Universidad de Navarra
Facultad de Ciencias

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

Project Nº 19

Title: *Enhancing CAR-T cell efficacy against the solid tumor microenvironment using innovative organ-on-chip models.*

Department/ Laboratory
Immunology and Immunotherapy program.
Lab 3.02. CIMA.

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Summary: Despite the unprecedented success of chimeric antigen receptor (CAR) T cells as adoptive cell therapies in hematological malignancies, poorer clinical responses are being obtained in solid tumors. The hostile tumor microenvironment (TME) heavily interferes with targeted T cell activity, hindering effective T cell infiltration and promoting severe immunosuppression, terminal exhaustion, and limited persistence. Furthermore, traditional static *in vitro* models fail to accurately recapitulate the complex physical, chemical, and cellular barriers of this dynamic ecosystem, significantly limiting the successful clinical translation of novel therapeutic strategies.

Goal: This project aims to design and evaluate enhanced CAR-T cell therapies capable of overcoming these TME barriers. By employing advanced, highly realistic *in vitro* modeling, we seek to obtain dynamic responses and functional readouts that more accurately mimic human patient physiology and tumor pathophysiology.

Methodology: To realistically simulate the 3D complexity of the solid TME, we will integrate cutting-edge organ-on-chip technology. The project involves standard *in vitro* cell culture methodologies, including DNA and viral vector production, targeted cell transduction, and comprehensive analysis of T cell effector functions via flow cytometry, ELISA, ELISPOT and cytotoxicity assays. Crucially, to properly evaluate cellular behavior within these microfluidic platforms, we will incorporate advanced imaging techniques, specifically confocal microscopy, time-lapse imaging, and immunofluorescence. This approach allows us to dynamically monitor CAR-T cell infiltration, spatial distribution, and tumor-killing interactions in real-time. Finally, the most promising therapeutic candidates will be tested and validated in *in vivo* experiments using appropriate immunocompetent tumor models.

yes	x
no	

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