



**UNIVERSITY: University of Navarre (UNAV)**

**WIT PROGRAMME'S RESEARCH LINE NAME:**

Hematology: advanced therapies and diagnostic innovation

**DOCTORAL PROGRAMME:** Doctoral program of applied medicine and biomedicine <https://en.unav.edu/web/doctoral-program-of-applied-medicine-and-biomedicine>

**COMPLETE DESCRIPTION OF THE LINE**

Our **main research line** is focused on CAR T therapies for hematological malignancies and solid tumors. By using CRISPR-based genome editing approaches, multimodal genomic technologies at single cell level, patient samples collected from clinical trials and *in vitro* and *in vivo* disease model, our **objectives** are:

- Develop innovative **CAR T therapies** with **improved persistence, efficacy and safety**, including:
  - Innovative non-viral gene delivery vectors
  - 4<sup>th</sup> generation CAR T cells (TRUCKs) expressing immunomodulatory molecules
  - Genome-edited CAR T cells with improved features
- Dissect the **molecular mechanisms** involved in the **antitumoral response, resistance and toxicities associated to CAR T therapies**, including:
  - Transcriptomic and epigenetic analysis at single cell level (scRNAseq, scATACseq) of both CAR T cells and tumor microenvironment
  - Implementation of novel computational tools for Gene Regulatory Network analysis
  - CRISPR/Cas9-based libraries for high throughput screenings



Our **multidisciplinary research group** brings together many different expertise, representing an added value for the development of our ambitious goals

**RESEARCH GROUP NAME:**

Molecular bases of hematological malignancies

**COORDINATOR:**

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**MEMBERS OF THE LINE RESEARCH:**

Felipe Prósper

Juan Roberto Rodríguez

Susana Inoges

Ascensión López

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Paula Rodríguez-Marquez

Maria Luisa Palacios

Ana Alfonso

Jose Rifon

Paula Rodriguez-Otero

Rebeca Martínez

Saray Rodríguez

Patricia Jaúregui

Patxi San Martín  
M<sup>a</sup> Erendira Calleja

### **ANOTHER RESEARCH LINES OF THE GROUP:**

- **Role of epigenetic alterations in the pathogenesis and treatment of hematological tumors:** Our general objective is to study and gain in-depth knowledge of both the altered epigenome and the aberrant regulation of the enzymes that regulate epigenetic mechanisms (DNA methylation and histone modifications) in the tumor cells of different hematological malignancies. This objective pursues the aim of better understanding the disease and detecting new targets, in this case epigenetic, for the development of new therapeutic strategies for the treatment and improvement of the quality of life of these patients.
- **Mechanisms of gene regulation in acute leukemia and myelodysplastic syndromes:** Studies in myelodysplastic syndromes (MDS) have focused on the characterization of the mutational profiles associated with this disease. However, few studies investigate the fundamental molecular basis at the origin of this pathology. Our group aims to further study the mechanisms that contribute to the development of MDS. Specifically, we focus on the study of the transcriptome of patients with MDS, both coding and non-coding, with the aim of identifying molecular pathways involved in the development of this disease. In addition, we aim to characterize the regulatory mechanisms at the transcriptional level in order to identify potential therapeutic targets for the treatment of this pathology.
- **Role of the hematopoietic niche in hematologic tumors:** In the laboratory, we are interested in understanding the different levels of organization and cellular relationships that occur in the bone marrow (BM) niche in homeostasis and after neoplastic transformation. To this end, we employ a systems biology strategy combined with the use of genetically modified animals, multi-parametric flow cytometry and multi-omics technologies. Another major interest of our laboratory is the development of hematopoietic stem cell



mobilization regimens, as well as the development of non-genotoxic conditioning agents that allow the use of hematopoietic progenitor transplantation in monogenic diseases and congenital and acquired immunodeficiencies.

- **Study of the complete transcriptome, epigenome and metabolism of multiple myeloma tumor plasma cells:** Our general objective is to study and to know in depth both the complete transcriptome (especially the one referring to long non-coding RNAs), the altered epigenome and the aberrant metabolism of tumor plasma cells of monoclonal gammopathy of uncertain significance and multiple myeloma. This objective pursues the aim to better understand the biology of the disease and to detect new targets for the development of new therapeutic strategies for the treatment and improvement of the quality of life of these patients.

