

Exploring the Genetic Origins of Macular Degeneration:

Math 295 - Final Project



Data:

- 2004 Science Paper:
- Found two SNPs of significant association.
- Came to me raw (and filled with errors)

Complement Factor H Polymorphism in Age-Related Macular Degeneration

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What is AMD?

- Effects 11 million people in the US alone.
- Blindness is caused by extracellular growths.
- Primarily seen in people aged 60+



Data form:

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146 1145794 0 0 1 1 G G A G T T G G T T G G G G C C C C C C A A C C C C C C A A C C C C G A G G T T G G G G T C G G G G G G A C C C A A G T G G T C C T C A
T T T T C T C C G A C C G G C C G G T T A G T T C C C T T T C C G A C C A G G A A A G G T T A C C C G G C C A A G G A A T T A G A G T C C T T T A A G G T
T A A C C G G T T G G C C T T A A C C C T G A T T G G T T G G T T T C C C G T G A A A T T A G T T A A A A C G A A A C C A A C C T T C C T T A A C C A A A
G T T T C C G G A C T C C T T C C C C C C C C C T G A T A G A G A C T C C G G T T C C G A C C A A C C C C A A T T A A G G T T A A A A T T G G C C T T C C
C T A A T T C C C C G G A A G G A A G G G C C C C A G T C G A C C G A G G C C G G A A T T A A G G A A A A 0 0 G A T C A A A A T A C T C T T G C C C C G G
G G A A C C G G G G T T C C G G C C A A T T G G G G A A A A G G A A G G G G G C T T T T G G C C A G C C G G G A G G G C G A T T G G T T G G T T G G T T A
A C C C C G G T T G G T T T C C C T T T T G G C C G G G G T T G G G A A G G A C T G G A A A A A A C C C T G G C C A A G C A A G G C C G G C C C C C T G C A
A A A A A T T C C G A C C C G A A C C C C A A C C C C T T C C A G G G G G T T G G A G G G T T A A A A C C C A T C G A C C A A C T A A T C A A C C G G C T
A T G G C G C C A A G G T T T C T C G A T T G A G G C T C G G A A G A A A A C C G G C C C C C G G G G G C A A A A T T A G C T 0 0 C C G G T T C C G G T T
T T C C C C G G G A A A G G T T C C T T T T T T A A C C G G T T A A A A C C G G G G A A C C G A C C A A 0 0 A G A A 0 0 A G G G C G T T G G C C G G G G A
A G G G G T T A G A A T C A A G G G G G G T T G G G G T T G G G G T T T T G G G G T T A A C C T T A A C C G G C T G G C C G A A A C C C C T T G G G A C C T
T G A A A C C C C G G A C A A C C C C T C G G T T C C C C G G G G G A T T A A C T A G T C A G G G C C A A G G G G G A T T C G A C T T G G A A T T A G T T
T T C C C T G G A A G G G G A A A A T T G G G G G A C C A A T T T T A A C C G G T T A A C T A C T T A A T G G G A A T T T T A A G G A G A G A C C C C G G
A A C C G G G T A T T G T T T T G G T T C T T T T T G G C C T T C C A A A A T T C T G G A C G G T C G G A C C C T C G G T C G A A T G G A A C C G G G A T
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- Too big to open in a text editor
- Two files: .map and .ped
- Messy...

Messy:

- Proprietary technologies result in problems
- There are a million nothings.
- No documentation.

