Disease Association Studies

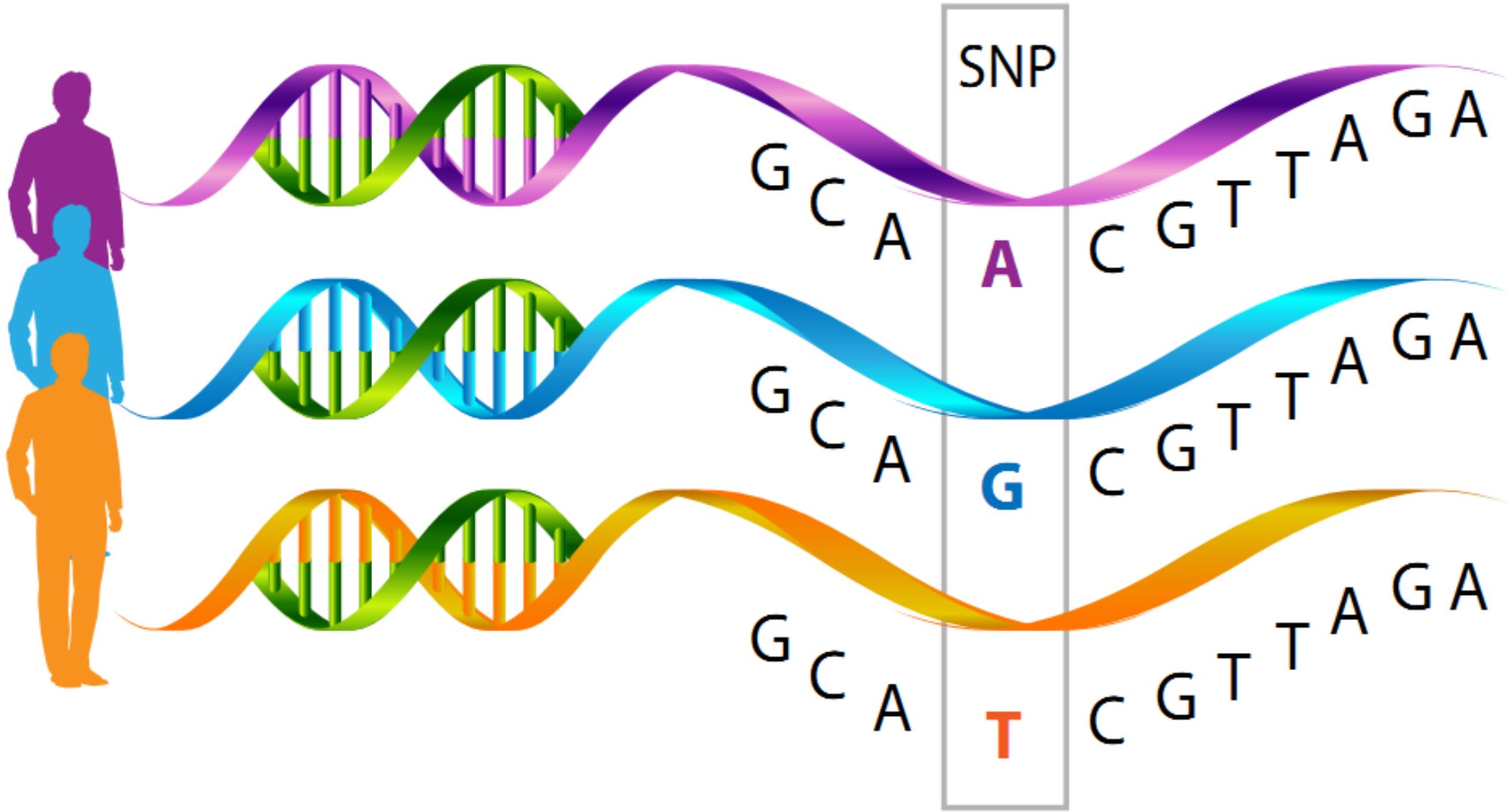
ICS 491

Upcoming guest lectures

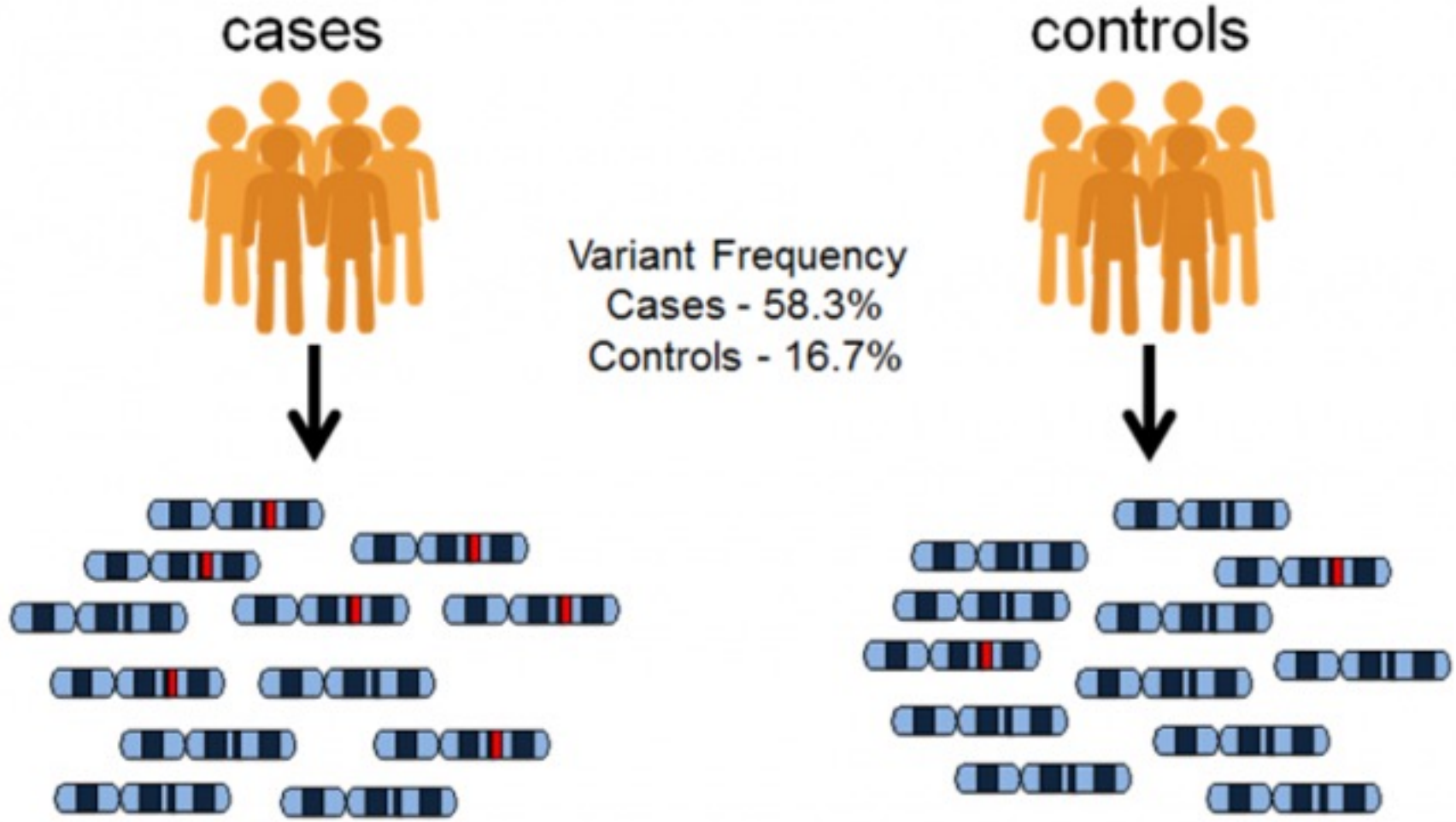
- November 14: Aekta Shah (Ex-Google) - Data Ethics

We may need to move around some discussion question presentations.

Review:
Single Nucleotide Polymorphisms (SNPs)

