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Targeting Glioblastoma Cells with Polymeric Nanoparticles in 3D Biomimetic Culture Models †

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Abstract: Glioblastoma is a tumor of the central nervous system (CNS) known as one of the most lethal cancers, with a median survival of fewer than two years after first diagnosis. Despite recent major progress made with the improvement of modern surgical approaches, pharmacological therapy for glioblastoma could still benefit from further development. One of the major particularities of CNS cancers, which also stands for a major therapeutic approach disadvantage, is that theBlood–brain barrier (BBB) blocks the access of active compounds to their target. Various active compounds and delivery methods are continuously designed and tested in this context to investigate their potential benefits. With this respect, on the one hand, polymeric nanocarriers are widely studied for their potential to actively deliver biological agents based on their size, size distribution, and surface chemistry, and on the other hand, new 3D biomimetic culture systems are developed to better mimic *in vitro* the physiological environment. We present here novel polymeric nanoparticles based on silk sericin grafted with poly(2-(dimethylamino)ethyl methacrylate)) (PDMAEMA) loaded with temozolomide and 5FU drugs. More, we show our progress in developing a 3D biomimetic culture system using the TwoLane OrganoPlate® from MIMETAS and the LN229 glioblastoma cells. We also present some preliminary studies on the cells viability within this culture system after the treatment with drug-loaded NPs. SEM and DLS showed PDMAEMA-silk sericin nanoparticles with narrow size distribution and low sizes (60-80nm). Regarding the biological investigations, we determined via the MTT spectrophotometric quantitative assay that in conventional culture systems, the inhibitory concentration 50 (IC50) of the Temozolomide or 5FU loaded NPs is 10 mg/ml. More, we observed after the Live/Dead assay performed by fluorescence microscopy that the cells viability in the 3D culture systems significantly decreased 24h post-treatment with Temozolomide and 5FU loaded NPs. These preliminary data allow us to continue developing the study by validating the delivery systems and the 3D culture system.

Keywords: non-viral vectors; temozolomide; 5FU; glioblastoma; 3D culture systems.

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Conflicts of Interest

The authors declare no conflict of interest.