Virtual KOL Event: Frontotemporal Dementia

June 11, 2021

ALECTOR

Forward Looking Statement

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this presentation, including statements regarding our future financial condition, results of operations, business strategy and plans, plans, timelines and expectations related to AL001 and our other clinical and pre-clinical programs, including with respect to the availability of data, the initiation of future clinical trials and plans and expectations regarding planned regulatory filings with respect to such programs; and objectives of management for future operations, as well as statements regarding industry trends, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potentially” “predict,” “should,” “target,” “will” or the negative of these terms or other similar expressions.

We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, among other things: the ability of our clinical trials to demonstrate safety and efficacy of our product candidates, and other positive results; the timing and focus of our future clinical trials, and the reporting of data from those trials; our plans relating to commercializing our product candidates, if approved; the expected potential benefits of strategic collaborations with third parties and our ability to attract collaborators with development, regulatory and commercialization expertise; our estimates of the number of patients who suffer from the diseases we are targeting; our ability to expand our product candidates into additional indications and patient populations; the beneficial characteristics, safety, efficacy, and therapeutic effects of our product candidates; our plans relating to the further development and manufacturing of our product candidates, including additional indications we may pursue; our continued reliance on third parties to conduct additional clinical trials of our product candidates, and for the manufacture of our product candidates for preclinical studies and trials; our plans and ability to obtain or protect intellectual property rights; the accuracy of our estimates regarding expenses, future revenue, capital requirements, and needs for additional financing; our financial performance; and the sufficiency of our existing cash and cash equivalents to fund our future operating expenses and capital expenditure requirements. These risks are not exhaustive. New risk factors emerge from time to time and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements, as discussed in greater detail in our filings with the Securities and Exchange Commission (SEC), including without limitation in our Quarterly Report on Form 10-Q, as filed on May 5, 2021 with the Securities and Exchange Commission (“SEC”). You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this presentation, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

This presentation contains statistical data based on independent industry publications or other publicly available information, as well as other information based on our internal sources. We have not independently verified the accuracy or completeness of the data contained in these industry publications and other publicly available information. Accordingly, we make no representations as to the accuracy or completeness of that data.

Agenda and speakers

Topic	Speaker	Timing
Introductory remarks	Shehnaaz Suliman, MD *President and Chief Operating Officer*	7:30 AM – 7:35 AM PST 10:30 AM – 10:35 AM EST
Immunoneurology and PGRN franchise overview	Arnon Rosenthal, Ph.D. *Chief Executive Officer and Co-Founder*	7:35 AM – 7:40 AM PST 10:35 AM – 10:40 AM EST
Alector's AL001 program in frontotemporal dementia	Robert Paul, MD, Ph.D. *Chief Medical Officer*	7:40 AM – 7:45 AM PST 10:40 AM – 10:45 AM EST
GRN-related FTD and trials	Jonathan Rohrer, Ph.D., FRCP	7:45 AM – 8:30 AM PST 10:45 AM – 11:30 AM EST
The FTD disease cascade and biomarkers	Henrik Zetterberg, MD, Ph.D.	8:30 AM – 9:15 AM PST 11:30 AM – 12:15 PM EST
Looking ahead to AAIC	Robert Paul, MD, Ph.D.	9:15 AM – 9:25 AM PST 12:15 PM – 12:25 PM EST
Closing remarks and Q&A	Shehnaaz Suliman, MD *President and Chief Operating Officer*	9:25 AM – 10:00 AM PST 12:25 PM – 1:00 PM EST

AL001 in frontotemporal dementia with progranulin gene mutation (FTD-GRN)

Results from Alector's Phase 2 study of AL001 in FTD-GRN patients to be presented at AAIC on July 29, 2021 at 8 AM MT

- 12-month data for FTD-GRN patients
- Cognitive outcome assessment data [CDR-NACC-FTLD]
- Disease-relevant biomarkers [plasma, CSF and vMRI]

Immunoneurology and PGRN franchise overview

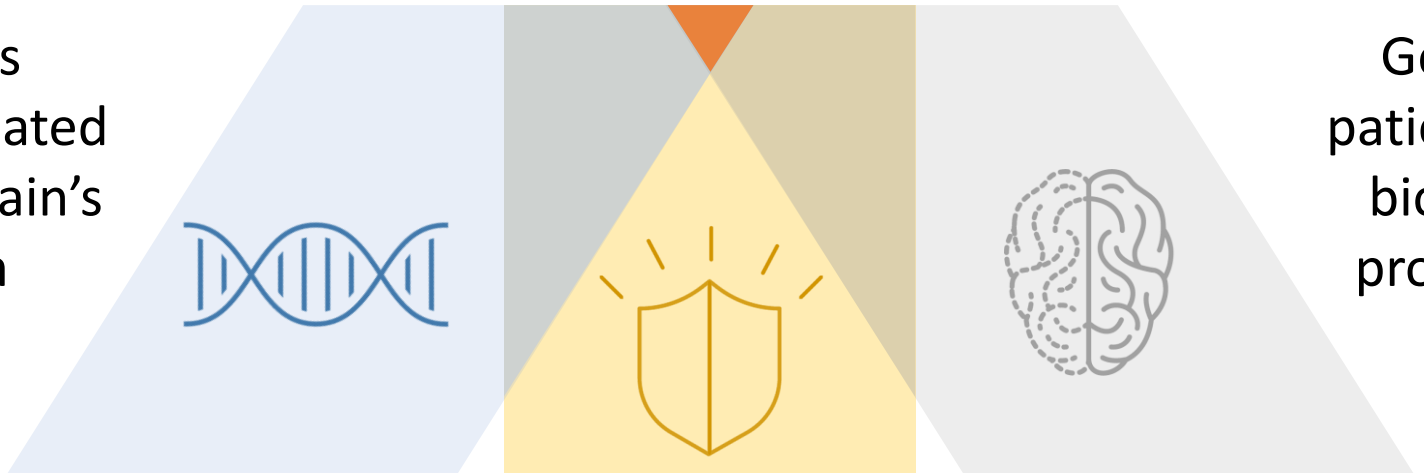
Arnon Rosenthal, Ph.D.
Chief Executive Officer & Co-Founder

Pioneering immuno-neurology

IMMUNO NEUROLOGY

Recruiting the brain's immune system
to cure neurodegeneration

Our therapeutics
are genetically validated
regulators of the brain's
immune system



Genetically defined
patient populations and
biomarkers enhance
probability of success

Human Genetics | Immunology | Neuroscience

Portfolio of product candidates targeting genetic causes of neurodegeneration

	TARGET	CANDIDATE	RESEARCH	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	PARTNER
Progranulin Franchise	**PGRN**	**AL001**	FTD-GRN (Followed by idiopathic FTD)					
		AL001	FTD-C9orf72					
		AL001	ALS- C9orf72 (Followed by idiopathic ALS)					
		AL101	Sub Q for PD / AD					
Alzheimer's Programs	**TREM2**	**AL002**	Alzheimer's disease					abbvie
	SIGLEC3	**AL003**	Alzheimer's disease					abbvie
	MS4A4A	**AL044**	Alzheimer's disease					
		AL044	Orphan neuro indication					
Oncology Programs	**SIRP-alpha**	**AL008**	Cancer					Innovent
	Multi-Siglec	**AL009**	Cancer					
*Single gene mutations that cause risk for **AD, PD, FTD, MS** and others*		**7+ programs**						

Progranulin loss of function constitutes risk for most neurodegenerative diseases

Homozygous mutations (100% LOF)

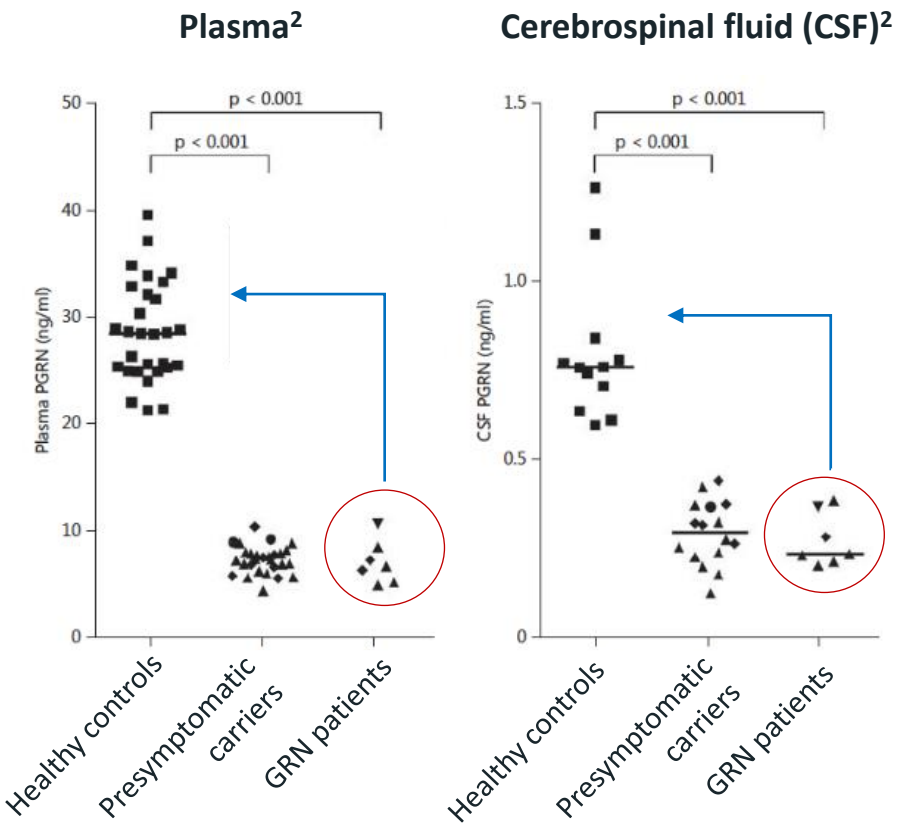
- Neuronal ceroid lipofuscinosis
- Dementia, ataxia, seizures, blindness[1]
- Onset 13 - 25 Yrs, 100% penetrance

Heterozygous mutations (50% LOF)

- Frontotemporal Dementia
- Changes to personality, language, decision making, behavior, and movement
- Avg. onset ~58 Yrs, >90% penetrance

Regulatory mutations (~10-20% LOF)

- Risk for ALS, FTD, LSD, AD, PD[3]
- Onset and symptoms vary



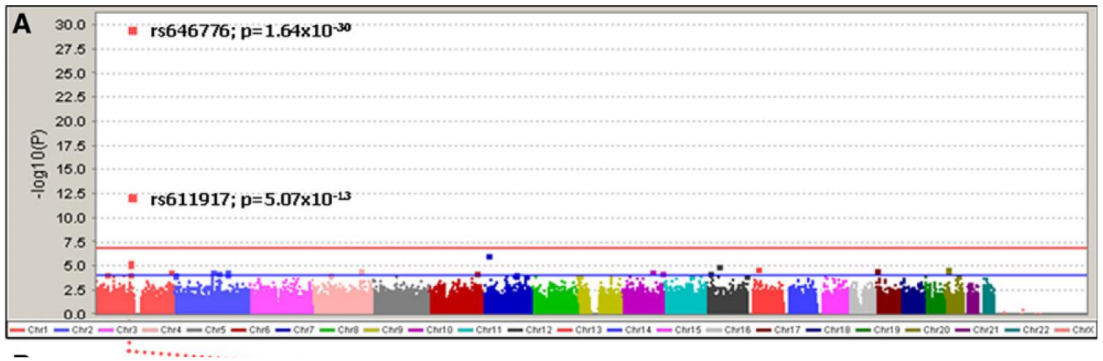
Common denominator: Pathologies are associated with dysfunctional microglia, lysosomes and misfolded proteins

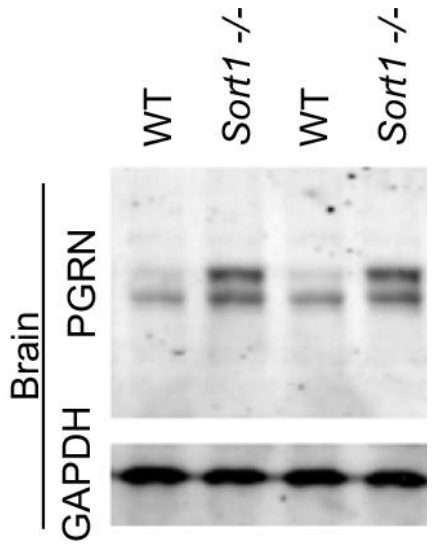
Note: LOF - loss of function. LSD – Lysosomal Storage Diseases

1. Sci Transl Med. 2017 Apr 12;9(385).
2. Dement Geriatr Cogn Disord Extra 2016;6:330-340.
3. Eur J Neurol. 2013 Dec;20(12):1571-3; Gene. 2014 Jun 1;542(2):141-5.

Immuno-neurology in action: AL001 and AL101 control progranulin (PGRN) levels

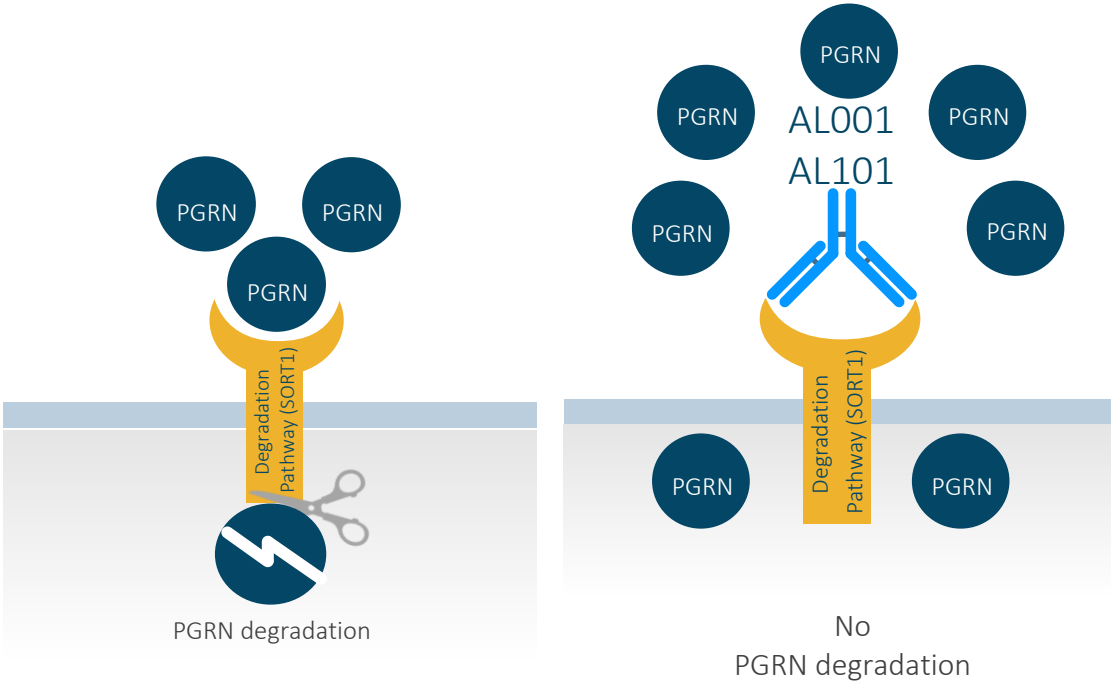
SORT1 expression levels inversely correlate with the levels of PGRN in humans





Genetic ablation of SORT1 raises PGRN in the mouse brain and serum without neurodegredation

AL001/AL101 blocks SORT1 PGRN interactions and raises the level of PGRN in human



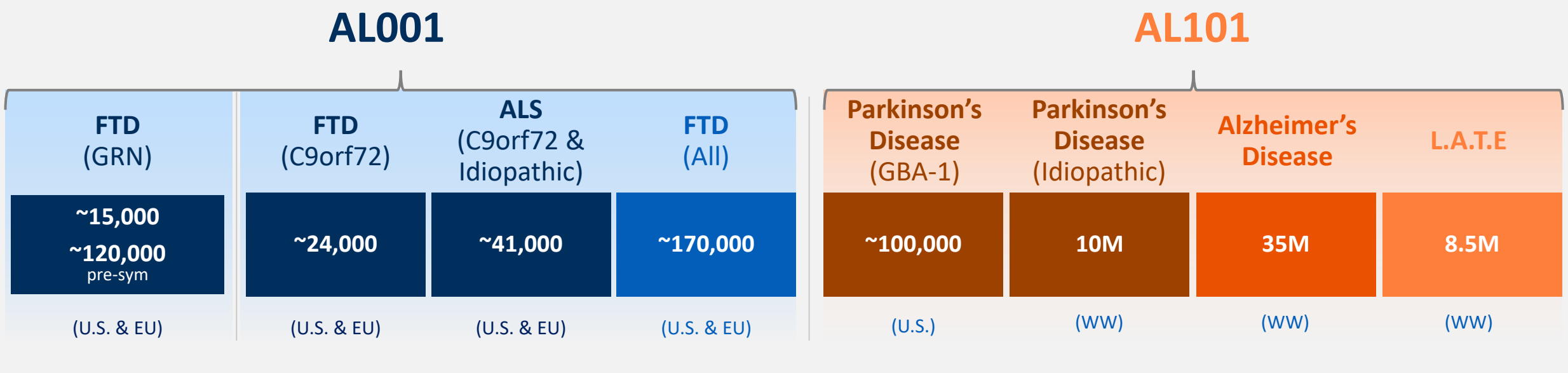
AL001/AL101 functionally mimicking the human genetic polymorphism in SORT1

Source(s): Carrasquillo et al, AJHJ 2010 Hu et al, Neuron 2020).

