

**FOUNDATION
FIGHTING
BLINDNESS**

About Genetic Testing
For Retinal Degenerative
Diseases: A Resource
Guide for Affected
Individuals, Families and
Health Care Providers

Resource Links for Patients and Families



For more information in lay language on genetics and genetic testing, there are many excellent websites. Following are a few offerings from academic, non-profit, and government resources.

University of Utah – Genetics: Tour of the Basics - *Confused by all the talk about DNA and genes? Take a tour of the basics.*

<http://learn.genetics.utah.edu/units/basics/tour/>

Genetics Home Reference – A service of the U.S. National Library of Medicine – *A thorough handbook on many aspects of genetic testing including a glossary and more helpful links.*

<http://ghr.nlm.nih.gov/handbook/testing?show=all>

University of Washington – GeneTests – Educational Materials –

A comprehensive website on available genetic tests including an explanation of the differences between types of tests: clinical, research and investigational.

www.genetests.org

National Society of Genetic Counselors – *The NSGC website features educational material such as Making Sense of Your Genes: A Guide to Genetic Counseling and a search tool for finding a genetic counselor in your area.*

www.nsgc.org

InformedDNA – *InformedDNA is a nationwide network of genetics experts available by telephone to help patients and providers with genetic health information.*

<http://informeddna.com>

American College of Medical Genetics Clinic Services Search Engine – *View all US Clinics, search for a specific center or genetic services.*

www.acmg.net/GIS

My Family Health Portrait - *The Surgeon General's "My Family Health Portrait" is an internet-based tool that makes it easy for you to record your family health history.* <https://familyhistory.hhs.gov/fhh-web/home.action>

Genetic Alliance – Publications – *Understanding Genetics: A Guide for Patients and Health Professionals is one of many downloadable publications Genetic Alliance makes available to patients and advocates.*

www.geneticalliance.org/publications

Genetic Alliance – Public Policy – Genetic Discrimination – GINA – *What does GINA mean? A Guide to the Genetic Information Nondiscrimination Act.*
www.geneticalliance.org/ginaresource.overview

National Institutes of Health – National Human Genome Research Institute
Frequently Asked Questions about Genetic Testing.
www.genome.gov/19516567

Foundation Fighting Blindness – *Visit the Foundation’s website often!*
www.FightBlindness.org

About Genetic Testing

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**FOUNDATION
FIGHTING
BLINDNESS**
Introduction to *About Genetic Testing*

This booklet from the Foundation Fighting Blindness contains valuable information about genetic testing for retinal degenerative diseases (RDDs). Over the past several years, research in RDDs has revealed much about the genetics of these diseases and, specifically, which genes are involved. This has prompted many affected individuals and their family members to question whether or not they should be genetically tested. The decision to have a genetic test can be complex and should involve a discussion with an informed clinician and/or a genetic counselor about the risks, benefits, and limitations of genetic testing and whether or not other family members should be tested.

The contents are meant to help you make an informed decision about genetic testing. It contains the following:

- **Information for affected individuals and their families about the role of genetic counseling.** The Foundation Fighting Blindness strongly recommends genetic counseling whenever genetic testing is being considered.
- **A list of frequently asked questions** about genetics, genetic testing, and inherited retinal diseases;
- **A decision tree** showing general options that a doctor and patient have when it comes to retinal degenerative diseases and courses of action if genetic testing becomes part of the management plan. Examples of options include: observation/monitoring; nutritional, medical or surgical treatment; referral to a low vision specialist; and genetic testing.
- **References and links** to additional resources for patients, doctors and their staff for more information on genetics and genetic testing.

This publication is intended to help a patient and doctor make a decision about genetic testing. The choice to proceed with genetic testing is highly personal and best made following discussions between affected individuals, their family members, and their health care provider. To help medical professionals respond to inquiries from their patients, the Foundation has included information about laboratories offering genetic testing for RDDs as well as links to the laboratories' websites or other contact information to obtain instructions for submitting blood samples for DNA testing.

FOUNDATION FIGHTING BLINDNESS

Information for Patients Genetic Counseling for Retinal Degenerative Diseases

The Foundation Fighting Blindness strongly recommends genetic counseling for patients and families before and after genetic testing. Genetic counseling includes discussions about: (i) personal and family health, (ii) potential benefits of genetic testing to the patient and family, (iii) types of information genetic testing can and cannot provide, and (iv) health and lifestyle implications based on the outcome of the genetic testing.

Genetic counseling is provided by professionals specially trained in the field (e.g., physicians, geneticists, genetic counselors).

Note about genetic testing outcomes: It is important that patients understand that even though genetic testing is available, it's possible an individual's genetic mutation will not be successfully identified by current testing.

Why is genetic counseling important?

It guides information gathering: Genetic testing is best undertaken with an accurate body of background information about the patient's medical condition(s) and family medical history. Obtaining this information often involves gathering and coordinating a body of data sufficient to construct a pedigree (i.e., a family tree that shows which individuals may or may not have a condition similar to the person being tested). A pedigree may aid decision-making, tailor the genetic testing, and improve the likelihood of finding a genetic mutation.

It guides patients and families as facts are imparted: Genetic counseling guides patients and families toward a clearer understanding of the limitations and benefits of genetic testing as well as the interpretation of test results. It is also designed to help patients and families learn to manage the potentially stressful and emotional aspects of the testing process and outcomes.

Why seek the services of a trained genetic counselor?

