Andrew Singleton, Chief of the Laboratory of Neurogenetics
Our Priority – Diseases of Aging

• Alzheimer’s disease
  • 5 million in the US currently affected ($203 billion)
  • 15 million by 2050 ($1.2 trillion)

• Parkinson’s disease
  • 1 million in the US currently affected ($25 billion)
  • 4 million by 2050 (~$150 billion)

• Amyotrophic Lateral Sclerosis
  • 30,000 in the US currently affected ($300 million)
Our Path

1. Identify the locus
2. Find the gene
3. Understand the pathobiology
4. Identify a target
5. Treatment
Genetics of Parkinson’s Disease

Frequency in the population

Risk of Disease

Genetics of Parkinson’s Disease

Frequency in the population

Risk of Disease


SNCA

PARK2

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National Institute on Aging
Turning discovery into health
Genetics of Parkinson’s Disease

Frequency in the population

Risk of Disease

SNCA  LRRK2
PARK2  PINK  DJ1

GBA


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Genetics of Parkinson’s Disease

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GBA  LRRK2  SNCA
Genetics of Parkinson’s Disease

Frequency in the population

Risk of Disease

SNCA  LRRK2
PARK2  PINK 1  DJ1
FBXO7  VPS35  ATP13A2
PLA2G6  SYNJ1

GBA
LRRK2

HLA  LRRK2
SNCA  MAPT  SYT11
GAK  STK39  STX1B
GPNMB  BST1
RAB7L1  LAMP3  HIP1R
SCARB2  STBD1  ACMSD  FGF20

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NIH
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Our Progress

• Massive international collaborative study
  • Collected DNA on 20,000 PD patients, and 80,000 people without disease

• Assessed variability in their genetic code (~20 million common changes)

• Looked for genetic variants that are more frequent in one group versus the other
Our Progress

• Took 3 years of work at sites across the US
• Lead by our laboratory within the Intramural Research Program of NIA
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MCC1  GAK  STK39  STX1B
SIPA1L2  GPNMB  BST1  GBA
SNCA  RAB7L1  LAMP3  HIP1R
INPP5F  SCARB2  STBD1
CCDC62  ACMSD  FGF20  HLA
Mir4697  DDRGK1  VPS13C  GCH1
RIT2

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Pathways of Disease

Risk of Disease

Frequency in the population

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Summary

• We have made incredible progress in the genetics of age related disease
  • Still a great deal to do
  • We have the infrastructure and knowhow to finish this task

• Concurrently we must work to understand the molecular processes that are disease
  • An incredible challenge, but our surest route to an effective treatment
Our People