

2019 CJD Foundation Family Conference

July 12-14, 2019

*“Assessing long-term stability of cerebrospinal fluid PrP levels
in genetic prion disease mutation carriers”*

Preparing for Prevention & Treatment

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Sonia Vallabh, PhD and Eric Minikel, PhD

Broad Institute of MIT and Harvard

Prion Diseases: *Fast Facts*

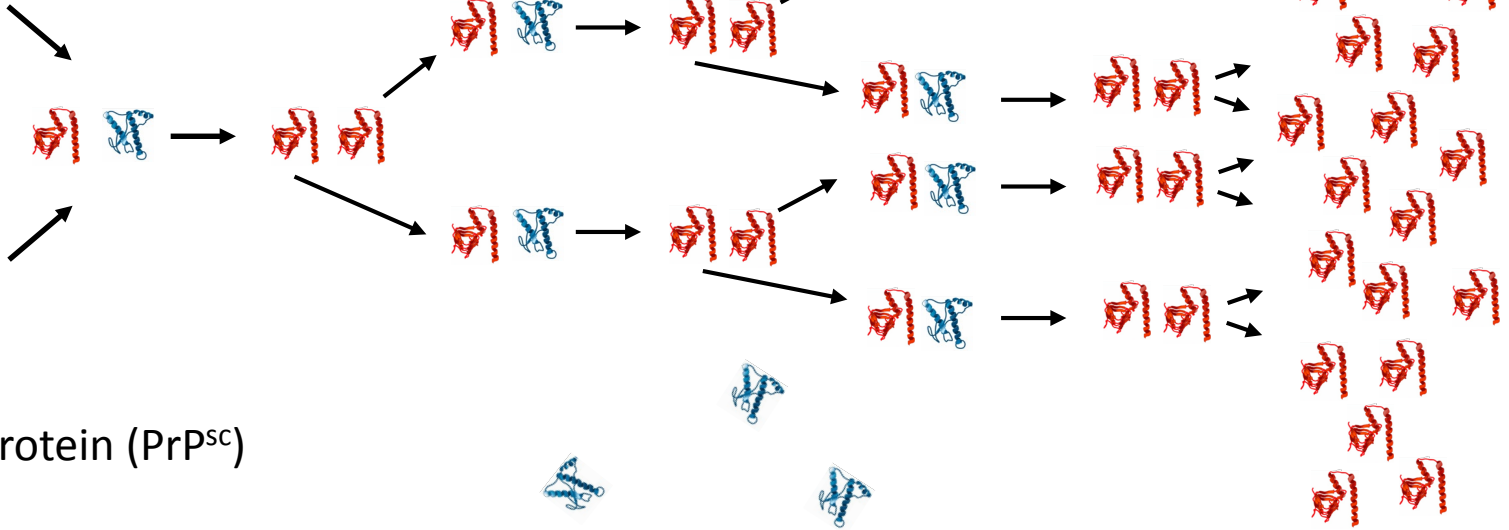
- **Creutzfeldt Jakob Disease:** 1 case/M/year, 85-95% sporadic, 5-15% autosomal dominant familial, <1% iatrogenic, average onset 57-62 (20->80s), rapidly progressive cognitive decline/ dementia, myoclonus +/- mood & neuropsychiatric, sleep, extrapyramidal, cerebellar, survival < 1year
 - **Gerstmann Straussler Scheinker Disease:** 1-10 cases/100M/year, autosomal dominant PRNP mutation, mid-life onset of cerebellar dysfunction → motor deterioration & variable dementia, survival 5 years
 - **Fatal Familial Insomnia:** Exceptionally rare, autosomal dominant PRNP in ~50 families worldwide, variable adult onset (20-73), malignant insomnia → autonomic instability, dementia/delirium, neuropsychiatric symptoms, survival 7-18 months
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Prion Disease

Normal Prion Protein (PrP^C)