Genetic counselors are specifically trained in genetics, all aspects of genetic testing, and psychological counseling. They hold graduate degrees and are typically a member of a health care team. A genetic counselor's main focus is to guide the patient and family through the complex process of genetic testing, as well as to be an informed conduit of information between the doctors, patients, laboratories, and many times insurance companies. Although rare, some ophthalmologists and primary care physicians have experience in genetic

counseling. Geneticists, who may also provide genetic counseling services, are often research scientists.

What happens during genetic counseling?

A genetic counselor works with the patient and their family over an extended period of time. Listed below is a typical course of action for a genetic counselor:

- Gather information about family history and medical history;
- Discuss the diagnosis affecting the patient and/or family;
- Explain typical inheritance patterns and provide risk assessment;
- Research what genetic tests are available for the particular disorder;
- Explain the benefits and limitations of genetic tests;
- Go through a decision-making process with the patient and family to help determine if genetic testing should be performed;
- Arrange for blood samples to be drawn and sent to the testing laboratory; and,
- Discuss the results of the genetic testing and their implications for health and lifestyle choices such as career and family planning.

Genetic counseling is available in most communities. Following are several resources:

The National Society of Genetic Counselors (NSGC) provides general information about genetic counseling and their website offers a search tool to help you find a certified genetic counselor in your area.

Phone: 312-321-6834

www.nsgc.org

InformedDNA offers phone-based genetic counseling sessions by certified genetic counselors experienced with inherited ophthalmic diseases.

Phone: 800-975-4819

<http://informeddna.com>

For help in finding a multi-disciplinary genetic clinic, the American College of Medical Genetics provides a search tool on their website:

<http://www.acmg.net/GIS/>

FOUNDATION FIGHTING BLINDNESS

FREQUENTLY ASKED QUESTIONS ABOUT: GENETICS, GENETIC TESTING, AND INHERITED RETINAL DISEASES

Preface

1. A Genetic Test Does Not Guarantee a Genetic Diagnosis.

It is important to understand that having a genetic test done does not guarantee you will receive a molecular (genetic) diagnosis for your retinal degenerative disease (RDD). At this relatively early stage in the development of genetic tests for RDDs, testing often does not identify the retinal degeneration causing gene mutation in an individual. Furthermore, genetic tests are not yet available for all inherited RDDs nor for every gene that has been identified. As research and genetic testing advance, availability and diagnostic methods will improve.

This document will be updated as new genes are identified and more tests become available. The Foundation Fighting Blindness (FFB) funding is helping move the field forward with the specific goal of being able to identify 90% of the RDD causing gene variants within 10 years.

2. Policies for Testing and Providing Results Differ by Facility Type.

Generally, when referring to “laboratory” or “testing facility” in this document we are referring to a CLIA (Clinical Laboratory Improvement Act/Amendment) approved facility where testing is provided for a fee and results are reported in writing to the referring ophthalmologist or genetic counselor. However, testing may also be provided by a research laboratory, with different policies and procedures, as explained below. Laboratories operating outside the United States are usually not subject to CLIA or other US government regulations and guidelines. They may be subject to similar regulations in the countries in which they operate.

a) A clinical laboratory examines specimens and reports results to healthcare providers for the purpose of diagnosis, prevention, or treatment. In the United States, laboratories performing clinical tests, the results of which can be used for treatment, must be CLIA approved.

b) A research laboratory examines specimens for the purpose of better understanding a medical condition and/or developing a clinical test. Some research laboratories will obtain CLIA certification so their research findings can be shared with study participants.

The following table highlights the basic differences that may be found between testing through a clinical laboratory and testing through a research laboratory.

	<u>Clinical Laboratory</u>	<u>Research Laboratory</u>
Test Costs:	There is usually a fee for the testing. The cost varies according to variables that can include the disease, the number of genes and/or possible mutations on the gene(s) and the method of testing. Payment is often requested at the time the sample is submitted.	Costs for the actual testing are generally covered by the research funding. Fees for the doctor or lab visit for a blood draw are usually the patient's responsibility.
Providing Results:	Test results are provided as a written report in a timely manner. The time between sample submission and reporting of results varies among laboratories and specific tests. However, fees and turn-around time for test results should be readily available to the patient and/or the medical care provider.	Test results are generally not given to patients or their providers. In some instances, a research laboratory will, at the patient's request, share potentially useful findings with a clinical laboratory so the patient's test results can be confirmed and a formal report issued. Some research facilities work with a CLIA-approved lab and can provide test results.
Regulation:	Subject to CLIA guidelines.	Not subject to CLIA regulation.

Q1: What is a gene?

Physically, a gene is a segment of DNA (deoxyribonucleic acid). DNA is in every cell of the body and is the blueprint that makes us who we are—human, male or female, blonde or brunette, tall or short, normally-sighted or vision-impaired, and so on.

Functionally, a gene is a recipe for the assembly of a specific protein. Proteins perform all the essential functions of the body. Genes get a lot of attention but it's really the proteins that perform most of the body's functions and make up the majority of a cell's structure.

Each cell of the body, with the exception of eggs, sperm, and mature red blood cells, contains the same number and arrangement of genes. In other words, all cells contain identical DNA except for the variant that causes disease. The [Human Genome Project](#) has estimated that humans have between 20,000 and 25,000 genes. Genes within cells are turned on and off according to the specific needs of that type of cell. For example, genes within muscle cells are turned on to produce proteins involved in muscle contraction while genes within retinal cells are turned on to produce proteins involved in vision.

