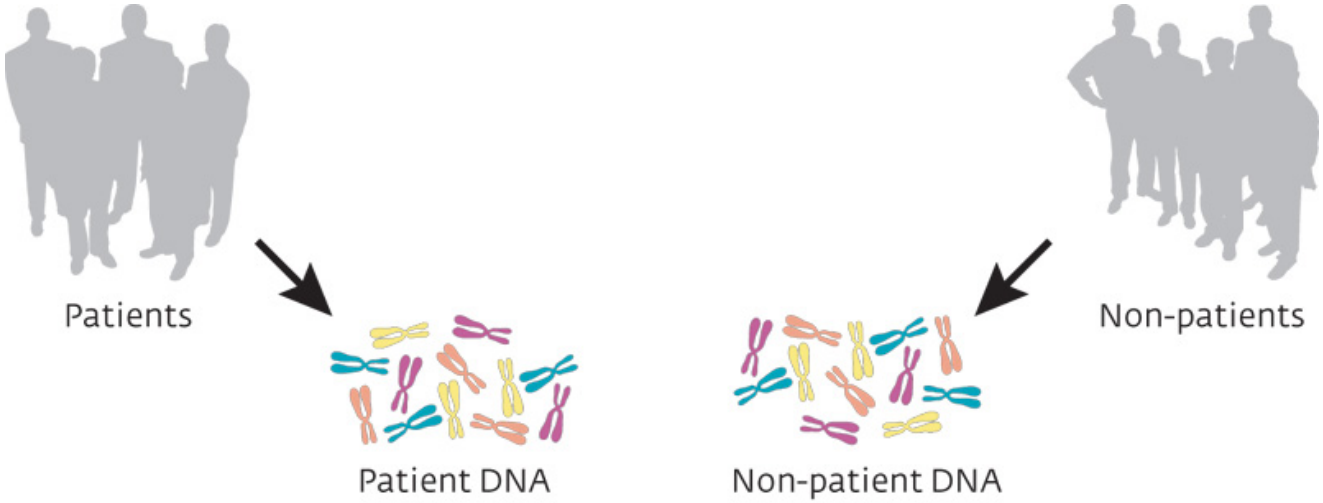
Genome-Wide Association Studies



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CSC 334
Fall 2015

Outline

- Background about GWAS
  - How it works
  - Benefits
- Background about HapMap
  - How it ties in with GWAS
- Accuracy of GWAS
  - Figure 1
- Association of disease
  - Statistics Terms
  - Figure 2
- Results and Discussion
  - Figure 4 and Figure 4 from another paper

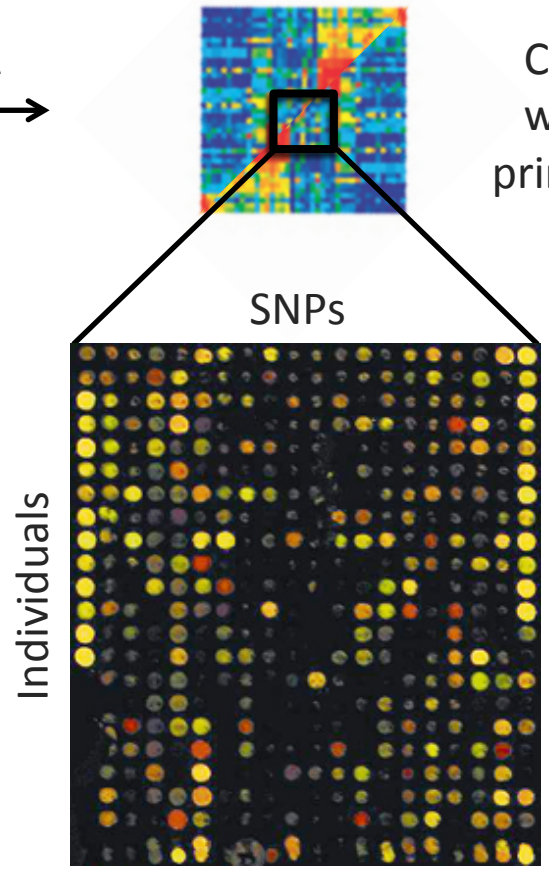
Background about GWAS

- An approach to find genetic variations associated with a particular disease
  - Compare SNPs
- Improvements
  - Builds better strategies with new genetic association
- Benefits
  - Ability to characterize an individual's state
  - Personalized medicine

