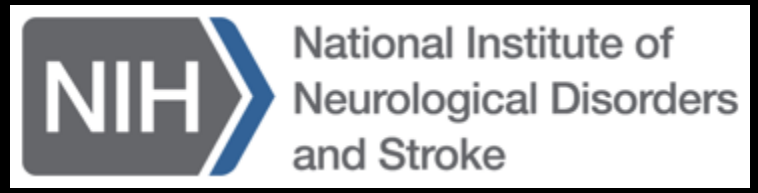
Future directions in the Genomics of ALS: importance of biobanking

Bryan J. Traynor

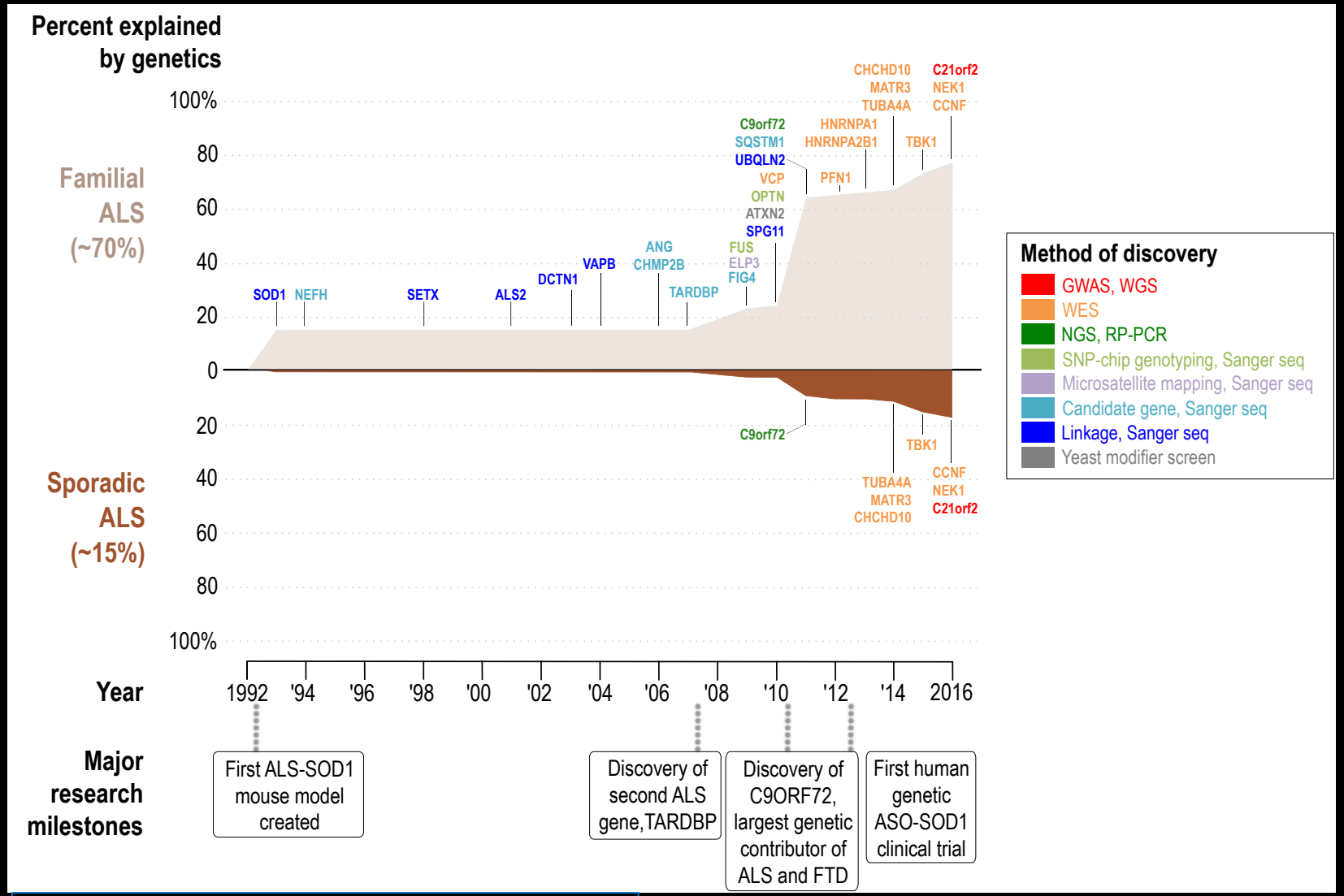
NIA

Funding



European and US patent on *C9orf72* testing and diagnostic applications

Timeline of ALS genetics



Chia *et al*, Lancet Neurology 2018

