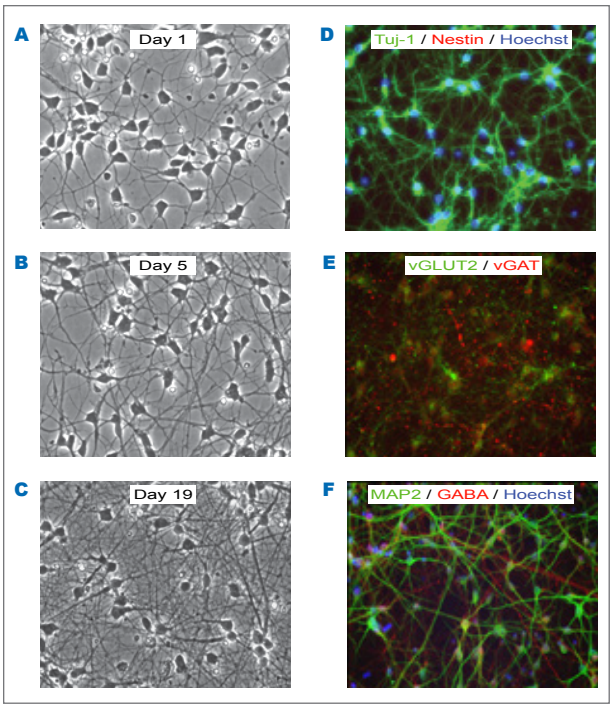
FUJIFILM
Cellular Dynamics

PRODUCT DATASHEET

# iCell® GABANeurons

iCell® GABANeurons from FUJIFILM Cellular Dynamics, Inc. (FCDI), are derived from human induced pluripotent stem (iPS) cells and provide a unique in vitro system for preclinical drug discovery, neurotoxicity testing, and disease research. A better and more biologically relevant alternative to current cell models, iCell GABANeurons offer access to commercial quantities of a high quality, highly pure, human-derived population that is comprised primarily of mature GABAergic neurons possessing typical phenotypic characteristics and functionality.

Historically, in vitro models have played an important role in the drug discovery process, including use during early stage disease modeling and candidate identification as well as pharmacokinetic and safety testing. Because of the complexity of the human brain, scientists currently use simplified models, such as primary cells isolated from rodent tissues and transformed cell lines. However, issues of biological relevance, reproducibility, and scalability can arise, and the reliance on inferior models may result in drug-induced neurotoxicity not being observed until late-stage clinical trials or after marketplace introduction. iCell GABANeurons overcome these limitations, providing a robust, well-characterized, highly reproducible in vitro model for preclinical drug discovery and safety testing.




▲ **Figure 1: iCell GABANeurons Exhibit Typical Morphology and High Purity**
*(A - C) iCell GABANeurons, post-thaw, develop branched networks within 24 hours and remain viable for an extended culture period (≥14 days). Additionally, iCell GABANeurons represent a highly pure population comprised primarily of GABAergic neurons with low levels of nestin as demonstrated by immunocytochemistry: (D) ß-III tubulin (tuj-1) and nestin, (E) synaptic markers vGAT and vGLUT2, and (F) MAP2 and GABA.**

## Advantages

- **Human cells:** iCell GABANeurons are terminally differentiated from human iPS cells and exhibit neuronal characteristics and functions.
- **Homogenous and reproducible:** iCell GABANeurons are highly pure, providing biologically relevant and reproducible results.
- **Acute and long-term testing:** iCell GABANeurons remain viable and pure in culture for weeks, enabling assessment of both acute and sub-chronic responses.
- **Easy to implement:** iCell GABANeurons are shipped cryopreserved with cell culture media specifically formulated for optimal cell performance. Simply thaw and use.

## Electrophysiological Characterization

Neurons are electrically active cells. Communication between neurons, and between neurons and other cell types and organs, is accomplished through electrical activity. Small molecule compounds can disrupt this communication, leading to decreased functionality of ion channels and ultimately altered synaptic transmission. iCell GABANeurons are spontaneously electrically active neurons, exhibiting typical electrophysiological and biochemical responses upon exposure to exogenous compounds for early assessment of potential effects.