How GWAS works

Sample of individuals with disease

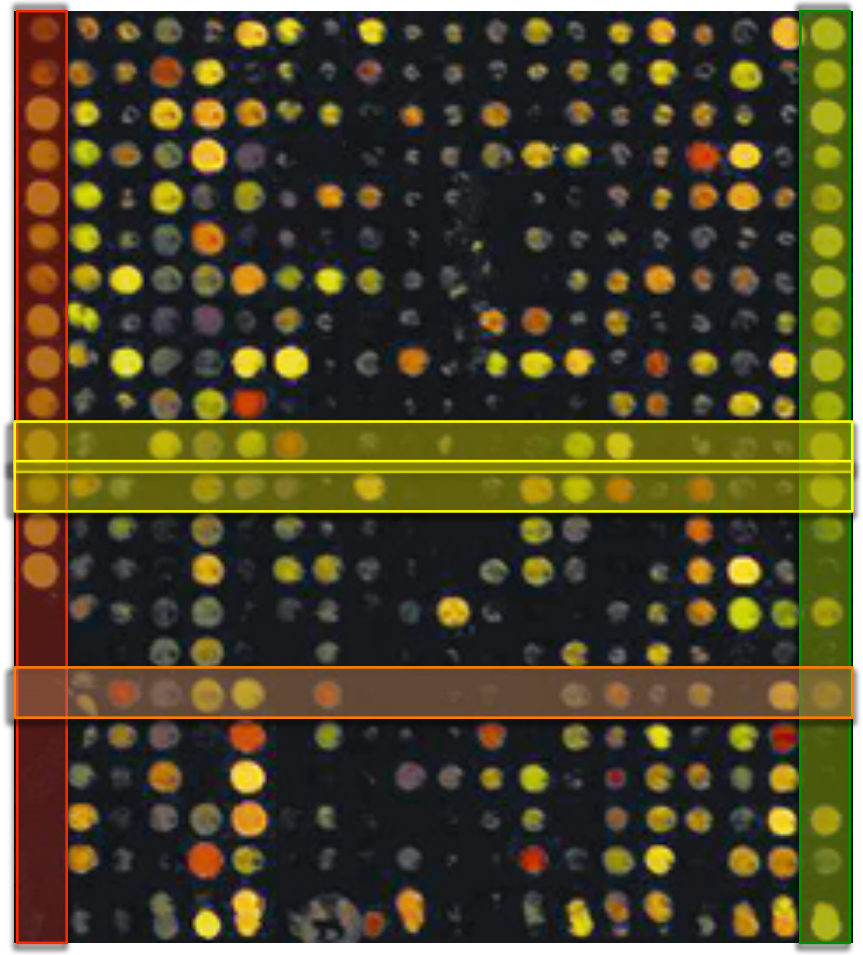
Sample DNA →



Chip with primers

Nalls et al.

How GWAS works



Haplotype

Nalls et al.

