

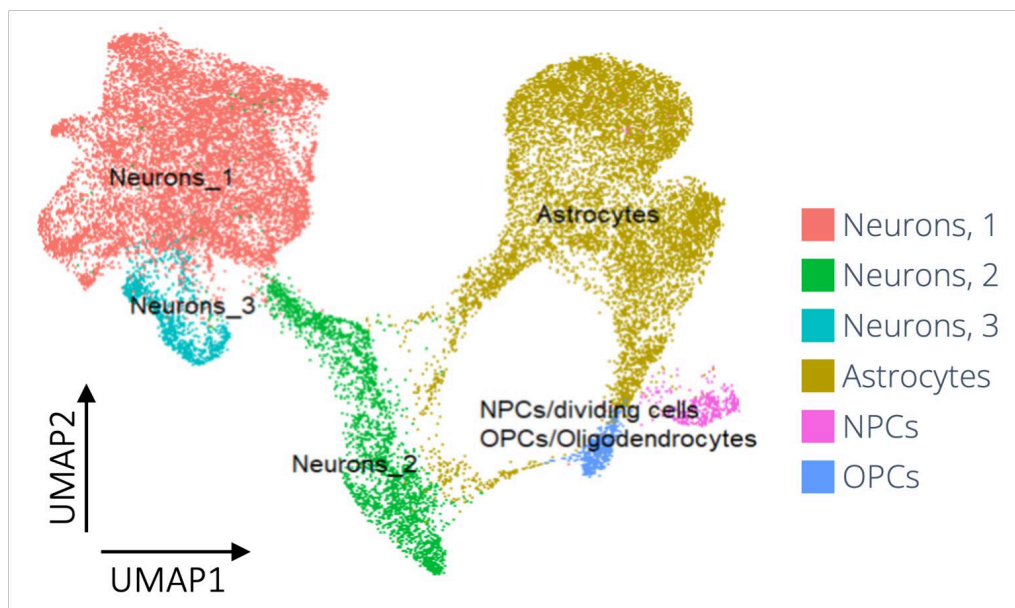
## CNS-3D Brain Organoids

Assay-ready human cortical organoids for functional studies of CNS safety and drug efficacy.

### Overview

CNS-3D Brain Organoids are human cortical organoids designed for predictive drug assessment. Derived from iPSC-based neural progenitor cells, they self-organize into balanced neuron-astrocyte co-cultures that form functional neural networks with spontaneous activity.

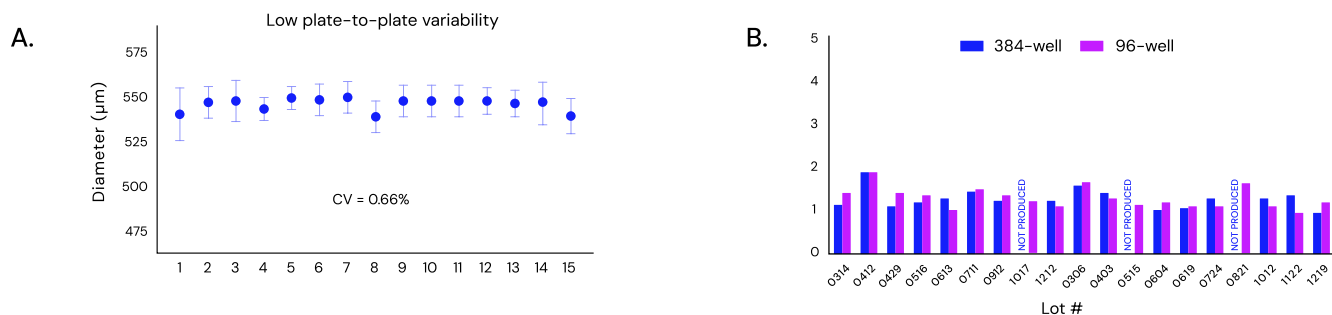
This activity is measured using calcium imaging to assess drug-induced changes in neuronal function and can be multiplexed with complementary endpoints spanning viability, imaging, and molecular analysis. CNS-3D Brain Organoids are available as assay-ready products for in-house workflows or through CNS Services for end-to-end study design, execution, and analysis.



Single-nucleus RNA-seq (snRNA-seq) confirms neuronal and astrocyte populations with limited progenitor cell (NPC) presence, consistent with human cortical tissue.