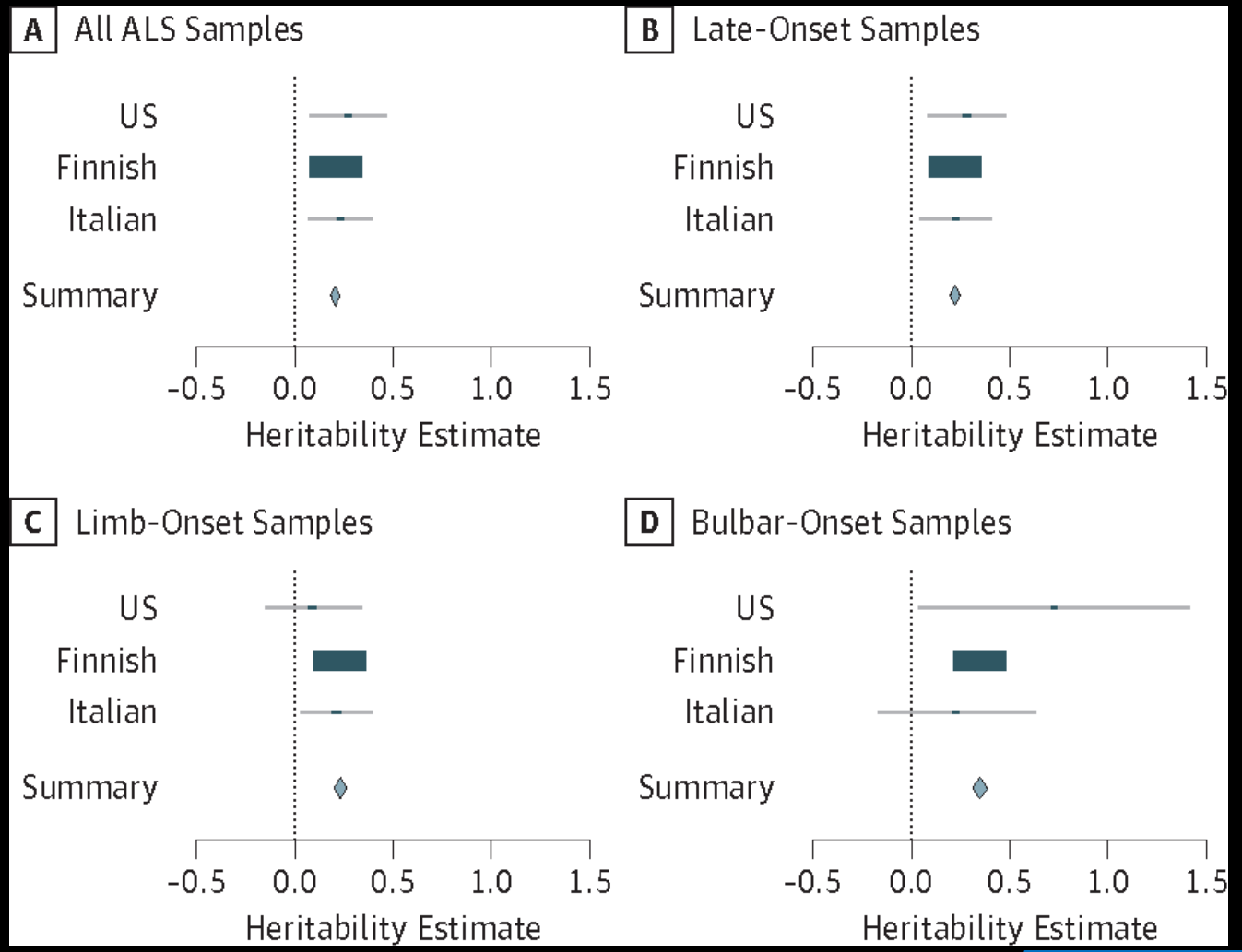
How did we get here?

Familial ALS	Sporadic ALS
• Collection of families • small numbers • Clues from pathology • Linkage/positional cloning • Exome sequencing • Whole genome sequencing	• Large cohorts • GWAS • Exome • Whole genome sequencing

When should we stop?

