CGT

Carrier Genetic Test

by Igenomix®

Igenomix®

PART OF VITROLIFE GROUP™

v. 2024

Carrier Genetic Testing (CGT)

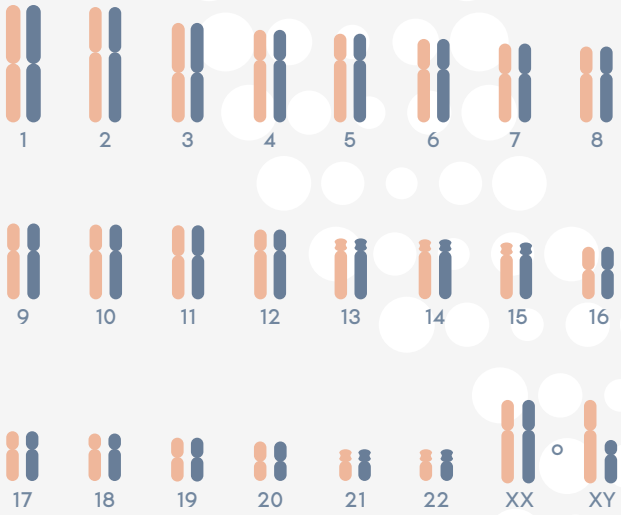
This handout is intended for individuals considering carrier genetic testing (CGT) with Igenomix. It provides information on the rationale for CGT, the process of testing, and possible results.

BASIC GENETIC CONCEPTS

Our genetic information (deoxyribonucleic acid or DNA) is organized in structures called chromosomes. Typically, we each have 23 pairs of chromosomes; one chromosome in each pair comes from our biological mother and the other comes from our biological father.

Chromosome pairs 1-22 contain the same information in males and females, and pair number 23 determine whether an individual is biologically male (XY) or female (XX).

These chromosomes contain genes, which are instructions for our bodies to work and grow. Just as we have two copies of each chromosome, we also have two copies of most genes.



WHAT IS AN AUTOSOMAL RECESSIVE GENETIC CONDITION?

For autosomal recessive genetic conditions, the gene in question is located on one of the 'autosomes' (chromosomes 1-22). A recessive genetic condition is caused by an individual having a harmful spelling mistake (or 'variant') in both copies of a particular gene. An affected individual does not have any working copies of the gene and therefore shows signs of the condition.

If an individual has one copy of the gene with a harmful variant and a second, working copy of the gene, they will be a 'carrier' of the condition. This generally does not have any health implications as the working copy of the gene is able to compensate for the faulty copy. It will, however, lead to an increased risk of having a child with the related genetic condition, if the other biological parent carries a harmful variant in the same gene. Research has shown that over 80% of people are carriers of at least one genetic condition, often without knowing it.

Some examples of autosomal recessive conditions include cystic fibrosis (CF), sickle cell anemia, and phenylketonuria (PKU).

TYPICAL GENE PAIR

CARRIER OF AN AUTOSOMAL RECESSIVE GENETIC CONDITION
(ONE FAULTY GENE COPY)

WHAT IS AN X-LINKED CONDITION?

X-linked conditions are caused by a harmful variant in a gene located on the X chromosome. As biological females have two X chromosomes, they usually have a second working copy of the gene which can compensate for the faulty copy. Females with one faulty copy of the gene are considered carriers and can pass the faulty copy on to the next generation. Typically, female carriers are not affected with X-linked conditions, though for some conditions they may develop mild symptoms.

As biological males have only one X chromosome, there is no second copy of the gene to compensate for a faulty copy. If they have a harmful variant in a gene on this chromosome, they will be affected with the related X-linked condition.

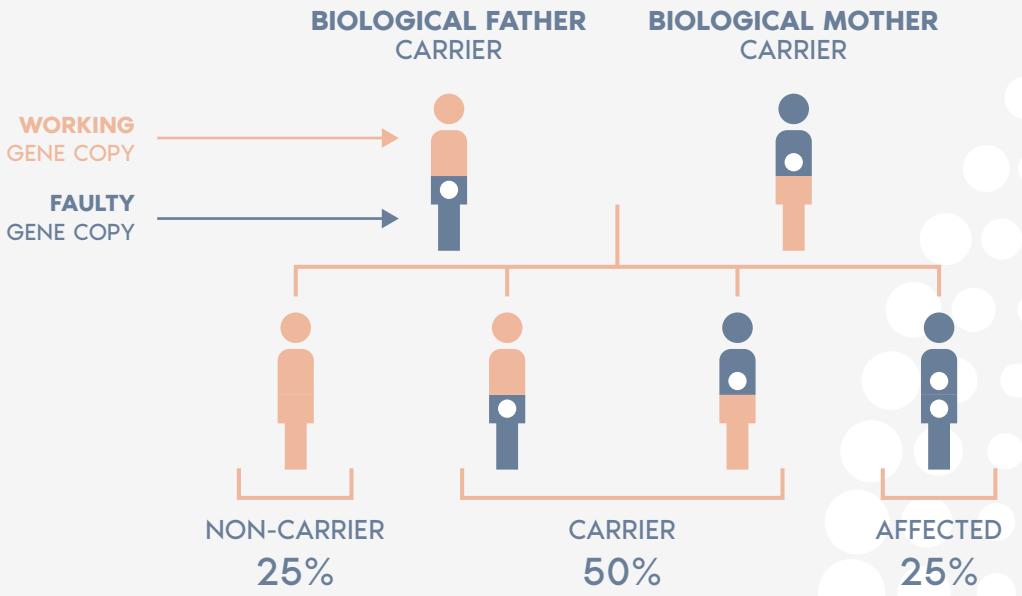
Some examples of X-linked conditions include hemophilia, Duchenne muscular dystrophy (DMD), and fragile X syndrome.

