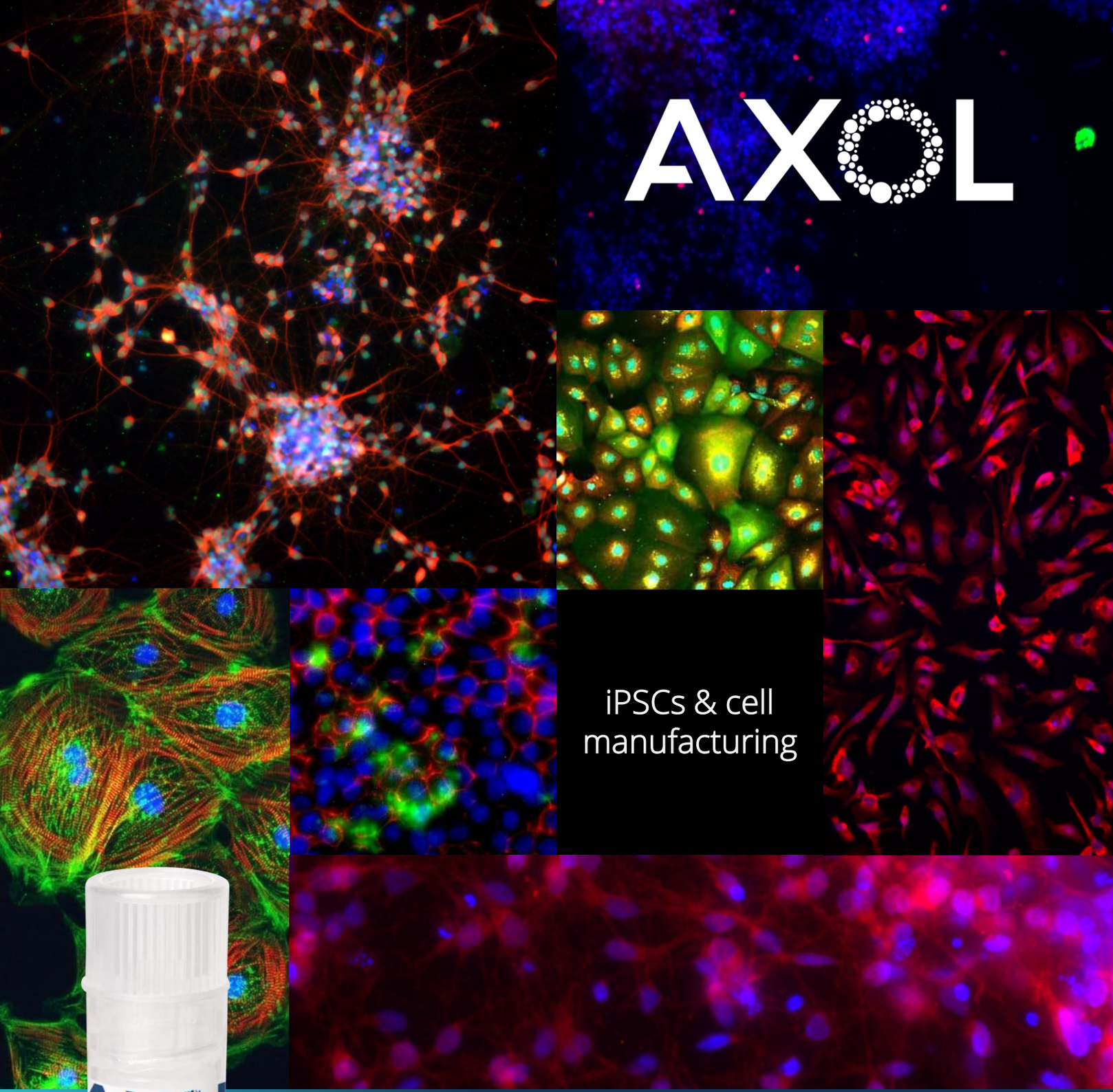


iPSCs & cell manufacturing

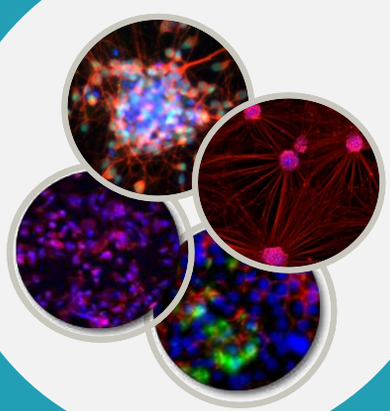
A library of donor iPSC axoLines™ and cell manufacturing capabilities

www.axolbio.com

Axol Bioscience's iPSC-derived **manufacturing** capabilities

01

From our axoLines™
or your iPSC lines



02

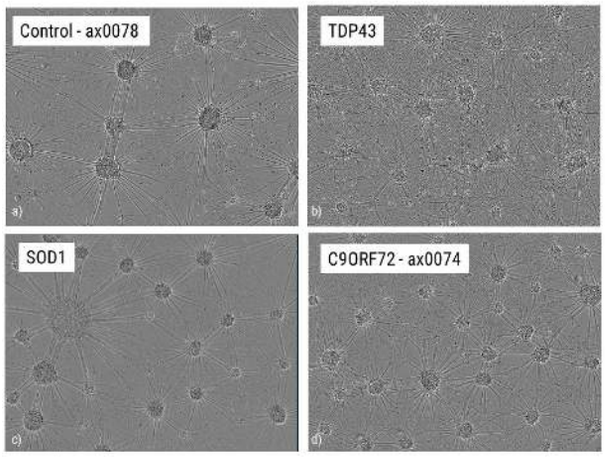
We can quality manufacture
11 different iPSC-derived cell types.

