

# qCarrier Test

## INFORMATION DOCUMENT

The qCarrier Test is a laboratory test developed by qGenomics, aimed at studying your genetic material. It is based on a targeted analysis of human genome fragments, to detect mutations that may be responsible for recessive genetic diseases, with different impact on the quality of life of patients. This analysis is performed by a specific study (capture and direct sequencing) of genes of interest using massively parallel sequencing techniques (next generation sequencing - NGS).

This document explains various basic aspects of genetics, and provides insights into the characteristics and scope of the test and the experimental approach behind it.

The test you are going to have is a study of your genetic material (DNA). As with any other medical procedure, you must receive appropriate counseling before and after the test, preferentially a professional with experience in human genetics (geneticist or genetic counselor), which should explain what the test is, its advantages, limitations and answer any questions that may arise in this regard; after that, you must provide written consent to have the test.

### WHAT ARE THE CHROMOSOMES AND GENES?

Every cell in our body contains structures called chromosomes where genetic information is stored. This information determines our appearance and controls the development of all organs in our body such as the brain, heart or kidneys. Most of our body cells contain 46 chromosomes arranged in 23 pairs, each consisting of a chromosome inherited from the father and one from the mother. The first 22 pairs are equal in males and females and are called **autosomes**, and the pair 23 is formed by the **sex chromosomes**, called XX in females and XY in males.

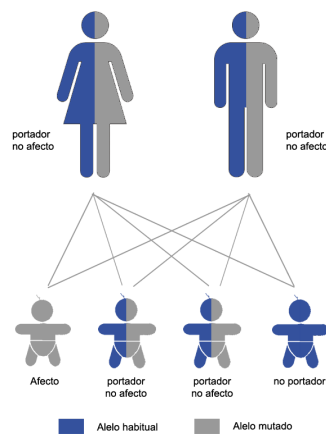
Chromosomes contain the genetic information packaged in the form of genes. There are over 20,000 genes in the nucleus of every cell of our body. Each gene plays one or more specific functions, but the function of many genes is still unknown. Each gene has two copies (alleles), one in each chromosome inherited from our parents, except for the genes on sex chromosomes X and Y, with a single copy in males. Genetic diseases occur when one or more genes exhibit some alteration (mutation). This dysfunction may originate in a missing piece of gene or because the information is altered. Identifying the alteration that causes the disease may be important to provide a correct diagnosis to the patient and relatives. The disruption of a gene can occur spontaneously (*de novo*) in an individual, or may be inherited from one or both parents. It is important to know that we all have a number of those alterations in our genes, that usually go unnoticed and only in certain circumstances can cause disease.

### WHAT ARE GENETIC RECESSIVE DISEASES?

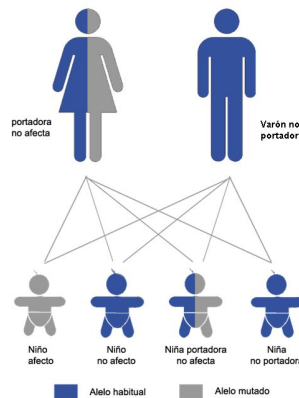
Autosomal recessive diseases occur when two mutated copies (or alleles) of the same gene are inherited. This requires that both the father and the mother are **carriers** of the disease, i.e. they both have an altered copy of the gene and, by chance, the two pass their mutated

copy to the offspring. A carrier of a genetic recessive mutation shows no symptoms of the disease and, indeed, we are all carriers of different mutations in recessive genes, without incurring in any clinical manifestation.

When both partners are carriers of recessive mutations in the same gene there is a 25% of conceiving and affected children, 50% of conceiving unaffected carriers, and 25% of mutation free (non-carriers) children.



In X-linked recessive diseases, the causative gene is located on the X chromosome. 50% of the offspring of a carrier mother will receive the mutated copy of the gene. The effects of this mutated copy will be very different if a boy or a girl is conceived. While male descendants receiving a mutated copy of the gene will be affected and manifest the disease, girls with one mutated copy will not usually present any clinical manifestation (although due to the phenomenon called X chromosome inactivation, it can not be totally ruled out the presence of symptoms).



For couples in which a risk of transmission is determined, the information can be used for family planning, as there are various reproductive options to minimize risks and conceive a

disease-free offspring. Genetic counseling provided by a professional in genetic medicine or human reproduction is necessary for correct interpretation of the test and planning future options.