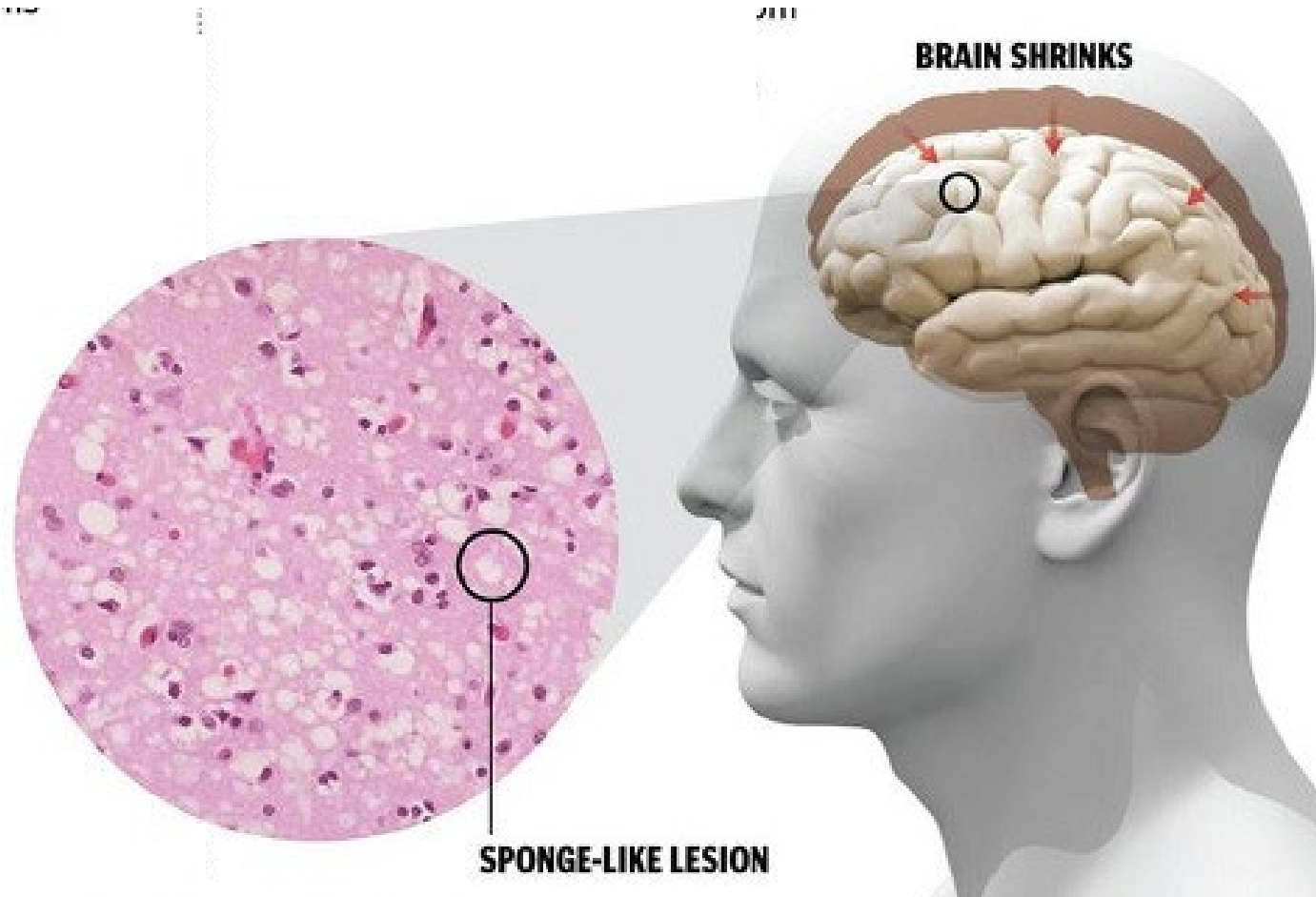


CHAIN REACTION OF MISFOLDING & SPREAD

