



Is Parkinson's Disease In Your Genes? Genetics and PD

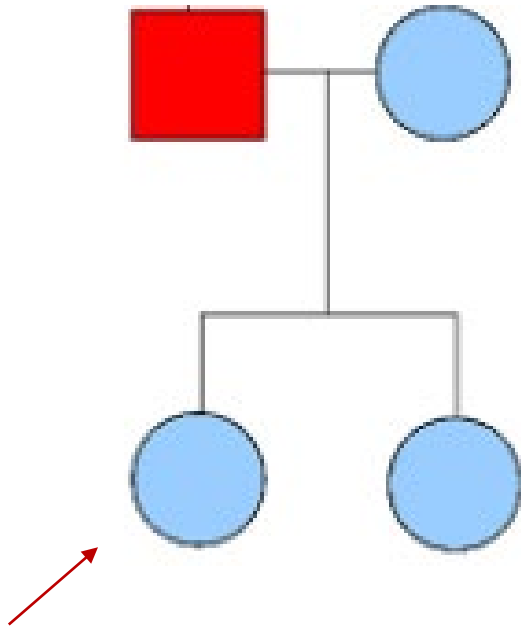
Allison Daley, MS, MPH
Licensed Genetic Counselor
Department of Neurology
The Ohio State University

Today's Objectives

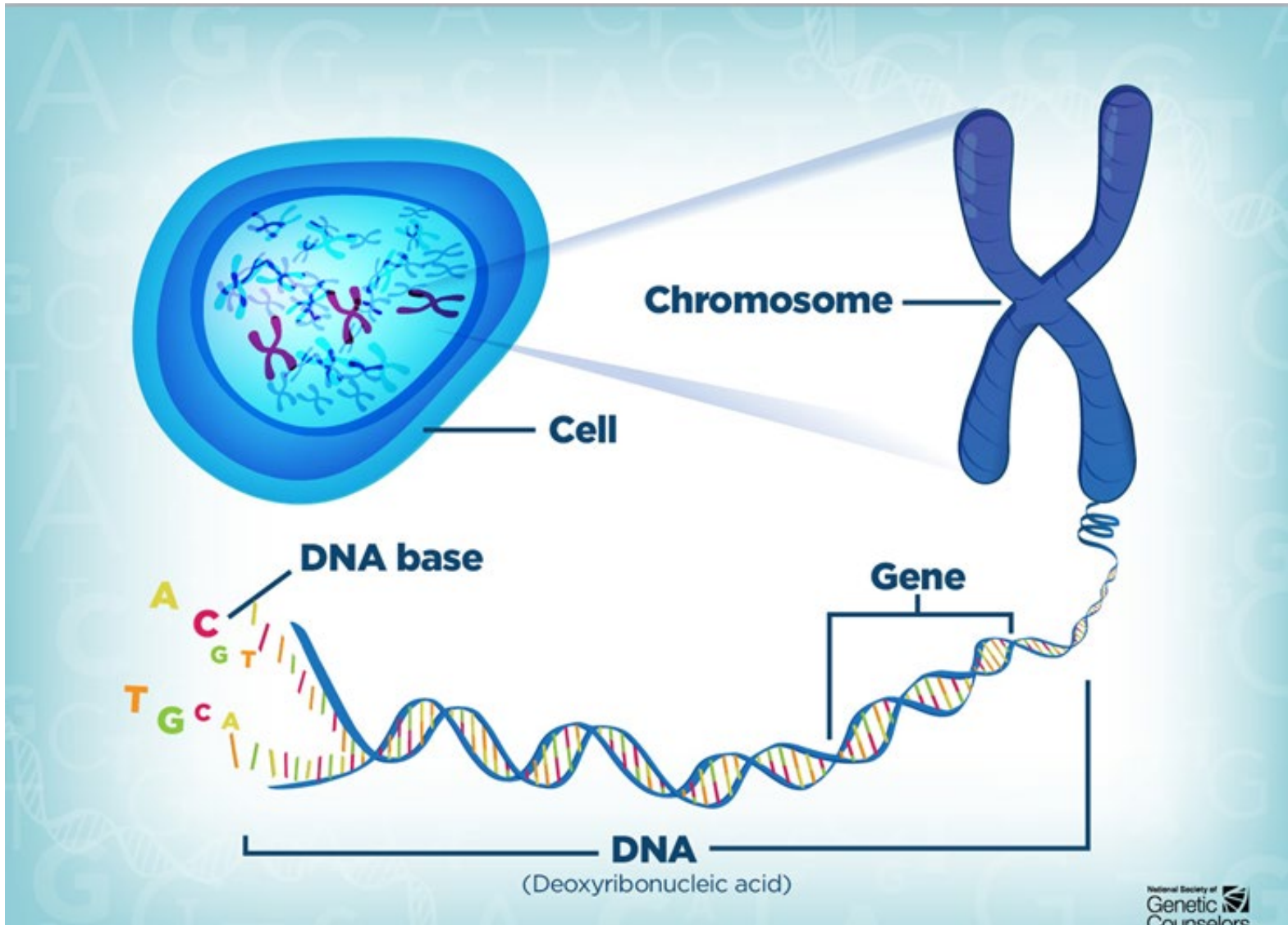
- Review the causes of PD focusing on the role of genetics in the risk for PD
- Explore how genetic variants influence PD risk
- Examine the role of genetic testing for PD

