



Genetic Testing For Retinal Degenerative Diseases: Information and Resources for Affected Individuals, Families and Health Care Providers

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Overview of Genetic Testing for Inherited Retinal Degenerative Diseases

Most rare retinal degenerative diseases (RDDs) - including retinitis pigmentosa, Stargardt disease, Usher syndrome and choroideremia - are inherited and usually caused by one or more defects (mutations) in a single gene.

Genetic testing is now available to attempt to identify the defective gene causing the RDD in an individual or family.

There are potential benefits to knowing the underlying genetic cause of a person's RDD:

- It may help confirm or refine a diagnosis.
- Knowing the mutated gene can help a person understand how the disease may affect their vision during their lifetime.
- Knowing the mutated gene can guide the testing of family members to identify those at risk of inheriting the condition.
- Knowing the genetic defect may help people qualify for clinical trials and inform them about which future therapies may be of benefit.

At the same time, the information revealed from a genetic test may not be immediately helpful to an individual or family. In some cases, the knowledge might create anxiety for some family members.

It is very important to remember, however, that a genetic test may not reveal the defective gene, which can be frustrating for a patient and their family.

The decision to undergo genetic testing should not be made lightly. Anyone interested in a genetic test is strongly advised to talk to a genetic counselor or retinal physician who is knowledgeable about the genetic testing process and the potential impacts of the results, before they decide to undertake the test.

The Genetic Testing Process

1. **Get a Thorough Clinical Exam** — Before blood is sent off to a laboratory for testing, a patient needs to get a thorough clinical exam conducted by a retinal specialist familiar with RDDs. Usually, a

clinical exam will give a strong indication of what the disease is — *e.g.*, Stargardt disease versus retinitis pigmentosa. This can greatly help the genetic testing lab narrow the scope of the search for the disease-causing gene mutation, saving time and money.

2. **Meet with a Genetic Counselor** — Genetic counseling is a critical part of the genetic testing process. A genetic counselor can help you decide if genetic testing makes sense for you and your family. A genetic counselor can also help determine the best genetic test for you, based on current test methodology, number of genes to be tested, detection rate, price of the test, and potential insurance reimbursement. The counselor can also tell you the likelihood that the genetic basis of your condition will be found and how discovering, or not discovering, the genetic defect might affect you and your lifestyle. In addition, the counselor will interpret the test results for you, and serve as your advocate throughout the genetic testing process.
3. **Submit a Blood or Saliva Sample** — The genetic testing lab will provide instructions for the doctor or clinical lab collecting the blood or saliva sample, including how much is required and where the sample should be sent. Getting blood drawn for a genetic test is not much different from getting blood drawn for other common tests.
4. **Receive and Interpret Results** — It can take several months for initial results to come back from a genetic testing lab. Sometimes the disease-causing gene is not found. The likelihood of finding the gene depends on several factors which your genetic counselor can discuss with you. Regardless of whether your gene mutation is found, your genetic counselor will help you understand the results and recommend next steps. In some cases, re-testing may be an option, perhaps at a later date.
5. **Costs of Genetic Testing and Counseling** — The costs associated with genetic testing and counseling can vary depending on who is providing the services and what disease is being investigated. Some insurance companies will reimburse for these expenses — others won't. If the expense is a concern, talk with your genetic counselor before you begin the process. He or she should be able to give you an estimate of how much the counseling will cost and whether your insurance will cover it.

This booklet provides additional information on the genetic testing process. While this booklet is not a substitute for a genetic counselor, it can help you better understand and prepare for the process. The last section of the booklet lists additional resources, which may also be helpful.

Overview of the Genetic Testing Booklet

This booklet contains 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 consider genetic testing. The decision to get a genetic test should involve a discussion with an informed clinician and/or a genetic counselor to discuss the risks, benefits, limitations, and whether other family members should be tested.

This booklet 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.
- References and links to additional resources where more information on genetics and genetic testing can be found.
- Genetic testing laboratory listings. To assist you and your medical professionals in finding the right resources, this booklet also includes information about: laboratories offering genetic testing for RDDs and links to the laboratories' websites and other contact information.

