GLOBAL NATURAL HISTORY STUDY (GNHS)

Expanding representation of Hispanic and Latin American populations in longitudinal ALS research

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Background

Hispanic and Latin American populations remain substantially underrepresented in ALS natural history studies, biorepositories, and biomarker discovery efforts, limiting understanding of disease heterogeneity across genetically diverse populations. The genetic heterogeneity of northern South American populations is especially relevant, as their long-standing and continuous admixture may favor the emergence of phenotypes with oligogenic architecture.

The Global Natural History Study (GNHS), originally established in 2021 as a six-site U.S. biomarker study, has expanded into an international longitudinal research platform designed to increase representation while generating standardized clinical, biospecimen, and genomic resources. We evaluated the impact of this expansion on enrollment, longitudinal participation, and biospecimen collection among Hispanic and Latin American participants.

Methods

GNHS is an ongoing prospective longitudinal study of individuals with ALS and healthy controls. Participants undergo standardized clinical, cognitive, respiratory, and genetic assessments and contribute blood, urine, and cerebrospinal fluid over approximately 18 months. Demographic characteristics, longitudinal participation, retention, and biospecimen collection were evaluated among participants self-identifying as Hispanic, Latino, or of Latin American ancestry, including those enrolled at U.S., Puerto Rican, and Colombian sites.

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

CLINIC VISITS — 0 · 4 · 8 · 12 · 16 mo

- **ALS** — 5 visits
- **Controls** — 2 visits (HC)
- **At home speech and motor function** — Optional, every two weeks

BIOFLUIDS AT EVERY CLINIC VISIT: CSF · Plasma · Serum · Urine

COLLECTED CLINICAL DATA

- ALSFRS-R/Harmonized
- Vital signs
- ALS-CBS/ECAS
- Family and medical history
- Vital capacity
- Neurologic exam
- Concomitant medications
- Epidemiological and environmental questionnaire

Aural Analytics	Speech	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

PARTICIPATING SITES



United States	Puerto Rico
Colombia	Israel
South Korea	Malaysia
India (2 sites)	Canada

Sites with Hispanic/Latino participants enrolled

Other active sites · Onboarding

Representation in Action: Hispanic/Latino Impact

- **80** Hispanic/Latino participants
- **374** completed study visits
- **45,823** individual aliquots contributed

ALS Global Research Initiative
POWERED BY TARGET ALS

Join the study ›
Scan to learn about participating in GNHS.

Únase al estudio ›
Escanee para saber cómo participar en el GNHS.

targetals.org/agri

Results

As of October 2026, GNHS has enrolled 398 participants across our 16 sites. Global study expansion increased the overall cohort diversity from approximately 8% to 34%, with Hispanic participants representing 23.4% of the ALS cohort.

Genetic results by ethnicity: participants with a genetic result

Hispanic/Latino participants in our cohort exhibit a higher prevalence of uncommon ALS-associated genetic variants compared with non-Hispanic/Latino participants.



Hispanic/ Latino
N = 31



Not Hispanic/ Latino
N = 154

	HISPANIC	NOT HISPANIC
SOD1	3 (9.7%)	35 (22.7%)
C9orf72	1 (3.2%)	24 (15.6%)
TARDBP	1 (3.2%)	0 (0.0%)
FUS	1 (3.2%)	1 (0.6%)
Other genes only	2 (6.5%)	8 (5.2%)
No positive result reported	23 (74.2%)	86 (55.8%)

