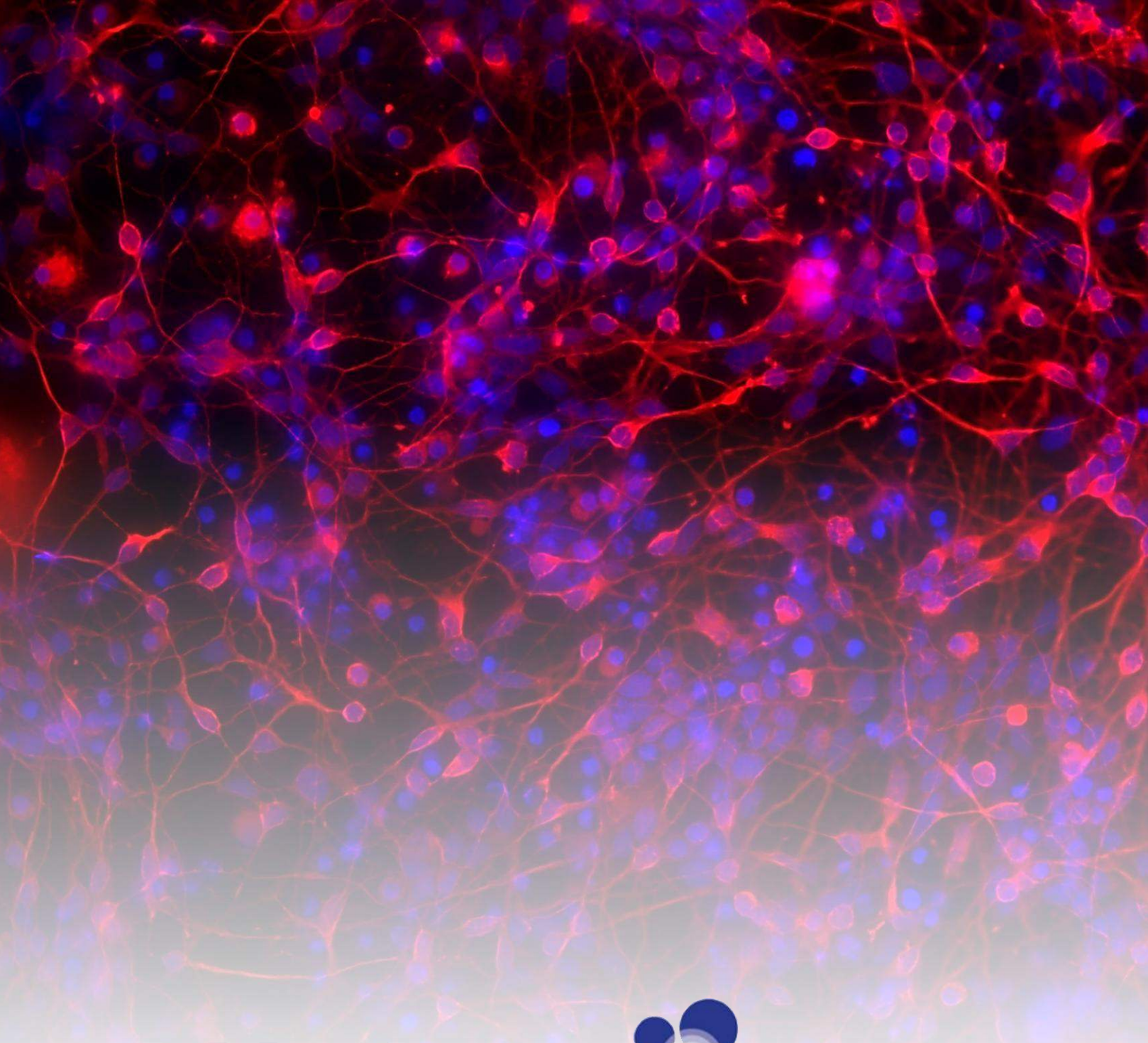


AXOL

RIGHT DRUG - RIGHT PATIENT - RIGHT TIME
STRATASTEM

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

Available for custom manufacturing and service projects

www.axolbio.com

www.stratastem.com

Axol Bioscience in partnership with **StrataStem** have released a collection of iPSC lines generated from primary materials donated from patients with sporadic Alzheimer's Disease (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.

