



Genetic Association Analysis of Essential Tremor

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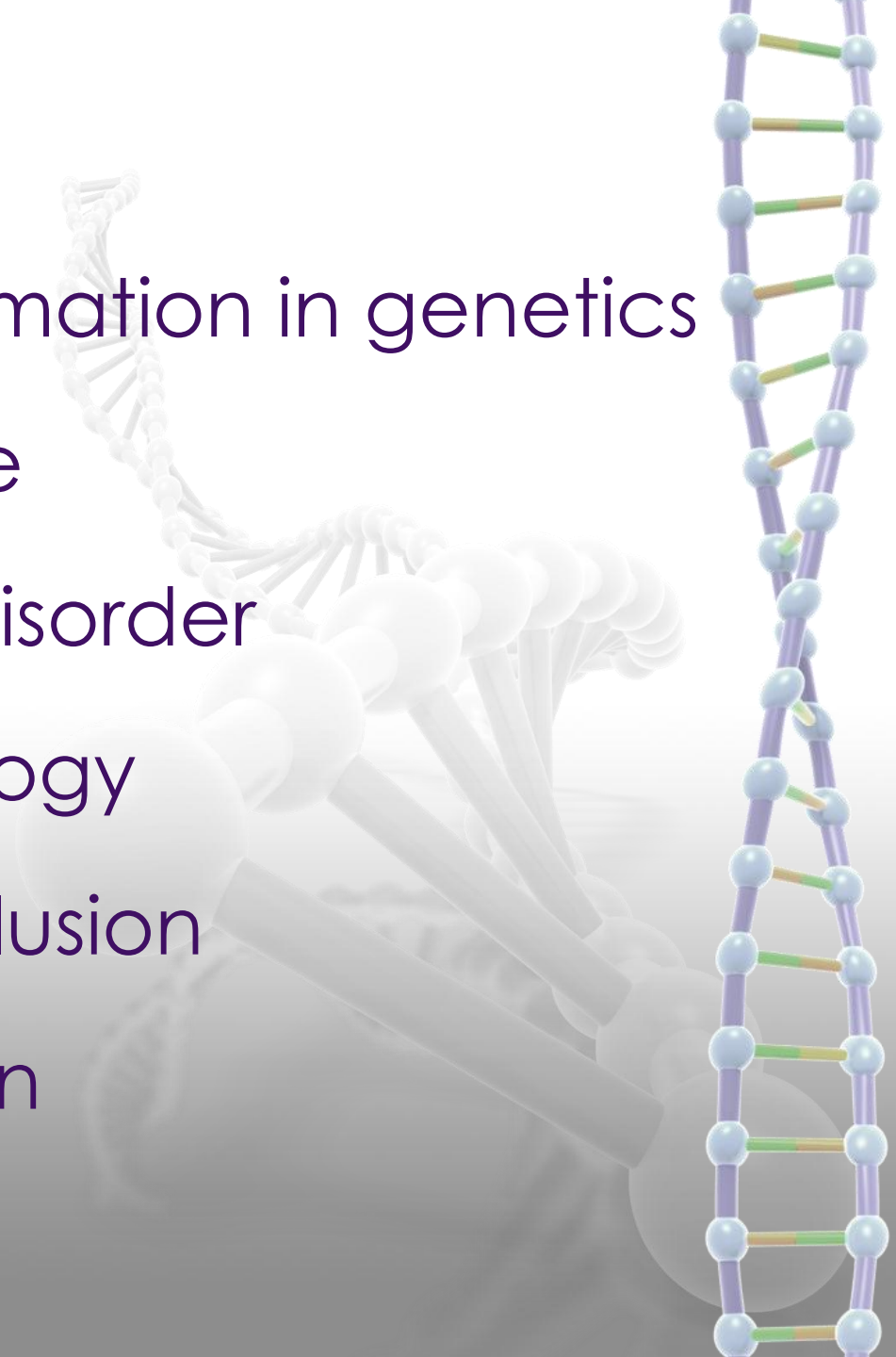
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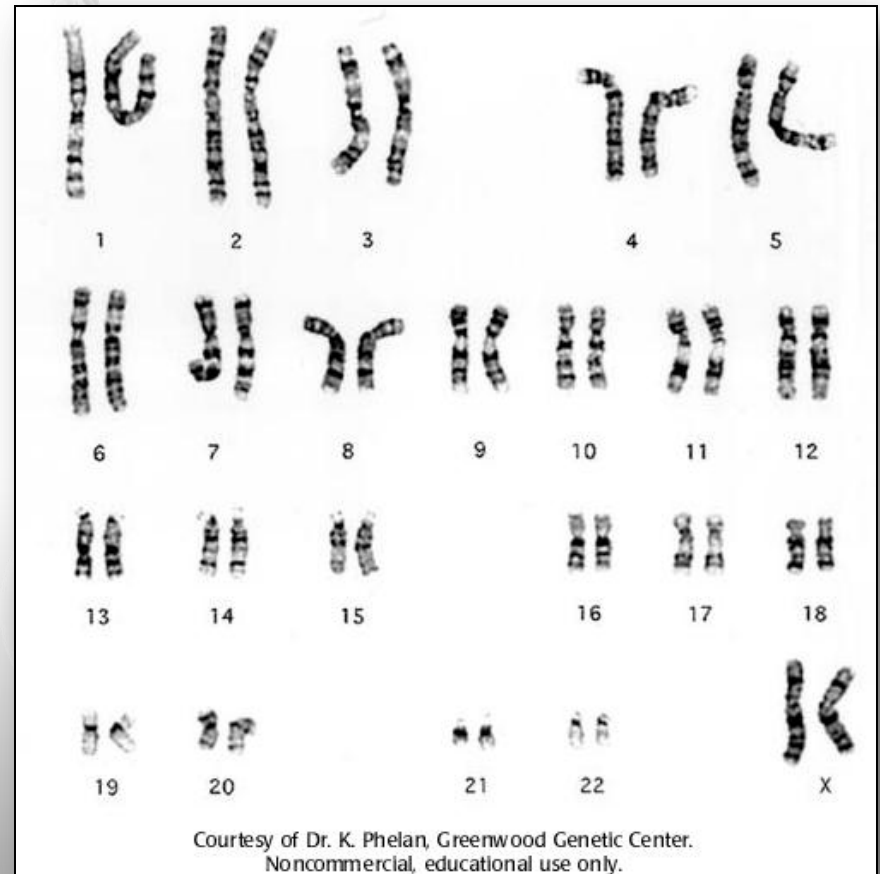
Overview

