A GENOME-WIDE ASSOCIATION STUDY OF GLAUCOMA AND AGE-RELATED MACULAR DEGENERATION

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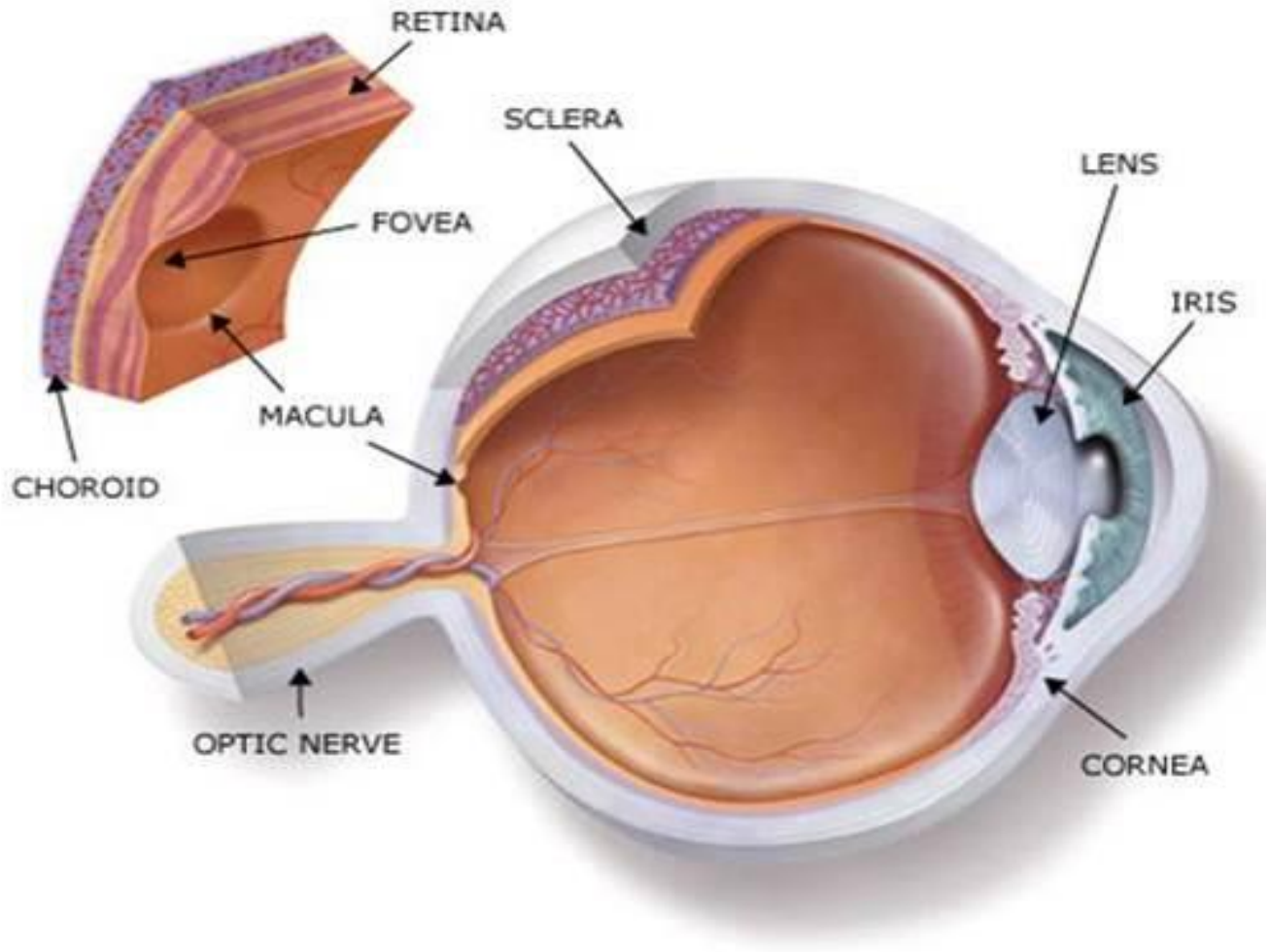
EYE ANATOMY

