Universidad de Navarra
Facultad de Ciencias

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

Project Nº 32

Title: *The Silent Saboteurs: Decoding Immune Evasion Mechanisms of Circulating Tumor Cells in Cancer Therapy*

Department/ Laboratory
Therapeutic Innovation, RNA Aptamer Therapeutics, CIMA

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Summary

Radiotherapy and certain chemotherapies can trigger immunogenic tumor cell death, creating a powerful opportunity for in situ tumor immunization. Yet, many patients eventually relapse, and current immunotherapies often fail to achieve durable clinical responses. Tumor recurrence and therapy resistance remain among the most pressing unmet needs in oncology.
At the core of this challenge lie circulating tumor cells (CTCs), rare but highly resilient cancer cells capable of surviving treatment and reinitiating disease. CTCs evade immune surveillance through various strategies. We propose that a key mechanism is the transient loss of immunodominant neoantigens, many of which originate from frameshift mutations. These neoantigens, however, are tightly regulated by the nonsense-mediated mRNA decay (NMD) pathway, which eliminates aberrant transcripts before they can be translated into immunogenic peptides. A recent work from our team (Meraviglia et al., Mol Cancer, 2022) has uncovered that NMD activity is modulated by intrinsic inflammatory signals frequently triggered by radiotherapy and chemotherapy.
We hypothesize that CTCs exploit therapy-induced systemic inflammation to enhance NMD activity, suppressing neoantigen expression and enabling immune evasion. This molecular shield may underlie the stealth-like, treatment-resistant phenotype of CTCs. This project seeks to unravel this immune escape program and expose new therapeutic vulnerabilities in CTCs.
The selected master's student will work with cutting-edge tools and models, including transgenic murine tumor systems, molecular biology (CRISPR, RNAi, aptamers), cell and tissue culture, flow cytometry, confocal microscopy, and state-of-the-art bioinformatics pipelines for omics analysis, such as single-cell RNA-seq and spatial transcriptomics.

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

yes	X
no	