Liverpool Women's
NHS Foundation Trust

Panel Genomic Testing

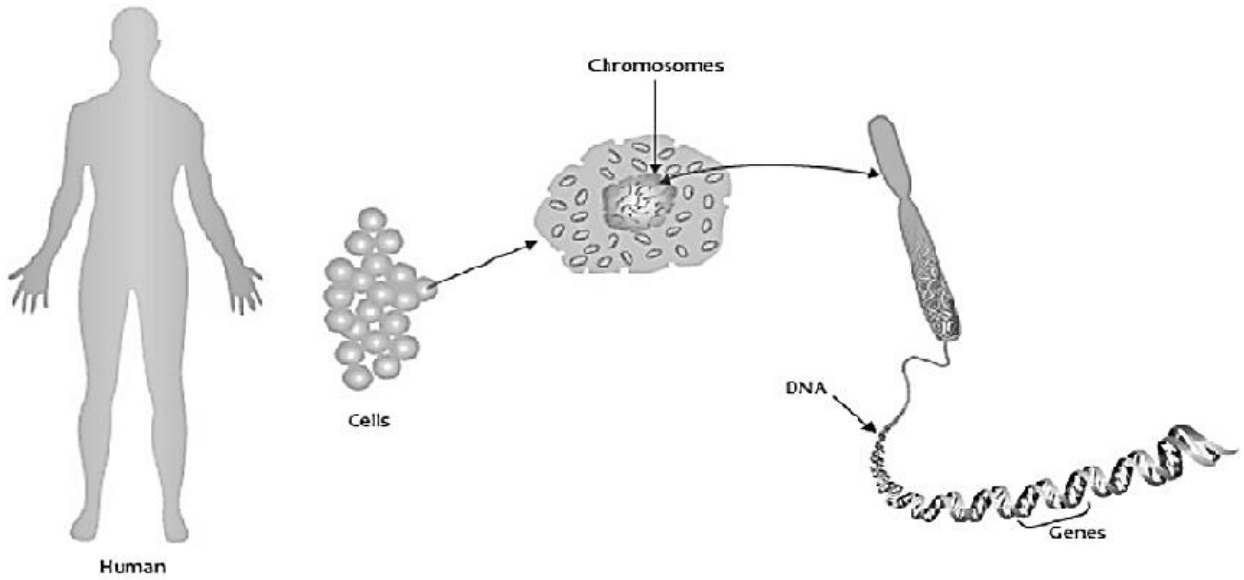
Information for people who are eligible for gene panel testing

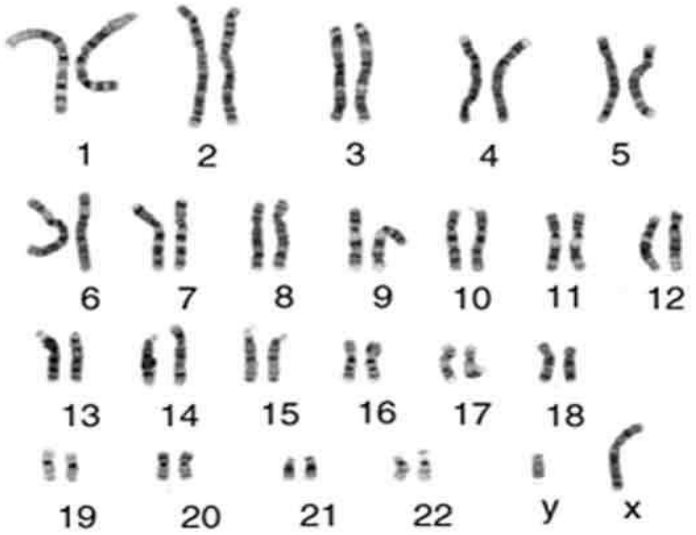
Introduction

For many people with a genetic condition finding out the cause of the condition can be important. Understanding the genetic basis of the condition might help health professionals to give you information about the progress of the condition, possible preventive actions or treatment. Individuals with a genetic condition may just find it helpful to know why their signs and symptoms occur.

What are genes and chromosomes?

