

Oncogenesis and Antitumour Drugs



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Main Lines of Research

- ▶ Development of novel animal models of disseminated disease in solid tumours and haematological neoplasms for the mechanistic study of metastases and preclinical drug development.
- ▶ Identification of prognostic biomarkers in head and neck squamous cell carcinoma and their functional validation in vivo.
- ▶ Development of nanoconjugates for targeted delivery of antitumour drugs or toxins to metastasis stem cells.

Challenges

- ▶ Obtain funding to ensure stable employment of senior researchers, attract post-doctoral fellows and reinforce current collaborations with clinicians.
- ▶ Develop molecular markers for therapeutic decision-making in head and neck carcinomas.
- ▶ Achieve antimetastatic effects by targeting antitumour drugs to metastasis stem cells in solid tumors and haematological neoplasias.
- ▶ Enhance international collaboration and participation in EU networks and industrial projects.

Collaborations with other IIB Sant Pau Groups

- ▶ Collaboration with Dra. Isolda Casanova and Aïda Falgàs in: Teràpia dirigida de Auristatina E o Ara-C a cèlulas de leucèmia mieloide aguda que expresen CXCR4, receptor implicado en adhesión al estroma y quimiorresistencia. PI14/00450. IP: Jordi Sierra Gil. Instituto de Salud Carlos III. Duration: 2015-2018. 172,000.00 €.
- ▶ Collaboration of Dr. Irene Arroyo with the research group of the Otorhinolaryngology Service led by the Drs. Miquel Quer and Xavier León in the study of prognostic factors in head and neck cancer.
- ▶ Collaboration of Drs. María Virtudes Céspedes and Patricia Álamo and de Rita Sala with the research groups of the Services of Pharmacy (led by Dra. María Antònia Mangués), Pathological Anatomy (led by Drs. Enrique Lerma and Alberto Gallardo), Surgery (led by Dr. Manuel Trias) and Medical Oncology (led by Drs. Agustí Barnadas and Antonio López-Pousa), and Àlex Bayés and Marta Valle groups at IIB-Sant Pau. Project: Targeted nanoconjugates for the selective elimination of stem cells in disseminated cancer. PIE15/00028. IP: Ramon Mangués. Instituto de Salud Carlos III. Duration: 2016-2018. 423,912.00 €.

National Collaborations

- ▶ Eduard Batlle, Biomedical Research Institute (IRB) and Barcelona Scientific Park (PCB).
- ▶ Antonio Villaverde, Departament de Microbiologia Aplicada, Universitat Autònoma de Barcelona (UAB).
- ▶ CB06/01/1031. Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN). Insti-

tuto de Salud Carlos III. 2008-2018. 90,000-117,000€/year.

- ▶ OncoCat. Member of the Catalan Cancer Research Network. Xarxa ConnectEU, Biocat, Generalitat de Catalunya.
- ▶ NanoBioMed. Member of the Catalan Network on Nanobiotechnology, Xarxa Connect-EU. Biocat.

International Collaborations

- ▶ Achilea Bittencourt. Visiting Researcher, International Cooperation with Brasil, MCT/CNPq 046/2010.
- ▶ Paolo Micheli, Institute for Cancer Research and Treatment, Candiol, Turin (Italy).
- ▶ Arne Östman, Cancer Center Karolinska, Karolinska Institutet, Stockholm (Sweden).
- ▶ Alberto Bardelli, University of Torino, Medical School, Turin (Italy).
- ▶ Ramon Mangués collaborates with the French Institute National du Cancer (INCa), by being Member of the Scientific Evaluation Committee of the Translational Cancer Research Programme (PRT-K) since 2016, Ministry of Health (DGOS) and
- ▶ ATMP-EATRIS, European Union. Member of the Working Group on Advanced therapies and biologicals of ATMP (Advanced Therapy Medicinal Products), EATRIS (European Infrastructure for Translational Medicine) Network.
- ▶ ETP Nanomedicine, European Union, Member of the European Technology Platform on Nanomedicine.
- ▶ TME-AACR member. Member of the Tumor Microenvironment Working Group, American Association for Cancer Research (AACR).

