Enlis Genomics

Report Date: **August 19, 2015**
Software Annotation Version: **8**

Phenotype Report

Name: **Greg Mendel**
Genome ID: **genome_Greg_Mendel_Dad**

Sequencing Provider: **23andMe**
Sequencing Type: **Genotyping SNP Array**

Phenotype: **Macular Degeneration**

Description:
Age-related macular degeneration is an eye disease that is a leading cause of vision loss in older people in developed countries. The vision loss usually becomes noticeable in a person's sixties or seventies and tends to worsen over time. Age-related macular degeneration mainly affects central vision, which is needed for detailed tasks such as reading, driving, and recognizing faces. The vision loss in this condition results from a gradual deterioration of light-sensing cells in the tissue at the back of the eye that detects light and color (the retina). Specifically, age-related macular degeneration affects a small area near the center of the retina, called the macula, which is responsible for central vision. Side (peripheral) vision and night vision are generally not affected. Researchers have described two major types of age-related macular degeneration, known as the dry form and the wet form. The dry form is much more common, accounting for 85 to 90 percent of all cases of age-related macular degeneration. It is characterized by a buildup of yellowish deposits called drusen beneath the retina and slowly progressive vision loss. The condition typically affects vision in both eyes, although vision loss often occurs in one eye before the other. The wet form of age-related macular degeneration is associated with severe vision loss that can worsen rapidly. This form of the condition is characterized by the growth of abnormal, fragile blood vessels underneath the macula. These vessels leak blood and fluid, which damages the macula and makes central vision appear blurry and distorted.

Modes of inheritance*: Autosomal Recessive
Polygenic Inheritance
Autosomal Dominant

Variation Summary:

Variant Classification	Num. Variants Found	Num. Positions Not Called (Missing data)	Num. Positions Matching Reference	Num. Variants Assessed
Pathogenic	1	7 (38.9%)	10 (55.6%)	18
Risk factor	3	4 (19.0%)	14 (66.7%)	21
Protective	2	0 (0.0%)	0 (0.0%)	2

Total number of phenotype variations assessed: **41**

Variation Details:

- **Chr20: 23,618,427 C>T** — **Pathogenic** ★☆☆☆☆†

  Zygosity: Heterozygous dbSNP ID: rs1064039
  Population Allele Frequency: 12.01%
  Gene Impact: **CST3** MISSENSE A-25-T
  Supporting Publications: http://www.ncbi.nlm.nih.gov/pubmed/11815350

- **Chr3: 39,307,256 C>T** — **Risk factor** ★☆☆☆☆†

Zygosity: Heterozygous dbSNP ID: rs3732379

Population Allele Frequency: 22.08%

Gene Impact: **CX3CR1** MISSENSE V-249-I
MISSENSE V-281-I

Supporting Publications: http://www.ncbi.nlm.nih.gov/pubmed/23716478
http://www.ncbi.nlm.nih.gov/pubmed/17909628
http://www.ncbi.nlm.nih.gov/pubmed/17909628 ... and 5 more

- **Chr10: 50,747,539 G>C** — Risk factor †

Zygosity: Heterozygous dbSNP ID: rs3793784

Population Allele Frequency: 23.78%

Gene Impact: **ERCC6-PGBD3** UTR5

Gene Impact: **ERCC6** UTR5

Supporting Publications: http://www.ncbi.nlm.nih.gov/pubmed/17854076
http://www.ncbi.nlm.nih.gov/pubmed/16754848

- **Chr19: 6,718,387 G>C** — Risk factor †

Zygosity: Homozygous dbSNP ID: rs2230199

Population Allele Frequency: 15.18%

Gene Impact: **C3** MISSENSE R-102-G

Supporting Publications: http://www.ncbi.nlm.nih.gov/pubmed/23455636
http://www.ncbi.nlm.nih.gov/pubmed/19259132
http://www.ncbi.nlm.nih.gov/pubmed/17767156 ... and 3 more

- **Chr6: 31,910,938 G>T** — Protective †

Zygosity: Heterozygous dbSNP ID: rs547154

Population Allele Frequency: 11.78%

Gene Impact: **C2** INTRON

Gene Impact: **CFB** INTRON

Supporting Publications: http://www.ncbi.nlm.nih.gov/pubmed/16936732
http://www.ncbi.nlm.nih.gov/pubmed/16518403