## Reproducibility

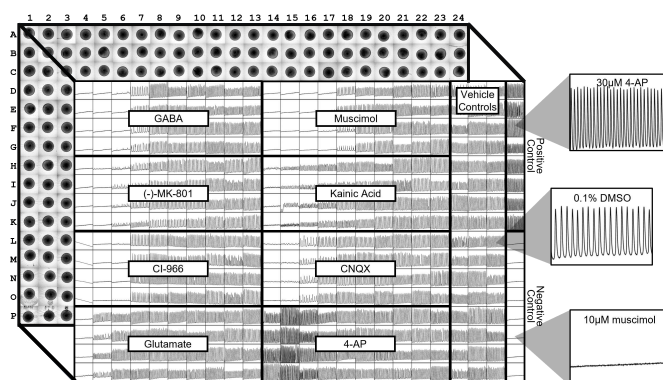
CNS-3D Brain Organoids deliver consistent, reproducible performance that overcomes the variability often seen in self-generated organoids. Stable pharmacological responses support longitudinal and chronic treatment paradigms over several weeks, with a validated four-week use window enabling flexible assay workflows while maintaining data quality.



**(A)** CNS-3D Brain Organoids exhibit uniform diameter within and across plates, minimizing morphological variability often seen in organoid models. **(B)** Batch-to-batch reproducibility in organoid diameter is maintained across 96- and 384-well formats, with CVs <5%.

## Quality Control

Organoids are batch-produced and subjected to rigorous quality control to ensure consistency across experiments. Brightfield imaging and functional characterization confirm uniform organoid size (500–800  $\mu\text{m}$  diameter, <5% CV within plate) and a high presence rate (98%). Immunocytochemistry (ICC) verifies the expected neuron-to-astrocyte ratio, while sterility testing confirms absence of mycoplasma, anaerobic, aerobic, and fungal contaminants. Each shipment includes a certificate of analysis, along with EC/IC50 values and Z-prime scores for FLIPR-based functional screening.



High-throughput functional readouts (e.g., FLIPR) capture dose-dependent responses across neuromodulators with strong replicate reproducibility, enabling studies with as few as 4 organoids per condition.

Application

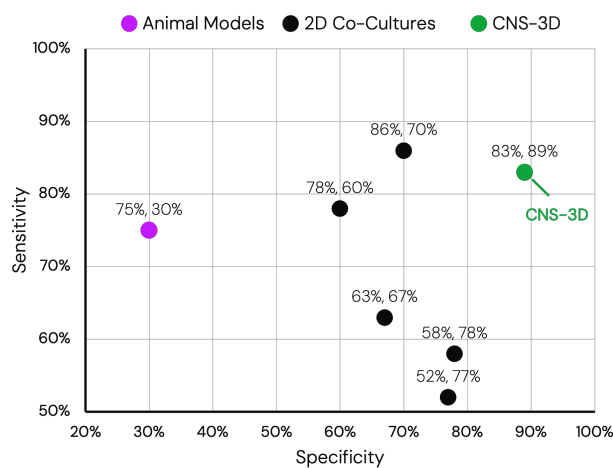
# CNS Toxicity

Predict CNS toxicity risk by measuring drug-induced changes in neuronal network activity. In small molecule and ASO toxicity studies, CNS-3D Brain Organoids have outperformed animal models and 2D assays, supporting more confident assessment of drug-induced neurotoxicity.

Use Case

## Small Molecule Toxicity

Accurately identify seizurogenic small molecules while minimizing the risk of eliminating clinically safe drugs. CNS-3D Brain Organoids combine functional neural activity with AI-based prediction to assess clinical seizure risk with high confidence. Across 66 small molecules with known clinical outcomes, CNS-3D achieved 83% sensitivity and 89% specificity.



Sensitivity and specificity comparison for small molecule seizure risk prediction, demonstrating superior performance of CNS-3D versus alternative models.

Use Case

## ASO Toxicity

In a study of 24 ASOs, CNS-3D Brain Organoids outperformed sequence-based prediction and 2D calcium assays, achieving 92% sensitivity and 92% specificity. By measuring functional activity in human 3D neural tissue, CNS-3D captures toxicity signals that sequence-based and 2D approaches can miss. Beyond identifying ASOs as toxic or safe, CNS-3D captures gradations of neurotoxicity, enabling more precise candidate rank ordering.

