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 3: RNA delivery in the treatment of neurodegerative diseases

Bioactive non-viral nanovectors for RNA delivery

The approval of therapies based on RNA underlines the mandatory role of lipid-based nanoparticles to avoid the use of viral vectors. A pivotal role of nanoparticle components (i.e. lipids) has been shown, influencing not only RNA uptake, but also interaction with blood components and nanoparticle biodistribution. Moreover, nanoparticle components with biological effects can be used to design “bioactive” nanoparticles that could support RNA delivery strategy for the development of combined novel and more powerful therapeutic approaches. With this in mind, bioactive lipid-based nanoparticles, namely lipid nanoparticles or lipid self-assembling nanoparticles, will be designed for RNA (siRNA, miRNA/antagomir or mRNA) delivery as potential novel therapeutical approach in the treatment of diseases, especially neurodegenerative diseases. Thus, lipid nanovectors encapsulating RNAs, enriched with bioactive compounds, will be prepared and fully (physically and biologically) characterized. The inclusion of physically or chemical conjugated ligands on the nanoparticle surface will be also evaluated for targeting of specific cells or for overcoming biological barriers, e.g. the blood-brain barrier. Physical stability during storage, stability in plasma or simulated plasma, as well as hemolytic activity will be evaluated. In vitro studies will be used to determine the cytotoxicity of the formulations. In vitro studies will also provide information on the biological effect of the bioactive formulation. RNA uptake by using the selected formulations will be studied on cell lines and/or primary cells providing further information for the optimization of nanoparticle formulations. Finally, the selected lipid-based nanoparticles encapsulating RNA will be tested on animal models, relevant for the selected neurodegenerative disease. The study will allow to advance the development of novel and efficient therapies based on RNA for the treatment of neurodegenerative diseases. Moreover, this project will represent the basis for a further optimization of lipid nanovectors to design novel therapeutical and combined approaches based on RNA.