Universidad de Navarra
Facultad de Ciencias

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

Project Nº 61

Title: Engineering human iPSC-derived immune systems to identify regulators of T-cell fitness in DLBCL immunotherapy

Department/ Laboratory
Biochemistry and Genetics Department (School of Science, UNAV)

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Summary

Diffuse large B-cell lymphoma (DLBCL) remains a clinically heterogeneous disease in which resistance to immunotherapy is often associated with impaired anti-tumor immunity and dysfunctional T-cell responses. This project aims to establish a human iPSC-based experimental platform to evaluate the role of one selected candidate gene in the fitness, differentiation and anti-lymphoma activity of the human T-cell compartment.

A well-characterized commercially available human iPSC line will be engineered to incorporate a hematopoietic/T-cell reporter and a Cas9-based perturbation system, enabling targeted knockout of a predefined gene of interest involved in T-cell persistence, activation, exhaustion or cytotoxic function. Engineered hiPSCs will be differentiated into CD34+ hematopoietic progenitors and subsequently toward the T-cell lineage using established directed differentiation protocols. Edited progenitors and derived immune populations will be characterized in vitro by flow cytometry, molecular validation of gene editing, differentiation assays and functional readouts of T-cell activation and cytotoxicity.

The functional impact of this targeted genetic perturbation will be evaluated in vivo using NSG-DKO immunodeficient mice humanized with edited human immune progenitors. These mice provide a suitable model for human immune-cell engraftment while reducing xenogeneic graft-versus-host disease. Humanized mice will be challenged with CDX models based on DLBCL-derived human lymphoma cell lines and exposed to immunotherapeutic strategies. Tumor burden, human immune reconstitution and T-cell phenotypes will be monitored by flow cytometry and complementary molecular analyses.

yes	X
no	

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