Collaborations

Active Grants

- ▶ Ramon Mangues Bafalluy. Grup d'oncogènesi i antitumorals (GOA). 2014 SGR 1041. Agència de Gestió d'Ajuts Universitaris i de Recerca. Duration: 2014-2017. 30,000.00 €.
- ▶ Ramon Mangues Bafalluy. Desenvolupament d un nanoconjugat antimetastàtic dirigit a cèl·lules mare metastàtiques CXCR4+. 2014 PROD 00055. Agència de Gestió d'Ajuts Universitaris i de Recerca. Duration: 2015-2017. 89,500.00 €.
- ▶ Ramon Mangues Bafalluy. Prevención de metástasis en cáncer colorrectal mediante terapia dirigida a células madre metastáticas y estromales. PI15/00378. Instituto de Salud Carlos III. Duration: 2016-2018. 172,000.00 €.
- ▶ Virtudes Céspedes Navarro. Contratos Miguel Servet I 2015. MS15/00163. Instituto de Salud Carlos III. Duration: 2016-2021. 202,500.00 €.
- ▶ Virtudes Céspedes Navarro. Nanoconjugates for targeted therapy against CXCR4+ cancer stem cells in pancreatic cancer. CP15/00163. Instituto de Salud Carlos III. Duration: 2016-2018. 121,500.00 €.
- ▶ Ramon Mangues Bafalluy. Targeted nanoconjugates for the selective elimination of stem cells in disseminated cancer. PIE15/00028. Instituto de Salud Carlos III. Duration: 2016-2018. 423,912.00 €.
- ▶ Rita Sala Faig. Contractes predoctorals de formació en investigació en salut 2016. FI16/00017. Instituto de Salud Carlos III. Duration: 2017-2020. 82,400.00 €.
- ▶ Ramon Mangues Bafalluy. Papel de las células natural killer y del receptor CXCR4 en el desarrollo de metástasis en cáncer colorrectal. IR16-P2. Fundació Privada Hospital de la Santa Creu i Sant Pau. Duration: 2017-2017. 7,000.00 €.
- ▶ Ugutz Unzueta Elorza. Contractes "Sara Borrell" 2014. CD14/00055. Instituto de Salud Carlos III. Duration: 2015-2018. 86,598.00 €.
- ▶ Ramon Mangues Bafalluy. Genotoxic nanoparticles targeting colorectal cancer stem cells. 20132030. Fundació La Marató de TV3. Duration: 2014-2017. 142,000.00 €.
- ▶ Ramon Mangues Bafalluy. Grup d'Oncogènesi i Antitumorals (GOA). 2017 SGR 865. Agència de Gestió d'Ajuts Universitaris i de Recerca. Duration: 2017-2019. 35,200.00 €.
- ▶ Carmen Cabrera Rodriguez. Ayudas para personal técnico de apoyo a infraestructuras. convocatoria 2013. Plataforma de Nanotoxicología. Centro de Investigación en Red en Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN). PTA2013-8426-I. MINECO. Duration: 2015-2017. 36,000 €.
- ▶ Ramón Mangues. Humanized antitumoral nanodrug for the treatment of CXCR4-positive cancers (CIBER-BBN Technology Transfer Program (coordinated project). Group PI and coordinator: Antonio Villaverde (NBT-UAB). Industrial Partner: Nanoligent SL. Finance Agencies: CIBER-BBN and Nanoligent SL. Nanotracer. BBN-TRF17. Duration: 2017-2018. 35,000 €.

Note: Total amount granted to PI. It does not include indirect costs.

