Universidad de Navarra
Facultad de Ciencias

MASTER'S DEGREE IN BIOMEDICAL RESEARCH
Research Project Proposal
Academic year 2023-2024

Project Nº 29

Title: Understanding the mechanisms of circulating tumor cells (CTCs) to evade the immune response in cancer immunotherapy.

Department/ Laboratory
Terapias Innovadoras, RNA Aptamer Therapeutics, CIMA

Director 1 *Fernando Pastor Rodríguez*
Contact: *fpasrodri@unav.es*
Codirector: Helena Villanueva
Contact: *evillanue@unav.es*

Summary

Radiotherapy and some chemotherapy drugs lead to immunogenic tumor cell death, which provides the optimal conditions to generate an in situ tumor immunization. Nevertheless, many patients relapse after standard treatments and current cancer immunotherapy is not fully successful. Tumor relapse and therapy resistance is still a main unmet clinical need in cancer. Circulating tumor cells (CTCs) are resilient cancer cells that are key for promoting therapy resistance and recurrence. CTCs hinder the effect of the immune response through multiple possible immune escape mechanisms. Among them we propose the transient loss of immunodominant antigens in CTCs as one of the main causes. Frameshift mutation, one of the most potent sources of neoantigens, is controlled under the action of the nonsense-mediated mRNA decay (NMD) and we have recently uncovered that the activity of NMD is circumvented to intrinsic inflammatory signals (Meraviglia et al Mol Cancer 2022) that can be triggered by standard radio/chemotherapy regimens. We hypothesize that CTCs acquire this highly resistant phenotype as they upregulate NMD activity in response to a systemic inflammation induced by radio/chemotherapy. We count with all the experimental tools to tackle this question including several in vivo tumor murine models.

The master's thesis student will be exposed to many technologies during the timeframe of the master's program: molecular biology techniques (cloning, RNAi, CRISPR and aptamer technology), cell and tissue culture, in vivo animal experiments, different immunoassay techniques, flow cytometry, image confocal microscopy, and different bioinformatic pipelines for omics analysis including scRNAseq.

yes	x
no	

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