Genetic Testing Results: What to Expect

It is important to understand that having a genetic test does not guarantee you will receive a genetic diagnosis for your retinal degenerative disease (RDD). Labs can only test for mutations in genes that are known to be associated with RDDs. Since not all of the genes that are associated with RDD have been discovered, testing may not identify the disease-causing gene mutation for any one individual. It can often take several months to get a result from genetic testing. It will take the same amount of time to report on a known gene mutation, as it will to report that your gene is not yet discovered, because the lab will have to test all known genes before it can conclude your gene is not amongst them. When a new RDD gene is discovered, it can take several months before a qualified genetic test is available.

The Genetic Testing Process

Before even discussing genetic testing, a patient should get a clinical evaluation from a physician familiar with RDDs. Based on the disease diagnosis or clinical evaluation, a genetic counselor and/or physician will determine where a patient's blood (DNA) should be sent for genetic testing.

For a genetic testing result to be given to a patient, the blood sample must be sent to a laboratory that meets quality control requirements mandated by the Centers for Medicare & Medicaid Services (CMS) that are overseen by each state. These labs meet criteria established in the Clinical Laboratory Improvement Amendment, 1988, or CLIA for short. They are called CLIA-certified labs. In these labs, testing is provided for a fee and results are reported in writing to the referring ophthalmologist or genetic counselor.

In addition to the CLIA-certified labs, research labs may also undertake gene discovery which may be loosely referred to as genetic testing. This discovery work should not be confused with genetic testing. If the researcher discovers a new gene, they cannot report the result to the participant, but they may be able to arrange for a CLIA-certified lab to develop a test and perform CLIA-certified testing. Typically there is no cost to donate your DNA to discovery research analysis.

There are two basic approaches to genetic testing. In one, the clinician guides the patient to a limited set of tests, based on the clinical findings. If the gene is not found, more tests can be ordered, again based on likelihood. This is cost-effective if your ophthalmic and family history indicates your mutation may be a common one. The other method tests for mutations in all known RDD genes at the same time. While a more complete test, this is also more expensive. Your clinician and genetic counselor will select the best strategy and appropriate testing laboratory for you.

The cost of the genetic test varies depending on the disease, lab and the breadth of the screening. If the lab is screening the DNA sample for several mutations in multiple genes, the cost of the testing may be higher than for more limited screening. Insurance may or may not cover the cost of genetic testing. Your genetic counselor can help you understand what your insurance will cover.

Laboratories operating outside the United States are usually not subject to CLIA or US government regulations and guidelines, although most reputable testing laboratories have equivalent standards. They may be subject to similar regulations in the countries in which they operate.

	<u>Clinical Laboratory (CLIA-accredited)</u>	<u>Research Laboratory</u>
Test Costs:	<p>There is a fee for the testing.</p> <p>The cost varies according to variables that can include the disease, the number of genes and/or possible mutations on the gene(s), the method of testing, and insurance coverage.</p>	<p>Costs for the research are generally covered by research funds available to the researcher.</p> <p>The researcher will often arrange for a sample submission at no cost to the patient.</p>

	<u>Clinical Laboratory</u>	<u>Research Laboratory</u>
	Payment is often requested at the time the sample is submitted for testing.	
Providing Results:	<p>Tests are ordered by a physician or a genetic counselor.</p> <p>Test results are provided as a written report in a timely manner to the professional ordering the test. They then provide the result to the patient.</p> <p>The time between sample submission and reporting of results varies among laboratories and specific tests.</p> <p>Fees and turn-around time for test results should be explained to the patient and/or the medical care provider at the time they provide blood.</p>	<p>Test results are not given to patients or their providers.</p> <p>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.</p>
Regulation:	Subject to CLIA guidelines.	Not subject to CLIA regulation

Critical Role of Genetic Counseling in the Testing Process

The Foundation Fighting Blindness strongly recommends genetic counseling for patients and families before and after genetic testing. Genetic counseling includes discussions about:

- Personal and family health
- Potential outcomes, risks and benefits of genetic testing for the patient and family
- The limitations of genetic testing
- Types of information genetic testing can and cannot provide
- Health and lifestyle implications based on the outcome of the genetic testing.

Genetic counselors are professionals, who hold a graduate degree in genetic counseling. They are trained health care professionals who combine their knowledge of basic science, medical genetics, epidemiological principles, and counseling theory with their skills in genetic risk assessment, education, interpersonal communication and counseling to provide services to clients and their families for a diverse set of genetic or genomic indications.

