

Oncogenesis and Antitumour Drugs

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DESCRIPTION

We are developing protein-based targeted nanoparticles and nanoconjugates to selectively ablate cancer stem cells and cancer-associated fibroblasts, as well as inhibitors of Immune checkpoints, to improve the current treatment of solid tumours and haematological neoplasms. We also generate immunosuppressed and immunocompetent, subcutaneous or orthotopic cancer mouse models to preclinically evaluate the anticancer effects and associated toxicities of these nanomedicines and their combinations for clinical translation and industrial transfer.

MAIN LINES OF RESEARCH

- To develop a humanised nanoconjugate of auristatin directed to leukemic stem cells for the treatment of Acute Myeloid Leukemia. Within this line, the activity of the nanoconjugate is being evaluated in new animal models derived from patient samples (PDX) and humanised murine models. We are also studying the ability of the nanoconjugate to activate the immune system and the possible synergies of its combination with other precision drugs (Casanova Rigat, Isolda).
- To design and develop protein nanodrugs for the treatment of cancer. This line seeks to offer innovative therapeutic proposals based on rational design and development of active targeted protein nanoparticles for the selective delivery of therapeutic protein domains or conjugated antitumor drugs to tumor cells (Unzueta Elorza, Ugutz).

- To develop and preclinical validation of tumor microenvironment targeted nanoparticles. This research line aims to target cancer-associated fibroblasts within solid tumors to reprogram the tumor microenvironment to reduce cancer cell aggressiveness and blocking metastatic dissemination (Alba Castellón, Lorena).
- To develop targeted nanoparticles, that incorporate bacterial toxins, to induce local tumor pyroptosis, to recruit and activate T cells in tumor and metastatic tissues, and their combination with Immune Checkpoint inhibitors and T Cell Receptor Agonists to reverse immune exhaustion, to fight microsatellite stable solid cancers (Mangues Bafalluy, Ramon).

SCIENTIFIC CHALLENGES

- To develop nanomedicines based on preclinical protocols able to achieve effective immunogenic cell death in solid tumors, which are currently resistant to Immunotherapy.
- To develop new protein nanoconjugates for targeted delivery of antitumor drugs with innovative mechanisms of action for the treatment of tumors resistant to standard drugs.
- To develop efficient protein nanovehicles for the targeted delivery of therapeutic nucleic acids to tumor cells in vivo as an alternative to viral vectors.
- To develop protein nanopharmaceuticals for the activation of the immune system against cancer as a more effective nano-immuno-oncology approach than current treatments.
- To develop targeted-nanotherapy to reprogram the tumor microenvironment to enhance its antitumor role.

ACTIVE & AWARDED GRANTS

- Alamo Vargas, Patricia Virginia. Multivalent presentation for enhanced drug-internalization and cytotoxicity of nanoparticles targeting CXCR4-overexpressing tumors. PTQ2021-

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- Alba Castellón, Lorena. Cancer-Associated Fibroblast-Targeted Nanoparticles to Improve Antimetastatic Therapy in Colorectal Cancer. POSTDOC AECC 2020. Asociación Española Contra el Cáncer (AECC). Duration: 2020-2025. 170.000,00 €
- Alba Castellón, Lorena. Contratos Miguel Servet 2024. CP24/00111. Instituto de Salud Carlos III (ISCIII). Duration: 2025-2029. 268.600,00 €
- Alba Castellón, Lorena. Safety and Efficacy Study of PDGFD-NT-H6, a Tumour Microenvironment-targeted Nanoparticle to treat Colorectal Cancer. INNOV247584ALBA. Fundación Científica de la Asociación Española Contra el Cáncer. Duration: 2024-2026. 172.000,00 €
- Mangues Bafalluy, Ramon. Eliminación selectiva de células madre de cáncer de colon mediante nanopartículas inductoras de poro, inflamación crónica e inmunidad antineoplásica (IMMUNO-FIRING). PI21/00150. Instituto de Salud Carlos III (ISCIII). Duration: 2022-2024. 244.420,00 €
- Mangues Bafalluy, Ramon. New protein-based nanodrugs for the development of targeted tumor-agnostic therapy. CPP2021-008946. Ministerio de Ciencia e Innovación (MICINN). Duration: 2022-2025. 439.367,01 €
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- Sierra Cruz, Marta. Contratos Sara Borrell 2024. CD24/00149. Instituto de Salud Carlos III (ISCIII). Duration: 2025-2027. 95.000,00 €

- Unzueta Elorza, Ugutz. Conjugación dirigida de nanomedicinas proteicas inteligentes para la mejora de la terapia selectiva del cáncer metastásico de colon. PI20/00400. Instituto de Salud Carlos III (ISCIII). Duration: 2021-2025. 171.820,00 €
- Unzueta Elorza, Ugutz. Eliminación selectiva de células madre metastásicas del cáncer colorrectal por bloqueo de la RNA polimerasa II. PI23/00318. Instituto de Salud Carlos III (ISCIII). Duration: 2023-2026. 230.000,00 €
- Unzueta Elorza, Ugutz. Nanoimmunoterapia de precisión contra células madre leucémicas CXCR4+ en Leucemia Mieloide Aguda. Fundació Investigació per a la Salut i el Progrés (FISP). FISP 2024. Duration: 2025-2026. 99.880,00 €
- Unzueta Elorza, Ugutz. Targeted Nano-immunotherapy Against CXCR+ Cancer Stem Cells. Fundació La Caixa. INPhINIT 2024. Duration: 2024-2028. 160.272,00 €
- SCIENTIFIC PRODUCTION
- Favaro MTP, Alamo P, Roher N, Chillon M, Lascorz J, Márquez M, Corchero JL, Mendoza R, Martínez C, Ferrer N, Ferreira LCS, Mangues R, Vázquez E, Parladé E, Villaverde A. Zinc-Assisted Microscale Granules Made of the SARS-CoV-2 Spike Protein Trigger Neutralizing, Antivirus Antibody Responses. ACS Materials Letters. 2024; 6(3). DOI:10.1021/acsmaterialslett.3c01643. IF:9,600 (Q1/2D). Document type: Article.
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- López H, Tsimbouri PM, Jayawarna V, Rigou I, Serna N, Voltà E, Unzueta U, Salmeron M, Vázquez E, Dalby MJ, Villaverde A. Hybrid Micro-/Nanoprotein Platform Provides Endocrine-like and Extracellular Matrix-like Cell Delivery of Growth Factors. ACS Applied Materials & Interfaces. 2024; 16(26). DOI:10.1021/acsami.4c01210. PMID:38888932. IF:8,300 (Q1/2D). Document type: Article.
- Parladé E, García A, Voltà E, Unzueta U, Mangues R, Casanova I, Villaverde A, Vázquez E. Paradoxical cell targeting of calreticulin-empowered, protein-only nanoparticles. EUROPEAN JOURNAL OF PHARMACEUTICS AND BIOPHARMACEUTICS. 2024; 202:114410. DOI:10.1016/j.ejpb.2024.114410. PMID:39004320. IF:4,400 (Q1/2D). Document type: Article.
- Sánchez JM, López H, Parladé E, Somma AD, Livieri AL, Alamo P, Mangues R, Unzueta U, Villaverde A, Vázquez E. Structural Stabilization of Clinically Oriented Oligomeric Proteins During their Transit through Synthetic Secretory Amyloids. Advanced Science. 2024; 11(21). DOI:10.1002/adv.202309427. PMID:38501900. IF:14,300 (Q1/1D). Document type: Article.
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