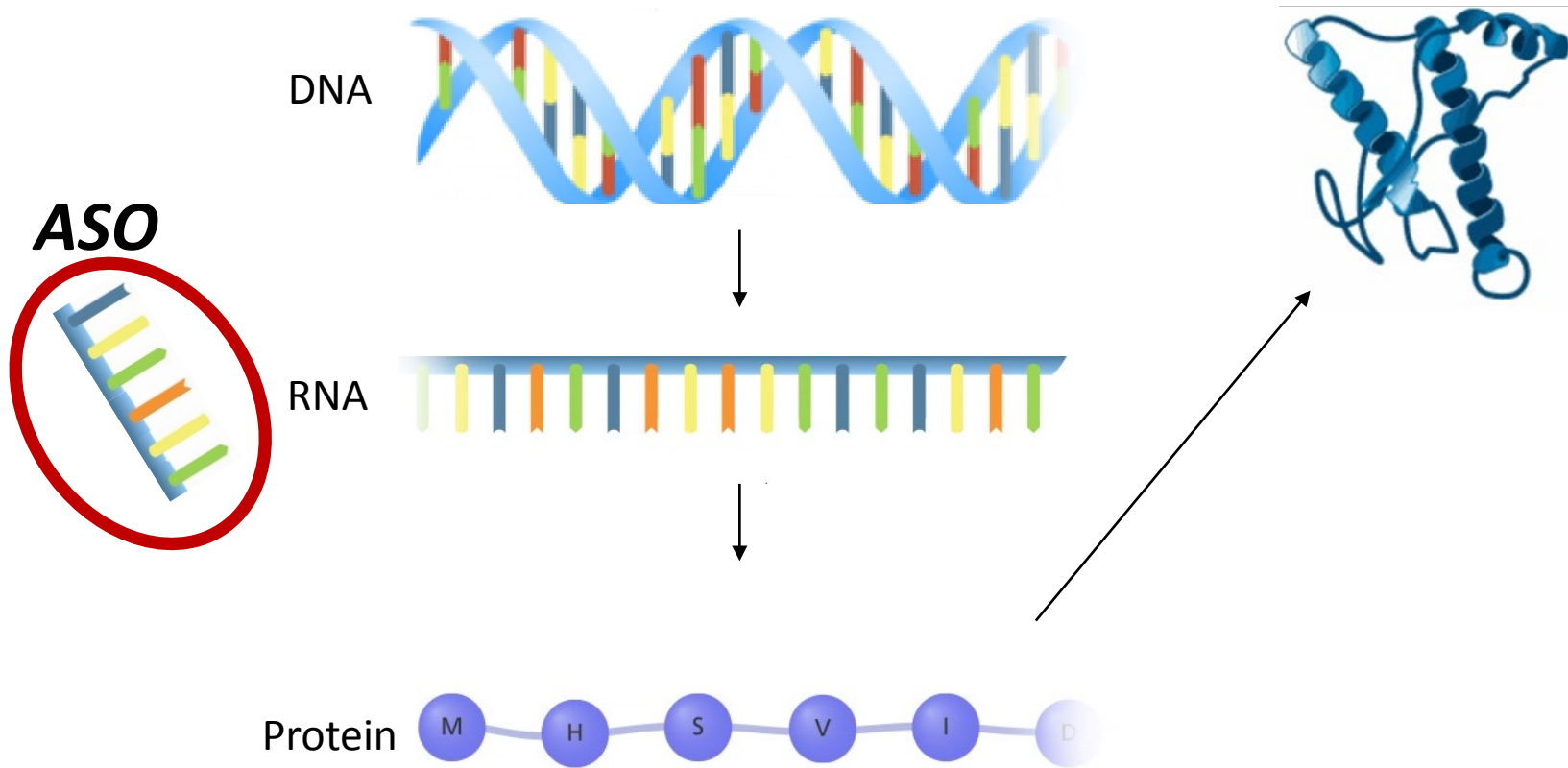


Misfolded Prion Protein (PrP^{Sc})

