NEUROMICS

Human iPSC - Motor Neurons (TDP-43 M337V, Homozygous)

Catalog #: IPS015

Cell #: >1.0x10^6 cells

Storage: Liquid Nitrogen until ready for culture.
While Culturing keep in 37°C CO_2 incubator

Product Format: Frozen Vial

GENERAL INFORMATION

These human spinal motor neurons (MNs) are derived from a genetically engineered induced Pluripotent Stem Cell (iPSC) line carrying a homozygous M337V mutation in the TARDBP gene, which encodes the TDP-43 protein. This mutation is strongly associated with familial and sporadic Amyotrophic Lateral Sclerosis (ALS) and Frontotemporal Dementia (FTD). The cells are differentiated using a robust, floor-plate directed protocol to generate a highly pure population of functional motor neurons.

This isogenic model provides a precise and powerful tool for studying TDP-43 proteinopathy, a pathological hallmark of nearly all ALS cases. These neurons robustly recapitulate key disease features, including cytoplasmic TDP-43 mislocalization, stress granule dynamics, increased sensitivity to proteotoxic stress, and altered mitochondrial function. They are indispensable for dissecting the mechanisms of TDP-43-mediated neurodegeneration and for high-content screening of targeted therapeutics.

*Differentiation efficiency may vary due to the inherent biological variability of the donor phenotype.

These cells exhibit biological characteristics associated with the donor phenotype, which may impact their growth, differentiation, and metabolic behavior compared to cells from health donors. It is the user's responsibility to determine the suitability of this product for their specific application.

Product is for Research use only.

Frozen Vials are shipped in a Dry Ice Package.

KEY FEATURES & BENEFITS

- **Precise Genetic Model:** Features a homozygous, well-characterized ALS/FTD-associated point mutation (M337V) in the TARDBP gene for consistent, mechanism-driven research.
- **Isogenic Control Available:** A genetically corrected, wild-type control line (isogenic) is available, enabling definitive attribution of phenotypes directly to the TDP-43 mutation.
- **Strong Disease Phenotype:** Consistently exhibits cytoplasmic TDP-43 mislocalization, particularly under stress conditions, providing a robust readout for drug screening.
- **High Purity & Functionality:** Differentiated into a highly pure population of spinal motor neurons expressing key markers and capable of firing action potentials.
- **Ready for Functional Assays:** Cryopreserved at a post-mitotic stage, ready for recovery and use in high-content imaging, electrophysiology, and biochemical assays.

APPLICATIONS

- **TDP-43 Proteinopathy Studies:** Investigate mechanisms of nuclear-to-cytoplasmic mislocalization, aggregation, and cleavage of TDP-43.

FOR RESEARCH USE ONLY

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- **High-Content Screening:** Screen for compounds that reduce TDP-43 mislocalization, enhance autophagy/proteasomal clearance, or improve neuronal survival.
- **RNA Metabolism & Stress Granules:** Study altered RNA binding, splicing, and stress granule dynamics in a disease-relevant context.
- **Electrophysiology:** Characterize functional deficits in neuronal excitability and synaptic transmission using patch-clamp or MEA.
- **Biochemical Pathway Analysis:** Investigate nucleocytoplasmic transport defects, mitochondrial dysfunction, and ER stress.

QUALITY CONTROL SPECIFICATIONS

Each lot is tested to meet the following release criteria:

Parameter	Specification	Test Method
Viability (Post-Thaw)	≥ 70%	Trypan Blue Exclusion
Cell Yield per Vial	≥ 1 Million Cells	Cell Count
Purity (MN Marker Expression)	≥ 70% ISL1+/HB9+	Immunocytochemistry (ICC)
Neuronal Marker Expression	Positive: β-III-Tubulin (Tuj1), MAP2	ICC
Genotype Verification	Confirmed Homozygous TARDBP c.1009A>G	Sanger Sequencing
TDP-3 Expression	Positive for Nuclear TDP-43 (basal state)	ICC
Pluripotency Marker Absence	Negative: Oct3/4	ICC
Microbiological Sterility	No Growth	USP <71>
Mycoplasma	Negative	PCR Method

TYPICAL DONOR DEMOGRAPHICS & CLINICAL HISTORY

Donors are carefully selected and characterized. A typical profile includes:

- **Gene:** TARDBP
- **Mutation:** c.1009A>G (p.Met337Val)
- **Zygosity:** Homozygous
- **Parental Line:** The engineered line is based on a well-characterized, karyotypically normal human iPSC background.
- **Isogenic Control:** The availability of a genetically corrected, otherwise identical control line is critical for validating mutation-specific effects.

HANDLING OF ARRIVING CELLS

1. Check all containers for leakage or breakage.

2. Remove the frozen cells from the dry ice packaging and immediately place the cells into a -80°C freezer for short-term storage or liquid nitrogen tank for long-term storage.

3. To ensure the highest level of viability, thaw the vial and initiate the culture as soon as possible upon receipt. If upon arrival, continued storage of the frozen culture is necessary, it should be stored in liquid nitrogen vapor phase and not at -70°C. Storage at -70°C will result in loss of viability.

4. When handling cell cultures, the application of stringent aseptic techniques is imperative. Maintaining a contamination-free environment is crucial for preserving the integrity and reliability of experimental results. This involves not only cleanliness but also the use of sterile tools, media, and working environments to prevent contamination from airborne particles, microbial agents, and other sources.

MEDIUM

We recommend Motor Neuron Maintenance Medium Kit (cat. HNM013) for these cells. The kit contains ingredients to support cell growth.

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PROTOCOL FOR THAWING THE CELLS

Note: If you have any questions or need clarification regarding the protocol for culturing these cells, please reach out to Dr. Jensen Auguste at (978) 608-1766 with your questions before beginning.

1. Pre-coat culture vessels overnight at 4°C or 1-2 hours at 37°C with AlphaBioCoat Solution (cat. AC001), followed by rinses with PBS before plating.

2. Quick Thaw: Remove the vial from liquid nitrogen and immediately place in a 37°C water bath. Gently agitate until only a small ice crystal remains (≈1-2 minutes).

3. Decontaminate: Spray the vial with 70% ethanol before transferring to a biosafety cabinet.

4. Transfer and Dilute: Gently transfer the cell suspension to a 15 mL conical tube. Slowly add 5-9 mL of pre-warmed IPSC Neuron Plating Medium (cat. HNM003) drop-wise to dilute the cryoprotectant (DMSO).

5. Centrifuge: Spin at 200 x g for 5 minutes.

6. Resuspend and Plate: Aspirate the supernatant and gently resuspend the cell pellet in fresh, pre-warmed IPSC Neuron Plating Medium.

    a. Recommended Seeding Density: 70,000 - 150,000 cells/cm².

7. Incubate: Place the culture vessel in a humidified 37°C incubator with 5% CO_2.

8. Medium Change: After 24-48 hours, carefully replace 50% of the medium with fresh Motor Neuron Maintenance Medium. Thereafter, perform a 50% medium change every 2-3 days.

MAINTENANCE & MATURATION

- **Maturation:** Allow 10-21 days in culture for full maturation and robust expression of TDP-43-related phenotypes.
- **Stress Induction:** To consistently induce cytoplasmic TDP-43 mislocalization, treat cells with mild stressors after 14 days in culture (e.g., 50-100 µM Sodium Arsenite for 30-60 min, or 1 µM Staurosporine for 6-24 hours). Optimize conditions for your specific assay.
- **Handling:** These are delicate neurons. Avoid mechanical disruption. Use pre-warmed media for changes to minimize temperature shock.

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