Master's Degree in Molecular Biology of Cancer
Course syllabus – Basic and Preclinical Oncology Research Methodologies

Basic data of the subject

Asignatura:	Basic and preclinical cancer research methodologies			
Type (Mand/Opt):	Mandatory			
ECTS credits:	3			
Semester:	1º			
Responsible departments:	Biochemistry and Molecular Biology			
Responsible teacher: (Nombre, Dep, e-mail, teléfono)	Dra. Paloma Bragado Domingo	Dept. of Biochemistry and Molecular Biology. F. Pharmacy, UCM	pbragado@ucm.es	913941853
Teachers:	Dr. Ángel Cuesta Martínez. Dept. of Biochemistry and Molecular Biology, F. Pharmacy, UCM angcuest@ucm.es Dr. Álvaro Gutiérrez Uzquiza. Dept. of Biochemistry and Molecular Biology, F. Pharmacy, UCM. alguuz@ucm.es Dra. María del Mar Lorente Pérez. Dept. of Biochemistry and Molecular Biology, F. Chemical Sciences, UCM mmlorent@ucm.es. Dra. María Salazar Rosa. Dept. of Biochemistry and Molecular Biology. F. Biological Sciences, UCM masala08@ucm.es			

Specific data of the subject

Descriptor:	The following contents will be covered in this subject: • Use of tumor cell models in two and three dimensions: monocultures, co-cultures with cells from the tumor microenvironment, organoids, etc. • Genetic modifications of tumor cells through gene silencing, CRISPR technology, etc. • Animal models: xenotransplantation of tumor cells (hetero- and orthotopically) in immunosuppressed mice, chemical induction of tumors in mouse models (with or without genetic modifications), etc.
Requirements:	None
Recommendations:	None

Learning Outcomes

Knowledge and content	• To know the basic molecular and cellular mechanisms whose dysregulation leads to the development of cancer, with special emphasis on oncogenic and tumor-suppressing mechanisms. • To know the molecular and cellular mechanisms involved in the reciprocal interactions that occur between the tumor and the tumor microenvironment and how they affect tumor progression. • To know the main genetic and environmental risk factors that predispose to the development of cancer, as well as the main molecular mechanisms responsible for the effects of these factors. • To know cancer research techniques, both classic and more innovative strategies, and to understand their advantages and limitations. • To learn about the main types of anti-tumor treatments with special attention to the use of advanced techniques of radiotherapy, cell therapy, immunotherapy, nanoencapsulation and targeted therapies.
Skills and abilities	• Ability to understand and apply concepts, tools and methodologies in cancer research allows them to develop an integrative vision of advances in scientific research in this field. • Ability to analyze and understand a scientific work from the hypothesis and the initial objective, preliminary approach to the conclusions obtained. • Ability to clearly and unambiguously express results from scientific research in the field of molecular biology of cancer in a clear and unambiguous report or scientific work in English.

- Ability to communicate the conclusions obtained from scientific works to specialized and non-specialized audiences in a clear and unambiguous way: developing, understanding, and transmitting knowledge, scientific results, and strategies, in English.
- Ability to use and appropriately apply the latest techniques for the analysis of the mechanisms underlying tumor development and progression, as well as to study the mechanism of action of antitumor treatments in cultured cells, tissues, or whole organisms.
- Ability to learn autonomously and perform critical analysis allows them to evolve professionally in a self-directed manner.

Competencies

Core Competencies (CB)

- **CB1.** That students acquire advanced knowledge and demonstrate a solid understanding of the theoretical and methodological foundations of biomedical research in oncology.
- **CB2.** Students should know how to apply the knowledge acquired to problem solving in research environments, developing new experimental approaches.
- **CB3.** Students are able to integrate knowledge and formulate critical judgments based on incomplete or limited information, considering its scientific and clinical impact.
- **CB4**. That students communicate scientific results and conclusions in a clear and rigorous way, both to specialized and non-specialized audiences.
- **CB5**. That students develop autonomous learning skills that allow them to continue their research training.

General Competencies (GC)

- **CG1.** Understand cancer research as a multidisciplinary process that integrates molecular biology, cell biology, genetics and experimental pharmacology.
- **CG2.** Critically analyze experimental designs and results of basic and preclinical research in cancer.
- **CG3.** Apply the scientific method in hypothesis, experimental design and validation of results in oncology.
- **CG4.** To make appropriate use of bibliographic sources and scientific databases specialising in cancer research.
- **CG5.** Act in accordance with ethical principles, scientific integrity and good practices in biomedical research.

