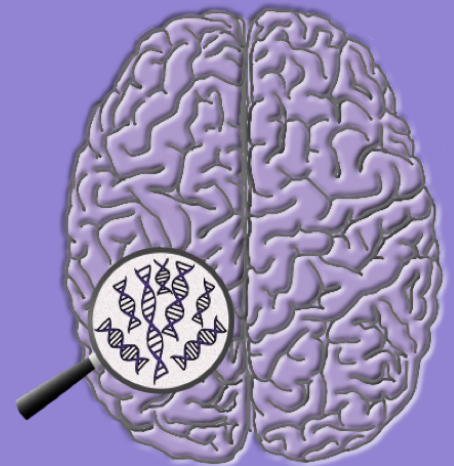


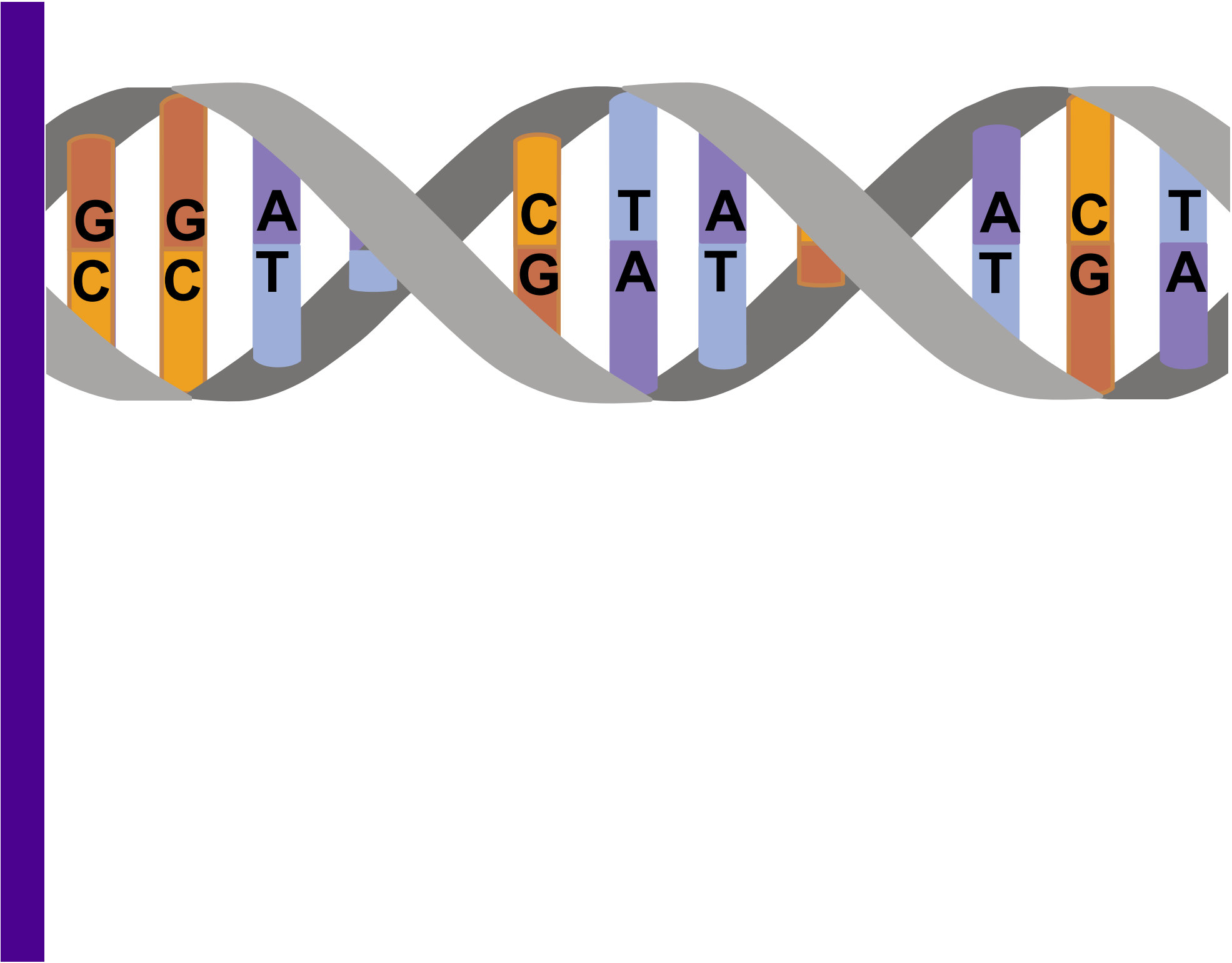
Single Nucleotide Polymorphisms (SNP) analysis

