



MÁSTER EN INVESTIGACIÓN BIOMÉDICA
Research Project Proposal
Academic year 2026-2027

Project Nº 20

Title: Exploiting RNA Modification Dependencies to Expand Precision Medicine in Ovarian Cancer

Department/ Laboratory: RNA Biology and Therapy- RNA and Senescence (4.03, CIMA).

Director 1 Marta Montes Resano

Contact: mmontesr@unav.es

Summary

High-grade serous ovarian cancer (HGSOC) remains the most lethal gynecologic malignancy, largely due to the limited therapeutic landscape for the 50% of patients who are homologous recombination (HR)-proficient. Unlike their HR-deficient counterparts, these patients do not respond to PARP inhibitors and quickly develop resistance to standard platinum-based chemotherapies. These tumors, often driven by CCNE1 amplifications, possess intact DNA repair mechanisms that allow them to bypass traditional targeted therapies.

There is an urgent need to identify synthetic lethal vulnerabilities unique to this non-HRD population. The "epitranscriptome", the collective group of RNA-modifying "writers," "erasers," and "readers", presents a frontier for discovery. Emerging evidence suggests cancer cells exploit RNA modifications to fine-tune gene expression under proteotoxic stress. By disrupting specific epitranscriptomic regulators, we may induce a state of "non-oncogene addiction," providing a precision medicine pathway for patients currently excluded from existing targeted regimens.

The primary objective of this project is to identify and validate RNA-modifying enzymes essential for the survival of HR-proficient HGSOC cells.

Aims 1: Functional Mapping of Dependencies. Utilize a targeted CRISPR-Cas9 dropout screen (targeting 407 RNA-modifying genes) across a panel of 2 stratified HGSOC cell lines to identify genes whose loss specifically induces lethality in HR-proficient backgrounds.

Aim 2: Preliminary Validation. Experimentally validate top candidate genes in ovarian cancer cells with different genetic backgrounds to determine if their inhibition re-sensitizes cells to platinum-based chemotherapy, laying the groundwork for future in vivo studies.

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