- 20 iPSC lines including sAD and unaffected donor controls
- Full ethical and commercial consent
- Gender mixed, age relevant to late-onset AD
- Reporting on ApoE genotype, gender, age, diagnosis, medical and family history.

iPSC	ApoE Genotype	CSF Abeta	Family & Medical History (Y/N)	Age	Sex	Diagnosis
CENSOi004-E	E2/E3	N/T	N	40-50	M	not affected at time of donation
CENSO-SS-i005-A	E2/E3	N/T	Y	73	M	not affected at time of donation
CENSO-SS-i007-A	E2/E3	N/T	Y	77	M	sAD
CENSOi070-A	E3/E3	N/T	N	59	F	sAD
CENSOi058-A	E3/E3	N/T	N	45	F	not affected at time of donation
CENSO-SS-i004-A	E3/E3	N/T	Y	81	M	not affected at time of donation
CENSO-SS-i006-A	E3/E3	N/T	Y	70	M	not affected at time of donation
CENSO-SS-i009-A	E3/E3	N/T	Y	80	M	sAD
CENSO-SS-i010-A	E3/E3	N/T	Y	83	M	sAD
CENSO-SS-i013-A	E3/E3	N/T	Y	79	F	sAD
CENSOi074-A	E3/E4	N/T	N	60	M	sAD
CENSOi077-C	E3/E4	N/T	N	52	F	sAD
CENSO-SS-i001-A	E3/E4	high	Y	70	M	sAD
CENSO-SS-i002-A	E3/E4	high	Y	77	M	sAD
CENSO-SS-i003-A	E3/E4	high	Y	72	M	sAD
CENSO-SS-i011-A	E3/E4	N/T	Y	74	M	sAD
CENSO-SS-i013-A	E3/E4	N/T	Y	82	M	sAD
CENSO-SS-i008-A	E4/E4	N/T	Y	69	F	sAD
CENSO-SS-i012-A	E4/E4	N/T	Y	76	F	sAD

Early Access axoCells™	ApoE Genotype	NSCs code	Diagnosis	Age	Sex
CENSO-SS-i009-A	E3/E3	ax0109	sAD	80	M
CENSOi070-A	E3/E3	ax0170	sAD	59	F
CENSOi074-A	E3/E4	ax0174	sAD	60	M
CENSOi077-C	E3/E4	ax0177	sAD	52	F
CENSO-SS-i008-A	E4/E4	ax0108	sAD	69	F
CENSO-SS-i012-A	E4/E4	ax0110	sAD	76	F

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

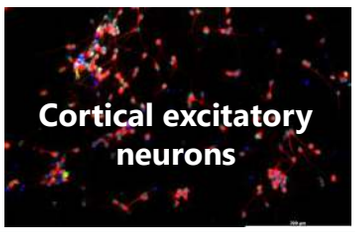
Exclusion criteria for patients:
- Patients or donors under 65 years of age
- Diagnosis of non-AD dementia or other neurodegenerative disease
- Any current or past severe psychiatric illness
- HIV, Hepatitis C or Hepatitis B positive viral screen

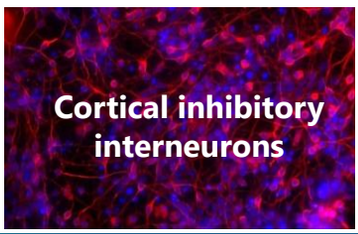
McKhann criteria section 4.1 was applied to all patients prior to samples being taken.

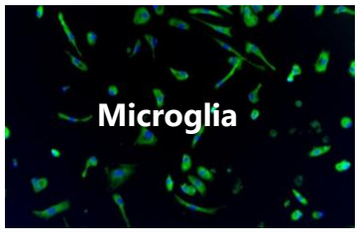
Unaffected donor lines:

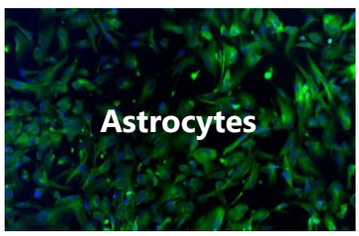
Inclusion criteria:
- Male or female donors aged 65 years or above, otherwise healthy

