Universidad de Navarra
Facultad de Ciencias

MÁSTER EN INVESTIGACIÓN BIOMÉDICA
Research Project Proposal
Academic year 2026-2027

Project Nº 27

Title: Impact of the Reorganization of the hepatic immune niche over Wilson's disease progression

Department/ Laboratory *Laboratorio terapias Avanzadas enfermedades hepaticas raras. División médicina de DNA y RNA. CIMA. Universidad de Navarra.*

Director 1 *Gloria Gonzalez Aseguinolaza*
Contact: *ggasegui@unav.es*
Codirector: *Oihana Murillo*
Contact: *omurillo@unav.es*

Summary

While in other liver pathologies such as MASLD macrophages and neutrophils play an important role not only in liver damage but also in regulating liver regeneration, their role in Wilson disease (WD) remains poorly explored. A better understanding of their interplay throughout the course of the disease might offer an opportunity to tailor existing treatment options and improve novel treatments such as gene therapy. Integrative analysis of single cell RNA sequencing analysis (scRNA-seq) revealed the macrophage and neutrophil populations and phenotypes were altered in all WD stages compared to the WT control. The transcriptomic profile of all macrophages also shifted, from a mixed pro- and anti-inflammatory state to a reparative and LAM-like phenotype. The emergence of this LAM-like phenotype was confirmed in human patients by re-analysing published scRNA-seq data. Regarding neutrophils, starting from week 16, there was increased recruitment to the liver, with a depletion of interferon-response populations and an increase in PD-L1+ immunoregulatory populations.

Thus, WD progression drives a reorganization of the hepatic immune niche, characterized by the emergence of macrophages with a LAM reparative phenotype and reprograming of neutrophils to an immunoregulatory state. The work of this TFM will be to better characterize these populations and to modulate them to better understand their role on WD liver pathology. scRNA seq and spatial transcriptomic analysis on WT and WD liver samples will be performed.

yes	X
no	

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