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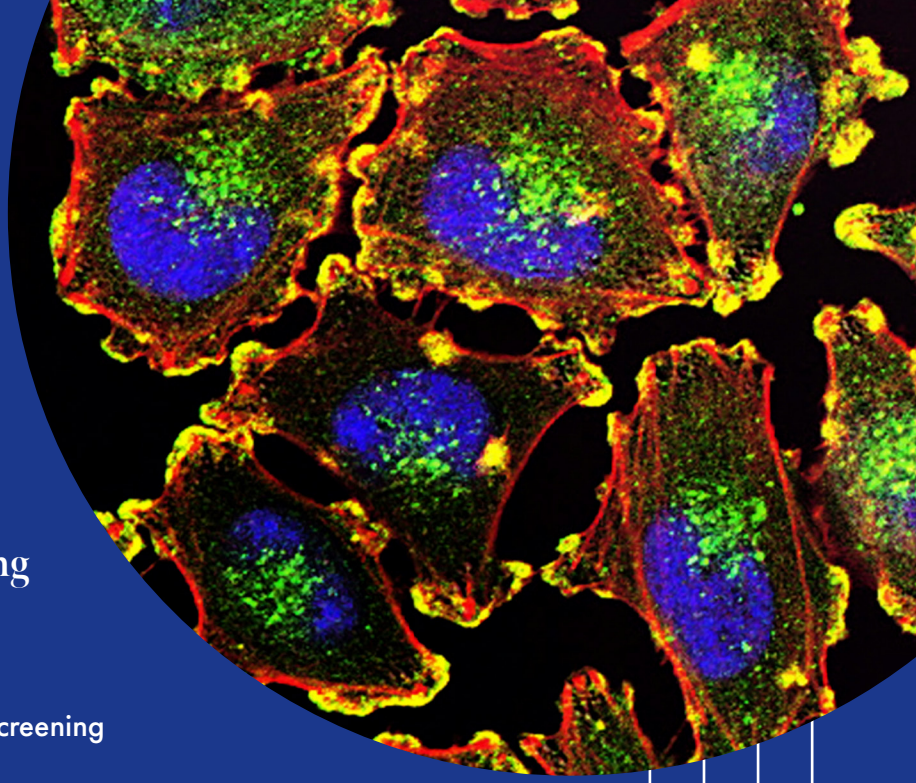
Application Note

Automated Organoid Culture at Scale:

Reducing Variability and Accelerating Compound Screening Workflows



Organoid Culture & Research-Use Compound Screening

For Research Use Only

INTRODUCTION

The Reproducibility Challenge in Three-Dimensional Cell Culture

Organoids are self-organizing, three-dimensional structures derived from adult stem cells or induced pluripotent stem cells (iPSCs) and have emerged as a compelling model system for early-stage drug discovery, disease modeling, and toxicity assessment. Unlike conventional 2D monolayers, organoids recapitulate the cellular architecture, gradient exposure, and intercellular signaling of native tissue, offering a more physiologically relevant platform for research-use compound evaluation.[1]

Despite their biological advantages, organoids have remained an emerging rather than an established technology, with the primary barrier to adoption being a lack of reproducibility inherent to manual workflows. Organoid culture is technically demanding, and seeding density, matrix composition, media exchange timing, and passage technique each introducing compounding variability across the workflow. This can make it difficult to distinguish genuine biological signal from experimental noise in drug screening assays.[2]

Inconsistent size and morphology can also yield variable drug responses — meaningful liability for research programs that depend on comparative data across multiple compounds and conditions. Addressing these limitations requires a systematic, instrument-level approach to process standardization.

Another hindrance to manual workflows is that they are inherently low throughput. Automation addresses this on two fronts: higher capacity per run, and continuous processing where successive batches can be initiated without waiting for the prior run to complete.

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This application note presents representative performance data across iPSC-derived organoid models using the Galatek Titan2000 Organoid Workstation and the Titan3000 Integrated Platform to address the reproducibility challenge through workflow automation, AI-driven protocol optimization, and end-to-end data traceability.

All applications described are intended for research use only. Not cleared or approved for clinical diagnostic use.

