Universidad de Navarra
Facultad de Ciencias

MÁSTER EN INVESTIGACIÓN BIOMÉDICA
Research Project Proposal
Academic year 2026-2027

Project Nº 22

Title: *Functional Study of the Epitranscriptomic Gene VIRMA and Its Potential as a Therapeutic Target in Multiple Myeloma*

Department/ Laboratory: *Laboratory of Epigenetics. Hemato-Oncology program. CIMA Universidad de Navarra.*

Director 1 *Xabier Agirre*
Contact: *xaguirre@unav.es*
Codirector: *Edurne San José-Enériz*
Contact: *esanjose@unav.es*

Summary

Multiple Myeloma (MM) is an aggressive hematological neoplasm characterized by the clonal proliferation of plasma cells, which accumulate in the bone marrow and produce a monoclonal antibody leading to organ damage and clinical complications. MM is the second most common hematological neoplasia and despite advances in research and therapy, MM remains incurable. In our previous projects we demonstrated that MM is characterized by extensive DNA hypomethylation (*Agirre X. Genome Research 2015*), *de novo* epigenomic activation (*Ordoñez R. Genome Research 2020; Valcárcel LV. Leukemia 2021*), the expression of novel lncRNAs (*Agirre X. Nature Communications 2019; Carrasco-León A. Leukemia 2021; Amundarain A. Am J Hematol 2022; Gomez-Echarte N. Haematologica 2025*), and alterations in the epitranscriptome of genes regulating the m6A post-transcriptional modification. Among these m6A regulating genes, we demonstrated that VIRMA, a recruiter of m6A methyltransferases, is essential for MM proliferation (manuscript under review). Therefore, the objective of our new proposal is to characterize the functionality of VIRMA in the regulation of transcription factors (TFs) and cellular metabolism, its role in the activity of m6A methyltransferases, and the development of innovative RNA-based therapeutic strategies targeting VIRMA. Using the CRISPR strategy, direct m6A-seq (nanopore), and metabolomics (LC-MS/MS), we will define the functionality of VIRMA in key TFs and genes involved in mitochondrial and cellular metabolism. Through CRISPR and untargeted proteomics (LC-MS/MS), we will study the anti-MM potential of dual inhibition of m6A methyltransferases and VIRMA. Finally, we will develop an RNA-based therapy using siRNAs encapsulated in nanoparticles (*Garbayo E. Adv Drug Deliv Rev. 2024; El Moukhtari SH. J Control Release. 2023; San José-Enériz E. Nature Communications 2024;*) and explore its combination, both in vitro and in vivo, with other therapeutic strategies identified in the analysis of VIRMA functionality, to improve the treatment and quality of life for MM patients.

Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator? **YES**.