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):

University of Naples Federico II – Department of Pharmacy – Via D. Montesano 49, 80131 Naples - Italy

TUTOR:

Prof. A. Randazzo

PROPOSED RESEARCH ACTIVITIES (max 300 words):

DNA exists in the form of a three-dimensional double helix, as stunningly discovered by James Watson and Francis Crick in 1953. Since then, science has notably evolved and DNA is now recognized as a structurally dynamic molecule which is also able to adopt alternative secondary conformations such as cruciforms, hairpins, G-quadruplexes (G4s), triplexes, and i-motifs (iMs), mainly depending on the nucleotide sequence.
G4s fall among the most widely investigated non-canonical DNA secondary structures. They occur in guanine-rich sequences and consist of stacked layers of G-tetrads, planar arrangements of four guanines held together by eight Hoogsteen hydrogen bonds.

The complementary cytosine-rich strand of a G4-forming sequence can fold into an i-motif, a four-stranded DNA conformation held up by hemi-protonated cytosine-cytosine+ base pairs.

Both G4s and iMs are highly prevalent in biologically relevant genomic regions such as telomeres, oncogene promoters, and replication initiation sites, thus being potentially involved in a number of critical cellular processes including genomic stability, gene transcription, and DNA replication.

Firstly, with the aid of a multi-omics approach including transcriptomic, proteomic and metabolomic analyses, this research project aims at dissecting the implications of non-canonical nucleic acids in the development of different types of disorders such as metabolic, neurodegenerative, inflammatory, genetic diseases or cancer. This might allow to identify unprecedented pathogenetic mechanisms G4s and iMs could participate in.

This project is also intended to provide a more in-depth knowledge about the specific roles of G-quadruplexes and i-motifs in the cellular environment, paving the way towards the use of G4-forming oligonucleotides in gene therapy, to manipulate the expression of target genes.

In conclusion, this investigation could directly impact the scientific community by providing fresh knowledge about the biology governing non-canonical nucleic acid structures and their role in the development of diseases, also making space for the rational design of new therapeutic strategies.