- Background information in genetics
- Pedigree structure
- Essential Tremor Disorder
- Project Methodology
- Results and Conclusion
- Further information

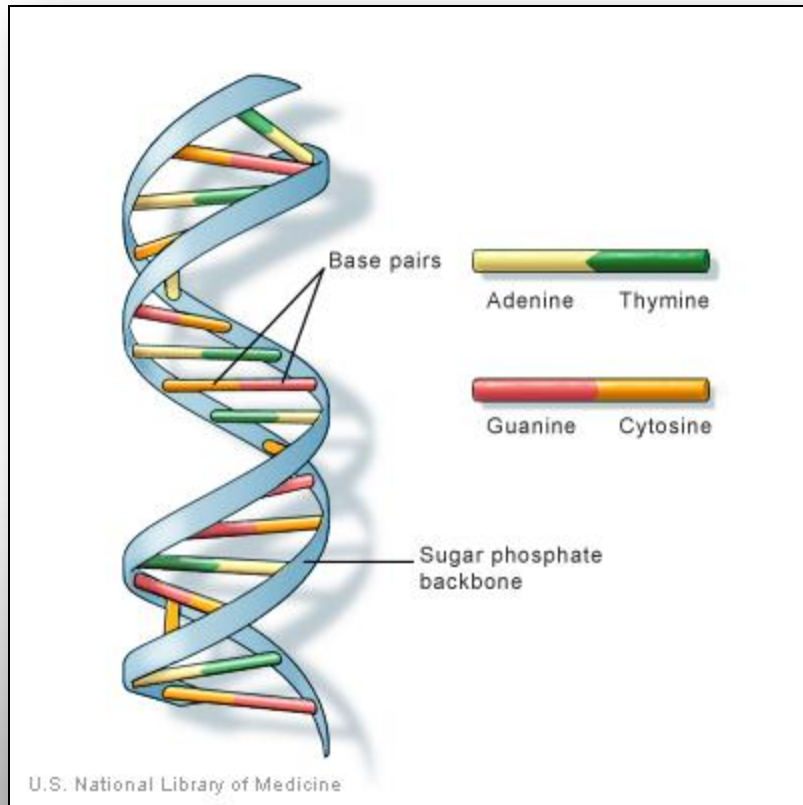


Cellular Basics

- Cells are one of the most basic structures of life.
- Each cell contains a full set of chromosomes.
- Karyotypes show all the chromosomes of an individual.
- Normal individual has of 22 chromosomes and a sex chromosome.

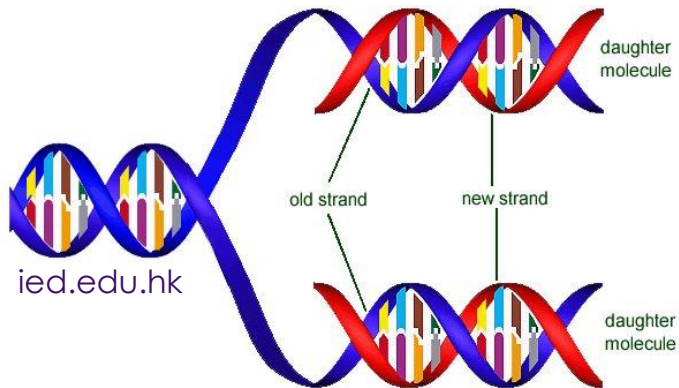


Genetic Composition- DNA



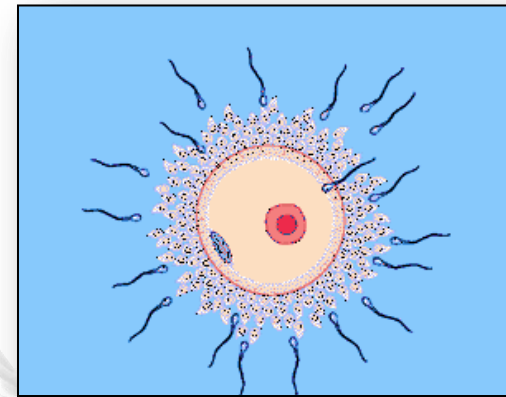
- Deoxyribonucleic acid.
- Consists of two long chains of subunits twisted around one another to form a double-strand helix.
- Contains four chemical components called bases:
 - Adenine (A) Thymine (T)
Guanine (G) & Cytosine (C)

Movement of genetic information



DNA Replication

- Helix separates and serves as a temple for replication.
- Results in two stands of DNA each contained one of the original strands.

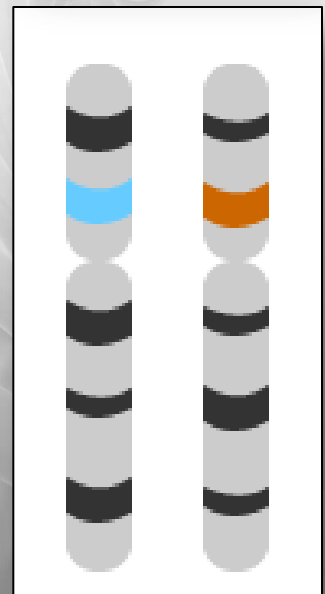
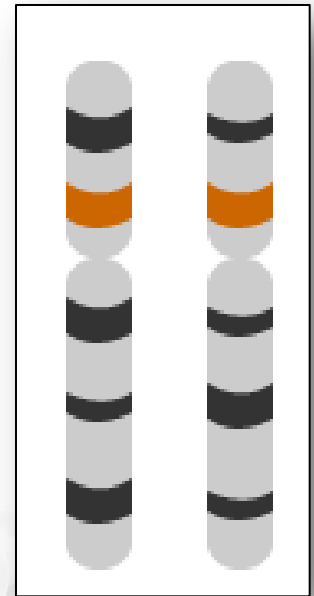


