

GENETIC DIAGNOSTIC LABORATORY
UNIVERSITY OF PENNSYLVANIA SCHOOL OF MEDICINE
DEPARTMENT OF GENETICS
Tel: (215) 573-9161 • Fax: (215) 573-5940
CLIA ID NUMBER 39D0893887
<http://www.med.upenn.edu/genetics/core-facs/gdl/>

Age-Related Macular Degeneration (ARMD)

- Background:** Age-related macular degeneration (ARMD) is the leading cause of visual impairment and irreversible blindness in older adults. ARMD is the result of age-related changes that occur in the outer retina of the eye. The etiology of ARMD remains largely unknown; however certain environmental risk factors, primarily smoking, have been shown to be associated with the development ARMD. Other known risk factors include hypertension, chronic inflammation, and a family history of ARMD. More recently, specific genetic alterations that are implicated in ARMD have been identified. While some of these alterations confer protection from developing the disease (*C2* & *BF*), the presence of others (*CFH* Y402H & *LOC387115* A69S) increases the risk to develop ARMD. *CFH*, *C2* and *BF* are genes in the complement cascade, a pathway in which dysregulation might contribute to drusen formation. *LOC387115* is an independent locus at chromosome 10q26; its precise function is not known.
- Assay:** SNP (Single Nucleotide Polymorphism) genotyping test based on real-time PCR for the presence or absence of four variants (*CFH* Y402H, *LOC387715* A69S, *C2*, and *BF*) associated with the risk for developing ARMD.
- Utility:** Risk assessment for developing ARMD in individuals who might be at risk due to environmental factors or family history. Risk assessment for developing advanced ARMD (wet form) in individuals who have been diagnosed with ARMD. *CFH* and A69S independently confer a 7 to 8-fold increase in risk, while a combination of variants in *C2* and *BF* confer a 3-fold decrease in developing ARMD. However, the overall contribution of these alleles to the risk of ARMD is still unknown due to multifactorial inheritance.
- Sensitivity:** Detection of these risk alleles is >99%.
- Turn Around:** 2 weeks
- Fee:** TEST A: Genotyping for risk of developing ARMD [*CFH*, *BF*, and *C2*]: \$220
TEST B: Genotyping for risk of advanced (wet) ARMD [*CFH* and A69S]: \$180
- CPT codes:** 83891, 83898, 83904, and 93912
- References:** Haines JL, Hauser MA, Schmidt S *et al*: Complement factor H variant increases the risk of age-related macular degeneration. *Science* 2005; 308:419-421.
- Gold B, Merriam JE, Zernant J *et al*: Variation in factor B (BF) and complement component 2 (C2) genes is associated with age-related macular degeneration. *Nat Genet* 2006; 38:458-462.
- Seddon J, Francis PJ, George S *et al*: Association of *CFH* Y402H and *LOC387715* A69S with progression of age-related macular degeneration. *JAMA* 2007; 297:1793-1800.

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Age-Related Macular Degeneration Testing
INSTRUCTIONS FOR SAMPLE SUBMISSION

Documentation: Each sample must be accompanied by:

1. A requisition for DNA analysis completed by the physician, nurse or genetic counselor requesting screening. ***Please note: ICD-9 code is required for billing purposes. If ICD-9 code is unknown, please provide patient's clinical symptom(s) or family history that prompted testing.***
2. The patient's pedigree including three generations, if possible.
3. An informed consent signed by the patient and the professional obtaining the consent. Please have the patient initial at the top of each page and send **all** pages of the consent.
4. A verification of blood tubes form signed by the patient. The form should be signed at the time of the blood draw.
5. A completed registration form with check, money order, credit card authorization or information for billing the referring institution.

