3.6.5 Translational Research in Maxillofacial Surgery and Head and Neck Cancer Group

Publications:5 | **Q1:**2

COMPOSITION

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- **José Luis del Castillo Pardo de Vera.** Facultativo Especialista de Área en Cirugía Oral y Maxilofacial. Hospital Universitario La Paz
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- **Marta Mascarque Checa.** Investigadora Postdoctoral. Contrato Sara Borrel. FIBHULP
- **María José Morán Soto.** Facultativo Especialista de Área en Cirugía Oral y Maxilofacial. Hospital Universitario La Paz
- **Marta María Pampín Martínez.** Facultativo Especialista de Área en Cirgía Oral y Maxilofacila. Hospital Universitario La Paz
- **César Pérez-Pérez Brotons.** Bioinformático. FIBHULP
- **Elena Ruiz Bravo-Bruguillos.** Facultativo Especialista de Área en Anatomía Patológica. Hospital Universitario La Paz
- **Alejandro San Lorenzo Vaquero.** Investigadora Predoctoral. FIBHULP
- **Rocío Sánchez Siles.** Investigadora Predoctoral. FIBHULP

STRATEGIC OBJECTIVE

- To improve the diagnosis and surgical treatment of patients with Oral Cancer using the latest technologies applied to the field of Head and Neck Oncology planning and treatment. Our goal is to establish a workflow in which technological and technical advances are included as part of the treatment protocol for patients with oral cavity cancer.
- The identification of biomarkers of cancer progression and therapy response in head and neck cancers (HNC). HNC are low frequent tumors with poor outcome and limited treatment options. This is due to a poor understanding on the initial steps in tumor initiation and progression, and the implication of the tumor microenvironment in these processes. Using mouse models and novel patient derived organoid models, we are defining the mechanism driving the most aggressive HNC and developing this knowledge into translational tools to guide patient management. In addition, we are applying novel functional genomics to identify genes involved in driving resistance to chemo and targeted therapies, to uncover biomarkers of treatment response and new therapeutic targets. Overall, our goal is to improve patient survival and to increase patient life quality.

RESEARCH LINES

1. Epigenetic characterization of oral tumors and their association with resistance to chemotherapies and immunotherapies, identification of new biomarkers that predict response: Oral squamous cell carcinomas are an aggressive type of HNC with 370.000 cases per year and 50% 5-year survival rate. This is due to the lack of understanding of the biology of the disease and, in consequence, sufficiently efficient therapies. In this line, we are carrying out an epigenetic characterization of these tumors, analyzing characteristics such as their transcriptome and enhancer landscape using novel massive sequencing techniques on patient samples. Through bioinformatics analysis and monitoring the evolution of patients, we uncovered a population of cancer cells that associates with the most aggressive cancers and predicts patients with worse outcomes. Currently we are evaluating the translational impact of these findings. This research line is funded by CP19/00063 and PI20/00329 (ISCIII) and a Luis Álvarez PI5102 grant (FIBHULP).
2. Search for vulnerabilities in oral carcinoma cells using functional genomics. To define the vulnerabilities of tumor cells, our group has established CRISPR/Cas9 screens to evaluate the function of genes involved in the response to different therapies such as chemotherapies or immunotherapies. These screens, which target all protein-coding genes, are allowing us to identify in an unbiased way mechanisms of action that will allow us to understand how cells survive chemotherapy or how they are able to escape the action of the immune system. In this way, we will be able to reuse drugs already approved for these targets or design new ones that will allow us to improve the quality of life of patients with oral tumors. This research line is funded by CP19/00063 and PI20/00329 (ISCIII).