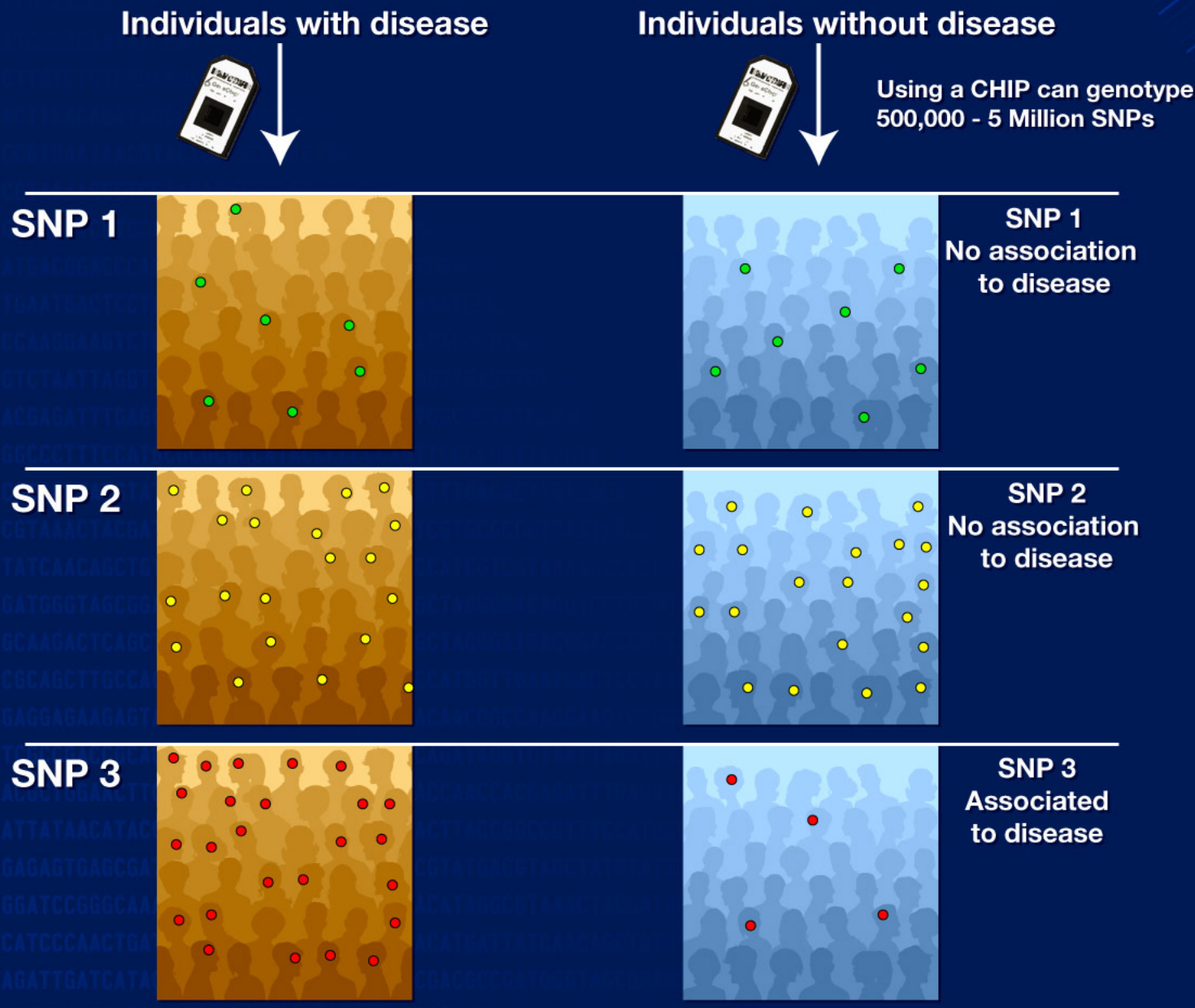


Genome Wide Association Study (GWAS)

