ARTICLE IN REVIEW:

HuBiogel™-based 3D microtumors are genetically similar to the gold standard, patient-derived xenografts

PUBLICATION: Cells, July 2019

TITLE: A Novel Assay for Profiling GBM Cancer Model Heterogeneity and Drug Screening[1]

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STUDY DESIGN: Benchtop

SUMMARY: Currently, drug safety and efficacy, chemical toxicity, and other important types of testing are performed in either two-dimensional (2D) cultures or animal models. However, these methods often fail to accurately represent the human *in vivo* environment and may lead to unsafe or ineffective therapies. Patient-derived xenografts (PDX), in which patient-derived tumors are grown in immunocompromised mice, are often considered the gold standard cancer model for human tumor representation; however, they lack the ability for high-throughput drug testing. Three-dimensional (3D) culture of microtumors in a fully human-derived HuBiogel extracellular matrix (ECM) may be a more relevant preclinical model because it more closely resembles the human tumor microenvironment and is capable of high-throughput assaying. This paper compared the genetic profiles of two 3D models of glioblastoma multiforme (GBM) – HuBiogel-based microtumors and spheroids – to cells from the current gold standard PDX model. Using a custom NanoString panel of 350 pan-GBM genes, 113 core genes were found to be common among the three models, indicating model-independence and suggesting tumor-specificity. No differentially expressed gene differences were observed between Temozolomide (TMZ) treatment of microtumors and PDX cells. Therefore, HuBiogel-based 3D microtumors show genetic similarity and similar drug sensitivity to the gold standard PDX model, potentially offering a more relevant preclinical model capable of high-throughput therapeutic screening and profiling of tumor-specific biology.

Preservation of native tumor physiology:

3D microtumors grown in HuBiogel more closely matched the tumor microenvironment of cells from the murine-implanted PDX tumors compared to spheroids. Microtumors recapitulated the GBM characteristics seen in the patient.

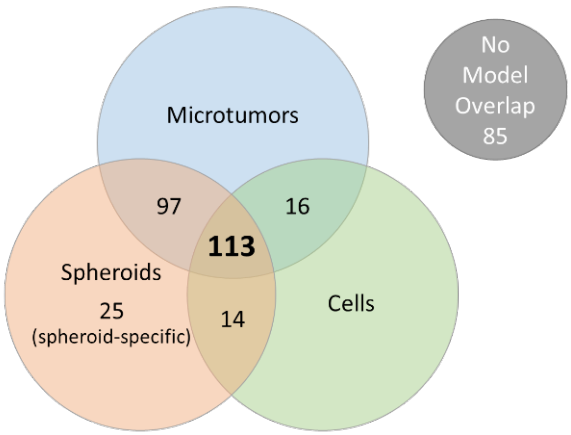
Model-independent core genes identified:

NanoString analysis identified 113 core genes that were common among all three models. These core genes indicate GBM tumor-specificity.

Targeted screening based on model-independent genes:

Model-independent genes can be used to profile tumor-specific biology and for targeted high-throughput therapeutic response screening using the HuBiogel-based 3D microtumors.

Model overlap identifies 113 tumor-specific, model-independent genes



Overlap of the 350 NanoString pan-GBM genes across the three models. Figure created from data presented in Figure 3A.[1]

Reference:

1. Stackhouse CT, Rowland JR, Shevin RS, Singh R, Gillespie GY, Willey CD. A Novel Assay for Profiling GBM Cancer Model Heterogeneity and Drug Screening. Cells. 2019;8(7):702. doi:10.3390/cells8070702

68-20-326.00

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