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Supervisor Expression of Interest
MSCA - Marie Sklodowska Curie Action - (PF) Postdoctoral Fellowship 2024

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Department Name: Department of Chemistry, Materials and Chemical Engineering&Department of Electronics, Information and Bioengineering

Research topic: Nanomedicine and Organ-on-chip

MSCA-PF Research Area Panels:

- ☐ECO_Economic Sciences
- X ENG_Information Science and Engineering
- ☐ENV_Environmental and Geosciences
- ☐LIF_Life Sciences
- ☐MAT_Mathematics
- ☐PHY_Physics
- ☐SOC_Social Sciences and Humanities
- X CHE_Chemistry

Brief description of the Department and Research Group (including URL if applicable):
This is a collaboration between two different research groups in different Departments with complementary expertise on cutting-edge research topics: NP synthesis and characterization for tumour targeting and development of tumour-on-a-chip. This synergy will enable to use a tumour-on-a-chip to elucidate NP delivery mechanisms to cancer tissues by a composition-structure-function approach. This project will be a unique opportunity for the candidate to acquire broad and diverse competences in chemistry and bioengineering on the development of new technologies for personalized and precision medicine.

TITLE of the project: Design of nanoparticle delivery strategy using a tumour-on-a-chip platform

Brief project description: Despite the extensive work done in the past decades on the development of nanoparticles (NP) for cancer treatment, their clinical translation is still limited[1].

This is due to the poor understanding of the mechanisms of NP delivery into solid tumours. The enhanced permeability and retention (EPR) effect, stating that NPs passively enter the tumours by gaps among endothelial cells and are retained thanks to reduced lymphatic drainage, has long been recognized as the main NP access mechanism to tumors[2]. EPR has dictated the rationale for designing anti-cancer NPs reducing size (smaller than interendothelial gaps) and prolonging circulation time to enhance accumulation. Recently, it has been shown that NPs enter tumours by an active transport and retention (ATR) principle[3]: NPs are actively internalized by endothelial cells, retained by interactions with tumour microenvironment (TME) components and exit by lymphatic routes. This novel concept sees EPR effect only as a secondary mechanism, fully revolutionizing the design of anti-cancer NP paradigm, which should be guided by the specific transport processes and TME. Thus, while conventional 2D in vitro models are not suitable for predicting NP in vivo response, it is unthinkable to "optimize" the NPs by in vivo experiments. Here our objective is to develop an ideal NP for the treatment of cholangiocarcinoma using a human 3D platform developed by MiMic Lab (https://www.biomech.polimi.it/mimiclab) in collaboration with Humanitas Hospital (Milan)[4]. This integrated engineered platform mimics complex in vivo tumour features at a microscale level, such as (TME), 3D tissue structure, and dynamic culture conditions. This platform will be used to study the delivery mechanisms (NP extravasation, NP tumor cell internalization, NP interaction with TME components) of tailored lipid NPs to cholangiocarcinoma tissues using different NP surface functionalization and lipid compositions, which should improve NP accumulation in tumour cells.

References

1 He, H. et al., Acc. Chem. Res. 2019, 52, 2445–2461
2 Ryoho, K. et al., Cancer Chemother. 1987, 14, 821–829; Peer, D. et al. Nat. Nanotechnol. 2007 2, 751–760
3 Nguyen, L. N. M. et al. Nat. Mater. 2023, 22, 1261–1272
4 Polidoro M.A. et. al., JHEP Reports 2024, 6, 1009104