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**

Tematica per SPOKE: 6 (RNA drug development)

Design, synthesis, structural characterization, and evaluation of the biological properties of therapeutic oligonucleotides based on DNA, RNA and analogs.

Therapeutic oligonucleotides are a new class of drugs chemically made up of nucleic acids (DNA and RNA). The main types of therapeutic oligonucleotides are those based on messenger RNA (mRNA), DNA or RNA antisense (ASO and anti-miRNA), RNA interference (siRNA and miRNA), and DNA or RNA aptamers. After nearly 40 years of research, oligonucleotide therapies are approaching significant clinical productivity.
One of the main advantages of oligonucleotides is that their distribution and efficacy are mainly derived from the chemical structure while their target is defined by the base sequence. Successful clinical development requires that the chemical structure of the oligonucleotide is optimized with a combination of modifications of the sugar-phosphate backbone, nucleobases, and 3' and 5' ends. To this end, a variety of chemical modifications can be used to impart pharmacological properties to the oligonucleotide, with minor structural alterations often resulting in major improvements in biological efficacy. Therefore, through the introduction of suitable nucleotide derivatives or the conjugation with other molecules, the present research project has the following targets: 1) improving the thermodynamic stability; 2) increasing resistance in biological environment; 3) enhancing the pharmacodynamic properties of interaction with the target; 4) improving the pharmacokinetic properties and, in particular, the specific organ-tissue delivery; 5) using the oligonucleotide as a carrier for small therapeutic molecules with a resulting synergistic effect; 6) facilitating structural investigations and interaction with the target.
In addition to the chemical synthesis procedures, the project includes steps of analysis and purification of the products, based mainly on chromatographic and electrophoretic techniques, and steps of analysis and structural characterization based on spectroscopic techniques (circular dichroism, UV and NMR).