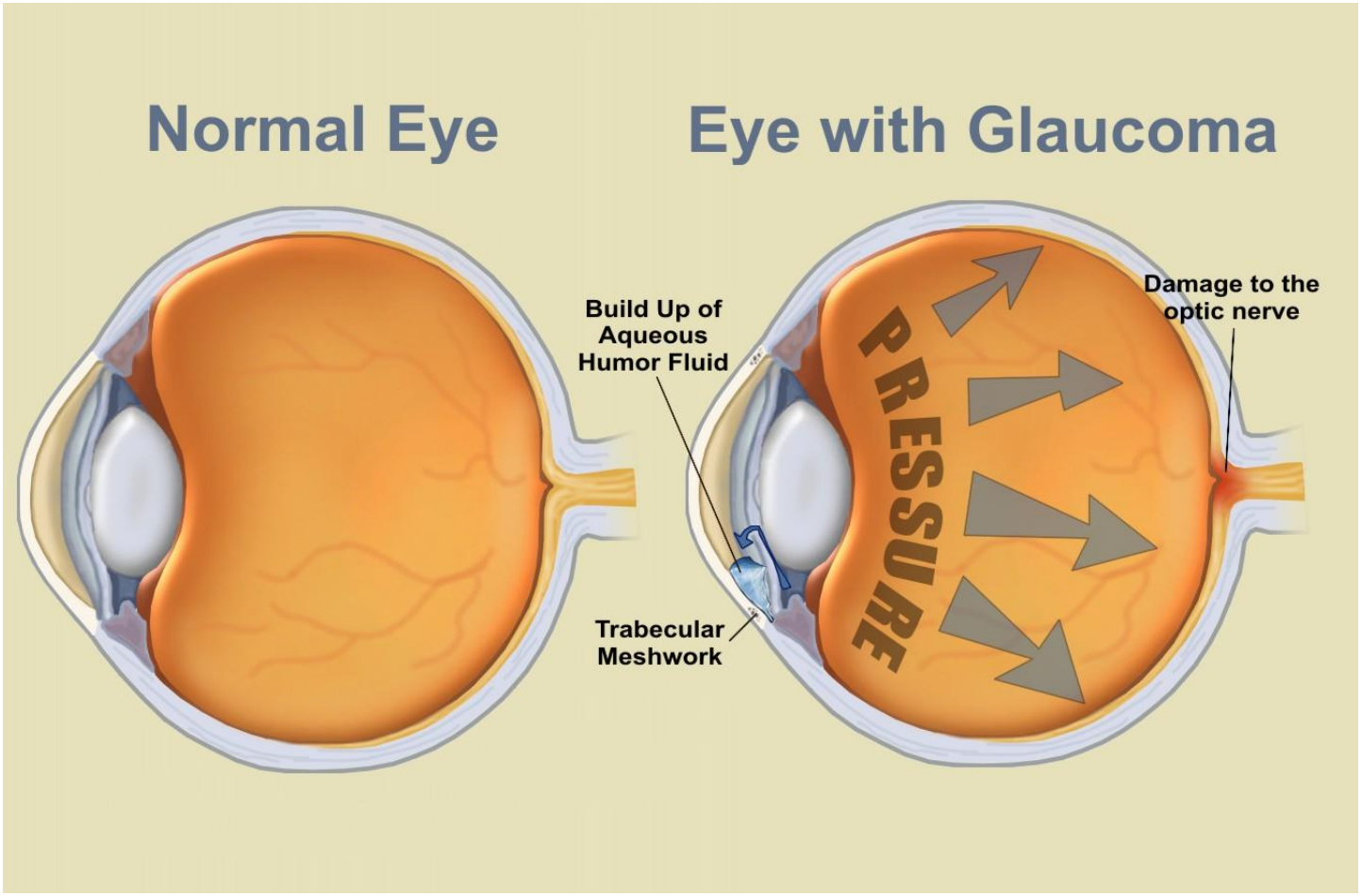


http://biotuesdays.com/2011/04/05/macuclear-seeking-financing-for-pivotal-dry-amd-trial/picture2-2/

WHAT IS GLAUCOMA?

