

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):

Federico II University, Department of Advanced Biomedical Sciences

TUTOR: Prof. C. Perrino C./G. Esposito

PROPOSED RESEARCH ACTIVITIES (max 300 words): RNA-based diagnostics and therapeutics represent exciting and growing fields of research, yet a still modestly exploited frontier in gene therapy for cardiovascular disease, as technical difficulties affecting their in vivo delivery have limited their clinical application in the past two decades. Small nucleolar RNAs (snoRNAs) are typically 60-300-nucleotide-long and broadly expressed in nucleated cells, reflecting their primary role in rRNA maturation. Although their canonical functions in modifying rRNA have been most studied, snoRNAs have been also associated with a wide variety of cellular processes, such as regulation of mRNA splicing, chromatin organization, or oxidative stress. In addition, there are many putative orphan snoRNAs that do not have known RNA targets, and recent reports suggest that even canonical snoRNAs can also be associated with noncanonical regulatory functions. Currently, the impact of snoRNAs on cardiovascular diseases is still poorly understood. Furthermore, snoRNAs are frequently released from cells and can be found and measured in the circulation. This feature makes them attractive as potential biomarkers of disease. In addition, early data suggest that vesicle-mediated transfer can shuttle snoRNA and other lncRNAs between cells or distant tissues, raising the possibility of functional signaling or biological actions at a distance. This PhD program will be focused on the

identification and mechanistic snoRNA-mediated regulation of cardiomyocyte survival and contractility under physiological and pathological conditions in vitro and in vivo, using wild-type and genetically modified murine models of cardiac disease, and possibly identifying novel RNA-based diagnostics and therapeutics for myocardial ischemia, infarction and ultimately heart failure.