Our progranulin franchise is founded on the dual rationale of strong human genetics and biology

AL001: Fast-to-market in FTD and ALS

AL101: Indication expansion in AD, PD, L.A.T.E

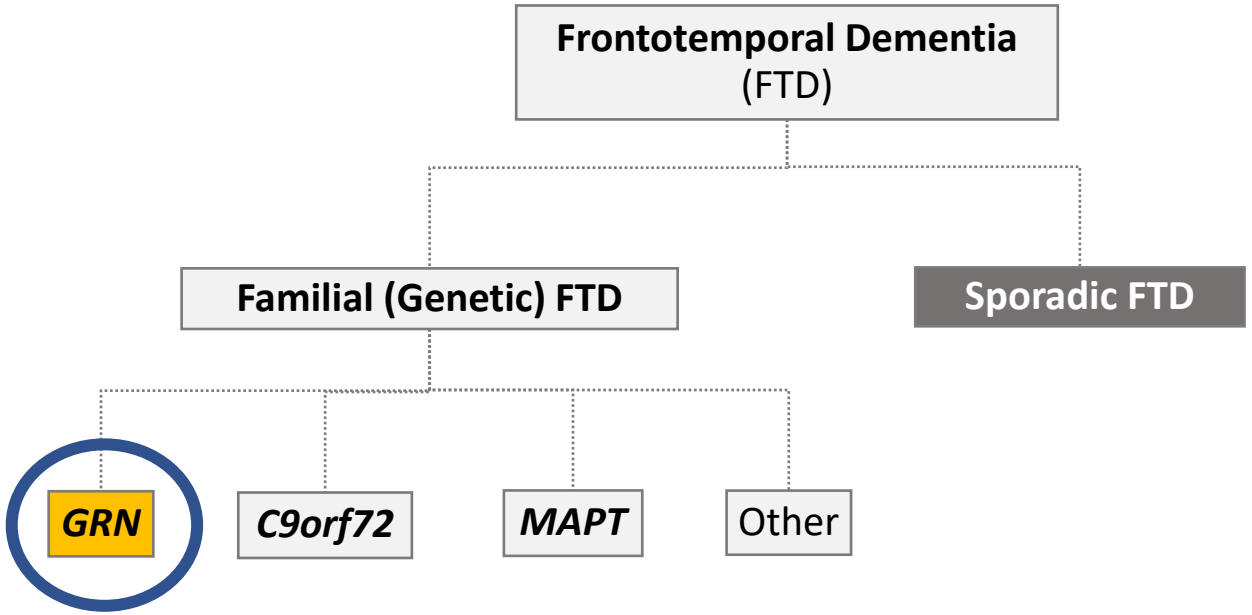


Alector's AL001 program in frontotemporal dementia

Robert Paul, MD, Ph.D.
Chief Medical Officer

Frontotemporal Dementia (FTD)
A rapidly progressive form of dementia with no treatment

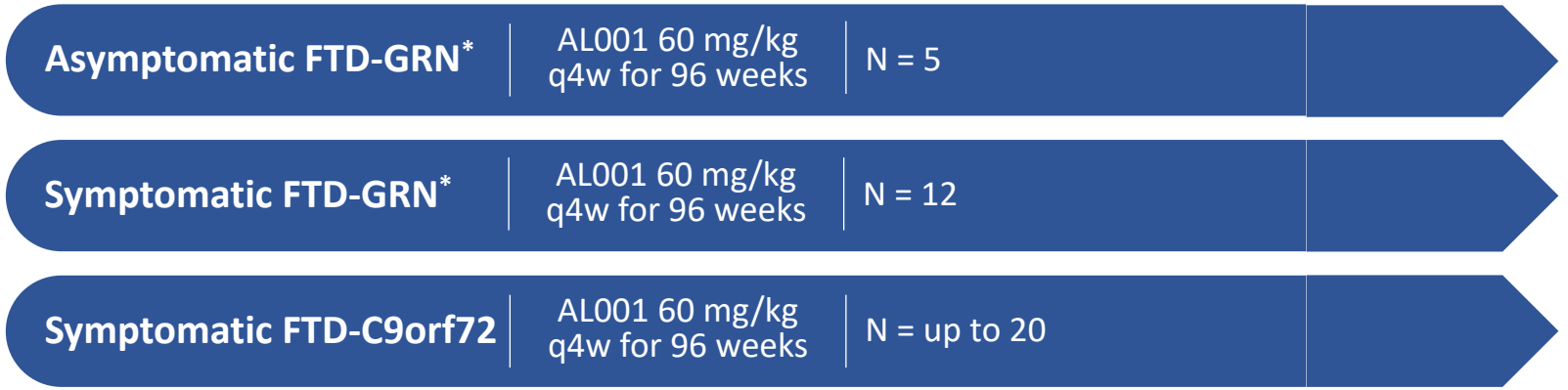
- Presents with compulsive behavior, lack of restraint, apathy, anxiety, and aphasia
- Symptom onset often under the age of 60
- Life expectancy after diagnosis 7 - 10 years
  - **~170,000 symptomatic FTD patients**
  - **~15,000 FTD-GRN patients**
  - **~24,000 FTD-C9orf72 patients**
- No approved disease modifying or symptomatic treatments available



A family history is present in up to 40% of FTD cases

FTD-GRN and FTD-C9orf72 Phase 2 INFRONT-2 study

Phase 2 Open-Label



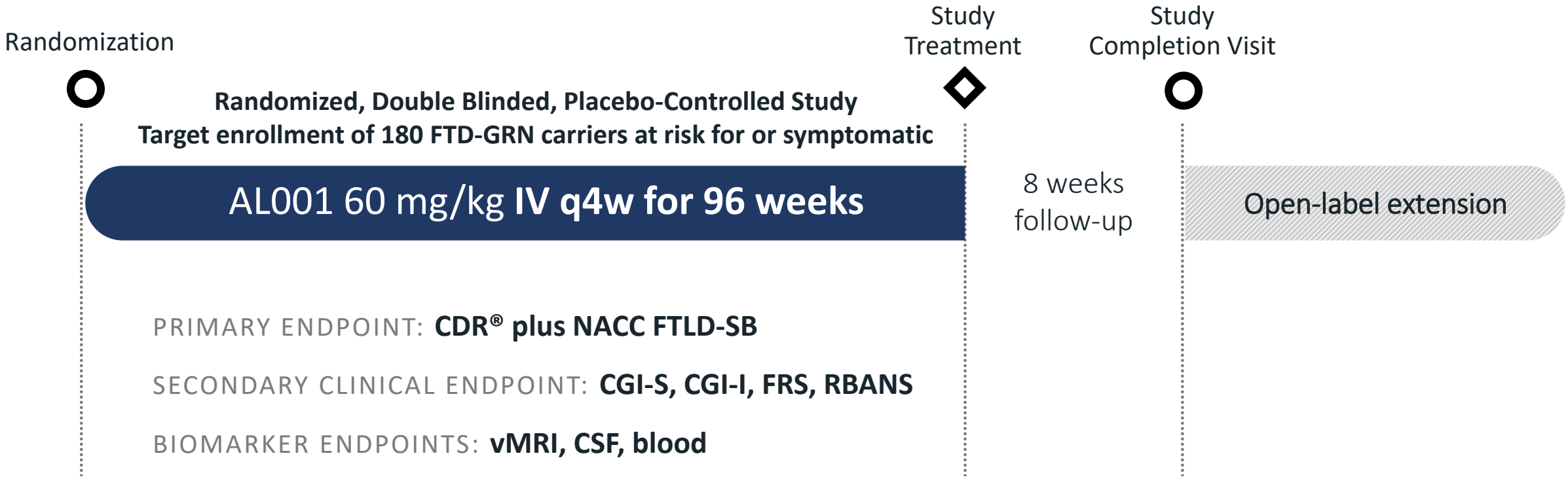
PRIMARY ENDPOINT: **Safety and tolerability**

SECONDARY ENDPOINT: **PK, PD**

EXPLORATORY: **Biomarkers in blood and CSF, volumetric MRI (vMRI), Clinical Outcome Assessments**

* Asymptomatic and Symptomatic FTD-*GRN* enrollment closed.

Pivotal Phase 3 INFRONT-3 study in FTD-GRN carriers



Study taking place at approximately 45 clinical centers in US, Europe and Australia

Enrollment on track

CDR® plus NACC FTLD-SB = Clinical Dementia Rating Dementia Staging Instrument PLUS National Alzheimer's Disease Coordinating Center Frontotemporal Lobar Degeneration Behavior and Language Domains Sum of Boxes; CGI-S = Clinician's Global Impression-Severity; CGI-I = Clinician's Global Impression-Improvement; FRS = Frontotemporal Dementia Rating Scale.

Genetic Frontotemporal Dementia Initiative (GENFI) Overview

- GENFI is a group of **research centers across Europe and Canada** focused on familial FTD and coordinated by Dr. Jonathan Rohrer at University College London

  - The aim of GENFI is to understand more about genetic FTD, particularly in those who have mutations in the **progranulin (GRN)**, microtubule-associated protein tau (MAPT) and **chromosome 9 open reading frame 72 (C9orf72)** genes

- GENFI investigates both people who have **developed symptoms and also people who have a risk of developing symptoms** in the future because they carry an abnormal genetic mutation

Source: https://www.genfi.org/study/.

GRN-related FTD and trials

Jonathan Rohrer, PhD, FRCP

Jonathan Rohrer, PhD FRCP

BRUK Senior Fellow, University College London, Dementia Research Centre

- Honorary consultant neurologist at the National Hospital for Neurology and Neurosurgery

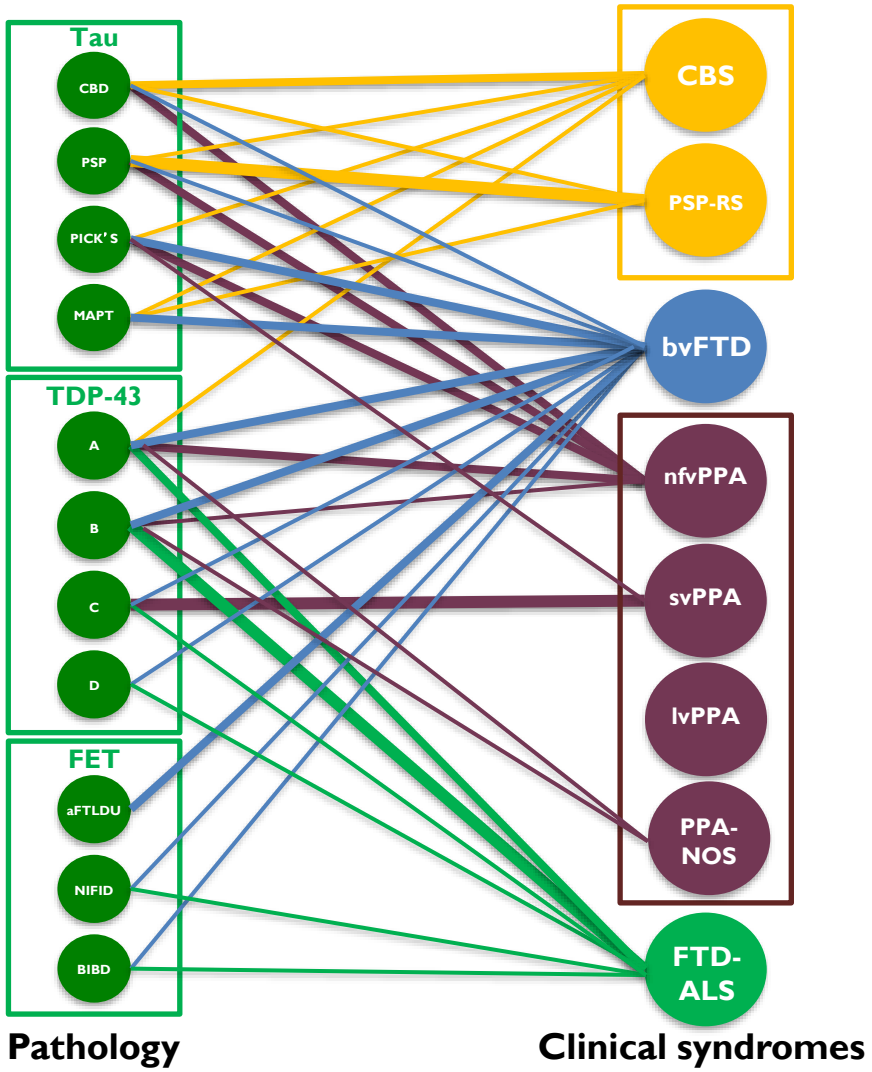
- Focused on biomarkers of frontotemporal dementia (FTD)
  - Coordinates the Genetic FTD Initiative (GENFI)
  - Co-lead for the FTD Prevention Initiative (FPI)
  - Established FTD UK annual meeting
  - >250 papers on FTD

GRN-related FTD and trials

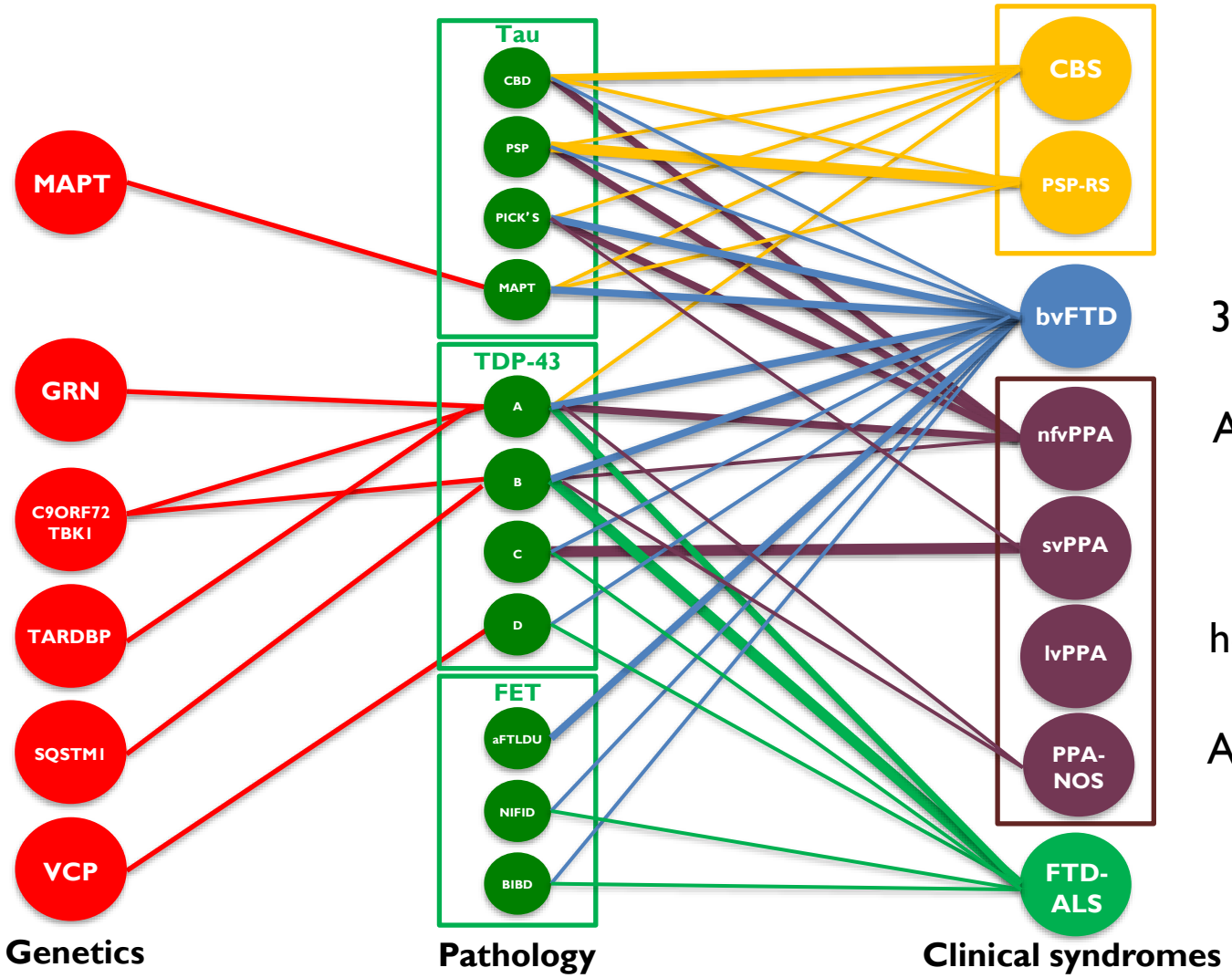
Dr Jonathan Rohrer

BRUK Senior Fellow

UCL Queen Square Institute of Neurology
National Hospital for Neurology and Neurosurgery



FTD is a complex and heterogeneous disease



So why focus on genetic FTD?