Which genes are turned on and which proteins are made can also be influenced by the environment. This includes diet and stressors like air pollution and cigarette smoking.

Q2: What is the relationship of a gene to a chromosome?

A: That's a good question, and one that a lot of people ask.

A gene is a segment of DNA, contained on a much longer strand of DNA known as a chromosome. Imagine a string of beads of varying sizes. The string of beads is the chromosome, with each bead representing a unique gene. Some genes are larger than others, which accounts for the different-sized beads.

Each cell in the body, with the exception of sperm and egg cells, contains 23 pairs of chromosomes. We get one chromosome of each pair from our mother and the other from our father.

Q3: How do genes cause disease?

A: Sometimes a gene contains a mutation or variant. A mutation is a permanent, physical change in the segment of DNA that is the gene. A gene has a precise and ordered structure (a sequence), much like the correct spelling of letters within a word. When the "spelling" is wrong, the gene is said to be mutated. Some mutations can occur randomly and are not inherited from a

parent, but most retinal degenerative disorders are due to a gene mutation that is inherited from one or both parents.

A gene with a mutation can instruct a cell to make a defective protein, the wrong amount of protein, or no protein at all. As a result, the cell functions abnormally and may even die. Not all gene mutations are harmful, but some cause medical conditions such as retinal degenerative diseases. It is important to remember that everyone carries the same genes; however, in someone with a retinal degenerative disorder, a particular gene is not working properly.

Q4: What is genetic testing?

A: Genetic testing is the process of determining the sequence (or “spelling”) of a person’s genes in an effort to determine the presence or absence of a disease-causing gene mutation. For retinal degenerative disorders, genetic testing is usually performed using DNA from cells found in a small blood sample.

It is important to realize that although genetic testing is available it’s possible an individual’s genetic mutation will not be successfully identified by current testing. (see the **Preface** to this Q&A). It is also important to know that having a gene mutation does not automatically mean that a person has a disorder, will develop it, or will pass it on to any offspring. Retinal diseases are complex and scientists are still researching which factors lead to their occurrence.

Q5: Has the gene for my retinal degenerative disease (RDD) been discovered?

A: New gene mutations for RDDs are being discovered at a rapid pace. So far, approximately 200 different genes—when working improperly—are known to cause retinal degenerative disease. Within many of these genes, more than one RDD-causing mutation has been discovered. More than 70 genes have been linked to retinitis pigmentosa and associated syndromes.

Gene mutations have been discovered for Bardet Biedl syndrome, cone or cone-rod dystrophy, Leber congenital amaurosis, Stargardt macular degeneration, Best disease, and Usher syndrome, among other retinal dystrophies. These genes are generally discovered as part of research studies. After these genes are thoroughly studied in a research lab, they may become available for development into a clinical genetic test. There are many more disease-causing genetic mutations yet to be discovered.

When a bona fide RDD-causing mutation is found in a research setting and is developed into a clinical laboratory test, it’s possible a patient’s existing blood sample may be used for the clinical test. If the blood sample has been exhausted or

the developing lab is different from the discovery lab, a new blood sample may be required along with the required fees for a clinical test.

[See Question 18 for a list of laboratories and available testing.]

Q6: How likely is it that the mutation in my family can be pinpointed?

With the genetic testing available today it is possible to find the underlying genetic cause in roughly one quarter to one half of individuals with inherited retinal disease. However, the chance of finding the cause depends on the specific disease involved, the test used, the country of origin of the affected individual, and other factors. Therefore, the chance of success in genetic testing varies from case-to-case, and cannot be given as a simple number.

This is especially true for individuals for whom there is no prior family history of disease or other information about the possible cause. However, if the person being tested is a member of a family in which the underlying genetic cause has been identified already or a clinical diagnosis obtained, then further testing is likely to determine whether the genetic cause is present in or absent from this additional family member.

Q7: Why would I want to be tested? Should I have my child tested?

A: There are a number of reasons to be tested, including the following:

- It may eliminate uncertainty about a diagnosis, which can be a relief.
- It may help with family planning.
- It may help a person make informed decisions about his or her future (e.g., career choices, place of residence).
- It may provide information for other at-risk family members.
- A positive test (one that confirms a gene mutation) sets up an opportunity for counseling.
- A positive test may also provide a motivation for using any preventive measures that may be known or subsequently discovered. One example would be to quit or not start cigarette smoking, which has been linked to macular degeneration.
- In some cases, a definitive diagnosis can lead to a direct medical benefit by providing a basis for making early decisions about treatment and allowing for referral to appropriate specialists. For example, a genetic diagnosis of Usher syndrome can initiate discussions about cochlear implants for young children developing their language skills. Individuals with Refsum disease can delay progression of their symptoms with dietary modifications.
- Having a precise diagnosis can help a person keep track of research advances for preventing, treating, or curing the particular disorder.

- It helps researchers identify people who may benefit from participation in research studies targeting their specific genetic disorder. The website of the [Foundation Fighting Blindness](#) contains a list of current clinical trials. The National Institutes of Health website [ClinicalTrials.gov](#) maintains a searchable registry of clinical trials. Visit either website to see if you qualify for enrollment in ongoing clinical trials.
- Although an individual's testing may not return a genetic diagnosis, the information gained from the test can add to the research knowledge base concerning the genetics of inherited retinal degenerative diseases and help refine genetic tests so all genes and genetic mutations can eventually be identified.

