Validation of Magnetic 3D Spheroid Bioprinting in Combination with a BlueWasher

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Abstract

Three-dimensional (3D) cell models are thought to better mimic the complexity of in vivo tumors. We have previously enabled an HTS-compatible method using cell-repellent plates combined with a magnetic force bioprinting technology that affords large scale testing of spheroids and organoids in flat-bottom 384 and 1536 well plates. This type of 3D biology requires tissue culture in suspension which makes feeding, media transfers, washing, etc., problematic. To address this we combined the 384 well formatted n3D technology with the utility of the BlueWasher equipped with magnetic spin features. We validated this system for rapid removal and replacement of media to facilitate adaptation of a non-homogeneous format within 3D HTS. Our work demonstrates the effectiveness of both the magnetic 3D (m3D) bioprinting system and the BlueWasher in the following aspects in 384 well plates: 1) Retention of 3D spheroids and their integrity 2) Precision and accuracy of liquid manipulation 3) Qualification in terms of compound controls, Z’ and S:B when using phenotypic 3D primary pancreatic tumor cell based assays.

BlueWasher Magnetic Spin Evaluation: Spheroid loss or disruption?

hT1-CAF Spheroids

Figure 2. (A) hT1-CAF spheroids cultured using m3D bioprinting technology in full plate at 24 hrs post-seeding imaged by Scirpss HIAPI imager and standard microscopy. Only 1 spheroid was lost after 3 times of medium change using BlueWasher magnetic spin method. From the 10X objective images, hT1-CAF spheroids stayed intact after 3 times of magnetic spin. (B) Concentration-response curves of 5 known chemotherapeutics on hT1-CAF spheroids with and without medium change using BlueWasher. Drug response of controls on hT1-CAF spheroids was not affected by medium change using magnetic spin. Assay statistics (S/N, Z and Z’) are listed for each CRC plate.

Conclusion

- m3D bioprinting technology incorporating magnetic force coupled with Greiner Bio-One cell repellent plate for 3D culture has been validated for HTS drug screening.
- m3D bioprinting technology in combination with BlueWasher magnetic spin for medium removal has been evaluated using two representative 3D pancreatic cancer cultures.
- BlueWasher magnetic spin for liquid removal does not cause destruction to 3D hT1-CAF spheroids or barely cause spheroid loss.
- 20% of hT1 cells are lost after magnetic spin, which are probably non-labeled cell.
- Cell loss in m3D plates does not follow the Center Row pattern.
- Medium change does not affect CRC of control drugs on 3D pancreatic cancer culture.
- Magnetic spin effectively removes liquid in Greiner 384 GNF compatible plates.
- BlueWasher magnetic spin method for medium removal works well with n3D bioprinting system.

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