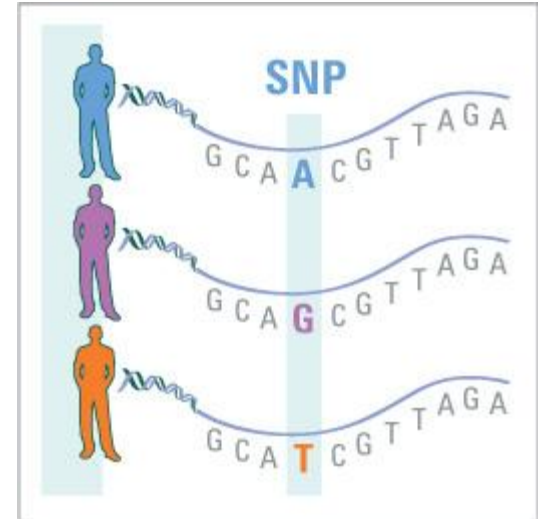
V10	V11	V12	V13
G	TRUE	TRUE	G
A	TRUE	TRUE	G
G	TRUE	TRUE	G
G	TRUE	TRUE	G
G	TRUE	TRUE	G



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What is a SNP?

- **S**ingle **N**ucleotide **P**olymorphism.
- The binary of biology.
- Come in pairs called genotypes.



Testing for association:

- Groups are made by phenotype (or trait).

phenotype	rs950122	rs1496555	rs1338382
TRUE	CG	GG	TT
TRUE	GG	AA	TT
TRUE	CG	GG	TT

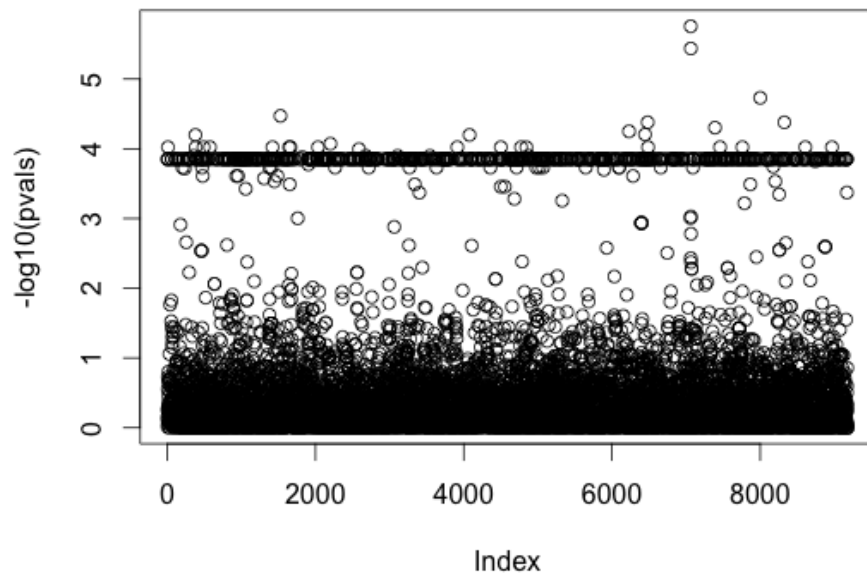
- A statistical test for association is run. (I used chi-square)

- Looped over all SNPs and plotted...

	rs1496555		
phenotype	AA	AG	GG
TRUE	4	15	75
FALSE	1	11	38

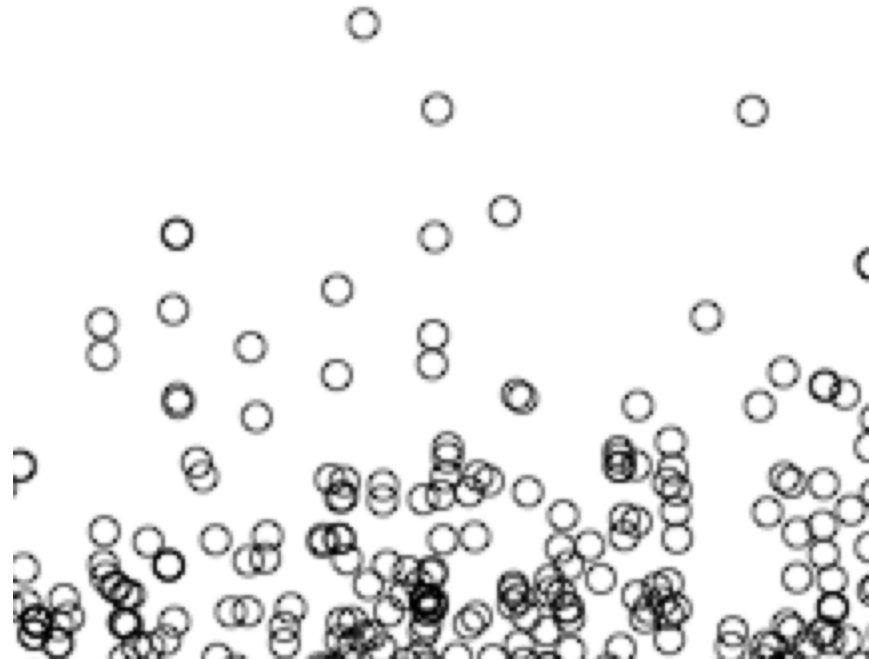
The manhattan plot:

- The big gun in genome wide association studies.
- $-\log_{10}(\text{p-value})$ - transforms p-values to magnitudes.
- Fantastic for seeing impacts.



The manhattan plot cont.

- Flawed...
- Hard to actually spot what's going on.
- Labeling is almost impossible...

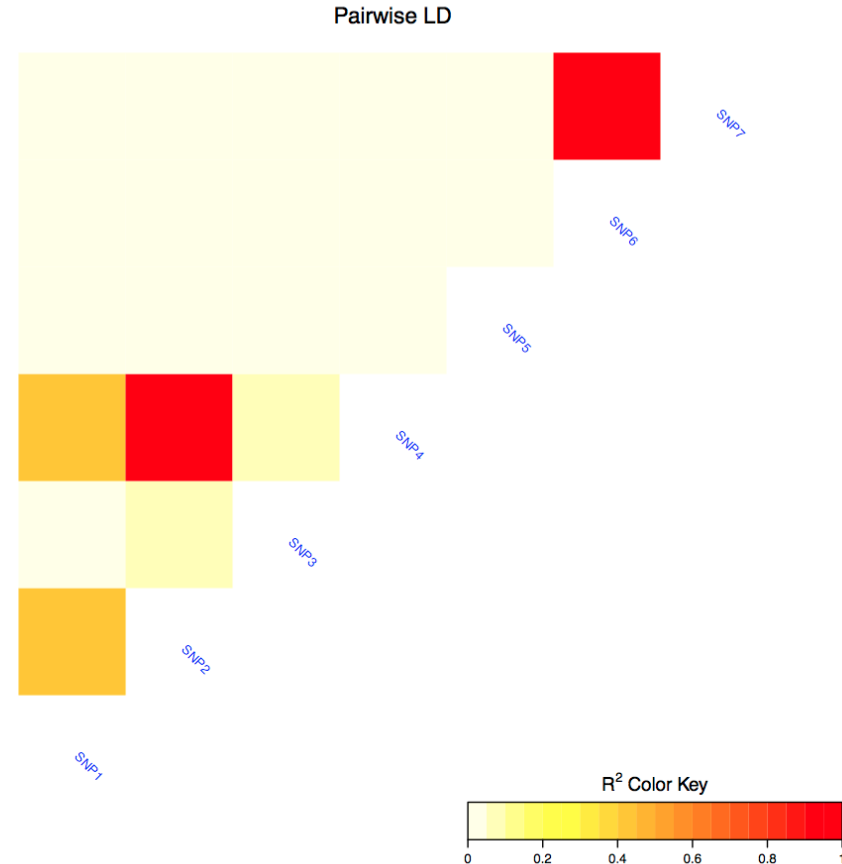


A new way:

www.uvm.edu/~nstrayer/dataFinal

Linkage Disequilibrium (LD):

- Gender differences!
- Much less LD than expected
- Tip of iceberg



Conclusion:

- New SNPs!
- A hypothesis driven follow up is necessary.
- Traits are complex.

