Nano4Glio

# Engineered nano-based device for glioblastoma multiforme therapy

Maria J. Ramalho[1,2], Stéphanie Andrade[1,2], Joana Peixoto[3], Kartikey Saxena[4,5], Manuel A.N. Coelho[1,2], Le T. Truong[6], Sabina P. Strand[6], Jorge Lima[3], Wilhelm R. Glomm[6], Andreas K.O. Åslund[6], Bjarne Winther Kristensen[4,5] Joana A. Loureiro[1,2], Maria C. Pereira[1,2],

[1] LEPABE - Laboratory for Process Engineering, Environment, Biotechnology and Energy, Faculty of Engineering, University of Porto, Rua Dr. Roberto Frias, 4200-465 Porto, Portugal

[2] ALiCE - Associate Laboratory in Chemical Engineering, Faculty of Engineering, University of Porto, Rua Dr. Roberto Frias, 4200-465 Porto, Portugal

[3] i3S – Instituto de Investigação e Inovação em Saúde, University of Porto, Rua Júlio Amaral de Carvalho 45, 4200-135 Porto, Portugal

[4] Department of Clinical Medicine and Biotech Research and Innovation Centre, University of Copenhagen, Copenhagen, Denmark

[5] Department of Pathology, The Bartholin Institute, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark

[6] Department of Biotechnology and Nanomedicine, SINTEF Industry, Sem Sælands Vei 2a, N-7034 Trondheim, Norway

* presenting author e-mail: jasl@fe.up.pt

Glioblastoma (GBM) is the most aggressive brain tumor, with poor prognosis. Standard treatment includes surgery, radiotherapy, and chemotherapy with temozolomide (TMZ). However, TMZ has poor blood-brain barrier (BBB) penetration, high toxicity and O6-methylguanine-DNA methyltransferase (MGMT)-mediated resistance.

Nano4Glio is developing an implantable hydrogel for sustained co-delivery of TMZ and an MGMT inhibitor via drug-loaded nanoparticles (NPs). Two NP formulations were designed: one functionalized with transferrin receptor (TfR) ligand (transferrin, Tf) and another with OX26 antibody against the TfR, both designed to enhance brain accumulation. The NPs show optimal properties for brain delivery, such as size <200 nm, low PDI, negative zeta potential, high stability, and controlled release.

Patient-derived GBM tumor spheroids BIT 14 and BIT 16 with MGMT unmethylated status were selected for *in vitro* studies. Concomitant treatment with TMZ and the MGMT inhibitor O6BG proved to be advantageous over single-TMZ treatment. Additionally, Tf-functionalized NPs showed superior efficacy over OX26-modified NPs.

Multiple polymer composite hydrogels and variations have been screened for suitable properties, such as, shear thinning, biocompatibility, recovery, density matching with tissue and release of NPs. Different types of NPs have been incorporated into the hydrogels to investigate both drug and NP release as well as the effect of NPs on the hydrogel properties.

This approach is expected to improve drug bioavailability in brain tumor cells, reduce toxicity, and overcome resistance, enhancing GBM treatment. In Nano4Glio, we aim at developing an implantable hydrogel device that will provide controlled, localized drug release for 6-weeks, reducing the need for frequent administration.

Project outcomes will be presented at the event through a poster and 10-minute oral presentation, focusing on the NPs, hydrogel formulation, NP incorporation, and impact on GBM therapy.

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