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3.5.3 Experimental Therapies and Biomarkers in Cancer



Publications: 12 | Q1: 7

COMPOSITION

Javier de Castro Carpeño.
Director Científico de IdiPAZ/Jefe de Sección de Oncología. Hospital Universitario La Paz/Profesor Asociado. Universidad Autónoma de Madrid
Olga Vera Puente.
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- **Ana Arauzo Cabrera.** *Investigadora Predoctoral. FIBHULP*
- **María José Beato Merino.** *Facultativo Especialista de Área en Anatomía Patológica. Hospital Universitario La Paz*
- **Miranda Burdiel Herencia.** *Investigadora Postdoctoral. FIBHULP*
- **César Casado Sánchez.** *Profesor Asociado. Universidad Autónoma de Madrid*
- **Patricia Cruz Castellanos.** *Facultativo Especialista de Área en Oncología Médica. Hospital Universitario La Paz*
- **Lucía de Dios Blázquez.** *Bioinformática. FIBHULP*
- **María Dolores Diestro Tejeda.** *Facultativo Especialista de Área en Ginecología y Obstetricia. Unidad de Ginecología Oncológica. Hospital Universitario La Paz*
- **María Isabel Esteban Rodríguez.** *Facultativo Especialista de Área en Anatomía Patológica. Hospital Universitario La Paz*
- **Álvaro García Guede.** *Profesor doctor. Universidad Europea de Madrid*
- **Laura Gutiérrez Sainz.** *Facultativo Especialista de Área en Oncología Médica. Hospital Universitario La Paz*
- **Óliver Higuera Gómez.** *Facultativo Especialista de Área en Oncología Médica. HULP*
- **Diego Jiménez Bou.** *Facultativo Especialista de Área en Oncología Médica. HULP*
- **Cristina Manguán García.** *Técnico de Laboratorio. IIB Sols Morreale*
- **Ander Paulo Mayor Ibarguren.** *Facultativo Especialista de Área en Dermatología. Hospital Universitario La Paz*
- **Rocío Moreno Velasco.** *Técnico de Laboratorio. FIBHULP*
- **Olga Pernía Arias.** *Investigadora Predoctoral. Universidad Autónoma de Madrid*
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- **Darío Sánchez Cabrero.** *Facultativo Especialista de Área en Oncología Médica. HULP*
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STRATEGIC OBJETIVES

- Genetic and epigenetic mechanisms play a significant role in tumor progression and the development of treatment resistance. The dynamic nature of tumors and their ability to adapt and resist therapies pose critical challenges in clinical practice. In our research, we have employed various strategies to address these challenges. First, we have focused on identifying novel markers throughout the course of lung cancer, aiming to uncover crucial indicators of disease evolution. Furthermore, we have pursued several approaches to identify specific targets involved in drug response, seeking to improve treatment efficacy. Our research has transcended the realm of theory, extending into the realm of clinical practice through the meticulous analysis of human samples. It is through this granular examination that we have unraveled the alterations that occur at the individual patient level. Moreover, we have successfully identified epigenetic changes in tumor suppressor genes that are strongly associated with drug resistance. Furthermore, we have made significant progress in understanding the role of epigenetic regulators in lung cancer and melanoma, particularly in the context of oxidative stress. These findings shed light on new avenues for therapeutic interventions and provide valuable insights into the complex interplay between genetic, epigenetic, and environmental factors in cancer progression and treatment resistance.
- By applying genomic, transcriptomic, and expression reactivation techniques, we have made significant progress in identifying a wide range of biomarkers, including genes and microRNAs. These biomarkers hold enormous potential for non-invasive cancer diagnosis, particularly in the context of non-small cell lung cancer (NSCLC). Our pioneering research has demonstrated the effectiveness of liquid biopsy as a reliable method for detecting these biomarkers, offering a promising avenue for early lung cancer detection and diagnosis. Furthermore, we have focused our attention on evaluating patients with chronic obstructive pulmonary disease (COPD) to establish the presence of early-stage lung cancer. By leveraging these advanced techniques, we have successfully unraveled the complex transcriptomic alterations at the miRNA level that occur during lung cancer development in COPD patients. These groundbreaking findings not only have great potential to improve the accuracy and efficiency of cancer diagnosis but also pave the way for personalized treatment approaches that can potentially improve patient outcomes.