It's important to be aware of the limits of genetic testing as well as the advantages. For example, even though genetic testing is available, not all genetic mutations will be identified. Talking with a geneticist, genetic counselor, or well-informed health care provider before and after testing is extremely helpful. It is especially important to discuss genetic testing of children before proceeding with testing. It is important to discuss such questions as: Would there be a medical benefit to knowing if my child carries a gene mutation? Would it be more appropriate to wait until my child is old enough to make the decision independently about having the testing done?

In the United States, genetic counseling is considered by most to be an important step in achieving an accurate molecular diagnosis and in interpreting test results. Outside the United States, genetic counseling can be regarded differently. For more information, you could visit the website to Retina International: <http://www.retina-international.org>.

Q8: What's involved in having a genetic test?

A: Genetic testing for retinal degenerative diseases is a relatively new specialty. Many physicians are just learning about it. Testing can usually be arranged either through your ophthalmologist or physician. It is advisable to also speak with a geneticist or genetic counselor.

The steps are basically these:

1. You or a family member is diagnosed with an inherited retinal disorder.
2. You discuss testing risks, benefits, and limitations with a well-informed health care provider.
3. After reviewing your current clinical diagnosis and medical and family history, your health-care provider orders a genetic test.
4. Your blood is drawn, usually from a vein in your arm.
5. The blood sample and required forms are mailed to a laboratory.
6. Genetic testing is performed on the DNA extracted from the blood.
7. Results from a CLIA-certified testing facility are available in several weeks to several months, depending on the test. Results from a research lab, if

they are made available to the patient, can take several months or several years. *Refer to the Preface and Question 5 for an explanation of research and clinical laboratories and gene discovery.*

8. A CLIA-approved clinical laboratory sends a report to the referring physician. At the time samples are submitted for genotyping to a research lab, if and how those results will be communicated to the patient should be investigated.
9. Your physician and/or genetic counselor explain the results and implications.

Q9: How do I decide whether or not to have genetic testing?

A: The Foundation Fighting Blindness has put together a “decision tree” to help people decide whether genetic testing is right for them. This tool, in addition to talking with your personal physician and a genetic counselor can be helpful.

Q10: How is genetic testing different from gene mapping?

Gene mapping is the identification of the location of a disease gene while genetic testing is the process of identifying the genetic cause of a disease in an individual patient (and counseling them about this finding).

Q11: Does everyone with the same diagnosis as mine have the same genetic mutation?

A: No, and this is one of the things that makes diagnosis and the development of gene-based treatments extremely complicated. Likewise, sometimes mutations in the same gene can cause similar yet different diseases.

Retinitis pigmentosa presents a good example. More than 50 different genes have been implicated in RP and associated syndromes, and some of these genes contain multiple mutations. Genetic tests that screen for all the mutations may have to be done to make a precise diagnosis. Also, in some cases, the same gene with different mutations can cause different retinal degenerative diseases.

Q12: I've heard the words "genotype" and "phenotype" used. What do they mean?

A: Genotype refers to a person's genetic make-up, like a blueprint. It is a personal, gene-dependent instruction guide for making us who we are. The instructions are really segments of DNA (genes) that are "read" to tell the cell how much and which type of protein to produce, how to construct cell components, and so on. In the context of talking about a RDD, your genotype would be your precise disease gene(s) and its mutation(s).

Phenotype refers to the physical, observable characteristics dictated by the genotype. Phenotype is also influenced by environmental factors, some known and some unknown. In other words, phenotype is the manifestation (what we can see and often measure) of the many instructions spelled out by the genotype.

A physician often makes a clinical diagnosis of a retinal degenerative disease based on phenotype—how the retina appears. It is now possible in many cases to confirm a clinical diagnosis, or get a more precise diagnosis, through genotyping.

Genotyping for RDDs is relatively new. Many physicians are not familiar with the procedures or specialized laboratories where the tests are being performed. Laboratories require, for example, that physicians provide a description of the phenotype and a patient's recent medical records along with the blood sample for genotyping.

Q13: If I have the genetic mutation for a particular RDD, does this automatically mean that I have the disease or will get it? Is there anything I can do to prevent it?

A: Having a genetic defect for a particular retinal degenerative disease does not necessarily mean you have the disease or will ever develop it. In addition, knowing that you have a genetic defect for a particular retinal degenerative disorder does not always tell you how mild or severe the disorder could be.

The same holds true for other non-retinal diseases. Consider the BRCA1 breast cancer susceptibility gene. (This has nothing to do with inherited retinal conditions. It's merely being used as an example of a genetic defect that does not always cause disease.) The risk for cancer in women and men who have the BRCA1 genetic mutation is high compared to the general population but not absolute. This uncertainty is another important reason for seeking genetic counseling both before and after testing.

Our knowledge about the genetics of RDDs is progressive and will advance as more people with a family history of a RDD have genetic testing. We do know

that a variety of factors involving other genes and the environment can influence disease. Cigarette smoking, for example, increases the risk of developing age-related macular degeneration.

Q14: I've heard the word "mutation" used to refer to genes. What does this mean?

A: The vast majority of genes in any individual are similar to those of everyone else. However, there can be slight differences in our genes—just as there can sometimes be variations in the spelling of the same word (e.g., color and colour); these variations are what make us unique. Everyone carries some gene changes in their genetic material (mutations), yet most of us never know about them because they cause minimal or no problems (silent mutations). Rarely, though, a significant change can occur in a gene and will cause a disease (just like a major spelling error can make a word unreadable) —this is called a "disease-causing mutation."

Q15: Should my family and I be genetically tested?

