

## **University of Naples Federico II Department of Pharmacy** *Doctoral Course in Pharmaceutical Sciences XL Cycle*



## NOVEL THERAPEUTIC STRATEGIES IN FIGHTING CANCER

Tutor Annapina Russo e Co-tutor Giulia Russo

Despite advancements in therapeutic strategies, development of drug resistance and metastasis remains a serious concern for the efficacy of chemotherapy against cancer. Evidence has emerged in recent decades regarding the close link between dysregulation in ribosomal proteins and cancer (1). We have demonstrated that the downregulation of the mRNA encoding for the ribosomal protein uL3 positively correlates with drug resistance in colon and lung cancer that contain mutant p53 or no p53 at all (2,3). The analysis of transcriptomes of colon and lung cancer patients has unveiled the strictly correlation between uL3 expression and patients' outcome. Specifically, the reduced uL3 levels were associated with poor response to therapeutic treatment and shorter progression-free survival (4).

All these studies have identified uL3 as an important player in response to chemotherapeutic drugs suggesting a possible application of uL3 as a predictive biomarker of treatment response in cancer.

This project aims to provide more in-depth knowledge of new important cellular pathways involved in tumorigenesis and chemoresistance, whose investigations will produce new biomarkers for the treatment of cancer; to study the efficacy of novel RNA therapeutics. The biocompatibility and therapeutic efficacy of novel therapies will be evaluated with the use of 2D, 3D models and an in vivo model using the chicken embryo chorioallantoic membrane (CAM) system.

## References

1. Pecoraro A, Pagano M, Russo G, Russo A. Ribosome Biogenesis and Cancer: Overview on Ribosomal Proteins. Int J Mol Sci. 2021 May 23;22(11):5496. doi: 10.3390/ijms22115496. PMID: 34071057; PMCID: PMC8197113.

2. Russo A, Saide A, Smaldone S, Faraonio R, Russo G. Role of uL3 in Multidrug Resistance in p53-Mutated Lung Cancer Cells. Int J Mol Sci. 2017 Mar 3;18(3):547. doi: 10.3390/ijms18030547. PMID: 28273808; PMCID: PMC5372563.

3. Pagliara V, Saide A, Mitidieri E, d'Emmanuele di Villa Bianca R, Sorrentino R, Russo G, Russo A. 5-FU targets rpL3 to induce mitochondrial apoptosis via cystathionine-β-synthase in colon cancer cells lacking p53. Oncotarget. 2016 Aug 2;7(31):50333-50348. doi: 10.18632/oncotarget.10385. PMID: 27385096; PMCID: PMC5226586.

4. Carotenuto P, Pecoraro A, Brignola C, Barbato A, Franco B, Longobardi G, Conte C, Quaglia F, Russo G, Russo A. Combining β-Carotene with 5-FU via Polymeric Nanoparticles as a Novel Therapeutic Strategy to Overcome uL3-Mediated Chemoresistance in p53-Deleted Colorectal Cancer Cells. Mol Pharm. 2023 May 1;20(5):2326-2340. doi: 10.1021/acs.molpharmaceut.2c00876. Epub 2023 Mar 28. PMID: 36976623; PMCID: PMC10155186.