

Course unit name: ANTI-TUMOR IMMUNOTHERAPY: FROM BIOLOGY TO CLINICAL APPLICATIONS

1.- General information

Code	303023	Plan		ECTS	3
Type	Elective	Course	2023/2024	Periodicity	2 nd Semester
Department	Cancer Research Center				
Virtual Platform	Platform:	moodle.usal.es			
	URL de Acces:	https://studium.usal.es/			

Faculty

Professor Coordinator 1	Dra. Julia M ^ª Almeida Parra				
Department	Medicine				
Research area	Immunology and Cancer				
Center	Cancer Research Center				
Office	Lab S3				
Tutorials	Appointment by email				
URL Web	https://www.cicancer.org/grupo?id=79				
E-mail	jalmeida@usal.es	Phone	+34 923294500 5816		

Professor Coordinator 2	Dr. Alberto Orfao de Matos Correia e Vale				
Department	Medicine				
Research area	Immunology and Cancer				
Center	Cancer Research Center				
Office	Laboratory 11				
Tutorials	Appointment by email				
URL Web	https://www.cicancer.org/grupo?id=27				
E-mail	orfao@usal.es	Phone	+34 923294811		

Professor	Dr. Miguel Vicente Manzanares		
Department	Not applicable (no USAL staff)		
Research area	Biofísica tumoral		
Center	Cancer Research Center		
Office	Laboratory 6		
Tutorials	Appointment by email		
URL Web	https://www.cicancer.org/grupo?id=69		
E-mail	miguel.vicente@usal.es	Phone	+34 923294806

Professor	Dr. Manuel Fuentes García		
Department	Medicine		
Research area	Molecular biology, proteomics, nanotechnology, and immunotechnology		
Center	Cancer Research Center		
Office	Laboratory 11		
Tutorials	Appointment by email		
URL Web	https://www.cicancer.org/grupo?id=81		
E-mail	jmfuentes@usal.es	Phone	+34 923294811

Professor	Dr. Alejandro Martín Sancho		
Department	Medicine		
Research area	Medicine (Hematology)		
Center	University Hospital of Salamanca		
Office	Service of Hematology (University Hospital of Salamanca)		
Tutorials	Appointment by email		
URL Web			
E-mail	amartingar@usal.es	Phone	+34 923294812

Professor	Dr. Juan Jesús Cruz Hernández		
Department	Medicine (Oncology)		
Research area	Clinical research in Medical Oncology		
Center	Cancer Research Center and Faculty of Medicine		
Office	Department of Medicine (Faculty of Medicine)		
Tutorials	Appointment by email		
URL Web	https://ibsal.es/es/canc-01-estudio-sobre-la-predisposicion-y-tratamiento-de-tumores-solidos-c		
E-mail	jjcruz@usal.es	Phone	+34 923294812

Professor	Dr. Martín Pérez de Andrés		
Department	Medicine		
Research area	Immunology and Cancer		
Center	Edificio I+D+i		
URL Web	https://www.cicancer.org/investigador?id=211c1d3e-bed9-4810-8fad-f00caf33b150		
Tutorials	Appointment by email		
E-mail	jmmmar@usal.es	Phone	+34 923294500 5505

Professor	Dra. M ^a Aránzazu Rodríguez Caballero		
Department	Medicine		
Research area	Immunology and Cancer		
Center	Cancer Research Center		
Office	Laboratory 11		
Tutorials	Appointment by email		
E-mail	arocab@usal.es	Phone	+34 923294811

Professor	Dr. Enrique Montalvillo Álvarez		
Department	Medicine		
Research area	Immunology and Cancer		
Center	Cancer Research Center		
Office	Laboratory 11		
Tutorials	Appointment by email		
E-mail	emontalvillo@usal.es	Phone	+34 923294811

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

Training Module
Fifth block (out of five) of master program organization.
General aim of the subject
<p>To contribute to provide comprehensive training for students on the field of Cellular Biology - in order they can start a research career, and to facilitate them their incorporation into a PhD program-, through acquisition of transversal (general) master competences (CG1 to CG4), as well as the following specific competences:</p> <ul style="list-style-type: none"> • CE2- Students will understand how a clinical trial is planned and its basic components: susceptible population, inclusion and exclusion criteria, and methods for evaluation of efficacy and toxicity. • CE4- Students will be able to recognize the genes and proteins involved in tumor process, and their basic mechanisms. • CE5- Students will be able to interpret basic biological data on tumor genes and proteins, and to translate it to the clinical level and in the development of diagnostic, prognostic or therapeutic applications. • CE6- Students will be able to recognize the specific clinical and molecular characteristics of the different types of cancer, diagnostic methods and therapeutic approaches. • CE7- Students will know, in a general way, the methods used for diagnosis and treatment of the different types of cancer. • CE8- Students will know how to access information and data on specialized areas of research on Molecular and Cellular Cancer Biology. • CE10- Students will be able to integrate new knowledge in the field of Molecular Cancer Biology, and develop their ability for self-learning. • CE11- Students will be able to discriminate between cause and consequence using biological experimentation. • CE12 – Students will recognize contents and how to access to the major sources of biological resources and biomolecular databases.
Professional specialization
Master Degree on Health Sciences.

