







# 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:

Lipid-based delivery strategies for the development of RNA-based therapeutics for the treatment of triple negative breast cancer

## SELECT ONE OF THE FOLLOWING RESEARCH AREA:

- □ Mechanisms of Diseases and Drug Target Identification
- X 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. Giuseppe De Rosa

#### PROPOSED RESEARCH ACTIVITIES (max 300 words):

Triple-Negative Breast Cancer (TNBC) is the most aggressive breast cancer with a poor prognosis due to the lack of effective therapies. Recently, the Telomere Repeat binding Factor 2 (TRF2) has been proposed as a valuable therapeutic target in TNBC since it contributes to tumor formation and progression. In this









context, a microRNA (miR-182-3p) capable of specifically inhibiting TRF2 has been identified and delivered by lipid nanoparticles (Dinami et al, 2022).

Building on our promising results (Dinami et al, 2022), within this project we aim at developing novel lipid-based nanoparticle formulations to maximize miR-182-3p delivery to TNBC cells and investigate potential synergistic effects with established chemotherapies and targeted therapies in advanced models of TNBC. In order to achieve cancer cell-specific miRNA delivery, the surface of the nanoparticles will be functionalized with peptides able to selectively bind receptors overexpressed in TNBC cells. We will explore the use of microfluidic mixing and tangential flow filtration to obtain miRNA-loaded nanoparticle formulations to facilitate their clinical translation and industrialization. The scale-up of the selected nanoparticle formulations will be performed at IBI's plant. The critical parameters related to the preparation and purification of the formulations at laboratory scales will be identified to define the design space necessary to obtain a final product with the required critical quality attributes at industrial scales. Analytical methods for formulation testing will be developed and a detailed protocol for batch production in GMP will be prepared.

The results achieved within this project will pave the way for the industrial development of a novel lipidbased formulation for miRNA delivery against TNBC which could be combined with current chemotherapies and targeted therapies. We expect the lead formulation to advance to a phase I clinical trial tailored to patients with metastatic TNBC who do not respond to the currently available therapies.