IdiPAZ Instituto de Investigación Hospital Universitario La Paz

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RESEARCH LINES

1. Identification of predictive epigenetic biomarkers for the development of treatment resistance in solid tumors.

- Among cancer markers, predictive markers are the most crucial for guiding therapies, as the vast majority of patients are diagnosed when the tumor requires treatment. Platinum-derived compounds are the standard treatment for high-incidence tumors such as those of the lung, ovary, and rectum; therefore, identifying markers of response to their use would allow for patient selection, optimizing treatment and associated healthcare costs.
- Lung cancer:
- In this area, we have identified the methylation of the IGFBP3 gene promoter, whose epigenetic silencing is related to platinum resistance, extending its validation to cohorts of lung cancer patients likely to benefit from its use. Furthermore, the efficacy of this biomarker is being tested in liquid biopsy as a non-invasive test. This line of research has resulted in three related publications (Oncogene 2010 PMID: 20023704, Oncogene 2013 PMID: 22543588, Epigenetics 2014 PMID: 25482372) and a patent in the joint exploitation phase with a Spanish biotechnology company that has licensed the patent. This patent has passed a Pre-Commercial Public Procurement process with the Galician Health Service (SERGAS), and its validation in national phases has been supported by two related RETOS projects.
- Brain Tumors:
- Regarding our work with brain tumors, we have been assessing the methylation status of the MGMT gene in glioblastomas as part of our clinical and research activities since 2014 in our laboratory, developing advanced, highly sensitive technology for its detection in liquid biopsies. The data obtained to date from more than 200 patients in a prospective trial has resulted in a recent publication (Clinical Epigenetics 2021 PMID: 33750464).
- Ovarian Cancer:
- We also have an open line in ovarian cancer, in which we have published a recent article (Clinical Epigenetics 2021 PMID: 34454589) and has allowed us to participate as leaders of work package in a European Transcan project led by Italy, which has just passed the first round of evaluation positively.
- Melanoma:
- In this emerging line of research, we are focusing on characterizing the oncogenic role of MAFG in the response to immunotherapy in melanoma. Dr. Olga Vera recently joined the group as a Sara Borrell postdoctoral researcher to lead this line of research. Olga's previous studies have identified MAFG as a potential oncogene in melanoma with possible therapeutic applications. The successful completion of our study will significantly advance our understanding of the role of MAFG in melanoma, identify new therapeutic targets, and open new lines of research focused on dissecting the oncogenic role of MAFG.

2. Study of the molecular mechanisms underlying simultaneous platinum resistance in cancer, through epigenetic regulation of regulatory non-coding RNAs.

- Along these lines, we are studying changes in the expression of microRNAs and lncRNAs in platinum-sensitive and platinum-resistant human cell lines of NSCLC and ovarian cancer established in our research group. We have identified 7 microRNAs whose expression appears to be under epigenetic regulation. One of them, miRNA-7, is under epigenetic regulation of its regulatory region and is a potential predictive biomarker of platinum response in ovarian cancer in terms of overall survival and time to progression. The development of this line of research has resulted in the publication of an article in the journal (Theranostics 2017 PMID: 29158814), as well as a patent currently in PCT phase. Based on these findings, in 2016 we initiated a collaboration with the Moffitt Cancer Center in Tampa, USA, to study long non-coding RNAs (lncRNAs) and their possible regulation through DNA methylation in these cell lines. With this project, we are evaluating changes in the expression of the This research focuses on lncRNAs and their epigenetic regulation at the level of DNA methylation, characterizing two groups of lncRNAs differentially regulated in the development of cisplatin resistance, thus paving the way for the identification of new ones. This collaboration has yielded highly innovative results in this field (Epigenetics PMID: 29436261 and Translational Research 2018, PMID: 30053382), and ongoing research focused on the characterization of these novel biomarkers is supported by funding from projects PI21/00145 and Caixa Impulse.

3. Identification of new therapeutic targets. In recent years we have also identified the direct regulation of the MAFG gene through miR-7 in our experimental models.

- The function of MAFG is associated with detoxification under oxidative stress, and our in vitro studies have demonstrated its involvement in the development of cisplatin-resistant phenotypes. Our translational approach suggests that MAFG could be a diagnostic marker in lung and ovarian cancer patients treated with platinum-based chemotherapy. To date, this line of research has yielded four articles (Translational Research 2018, PMID: 30053382; Cell Biosci. 2019 PMID: 31406565; Arch Bronconeumol (Engl Ed). 2020. PMID: 31780284; Antioxidants (Basel). PMID: 32492865) and a European patent, which has just been extended to national phases in the US and Europe, describing the clinical use of MAFG in lung and ovarian cancer patients. Currently we have addressed the study and use of MAFG as a therapeutic target through in vitro and in vivo assays after editing the MAFG gene using CRISPR/Cas9 technology, a project funded by the ISCIII (PI18/00050, P21/000145) in addition to expanding and validating its use with the potential development of a kit for clinical use thanks to obtaining a RETOS project (RTC2019-007229-1) from the 2019 call and which is underway with the collaboration of the H. Ramón y Cajal and the companies Aptus and Atrys.

4. Identification of biomarkers in exosomes as a liquid biopsy in patients with lung and ovarian cancer.

- This line of research aims, through an initial basic approach, to characterize and compare the protein and microRNA content of secretome exosomes from paired, sensitive, and resistant lung cancer cell lines. In the translational study of this project, the candidates identified in the cell lines are being validated in circulating exosomes from samples obtained from lung and ovarian cancer patients, which has yielded several results. On the one hand, two candidate miRNAs with prognostic significance in this disease have been identified, and on the other hand, a miRNA with potential universal value as an endogenous agent capable of normalizing the exosomal miRNA content has been identified, both in healthy individuals and in individuals with different tumor types. These results have led to a European patent that is in national phases and to obtaining a Caixa Impulse Validate project for the constitution of a Spin-off, in our institution focused on the development of a first RUO product for the normalization of the exosomal content in human blood samples, in addition to two manuscripts in preparation, as well as the defense of Julia Jiménez's thesis in July 2019.

5. Identification of pharmacogenetic biomarkers associated with the efficacy and toxicity of cancer treatments.

- Led by Dr. R. Rosas. Pharmacogenetics is the field of knowledge that seeks to identify genetic variants to provide information that allows for a better understanding of drug response in terms of efficacy and toxicity, thus contributing to personalized precision medicine. Despite advances in the research and

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development of new cancer treatments, the efficacy and safety of these drugs vary considerably from patient to patient. In this context, this line of research aims to understand how genetic variations in individuals can influence the efficacy and toxicity of cancer treatments. The use of pharmacogenetic biomarkers is a reality in routine clinical practice and has been shown to improve the efficacy and reduce the side effects of treatments, resulting in a better quality of life for patients and reduced costs for the national healthcare system. Our ultimate goal is to identify new pharmacogenetic biomarkers that will allow for better selection of cancer treatments for each patient, thus advancing the medicine of the future with a personalized and individualized approach. This line of research currently includes two projects awarded through competitive public (PI22/00128) and private (José Luis Castaño Foundation-SEQC) funding calls, led by Dr. Rocío Rosas.

