

**Course unit name: MOLECULAR BASES OF TUMORAL VARIABILITY: MODIFIER GENES OF THE SUSCEPTIBILITY AND EVOLUTION OF CANCER**

**1.- General information**

Code	303012	Plan		ECTS	3
Type	Elective	Course	2021/2022	Periodicity	2 <sup>nd</sup> Semester
Department	Cancer Research Center				
Virtual Platform	Platform:	CICLOUD			
	URL de Acces:	<a href="http://cicloud.dep.usal.es/index.php/s/Gp0vghR305Y6glo/authenticate">http://cicloud.dep.usal.es/index.php/s/Gp0vghR305Y6glo/authenticate</a>			

**Faculty**

Professor Coordinator	Dr. Jesús Pérez Losada				
Research area	Genetic determinants of the cancer susceptibility, evolution, and treatment response				
Center	Cancer Research Center				
Office	Laboratory 7				
URL Web	<a href="https://www.cicancer.org/grupo?id=60">https://www.cicancer.org/grupo?id=60</a>				
E-mail	<a href="mailto:jperezlosada@usal.es">jperezlosada@usal.es</a>	Phone	+34 923294807		

Professor	Dra. M <sup>a</sup> Purificación Galindo Villardón				
Center	Medicine Faculty				
Office	Statistics Department.				
URL Web	<a href="https://diarium.usal.es/pgalindo/">https://diarium.usal.es/pgalindo/</a>				
E-mail	<a href="mailto:pgalindo@usal.es">pgalindo@usal.es</a>	Phone	+34 923291921		

Professor	Dr. Manuel A. Sánchez Martín		
Department	Medicine		
Area	Medicine		
Center	Faculty of Medicine, Medicine Department.		
URL Web	<a href="https://nucleus.usal.es/es/transgenesis/contacto">https://nucleus.usal.es/es/transgenesis/contacto</a>		
Office	Lab. Transgenic, Basement -3, CIC.		
Tutorials	16.00-18.00		
URL Web	<a href="http://www.cicancer.org/uploads/master/Optativas/1Semestre/modelos_cancer_ratones.pdf">http://www.cicancer.org/uploads/master/Optativas/1Semestre/modelos_cancer_ratones.pdf</a>		
E-mail	<a href="mailto:adolsan@usal.es">adolsan@usal.es</a>	Phone	+34 923294500-3015

Professor	Dr. Javier Cañueto Álvarez		
Department	Medicine		
Center	University Hospital of Salamanca		
URL Web	<a href="https://fhgst.es/especialidad/dermatologia/">https://fhgst.es/especialidad/dermatologia/</a>		
E-mail	<a href="mailto:canueto@yahoo.es">canueto@yahoo.es</a>	Phone	+34 923294807

Professor	Dr. Isidro Sánchez-García		
Research area	Experimental and Translational Oncology Laboratory: Stem Cells, Cancer Stem Cells, and Cancer		
Center	Cancer Research Center		
Office	Laboratory 13		
Tutorials	Appointment by email		
URL Web	<a href="https://www.cicancer.org/grupo?id=53">https://www.cicancer.org/grupo?id=53</a>		
E-mail	<a href="mailto:isg@usal.es">isg@usal.es</a>	Phone	+34 923294813

Professor	Dra. M <sup>a</sup> del Carmen Patino Alonso		
Center	Medicine Faculty		
Office	Statistics Department.		
URL Web	<a href="https://www.usal.es/departamento-de-estadistica">https://www.usal.es/departamento-de-estadistica</a>		
E-mail	<a href="mailto:carpatino@usal.es">carpatino@usal.es</a>	Phone	+34 923291921

Professor	Dr. Carlos Prieto		
Center	Nucleus.Bioinformatics Unit. University of Salamanca		
Office	Bioinformatics Unit		
URL Web	<a href="http://bioinfo.usal.es/">http://bioinfo.usal.es/</a>		
E-mail	<a href="mailto:Bioinformatica@usal.es">Bioinformatica@usal.es</a>	Phone	+34 923291921

Professor	Dr. Marina Mendiburu-Eliçabe		
Center	Cancer Research Center		
Office	Laboratory 7		
E-mail	<a href="mailto:marinamendiburu@usal.es">marinamendiburu@usal.es</a>	Phone	+34 923294807

## 2.- The course in the context of the Master's Program

Training Module	The five block (out of five) of master program organization.
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## 3.- Previous recommendations

No prior requirements.

## 4.- Aims of the subject

-To understand cancer as a systemic and complex genesis disease, which develops in the context of a complex organism. Cancer, as a complex trait, there are multiple intermediate phenotypes or subphenotypes at different levels (molecular, cellular, tissue, and systemic) that participate in their pathogenesis and pathophysiology.

-To comprehend the molecular and physiological crosstalks between the tumor and the organism in which it is generated. Cancer destabilizes the physiology of the organism producing the disease, and, simultaneously, the evolution of cancer is greatly influenced and sometimes determined by the organism's physiology. These facts contribute to the generation of clinical variability and the evolution of disease among patients.

-To recognize the concept of interaction between different compartments of the organism (physiological and molecular ones) and its role in the variability of tumor susceptibility and evolution.

-To understand the relationship between different physiological states (e.g., age and menopause) and pathophysiological (e.g., obesity and pro-inflammatory states.) and different tumor evolution among patients.

-To realize the concept of Systems Biology and the main Biostatistics strategies that allow to integrate variables of different levels, including DNA, protein, other molecules, cells, tissues, systemic factors, and explain a complex phenotype.