Genetic counseling is a critical part of the testing process because:

It guides information gathering: Genetic testing is best undertaken with accurate and thorough 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 family tree that shows which individuals may or may not have a condition similar to the person being tested. The family tree 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 their life and the lifestyle implications.

Benefits of working with a certified genetic counselor

Genetic counselors are specifically trained in genetics, all aspects of genetic testing, and counseling. They hold graduate degrees and are typically members 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 serve as a conduit of information between the doctors, patients, laboratories, and in many cases, insurance companies. Occasionally, some ophthalmologists and primary care physicians have experience in genetic counseling.

What the genetic counselor will do

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:

- Gathers information about family history and medical history;
- Discusses the diagnosis affecting the patient and/or family;
- Explains typical inheritance patterns and provides risk assessment;
- Researches the genetic tests, which may be available for the condition;
- Explains the benefits and limitations of genetic tests;
- Goes through a decision-making process with the patient and family to help determine if genetic testing should be performed;
- Arranges for blood or saliva samples to be drawn and sent to the testing laboratory; and
- Discusses the results of the genetic testing and their implications for health and lifestyle choices.

Genetic counseling is available locally in most communities, and nationally through telephone-based counseling services. A select listing of a few of the resources for finding a genetic counselor include:

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 is one of several genetic counseling services which offers phone-based genetic counseling sessions by certified genetic counselors experienced with inherited ophthalmic diseases.

Phone: 800-975-4819

www.informeddna.com

American College of Medical Genetics provides a search tool for finding a genetics clinic and/or genetic counselor on their website:

<https://www.acmg.net/>

For more resources, you may like to use the internet to look-up “genetic counseling services.”

Frequently Asked Questions: Basic Concepts & Terminology

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 blood cells, contains the same number and arrangement of genes. In other words, all cells contain identical DNA. 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. It is the specific combination of genes that are turned on in each cell that makes a cell unique. For example, specific combinations of genes within muscle cells are turned on to produce proteins involved in muscle contraction while a different combination of genes within retinal cells are turned on to produce proteins involved in vision.

The environment can chemically alter DNA and alter how they are turned on and off. This includes diet and stressors like ultra-violet light, air pollution and cigarette smoke.

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

If you think of a gene as functionally being like a recipe, then a chromosome is like a book chapter, a collection of recipes, while the genome is the entire book – a collection of 23 chapters (23 chromosomes). Each cell in the body 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?

Sometimes a gene contains a mutation or variant. A mutation is a physical alteration in the gene. A gene has a precise and ordered structure (a sequence), much like the arrangement 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 RDDs. It is important to remember that everyone carries the same genes; however, in someone with a retinal degenerative disorder, a particular gene is altered.

Q4: What do the words “genotype” and “phenotype” mean?

Genotype refers to a person’s genetic make-up. It is like the blueprint — or large collection of recipes — for making us who we are. In the context of talking about an 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. It is the manifestation (what we can see and often measure) of the many instructions spelled out by the genotype. As such, phenotype is also influenced by environmental factors.

A physician often makes a clinical diagnosis of a retinal degenerative disease based on phenotype — how the retina appears. In the cases where the gene is known, the physician confirms the phenotype-based diagnosis using the genotype (i.e., genetic testing).

Most genetic testing laboratories require that physicians provide a description of the phenotype and a patient’s recent medical records along with the blood sample for genotyping. The phenotype gives the testing laboratories important clues about what the genotype might be.

Frequently Asked Questions: Genetic Testing Process

Q5: What is genetic testing?

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 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. 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.

Q6: Has the gene for my retinal degenerative disease (RDD) been discovered?

New gene mutations for RDDs are being discovered at a rapid pace. So far, approximately 260 different genes — when working improperly — are known to cause retinal degenerative disease.

For any given RDD gene, different people may have slightly different “spellings”. Showing that a particular spelling actually causes the disease, as opposed to being just a variant (like differences in English and American spelling of a word) is an ongoing challenge for researchers. Different ethnicities often have different spellings which do not affect the function of a protein.

Gene mutations have been discovered for all of the diseases the Foundation works with, but not all of the genes that cause RDDs have been found. Those “missing” 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. 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. When new CLIA tests are developed there is normally a fee for the new clinical test.

