

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

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):

University of Milan, Department of Pharmaceutical Science

TUTOR:

Prof. Paola Minghetti

PROPOSED RESEARCH ACTIVITIES (max 300 words):

The research activities will be focused on the pharmaceutical technology and regulatory aspects of synthetic and biological lipid vesicles for the skin delivery of DNA and/or RNA.

The delivery to the skin of DNA and RNA can be useful in different pathologies. The research will be focused to the design of synthetic and biological lipid vesicles as well as on the individuation of critical aspects also considering the regulatory point of view. In a first step different formulations will be designed to identify the best composition for the transfection of keratinocytes, melanocytes or dendritic cells using GFP-DNA or GFP-mRNA as models. Afterwards, their ability to penetrate the skin after a pretreatment with a microneedle array will be assessed using explanted human skin. In particular, in the case of synthetic vesicle the possible relationships between the

nanoparticle physical properties (e.g. zeta potential, size, structure and deformability) and the lateral diffusion in the tissue will be explored using explanted human skin as in vitro model with aim to identify the quality attributes critical for a specific delivery of genetic material to a specific skin layer. As far as the biological vesicles is concerned, considering that very few information on their possible use as carrier for skin delivery, the feasibility to use extracellular vesicles isolated from cells obtained by human skin samples will be explored evaluating their ability to transfect specific cell lines of the skin. Overall, the experimental data related to the definition of critical quality attributes of such delivery systems will be used to elaborate a general guideline for these typologies of products.