



Research Project Proposal
Academic year 2021-2022
Máster en Investigación Biomédica

Project Nº 16 ASIGNADO

Title: Identification of novel epigenetic targets and development of new epigenetic inhibitors 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, alterations in Epigenetic mechanisms (DNA methylation, histone modifications) 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).

The main goal of this project is find new epigenetic targets and develop novel therapies against them. Base on our previous transcriptome-epigenome data in MM, we will select epigenetic enzymes and epigenetically modified genes and we will check their expression by Q-PCR and Western Blot and in 1000 MM patient samples from CoMMPass-dataset to study their prognosis potential. Next, we will validate the selected targets using CRISPR strategy. Then, we will develop a therapy against the selected targets using small molecules and fragment-based drug-design 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 or ChIP-seq analyses in order to elucidate the mechanism of action of our novel inhibitors.

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?