03

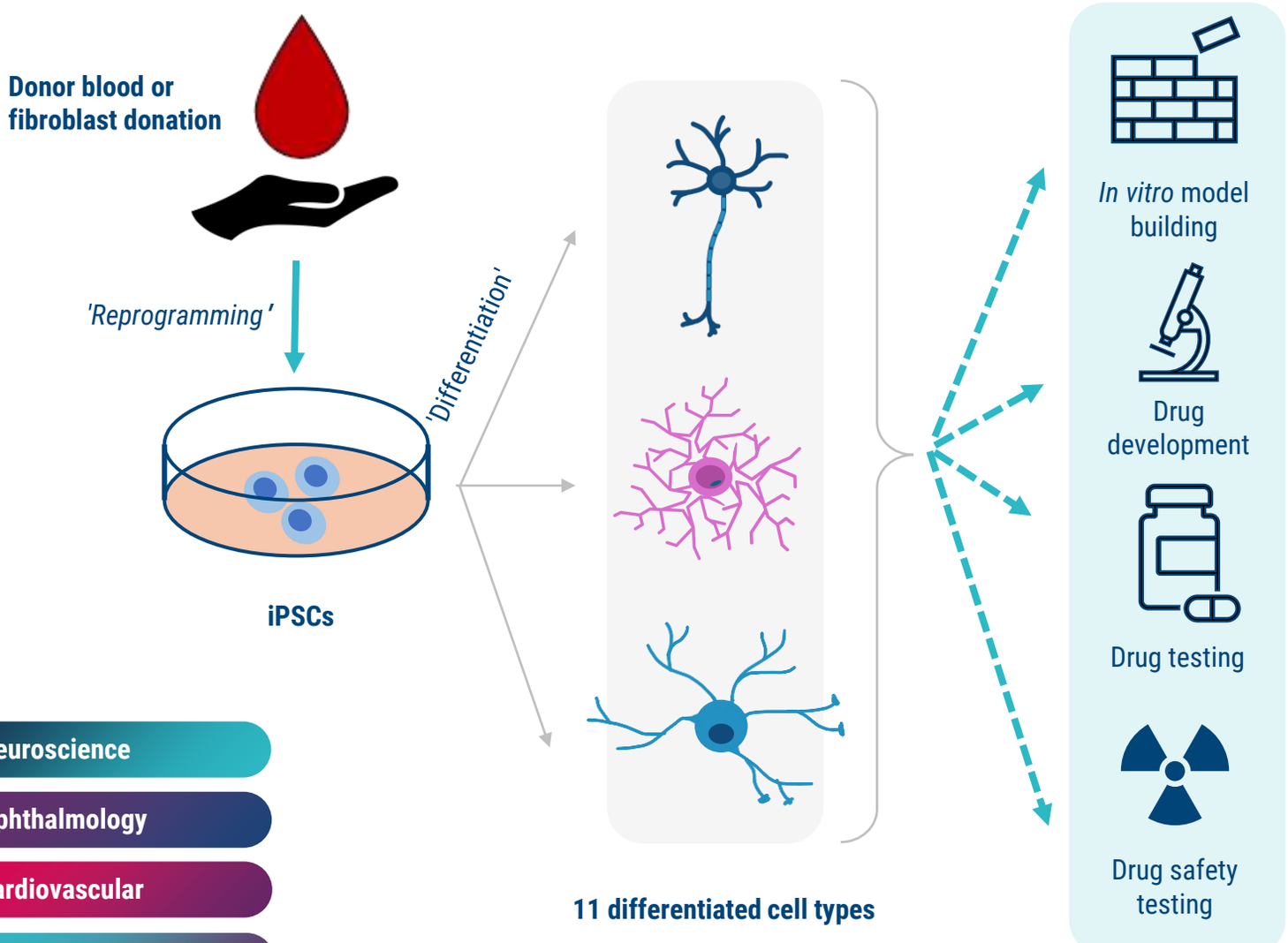
And supply in flexible volumes
and delivery patterns to suit your
research program.

iPSC-derived cells for *in vitro* research and drug discovery

Axol Bioscience is a market leader in the manufacturing of iPSC-derived cells to support drug discovery and research. iPSCs are induced pluripotent **stem cells** created from mature cells **donated** by a patient or often a relative. The donation can be a blood sample or fibroblast. The sample is '**reprogrammed**' into an iPSC using technology first created by Professor Yamanaka, winner of the 2012 Nobel Prize. Through the **differentiation** process, iPSCs can be turned into **motor neurons** and other cell types. Importantly, the end cell-type can carry the traits seen in the original human donor making iPSC-derived cells more '**human relevant**' than other cell types. Endpoint cells can be manufactured at scale and in a reproducible manner with defined functional quality controls.



Example, phase contrast image of motor neurons derived from iPSCs generated from 4 donors, 3 of whom had ALS.



axoLines donor iPSC Library

Axol Bioscience maintains a library of iPSC lines for use in cell manufacturing. The lines have been created from donated primary material (PBMCs or fibroblasts) and carry with them consent and ethics for use.