6. Identification of microRNA hypermethylation patterns associated with an increased risk of developing non-small cell lung cancer in patients with mild COPD and moderate to high tobacco use.

- In recent years, the potential role of epigenetic alterations in the development of lung cancer in patients with COPD has gained particular importance. This development is mediated by changes in the activity of various microRNAs, small non-coding RNA molecules (19-25 nucleotides) with a regulatory function in gene expression, which induce the degradation of messenger RNA or inhibit its translation. Therefore, it is interesting to consider whether there may be hypermethylation profiles of different microRNAs that are associated with an increased risk of lung cancer in patients with COPD, which would facilitate appropriate risk selection for screening programs. This line of research currently has one project, awarded through a competitive public call (PI22/001764), under the co-direction of Olga Pernía Arias.

7. Development of high-throughput techniques available to the National Health System (NHS).

- NGS and DNA methylation status characterization. Implicit in the group's cross-cutting lines and in our commitment to supporting the implementation of technological advances derived from our research activity within the NHS, we have developed the characterization of DNA methylation status at the PAZ genetics facilities. This is achieved through the use of these new aspects of NGS applied to the field of epigenetics, both from a global perspective and limited to specific regions, to implement its potential clinical applicability in cancer patients through customized panels for solid tumors, including glioblastomas, using Methylseq technology and 850K EPIC arrays. Furthermore, in recent years we have developed the use of commercial NGS panels in strict compliance with quality standards to address the genetic profiling of tumors in lung cancer patients. Thanks to the addition of Dr. Rocío Rosas and Juan Rodés to our team in 2022, we are beginning the hospital implementation phase, in which we have already tested runs with several platforms from different vendors. Its fine-tuning will allow its use for both research activities and its future application in healthcare, especially in the classification of brain tumors. This activity is funded by the Spanish Group for Transversal Oncology and Rare Orphan Tumors (GETHI), which recently awarded the group a competitive grant for this purpose. Given the group's experience in using big data, we have been able to participate in the EU's ISIDORE project and have begun studying bioinformatics matrices that predict response to platinum-based treatment. We intend to combine information available in public domain databases with relevant clinical information associated with our own experimental results (methylation and gene expression microarrays and microRNAs, bisulfite sequencing, RNAseq, and miRNAseq) to generate a predictive matrix of treatment response. With these analytical models, we aim to identify "global markers" that define a predictive profile for platinum-based treatment in lung and ovarian cancer, based on the transcriptome, microRNome, and/or methylome. This line of research is led by Carlos Rodríguez Antolín, a bioinformatician in the group.

RESEARCH ACTIVITY

Doctoral Theses

- **García Guede A.** Estudio de MAFG como biomarcador en Cáncer de Pulmón No Microcítico: Causa y consecuencia en la regulación de factores implicados en cáncer[dissertation]. Madrid: UAM: 2025(24/07/2025). Director: Vera Puente O

Master Theses

- **Ruiz Buceta S.** Caracterización de los cambios no genéticos en el desarrollo y progresión del melanoma.[dissertation]. Madrid: UCM: 2025(07/07/2025). Director: Vera Puente O
- **Lumbreras García C.** Evaluación del papel de MAFG y sus genes diana en la progresión del melanoma cutáneo[dissertation]. Madrid: UAM: 2025(30/09/2025). Director: Vera Puente O
- **Heredia G Cantón PM.** Desarrollo e implementación de un Beacon Fhir para la interoperabilidad y el acceso seguro a la información genética procedente de estudios de secuenciación masiva.[dissertation]. Madrid: UAM: 2025(23/06/2025). Director: Rodriguez Antolin C.
- **Sánchez Lara C.** Optimización de la detección de CNVS en paneles y exomas mediante secuenciación masiva: implementación y validación clínica[dissertation]. Madrid: UAM: 2025(23/06/2025). Director: Rodriguez Antolin C.

Final Degree Theses

- **Fernández Fernández M.** Estudio de la inducción de MAFG por radiación ultravioleta como evento iniciador en la transformación melanocítica[dissertation]. Madrid: Universidad Francisco de Vitoria: 2025(07/07/2025). Director: Vera Puente O. CP24/00005
- **Ramos López M.** Identificación de biomarcadores farmacogenéticos predictivos de toxicidad a tratamiento en cáncer de colon. [dissertation]. Madrid: Universidad Francisco de Vitoria: 2025(09/06/2025). Director: Rosas Alonso R.

