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Abstract: P-303

Validation of long-term 3D glioblastoma cell culture as a novel biomimicking model system for preclinical drug testing

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Introduction

Various three dimensional (3D) biomimicking human glioblastoma cell culture models have been developed in the last decade. However, all these models have limited duration of viable cell cultures, which is necessary for reliable drug response studies. Therefore, we are developing a novel long-term 3D glioblastoma biomimicking model system that would enable optimal drug testing at clinically relevant duration.

Material and Methods

3D culture of human U87 glioblastoma cells in alginate microfibers was followed for 28 days under static and dynamic conditions. To characterize this culture, cell growth and viability were assessed by trypan blue dye exclusion test every seven days, until 28th day. At the same time points, cell morphology and aggregation were analyzed by fluorescent and confocal microscopy upon calcein-AM/propidium iodide staining. Drug testing was validated by comparing effects of two different TMZ treatment modalities on cell viability, morphology, aggregation and resistance-related gene expression (*MGMT* and *ABCB1)*. Specifically, effects of 3 treatments with 100 μM TMZ, starting from day 7 (X=7), were compared between subsequent treatment modality (day by day treatments, X+1) and protractive treatment modality (every 7 day, X+7).

Results and Discussions

Within the newly established static 3D model system, U87 glioblastoma cells remained viable up to 28 days. The number of cells increased over time, while the cell death rate was low. At day 7, cells formed visible aggregates oriented to microfiber periphery, towards the source of oxygen and nutrients. Importantly, both

TMZ treatment modalities had the same effect on cell viability in the static long-term 3D culture. However, protractive treatment reduced the expression of *MGMT* and *ABCB1*observed with subsequent treatments.
Further work will be focused on the development of dynamic long-term 3D cell culture in perfusion bioreactor. In this advanced model system, U87 cells in alginate microfibers will be exposed to continuous media flow for 28 days. Introduction of media flow, as the tumor microenvironment factor, may promote different glioblastoma phenotype making it more reliable *in vitro* model for drug testing.

Conclusion

Based on the results obtained so far, we can conclude that our model system could be suitable for drug testing in glioblastoma gaining relevant results for future clinical studies.