A: This is a common question, and one for you, your family, doctor, and/or a genetic counselor to answer together. This Genetic Testing Information Packet includes a "decision tree," which may help you reach the best answer for your particular circumstances.

It is important to understand what a genetic test can and cannot tell you. That's why you should speak to a professional who is knowledgeable about genetic testing.

Q16: I think I am a carrier of a retinal degenerative disorder and would like to have children. What does this mean? How can I understand whether my offspring would have the genetic defect?

A carrier is a term that implies that while you may have a disease-causing gene defect (mutation), you do not show symptoms of the disease and likely never will. People who are carriers can exist because of the nature of the pattern by which the disease gene is passed down through generations, i.e., its inheritance pattern. Most carriers will have a gene for an RDD disease whose defect gets passed on via a recessive inheritance pattern, meaning it requires two copies of a disease mutation to cause the disease, i.e. - one from each parent.

Under some circumstances, the gene defect can be passed along to children who may also become carriers. However, some children may be affected with the condition if they also get a disease causing mutation from their other parent.

In a dominant inheritance pattern, which requires only one copy of a disease mutation to cause the disease, people with the disease mutation are either affected or are predisposed to develop the condition (such as the BRCA1 gene carriers discussed above, in Question 13). In an X-linked recessive inheritance pattern, such as for X-linked retinitis pigmentosa (RP), female carriers of the condition usually are not affected with RP (although exceptions exist), while males are.

Be sure to tell your doctor if you think you are a carrier of a gene for an RDD. Your doctor may recommend that you speak with a genetic counselor as a first step.

Some labs may be able to perform prenatal testing for certain genetic diseases, but not all genetic testing labs have this capability.

Q17: Could a genetic test be wrong?

A: Like any medical test, genetic testing is subject to human and machine error. While it is possible that a test could give a “false positive” or “false negative,” the chances of this happening are very low.

Q18: What is known about the gene for my type of RDD? Is there a genetic test for it, and if so, where could I have testing performed?

A: Genetic testing for retinal degenerative diseases is relatively new. Several laboratories in the United States and elsewhere test for different retinal degenerative disorder causing genes. Because not all the RDD causing genes have been identified and not all the variations in a gene that could be causing a particular RDD have been discovered, it is possible that, even if tested, you may not receive a definitive diagnosis. For example, one experienced testing laboratory detects the genetic defect in only about 50% of blood samples from patients who have a clinical diagnosis of Usher type 1. A clinical diagnosis based on retinal phenotype and a consultation with a genetic counselor can give a clearer indication of the likelihood of finding the mutation that is causing your disorder.

It is recommended that you use a known and dependable laboratory and not be tempted by genetic testing kits that may be marketed directly to the public. In the United States, there is a rigorous review and inspection process for a genetic testing research laboratory to become certified to provide genetic testing. This certification, known as CLIA (Clinical Laboratory Improvement Act/Amendments), is meant to ensure quality and consistency in laboratory testing.

Testing Laboratories:

Below, you will find contact information for several CLIA-certified genetic testing laboratories in the United States that perform testing for inherited retinal diseases.

Test requisitions and samples are accepted only through a qualified physician or genetic counselor. Results are then returned to the same physician or counselor and it is the responsibility of that healthcare provider on record to explain the results to the patient or employ the services of a genetic counselor to do so.

Baylor Medical Genetics Laboratory

Baylor College of Medicine

Website: <https://www.bcm.edu/geneticlabs/index.cfm?PMID=0>

Email: geneticstest@bcm.edu

Phone: 800-411-GENE

John and Marcia Carver Nonprofit Genetic Testing Laboratory

University of Iowa

Website: www.carverlab.org

Email: carverlab@uiowa.edu

Phone: 319-335-8270

Casey Eye Institute Molecular Diagnostic Laboratory

Oregon Health & Science University

Website: <http://www.ohsu.edu/xd/health/services/casey-eye/healthcare-professionals/cei-diagnostics/index.cfm>

Email: ceidiagnostics@ohsu.edu

Phone: 503-494-5838

Emory Genetics Laboratory

Emory University

Website: <http://genetics.emory.edu/eql/>

Email: eqlqc@emory.edu

Phone: 404-778-8499

eyeGene™

National Ophthalmic Disease Genotyping Network

National Eye Institute, National Institutes of Health

Website: <http://www.nei.nih.gov/resources/eyegene.asp>

Email: eyeGENEinfo@nei.nih.gov

GeneDx

Website: www.genedx.com

Email: genedx@genedx.com

Phone: 301-519-2100

Ocular Genomics Institute, Massachusetts Eye & Ear Infirmary, Harvard Medical School

Website: <http://ocular-genomics-institute.org/>

Email: OGI_Diagnostics@meei.harvard.edu

Phone: 617-573-6906

Partners HealthCare Center for Personalized Genetic Medicine (PCPGM), Laboratory for Molecular Medicine, Harvard Medical School

Website: <http://pcpgm.partners.org/LMM/>

Email: imm@partners.org

Phone: 617-768-8500

Molecular Pathology Laboratory

Columbia University – Department of Pathology

Website: <http://pathology.columbia.edu/consents/>

Phone: 212-305-9706

Shiley Eye Center

University of California, San Diego

Website: <http://shileyeye.ucsd.edu/specialties/genetics-research>

Email: eyeDNAtest@ucsd.edu

Phone: 858-534-5362

Denver Genetic Laboratories

UCD DNA Diagnostic Laboratory

Website:

<http://www.ucdenver.edu/academics/colleges/medicalschool/programs/genetics/Pages/DenverGenetics.aspx>