Unaffected donors iPSCs / 'Control lines'

Donor	Lines available
Unaffected by disease at time of donation	Male, 74, ApoE: E2/E2 Male, 40-50, APOE: E2/E3 Female, 45, APOE: E3/E3; ATN: 12/13 CAG repeats Male, 70, ApoE: E3/E3 Male, 81, ApoE: E3/E3 Male, 73, ApoE: E2/E3 Male, 44, FXN: 8 GAA repeats Male, Newborn, ApoE: E3/E4 Female, Newborn, ApoE: E3/E4

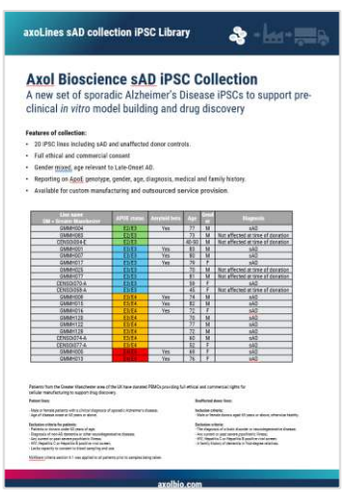
Patient donor iPSCs

Donor Condition		Lines Available
Amyotrophic Lateral Sclerosis (ALS)		Female, 44, C9orf72: >100 G4C2 (Asymptomatic Carrier) Female, 61, SOD1: Het. D109Y Female, 64, C9orf72: >145 G4C2 Male, 62, C9orf72: >145 G4C2 (Asymptomatic Carrier)
Alzheimer's Disease		Male, 77, ApoE: E2/E3 Female, 59, ApoE: E3/E3 Female, 79, ApoE: E3/E3 Male, 80, ApoE: E3/E3 Male, 83, ApoE: E3/E3 Female, 52, ApoE: E3/E4 Female, 72, ApoE: E3/E4 Male, 60, ApoE: E3/E4 Male, 70, ApoE: E3/E4 Male, 72, ApoE: E3/E4 Male, 74, ApoE: E3/E4 Male, 77, ApoE: E3/E4 Male, 82, ApoE: E3/E4 Female, 69, ApoE: E4/E4 Female, 76, ApoE: E4/E4
FTD	Behavioural variant frontotemporal dementia (bvFTD)	Male, 65, MAPT: Het. c.1920+16C>T Male, 68, MAPT: Het. c.1920+16C>T Male, 59, MAPT: Het. c.1920+16C>T
	ALS/FTD	Female, 64, TARDBP: A382T
	FTD, Paget's Disease	Female, 31, Progranulin: R493X Male, 65, Progranulin: C31FS Female, 46, MAPT: Het. c.1920+16C>T (Asymptomatic Carrier) Female, 54, MAPT: Het. c.1920+16C>T Female, 42, MAPT: Het. c.1920+16C>T Male, 35, MAPT: Het. c.1920+16C>T Female, 43, VCP: Het. VCP R155C Male, 42, VCP: Het. VCP R191Q
Charcot-Marie-Tooth Disease, Type 4J		Male, 27, FIG4: Het. c.122T>C p.(I41T) exon 2
Dentatorubral-pallidoluysian atrophy (DRPLA)		Male, 16, ATN1: 13/66 CAG Male, 51, ATN1: 17/57 CAG Female, 45, ATN1: 12/13 CAG (Asymptomatic Carrier)
Friedreich's Ataxia		Male, 21, FXN: >75 GAA Female, Unknown , FXN: >75 GAA (Asymptomatic Carrier) Male, 44, FXN: 8 GAA (Asymptomatic Carrier) Female, 17, FXN: >75 GAA Male, 23, FXN: >66 GAA Male, 34, FXN: >75 GAA

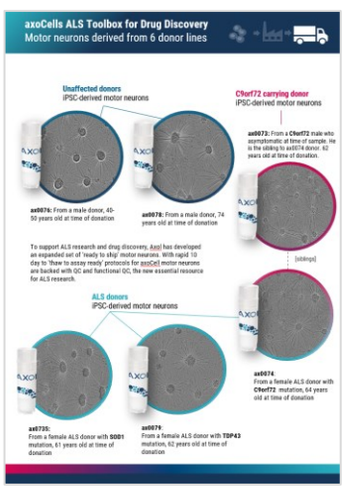
axoLines donor iPSC Library

Patient donor iPSCs

Donor Condition	Lines Available
Huntington's Disease	Female, 40-50, HTT: 18/39 CAG
	Female, 51, HTT: 42/17 CAG
	Female, 7, HTT: 127/14 CAG
	Male, 16, HTT: 28/66 CAG
	Male, 64, HTT: 17/38 CAG (Asymptomatic Carrier)
Mucolipidosis IV (ML4)	Female, 36, MCOLN1: Het. c.785T>C (Asymptomatic Carrier)
	Female, 10, MCOLN1: Hom. c.406-2A>G
	Male, 45, MCOLN1: Het. c.406-2A>G
	Male, 7, MCOLN1: Het. c.694A>C p.(T232P); Het. c.785T>C p.(F262S)
Nasu-Hakola Disease	Female, 41, TREM2: Hom. c.150G>T p.(W50C)
	Female, 69, TREM2: Het. c.150G>T p.(W50C) (Asymptomatic Carrier)
	Male, 68, TREM2: Het. c.150G>T p.(W50C) (Asymptomatic Carrier)
Parkinsonism/Machado-Joseph disease/SCA3	Male, 50, ATXN3: 14/69 CAG
	Female, 53, ATXN3: 26/70 CAG
Parkinson's Disease	Female, 48, PINK1: W90Lfsx12 & PARKIN: R275W
	Male, 75, Het. PARK1 & PARK2 Variant
	Female, 52, PINK1: Hom. W90Lfsx12
Spinal and bulbar muscular atrophy (SBMA)	Male, 66, AR: >47 CAG
Spinocerebellar ataxia	Male, 41, ATXN2: 22/38 CAG
	Male, 58, ATXN2: 22/36 CAG
	Female, Unknown , ATXN2: 22/39 CAG
	Female, 22, ATXN3: 14/75 CAG
	Female, 63, CACNA1A: Het. 23 CAG
	Female, 61, ATXN7: 10/39 CAG