3.- Previous recommendations

To meet the following general requirements, as regards admission into "Cancer Biology and Clinic University Master": i) Have completed at least one bachelor degree on Biology, Biotechnology, Pharmacy, Medicine or any other degree on Biomedicine; ii) interest in scientific production; iii) a high English level is recommended.

4.- Aims of the subject

To get inside into the general principles of current and future cancer treatment strategies based on immunotherapy, that is, all those therapeutic approaches aimed at enhancing or improving patient's immune system to attack and destroy tumor cells.

This subject is structured into three thematic blocks: the first one aims to go in depth in cellular and molecular mechanisms involved in the relationship between tumor and immune system; the second block focuses on new strategies to enhance the response of immune cells against the tumor, as well as on the identification of new cellular and molecular biomarkers to be used as targeted therapies; finally, in the third block, information of the most recent advances in anti-tumor immunotherapy (in different models of solid and hematological tumors) is provided.

Specific purposes:

- To get knowledge on the biological bases of anti-tumor immune response.
- To recognize all the different immune components and mechanisms involved in anti-tumor immunity.
- To understand the mechanisms of tumor immune escape, with special focus on tumor microenvironmental escape.
- To understand the bases and principles of anti-tumor immunotherapy.

To know the major results derived from clinical application of the new anti-tumor immunotherapy strategies.

5.- Contents

Theory:

I – IMMUNE SYSTEM AND CANCER: GENERAL PRINCIPLES OF TUMOR IMMUNITY:

Lesson 1.- Immunobiology of cancer immunosurveillance.

Lesson 2.- Molecular mechanisms of immune response: co-stimulatory and inhibitory immune molecules and their roles as therapeutic targets in cancer.

Lesson 3.- Tumor antigens.

Lesson 4.- Mechanisms of tumor immune escape.

Lesson 5.- Role of tumor microenvironment on local tumor progression.

Lesson 6.- Role of tumor microenvironment on tumor metastatization.

II – ANTI-TUMOR IMMUNOTHERAPY: PRINCIPLES AND STRATEGIES:

Lesson 7.- Anti-tumor immunotherapy: general principles and classification of anti-tumor treatment strategies based on immunotherapy.

Lesson 8.- Application of immune checkpoint targeted therapies on anti-tumor treatment.

Lesson 9.- Monoclonal and bi(tri)specific antibodies in cancer therapy: cellular and molecular basis.

Lesson 10.- Principles of anti-tumor vaccination using tumor antigens and/or dendritic cells.

Lesson 11.- Anti-tumor cell-based therapies: from TIL to NK- and CART-cells.

Lesson 12.- Tumor microenvironment: future perspectives as antitumor targeted therapies.

Lesson 13.- Proteomics strategies to identify biomarkers for anti-tumor immunotherapy.

Lesson 14.- Proteomic strategies to identify molecular targets for anti-tumor immunotherapy.

III – CLINICAL APPLICATIONS OF ANTI-TUMOR IMMUNOTHERAPY:

Lesson 15.- Combination of anti-tumor treatment strategies (i.e. immunotherapy combined with conventional therapies).

Lesson 16.- Anti-tumor therapy-related toxicity.

Lesson 17.- Anti-tumor immunotherapy applied to solid tumors: clinical trials.

Lesson 18.- Anti-tumor immunotherapy using monoclonal antibodies in hematological malignancies.

Lesson 19.- Adoptive cell-therapy in hematological malignancies: current and future perspectives of CART-cell-based therapies.

Lesson 20.- Immune monitoring of anti-tumor immunotherapy.

Lab training / data analysis with specific software programs:

Lesson 1. Flow cytometer. Techniques for staining membrane surface molecules of immune cells.

Lesson 2. Software programs for analysis of flow-cytometry data: application on immune monitoring.

Lesson 3: Immunohistochemistry in cancer diagnosis

Lesson 4: Proteomics.

Seminars:

Students will individually present scientific papers either on hot / controversial aspects in the field of "Immunology and Cancer" or on other contents of the subject directly related with their master theses. After oral presentation, the presented study will be collectively discussed.

Scientific lectures:

Attendance and academic use (to be evaluated) to at least one scientific lecture on "anti-tumor immunotherapy", given by prestigious speakers invited by the teachers responsible for the subject.

6.- Skills to be acquired

Basic skills

- Understanding the basic principles of tumor immunology. Improve knowledge on immunotherapy basis applied for cancer treatment. Ability to understand and critically comment on scientific results on the field of cancer immunology. Ability to integrate all the information on this field, to understand the clinical application of cancer immunology.
- Ability to critically analyze, orally present and discuss relevant research papers published on cancer immunology and anti-tumor immunotherapy.