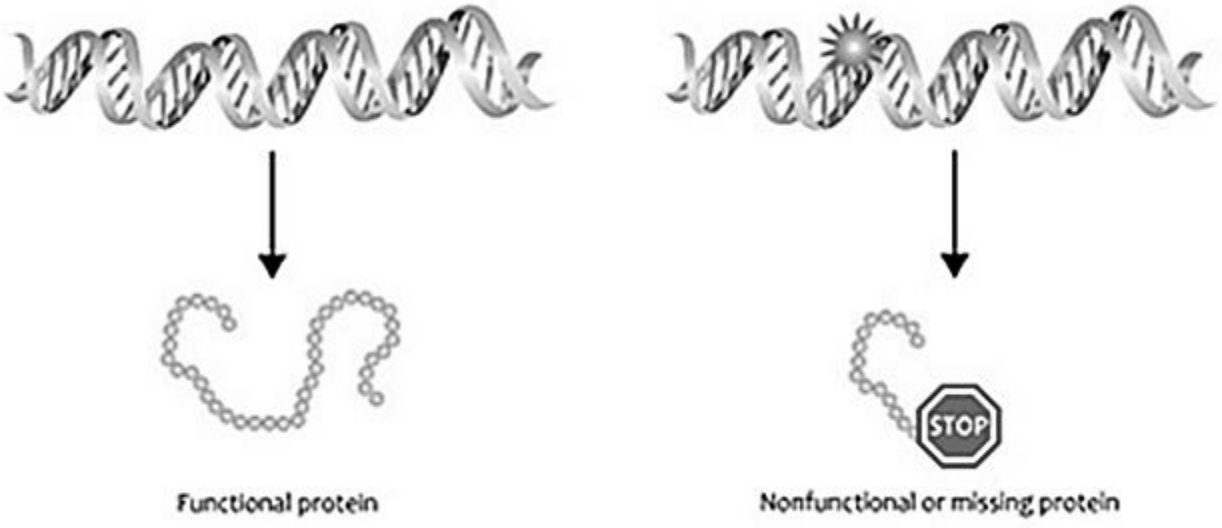
Humans are made up of trillions of cells. At the centre of almost all of our cells is a ball-shaped structure called the nucleus, inside of which are 46 thread-like structures called chromosomes. Chromosomes are long strands of DNA (**D**eoxyribo**N**ucleic **A**cid). It is estimated that if a strand of DNA was stretched out it would be around two metres long, even though the average cell is smaller than a pinhead.





We have 23 pairs of chromosomes; one of each pair is inherited from your mother and one of each pair from your father. Chromosomes 1-22 are arranged in size order with number 1 being the largest and 22 the smallest. The 23rd pair of chromosomes determines if you are a male or female. Males are XY and females are XX. Chromosomes contain an estimated 20-30,000 pairs of genes that make us who we are. As we have pairs of chromosomes we therefore have pairs of genes.

Genes are often called the blueprint for life because they tell each of your cells what to do and when to do it. For example, some genes determine how tall you will be; some what colour your hair will be; some genes are responsible for maintenance in our bodies and some for our development, and so on. Genes do this by making proteins. In fact, a gene may act by being a 'recipe' or a code for making a certain protein. In order for a gene to do the job it is supposed to do, the 'recipe' or code needs to be written correctly. If the 'recipe' is wrong, the protein is either not made or is made incorrectly so cannot do the job it is supposed to do. This is sometimes called a gene alteration, a spelling mistake or a gene mutation.



What is panel testing?

Traditionally genetic tests were targeted at just one gene. This meant that the health professional providing your care needed to have a strong idea of what was causing the condition in order to choose the correct test. This is not always possible with conditions that may not fit an obvious pattern or when the condition could be caused by changes in one of a large number of genes. In many instances that meant multiple tests of several genes over a period of time, and more laboratory time and effort was needed to obtain a result. With new technologies it is possible to examine many different genes at the same time.

Targeted panel testing is a technique in which a number of specific genes that are linked to a particular genetic condition are examined at the same time. Examples of conditions for which targeted gene panels have been developed are hearing impairment, epilepsy and eye disorders, which may be caused by alterations in one of many separate genes. With this test, even though we might be looking at a number of different genes, the analysis is targeted on the specific condition present in the family.

It is important to remember that the genes we test can also be associated with a range of other problems that can impact your health and may mean you need additional screening or other tests.

If I undergo panel testing, what will my results show?

Your results will show one of 3 things:

1. **A gene alteration is identified in your sample that is known to be disease causing (pathogenic).** This is highly likely to be the cause of your condition or contributes to it in some way. Usually we know this because it has been found in many others with the same condition. Finding a gene alteration allows other family members to be offered predictive testing. Predictive testing is offered to family members who are known to be at risk of inheriting a gene alteration that has been identified in the family but are currently well.

2. **No pathogenic gene alteration is identified.** This does not necessarily mean there is not an inherited genetic explanation for your condition but it may be that, within the confines of current technology, we have been unable to detect a gene alteration. Alternatively, there may be an alteration in a gene that we do not yet know about and therefore, cannot test for. Regardless of the results of any genetic testing we may still make screening recommendations for family members based on the family history to help protect their health.

