MANIPULATING AND ANALYZING CELLS WITH MAGNETIC 3D CELL CULTURE

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3dcellculture.gbo.com

GREINER BIO-ONE

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ABSTRACT:

The speed of adopting 3D cell culture models is often limited by technical challenges in handling, processing, and scalability to high-throughput applications. To meet these challenges, we use our platform, magnetic 3D cell culture (M3D), in which cells are individually magnetized and assembled with magnetic forces. In magnetizing cells, not only do we make routine cell culture and experiments feasible and scalable, but we also gain control in the formation and manipulation of spheroids and more complex structures. This poster will focus on recent developments using this platform. Specifically, we will present a tool for manipulating cells and phenotypic profiling of 3D cell culture.

TECHNOLOGY:

The core technology of Greiner Bio-one's magnetic 3D cell culture is the magnetization of the cells with NanoShuttle™-PL. The cells can be aggregated with magnetic forces, either by levitation or bioprinting, to form structurally and biologically representative 3D models in-vitro.
NanoShuttleTM-PL consist of gold, iron oxide and poly-L-Lysine and is electrostatically attaching to the cell membrane during an overnight static incubation.
NanoShuttleTM-PL is biocompatible, showing no effects on metabolism, viability, proliferation and inflammatory stress.

Figure 1: **384 Well 3D Bioprinting Kid**

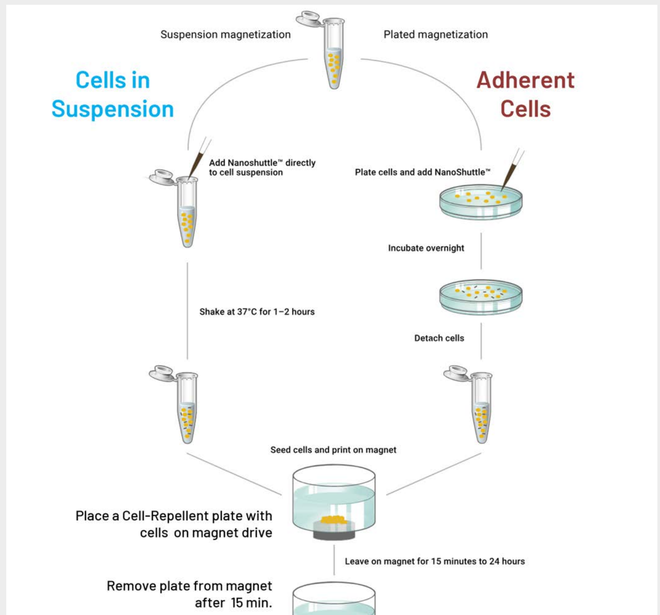


Figure 2: **Mignatizing cells with NanoShuttle™-PL to form structurally and biologically representative 3D models in-vitro**

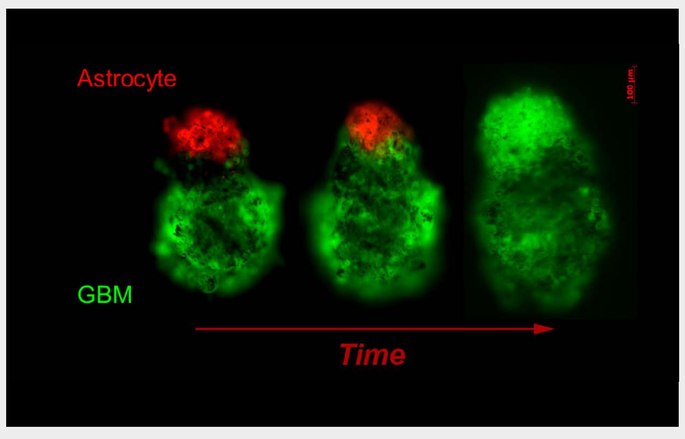


Figure 3: **Co-culture of Glioblastoma (LN229; Green) with Normal Human Astrocytes (red).**

DETECTION OF SPECIFIC TARGETING AND KILLING OF CD19+ NALM-6 CELLS:

