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):

Dept. of Molecular Biotechnology and Health Sciences, University of Torino
https://www.dbmss.unito.it/do/home.pl/View?doc=Gruppi_ricerca/Regenerative_Medicine_group_copy.html

TUTOR: Benedetta Bussolati, MD PhD

PROPOSED RESEARCH ACTIVITIES:

Targeted renal cell therapy using engineered blood-derived extracellular vesicles.

Cell-released biological nanoparticles, that is, extracellular vesicles (EVs), are emerging drug carriers with high complexity (Yu et al. 2020). This PhD project aims to develop a new RNA drug delivery system based on engineering of natural circulating EVs, including red blood cell or platelet derived vesicles. The aim will be to set up a new therapeutic strategy of RNA delivery for renal regeneration, with the main goal to foster the repair of kidneys not suitable for donation, exploiting the possibility to provide a regenerative therapy during the period of graft ex vivo normothermic reperfusion. EV will be functionalized using tissue damage-binding peptides using click chemistry (i.e KIM1). In addition, EVs will be engineered with RNA species prone to stimulate regenerative processes, including transcription factors and mitochondrial oxidative pathway, as described (PMID: 30788382, PMID:34111564). The effects of different RNA-carrying EVs will be tested in models of acute and chronic kidney damage. In particular, in vitro potency tests for inhibition of renal cell apoptosis, fibrosis and for induction of pro-regenerative pathways will be evaluated. Ex vivo, EVs will be tested in a non-survival ex vivo porcine model mimicking the donation after cardiac death (DCD) renal transplantation scenario. The effects will be evaluated with standard pathology, immunohistochemistry and RNA sequencing analysis. This project will form the PhD student in developing a new RNA-based therapy based on targeted compatible EV sources with important clinical translational implications.