

AXOL

eBook

axoCells™

Human iPSC-derived

MICROGLIA

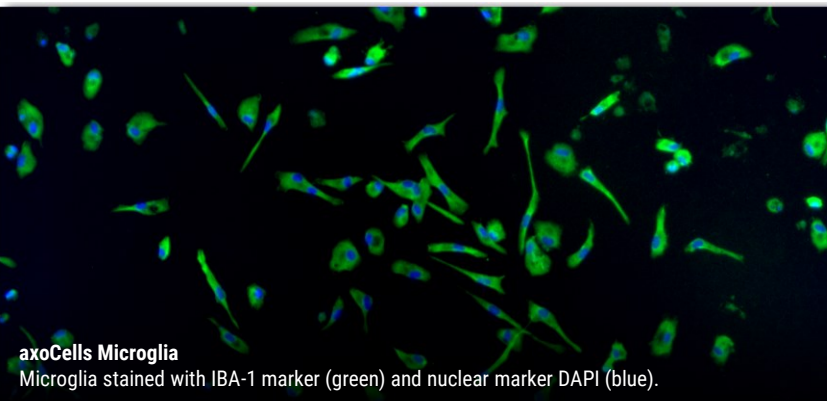
Supporting biopharma with better human disease models



Microglia, a high-profile target for drug discovery

Neurodegenerative diseases affect around 15% of people worldwide¹, with rates increasing due to our aging population. Research into these conditions has identified neuroinflammation as a key disease driver, so the drug discovery industry has turned to the brain's main immune cell, microglia, in search of new therapeutic targets.

First identified in the late 19th century by Frank Nissl (and his eponymous staining technique), microglia are becoming an increasingly vital component in human-relevant drug development platforms.



Microglia are the main immune cell of the central nervous system, making up around 10% of all cells in the brain². They play key roles in brain development, neurogenesis, synaptic pruning and maintenance of the normal homeostatic environment³.

Research has also revealed a key role for microglia in neurodegenerative diseases including Alzheimer's Disease, Amyotrophic Lateral Sclerosis (ALS) and Parkinson's Disease.

Microglia derived from human induced pluripotent stem cells (iPSCs) can be produced consistently and incorporated into model systems. Human iPSC-derived microglia are made by differentiating iPSCs from reprogrammed donor blood samples. They therefore retain the phenotypic characteristics of the donor, producing a more human-relevant model system. This also opens up exciting applications of disease-derived microglia to test potential therapies in specific human disease models.

iPSC-derived microglia can also be produced in large volumes, optimizing cell consistency while adjusting the price point for larger-throughput platforms.

References

- 1 Feigin V.L., Vos T., Nichols E., O Owolabi M., Carroll W.M., Dichgans M., Deuschl G., Parmar P., Brainin M., Murray C. The global burden of neurological disorders: Translating evidence into policy. *Lancet Neurol.* 2019;19:255–265. doi: 10.1016/S1474-4422(19)30411-9.
- 2 Colonna M, Butovsky O. Microglia Function in the Central Nervous System During Health and Neurodegeneration. *Annu Rev Immunol.* 2017 Apr 26;35:441-468. doi: 10.1146/annurev-immunol-051116-052358. Epub 2017 Feb 9. PMID: 28226226; PMCID: PMC8167938.
- 3 Gao, C., Jiang, J., Tan, Y. et al. Microglia in neurodegenerative diseases: mechanism and potential therapeutic targets. *Sig Transduct Target Ther* 8, 359 (2023). <https://doi.org/10.1038/s41392-023-01588-0>

Axol Bioscience supporting the use of microglia in biopharma drug discovery



“With over a decade of experience in the iPSC industry, we’re working towards a mission of building better, more human-relevant models for drug discovery. We’re using that expertise to unlock the utility of iPSCs for biotech companies, allowing them to focus on the science and accelerate drugs through the development pathway. Ultimately, that will translate to better treatments for patients worldwide.”

- **Liam Taylor**, CEO, Axol Bioscience

Here to help your science



We want to run a microglia screen in-house.



We want to use a more 'human-relevant' microglia model in our lab.



Can you run a compound screen for us using microglia?