See 'sAD Line Collection' information



See 'ALS Toolbox' information

axoCells™
Pre-manufactured and ready-to-ship

Category / cell type	Product name	iPSC-derived cells only	Cells, media, supplements bundle kit
Neuroscience			
Cortical Excitatory Neurons	axoCells™ Human iPSC-Derived Neural Stem Cells, newborn male donor, ≥1.5 million cells	ax0015	ax5115
	axoCells™ Human iPSC-Derived Neural Stem Cells, male donor, ≥1.5 million cells	ax0018	ax5118
Striatal neurons	axoCells™ Human iPSC-Derived Neural Stem Cells, newborn male donor, ≥1.5 million cells	ax0015	ax3115
	axoCells™ Human iPSC-Derived Neural Stem Cells, male donor, ≥1.5 million cells	ax0018	ax3118
Cortical Inhibitory Interneurons	axoCells™ Human iPSC-Derived Inhibitory Interneurons, male donor, ≥2 million cells	ax0662	-
	axoCells™ Human iPSC-Derived Inhibitory Interneurons, male donor, ≥2 million cells	ax0667	-
Motor Neurons	axoCells™ Human iPSC-Derived Motor Neurons, ALS (C9orf72) asymptomatic male donor, ≥2 million cells	ax0073	ax0183
	axoCells™ Human iPSC-Derived Motor Neurons, ALS (C9orf72) female donor, ≥2 million cells	ax0074	ax0184
	Human iPSC-Derived Motor Neurons (unaffected male 1)	ax0076	ax0186
	Human iPSC-Derived Motor Neurons (female, ALS, SOD1)	ax0735	ax01835
	Human iPSC-Derived Motor Neurons (female, ALS, TDP43)	ax0079	ax0189
	axoCells™ Human iPSC-Derived Motor Neurons, male donor, ≥2 million cells	ax0078	ax0178
Microglia	axoCells™ Human iPSC-Derived Microglia, male donor, ≥1 million cells	ax0664	ax0679
Astrocytes	axoCells™ Human iPSC-Derived Astrocytes, male donor, ≥1 million cells	ax0704	-
Pain and Sensation			
Sensory Neurons	axoCells™ Human iPSC-Derived Sensory Neurons, male donor, ≥3.2 million cells	ax0555	-
	axoCells™ Human iPSC-Derived Sensory Neurons, male donor, 1million cells	ax0055	ax0157
	axoCells™ Human iPSC-Derived Sensory Neuron Bundle Kit -XF, 3.2 million cells	ax0555	ax4555
	axoCells™ Human iPSC-Derived Sensory Neuron Bundle Kit -XF, 1 million cells	ax0555	ax4055
Cardiovascular			
Ventricular Cardiomyocytes	axoCells™ Human iPSC-Derived Ventricular Cardiomyocytes, male donor, ≥1 million cells	ax2508	ax2500
Atrial Cardiomyocytes	axoCells™ Human iPSC-Derived Atrial Cardiomyocytes, male donor, ≥1 million cells	ax2518	ax2510
Ophthalmology			
Retinal Pigment Epithelial cells	Human iPSC-derived RPE, Caucasian donor,≥ 1 million cells	PCi-RPE_CAU	PCi-RPE_KIT
Microglia	axoCells™ Human iPSC-Derived Microglia, male donor, ≥1 million cells	ax0664	ax0679
Dermatology			
Sebocytes	Human iPSC-derived Sebocytes, Caucasian donor,≥ 2 million cells	PCi-SEB_CAU	PCi-SEB_CAU_KIT
Melanocytes	Human iPSC-derived Melanocytes, Caucasian donor,≥ 1 million cells	PCi-MEL_CAU_1M	PCi-MEL-CAU_KIT
Sensory Neurons	axoCells™ Human iPSC-Derived Sensory Neurons, male donor, ≥3.2 million cells	ax0555	-
	axoCells™ Human iPSC-Derived Sensory Neurons, male donor, >0.5 million cells	ax0055	ax0157
	axoCells™ Human iPSC-Derived Sensory Neuron Bundle Kit -XF, 3.2 million cells	ax0555	ax4555
	axoCells™ Human iPSC-Derived Sensory Neuron Bundle Kit -XF, 1 million cells	ax0555	ax4055

Custom manufacturing iPSC-derived cells

With over a **decade of experience** in the human iPSC space, we understand that high-quality differentiation is challenging, with significant risks and costs if not performed well. But like you, we also see the enormous value of human iPSCs for building **better, more physiologically relevant** models of human disease.

That's why we offer our iPSC expertise to leading biopharma and research organizations globally. We've developed a **tried-and-tested workflow** to provide **full-service differentiation** from iPSCs to end-point cells, with robust characterization and ongoing support from our expert scientists.

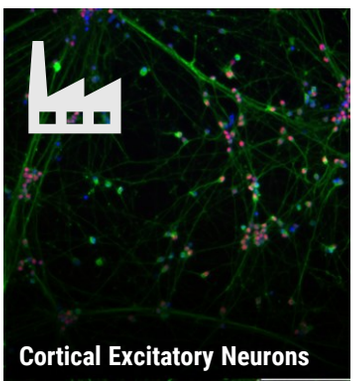
Clients who work with Axol share our obsession with doing it once and doing it well.

We prioritize **quality** control and characterization, always built-in as standard in our projects, to ensure there are no surprise challenges (or costs), maximizing project success. That gives you more confidence, time and resource to focus on your research and produce better human disease models for drug discovery and beyond.

