

PREVENT ALL ALS: Design for a national ALS gene carrier natural history study

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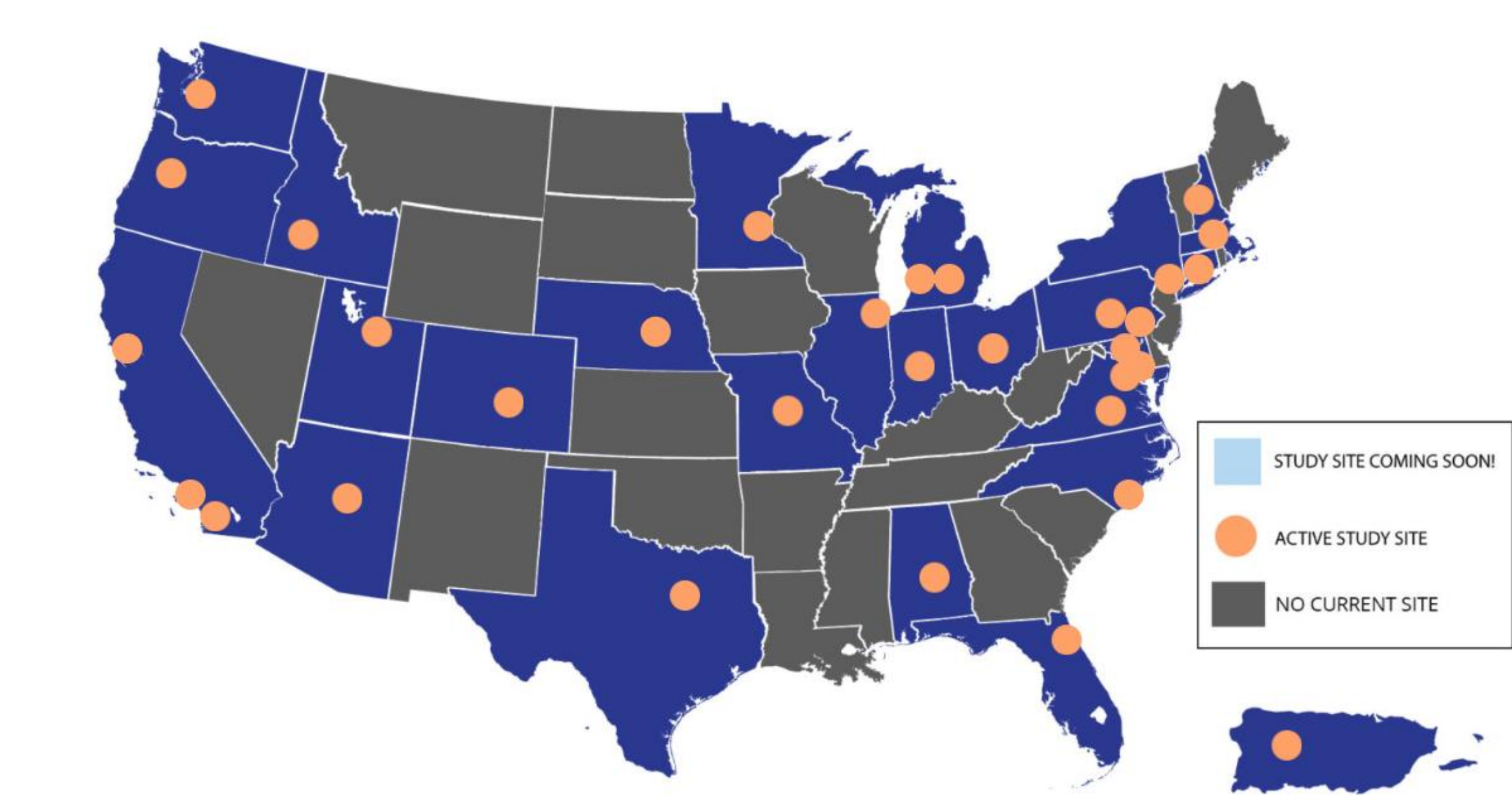
Background

- 10-15% of ALS is associated with Mendelian-inherited gene variants.
- Biomarkers changes are detectable prior to ALS/FTD onset and may provide a window to initiate preventative therapy.
- Research into pre-symptomatic ALS/FTD has been limited by small sample sizes and a lack of open-access longitudinal samples and clinical data from persons at genetic risk for ALS.