No problem, we can supply you with the cells*, media and supplements you need.



No problem, we can supply you with cells or we can build and test the model here, and then tech transfer to you.



Yes, we can run that screen for you.



Your lab does the screen with axoCells iPSC-derived microglia.

We handle the technical complexities and then you take over the running of the model.

You get the data (plus cell lysates).

What does a typical project look like?



1. Kick off

- Open discussions
- Rapid follow-up with competitive quote



2. Execution

- Ongoing communication
- Focus on quality of output guided by in-house expertise



3. Output

- Debrief meeting
- Data sharing
- Ongoing support

Want to discuss a project, including timelines and ballpark costings?
[Click here to speak to our scientists.](#)

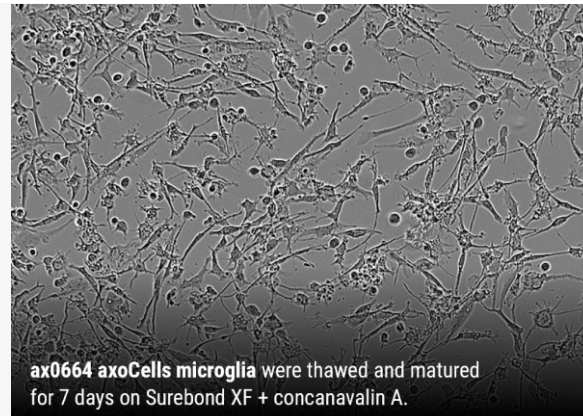
*We can supply microglia "off-the-shelf" or made-to-order, either from our extensive iPSC library or from your own iPSCs

The data behind axoCells™ iPSC-derived microglia

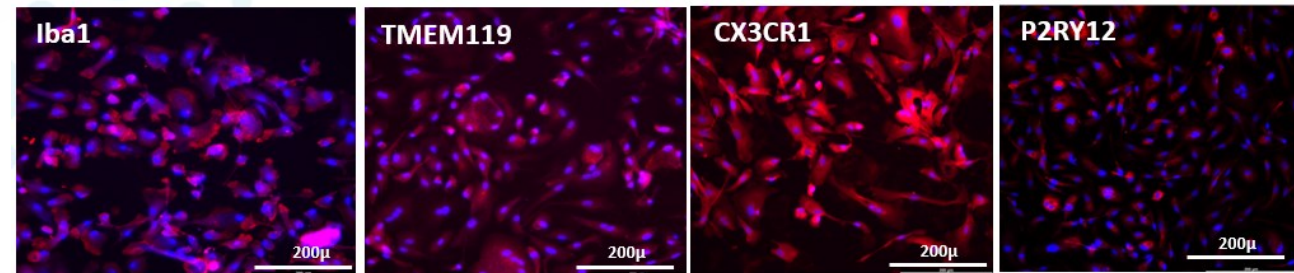
We've **extensively characterized** our axoCells microglia to ensure the **correct morphology**, expression of **key cell markers** and **functional relevance**. We manufacture them to ISO 9001 standards to ensure **high quality and consistency**, at scale, to fuel robust *in vitro* neurodegenerative disease models.

We conduct robust characterization

axoCells microglia showing expected morphology, with different phenotypes demonstrating sub-populations with specified functions.



Expression of key markers (Iba1, TMEM119, CX3CR1 and P2RY12) on immunocytochemistry (ICC).

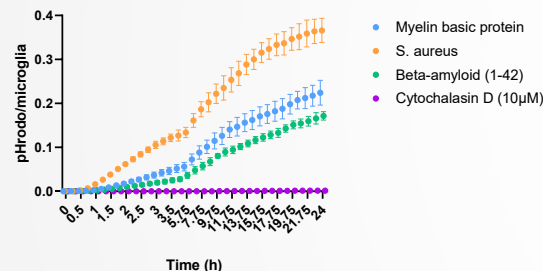


axoCells iPSC-derived microglia were thawed and matured for 7 days. Cells were fixed and stained for the relevant markers and imaged using a Leica microscope. Key microglia markers Iba1, TMEM119, CX3CR1 and P2RY12 were used as standard quality control. Red: Marker of interest, Blue: DAPI

