PNRR Missione 4, Componente 2, Investimento 1.4 "Potenziamento strutture di ricerca e creazione di "campioni nazionali di R&S" su alcune Key Enabling Technologies"
Iniziativa finanziata dall'Unione europea –- NextGenerationEU.
National Center for Gene Therapy and Drugs based on RNA Technology
Sviluppo di terapia genica e farmaci con tecnologia a RNA
Codice progetto MUR: **CN00000041** – CUP UNINA: **E63C22000940007**

Doctorate of National Interest

RNA THERAPEUTICS AND GENE THERAPY

SELECT ONE OF THE FOLLOWING RESEARCH AREA:

☒ **Mechanisms of Diseases and Drug Target Identification**

☐ **Design and Delivery of New Gene Therapy and RNA-Based Medicines**

☐ **Validation and Safety In Preclinical and Clinical Studies**

LOCATION OF THE RESEARCH ACTIVITY (INSTITUTION/DEPARTMENT):

Institute of Clinical Physiology (CNR)

URT presso ISPRO, viale Gaetano Pieraccini 6, 50139 Firenze

TUTOR:

Silvestro Conticello

PROPOSED RESEARCH ACTIVITIES (max 300 words):

Synthetic lethality, a promising therapeutic approach to target cancer cells, has been hindered by the difficulty to identify and block exploitable patient-specific processes.

Aim of the project is the development of programmable RNA editing as a tool to interfere with specific cellular processes and trigger cell death in cancer: enzymatic deamination by programmable RNA editing can alter specific transcripts through recoding and stability alterations; as RNA editing does not introduce permanent alterations in the genetic information of the cell, it poses lower risks on bystander cells compared to DNA-targeting technologies. Moreover, RNA

targeting based on the characteristics of the individual tumor makes this approach much more versatile than a drug-based one. Selective cell death will be achieved by targeting cellular processes in a synthetically lethal relationship with processes already altered in cancer cells. We will thus use cancer genome-based information to define exploitable targets for programmable RNA editing.

As we are testing alternative RNA editing approaches and developing selective induction of cancer cell death using established synthetically lethal pairs, the PhD student involved in the project will work at the selection of patient-specific targets.

To this aim, the student will establish tools to identify exploitable targets using genomic, epigenetic, and transcriptomic information from individual patients, both from primary/metastatic tissue and from cell-free DNA obtained from liquid biopsy.

The project rests on the expertise of the proponent lab on the study and exploitation of DNA/RNA editing technologies, and on the development of novel approaches to characterize the genomic/epigenetic features of cancer. Ongoing collaborations with national and international research groups will facilitate the professional growth of the doctoral student and the implementation of the project.