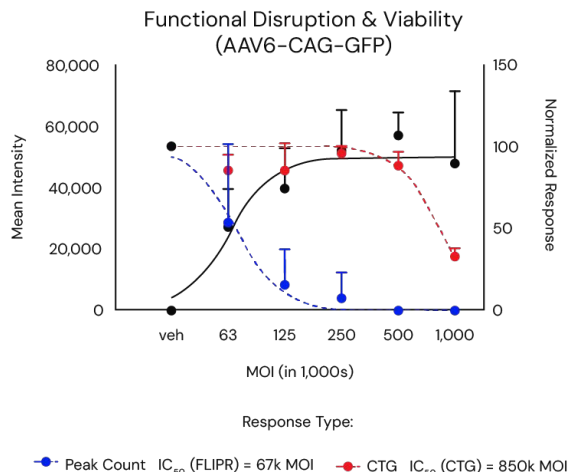
		Neurotoxic	Safe
CNS-3D	Neurotoxic	11 True Positives	1 False Positives
	Safe	1 False Negatives	11 True Negatives
ASO Sequence-Based Prediction	Neurotoxic	8 True Positives	5 False Positives
	Safe	4 False Negatives	7 True Negatives
2D Calcium Oscillation	Neurotoxic	7 True Positives	4 False Positives
	Safe	5 False Negatives	8 True Negatives

CNS-3D ASO neurotoxicity predictions compared with sequence-based and 2D calcium assay results, showing improved sensitivity and specificity across 24 ASOs.

Use Case

AAV Toxicity

CNS-3D Brain Organoids detect functional disruption at doses below overt viability loss, enabling more sensitive safety assessment than viability assays alone. By integrating expression, neuronal network activity, and viability assessment, CNS-3D helps identify vectors that balance transduction efficiency with functional safety.

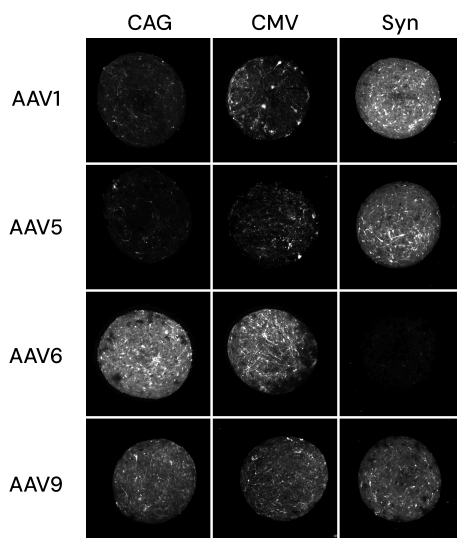


Functional calcium imaging detects AAV-associated disruption of neuronal network activity before ATP-based viability loss, supporting more sensitive assessment of vector impact than viability endpoints alone.

Application

Gene Therapy

Prioritize gene therapy vectors through integrated assessment of expression, toxicity, and neural function. CNS-3D Brain Organoids integrate assessment of transduction efficiency, toxicity, and functional impact in a single model. In AAV studies, this approach resolves serotype- and promoter-dependent differences in vector performance and detects disruption of neuronal network activity before overt viability loss.



Representative images of AAV transduction in CNS-3D Brain Organoids, demonstrating clear serotype- and promoter-dependent GFP expression.

## Technical Specifications

Specification	Details
Organoid Size	500–800 $\mu\text{m}$ diameter; CV <5% within and across plates
Cell Composition	50% neurons (~90% glutamatergic, ~10% GABAergic) and 50% astrocytes
Validated Assay Window	Weeks 6–10 of maturation
Assay	Multiplexed functional and molecular endpoints, including calcium imaging (e.g., FLIPR), viability (CellTiter-Glo), cytotoxicity (LDH-Glo), protein biomarker analysis (e.g., MSD, Ella), high-content imaging, and transcriptomic profiling.

## Ordering Information

CNS-3D Brain Organoids are produced monthly to ensure reliable supply and are delivered assay-ready in 24-, 48-, 96-, and 384-replicate formats. A proprietary hibernation media enables shipment to laboratories worldwide.

Product Name	Replicates per Plate	Plate Format	Catalog Number
CNS-3D Brain Organoids	24	24-well	P-C3S-24-V1
	48	48-well	P-C3S-48-V1
	96	96-well	P-C3S-96-V1
	384	384-well	P-C3S-384-V1