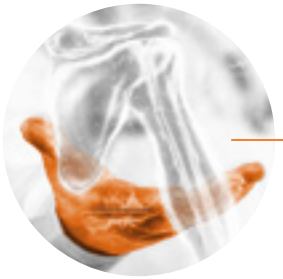


3.6.5 Translational Research in Maxillofacial Surgery and Head and Neck Cancer Group

Publications: 4
Q1: 2

COMPOSITION

José Luis Cebrián Carretero. Jefe de Servicio de Cirugía Oral y Maxilofacial. Hospital Universitario La Paz

Ana Sastre Perona. Investigadora senior. FIBHULP

Lucía Acero Riaguas. Investigadora Predoctoral. FIBHULP

Estefanía Alonso Rodríguez. Facultativo Especialista de Área en Cirugía Oral y Maxilofacial. Hospital Universitario La Paz

Sara María Fernández Díaz. Técnico de Grado Superior. FIBHULP

Javier González Martín-Moro. Facultativo Especialista de Área en Cirugía Oral y Maxilofacial. Hospital Universitario La Paz

Ana Belén Griso Acevedo. Investigadora Predoctoral. FIBHULP

José Luis del Castillo Pardo de Vera. Facultativo Especialista de Área en Cirugía Oral y Maxilofacial. Hospital Universitario La Paz

María José Morán Soto. Facultativo Especialista de Área en Cirugía Oral y Maxilofacial. Hospital Universitario La Paz

Pedro Manuel Losa Muñoz. 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

Elena Ruiz Bravo-Bruguillos. Facultativo Especialista de Área en Anatomía Patológica. Hospital Universitario La Paz

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

- 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).
- 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).
- 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.
- 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).
- 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.
- 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.
- Use of radiotracers and fluorescence with indocyanine green for sentinel node detection in squamous tumors and melanoma of the head and neck.

RESEARCH ACTIVITY

Doctoral theses

Master Theses

Griso AN. Model establishment and optimization: Assessment of tumor-CAF interplay in Oral Squamous Cell Carcinomas [dissertation]. Madrid: UCM: (07/08/202).
Director: Sastre Perona A.

Final Degree Theses

Rodriguez S. Implicación de la fosfatasa DUSP1 en la iniciación y progresión de carcinomas escamosos cutáneos [dissertation]. Madrid: UAM: (30/06/2022).
Director: Sastre Perona A.

Posse I. Identificación de nuevos mecanismos de resistencia a cisplatino en tumores de cabeza y cuello [dissertation]. Madrid: UAM: (30/06/2022).
Director: Sastre Perona A.

Publications

- Michel M, Benítez-Buelga C, Calvo PA, Hanna BMF, Mortusewicz O, Masuyer G, Davies J, Wallner O, Sanjiv K, Albers JJ, Castaneda-Zegarra S, Jemth AS, Visnes T, Sastre-Perona A, Danda AN, Homan EJ, Marimuthu K, Zhao ZJ, Chi CN, Sarno A, Wiita E, von Nicolai C, Komor AJ, Rajagopal V, Muller S, Hank EC, Varga M, Scaletti ER, Pandey M, Karsten S, Haslene-Hox H, Loevenich S, Marttila P, Rasti A, Mamonov K, Ortis F, Schomberg F, Loseva O, Stewart J, D'Arcy-Evans N, Koolmeister T, Henriksson M, Michel D, de Ory A, Acero L, Calvete O, Scobie M, Hertweck C, Vilotijevic I, Kalderen C, Osorio A, Perona R, Stolz A, Stenmark P, Berglund UW, de Vega M, Helleday T. Small-molecule activation of OGG1 increases oxidative DNA damage repair by gaining a new function. Science. 2022; 376(6600): 1471-6. Article. IF: 56,9; D1
- Peña-Cardelles JF, Pozo-Kreilinger JJ, Roncador G, Esteban-Hernández J, Moro-Rodríguez JE, Sastre-Perona A, Castelo-Fernandez B, Cebrián-Carretero JL. Prognosis value of immunoregulatory molecules in oral cancer microenvironment: an immunohistochemical study. Biomedicines. 2022; 10(3): 710. Article. IF: 4,7; Q1

- Griso AB, Acero-Riaguas L, Castelo B, Cebrián-Carretero JL, Sastre-Perona A. Mechanisms of cisplatin resistance in hpv negative head and neck squamous cell carcinomas. Cells. 2022; 11(3): 561. Review. IF: 6; Q2
- Rodríguez-Fanjul V, Guerrero-López R, Fernández-Varas B, Perona R, Sastre-Perona A, Sastre L. Comparison of colorectal cancer stem cells and oxaliplatin-resistant cells unveils functional similarities. Cells. 2022; 11(3): 511. Article. IF: 6; Q2

Research projects

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 (2022-MM-Cebrián). Fundación Mutua Madrileña. 2022-Ongoing.

