



Did you know that two people who are living with the “same” diagnosis, such as retinitis pigmentosa (RP), may have different mutations in the same gene or even different mutations in different genes? In many cases, the location of these genes and mutations can be identified. Today, more than 250 genes related to retinal dystrophies have been identified. Each gene is made up of thousands of DNA subunits called base pairs. Mutations can occur anywhere in this string of base pairs, so even when two people have vision loss due to an error in the same gene, they may have completely unique mutations.

A variety of different inherited eye disorders can lead to uncorrectable low vision or total blindness. Clinicians often describe these conditions, which are caused by disordered retinal tissue at the back of the eye, as retinal dystrophies. Although there are important differences among the types of retinal dystrophies, they share some things in common: 1) vision loss ultimately results from damage to the retina at the back of the eye (where photoreceptors, the eye’s critically important light-sensing cells are located); and 2) this damage is caused by genetic mutations (errors). There are other inherited eye disorders that are due to disordered anterior segment tissues found at the front of the eye. Examples include corneal dystrophies and aniridia.

What is genetic testing?

Genetic testing involves taking a sample of your DNA (usually from a blood sample) and examining it in a laboratory. This process can be initiated by your ophthalmologist specializing in ocular genetics and involves genetic counselling. It may also require a referral by your ophthalmologist to another physician specializing in medical genetics. It is important to work with your vision care team because genetic testing does not always deliver a clear result. This is because even though there have been remarkable advances over the past 10 years, many genes associated with vision loss remain unidentified or have not been characterized well enough yet. **Genetic counselling will help you to understand the purpose, benefits, risks, limitations and the results of your genetic test and provide guidance about possible next steps.**

Why is genetic testing done?

Successful genetic testing can teach you about your condition. It can confirm your diagnosis and provide a more accurate estimate of the chances a family member would develop the same condition. Knowing whether you have a disease-causing mutation (or not) might also change



how you manage your disease. For example, it will help to determine if you are eligible to participate in experimental studies related to emerging treatments.

Most people who contact the Foundation Fighting Blindness about genetic testing are interested to get involved with clinical trials, which are designed to test emerging therapies. There are many approaches to vision research now under way. Therapies that are based on specific genetic mutations are only one approach. When a therapy is developed for a specific genetic subtype ONLY people with a mutation in that specific gene will be eligible for the trial and only people with mutations in that specific gene will be able to benefit, if the therapy is approved.

Will genetic testing identify my mutation?

Your genetic counsellor can provide you with an estimate of success specific to you. S/he can also identify the most appropriate laboratories to test your sample based on your condition and family history.

The likelihood of receiving an answer from genetic testing depends on an accurate diagnosis of your clinical condition (usually made by an ophthalmologist with expertise in genetic eye conditions). Some conditions are associated with only a small number of genes and the genes are well known. In other cases, there are many possible mutations in many different genes – and testing will be more difficult.

In general, people living with x-linked retinoschisis or choroideremia or X-linked recessive retinitis pigmentosa are most likely to get an informative result, people with autosomal dominant retinitis pigmentosa or Leber congenital amaurosis (LCA) or Stargardt macular dystrophy are next, while autosomal recessive retinitis pigmentosa (RP) is likely to be more challenging.

For example, if you have x-linked retinoschisis, there is a 90% detection rate to identify a mutation in the RS1 gene. If you have choroideremia, there is a 95% detection rate with the CHM gene. In contrast, the detection rate for LCA is approximately 60%. In Stargardt disease, there is an 80% detection rate for the common gene ABCA4, however there are 4 – 5 other genes that cause similar vision symptoms that have a much lower detection rate. In RP, the form with the highest detection rate is X-linked RP. This is because mutations in the RPGR and RP2 genes account for approximately 90% of all cases. There is a 60% detection rate for people living with an autosomal dominant form of RP with about 25 different genes that have been identified. The detection rate for the autosomal recessive form of RP is about 35% and has been associated with 33 different genes so far.



How can I arrange to have genetic testing?

A genetic counsellor can work with you to arrange testing. Unfortunately, this is still difficult in many parts of the country. We recognize that genetic counselling for eye conditions is not widely available across Canada. However many large Canadian cities have a retinal dystrophy clinic or a Medical Genetics Clinic where you may be able to connect with a genetic counsellor. It is important to remember that many genetic counsellors do not have a specialty in ocular genetics but are capable of arranging appropriate testing with enough information.