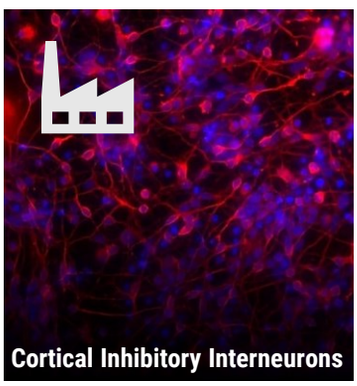
From your lines or from ours, our custom manufacturing service is designed to support research and drug discovery in the provision of functionally active, human iPSC-derived cells.

iPSC-derived cells for Neuroscience

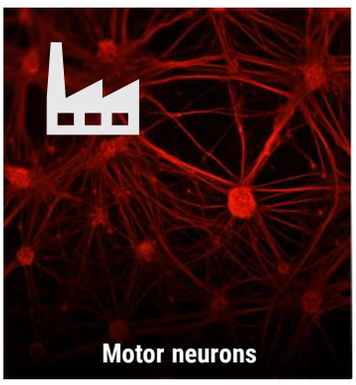
Neuronal cell types



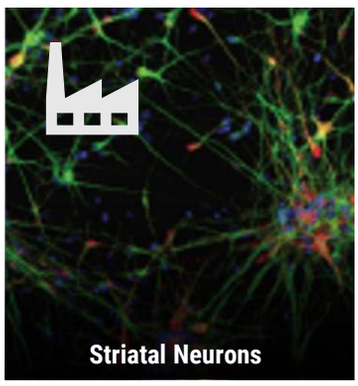
Ideal for research into **Alzheimer's Disease**
- Assay ready in 20 days
- Express over 12 of the key markers including CTIP2, TUJ1, CUX1 and MAP2.
- Demonstrated functionality in advanced *in vitro* models including co-culture and tri-culture



Ideal for research into **Alzheimer's Disease**
- Assay ready in 20 days
- Express the key markers including GAD65, Parvalbumin-B, GABA and Somatostatin
- Demonstrated functionality in advanced in vitro models including co-culture and tri-culture



Ideal for research into **ALS** and **Motor Neuron Disease**
- Assay ready in 10 days
- Express the key markers including TUJ1, ChAT, HB9, Islet1 and SMI32
- Demonstrated functionality in advanced in vitro models

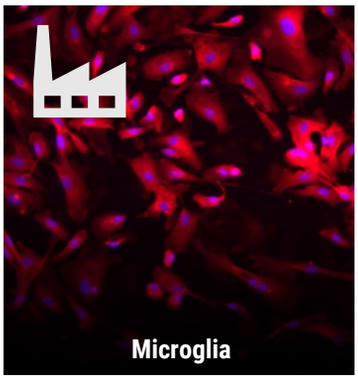


Ideal for research into **Huntington's Disease**
- Assay ready in 31 days
- Express the key markers including DARPP32, CTIP2, and GABA
- Designed for use in advanced in vitro models

Custom manufacturing iPSC-derived cells

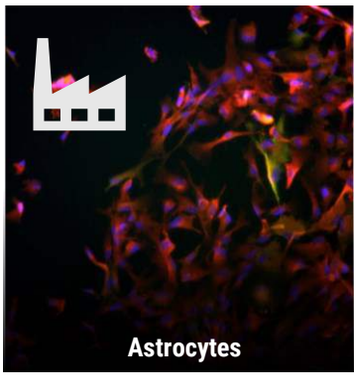
iPSC-derived cells for Neuroscience

Glial and neuroinflammatory cell types



Ideal for research into **a range of neurodegenerative diseases**

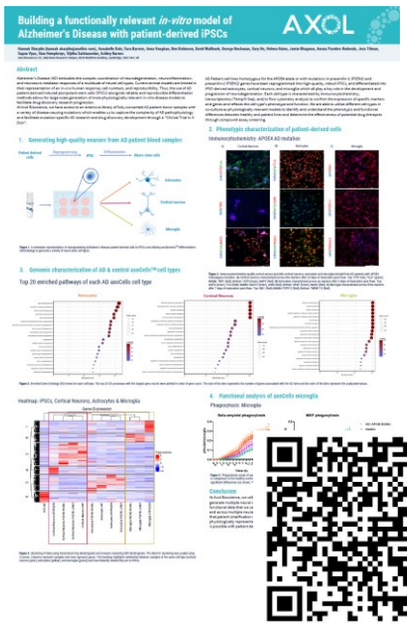
- Assay ready in 7 days
- Express the key markers including IBA-1, TMEM119 and P2RY12
- Demonstrate robust functional activity, measured by cytokine release, phagocytosis and chemotaxis

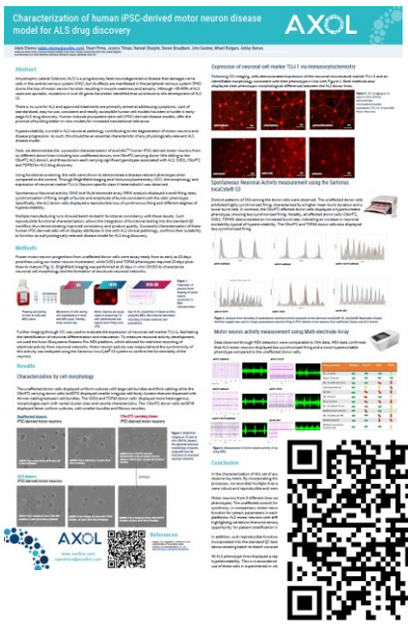


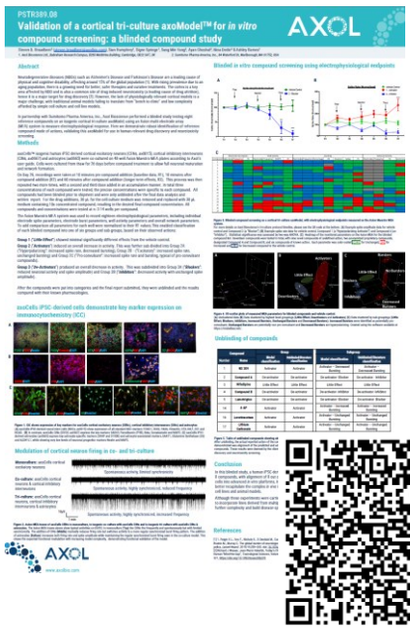
Ideal for research into **a range of neurodegenerative diseases**

