High-throughput spheroid formation in a 384-well format using magnetic 3D bioprinting

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Background

Three-dimensional (3D) cell culture can recreate native tumor microenvironments in vitro. However, technical limitations in speed, handling, and sample retention have prevented its widespread incorporation into high-throughput compound screening processes.

A solution for this unmet need is magnetic 3D bioprinting. where cells are magnetized with biocompatible magnetic nanoparticles (NanoShuttle™). Once magnetized, these cells can be rapidly aggregated and formed into spheroids and other shapes using magnetic forces.

These spheroids:
- are rapidly formed (15 min - few hours)
- easy to handle/hold down with magnets to retain samples
- are viable, with no effect of NanoShuttle™ and/or magnetic fields on cell behavior
- can be made with most cell types
- do not require specialized equipment, media
- fluoresce without interference from NanoShuttle™
- scale down in size for high-throughput formats (384- and 1536-well)

Magnetic 3D Bioprinting

- Cells are magnetized by incubating with NanoShuttle™ overnight.
- The next day, magnetized cells are detached, counted, and resuspended in media.
- Cells are distributed into a low-binding 384-well microplate (CELLSTAR® Cell Repeilient Surface, Greiner).
- Plate is then placed on magnetic drive to form spheroids anywhere between 15 min to overnight.
- Plate can then be removed off magnet to culture and assay.

High-Throughput Spheroid Printing

Magnetic 3D bioprinting rapidly prints spheroids by using magnetic forces to accelerate spheroid aggregation. With fixed magnet sizes, spheroid size is reproducible and scalable for high-throughput testing. These spheroids are viable and growing, and represent native tumor microenvironments.

Toxicity Screening - BiO Assay™

Spheroids will contract immediately (< 24 h) in a manner related to viability, where healthy spheroids will contract, while unhealthy ones will not. We use spheroid size over time as a simple metric to measure the efficacy of a compound in killing cancer cells. Contraction is measured in real-time using an iPod (Apple Computer) that captures whole plates of spheroids with sufficient resolution (200 µm) at programmed intervals (< 1 s), forgoing the need to image and measure each individual spheroid under a microscope.

Acknowledgements

This work was supported by Small Business Innovation Research Grants from the National Institute of Environmental Health Sciences (Phase I - ES024644) and the National Science Foundation (Phase I - 0945954, Phase II 1127551).

References