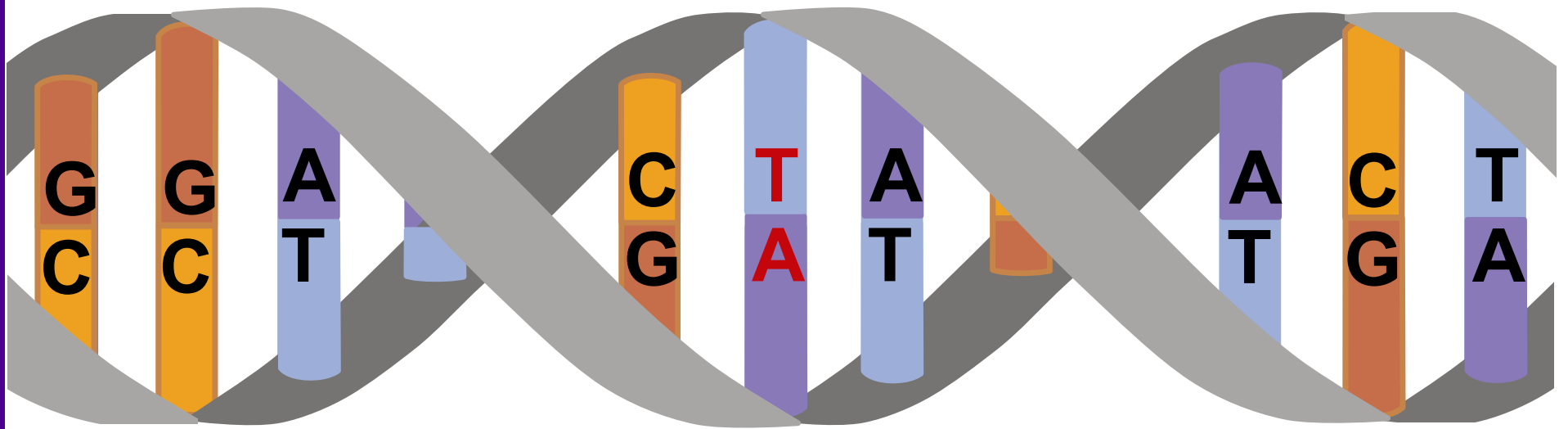
Yuetiva Robles, PhD

Basics of Genetic Analysis: SNP analysis and GWAS

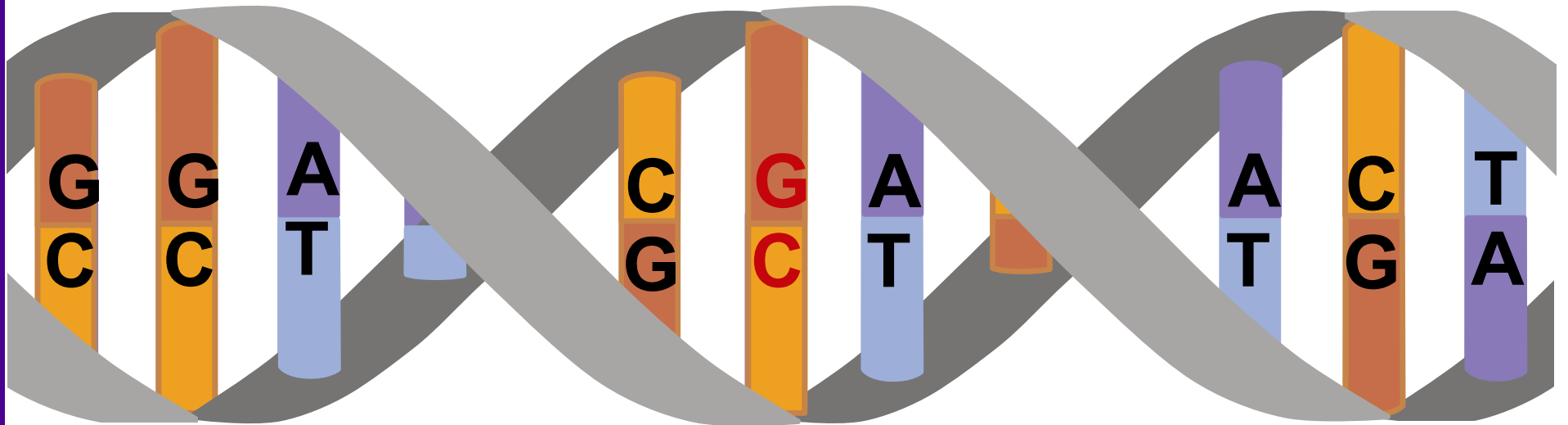
July 25, 2025



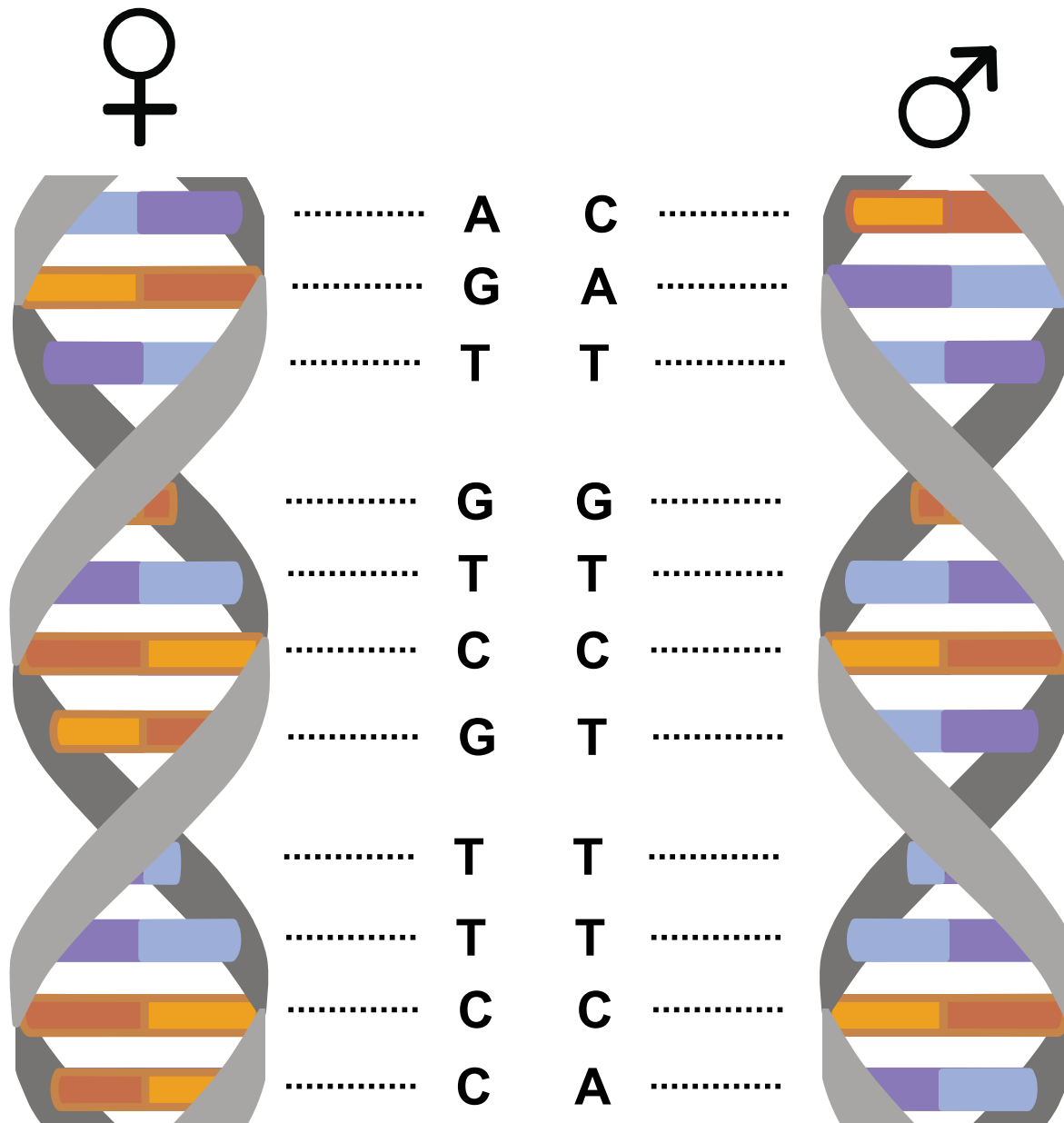




Single Nucleotide
Polymorphism

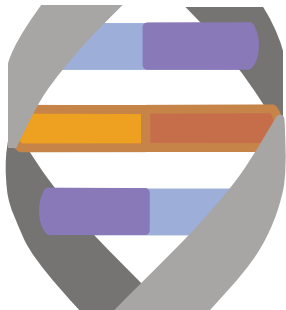












Genotype: Allele pairs



*flipped strand to mirror alleles

Genotype: Allele pairs

♀			♂	minor allele	#minor alleles
	A C	C	1
	G A	G	1
	T T	G	0
	G G	G	2
	T T	T	2
	C C	A	0
	G T	G	1
	T T	T	2
	T T	G	0
	C C	C	2
	C A	A	1

*flipped strand to mirror alleles

SNP Analysis