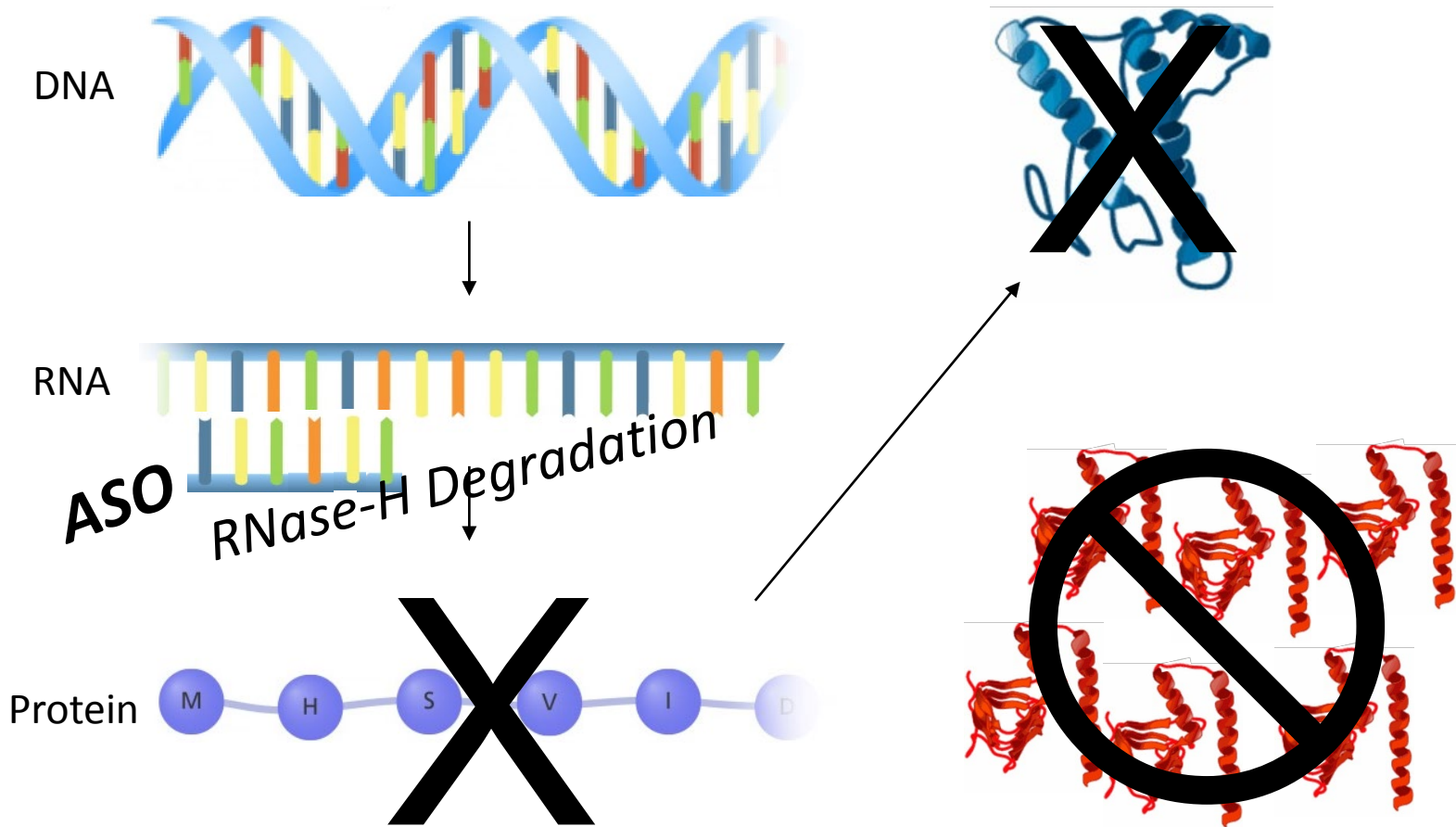
Spongiform Encephalopathy



Rationale for ASO Prevention (& Therapy) in Prion Disease



Rationale for ASO Prevention (& Therapy) in Prion Disease



How will we know if an ASO is working?

Clinical Outcomes

Disease Onset
Disease Progression
Survival

Biomarkers

Neuropsychology
Neurophysiology
Neuroimaging
Biofluids (Blood, CSF)



*“Assessing long-term stability of cerebrospinal fluid PrP^C levels
in genetic prion disease mutation carriers”*

Study Participant Characteristics

Whole Sample with at least Baseline Assessment

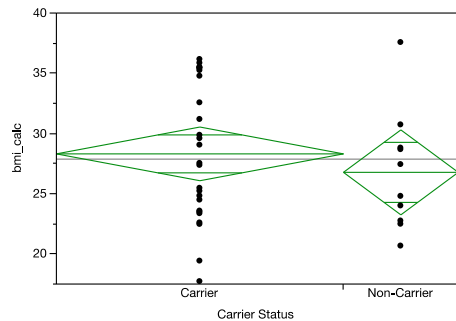
n	43
Age	44.3 (SD=14.1, Range 22 – 75)
Sex	28 Female, 15 Male
Education	15.6 (SD=2.5, Range 12 – 20)

	<u>Carriers</u>	<u>Non-Carriers</u>	<u>Pending</u>
N	27	11	5
Age	43.6 (14.9)	45.1 (13.6)	46.1 (13.6)
Sex	17F/10M	7F/4M	4F/1M
Education	15.4 (2.3)	15.7 (3.1)	16.2 (2.0)
Phenotype:	CJD 45%		
	FFI 30%		
	GSS 25%		