Publications

- **Alameda-Guijarro M, Rueda-Lara A, Martín-Montalvo G, Higuera O, Gutiérrez-Sainz L, Jimenez-Bou D, Villamayor J, de Castro J, Custodio A, Pérez-Wert P.** Novel therapies targeting delta-like ligand 3 (DLL3) in pulmonary and gastroenteropancreatic neuroendocrine carcinomas. Cancer Treat Rev. 2025; 140: 103022. Review. IF: 10.6; Q1
- **de Castro J, Alonso-Fernández P, Castrodeza JJ, Gayete A, Hernando F, Martínez-Olmos J, Massuti B, Paz-Ares L, Sisó-Almirall A, Vicente D, Molins L.** Monitoring of the oncological process for lung cancer in Spain: an expert consensus report. Clin Transl Oncol. 2025; 27(10): 3867-76. Article. IF: 2.7; Q3
- **Sánchez CV, Rodríguez MIE, García AP, Taravilla-Loma M, Rodríguez-Domínguez V, Rodríguez-Antolín C, Rosas-Alonso R, Losantos-García I, Guerrero AI, Gandía-González ML.** Clinical impact of a next-generation sequencing approach for glioblastoma patients. Cancers (Basel). 2025; 17(5): 744. Article. IF: 4.8; Q2
- **Yang JCH, Wang MZ, Doucet L, Fan Y, Lv DQ, Sun ML, Huang DZ, Greillier L, Planchard D, Hong QY, Mazieres J, Felip E, Li XY, Hu Y, Fang J, Bazhenova L, Ghiringhelli F, Dols MAC, Rodríguez LPA, Bearz A, Pellini B, Kim YJ, Bosch-Barrera J, Shim BY, Luo YH, Tiseo M, Yang TY, Carcereny E, Memmott RM, Zalcman G, Carpeño JD, Di Noia V, Parra HS, Streich G, Lee DH, Shum E, Han JY, Jaime JC, Brungs D, John T, D'Arcangelo M, Joaquin AB, Liu GF, Antonuzzo L, Hinojal GF, Le XN, Zheng L, Jänne PA.** Phase II dose-randomized study of sunvozertinib in platinum-pretreated non-small cell lung cancer with epidermal growth factor receptor exon 20 insertion mutations (WU-KONG1B). J Clin Oncol. 2025; 43(29): 3198-208. Article. IF: 44.7; D1

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- **Rosas-Alonso R, Salas NR, Wert PP, Hoyo A, Martín-López S, Martínez-Pérez D, Ruiz-Gutiérrez I, Jimenez-Bou D, Peña J, Arias P, Custodio A, Losantos-García I, Borobia AM, Feliu J, Ghanem I.** DPYD-guided fluoropyrimidine dose adjustment in colorectal cancer DPYD carriers: start slower to finish stronger. Front Pharmacol. 2025; 16: 1645188. Article. IF: 5.4; Q1
- **Chadourne M, Griffith C, Jasani N, Xu XN, Brennan E, Vera O, Mecozzi N, Wang KZ, Jaeger AM, Karreth FA.** CDH3-AS1 antisense RNA enhances P-cadherin translation and acts as a tumor suppressor in melanoma. Cell Rep. 2025; 44(10): 116362. Article. IF: 7.7; Q1
- **Rodero BS, Martínez-Toledo C, Nadal E, Molina-Alejandre M, Campelo RG, Gil-González A, Massuti B, García-Grande A, Dómine M, Insa A, Carpeño JD, Vence GH, Majem M, Martínez-Marti A, Megias D, Lobato D, Collazo-Lorduy A, Calvo V, Provencio M, Cruz-Bermúdez A.** Peripheral memory B cell population maintenance and long-term survival after perioperative chemoimmunotherapy in NSCLC (NADIM trial). Oncoimmunology. 2025; 14(1): 2513109. Article. IF: 6.2; Q1
- **Ospina-Serrano AV, González-Larriba JL, Nadal E, Trancho FH, Bosch-Barrera J, Calvo V, Bolufer-Nadal S, de la Cruz JLCC, Macía-Vidueira I, Álvarez-Kindelán A, Del Barco-Morillo E, Bernabé-Caro R, Casal-Rubio J, Cilleruelo-Ramos A, Cobo-Dols M, Dómine-Gómez M, Figueroa-Almánzar S, Insa-Mollá A, Jarabo-Sarceda JR, Jiménez-Maestre U, López-Castro R, Majem M, Martínez-Marti A, Téllez EM, Sánchez-Lorente D, López-Valcárcel M, Couñago F, García-Campelo R, de Castro J, Massuti-Sureda B, Provencio M.** Multidisciplinary approach for patients with early and locally advanced non-small cell lung cancer (NSCLC): 2nd Spanish Lung Cancer Group (GECP) expert consensus statement. Transl Lung Cancer Res. 2025; 14(9): 3299-322. Article. IF: 3.4; Q2
- **Remon J, Bironzo P, Girard N, Bigay-Game L, Juan-Vidal O, de Castro J, Reguart N, Greillier L, Cousin S, Dansin E, Majem M, Bernabe R, Martínez JM, Díaz M, Meya A, Alcalá-López D, García-Sanz A, Righi L, Novello S, Besse B.** Lenvatinib plus pembrolizumab in pretreated metastatic B3 thymoma and thymic carcinoma (PECATI): a single-arm, phase 2 trial. Lancet Oncol. 2025; 26(9): 1215-26. Article. IF: 33.7; D1
- **Gutiérrez-Sainz L, Rosas-Alonso R, Rodríguez-Antolín C, Rodríguez-Jiménez C, Rodríguez IE, Peláez R, Gomez OH, Villamayor J, Cruz-Castellanos P, Peláez-García A, de Cáceres II, Carpeño JD.** A Novel Exon 19 EGFR mutation in a patient with lung adenocarcinoma: A Case Report and Literature Review. Curr Probl Cancer Case Rep. 2025; 18: 100374. Review. IF: 0.5; Q4
- **Calles A, Alonso M, Martín-Martorell P, Gómez A, de Castro J, Martínez-Aguillo M, Estival A, Mosquera J, Martínez-Banaclocha N, Majem M, Reyes R, Azkona E, Ortega AL, Aguin S, Santos A, Aguilar A, Cucurull M, Blasco A, Calvo V, Isla D, Nadal E, Aguado C, Sais E, Juan-Vidal O, Diz-Taín M, Taus A, Villanueva N, Bayona C, Amenedo M, Mielgo X, Arriola E, Baena J.** Efficacy and safety of lorlatinib in patients with ALK-and ROS1-rearranged metastatic non-small cell lung cancer treated within the compassionate use program in Spain. Cancer Treat Res Commun. 2025; 43: 100905. Article. IF: 3.5; Q2
- **Jasani N, Xu XN, Posorske B, Kim Y, Wang KZ, Vera O, Tsai KY, Denicola GM, Karreth FA.** PHGDH induction by MAPK is essential for melanoma formation and creates an actionable metabolic vulnerability. Cancer Res. 2025; 85(2): 314-28. Article. IF: 22.6; D1