- Glaucoma refers to a group of eye conditions characterized by injury to the optic nerve and a corresponding pattern of visual loss
- One of the leading causes of blindness in the U.S.; accounts 10% of all blindness in the U.S.
- 2.2 million Americans suffer from glaucoma
- Most common form of glaucoma in the United States is primary open angle glaucoma (POAG)
- Risk factors for glaucoma include advanced age, ethnicity, elevated intraocular pressure (IOP), and family history
- Individuals with relatively thin corneas have been shown to have an increased risk of developing glaucoma than individuals with normal corneal thickness

NORMAL EYE COMPARED TO EYE WITH GLAUCOMA



http://www.improveeyesightfast.com/diabetes-and-eye-problems/

WHAT IS AGE-RELATED MACULAR DEGENERATION(AMD)?

- AMD gradually destroys the macula; which is the part of the eye that provides sharp and central vision
- One of the leading causes of vision loss among individuals age 50 and older
- 2 million Americans have AMD
- AMD does not cause complete blindness as individuals with the disease are able to use their side (peripheral) vision
- Risk factors include smoking, race (Caucasians are more likely to contract AMD than people of African descent), and family history

- How a Glaucoma patient sees

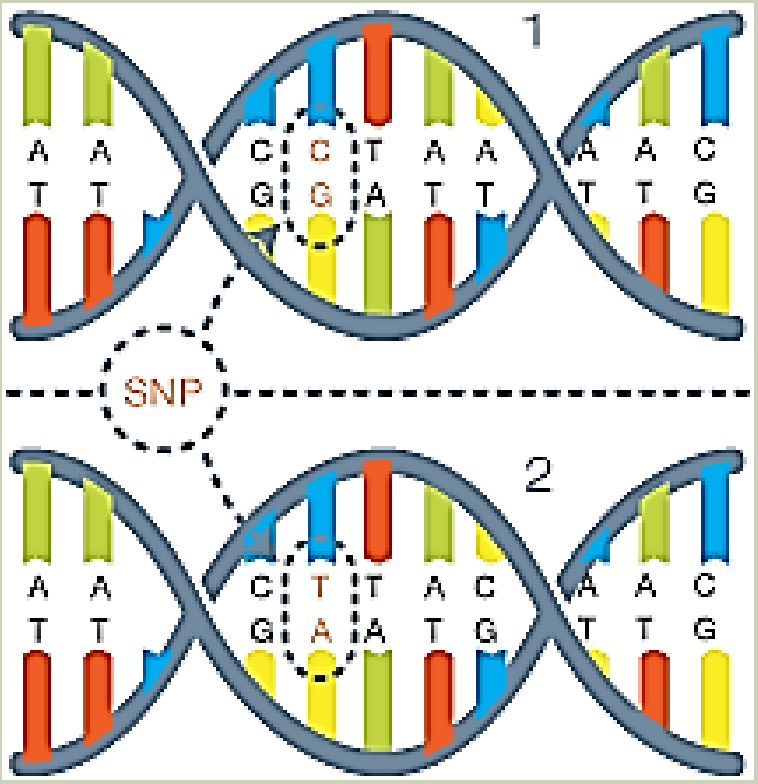
http://www.optos.com/en-us/Patients/Eye-conditions/Glaucoma/

- How an AMD patient sees

http://www.optos.com/en-us/Patients/Eye-conditions/Age-related-macular-degeneration-AMD/

METHODS

- GWAS
- 400 POAG patients / 400 AMD patients
- 500,000 single nucleotide polymorphisms (SNPs)
- There are 3 possible genotypes at each SNP, denoted by 0,1, and 2



http://www.siriusgenomics.com/technology/

- One contingency table for each SNP
- Analyzed each table with the Pearson's Chi-Squared Test