#### **ENTITIES INVOLVED IN RESEARCH LINES AND CONTACT PERSON:**

##### **Academic entities:**

- Marc Guell: Universitat Pompeu Fabra (<https://www.upf.edu/web/synbio/research>)
- Lars Bullinger : Charité University Medicine Berlin ([https://haema-onko-cvk.charite.de/forschung/arbeitsgruppen/ag\\_bullinger/](https://haema-onko-cvk.charite.de/forschung/arbeitsgruppen/ag_bullinger/))
- Leonor Puchades : Instituto de Investigación Sanitaria La Fe (<https://www.iislafe.es/es/investigacion/lineas-de-investigacion/grupo/170/unidad-de-descubrimiento-de-farmacos-udf>)
- André Catic: Baylor College of Medicine (<https://www.bcm.edu/research/faculty-labs/andre-catic-lab>)
- Maria Diez Campelo: Hospital Universitario de Salamanca (<https://hematosalamanca.es/proyectos-de-investigacion/>)
- David Valcarlel: Vall d'Hebron Instituto de Oncología (<https://www.vhio.net/es/programas-y-grupos/investigacion-clinica/grupo-de-hematologia-experimental/>)
- Josep Solé: Josep Carreras Research Institute ([https://www.carrerasresearch.org/en/Myelodysplastic\\_Syndromes](https://www.carrerasresearch.org/en/Myelodysplastic_Syndromes))
- Kevin Rouault: Pierre: Cancer Research UK Barts Center (<https://www.bartscancer.london/staff/dr-kevin-rouault-pierre/>)



- Jude Fitzgibbon: Cancer Research UK Barts Center  
(<https://www.bartscancer.london/staff/professor-jude-fitzgibbon/>)
- Luca Malcovati: IRCCS Fondazione San Matteo / University of Pavia  
(<http://medmol.unipv.eu/site/home/persona/docenti---ricercatori/scheda870004702.html>)
- Iñaki Martín Subero: IDIBAPS – Fundación Clinic  
(<https://www.clinicbarcelona.org/idibaps/areas-de-investigacion/oncologia-y-hematologia/epigenomica-biomedica>)
- Francis Planes: Tecnun - Universidad de Navarra  
(<https://www.unav.edu/en/web/departamento-de-ingenieria-biomedica-y-ciencias/investigacion/computational-biology>)
- Brian Huntly: University of Cambridge (<https://www.unav.edu/en/web/departamento-de-ingenieria-biomedica-y-ciencias/investigacion/computational-biology>)
- Jesper Tegnér: KAUST King Abdullah University of Science and Technology  
(<https://www.kaust.edu.sa/en/study/faculty/jesper-tegner>)
- Fernando Pastor: CIMA Universidad de Navarra  
(<https://cima.cun.es/investigacion/programas-investigacion/programa-investigacion-terapias-moleculares/grupo-investigacion-aptameros>)
- José Ángel Martínez-Climent: CIMA Universidad de Navarra  
(<https://cima.cun.es/investigacion/programas-investigacion/programa-investigacion-hemato-oncologia/grupo-investigacion-sindromes-linfoproliferativos>)
- María Blanco: Universidad de Navarra (<https://www.unav.edu/en/web/grupo-investigadores/nanomedicines-and-drug-delivery>)
- Ari M. Melnick: Weill Cornell Medical College (<https://melnicklab.weill.cornell.edu/>)
- Jesús M. Paramio. CIEMAT-Hospital 12 de Octubre  
(<http://rdgroups.ciemat.es/web/oncomol/>)
- Esteban Ballestar: Josep Carreras Research Institute  
([https://www.carrerasresearch.org/es/epigen%C3%A9tica-y-enfermedades-inmunitarias\\_124402](https://www.carrerasresearch.org/es/epigen%C3%A9tica-y-enfermedades-inmunitarias_124402))
- Cynthia Zahnow: Johns Hopkins University (<https://cmm.jhmi.edu/index.php/cmm-faculty/cynthia-a-zahnow-phd/>)
- Karine Breckpot: Vrije Universiteit Brussel (<https://lmct.research.vub.be/en>)
- Anna Mondino. IRCCS San Raffaele Scientific Institute  
(<https://research.hsr.it/en/divisions/immunology-transplantation-and-infectious-diseases/lymphocyte-activation.html>)



## **Industrial entities:**

- María Peñas: Recombina Biotech (<https://www.recombina.com/es/>)
- Ernesto Ruiz: NASERTIC (<https://hpc.nasertic.es/>)
- Natalia Elizalde: VIVEBiotech (<https://www.vivebiotech.com/en/>)

## **GROUP REVIEW**

Dr. Felipe Prosper is Director of the Cell Therapy Area and the Department of Hematology and Hemotherapy of the Clinica Universidad de Navarra and the Director of the Programs of Hemato-Oncology and Regenerative Medicine at CIMA Universidad de Navarra. Dr. Prosper's group has published more than 400 articles in top journals and his laboratory is funded through national and international grants. The group have a long-track training record with more than 30 mentored PhD students and postdocs.