Clinical Characteristics

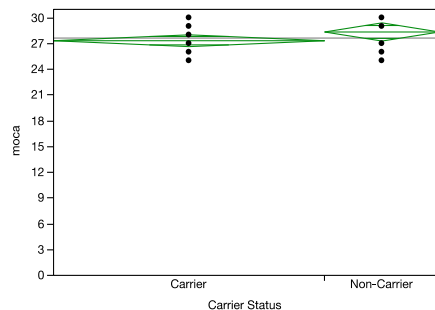
General Health

Body Mass Index



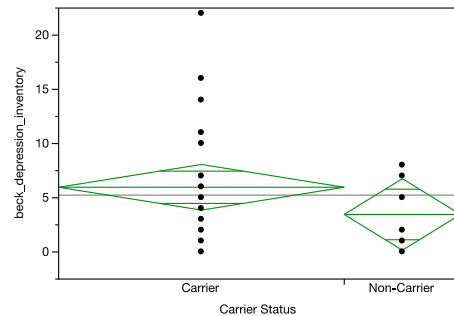
Cognitive

Montreal Cognitive Assessment

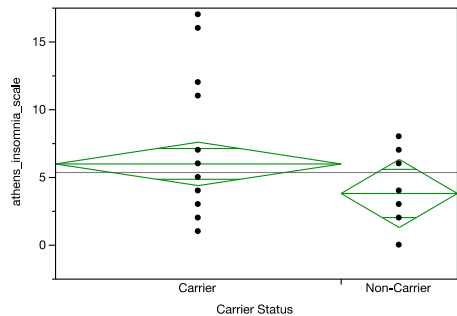


Neuropsychiatric

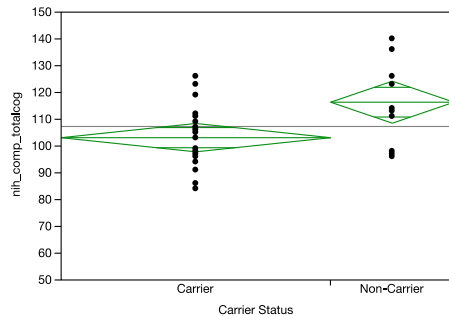
Beck Depression Inventory



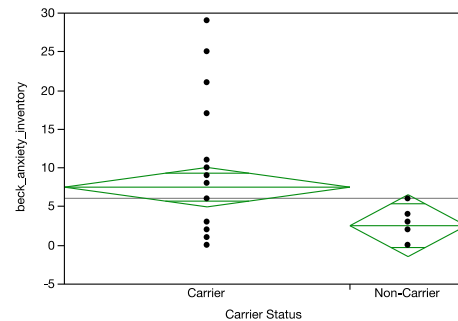
Athens Sleep



NIH Toolbox Composite