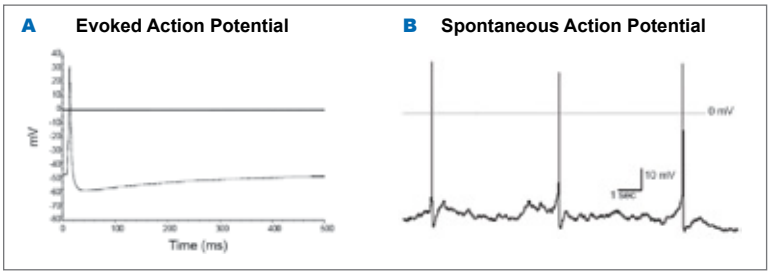
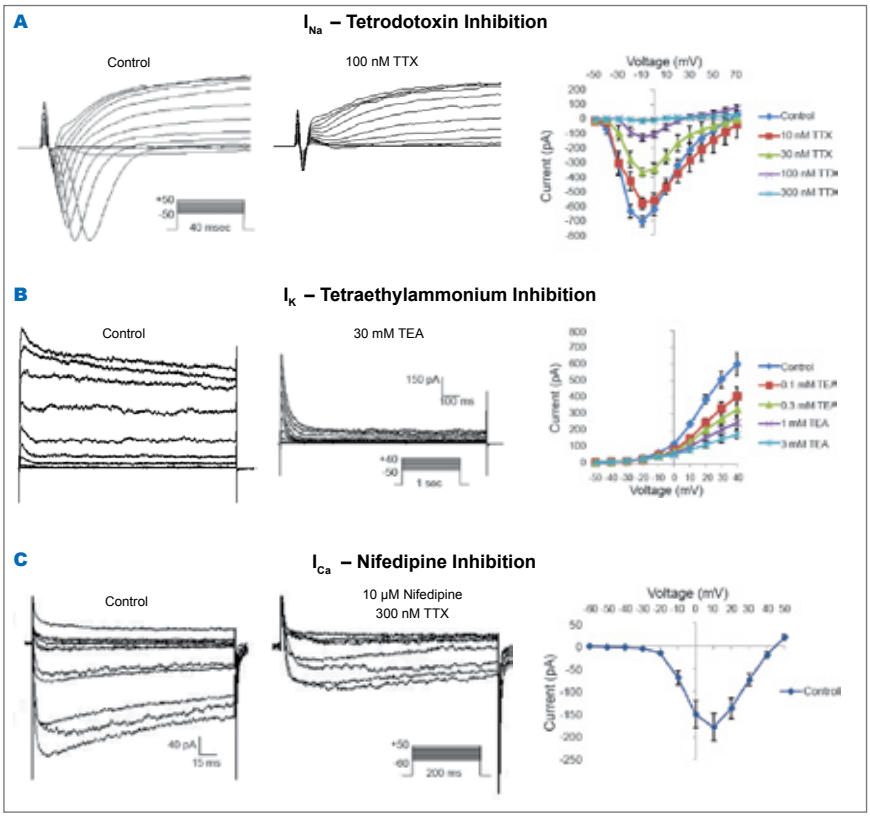



**Figure 2: iCell GABANeurons Demonstrate Characteristic Action Potentials**
*Evoked and spontaneous action potentials were recorded from iCell GABANeurons (9 and 14 days post-thaw, respectively) using whole-cell current clamp techniques. The representative action potentials demonstrate an overshoot of the depolarization phase above 0 mV and an undershoot of the repolarization phase below the baseline.**

**Figure 3: iCell GABANeurons Respond to Ion Channel Blockers**
*The addition of classical neuron ion channel antagonists tetrodotoxin (TTX), tetraethylammonium (TEA), and nifedipine blocks (A) inward sodium currents, (B) outward potassium currents, and (C) inward calcium currents, respectively, in iCell GABANeurons (12 - 19 days post-thaw) as measured (12 - 19 days post- thaw) as measured using whole cell patch clamp.**



## Toxicity Characterization

iCell GABANeurons' typical neuronal physiological functions and responses make them a viable model for in vitro toxicity screening and drug development. They exhibit stable transcriptional and phenotypic profiles over an extended period of time, thus enabling assessment of both acute and sub-chronic responses.

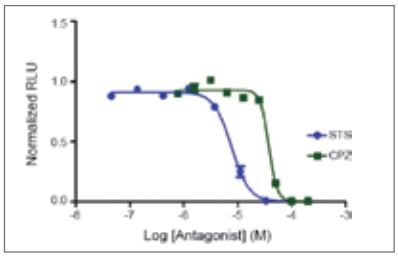



**Figure 4: iCell GABANeurons Display Cytotoxicity Dose Response to Known Compounds**
*iCell GABANeurons were cultured for 7 - 14 days post-thaw and exposed to staurosporine (STS), an ATP competitive kinase inhibitor, and chlorpromazine (CPZ), a phenothiazine antipsychotic. They were subsequently assayed using the CellTiter-Glo® Luminescent Cell Viability Assay (Promega Corp.).**

