in epigenetic regulation, due to expansion of triplets and by mutations altering the cell cycle thus being related to cancer.

Know and identify methodological approach is that of choice for molecular and genetic characterization of a particular genetic disease.

Knowing when applied genetic diagnosis and what strategies can be followed according to the available knowledge of the disease.

Knowing when it is indicated genetic counseling and how to calculate the risk of recurrence of an inherited disease in a family.

Know the different screening programs and the characteristics required of the disease and the test employed.

Know the main experimental therapeutic strategies for the treatment of distinct genetic diseases.

DESCRIPTION OF CONTENTS

1. Initial theme: The human genome. Chromosomes. Mutation and polymorphism.

The human nuclear genome. Results derived from the genome project. HapMap and 1000 genomes projects. Mutation and polymorphism. General classification and types of mutations. Distinctive features of the diseases caused by altering the mitochondrial DNA.

2. Block 1: Chromosomopathies.

In this block we study the karyotype and the main techniques for its realization as the traditional banding, chromosome painting or novel CGH-Array (comparative genomic hybridization-Array). The goal is to understand the different techniques currently available and their application for diagnostic in the clinical practice. This will enable us to know how to select the appropriate technique for the diagnosis of a specific patient and obtain a rapid, accurate and economical diagnostic. We study diverse numerical and structural chromosomal pathologies analyzing the causes that trigger them. Euploidy and aneuploidy. Down syndrome, Turner syndrome, Klinefelter syndrome. Uniparental disomy. Structural abnormalities. Translocations. Microdeletion/microduplications syndromes.

3. Block 2: Monogenic Pathologies.

-Patterns of inheritance and models of disease inheritance: Genetic heterogeneity: Retinosis Pigmentaria and Charcot-Marie-Tooth neuropathy. Allelic diseases: Duchenne/ Becker Muscular Dystrophy. Founder mutations: Cystathioninuria and founder mutations in Gypsy population. Autosomal dominant inheritance: Marfan syndrome, Neurofibromatosis and Achondroplasia. Autosomal recessive inheritance: Cystic Fibrosis, Tay-Sachs disease and Spinal Muscular Atrophy. X-linked inheritance: Hemophilia and Rett Syndrome. Y-linked inheritance: Hypertrichosis Pinnae Auris

- Epigenetic diseases (Beckwith-Wiedemann syndrome) and epigenomic (Rett syndrome or ICF syndrome (Immunodeficiency/centromeric instability/facial anomalies).
-Pathologies by alteration of mitochondrial DNA (Leber's hereditary optic neuropathy and Pearson syndrome).
- Pathologies caused by microsatellite expansions: CUG trinucleotide expansions (spinocerebellar ataxia type 8 and myotonic dystrophy type 1) CAG (Huntington's disease and spinocerebellar ataxia type 3) CGG (fragile X syndrome) and GAA (Friedreich ataxia). Pathologies caused by expansions of tetranucleotides (myotonic dystrophy type 2) and hexanucleotides (amyotrophic lateral sclerosis and frontotemporal dementia).
-Identification of genes responsible for monogenic diseases: Polymorphism and their types. Gene mapping and genetic linkage. Strategies for the identification of genes. Genetic analysis methods. New approaches based on massive sequencing. Practical cases of discovering of new genes involved in hereditary disorders.
-Phenotypic effects of mutations: Punctual mutation: missense, premature stop, (Nonsense Mediated Decay, NMD), insertion/deletion/indel. Non-exonic mutation. Deleterious, lethal and beneficial mutations. Mutation with gain or loss of function. Dominant negative mutation. Novel mutations, how prove that they are the cause of the disease?

4. Block 3: multifactorial diseases.

In this block, different methodological approaches for identify susceptibility genes in complex disease such as twins studies, parametric and nonparametric linkage studies, and association studies with and without prior hypothesis, are analysed. Linkage disequilibrium and haplotypes: the HapMap project. Common disease common variant hypothesis. Where to look for the missing heritability? Rare variants and complex disease. Epigenetics and complex disease. Postmenopausal osteoporosis as an example of multifactorial disease. Searching for genes involved in the response to drugs: pharmacogenetics and pharmacogenomics.