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









To learn more about the collection please contact **operations@axolbio.com**

Apolipoprotein E and Alzheimer's disease

The Apolipoprotein E (*APOE*) gene plays a critical role in the development and progression of Alzheimer's disease (AD), particularly through its *APOE* ε4 allele, which is the strongest genetic risk factor for late-onset AD. *APOE* encodes a protein responsible for lipid transport and metabolism in the brain, helping to clear amyloid-beta (Aβ) peptides, a key component of the plaques that accumulate in AD. Individuals carrying one or two copies of the *APOE* ε4 variant have an increased likelihood of developing AD compared to those with the more common *APOE* ε3 allele. This heightened risk is attributed to the inefficient clearance and increased aggregation of Aβ in the brains of ε4 carriers.

In addition to its role in amyloid pathology, *APOE* influences tau pathology, another hallmark of AD. Tau proteins normally stabilize microtubules in neurons, but in AD, they become hyperphosphorylated, leading to neurofibrillary tangles that contribute to neurodegeneration. Studies suggest that *APOE* ε4 exacerbates tau pathology, particularly in combination with amyloid deposition. This interaction accelerates neuronal damage and cognitive decline, emphasizing the multifaceted role of *APOE* in AD beyond amyloid processing alone.

The presence of *APOE* ε4 also affects neuroinflammation, another key contributor to AD progression. Microglia, the brain's resident immune cells, play a role in clearing amyloid deposits and maintaining neural homeostasis. However, in *APOE* ε4 carriers, microglial function appears to be impaired, leading to chronic inflammation and exacerbation of neuronal damage. This pro-inflammatory environment contributes to synaptic dysfunction and accelerates cognitive impairment, making inflammation a crucial pathway through which *APOE* ε4 increases AD risk.

Despite the strong association between *APOE* ε4 and AD, not all carriers develop the disease, suggesting that additional genetic, lifestyle, and environmental factors influence disease onset and progression. For example, physical activity, diet, and cognitive engagement may help mitigate the risks associated with *APOE* ε4. Furthermore, other *APOE* isoforms, such as *APOE* ε2, are associated with a reduced risk of AD, possibly due to enhanced clearance of Aβ and neuroprotective effects. This highlights the complex interplay between genetics and modifiable risk factors in AD development.

Given the significant role of *APOE* in AD, researchers are exploring therapeutic strategies targeting its effects. Potential interventions include reducing *APOE* ε4 expression, enhancing lipid metabolism to improve amyloid clearance, and modulating neuroinflammatory responses. Additionally, gene-editing techniques such as CRISPR are being investigated to modify *APOE* alleles and potentially reduce AD risk. As our understanding of *APOE*'s involvement in AD deepens, these approaches may offer new avenues for prevention and treatment, providing hope for those at risk of developing the disease.

APOE genotypes	Association with AD
APOE ε2	The rarest allele, associated with a **reduced risk** of AD. It may offer some neuroprotective effects, though carriers can still develop the disease, particularly if they have other risk factors.
APOE ε3	The most common allele, considered **neutral** in terms of AD risk. It does not significantly increase or decrease the likelihood of developing AD.
APOE ε4	The strongest genetic risk factor for AD. A single **ε4 copy** increases the risk **3-4 times**, while two copies (**ε4/ε4**) can raise the risk **8-12 times**. APOE4 is also linked to an **earlier onset** of symptoms and greater amyloid plaque accumulation in the brain.

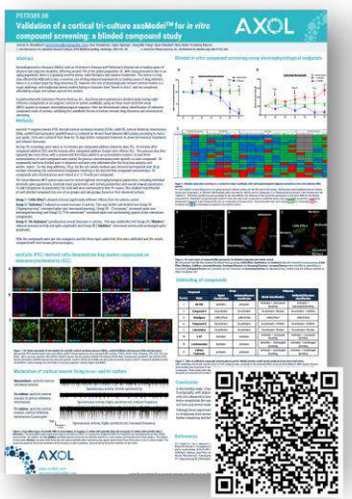
Induced pluripotent stem cell (iPSC) models are revolutionizing Alzheimer's disease (AD) research by providing a patient-specific, physiologically relevant platform to study disease mechanisms and test potential therapies. iPSCs are derived from adult cells, such as skin or blood cells, which are reprogrammed into a pluripotent state and then differentiated into brain-relevant cell types, including cortical excitatory neurons, inhibitory neurons, astrocytes, and microglia.