30-50% of FTD is genetic

Able to accurately define molecular pathology

Study of more homogeneous population

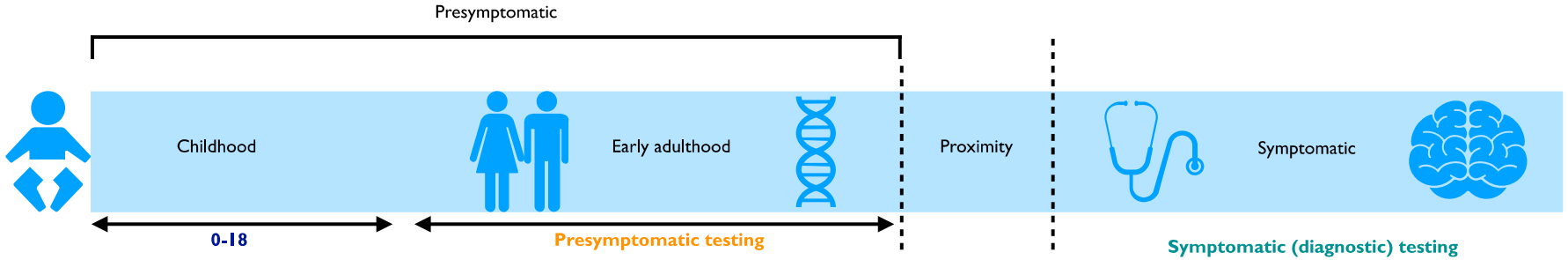
Allows window into early disease

GRN-related FTD

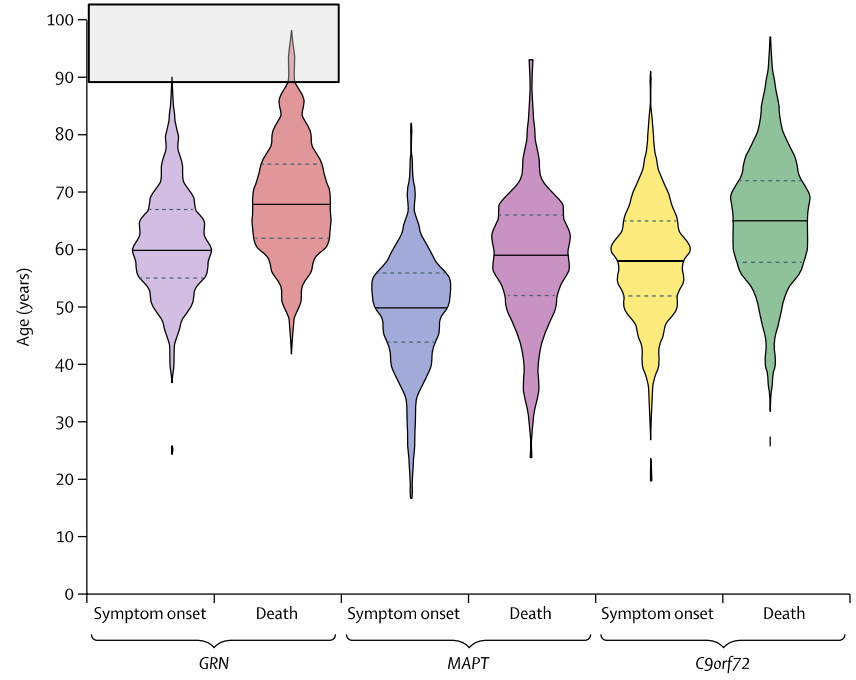
- >170 known pathogenic LOF mutations: https://www.ftdtalk.org/what-is-ftd/genetics/grn-mutations/
- Heterozygous mutations cause FTD, homozygous mutations cause NCL-like lysosomal storage disorder
- Majority of missense mutations unlikely to be pathogenic
- Very variable age at onset
- Usually causes bvFTD, but also other phenotypes: PPA, CBS…
- Final pathology – TDP-43 type A
- Currently no disease modifying therapies – large unmet need

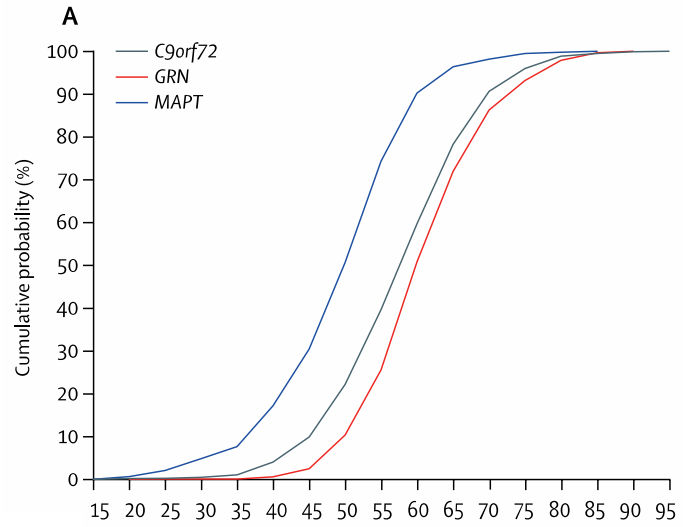
Prevalence

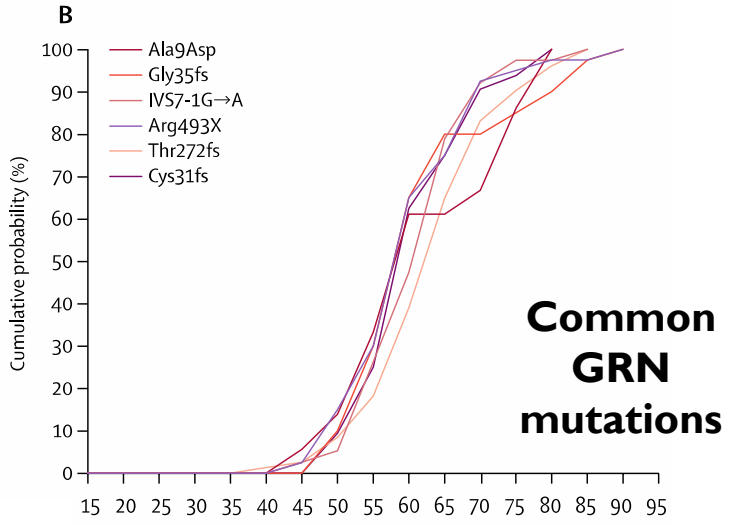
- FTD prevalence 10.8/100,000 *(Coyle-Gilchrist et al, Neurology, 2016)*
- *GRN*-related FTD is ~10% of all FTD
- *GRN*-related FTD prevalence therefore ~1/100,000 = symptomatic carriers
- Larger population of presymptomatic carriers
- Mean disease duration 7.1 (3.9) years
- Experience of being an at-risk family member is difficult, particularly if you find out when young:



Variable age at symptom onset

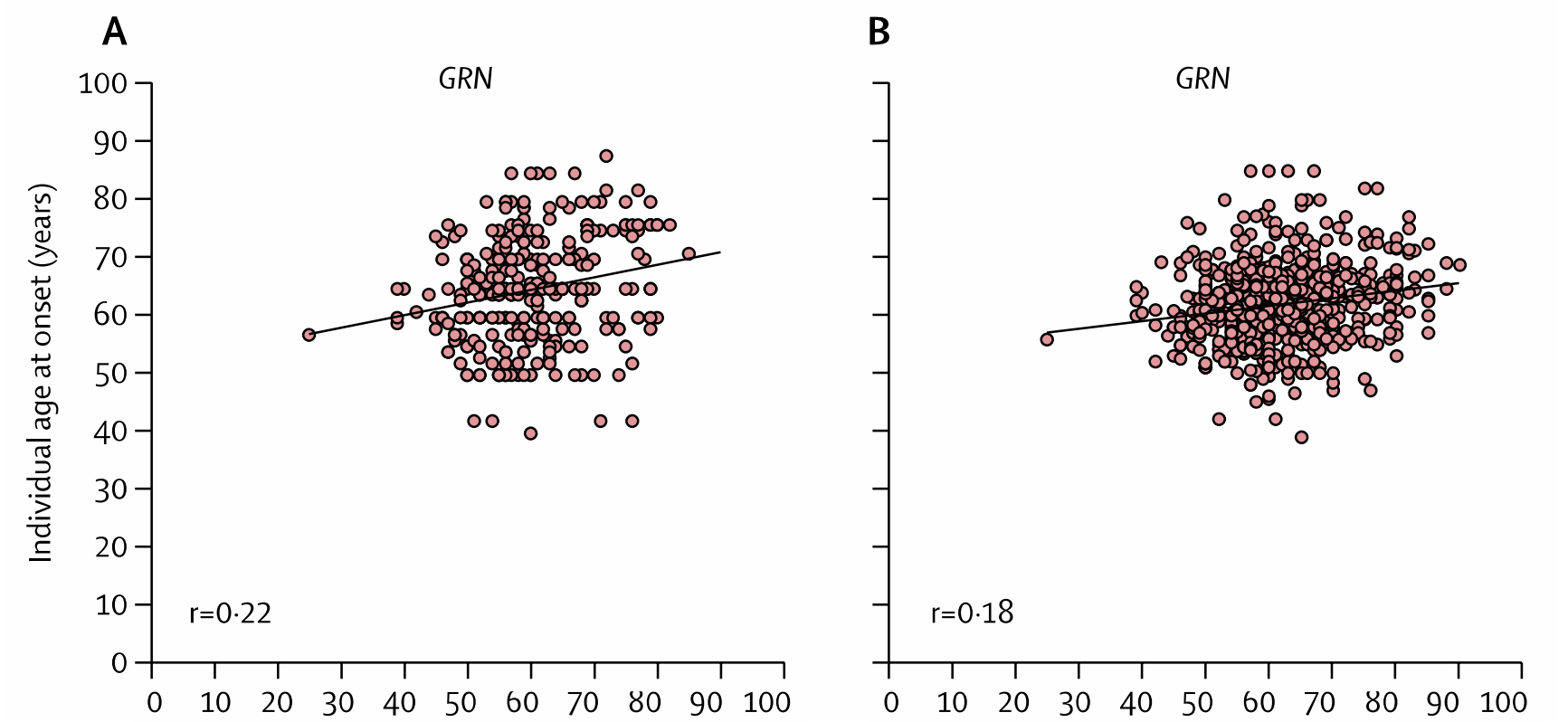






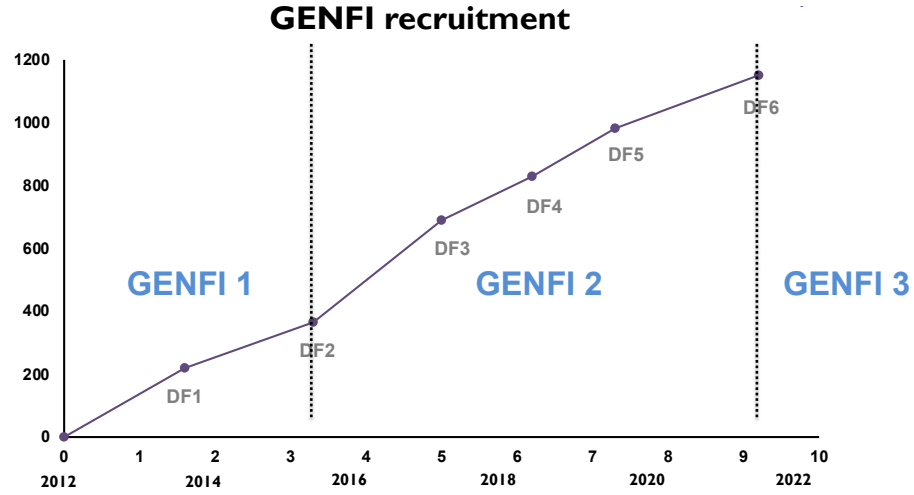
Common GRN mutations

Average age of onset correlation with parental or mean family onset is poor



GENFI

- Multicentre natural history study, running since Jan 2012
- At-risk and symptomatic *GRN* (and *C9orf72*/*MAPT*) mutation carriers
- Currently 30 centres
- >1200 subjects seen longitudinally on an annual basis – currently >2500 visits in total
- Core infrastructure:
  - Clinical history and examination
  - Functional questionnaires
  - Neuropsychology battery
  - MR imaging
  - Blood sampling
    - DNA, RNA, serum, plasma
  - CSF sampling



Clinical measures

- CDR plus NACC FTLD = Clinical Dementia Rating scale with addition of language and behaviour scores
- 8 items scored 0, 0.5, 1, 2 or 3:
  - Memory
  - Orientation
  - Judgment and problem solving
  - Community affairs
  - Home and hobbies performance
  - Personal care
  - **Behaviour**
  - **Language**

CDR

CDR plus NACC FTLD

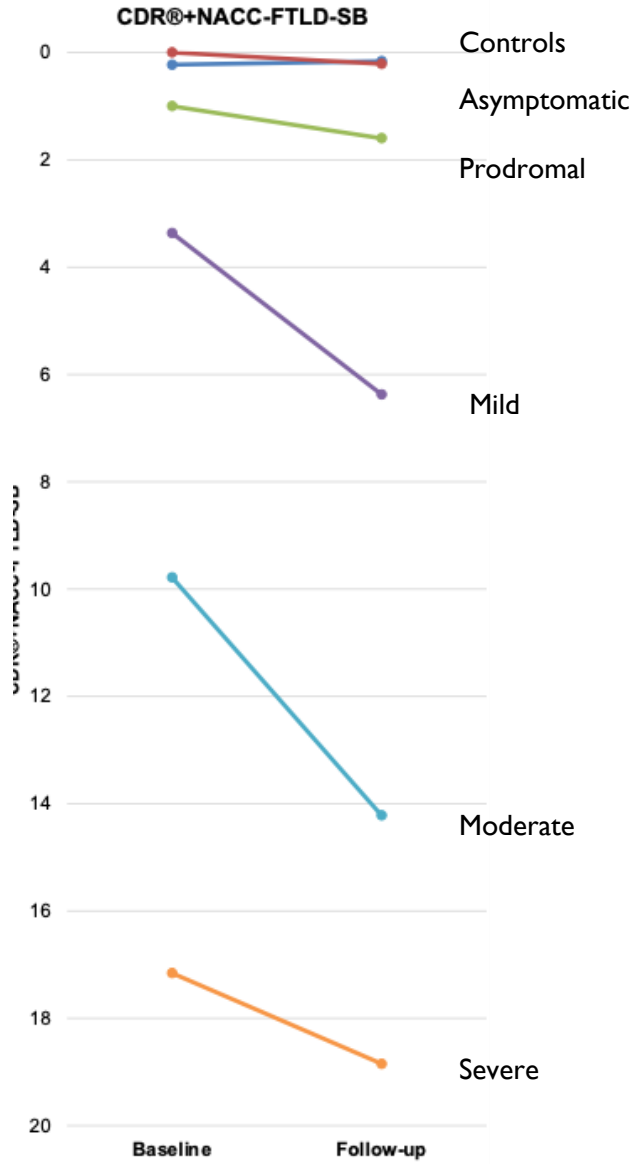
- **Sum of boxes score** – addition of all scores
- **Global score** allows stratification into:
  - 0: not symptomatic
  - 0.5: very mild symptomatic/prodromal
  - 1,2,3: symptomatic (mild/moderate/severe)

References:
- Knopman et al, Brain 2008
- Miyagawa et al, Alzheimer's and Dementia 2020

Clinical measures

- CDR plus NACC FTLD shows measurable decline during 1 year follow up in prodromal and symptomatic participants

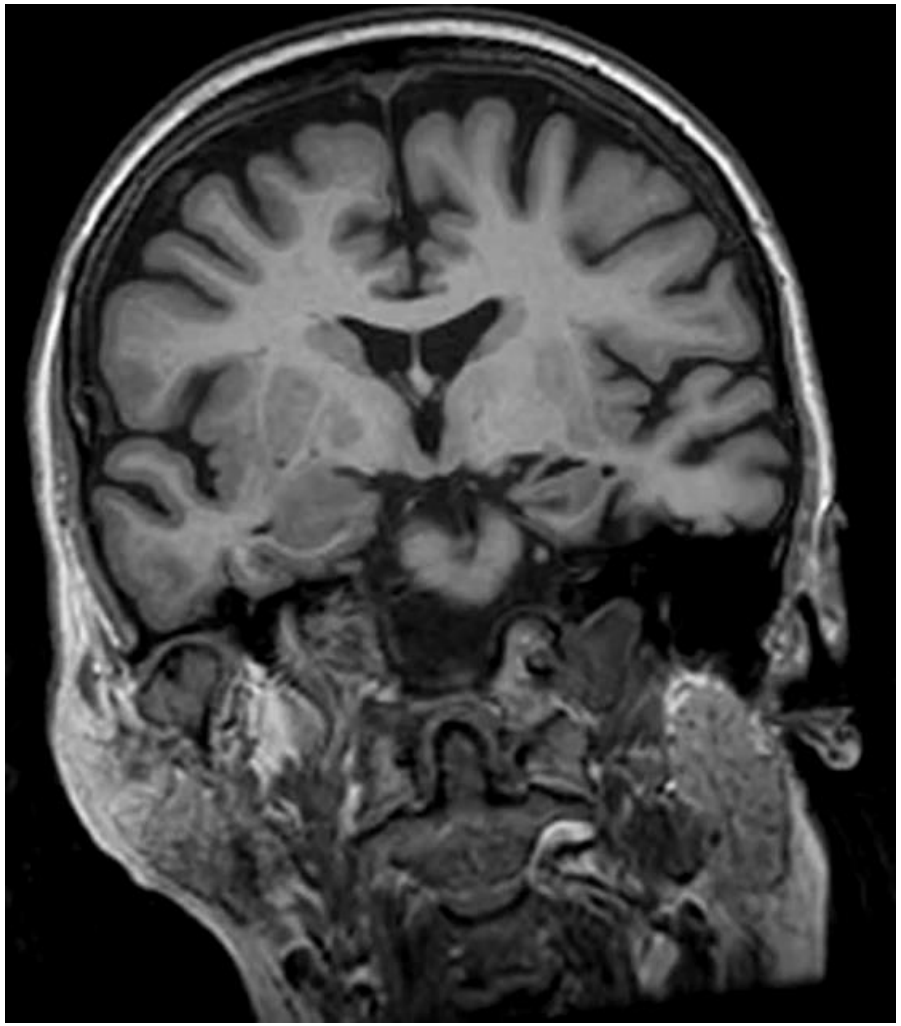
- Other measures in GENFI:
  - FTD Rating Scale (FRS)
  - Revised Self Monitoring Scale (RSMS)
  - Modified Interpersonal Reactivity Index (mIRI)

