Finanziato dall'Unione europea NextGenerationEU
Ministero dell'Università e della Ricerca
Italiadomani PIANO NAZIONALE DI RIPRESA E RESILIENZA
Università degli Studi di Napoli Federico II

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

TITLE OF THE RESEARCH PROJECT

Design and Synthesis of Ligands for RNA-based therapies

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):

Department of Pharmacy, University of Naples Federico II

TUTOR: Paolo Grieco

PROPOSED RESEARCH ACTIVITIES (max 300 words):

Dysregulation of miRNA expression has been implicated in the development and progression of a wide range of human diseases, including cardiovascular diseases (CVD), neurodegenerative diseases, dermatological conditions, and cancer.

Recently, peptides have attracted increasing interest in the fields of gene therapy as they could be used as modulators of miRNA expression.

Furthermore, thanks to their characteristics and size they can occupy a larger area than small molecules, and therefore can compete more easily in RNA and RNA-protein interactions.

The use of peptides in the regulation of miRNA expression is, however, largely underexplored. Recent studies have demonstrated that macrocyclic peptides, compared to their linear peptide counterparts,

exhibit high binding affinities for target RNAs. This is likely due to the fact that peptide cyclization limits conformational flexibility, which in turn reduces the entropic penalty paid by RNA binding and increases their selectivity for the RNA binding site.

Finally, our research group demonstrated that peptides would also be able to recognize G-quadruplex structures and therefore be able to develop new peptide-based G-quadruplex ligands with greater selectivity and anti-tumor activity. These results highlight the therapeutic potential of peptide-based ligands and pave the way for the development of new targeted therapeutic strategies in gene therapy. The research activity will be aimed at identifying peptides capable of acting as potential agents targeted toward gene therapy.