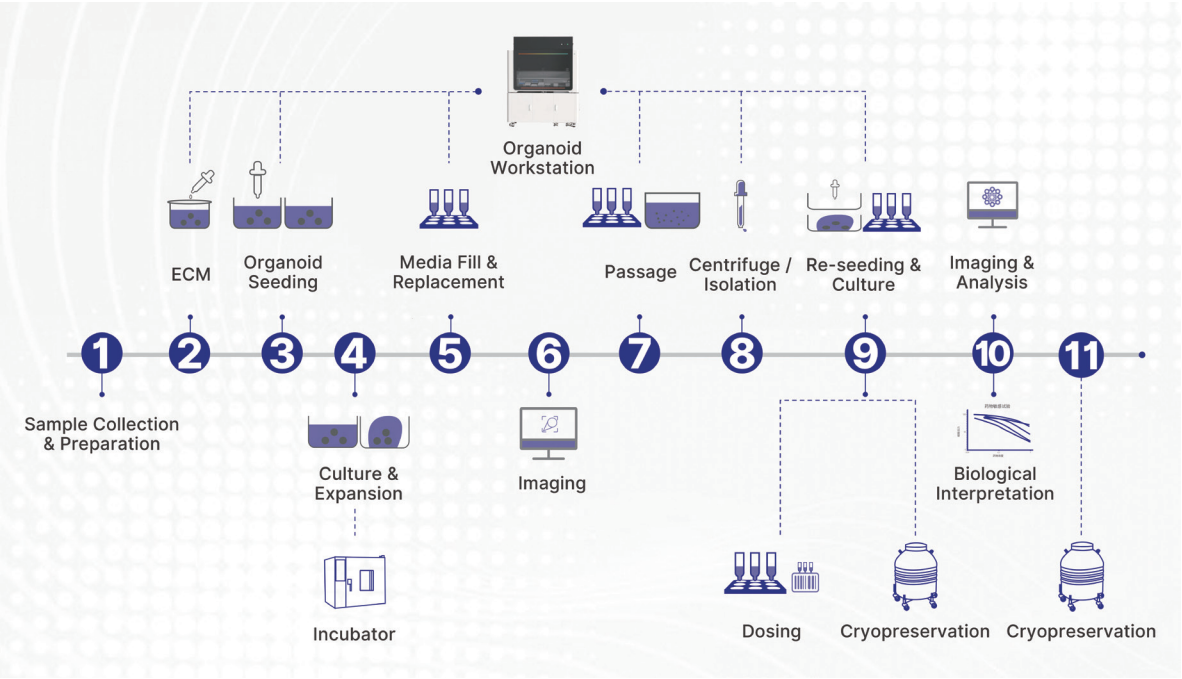
METHODS

Materials

The iPSC-Derived Cerebral Organoid Culture Kit (Cat# M-iHBOK) underwent rigorous QC including cell-based validation and sterility and mycoplasma testing prior to use. Previous characterization of Galatek's organoid kits has demonstrated intra-assay reproducibility of <10% CV.

The validated organoid kit provides the biological foundation for the workflow, while automated handling supports consistent execution of repeated culture steps. Performance data were validated by imaging, H&E staining, immunofluorescence, and immunohistochemistry. The AI-powered R&D process underlying Galatek's organoid kit incorporates small-sample learning and transfer learning across organoid data from diverse cancer types and patient samples, enabling rapid convergence on optimal media formulations, including customized protocols for staging, concentration, and culture duration.

Organoid Culture and Drug Screening Workflow:



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Organoid Culture and Drug Screening Workflow:

Experiments were conducted using the Galatek Titan2000 Organoid Workstation and, where whole-process automation was required, the Titan3000 Integrated Platform. Both systems operate within a positive-pressure HEPA-filtered environment and support the full organoid workflow from initial seeding through compound screening readout.

Features	Titan2000	Titan3000
Pipetting Module	8-Channel independent operation	8-Channel independent operation
Heating/Cooling	✓	✓
Positive Pressure HEPA	✓	✓
Centrifuge	✓	✓
Media Replacement Module	✓	✓
Incubator		✓
High Content Imaging System		✓
Microplate Reader		✓
Consumable Stacker		✓
Sample Transfer Robotic Arm		✓
AI-Driven Software	✓	✓

Pipetting was performed using a flexible 8-channel liquid handling module (adjustable spacing 9–18 mm) with air displacement mechanics, delivering pipetting precision of 0.75% CV at 1 mL and 3.00% CV at 10 µL (10 µL tip).