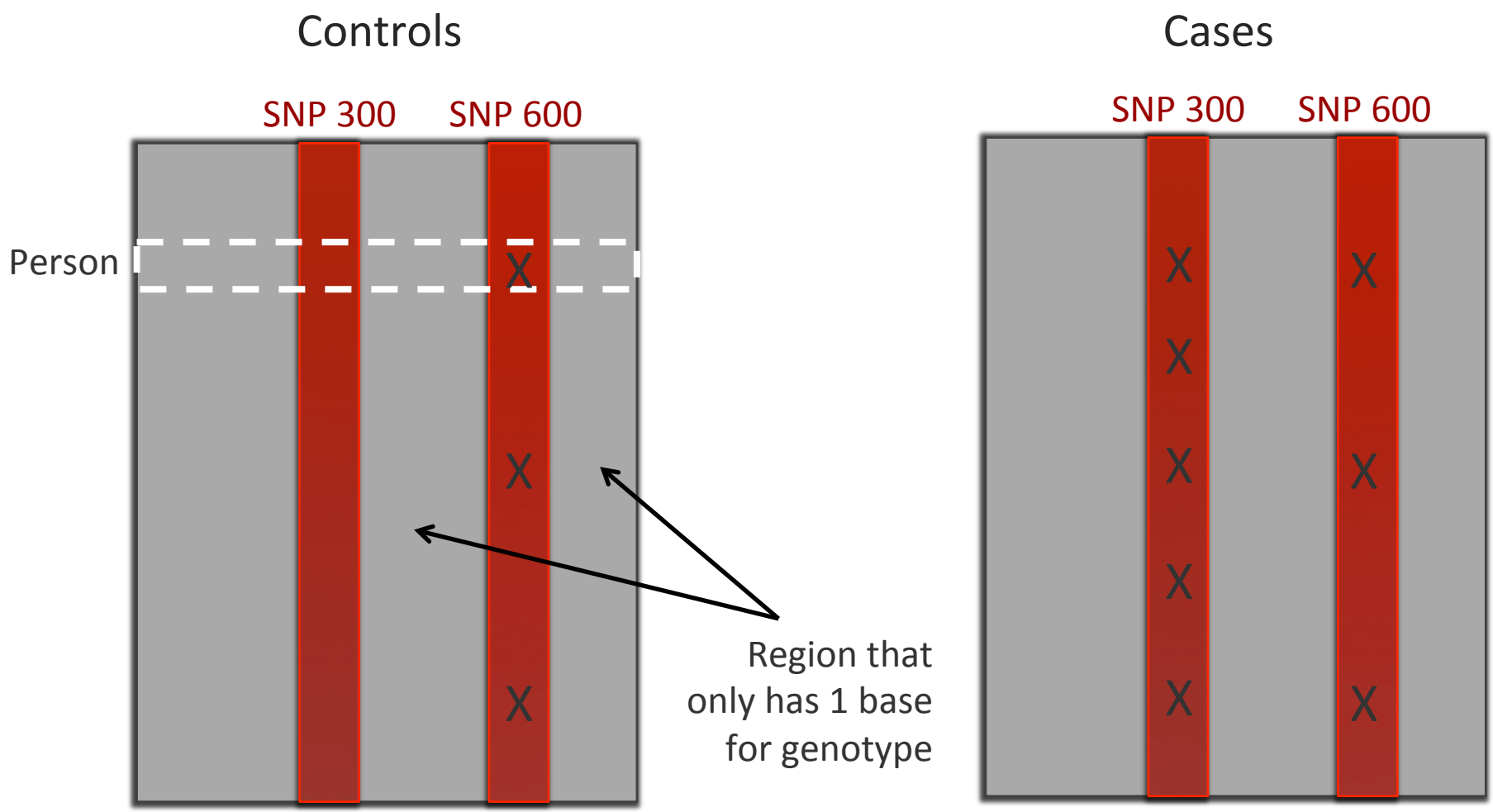
How GWAS works

Repeat for sample of individuals without disease

- What would you expect to see?

No particular pattern!