3. The implication of the tumor microenvironment in the acquisition of metastatic capacity of oral tumors. In this research line we are analyzing the connection between tumor microenvironment and the induction cancer progression programs. To this end, we are using novel co-cultures of paired organoids and TME cells from patients and measuring the influence at the level of chromatin remodeling and gene expression. This research is financed by an international competitive grant funded by the Worldwide cancer research and Scientific Foundation of the "Asociación Española Contra el Cáncer" (WWRC-23-0272), and FIBHULP Luis Álvarez grant.
4. Salivary glands malignancies. Salivary gland tumors are rare tumors that account for 5% of head and neck tumors. Their histological diversity and the lack of knowledge of the molecular basis of the disease make their treatment complex. Using NGS techniques we are characterizing the mutations, methylation profiles and tumor heterogeneity of these tumors to identify biomarkers of progression, mutations with targeted therapies and possible targets within the tumor microenvironment. Funding PI22/01512, (ISCIII) and Gilead (GLD22/00166).
5. Study of mechanism of initiation and progression of cutaneous squamous cell carcinoma (cSCC): In this research line, we are exploring the function of several tumor suppressor genes and how their loss of expression affects the composition on the tumor microenvironment and the response to therapy. This project is done in collaboration with L. Sastre, at IIBM Alberto Sols.
6. Application of 3D Medicine in the planning and treatment of head and neck cancer. Virtual design and segmentation of facial structures for generation of biomodels, cutting guides and custom implants. Surgery and personalized medicine. Mutua Madrileña 2022 grant funding.
7. Use of radiotracers and fluorescence with indocyanine green for sentinel node detection in squamous tumors and melanoma of the head and neck.

RESEARCH ACTIVITY

Master theses

- **Ibáñez Herrera B.** Caracterización del papel del gen DUSP1 en la progresión de cáncer escamoso de glándula salival[dissertation]. *Madrid: UCM: 2023(03/01/2023). Director: Sastre Perona A.*

Final Degree Theses

- **San Lorenzo A.** Regulación de la transición epitelio mesénquima parcial en cáncer oral: el papel de TGFβ y los fibroblastos asociados al cáncer [dissertation]. *Madrid: UAM: 2023(14/06/2023). Director: Sastre Perona A.*
- **López García I.** Identificación de mecanismos de resistencia a quimioterapias en tumores de cabeza y cuello [dissertation]. *Madrid: UAM: 2023(30/06/2023). Director: Sastre Perona A.*

Publications

- **Burdiel M, Jiménez J, Rodríguez-Antolín C, García-Guede A, Pernía O, Sastre-Perona A, Rosas-Alonso R, Colmenarejo J, Rodríguez-Jiménez C, Diestro MD, Martínez-Marín V, Higueras O, Cruz P, Losantos-García I, Peinado H, Vera O, de Castro J, de Cáceres II.** MiR-151a: a robust endogenous control for normalizing small extracellular vesicle cargo in human cancer. Biomark Res. 2023; 11(1): 94. Letter. IF: 9.5; D1
- **Cuéllar CN, Urmeneta AS, Marcos RL, Antúnez-Conde R, López AL, de Vera JLDP, Martín-Moro JG, Carretero JLC, Serrano FA, Orabona GD, Zamorano-León JJ, Cuéllar IN.** Prognostic value of lymph node density in lingual squamous cell carcinoma. Appl Sci(Basel). 2023; 13(9): 5611. Article. IF: 2.5; Q2
- **Cuéllar IN, Alonso SE, Serrano FA, Herrera IH, León JJZ, de Vera JLDP, López AML, Muela CM, de Frutos GA, Caicoya SO, Rial MT, Sevilla AG, Antúnez-Conde R, Carretero JLC, Alonso MIGH, Escobar JIS, García MB, Vila CN, Cuellar CN.** Depth of invasion: Influence of the latest TNM classification on the prognosis of clinical early stages of oral tongue squamous cell carcinoma and its association with other histological risk factors. Cancers (Basel). 2023; 15(19): 4882. Article. IF: 4.5; Q1
- **de Vera JLDP, Calleja JMLA, Albertos CSG, de Cevallos JGD, Carretero JLC.** Wooden clothes' pin device for trismus treatment. Brit J Oral Max Surg. 2023; 61(2): 181-2. Editorial Material. IF: 1.7; Q3
- **de Vera JLDP, Martínez MP, Niño IA, Blanco MB, Carretero JLC.** Temporomandibular joint meniscopexy using the JuggerKnot® Soft Anchor System. Brit J Oral Max Surg. 2023; 61(4): 327-8. Article. IF: 1.7; Q3