We measure functional relevance

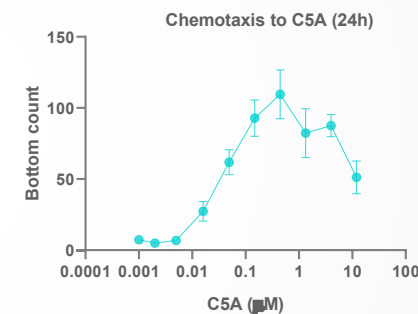
Phagocytosis

axoCells microglia were thawed and matured for 7 days before addition of pHrodo labelled bait. Baits were added to the cells and phagocytosis monitored over 24h using an IncuCyte S3, showing a steady increase over time. Cytochalasin D (10μM) was used as a negative control and showed complete inhibition of phagocytosis.



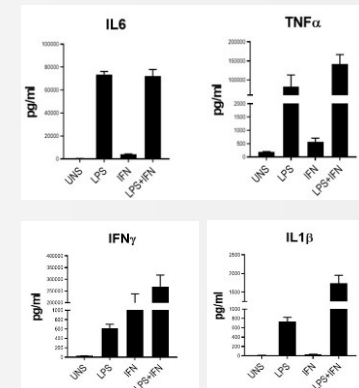
Chemotaxis

Chemotaxis by fresh axoCells microglia to various concentrations of C5a. iPSC-derived microglia were matured for 7 days before re-plating into chemotaxis plates. Cell movement was measured using an IncuCyte S3. Values represent the number of cells moving from the top chamber to the bottom, towards C5a, after 24h. Data are n=4 +/- SEM.



Cytokine release

Cytokine release from fresh axoCells microglia following 24 h stimulation with LPS, INFγ or both (n=3). UNS= unstimulated. The expected pattern of cytokine release demonstrates functional relevance.



How we bulk manufacture high-quality microglia

Our approach to microglia Quality Control (QC)

From our manufacturing facility in Roslin, we work to ISO 9001 standards to ensure our cells are **high-performing, functionally relevant** and **consistent** - even in bulk quantities. We have rigorous QC across the following parameters:

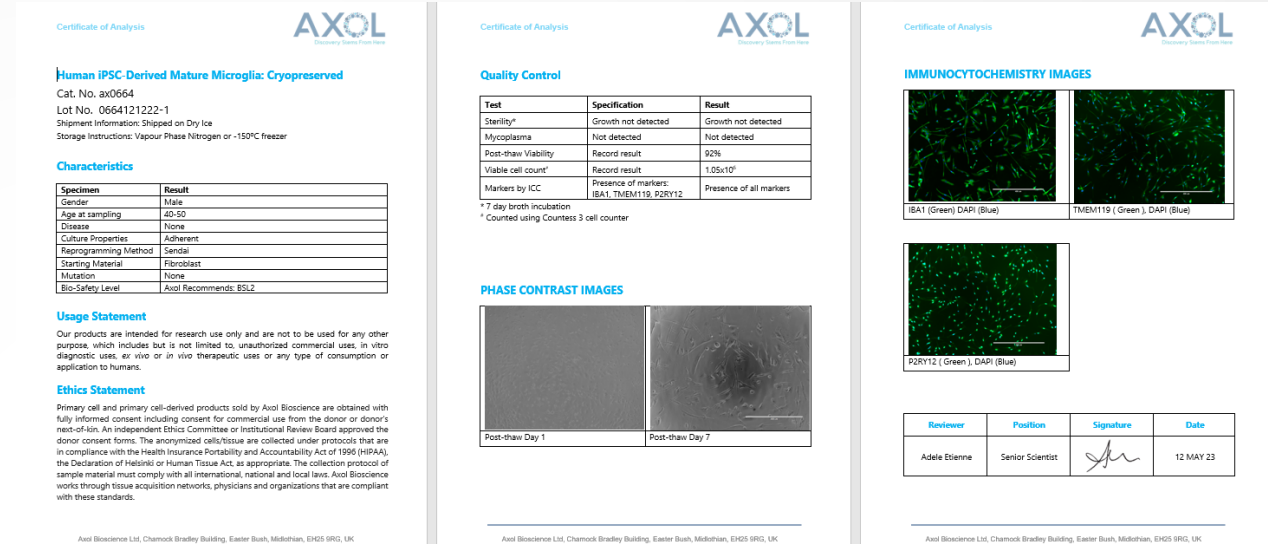
Quality Control

Test	Specification
Flow Cytometry	Presence of lineage-specific markers and absence of pluripotency marker
Sterility*	Growth not detected
Mycoplasma	Not detected
Post-thaw Viability	Record result
Viable Cell Count**	Record result
Markers by ICC	Presence of markers: IBA1, TMEM119, P2RY12, Cx3CR1

*7 day broth incubation

**Counted using Countess™ 3 Automated Cell Counter

We also offer custom functional QC as an add-on, comprising **phagocytosis, chemotaxis** and **cytokine release**.



Supporting quality and consistency

We want our customers to have confidence in using our microglia in their neural workflows. That's why our production facility works to **ISO 9001 standards**, guided by our rigorous quality control procedures and decades of scientific experience. All cells come with a full **Certificate of Analysis** (as shown above) and are [officially certified by HPScreg®](#), to ensure ethical and biological conformity for your peace of mind.

Do you have any questions about our **shipping and logistics** capabilities? Visit our website to look at our **comprehensive shipping FAQs**.

[Read our shipping FAQs](#)

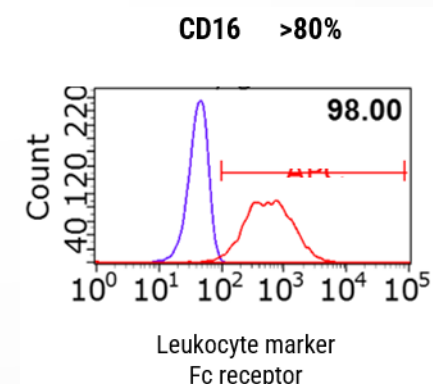
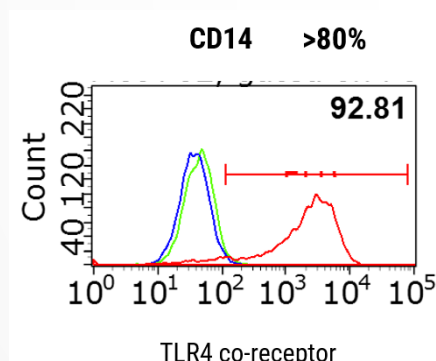
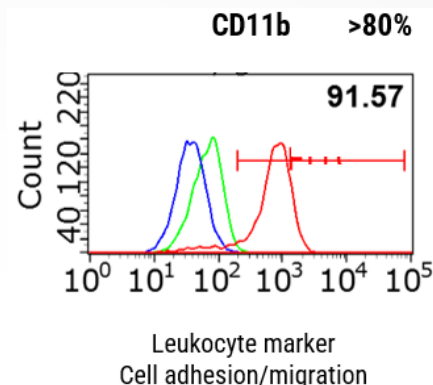
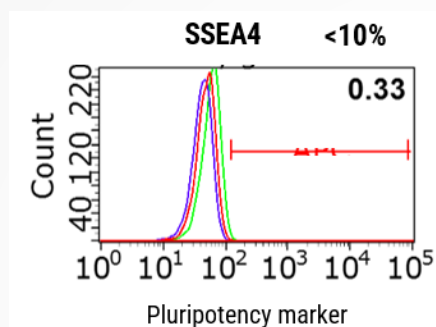
How we bulk manufacture high-quality microglia

Flow Cytometry

We use flow cytometry to assess progenitor cells for a standard panel of lineage-specific markers, ensuring **high levels of quality control**. SSEA4 is used as a negative control to detect markers of pluripotency.