Family History: Clues for a Genetic Cause

- 15% of people with PD have a first degree relative with PD
- Risk for first degree relatives ~8%



What are genes?

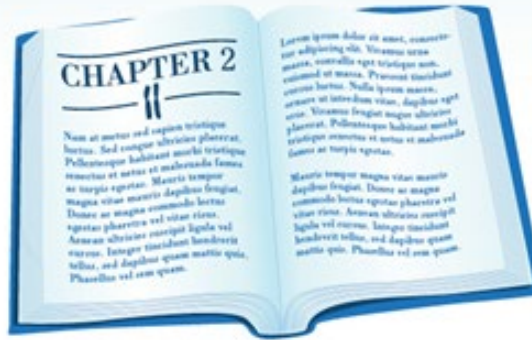


National Society of
Genetic
Counselors

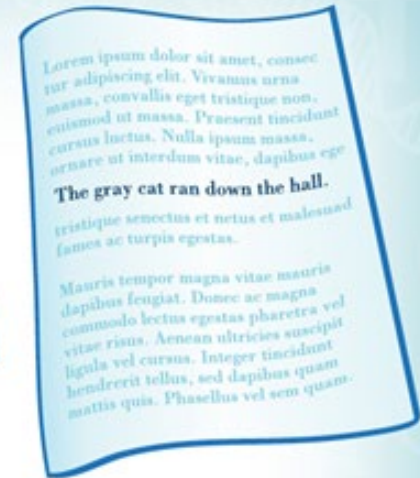




BOOK - GENOME

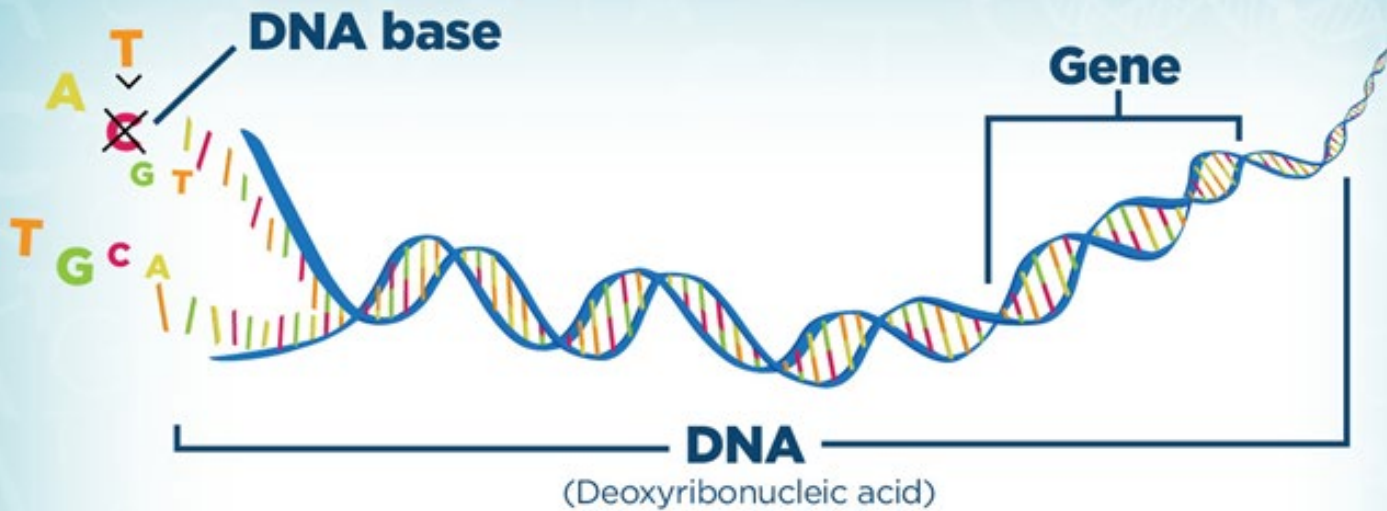


CHAPTERS - CHROMOSOMES



SENTENCE - GENE





The gray cat ran down the hall.
The gray cat ran down the ball.

Changes in DNA might change the way a gene works.



A Genetic Link In Parkinson's Disease?

