

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):

Department of Pharmacy, University of Salerno, Laboratory Bio Open Lab

TUTOR: Prof. Eduardo Maria Sommella

PROPOSED RESEARCH ACTIVITIES (max 300 words): Mass Spectrometry-based omics for Disease and Drug mechanism elucidation

In the current early drug development stage potential drug candidates are evaluated to confirm and validate their target engagement (TE) markers as well as elucidation of the mode of action (MoA). In these stages is crucial to apply different bioanalytical methodologies and strategies, that allow to investigate pharmacokinetics and pharmacodynamics. Mass spectrometry (MS) has emerged as a highly versatile and valuable tool crucial to many aspects of modern drug development. In particular MS based omics provide the comprehensive study of the biochemical composition of an organism and has the potential to accelerate drug development at several stages such target engagement and mechanism of action, safety and efficacy as well as possible future applications such as in drug repurposing. In the context of modern drug discovery there is a rising interest in mRNA drugs for the treatment of different diseases, with several examples currently being used in clinical fields. Nevertheless, their development includes several challenges. In order to better understand their pharmacodynamics and underlying molecular mechanisms, omics sciences, in particular Metabolomics and Lipidomics, stand as a useful supporting tool. The aim of this project is an extensive application of mass spectrometry-based multi-omics approaches to supporting and assist early and innovative drug discovery, such as the development and validation of new mRNA-based

drugs. The project will be focused in develop new analytical solutions able to decipher the complex molecular events that follow drug administration, in conventional and innovative screening systems such as 3D cell cultures, patient derived organoids (PDO) and tissues. Different and integrated advanced MS strategies (HRMS, ion mobility, MALDI-imaging) will assist the development of novel technological solution for drug delivery to evaluate the ability of precision targeting, and bio-informatics will be used to build predictive models and extract markers of efficacy or toxicity, to be used for prognostics and drug-monitoring.