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**

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 Surgical, Medical and Molecular Pathology, and Critical Care Medicine (primary location)

Center for instrument Sharing (CISUP)

Department of Chemistry and Industrial Chemistry

Department of Physics

Department of Pharmacy

TUTOR:

Prof. Ranieri Bizzarri

PROPOSED RESEARCH ACTIVITIES (max 300 words):

In DNA/RNA therapy it is crucial to tackle the fate and efficacy of the delivery systems in living cells. In this scenario, we shall target a versatile pre-clinical platform combining state-of-the-art intelligent

probes with optical nanoscopy, to enable live functional imaging of how the nanoformulation properties determine its cellular fate and downstream activity. Goals will be: 1) the assessment of how the physicochemical features of formulations tailor their drug targeting/delivery capabilities; 2) the development of intracellular fluorescent nanosensors able to follow biochemical pathways targeted by DNA/RNA therapeutic systems. The experimental activity will be primarily devoted to characterizing *ex vivo* and *in cellulo* the activity of the delivery systems. This will be accomplished by functionalising delivery systems by suitable fluorescent groups, enabling the nanoscale imaging of treated/untreated cells. Much interest will be devoted to transcription pathways modulating the cell phenotypes in pathologies such as cancer and diabetes. Here, a crucial role is played by the polycomb protein family, whose ability to shape the hierarchical organization of chromatin is presently under intense study in the quest of innovative epigenetic drugs. For this purpose, we shall apply super-resolution fluorescence imaging techniques (such as STORM, ISM, STED-FLIM, FRET/TR-FRET) which are intimately suited to address the meso- and nanoscale of chromatin organization by reporting on functional molecular parameters, such as the formation of condensed nanophases, the local chromatin topology, and the diffusion/binding processes.

The student will be encouraged to participating to all the activities of Spoke8 @Unipi, to develop a broader understanding of crucial principles and methods of relevance for the challenge of CN3, including DNA/RNA manipulation, “omics” techniques, protein engineering, super-resolution imaging of biological specimens. This purposedly multidisciplinary education will provide the young investigator with a wide scientific background, fostering her/his personal capabilities as future independent scientist.