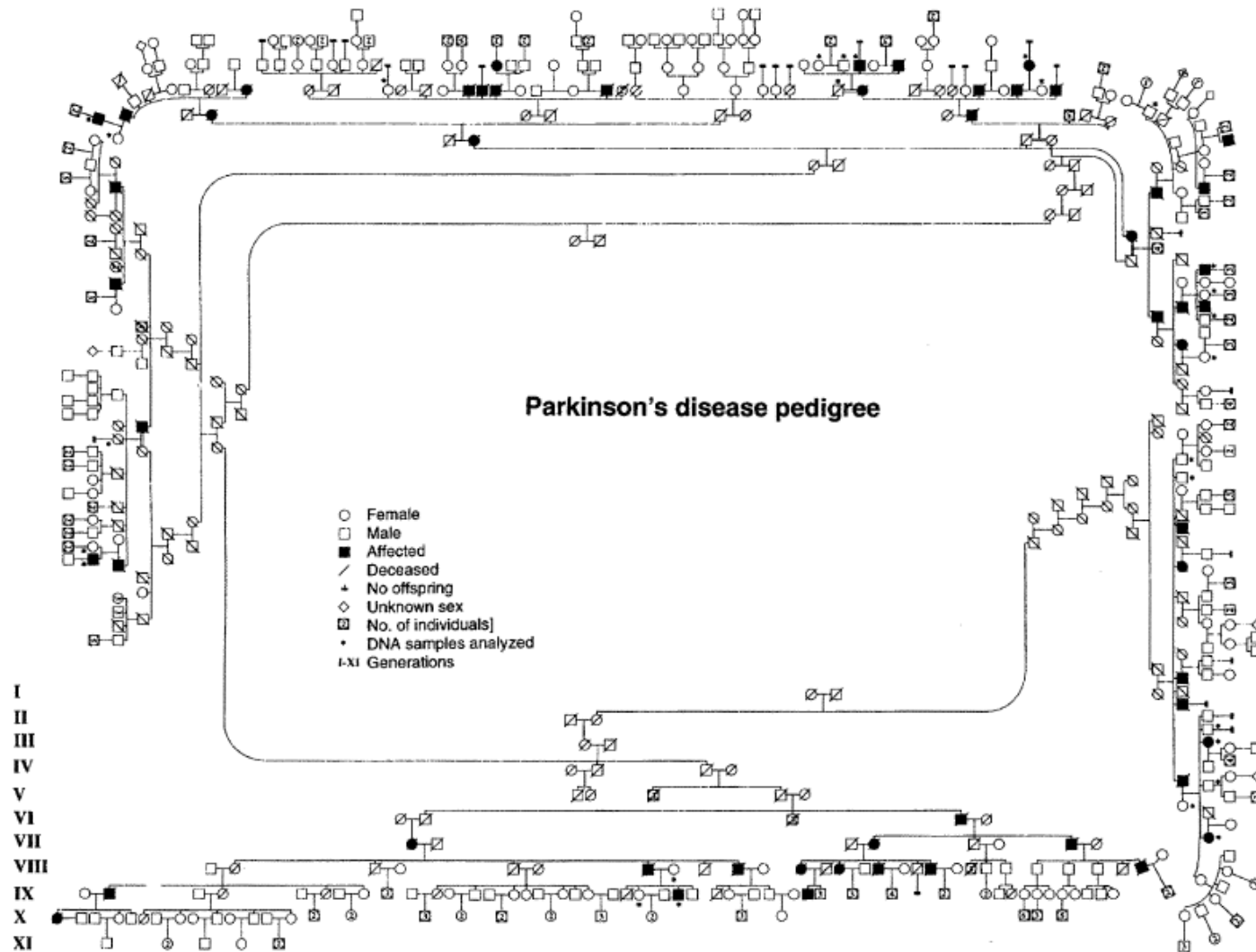