- Assay ready in 2 days
- Express the key markers (GFAP and S100) with low expression of Nestin (a NSC marker) and TUJ1 (a neuronal marker)
- Designed for use in advanced in vitro models

Learn more







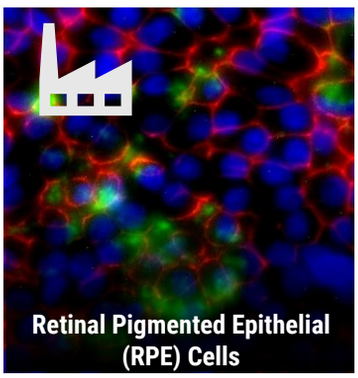
Example manufacturing production runs:

- **For ALS studies –** for instance, generating motor neurons from 3 ALS patients with matched 'unaffected donor' derived cells
- **For Alzheimer's** studies - for instance, generating cortical neurons from multiple lines with different ApoE status with matching microglia
- **For Huntington's studies –** for instance, striatal neurons from donors with different CAG repeat lengths

Custom manufacturing iPSC-derived cells

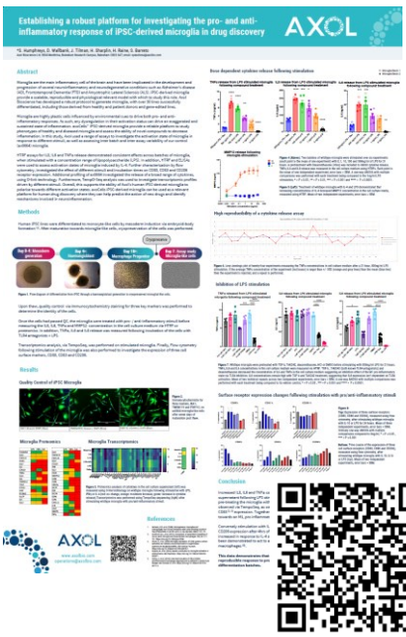
iPSC-derived cells for Ophthalmology

Epithelial and neuroinflammatory cell types



Ideal for research into **Dry-AMD and gene-therapy modeling**

- Typical pigmented and cobblestone morphology
- Expression of key markers (MITF, ZO-1, PMEL17) by immunostaining
- High purity, with >95% PMEL 17 expression on flow cytometry

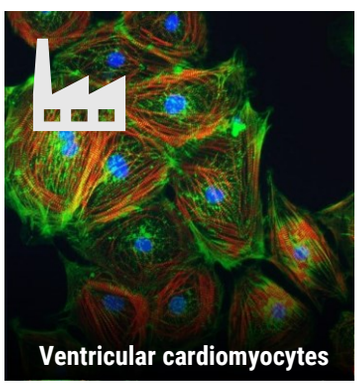


Ideal for research into **ophthal-inflammatory** studies and co-culture

- Assay ready in 7 days
- Express the key markers including IBA-1, TMEM119 and P2RY12
- Demonstrate robust functional activity, measured by cytokine release, phagocytosis and chemotaxis

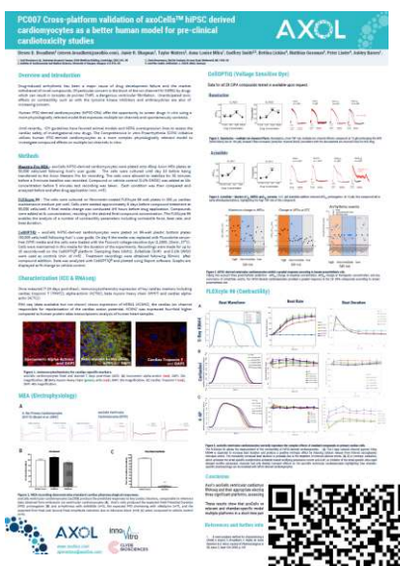
iPSC-derived cells for Cardiovascular toxicity and research

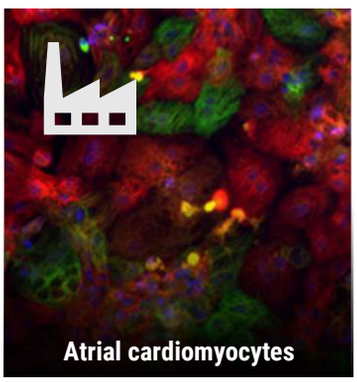
Cardiac muscle cells



Ideal for *in vitro* **cardiotoxicity** studies, ion channel studies and disease specific **cardiology** research

- Spontaneously beat 3 days post-thaw and assay-ready in just 7 days
- Validated against all 28 CiPA compounds
- Demonstrate functional responses in a range of assay formats including patch clamp, electrophysiology and voltage-sensitive dyes





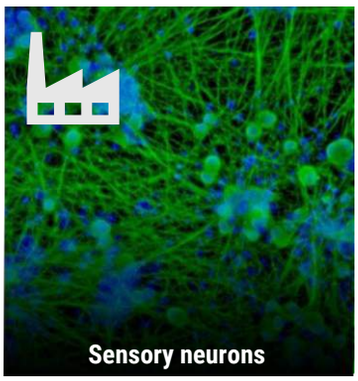
Ideal for *in vitro* **cardiotoxicity** studies, ion channel studies and disease specific **cardiology** research

- Spontaneously beat 3 days post-thaw and assay-ready in just 7 days
- No evidence of endogenous arrhythmias
- Demonstrate functional response to atrial-specific compounds including carbachol