Sexual Reproduction

- Combination of Sperm and Egg each which each contain 23 chromosomes.
- Form Zygote with 23 chromosomal pairs.
- Offspring Characteristics
 - Phenotype : Physical Characteristics
 - Genotype : Genetic Characteristics

Genetic Markers

- A strand of polymorphic DNA.
- Alleles are particular forms of genetic markers.
- Single Nucleotide Polymorphism are markers that only differ at a single nucleotide.
- Each has two alleles, one from the maternal and the other from the paternal chromosome.
- The two alleles are called an individual's genotype.
- Homozygous
 - Two alleles are the same
- Heterozygous
 - Two alleles are not the same



Genetic Inheritance



MENDELIAN GENETICS

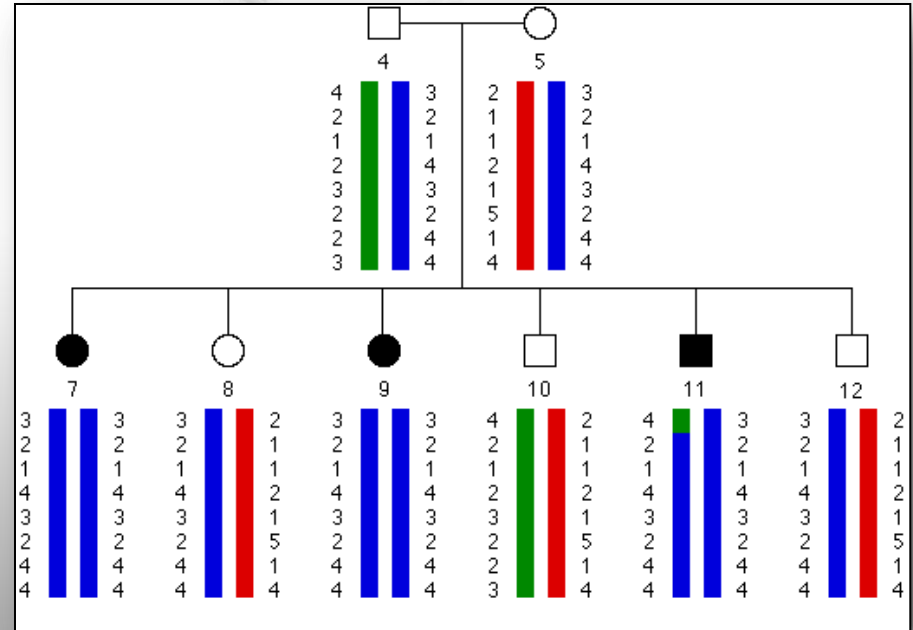
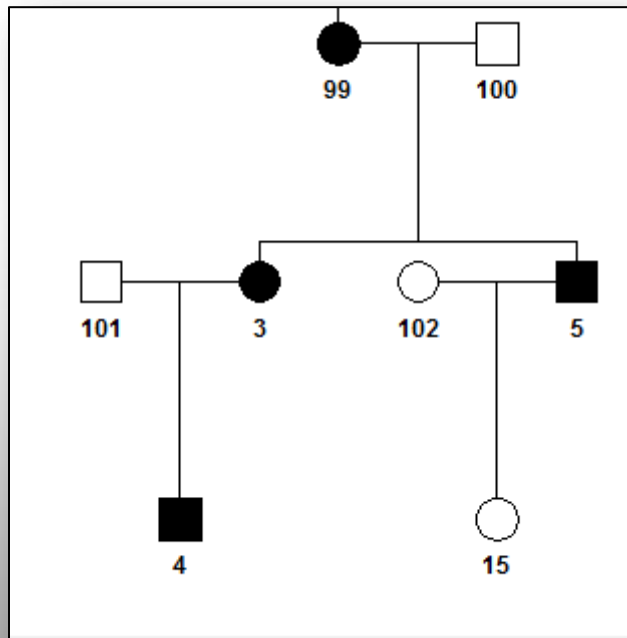
- In gamete formation, allele separate in such a way that each gamete is equally likely to contain any allele.
- Leads to easy straightforward predictions of offspring's characteristics.