WHAT IS THE RISK OF HAVING AN AFFECTED CHILD?

Studies have shown that approximately 1-5% of reproductive couples are at risk of having an affected child, either because they are both carriers of the same autosomal recessive condition, or because the egg-source is a carrier of an X-linked condition.

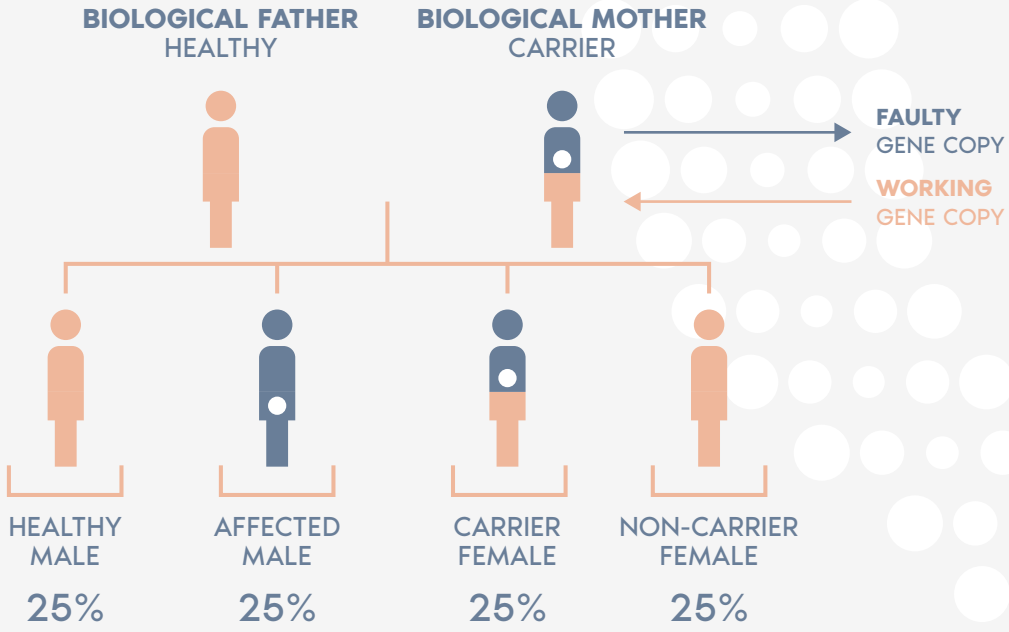
AUTOSOMAL RECESSIVE INHERITANCE

If both biological parents (individuals who provide the sperm and egg) carry a harmful variant in the same gene, with each pregnancy there is a 25% or 1 in 4 chance that the child will inherit two harmful variants (one from each biological parent) and be affected with the condition.



X-LINKED INHERITANCE

If the biological mother (individual providing the egg) is a carrier of an X-linked condition, there is a 25% or 1 in 4 chance of having an affected male and a 25% or 1 in 4 chance of having carrier female.



WHAT IS CARRIER GENETIC TESTING (CGT) WITH IGENOMIX?

Carrier Genetic Testing with Igenomix analyzes an individual's DNA to determine if they are a carrier of a range of autosomal recessive genetic conditions. In biologically female individuals, carrier screening may also include the analysis of genes associated with X-linked conditions. This information can be useful in understanding the risk of having a child with a genetic condition.

Carrier screening is available to anyone who wants to learn more about their risk of being a carrier of a genetic condition, including couples who are planning to conceive naturally, individuals/couples who are pursuing assisted reproduction, sperm/egg donors, and intended recipients of donor sperm/eggs.

Some genetic conditions occur more often in people who trace their ancestry to a particular geographic area. For example, Gaucher disease more frequently affects people of Ashkenazi Jewish ancestry, and sickle cell disease more frequently affects people of African descent. These conditions, however, are not restricted to these groups, and anyone can be a carrier.