The Cell Therapy Area encompasses one of the largest clinical hematological programs and one of the most active cell therapy and immunotherapy programs in Spain, with a GMP accredited laboratory with experience in ATMP products. Moreover, our CAR T cell program aims to provide clinically relevant results. Thus, the group is actively participating in several national projects (TranspoCART, DESCARThES, ARI0002h), international initiatives (CARAMBA, T2Evolve) and clinical trials involving CAR T therapies for hematological diseases, with the envision to accelerate the development and the access to innovative immunotherapeutic strategies.

## **LINK OF THE GROUP TO THE "PORTAL OF SCIENTIFIC PRODUCTION"**

<https://cima.cun.es/en/research/research-programs/research-programs-hematology-oncology>





## LINKS TO ACADEMIC OR INDUSTRIAL PARTNERS RELATED TO THE PROPOSAL

### Academic partners:

- Michael Hudecek: University Hospital Würzburg (<https://www.ukw.de/research/research-hudecek-lab/home/>)
- Zolta Ivics: Paul-Ehrlich-Institut (PEI) (<https://www.pei.de/EN/research/groups/medical-biotechnology/medical-biotechnology-research-node.html;jsessionid=E60EBE4E70C03EBE6DB66BE2439CCFC8.intranet242>)
- Toni Cathomen: Institute for Cell and Gene Therapy, Medical Center - University of Freiburg (<https://www.uniklinik-freiburg.de/itg-en.html>)
- John Maher: King's College London (<https://www.kcl.ac.uk/research/car-mechanics-group>)
- Christoph Bock: CeMM - Research Center of Molecular Medicine of the Austrian Academy of Sciences (<https://cemm.at/research/groups/christoph-bock-group>)
- David Gomez-Cabrero: Navarrabiomed (<https://www.navarrabiomed.es/es/directorio/gomez-cabrero>) & KAUST- King Abdullah University of Science and Technology (<https://www.kaust.edu.sa/en/study/faculty/david-gomez-cabrero>)
- Mikel Hernaez: CIMA Universidad de Navarra (<https://cima.cun.es/investigacion/programas-investigacion/programa-investigacion-biologia-computacional>)
- Antonio Pineda: CIMA Universidad de Navarra (<https://cima.cun.es/investigacion/programas-investigacion/programa-investigacion-terapias-moleculares/grupo-investigacion-quimica-medica>)
- Bruno Paiva: CIMA Universidad de Navarra (<https://cima.cun.es/investigacion/programas-investigacion/programa-investigacion-hemato-oncologia/grupo-investigacion-mieloma-multiple>)
- Juan José Lasarte: CIMA Universidad de Navarra (<https://cima.cun.es/investigacion/programas-investigacion/programa-inmunologia-inmunoterapia/grupo-investigacion-inmunomodulacion-microambiente-tumoral>)
- Juan Bueren: CIEMAT - Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas (<http://rdgroups.ciemat.es/web/terapias-innovadoras>)
- Fermín Sánchez-Guijo: IBSAL - Instituto de Investigación Biomédica de Salamanca (<https://ibsal.es/es/tgyc-01-medicina-regenerativa-c>)
- Margarita Redondo: CHN – Complejo Hospitalario de Navarra ([http://www.navarra.es/home\\_es/Gobierno+de+Navarra/Organigrama/Los+departamentos/Salud/Organigrama/Estructura+Organica/?idunidadactual=10007319](http://www.navarra.es/home_es/Gobierno+de+Navarra/Organigrama/Los+departamentos/Salud/Organigrama/Estructura+Organica/?idunidadactual=10007319))



- José María Moraleda: Hospital Universitario Virgen de la Arrixaca – IMIB (<https://www.imib.es/web/personal.jsf?id=171>)
- Alvaro Urbano: Hospital Clinic de Barcelona – IDIBAPS (<https://www.clinicbarcelona.org/idibaps/areas-de-investigacion/oncologia-y-hematologia/trasplante-de-progenitores-hemopoyeticos>)
- Carlos Fernández de Larea: Hospital Clinic de Barcelona – IDIBAPS (<https://www.clinicbarcelona.org/idibaps/areas-de-investigacion/oncologia-y-hematologia/mecanismos-de-progresion-en-gammapatias-monoclonales>)
- Manel Juan: Hospital Clinic de Barcelona – IDIBAPS (<https://www.clinicbarcelona.org/idibaps/areas-de-investigacion/agresion-biologica-y-mecanismos-de-respuesta/inmunogenetica-en-la-respuesta-autoinflamatoria>)
- Francisco Martín: Centro Pfizer – Universidad de Granada – Junta de Andalucía de Genómica e Investigación Oncológica (GENYO) (<https://www.genyo.es/research-groups/gene-and-cell-therapy/?lang=en>)

### **Industrial partners:**

- Recombina Biotech (<https://www.recombina.com/es/>)
- VIVEBiotech (<https://www.vivebiotech.com/en/>)
- LentiStem (<https://lentistem.weebly.com>)