PRACTICAL GENETICS

- Many alleles and traits are linked so they do not segregate independently.
- Not all alleles are dominant or recessive
- Interactions between genes.
- Makes it more difficult to predict and trace traits.

Pedigree Structure

- Pictorially shows a trait in a group of related individuals.
- Can show genotypes and/or phenotypes.



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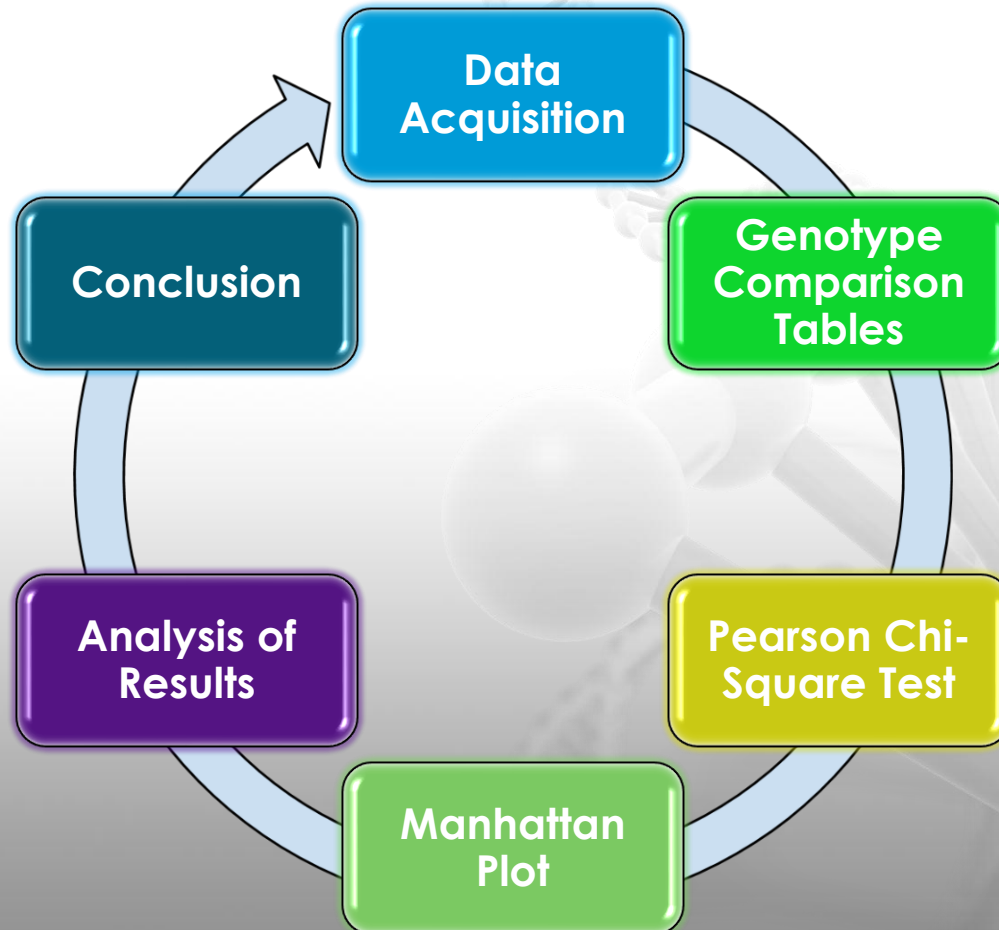
Essential Tremor

- Neuromuscular disorder that causes shaking of the hands, head, and voice.
- Usually a dominant trait.
- Most common in people older than 65.*
- Affects 4% to 5% of people age 40 to 60.*
- Affects 6.3% to 9%. Of people 60 and older. *
- Exact cause is unknown.
- Believed to have both neurological and genetic component.