3. **A gene alteration has been found but we are not sure if it is significant or not.** This is also sometimes called a variant of unknown significance (VUS) or an unclassified variant (UV). Finding this may mean we have to undertake more testing in the family or that we may need to look at the VUS again sometime in the future to see if any further information about it is available. This will be discussed with you in more detail should this be the case.

*****NB: *The finding of a pathogenic (disease-causing) gene alteration is based on current knowledge. Very occasionally, new information in the future may mean that our understanding of the significance of a specific gene alteration may change.******

It is very important to remember that the genes we test can also be associated with a whole range of other problems that can impact your health and may mean you need additional screening or other tests.

In general, your genetic counsellor or doctor may think it is helpful to tell you about anything that is found that is actionable. This means that there is known to be a risk to your health and your genetic counsellor or doctor can advise you about screening or treatment that could be helpful to prevent or treat the condition.

There is also a possibility that you could be found to have a gene alteration that does not affect your own health but may result in an increased risk of having an affected child. For example, some genetic conditions (called autosomal recessive conditions) arise when a child inherits a gene alteration from both parents and has no normal copy of that gene. Healthy carrier parents have one normal and one faulty copy of the gene and do not usually have any problems associated with the condition. A genetic test may indicate you are a healthy carrier of a condition, and if so you will be given information about what this means for your family.

How are gene alterations passed down (inherited) through families?

Gene alterations can be passed down by several different patterns of inheritance. The specific inheritance pattern helps us to inform the chance of other family members being found to have the same gene alteration and therefore their chance of developing a particular condition.

Your genetic counsellor or doctor will provide you with information and additional leaflets about the inheritance patterns relevant to the genes in the panel test that is being offered to you.

What are the issues to think about when deciding whether or not to go ahead with genetic testing?

A genetic test can establish whether you have an alteration in a gene which could affect your health. It can be difficult to make a decision about whether or not to have a genetic test. We all have gene alterations and many of these do not affect our health. It is still quite unusual for a person to know they have an alteration in a specific gene.

There are reasons for and against having a genetic test. Within one family relatives often have different views. You should try to make your own decision without feeling pressured from relatives or other influences. You will have plenty of opportunity to talk through the issues surrounding the test with the genetic counsellor or doctor. Some of the things people may consider include:

- **Do I need to tell people I am considering genetic testing?**

It is entirely up to you whether or not you choose to tell anyone you are going ahead with genetic testing. It is often useful to have someone to accompany you to your appointments so that you have another 'set of ears' to hear the information and discussions that you have had. They can also be useful as a support for any discussions away from the appointment and should be someone you trust.

People often choose this to be their partner, a close friend or another family member. However, if you choose to bring a family member it is important to remember the discussions you have in clinic are likely to have implications for them as well and they may not be prepared for this. Our experience, however, has demonstrated that families are often aware of the family history and may already be asking questions about why and so it may be that an opportunity to discuss this within the family could happen quite naturally anyway.

Other people would rather wait until there is something to know before discussing things with the wider family, whilst other people prefer to discuss things as the process goes along to help prepare the family for any news. There are no right or wrong answers and we are happy to discuss how to involve your family if you wish.

- **Do my family need to know about any results I receive from genetic testing?**

Genetic testing provides information for the individual but will also provide information for the rest of the family. If genetic testing identifies a gene alteration in you we would assume that you had inherited it from either your mother or father. Altered genes can often be passed down through families over generations without being noticed. Therefore, finding a gene alteration in you will have implications for other family members as well and so sharing genetic information in a family is really important. It can provide family members with a real opportunity to protect their health, for example, by enrolling in screening programmes or even surgical options.

Sometimes people may think if genetic testing does not show anything then there is nothing to tell anyone. However, knowing what is happening in the family can prevent work being repeated as sometimes lots of family members are asking the same questions. It is also very important to remember that, regardless of the results of any genetic testing, the family history itself may mean family members are at a higher risk of a condition anyway and opportunities to protect their health can be offered to them.

- **How can I share this information?**

On a practical level you will have this leaflet to share with them and we will also provide a letter after your clinic appointment detailing any other issues discussed.

If a gene alteration is found we will provide you with a 'Dear Family Member Letter' detailing that a gene alteration has been identified in the family, that they are at risk and how to access testing. We will also guide you as to whom the letter should be passed on to.

On an emotional level telling family members may be more difficult. You may be worried about upsetting them or have trouble deciding when the right time is. There really is no right or wrong answer to this but it is really useful to think about this before you get your test results and we are more than happy to discuss this with you further.