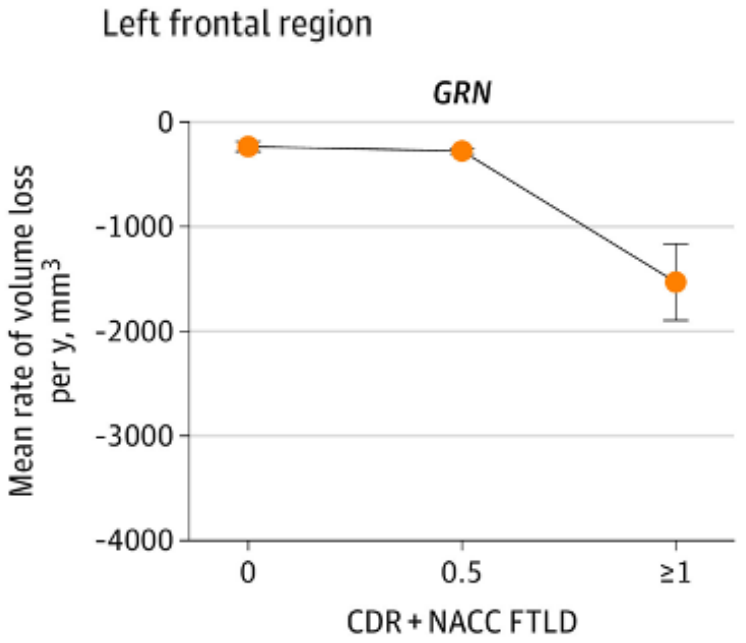


Structural imaging

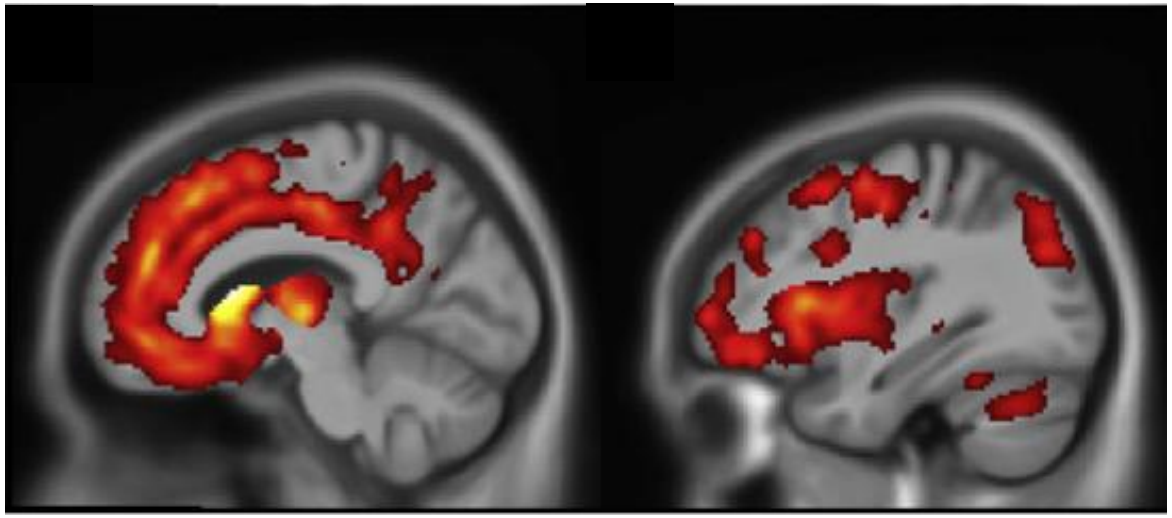
- Volumetric T1 MRI
  - Patterns/Rates of brain atrophy
- Volumetric T2 MRI
  - White matter hyperintensity volumes
- Other: DTI/rsfMRI/ASL – too variable; problems across multicentres

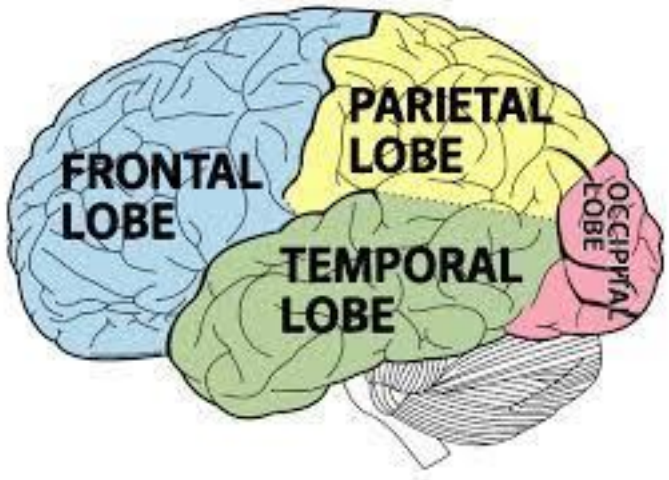
T1 imaging shows progressive atrophy





Pattern of atrophy is regional and disease specific





T1 imaging shows atrophy prior to symptom onset

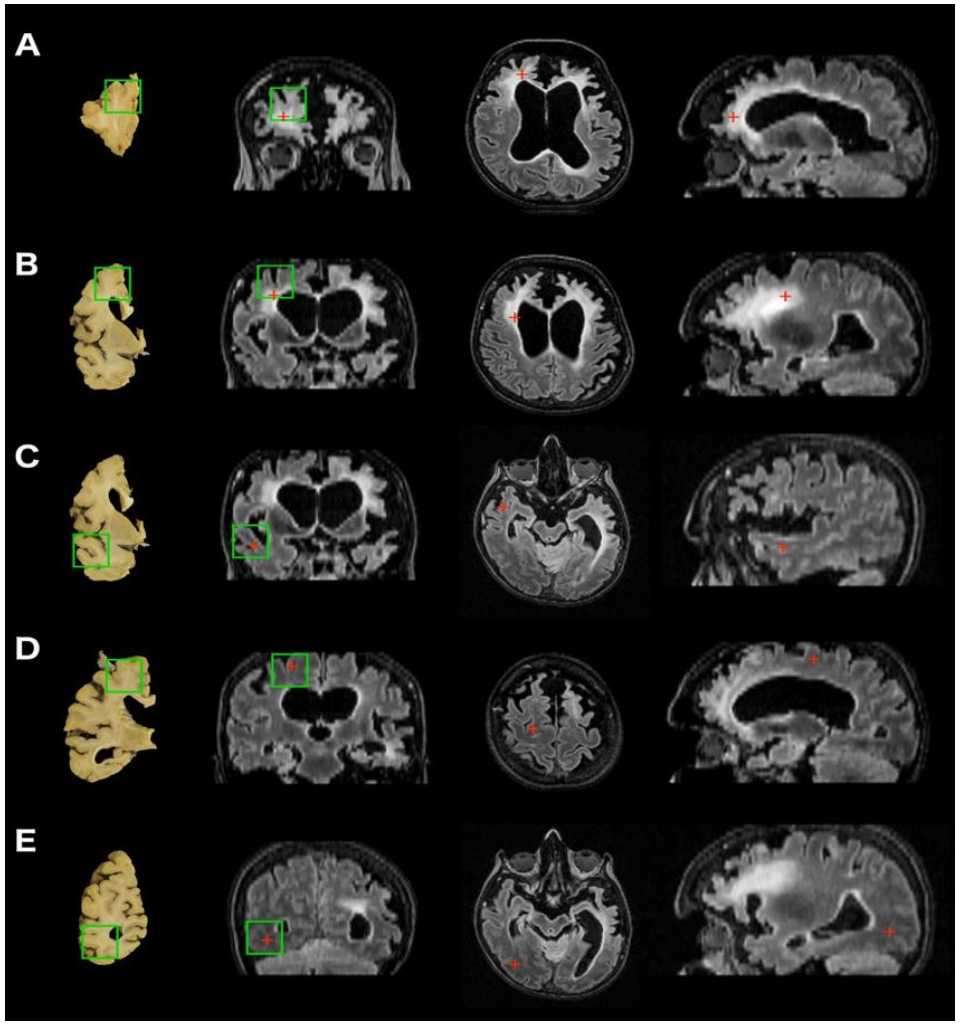
	-25 years	-20	-15	-10	-5	0	5	10
Frontal								
Temporal								
Parietal								
Occipital								
Insula								
Cingulate								
Striatum								
Thalamus								

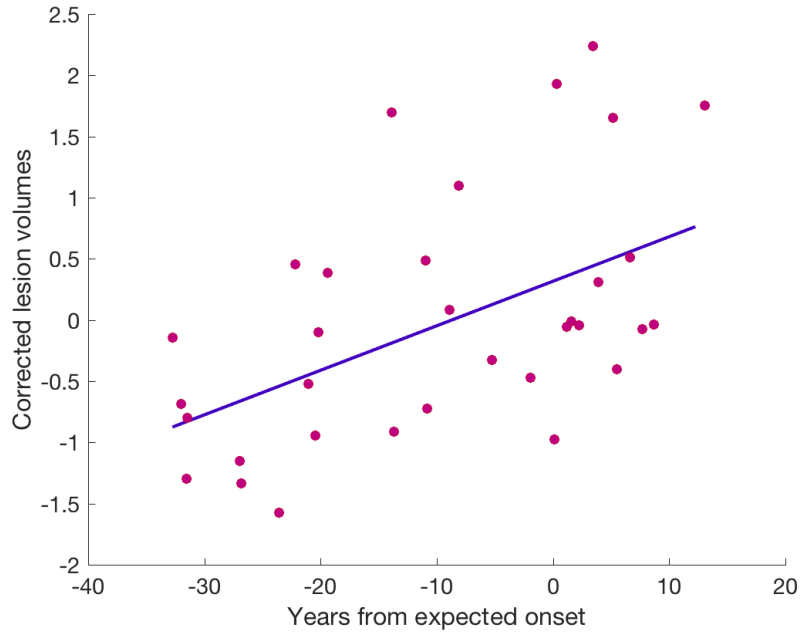
Symptom onset

Rates of atrophy increase with disease progression

	Annualized whole brain atrophy rate (%)
Symptomatic mutation carrier	3.5 (1.5)
Late presymptomatic mutation carriers	1.4 (2.1)
Early presymptomatic mutation carriers	0.5 (1.5)
Mutation negative non carriers	0.3 (0.6)

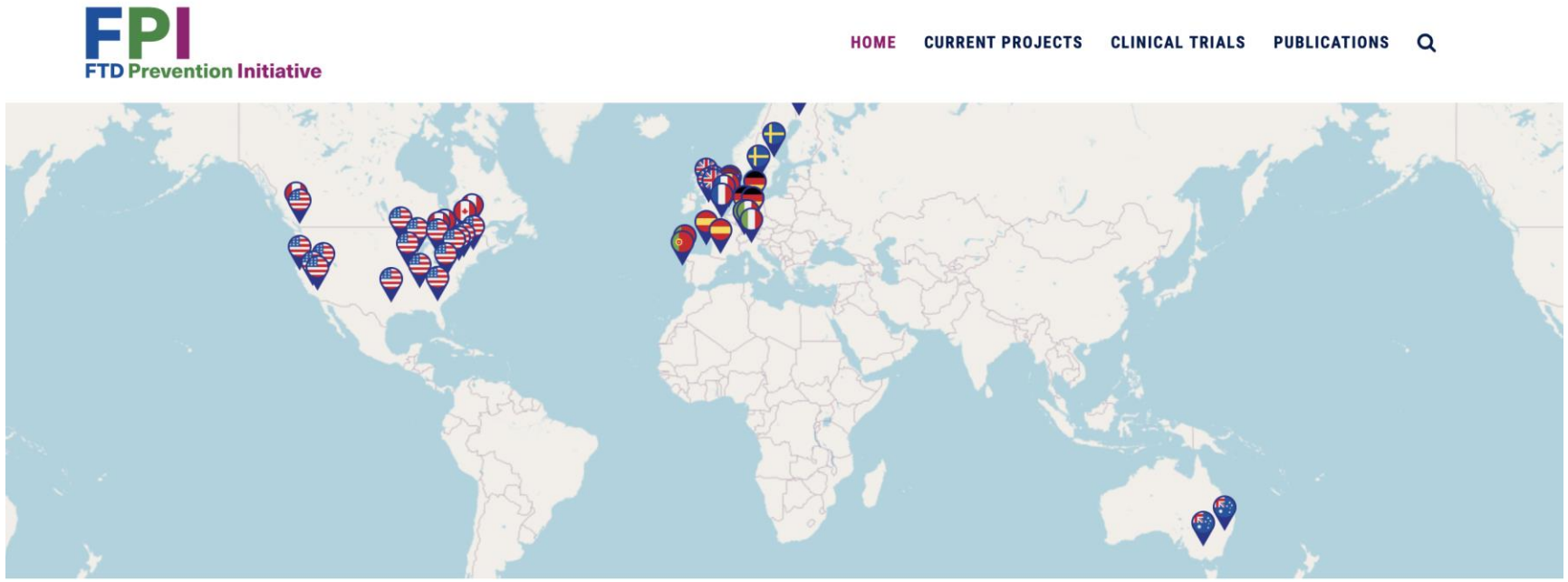
T2 MRI: white matter hyperintensities





Potential MR marker of inflammation

www.thefpi.org



The FTD Prevention Initiative (FPI) brings together genetic FTD cohorts from across Europe, North America, South America and Australasia.

It is is led by Dr Jonathan Rohrer at UCL in the UK, and Professor Adam Boxer at UCSF in the US.

The Genetic FTD Initiative (GENFI) in Europe and Canada and the ALLFTD study in US and Canada were the founding members of the FPI. Other members include the Australian Dominantly Inherited Non-Alzheimer Dementias (DINAD) and Research Dementia Latin America (ReDLat) studies.

Goals

Our overall aim is to promote clinical trials of new therapies to prevent FTD.

Key goals:

- Create uniform standards for conduct of clinical trials in familial FTD syndromes.
- Create an international database of familial FTD research participants who might be eligible for clinical trials.
- Promote responsible data sharing within the context of observational studies and trials in familial FTD.

The future

- Worldwide collaboration is the way forward – this is a rare disease with a need for working together across patients, families, academia and industry.

- The goal of the FPI is to provide the best science and the best opportunities for patients and families that will eventually lead to a cure for FTD.

Acknowledgments

To all the participants, carers and family members who take part in the GENFI study

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- Firenze: Sandro Sorbi
- Stockholm: Caroline Graff
- Quebec: Robert Laforce
- Lisboa: Alexandre Mendonca
- Leipzig: Matthias Schroeter
- Oulu: Anne Remes
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- Paris: Isabelle Le Ber
- Lille: Florence Pasquier
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- Tubingen: Matthis Synofzik
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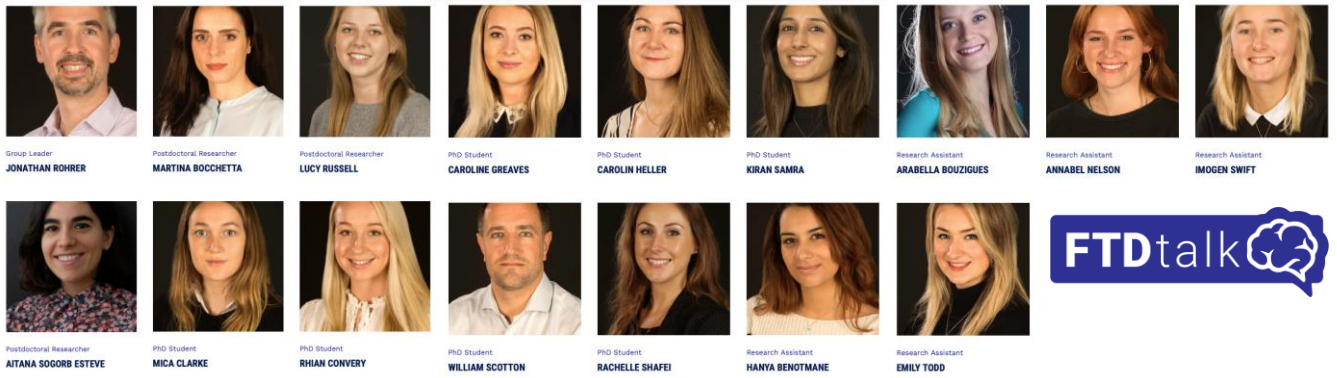
- Adrian Isaacs
- Pietro Fratta
- Jason Warren
- Cath Mummery



The FTD disease cascade and biomarkers

Henrik Zetterberg, MD, Ph.D.