Email: Elaine.Spector@ucdenver.edu

Phone: (303) 724-3801

Prevention Genetics

Website: <http://www.preventiongenetics.com/>

Email: clinicaldnatesting@preventiongenetics.com

Phone: 715-387-0484

Overview of Currently Available Retinal Degenerative Disease Tests and Laboratories: *(This list is updated by checking the individual lab websites and/or the NIH Genetic Testing Registry. Labs and tests are added and dropped frequently. For the most up-to-date information visit the NIH Genetic Testing Registry. <http://www.ncbi.nlm.nih.gov/gtr/>)*

- Achromatopsia [Carver, Casey, Denver, GeneDx, OGI, & Prevention
- Bardet Biedl syndrome [Baylor, Carver, Casey, Denver, Emory, OGI, & Prevention]
- Best disease [Carver, Casey, GeneDx, eyeGENE, OGI, & Shiley]

- Blue Cone Monochromacy [OGI and Carver]
- Choroideremia [Carver, Casey, GeneDx, eyeGENE, OGI]
- Cone-rod dystrophy [Baylor, Carver, Casey, Columbia, eyeGENE, GeneDx, OGI, Prevention & Shiley]
- Congenital Stationary Night Blindness [Casey, eyeGENE, GeneDx, OGI, Prevention & Shiley]
- Enhanced S-Cone Syndrome [Carver, Casey, eyeGene, OGI]
- Jewish Retinal Degeneration Panel [Carver]
- Jewish Panel for Usher Syndrome [PCPGM]
- Late Onset dominant macular degeneration [Shiley]
- Leber congenital amaurosis [Baylor, Carver, Casey, GeneDx, OGI, Prevention & Shiley]
- Malattia leventinese/Doyne honeycomb macular dystrophy [Carver, Casey, eyeGENE, OGI Shiley,]
- Retinitis Pigmentosa - dominant [Baylor, Carver, Casey, Emory, eyeGENE, GeneDx, OGI, Prevention & Shiley]
- Retinitis Pigmentosa – recessive [Baylor, Carver, Casey, Columbia, Emory, EyeGene GeneDx, OGI, Prevention & Shiley]
- Retinitis Pigmentosa – x-linked [Carver, Casey, Emory, eyeGene, GeneDx, OGI & Prevention]
- Retinoschisis [Carver, eyeGENE, GeneDx, OGI]
- Sorsby fundus dystrophy [Carver, eyeGene, OGI, Prevention & Shiley]
- Stargardt disease [Baylor, Carver, Casey, Columbia, Denver, eyeGENE GeneDx, OGI & Shiley]
- Usher Syndrome [Baylor, Carver, Casey, eyeGENE, GeneDX, OGI, Prevention & PCPGM]

Q19: What must I do to get genetically tested?

A: The Foundation strongly recommends you begin by discussing the benefits, risks and limitations of genetic testing with an ophthalmologist, retinal specialist or a genetic counselor. If you and your healthcare provider agree to go ahead with testing, the doctor or genetic counselor orders a blood test and fills out forms provided by the testing laboratory. Some genetic testing laboratories also require the doctor or counselor to inform the lab by phone or email to expect your sample. You may be required to sign a consent form for DNA testing. Many doctors are just learning about genetic testing for RDDs. You may want to share this packet with your physician.

Instructions from the laboratory will tell the doctor how much blood is needed (usually 5–9 milliliters (ml) for adults, which is roughly equivalent to one or two large spoonfuls; less for children), the type of blood vial to use, and shipping instructions.

The response time depends on several factors:

- whether your blood is submitted to a CLIA-approved, fee-for-service laboratory or to a research setting;
- your clinical diagnosis; and,
- whether or not more than one test is needed.

It can take several weeks to months in a CLIA lab or several years in a research setting.

Q20: How would I find out the results of a genetic test?

A: CLIA laboratories send test results to physicians and/or genetic counselors depending upon whom you say should receive the results. Your doctor or counselor should contact you with the results of your test. If you have not received a result within the promised time period, contact the doctor or genetic counselor that arranged the test.

When you submit a blood sample to a research laboratory, read the consent documents carefully for information on whether or not results from the research will be disclosed to individuals under that research protocol. The type of lab used, state and federal regulations, as well as the internal review board for that particular institution and specific research project, can affect if and how results are disclosed and to whom and for what purpose.

Q21: What is the cost of genetic testing?

A: This depends on several factors. In considering the total cost of genetic testing you should include your visit(s) to your physician or genetic counselor, the blood draw itself and shipping your sample to the testing laboratory. Actual testing costs can be from about \$100 to over \$2,000 depending on the number of genes being tested, the number of tests needed and the methodology used for the test(s). Payment is usually due at the time the blood sample is submitted to the lab. There is no fee for testing through the National Eye Institute's eyeGene program. However, other fees such as office visits, blood drawing and shipping are still the responsibility of the patient.

Q22: Is genetic testing covered by insurance?

A: Some insurance companies are now offering limited coverage for certain types of genetic testing. Check your personal healthcare insurance policy and talk to your physician and/or insurance carrier. Each lab has its own policy on whether they will bill insurance companies or require payment in advance. Read the test requisition information carefully.

Q23: What is gene therapy? Am I eligible?

Gene therapies are treatments for correcting defective genes and the physical problems they cause. Researchers are experimenting with several approaches:

- trying to insert a good gene to make up for lack of function of a defective gene;
- trying to repair the defective gene; and,
- trying to control the activity level of the defective gene.