- **Should I tell my children?**

As parents, we want to protect our children from things that we believe can harm them and sometimes this means that we try and 'hide' things we think may be difficult for them to cope with. However, we tend to underestimate what children have already picked up on and they are often aware of something going on anyway. They may have noticed letters from the hospital or overheard conversations, they may also pick up cues from adults that they should not ask any questions.

Children in this situation may imagine something really awful is going on, often much worse than the reality, and may even believe it is something bad they have done. Children value being included and are helped by adults who are honest and direct with communication. It is not always easy but children often cope a lot better than we give them credit for. Our experience has also shown us that the parents of adult children often do the same.

We are happy to talk to you about sharing information with your children during your appointment.

- **Who else should I tell?**

That is entirely up to you. There is generally no obligation to tell your employer but it might be useful if you anticipate you may need time off work to have screening.

Having friends to discuss this with is helpful for some people but it is important to be aware that people may have differences of opinion that could be in conflict with any decisions you have made. However, for the majority of people, having discussions with other people is helpful and supportive.

- **What happens if I choose to go ahead and have a test?**

After you have discussed what genetic testing could mean for you, you may decide to go ahead with testing. We will ask you to provide your consent and we will arrange for you to have a blood sample taken.

The laboratory team will then extract the DNA from your blood sample. They will search through the DNA of the specific set of genes on the panel to see if the code in any of these genes differs from that of a normal gene. Often, genes are large and can take a long time to be looked through. The time that we would expect results to be ready differs between panel tests and your genetic counsellor or doctor will advise you on this.

You can discuss with your genetic counsellor or doctor how you wish to receive your results. Some people want their results by letter or over the telephone with the opportunity of a follow-up appointment to discuss any findings whereas others prefer to come into clinic to have the opportunity to discuss the implications of any findings and next steps. This is entirely up to you and will be discussed during your appointment.

IF, FOR SOME REASON, YOU HAVE NOT RECIEVED YOUR RESULTS WITHIN THE EXPECTED TIMEFRAME GIVEN TO YOU PLEASE CALL THE LIVERPOOL CENTRE FOR GENOMIC MEDICINE ON 0151 802 5008. Please remember to have your G number and W number handy for this call so we can quickly and correctly identify you. These numbers can be found on any letter sent from the Genetics Department.

- **What happens if I choose not to go ahead with having a test?**

We will not be able to offer predictive testing to your relatives but we may be able to make screening recommendations for your relatives based on the family history.

Attending your appointment with Genomic Medicine does not oblige you to go ahead with testing and, if you do go ahead and change your mind about receiving your results, you can do so until you are ready.

Insurance and Genetics

For some types of insurance it is necessary to provide medical information, including genetic information, to the insurers in order for them to set up your policy and work out your premiums. The types of policy that require a medical history or genetic test are likely to be, life cover, critical illness insurance and income protection insurance.

We would suggest that if yourself or family members are considering taking out new insurance policies in the future that consideration be given to the possible affect genetic test results could have on the ability to gain insurance or the premiums charged. Genetic Test results do not affect insurance policies already in place.

The Association of British Insurers (ABI) has a Code of Practice 'The Concordat and Moratorium on Genetic and Insurance'.

- *Insurance companies cannot ask for the **Predictive Genetic Test** results of individuals or family members* (unless for Huntington Disease over £500,000). *A Predictive Genetic Test is where an individual has a family member with a genetic condition, but who personally has no symptoms, signs or abnormal medical tests consistent with the condition at time of testing.*
- *If a family member has been diagnosed with a genetic condition based on a **Diagnostic Genetic Test** then you or family members will need to mention this when asked to provide your family's medical history. In many cases Diagnostic Genetic Testing is used to confirm a diagnosis when a particular condition is suspected because of symptoms, signs or abnormal non-genetic tests including unusual findings on a routine blood test or other test.*

Sources of Further Information Include

The Association of British Insurers Genetics Frequently Asked Questions https://www.abi.org.uk/products-and-issues/topics-and-issues/genetics/genetics-faqs/

Genetic Alliance UK (Charity) Genetics & Insurance
http://www.geneticalliance.org.uk/information/living-with-a-genetic-condition/insurance-and-genetic-conditions/

We hope you find this leaflet useful and please do not hesitate to discuss any of the issues identified in this leaflet with the genetics practitioner that is looking after you.

Useful websites

Genetic Alliance UK
www.geneticalliance.org.uk

All images in this leaflet were provided by **NHS National Genetics and Genomics Education Centre**

This leaflet can be made available in difference formats on request. If you would like to make any suggestions or comments about the content of this leaflet, then please contact the Patient Experience Team on 0151 702 4353 or by email at pals@lwh.nhs.uk

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