ALECTOR

Henrik Zetterberg, MD, P.hD.

Professor of Neurochemistry, University of Gothenburg

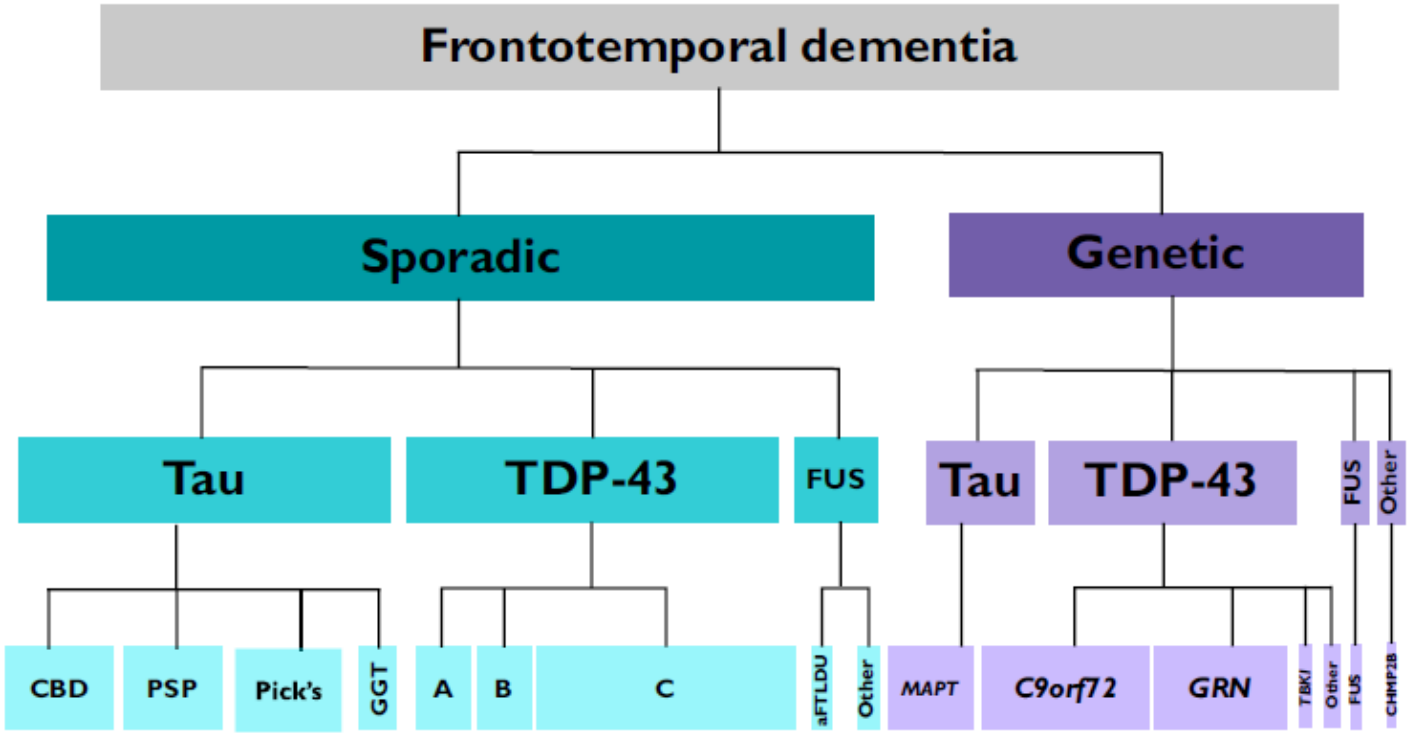
- Head of the Department of Psychiatry and Neurochemistry at Sahlgrenska Academy at the University of Gothenburg
- Professor of Neurochemistry, University of London
- Focused on the development of biomarkers for Alzheimer's disease and other brain disorders
  - Developed new diagnostic tests for Alzheimer's disease
  - Published >1400 scientific articles
  - Recipient of the Erik K. Fernström and Inga Sandeborg prizes for research

The FTD cascade and biomarkers

Henrik Zetterberg, MD, PhD
Professor of Neurochemistry
University of Gothenburg and University College London

The Sahlgrenska Academy

The challenge:

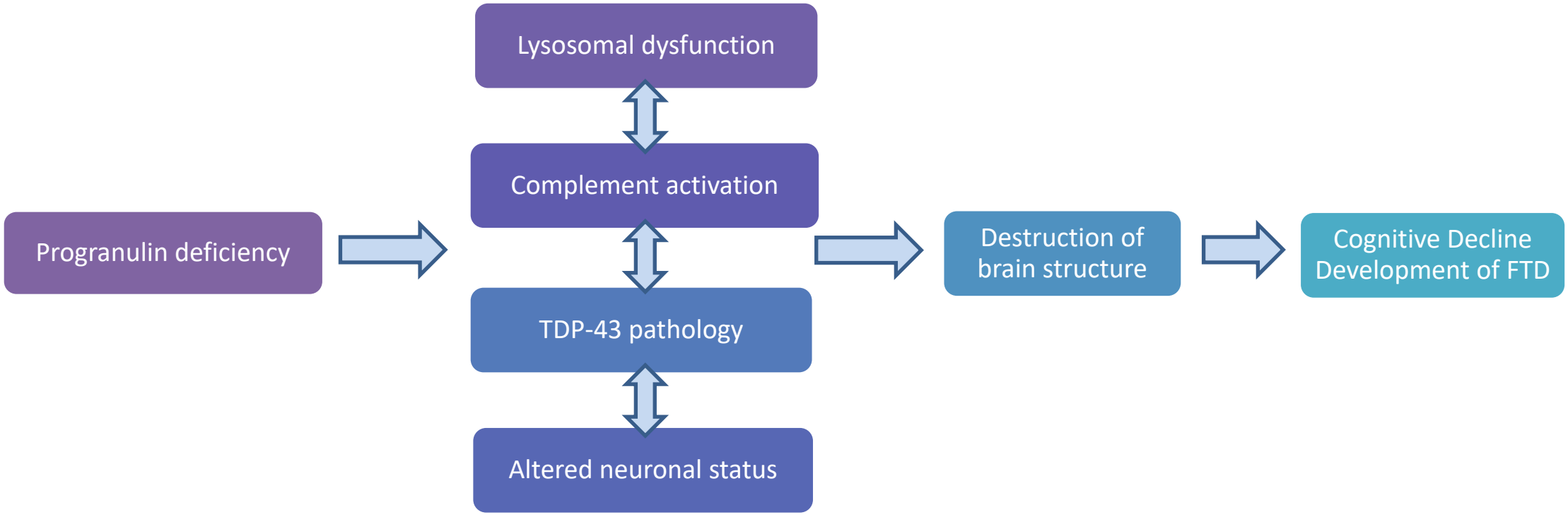


Greaves and Rohrer, Neurology, 2019

The solution:

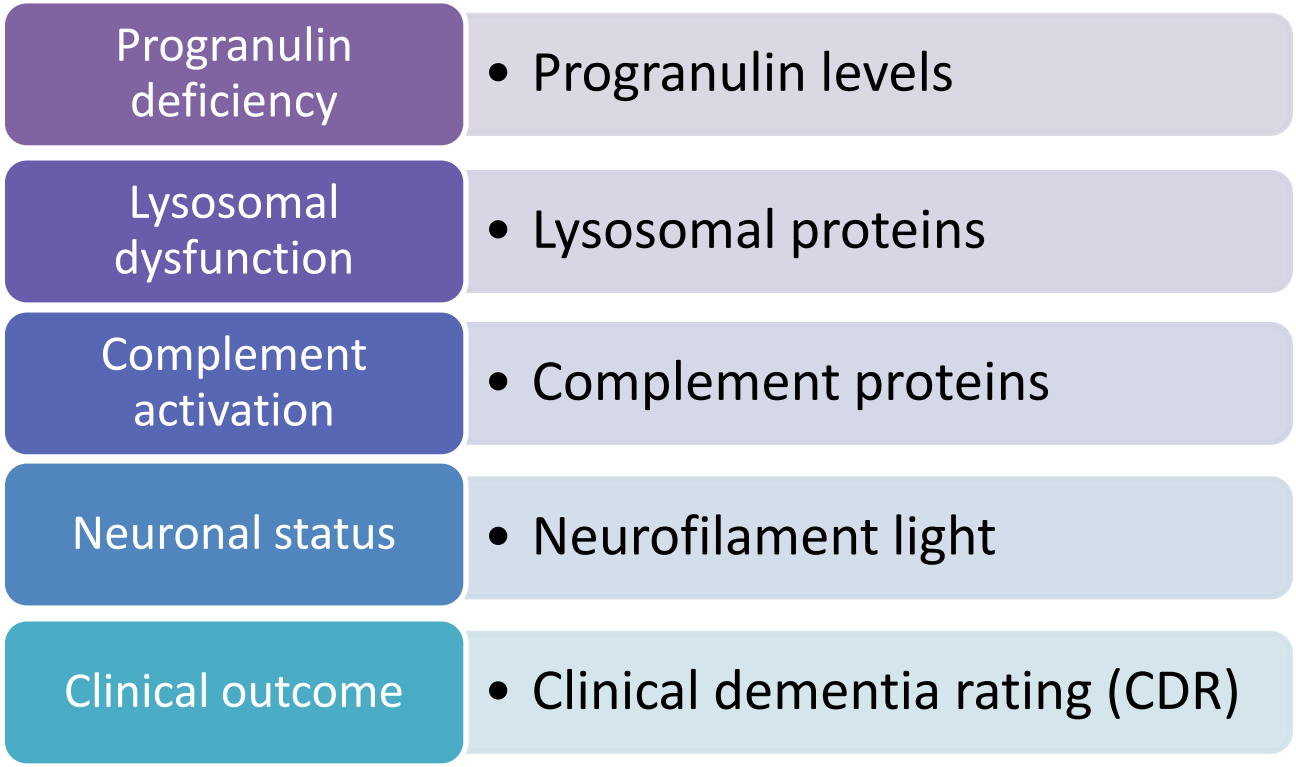
Focus on a well-known pathophysiological mechanism and then zoom out

Working hypothesis of the FTD-*GRN* disease cascade



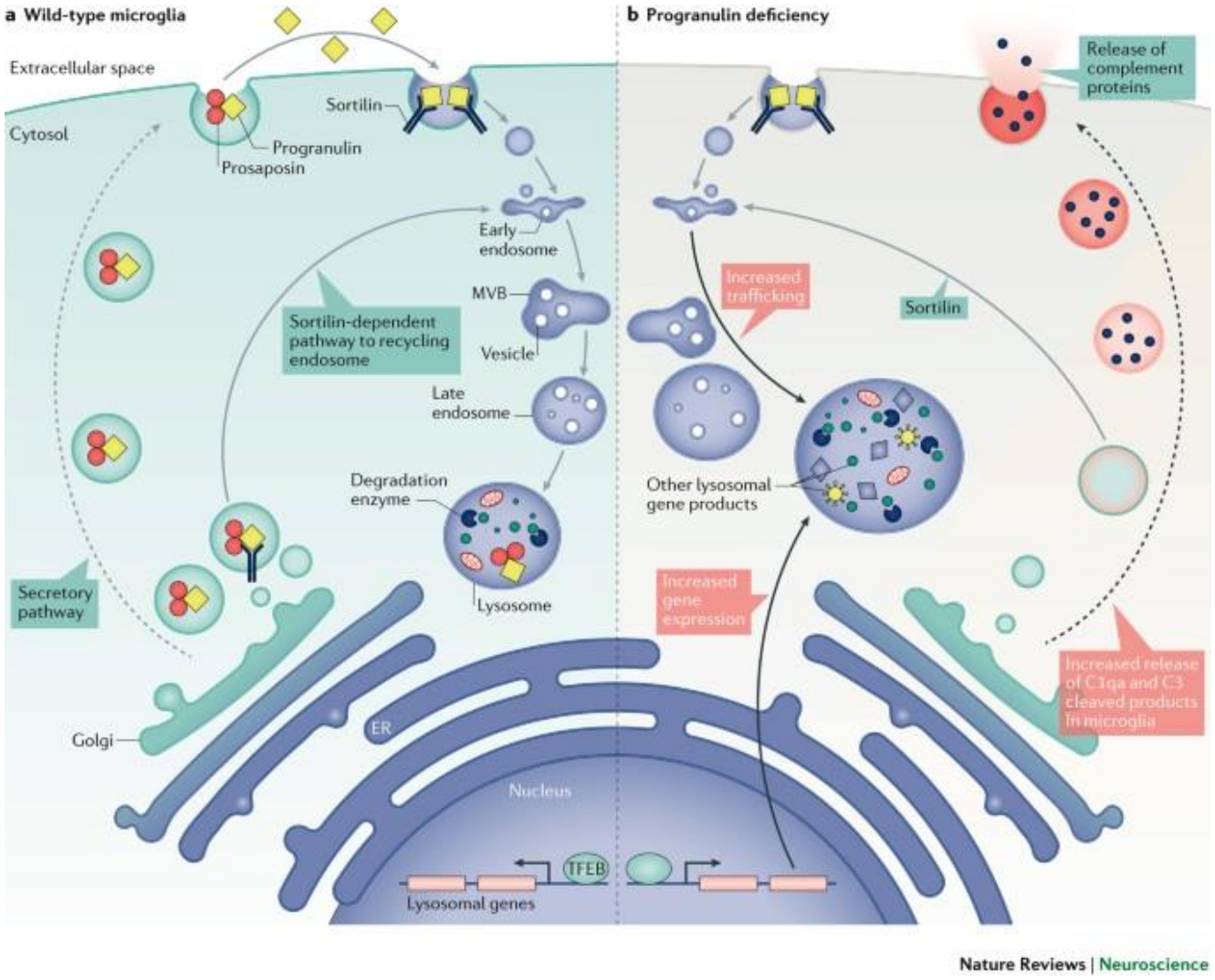
- PGRN deficiency leads to lysosomal dysfunction, increased complement activation, TDP-43 pathology, and altered neuronal status
- Ultimately, these changes lead to destruction of brain structures and cognitive decline resulting in the development of FTD

Key nodes of FTD-*GRN* pathophysiology assessed by fluid biomarkers and clinical outcome assessments



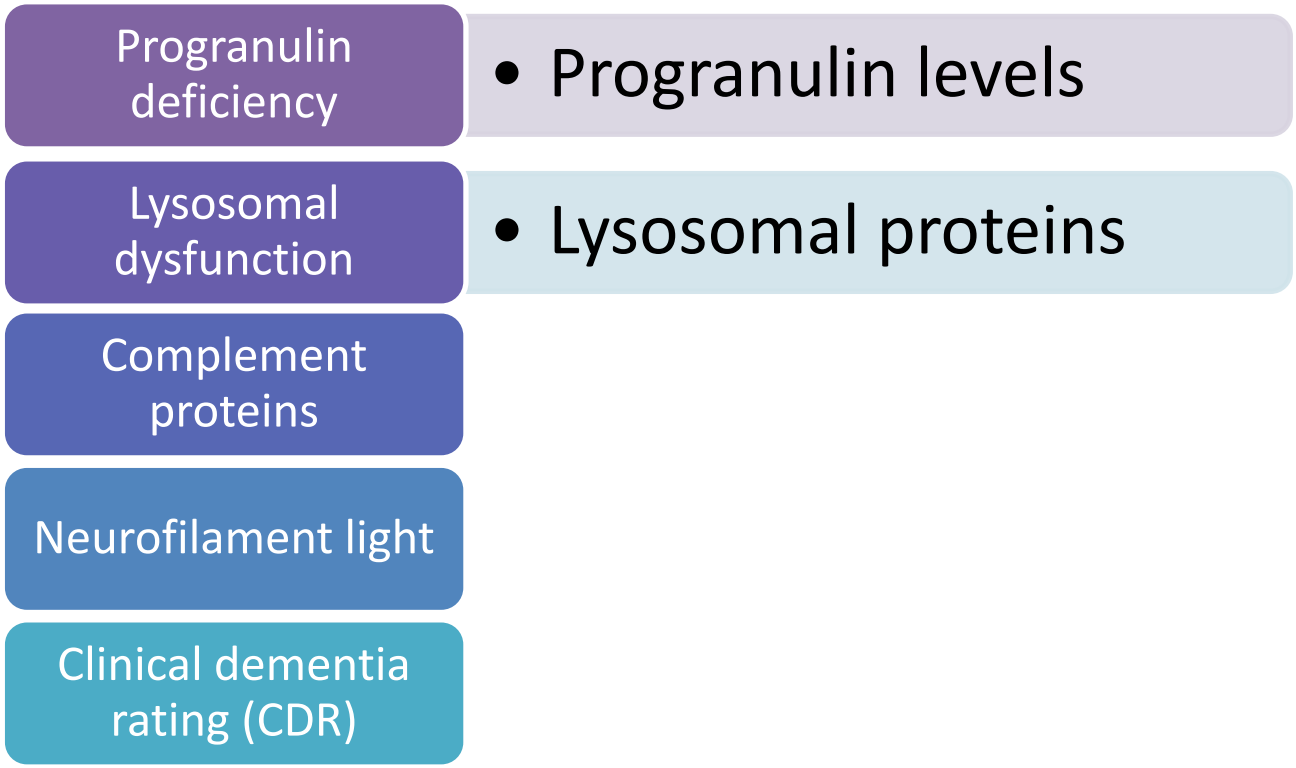
- The FTD-*GRN* disease cascade can be assessed by fluid biomarkers representing key nodes of the pathophysiology
- Clinical outcome data bolstered by fluid biomarker data can reveal potential treatment impact on disease progression

