



MASTER'S DEGREE IN BIOMEDICAL RESEARCH

Research Project Proposal

Academic year 2024-2025

Project Nº 32

Title: Identification of key transcriptional regulators as novel therapeutic targets in myeloid malignancies

Department/ Laboratory *Laboratory of myeloid malignancies. Lab. 1.04. Hematology/Oncology, CIMA.*

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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*

Myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML) represent hematological malignancies characterized by alterations in the differentiation and proliferation of hematopoietic progenitor cells. Genetic alterations do not fully explain the molecular pathogenesis of these diseases, indicating that other types of lesions play a role in their development. Our group uses sequencing techniques paired with functional analyses in order to characterize transcriptional alterations that contribute to these diseases, and that, due to the reversible nature of transcriptional events, are amenable of therapeutic intervention.

Firstly, using single-cell RNA-seq data from bone marrow primary samples, the student will be able to identify transcription factors/chromatin regulators that act as master regulators of the transcriptional profile of these patients. Secondly, the student will interrogate the potential functional involvement of candidate factors in the promotion of an MDS/AML phenotype. To do so, the student will use an ex-vivo myeloid differentiation system starting from primary cells (HSCs from healthy donors). This system allows us to model early stages of hematopoietic differentiation in vitro, where the expression of specific genes can be manipulated. The candidate will generate lentiviruses to overexpress the factor of interest and use the differentiation system and flow cytometry analyses to evaluate the effect of the altered factor on normal hematopoietic differentiation.

All in all, the candidate will acquire the following expertise:

- State of the art transcriptome profiling techniques: including single cell transcriptome profiling by scRNA-seq analyses and bulk transcriptome profiling of small cell populations by low input RNA-seq.
- Human hematopoiesis cell biology.
- HSCs isolation, differentiation and culture.
- Ex-vivo myeloid differentiation system.
- Cloning and production of lentiviruses.
- Flow cytometry analyses of hematopoietic differentiation.



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yes	
no	X

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