Beck Anxiety Inventory

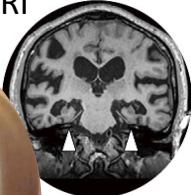


Biomarkers

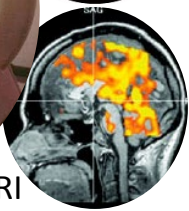
MRI



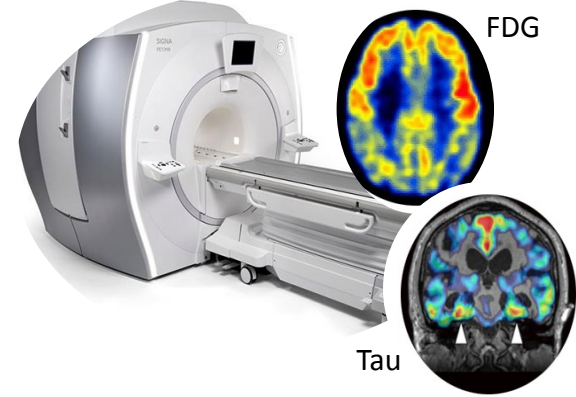
vMRI



fMRI



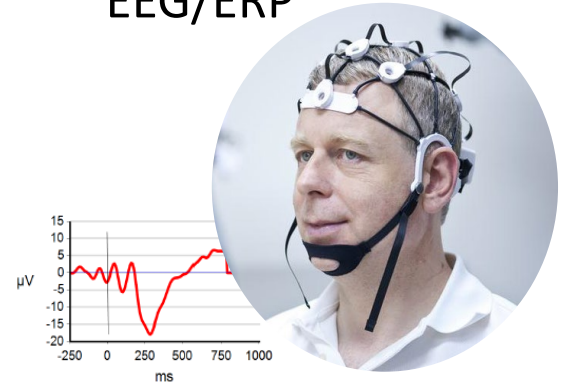
PET-MRI



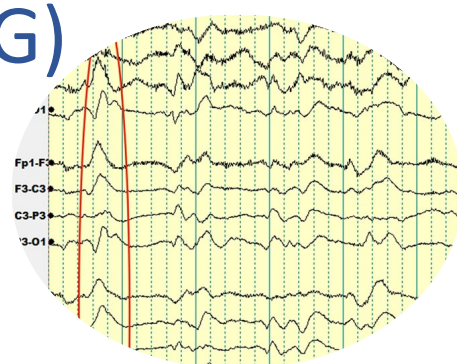
Blood



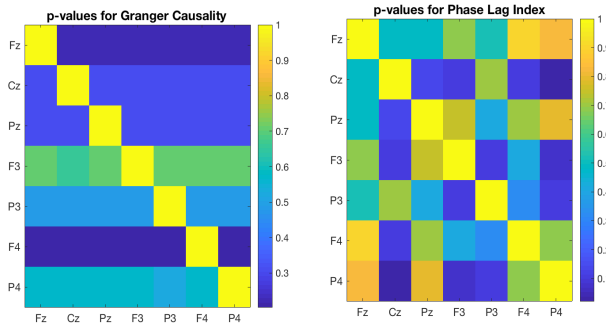
EEG/ERP



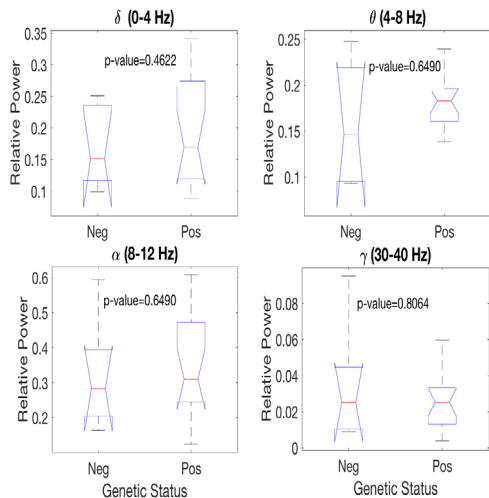
Electroencephalography (EEG)