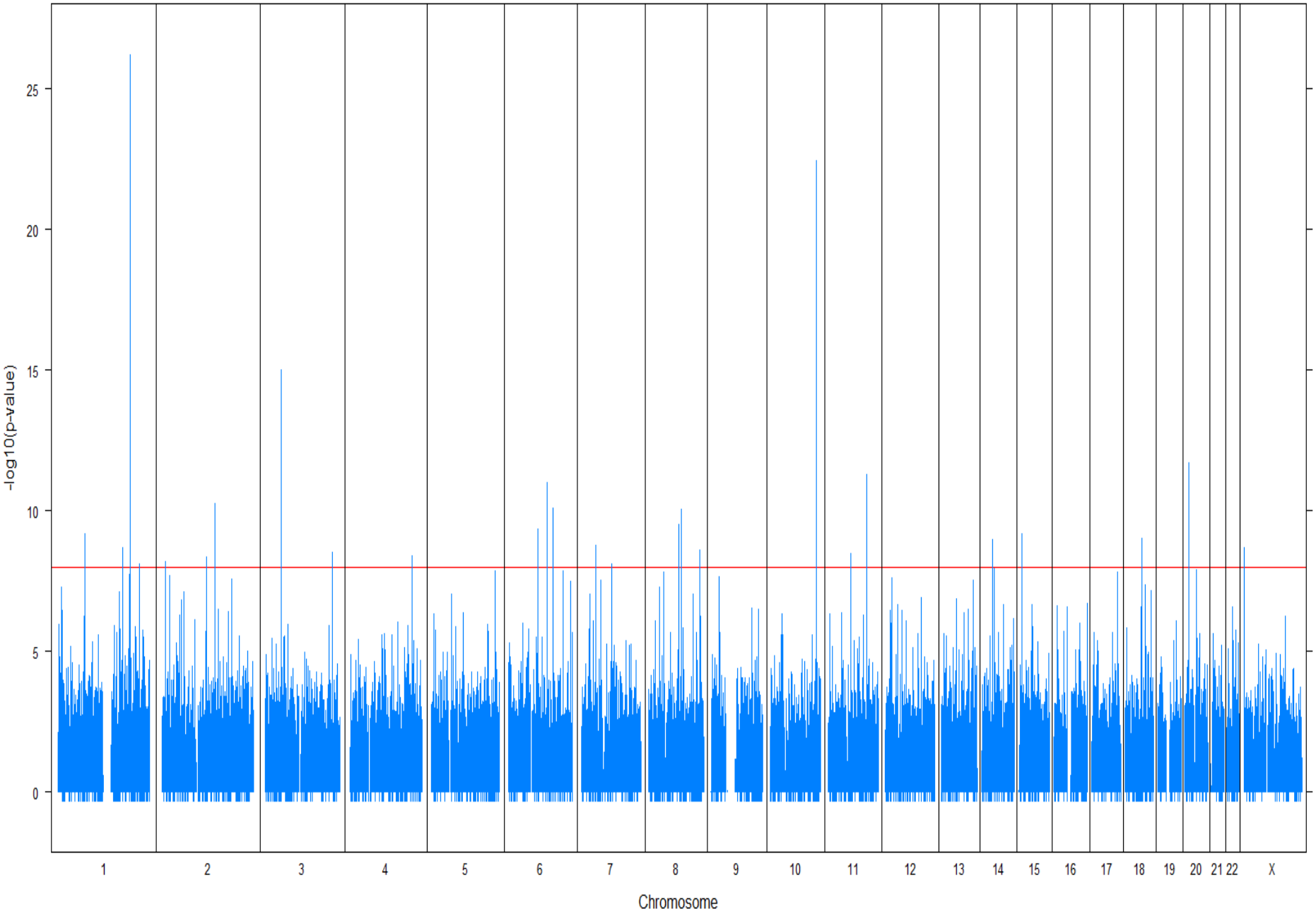
	Genotype		
	0	1	2
POAG	73	187	133
AMD	10	109	280

