



**MASTER'S DEGREE IN BIOMEDICAL RESEARCH**

**Research Project Proposal**

Academic year 2024-2025

**Project Nº 35**

**Title:**

*Blockade of an RNA surveillance mechanism in resilient tumor cells to counteract antigen immune escape and tumor relapse.*

**Department/ Laboratory:**

*CIMA, Enable Technologies, Aptamer Unit.*

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**Summary**

As tumors evolve, they acquire new capabilities that allow them to survive pressing antitumor forces. They achieve this by displaying high levels of genomic and transcriptomic plasticity. However, as they acquire new genomic driver mutations, they become more antigenic and are easily recognized by the immune system. We have proved that tumors take advantage of rewiring an RNA surveillance mechanism to prevent the expression of neoantigens derived from this newly acquired mutations (Meraviglia et al Mol Cancer 2022). We hypothesize that this process is critical in tumor metastasis and confer resistance to standard cancer treatments. We propose the use of selective drugs to target the inhibition of this RNA surveillance pathway in resilient tumor cell to counteract relapse.

During the master's program, the student will learn various technologies, including molecular biology techniques like cloning, RNAi, CRISPR, and aptamer technology, as well as cell and tissue culture, in vivo animal experiments, flow cytometry, image confocal microscopy, and different bioinformatics pipelines for omics analysis, including scRNAseq. She/he will use bioinformatics analysis of the tumor mutation landscape and transcriptomics to interrogate the existence of RNA surveillance forces that coopt the expression of neoantigens. The student will evaluate the outcome of this RNA-immunoediting mechanism in different metastatic murine tumor models treated with standard immune-checkpoint blockade therapies and radiotherapy. The student will also determine the modulation of immune responses by this RNA surveillance process through different in vitro and in vivo immune assays.

yes	<input checked="" type="checkbox"/>
no	<input type="checkbox"/>

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