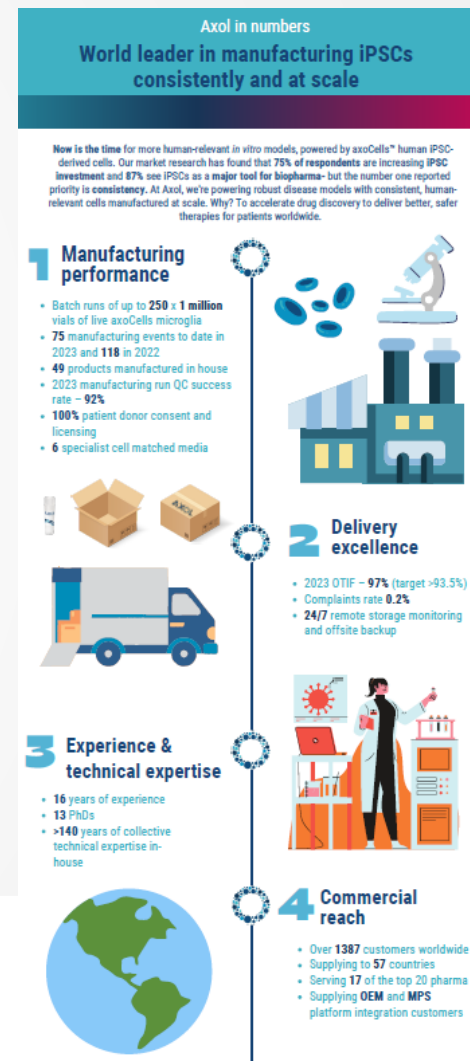
With our quality-focused approach, we've developed the manufacturing capabilities to produce high-quality microglia at scale, with excellent functional consistency.

Example flow cytometry QC for fresh macrophage progenitors, demonstrating the presence of lineage-specific markers CD14, CD11b and CD16 above threshold levels, and negative control SSEA4 below threshold. This batch would therefore pass this stage of QC. Our standard panel also includes CD206 and CD163 as lineage-specific markers. *Unstained, Isotype (control), Marker of interest.*



[Download our infographic](#)

If you'd like to **explore the impressive numbers** behind our manufacturing and logistics performance, download our latest infographic.



Powering your platform with high-quality, consistent cells

Supporting high-volume customers



Whether you want to **scale up** in size or complexity, run large **screening platforms**, or just want to ensure **consistency for the future**, we've developed the manufacturing capabilities to support your bespoke experimental designs.

We can produce microglia from several **disease lines** (including Alzheimer's Disease) and can manufacture **large batches** (up to 250 x 1 million vials as standard, and more if needed) for individual customers to source from, with custom QC, to enable **better continuity** of cell quality and supply.

For BioPharma

For Contract Research Organizations

Excellent compliance with ISSCR Standards

We conducted a **thorough analysis of our quality operations** against the ISSCR Standards Document 2023 demonstrating **excellent compliance**, a testament to our focus on quality and consistency.

[Read our compliance statement](#)

Standards
for Human
Stem Cell
Use in
Research

JUNE 2023

www.isscr.org

SUPPORTED BY



axoCells™ microglia production information

axoCells microglia production information

To ensure simplicity and effectiveness, we've developed a kit containing iPSC-derived cells that have been directed down a microglia end-type lineage. Using the easy-to-follow protocol, you can rapidly mature these cells into functional microglia **in just 7 days**.

- You'll need a Microglia kit [ax0679](#)
- In this you'll find Microglia cells [ax0664](#) and all reagents*
- Follow the [protocol](#)
- **7 days** later you will have highly functional microglia

*Additional third-party components are required. Be sure to check the protocol before you start using the microglia kit.

Donor gender	Donor age	Source	Condition	Product code	Cells/vial	Kit
Male	40-50 yr	Fibroblasts	Healthy	ax0664	≥1 million	ax0679

FAQs

What applications are there for axoCells microglia?

Our microglia have been used extensively in **mono-, co- and tri-culture** with Axol's cortical excitatory neurons, astrocytes, and/or inhibitory interneurons to produce more relevant models of human neurodegenerative diseases, which include Alzheimer's Disease, ALS and Parkinson's Disease.

Do you have protocols available?

Protocols for incorporating microglia into co- and tri-culture with neurons are available as well as for microglia in monoculture.

How do you ensure manufacturing quality?

We work to ISO:9001 standards, guided by our rigorous quality control procedures and decades of scientific experience. All cells come with a full Certificate of Analysis and are officially certified by HPSCreg®, to ensure ethical and biological conformity for your peace of mind.

