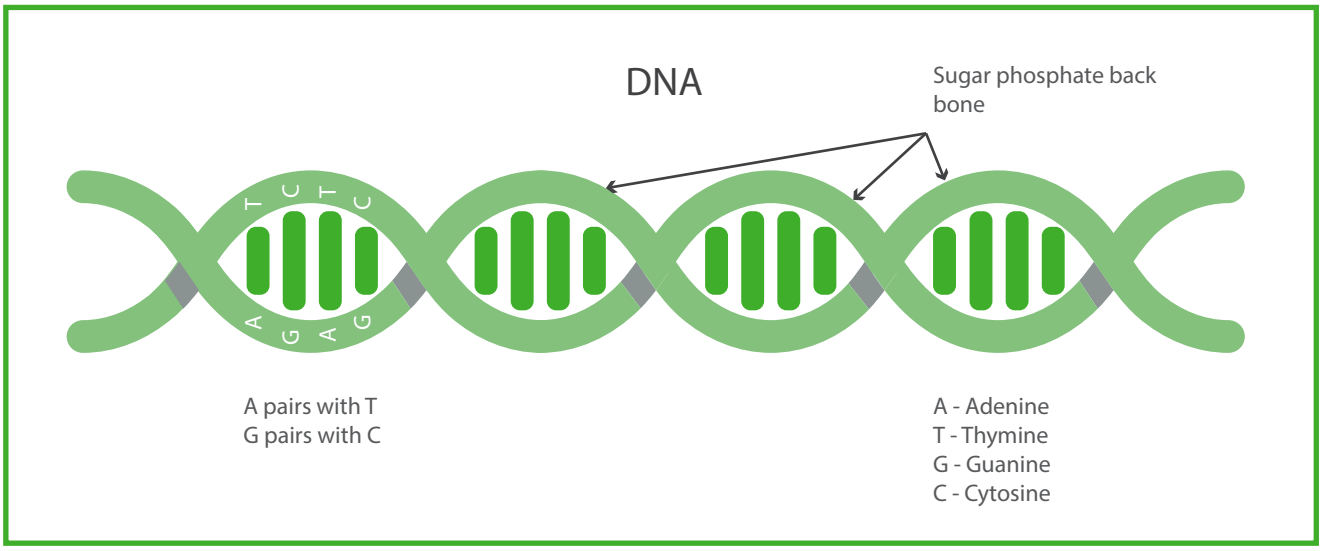
# GENETIC TESTING FOR MITOCHONDRIAL DISEASE

## KEY POINTS

- Genes help our mitochondria function. When a change occurs in one of these important genes and stops it from working properly, it can lead to mitochondrial disease (mito)
- Genetic changes that can cause mito can occur in the nuclear DNA or the mitochondrial DNA
- Genetic testing can look for these changes. Testing can be performed using a urine sample, blood sample or a muscle or tissue biopsy
- For people with suspected mito, your doctor will consider your symptoms and family history, and decide which kind of genetic test is the most suitable
- Genetic test results can explain if a genetic variant has been found and if it is likely to cause mito
- Sometimes genetic testing can have uncertain results. Our understanding of these results can change over time with new research

## GENES AND DNA

Our genetic material is made up of deoxyribonucleic acid (DNA). DNA is made up of nucleosides, or 'building blocks' called adenine (A), thymine (T), guanine (G), and cytosine (C). They make a 'code' or 'sequence' that our body reads to make proteins and other things it needs.

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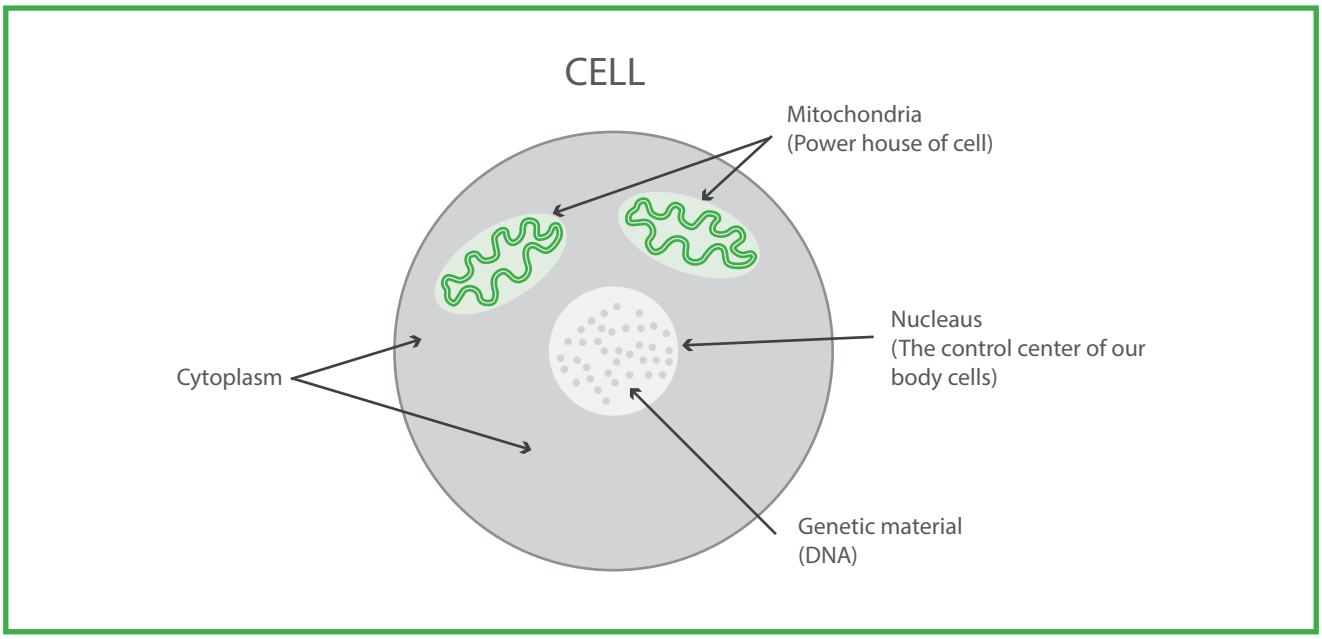
Our DNA is very long - there are three billion letters that spell out our genetic code. Our body doesn't read these letters all at one time. Instead, it reads small parts of our DNA called genes. Genes tell our body to make a protein. They make up the coding portion of DNA. The parts of DNA that are not often read are called non-coding DNA.