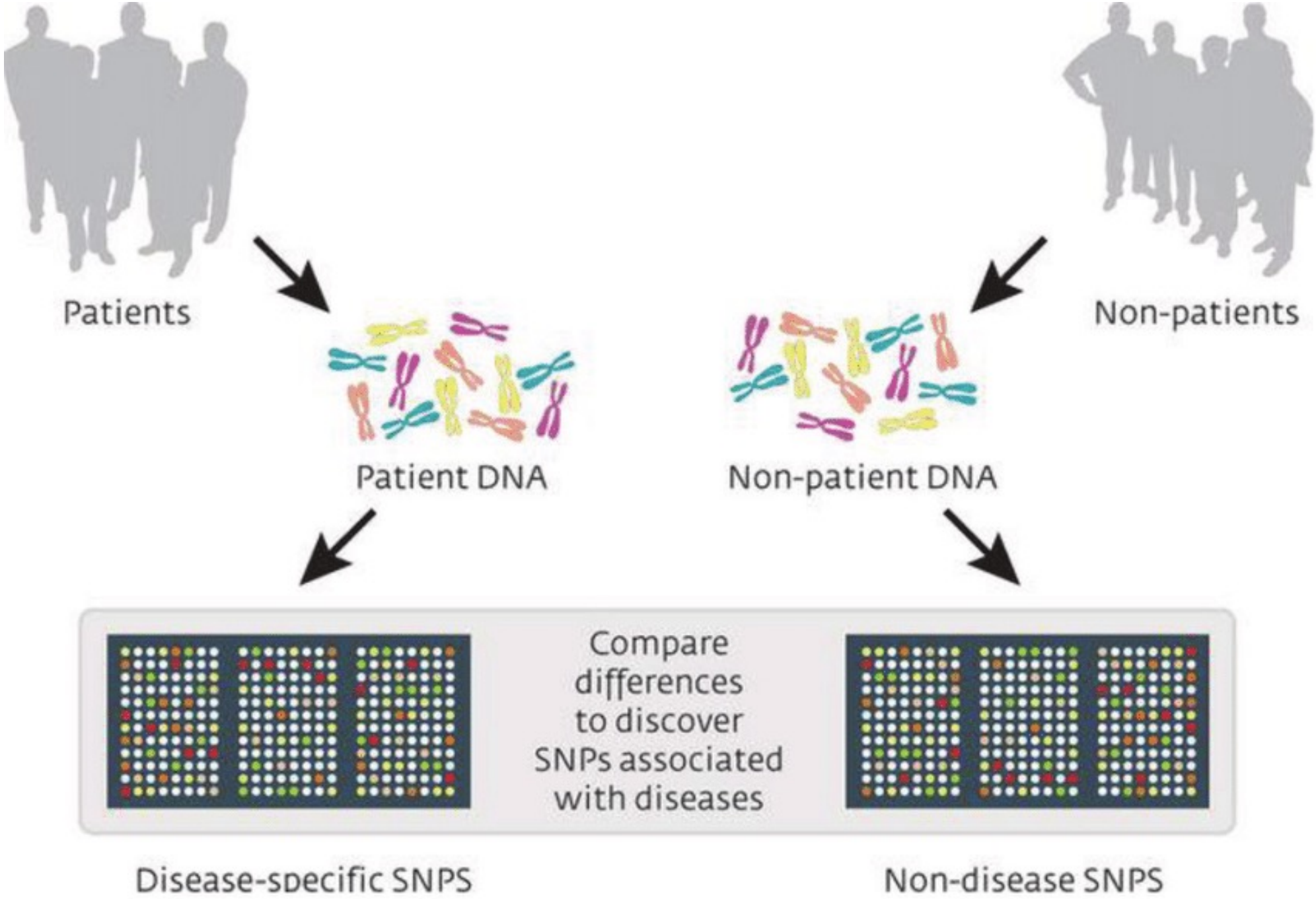


GWAS – Genome-wide Association

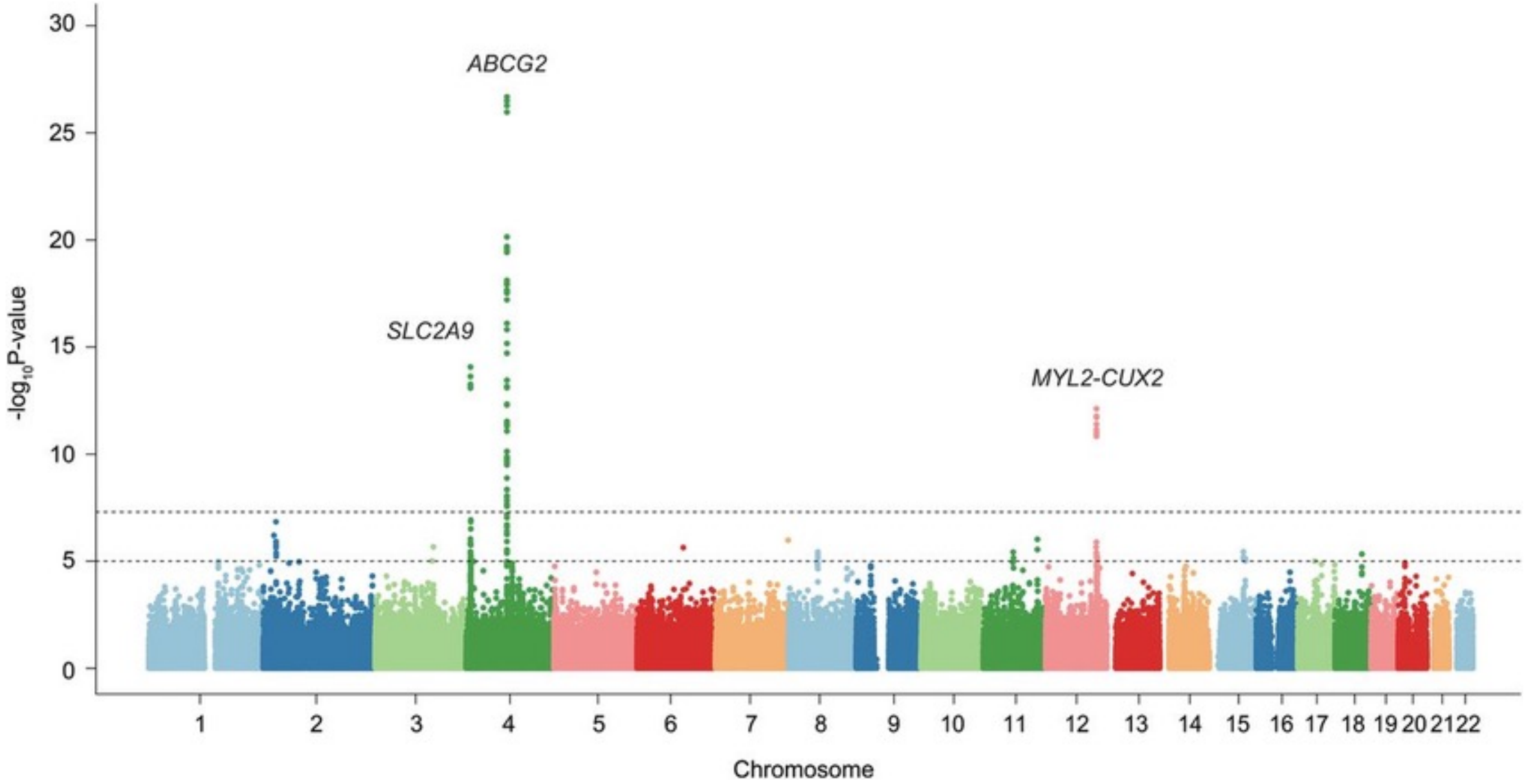
