



UNIVERSITY: CIMA Universidad de Navarra

WIT AREA:

Automotive, Mechatronics and Advance Manufacture

Health

Energy

IA

WIT PROGRAMME'S RESEARCH LINE NAME: Hemato-Oncology

DOCTORAL PROGRAMME:

<https://www.unav.edu/web/programa-de-doctorado-de-medicina-aplicada-y-biomedicina>

COMPLETE DESCRIPTION OF THE LINE (max. 1000 characters)

In spite of the advances in Multiple Myeloma (MM) research and therapy, MM is still an incurable disease. As others and we have demonstrated, epigenetic alterations contribute to the pathogenesis of MM. In addition, due to the reversibility of epigenetic, targeting the epigenetic enzymes becomes a crucial area for the development of anti-cancer drugs.

Based on our preliminary results obtained in MM cells using a CRISPR/Cas9 library against 61 epigenetic enzymes, we have identified distinct epigenetic enzymes essential for Mm survival for continue with the project. Next, we will validate the selected targets using CRISPR strategy and we will develop a therapy using PROTAC strategies. We will determine their in-vitro efficacy (dot-blot, western blot or ChIP-PCR) analyzing the cell cycle, proliferation and apoptosis and their in-vivo potential in MM transgenic models. Finally, we will carry out RNA-seq, Bis-seq, ATAC-seq and ChIP-seq analyses in order to elucidate the mechanism of action of our novel Epi-PROTACs.

We hope this work will be the basis for a new epigenetic therapy that will improve the treatment and quality of life of patients with MM.

RESEARCH GROUP NAME: Epigenetics



COORDINATOR:

- Last and first name; link to the "Portal of scientific production":
Xabier Agirre (<https://cima.cun.es/investigacion/programas-investigacion/programa-investigacion-hemato-oncologia/grupo-investigacion-mieloma-multiple>)
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MEMBERS OF THE LINE RESEARCH:

Xabier Agirre (Researcher)
Eduarne San José-Enériz (Associated researcher)
Arantxa Carrasco-León (post-doc)
Estíbaliz Miranda (Research assistant)
Leire Garate (Research assistant)
Ane Amundarain (pre-doc)
Nahia Gómez (pre-doc)
Estíbaliz Urizar (pre-doc)
Naroa Barrena (Bioinformatician)

ANOTHER RESEARCH LINES OF THE GROUP: list of them

- Study of the epigenome in the transformation from a benign stage (MGUS, SMM) to the lethal stage of MM
- To delve into the role that transcription factors can play in aberrant epigenomic regulation in MM
- Decipher the role of the transcriptome, and specifically the transcriptome of the lncRNAs in the MM
- Study of the role played by the epitranscriptomic m6A genes in multiple myeloma
- Develop new therapeutic strategies based on PROTACs against altered coding genes in MM
- Develop new RNA-based therapeutic strategies, through the use of aptamers and nanoparticles, against coding and non-coding RNA transcripts altered in MM

Entities involved in research lines and contact person:

✓ Academic entities:

- Iñaki Martín Subero: IDIBAPS – Fundación Clinic
(<https://www.clinicbarcelona.org/idibaps/areas-de-investigacion/oncologia-y-hematologia/epigenomica-biomedica>)
- Ari M. Melnick: Weill Cornell Medical College (<https://melnicklab.weill.cornell.edu/>)
- Francis Planes: Tecnun - Universidad de Navarra
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- Antonio Pineda: CIMA Universidad de Navarra
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- Bruno Paiva: CIMA Universidad de Navarra
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- 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>)
- Fernando Pastor: CIMA Universidad de Navarra
(<https://cima.cun.es/investigacion/programas-investigacion/programa-investigacion-terapias-moleculares/grupo-investigacion-aptameros>)
- Jesús M. Paramio: CIEMAT-Hospital 12 de Octubre
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- Esteban Ballestar: Josep Carreras Research Institute
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- Laura Belver: Josep Carreras Research Institute
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- Cynthia Zahnow: Johns Hopkins University (<https://cmm.jhmi.edu/index.php/cmm-faculty/cynthia-a-zahnow-phd/>)
- 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>)



✓ Industrial entities:

- Joint supervision of doctoral thesis with international universities or non-academic institutions:

- Brief group overview (max. 1000 characters)

The main research interest of the group is 1) to study the role of the epigenome, transcriptome and epitranscriptome in the genesis, pathophysiology and clinical behavior of hematological tumors, especially Multiple Myeloma (MM), from benign gammopathies to final lethal status, and 2) Identify new therapeutic targets and design new drugs for the most effective treatment of hematological tumors. The group has generated the first DNA methylomes and epigenomes on MM (Agirre 2015; Ordoñez 2020; Valcárcel 2021), the lncRNA transcriptome of B cell differentiation and MM (Agirre 2019; Carrasco-León 2021; Amundarain 2022), have participated in the generation of hydroxymethylome of MM (Martinez-Calle 2019), first DNA methylome and epigenome of normal and neoplastic B cells (Kulis 2015; Beekman 2018; Duran-Ferrer 2020). Based on these alterations in the epigenome and transcriptome we have validated new targets involved in the pathogenesis of different human tumors and generated new chemical compounds that target epigenetic enzymes that have demonstrated potent activity and efficacy *in vitro* and *in vivo* (San José-Enériz 2017; Segovia 2019; Fresquet 2021).

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

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

ACADEMIC REQUIREMENTS:

At the deadline for the submission of proposals, researchers (*):



- Shall be in possession of a bachelor's and master degree awarded between 2020 and 2022.

ADDITIONAL REQUIREMENTS:

- Fundamental knowledge of Molecular and Cellular Biology techniques.
- Knowledge about massive sequencing techniques.
- Knowledge about approaches based on CRISPR.
- Experience with programming languages (as R, Matlab, Python or Perl).
- Basic knowledge of data analysis of high-throughput experiments (RNA-seq, ChiP-seq, ATAC-seq).
- Fundamental knowledge of statistics.