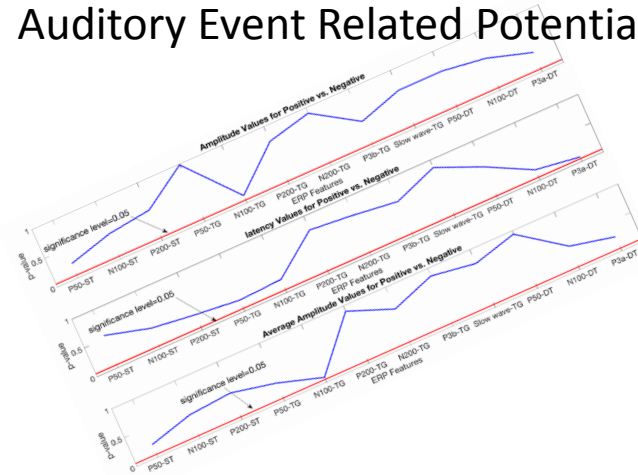
EEG Synchrony



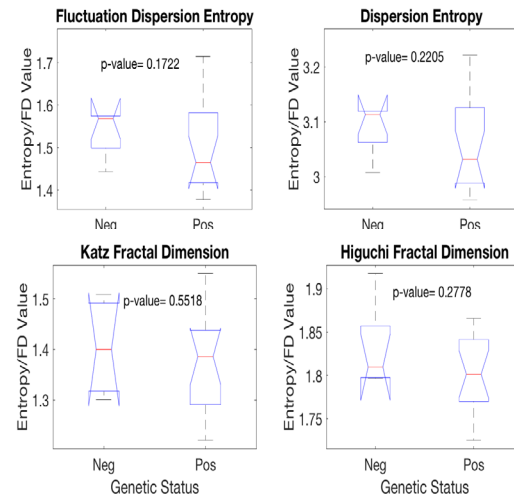
Power Spectral Density



Auditory Event Related Potential



EEG Complexity

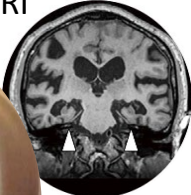


Biomarkers

MRI



vMRI

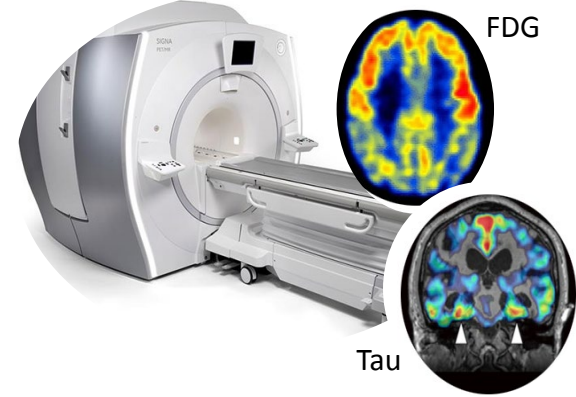


fMRI



Cerebrospinal Fluid (CSF)

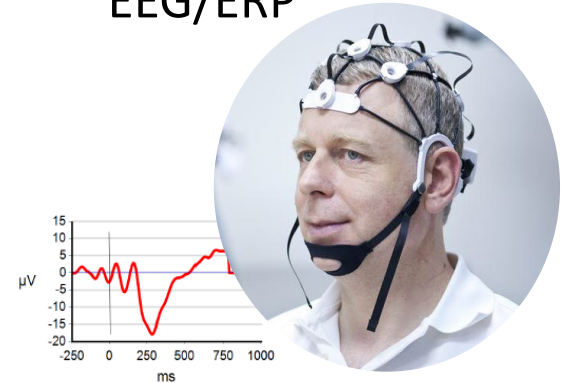
PET-MRI



Blood



EEG/ERP

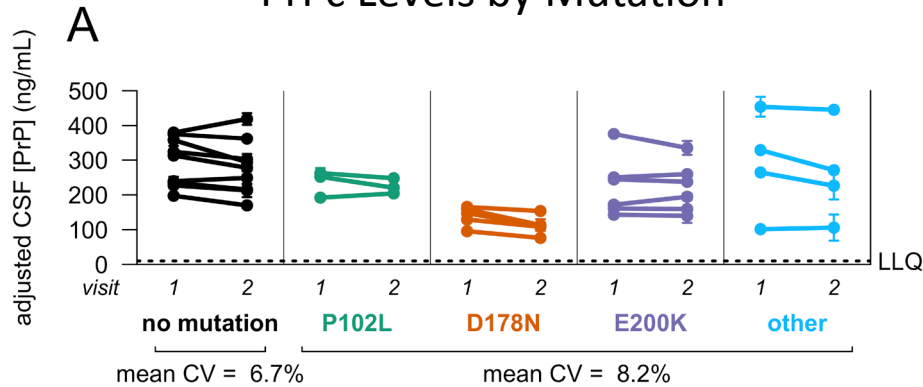


Spinal Fluid (CSF) Testing

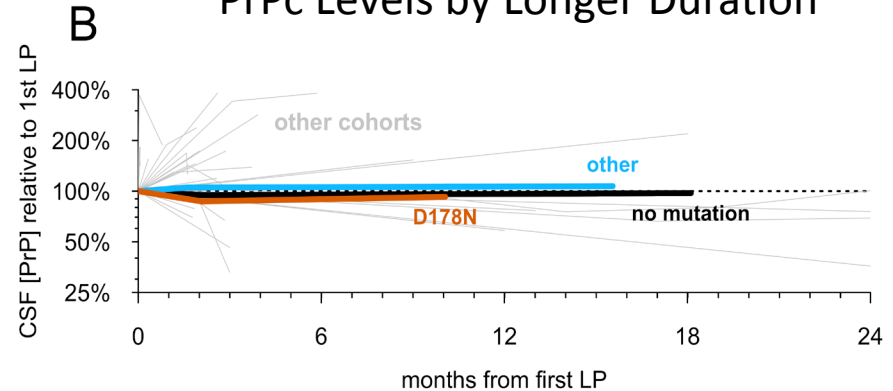
Biotemporal Stability of Prion Protein (PrPc)
Levels in Carriers and Non-Carriers Over 8 Weeks