- Usually logistic or linear regression
- SNP usually coded as an additive 0, 1, 2 based on number of minor alleles a person has

Outcome = Intercept + SNP + covariates

SNP regression results - example

CSF $A\beta_{42}$ = Intercept + rs429358_C + age_lp + sex + Summary_Diagnosis
(aka APOE $\epsilon 4$)

Residuals:

Min	1Q	Median	3Q	Max
-744.07	-232.79	-31.43	211.44	925.44

Coefficients:

	Estimate	Std. Error	t value	Pr(> t)	
(Intercept)	676.957	189.692	3.569	0.000404	***
rs429358_C	-130.776	28.540	-4.582	6.24e-06	***
age_lp	-1.654	2.379	-0.695	0.487261	
genderMale	-18.938	35.069	-0.540	0.589505	
Summary_DiagnosisMCI-AD	183.143	82.101	2.231	0.026280	*
Summary_DiagnosisNormal	378.629	67.587	5.602	4.05e-08	***

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 330.4 on 383 degrees of freedom
(25 observations deleted due to missingness)

Multiple R-squared: 0.2019, Adjusted R-squared: 0.1915

F-statistic: 19.38 on 5 and 383 DF, p-value: < 2.2e-16

SNP regression results - example

CSF A β ₄₂ = Intercept + rs429358_C + age_lp + sex + Summary_Diagnosis

(aka APOE ϵ 4)

Note the allele here
results = effect of # C alleles

Residuals:

