



UNIVERSITY:

Universidad de Navarra

WIT AREA:

Automotive, Mechatronics and Advance Manufacture

Health

Energy

IA

WIT PROGRAMME'S RESEARCH LINE NAME:

Hematology: advanced therapies and diagnostic innovation

DOCTORAL PROGRAMME:

Applied Medicine and Biomedicine

COMPLETE DESCRIPTION OF THE LINE (max. 1000 characters)

Hematopoiesis is the process by which blood lineages are formed from a common and undifferentiated cellular precursor, the hematopoietic stem cell. Alterations in the molecular mechanisms that control hematopoiesis lead to an abnormal differentiation and to the development of various hematological disorders, such as myelodysplastic syndromes and acute myeloid leukemia. Molecular studies have focused on the mutational status of these diseases, however, they not fully explain their pathogenesis and progression. In our lab, we take an integrative approach in the study of these pathologies, performing low-input transcriptome, epigenetic and chromatin architecture profiling of hematopoietic progenitors. These patients are also analyzed by single-cell technologies (RNA and DNA-seq), allowing for the identification or relevant subpopulations and of transcriptional lesions that may be responsible for aberrant hematopoiesis, in a more precise and personalized manner. With all



these data, we use human ex vivo myeloid differentiation systems to identify the lesions that are functionally relevant, and that could represent therapeutic targets for the treatment of these patients.

RESEARCH GROUP NAME:

Transcriptional deregulation of myeloid malignancies

COORDINATOR:

Name: Prosper Cardoso, Felipe

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MEMBERS OF THE LINE RESEARCH:

Felipe Prósper

Teresa Ezponda

Mikel Hernáez

Amaia Vilas

Nerea Berástegui

Paula García

Marina Ainciburu

Aintzane Díaz

Ana Alfonso

Sofía Huerga

ANOTHER RESEARCH LINES OF THE GROUP: list of them

- 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.

- Adoptive Cell Therapy: 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, we aim to a) Develop innovative CAR T therapies with improved persistence, efficacy and safety; b) Dissect the molecular mechanisms involved in the antitumoral response, resistance and toxicities associated to CAR T therapies.

- 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 (lncRNAs)), 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:

- 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>)
- 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/)
- 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)
- 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>)



- Christoph Bock: CeMM - Research Center of Molecular Medicine of the Austrian Academy of Sciences (<https://cemm.at/research/groups/christoph-bock-group>)
- Mikel Hernaez: CIMA Universidad de Navarra (<https://cima.cun.es/investigacion/programas-investigacion/programa-investigacion-biologia-computacional>)
- Jesper Tegnér: KAUST King Abdullah University of Science and Technology (<https://www.kaust.edu.sa/en/study/faculty/jesper-tegner>)
- Antonio Pineda: CIMA Universidad de Navarra (<https://cima.cun.es/investigacion/programas-investigacion/programa-investigacion-terapias-moleculares/grupo-investigacion-quimica-medica>)
- 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>)
- 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>)
- 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)
- 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/>)

- Joint supervision of doctoral thesis with international universities or non-academic institutions:
- Brief group overview (max. 1000 characters)

The research group is a multidisciplinary team formed by experts in basic research, clinical practice in hematology, and computational analysis. The group is led by Dr. Felipe Prósper, head of the Hematology Service of the Clínica Universidad de Navarra and the Hematology department at CIMA Universidad de Navarra. Since 2001, the group has focused his research activity on the study of the role of transcriptional and epigenetic alterations in the pathogenesis, prognosis and treatment of hematological tumors, including myeloid neoplasms. The basic research part of the team is formed by Dr. Teresa Ezponda, Dr. Paula García, Dr. Amaia Vilas, and PhD students Nerea Berastegui and Aintzane Diaz, which have ample expertise in the use of NGS technologies as in cellular and molecular experiments both with cell lines and primary samples. Together with Dr. Prosper, the hematologists Dr. Ana Alfonso and Dr. Sofía Huerga, experts in MDS and AML, comprise clinical part of the group. Finally, the computational analysis of the generated data is carried out by Dr. Mikel Hernández, head of the computational department at CIMA, and by Dr. Marina Ainciburu.

- Link of the group to the “Portal of scientific production”

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

- Pictures, links... to academic or industrial partners (if any)

- 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: Instituto Jose Carreras
(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>)

ACADEMIC REQUIREMENTS:

Degree in Biology, Biochemistry, or computational sciences.

ADDITIONAL REQUIREMENTS:

Expertise in molecular biology (cloning and basic techniques), culture and cellular assays (i.e: proliferation, survival, differentiation status...) of cell lines and primary cells, as well as computational knowledge are welcome although they are not required.