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
Role of miRNA loaded MSC-derived MVs in pediatric Immune Thrombocytopenia

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):

University of Campania "Luigi Vanvitelli"/Department of Woman, Child and General and Specialist Surgery

TUTOR: Prof.ssa Francesca Rossi

PROPOSED RESEARCH ACTIVITIES (max 300 words):

Immune thrombocytopenia (ITP) is the most common childhood piastrinopenia (platelet count<100×10^9/L). It is an autoimmune disorder caused by platelets destruction mediated by autoantibodies, leading to symptoms ranging from asymptomatic to severe bleeding. ITP causes immune system dysfunction, including a prevalence of pro-inflammatory M1 macrophages, an elevated Th1/Th2 ratio, and impairment of mesenchymal stromal cells (MSCs) functions.
MSCs, known for their immunosuppressive and anti-inflammatory properties, are impaired in ITP patients, exhibiting abnormal morphology, reduced proliferation, increased apoptosis, and loss of immunosuppressive functions. First-line treatment with corticosteroids can manage ITP but has long-term side effects like hypertension and cognitive impairments. Recent research suggests that co-administering dexamethasone with a CB2 receptor agonist can improve MSCs' survival and restore their properties.
MSCs exert effects through secretome production, including extracellular vesicles (EVs) like microvesicles (MVs) and exosomes, which facilitate intercellular communication. MSC-derived EVs have shown promise in treating autoimmune disorders due to their immunomodulatory properties.

This study aims to explore a new therapeutic strategy for pediatric ITP using MSC-derived MVs loaded with miRNA implicated in ITP pathogenesis.
The study will enroll newly diagnosed ITP patients and healthy donors, collecting bone marrow and peripheral blood samples to obtain MSCs, lymphocytes, and macrophages. Various *in vitro* co-cultures will be established to analyze the effects of MSC-derived MVs on lymphocyte and macrophage viability, cytokine release, and phenotype switching. Additionally, small-RNA sequencing will identify miRNAs differentially expressed in MSC-derived MVs from ITP patients, and these miRNAs will be tested for their therapeutic potential.
In vivo experiments on a murine ITP model will assess the efficacy of miRNA-loaded MSCs, alone and combined with dexamethasone, in improving clinical parameters like platelet count and inflammatory state. This study aims to be the first to investigate miRNA-loaded MSCs in pediatric ITP, potentially offering a safer and more effective treatment option.