Min	1Q	Median	3Q	Max
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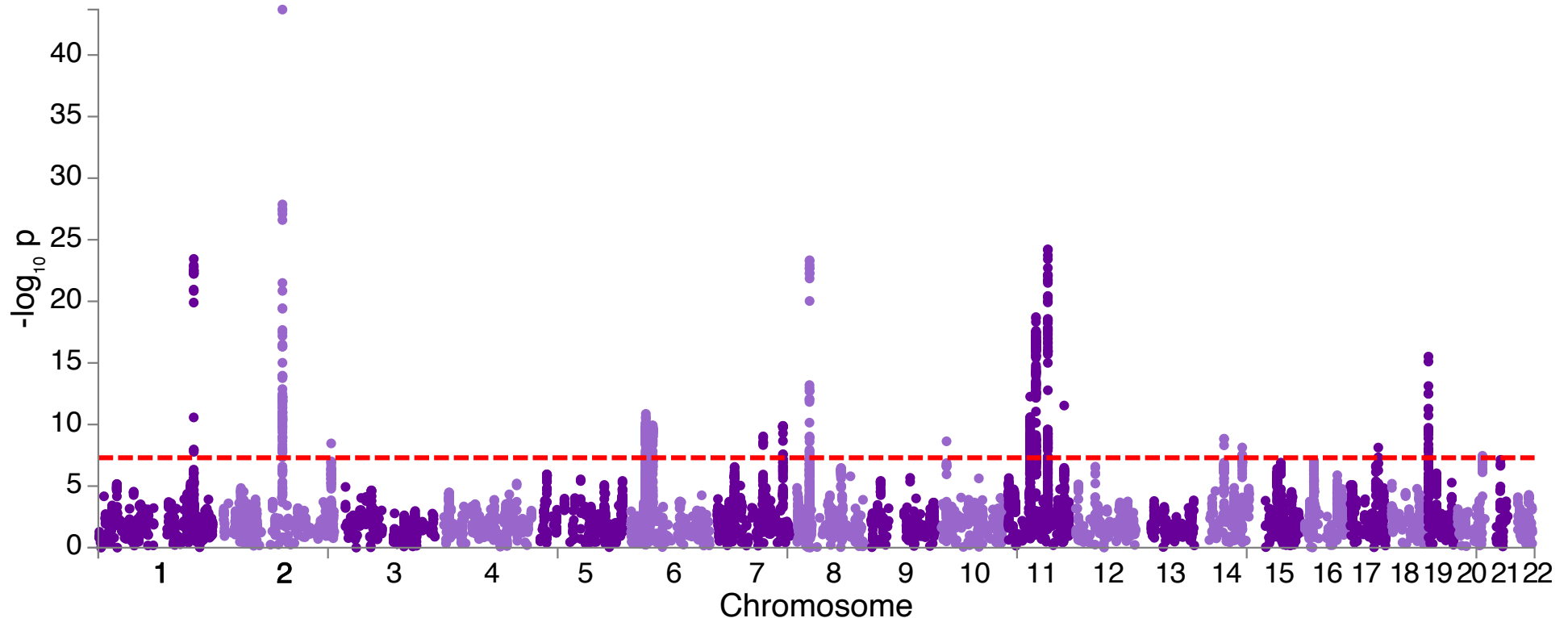
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Genome-Wide Association Studies (GWAS)

GWAS – multiple testing

- Individual SNP tests repeated hundreds of thousands to millions
- Traditional Bonferroni threshold 5×10^{-8} based on assumption of 1 million independent tests
- Alternatives available including FDR, permutation, etc

Manhattan plot created from GWAS published by Kunkle et al, 2019



- Results from meta-analysis of logistic regressions (AD case/control defined by clinical status)
- Each dot represents a SNP, x-axis genomic location, y-axis $-\log_{10} p$
- Dotted line is the genome-wide significance threshold (5×10^{-8})