UNIVERSITÀ DEGLI STUDI DI MILANO-BICOCCA

DOTTORATO DI RICERCA IN Tecnologie Convergenti per i Sistemi Biomolecolari – XLII CICLO

Research Topic ID: XLII – 1.6

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Project Supervisor: Lucia Salvioni

Project Title: Crossing the blood–brain barrier for improved diagnosis and therapy of brain diseases

Scientific background & Objectives

The blood–brain barrier (BBB) remains a major obstacle to effective drug delivery and to the identification of reliable circulating biomarkers for brain diseases. Overcoming this selective endothelial interface is crucial to advance both therapeutic and diagnostic strategies.
This project aims to characterize the biological processes underlying nanoscale transport across the BBB through in vitro models and in vivo animal studies. Engineered organic nanocarriers and extracellular vesicles (EVs) will be investigated for their ability to transport biologically active molecules into the brain. EVs have demonstrated the capacity to traverse the BBB and represent promising candidates both as drug delivery vehicles and as minimally invasive liquid biopsy biomarkers. However, the molecular mechanisms regulating their transcytosis across brain endothelium remain insufficiently understood.
In this context, the specific objectives of this project will be: 1) to assess the effective potential of organic nanocarriers and EVs for brain-targeted delivery of therapeutic molecules; 2) to elucidate the molecular pathways and transcytosis mechanisms governing BBB crossing. In vitro BBB models and in vivo animal studies will be employed to validate the feasibility and translational potential of the proposed project.

Project's Networks, Sustainability & Mobility

a) the coherence of the suggested project with competences/tools of the hosting lab
b) intradepartmental or external collaborations
c) at least one pertinent research article published by the proposer/s
d) 1 (or more) putative foreign institutions for achieving the required ordinary mobility (6 months)

a) The project is fully coherent with the competences of the hosting lab, the Laboratory of Advanced Cell Models, specialized in the production of complex in vitro models, including biological barriers, and in the interaction of biologically active nanoparticles with these systems. In addition, the research group has consolidated expertise in in vivo experimentation and direct access to the animal facility of the BtBs Department, ensuring the effective implementation of animal studies

b) A strong and well-established collaboration is already in place with NanoBioLab, which has resulted in several joint publications, including studies on the interaction and trafficking of anti-tumor nanoparticles in both in vitro and in vivo tumor models. This collaboration has also led to previous work investigating the permeation of brain-targeting nanoformulations across the blood–brain barrier.
A new collaboration will be also activated with Prof. Marzia Del Re of Saint Camillus International University of Health and Medical Sciences (Rome) and Fondazione Policlinico A. Gemelli IRCCS (Rome). Prof. Del Re has recognized expertise in liquid biopsy and

circulating biomarkers in oncology, including those potentially relevant to brain malignancies.

c) Fiandra L, Colombo M, Mazzucchelli S, Truffi, M, Santini B, Allevi R, Nebuloni M, Capetti A, Rizzardini G, Prosperi D, Corsi F. Nanoformulation of antiretroviral drugs enhances their penetration across the blood brain barrier in mice. Nanomedicine, 2015; 11(6): 1387-1397.

Fiandra L, Mazzucchelli S, Truffi M, Bellini M, Sorrentino L, Corsi F. In vitro permeation of FITC-loaded ferritins across a rat blood-brain barrier: a model to study the delivery of nanoformulated molecules. Journal of Visualized Experiments. 2016; 114: e54279

d) A putative foreign institution includes the Silesian University of Technology (Poland), and the research group of Prof. Ilona Wandzik, dealing with the production of polymeric nanoparticles for the treatment of neurodegenerative disorders.