WHICH CARRIER GENETIC TEST (CGT) IS RIGHT FOR ME?

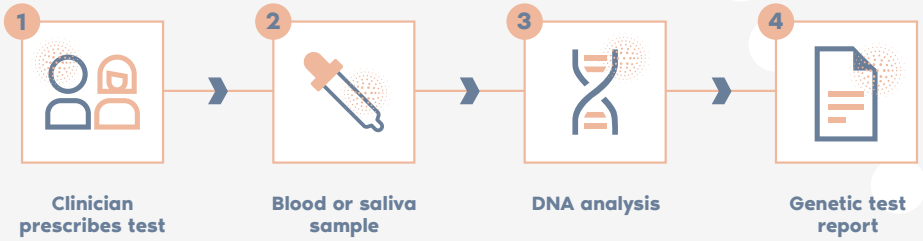
Your ordering provider will determine which carrier screening panel will be requested. There are three main types of carrier screening tests offered by Igenomix: CGT Plus, CGT Mirror, CGT Sequential.

- **CGT Plus** examines a larger list of genes associated with over 500 genetic conditions. This panel-based test is recommended when both individuals in a reproductive couple are seeking CGT to find out if they might be carriers of the same genetic condition(s), or when individuals are looking to donate eggs/sperm.

- **CGT Mirror** is a test that facilitates "mirroring" a carrier screening test performed by a different genetic testing laboratory to ensure that the two panels include the same genes. Panels can vary between laboratories and over time. CGT Mirror can be considered when one member of the reproductive couple has already had carrier screening and the other member wishes to have a similar panel of genes tested.

- **CGT Sequential** may be considered when one individual in a reproductive couple (one partner or a sperm/egg donor) is a known carrier of one or more autosomal recessive genetic conditions. CGT Sequential can be ordered for the reproductive partner and includes analysis of the gene(s) of interest. The optional analysis of X-linked conditions is available for biologically female patients.

WHAT CAN I EXPECT FROM CGT?



Carrier genetic testing can be done using DNA from a blood or saliva sample. Pre-test genetic counselling is recommended to discuss the testing process in more detail including the benefits and limitations, possible results and implications, and address any questions or concerns. Post-test genetic counselling is also available to discuss the test results, which are generally available within 28 calendar days from receipt of the DNA sample in our laboratory.

WHAT DO THE RESULTS MEAN?

If an individual receives a **negative** CGT result, this means they have not been found to be a carrier of any of the conditions included in the test. This does not exclude the possibility that the individual carries a harmful variant in a gene that was not tested.

If one or both biological parents have completed CGT and are found to be carriers of **different** autosomal recessive genetic conditions, their risk of having an affected child is significantly reduced. Any children will have a 50% or 1 in 2 risk of being a carrier of each condition, and they could consider carrier testing when they reach adulthood.

If **both** biological parents are found to be carriers of the **same** autosomal recessive condition, or the biological mother is a carrier of an X-linked condition, there is an increased risk of having an affected child (see 'What is the risk of having an affected child?' above). In this situation, a follow-up genetic counselling session is available to explore potential reproductive options. These options may include:

- Continuing with reproductive plans with an understanding of the risk
- Sperm/egg donation or selection of an alternative donor
- Genetic testing of embryos and selection of unaffected embryos for transfer (pre-implantation genetic testing)
- Genetic testing in pregnancy to determine whether the developing fetus is affected (prenatal testing)
- Adoption

If an individual is found to be a carrier of a particular condition, their relatives may also be at risk of being a carrier. We recommend sharing the results with relatives so that they can consider the option of carrier testing. If they are interested, carrier screening could be coordinated by their primary care provider or a local genetic counselor.

LIMITATIONS OF CGT

- There is a 1-2% misdiagnosis risk for CGT. This refers to the chance of a harmful variant being reported that is not actually present or vice versa.
- There is a small chance that the individual who is undergoing testing may carry a much rarer variant that we have not been able to identify. A negative result would therefore not exclude the risk of being a carrier entirely but would significantly reduce the chance. The precise detection rate varies by gene and is available on request.
- CGT Mirror, CGT Plus, and CGT Exome are targeted tests, meaning they will only examine the gene(s) included in the test. CGT therefore cannot 'rule out' the risk of having a child with other genetic conditions that are not included in the test.
- There is a small chance that the DNA extraction from a blood/saliva sample may be unsuccessful, and we may need to arrange for a new sample to be provided.

CONTACT US

If you have questions or concerns about CGT, or would like further information, please get in touch with our genetic counselling team at gc@igenomix.com.

Igenomix®
PART OF VITROLIFE GROUP®

Follow us on social media
@Igenomixusa

(305) 501-4948

infousa@igenomix.com
www.igenomix.com

V. 2024