Q7: 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 65% of individuals with inherited retinal disease. However, the chance of finding the cause depends on the specific disease involved, the test used, the ethnicity of the affected individual, and other factors. Therefore, the chance of success in genetic testing varies from case-to-case, and is best discussed with a genetic counselor.

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 and a clinical diagnosis obtained, then the genetic test is usually of lower cost and more straightforward.

Q8: Why would I want to be tested?

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 may also provide a motivation for using any preventive measures that may be known or subsequently discovered. 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. Individuals with Stargardt disease should not take Vitamin A supplements.

- Having a precise diagnosis can help a person keep track of research advances for preventing, treating, or curing their particular disorder.
- It helps researchers identify people who may benefit from participation in clinical trials targeting their specific genetic disorder.
- 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.

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 for Retina International: www.retina-international.org.

Q9: Should I have my child tested?

It is especially important to discuss the potential genetic testing of children with a genetic counselor. It is important to pose questions such 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?
- What impact might a diagnosis have on my child psychologically?

Q10: What's involved in having a genetic test?

Genetic testing for retinal degenerative diseases is a relatively new specialty. Many physicians are just learning about it. Testing can usually be arranged through a genetic counselor you are referred to by your ophthalmologist or physician. If you are not referred to a genetic counselor, the Foundation recommends you ask to speak to one. They will take the time to carefully explain the process and answer all of your questions.

Here are the basic steps:

1. You or a family member is diagnosed with an inherited retinal disorder.
2. You discuss testing risks, benefits, and limitations with a genetic counselor and/or a well-informed health care provider. This should not be a rushed conversation, but one in which you have time to completely understand the process, outcomes, and implications
3. You consent to a genetic test and a test is ordered.
4. Either a sample of your saliva (“spit”) is collected or a sample of your blood is drawn from a vein in your arm.
5. Your sample and required forms are mailed to a laboratory.
6. The laboratory extracts DNA from your sample and performs the genetic test.
7. The results from a CLIA-certified testing facility are returned to the person who ordered the test and your genetic counselor. This process may take several months.
8. Your genetic counselor explains the results and implications to you.
9. Sometimes your clinician may be also be your genetic counselor

Q11: What is the difference between gene mapping, finding a gene and genetic testing?

Gene mapping is the identification of the location of a disease gene, it is often the first step in a process. This is a way to find roughly where a gene is – like saying a person lives in Baltimore. Finding the gene means looking at the location of the gene that has been mapped and finding exactly where it is – like finding a specific house address in Baltimore. Genetic testing asks if the gene that is found is mutated – does the house have a problem?

Q12: Does everyone with the same diagnosis as mine have the same genetic mutation?

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 100 different genes have been implicated in RP. For any two people who know they have a mutation in a particular gene, they may have different mutations – think of the analogy that if the gene is a word, there are many ways to misspell that word. Different people may have the same or different spellings (mutations), 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.

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?

Having a genetic defect for a particular retinal degenerative disease does not necessarily mean you have the disease or will ever develop it. Sometimes you have to have two diseased genes to get a disease, sometimes one diseased gene is sufficient. This is where a genetic counselor can help you understand your own particular risk. In addition, knowing that you have a genetic defect for a particular retinal degenerative disorder rarely tells you how mild or severe your loss of visual function will be.

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 including the influence of other genes and the environment can affect disease.

Q14: 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. 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.

Q15: 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?

The term "carrier" implies that you have a disease-causing genetic defect (mutation), but do not show symptoms of the disease and likely never will. A carrier may pass the mutated gene on to their offspring.

If you carry a mutation for a recessive disease, the offspring will only develop the disease **if** the child inherits your mutated gene **and** their other parent is also a carrier **and** also passes on a mutated gene. The child must get 2 copies of the mutated gene – one from each parent.

In an X-linked inheritance pattern, sometimes also called a sex-linked inheritance, such as X-linked retinitis pigmentosa (RP), females may be carriers and are often less severely affected or even unaffected with RP (although several exceptions exist). A male child can only inherit the mutated gene from the mother. If a female child inherits the mutated gene from the mother she will be a carrier also. It is important to understand a male cannot be a carrier of X-linked RP. If a male has the mutated gene he will be affected.

