

## **Patient information about exome sequencing**

Exome sequencing is a new form of genetic testing. This information sheet tackles the following points regarding this new genetic testing approach.

- What are chromosomes and genes?
- Why sequencing the exome?
- Which genes will be tested?
- What are the possible outcomes of testing by exome sequencing?
- The impact of increasing genetic information on exome sequencing.
- What is required for exome sequencing?
- The use of exome sequencing results for research
- Contact details for further questions

### **What are chromosomes and genes?**

Each body cell contains chromosomes in which genetic information is stored. This genetic instructions determine our appearance and control the development of all organs, such as the brain, heart or kidneys. Most of our body cells contain 46 chromosomes, arranged in 23 pairs. One of each of these pairs is inherited from our father and the other from our mother. 22 of the chromosome pairs are similar in men and women, while the 23rd pair is called the sex chromosomes. These are called XX in women and XY in men.

Chromosomes contain genetic instructions that are packed in the form of **genes**. There are about 20,000 genes in each cells. All genes have specific functions, although at present some genes have an unknown function. We have two copies of each gene, one from each parent. A genetic condition may occur if one or more genes do not function properly. This may be due to missing parts of the gene or to an alteration of the information within the gene. It can be important to

identify the DNA alteration responsible for the disease both for diagnosis in you and in other family members. A non-functioning gene may occur either for the first time in a person or be inherited from one or both parents. Such gene alterations are commonly known as gene mutations. Such mutations are present in all people and sometimes are associated with disease.

**Why sequencing the exome?**

Previously, only one gene at a time could be tested, thus it could take years to identify the cause of a disease caused by one of many genes. It is now possible to test all 20,000 genes at a time by exome sequencing. This means that the genetic cause of a disease maybe detected within a shorter period of time.

**Which genes will be tested?**

For most conditions, only the genes known to cause a disorder, rather than all 20,000 genes, will be tested in first instance. If no gene alteration is identified, the remaining genes will then be tested. In this situation we cannot predict whether (or when) a cause will be identified, as the specific gene causing the condition will not be known. All genes will be tested initially for some specific conditions. Should this apply to the condition being investigated in your family, this will be discussed with you appropriately.

**What are the possible outcomes of testing by exome sequencing?**

There are four possible outcomes after exome sequencing:

1. One or more gene alterations are identified that are assessed as explaining the condition in you. In this situation, our trained personnel will be available to discuss there results with you.
2. One or more gene alterations are identified where the significance

is not immediately clear. In this case, additional testing in other family members may be required to determine if the result is relevant to the condition. It is your choice whether you will inform your family and/or request that other family members participate in the genetic study. Your family will not be approached by your healthcare providers.

3. No gene alterations are identified that could explain the condition. In this situation, testing would continue for possible causes of the condition under inspection as more information regarding associated genes is identified. Additional results would be discussed with you should they be identified.
4. When all genes are tested, there is a small chance that alterations could be identified by chance in genes not directly related to the disorder being investigated. These are called incidental findings. An example of this could be a gene alteration associated with an increased risk of cancer or a neurological disease in you or your child. This could have important consequences for you and/or other family members.

Any incidental finding will be assessed by an independent committee of experts to determine if they are to be reported. You will have to decide whether you want to be informed of such findings. In exceptional cases, the committee may, in consultation with your doctor, decide that it is in your best interest to inform you about incidental findings. In all situations, you will be informed of the results of the exome sequencing by your genetic counselor / physician.

**The impact of increasing genetic information on exome sequencing.**

Knowledge of the function of genes and diseases is increasing rapidly. Should the cause of the condition tested not be identified now, it could still be identified

in the future as knowledge increases. A gene alteration identified today by exome sequencing could be assessed as having an unknown effect but this interpretation could be revised as knowledge increases in the future. Your doctor will contact you if such new information becomes available. It is recommended that you contact your doctor two years after the discussion of results if the exome sequencing result is unclear, in case any new information becomes available.

**What is required for exome sequencing?**

A blood sample will be required from you (5-20mL, 1-2 tubes) from which DNA will be extracted. In some cases it may also be necessary to draw blood samples from your parents. The remaining DNA will be stored de-identified at qGenomics for quality checking and validation purposes. Your written consent will be needed prior to any testing being done. You have the right at any time to withdraw your consent, without affecting the quality of your treatment.

**The use of exome sequencing results for research**

The information obtained from exome sequencing is also important to assist in the understanding of the causes of the hereditary conditions. Your test results will be stored at qGenomics. This information will be de-identified and only your doctor will have access to a reidentification code. Your results may therefore be shared anonymously with other research groups. Should there be anything of potential importance to you identified through this research, it will be reported to your doctor. He/she will then discuss with you.

**Contact details for further questions**

If you have any questions or wish to alter details of your consent, please contact your doctor or contact us.





INFORMED CONSENT FORM FOR EXOME SEQUENCING

**PATIENT**

NAME	
SURNAME	
ADDRESS	
	ZIP
BIRTH DATE	PHONE

**PARENT OR GUARDIAN**

NAME	
SURNAME	
ADDRESS	
	ZIP
BIRTH DATE	PHONE

TO BE COMPLETED BY THE HEALTH PROFESSIONAL
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I, \_\_\_\_\_, have informed this patient/parent/guardian regarding results and limitations of exome sequencing. We have discussed the consequences and procedures involved in testing and the storage of patient data.

TO BE COMPLETED BY THE PATIENT / LEGAL GUARDIAN
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1. I wish that DNA from **me/ my child / person under my legal guardianship** will be stored and tested by exome sequencing for the following condition:

\_\_\_\_\_

YES

NO

2. I understand that only genes known to cause the condition in question will be analyzed initially (or all genes will be analyzed initially for some specific conditions). The test results will be discussed with me on completion of the analysis. If this initial testing does not identify a cause, all genes will then be analyzed (exome sequencing). I will also be informed if findings relevant to the condition in question are identified by exome sequencing.

YES

NO

3. I understand that there is a small chance that incidental findings not related to the specific condition in question may be identified. I understand that any incidental findings will be assessed by an independent expert committee. Such incidental findings may be of medical importance. If so, the committee in consultation with my doctor, may inform me of these incidental findings. This will occur only if the incidental findings could have a significant impact on my health / the health of my child.

I want to be informed /  I do NOT want to be informed

4. I understand that the knowledge of genetic conditions is likely to improve in the future. I would like to be contacted if further information becomes available about the exome sequencing results relating to the genetic condition in my family.

YES

NO

5. I understand that the information from the exome sequencing will be stored at qGenomics and that it may be shared with researchers in other research institutes after it is de-identified.

YES

NO

6. I understand that I have the ability to withdraw my consent at any time without influencing **my management /the management of my child/my ward.**

YES

NO

7. I have had the opportunity to ask additional questions I and am satisfied with the explanations.

YES

NO

Signature of patient / guardian	Signature of Health Professional
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In \_\_\_\_\_, on \_\_\_\_\_, 20\_\_