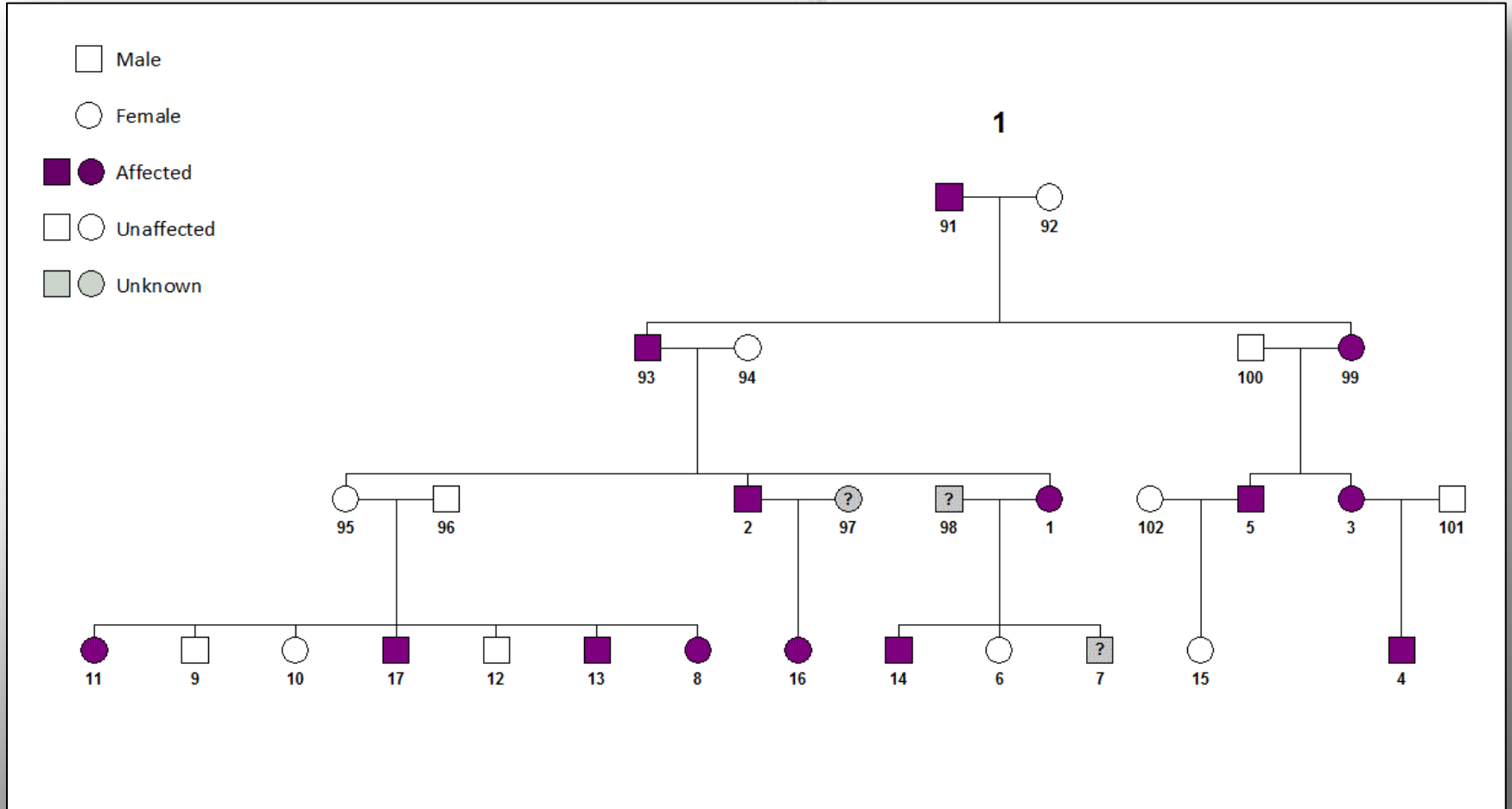
*Statistics from National Center for Biotechnology Information

Methodology

Purpose: To identify possible single nucleotide polymorphisms linked to Essential Tremor through genotype analysis.



