ARTICLE IN REVIEW:

HuBiogel™-based 3D microtumor model for high-throughput drug screening

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TITLE: Combinatorial Drug Testing in 3D Microtumors Derived From GBM Patient-Derived Xenografts Reveals Cytotoxic Synergy in Pharmacokinomics-informed Pathway Interactions[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 animal models or two-dimensional (2D) cell cultures. However, these methods often fail to accurately represent the human *in vivo* environment and may lead to ineffective therapies. Patient-derived xenografts (PDX), in which patient-derived tumors are grown in immunocompromised mice, have offered attractive cancer models for human tumor representation; however, they lack the ability for high-throughput drug testing. This paper reports the use of a fully human-derived HuBiogel extracellular matrix (ECM) to develop a three-dimensional (3D) microtumor model of glioblastoma mutliforme (GBM) PDX tumor cells, which mimics the human microenvironment. GBM microtumors closely resembled murine-implanted tumors and displayed global kinase (kinomic) and morphological diversity. Drug response screening could be reproducibly performed in a 96-well format using 4 small molecules, singularly and in combination. Therefore, the fully human-derived HuBiogel-based 3D microtumor model is effective for high-throughput combinatorial drug screening in order to evaluate therapeutic effectiveness.

Preservation of native tumor physiology:

3D microtumors grown in HuBiogel maintained their native proliferative capacity and morphological characteristics (colony-like formation and invasive properties) similar to murine-implanted tumors.

Biological diversity of 3D microtumors:

3D microtumors exhibited reproducible kinomic diversity. The HuBiogel ECM allowed signaling of the embedded tumor cells.

Effective model for high-throughput drug screening:

Individual and combinatorial high-throughput drug screening was reproducibly performed on the 3D microtumors grown in HuBiogel.

GBM PDX cells form 3D microtumors in HuBiogel

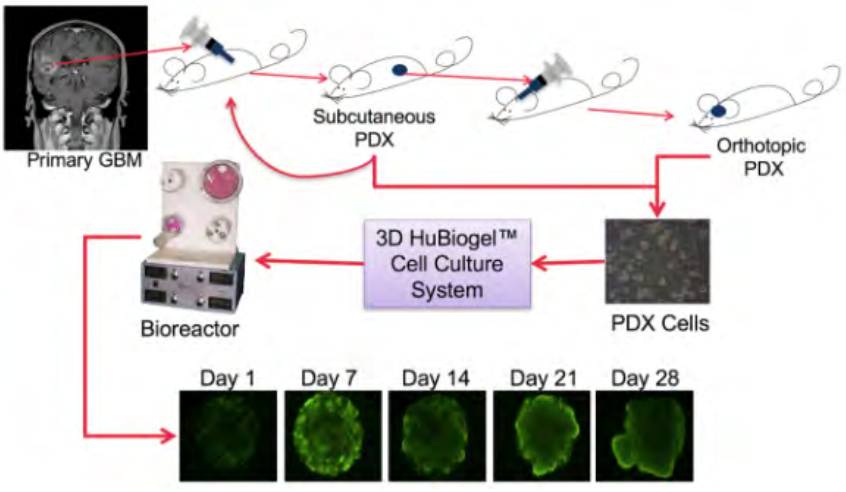

Figure 2A. Reproduced with permission under an open access license.[1]

Reference:

1. Gilbert AN, Anderson JC, Duarte CW, et al. Combinatorial Drug Testing in 3D Microtumors Derived from GBM Patient-Derived Xenografts Reveals Cytotoxic Synergy in Pharmacokinomics-informed Pathway Interactions. Sci Rep. 2018;8(1):8412. doi:10.1038/s41598-018-26840-4

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