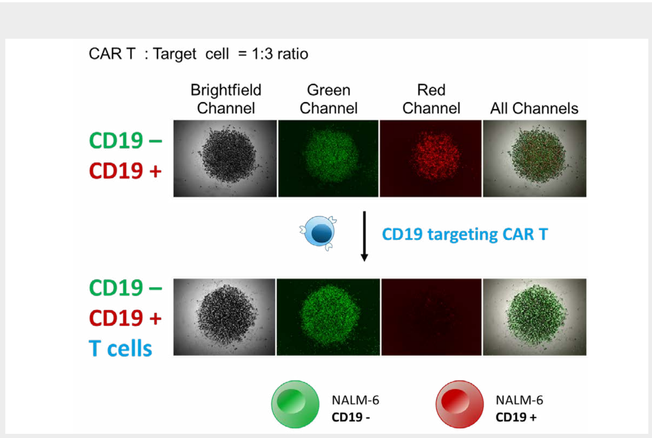


Figure 4: **Magnetically bioprinted dots of cells**

Magnetically bioprinted dots of Leukemia cells (NALM-6) as a co-culture of CD19 positive (red) and negative (green) mixed CAR T targeting CD19 (blue).
CD19 positive NALM-6 cells disappeared from the after 24 hours culture as a result of the targeted killing of the CAR T. cells. NALM-6 cells assembled into a spheroid shape but they did not form a tight 3D structure. The ratio of NALM-6 to CAR T was 3:1 and this assay was performed with 384 well flat bottom.

3D IN A 2D WORKFLOW:

- Rapid spheroid formation (<24 h)
- Easy of exchanging media
- Magnetized spheroids easy to hold down during manipulation
- Scalable, up/down, in size from 6- to 1536-well formats
- Bioprint, culture, co-culture, stain, and image spheroids in same plate
- Non-specific to any cell type
- No effect of NS or magnetic field on cell viability and function
- No interference on any endpoint (fluorescence, qRT-PCR, etc)
- No special equipment/media required.
- Magnetized spheroids can be centered in the well
- All experimental steps of culturing, bioprinting, staining and imaging the 3D cell culture can be done in one plate.
- Spheroids can also be easily captured and transferred between vessels using the magnetic tools such as the MagPen.

INFLAMMATORY BREAST CANCER COMPARISON: IN VIVO PDX VS. M3D CELL CULTURE:

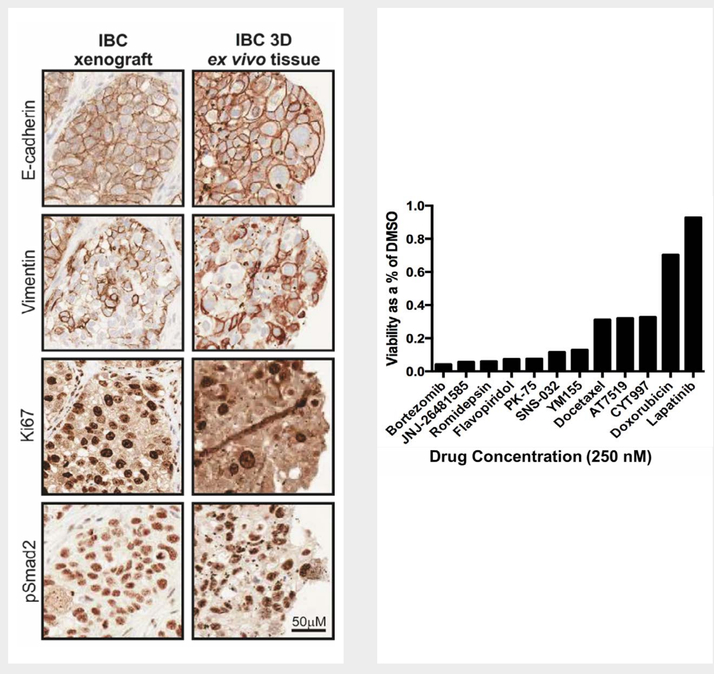
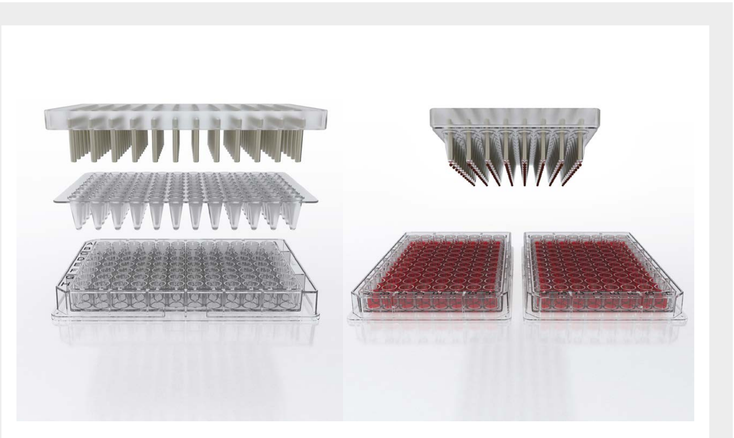