### **WHAT IS THE qCARRIER TEST FOR?**

The qCarrier Test is able to analyze more than 4,000 mutations causing more than 200 recessive genetic diseases, classified into four groups:

- serious illness with serious implications for health, that usually have a negative impact on life expectancy and quality of life of patients.
- diseases of varying severity, with a variable range from mild to subclinical conditions that can affect overall quality of life, but not decisively affect the life expectancy.
- very rare diseases, with serious implications for health that are present with high incidence in certain populations of the world, especially in populations of Jewish origin, Nordic and areas surrounding the Mediterranean sea.
- X-linked, diseases include diseases that, by their nature could be included in any of the three above groups, but having this particular pattern of inheritance.

### **HOW DOES THE qCARRIER TEST WORKS?**

Parental DNA is obtained from a biological sample, typically blood vein or saliva. The risks of complications in obtaining these samples are low, and mainly inherent to the blood sample drawing, which are very rare and mild (hematomas, phlebitis, dizziness, vagal syncope ...), unless you are affected by a blood disorder.

Blood or saliva is the processed in our laboratory to obtain the DNA of cells. The qCarrier Test uses massively parallel sequencing technologies to identify specific mutations in certain genes, as well as most prevalent types of mutations in coding regions of genes causing recessive diseases prevalent in our geographic area.

Unlike conventional methods, massively parallel sequencing allows us to analyze millions of different DNA fragments at a time, allowing the study of such a large number of genes and mutations in a single experiment.

Although the number of potentially detectable mutations is very large, the qCarrier Test can not detect ALL disease-causing mutations, either due to technical limitations or to biological phenomena. Thus, a normal result of this test for the causative gene of a particular disease, does not guarantee hundred percent a disease-free offspring.

### **WHAT RESULTS SHOULD I EXPECT FROM THE qCARRIER TEST?**

The test is able to identify disease-causing genetic variants in any of the genes analyzed, determining your carrier status, and thus the likelihood of transmitting this variant to your offspring.

Although among the regions analyzed there are thousands of known benign genetic variants (called polymorphisms) and more than 4,000 known mutations, it can not be ruled out the possibility that other variants for which no population information is available and, therefore, is not possible to know if they are or not related to disease (variants of uncertain significance or VUS). There is also the possibility of finding genetic variants of uncertain significance despite having been reported in the literature, because of incomplete or contradictory evidences about their pathogenicity. In these cases, it will only be possible to discuss the evidences with you, but it does not exist the possibility to make medical decisions based on this information. Thus, you must decide whether you want to be informed in case of detecting genetic variants of uncertain significance, knowing that as of today this information will not be able to change clinical practice guidelines.

There is also the possibility to identify mutations that reveal the existence of a not yet evident genetic disease. An example of this might be the identification of mutations in a gene that causes a disease with variable expressivity or late onset, and so far undiagnosed because no specific symptoms have yet appeared. The identification of a recessive genetic disease, so far undiagnosed, may have important implications both for you and your family.

You must decide whether you want to be informed in case of serendipitous findings that have a proven clinical impact.

In any case, clinical data from the test, the geneticist be provided in order to continue its assistance. This will be done respecting patient confidentiality and following the guidelines of the Organic Spanish Law on Data Protection and the Spanish Law of Biomedical Research.

### **IMPACT OF KNOWLEDGE ADVANCES ON THE RESULTS OBTAINED WITH THE qCARRIER TEST**

The knowledge of gene function and its relationship with diseases has increased precipitously in recent years, but we are still far from a complete understanding of the meaning of the sequence of the genetic material and its variations. Thus, it is possible that the qCarrier Test might detect a previously unknown genetic variant, not present in other individuals, and that should be considered of **unknown or uncertain significance**. On the other hand, even if today it might not be possible to determine the genetic cause of a certain disease, it is hoped that it will be possible as knowledge advances, which nowadays takes place very quickly. This means that a genetic alteration that is identified and today is classified as of unknown significance, may be reclassified in the future, when knowledge advances, as pathogenic. Shall this happen, you will be recontacted by your physician.

### **WHAT IS NEEDED TO PERFORM THE qCARRIER TEST?**

We will need to obtain a blood sample (1 tube with 5-8mL) from which to extract DNA to perform the test. It is also possible to perform the test from saliva samples, at an extra cost.

The remaining DNA will be preserved for future validation studies. Although we will preserve it for security reasons, you will always be asked to provide a written consent to perform any other type of analysis with your sample. You have the right to decline this consent at any time, without giving any explanation and without having any impact in the quality of the treatment you might need.