Research projects

- **Cruz Castellanos P.** APP Respira. Boehringer Ingelheim España S.A. 2019-Ongoing. Managment centre: FIBHULP
- **Vera Puente O.** Primera bioherramienta para la normalización del contenido exosomal en biopsia líquida y su aplicabilidad clínica para la estratificación y diagnóstico de pacientes con cáncer de pulmón. FIBHULP. 2021-Ongoing. Managment centre: FIBHULP
- **Vera Puente O.** Early molecular nanodiagnostics of brain tumors using inmune-pet (PLEC2021-008034). MICINN. 2021-2025. Managment centre: FIBHULP
- **de Castro Carpeño J.** Estudio de la plasticidad tumoral epigenética a través de la carcinogénesis y progreción del CPNM en biopsia líquida setup (PI21/00145). ISCIIII. 2022-2026. Managment centre: FIBHULP
- **de Castro Carpeño J.** INtegrative GENomic, digital Imaging and clinical information towars Precision Oncology Optimization – INGENIO. (PMP21/00107). ISCIIII. 2022-2026. Managment centre: FIBHULP
- **Vera Puente O.** Integrated services for infectious diseases outbreak research. UE. 2022-2025. Managment centre: FIBHULP
- **de Castro Carpeño J.** Identificación de nuevos mecanismos genéticos y epigenéticos de resistencia a la inmunoterapia de primera linea en pacientes con cáncer de pulmón no microcítico metastásico (CPNMm) con alta expresión pd-l1. Estudio KEYPREDICT. Fundacion Mutua Madrileña. 2022-2027. Managment centre: FIBHULP
- **Rosas Alonso R.** Estudio de nuevas variantes asociadas a toxicidad por fluoropirimidinas (2022.184). Fundación José Luis Castaño para el Desarrollo del Laboratorio Clínico. 2022-Ongoing. Managment centre: FIBHULP
- **Rodríguez Antolín C.** Evaluación del perfil de hipermetilación de micrornas para la estimación de riesgo de cáncer de pulmón en pacientes con EPOC (PI22/01764). ISCIIII. 2023-2026. Managment centre: FIBHULP
- **Rosas Alonso R.** Farmacogenética de inhibidores tirosina-quinasa en cáncer de pulmón: medicina de precisión más allá de un solo gen (PI22/00128). ISCIIII. 2023-2026. Managment centre: FIBHULP
- **de Castro Carpeño J.** SurvAI: plataforma web para la automatización de la anotación, clasificación e interpretación de variantes genéticas en cáncer a través de algoritmos basado en deep learning. predicción de supervivencia y efecto de variantes de significado incierto (DTS22/00145). ISCIIII. 2023-2027. Managment centre: FIBHULP
- **Vera Puente O.** Validación clínica en biopsia líquida de una firma genética y epigenética como herramienta pronóstica frente a quimioinmunoterapia en pacientes con cáncer de pulmón (CPP2022-009545). ISCIIII. 2024-2026. Managment centre: FIBHULP
- **Vera Puente O.** Dinamización de ciencia disruptiva en predictores de enfermedades tumorales, infecciosas y hereditarias como base de la medicina personalizada (FORT23/00006_GRUPO III). ISCIIII. 2024-2027. Managment centre: FIBHULP
- **Vera Puente O.** Caracterización de las funciones inmunosupresoras de mafg en melanoma y sus potenciales implicaciones para la terapia del cáncer (GEM2023_OVP). Grupo Español Multidisciplinar de Melanoma. 2024-2025. Managment centre: FIBHULP
- **de Castro Carpeño J.** cáncer de pulmón de célula pequeña. de las redes biológicas a la terapia personalizada: apoyo a iniciativas dirigidas a pacientes, prevención y divulgación. Fundación Asociación Española Contra el Cáncer. 2024-2025. Managment centre: FIBHULP
- **de Castro Carpeño J.** The European Comprehensive Cancer Centre Network. UE. 2024-2028. Managment centre: FIBHULP
- **Vera Puente O.** Caracterización de epi-marcadores de la rigidez del estroma tumoral en vesículas extracelulares en cáncer de pulmón no microcítico (PI24/00291). ISCIIII. 2025-2027. Managment centre: FIBHULP
- **Rosas Alonso R.** Optimización del tratamiento con inmunoterapia en pacientes con cáncer de pulmón mediante la integración de biomarcadores farmacogenéticos y proteómicos (optinmun) (2025.325). FIBHULP. 2025-Ongoing. Managment centre: FIBHULP

Ciber and Retics

- **de Castro Carpeño J.** Dinamización e innovación de las capacidades industriales del SNS y su transferencia al sector productivo. ISCIII. (31/12/2026). FIBHULP
- **de Castro Carpeño J.** The European Comprehensive Cancer Centre Network. (EUnetCCC). ISCIII. (46387). FIBHULP