Pedigree



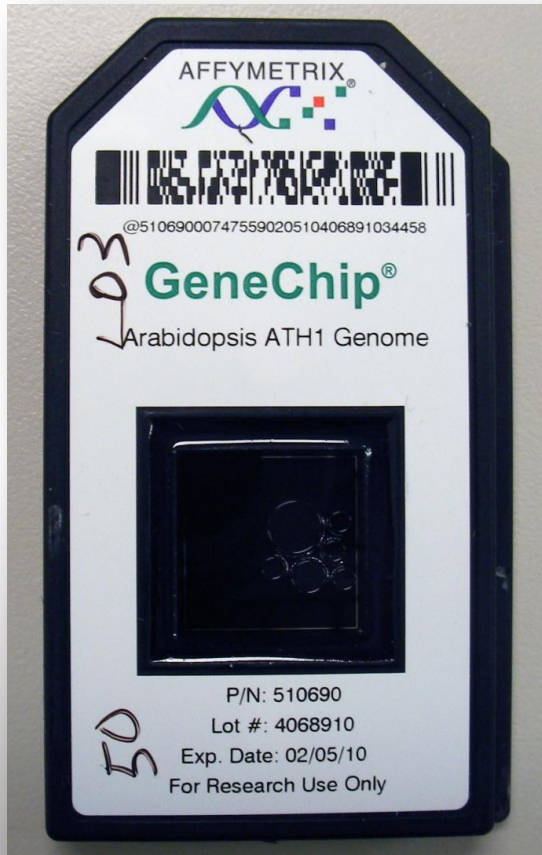
Data Acquisition

Genotype Data

probeset_id	15	2	7	8	9	10	11
SNP_A-2131660	1	2	2	2	2	2	2
SNP_A-1967418	1	2	2	2	2	2	2
SNP_A-1969580	2	2	2	2	2	2	2
SNP_A-4263484	2	2	1	1	2	2	1
SNP_A-1978185	0	0	0	0	0	0	0
SNP_A-4264431	0	1	0	0	0	0	0
SNP_A-1980898	1	1	2	2	2	2	2

Map File

#_AFFY_ID	<u>dbSNP_ID</u>	CHR	<u>Sex-averaged cM</u>	NCBI36.1_bp
SNP_A-8575125	rs10458597	1	0.654573674	554484
SNP_A-8575115	rs9629043	1	0.654753112	554636
SNP_A-8575371	rs11510103	1	0.658271037	557616
SNP_A-8709646	rs12565286	1	0.839523263	711153
SNP_A-8497791	rs12082473	1	0.862622336	730720
SNP_A-1909444	rs3094315	1	0.876444948	742429
SNP_A-8358063	rs2286139	1	0.887265518	751595
SNP_A-8329892	rs11240776	1	0.891440988	755132
SNP_A-8408912	rs2980319	1	0.905433593	766985
SNP_A-8294056	rs2977613	1	0.90886298	769890
SNP_A-1886933	rs2980300	1	0.915901191	775852
SNP_A-2236359	rs2905036	1	0.923563892	782343
SNP_A-8515688	rs11240777	1	0.931212427	788822



Genotype Comparison Tables

	Genotype			Total
	AA	AB	BB	
Unaffected Individuals	0	2	3	5
Affected Individuals	0	4	4	8
Total	0	6	7	13