**IN THE EVENT THAT ALL PROPERLY COMPLETED FORMS DO NOT ACCOMPANY
THE SPECIMEN, YOU WILL BE NOTIFIED, AND TESTING WILL BE HELD UNTIL
PAPERWORK IS COMPLETE.**

Preparing Sample:

- Obtain 2 EDTA tubes (lavender top) of blood - approx. 4 mL per tube
- Label each tube with the patient's name and date sample was obtained
- We accept banked or recently extracted DNA; please include the concentration

Shipping Sample:

Ship at room temperature via Federal Express or other overnight courier that guarantees AM delivery to arrive Monday-Friday. There is no one in the laboratory evenings and weekends to receive samples. If sample is drawn on a Friday, please refrigerate it until shipment on the following business day.

Shipping Address:

Genetic Diagnostic Laboratory
University of Pennsylvania
415 Anatomy-Chemistry Building
3620 Hamilton Walk
Philadelphia, PA 19104

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REQUEST FOR AGE-RELATED MACULAR DEGENERATION TESTING

PATIENT FIRST NAME _____ PATIENT LAST NAME _____

BIRTH DATE _____ SEX _____ RACE _____ ETHNICITY _____

STREET ADDRESS _____

CITY _____ STATE _____ ZIP _____ HOME PHONE _____

Has the PATIENT been diagnosed with AGE-RELATED MACULAR DEGENERATION? YES _____ NO _____
IF YES, HAS IT BEEN DIAGNOSED IN ONE EYE _____ OR BOTH EYES _____?

HISTORY OF SMOKING? **NO** **YES** HOW LONG? _____

HISTORY OF HYPERTENSION? **NO** **YES**

HISTORY OF CHRONIC INFLAMMATION IN THE EYES? **NO** **YES** CAUSE? _____

ARE THERE ANY FAMILY MEMBERS WITH AGE-RELATED MACULAR DEGENERATION? **NO** **YES**
IF YES, WHAT IS THE RELATIONSHIP TO THE PATIENT?

REFERRING PHYSICIAN _____ PHONE _____ FAX _____

GENETIC COUNSELOR _____ PHONE _____ FAX _____

EMAIL ADDRESS FOR COUNSELOR OR PHYSICIAN _____

INSTITUTION and
DEPARTMENT _____

STREET ADDRESS _____

CITY _____ STATE _____ ZIP _____ COUNTRY _____

ICD-9 CODE: _____ 362.50 (macular degeneration, senile, unspecified > use for affected patient)
_____ V19.1 (family history of blindness or visual loss > use for unaffected at-risk family member)
_____ other _____

TEST REQUESTED: _____ Test A: Risk for Developing ARMD [CFH, BF, C2]

_____ Test B: Risk for Developing Advanced (wet) ARMD [CFH and A69S]

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Patient Registration Form

Please provide the following information. We cannot perform your test without ALL of this information. PLEASE PRINT ALL ANSWERS

PATIENT INFORMATION

LAST FIRST MI _____ PATINET'S MAIDEN NAME IF PREVIOUS TESTING WAS PERFORMED _____

Date of Birth: _____ *Gender:* ___ Male ___ Female

Patient Address: _____
STREET/APT NO.

CITY, STATE, ZIP _____ COUNTRY IF OUTSIDE UNITED STATES _____ HOME TELEPHONE _____

REFERRING PHYSICIAN

NAME MD DO OTHER _____ INSTITUTION _____

STREET ADDRESS _____ CITY, STATE, ZIP _____

TELEPHONE _____ FAX _____

PAYMENT OPTIONS (must choose one) [a receipt will be mailed to the patient for self-pay options]

_____ I have enclosed a check payable to the "Genetic Diagnostic Laboratory" for \$ _____

_____ Please charge my credit card for the amount of \$ _____
___ VISA ___ Master Card ___ Discover ___ American Express

Card Number: _____ Exp date: _____

Name as it appears on card: _____

_____ I have Pennsylvania Medicaid. A copy of my Medicaid card is attached.

_____ INSTITUTIONAL BILLING: The Institution where my testing originated has agreed to pay all charges for the testing. INCLUDE Billing Address, Person Authorizing Payment, Telephone, and Fax below:

BILLING ADDRESS _____

BILLING ADDRESS _____

PERSON AUTHORIZING PAYMENT _____ PHONE _____ FAX _____

Verification of Correctly Identified Blood Tubes

I am a participant in genetic DNA testing.

