Universidad de Navarra
Facultad de Ciencias

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

Project Nº 31

Title: Multi-Omic characterization at single cell level of Transposon-Based CAR-T therapies in B-cell Malignancies

Department/ Laboratory Immune Therapy group (lab 1.04), Hemato-Oncology Program, Cancer Division. Cima Universidad de Navarra.

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Summary
CAR-T cell therapies have revolutionized treatment of B-cell malignancies; however, their long-term efficacy remains limited by T-cell exhaustion, suboptimal persistence, and therapy-associated toxicities. Current manufacturing strategies based on lentiviral (LV) vectors often generate highly differentiated T-cell populations with reduced functional durability. Emerging evidence suggests that non-viral, transposon-based systems such as Sleeping Beauty (SB) may overcome these limitations by promoting a stem-like, metabolically flexible phenotype with enhanced persistence and antitumor activity. This project aims to comprehensively characterize the molecular and functional determinants underlying the superior fitness of SB-generated CAR-T cells. The central hypothesis is that SB-based CAR-T cells establish a distinct regulatory architecture that preserves cellular plasticity, prevents exhaustion, and enhances adaptability to the tumor microenvironment. To address this, we will integrate longitudinal patient-derived samples with state-of-the-art multi-omic technologies at single-cell resolution. Specifically, we will combine transcriptomic and epigenomic profiling (Multiome), gene regulatory network inference, metabolic characterization (SCENITH), and spatial proteomics (Pixelgen) to generate a holistic map of CAR-T cell states and dynamics.
The main objectives are:
- to define transcriptional and epigenetic programs driving CAR-T cell fitness
- to quantify metabolic dependencies and flexibility
- to resolve the spatial organization of signaling receptors
- to identify and functionally validate key regulatory nodes using CRISPR-based perturbation.
The novelty of this proposal lies in its integrative, systems-level approach to CAR-T biology, moving beyond descriptive analyses to mechanistic insights. Its impact is both scientific and translational, enabling the rational design of next-generation CAR-T therapies with improved efficacy, reduced toxicity, and broader clinical accessibility.

yes	X
no	

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