

In the past 40 years, there has been a complete shift in the way that clinicians and researchers categorise inherited retinal diseases (IRDs). Prior to the 1980s, very little was known about the genes that cause IRDs – in fact, the first IRD gene to be identified wasn't until 1984.⁽¹⁾ Since this time, the rate of gene discovery has accelerated, and we now know of over 300 genes that can cause an IRD.

What is genetic testing?

Genetic testing, also known as DNA testing, is a medical process undertaken to examine a person's DNA, to identify changes in genes which can be used to confirm or rule out a genetic condition.

It is the only way to be certain about what genetic mutation is causing a person's inherited retinal disease (IRD). Testing is also sometimes referred to as obtaining a "molecular diagnosis".

To have a genetic test, you need to give a DNA sample. This can be collected from a blood test, saliva sample, or a buccal swab (using a cotton bud to collect some of the cells from inside your cheek). The doctor will then send your sample to a testing laboratory, which is usually overseas.

How do I get a genetic test?

Genetic testing can be ordered through your ophthalmologist or a clinical geneticist. There are specialist ocular genetics clinics at many of our main eye hospitals in Australia, including the Royal Victorian Eye and Ear Hospital, the Sydney Eye Hospital, Royal Adelaide Hospital and the Perth Lions Eye Institute/Perth Hospital.

Results can take months to be returned, and are not always conclusive. In fact, four out of ten people won't get a genetic answer from current testing methodologies.⁽²⁾ This is because we still do not know all the genes that cause IRDs and, in some cases, our testing is not sensitive enough to detect certain changes in the genetic information.

You should feel comfortable to ask as many questions as you like about the genetic testing process, including implications on life insurance, and what will happen if unexpected results are discovered.

What are the different types of genetic tests?

There are many different types of genetic tests available. Your doctor will select the most appropriate type depending on your condition.

The test types can be categorised into three general levels – from cheapest and easiest, to more expensive and complex. These are:

1. Single gene testing

- Also called “Sanger sequencing”, these tests only look for mutations in a single gene.
- This type of test is the cheapest and quickest option, and is useful when your doctor knows the gene that is present in other members of your family, or if they are specifically testing to see if you are eligible for a clinical trial.

2. Panel testing

- In a panel test, over 300 known genes that can cause an IRD are tested at once.
- This is the most common type of initial genetic test completed
- if there is no known gene in the family and no clear indication of the possible gene from the clinical presentation.

3. Genomic testing

- The most comprehensive is whole genome sequencing but it comes at a high cost and resource demand.
- Genomic testing allows the testing of the entire genome (a person’s complete set of genetic information), at once which is useful when there are several genes associated with a condition, or it is unknown which gene may be the cause.

How much does genetic testing cost?

The cost of a genetic test varies significantly depending on the test type (as described above), from hundreds to thousands of dollars.

Australians have a choice to fund this testing privately (i.e. pay out of your own pocket), or through the public health system (which covers the costs for some patients through government funding programs).

There have previously been sponsored genetic testing programs for people with IRDs to access no-cost testing, but as of January 2024 there are no active programs in Australia. Your doctor will be able to provide the best information on the cost, and best pathway for your circumstances.

Reasons why you might consider having a genetic test

Not everyone will want, or need, to have genetic testing. Some of the reasons that you might consider having a test include:

- A positive disease diagnosis may assist in making more informed medical and lifestyle decisions.
- Family planning. If someone in the family has been diagnosed with an IRD, having a genetic test may provide some insight as to your potential disease risk, and also carrier identification. Some people choose to investigate in-vitro fertilisation as an option.
- A positive disease diagnosis will enable participation in research studies and clinical trials for potential future treatments. Registering on a research database will assist in this opportunity. These include the AIRDR, VENTURE study, WARD study and Save Sight Institute Registry, all which can be found on Retina Australia's [IRD Research Project and Clinical Trial Register](#).
- In some syndromic IRDs, such as [Refsum disease](#), there are dietary modifications that may be needed, so your doctor may advise you to have a genetic test to confirm that syndrome, so that you receive the most targeted management and counselling.

Reasons that you may NOT want to have a genetic test

The decision to have a genetic test is very personal and should be considered carefully. It is always advised to have genetic counselling prior to making the decision as the counsellor or doctor can outline the implications of having a test.