Most current gene therapies are experimental and have only been applied in preclinical settings (i.e., basic research and/or animal studies). A few have progressed to Phase 1 (safety) and Phase 2 (further safety and efficacy) studies. Announcements and updates on enrollment can be found on the Foundation's website, www.fightblindness.org, and on the National Institutes of Health's clinical trials registry, www.clinicaltrials.gov

Q24: What is the relationship of the Foundation Fighting Blindness to genetic testing and gene therapy?

The Foundation Fighting Blindness supports research to save and restore sight. For the past four decades, FFB funding has helped advance a majority of the important discoveries in the field of retinal degenerative disease, including funding laboratories finding the genes responsible for RDDs and funding laboratories doing genetic testing.

Q25: If they don't find my gene when my sample is tested, will it automatically be re-tested when new genes are identified OR will I have to go through the whole process and re-submit at another time, when more genes have been identified?

Each laboratory has its own policy for retesting (or not) depending on whether it's a fee-for-service diagnostic laboratory or in a research setting, the disease in question, and other factors.

When you submit a sample to a CLIA-approved diagnostic lab, you are usually requesting a specific test for one gene or several closely related genes for one disease or several related diseases (a panel). However, generally speaking, samples can be retested until the lab runs out of DNA. Retesting will usually require submission of additional paperwork and fees. In certain cases, the diagnostic laboratory may contact the referring clinician to let the doctor know of the availability of a more appropriate test for their patient's condition. There may be many clues in a patient's medical history and family tree that can point the way to the appropriate test. This reinforces the need for a good clinical diagnosis and genetic counseling.

If you submit a blood sample as part of a research program, you should read the consent documentation carefully to find the laboratory's policy on continuation of testing as new genes are identified. Retesting may depend on the goals of the research project and available funding.

If in doubt, ask the laboratory manager or investigator about their retesting policy and how it might be applied to your individual situation.

Q26: I know I'll have more questions. How can I learn more about genes and the progress being made to identify and treat my retinal disorder?

You might want to visit the Foundation Fighting Blindness website, www.fightblindness.org, and subscribe to FFB's free electronic newsletter.

FOUNDATION FIGHTING BLINDNESS

DECISION TREE

For Doctors and Patients Considering Genetic Testing for Retinal Degenerative Disorders

The Foundation Fighting Blindness *Decision Tree* is designed to demonstrate the options for the diagnosis and treatment of retinal degenerative diseases (RDDs).

Genetic testing can sometimes reveal the DNA mutations causing retinal degenerative disorders. More and more patients are asking about genetic testing. Some may want to know the risk of the disease for family members, while others may want to identify their specific genetic disorder in order to keep up with research and clinical updates. There are other reasons too, such as an interest in participating in future clinical trials.

Today, much genetic testing is research-based – to discover new RDD genes and explain their effect, to develop gene therapy and other treatments, and to explain the interactions of genetic and environmental influences.

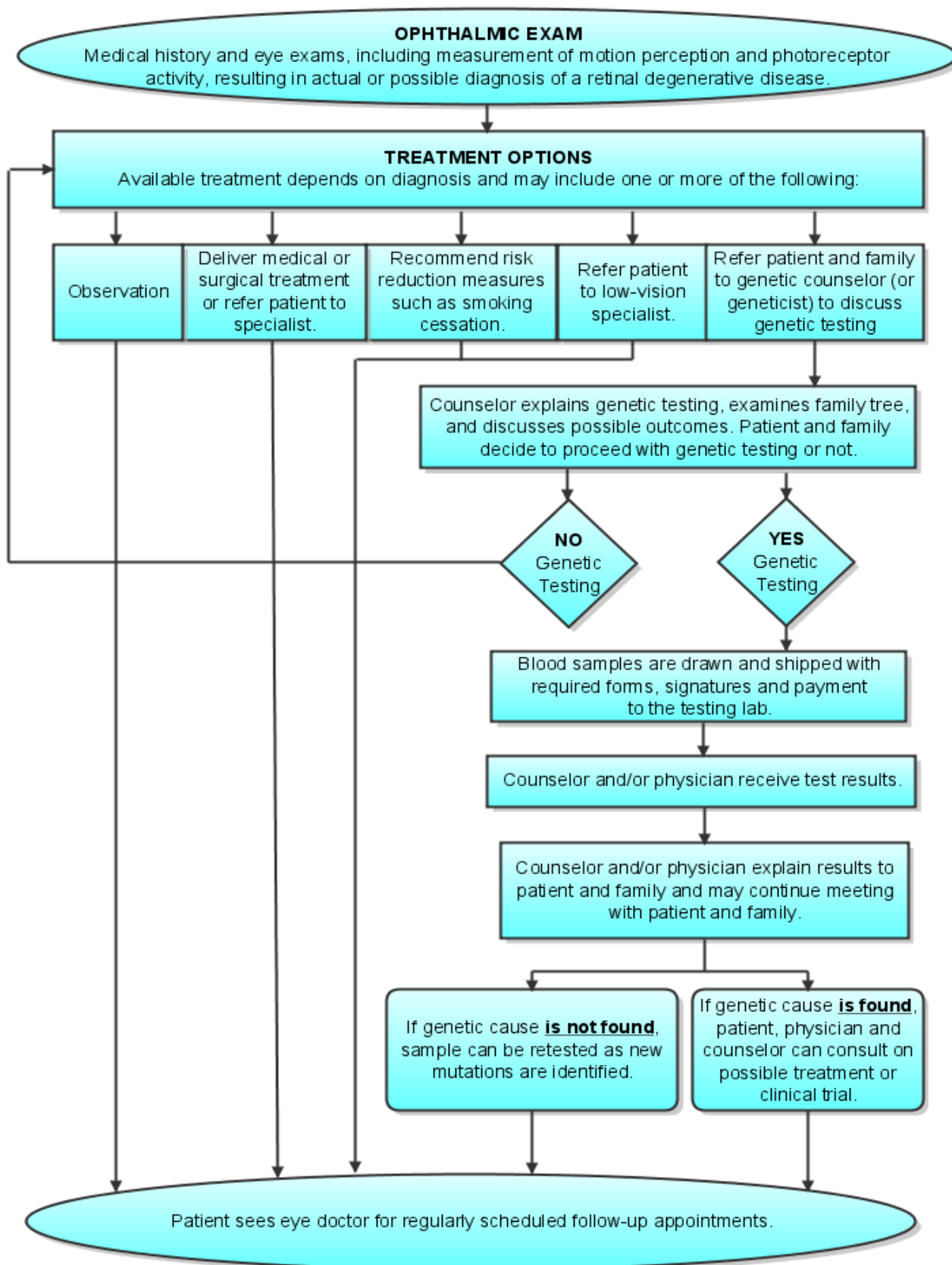
An increasing number of clinical genetic testing laboratories are equipped to test DNA from blood samples from patients with a diagnosis of a retinal degenerative disease and their family members. If a genetic variation is confirmed for an affected person, unaffected family members may want to be tested to discover whether or not they carry the same genetic variation.