Contingency table for SNP_A-2171106

RESULTS

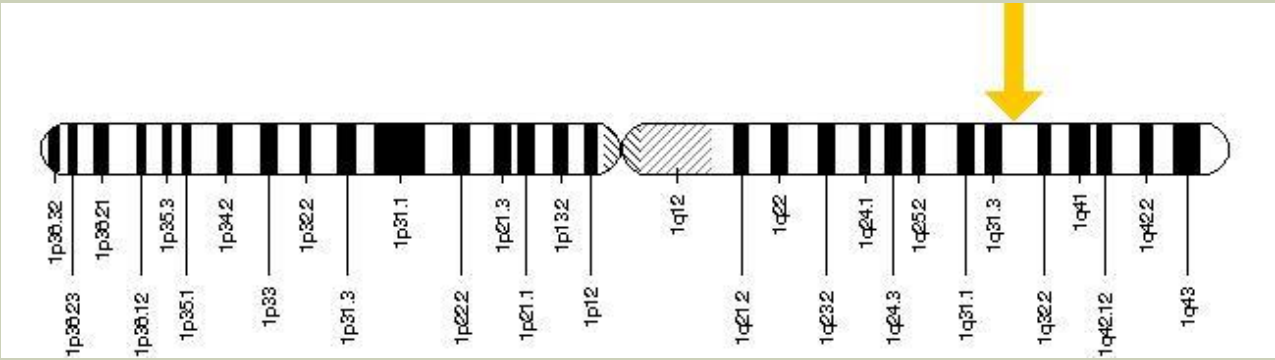
- R used for data analysis: finding p-values of each SNP for each contingency table
- 44 SNPs significant at p-value of 10^-8

SNP	RS name	p-value	Chr	Base pair position
SNP_A-2171106	rs10737680	6.31e-27	1	193411112
SNP_A-1841655	rs3750848	3.67e-23	10	124205305
SNP_A-2006209	rs10490924	2.49e-22	10	124204438
SNP_A-4206823	rs395544	1.65e-22	1	193429929
SNP_A-4290423	rs10733086	8.72e-21	1	193408592
⋮	⋮	⋮	⋮	⋮


-log10(p-value)
25
20
15
10
5
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
X
Chromosome

GENE NAMES

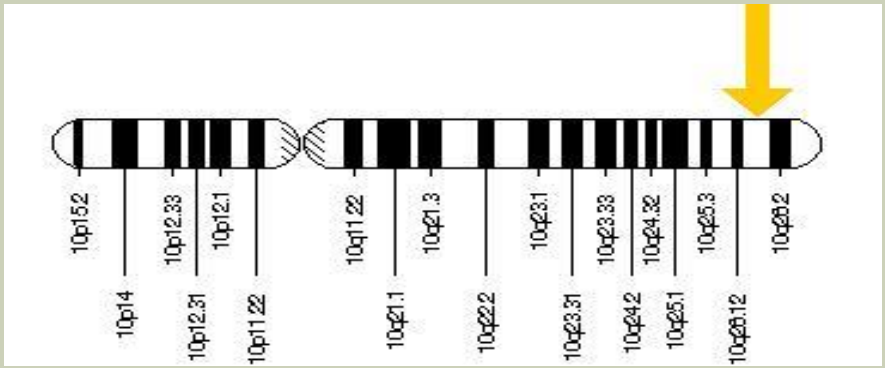
- Chr 1: Complement Factor H (CFH)
  - CFH is a key regulator for the complement system of immunity that protects against infection and spares healthy cells.
- Chr 10: ARMS2
  - ARMS2 is a mitochondrial protein thought to play roles in diseases in the elderly.



http://ghr.nlm.nih.gov/gene/CFH

Chromosome 1:

CFH



http://ghr.nlm.nih.gov/gene/ARMS2

Chromosome 10:

ARMS2

CONCLUSION

This study used two separate populations in which one is the control of the other (POAG and AMD) allowing the investigators to assess genetic associations. The investigators concluded that there is a genetic association between AMD and CFH gene on chromosome 1 and between AMD and ARMS2 gene on chromosome 10. These findings are consistent with previous findings reported in the literature.

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ACKNOWLEDGEMENTS

- Dr. Kai Wang
- Dr. Gideon Zamba
- Terry Kirk
- Dr. Val Sheffield (for generating data)
- Dr. Ed Stone (for generating data)
- Dr. Todd Scheetz (for bioinformatics support)
- ISIB Program Faculty and Students