Bridging Clinical and Molecular Insights in ALS: The Target ALS PMTC & the Power of Paired Pre- and Postmortem

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Abstract

Background. The Target ALS Postmortem Core (PMTC) and Target ALS Global Natural History Study (GNHS) are complementary leading research studies designed to accelerate ALS therapeutic development. The studies utilize high-quality, extensively annotated biofluids collected during life and post-mortem tissues, from individuals with ALS, and non-neurological controls. Longitudinally collected blood, CSF, and urine samples paired with postmortem brain and spinal cord tissue are made available to researchers, along with neuropathological evaluation through the TALS Data Engine. This approach enables researchers to correlate molecular changes identified in postmortem tissues with biomarkers measured throughout disease progression, providing a critical framework for biomarker validation and disease mechanism discovery.

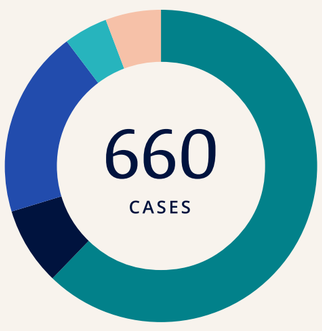
Objective. By providing researchers with access to paired biospecimens and comprehensive clinical and molecular data, the TALS PMTC and GNHS represent the most comprehensive resource of their kind, supporting both academic and industry investigators to accelerate the translation of scientific discoveries into future therapies for ALS.

Methods. Biofluid and tissue collections, sample storage, and disbursement for dual enrollment are performed across five different sites. Site inventories and the corresponding metadata are linked by a secure, cloud based software. Biofluids, frozen tissue, FFPE slides, and associated de-identified data are provided to academic researchers without intellectual property requirements and free of charge, and to industry researchers on a cost recovery basis. Multi-omic datasets are generated across tissue regions, blood, and CSF from every participant. PacBio HiFi sequencing is generated on all C9orf72 cases and other familial forms of ALS.

Results. The PMTC repository currently includes 660 cases and GNHS has enrolled nearly 400 participants. Together, these complementary programs have established a unique longitudinal cohort that links clinical, biomarker, and molecular data collected during life with postmortem tissue donation. To date, 53 GNHS or ALL ALS ASSESS participants have pre-enrolled or expressed interest in participating in the PMTC.

Conclusion. We've performed nearly 700 tissue procurements and banked 100,000+ biosamples from our two studies. We've provided biosamples to over 500 academic and industry labs worldwide, facilitating hundreds of research projects. We're positioned as a global leader in enabling translational science, reflecting our commitment to advancing the field through collaboration and innovation.

Postmortem core tissue collection



660 postmortem cases available

TARGET ALS POSTMORTEM CORE (PMTC)

ALS	**410**	62%
ALS-FTLD	**53**	8%
Healthy controls	**128**	19%
FTLD (all subtypes)	**30**	5%
Pending neuropathological report	**39**	6%

Available to academic and industry researchers worldwide

Global Natural History Study collection



392 participants enrolled

TARGET ALS GLOBAL NATURAL HISTORY STUDY (GNHS)

ALS participants	**223**	57%
Healthy controls	**169**	43%

55,000+
biofluid vials collected

7,500+
biofluid vials distributed

Dual enrollment case collection

PRE-CONSENTED OR EXPRESSED INTEREST

53

participants with biofluid samples already collected who have enrolled in or are expected to enroll in PMTC

→

DUAL ENROLLED

3

participants have made invaluable contributions to both the GNHS and PMTC collections, providing researchers matched samples from each participant across both collections

Participant perspective

targetals.org/agri

Not only will my CSF, blood, and urine samples be available for researchers, but upon my death, so will my brain, muscle, and spinal cord tissues. ***I truly am ALL IN on finding a cure so that no future generations will have to experience the loss of abilities, the loss of life plans, the loss of life that I am experiencing.*** *The best gift I can give to my children, grandchildren, nieces, nephews, etc, is to be involved in research.*

- Laura Woods, Global Natural History Study and Brain and Spinal Cord Donation participant

Global Natural History Study to Postmortem Tissue Core

One participant, followed in life and after death

Target ALS Global Natural History Study (GNHS) samples paired with the Postmortem Core (PMTC) samples

During life: GNHS

Clinic visits with biofluid collection, plus optional at-home assessments

CLINIC VISITS

ALS
5 visits
0 mo · 4 mo · 8 mo · 12 mo · 16 mo

Controls
2 visits (HC)
0 mo · 12 mo

BIOFLUIDS COLLECTED AT EVERY CLINIC VISIT

CSF · Plasma · Serum · Urine

MEASURES AT EACH VISIT

- ALSFRS-R/Harmonized
- Vital capacity
- Neurologic exam
- ALS-CBS/ECAS
- Medications
- Family history
- Environmental questionnaire*

*Epidemiological and environmental questionnaire added in 2024 (118 completed to date); updated in 2026 for more quantitative data capture

OPTIONAL AT-HOME ASSESSMENTS, EVERY TWO WEEKS

Aural Analytics
Speech and motor function
100 ALS, 50 HC
COMPLETED

modality.ai
Speech and motor function
100 ALS, 50 HC
IN PROGRESS

ZEPHYRx
Respiratory measures
100 ALS and HC
COMPLETED

→ TISSUE DONATION

After death: PMTC

Brain and spinal cord tissue banked

~45
brain regions collected: frontal, parietal, temporal, occipital

Spinal cord: all three regions
Cervical, thoracic, lumbar

Frozen tissue · FFPE slides

Short fixation (<24 hours) FFPE blocks and TMAs are available upon request from certain cases.

