

# **PRODUCT DATASHEET**

# iCell<sup>®</sup> Sensory Neurons

Sensory neurons that innervate the skin and internal organs are responsible for relaying sensory information into the central nervous system, including noxious/painful stimuli. These neurons are also the target of off-target toxicity for many common chemotherapeutic treatments for cancer, resulting in acute or chronic peripheral neuropathy. Consistent and effective human cell culture models are desperately needed to speed up and improve translational success for the next generation of pain therapeutics and chemotherapeutics.

# iCell Sensory Neurons offer a robust and consistent source of human induced pluripotent stem cell (iPSC) derived sensory neurons for use in pain and chemotherapy-induced peripheral neuropathy (CIPN) drug screening and discovery research. These highly pure human sensory neurons express nociceptor-specific ion channels (Nav1.7, Nav1.8) and sensory receptors (TRPV1, P2RX3, TRPM8). iCell Sensory Neurons have proven sensitivity to sensory agonists (capsaicin, menthol, ATP) and cytotoxicity to chemotherapeutic drugs, making them ideal for pain and CIPN-related research.

### **Consistent Function and Purity**

The iCell Sensory Neurons manufacturing process results in cells that are robust, scalable, and have reproducible performance. These characteristics make human sensory neurons a trustworthy and consistent product that is ideal for groups that want to focus on research and discovery, not cell manufacturing.



Figure 1: iCell Sensory Neurons purity analysis across multiple manufactured lots (combined 01279 and 21527 donors) shows high % positivity for BRN3A and UCHL1 (left). Representative image showing BRN3A (green) and  $\beta$ -III Tubulin (red) staining in iCell Sensory Neurons at d14 post (right).

#### **Benefits**

- Consistent lot-to-lot purity and performance results in reproducible experiments.
- Express nociceptor genes (TRPV1, Nav1.7, Nav1.8) enabling pain therapeutic studies.
- Functional responses to sensory agonists (capsaicin, menthol, ATP) within 21 days of culture.
- Low spontaneous activity mirroring quiescent basal activity in human DRG neurons.
- Sensitive to chemotherapeutics allowing for chemotherapeutic-induced peripheral neuropathy (CIPN) modeling.
- Male and Female cell lines enable studies on sex differences for pain.
- Flexible plating density supports staining, neurite outgrowth, calcium influx, electrophysiology studies.

#### **Responsive to Known Sensory Agonists**

iCell Sensory Neurons express characteristic sensory receptors, including TRPV1, TRPM8, P2RX3, and PIEZO1/2. Responses to sensory agonists are observed withing 21 days post-thaw, enabling quick functional assay time frames for drug discovery and compound validation.

**Figure 2:** iCell Sensory Neurons cultured for 21 days demonstrate increased calcium influx in response to known sensory channel agonists, including TRPV1 (yellow; Capsaicin), TRMP8 (red, Menthol), and P2RX3 (green, ATP). Potassium chloride is the positive control (blue; KCI).



# Applications

iCell Sensory Neurons are designed to support pain and chemotherapy-induced peripheral neuropathy (CIPN) drug screening and discovery research.



# High Throughput CIPN Compound Testing

Chemotherapy-induced peripheral neuropathy (CIPN) is a toxic side effect associated with many cancer treatment strategies. Access to reliable in vitro human cell models will improve identification of next generation chemotherapeutics with less off-target toxicity. iCell Sensory Neurons provide a relevant human cell source for high throughput CIPN drug discovery and validation workflows.

Figure 4: iCell Sensory Neurons were cultured for four days followed by a 3-day treatment with varying does of Paclitaxel, a chemotherapeutic with known CIPN-inducing side effects. iCell Sensory Neurons display a dose-response neurite degeneration to Paclitaxel.

#### **Evaluate and Modulate Excitability**

iCell Sensory Neurons mirror the quiescent basal activity of human dorsal root ganglion sensory neurons, displaying low frequency of spontaneous action potentials. This feature enables the investigation of pain mechanisms for hyperalgesia and allodynia.

**Figure 3:** iCell Sensory Neurons display low spontaneous activity as displayed by patch clamp and multielectrode array (MEA). Patch clamp shows few neurons with spontaneous action potentials in 3- and 4-week cultures for both donors (**left**). MEA raster plots show low baseline activity of sensory neurons compared to the synchronized network bursting observed in iCell GlutaNeurons (**right**).





# **Contribution of Sex Differences to Pain**

Pre-clinical and clinical data suggests differences in sensitivity and prevalence of pain between men and women. iCell Sensory Neurons from male (01279) and female (21527) donors enable the exploration of sex differences at the cellular and molecular level.

**Figure 6:** iCell Sensory Neurons from both 01279 (male) and 21527 (female) cell lines were cultured for 21 days and a dose-response to capsaicin, using calcium imaging, was performed. Data show similar response kinetics between 01279 and 21527 donors.

# **Nociceptor Sodium Channel Analysis**

Nav1.7 and Nav1.8 sodium channels are present in iCell Sensory Neurons as detected by RNA-seq, immunocytochemistry, and patch clamp. The presence of Nav1.7 and Nav1.8 in these iPSC-derived sensory neurons makes these cells ideal for researching the role of sodium channels in nociception and pain.

Figure 5: iCell Sensory Neurons from 01279 (male) and 21527 (female) donors were cultured for 3 weeks prior to patch clamp experiments to measure sodium currents. Robust sodium currents were detected in both donors. TTX treatment revealed TTX-sensitive and TTX-resistant sodium currents (post-TTX).





# **Model Peripheral Neuroinflammation**

Peripheral inflammation is a contributor to neuropathic pain. Human relevant in vitro models are needed to elucidate mechanisms of inflammatory pain and to identify new targeted therapeutics. Co-culture of iCell Sensory Neurons with isogenic human iPSC-derived immune cells, such as iCell Macrophages 2.0, make modeling peripheral neuroinflammation possible.

Figure 7: iCell Sensory Neurons, 01279 (magenta) were cultured with isogenic iCell Macrophages 2.0, 01279 (green) using Complete Sensory Neurons Medium. Counterstained with DAPI (blue)

#### **Product Specifications**

Cell Type	Peripheral Sensory Neurons	
Organism	Human	
Source	Differentiated from an FCDI reprogrammed human iPSC cell lines (01279 and 21527)	
Quantity	≥1.0 x 10 <sup>6</sup> or ≥6.0 x 10 <sup>6</sup> viable cell per vial	
Shipped	Frozen	
Media	Serum-free base medium and supplement provided with each kit	

# **Ordering Information**

Item	Component(s)*	Catalog Number
iCell Sensory Neurons, 01279 (male)	≥ 1 x 10 <sup>6</sup> viable cells	R1251
iCell Sensory Neurons, 01279 (male)	$\geq$ 6 x 10 <sup>6</sup> viable cells	R1250
iCell Sensory Neurons, 21527 (female)	≥ 1 x 10 <sup>6</sup> viable cells	R1253
iCell Sensory Neurons, 21527 (female)	≥ 6 x 10 <sup>6</sup> viable cells	R1252

\*Kits are provided with iCell Sensory Neurons Base Medium (100 ml) and iCell Sensory Neurons Supplement (100X) (1 ml)

\*\*A User's Guide is provided in each iCell Sensory Neurons Kit

#### 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, cardiac fibroblasts, cardiac progenitor cells, GABAergic, glutamatergic, dopaminergic, motor, and induced excitatory neurons, hepatocytes, endothelial cells, astrocytes, hematopoietic progenitor cells, macrophages, blood-brain barrier models and others.

Visit the <u>FCDI website</u> for the most current list of supported cell types.





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