I have been shown the tubes containing my blood for this genetic testing and my name has been correctly placed on each one of these tubes.

I have signed a copy of the consent form regarding this genetic testing to be sent along with my blood samples. If requested, I have been given a copy of the consent form to keep.

Participant Name: _____

Participant Signature: _____

Date: _____

INITIALS _____

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Informed Consent for Age-Related Macular Degeneration Genetic Testing

I, _____, hereby request testing for the genetic variants associated with **age-related macular degeneration (ARMD)**, using a molecular test. According to several published research studies, certain variants have been associated with an increased risk of developing ARMD and for developing the advanced (wet) form of ARMD.

I understand that:

1. The molecular test directly detects single nucleotide polymorphisms (a variation in sequence) in the DNA in the following gene loci: *CFH*, *BF/C2*, and *LOC387715*. The test is >99% accurate.
2. The molecular analysis performed at the University of Pennsylvania Genetic Diagnostic Laboratory in no way guarantees my health.
3. A sample of blood will be drawn from my arm. This procedure carries little risk, with one risk being the formation of a small bruise. Infection is possible but very rare.
4. Test results will be reported as the fold risk (or increase in risk). An increased risk **does not mean** that I will definitely develop ARMD. Rather the risk results give the relative likelihood of my developing ARMD compared to the general population. Any reported increase in risk is in addition to the impact of other risk factors for developing ARMD. However, evidence indicates that preventative measures and/or regular disease screening may prevent some cases of ARMD from developing and/or facilitate early diagnosis and treatment. The increase in risk identified through this molecular test is based on the current understanding of risk and risk factors. New information may change the current understanding of risk and risk factors.
5. Results that do not identify a significant increase in risk or results that identify a risk lower than that of the general population **do not mean** that I will never develop ARMD. Even with negative results from this molecular test, it is important to follow advice from my physician or other health care provider and take steps that reduce the risk of ARMD. These steps may include regular screening. This molecular test is **not** a diagnostic test, but rather a risk assessment test. The presence of ARMD will not be detected by this molecular test. Even after completing this molecular test, it is important to be examined by my physician or other health care provider for ARMD if I have been determined to be at risk based on my family history or my personal risk factors.
6. These tests are relatively new and are subject to change periodically to improve or expand the utility of the test. The tests are not considered research but are considered to be the best and newest laboratory service available. This testing is often complex and utilizes special materials so that there is a small possibility that the test will not work properly or that an error will occur. My signature below acknowledges my voluntary participation in this testing, but in no way releases the laboratory and staff from their professional and ethical responsibility to me.
7. Because of the complexity of molecular based testing and the important implications of the testing results, results will be reported to me **only** through the physician or genetic counselor who requested the testing.

The results are confidential; they will only be released to other medical professionals or other parties with my written consent. Participation in molecular testing is completely voluntary.

- 8. Any blood or tissue specimens obtained for the purposes of this molecular testing becomes the exclusive property of the Genetic Diagnostic Laboratory. After the specific tests requested have been completed and reported, the Laboratory may dispose of, retain, or preserve these specimens and may use these specimens for research. I understand that my identity will be protected and that research results will not be provided to me or to any other party. If use of this genetic material results in a scientific publication, it will not contain any identifying information. I understand that the Genetic Diagnostic Laboratory is not a DNA banking facility and my DNA sample may not be available for future clinical studies.

Print Patient's Name _____

Patient's Signature _____

Patient's Birth Date _____ Date Signed _____

Physician's/Counselor's Statement: I have explained molecular testing to this individual. I have addressed the limitations outlined above, and I have answered this individual's questions.

Print Name of Professional Obtaining Consent _____

Signature _____

Date _____