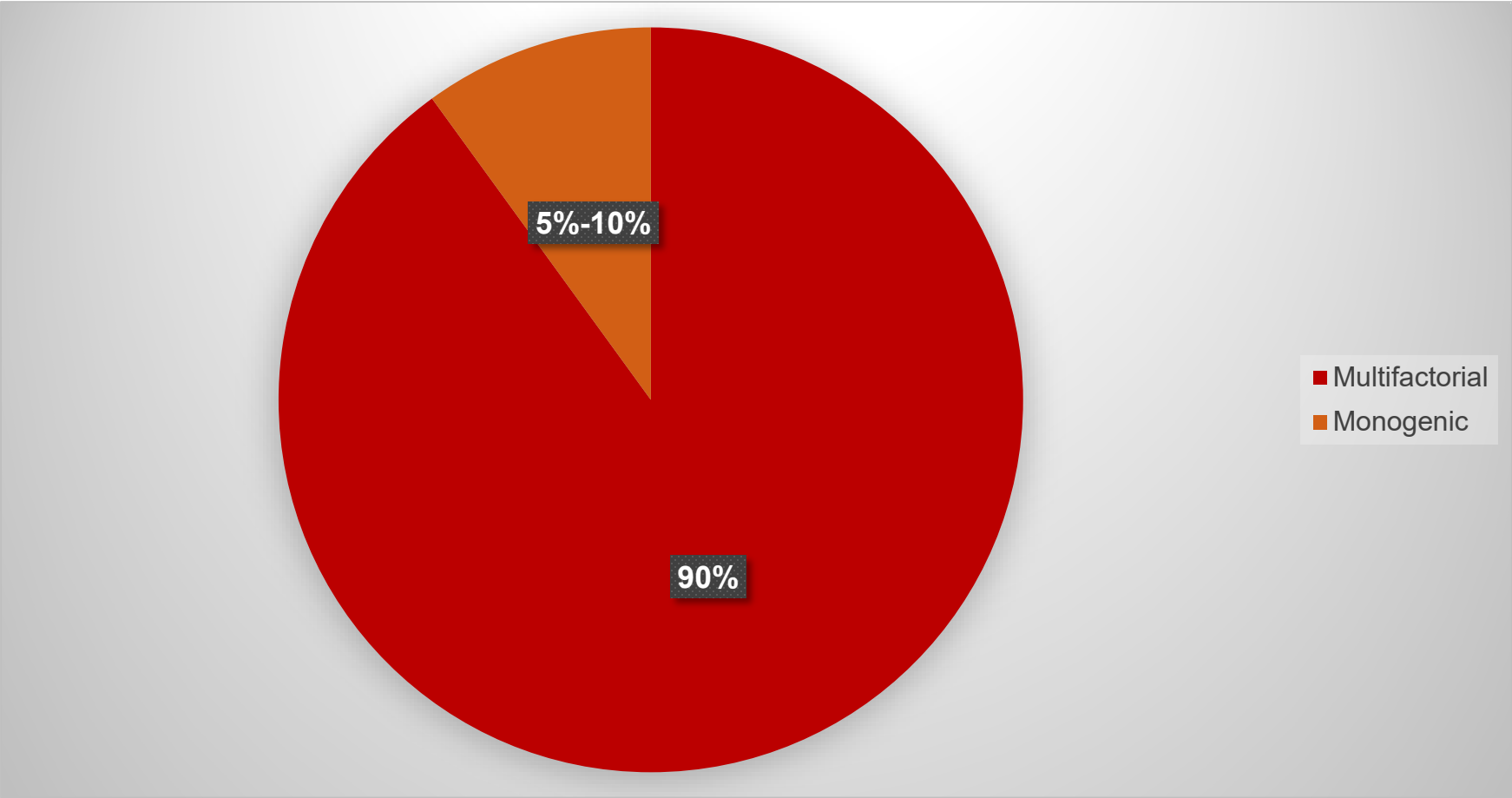