Research projects

- **Cebrián Carretero JL.** Identificación de nuevos biomarcadores de predicción de progresión en pacientes con tumores adenoides císticos y ductales de glándula salivar (PI22/01512). ISCIII. 2023-2025. *Managment centre: FIBHULP*
- **del Castillo Pardo de Vera JL.** Determinación de la relación causal entre el empleo de bifosfonatos y el desarrollo de osteonecrosis en los maxilares. Aplicación de células madre mesenquimales para su tratamiento sobre modelo experimental animal. Varios Financiadores. 2015-Ongoing. *Managment centre: FIBHULP*
- **del Castillo Pardo de Vera JL.** Expresión de moléculas inmunoreguladoras pd1/ pd-llen el carcinoma oral de células escamosas. Osteoplac Innovations S.L.U.. 2021-Ongoing. *Managment centre: FIBHULP*
- **del Castillo Pardo de Vera JL.** Repositorio de biomodelos en traumatología: una biblioteca 3D multidisciplinar y colaborativa (AP180652022). Fundación Mutua Madrileña. 2022-2024. *Managment centre: FIBHULP*
- **Sastre Perona A.** Contrato garantía juvenil Ayudante de Investigación (PEJ-2020-AI/BMD-17846). CM. 2021-2023. *Managment centre: FIBHULP*
- **Sastre Perona A.** Contrato garantía juvenil Ayudante de Investigación (PEJ-2023-AI/SAL-GL-27700). CM. 2023-2025. *Managment centre: FIBHULP*
- **Sastre Perona A.** Contrato garantía juvenil Técnico (PEJ-2021-TL/BMD-21631). CM. 2022-Ongoing. *Managment centre: FIBHULP*
- **Sastre Perona A.** Desarrollo de herramientas predictivas y terapeúticas para combatir la resistencia a cisplatino en carcinomas escamosos de cabeza y cuello (PI20/00329). ISCIII. 2021-2023. *Managment centre: FIBHULP*
- **Sastre Perona A.** Desarrollo de métodos de predicción de la respuesta a inmunoterapia en tumores orales. (PI-5102). FIBHULP. 2022-Ongoing. *Managment centre: FIBHULP*
- **Sastre Perona A.** Devoloping therapeutic and predictive tools to overcome cisplatin resistance in head and neck squamous cell carcinomas (CP19/00063). ISCIII. 2020-2023. *Managment centre: FIBHULP*
- **Sastre Perona A.** Dinamización de Ciencia Disruptiva en Predictores de Enfermedades tumorales, infecciosas y hereditarias como base de la Medicina Personalizada (FORT23/00006). ISCIII. 2024-2027. *Managment centre: FIBHULP*
- **Sastre Perona A.** Integración de las características moleculares, genómicas, morfológicas, y ambientales para mejorar el diagnóstico y tratamiento de precisión en enfermedades pulmonares intersticiales difusas fibrosantes(PRECISION-EPID) (PMP22/00083). ISCIII. 2023-2025. *Managment centre: FIBHULP*
- **Sastre Perona, A.** Contrato Sara Borrel (CD23/00167). ISCIII. 2024-2026. *Managment centre: FIBHULP*
- **Sastre Perona, A.** Defining CAF-induced tumor cell plasticity as a positive switch for tumor progression and therapy resistance. (WWCR-23-0272). Worldwide Cancer Research AECC. 2023-2025. *Managment centre: CSIC*

Clinical trials

- **Cebrian Carretero JL.** A randomized, double-blind, multi-center, placebo-controlled, parallel-group phase 3 study to compare the efficacy, acceptability, and safety of tranexamic acid oral solution with placebo in the prevention of clinically relevant bleeding events in subjects treated with direct oral anticoagulants or vitamin k antagonists and undergoing a single or multiple tooth extraction.
  Type/Phase: III
  Sponsored by: Hyloris Developments S.A.
  Signed date: 18/10/2023
- **Cebrian Carretero JL.** Ensayo clínico aleatorizado, doble ciego, controlado con placebo y con tratamiento activo, para evaluar la eficacia analgésica y la seguridad de una combinación oral de ibuprofeno (arginina)-tramadol hcl administrada a pacientes con dolor moderado a severo tras someterse a cirugía dental.
  Type/Phase: III
  Sponsored by: Farmalider S.A.
  Signed date: 17/04/2023