Hypothesis

- PREVENT ALL ALS (NCT06581861) will obtain longitudinal biofluid samples and natural history data from the largest cohort of individuals carrying ALS causative gene variants.
- Launched in 2024 as part of the ALL ALS Consortium at 32 study sites across the United States
- Samples and data will be made broadly available to the ALS research community through the AMP-ALS Knowledge Portal (ampals.synapse.org)

Figure 1: Prevent ALL ALS Study Sites



Methodology

Study Population: Asymptomatic individuals who carry or are at-risk for carrying an ALS disease causative gene variant

Study Design: Observational natural history study with at least 3 years of follow up

- In Person Visits: Every 12 months
- Remote Follow Up Visits: Every 4 months

Key Inclusion Criteria:

- Age 18+
- Genetically at risk for ALS based on any of the following:
 - Known carrier of any ALS causative gene variant
 - First degree relative of a known or obligate carrier of any ALS causative gene variant
 - First degree relative with ALS or FTD and a “compelling family history” of ALS/FTD

Key Exclusion Criteria:

- Neurologic signs or symptoms concerning for ALS/FTD

Data and Sample Storage:

- Biofluid samples from all sites are stored at BioSEND biorepository at Indiana University
- Clinical Data stored in NeuroBANK™ and will be sent to AMP-ALS knowledge portal

Table 1: PREVENT ALL ALS Study Assessments

Visit Type	In-Person Visits	Remote Follow Up Visits
	Every 12 months	Every 4 months
Medical History, Family History, Medications	X	
Height, Weight	X	
Neurologic examination	X	
Dynamometry (HHD, Grip)	X	
Vital Capacity	X	
ECAS	X	
Multidomain Impairment Rating Scale (MIR)	X	
Blood collection (plasma, serum, whole blood)	X	X
Blood collection (RNA, PBMCs)	Screening visit only	
CSF Collection (Optional)	X	
EMG/NCS (Optional, available at limited sites)	X	
ALS Symptom Questionnaire	X	X
Speech recordings		X
ePRO questionnaires (Environmental Exposures)		X

Genetic Testing Substudy

- Optional, confidential genetic testing is offered following remote consultation with study genetic counselors
- Genetic Psychosocial Risk Instrument (GPRI) is used to screen for risks of psychological harm following testing

