

Consent for Next Generation Sequencing (NGS)

What is next-generation sequencing?

'DNA' is a genetic molecule that provides instructions for cells to function correctly. 'Genes' are pieces of DNA that provide instructions for building the proteins that allow our bodies to function.

Sometimes spelling mistakes can occur in these DNA instructions. These mistakes are called 'mutations'. When mutations keep occurring they can sometimes lead to cancer.

At present laboratories routinely test cancer samples for mutations that are important for that particular type of cancer. Usually only a small number of genes are tested.

Next-generation sequencing (NGS) is method of genetic testing where a large number of genes, sometimes hundreds, are 'sequenced' (looked for and tested) at the same time.

Why is my doctor recommending this test?

In certain situations we may recommend sending a sample of your cancer, or your child's cancer, for NGS.

Testing a larger number of genes in a cancer sample is sometimes helpful. Finding or excluding certain mutations may be useful to confirm a diagnosis, help us understand the possible course of a cancer, and guide treatment decisions. For instance NGS may identify a cancer mutation that we can 'target', or treat with a medicine.

The benefits and risks of NGS in paediatric cancer are constantly evolving, and may vary for different cancers and situations. Your consultant will explain the goals of NGS in your situation.

Will this test improve treatment?

There are situations where NGS has identified a cancer mutation that can be targeted with a particular medicine, and that medicine leads to meaningful clinical improvement.

However, at the present time, cancer NGS does not change treatment, or the ultimate outcome of the disease, in the majority of paediatric cancers. For instance, NGS may not find any relevant mutations, or it may discover Variations of Unknown Significance (VUS) - genetic changes that are not fully understood, nor linked to a specific medicine.

Sometimes a cancer mutation is discovered but there may be a reason that a patient does not receive the associated medicine. For instance the medicine may not be available, there may be no safe paediatric dose, the clinical situation may have changed, or there may be a better treatment option. Like all tests, cancer NGS results also have the potential to be incorrect.

This means that if even if a cancer causing mutation is present, and this mutation is associated with response to an anti-cancer medicine, we cannot guarantee you or your child will receive the medicine.

How is the testing done?

The hospital will send the cancer sample to a laboratory overseas where the testing is done. Different cancer NGS tests have different strengths and weaknesses, and NGS tests are rapidly developing. If you wish, your haematologist-oncologist can explain why a particular NGS test was selected.

Sometimes we will also send a sample of your blood, or your child's blood, at the same time. The blood sample is used to provide DNA from healthy cells. By comparing DNA from healthy blood cells to the cancer sample, we can often distinguish whether the patient was born with a genetic mutation and confirm whether the mutation is related to the cancer.

The samples may be sent to a laboratory overseas. Some laboratories store unused genetic material for a period of time but they cannot use this for research, and patient confidentiality is protected by strict laws.

How is the test interpreted?

The DNA in the cancer is compared to a 'reference' or 'normal' DNA sequencing result to identify genes with mutations that are important in cancer diagnosis and/or treatment.

Your haematologist or oncologist is best placed to discuss the significance of test results in your particular situation.

What is a cancer predisposition?

NGS can sometimes detect genetic 'risk factors' that may indicate why you or your child developed cancer. This is known as a 'germline cancer predisposition', which can be inherited. Individuals who have the mutation are at a greater risk of developing cancers compared to individuals without the mutation.

NGS may discover a genetic result that does not explain why you or your child developed their particular type of cancer. NGS may also discover a genetic risk factor that increases the chances of developing another type of cancer, or a disease other than cancer.

If cancer sample NGS shows a genetic mutation that is associated with a predisposition to cancer, then further testing may be required to determine if you or your child were born with the mutation. If the mutation is not present in healthy cells then there is no cancer predisposition in you or your child. However, if the mutation is present in healthy cells and cancer cells then a predisposition to cancer is present.

In these situations we will offer to refer you to the Genetic Services for a more in-depth discussion and to determine if further testing is required.

If a predisposition to cancer or other disease is detected your relatives might want to know so that they can decide whether to get tested or followed up in other ways. It is also possible that they might not want to know. You may wish to discuss this with them beforehand, but your genetic health information is confidential and you cannot be forced to share the information. The presence of a cancer predisposition may be very distressing for some families, but may also potentially help some families to stay healthy.

Do you always know what the results mean?

No. The DNA of every person is unique and these differences usually do not cause medical problems. However, the complete human 'genome' of DNA (all human genes) is extremely large and complex. Very frequently testing will find DNA variations of uncertain significance (VUS) meaning that doctors do not know what the variations mean. VUS can occur both in the cancer sample, and in the genes that are inherited from parents. Your haematologist-oncologist may need to discuss the results of VUS with other specialists and scientists.

Medical knowledge is constantly advancing and so the meaning of DNA mutations and DNA variations may change over time in ways that are medically important. At this time we do not have a mechanism to update you if and when new information arises. If you want your genetic tests results re-interpreted in the future it is up to you to request a copy of your cancer NGS report. If the Starship Blood and Cancer Centre sent your cancer sample for testing then results of testing will be stored at Auckland DHB. If Christchurch Haematology Oncology Centre sent your sample for testing the results will be stored at Canterbury DHB. To request a copy of the test you can ask your haematologist-oncologist, or request a copy of your medical record from DHB.

Does the test always work?

No. Sometimes we cannot obtain high quality samples and testing fails. Other times the sample is high quality but something goes wrong with testing. We select laboratories where the risk of technical failure is very low, but it is never zero.

Who can I ask for more information?

Your haematologist-oncologist is best placed to give you advice on additional sources of information that relate to your particular situation. You can also ask your doctor for additional information, or to explain things again in the future.

If you require Māori cultural support talk to your whānau in the first instance. Alternatively you may contact the administrator for He Kamaka Waiora (Māori Health Team) by telephoning (09) 486 8324 ext 2324.

Place patient sticker here

Consent form

- I consent to my cancer tissue, or my child's cancer tissue being sent for next-generation sequencing (NGS).
- I understand that my blood, or my child's blood, may also be sent for testing.
- I have read and understood the attached information, and I have had the opportunity to ask questions.
- I understand that I can ask further questions in the future, and request a copy of my results.
- I understand that NGS may detect findings of uncertain significance.

Please circle: Y / N _____(initial)_____(date)

- I understand that these results do not guarantee access to any medicines, and may not result in treatment, cure, or prognostic information.

Please circle: Y / N _____(initial)_____(date)

- I would like to learn of genetic findings that indicate a predisposition to cancer.

Please circle: Y / N _____(initial)_____(date)

- If I do not wish to know about a cancer predisposition, I acknowledge that the treating team may be obliged to disclose the results regardless, if the results significantly alter treatment recommendations.

_____(initial)_____(date)

- I would like to learn of findings that predispose me, or my child, to conditions other than cancer.

Please circle: Y / N _____(initial)_____(date)

- I understand that results may impact the health of other family members.

Please circle: Y / N _____(initial)_____(date)

PATIENT'S NAME _____

SIGNATURE OF PATIENT/ PARENT OR GUARDIAN

DATE

SIGNATURE OF SENIOR MEDICAL OFFICER OBTAINING CONSENT

DATE