Embedded AI-driven software managed protocol selection and real-time optimization. The system mined accumulated experimental data and published literature to recommend media formulations, flag protocol adjustments, and monitor organoid morphology, diameter, and quantity continuously during culture, without the need for manual operator input between scheduled events.

For Titan3000 experiments, a robotic arm coordinated physical sample transfers between the workstation, incubator, high-content imaging system, and microplate reader, enabling uninterrupted automation across the full culture-to-readout pipeline.

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RESULTS

Representative Performance Data

iPSC-derived cerebral organoid differentiation was assessed across multiple extracellular matrix (ECM) surrogate concentrations (2.5%, 5%, 7.5%, 100%) at Days 10, 17, and 23 post-induction using the automated seeding and culture protocol.

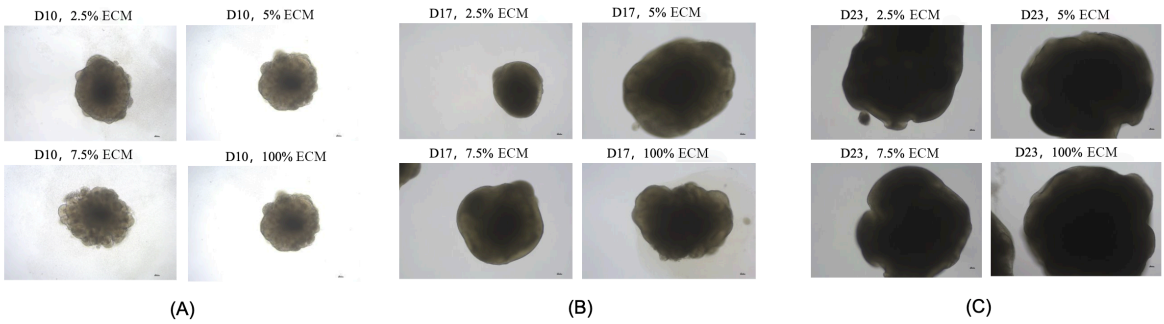

Figure 1. Differentiation and culture of iPSC-Derived Cerebral Organoids, Days 10–23
Brightfield images at Days 10, 17, and 23 across ECM surrogate concentrations using the iPSC-Derived Cerebral Organoid Culture Kit.

Neuroepithelial rosette structures consistent with native nerve tissue architecture were confirmed by H&E staining at Day 16. By Day 35, distinct neural rosette formation was observed across replicates.

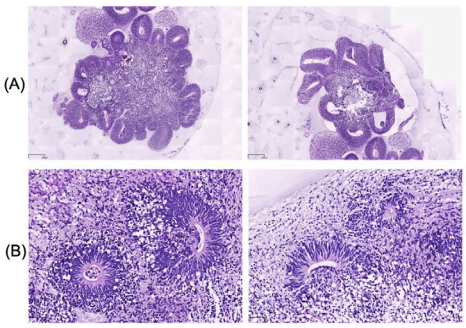

Figure 2. iPSC-Derived Cerebral Organoid Morphology
H&E staining at Days 16 (A) and 35 (B) confirmed neuroepithelial rosette formation, consistent with the physiological structure of nerve tissue.

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Immunofluorescence at Day 16 confirmed expression of SOX2 (neural progenitor marker), Nestin (intermediate progenitor marker), and NeuN (neuron marker).

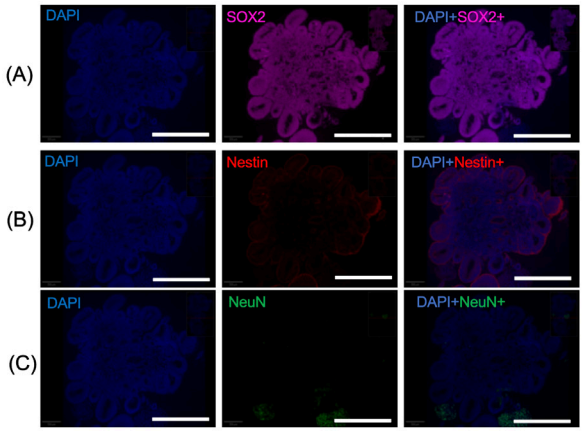

Figure 3. Differentiation of iPSC-Derived Cerebral Organoids at Day 16

Differentiation effects of iPSC-derived Cerebral Organoids were characterized by immunofluorescence staining of cell-type-specific markers merged with DAPI. (Scale bar: 500 μm)

(A) SOX2 (neural progenitor cell marker), (B) Nestin (intermediate progenitor cell marker), and (C) NeuN (neuron marker).