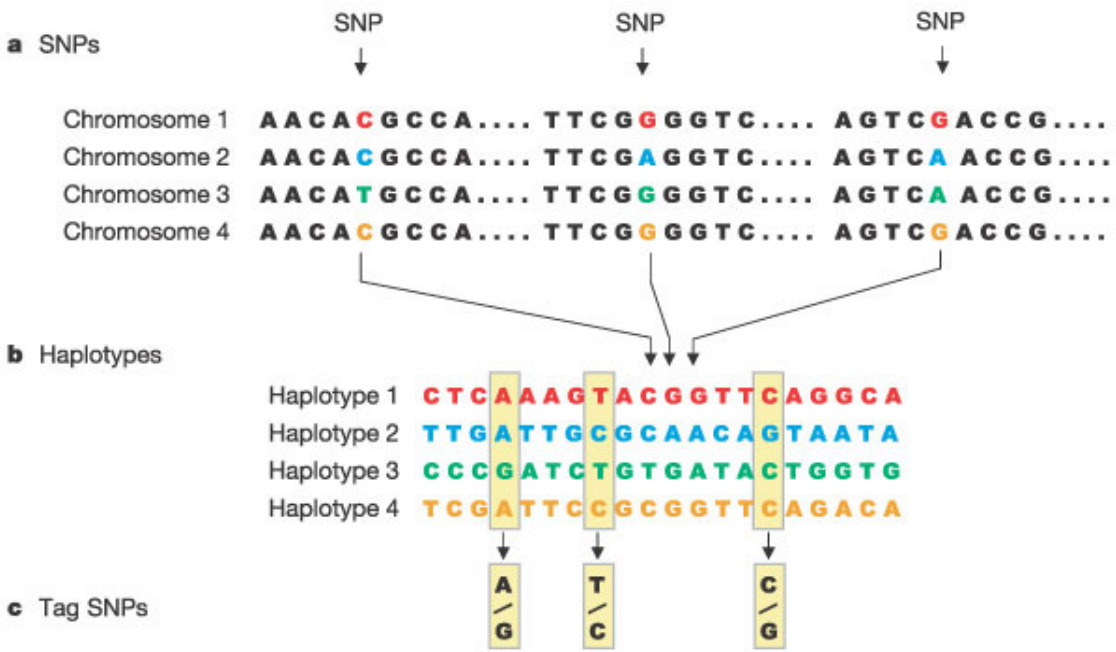
Recap


Controls
Cases
SNP 300
SNP 600
SNP 300
SNP 600
Person
X
X
X
X
X
X
X
X
X
X
Region that
only has 1 base
for genotype