Grants Awarded in 2017

- ▶ Aida Falgas Comamala, Avaluació de l'activitat antitumoral de nous nanoconjugats dirigits al receptor CXCR4 en Limfoma Difús de Cèl·lules Grans B (LDCGB). 2017 FI_B 00680. Agència de Gestió d'Ajuts Universitaris i de Recerca. Duration: 2017-2020. 40,806.00 €.
- ▶ Virtudes Céspedes Navarro. Terapia dirigida para la eliminación selectiva de células madre metastáticas CXCR4+ en cáncer de endometrio. FMM 2017. Fundación Mutua Madrileña. Duration: 2017-2020. 133,333.33 €.
- ▶ Virtudes Céspedes Navarro. Nanoterapia dirigida y radioterapia SBRT combinada para la eliminación selectiva de células madre tumorales en cáncer de páncreas. PI17/00150. Instituto de Salud Carlos III. Duration: 2018-2020. 123,000.00 €.
- ▶ Ramon Mangues Bafalluy. Émbolos tumorales circulantes hCXCR4/SerpinE1 en el pronóstico del cáncer de cabeza y cuello. PI17/00584. Instituto de Salud Carlos III. Duration: 2018-2020. 90,000.00 €.
- ▶ Ramon Mangues Bafalluy. Implicación de la vía CXCR4/CXCL12/CXCR7 en la resistencia, recidiva y fenotipo de célula madre de la leucemia mieloide aguda. PI17/01246. Instituto de Salud Carlos III. Duration: 2018-2020. 108,000.00 €.

Note: Total amount granted to PI. It does not include indirect costs.

Theses

- ▶ Irene Arroyo Solera. Estudio del valor pronóstico de Serpina E1 y su papel en el crecimiento y la diseminación metastática del carcinoma escamoso de cabeza y cuello. Universitat de Barcelona. Directors: Ramon Mangues and Miguel Angel Pavón. Date of defense: 24/06/2017.

Transfer Products

- ▶ Company: NANOLIGENT, SLU. (B-66970088). Spin-off of the Biomedical Research Institute Sant Pau. Founding members: M. Rodríguez-Mariscal, Ramon Mangues, Antonio Villaverde, and Esther Vázquez. Date of constitution: 03/13/2017.

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Patents

- ▶ Inventors: Antonio Villaverde, Esther Vázquez, Ugutz Unzueta, Ramon Mangues, María Virtudes Céspedes, Isolda Casanova. Owner Companies: Universitat Autònoma de Barcelona, Fundació Privada Institut de Recerca de l'Hospital de la Santa Creu i Sant Pau and Centro de Investigación Biomédica en Red. Therapeutic Nanoconjugates And Uses Thereof. European Patent Office. Application number: EP17382461, PCT. 14/07/2017.
- ▶ Inventors: Antonio Villaverde, Esther Vázquez, Naroa Serna, Laura Sánchez García, Ugutz Unzueta, Ramon Mangues, María Virtudes, Céspedes Isolda Casanova. Owner Companies: Universitat Autònoma de Barcelona, Fundació Privada Institut de Recerca de l'Hospital de la Santa Creu i Sant Pau and Centro de Investigación Biomédica en Red. Nanostructured Proteins And Uses Thereof. European Patent Office. Application Number: 17169722.0 - 1401, PCT. 05/05/2017.
- ▶ Inventors: Esther Vázquez, Ugutz Unzueta, Neus Ferrer, Antonio P. Villaverde, María Virtudes Céspedes, Isolda Casanova and Ramon Mangues. Owner Companies: Universitat Autònoma de Barcelona, Fundació Privada Institut de Recerca de l'Hospital de la Santa Creu i Sant Pau and Centro de Investigación Biomédica en Red en Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN). Methods and reagents for efficient and targeted delivery of therapeutic molecules to CXCR4 cells. European Patent: EP2663336. Reference: P6461EPPC. European Patent, PCT. 17/09/2017.

