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
Development of innovative mRNA delivery systems for rare pathologies involving lungs.

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: Prof.ssa Stefania Galdiero

PROPOSED RESEARCH ACTIVITIES: Design, synthesis, and characterization of self-assembling peptide nanosystems for the targeted, controlled, and guided delivery of mRNA to lung cells, carrying bioinspired components for a more efficient administration. The nanoplatform to develop will be highly versatile and modular and suitable to be exploited for personalized medicine and used for the treatment of different types of pathologies simply by modifying the molecules exposed on its surface. By means of a single-step self-assembly process, amphiphilic peptides will be used to afford the generation of nanofibers decorated on their surface with selected moieties. The central hypothesis is that precise control of nanosystem design will lead to a unique delivery platform able to cross the mucus barrier encountered in several of these pathologies (such as cystic fibrosis, primary ciliary dyskinesia, and bronchiectasis) to have access to the target. In particular, the nanosystem will be functionalized with i) cell penetrating peptides as delivery moiety; ii) targeting moieties; iii) antimicrobial peptides and /or molecules; iv) mRNA. The developed nanoplatform will be characterized though biophysical techniques, including circular dichroism (CD), dynamic light scattering (DLS), transmission electron microscopy (TEM), nuclear magnetic resonance (NMR), fluorescence-based assays, atomic force microscopy (AFM) and scanning electron microscopy (SEM). The internalization in normal Human Bronchial Epithelial (NHBE) cells (in 2D and 3D) and cytotoxicity of the nanoplatform will be evaluated; the antimicrobial properties provided by the AMPs fused on the surface of the vector will be analyzed by co-culturing spheroids in presence of bacteria usually found in lungs; the synergistic action of mRNA and antimicrobial moieties will be determined. Once administered, our nanomedicine should: • pass several barriers allowing accumulation of mRNA to the designated sites of action, • enhance cell uptake, • protect the drug from its easy degradation and random diffusion• be responsive to the environment • be biodegradable.