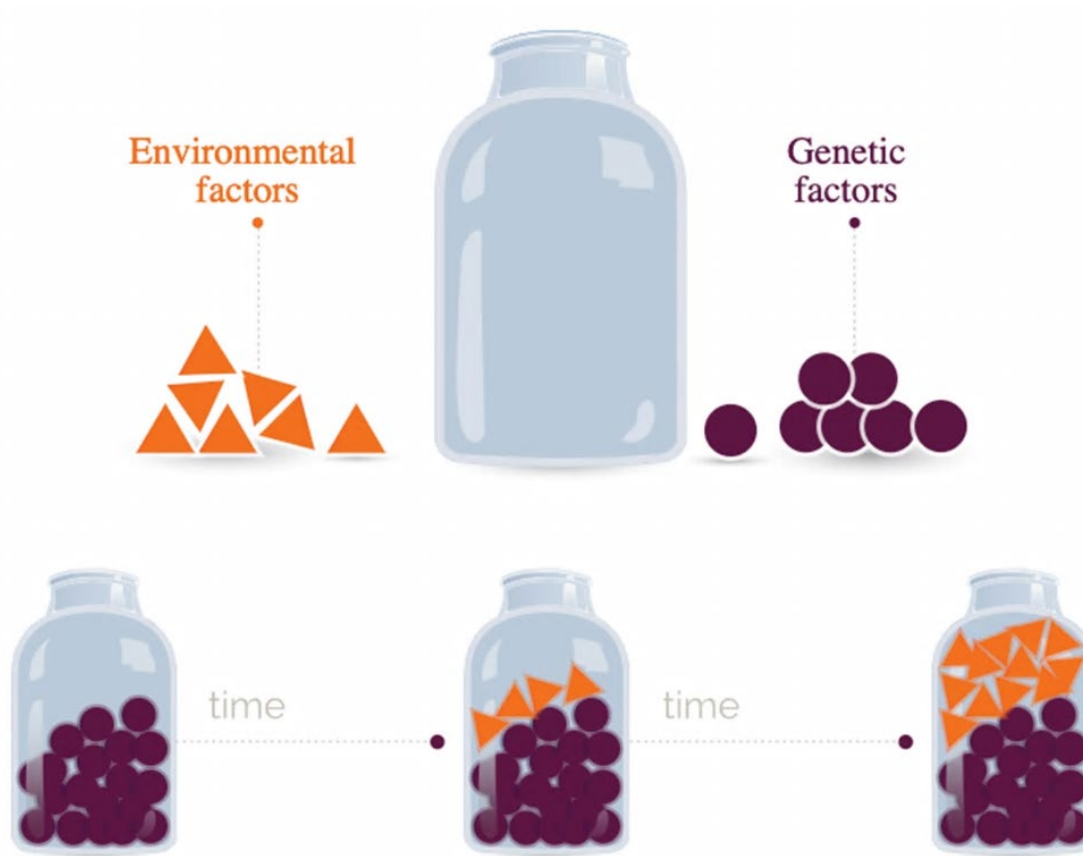


