Universidad de Navarra
Facultad de Ciencias

MÁSTER EN INVESTIGACIÓN BIOMÉDICA
Research Project Proposal
Academic year 2025-2026

Project Nº 09
Title: *Boosting CAR-T Cell Therapy in Solid Tumors with RNA-Based Vaccines*
Department/ Laboratory *Laboratorio de "Terapia celular adoptiva" del Programa de "Inmunología e Inmunoterapia". Centro de investigación Médica Aplicada (CIMA).*
Director 1 *Sandra Hervás-Stubbs* **Contact:** *mshervas@unav.es* **Codirector:** **Contact:**
Summary Chimeric Antigen Receptor (CAR) T cells are a powerful therapy for blood cancers, but their efficacy in solid tumors is still limited due to the immunosuppressive tumor microenvironment (TME), which hinders CAR-T activation and persistence. This project explores a novel strategy to enhance CAR-T cell function by combining it with RNA-based vaccines that express the CAR-target antigen (CAR-Ag). We hypothesize that presenting CAR-Ag outside the tumor could safely "boost" CAR-T cells, improving their expansion and antitumor activity. To test this approach, we will use self-amplifying RNA (saRNA) and conventional mRNA vaccines, both formulated in lipid nanoparticles (LNPs). saRNA offers a significant advantage by generating higher protein levels per dose. LNPs are essential for protecting the RNA and facilitating its cellular delivery. Objectives include: (i) Designing and producing saRNA and mRNA vaccines encoding CAR-Ag or luciferase; (ii) Assessing in vivo protein expression via bioluminescence imaging; (iii) Evaluating the vaccine's boosting effect on CAR-T cells; and (iv) Testing therapeutic efficacy in mouse models of breast cancer. For objectives (ii)–(iv), we will compare saRNA and mRNA vaccine platforms. What you'll learn: (1) RNA vaccine design (mRNA, saRNA); (2) Molecular biology, cloning, and cell culture; (3) Flow cytometry and immune assays; and. (4) Animal handling and in vivo imaging This project is ideal for highly motivated students pursuing a career in translational research or cancer immunotherapy.
<table><tr><td>yes</td><td>X</td></tr><tr><td>no</td><td></td></tr></table>Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator? YES