- **Chr6: 31,914,180 G>A** — Protective †

Zygosity: Heterozygous dbSNP ID: rs641153

Population Allele Frequency: 9.77%

Gene Impact: **CFB** MISSENSE R-534-Q
INTRON
MISSENSE R-32-Q

Supporting Publications: http://www.ncbi.nlm.nih.gov/pubmed/16936732
http://www.ncbi.nlm.nih.gov/pubmed/16518403

Limitations:

There are several limitations to the results presented here:

- 11 variation(s) known to be related to this phenotype were not called in the sequencing data. This data is missing and would likely require additional sequencing to determine.
- The quality of the sequencing data has not been verified by Enlis. It is possible that variations listed here do not actually exist in the listed genome, and it is possible that positions listed as matching reference are actually variant.
- Knowledge of the genomic factors that relate to this phenotype are incomplete and may be incorrect. New variations and genes that relate to this phenotype may be discovered in the future. Variations and genes currently thought to be related to this phenotype may be found to be incorrect. Care should especially be taken in the interpretation of variations with confidence star levels of only 1 or 2.
- The Enlis Genome Research application, and all associated communication (Enlis Products) are for research and educational purposes only. Enlis Products together and separately do not constitute medical advice and should not be used as a source of professional medical advice or diagnosis.

Notes

* Mode of inheritance defintions:

Autosomal Dominant
Autosomal dominant inheritance refers to genetic conditions that occur when a mutation is present in one copy of a given gene (i.e., the person is heterozygous).

Autosomal Recessive
Autosomal recessive inheritance refers to genetic conditions that occur only when mutations are present in both copies of a given gene (i.e., the person is homozygous for a mutation, or carries two different mutations of the same gene, a state referred to as compound heterozygosity).

Polygenic Inheritance
A phenotypic outcome (physical characteristic or disease predisposition) that is determined by many genes.

† Confidence Star Levels:


Review Status: Classified by single submitter with no evidence provided, or multiple conficting interpretations


Review Status: Classified by single submitter with evidence


Review Status: Classified by multiple submitters


Review Status: Reviewed by expert panel


Review Status: Reviewed by professional society

Human genome reference version: HomoSapiens_GRCh37

Appendix - Full Position List:

Position and Variation	dbSNP ID	Gene	Clinical Significance	Phenotype	Variation Found	Position Not Called	Position Matches Reference
Chr1: 94,463,617 >T	rs1800555	ABCA4	Risk factor	Macular degeneration, age-related, 2, susceptibility to			Reference
Chr1: 94,473,807 >T	rs1800553	ABCA4	Risk factor	Macular degeneration, age-related, 2, susceptibility to			Reference
Chr1: 94,496,666 >A	rs61750130	ABCA4	Risk factor	Macular degeneration, age-related, 2, susceptibility to			Reference
Chr1: 94,508,969 >A	rs61751374	ABCA4	Risk factor	Macular degeneration, age-related, 2, susceptibility to			Reference
Chr1: 94,512,565 >T	rs1801581	ABCA4	Risk factor	Macular degeneration, age-related, 2, susceptibility to			Reference
Chr1: 94,544,895 >A	rs61748550	ABCA4	Pathogenic	Age-related macular degeneration 2			Reference
Chr1: 186,147,638 >G	rs121434382	HMCN1	Risk factor	Macular degeneration, age-related, 1, susceptibility to		Missing Data	
Chr1: 196,642,233 >A	rs800292	CFH	Risk factor	Age-related macular degeneration 4			Reference
Chr1: 196,659,237 >C		CFH	Risk factor	Age-related macular degeneration 4			Reference
Chr1: 196,682,947 >C	rs2274700	CFH	Risk factor	Age-related macular degeneration 4			Reference
Chr1: 196,683,035 >G		CFH	Risk factor	Age-related macular degeneration 4		Missing Data	
Chr1: 196,696,933 >G		CFH	Risk factor	Age-related macular degeneration 4			Reference
Chr1: 196,716,375 >T	rs121913059	CFH	Risk factor	Age-related macular degeneration 4			Reference
Chr3: 39,307,162 >A	rs3732378	CX3CR1	Risk factor	Macular degeneration, age-related, 12, susceptibility to			Reference