NHGRI FACT SHEETS
genome.gov



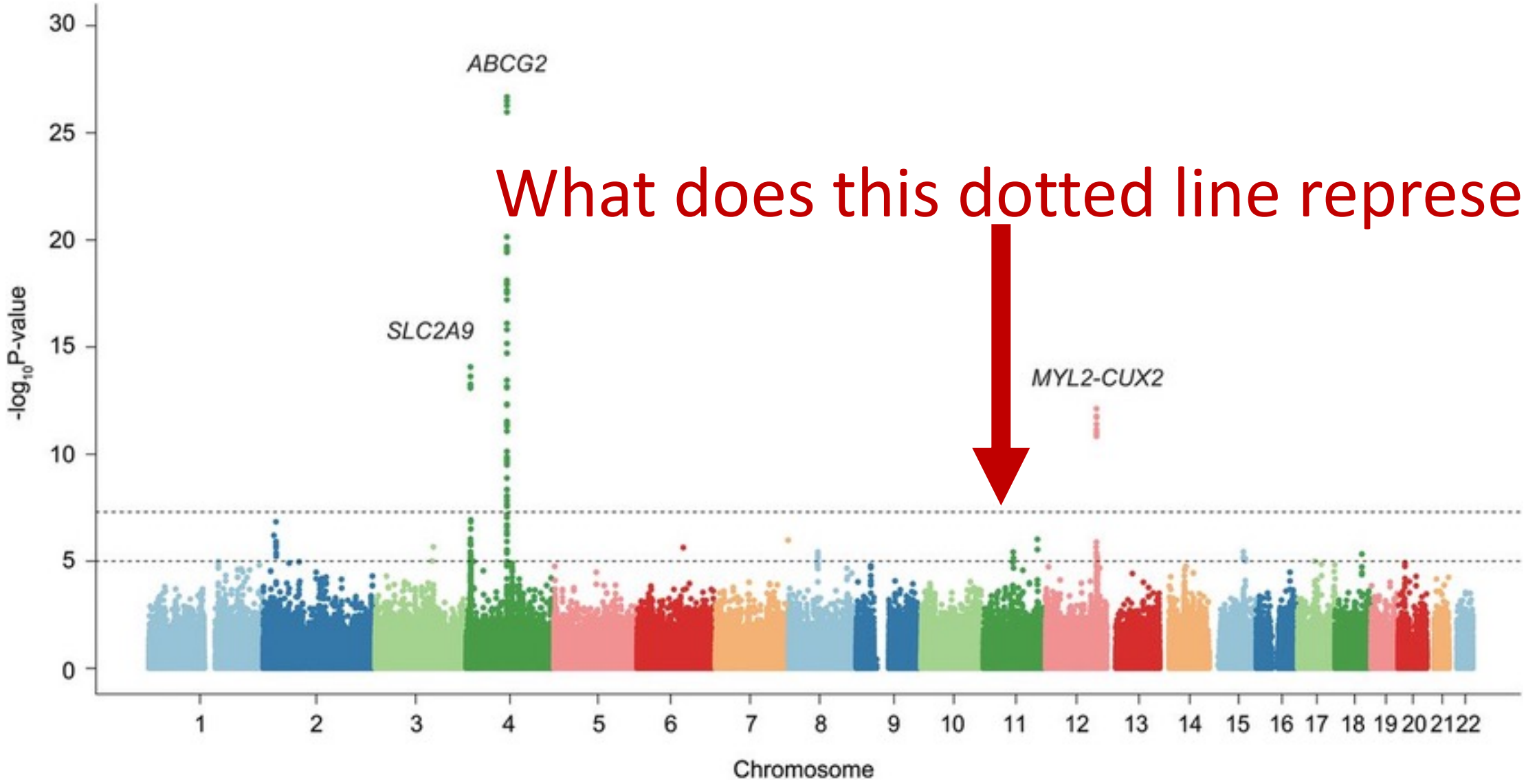
National Human Genome Research Institute