Results

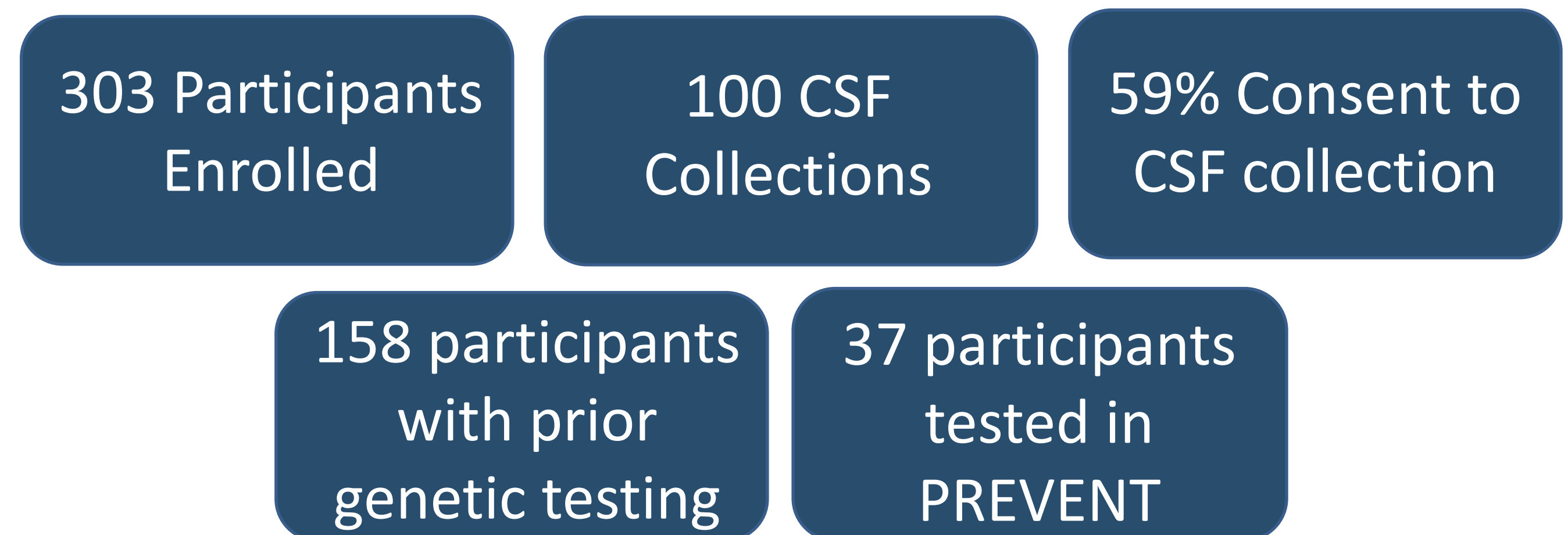
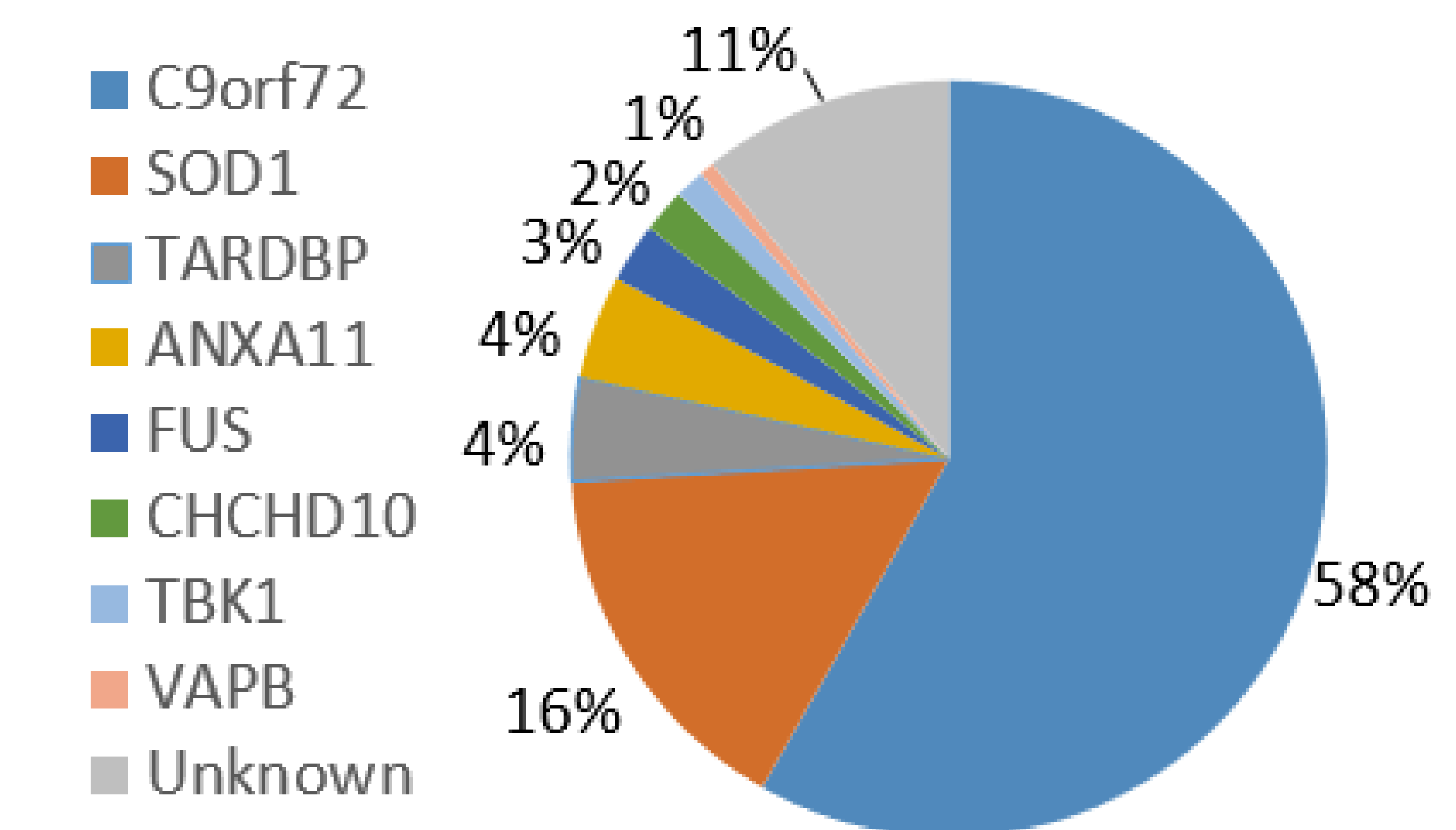


Figure 2: Genotype Frequency in PREVENT



Conclusion

- Samples and clinical data from PREVENT will be a valuable community resource to evaluate pre-symptomatic ALS and FTD disease states

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