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.

Q16: Could a genetic test be wrong?

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. To ensure testing is kept to a high standard, only CLIA-certified labs, that are required to maintain high quality standards, are allowed to return a genetic test result to you.

Genetic test results are complex, and results are not always a clear-cut positive or negative. There can be some level of uncertainty in the reported result, which is again why it is critical to build a relationship with a genetic counselor who can explain this type of result to you and clarify the interpretation and limitations of the test.

Q17: 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?

Genetic testing for retinal degenerative diseases is relatively new. Several laboratories in the United States and elsewhere test for different retinal disease-causing genes. Because not all the RDD-causing genes and related variations have been identified, 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. This same information can help lead your physician and/or genetic counselor to the laboratory test that may be right for you and your family.

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.

Test requisitions and samples are accepted only through a qualified physician or genetic counselor. Results are then returned to the same physician or counselor.

Testing resources for health care professionals can be found in the back of this booklet.

Q18: What must I do to get genetic testing?

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 booklet with your physician.

Instructions from the laboratory will tell the doctor how much saliva or blood is needed – typically the equivalent to one or two spoonfuls; (less for children) – and what container to collect the saliva or blood sample in, along with 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 months for a CLIA lab to return a result, but for a research lab the time is often much longer, and could be several years before you learn of any result.

Q19: How would I find out the results of a genetic test?

CLIA laboratories send test results to physicians and genetic counselors. 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.

Q20: Will knowing my genetic mutation qualify me for a research study or clinical trial?

Knowing your genetic mutation does not automatically qualify you for a research study or clinical trial. However, clinical trials may specify a particular genetic mutation as one element of their multiple inclusion criteria. If you have a mutation a trial is looking for you will still have to meet all the other criteria of the trial such as stage of progression and other retinal function measures.

If you register with My Retina Tracker, the Foundation Fighting Blindness supported registry for individuals with inherited retinal degenerative disease, you will be part of a database researchers can access when they need to reach out to individuals who have indicated they want to receive information about clinical trials and research studies.

The National Institutes of Health website [ClinicalTrials.gov](https://www.clinicaltrials.gov) maintains a searchable registry of clinical trials. Visit the website to see if you qualify for enrollment in ongoing clinical trials based on your genetic testing results and other factors. However, always talk to your retinal health care provider, or contact the Foundation to guide you to an appropriate clinician, before you commit to a clinical trial that is listed on ClinicalTrials.gov. This is particularly important for any cell or stem-cell therapy listed on ClinicalTrials.gov.

Q21: What is the cost of genetic testing?

This depends on several factors. In considering the total cost of genetic testing you should include your visit(s) to your physician, your genetic counseling session(s), the sample collection itself and shipping your sample to the testing laboratory. Actual testing costs can be from about one hundred dollars to several thousand dollars 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 sample is submitted to the lab.

Q22: Is genetic testing covered by insurance?

Some insurance companies are now offering 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.

Q23: What is gene therapy? Am I eligible?

A gene therapy is a treatment for correcting a defective gene and the physical problems it causes. Researchers are experimenting with several approaches, all of which are called a gene therapy. These include:

- Inserting a good gene to make up for lack of function of a defective gene;
- Repairing the defective gene; and,
- Controlling 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 human studies. These studies progress systematically starting with Phase 1 (safety) then Phase 2 (further safety and efficacy) studies. Announcements and updates on enrollment can be found on the Foundation's website, www.FightingBlindness.org, and on the National Institutes of Health's clinical trials registry, www.clinicaltrials.gov.

If you are in the Foundation registry, My Retina Tracker[®], which is free and accessible online at www.MyRetinaTracker.org, researchers may identify you for further screening if there is a clinical trial that you may be eligible for.

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, Foundation funding has helped advance a majority of the important advances in the field of retinal degenerative disease, including the discovery of genes responsible for RDDs and our support of that work continues.

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?

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.

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?

Visit the Foundation Fighting Blindness website, www.FightingBlindness.org, and register to receive free information about your disease and research efforts to find treatments and cures.