Fig. 1. A large family with PD. The clinical and pathological features of some members of this kindred were previously reported (11).

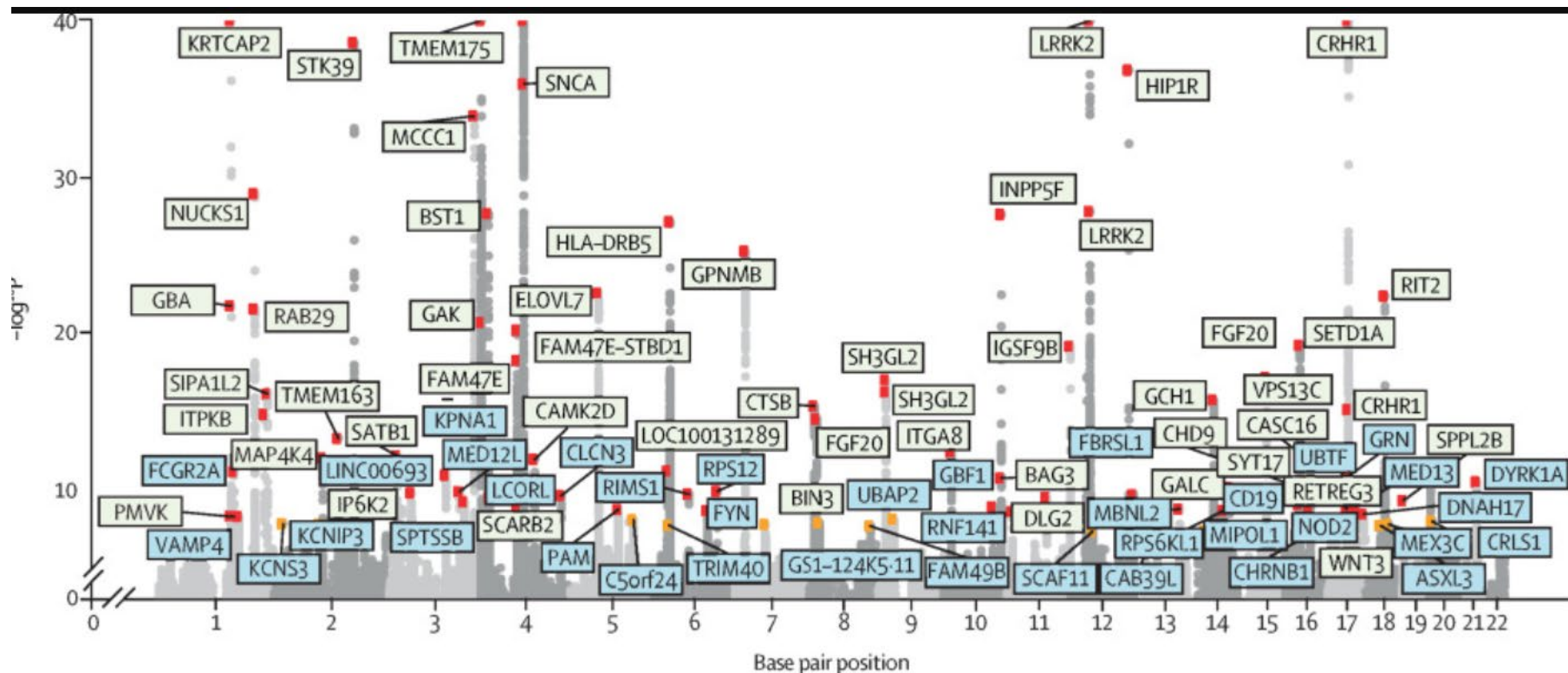
