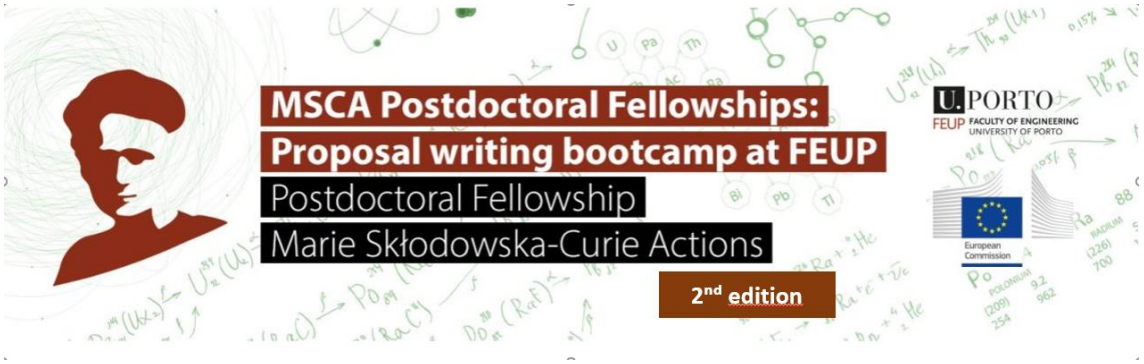

SUPERVISOR INFORMATION	
First and Last name	Maria do Carmo Pereira Maria João Ramalho
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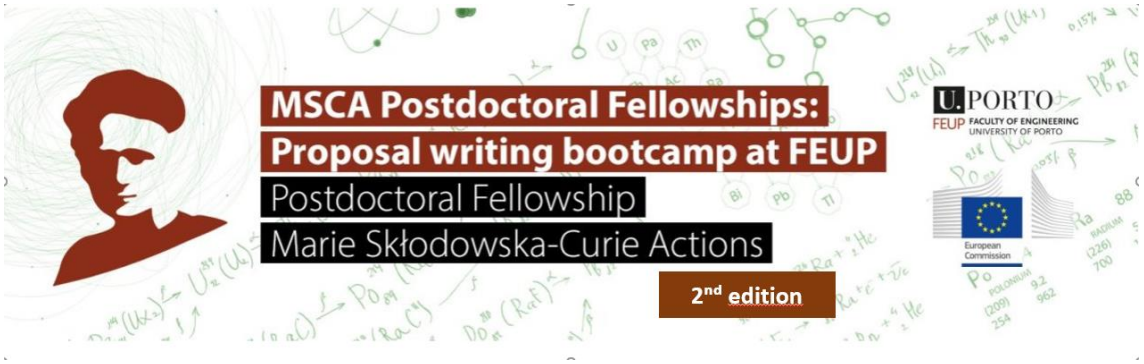
Department	Departement of Chemical Engineering
Field(s) of research	Nanomedicine
PROJECT PROPOSAL	
Title (optional)	Glioblastoma-Targeted Nanoparticles: A Dual Approach to Overcome the Blood-Brain Barrier

Brief project description

Glioblastoma multiforme (GBM) is the most common and invasive type of brain cancer with high morbidity and mortality. The currently used therapeutic strategies are not curative, only modestly increasing the patient's survival time. Therefore, is urgent to find new treatments. However, the blood-brain barrier (BBB) represents a major challenge for the delivery of drugs to the brain. Despite several drugs exhibiting a potential therapeutic effect for brain diseases, this barrier is an additional obstacle to therapeutic success. The BBB is a highly selective and active barrier that is fundamental for regulating the movements of molecules between the systemic circulation and the brain tissue, protecting the brain from undesired exposure to exogenous molecules. However, it is reported that the BBB is impermeable to 100% of the larger molecules and to approximately 98% of the smaller molecules (<500 Da). Thus, a promising strategy is the use of nanoparticles (NPs) that are able to cross the BBB and deliver drugs to the brain tumor tissue. An active targeting strategy can be used by attaching ligands to the NPs surface that bind specifically to the BBB receptors. Different moieties can be used to target the BBB, such as natural ligands (transferrin, folate, etc), antibodies and cell-penetrating peptides (CPP). After reaching the brain tissue, the NPs should be able to be taken up by the target cells. For that, the NPs can also be modified with ligand with affinity for the GBM cells. Several biomarkers are overexpressed at the GBM cells, and therefore can be used as targets. Thus, in this project it is intended to develop dual-targeted NPs with affinity for the BBB and GBM cells to increase their specificity and therapeutic efficacy. For that, NPs will be modified with ligands for BBB transport and for GBM recognition, The NPs will be also loaded with a model anticancer agent for therapeutic effect.

The main objectives of this work are:



- Production and characterization of NPs for the encapsulation of chemotherapeutic agents

- Surface modification of the NPs with ligands for BBB targeting

- Surface modification of the NPs with targeting moieties with affinity for tumor cells

- Optimization of the NPs production process using experimental design

- Physicochemical characterization of the developed NPs (mean size, polydispersion index, zeta potential)

- Evaluation of the release profile of the prepared NPs

- Evaluation of the colloidal stability of the NPs in storage and physiological conditions

- Evaluation of the uptake of the NPs in cell models

- Evaluation of the biocompatibility and therapeutic efficacy of the NPs in GBM cells