PROGRANULIN DEFICIENCY



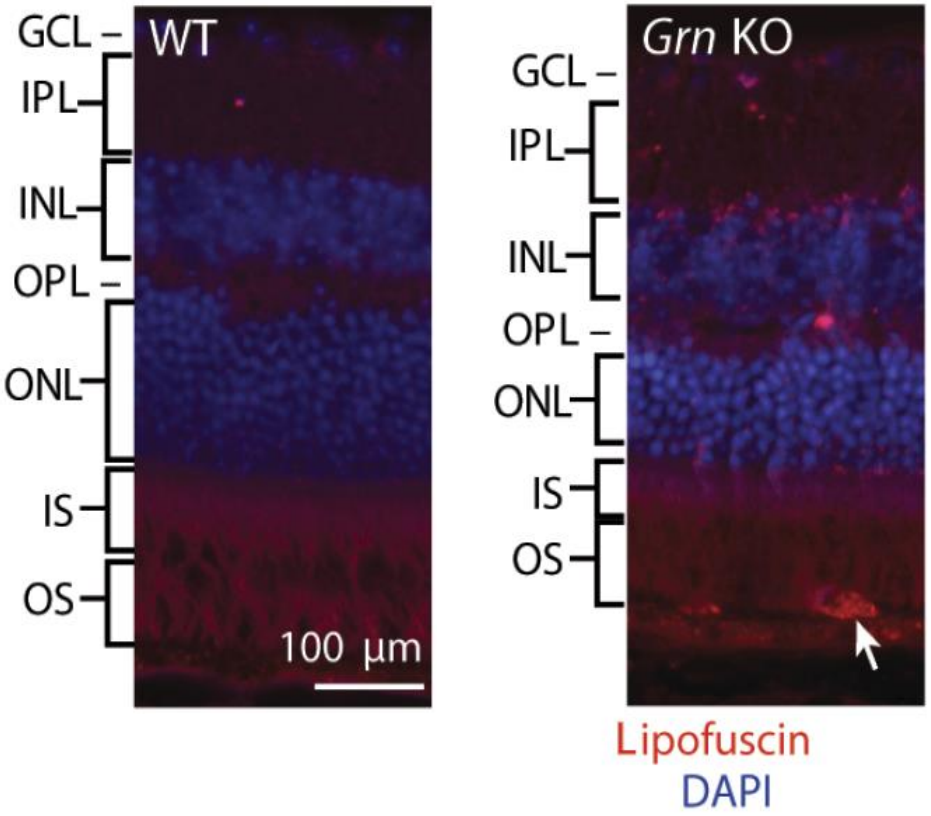
- Normal progranulin levels maintains homeostasis in the brain
- PGRN deficiency leads to lysosomal dysfunction, aberrant microglia activation, TDP-43 pathology, and neuronal death

Kao et al., Nature 2017

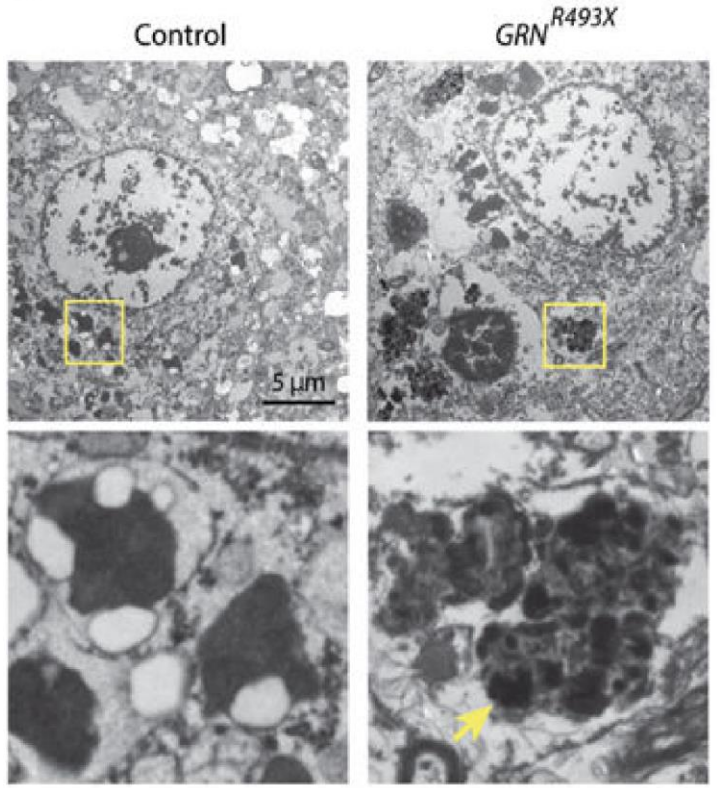

Progranulin deficiency
• Progranulin levels
Lysosomal dysfunction
• Lysosomal proteins
Complement proteins
Neurofilament light
Clinical dementia rating (CDR)

GRN mutations and lysosomal dysfunction

- Deficiency in PGRN leads to lysosome dysfunction
  - Homozygous *GRN* mutation leads to neuronal ceroid lipofuscinosis (NCL), a lysosomal storage disease
  - Heterozygous *GRN* mutation carriers exhibit features of NCL including accumulation of storage material in neurons



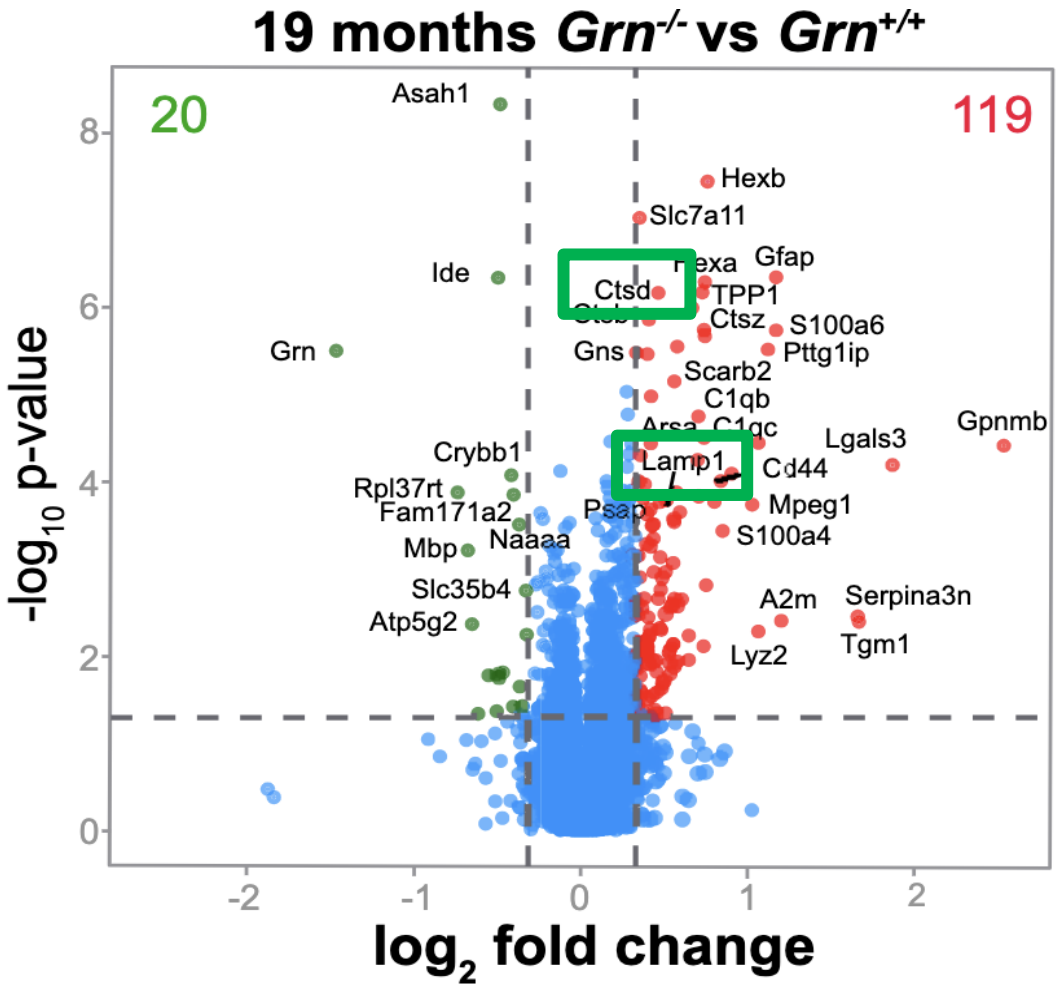
Accumulation of lipofuscin in the retina of *GRN* KO mice



Accumulation of storage material in post-mortem brain of *GRN* mutation carriers

Ward et al Sci Transl Med. 2017

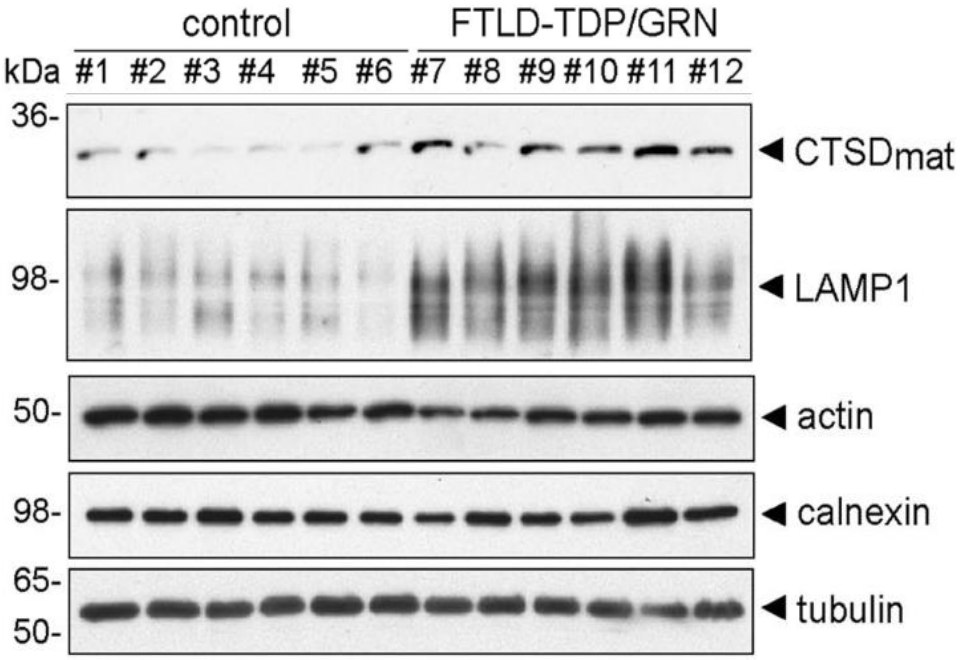
PGRN deficiency leads to increased expression of lysosomal proteins

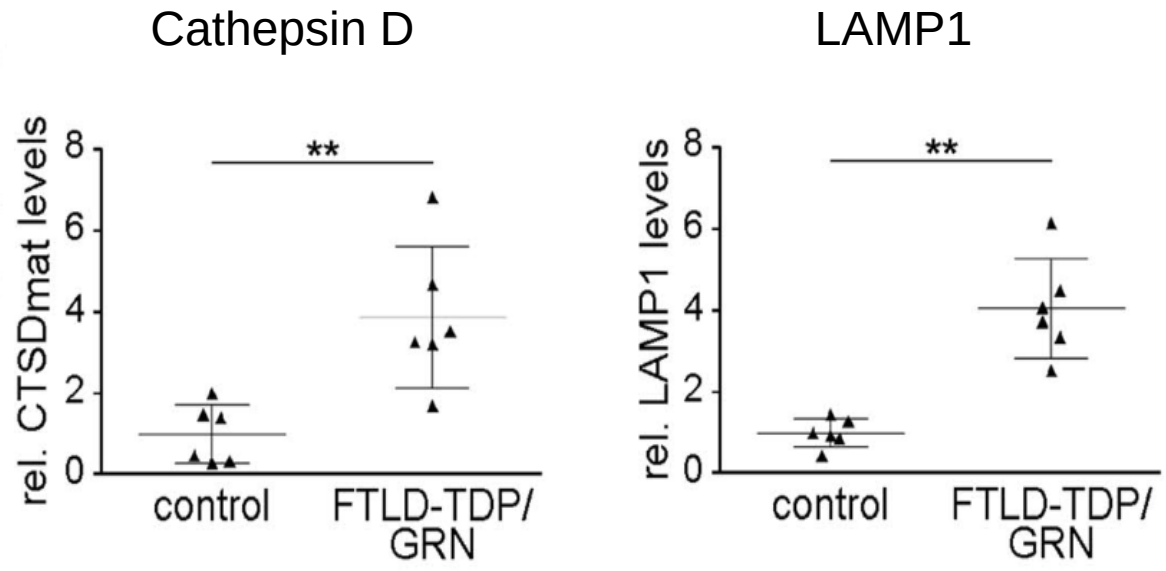


- PGRN deficiency leads to lysosomal dysfunction that results in cellular overexpression of lysosomal proteins in an attempt to compensate
- Lysosome proteins such as cathepsin D (Ctsd) and Lamp1 are increased in the brains of *GRN* knockout mice

Huang et al Acta Neuropath Comm 2020

PGRN deficiency leads to increased expression of lysosomal proteins

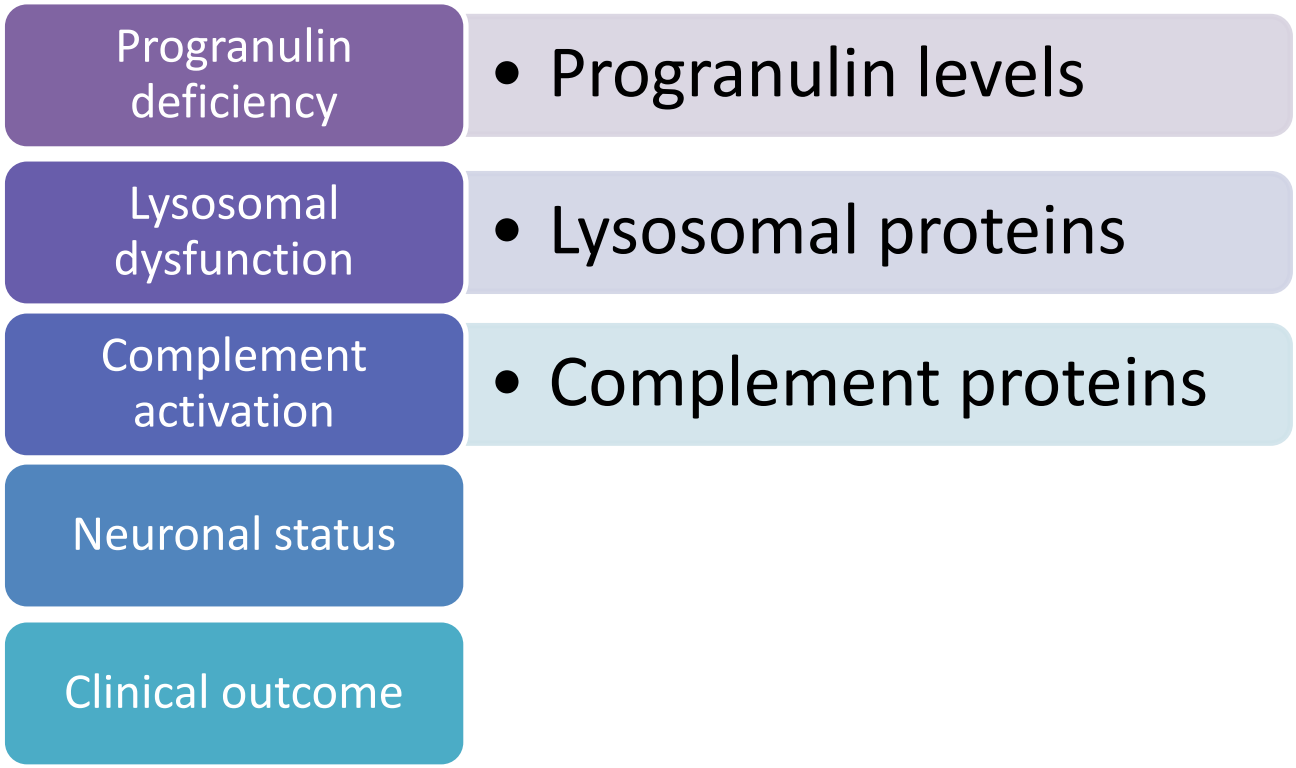




CTSDmat: Mature Cathepsin D; LAMP1: Lysosome associated membrane protein 1

Lysosome proteins such as cathepsin D and LAMP1 are increased in the brains of FTD-*GRN* patients