If you do not have access to an ocular genetic counsellor in your city, ask your family doctor and/or ophthalmologist to connect you with someone.

It is important that you work with your ophthalmologist and a genetic counsellor to arrange for testing. **Do not attempt to go through a private testing company.** These companies (for example, 23andme) are increasingly affordable and easy to access online. These companies do not have the resources to provide you with the answers that you are looking for.

Ask your ophthalmologist to refer you to the clinical genetics service in your area. The Canadian Association of Genetic Counsellors offers a listing of these clinics at <http://cagc-accg.ca> (click on Genetic Clinics). Genetic counsellors in Canada have access to many professional resources to keep them updated about the latest possibilities for genetic testing and to identify international labs testing for specific genes.

Be your own advocate.

If you are having trouble getting access to a genetic counsellor and/or genetic testing, remember: you must be your own best advocate. What does this mean? KEEP ASKING FOR THE CARE THAT YOU NEED.

Explain why genetic testing is important for your care.

Explain to your doctor that a genetic diagnosis is an important part of managing your condition.

Explain that there are now over 250 different genes related to inherited retinal dystrophies and that genetic testing of these genes can potentially help secure an accurate diagnosis for you.

Explain that you would like to join the FOUNDATION FIGHTING BLINDNESS PATIENT REGISTRY so that you can become involved if there are any Canadian clinical trials that target your specific genetic eye condition.

Print out this resource and share it with them.



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Genetic testing and counselling are an important part of your vision care pathway. We know that it is sometimes hard to get access to this care. The FFB is advocating for better access. Please share your stories with us. These stories are powerful and will help us to show the government that ocular genetics is important for people living with blinding eye diseases.

What information needs to be in the Clinical/Medical Genetics referral from my doctor?

- Name
- Address and phone number
- Present diagnosis
- Information about other family members with vision problems
- Details of first symptoms and the age at which they started
- The results of tests such as ERG, VEP, OCT, visual fields & visual acuity tests

How long will it take?

After a sample has been submitted for molecular genetic testing, it may take months to receive a result. Even Canada's largest centres will likely send your sample out to one or more international laboratories for testing. **Ask your genetic counsellor how you will be informed about the results when they do arrive.** If your genetic result is inconclusive or does not help to confirm your clinical diagnosis, it may be possible for your DNA specimen to be stored and retested again as researchers learn more about the eye condition and more genes are identified. Ask your genetic counsellor about the possibilities for holding and retesting your specimen and the length of time the specimen might be held.

Will my provincial health plan pay?

In some provinces, your genetic counsellor can complete an application for coverage of genetic testing. It may take months for such a claim to be processed and not all provinces have this option.

Can I pay for it myself? What will it cost?

Depending on the regulations in your province, you may be able to pay for testing yourself. In some cases, this will be the only option. The cost will depend on your condition, the number of genes to be tested and the methods used. The range is between \$400 and \$3000. Tests are constantly being updated, and are becoming faster and less costly.



Most recently, it is now possible to look at much more of your genome, thanks to scientific developments that have led to a process called **whole exome sequencing (WES)**. In theory, this process makes it possible to find almost any mutation, but it is also more costly and time intensive, and it is still not possible to *guarantee* a result. This is because your mutation might not be known. WES is very helpful in a clinical research setting to learn more about a particular patient's unusual symptoms. WES is often used test the patient as well as the parents to see if we can identify new genes and/or pinpoint the specific causal mutation(s).

Will the availability and efficacy of testing improve?

Yes, we anticipate that testing will improve in the next few years. With your support, Canadian scientists discover new genes each year; other scientists around the world are doing the same. The tools for performing these tests are continually being updated, and becoming more affordable. In the future, we anticipate that genetic testing will be able to identify most mutations and will become a more routine option for Canadians living with vision loss.

Updated on April 29, 2016 by Dr. Mary Sunderland, Director of Research & Education at the Foundation Fighting Blindness, reviewed by Stephanie Chan, Ocular Genetic Counsellor at the Royal Alexandra Hospital. This fact sheet was originally issued on October 14, 2011, and was reviewed by Joanne Sutherland and Megan Day, Ocular Genetic Counsellors, Sick Children's Hospital.