Pearson Chi-Square Statistics Test

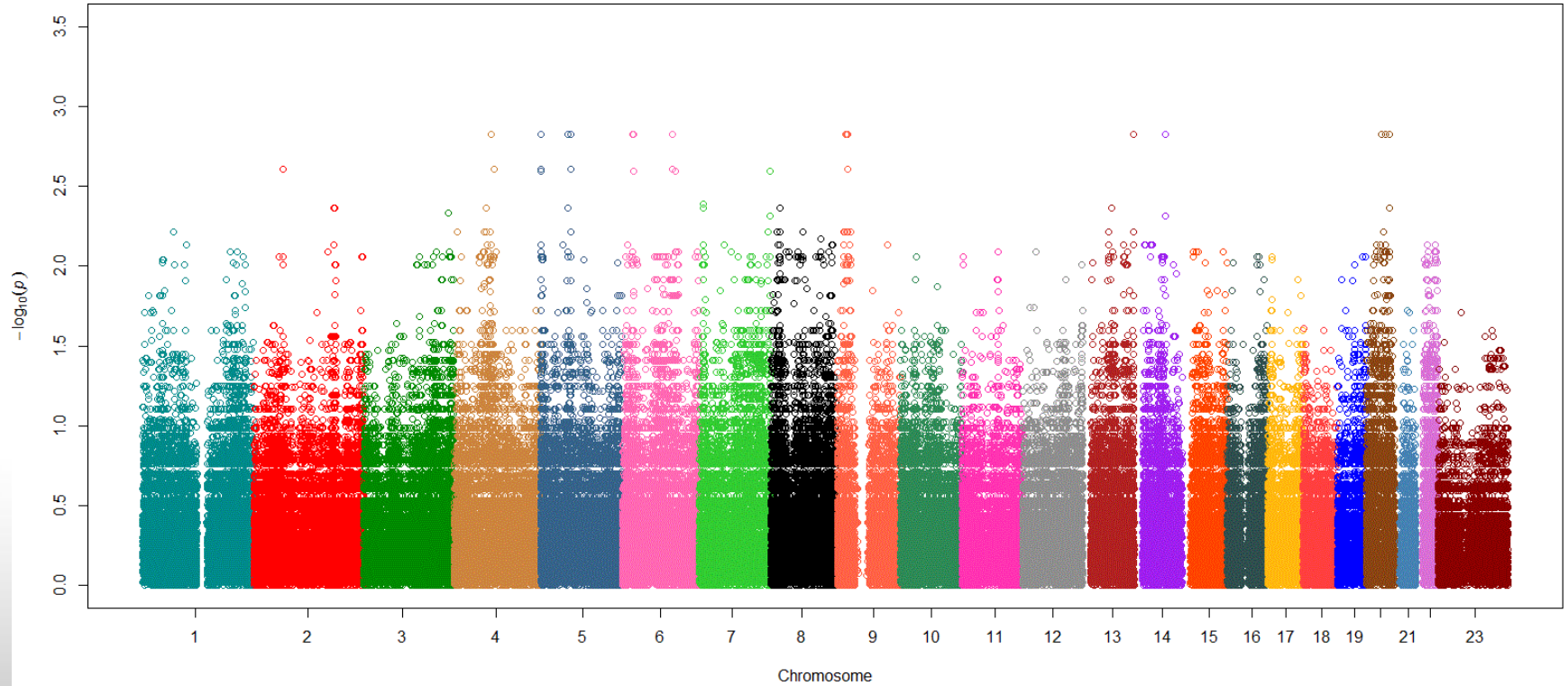
- Tests for independence between the row and the column
- If no interaction the same proportion should be in each column
- Follows Chi-Square distribution with 2 degrees of freedom

Test Statistic

$$\sum_{6 \text{ cells}} \frac{(\text{Observed} - \text{Expected})^2}{\text{Expected}}$$

Manhattan Plot

Manhattan Plot for Study of Essential Tremor



- Plot of P-value vs SNP location

Results and Conclusion

- No p-values are significant at genome wide significance level (1×10^{-8}).
- Some suggestive locations.

Chromosome	Gene name	Function
5	DEP1B	Regulation of GTPase activity
14	RAD51 homolog B	DNA repair protein
6	GPR6	Nerve growth and myelin

- More study need on this disorder in genetics and neurobiology.

Further Information



[International Essential Tremor Foundation](#)

[National Center for Biotechnology Information](#)