How HapMap works

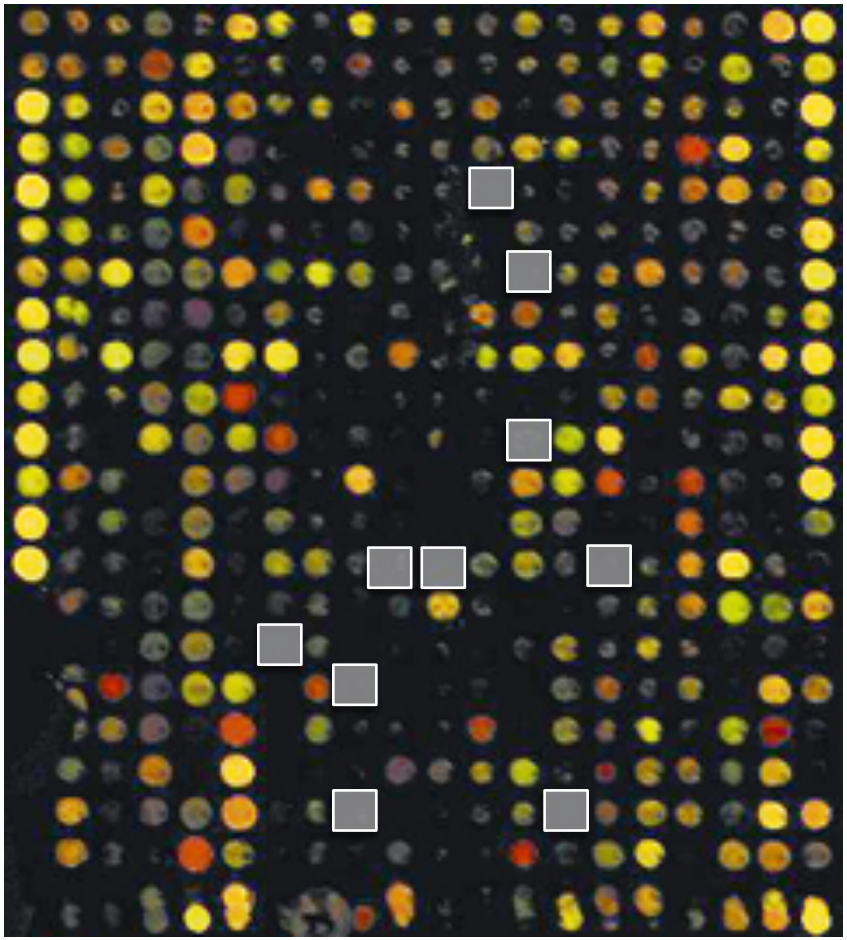
HapMap

- Reference panel for common genetic variants that occur in human beings



International HapMap Project

How HapMap ties in with GWAS

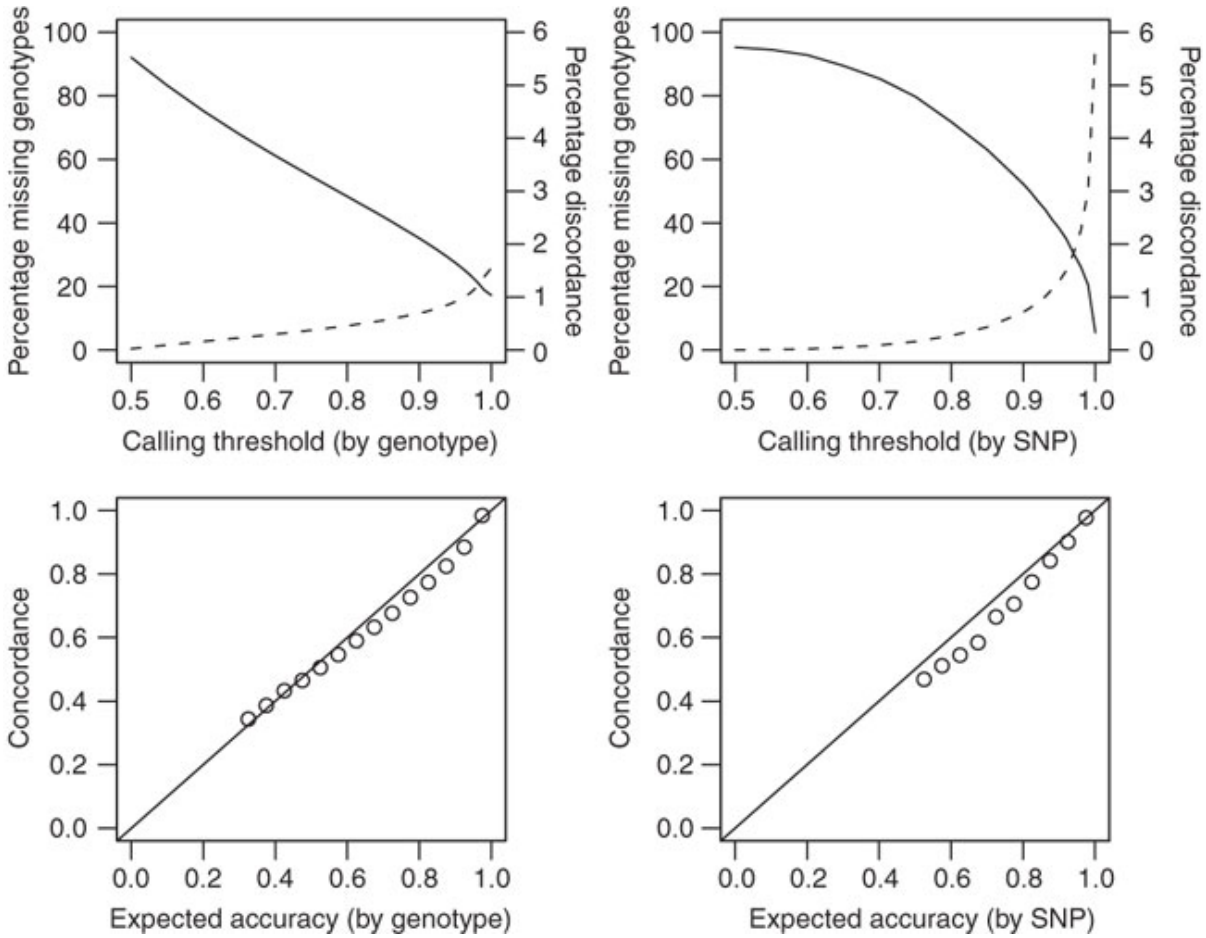


Nalls et al.

Filling in the blanks using HapMap

Imputation of missing data

Accuracy of GWAS with HapMap



Marchini, (Figure 1)