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Clinical trials

- **de Castro Carpeño J.** Estudio en fase II abierto, de un solo grupo y multicéntrico para evaluar la eficacia y la seguridad de taletrectinib en pacientes con cpnm ros1 positivo avanzado o metastásico y otros tumores sólidos.
  Type/Phase: II
  Sponsored by: Anheart Therapeutics Inc.
  Signature date: 15/08/2025
- **de Castro Carpeño J.** A phase III, randomized, double-blind, multicenter, global study of rilvegostomig or pembrolizumab in combination with platinum-based chemotherapy for the first-line treatment of patients with metastatic non-squamous non-small cell lung cancer whose tumors express pd-l1 (artemide-lung03)".
  Type/Phase: III
  Sponsored by: Astrazeneca Ab.
  Signature date: 30/10/2025
- **de Castro Carpeño J.** Estudio fase III, aleatorizado, doble ciego, controlado con placebo que evalúa la eficacia y seguridad de pembrolizumab más quimioterapia basada en doblete de platino con o sin canakinumab, como terapia de primera línea para pacientes con cáncer de pulmón de células no pequeñas escamoso o no escamoso, localmente avanzado o metastásico (canopy-1) c".
  Type/Phase: III
  Sponsored by: Novartis Farmaceutica, S.A..
  Signature date: 23/06/2025
- **de Castro Carpeño J.** Estudio de fase ib/II, abierto y aleatorizado de vudalimab en combinación con quimioterapia o pembrolizumab en combinación con quimioterapia como tratamiento de primera línea en pacientes con cáncer de pulmón no microcítico avanzado.
  Type/Phase: II
  Sponsored by: Xencor Inc.
  Signature date: 15/07/2025
- **de Castro Carpeño J.** Estudio de fase III aleatorizado, controlado y multirregional de ivonescimab en combinación con quimioterapia frente a pembrolizumab en combinación con quimioterapia para el tratamiento de primera línea del cáncer de pulmón no microcítico escamoso metastásico (harmoni-3).
  Type/Phase: III
  Sponsored by: Summit Therapeutics, Inc.
  Signature date: 06/06/2025
- **de Castro Carpeño J.** Estudio en fase III, multicéntrico, aleatorizado y sin enmascaramiento de ifinatamab deruxtecán (i-dxd), un conjugado anticuerpo-fármaco (caf) b7-h3 frente al tratamiento elegido por el médico (tpc) en participantes con carcinoma pulmonar de células pequeñas (cpcp) recidivante (ideate-lung02)".
  Type/Phase: III
  Sponsored by: DaIIchi Sankyo Inc.
  Signature date: 07/08/2025
- **de Castro Carpeño J.** Phase 1/2, open-label, multicenter, first-in-human study of ds-3939a in subjects with advanced solid tumors.
  Type/Phase: I
  Sponsored by: DaIIchi Sankyo Inc.
  Signature date: 17/10/2025
- **Gutiérrez Sainz L.** Estudio descriptivo de la evolución en el diagnóstico y tratamiento de pacientes con cáncer microcítico de pulmón en españa" con código clarisse.
  Type/Phase: EOm no prospectivo
  Sponsored by: Investigacion Sobre Cancer De Pulmones En Mujeres Icapem.
  Signature date: 14/08/2025
- **de Castro Carpeño J.** Phase 1b/2 trial of omtx705, an anti-fibroblast activation protein antibody-drug conjugate, in combination with carboplatin, pemetrexed and tislelizumab in patients with advanced/metastatic non-squamous non-small cell lung cancer.
  Type/Phase: I
  Sponsored by: Oncomatryx Biopharma, S.L.
  Signature date: 25/11/2025
- **de Castro Carpeño J.** Estudio en fase I, abierto, de escalada y ampliación de la dosis para evaluar la seguridad, la tolerabilidad, la farmacocinética, la farmacodinámica y la eficacia preliminar de d3s-001 en monoterapia en sujetos con tumores sólidos avanzados con mutación p.g12c en kras.
  Type/Phase: I
  Sponsored by: D3 Bio.
  Signature date: 20/06/2025
- **de Castro Carpeño J.** An open-label, randomized phase 3, global multi-center trial to assess the efficacy and safety of zipalertinib (tas6417) plus pemetrexed and cisplatin or carboplatin, versus pemetrexed and cisplatin or carboplatin, in patients with previously untreated, locally advanced or metastatic non-squamous non-small cell lung cancer (nsclc) with epidermal growth factor receptor (egfr) exon 20 insertion (ex20ins) mutations.
  Type/Phase: III
  Sponsored by: Taiho Oncology, Inc.
  Signature date: 13/06/2025
- **de Castro Carpeño J.** Estudio de fase III aleatorizado, abierto, para evaluar la eficacia y seguridad de divarasib y pembrolizumab comparado con pembrolizumab y pemetrexed más carboplatino o cisplatino en pacientes con cáncer de pulmón no microcítico no escamoso con mutación kras g12c, avanzado o metastásico, no tratados previamente (krascendo 2).
  Type/Phase: III
  Sponsored by: F.Hoffmann-La Roche Ltd.
  Signature date: 17/10/2025
- **de Castro Carpeño J.** Ensayo abierto, multicéntrico, aleatorizado, de fase III de trastuzumab deruxtecán en combinación con pembrolizumab frente a quimioterapia basada en platino en combinación con pembrolizumab como tratamiento de primera línea en participantes con cáncer de pulmón no microcítico, no escamoso, localmente avanzado irresecable o metastático, con sobreexpresión de her2 y tps de pd-l1 <50 % (destiny-lung06).
  Type/Phase: III
  Sponsored by: DaIIchi Sankyo Inc.
  Signature date: 02/09/2025
- **de Castro Carpeño J.** Estudio en fase III, aleatorizado y abierto para evaluar zimberelimab y domvanalimab en combinación con quimioterapia frente a pembrolizumab con quimioterapia, como tratamiento de primera línea de pacientes con cáncer de pulmón no microcítico metastásico sin aberraciones tumorales genómicas del receptor del factor de crecimiento epidérmico ni de la quinasa del linfoma anaplásico.
  Type/Phase: III
  Sponsored by: Gilead Sciences Inc.
  Signature date: 27/03/2025
- **Rosas Alonso R.** optimización del tratamiento con inmunoterapia en pacientes con cáncer de pulmón mediante la integración de biomarcadores farmacogenéticos y proteómicos (optinmun).
  Type/Phase: EPA-SP
  Sponsored by: Rosas Alonso, Rocío.
  Signature date: 19/05/2025
- **de Castro Carpeño J.** A randomized, double-blind, placebo-controlled, multi-regional phase III clinical study of toripalimab alone or in combination with tifcemalimab (js004/tab004) as consolidation therapy in patients with limited-stage small cell lung cancer without disease progression following chemoradiotherapy.
  Type/Phase: III
  Sponsored by: Shanghai Junshi Biosciences Co, Ltd.
  Signature date: 03/03/2025
- **de Castro Carpeño J.** Estudio de fase 2, multicéntrico, de linfocitos infiltrantes de tumores autólogos (In-145) en pacientes con cáncer de pulmón no microcítico metastásico.
  Type/Phase: II
  Sponsored by: Iovance Biotherapeutics, Inc..
  Signature date: 09/07/2025
- **de Castro Carpeño J.** A phase IIIb study of durvalumab as consolidation treatment for patients diagnosed with limited stage small cell lung cancer who have not progressedfollowing definitive concurrent or sequential platinum-based chemoradiation therapy in spain (alboran).
  Type/Phase: IIIb
  Sponsored by: Astrazeneca Farmaceutica Spain S.A..
  Signature date: 09/06/2025
- **de Castro Carpeño J.** Estudio de fase II, multicéntrico, aleatorizado, abierto, para evaluar la seguridad y la eficacia de bms-986504 en monoterapia en participantes con cáncer de pulmón no microcítico (cpnm) avanzado o metastásico con deleción homocigótica de mtap después de la progresión a tratamientos previos.
  Type/Phase: II
  Sponsored by: Bristol Myers Squibb S.A.U..
  Signature date: 01/10/2025