Heritability estimates

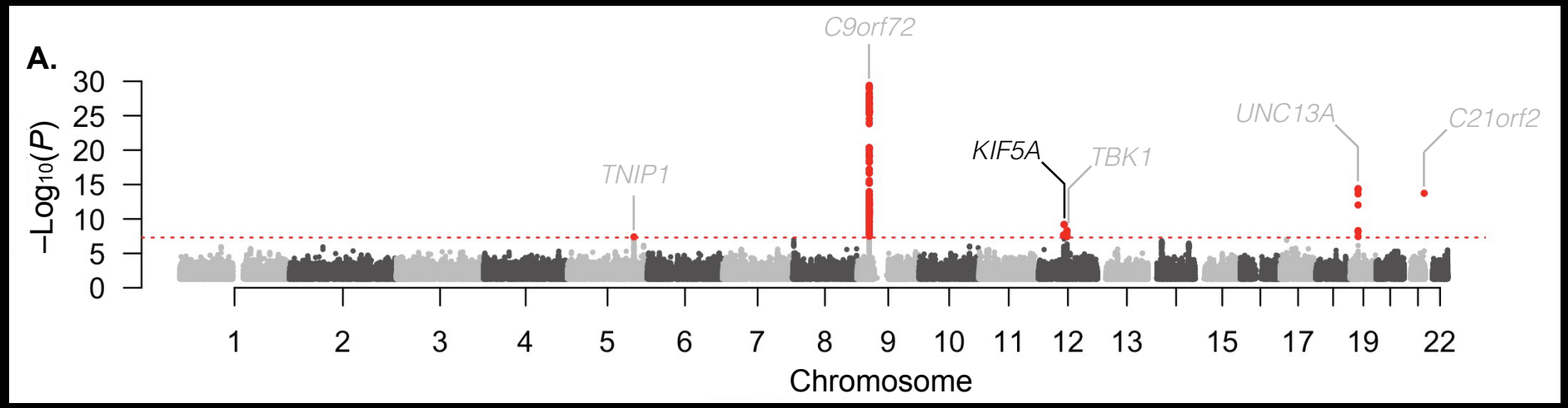
GWAS = 4.2%



Floor estimate!

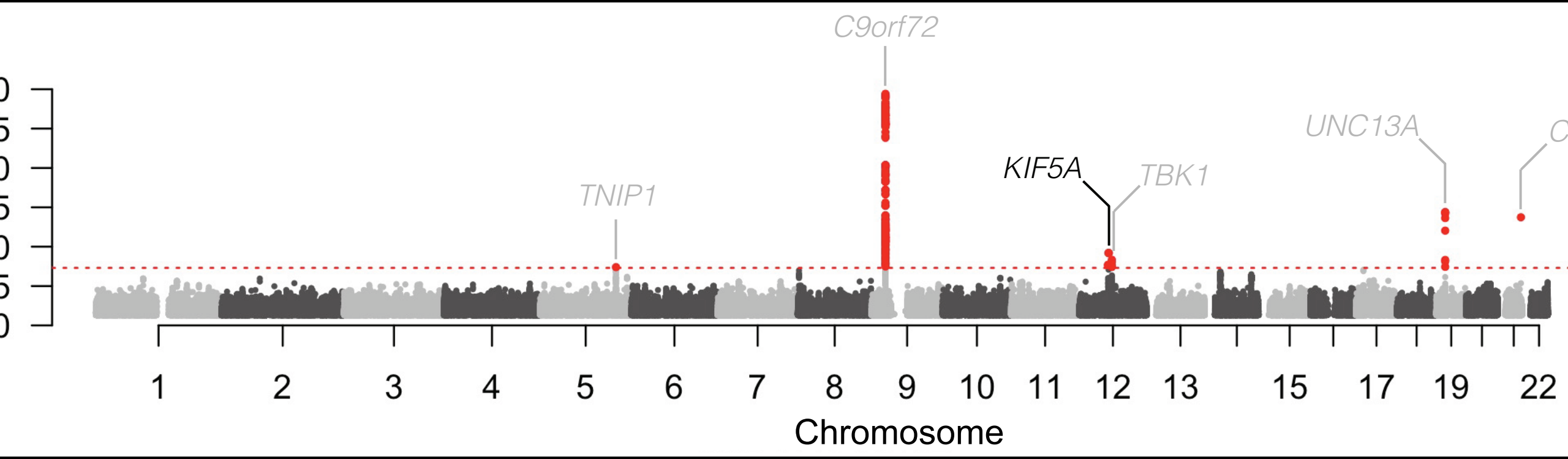
Keller *et al*, JAMA Neurology 2014

Look at the sub-significant peaks



20,806 ALS cases and 59,804 controls

Look at the sub-significant peaks



What is the key value of brain bank?

