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
<table>
<thead>
<tr>
<th>Familial ALS</th>
<th>Sporadic ALS</th>
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<tbody>
<tr>
<td>• Collection of families</td>
<td>• Large cohorts</td>
</tr>
<tr>
<td>• small numbers</td>
<td>• GWAS</td>
</tr>
<tr>
<td>• Clues from pathology</td>
<td>• Exome</td>
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<tr>
<td>• Linkage/positional cloning</td>
<td>• Whole genome sequencing</td>
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When should we stop?

Heritability estimates

GWAS = 4.2%

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
What is the future of brain banks?

• Electronic health records
BrainbankSeq

Resource building

Discovery acceleration
Two U.S. Brain Banks
Include VA Brain Bank

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