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**

SPOKE 4: Metabolic and cardiovascular diseases

Design and Synthesis of antisense oligonucleotides (ASOs) modified with small molecules.

MicroRNAs (miRNAs) are a kind of high conserved non-coding small RNAs that bind to the 3'-untranslated region (3'-UTR) of target gene's mRNA and regulate gene expression at post-transcriptional level. In immune responses, miRNAs act as signal-regulating molecules after immune-related receptors activation, and affect the expression of immune-related genes, thus extensively participating in various aspects of immune response. MiR-214 is a key miRNA that regulates the functions and characteristics of a variety of immune cells including T cells, natural killer (NK) cells, and macrophages, and widely participates in immune response processes. Recently, the functional role of miR-214 in the induction of perivascular fibrosis and vascular stiffening driven endothelial dysfunction was elucidated. miR-214 has been shown to affect several pathways involved in atherosclerosis development and progression. Thus, the main goal of the research is to target miR-214 for the control of hypertension and hyperlipidaemia concurring to metabolic syndrome. Synthetic anti-microRNA oligonucleotides are a form of steric-blocking antisense oligonucleotides (ASOs) that inhibit miRNA function through high-affinity binding and subsequent inactivation and/or degradation of the targeted miRNA. Specifically, the pursued objectives of the project are:

- Design and synthesis of antisense oligonucleotides.
- Chemical modifications proposal to improve pharmacological characteristics.

ASOs are ~18-30 nucleotide long, single-stranded, synthetic polymers of nucleic acids with diverse chemistries. The ASOs target mRNAs based on complementary base pairing and interfere with different aspects of gene expression and regulation. Their incredible versatility is the key to manipulating several aspects of nucleic acid function as well as their process. A large number of chemical modifications have now been applied to ASOs, resulting in improved pharmacological characteristics. Starting from these considerations, the aim of this project is to design and synthesize ASOs and/or ASOs small molecules conjugates through a structural approach.