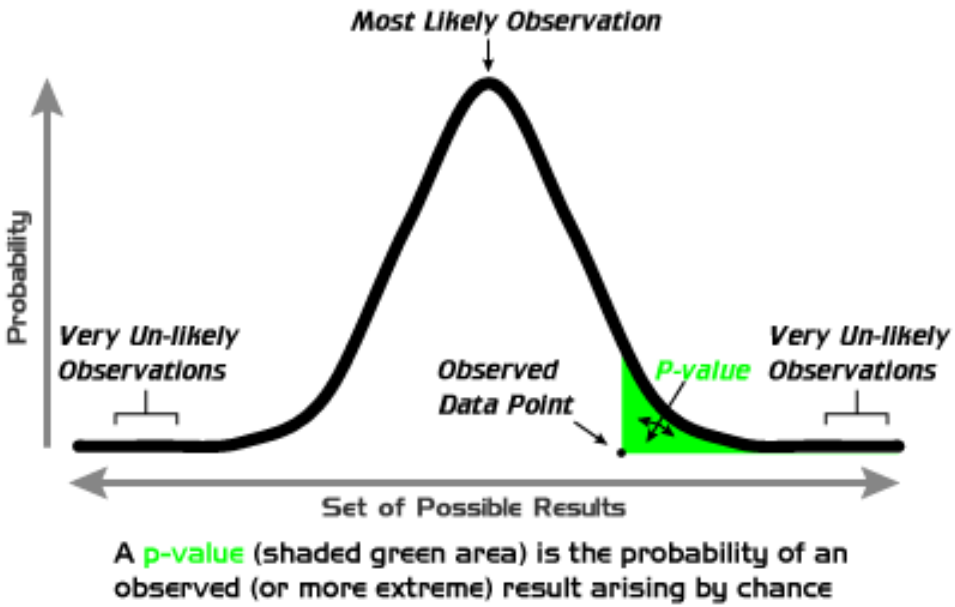
How HapMap ties in with GWAS

If certain genetic variations are observed more often in those with the disease, then the variations are **associated** with the disease.

What is an association?

Relevant terms in statistics

- Hypothesis testing
  - Null hypothesis (H_0)
  - Alternative hypothesis (H_A)
- Alpha-value
- p-value
- Association
- Bayes factor
- Type I and II error
  - Type I: false positive
  - Type II: false negative



Wikipedia

Bayes Factor and Type I error

Bayes Factor:

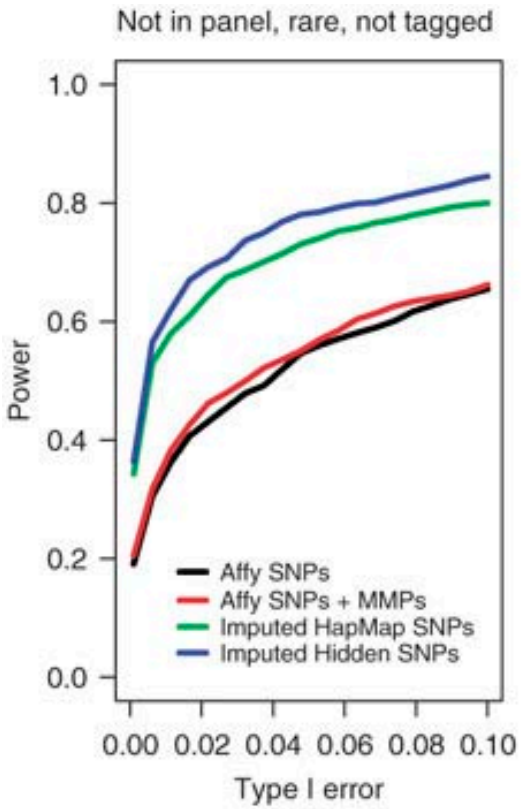
- $P(\text{Data}|\text{Model}) = P(M_1|D)/P(M_0|D)$

Type I error:

- $P(\text{reject } H_0|H_0 \text{ is true})$
- Best case: low value

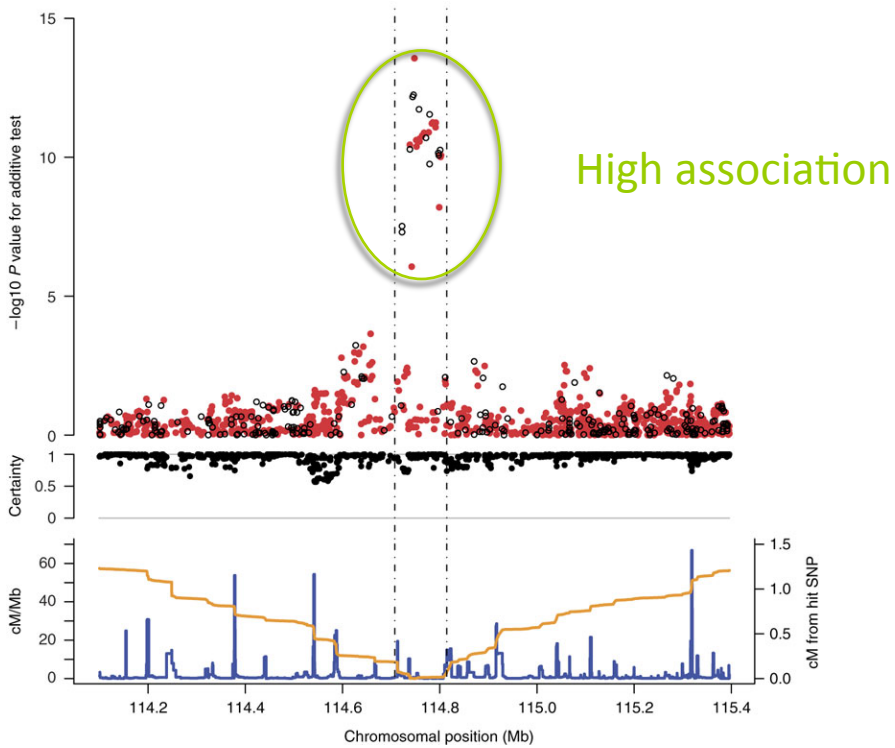
Power:

- $P(\text{reject } H_0|H_1 \text{ is true})$
- Best case: high value

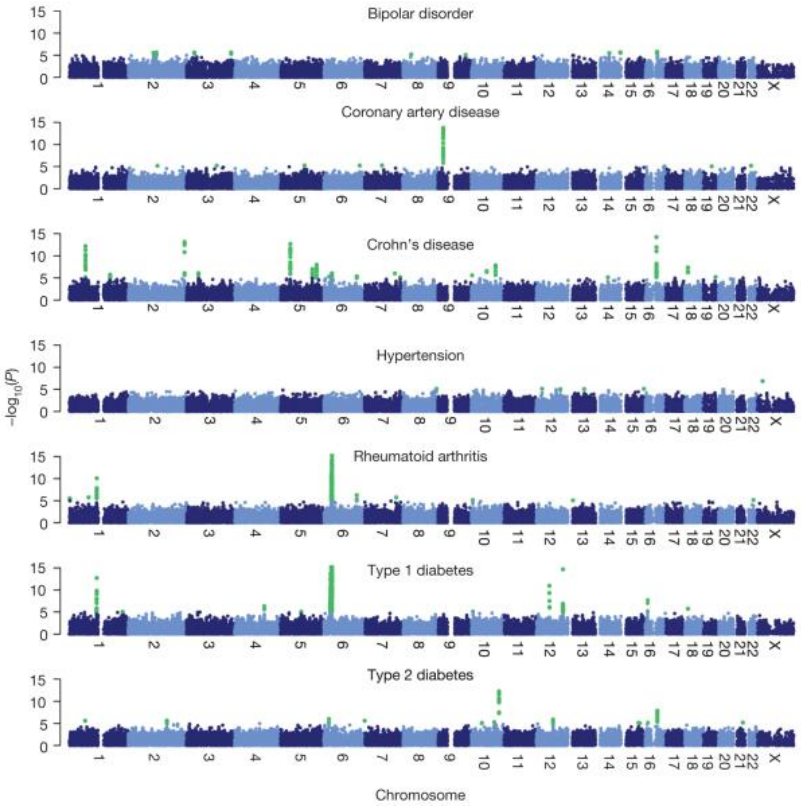


Marchini, (Figure 2)

Results



Marchini, (Figure 4)



Burton, (Figure 4)

Discussion

GWAS

- Can be used to find the genetic variations associated with other diseases
- Utilizes databases that contain the HapMap to refine haplotypes
- Is a promising technique for personalized medicine
- Needs to account for false positives
- Needs improvement in cost reduction

Questions / Comments?

G.W.A.S.

Citations

1. Burton, Paul R., et al. "Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls." *Nature* 447.7145 (2007): 661-678.
2. Marchini, Jonathan, et al. "A new multipoint method for genome-wide association studies by imputation of genotypes." *Nature genetics* 39.7 (2007): 906-913.
3. Nalls et al. “Large-scale meta-analysis of genome-wide association data identifies six new risk loci for Parkinson’s disease” *Nat. Genetics*, July 27, 2014. DOI: 10.1038/ng3043
4. Pasieka, Science Photo Library. https://www.mpg.de/10680/Modern_psychiatry
5. International HapMap Project. http://hapmap.ncbi.nlm.nih.gov/whatishapmap.html.
6. Genetics Science Learning Center. University of Utah. 2015. http://learn.genetics.utah.edu/content/pharma/snips/