Custom manufacturing iPSC-derived cells

iPSC-derived cells for pain & sensation studies

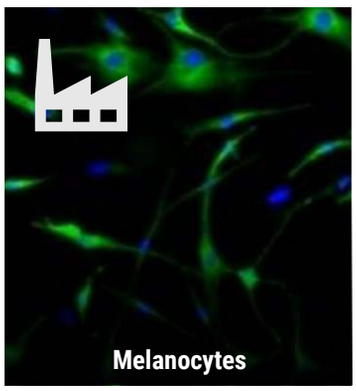
Sensory neurons



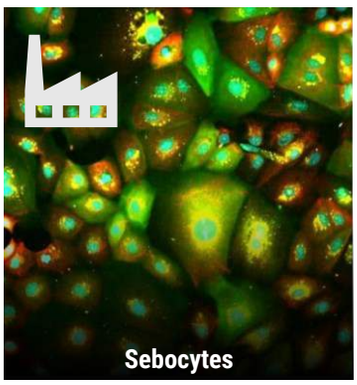
Ideal for *in vitro* models of pain, sensation, itch and touch
- Assay ready in 21 days
- Express 50 of the key ion channels including Nav1.7, Nav1.8, Nav1.9, TRPV1 and TRPA1
- Designed for use in microfluidics platforms and organ-on-chip devices for models of pain and peripheral neurotoxicity

iPSC-derived cells for dermatology and cosmetics

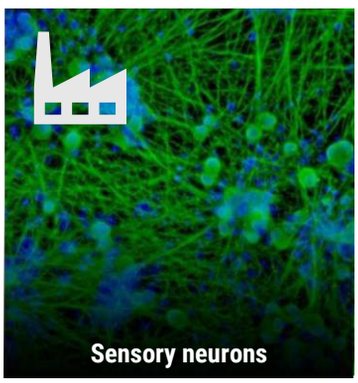
Skin and sensory cell types



Use for studying cell proliferation, toxicity, lightening and tanning
- Assay ready in 5 days
- Express the typical markers PAX3, MITF, PMEL17 and TYRP1
- Produce melanin and demonstrate melanosome transfer to keratinocytes



Ideal for studies of acne and hyperseborrhea
- Assay ready in 4 days
- Express the typical markers MUC1 and KRT7
- Produce sebum and exhibit functional responses to testosterone and linoleic acid



Ideal for *in vitro* models of pain, sensation, itch and touch
- Assay ready in 21 days
- Express 50 of the key ion channels including Nav1.7, Nav1.8, Nav1.9, TRPV1 and TRPA1
- Designed for use in microfluidics platforms and organ-on-chip devices for models of pain and peripheral neurotoxicity

Axol Bioscience sAD iPSC Collection

A new set of sporadic Alzheimer's Disease iPSCs to support pre-clinical *in vitro* model building and drug discovery

Features of collection:

- 20 iPSC lines including sAD and unaffected donor controls.
- Full ethical and commercial consent
- Male and female donors, age relevant to Late-Onset AD.
- Reporting on ApoE genotype, gender, age, diagnosis, medical and family history.
- Available for custom manufacturing and outsourced service provision.

Line name GM = Greater Manchester	APOE status	Amyloid beta	Age	Gender	Diagnosis
GMMH004	E2/E3	Yes	77	M	sAD
GMMH083	E2/E3		73	M	Not affected at time of donation
CENSOi004-E	E2/E3		40-50	M	Not affected at time of donation
GMMH001	E3/E3	Yes	83	M	sAD
GMMH007	E3/E3	Yes	80	M	sAD
GMMH017	E3/E3	Yes	79	F	sAD
GMMH025	E3/E3		70	M	Not affected at time of donation
GMMH077	E3/E3		81	M	Not affected at time of donation
CENSOi070-A	E3/E3		59	F	sAD
CENSOi058-A	E3/E3		45	F	Not affected at time of donation
GMMH009	E3/E4	Yes	74	M	sAD
GMMH015	E3/E4	Yes	82	M	sAD
GMMH016	E3/E4	Yes	72	F	sAD
GMMH120	E3/E4		70	M	sAD
GMMH122	E3/E4		77	M	sAD
GMMH129	E3/E4		72	M	sAD
CENSOi074-A	E3/E4		60	M	sAD
CENSOi077-A	E3/E4		52	F	sAD
GMMH005	E4/E4	Yes	69	F	sAD
GMMH013	E4/E4	Yes	76	F	sAD

Patients from the Greater Manchester area of the UK have donated PBMCs providing full ethical and commercial rights for cellular manufacturing to support drug discovery.

Patient lines:

- Male or female patients with a clinical diagnosis of sporadic Alzheimer's disease;
- Age of disease onset at 65 years or above.

Exclusion criteria for patients:
- Patients or donors under 65 years of age;
- Diagnosis of non-AD dementia or other neurodegenerative disease;
- Any current or past severe psychiatric illness;
- HIV, Hepatitis C or Hepatitis B positive viral screen;
- Lacks capacity to consent to blood sampling and use.

McKhann criteria section 4.1 was applied to all patients prior to samples being taken.

Unaffected donor lines:

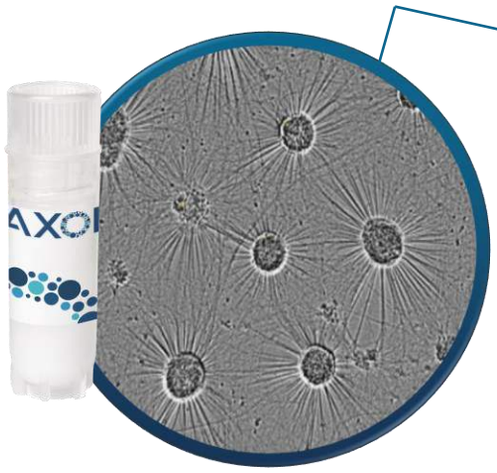
Inclusion criteria:
- Male or female donors aged 65 years or above, otherwise healthy.