Do you have licenses and consent in place?

Axol has obtained all relevant licenses for reprogramming donor samples into iPSCs and differentiating these into microglia for commercial use. Patient samples used to create these cells have been ethically sourced and consented for research and commercial use. All cells come with a full Certificate of Analysis and are [officially certified by HPSCreg®](#), to ensure ethical and biological conformity for your peace of mind.

Do you have specialized media and reagents available?

A ready-to-go kit containing microglia cells and optimized media is available [Microglia Complete Cells and Media \(ax0679\)](#) or media is available as a standalone item [Microglia maintenance media kit \(ax0660\)](#).

Product highlights

axoCells™ microglia: From thaw to assay-ready in just 7 days



- High-quality, relevant microglia that **express the three key markers** (IBA-1, TMEM119 and P2RY12) and demonstrate robust functional activity measured by **cytokine release, phagocytosis and chemotaxis**
- Save time with functionally mature cells available in just **7 days**
- Ensure confidence with high-quality cells manufactured to **ISO:9001 standards** under rigorous quality control procedures

For more information on product features, highlights and data, take a look at our axoCells microglia product page.

[Check out the product page](#)

We're here to help with our **kit, protocol and support**

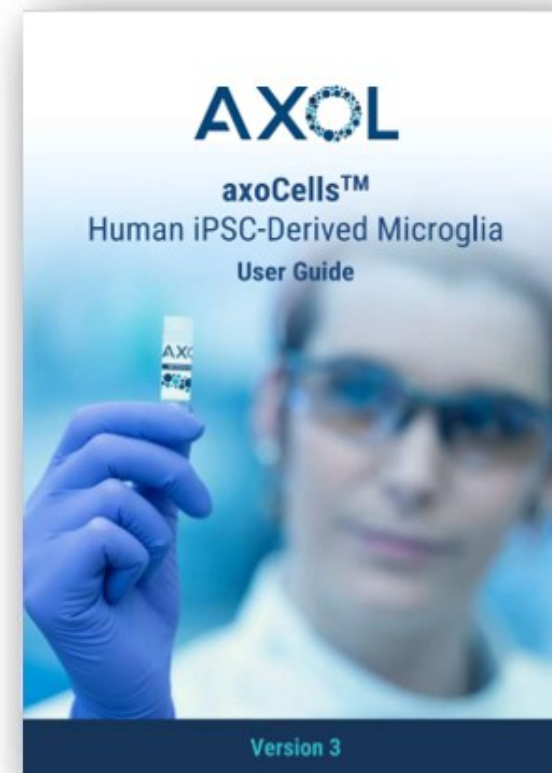


Media



Supplements

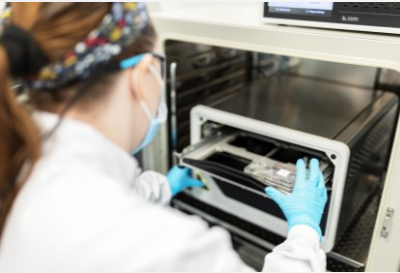
Progenitor cells



Protocol

axoServices microglia compound screening

Check out
axoServices™



Across our comprehensive suite of **custom lab assays**, compound screening is one of our main focus areas. We use our iPSC expertise to do the **technically challenging 'heavy lifting'**, allowing you to focus on the science and gather **high-quality *in vitro* data** for your compound.

We can **tailor the experimental design** to your needs, from simple mono-culture to complex co-culture (with astrocytes, cortical excitatory neurons and/or inhibitory interneurons), **scaled up** to your requirements.