Parkinson Disease Cases



Multifactorial Inheritance and PD

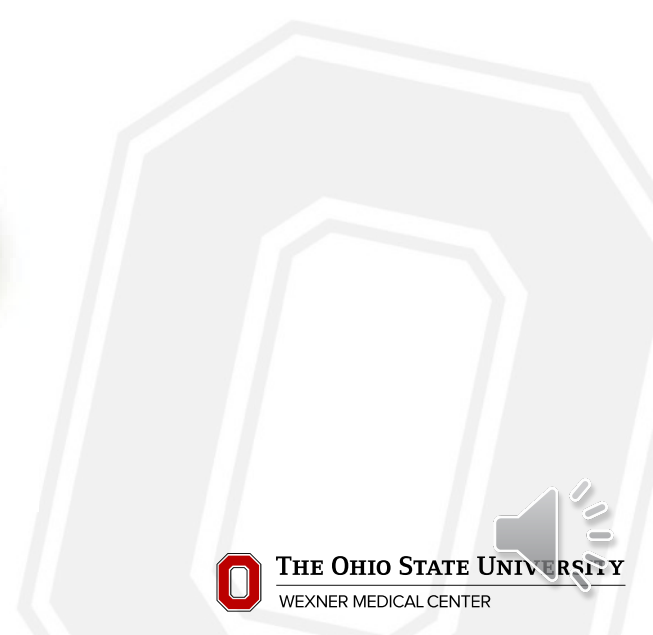
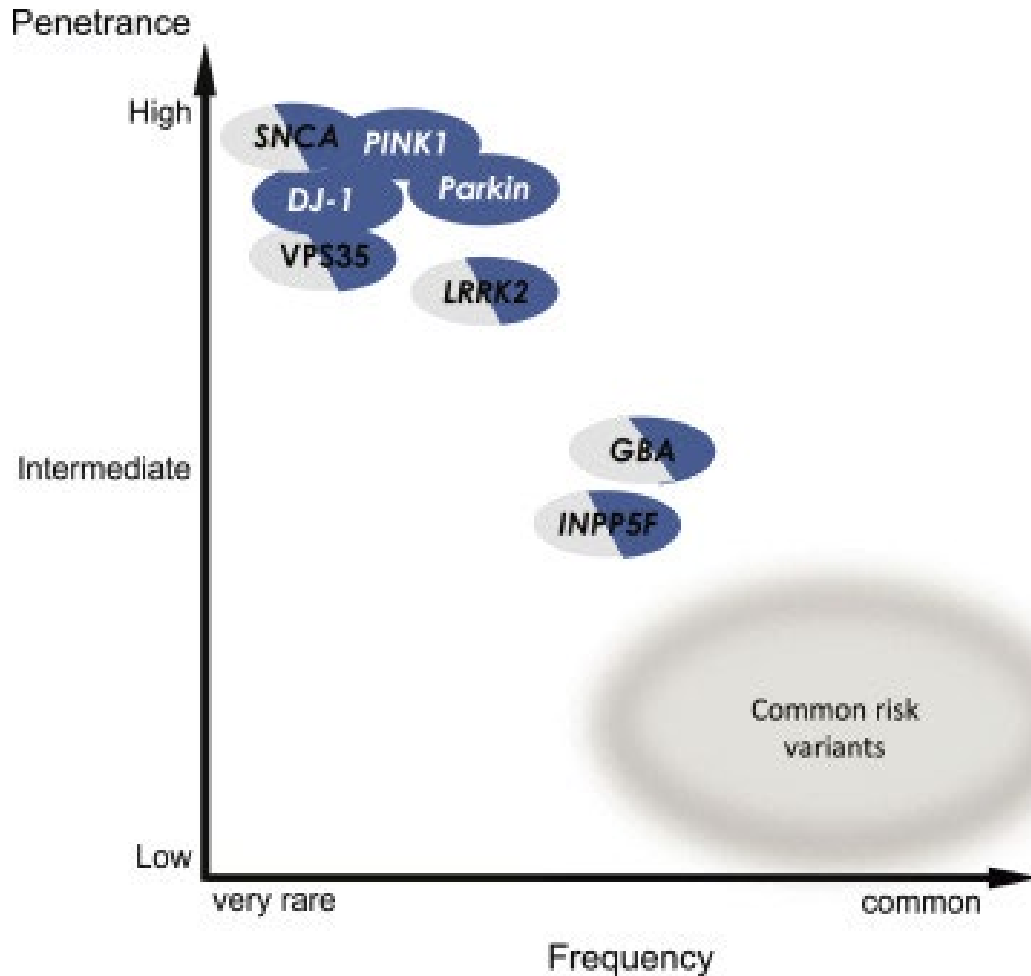


