Universidad de Navarra
Facultad de Ciencias

MÁSTER EN INVESTIGACIÓN BIOMÉDICA
Research Project Proposal
Academic year 2022-2023

Project Nº 26

Title: Development of Epi-PROTACs for the cure of Multiple Myeloma.

Department/ Laboratory *Multiple Myeloma-Myeloid malignancies (Lab 1.02), Hematology-Oncology Program, CIMA*

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Summary

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 (Agirre X. Genome Research 2015; Ordoñez R. Genome Research 2020; Carrasco-León A. Leukemia 2021; Valcarcel LV. Leukemia 2021). In addition, due to the reversibility of epigenetic, targeting the epigenetic enzymes becomes an important area for the development of anti-cancer drugs (San José-Enériz E. Nature Communications 2017; Segovia C. Nature Medicine 2019; Fresquet V. Cancer Discovery 2021; García-Gómez A. Nature Communications 2021).
Based on our results obtained in 3 lines of MM using a CRISPR/Cas9 library against 61 epigenetic enzymes, we will select 2 epigenetic target candidates for continue with the project. Next, we will validate the selected targets using CRISPR strategy. Then, we will develop a therapy against the selected targets using PROTAC strategies. We will determine their in-vitro efficacy analyzing the cell cycle, proliferation and apoptosis and their in-vivo potential in MM transgenic models. We will validate, both in-vitro an in-vivo, the correct inhibition of the epigenetic target by dot-blot, western blot or ChIP-PCR. 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.

yes	X
no	

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