Exclusion criteria:
- The diagnosis of a brain disorder or neurodegenerative disease;
- Any current or past severe psychiatric illness;
- HIV, Hepatitis C or Hepatitis B positive viral screen;
- A family history of dementia in first-degree relatives.

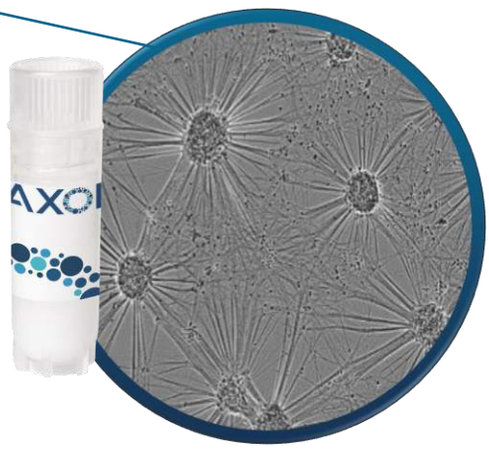
axoCells ALS Toolbox for Drug Discovery

Motor neurons derived from 6 donor lines

Unaffected donors
iPSC-derived motor neurons



ax0076: From a male donor, 40-50 years old at time of donation



ax0078: From a male donor, 74 years old at time of donation

C9orf72 carrying donor
iPSC-derived motor neurons

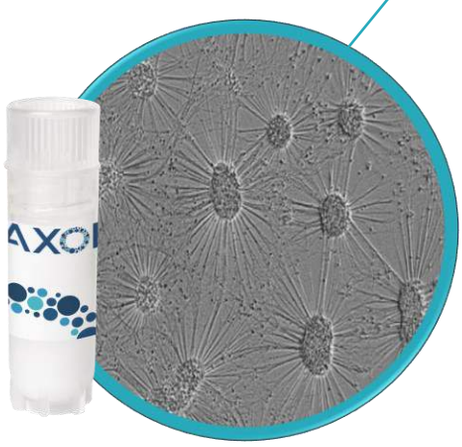
ax0073: From a **C9orf72** male who was asymptomatic at time of donation. He is the sibling of ax0074 donor. 62 years old at time of donation.

[siblings]

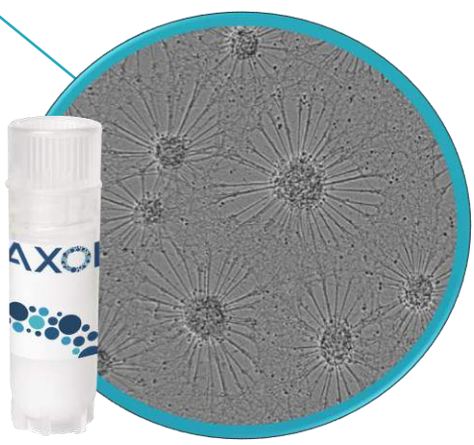
ax0074:
From a female ALS donor with **C9orf72** mutation, 64 years old at time of donation

To support ALS research and drug discovery, Axol has developed an expanded set of 'ready to ship' motor neurons, with rapid 10 day 'thaw to assay ready' protocols. axoCell motor neurons are backed with QC and functional QC and are the new essential resource for ALS research.

ALS donors
iPSC-derived motor neurons



ax0735:
From a female ALS donor with **SOD1** mutation, 61 years old at time of donation



ax0079:
From a female ALS donor with **TDP43** mutation, 62 years old at time of donation

A focus on quality

Our Quality Management System is the bedrock for our daily work, driving quality and consistency for every one of our customers.

Our Quality Management System:

- Bulk / same batch manufacturing and storage are available
- Our manufacturing facilities are ISO 9001:2015 accredited
- We conduct in-depth iPSC characterization, both pre- and post-differentiation
- Our Certificates of Analysis report on the quality testing methods and result
- We provide full batch control and ownership options
- There is full traceability of material origin and source
- We utilize a Q-Pulse Quality Management System for compliant audit-trail operation

The ISSCR Standards Document 2023

Our scientists have conducted a thorough analysis of our current processes to match against the ISSCR Standards Document

Patient stratification models - engaging in complexity and diversity with iPSC models

Many neurological conditions are complex in genetics, definition and causation. So called 'sporadic' cases, where there is no strong family history, account for the majority of ALS cases and late onset Alzheimer's. This ambiguity leads to challenges in drug design and clinical trial design. Patient stratification ('clinical trial in a dish') models may provide a way forward.

Age relevant, gender balanced, patient group providing a primary sample (PBMC), consent and clinical history

→ **1.** Multiple iPSCs created from multiple people.

→ **2.** From each iPSC, manufacture multiple relevant cells types so that each well represents a different individual.

→ **3.** Grasp the complexity of polygenic diseases to drive drug discovery insights and smarter, more successful clinical trial designs

To learn more about our cell manufacturing capabilities, timelines and quotations, contact operations@axolbio.com

About Axol Bioscience

Like you, we believe that having more human-relevant disease models will **expand scientific knowledge** and **de-risk drug development**. We use human iPSCs to achieve this and have been doing so for over a decade.

We take cells from patient and healthy donors and, using our **leading iPSC technology**, work with researchers to build physiologically-relevant *in vitro* models. We have a special focus on neurodegenerative diseases (like Alzheimer's Disease) as well as cardiotoxicity to promote drug safety.

Our customers benefit from our **extensive experience**, meaning we can do the scientific "heavy lifting" to unlock the benefits of iPSC technology. That ultimately means **more confidence** in the data outputs of advanced *in vitro* models, along with **better insights** and **reduced costs**.

So we ask you: iPSCs? What can we do to help?

www.axolbio.com