Resource Links for Patients and Families

The following academic, government, and nonprofit websites provide non-technical, easy-to-understand information on genetics and genetic testing:

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/content/basics/>

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>

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 genetic experts available by telephone to help patients and providers with genetic counseling and health information.*

www.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

Genetic Alliance – Publications – The [Genetic Alliance](http://www.geneticalliance.org) is a network that consists of disease-specific advocacy organizations, academic groups, private companies, government agencies, and public policy organizations. *Understanding Genetics: A Guide for Patients and Health Professionals is one of many downloadable publications that the Genetic Alliance makes available to patients and advocates.*

www.geneticalliance.org/publications

Information on GINA – The Genetic Alliance website provides an [overview of GINA](#) as well as an [interactive help site](#). The Genetic Alliance led the “Coalition for Genetic Fairness” which worked for over 12 years to pass the GINA bill. <http://www.ginahelp.org/>

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 for research news and updates. www.FightingBlindness.org

Eye on the Cure – A science blog authored by Dr. Stephen Rose, the Foundation’s chief research officer, and other contributors, the Eye on the Cure provides an insider view of the retinal research field, which, over the past decade, has exploded with scientific discoveries and advancements.
www.FightingBlindness.org

My Retina Tracker – The Foundation Fighting Blindness sponsored registry for individuals and families affected by inherited retinal degenerative diseases. www.MyRetinaTracker.org – FAQ and Documents – Genetic Testing Study <https://www.myretinatracker.org/help.html>

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 the NIH Genetic Testing Registry (GTR) as a primary resource for available genetic tests and laboratory contact information.

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/>

Gene Reviews - *GeneReviews*, is an international point-of-care resource for busy clinicians, provides clinically relevant and medically actionable information for inherited conditions in a standardized journal-style format, covering diagnosis, management, and genetic counseling for patients and their families. <https://www.ncbi.nlm.nih.gov/books/NBK1116/>

AAO Recommendation for Genetic Testing of Inherited Eye Disease - *A statement from the American Academy of Ophthalmology Task Force on Genetic Testing, February 2014*

<https://www.aao.org/clinical-statement/recommendations-genetic-testing-of-inherited-eye-d>

National Society of Genetic Counselors – *The NSGC website offers educational materials and events and an online search tool for finding genetic counselors in your area.*

www.nsgc.org

InformedDNA – *InformedDNA is a nationwide-network of genetics experts with a dedicated ophthalmic team 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 – A service of the ACMG that allows for the search for a specific genetics center or genetic services. www.acmg.net

Foundation Fighting Blindness – Visit the Foundation’s website often for research news and updates. www.FightingBlindness.org

Eye on the Cure – A science blog, the Eye on the Cure provides an insider view of the retinal research field, which, over the past decade, has exploded with scientific discoveries and advancements.
www.FightingBlindness.org

My Retina Tracker – The Foundation Fighting Blindness sponsored registry for individuals and families affected by inherited retinal degenerative diseases. www.MyRetinaTracker.org –
<https://www.myretinatracker.org/help.html>

CLIA Approved Laboratories Providing Tests for Retinal Degenerative Diseases

The following list of laboratories providing tests for inherited retinal degeneration diseases was compiled 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/>

Baylor Medical Genetics Laboratory

Baylor College of Medicine

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

Blueprint Genetics

www.BlueprintGenetics.com

John and Marcia Carver Nonprofit Genetic Testing Laboratory

University of Iowa

www.carverlab.org

Casey Eye Institute Molecular Diagnostic Laboratory

Oregon Health & Science University

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

Emory Genetics Laboratory

Emory University

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

eyeGene®

National Ophthalmic Disease Genotyping Network

National Eye Institute, National Institutes of Health

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

NOTE: Sample collection has been suspended as of December 31, 2015. For more information, visit the eyeGene

website: https://nei.nih.gov/eyegene/eyegene_notification

GeneDx

www.genedx.com

Ocular Genomics Diagnostic Laboratory

Massachusetts Eye and Ear Infirmary, Harvard Medical School

<http://oculargenomics.meei.harvard.edu/index.php/dt>

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

<http://personalizedmedicine.partners.org/laboratory-for-molecular-medicine/tests/default.aspx>

Molecular Pathology Laboratory

Columbia University – Department of Pathology

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

Shiley Eye Center

University of California, San Diego

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

Denver Genetic Laboratories

UCD DNA Diagnostic Laboratory

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

Prevention Genetics

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



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