Specific competences (EC)

- **CE1.** To know and apply the main experimental methodologies used in basic and preclinical cancer research.
- **CE2.** Select and use experimental models (cellular, organoid, and animal) suitable for the study of tumor processes and the evaluation of antitumor therapies.
- **CE3.** Design preclinical studies aimed at the identification and validation of therapeutic targets and biomarkers in cancer.
- **CE4.** Interpret results derived from molecular, cellular, and genetic biology techniques in the context of oncogenesis and tumor progression.
- **CE5.** To evaluate the translational relevance of preclinical studies and their potential clinical application.
- **CE6.** Apply current regulations and the principles of the 3Rs in the use of animal models in cancer research.

Objectives

The general objective of the course is to provide students with solid and up-to-date training in the main methodologies used in basic and preclinical cancer research, with special emphasis on their application to the study of the molecular mechanisms of cancer and the development of new therapeutic strategies.

Specifically, the subject aims to enable students to:

- **Understand the conceptual and experimental foundations** of basic and preclinical cancer research, as well as its role in the translation of knowledge from the laboratory to the clinic.
- **Know and analyse the main techniques and experimental models** used in the study of cancer, including cell, organoid and animal models, as well as their advantages, limitations and selection criteria.
- **Apply molecular, cellular, and genetic biology methodologies** for the characterization of key processes in oncogenesis, tumor progression, and response to treatments.
- **To design and evaluate preclinical experimental strategies** aimed at the study of therapeutic targets, biomarkers and antitumor drugs.
- **Develop competencies in the critical analysis of scientific literature**, identifying the methodological quality, reproducibility and impact of preclinical studies in oncology.

- **To promote an ethical and responsible attitude** in the use of experimental models, especially in animal research, in accordance with current regulations and the principles of the 3Rs (replacement, reduction and refinement)

Methodology

Description:

The teaching activity will follow a combined methodology, which will make use of collaborative learning and individual learning. The face-to-face activities are structured in theory classes, exhibitions or seminars and tutorials.

In the **theoretical classes** , the student acquires knowledge through master classes given by the professor and, eventually, by guest speakers who are specialists in a specific aspect of the subject program. In this type of class, the teacher will inform the student of the content of the subject. The theoretical concepts and some experimental data will be presented that allow the student to obtain a global and comprehensive vision of the subject. At the beginning of each topic, the content and main objectives of that topic will be presented. At the end of the topic, new proposals may be made that allow the interrelation of content already studied with that of the rest of the subject or with other subjects. To support the theoretical explanations, students will be provided with the appropriate teaching material (slides, videos, applications, etc.) through the Virtual Campus.

In **the exhibition or seminar classes,** students will make an exhibition of research works related to the subject program. These lectures/seminars aim to apply the knowledge gained to the discussion, for example, of scientific research articles that will be presented by students and then critically debated by students and teachers.

Tutorials, which will try to delve into specific aspects of the syllabus to facilitate learning.

Assessment: Oral or written tests to assess learning outcomes.

Autonomous work: The student's personal work is an essential part of the learning process, including studying, solving exercises and preparing individual or group work and reports. Other individual work of the student includes reading bibliographic material provided by the teacher, preparing for exams, etc.

Distribution of teaching activities

	Hours	% attendance
Theoretical classes:	14	100
Exhibitions and/or seminars:	6	100
Tutorials	2	100
Evaluation:	2	100
In-class work:	24	100
Independent student work:	51	0
Total:	75	

Evaluation

Applicable criteria:

The assessment of this subject will combine:

- **Final exam (60% of the overall grade of the subject):** It will consist of a written test that will evaluate the integrated understanding of the theoretical and applied content addressed throughout the course. This test may include development questions, case analysis, interpretation of experimental data, and problem solving.
- **Continuous assessment (15% of the overall grade of the subject):** Continuous assessment will include the monitoring of the work carried out by students during the course, including their active participation in seminars, workshops, internships, collaborative activities, midterm tests and other complementary training tasks.
- **Presentation and discussion of research works (25% of the overall grade of the subject):** A significant part of the evaluation will focus on the **presentation, defense and critical discussion** of research works, both individually and in groups. These activities will assess the students' ability to interpret scientific literature, communicate ideas clearly and argue rigorously, promoting essential skills in the field of research.

Students must participate actively and responsibly in at least 70% of face-to-face training activities.

The grades will be based on an absolute score of 0 to 10 points in accordance with the scale established in RD 1125/2003.

Semi-annual organization

The subject will be taught in the first semester

Syllabus

Theoretical program:

Block 1: In vitro tumor models
This block addresses the main in vitro experimental models used in cancer research, highlighting their usefulness for the study of the molecular mechanisms of cancer and the preclinical evaluation of antitumor therapies.

