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Abstract

Development of a 3D-bioprinted drug screening system for personalized glioblastoma treatment

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Central Nervous System WHO grade 4 glioblastoma is a highly malignant brain tumor with a poor prognosis. The complex three-dimensional architecture of glioblastoma, consisting of cell-cell and cell-matrix assemblies of tumor cells, stromal cells, and extracellular matrix contributes to a highly dynamic microenvironment that resists current therapeutic approaches. Here, we established a 3D biomimetic bioprinting approach with patient-derived glioblastoma cell lines to mimic the natural tumor microenvironment for preclinical targeted therapy.

Two different hydrogels (Alginate/Gelatine 3%/15%, GelMa, 4%) were used to evaluate biocompatibility. Patient-derived iRFP-680-transduced glioblastoma cells were suspended in the hydrogels and printed into scaffolds. Tumor cell growth and viability within the scaffolds were monitored for 28 days. Scanning electron microscopy was performed for structural analysis. A preliminary treatment approach was done with the standard of care drug temozolomide (TMZ 10 µM) and the CDK4/6 inhibitor abemaciclib (1 µM). Viability and LDH release were quantified.

The hydrogel compositions showed good printability. A direct comparison between the two hydrogels showed a comparable growth pattern, i.e. constant growth over a period of 21 days and a steady state until day 28. Scanning electron microscopy confirmed cellular integrity within the scaffold and the formation of small cell clusters with large pores within the matrix. In a preliminary drug response analysis, we successfully confirmed our previous results from 2D and 3D cultures. The preliminary 3D biomimetic bioprinting model proved to be a promising platform with good cell-material interaction for nutrient and substance exchange. For advanced preclinical drug screening, we aim to improve the culture conditions by incorporating vessels, non-malignant microglia and astrocytes, and by applying dynamic cell culture conditions.

AUTHOR'S STATEMENT

Conflict of interest: Authors state no conflict of interest. Informed consent has been obtained from all individuals included in this study. Ethical approval: The research related to human use complies with all the relevant national regulations, institutional policies and was performed in accordance with the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee [Ethics Registration ID: A2018-0167]. Acknowledgments: The project was funded by the German Federal Institute for Risk Assessment Grant Agreement Number 60-0102-01.P640.

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