The differences between genetic testing for research and for clinical applications is explained in the Preface to *Frequently Asked Questions* on page . It is important to know these differences since the type of testing will likely affect how the information is released and whether or not it can be used for treatment or participation in a clinical trial.

Although genetic testing is done carefully and thoroughly, disease-causing genetic defects are not found for many people. Even in instances where specific disease-causing gene variants are found, it is impossible to say if a person will develop a related disease or to what extent. Currently, there are few treatment options available (see following *Decision Tree*), raising important questions about the usefulness of genetic testing for some individuals.

Because of the many variables that can be involved in genetic testing, the Foundation Fighting Blindness recommends that a genetic counselor or other trained expert such as a geneticist be involved with patients and families considering genetic testing. See *Information for Patients - Genetic Counseling for RDD* on page 5.

Foundation Fighting Blindness Genetic Testing Decision Tree



Resource Links for Health Care Providers



For specific information on genetic tests available and the requirements for submitting samples, visit the laboratory websites. There are many more laboratories than can be listed here. The Foundation suggests GeneTests and the NIH Genetic Testing Registry (GTR) as primary resources for available genetic tests and laboratory contact information. The GTR will replace the laboratory directory component of GeneTests by early 2013.

National Institutes of Health Genetic Testing Registry - *The National Institutes of Health (NIH) has created the Genetic Testing Registry (GTR), a public database of test information submitted voluntarily by genetic test providers (e.g., laboratories conducting the test).* <http://www.ncbi.nlm.nih.gov/gtr/>

Introduction to the GTR - <http://oba.od.nih.gov/gtr/gtr.html>

GeneTests – *With funding support from the National Institute of Health, the University of Washington, Seattle, provides healthcare providers with laboratory and clinic directories, educational materials and tools for searching for genetic tests available for clinical use.* www.genetests.org

National Society of Genetic Counselors – *The NSGC website offers educational materials and events and an on-line search tool for finding genetic counselors in your area.* - www.nsgc.org

InformedDNA – *InformedDNA is a nationwide-network of genetics experts available by telephone to help patients and physicians by providing information or counseling.* www.informeddna.com

American College of Medical Genetics Clinic Services Search Engine – View a list of US Clinics, search for a specific center or genetic services. www.acmg.net/GIS

CLIA Approved Laboratories Providing Tests for Retinal Degenerative Diseases

Baylor Medical Genetics Laboratory, Baylor College of Medicine
<https://www.bcm.edu/geneticlabs>

John and Marcia Carver Nonprofit Genetic Testing Laboratory, U. of Iowa - www.carverlab.org

Casey Eye Institute Molecular Diagnostic Laboratory
www.ohsu.edu/xd/health/services/casey-eye/healthcare-professionals/cei-diagnostics/index.cfm

Denver Genetic Laboratories, University of Colorado

<http://www.ucdenver.edu/academics/colleges/medicalschool/programs/genetics/Pages/DenverGenetics.aspx>

Emory Genetics Laboratory, Emory University

<http://genetics.emory.edu/egl/>

National Ophthalmic Disease Genotyping Network (eyeGENE™), National Eye Institute, National Institute of Health -

<http://www.nei.nih.gov/resources/eyegene.asp>

Harvard Medical School - Partners HealthCare Center for Genetics & Genomics

Laboratory for Molecular Medicine <http://pcpgm.partners.org/LMM/>

Molecular Pathology Laboratory, Columbia University – Department of Pathology

<http://pathology.columbia.edu/consents/>

Ocular Genomics Institute, Massachusetts Eye and Ear Infirmary, Harvard –

<http://ocular-genomics-institute.org/index.php/gdt>

Prevention Genetics - <http://preventiongenetics.com/>

Shiley Eye Center, University of California, San Diego -

<http://eyesite.ucsd.edu/genetics/index.htm>

GeneDx - www.genedx.com

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