### **USE OF SEQUENCING RESULTS FOR RESEARCH**

qGenomics is a company committed to the progress of knowledge and collaborates with researchers of national and international reputation in the finding of genetic basis of Rare Diseases. The information obtained from this DNA analysis is very important for the global advance of knowledge of genetic diseases and may help many other people. If not stated otherwise, the results of your analysis will be kept completely anonymous and only your doctor will have the key to undo anonymity. Thus, the data may be shared only in aggregate and anonymous way with accredited researchers. If as a result of these investigations an important discovery for a genetic condition that may affect you occurs, your doctor will be informed and he shall contact you to convey such information.

### **CONTACT FOR MORE INFORMATION**

If you have any questions or want to change your details, contact your doctor or genetic counselor:

Name & surnames:

Street Address:

Contact Phone:

e-mail:

## INFORMED CONSENT FOR qCARRIER TEST

Medical record # .....

Mr./Ms. ....  
(NAME AND SURNAME)

Residing in ....., and with ID/Passport  
number .....

### I DECLARE

That Dr. ....  
(NAME AND SURNAME OF MEDICAL GENETICIST OR GENETIC COUNSELOR)

Has informed me about the risks, limitations and expected results of qCarrier Test. We have discussed procedures and consequences of the analysis, as well as regarding the storing of the results and use thereof.

I received the above information and have read and understood the attached briefing in this informed consent form, and therefore:

1. I consent my DNA to be tested using the qCarrier Test for the presence of recessive mutations known to cause genetic diseases.  

YES       NO
2. I consent that the remaining DNA is stored for future genetic studies, for which I will be previously asked to provide a specific consent.  

YES       NO
3. I understand that a normal result for this test does not guarantee a genetic disease-free offspring.  

YES       NO
4. I understand that there is a certain probability that incidental findings might occur and that they can have a significant impact on my health and/or on that of my family  

I decide TO BE INFORMED / NOT TO BE INFORMED about such findings.

Even if I decide not to be informed, I understand that if this information is necessary to prevent serious harm to the health of my biological family, at the discretion of the attending physician, it will be possible to inform the at risk individuals or their legally authorized representatives. In any case, communication will be strictly restricted to the information and data needed for these purposes. (Art. 49.2 Biomedical Research Act)

5. I understand that it is possible to identify genetic variants of uncertain significance (VUS), for which there is no population information or for which there are incomplete or contradictory evidences about their pathogenicity in the scientific literatura, and that to date these findings will not be considered to modify clinical practice guidelines.

I decide TO BE INFORMED about such findings.

YES  NO

6. I understand that it is very likely that current knowledge on analytical methods and genetic diseases will improve in the future. I want to be recontacted if new data can be generated or can be reinterpreted in relation to diseases under study using the qCarrier Test.

YES  NO

7. I understand that the information generated in the study by qCarrier Test will be preserved and could be shared, in a completely anonymized way, with other accredited researchers for research purposes, only after I provide specific consent to do so.

YES  NO

8. I understand that I have the right to decline this consent that I grant now at any time, without influencing at all in the medical care I receive.

YES  NO

9. I have had the opportunity to ask all the questions I felt like, and I am satisfied with the explanations I received.

YES  NO

In view of the above, I freely give my consent to submit my DNA for testing using qCarrier Test.

In .....  
(PLACE AND DATE)

Signed by PHYSICIAN or  
GENETIC COUNSELOR  
Certified number:  
Name & Surname:

Signed by: PATIENT  
  
Name & Surname:

In accordance with the provisions in force regarding the protection of personal data, and in particular by Organic Law 15/1999 on Personal Data Protection (LOPD), QUANTITATIVE GENOMIC MEDICINE LABORATORIES, S.L. is obliged, in relation to the personal data to which might have access to for the provision of contracted services, to: i) Treat the data only according to the instructions of the client; (ii) not apply or use data for purposes other than those contained in this undertaking; (iii) not to communicate the data to third parties, even for its preservation; iv) implement the security measures that are applicable, in order to preserve the integrity, confidentiality and availability of data; and v) destroying or returning the data to the client, as well as any support or document in which any data that has been subject to the treatment can be recorded once the service is finished.

We also inform you that the data you provide during the provision of contracted services will be stored in files under responsibility of Quantitative Genomic Medicine Laboratories, SL, in order to maintain, renew, extend or modify, where appropriate, the business relationship that mediates between the parties or the part that you represent, which expressly includes the commercial promotion of our products and services. You may exercise your rights of access, cancellation, rectification or opposition by contacting Quantitative Genomic Medicine Laboratories, S.L., C / Joan XXIII, 10, Esplugues del Llobregat, or by e-mail to [info@qgenomics.com](mailto:info@qgenomics.com).