



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

Publications: 17 | Q1: 6

### COMPOSITION

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- **César Pérez-Pérez Brotons.** Bioinformático. FIBHULP
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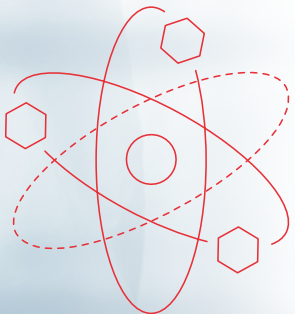
### STRATEGIC OBJETIVES

- 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.

3 Research areas and groups



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

### Publications

- Acero-Riaguas L, Griso-Acevedo AB, SanLorenzo-Vaquero A, Ibáñez-Herrera B, Fernández-Díaz SM, Mascaraque M, Sánchez-Siles R, López-García I, Benitez-Buelga C, Bravo-Burquillos ER, Castelo B, Cebrián-Carretero JL, Perona R, Sastre L, Sastre-Perona A. DUSP1 and SOX2 expression determine squamous cell carcinoma of the salivary gland progression. *Sci Rep-Uk*. 2024; 14(1): 15007. Article. IF: 3.9; Q1
- Álvaro-Martínez M, Cuesta-Urquía C, Ortiz-Peces L, Noguera-Tomas J, González-Otero T, Cebrián-Carretero JL. Venous malformation differential diagnosis with an odontogenic abscess on a pediatric patient. Case report and review of the literature. *J Clin Exp Dent*. 2024; 16(3): e387-90. Case Reports. Not Indexed
- Anguita MB, de Vera JLDP, Khayat S, López AML, Moro JGM, de Frutos GA, Hidalgo RAC, Martínez MP, Larren EG, Cuéllar CN, Carretero JLC, Cuéllar IN. Mandibular Fractures in Edentulous Patients with Bone Atrophy and Osseointegrated Dental Implants: Therapeutic Management in a Case Series. *Med Lith*. 2024; 60(11): 1835. Article. IF: 2.4; Q1
- Aragón-Niño I, Del Castillo-Pardo-de Vera JL, Gutiérrez-Venturini A, Pampín-Martínez MM, López-Martínez C, Cebrián-Carretero JL. Surface scanned 3D designed customized chinstrap for the treatment of intraoral dehiscence in polytraumatized patient. Technical note. *J Clin Exp Dent*. 2024; 16(2): e240-2. Article. Not Indexed
- Aragón-Niño I, Pardo-de Vera JLC, Garrido-Martínez P, Losa-Muñoz PM, Moreiras-Sánchez AD, Cebrián-Carretero JL. Interdisciplinary innovative approach to an aggressive ossifying fibroma case: Integrating 3D surgery and customized reconstruction in maxillofacial and dental care. *J Clin Exp Dent*. 2024; 16(5): e661-5. Article. Not Indexed
- Arranz-Martín B, del-Castillo-Pardo-de-Vera JL, Cebrián-Carretero JL, Rouco-García D, Fernández-Oliva C, Gil-Martínez A. Quality of life, craniomandibular function, and psychosocial factors related to pain and movement in patients with head and neck cancer. *Support Care Cancer*. 2024; 32(6): 334.

Article. IF: 3; D1

- Cobos MT, Salinas BT, Venturini AG, Nino IA, de Vera JLDP, Carretero JLC, Orejon RU. The application of three-dimensional printing in the management of a difficult airway due to Treacher Collins syndrome. *Anaesth Rep*. 2024; 12(1): e12290. Article. IF: 0.8; Q3
- de Vera JLDP, Carretero JLC, Niño IA, Martínez MMP, Gómez JTB, Cuéllar IN, López AML, Larren EG, Vila CN, Fernández-Micheltoarena PM, Sala AP, Cuéllar CN. Virtual Surgical Planning for Temporomandibular Joint Reconstruction with Stock TMJ Prostheses: Pilot Study. *Med Lith*. 2024; 60(2): 339. Article. IF: 2.4; Q1
- Gil FM, Artal PM, de Llano ACO, Guerra MM, Ballester DG, Arcas JML, Cedrun JLL, Pérez JLG, Martín-Granizo R, de Vera JLDP, Medina BG, González-García R, Sánchez MM, Rodríguez EV, SanRomán JF, Martos RL, Cagigal BP, Alamillos MR, Mas MM, Gil CS, Medina BR, Ontanon AV, Gridilla JM, Ferrer AD. Consensus Report and Recommendations on the Management of Late-stage Internal Derangement of the Temporomandibular Joint. *J Clin Med*. 2024; 13(11): 3319. Article. IF: 2.9; Q1
- López-Martínez C, Pampín-Martínez MM, García-López-Chicharro A, Aragón-Niño I, Cebrián-Carretero JL. Application of 3D technology for the design of a guidewire for deep cervicofacial collections percutaneous management. *J Clin Exp Dent*. 2024; 16(3): e383-6. Article. Not Indexed
- Niño IA, Carretero JC. Robotic surgery: A pending subject in oral and maxillofacial surgery. *J Dent Sci*. 2024; 19(2): 1282-4. Editorial Material. IF: 3.1; Q1
- Niño IA, Urquía CC, Chicharro AGL, Martínez CL, Moro JGM, Carretero JLC. Resident scientific meetings as part of the residency training curriculum: Just a hassle for the resident? *J Healthc Qual Res*. 2024; 39(3): 199-201. Letter. IF: 1.0; Q4
- Ortiz-Peces L, Álvaro-Martínez M, de Uribe-