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- **de Castro Carpeño J.** Rasolve 301: phase 3 multicenter, open label, randomized study of rmc-6236 versus docetaxel in patients with previously treated locally advanced or metastatic ras[mut] nsclc.
  Type/Phase: III
  Sponsored by: Revolution Medicines Inc.
  Signature date: 08/10/2025
- **de Castro Carpeño J.** A phase III, open-label, sponsor-blind, randomized study of dato-dxd with or without osimertinib versus platinum-based doublet chemotherapy for participants with egfr-mutated locally advanced or metastatic non-small cell lung cancer whose disease has progressed on prior osimertinib treatment (tropion-lung15).
  Type/Phase: III
  Sponsored by: Astrazeneca Ab.
  Signature date: 12/06/2025
- **de Castro Carpeño J.** Estudio pantumoral para el tratamiento a largo plazo de pacientes de cáncer que han participado en ensayos de investigación patrocinados por bms de nivolumab y otros tratamientos contra el cáncer.
  Type/Phase: II
  Sponsored by: Bristol Myers Squibb S.L.
  Signature date: 26/06/2025
- **de Castro Carpeño J.** Estudio fase 3 aleatorizado de la combinación de amivantamab y lazertinib frente a osimertinib como tratamiento de primera línea en pacientes con cáncer de pulmón no microcítico ocalmente avanzado o metastásico con mutación del egfr. mariposa.
  Type/Phase: III
  Sponsored by: Janssen Cilag International Nv.
  Signature date: 25/12/2025
- **de Castro Carpeño J.** Estudio de plataforma de fase 2, aleatorizado, abierto que utiliza el protocolo maestro para evaluar nuevas combinaciones con inmunoterapia en participantes con cáncer de pulmón no microcítico localmente avanzado/metastásico, seleccionados según la expresión del ligando de muerte programada 1, que no han recibido tratamiento previo.
  Type/Phase: II
  Sponsored by: Glaxosmithkline Research And Development Limited ,.
  Signature date: 13/01/2025
- **de Castro Carpeño J.** A phase III, randomized, double-blind, multicenter, global study of rilvegostomig or pembrolizumab in combination with platinum-based chemotherapy for the first-line treatment of patients with metastatic non-squamous non-small cell lung cancer whose tumors express pd-l1 (artemide-lung03)".
  Type/Phase: III
  Sponsored by: Astrazeneca Ab.
  Signature date: 25/04/2025
- **de Castro Carpeño J.** A phase i/IIa first-in-human single-arm open-label multicentre clinical trial to investigate the safety, tolerability, pharmacokinetics and anti-tumour activity of ascending doses of a cisplatin-based formulation administered as dry powder for inhalation in combination with first line standard of care in patients with stage iv non-small cell lung cancer.
  Type/Phase: IIa
  Sponsored by: Inhatarget Therapeutics, Srl.
  Signature date: 08/01/2025