High-quality compound screening with clear, measurable endpoints

A crucial component of any compound screening project is generating high-quality assay data. With microglia featuring in over 40% of our axoServices projects, we've developed the following assays for microglia compound screening:

Real-time imaging

- Phagocytosis
- Chemotaxis
- Cytokine release

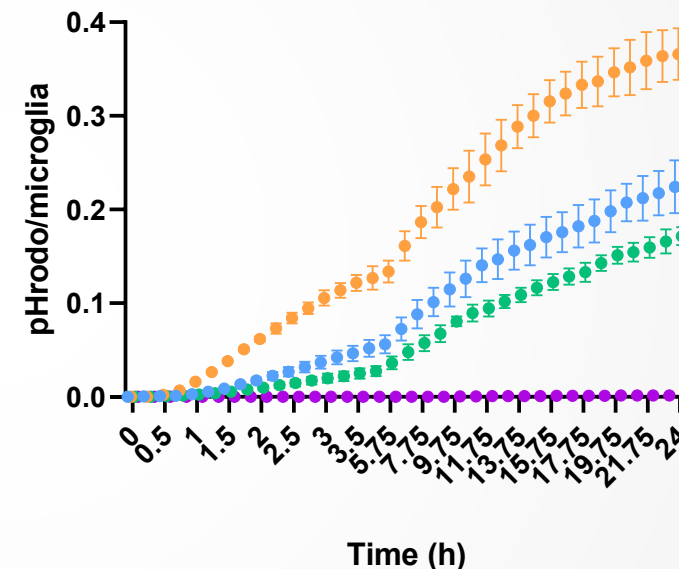
Electrophysiology (multi-electrode array)

Measurement of neuronal activity in co-culture models

In-house expertise with phagocytosis assays

We have extensively characterized our phagocytosis assays with a wide range of pHrodo-labelled baits, including ***E. coli*, zymosan beads, beta-amyloid, TAU, myelin basic protein, dead neurons, alpha-synuclein and *S. aureus***. Whatever your specific experimental need, we can help.

ax0664 Phagocytosis



- Myelin basic protein
- *S. aureus*
- Beta-amyloid (1-42)
- Cytochalasin D (10µM)

axoCells microglia were thawed and matured for 7 days before addition of pHrodo labelled bait. Baits were added to the cells and phagocytosis monitored over 24h using an IncuCyte S3, showing a steady increase over time. Cytochalasin D (10µM) was used as a negative control, and showed complete inhibition of phagocytosis.

Microglia compound screening at scale

We recently announced our collaboration with Sygnature Discovery to incorporate **axoCells human iPSC-derived microglia** into their high-content imaging *in vitro* screening workflows. This will enable researchers to gain a **deeper understanding** of the cellular response to drug candidates and identify **potential therapeutic targets** with higher precision and accuracy.

[Read more about it here](#)



Sygnature Discovery > News and Resources > News > News > Sygnature Discovery collaborates with Axol Bioscience to utilize human iPSC-derived microglial cells in high-content imaging drug discovery screening workflows.

Sygnature Discovery collaborates with Axol Bioscience to utilize human iPSC-derived microglial cells in high-content imaging drug discovery screening workflows.

On 10th October 2023, Sygnature Discovery, a world-leading integrated drug discovery provider and non-clinical solutions provider, has announced a scientific collaboration with human induced pluripotent stem cell (iPSC) experts, Axol Bioscience.

The collaboration aims to explore the incorporation of human [iPSC-derived microglia](#) into high-content imaging *in vitro* screening workflows. Human iPSC-derived cells are stem cells derived from patient donors that are a powerful tool in biomedical research due to their ability to differentiate into various cell types found in the human body. Microglia are neuro-inflammatory cells that constitute ~10% of the brain's cell population and are a key therapeutic target in the development of adequate treatments for Alzheimer's Disease and other neurodegenerative conditions.

By collaborating with [Axol Bioscience](#), Sygnature Discovery aims to enhance its drug discovery

“Our collaboration highlights the importance of leveraging **innovative technologies** and **expertise** to enhance the efficiency and effectiveness of the drug discovery process.

Axol's extensive practical experience in handling human iPSCs will **accelerate our ambition** to offer high-content-based imaging assays to customers in the neuroscience therapeutic area.”

- **Tim Phillips**, Associate Director (Bioscience) at Sygnature Discovery

axoModels™ advanced test systems using microglia

From Alzheimer's and Parkinson's Disease to ALS and epilepsy, microglia have been implicated in a range of neurodegenerative diseases. So we're applying our **technical expertise** to develop a new type of neuroinflammatory test system – more **human-relevant** than animal models, more **sophisticated** than simple cell culture, and more **consistent** and **scalable** than primary cells. Build in **measurable endpoints**, and you have a new generation of *in vitro* models for microglial compound screening.