At Day 82, extended culture-maintained marker expression was observed across multiple cell differentiation markers. Clustering revealed cortical neurons, cortical progenitor cells, excitatory neurons, intermediate progenitors, and radial neurons. Inter-organoid homogeneity was favorable, with slight variation in cell type ratios across individual organoids.

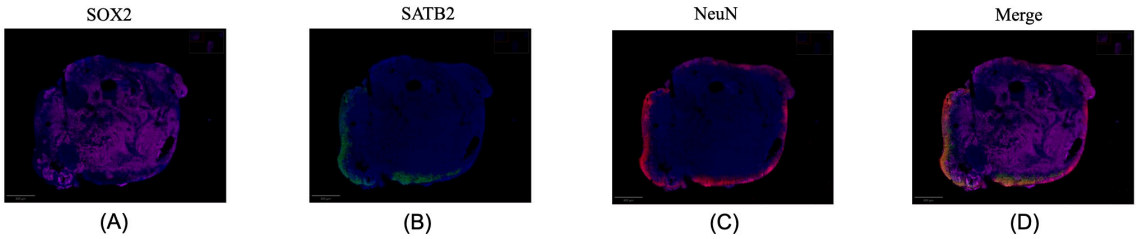

Figure 4. Differentiation of iPSC-Derived Cerebral Organoids at Day 82

Differentiation effects of iPSC-Derived Cerebral Organoids were characterized by immunofluorescence staining using DAPI and cell-type-specific markers (Scale bar: 800 μm).

(A) SOX2, (B) SATB2 (deep-layer neuron marker), (C) NeuN, and (D) Merged immunofluorescence staining of SOX2 (pink), SATB2 (green), and NeuN (red), with DAPI stained cell nuclei in blue.

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DISCUSSION

Automation as a Systematic Response to Process Variability

The data presented here demonstrate that the combination of standardized automated culture protocols, AI-driven real-time optimization, and validated organoid culture media can produce consistent, biologically meaningful results for iPSC-derived neural tissue.

In manual workflows, passage-to-passage variability in pipetting mechanics, centrifugation parameters, and replating density is a known source of culture drift. Automated handling eliminates these sources systematically, allowing the biological behavior of the organoid model to be observed without confounding process noise. These data support biological consistency within the demonstrated workflow and highlight the value of standardized handling when scaling organoid culture.

For research organizations running high-throughput compound screening panels, these properties translate into operational advantage. Consistent organoid size and morphology are expected to support more reliable downstream compound response measurements, including IC50 determinations when implemented in screening workflows. Automated work logs and full data traceability simplify cross-experiment comparisons and support documentation requirements where applicable.

It is worth noting that the regulatory landscape for organoid-based evidence packages is evolving. The FDA's New Approach Methods initiative[3] and April 2025[4] announcement regarding reduced animal testing requirements for certain drug classes[4]have raised the profile of human-relevant models in preclinical development. In late 2025, the first IND approval based solely on human vascularized organoid efficacy data established a meaningful precedent for the evidential weight such data can carry.[5,4]Well-documented, reproducible organoid data generated on validated platforms may therefore have value beyond discovery-stage screening.

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CONCLUSION

Reproducible Organoid Research at Practical Scale

The Titan2000 Organoid Workstation and Titan3000 integrated platform deliver end-to-end workflow automation across the full organoid culture and research-use compound screening pipeline. Combined with AI-driven protocol optimization and a validated organoid kit portfolio spanning 26+ model types, the platform addresses the reproducibility challenge that has limited organoid adoption in research settings.

Performance data across iPSC-derived cerebral organoids confirm stable, marker-validated culture over extended passages, consistent morphology, and high inter-organoid homogeneity - outcomes that support more reliable research-use compound screening and disease modeling applications.

For research organizations seeking to integrate organoid workflows at scale, the Galatek platform provides an accessible, well-characterized solution that reduces manual intervention without compromising experimental control.

All products and applications described in this application note are intended for research use only.
Not cleared or approved for clinical diagnostic use.

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