Whilst not a comprehensive list, some considerations include:

- The risk of receiving a negative result, with no answer to your questions. Despite significant improvements in genetic testing technologies in the past decade, it is still not possible to identify the responsible gene for everyone. In fact, about 4 out of 10 IRD genetic tests will be inconclusive.⁽²⁾
- Emotional implications. Sometimes the news of a causative gene for your eye condition can be a relief, with positive emotional outcomes. However, sometimes it can also raise feelings of stress, guilt and trepidation for the future. It is highly recommended that you have good genetic counselling in place to help with the emotions involved with genetic testing.
- Life insurance implications. Since 2019, Australia's life insurance industry has had a partial moratorium on the requirement to tell your life insurance company your genetic test results, but this may change in the future. It is important to get up to date advice on whether completing genetic testing is likely to change your ability to access affordable life [insurance](#).

- Unexpected results. Sometimes the test will uncover unexpected information, such as challenging family structure (for example, discovering that a parent is not biologically related to you), or identifying other aspects to your condition, such as the possibility of future hearing loss. These can be challenging to process, and again, require good counselling support in place.

Who can get a genetic test?

Genetic testing for IRDs is usually for an individual with signs and symptoms of the condition (often called “proband testing”). Sometimes your doctor will ask family members to also undergo testing, to confirm the genetic diagnosis.

In some cases, “genetic screening” can be completed for people who are planning to have children, if there is a known IRD in their family. This is completed through prenatal testing which identifies whether the parents carry the gene that can cause the IRD. This allows parents to make informed decisions about family planning. It is also possible to test for IRD genes through an amniocentesis, where cells are taken from the baby in a woman who is already pregnant.

Other people who may be eligible for a genetic test are those who are suspected to have the gene mutation, but are currently asymptomatic. This can often be children who have not yet shown any signs of the condition.

Genetic counselling is vital for making these decisions – these professionals can help advise you on the risks and benefits of deciding to take any of these testing routes.

What does a genetic test involve?

If you are interested in obtaining a genetic test, the first person to speak to is your ophthalmologist. You will usually need a referral from a general practitioner or optometrist before you can visit an ophthalmologist. They will be able to advise on whether a genetic test is suitable for you, and explain the potential costs, risks and benefits. If you would like to see another healthcare professional (i.e. a clinical geneticist, or a specialised ocular genetics clinic), your doctor can arrange a referral.

Before providing a sample for a genetic test, you will undertake counselling with either your doctor or a specialised genetic counsellor. They will inform you of the details of the process, and ask you to sign a form to acknowledge you consent to the procedure.

You will then be asked to supply a sample of either blood, saliva, or a cheek swab. The sample is then sent to a testing laboratory, where the genes of most likely involvement are tested.

The other information which is vital to genetic testing is knowledge of your family history. Before you start the process, it is important to find out if anyone else in your family has an IRD. You will be asked to provide this information to your doctor, as it helps them identify the most likely gene to test for.

What happens when the results are ready?

Results can take months to be returned and are not always conclusive. In fact, four out of ten people won't get a genetic answer from current testing methodologies.⁽²⁾

When the ordering doctor (geneticist or ophthalmologist) receives the results from the laboratory, they will arrange an appointment with you to discuss the results. This may either be with them, or with a genetic counsellor in their team.

Genetic counsellors are highly trained in explaining test results and can provide you information on the gene and what it might mean for you and your family. That may involve learning about who in the family may be at risk of developing the IRD, and advice on family planning. Genetic counsellors also provide emotional and practical support to help people adjust to living with, or being at risk for, a genetic condition.

If I didn't get a result on the first test, what are my next options?

If the genetic test did not give an answer, sometimes the doctor will discuss other test types and/or ask your family members to be tested as well to help solve the case. Sometimes, they will advise you to wait for a few years and then take another test.

If you have had a genetic test, the laboratory will hold your results and, if at a later date they learn that a particular gene mutation may be related to your IRD (which wasn't previously known), then they will contact your doctor to advise you of the update.

How do I access genetic testing?

Genetic testing can be ordered through a clinical geneticist, or an ophthalmologist with a special interest in IRDs. There are several clinical centres around Australia

with special interest in genetic eye diseases, where you can access a multidisciplinary team for care. To access these clinics, you will need a referral from your GP, optometrist or ophthalmologist.