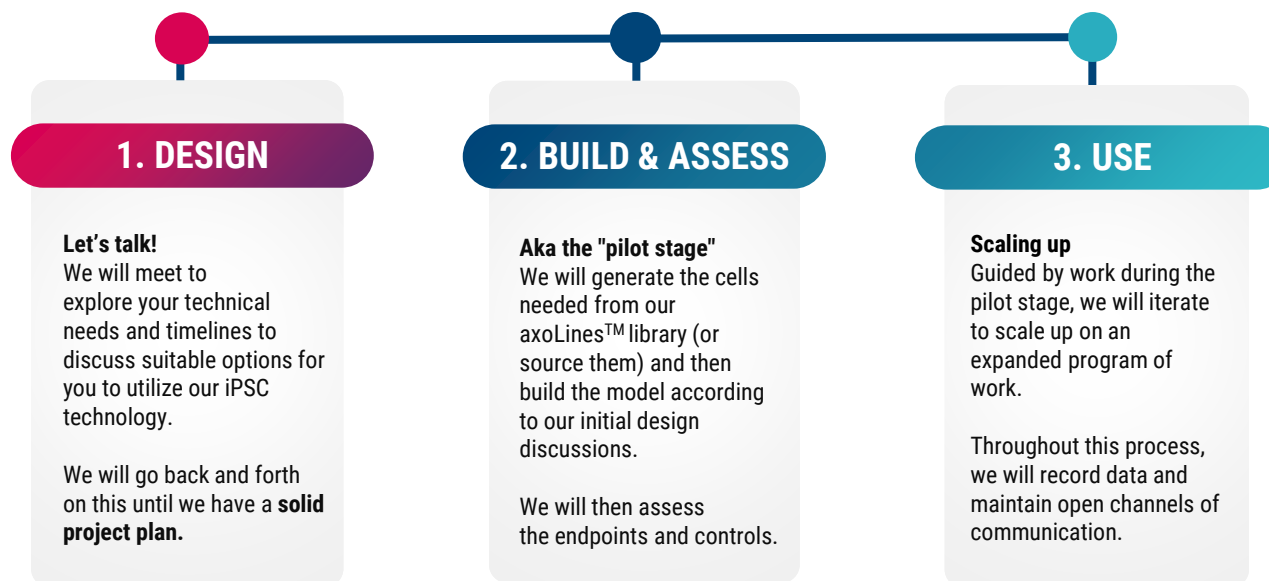
With axoModels, we partner with biopharma organizations who are looking to exploit **iPSC test model systems**. We work collaboratively to build, assess, and execute projects using [patient and healthy control-derived iPSCs](#) to offer a new and better platform to test novel therapeutics. If you'd like to discuss building a human-relevant model for neurodegenerative drug discovery, get in touch to discuss working with us on an axoModels project.

What are the components of a robust, human-relevant model?

1. High-quality, functional cells
2. An appropriate format (monoculture, co-culture, microfluidics)
3. Measurable assay endpoints

We work collaboratively to build model types to suit your experimental needs. We are also developing core neuroinflammatory and ALS models in-house to support drug development.

At Axol, we have a team of iPSC technical experts. If you'd like to access iPSC-based model systems to test your therapeutic, we can help. axoModels are created in partnership with our clients through a three-stage process:*



Our Location

Axol Bioscience operates globally but is based in the UK and US. Our R&D and manufacturing hubs are situated at sites of biotechnological excellence and innovation within the United Kingdom.

Research and Development Hub

B260 Meditrina, Babraham Research Campus, Cambridge, CB22 3AT, United Kingdom

Manufacturing Facility

Roslin Innovation Centre, Charnock Bradley Building, Easter Bush Campus, Easter Bush, EH25 9RG, United Kingdom

US Hub

147 Alhambra Circle, Suite 220, Coral Gables, FL 33134, United States

Contact Us

If you have any thoughts, ideas, questions, or concerns then please reach out via the channels below.

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Get in touch



Let's work together

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