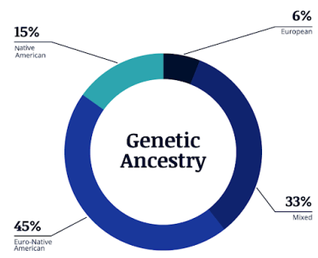
OTHER ALS GENES, HISPANIC

BCHE · *HFE* · *SPG11* · *SYNE1* · *VRK1* · *TAF15* VUS · *VRK1* VUS

OTHER ALS GENES, NOT HISPANIC

ANXA11 · *ATXN2* · *CHCHD10* · *GAA* · *MTHFR* · *NEB* · *NEK1* · *NEFH* · *TBK1* ×2 · *UBQLN2*

Genetic ancestry for Hispanic participants



MIXED ANCESTRY: TOP-THREE COMPONENTS

Ordered top three	n	%
Native American > European > East Asian	5	45.5%
Native American > European > African	2	18.2%
Native American > European > South Asian	1	9.1%
European > Native American > African	1	9.1%
European > Native American > South Asian	1	9.1%
European > Native American > East Asian	1	9.1%
Total	**11**	**100%**

Untested or no result: 14 Hispanic/Latino, 78 not Hispanic/Latino.

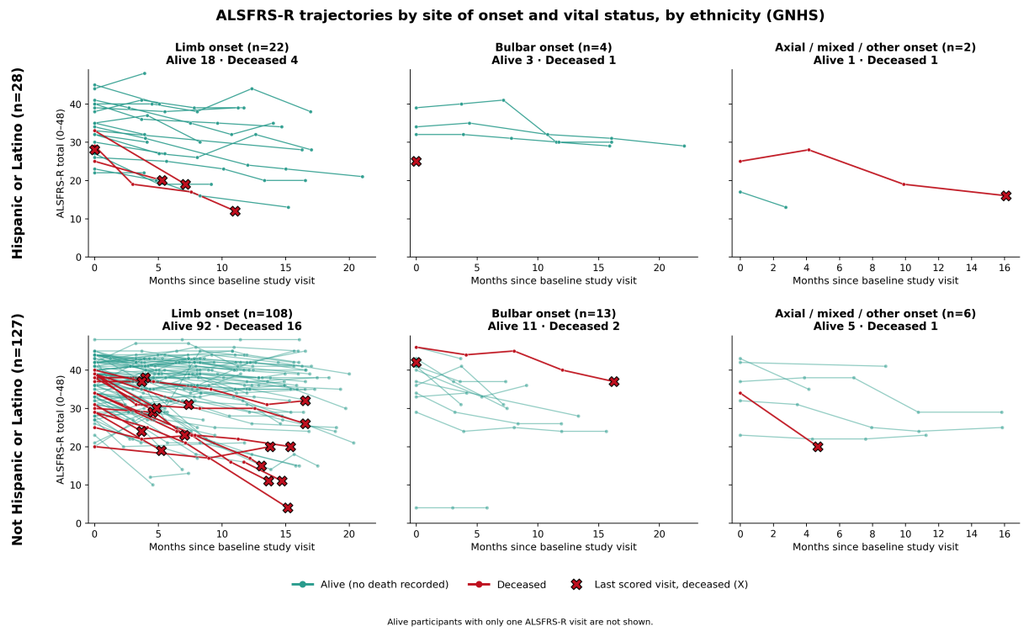
Mutation results include asymptomatic mutation carriers.

3 Hispanic/Latino *SOD1* participants lack tofersen access (unavailable in Colombia).

No Hispanic/Latino *SOD1* participants are from Puerto Rico.

ALSFRS-R trajectories by ethnicity in the GNHS cohort

Hispanic or Latino participants entered the study with lower ALSFRS-R scores than non-Hispanic or Latino participants (mean 30.7 vs 35.5), but declined at a similar rate during follow-up (mean ~0.7 vs ~0.6 points/month)



Alive participants with only one ALSFRS-R visit are not shown.

Conclusion

Strategic global expansion has increased Hispanic/Latino representation in the GNHS, creating a diverse longitudinal cohort with standardized clinical, biospecimen, and genomic data. Preliminary findings highlight variability in ALS progression, reinforcing the importance of studying disease heterogeneity. Ongoing long-read sequencing, NfL, and proteomics analyses will support the identification of novel biomarkers and biological factors associated with disease progression, advancing more inclusive precision medicine and future clinical trial design.