Course unit name: MOLECULAR CYTOGENICS IN ONCOLOGY

1.- General information

Code	303005	Plan		ECTS	
Type	Elective	Course	2021/2022	Periodicity	1st Semester
Department	Cancer Research Center				
Virtual Platform	Platform:	CICLOUD			
	URL de Acces:	http://cicloud.dep.usal.es/index.php/s/Gp0vghR305Y6glo/authenticate			

Faculty

Professor Coordinator	Dr. Jesús M. Hernández Rivas		
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Research area	Haematology		
Center	Cancer Research Center		
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Professor	Dra. Paola S. Dal Cin.		
Department	Harvard Medical School		
Research area	Pathology		
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Professor	Dra. M Rocío Benito Sánchez Dr. Juan Luis García Hernández Dra. Norma Gutierrez Dr. Ignacio García Tuñón Dra. Ana E Rodriguez Vicente Dra. María Hernández Sánchez Dra. Teresa González Dra. Inmaculada Serramito Gómez Dra. María Abaigar Alvarado

<table>
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2.- The course in the context of the Master´s Program

Treaning Module
Second block of five in which the academic year is divided.

General aim of the subject
To teach the role played by genes in both the onset and development of cancer.

Professional specialization
Train professional experts in cancer genetics. Aimed at graduates in Health Sciences and Biomedical Sciences (Biology, Biotechnology, Pharmacy, Biochemistry, Medicine, Veterinary, Genetics).

3.- Previous recommendations

The student must attend the theoretical sessions having previously read and understood both the recommended bibliography, and the presentations that will be explained later. The first session will be focoused on the sessions organization. Doubts and students comments will be discussed during this opening session. In the following sessions, the programme described below will be developed.

4.- Aims of the subject

To understand: 1. Genes and genetic alterations involved in the cancer development. 2. Epigenetic mechanisms involved in cancer development. 3. RNA mutations in tumor cells involved in cancer initiation, development and dissemination. 4. Genetic alterations study models (genomic editing, next generation sequencing and *in vivo* models).

To Know: 1. Methodologies frequently used in molecular cytogenetics: conventional cytogenetics, FISH, multicolored FISH, DNA arrays, expression arrays, next generation

sequencing: NGS (genome, exome, transcriptome directed sequencing). 2. Cytogenetic alterations involved in cancer: numerical (gains and losses), structural alterations (translocation, inversion). 3. Genes undergoing methylation or acetylation in different types of cancer. 4. That genome and transcriptome analysis identifies cellular processes responsible for cancer development and metastases. 5. The role of molecular alterations in cancer diagnosis. 6. Llimitations of these methodologies, identifiying which of them are used at a diagnostic level and which are in a experimental phase. 7. The role of cancer of genome and transcriptome alterations in patients prognosis. 8. Genomic editing (CRISPR / Cas9) in the study and treatment of genetic alterations. 9. The main in vivo models in the study of molecular alterations. 10 Bioethical aspects.

5.- Contents

Program:

Theoretical classes:

Block 1. Methodology

Unit 1. Introduction to molecular cytogenetics in oncohematology. History, main methodologies. Conventional techniques in molecular cytogenetics: chromosomal study and fluorescence "in situ" hybridization (FISH). Multicolored FISH and comparative genomic hybridization.
Unit 2. Methodologies of genome analysis: microarrays and massive sequencing NGS.
Unit 3. Introduction to Sequencing. Classic sequencing methods. Next Generation Sequencing (DNA and RNA-seq)
Unit 4. The cytogenetic study in cancer diagnosis and prognosis. Main applications
Unit 5. NGS applications in hematology and Oncology.

Block 2. Clinical Aspects

Unit 6. Cytogenetic and molecular analysis in the study of acute leukemias
Unit 7. Cytogenetic and molecular analysis in the study of chronic hemopathies
Unit 8. Cytogenetic and molecular analysis of multiple myeloma.
Unit 9. Molecular cytogenetics of solid tumors. Soft tissue tumors.
Molecular alterations of sarcomas: classification. Ewing's tumor
Unit 10. Chromosomal study of solid tumors: problems. Molecular analysis of epithelial tumors.
Unit 11. Carcinomas: genomic studies.
Unit 12. Molecular analysis of other solid tumors: neuroblastoma, central nervous system tumors.
Unit 13. Pharmacogenetics and Pharmacogenomics in cancer. From genomic research to personalized therapy. Precision medicine. Pharmacogenes

Block 3. Genome editing

Unit 14. Animal models in the molecular study of cancer. Mouse models in the study of sarcomas.
Topic 15: Introduction to genome editing. Genome editing models: CRISPR. Generation of in vitro and in vivo models by CRISPR.
Topic 16: CRISPR applications in Oncology and hematology. Hematopoietic stem cell edition.

