Universidad de Navarra
Facultad de Ciencias

MASTER'S DEGREE IN BIOMEDICAL RESEARCH
Research Project Proposal
Academic year 2025-2026

Project Nº 29

Title: Effect of extracellular matrix properties in CAR-T adoptive therapy

Department/ Laboratory *Microphysiological Systems and Quantitative Biology / Biomedical Engineering / Advanced Technologies Division / CIMA University of Navarre*

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Traditional 2D cell cultures and basic 3D cultures, such as tumor spheroids, often fail to accurately recapitulate the complex interactions between tumor cells and the tumor microenvironment (TME). In contrast, tumor organoids are more advanced 3D structures grown on biomimetic scaffolds using hydrogels that allows for replicating tumor complexity in vitro, enabling the study of key interactions cells-TME that plays a key role in the tumor phenotype, progression, and resistance to therapies. Improved organoid models have been developed using air-liquid interface (ALI) systems, in which tumor cells are embedded in hydrogels exposed to both air and culture medium. These devices ensure an optimal oxygen supply, allow long-term studies, and enable the inclusion of immune components. In this project, we propose the optimization and use of a custom-made ALI device designed to culture explant-based tumor organoids within a pseudo-immune-competent microenvironment, aiming to study how the properties of the extracellular matrix (ECM) modulate the antitumor effects of immune responses.

Specifically, we will study the in vitro dynamics of CAR-T cells in tumor explants extracted from tumors grown in syngeneic mice by implanting PDAC organoids subcutaneously and administering intravenous CAR-T cells. Additionally, we will analyze interactions between co-cultivated CAR-T cells and tumor explants extracted from syngeneic models implanted with PDAC organoids without CAR-T cells.

To achieve these objectives, we will use an interdisciplinary approach combining cell culture, microfluidics, and fluorescence microscopy techniques. The experiments will consist of culturing explant-derived PDAC organoids in lattices of different rigidity—composed of Collagen I, Matrigel, or a mixture of both—within our custom-made PDMS ALI device. Organoid growth and CAR-T cell interactions will be monitored using confocal and/or multiphoton microscopy.

To achieve our scientific objectives, the following tasks are proposed: **i)** Fabricate biomimetic hydrogels; **ii)** Optimize and fabricate ALI microfluidic devices; **iii)** Culture explant-derived organoids within the hydrogels and devices; **iv)** Adapt staining protocols, microscopy, and image analysis tools to characterize organoid growth and CAR-T cell dynamics.

yes	
no	X

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