TALS DATA ENGINE PAIRS SAMPLES WITH CLINICAL AND MULTIMODAL DATA

Bulk RNA-Seq · Single-Nucleus RNA-Seq · Spatial RNA-Seq · Short-Read WGS · Long-Read WGS · pTDP-43-stained, digitized images · Semiquantitative pTDP-43

Explore the Data Engine

Postmortem Tissue Core regions collected

Frozen regions (45 regions · varies by case)		
Lateral Motor Cortex	Middle Motor Cortex	Motor Root
Frontal Cortex (BA9)	Occipital Cortex	Temporal Cortex
Parietal Cortex	Sensory Cortex	Midbrain
BA6	BA8	Broca's area
Globus Pallidus	Lateral Ventricular Zone	Corpus Callosum
Amygdala	Skin	Subcutaneous Fat
Liver	Paraspinal Muscle	Diaphragm Muscle
Quadricep Muscle	Bicep Muscle	Psoas Muscle
Deltoid Muscle	Thalamus	Hypothalamus
Cingulate Gyrus	Striatum	Pineal Gland
Basal Ganglia	PM CSF	Caudate Putamen
Cerebellum	Pons	Medulla
Cervical Spinal Cord	Thoracic Spinal Cord	Lumbosacral Spinal Cord
Hippocampus	postCG	Periventricular Zone
R/L Whole Eye	Dura	Pituitary Gland

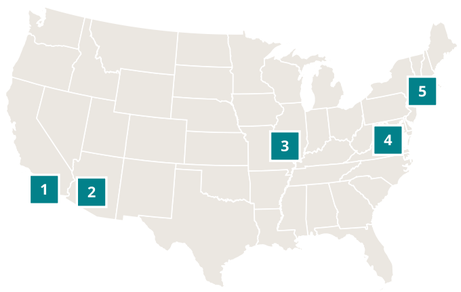
Paraffin regions (28 regions · varies by case)	
Lateral Motor Cortex	Medial Motor Cortex
Middle Motor Cortex	Frontal Cortex (BA9)
Occipital Cortex	Temporal Cortex
Parietal Cortex	Sensory Cortex
Midbrain	BA6
BA8	Cerebellum
Pons	Medulla
Deltoid Muscle	Thalamus
Basal Ganglia	Globus Pallidus
Lateral Ventricular Zone	Periventricular Zone
Cervical Spinal Cord	Thoracic Spinal Cord
Lumbosacral Spinal Cord	Hippocampus
Paraspinal Muscle	Bicep Muscle
Quadricep Muscle	Psoas Muscle

Frozen and paraffin regions collected. Across the 660 cases we have collected, we offer investigators a wide array of tissue regions. For fresh frozen specimens, we collect tissue from over 40 regions, providing comprehensive coverage for diverse research needs. Additionally, nearly 30 distinct regions are collected for paraffin embedding, allowing for the creation of slides to support various histological analyses. This extensive collection serves as a valuable resource for advancing research efforts.

Power of paired samples for ALS research

- **Impact on research community:** 378 academic and industry labs worldwide have received Target ALS tissue, and we are currently averaging about one tissue request per week. These samples enable high quality translational research for disease biomarkers and therapeutics.
- **A continuous line of discovery:** Pairing biofluids and clinical measures collected during life (blood, urine, CSF, motor, speech, respiratory, and cognitive data over roughly 18 months) with postmortem brain and spinal cord tissue lets researchers trace ALS across its whole arc, at depths no scan, blood test, or exam alone can reach.
- **Tracing when and why ALS changes occur:** When tissue is linked to data gathered during life, researchers can pinpoint when a biological change began, not just that it happened. Because autopsy remains the gold standard for classifying ALS, donated tissue also validates findings from biofluid samples. Together, these insights may help explain why ALS differs so widely from person to person and reveal potential targets for future therapies.
- **Better biomarkers for earlier detection:** Connecting molecular changes seen in postmortem tissue with blood and CSF samples collected over time lets researchers evaluate potential biomarkers, which could contribute to future tests that identify ALS earlier.
- Tissue samples and data sets upon request: www.targetals.org/resource/human-postmortem-tissue-core/

Dual enrollment sites



1. **UC San Diego** — San Diego, CA
2. **Barrow Neurological Institute** — Phoenix, AZ
3. **Washington University in St. Louis** — St. Louis, MO
4. **Georgetown University** — Washington, DC
5. **Columbia University** — New York, NY

Geographic locations. Target ALS has 22 sites globally across our Postmortem and Global Natural History studies. Five of these are dual-enrollment sites, distributed across the United States, that allow participants to enroll in both the GNHS and Postmortem studies at the same location.

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