Block 4. Genetics, cancer and bioethics

Unit 17. Tumor heterogeneity and clonal evolution.
Unit 18. Ethical Implications of Personal Data Usage. Data protection regulation: research and clinical trials.

Teaching Practices:

1. Tumor cytogenetics: culture, collection and cell preparations. Staining, visualization and observation under the microscope.
2. Preparation and hybridization of specific fluorescent probes. Results analysis.
3. NGS sequencing. Data analysis.
4. Genome editing by CRISPR / Cas9.

Seminars:
Each group of students (2-3) will elaborate an oral presentation about one gene involved in cancer. For the seminar preparation, students should be documented with relevant scientific articles published recently. They can also make use of the documentation provided and discussed in the previous sessions. Presentations will be made and discussed with the participation of all students enrolled in the course.

6.- Skills to be acquired

Basic skills

Acquire an exhaustive view of the classic and modern cytogenetic techniques applied to the diagnosis, prognosis and study of tumor molecular alterations

Specific skills

-Recognize the tools for genomic and transcriptomic analysis of cancer.

- To Know how a cytogenetic study, a study of FISH, biochips, NGS and a basic bioinformatic analysis of samples of patients with leukemia or lymphomas, are done.

- To interpret a FISH study and an analysis of NGS data including, filtering, interpretation and classification of variants.

- To Know how a genome editing study by CRISPR is carried out in a leukemia model. To understant the implications of genome editing both as a study tool and as a therapeutic tool.

Transversal skills

Team work. Results presentation. Discussion in small groups.

7.- Teaching methodology

The student must attend the assesable theoretical sessions having previously read and understood both the recommended bibliography, and the presentations that will be explained later. The first session will be focoused on the sessions organization. Doubts and students comments will be discussed during this opening session. In the following sessions, the programme described in the corresponding section will be developed.

Organization of the students in working groups that will consist of 2-3 students per group and that should prepare a class of those sessions included in the agenda. The selected classes will be adapted to the characteristics of the students to facilitate their involvement in the study.

The student must attend the seminars (6 hours) in which each group will present a published research paper on any of the topics discussed in the course and a critical evaluable dialogue will be established.

Two clinical cases will be showed to the students. Students should resolve these cases by using the contents showed in the sessions. They can make use of the bibliographic sources available, especially the internet addresses provided in the theretical sessions

8.- Estimated learning time

		Hours tutored by the teacher		Individual work (hours)	TOTAL HOURS
		Attendance required (hours)	Distance learning (hours)		
Lectures		10			10
Practices	- Clasroom				
	- Laboratory		8		8
	- Computer room				
	- De campo		6		6
	- De visualización (visu)				
Seminars					
Work presentations and debates		10	10		20
Tutorials		2			2
Online activities			5		5
Work preparation			10		10
Other activities			5		5
Exams - evaluation		1	8		9
TOTAL		**23**	**38**	**14**	**75**

9.- Materials

Books

Cancer Cytogenetics: Chromosomal and Molecular Genetic Aberrations of Tumor Cells, Fourth Edition. Editor(s): Sverre Heim and Felix Mitelman. 26 June 2015. Wiley Blackwell

Print ISBN:9781118795538 |Online ISBN:9781118795569 |DOI:10.1002/9781118795569.

Other bibliographical, electronic references or any other type of resource

1. Atlas of Genetics and Cytogenetics in Oncology and Haematology. http://atlasgeneticsoncology.org/
2. GeneCards®: The Human Gene Database. https://www.genecards.org/
3. PharmGKB. https://www.pharmgkb.org/
4. Wellcome Sanger Institute. https://www.sanger.ac.uk/

10.- Assessment

Assessments on the performance of the student

Class attendance is mandatory to be evaluated.

Participation in theoretical sessions and debates (50% of the final grade).
Evaluation of the course in writing (50% of the final grade)

Recommendations