PrPc Levels by Mutation



PrPc Levels by Longer Duration

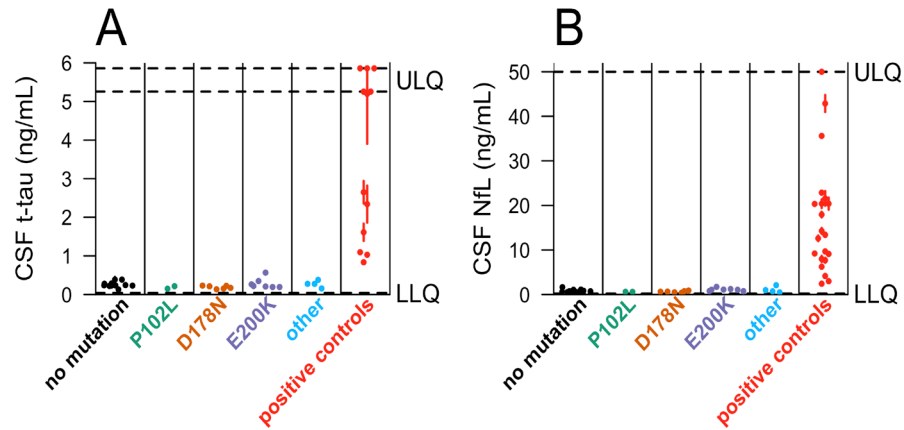


Spinal Fluid (CSF) Testing

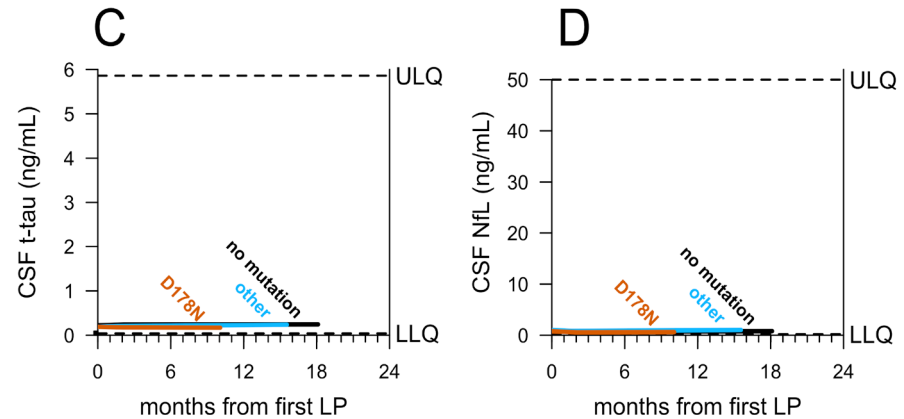
Biomarkers of Neurodegeneration
Tau & Neurofilament-Light



Tau and NfL by Mutation



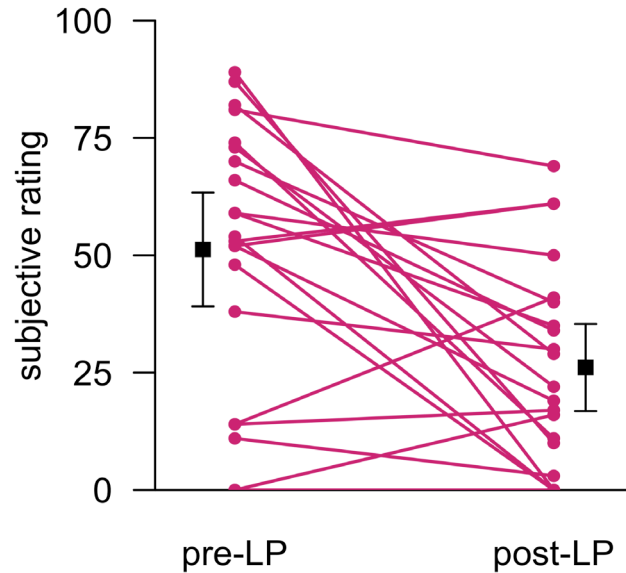
Tau and NfL by Longer Duration



Spinal Fluid (CSF) Testing



Subjective Experience of Anxiety About Spinal Fluid Testing Procedure



3. During today's visit, how did you feel before the lumbar puncture procedure?



4. Did you find today's lumbar puncture painful?



5. Based on today's experience, how do you currently feel about the prospect of a future lumbar puncture?



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Kathy Baxley

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CREUTZFELDT-JAKOB DISEASE
FOUNDATION, INC.

Supporting Families Affected by Prion Disease