- Vloria M, Andura-Correas M, Vázquez-Salgueiro E, Cebrián-Carretero JL. Epithelioid Hemangiioendothelioma of Mandibular Gingiva: A Challenging Diagnosis. *J Clin Exp Dent*. 2024; 16(9): e1151-6. Article. Not Indexed
- Rodríguez-Molinero J, Pozo-Kreiling JJ, Ruiz-Roca JA, López-Sánchez AF, Cebrián-Carretero JL. Clinical and Pathological Features of Osteosarcomas of the Jaws: A Retrospective Study. *Clin Pract*. 2024; 14(3): 965-79. Article. IF: 2.2; Q2
- Urquía CC, Martín-Moro JG, Niño IA, de Villota MH, Carretero JLC. Re: Re: Static retractor made from vessel loop. *Brit J Oral Max Surg*. 2024; 62(7): 661. Editorial Material. IF: 1.9; Q2
- Urquía CC, Martín-Moro JG, Niño IA, de Villota MH, Carretero JLC. Static retractor made from vessel loop. *Brit J Oral Max Surg*. 2024; 62(3): 304-5. Editorial Material. IF: 1.9; Q2
- Weng ZC, Salinas BT, Tomas JN, De Vera JLDP, Molina JDD. Anesthetic Management of a Patient with Madelung's Disease Presenting with a Giant Cervical Lipoma: A Case Report. *A Pract*. 2024; 18(4): e01779. Article. IF: 0.6; Q4

### Research projects

- Castrelo Fernández B, Sastre Perona A. Characterization of cancer-cell plasticity in head and neck cancers: discovery of new therapeutic targets and biomarkers for disease progression and treatment response (PI23/00192). ISCIII. 2024-2026. **Managment centre: FIBHULP**
- 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**
- Cebrián Carretero JL. Repositorio de biomodelos en traumatología: una biblioteca 3D multidisciplinar y colaborativa (AP180652022). Fundación Mutua Madrileña. 2022-2024. **Managment centre: FIBHULP**



## 3 Research areas and groups

### 3.6. Surgery, Transplant and Health Technologies Area

- **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 inmunoregulatoras pd1/ pd-l1 en el carcinoma oral de células escamosas. Osteoplac Innovations S.L.U. 2021-Ongoing. **Managment centre:** FIBHULP
- **Mascaraque Checa M.** Contrato Sara Borrel (CD23/00167). ISCIII. 2024-2026. **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 Ayudante de Investigación (PEJ-2023-AI/SAL-GL-27700). CM. 2024-2026. **Managment centre:** FIBHULP
- **Sastre Perona A.** Contrato garantía juvenil Técnico (PEJ-2021-TL/BMD-21631). CM. 2022-Ongoing. **Managment centre:** FIBHULP
- **Sastre Perona A.** Contrato PFIS Ana Belén Griso (FI24/00184 ). ISCIII. 2025-2028. **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
- **Sastre Perona A.** Desarrollo de herramientas predictivas y terapéuticas para combatir la resistencia a cisplatino en carcinomas escamosos de cabeza y cuello (PI20/00329 ). ISCIII. 2021-2024. **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.** Developing therapeutic and predictive tools to overcome cisplatin resistance in head and neck squamous cell carcinomas

(CP19/00063). ISCIII. 2020-2024. **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

#### Clinical trials

- **Cebrián 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 Sa  
**Signature date:** 29/05/2024

#### Patents and trademarks

- **Cuéllar Navarro C, Cebrián JL, Magaña Menéndez J, inventors; Hospital General Universitario Gregorio Marañón and Hospital Universitario La Paz, assignees.** Dispositivo de determinación de avance mandibular para un usuario con apnea. P202430809; 2024 October 8.