

A new pathway for cancer gene testing successfully completes pilot

Information Pack

Key points

- The Royal Marsden NHS Foundation Trust has completed a 6 month pilot of a new 'oncogenetic' gene testing pathway which is much faster and less costly than the previous pathway.
- The oncogenetic pathway brings gene testing directly to the patient through their existing oncology appointments. Previously, patients could only have a gene test via referral to genetics departments.
- Over 100 cancer patients have had *BRCA1* and *BRCA2* gene testing through the new pathway. The response from patients and the cancer and genetic clinicians has been overwhelmingly positive.
- The gene testing is being performed in the new TGL clinical laboratory which has state-of-the-art gene sequencing equipment which can do many more tests, much faster and at much lower cost than traditional testing methods.
- In 2013, NICE recommended people with >10% chance of having a mutation in either the *BRCA1* or *BRCA2* gene should be offered testing. This includes >10,000 cancer patients per year.
- The limited capacity and high costs of traditional gene testing pathways limits the *BRCA1* and *BRCA2* testing doctors are currently able to provide. The oncogenetic pathway could be used to deliver the NICE recommendations cost-effectively.
- The new laboratory test and clinical testing pathway is now ready for roll-out to other hospitals.

Speakers:

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A Case Study: How patients can benefit from the 'oncogenetic' gene testing pathway

Patient C was diagnosed with breast cancer in 1999 at the age of 36. Following consultation with her doctors she decided to undergo a bilateral mastectomy and treatment with chemotherapy.

14 years later, Patient C was diagnosed with ovarian cancer and was treated with surgery and chemotherapy. Patient C was also offered gene testing by her oncologist through the 'oncogenetic' pathway pilot.

Patient C's gene test identified a mutation in the *BRCA1* gene. The identification of this mutation, at this stage of her treatment, meant Patient C was eligible for treatment as part of a PARP inhibitor maintenance study.

Patient C is now undergoing treatment with a PARP inhibitor directly as a result of her gene testing through the 'oncogenetic' gene testing pilot.

Patient C has also had an appointment with the Genetics team. Finding out that her cancers were due to a *BRCA1* mutation now provides other members of the family with an opportunity to have a test to see if they also carry the mutation, should they wish to. For some this will show they have not inherited the mutation and are not at increased risk of cancer. For others it will show they have inherited the mutation. They will be at increased risk of cancer and can discuss and access surveillance and cancer risk-reducing interventions.

Patient survey of the 'oncogenetic' gene testing pathway: results to date

A survey of patients who have undergone gene testing via the 'oncogenetic' gene testing pathway is being carried out by The Royal Marsden. The evaluation is still ongoing, but the responses have been very positive. In particular, amongst the 30 patients that have thus far responded to the survey:

- 100% of patients agreed or strongly agreed with the statement: 'I am pleased I had the genetic test.'
- 100% of patients agreed or strongly agreed with the statement: 'I was happy to have the genetic test at one of my existing Oncology appointments rather than in a separate appointment with the Genetics team.'

Cancer Genetics – some basic facts

What is the genome?

The term 'genome' is used to describe our entire genetic information present in each of our cells. The genome is made of DNA which is itself made of 4 building blocks denoted by the letters A, C, G, T. The order and position of the letters determines the function of that part of the genome. The human genome contains over 3 billion letters.

What is a gene?

Genes are the parts of the genome that code for proteins, which in turn provide the instructions that make our bodies work. There are about 20,000 genes in the genome. The genes only take up 1% of the genome.

What does sequencing mean?

The order of letters in the DNA code is the 'sequence'. The term sequencing has come to mean the reading of the DNA code, either of selected parts or the whole genome. There has been a major advance in sequencing over the last five years. Previously the code had to be read one letter at a time. The newer methods, which are sometimes called next-generation sequencing or NGS, can read millions of sections of the genome simultaneously. This has made the process of sequencing much, much faster and cheaper.

What is a mutation?

A mutation is a change in the DNA code. There are many different types of mutation. For example single letter changes, removal or insertion of letters or rearrangement of letters. We all have many thousands of mutations but they are almost all innocuous.

How are gene mutations involved in cancer?

There are two ways in which gene mutations can be important in cancer.

- 1) Mutations in the DNA of the cancer cells can help cancers to grow and spread. These mutations are not present in normal cells; they are restricted to the cancer. They are sometimes called 'somatic' mutations.
- 2) Mutations that are present in every cell in the body and make it more likely that a normal cell will turn into a cancer cell. Such mutations are either inherited or can start for the first time at conception. Sometimes they can be passed on to offspring. Such mutations are called 'germline' or 'constitutional' mutations.

What is a cancer predisposition gene?

Genes in which germline mutations can increase the risk of cancer are called 'cancer predisposition genes'. These mutations do not cause cancer (otherwise every cell in the body would be a cancer), but they do predispose to cancer as they make it much more likely that at least one of the cells in the body will turn into a cancer cell. There are currently over 100 known cancer predisposition genes, together predisposing to about 35 different cancers. These mutations are important cause of certain cancers. For example about 1 in 7 women with ovarian cancer have a cancer predisposition gene mutation and about 1 in 4 people with certain endocrine cancers.

How many cancers are genetic?

It depends what one means by 'genetic'. Somatic mutations are a hallmark of cancer. The great majority of cancers will have some mutations in the cancer cells, and therefore could be considered 'genetic'. However, most people use 'genetic' to mean 'hereditary'. Somatic mutations are not hereditary. Germline mutations in cancer predisposition genes are often hereditary. Overall about 2% of cancers (~7000 people each year) develop because of a cancer predisposition gene mutation. This is not evenly distributed between cancers. For example ~40% of some childhood cancers, ~15% of ovarian cancers but only a very small number of lung cancers are due to currently known cancer predisposition gene mutations.

How can gene testing benefit people with cancer?

Knowing if a person's cancer is due to a mutation in their genetic blueprint is very important. For example it can impact on which treatments may be more, or less, successful. It also gives information about future risks of cancer. People with cancer predisposition gene mutations are often at risk of getting another cancer and may choose to have more comprehensive surgery, or may need extra monitoring.

How is cancer gene testing currently undertaken in NHS?

Currently, all cancer gene testing is undertaken by geneticists, doctors who are specialised in diagnosing genetic conditions. If a patient with cancer meets certain eligibility criteria, they can be referred to genetics departments by their cancer team for cancer gene testing.

However, the eligibility criteria are complex and the information required to decide if someone is eligible is not always available, meaning that not everyone who should benefit from a gene test is able to have one. There can also be delays for appointments in genetics departments all of which can impede provision of the best clinical management for the patient.

How is the oncogenetic pathway different?

The 'oncogenetic' pathway allows cancer gene testing to be undertaken by the cancer team. If the cancer team member has completed the online training they can take a sample for gene testing, rather than referring the patient to genetics to have the test. The test result is still reviewed and interpreted by the genetics team who inform the cancer team of the result so it can be used to aid management of the patient's cancer. If a gene mutation is found the patient is automatically sent a genetics appointment to discuss any additional implications for themselves and how the information may be helpful for their families.

Any patient that requires more detailed discussions, at any stage, either before or after the test, can be referred for a genetics appointment.

This pathway provides a more flexible, patient-centred gene testing service that is also considerably faster and more cost-effective than the current pathway.