Changes in our DNA code are natural, but sometimes genetic changes can stop a gene from working properly. In the case of mito these changes can occur in our mitochondrial DNA (mtDNA) or our nuclear DNA (nDNA). nDNA is much bigger and is found inside the nucleus of a cell. mtDNA is relatively small, and is found inside the mitochondria.




## WHAT IS GENETIC TESTING AND WHEN IS IT ADVISED?

Genetic testing examines the DNA sequence of A, G, C and T. Tests will look for changes in the sequence that might stop the gene from working properly. This is like looking for spelling mistakes in a sentence.

Your doctor can use your genetic test result with other tests, such as a blood test or muscle biopsies, to make an accurate diagnosis. As mito can be difficult to diagnose, genetic testing can be very helpful. The result can also explain how the condition might be inherited in your family. Sometimes a genetic change is a new change that has not been inherited, this is called a sporadic, or *de novo* mutation.

## WHICH GENES WILL BE TESTED?

A genetic test can look at our mtDNA, which has 37 genes. The letters across these 37 genes will be read and checked for any changes. This is referred to as the sequencing of the mitochondrial genome.

nDNA has 20,000-25,000 genes that all have different jobs in our body. Of these genes, approximately 1,500 genes are known to help mitochondrial function.

If these genetic tests do not find a genetic change that explains your symptoms, your doctor might suggest whole exome sequencing. This reads the coding sequence in all 20,000-25,000 genes for a genetic change *Whole genome sequencing* is also starting to become an option for genetic testing; it reads all three billion letters of our genetic code, including all the nuclear and mtDNA genes. Both whole exome and whole genome sequencing provide lots of information, but sometimes it can be difficult to know if the genetic changes found cause a disease.

## AM I AT RISK OF MITO?

If you have a close relative who has a genetic change that can cause mito, your doctor can test for this specific genetic change. Your doctor may refer you for genetic counselling and possible genetic testing to see if you are at risk of developing mito.

Find out more about genetic counselling.

## WHAT IS TESTED?

Your doctor might ask for a blood sample, urine sample or arrange for a muscle or tissue biopsy. Initially, your doctor will arrange for genetic testing to be performed on a blood sample. However, sometimes urine or tissue samples can give more information about potential genetic changes.

## HOW LONG DOES GENETIC TESTING TAKE?

The time it takes to receive a genetic test result after a biological sample has been taken can vary depending on the patient and the facility. Generally, it can take several months, although in some cases it can take years.

## HOW MUCH DOES GENETIC TESTING COST?

The out-of-pocket cost of genetic testing varies between the different states and territories depending on state health funding schemes. Genetic tests for mito are not currently funded through the Medicare Benefits Schedule (MBS). In some instances, costs can be fully covered, and in others can cost the patient thousands of dollars.

Some patients may be able to access genetic testing through research programs at no out-of-pocket cost. AMDF has co-funded the Australian Genomics Health Alliance (AGHA) Mitochondrial Disease Flagship, which will allow eligible patients with suspected mito to access genetic testing. Click here to read more about the AGHA.

Your specialist will be able to provide you with further information about the cost of testing.

## WHAT IS DIRECT-TO-CONSUMER GENETIC TESTING?

Direct-to-consumer genetic testing involves companies selling genetic testing services direct to the public without the involvement of a medical professional. Laboratories for these testing services are often overseas and, therefore, are not required to adhere to strict regulations that apply to Australian services, which are accredited by The National Association of Testing Authorities (NATA). AMDF encourages patients to work with their medical team for genetic testing to ensure that they receive accurate results and evidence-based information.

## WHAT DOES MY GENETIC TEST RESULT MEAN?

The test result will explain if a genetic change has been found, and if this change is likely to cause mito.

A genetic change that is known to stop the gene from working properly is referred to as a pathogenic variant or change. Pathogenic means that it can cause disease. This means that the genetic change can lead to mito. It can also be called a mutation or deleterious variant.

Genetic testing might find a genetic change that does not cause mito. This is called a benign variant.

Sometimes, the genetic test result will be uncertain. An uncertain variant means that a genetic change has been found, but it is unclear whether it causes mito.  This happens because our DNA contains lots of information and it can, at times, be hard to interpret the genetic code.

Genetic test results can be reclassified, meaning the result might change over time. This happens when additional information or research gives the laboratory new clues about a genetic change or variant. If you have received an uncertain test result, this result might change in the future.

Your doctor will interpret your genetic test results. They will also consider other test results, such as blood or tissue tests and your family history.

For further information, speak to your specialist.