



Research Project Proposal
Academic year 2018-2019

Project Nº 19

Title: *Innovative differentiating epigenetic therapy for the cure of Acute Myeloid Leukemia*

Department/ Laboratory *Mecanismos Epigenéticos del Cáncer. Área de Hemato-Oncología. CIMA. Universidad de Navarra.*

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Summary *Short summary of the project with a **maximum extension of 250 words**, including the goals and the methodology that will be used.*

Acute myeloid leukemia (AML) is a malignant disease characterized by the uncontrolled proliferation, differentiation and accumulation of immature myeloid progenitors. Although clinical advances in AML have been made, treatment failure remains high. Since the 1970s, various studies have demonstrated that the strategy of inducing malignant cells to overcome their blocked differentiation was an elegant alternative to killing cancer cells. The potential for differentiation-therapy to improve cure rates in AML is exemplified by the development of ATRA for the targeted treatment of acute promyelocytic leukemia (APL). However, other subtypes of AML display resistance to ATRA and the differentiation-inducers in clinical use are still very limited. Therefore, the identification of new therapeutic-agents that lead tumor differentiation is tremendously important for the improvement of treatment of AML.

Epigenetic alterations contribute to the pathogenesis of AML. In preliminary studies of our group, we have developed different novel epigenetic small molecules which include G9a-DNMT-HDACs, DNMT-HDACs or HDACs, finding interestingly, several with high capacity to promote cell differentiation in AML cell.

In this study we will perform a complete characterization of the myeloid differentiation inducing capacity of our novel epigenetic inhibitors in AML and elucidate with maximum depth its molecular mechanism at RNAseq, ChIPseq and protein modification level. The results obtained indicate that this differentiation-therapy may be beneficial and very important key for the cure of most subtypes of AML. We hope this work will be the basis for a new differentiation-based therapy that will improve the treatment and quality of life of patients with AML.

yes	<input type="checkbox"/>
no	<input checked="" type="checkbox"/>

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