*TIF: 74.365 **MIF: 6.760

Scientific Production

- Body S., Esteve-Arenys A., Miloudi H., Recasens-Zorzo C., Tchakarska G., Moros A., Bustany S., Vidal-Crespo A., Rodriguez V., Lavigne R., Com E., Casanova I., Mangues R., Weigert O., Sanjuan-Pla A., Menendez P., Marcq B., Picquenot J.-M., Perez-Galan P., Jardin F., Roue G., Sola B., Cytoplasmic cyclin D1 controls the migration and invasiveness of mantle lymphoma cells (2017) SCI REP-UK, 7 (1). **IF: 4.122**
- Mira A., Morello V., Céspedes M.V., Perera T., Comoglio P.M., Mangues R., Michieli P., Stroma-derived HGF drives metabolic adaptation of colorectal cancer to angiogenesis inhibitors (2017) ONCOTARGET, 8 (24), 38193-38213. **IF: 5.1680**
- Pallares V., Hoyos M., Chillón M.C., Barragan E., Conde M.I.P., Llop M., Céspedes M.V., Nomdedeu J.F., Brunet S., Sanz M.A., Gonzalez-Diaz M., Sierra J., Casanova I., Mangues R., NEDD 9 an independent good prognostic factor in intermediaterisk acute myeloid leukemia patients (2017) ONCOTARGET, 8 (44), 76003-76014. **IF: 5.1680**
- Pesarrodona M., Crosas E., Cubarsi R., Sanchez-Chardi A., Saccardo P., Unzueta U., Rueda F., Sanchez-García L., Serna N., Mangues R., Ferrer-Miralles N., Vazquez E., Villaverde A., Intrinsic functional and architectonic heterogeneity of tumor-targeted protein nanoparticles (2017) NANOSCALE, 9 (19), 6427-6435. **IF: 7.233**
- Sanchez-García L., Serna N., Mattanovich M., Cazzanelli P., Sanchez-Chardi A., Conchillo-Sole O., Cortes F., Daura X., Unzueta U., Mangues R., Villaverde A., Vazquez E., The fusogenic peptide HA2 impairs selectivity of CXCR4-targeted protein nanoparticles (2017) CHEM COMMUN, 53 (33), 4565-4568. **IF: 6.290**
- Sanchez-García L., Serna N., Mattanovich M., Cazzanelli P., Sanchez-Chardi A., Conchillo-Sole O., Cortes F., Daura X., Unzueta U., Mangues R., Villaverde A., Vazquez E., The fusogenic peptide HA2 impairs selectivity of CXCR4-targeted protein nanoparticles (2017) CHEM COMMUN, 53 (33), 4565-4568. **IF: 6.290**
- Serna N., Céspedes MV, Unzueta U, Sala R, Sánchez-Chardi A, Sánchez-García L, Cortés F, Ferrer-Miralles N, Mangues R, Vázquez E, Villaverde A. Peptide-based nanostructured materials with intrinsic pro-apoptotic activities in CXCR4+ solid tumors. Adv Funct Mat 2017. **IF: 13.325**
- Serna N., Sanchez-García L., Sanchez-Chardi A., Unzueta U., Roldan M., Mangues R., Vazquez E., Villaverde A., Protein-only, antimicrobial peptide-containing recombinant nanoparticles with inherent built-in antibacterial activity (2017) ACTA BIOMATER, 60, 256-263. **IF: 6.383**
- Serna N., Sanchez-García L., Unzueta U., Diaz R., Vazquez E., Mangues R., Villaverde A., Protein-Based Therapeutic Killing for Cancer Therapies (2017) TRENDS BIOTECHNOL. **IF: 13.578**
- Unzueta U., Seras-Franzoso J., Céspedes M.V., Saccardo P., Cortes F., Rueda F., Garcia-Fruitos E., Ferrer-Miralles N., Mangues R., Vazquez E., Villaverde A., Engineering tumor cell targeting in nanoscale amyloid materials (2017) NANOTECHNOLOGY, 28 (1). **IF: 3.404**
- Unzueta U., Serna N., Sanchez-García L., Roldan M., Sanchez-Chardi A., Mangues R., Villaverde A., Vazquez E., Engineering multifunctional protein nanoparticles by in vitro disassembling and reassembling of heterologous building blocks (2017) NANOTECHNOLOGY, 28 (50). **IF: 3.404**