Patients
Non-patients
Patient DNA
Non-patient DNA
Compare differences to discover SNPs associated with diseases
Disease-specific SNPS
Non-disease SNPS

Manhattan Plots



Manhattan Plots



Bonferroni Correction!

- When we test many SNPs, a p-value of 0.05 is easily achievable just by random chance
- So, we make an adjustment: 0.05 / (number of SNPs tested)

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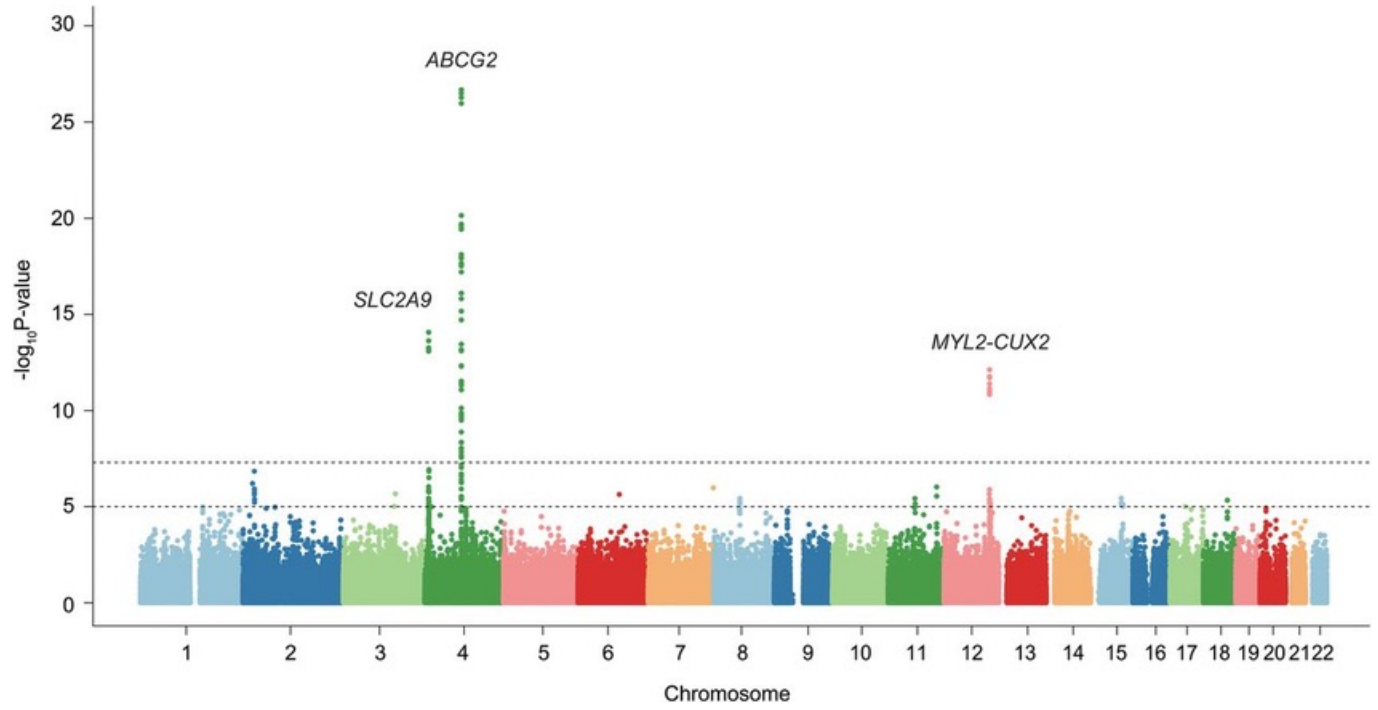
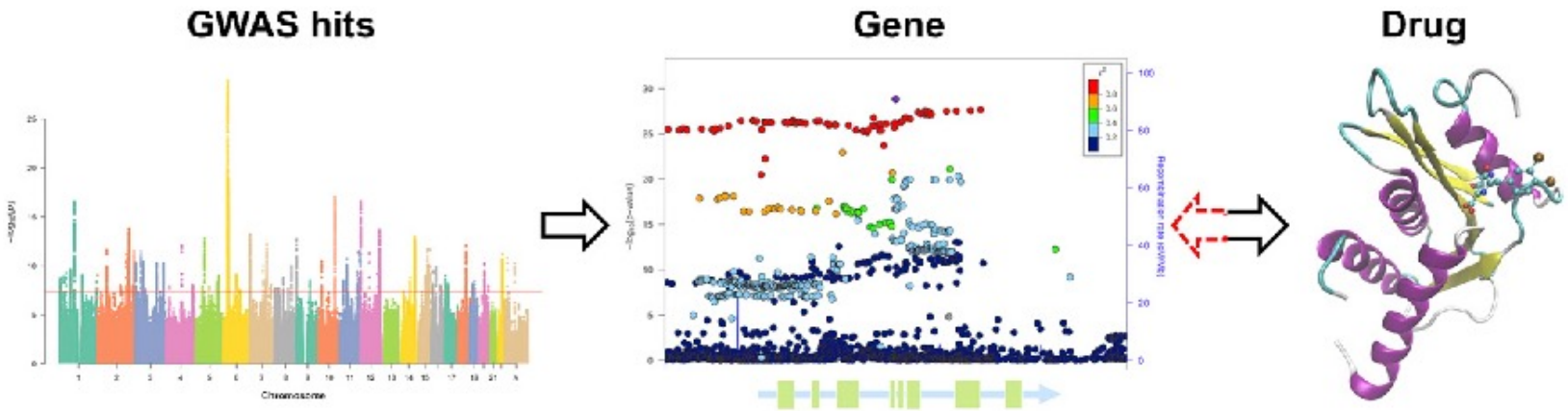
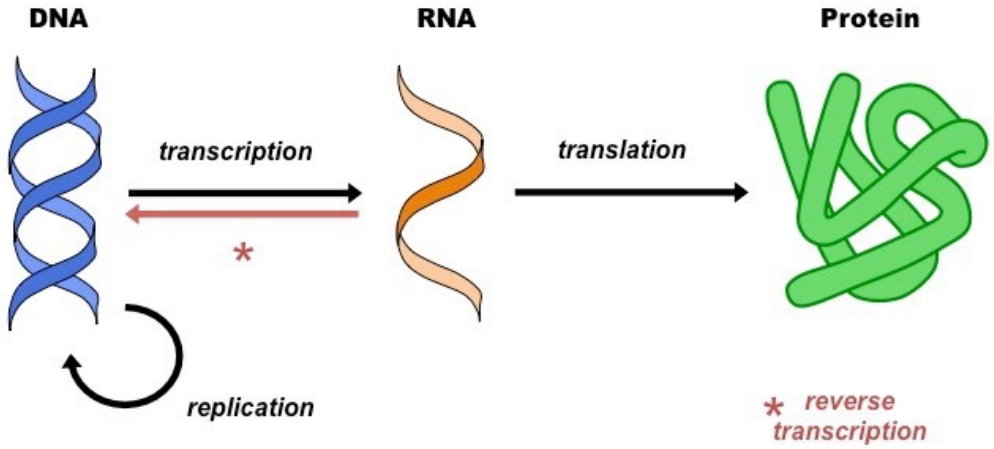