Position and Variation	dbSNP ID	Gene	Clinical Significance	Phenotype	Variation Found	Position Not Called	Position Matches Reference
Chr3: 39,307,256 >T	rs3732379	CX3CR1	Risk factor	Macular degeneration, age-related, 12, susceptibility to	Zygosity 1		
Chr5: 39,331,894 >A	rs34882957	C9	Risk factor	Macular degeneration, age-related, 15		Missing Data	
Chr5: 127,671,254 >G	rs149054177	FBN2	Pathogenic	Macular degeneration, early-onset		Missing Data	
Chr5: 127,674,667 >T	rs200060005	FBN2	Pathogenic	Macular degeneration, early-onset		Missing Data	
Chr6: 31,903,804 >C	rs9332739	C2,CFB, CFB	Pathogenic	Age-related macular degeneration 14			Reference
Chr6: 31,910,938 >T	rs547154	C2,CFB, CFB	Protective	Age-related macular degeneration 14	Zygosity 1		
Chr6: 31,914,024 >A	rs4151667	CFB,CFB	Pathogenic	Age-related macular degeneration 14			Reference
Chr6: 31,914,180 >A	rs641153	CFB,CFB	Protective	Age-related macular degeneration 14	Zygosity 1		
Chr9: 120,475,302 >G	rs4986790	TLR4	Risk factor	Macular degeneration, age-related, 10, susceptibility to			Reference
Chr10: 50,747,539 >C	rs3793784	ERCC6, ERCC6-PGBD3	Risk factor	Age-related macular degeneration 5	Zygosity 1		
Chr10: 124,214,448 >T	rs10490924	ARMS2	Risk factor	Age-related macular degeneration 8			Reference
Chr10: 124,220,544 >A	rs11200638	HTRA1	Risk factor	Age-related macular degeneration 7			Reference
Chr14: 92,336,680 >T	rs121434303	FBLN5	Pathogenic	Age-related macular degeneration 3			Reference
Chr14: 92,343,929 >T	rs121434302	FBLN5	Pathogenic	Age-related macular degeneration 3			Reference
Chr14: 92,343,965 >A	rs28939073	FBLN5	Pathogenic	Age-related macular degeneration 3			Reference
Chr14: 92,357,678 >G	rs28939072	FBLN5	Pathogenic	Age-related macular degeneration 3			Reference
Chr14: 92,403,411 >A	rs121434301	FBLN5	Pathogenic	Age-related macular degeneration 3		Missing Data	
Chr14: 92,403,458 >T	rs121434300	FBLN5	Pathogenic	Age-related macular degeneration 3			Reference
Chr14: 92,403,492 >G	rs121434299	FBLN5	Pathogenic	Age-related macular degeneration 3			Reference

Position and Variation	dbSNP ID	Gene	Clinical Significance	Phenotype	Variation Found	Position Not Called	Position Matches Reference
Chr16: 68,714,984 DEL		CDH3	Pathogenic	Juvenile macular degeneration and hypotrichosis		Missing Data	
Chr16: 68,719,191 >A	rs121434542	CDH3	Pathogenic	Juvenile macular degeneration and hypotrichosis			Reference
Chr19: 3,770,830 >T	rs398124431	RAX2	Pathogenic	Age-related macular degeneration 6		Missing Data	
Chr19: 3,770,914 >T	rs121908280	RAX2	Pathogenic	Age-related macular degeneration 6		Missing Data	
Chr19: 6,718,146 >G	rs147859257	C3	Risk factor	Macular degeneration, age-related, 9, susceptibility to		Missing Data	
Chr19: 6,718,387 >C	rs2230199	C3	Risk factor	Macular degeneration, age-related, 9, susceptibility to	Zygosity 2		
Chr20: 23,618,427 >T	rs1064039	CST3	Pathogenic	Age-related macular degeneration 11	Zygosity 1		
ChrM: 3,243 >G		MT-TL1	Pathogenic	Age-related macular degeneration 2		Missing Data	