Gotzl et al Acta Neuropathol 2014


Progranulin deficiency
• Progranulin levels
Lysosomal dysfunction
• Lysosomal proteins
Complement activation
• Complement proteins
Neuronal status
Clinical outcome

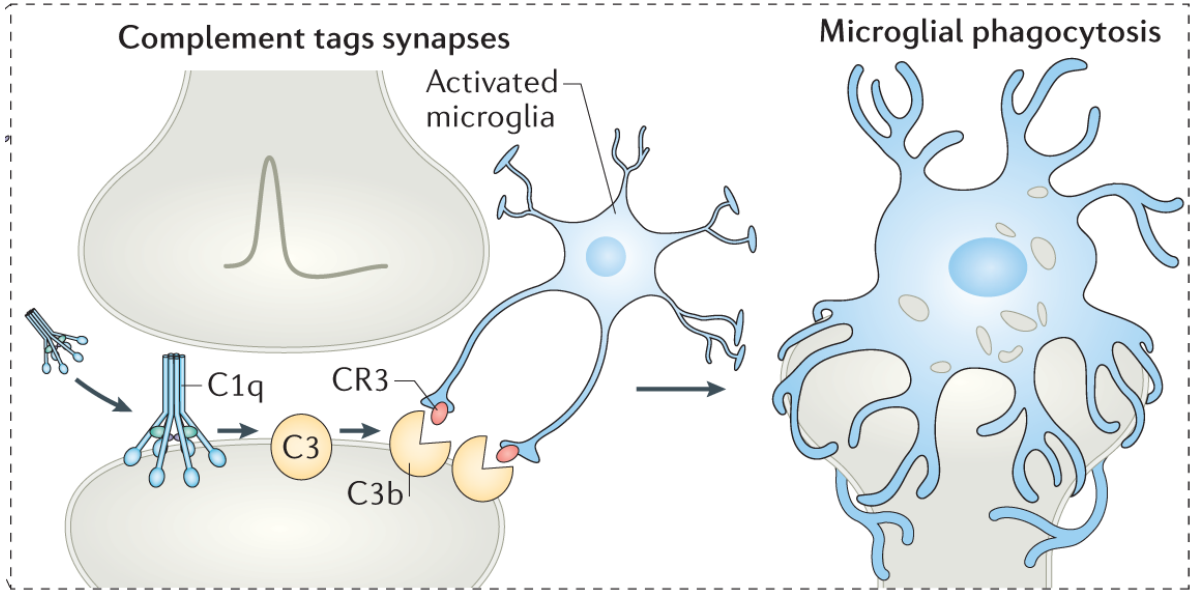
The complement cascade- a key mediator in neurodegeneration and FTD

The complement cascade

Proteolytic cascades of more than 30 proteins

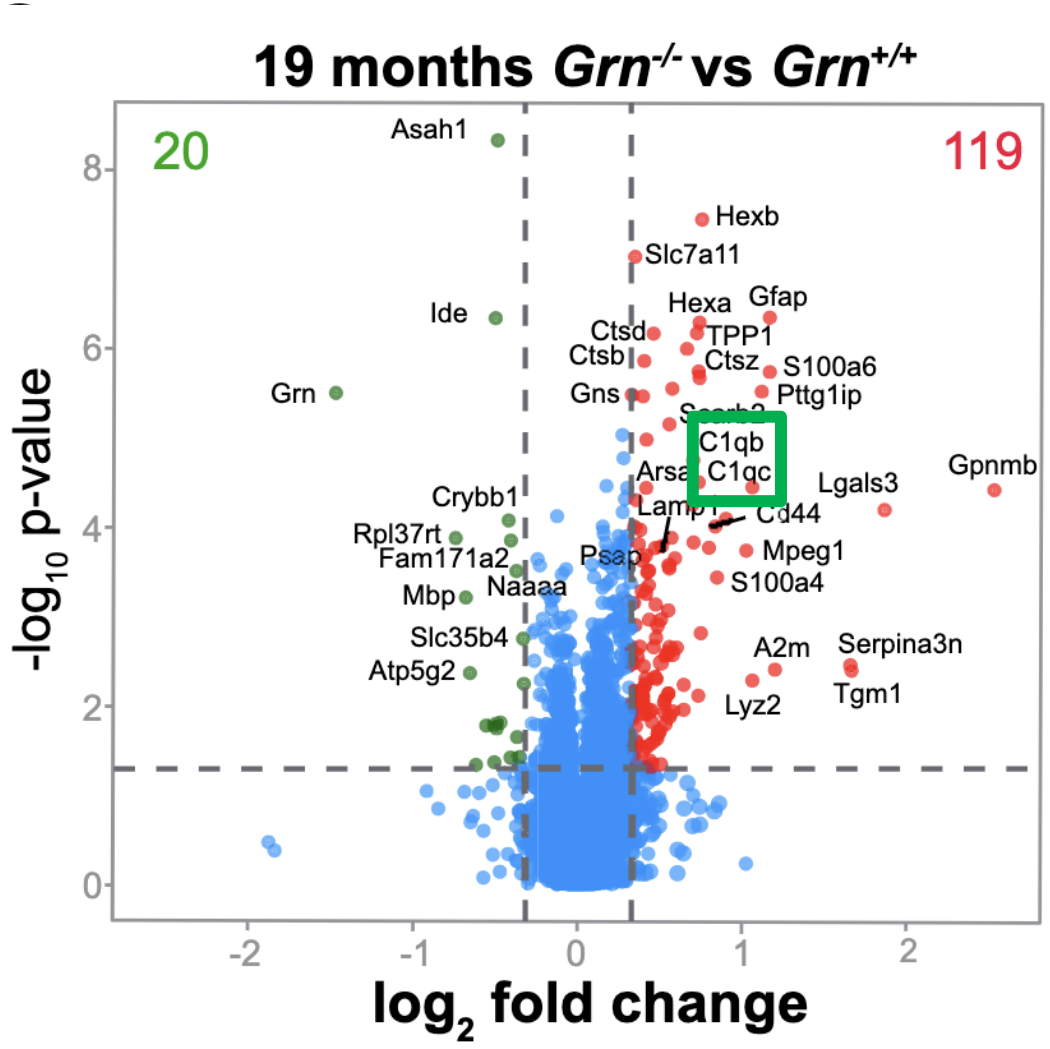
- Generation of proinflammatory mediators
- Opsonization and lysis of pathogenic surfaces
- Pruning and destruction of synapses
- Accumulation of pathological TDP-43 granule

Complement mediates synaptic destruction



Dalakas et al. Nat. Rev. Neurol 2020

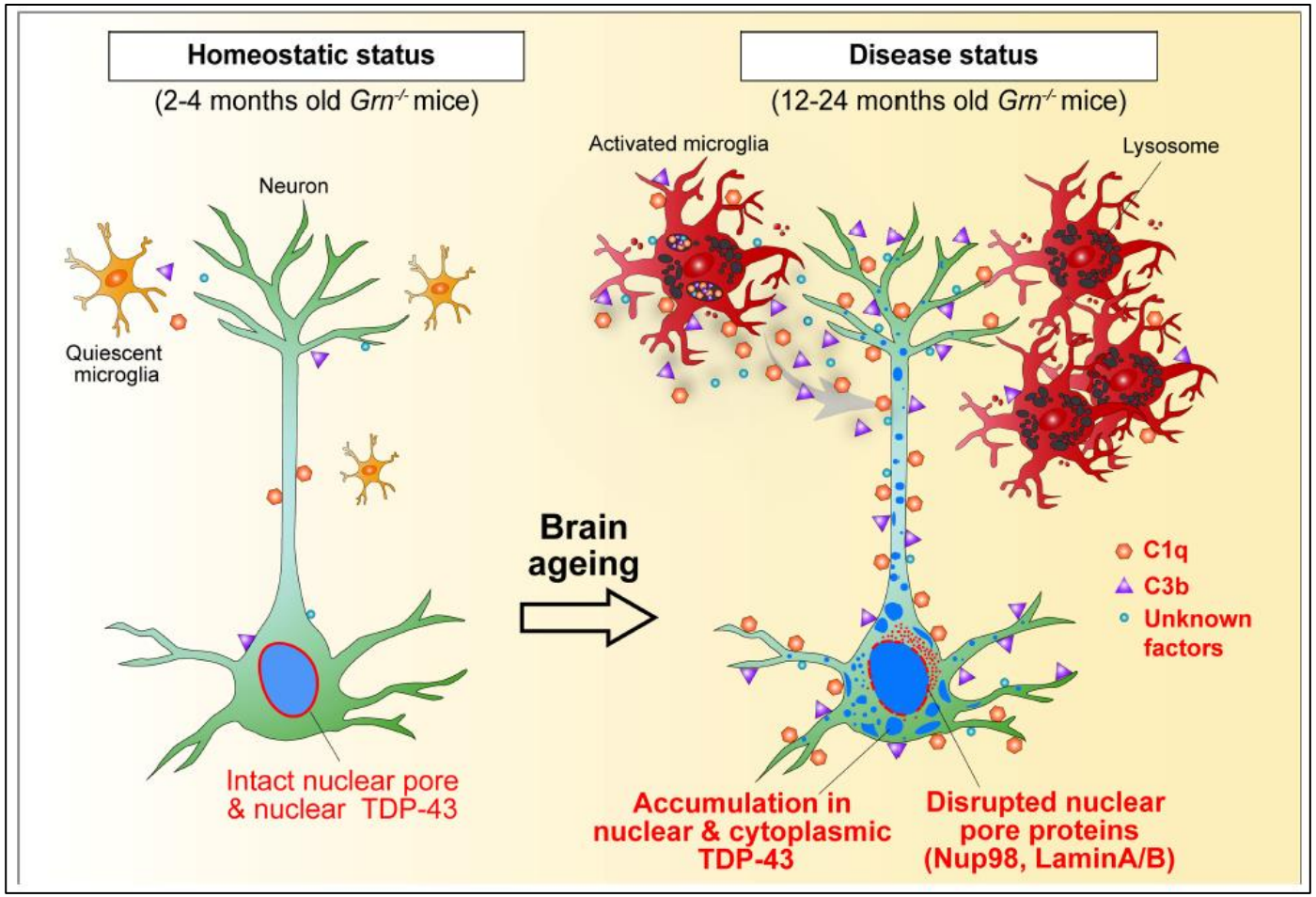
PGRN deficiency leads to increased expression of complement proteins



C1qb and C1qc (subunits that make up the complement protein C1q) are increased in the brains of *GRN* knockout mice

Huang et al Acta Neuropath Comm 2020

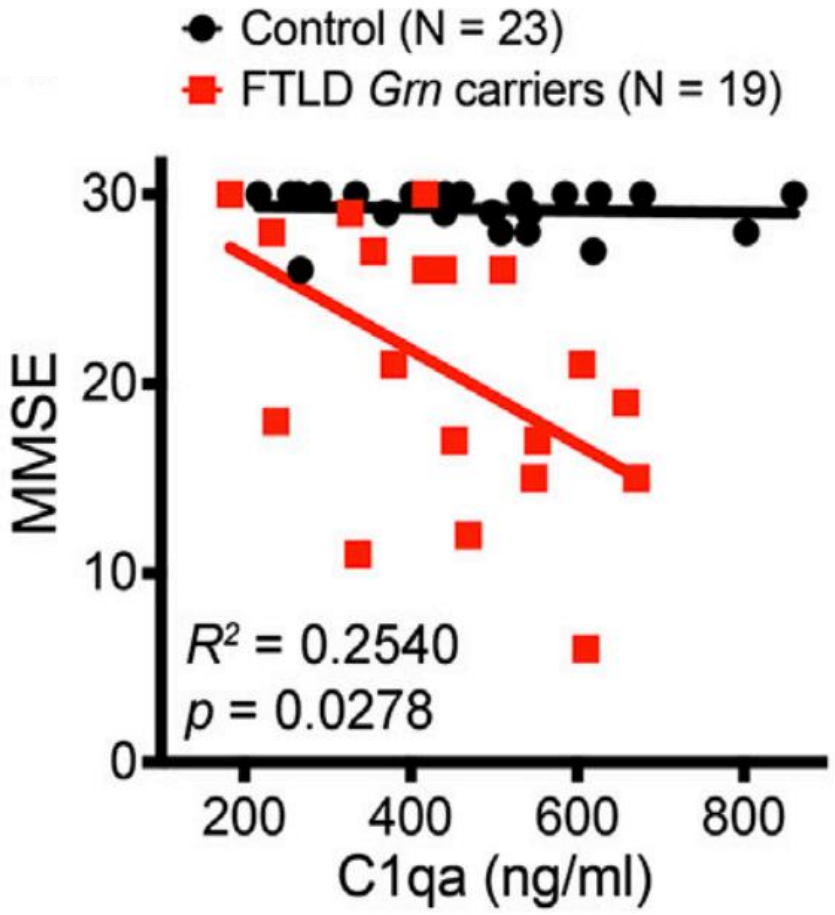
Complement proteins are thought to mediate development of TDP-43 pathology



Increased production of complement promotes TDP-43 granule development in mice

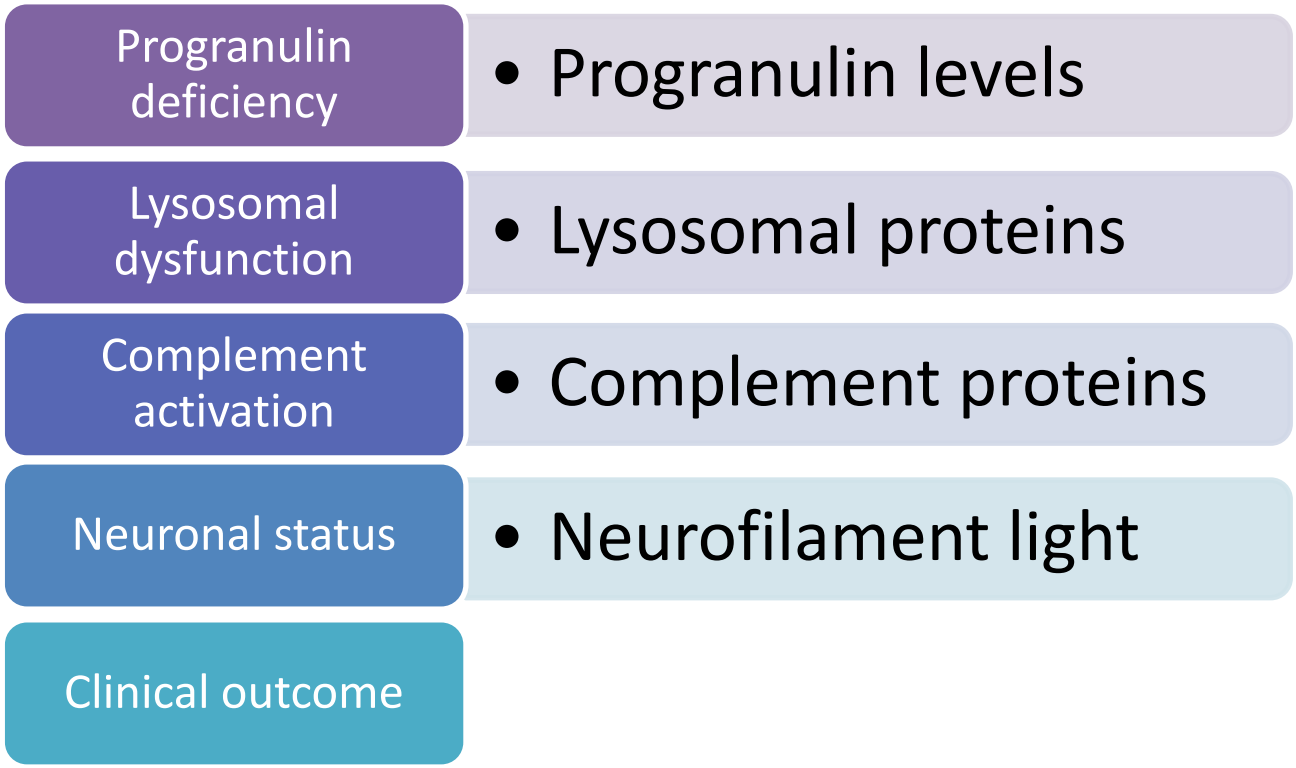
Zhang et al Nature 2020

Complement proteins in CSF of FTD-*GRN* carriers is correlated with clinical state