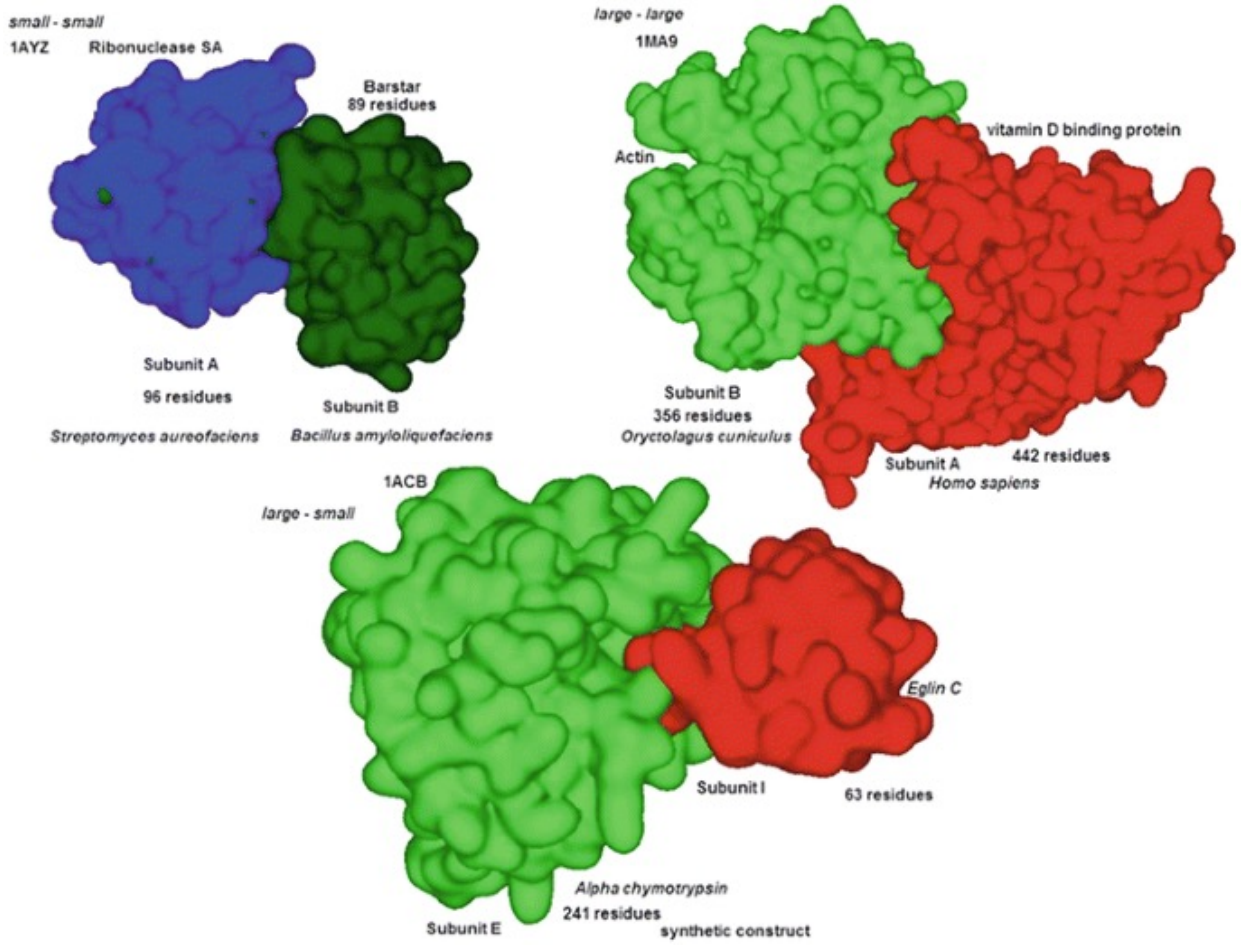
Discoveries enabled by GWAS



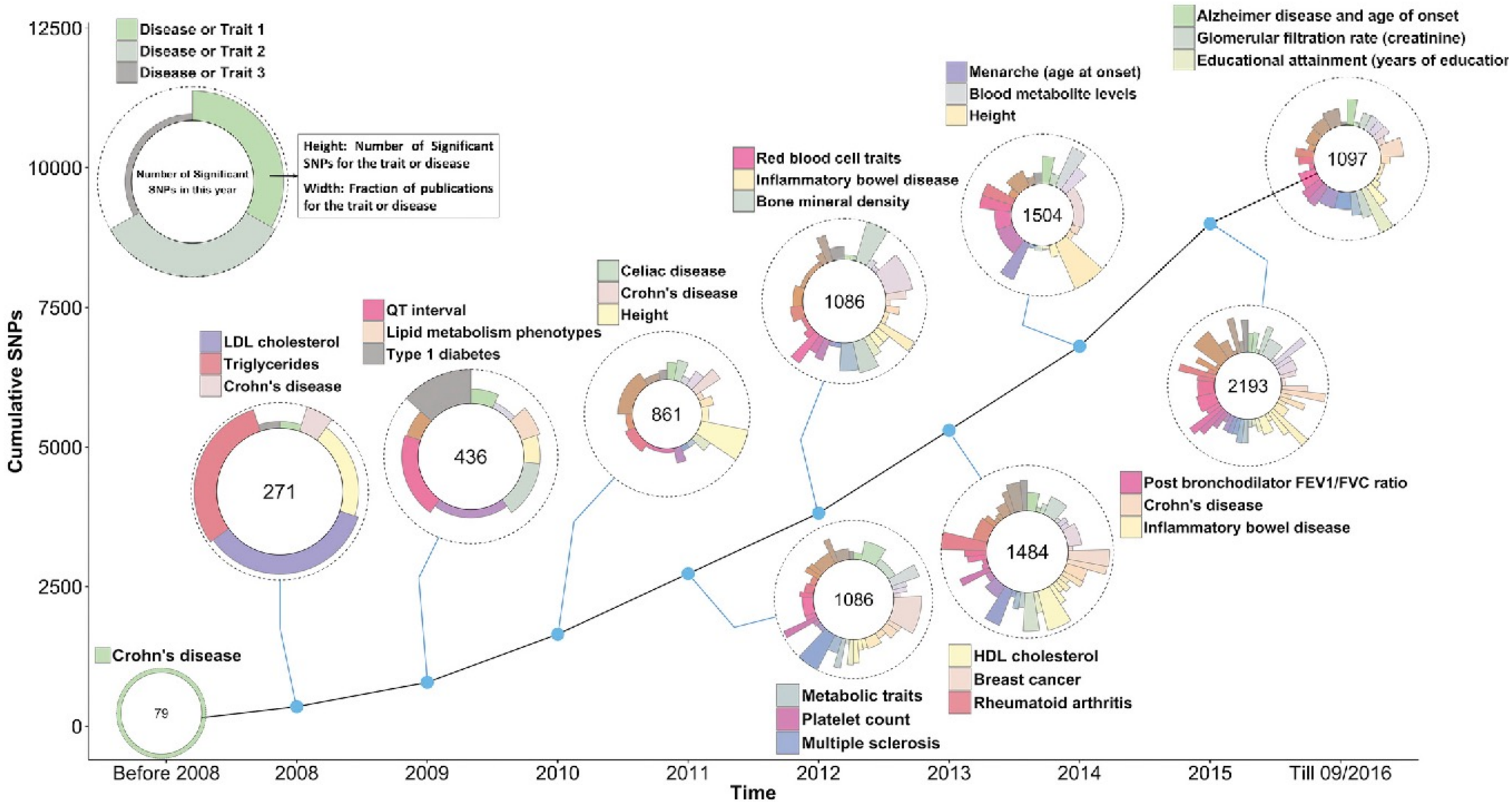
Trait	Gene with GWAS hits	Known or candidate drug
Type 2 Diabetes	*SLC30A8/KCNJ11*	ZnT-8 antagonists/Glyburide
Rheumatoid Arthritis	*PADI4/IL6R*	BB-Cl-amidine/Tocilizumab
Ankylosing Spondylitis(AS)	*TNFR1/PTGER4/TYK2*	TNF-inhibitors/NSAIDs/fostamatinib
Psoriasis(Ps)	*IL23A*	Risankizumab
Osteoporosis	*RANKL/ESR1*	Denosumab/Raloxifene and HRT
Schizophrenia	*DRD2*	Anti-psychotics
LDL cholesterol	*HMGCR*	Pravastatin
AS, Ps, Psoriatic Arthritis	*IL12B*	Ustekinumab

