

LC Sciences collaborates with n3D Biosciences to validate their high-throughput spheroid assay for toxicity screening in 3D environments.

A collaboration between LC Sciences, a leading developer of genomics and proteomics technologies, and n3D Biosciences has yielded a validated spheroid toxicity assay based on n3D's proprietary magnetic 3D bioprinting technology. The new assay represents a simple, biologically relevant, and label-free drug toxicity assay that more closely mimics *in vivo* conditions than assays performed in 2D environments such as the standard methylthiazolyl tetrazolium (MTT) assay.

n3D develops 3D assays (Three-dimensional (3D) *in vitro* systems) that address the shortcomings of 2D systems, which inadequately mimic tissue environments found *in vivo* and overcome the technical challenges of other 3D cell culture systems with limited potential. Modeling *in vivo*-like environments, cell-cell and cell-extracellular matrix (ECM) interactions that are crucial to the regulation of cell behavior and function in real-time, these assays reveal more information about toxic mechanisms or drug interactions than was previously possible.

3D cell cultures (spheroids) are formed by magnetic 3D bioprinting where cells are magnetized with a biocompatible, magnetic nanoparticle assembly and directed by a cylindrical magnet to form a spheroid at the bottom of a multiwell plate. The n3D researchers discovered that after formation, the spheroids begin contracting immediately as cells rearrange and compact the spheroid in relation to viability, cytoskeletal organization, and proliferation. They further discovered that cytotoxicity affects the ability of cells to migrate, interact with other cells, and form the spheroid. They reasoned that spheroid size, which can be tracked visually, could be used as a simple metric for toxicity.

3T3 cells were successfully printed into spheroids and their dose-dependent contraction in response to 5 toxic compounds was imaged over time using a mobile device-based imaging system. Indeed, spheroids exposed to higher concentrations contracted at a slower rate than spheroids exposed to lower concentrations.

In order to validate spheroid contraction as a cytotoxic endpoint, n3D collaborated with LC Sciences to investigate the assay results at the genomic level. Gene expression analysis, performed by LC Sciences genomics services division demonstrated differences between spheroids in the presence or absence of compounds that support the assay's findings of toxicity. Specifically, increased expression of genes promoting apoptosis and decreased expression of apoptosis inhibitors, as well as genes related to regulation of the actin cytoskeleton was found. Additionally, when comparing gene expression in spheroids to *in vivo* tissue as reported in literature, significant changes in expression of genes that regulate actin was similar in both environments.



According to n3D's CSO Glauco Souza, the data generated by LC Sciences "made a big difference" in the eventual validation of the assay.

Immunohistochemistry was performed along with the genomic analysis and the results further supported the assay results. Overall, these results demonstrate that toxic responses can be seen in spheroid contraction, and reflect spheroid viability, organization, and gene expression similar to *in vivo* results. The results were recently published in the journal [Scientific Reports](#), a Nature publication.

For over 10 years, LC Sciences has been providing researchers with access to the latest innovative technologies that are enabling significant discoveries in the life sciences, as demonstrated by the successful result of this

collaboration. The assay's modeling of general cytotoxicity and high-throughput format address the major challenge in biomedical research and drug development of predicting *in vivo* responses to drugs.

Reference

Tseng H et al. (2015) **A spheroid toxicity assay using magnetic 3D bioprinting and real-time mobile device-based imaging.** *Sci Rep* 5:13987. [[article](#)]

About LC Sciences

LC Sciences is a global biotechnology company that provides products and services to genomics and proteomics researchers across an array of markets for nucleic acid/protein analysis, biomarker-discovery and drug development. The company's innovative products and comprehensive services are based on several unique, in-house developed core technology platforms. For more information please visit <http://www.lcsciences.com/> or [@LCSciences](#)



About n3D Biosciences

Biomedical research is gravitating towards 3D cell culture models and tissue printing. n3D provides kits and services for 3D cell culture. The company's core technology is the magnetization of cells, which can then be directed using magnetic forces. In this manner, it is possible to either levitate or bioprint cells. These cultures are faster to assemble than other systems and easier to handle with magnets without losing samples. For more information on this technology, check out: <http://www.n3dbio.com/>



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