-To understand the concept of polygenic control and intergenic interaction in tumor susceptibility and evolution, together with the concept of Quantitative Trait Loci (QTL) and expression-QTL (eQTL) and its role in the different cancer susceptibility and evolution. To understand the concept of cancer-modifying genes and the role they have in susceptibility and tumor evolution.

To comprehend the role of genetic variants of higher impact genes and the idea of low-penetrance and low expressive genes (polygenes) and their role in tumor susceptibility and evolution.

## 5.- Contents

### Theoretical classes

- Lesson 1. Cancer as a complex trait disease (I): Cancer is a systemic disease in the context of the physiology and pathology of the organism. Systems Biology and cancer. Interaction between the environment and the genetic background. Polygenic influence of susceptibility and tumor evolution. Quantitative Trait Loci (QTL). Modifier genes: allelic forms of higher-effect, low-penetrating genes. Intrinsic or autonomous-cellular and extrinsic or non-self-contained-cellular modifier genes. Duration: 1 hour.

- Lesson 2. Cancer as a complex trait disease (II). Cancer as a result of the interaction between the genome and the environment: Strategies for identifying genes that modify tumor evolution. Cancer as an evolutionary and adaptive process under selection pressure: Intrinsic modifier genes of tumor evolution. Allele-specific mutations. Intrinsic modifier genes, according to the intracellular functional compartment. Duration: 1 hour.

- Lesson 3. Mouse strains for the generation of models of high but simplified genetic variability in the mouse. Genetic background. Intercross and backcross concepts. Studies in syngeneic mice. Genetic standardization. Collaborative cross. Duration: 2 hours.

- Lesson 4. Main biostatistics strategies to integrate variables of different levels and explain complex traits. Duration: 4 hours.

- Lesson 5. Involvement of extrinsic compartments to the tumor cell in the growth and spread of the tumor. Duration: 1 hour.

- Lesson 6. Stem cell and origin and tumor variability. Role of reprogramming at the source of cancer. Duration: 1 hour.

- Lesson 7. Strategy for identifying genetic and molecular determinants of tumor evolution at different levels, including molecular, cellular, tissue, and systemic ones. Identification of part of the missing heritability. Duration: 1 hour.

- Lesson 8. Strategies to identify intrinsic and extrinsic genetic and molecular determinants of response to chemotherapy. Duration: 1 hour.

- Lesson 9. Influence of physiological states on the susceptibility and tumor evolution: Identification of genetic and molecular determinants of cancer and aging. Duration: 1 hour.

- Lesson 10. Integration of different semiological, histopathological, and molecular levels to define cardiotoxicity by chemotherapy. Duration: 1 hour.

•Lesson 11. Integration of different semiological, histopathological, and molecular levels to define the prognosis of squamous skin cancer in patients. Duration: 1 hour.

#### **Practices**

Practice 1. To design and organize a backcross database. To evaluate the distribution of genotypes and tumor pathophenotypes in a backcross cohort that develops breast cancer.

Practice 2: To analyze the distribution of different phenotypes in a backcross cohort of mice genotyped by the Illumina platform. Identification of QTLs.

#### **Seminars**

The articles for discussion and presentation by the students will be chosen from the classic works of the field, which best illustrate the course's concepts.

#### **Tutorial meetings**

The course tutor will be available to students in the CIC, Lab 7, preferably by email appointment

## **6.- Skills to be acquired**

#### **Specific skills**

-To design and organize a model of genetic and phenotypic variability with a mouse backcross. The purpose is to analyze tumor evolutionary and pathophenotypes and subphenotypes of tumor variability between mice. Identification of QTLs

-To interpret studies of allele-specific mutations in the context of tumor variability for the analysis of intrinsic modifier genes.

-To interpret the manuscript where genetic and molecular determinants of tumor variability are studied.

## **7.- Teaching methodology**

-The classes will be taught totally or partially in English.

-The student must attend the evaluable theoretical classes of the course (13 hours), having read and understood the recommended bibliography previously.

-The student must attend the seminars (12 hours) in which each student will present a published research work related to the course. An evaluable critical dialogue will be established.

To assist in the evaluable practices (4 hours, organized in 2 days), evaluate a backcross, and identify QTL. The practice will take place in a computer classroom.

## 8.- Estimated learning time

		Hours tutored by the teacher		Individual work (hours)	TOTAL HOURS
		Attendance required (hours)	Distance learning (hours)		
Lectures		13		20	33
Practices	- In classroom				
	- In laboratory			4	
	- In computer classroom				
	- Countryside				
	- Visualization classroom				
Seminars		12		12	24
Work presentations and debates					
Tutorials		5			5
Online activities					
Work preparation				8	8
Other activities					
Exams - evaluation		1			1
<b>TOTAL</b>		<b>31</b>		<b>44</b>	<b>75</b>

## 9.- Materials

Books
Other bibliographical, electronic references, or any other type of resource

## 10.- Assessment

<p><b>Assessments on the performance of the student</b></p> <ul style="list-style-type: none"> <li>-Presentation of a research article of the field by PowerPoint (20 slides maximum): the quality of the display and exposure will be evaluated. It is essential to be able of understating the scientific problem that is intended to be solved, preceded by the introduction that justifies it, the working hypothesis, with what objectives the hypothesis is designed to respond to, results and its discussion with a focus on new questions, conclusions (50% of the final qualification).</li> <li>- Attendance and participation in theoretical sessions, practices, and seminars (30% of the final qualification).</li> <li>- Exam: test type (20% of the final grade).</li> </ul>
<p><b>Recommendations</b></p>