Biomedical research has gravitated towards three-dimensional (3D) cell culture platforms that replicate native tissue environments in vitro better than traditional two-dimensional (2D) platforms. These platforms can replicate tissue stiffness, extracellular matrix (ECM) composition, heterogeneity, and access to nutrients and compounds. However, technical issues in handling and speed have so far limited the expansion of 3D cell culture platforms into high-throughput screening.

A platform that addresses these issues is magnetic 3D bioprinting. The core principle behind this platform is the magnetization of cells with bio-compatible magnetic nanoparticles (NanoShuttle™), which attaches electrostatically to cell membranes. These cells are then subsequently printed into spheroids with mild magnetic forces. These spheroids escape the limitations of other platforms in high-throughput screening by being:

- rapidly formed (few hours - overnight)
- unattached to any stiff substrate
- easy to handle, held down with magnets to retain spheroids
- reproducible in size with fixed magnets
- viable, with no effect of NanoShuttle™ and magnetic fields on cell behavior
- unlimited to any cell type
- fluorescent without interference from NanoShuttle™
- scalable in size for high-throughput formats (384- and 1536-well)

In this study developed functional assays for cardiotoxicity (beating in cardiomyocytes) and drug-drug interactions (CYP450 inhibition/induction in hepatocytes).

**Methods**

- Cardiomyocytes (iPSC, Cellular Dynamics) and hepatocytes (primary, BioreclamationIVT) are thawed and magnetized by mixing with NanoShuttle™ (1 µL/10,000 cells) for 2 h
- MagNetized cells are detached, counted, resuspended in media, and distributed into a cell-repellent 384-well plate (CELLSTAR®, Greiner Bio-One)
- Cells are printed into spheroids by placing the plate atop a magnetic spheroid drive of 384 magnets (Nano3D Biosciences), that aggregate cells into spheroids at the bottom of the well
- Spheroids are left on the plate overnight to interact and build a mature spheroid with ECM

**Results**

We successfully printed cardiomyocyte spheroids that beat to track functional changes in beating and calcium signaling in response to cardiotoxic compounds.

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**References**