Figure 5 & 6: **(Left) Immunohistochemistry analysis and comparison of PDX tumor and magnetically 3D cultured PDX-derived ex-vivo tissue, which shows remarkably similar tissue architecture and expression distribution of E-cadherin, Vimentin, Ki67 and pSMAD2. (Right) Screening results of potential therapeutic agents for triple negative inflammatory breast cancer (340 compound anticancer drug library). Seven of the top 9 drug candidates had a stronger antitumor effect compared to the standard of care drugs.**

MULTI-MAGPEN – TOOL FOR TRANSFERRING 3D CELL CULTURES (COMING SOON):



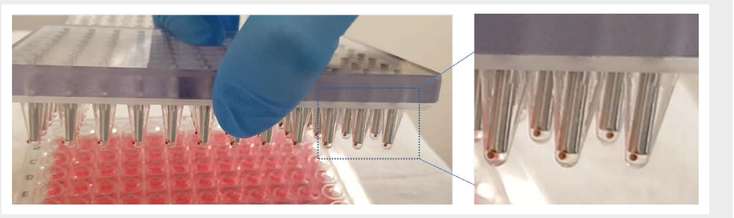


Figure 7 & 8: **(Left) 96 Well Multi-MagPen with Multi-MagPen Drive, Multi-MagPen Sleeve and Cell Repellent Plate; (Right) Transfer of 3D cell cultures by a simple pick-up-and-drop step**
Figure 9 & 10: **Enabling tool for magnetically transferring and layering 3D cell cultures without disrupting tissue organization**

REAL-TIME AND HIGH-THROUGHPUT IMAGING FOR MEASURING COMPOUND ACTIVITY & COLLECTIVE PHENOTYPICAL CHANGES; PANCREATIC CANCER (PANC-1) VS. DOXORUBICIN:

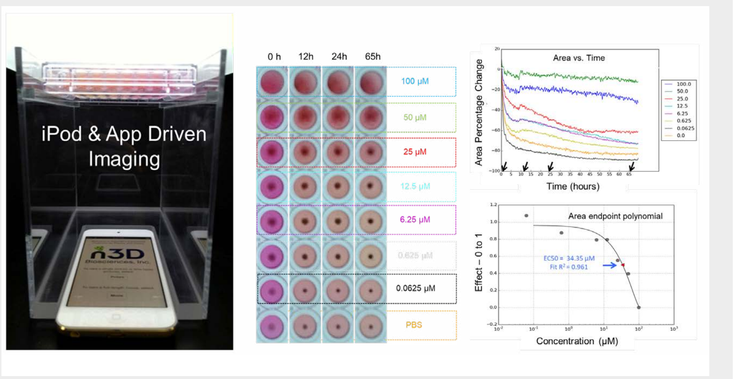


Figure 10: **Magnetically 3D bioprinted dots of 3T3 Fibroblast cells and Mobile device-based imaging the effect of Retinoic Acid killing effect by delaying natural 3D cell culture assembly. (12 hours)**
Tseng et al. Scientific Reports Sci. Rep. 5, 13987 (2015)

ACKNOWLEDGEMENTS & REFERENCES:

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