



Research Project Proposal
Academic year 2020-2021
Máster en Investigación Biomédica

Project Nº 23_ASIGNADO	
Title: Development of new epigenetic inhibitors for the cure of Multiple Myeloma.	
Department/ Laboratory <i>Multiple Myeloma-Myeloid malignancies (Lab 1.02), Hematology-Oncology Program, CIMA</i>	
Director 1 <i>Xabier Agirre Ena</i>	Contact: <i>xaguirre@unav.es</i>
Codirector: <i>Edurne San José-Enériz</i>	Contact: <i>esanjose@alumni.unav.es</i>
Summary:	
<p>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 essential Epigenetic mechanisms (DNA methylation, histone modifications) contribute to the pathogenesis of MM (Agirre X. Genome Research 2015; Ordoñez R. BioRxiv 2020). In addition, due to the reversibility of epigenetic modifications, targeting the epigenetic enzymes becomes an important area for the development of anti-cancer drugs (San José-Enériz E. Nature Communications; Segovia C. Nature Medicine 2019).</p> <p>The main goal of this project is find and validate new epigenetic targets and develop novel therapies against them. Base on our previous whole transcriptome-epigenome data in MM, we will select several epigenetic enzymes and we will check their expression in MM cell-lines by Q-PCR and Western Blot and in 650 MM patient samples from CoMMPass-dataset to study their prognosis biomarker 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 <i>in-vitro</i> efficacy analyzing the cell cycle, proliferation and apoptosis. Their <i>in-vivo</i> potential will be studied in subcutaneous mouse models using MM celllines and in MM transgenic models developed at CIMA. We will validate, both <i>in-vitro</i> an <i>in-vivo</i>, 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.</p> <p>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.</p>	
yes	<input checked="" type="checkbox"/>
no	<input type="checkbox"/>
Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?	