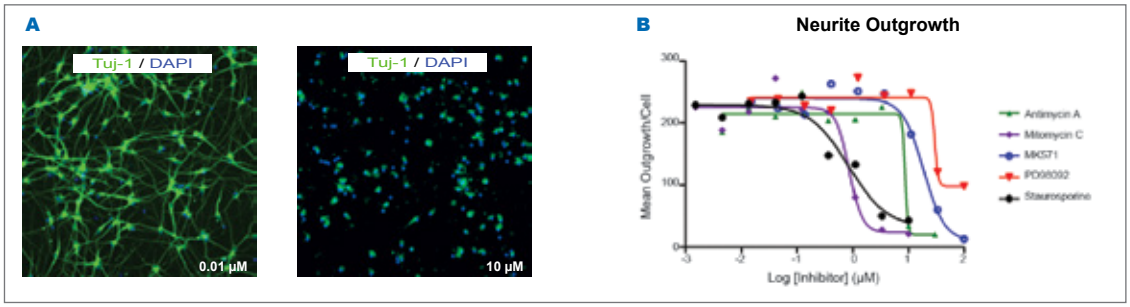



**Figure 5: Compound Toxicity Was Determined through Neuronal Network Disintegration in iCell GABANeurons**
*iCell GABANeurons that were treated with increasing concentrations of antimycin A, mitomycin C, MK571, PD98092, or staurosporine were (A) stained for ß-III tubulin (tuj-1) and nuclei (DAPI) and analyzed using the ImageXpress™ Micro High Content System and MetaXpress™ Software. (B) The resultant dose response curves assess neurite outgrowth to cytotoxic compounds. Images are of cells treated with increasing concentrations of mitomycin C. (Data were generated by Molecular Devices, Inc.)**

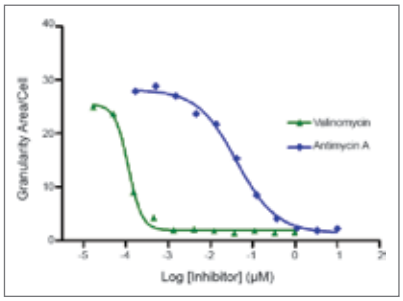



**Figure 6: Mitochondrial Damage Was Observed in iCell GABANeurons after Treatment with Cytotoxic Compounds**
*The mitochondrial membrane potential of iCell GABANeurons was monitored after treatment with mitochondrial active dye JC-10 and exposure to antimycin A or valinomycin. These iCell GABANeurons were then imaged using the ImageXpress Micro High Content System. Mitochondrial damage and the loss of the mitochondrial membrane potential were analyzed using the MetaXpress Software. (Data were generated by Molecular Devices, Inc.)**

## Applications

iCell GABANeurons are amenable to a variety of uses including:

**Cell-based Assays**

- Apoptosis
- ATP production
- Cell viability
- Oxidative stress
- Mitochondrial dysfunction
- Neurite outgrowth/sprouting

**Electrophysiological Applications**

- Conventional patch clamp recording
- Microelectrode (MEA) recording

## Specifications

| | |
|---|---|
| **Cell Type** | Neurons |
| **Organism** | Human |
| **Source** | Differentiated from an FCDI reprogrammed human iPS cell line |
| **Quantity** | ≥4.0 x $10^6$ viable cells per vial |
| **Shipped** | Frozen |

## Ordering Information

| Kit | Component(s)[1] | Catalog Number |
|---|---|---|
| iCell GABANeurons Kit, 01434 | ≥4.0 x $10^6$ viable cells<br>100 ml Neural Base Medium 1<br>2 ml Neural Supplement A | R1013 |
| iCell GABANeurons Kit, 01279 | ≥4.0 x $10^6$ viable cells<br>100 ml Neural Base Medium 1<br>2 ml Neural Supplement A | R1011 |
| iCell Neural Base Medium 1 | 100 ml Neural Base Medium 1 | M1010 |
| iCell Neural Supplement A | 2 ml Neural Supplement A | M1032 |

1 A User's Guide is provided in each kit.

## For More Information

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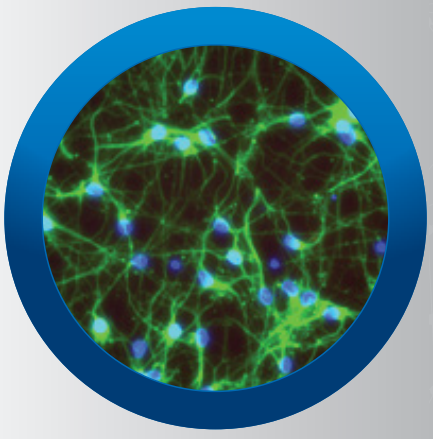
### iCell Products

Provide access to biologically relevant, human iPS cells for disease modeling, drug discovery, toxicity testing, and regenerative medicine. FCDI's rapidly growing portfolio of iCell products includes human cardiomyocytes, GABAergic, glutamatergic, dopaminergic and motor neurons, hepatocytes, endothelial cells, astrocytes, hematopoietic progenitor cells, skeletal myoblasts, macrophages, and others.

Visit the FCDI website for the most current list of supported cell types.



* Images and data are representative of iCell GABANeurons derived from two different genetic backgrounds (donors 01434 and 01279).

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