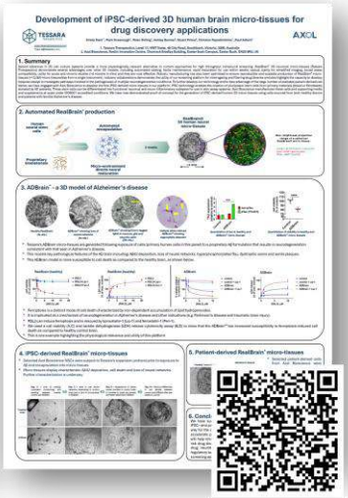
We also see the complexity of iPSC AD models on the rise with increasing use of multiple cell types (co-culture), multiple lines (patient stratification models) in a range of 2D and 3D formats.

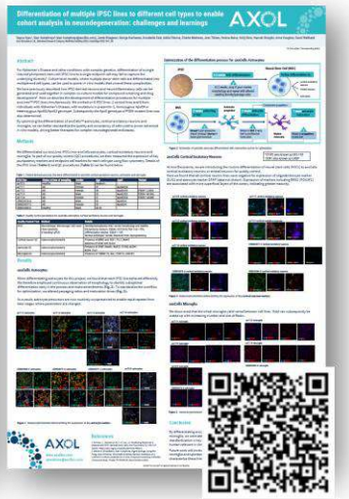
A gap has existed in the availability of high quality iPSCs from sporadic AD patients. The Axol Bioscience-Stratastem sporadic Alzheimer's Disease iPSC line collection provides the first opportunity to develop new models *in vitro* of complex sAD with a relevant genetic background to support drug discovery and research.

Resources

Recent posters:







- Validation of a cortical tri-culture axoModel™ for *in vitro* compound screening: a blinded compound study
- Development of iPSC-derived 3D human brain micro-tissues for drug discovery applications
- Differentiation of multiple iPSC lines to different cell types to enable cohort analysis in neurodegeneration

References and further reading:

1. Raulin AC, Doss SV, Trottier ZA, Ikezu TC, Bu G, Liu CC. ApoE in Alzheimer's disease: pathophysiology and therapeutic strategies. *Molecular Neurodegeneration* 2022; 17(1):72. <https://doi.org/10.1186/s13024-022-00574-4>** [\[link.springer.com\]](https://link.springer.com/article/10.1186/s13024-022-00574-4), [\[mayoclinic...erpure.com\]](https://mayoclinic.elsevierpure.com/en/publications/apoe-in-alzheimers-disease-pathophysiology-and-therapeutic-strate/)

2. Serrano-Pozo A, Das S, Hyman BT. APOE and Alzheimer's disease: advances in genetics, pathophysiology, and therapeutic approaches. *The Lancet Neurology* 2021; 20(1):68–80. <https://doi.org/10.1016/S1474-4422(21)00004-1>** [\[europepmc.org\]](https://europepmc.org/article/MED/33340485)

3. Jackson RJ, Hyman BT, Serrano-Pozo A. Multifaceted roles of APOE in Alzheimer disease. *Nature Reviews Neurology* 2024; 20(8):457–474. <https://doi.org/10.1038/s41582-024-00988-2>** [\[nature.com\]](https://www.nature.com/articles/s41582-024-00988-2.pdf), [\[europepmc.org\]](https://europepmc.org/article/MED/38906999)

Axol Bioscience

Axol Bioscience, acting with urgency to support drug discovery and research. With over a decade of hard-earned experience in the iPSC space, we are recognized as leaders in the manufacture of high quality, functional iPSC-derived cells and offer a range of outsourced services including disease model creation, compound screening, assay development, reprogramming and gene editing.

StrataStem

StrataStem identifies, collects, and processes tissues from patients with neurological disease. Proprietary patient and antecedent clinical history are obtained for each patient, and they are genotyped for disease-associated variants. Our disease models are suitable for drug screening, target identification, target validation, toxicity screening, patient stratification, and deciphering disease mechanisms.

To learn more about the collection please contact **operations@axolbio.com**

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