Specific skills

Acquisition of skills and ability to interpret laboratory results derived from the study of tumor cells, of interest in the field on immunotherapy.

Transversal skills

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7.- Teaching methodology

The student must attend the theory classes, after having previously read and understood the recommended bibliography. In the first day, a general overview on how the subject is structured will be given, as well as the contents of the subject. The student must attend all the lab and data analysis training. The student must attend the seminars, in which each of them will individually present a recent or controversial paper already published (of interest in cancer immunobiology and/or anti-tumor immunotherapy) and then will collectively discussed with the teacher and the other students. Likewise, the student must attend and participate in the scientific lectures (related with the objectives of this matter) organized by Cancer Research Center.

8.- Estimated learning time

	Hours tutored by the teacher		Individual work (hours)	TOTAL HOURS
	Attendance required (hours)	Distance learning (hours)		
Lectures	15		30	45
Practices	- In classroom			
	- In laboratory	3	1	4
	- In computer classroom	1		1
	- Countryside			
	- Visualization classroom			
Seminars				
Work presentations and debates	1			1
Tutorials	0.5	0.5		1
Online activities			6	6
Work preparation			5	5
Other activities	1			1
Exams - evaluation	1		10	11
TOTAL	22.5	0.5	52	75

9.- Materials

Books

Not applicable

Other bibliographical, electronic references or any other type of resource

- Almagro JC, Daniels-Wells TR, Perez-Tapia SM *et al.* Progress and challenges in the design and clinical development of antibodies for cancer therapy. *Front Immunol* 2018; 8: art 01751.
- Ben Khelil M, Godet Y, Abdeljaoued S, *et al.* Harnessing Antitumor CD4+ T Cells for Cancer Immunotherapy. *Cancers (Basel)* 2022;14: 260.
- Borst J, Ahrends T, Babala N, *et al.* CD4+ T cell helper in cancer immunology and immunotherapy. *Nat Rev Immunol* 2018; 18: 635.
- Cuesta-Mateos C, Alcaraz-Serna A, Somovilla-Crespo B, *et al.* Monoclonal antibody therapies for hematological malignancies: not just lineage-specific targets. *Front Immunol* 2018; 8: art 01936.

- Farhood B, Najafi M, Mortezaee K. CD8+ cytotoxic T lymphocytes in cancer immunotherapy: A review. *J Cell Physiol* 2019; 234: 8509.
- Gao J, Bernatchez C, Sharma P *et al.* Advances in the development of cancer immunotherapies. *Trends in Immunology* 2013; 34: 90.
- Kartikasari A, Prakash M, Cox M, *et al.* Therapeutic cancer vaccines - T cell responses and epigenetic modulation. *Front Immunol* 2019; 9: art 03109
- Koury J, Lucero M, Cato C *et al.* Immunotherapies: exploiting the immune system for cancer treatment. *J Immunol Res* 2018; Vol 2018, art ID 9585614, 16 pages, 2018.
- Marabelle A, Tselikas L, de Baere T, *et al.* Intratumoral immunotherapy: using the tumor as the remedy. *Ann Oncol* 2017; 28: xii33.
- Meric-Bernstam F, Larkin J, Tabernero J, Bonini C. Enhancing anti-tumour efficacy with immunotherapy combinations. *Lancet*. 2021 Mar 13;397(10278):1010-1022.
- Mohme M, Riethdorf S, Pantel K. Circulating and disseminated tumour cells – mechanisms of immune surveillance and scape. *Nat Rev Clin Oncol* 2017; 14: 155.
- Spranger S. Mechanisms of tumor escape in the context of the T-cell-inflamed and the non-T-cell-inflamed tumor microenvironment. *Int Immunol* 2016; 28: 383.
- Taylor BC, Balko JM. Mechanisms of MHC-I Downregulation and Role in Immunotherapy Response. *Front Immunol* 2022;13: 844866.

10.- Assessment

Assessments on the performance of the student

Continuous assessment system:

- Attendance to theory classes, seminars, practical sessions and tutorials.
- Active participation in all programmed activities
- Continuous evaluation

Written exam: exam consisting of multiple-choice questions.

Personal (individual) preparation and oral presentation and debate of a previously published paper in this field.

Assessment criteria:

Written final exam of the contents of theory lessons (45% of the final grade).

Active participation in all the programmed activities (20% of the final grade).

Personal (individual) preparation and oral presentation and debate of a previously published paper in this field (30% of the final grade).

Evaluation of the subject by the student (5% of the final grade).

Recommendations

Students who have not passed the subject (a mark of minimum 5 out of 10) will have only to submit to a new written exam, but the grade obtained in continuous evaluation and oral presentation will be maintained.