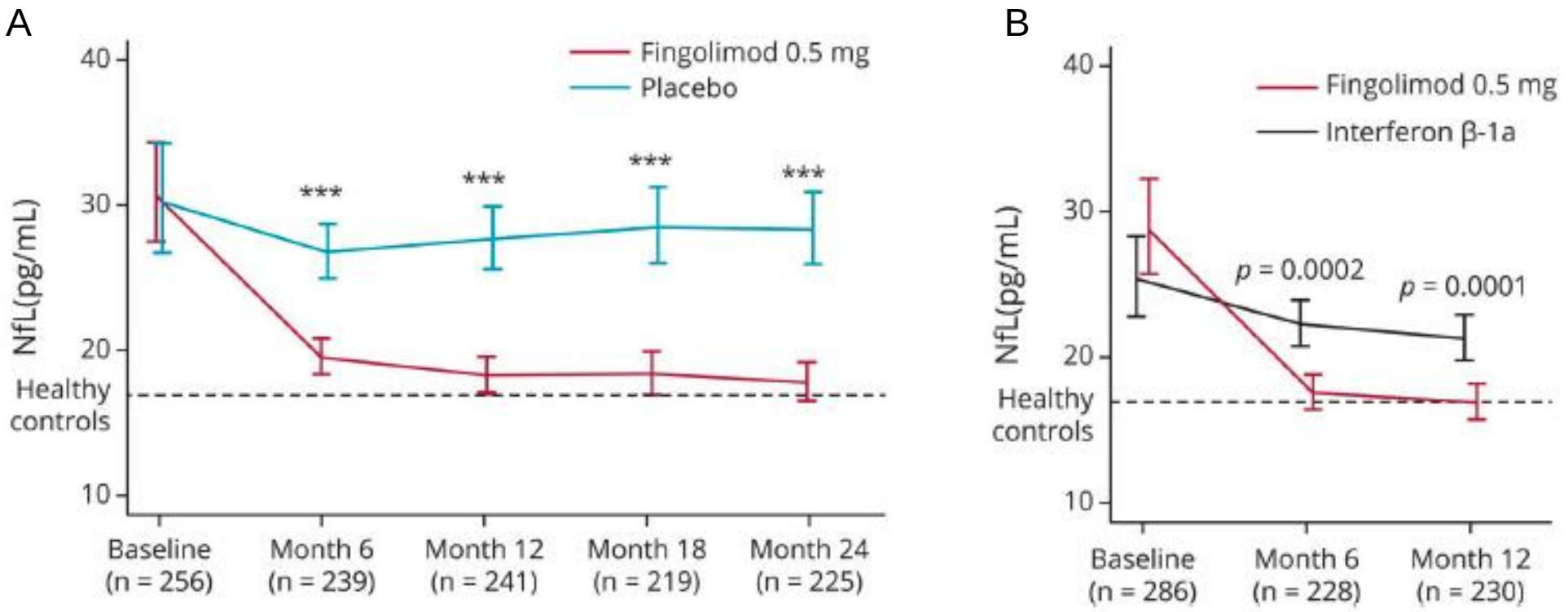


C1qa (a subunit of the C1q protein) levels increase as cognitive function declines (assessed by MMSE score) in FTD-*GRN* carriers

Lui et al Cell 2016


Progranulin deficiency
• Progranulin levels
Lysosomal dysfunction
• Lysosomal proteins
Complement activation
• Complement proteins
Neuronal status
• Neurofilament light
Clinical outcome

Effect of Fingolimod on blood NfL levels in Multiple Sclerosis – FREEDOMS trial (A) and TRANSFORMS trial (B)



Kuhle et al, Neurology 2019

Clinical efficacy in ALS without a change in plasma neurofilament

Table 2. Efficacy Results (Modified Intention-to-Treat Population).*

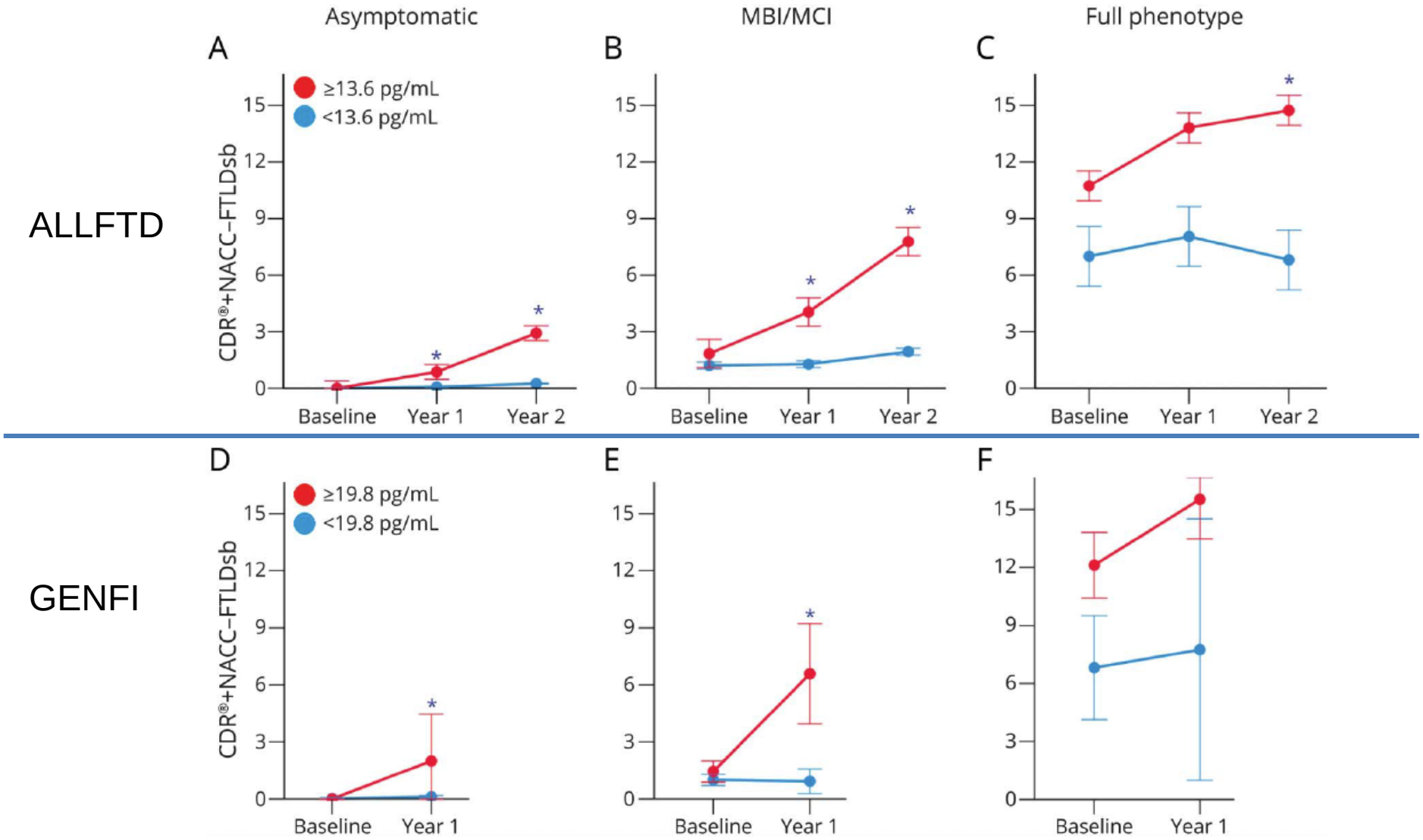
Outcome	Least-Squares Mean Change per Month†		Least-Squares Mean at Week 24†			Estimated Percentage of Patients with Event		Hazard Ratio (95% CI)‡
	Sodium Phenylbutyrate–Taurursodiol (N=87)	Placebo (N=48)	Sodium Phenylbutyrate–Taurursodiol (N=87)	Placebo (N=48)	Least-Squares Difference (95% CI)†§	Sodium Phenylbutyrate–Taurursodiol (N=87)	Placebo (N=48)	
Primary outcome								
ALSFRS-R total score	−1.24±0.12	−1.66±0.16	29.06±0.78	26.73±0.98	2.32 (0.18 to 4.47)¶			
Secondary outcomes: continuous								
ATLIS total score — % of predicted normal value‖	−3.03±0.19	−3.54±0.26	39.08±1.99	36.26±2.22	2.82 (−0.67 to 6.31)			
ATLIS upper-limb score — % of predicted normal value‖**	−3.04±0.23	−3.81±0.31	36.63±2.32	32.36±2.59	4.27 (0.16 to 8.38)			
ATLIS lower-limb score — % of predicted normal value‖**	−2.98±0.24	−3.36±0.33	41.17±2.37	39.09±2.66	2.09 (−2.23 to 6.41)			
Plasma pNF-H level — pg/ml	3.58±3.19	−2.34±4.20	406.95±35.82	374.25±38.81	32.70 (−24.34 to 89.75)			
Slow vital capacity — % of predicted normal value	−3.10±0.31	−4.03±0.42	66.17±2.33	61.06±2.81	5.11 (−0.54 to 10.76)			
Secondary outcomes: survival								
Death, tracheostomy, or hospitalization††						19.3±4.2	33.1±6.9	0.53 (0.27 to 1.05)
Death or tracheostomy††						2.8±1.7	4.4±3.0	0.63 (0.11 to 3.92)
Hospitalization						17.5±4.1	29.7±6.6	0.54 (0.27 to 1.12)

- Sodium phenylbutyrate–taurursodiol resulted in slower functional decline than placebo as measured by the ALSFRS-R score over a period of 24 weeks.

- The mean rate of change in plasma pNF-H levels did not differ significantly between the two groups over the 24-week trial duration.

Pagnoni et al, N Engl J Med 2020

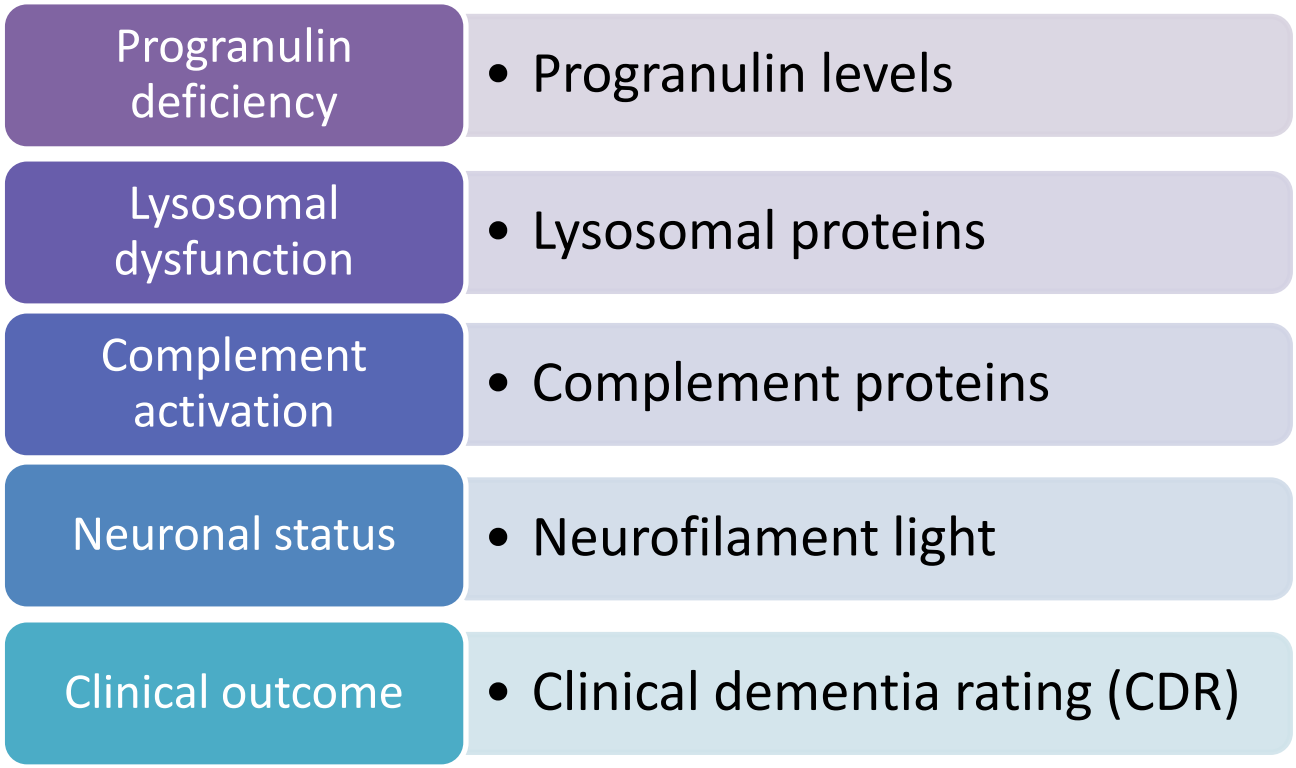
Prediction of clinical progression by plasma NfL in familial FTLD



CDR+ NACC-FTLD can stratify patients by level of global impairment, delineating MBI/MCI a prodromal state of mild disease between asymptomatic and full phenotype

Rojas JC *et al.*, Neurology 2021

Biomarker data in combination with clinical outcome may reveal clinical efficacy of treatment



- The totality of the biomarker data may provide evidence for treatment impact on the key nodes of the pathophysiology of FTD
- Treatment impact on different nodes of the disease cascade may be evident on different timescales
- Biomarker data may bolster confidence in what is observed with the clinical outcome data

Thanks!!

UNIVERSITY OF GOTHENBURG

Looking ahead to AAIC

Robert Paul, MD, Ph.D.

Chief Medical Officer

ALECTOR

Measuring the effects of AL001 on disease cascade

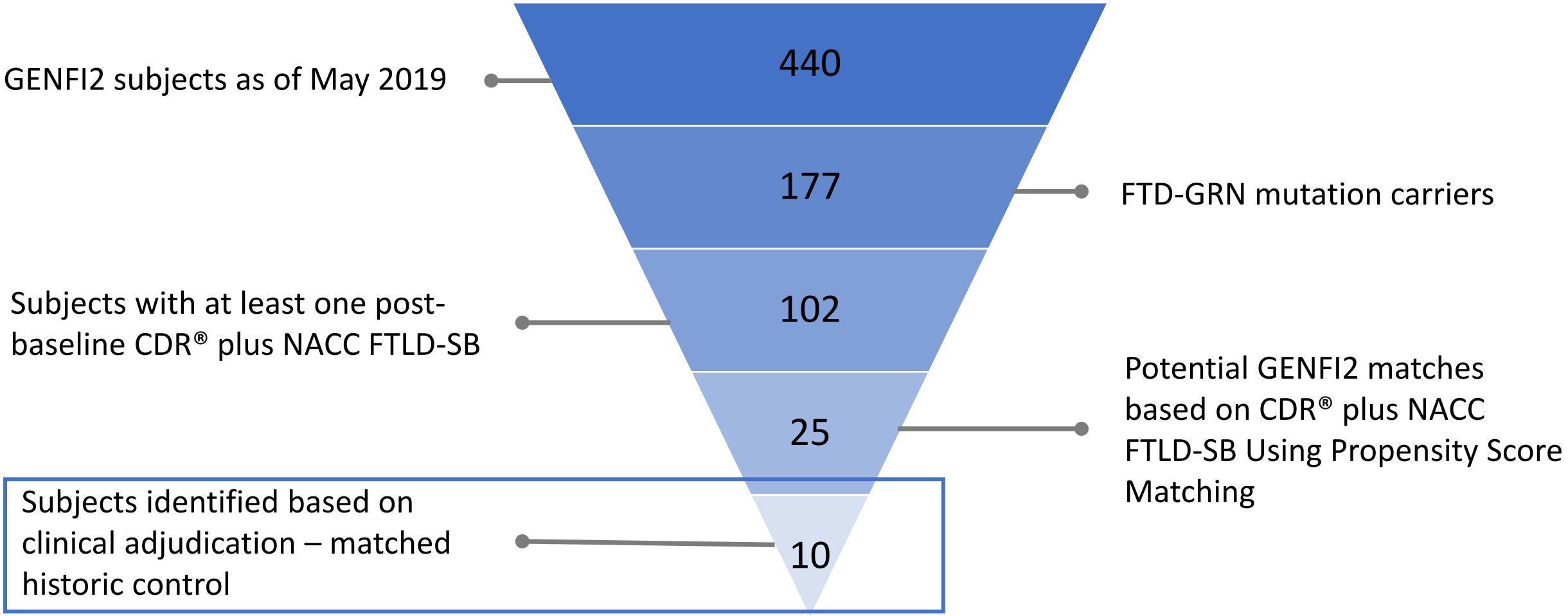
Proof of mechanism

Biomarkers of activity

Proof of efficacy

PGRN in plasma and CSF	**E.g. Cathepsin D & LAMP1**	**E.g. C1QB**	**NfL vMRI**	**CDR® plus NACC FTLD-SB**
• Proof of mechanism	• Lysosomal dysfunction and impaired proteostasis are a hallmark of FTD-GRN brains	• Complement proteins are known to correlate with cognitive decline	• Neurofilament light chain is a measure of axonal damage • vMRI is a measurement of brain atrophy	• Current gold standard for measuring decline in FTD

Creating a matched historic control from GENFI



AL001 Phase 2 data set to be presented at AAIC

12-month data in symptomatic FTD-GRN patients

Primary endpoint

- Safety and tolerability in symptomatic FTD-GRN patients

Secondary endpoint

- Progranulin level changes in plasma and cerebrospinal fluid (CSF)

Exploratory endpoints

- Changes in CDR-NACC-FTLD-SB scale at 12 months with GENFI matched controls
- Changes in biomarkers of lysosomal dysfunction, complement activation and neuronal health at 12 months
- Changes in volumetric MRI with GENFI matched controls

Q&A
Shehnaaz Suliman, MD
President and Chief Operating Officer