5. Block 4: Cancer as a genetic disease.

This block examines the relationship between the loss of control of cell division and cancer. This theme studied examples of diseases associated with mutations in proto-oncogenes and activation mechanisms in tumour suppressor genes and genes involved in the detection, signalling and repair of DNA damage. Examples: Ataxia Telangiectasia, Xeroderma pigmetosa, retinoblastoma, and Li-Fraumeni syndrome.

6. Block 5: Clinical Genetics.

This block is dedicated to the analysis of the possibilities of intervention in the treatment of different genetic pathologies, with special emphasis on hereditary diseases. It is also dedicated to the study of Pharmacogenetics and Pharmacogenomics. Examples of molecular treatments, as well as based on the Pharmacogenetics, of certain genetic pathologies, will be proposed.

WORKLOAD

ACTIVITY	Hours	% To be attended
Theory classes	21,00	100
Tutorials	7,00	100
Other activities	2,00	100
Preparation of evaluation activities	30,00	0
Preparing lectures	15,00	0
TOTAL	**75,00**	

TEACHING METHODOLOGY

The course is structured in three weekly sessions of one hour. In each session, the teacher will present the contents of the agenda items for about 50-55 minutes and the rest of the time will be dedicated to questions and discussion at the classroom. The concepts studied in the lectures will serve as a basis for the reading and understanding of scientific papers by students.

The teacher will provide a series of articles that represent all the pathologies studied, with the objective of reinforcing what has been learned at the classroom in terms of the basic principles of inheritance, diagnosis, technology used and genetic counseling and for the student to become familiar with this type of studies. Some of these articles will be discussed at the classroom in detail. The teacher may propose the preparation of voluntary reviews of the articles, discussed at the classroom or not, and their assessment will be taken into account for the student's portfolio.

EVALUATION

The evaluation of students' learning will be made through the assessment of the following sections:

1) An exam in a single call to be made in the classroom. This test will be worth 100% of the grade and will be done after the end of classes, in the month of January.

NOTE: at the beginning of the course students will be offered the possibility of taking two exams. In case of accepting, the first exam (50% of the grade and of an eliminatory nature) would evaluate the contents of the first 3 blocks of the subject and would be carried out in the second half of November. The second exam would evaluate the rest of the subject content and would be held in January.

2) In addition, the student will have a portfolio where it can accumulate points associated with the assessment that the teacher makes about his interest in the subject. Participation in class, attendance at personal tutorials, delivery of voluntary summaries of articles proposed or discussed in class by the teacher, and/or any other type of activity carried out by the student in relation to the subject will be considered. It can get up to 10% in the final grade of the subject.

To pass the course it will be necessary to get a score of at least 5 points out of a total of 10 on the exam. The final grade of the subject will be the sum of the obtained in the exam and the portfolio. The portfolio will only add if the student passes the exam (at least 5 points out of 10).

REFERENCES

Basic

- Nussbaum RL, McInnes RR and Willard HF (2004). Thompson and Thompson Genetics in Medicine. 6th edition. Sauders.
-Solari AJ (2004). Genética Humana. Fundamentos y aplicaciones en Medicina. Editorial Médica Panamericana.
-Strachan T and Read AW (2004). Human Molecular Genetics 3rd edition. Garland Publishing Publishers Ltd.
-Allis CD, Jenuwein TH, Reinberg D, and Caparros ML. Epigenetics. Cold Spring Harbor Laboratory Press, 2007.
-Epstein RJ (2002). Human Molecular Biology: An Introduction to the Molecular Basis of Health and Disease. Cambridge University Press.
-Uhlmann WR, Schuette JL, Yashar B (2009). A Guide to Genetic Counselling. 2009 (2nd edition).
-Haines JL, and Pericak-Vance MA (2006). Genetic Analysis of Complex Disease, 2006.
-Mckusick VA (1998). Mendelian inheritance in man. Catalogue of human genes. 1998. Johns Hopkins Univ.Press. La versión electrónica OMIM (Online Mendelian Inheritance In Man) es accesible en la dirección de internet: http://www.ncbi.nlm.nih.gov/entrez/Omim (revisada diariamente).
-Ott J. (1999). Analysis of human genetic linkage (3ª ed). Johns Hopkins Univ. Press.
-R. J. M. Gardner, Grant R.(2004) Sutherland. Chromosome Abnormalities and Genetic Counseling.
-Martha B. Keagle,Steven L. Gersen (2005). The Principles of Clinical Cytogenetics.