Universidad de Navarra
Facultad de Ciencias

MASTER'S DEGREE IN BIOMEDICAL RESEARCH
Research Project Proposal
Academic year 2024-2025

Project Nº 13

Title: Phenotypic and functional characterization of the immune cell repertoire in patients with myelodysplastic syndromes

Department/ Laboratory *Laboratory where the project will be carried out indicating Department, Area, Faculty, CUN, CIMA etc.*
Myeloid Neoplasia laboratory, Hematology-Oncology program, CIMA

Director 1 *Name and surname of the director (If there will be two co-directors indicate both)*
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Codirector:
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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) are aging-related hematologic malignancies that arise from the expansion of aberrant hematopoietic stem cell (HSC) clones in the bone marrow (BM) and are characterized by inefficient blood cell production. Our incomplete understanding of the pathogenic mechanisms of MDS translates into a scarcity of effective frontline pharmacological therapies for the patients. Specifically, how MDS HSCs escape immune surveillance is unknown.

Aging induces a progressive decline in the immune system's function. Further, our previous studies showed that clonal preleukemic conditions preceding MDS induce functional defects in cytotoxic innate immune cell subsets. Therefore, we hypothesized that immune cell dysfunction plays a key role in MDS maintenance and progression.

The overarching goal of this project is to dissect the cellular and functional characteristics of the BM immune niche of patients with MDS to ultimately identify therapeutic intervention opportunities. To do so, we will perform flow cytometry and gold-standard *in vitro* functional assays for cytokine secretion, degranulation and cytolysis in primary BM samples collected from MDS patients and from age-matched healthy donors. Our results will uncover quantitative and qualitative changes in the MDS immune cell repertoire.

Collectively, we expect our characterization of the MDS immune microenvironment to shed light on the mechanisms that contribute to MDS pathogenesis and provide a rationale for the development of immune-reprogramming approaches to arrest disease evolution in MDS patients.

yes	
no	X

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