Topic 1: Two-dimensional cell cultures and functional assays:
Introduction to cell cultures as a basic tool in cancer research. The general characteristics of cell cultures, the requirements for maintenance and the basic techniques for handling them in sterile conditions will be studied. The differences between primary cultures and established cell lines will be analyzed, as well as the processes of immortalization and cell transformation. The main functional assays used to evaluate key tumor processes will also be reviewed, including cell survival and proliferation analyses, apoptosis study, and migration and invasion assays. Finally, the use of co-cultures with cells from the tumor microenvironment will be addressed for the study of cell-cell interactions and their relevance in tumor progression.

Topic 2: Three-Dimensional Cultures
The conceptual and methodological bases of three-dimensional cultures as the most representative models of tumor architecture *in vivo* will be presented. The main techniques for generating and maintaining 3D cultures will be described, as well as their applications in cancer research. The use of advanced technologies such as bioprinting and organ-on-a-chip systems will be introduced, highlighting their potential in functional studies and in the development of preclinical screening platforms

Topic 3: Tumor Organoids
The use of tumor organoids derived from patient tissues as advanced models of cancer will be analyzed. Its applications in the study of tumor heterogeneity, response to treatments and personalized medicine will be discussed, as well as its technical limitations and current challenges.

Block 2: Genetic modification of tumor cells
This block focuses on the main genetic manipulation strategies used for the functional study of genes involved in oncogenesis and tumor progression.

Topic 4: Viral vectors and gene expression
The different types of viral vectors used in cancer research (retroviral, lentiviral, adenoviral and adeno-associated), their mechanisms of action and applications in stable or transient gene expression in tumor cells will be studied.

Topic 5: Gene silencing using RNAi
The fundamentals of RNA interference-based gene silencing (RNAi), including siRNA and shRNA, its experimental applications, and limitations in the study of gene function in tumor models will be addressed.

Topic 6: CRISPR/Cas9 technology
CRISPR/Cas9 technology as a gene editing tool, its molecular principles, applications in basic and preclinical oncology, as well as the technical and ethical considerations associated with its use will be analyzed.

Block 3: Animal Models in Oncology
This block addresses the main *in vivo* models used in cancer research, which are fundamental for the preclinical validation of hypotheses and therapeutic strategies.

Topic 7: Murine models
The different types of murine models used in oncology will be studied, including heterotopic and orthotopic xenografts in immunodeficient and immunocompetent mice. Chemically induced mouse tumor models and genetically modified models, such as transgenic mice, *knockout* (KO), and models based on CRE-LOXP and CRISPR systems, will be reviewed. Its applications, advantages and limitations, as well as aspects of experimental design, will be analyzed.

Topic 8: Other *in vivo models*
Alternative models used in cancer research will be introduced, such as *Drosophila melanogaster*, zebrafish (*Danio rerio*) and the CAM (chorioallantoic membrane) assay, highlighting their usefulness in studies of tumour development, angiogenesis and drug screening.

Seminars:

Students will be proposed, organized in groups, a scientific article focused on an innovative methodological technique in the field of biomedical research. Each group will be responsible for

	preparing a presentation in PowerPoint format explaining the fundamentals, applications and advantages of the technique described in the article, as well as its relevance in the current context of the research. During the seminar session, each group will present their work to the rest of the class. After each presentation, the other students must ask at least one question per group, with the aim of encouraging critical spirit, active participation and scientific debate. **Workshop/Seminar 1:** Cancer 3D models **Workshop/ Seminar 2:** Cancer in vitro models and functional assays **Workshop/Seminar 3:** Cancer in vivo models I **Workshop/Seminar 4:** Cancer in vivo models II
Bibliography:	**1.** Alberts et al. (2022) "Molecular Biology of the Cell". Editorial Norton & Co. ISBN-10: 0393884848 / ISBN 13: 978-0393884845. **2.** Hanahan D, Weinberg RA. The hallmarks of cancer. Cell 2000; 100:57–70. **3.** Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. Cell 2011; 144:646–74. **4.** Robert A. Weinberg; Richard A. Goldsby; Michael Hemann; Tyler Jack. The Biology of Cancer. Norton & Company. (ISBN: 9780393887662). **5.** Seema Nayak, Anupam Kumar Sriwastava. Concepts and Methodology in Cancer Diagnostics: An Immunological, Biochemical and Molecular Approach. Elsvier **6.** Beverly A. Teicher. Tumor Models in Cancer Research. Springer Science+Business Media, LLC 2011. ISBN: 978-1-60761-968-0 **7.** Nima Rezaei. Cancers in Different Conditions, Cancer Research Methods and Diagnosis: An Interdisciplinary Approach. Springer Cham. ISBN: 978-3-031-93522-0 *In the classes and practical sessions, specific bibliography of each of the topics to be dealt with will be recommended*