- Currently
- Genomics

- When we find a gene in the big cohorts, the first thing we do is use a cheaper technology to screen additional sample

- Then if we get lucky enough to find a mutation in the gene of interest, then we ask Kit or Thor to look at the pathology

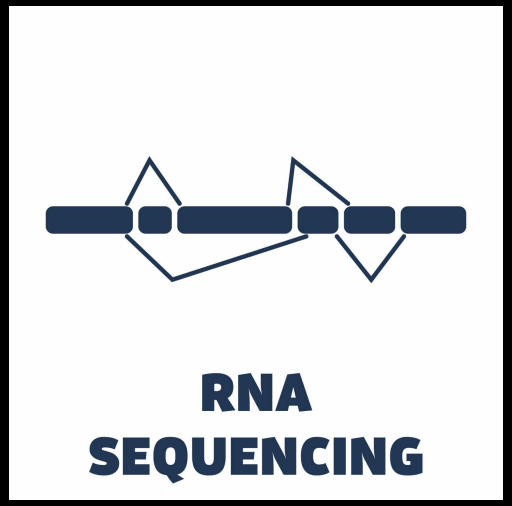
- This has happened several times recently!

What is the future of brain banks?

Increase cohort size

Controls

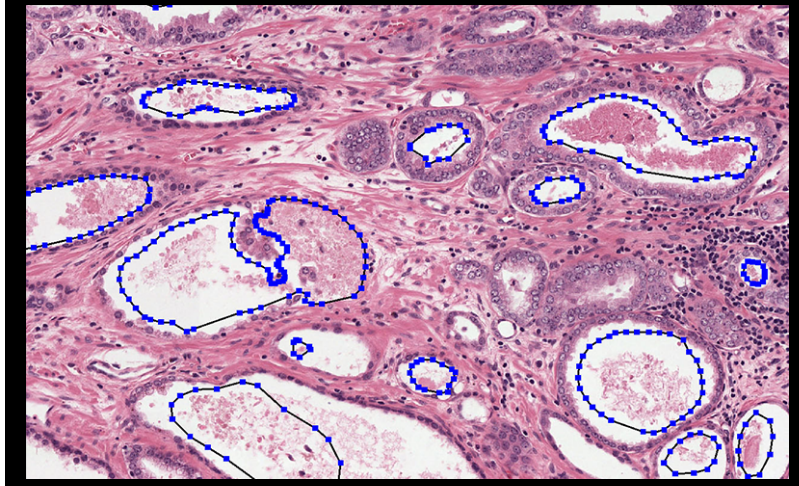
What is the future of brain banks?



Molecular characterization

What is the future of brain banks?

Automated quantitative pathology



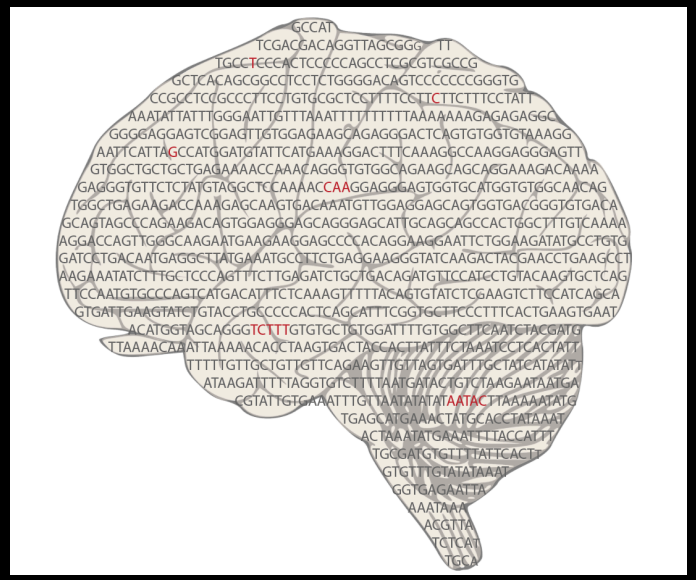
Automated image analysis

Automated quantitative pathology

What is the future of brain banks?

- Electronic health records

BrainbankSeq



- Resource building
- Discovery acceleration

Two U.S. Brain Banks

Banner Health Brain Bank

Johns Hopkins BRC

Image source: Harvard Brain Tissue Resource Centre

Include VA Brain Bank

- Whole genome sequence data
- n = 300 brains
- Sequencing at Uniformed Services University
- Timeline = early 2021

VA | U.S. Department of Veterans Affairs

Questions