New Drugs based on GWAS



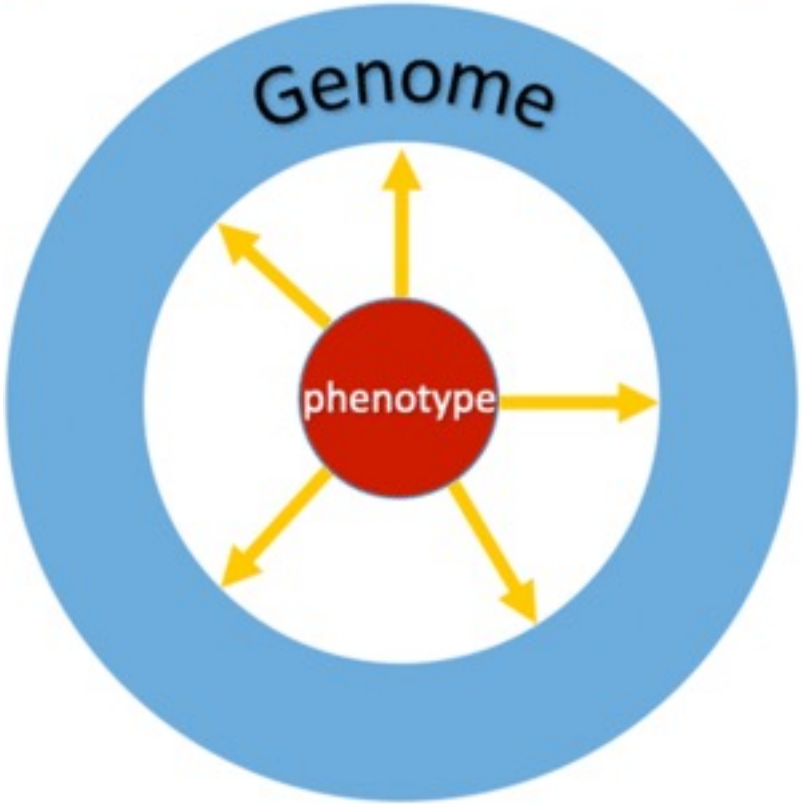


GWAS Discoveries over Time

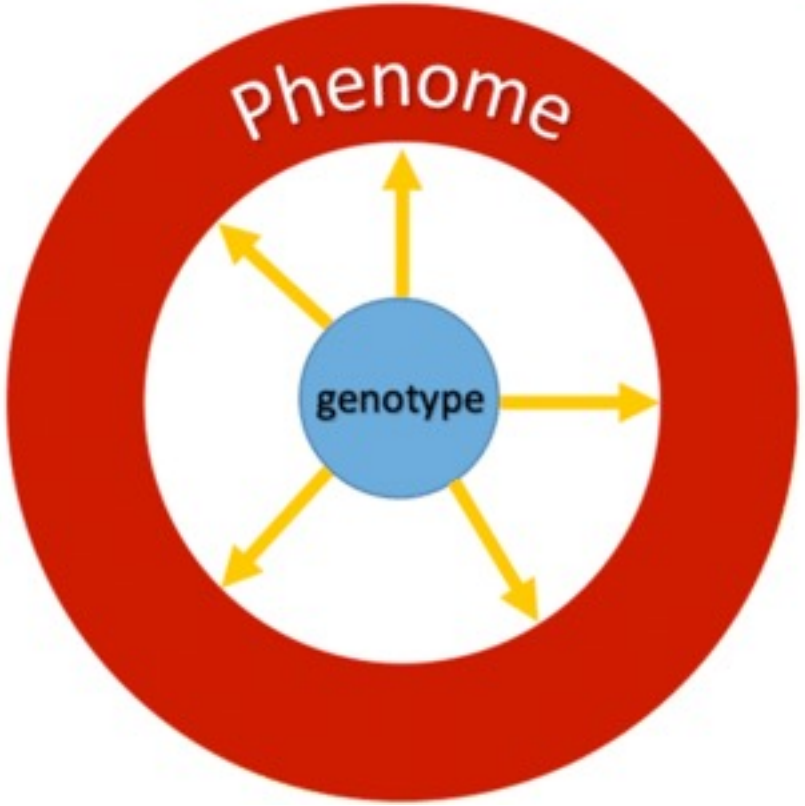


GWAS vs PheWAS

GWAS: examines associations between specific phenotypes and genetic variants across the genome



PheWAS: examines associations between specific genetic variants and a large number of different phenotypes (phenome)



Use cases of GWAS vs PheWAS