Managment centre: FIBHULP

Ramírez García E, Cebrián Carretero JL. Cohorte de pacientes quirúrgicos de hulp en situación de pandemia covid-19. Versión 01 de 23.10.2020 (HULP-QoV-2020). FIBHULP. 2020-2022.

Managment centre: FIHULP

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 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.

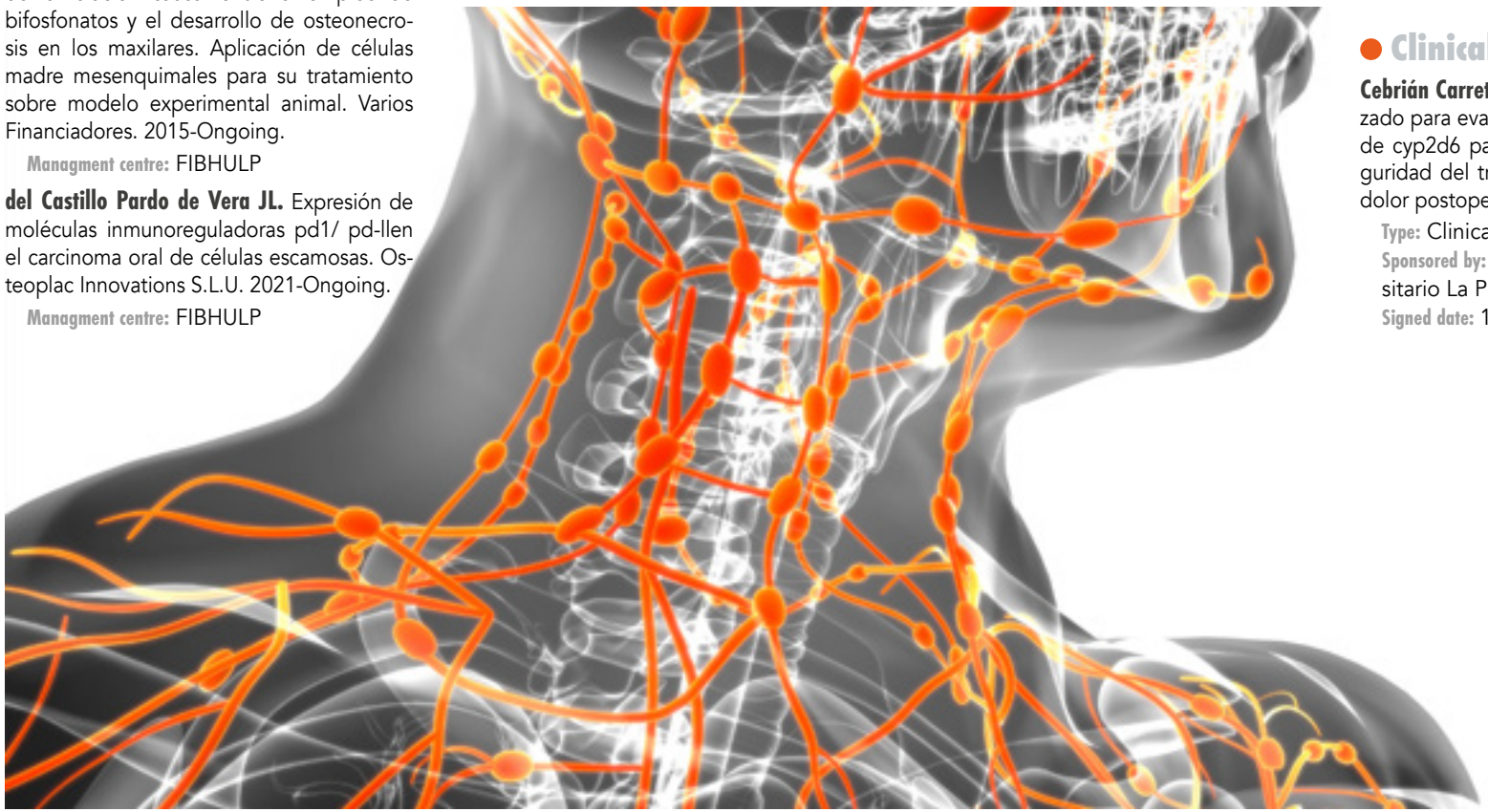
Managment centre: FIBHULP

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



Clinical trials

Cebrián Carretero JL. Ensayo clínico aleatorizado para evaluar la utilidad del genotipado de cyp2d6 para mejorar la eficacia y la seguridad del tramadol en el tratamiento del dolor postoperatorio agudo.

Type: Clinical Trials, phase IV. 6107.
Sponsored by: Fundacion Hospital Universitario La Princesa.
Signed date: 10/08/2022