Below is a list of public clinical IRD genetic testing providers in Australia (current January 2024). In some cases, these clinics will be able to access government subsidies to cover costs of genetic testing – please speak to your ophthalmologist regarding your own situation for the best advice on referrals.

- **Victoria.** Royal Victorian Eye and Ear Hospital – Contact Outpatient Booking Unit
- **New South Wales.** The Sydney Children's Hospital Network – Phone (02) 9845 3273 ,Email SCHN-CHW-ClinicalGenetics@health.nsw.gov.au
- **Queensland.** Princess Alexandra Hospital – Ophthalmology clinic – Phone 1300 364 155
- **South Australia.** Women and Children's Hospital – Associate Chris Barnett, Clinical Genetics Service Phone (08) 8161 7375 (for women and children). Royal Adelaide Hospital – Dr Nicola Poplawski, Adult Genetics Unit Phone (08) 7074 2697 (for adults)
- **Tasmania.** Royal Hobart Hospital – Phone (03) 6166 8296
- **Western Australia.** Lions Eye Institute – Phone (08) 9381 0777, Email – carecentre@lei.org.au
- **Northern Territory.** Northern Territory Genetics Services (Victorian Clinical Genetics Services providing visiting services to Northern Territory) – Dr Chloe Stutterd, Email: ntgenetics@vcgs@ord.au
- **National biobank.** Australian Inherited Retinal Disease Registry and DNA Bank (AIRDR) – Phone (08) 6457 2866, Email scghmtp@health.wa.gov.au

What is the future for genetic testing in IRDs?

There are many exciting advances happening in the field of genetic testing for IRDs, including the development of new testing methodologies, and better interpretation of existing results.

Retina Australia has been proud to fund a number of research studies into genetic testing, including:

- Looking for disease causing mutations in families with dominant RP pedigrees. Associate Professor Fred K Chen – Centre for Ophthalmology and Visual Sciences, The University of Western Australia \$40,000 ([2021](#))
- Finding genetics answers for Leber congenital amaurosis using next-generation sequencing. Associate Professor Robyn Jamieson – Eye Genetics Research Group, Sydney \$40,000 ([2014](#))

The Australian Inherited Retinal Disease Register and Biobank

In addition to the clinical genetic testing services listed above, people with IRDs and their families can also supply DNA samples to the Australian Inherited Retinal Disease Register and Biobank (AIRDR). This research platform is characterising the genetic spectrum of IRDs in Australia in order to guide research into treatments and cures. Genetic results are returned to participants where possible, via their clinicians, thereby improving disease management for those participants.

Retina Australia has been a key supporter of the AIRDR, including initial setup costs and provision of grants including:

- Provision of genetic research reports to research participants via their nominated ophthalmologists or clinical geneticists. Jennifer Thompson – Sir Charles Gairdner Hospital. \$20,000 (2021)
- Provision of genetic research reports to Australian Inherited Retinal Disease Registry participants via their nominated ophthalmologist or clinical geneticist. Jennifer Thompson – The Australian Inherited Retinal Disease Registry & DNA Bank, Perth. \$40,000 (2020)
- Report to Retina Australia on research carried out by the Australian Inherited Retinal Disease Registry and DNA Bank for the period 1 April 2018 to 31 March 2019. Dr John De Roach – Australian Inherited Retinal Disease Registry and DNA Bank, Perth \$100,000 (2018)
- Australian Inherited Retinal Diseases Register and DNA Bank. Dr Tina Lamey – Australian Inherited Retinal Diseases Register and DNA Bank, Perth. \$110,000 (2016)

To contact the AIRDR, call (08) 6457 2866, or email scghmtp@health.wa.gov.au.

References

- (1) Hattacharya SS, Wright AF, Clayton JF, et al. Close genetic linkage between X-linked retinitis pigmentosa and a restriction fragment length polymorphism identified by recombinant DNA probe L1.28. *Nature*. May 17-23 1984;309(5965):253-5. doi:10.1038/309253a0
- (2) Britten-Jones AC, Gocuk SA, Goh KL, Huq A, Edwards TL, Ayton LN. The Diagnostic Yield of Next Generation Sequencing in Inherited Retinal Diseases: A Systematic Review and Meta-analysis. *Am J Ophthalmol*. May 2023;249:57-73. doi:10.1016/j.ajo.2022.12.027

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