Genetic Risk Factors for PD



Nalls, M.A. et al (2019) Identification of novel risk loci, causal insights, and heritable risk for Parkinson's disease: a meta-analysis of genome-wide association studies. *The Lancet. Neurology*, 18(12), 1091–1102. [https://doi.org/10.1016/S1474-4422\(19\)30320-5](https://doi.org/10.1016/S1474-4422(19)30320-5)

Genetic Variants and PD Risk



PD and Genetic Testing – Commercial Testing

- Done in clinic and ordered by clinician or genetic counselor
- Recommendations for clinical testing in PD:
 - Positive family history (first degree relatives, multiple generations)
 - High-risk ethnicity (ex. Ashkenazi Jewish, North African Berber)
 - Young onset
- Testing for more common, lower risk variants not widely available or clinically useful
- Genetic testing in PD is expanding

Risks and Limitations to Genetic Testing

- Risks and limitations
 - Testing may be incomplete/penetrance may be low
 - Significance of results may be unclear
 - Does not alter medical management
 - Results may have psychological, social, professional implications
- Genetic Counseling Recommended

Genetic Testing for PD – Direct-to-Consumer

- *GBA*
 - Gaucher Disease (recessive)
 - N370S variant
 - Common in Ashkenazi Jewish populations
 - Incomplete penetrance → Not all carriers develop PD
- *LRRK2*
 - G2019S variant
 - Common in Ashkenazi Jewish and North African Arab populations
 - Incomplete penetrance → Not all carriers develop PD



Genetic Testing for PD – Research

- Testing done in the context of a research study
- May or may not receive results



PD GENERation:
Mapping the Future of
Parkinson's Disease
Help us change the course of Parkinson's

parkinson.org/PDGENERation



Why Genetic Testing in PD?

- Individuals
 - Provide a causal explanation of PD *in a minority of people*
 - Clarify genetic risks to family members
 - Provide prognostic information
 - Clinical trial participation
 - Future potential to guide treatment
- Larger Implications
 - Increase knowledge of underlying disease
 - Identify targets for treatments
 - Development of risk assessments tools



Genetic Testing Guide

- Talk to your PD doctor
- See a genetic counselor
- Participate in a research study

Genetics and PD Summary

- Most PD is caused by both genetic and environmental factors
- Knowledge Genetics of PD is quickly evolving
- Genetic testing is available on a clinical and research basis
- Genetic testing can increase our understanding of PD and may lead to the development of new treatments

Thank You



wexnermedical.osu.edu