Patents and trademarks

- **Perona Abellón R, Sánchez Pérez I, Machado Pinilla R, Sastre Garzón L, Murguía Ibáñez JR, inventors; CSIC, UAM, Universidad Politécnica de Valencia, assignees.** Sequence of nucleotides and peptides GSE 24.2 of dyskerin, which can induce telomerase activity, method for obtaining same, therapeutic compositions and applications thereof. P200502511, PCT/ES2006/070152, EP1947175, US20090202503, US2015337022, AT469212, CA2625981, DK1947175, JP2009511036, JP5560398, PT1947175; 2005 October 14.
- **Perona Abellón R, Sastre Garzón L, Machado Pinilla R, Sánchez Pérez I, inventors; CSIC, UAM, assignees.** Use of inductor agents GSE24.2 for producing pharmaceutical compositions for treating illnesses relating to cellular senescence. P200703106, PCT/ES2008/070212, EP2216043, US2011300115, JP2011504483, CA2706467; 2007 November 23.
- **Cejas Guerrero P, González Barón M, Casado Sáenz E, Sánchez Hernández JJ, Perona Abellón R, inventors; FIBHULP, UAM, CSIC, assignees.** Use of trefoil factor family 3 (TFF3) in the prognosis of patients diagnosed with colorectal cancer. P200703230, PCT/ES2008/000757, EP2236625; 2007 December 04.
- **Cejas Guerrero P, Belda Iniesta C, Feliú Batlle J, González Barón M, de Castro Carpeño J, Casado Sáenz E, Sánchez Hernández JJ, inventors; FIBHULP, UAM, assignees.** Genomic fingerprint for the prognosis of the evolution of colorectal adenocarcinoma. P200703229, PCT/ES2008/000756, EP2236626; 2007 December 04.
- **Cejas Guerrero P, Belda Iniesta C, Feliú Batlle J, de Castro Carpeño J, Moreno García V, Burgos Lizalde E, Casado Sáenz E, Sánchez Hernández JJ, inventors; FIBHULP, UAM, Empresa Pública Hospital del Norte, assignees.** Genomic fingerprint for predicting the clinical response to an antitumor therapy in colorectal cáncer. P201130863, PCT/ES2012/070379; 2011 May 26.
- **Martínez Máñez R, Murguía Ibáñez JR, Perona Abellón R, Agostini A, Mondragón Martínez L, Moreno Torres M, Manguán García C, Marcos Martínez MD, Soto Camino J, Sancenón Galarza F, inventors; Universidad Politécnica de Valencia, CSIC, Centro de Investigación Biomédica en Red en Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Centro de Investigación Biomédica en Red de Enfermedades Raras (CIBERER), assignees.** Release of substances into senescent cells. P201231370, PCT/ES2013/070581, EP2893923, JP2015529216, US2015306037; 2012 September 04.
- **Ibáñez de Cáceres I, Belda Iniesta C, Pernía Arias O, Perona Abellón R, Cortés Sempere M; inventors.** FIBHULP, CSIC, UAM, Fundación Hospital de Madrid, assignees. Method for predicting the response to a treatment consisting of radiotherapy combined with cisplatin-based chemotherapy. P201330783, PCT/ES2014/070433, EP3006572, US20160122828; 2013 May 29.
- **Perona Abellón R, Sastre Garzón L, Pintado Berninches L, Carrillo García J, Molina Pachón A, Irradiccio Silva L, Manguán García C, inventors; CSIC, UAM, Advanced Medical Projects, Centro de Investigación Biomédica en Red (CIBER), assignees.** Peptides derived from GSE 24.2 for treating diseases caused by oxidative stress and damage to DNA. P201331573, AU2014338820, CA2931429, EP3061815 PCT/ES2014/070803; 2013 October 25.
- **Ibáñez de Cáceres I, Pernía Arias O, de Castro Carpeño J, Vera Puente O, Jiménez Hernández J, Perona Abellón R, Rojo Todo F, inventors; FIBHULP, CSIC, UAM, Instituto de Investigación Sanitaria FJD, assignees.** Determination of methylation and miRNA levels in response to a platinum-based antitumor compound. P201530997, PCT/ES2016/070516; 2015 July 09.
- **Ibáñez de Cáceres I, de Castro Carpeño J, Vera Puente O, Pernía Arias O, Rodríguez Antolín C, González Muñoz VM, Martín Palma ME, Salgado Figueroa AM, inventors; FIBHULP, FIBIOHRC, assignees.** MAFG as a potential therapeutic target to restore chemosensitivity in platinum-resistant cancer cells. EP17382610.8 (Publication Number pending), PCT/EP2018/068156; 2017 September 15.
- **Ibáñez de Cáceres I, de Castro Carpeño J, Jiménez Hernández J, Rodríguez Antolín C, Rodríguez Jiménez C, Rosas Alonso R, Cruz Castellanos P, Burdiel Herencia M, Pernía Arias O, Diestro Tejada MD, Esteban Rodríguez MI, inventors; FIBHULP, assignee.** miR-151A-3p as an universal endogenous control for exosome cargo normalization. EP19382252.5 (Publication Number pending); 2019 April 05.
- **Ibáñez de Cáceres I, de Castro Carpeño J, Rosas Alonso R, Pernía Arias O, Martínez Marín V, Esteban Rodríguez MI, inventors; FIBHULP, assignee.** Method for determining the percentage of methylation of the promoter of the gene O6-methylguanine-DNA methyltransferase (MGMT) in circulating exosomes. EP19382299.6 (Publication Number pending); 2019 April 16.
- **Ibáñez de Cáceres I, de Castro Carpeño J, Jiménez Hernández J, Rodríguez Antolín C, Vera Puente O, Rosas Alonso R, Pernía Arias O, Losantos García I, inventors; FIBHULP, assignee.** Method for determining the response to treatment of a patient affected by non-small cell lung carcinoma (NSCLC). EP19382614.6 (Publication Number pending); 2019 July 19.

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