ANTI-TUMOR IMMUNOTHERAPY: FROM BIOLOGY TO CLINICAL APPLICATIONS

| 1 General information | | | | | | | |
|-----------------------|--------------------------|--------|-----------|-------------|--------------------------|--|--|
| Code | 303023 | Plan | | ECTS | 3 | | |
| Туре | Elective | Course | 2025/2026 | Periodicity | 2 st Semester | | |
| Language | | | | | | | |
| Department | Cancer Research Center | | | | | | |
| Virtual Platform | https://studium.usal.es/ | | | | | | |

| 1.1 Faculty | | | | | |
|-----------------------|--------------------------------------|---|--|--|--|
| Professor Coordinator | Dra. Julia Mª Almeida Parra | | | | |
| Department | Medicine | | | | |
| Research area | Immunology and Cancer | | | | |
| Center | Cancer Research Center | | | | |
| Office | Lab S3 | | | | |
| Tutorials | Appointment by email | | | | |
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| Professor Coordinator | Dr. Alberto Orfao de Matos Correia e Vale | | | |
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| Department | Medicine | | | |
| Research area | Immunology and Cancer | | | |
| Center | Cancer Research Center | | | |
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| Professor | Dr. Miguel Vicente Manzanares | | | |
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| Research area | Biofísica tumoral | | | |
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| URL Web | https://www.cicancer.org/grupo?id=69 | | | |
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| Professor | Dr. Manuel Fuentes García | | | | |
|---------------|---|----------|---------------|--|--|
| Department | Medicine | Medicine | | | |
| Research area | Molecular biology, proteomics, nanotechnology, and immunotechnology | | | | |
| Center | Cancer Research Center | | | | |
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| Professor | Dr. Alejandro Martín Sancho | | | |
|---------------|--|-------|---------------|--|
| Department | Medicine | | | |
| Research area | Medicine (Hematology) | | | |
| Center | University Hospital of Salamanca | | | |
| Office | Service of Hematology (University Hospital of Salamanca) | | | |
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| Professor | Dr. Juan Jesús Cruz Hernández | | | | |
|---------------|---|---------------------------------------|---------------|--|--|
| Department | Medicine (Oncology) | Medicine (Oncology) | | | |
| Research area | Clinical research in Medic | Clinical research in Medical Oncology | | | |
| Center | Cancer Research Center and Faculty of Medicine | | | | |
| Office | Department of Medicine (Faculty of Medicine) | | | | |
| Tutorials | Appointment by email | | | | |
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| Professor | Dr. Martín Pérez de Andrés | | | | |
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| Department | Medicine | Medicine | | | |
| Research area | Immunology and Cancer | | | | |
| Center | Edificio I+D+i | | | | |
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| Professor | Dra. M ^a Aránzazu Rodríguez Caballero | | | | | |
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| Research area | Immunology and Cancer | | | | | |
| Center | Cancer Research Center | | | | | |
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| Professor | Dr. Enrique Montalvillo Álvarez | | | |
|---------------|--|--|--|--|
| Department | Medicine | | | |
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| Tutorials | Appointment by email | | | |
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2.- 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; ii) a high English level is recommended.

3.- 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.

4.- Skills to be acquired / Learning outcomes

Skills

4.1: 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.

4.2: 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.

4.3: Transferable skills:

5.- Contents (Syllabus)

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.- Anti-tumor therapy-related toxicity.

Lesson 16.- Anti-tumor immunotherapy applied to solid tumors: clinical trials.

Lesson 17.- Anti-tumor immunotherapy using monoclonal antibodies in hematological malignancies.

Lesson 18.- Adoptive cell-therapy in hematological malignancies: current and future perspectives of CART-cell-based therapies.

Lesson 19.- 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.- 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.

| 6.1 Estir | nated learning time | | | | |
|--------------------|-------------------------|-----------------------------------|---------------------------------|-----------------|----------------|
| | | Hours tutored b | by the teacher | Individual | TOTAL HOURS |
| | | Attendance required (hours) | Distance learning (hours) | work (hours) | |
| Lectures | | 15 | | 30 | 45 |
| | - In classroom | | | | |
| | - In laboratory | 3 | | 1 | 4 |
| Practices | - In computer classroom | 1 | | | 1 |
| | - Countryside | | | | |
| | - Others (specify) | | | | |
| Seminars | | | | | |
| Work pres | entations 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 |

7.- Materials, other bibliographical, electronic references or any other type of resource

• Almagro JC, Daniels-Wells TR, Perez-Tapia SM et at. 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.

• Jiani W, Qin T, Jie M. Tumor neoantigens and tumor immunotherapies. Aging Med (Milton). 2024;7(2):224-230. Published 2024 Apr 12. doi:10.1002/agm2.12295

• 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.

• Ma R, Li Z, Chiocca EA, Caligiuri MA, Yu J. The emerging field of oncolytic virus-based cancer immunotherapy. Trends Cancer. 2023;9(2):122-139. doi:10.1016/j.trecan.2022.10.003

• 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.

• Tay C, Tanaka A, Sakaguchi S. Tumor-infiltrating regulatory T cells as targets of cancer immunotherapy. Cancer Cell. 2023;41(3):450-465. doi:10.1016/j.ccell.2023.02.014

• Taylor BC, Balko JM. Mechanisms of MHC-I Downregulation and Role in Immunotherapy Response. Front Immunol 2022;13: 844866.

• Waldman AD, Fritz JM, Lenardo MJ. A guide to cancer immunotherapy: from T cell basic science to clinical practice. Nat Rev Immunol. 2020;20(11):651-668. doi:10.1038/s41577-020-0306-5

8.- Assessment

8.1: Assessment Criteria:

8.2: Assessment Systems:

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).

8.3: General Considerations and Recommendations for Assessment and Resit:

Continuous assessment system:

-Attendance to theory clases, 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.

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.

9.- Weekly Teaching Schedule