Fragile X syndromepatient information

It is important that you discuss the benefits and limitations of genetic testing with your physician, a medical geneticist or a genetic counsellor before you have genetic testing.

Why is my physician recommending genetic testing?

Your physician (or other healthcare provider) may be ordering genetic testing, as some of the symptoms of your child may be suggestive of a genetic condition. It is possible that this test may help diagnose a genetic condition. If a genetic condition is diagnosed it can lead to a change in treatment and an understanding on what to expect in the future. Early diagnosis can help with finding the correct therapies for your child, prevent further complications before they happen, and/or stop any additional, unnecessary, diagnostic workup. Identification of a genetic disorder can also help determine if there is a risk for future pregnancies.

To understand how genetics impacts our health, it is important to understand the basics of genetics.

What is DNA?

DNA is the basic unit of genetics. It is the genetic material that we inherit from our parents and pass to our children. DNA is comprised of four separate molecules (chemicals) that are called bases. Each base is assigned a different letter. These letters are A (adenine), T (thymine), G (guanine), and C (cytosine). These four bases are joined together in very long strings of DNA within our cells. These long strings of DNA are called DNA sequences (also called the DNA code or the genetic code). DNA is what genes are composed of.

What is a gene?

A gene is a specific pattern of DNA bases; this pattern is called a DNA sequence. We have approximately 20,000 genes and each gene has a specific function within our body. Each gene creates a different protein, which are the building blocks for our body. Our genes determine how our bodies develop and function from hair and eye colour to how our brain cells communicate and how we develop during pregnancy. Our genes are located within structures called chromosomes.

What is a chromosome?

Chromosomes are structures that contain all of the DNA in our cells. We have 23 pairs of chromosomes. One copy of each pair is inherited from our mother while the other copy is inherited from our father. As we have two copies of each chromosome, we therefore have two copies of every gene. Each pair of chromosome are unique. Chromosome 1 is the largest and the remaining chromosomes are named by descending size, chromosome 22 is the smallest. Chromosome pair 23 are called the sex chromosomes. In general, sex chromosomes determine the gender of the individual. A pair of XX typically result in a female while a pair of XY chromosome typically result in a male. All of the chromosomes are found in the nucleus of the cell.

What is Fragile X syndrome?

Fragile X is a genetic condition that can cause multiple developmental issues including developmental delay, speech delay, mild to moderate intellectual disability, abnormal behaviour and autism spectrum disorder. Patients often have distinctive facial features. Typically, males are more severely affected than females.

What is the cause of fragile X?

Fragile X is caused by a mutation in a gene called FMR1. The FMR1 gene is found on the X chromosome. The X chromosome is one of the sex chromosomes, the other sex chromosome is the Y chromosome. A female is typically XX and a male is typically XY. Since males only have one X chromosome, they have only one copy of the FMR1 gene. Females have two X chromosomes, and therefore have two copies of the FMR1 gene. When females are affected, they have a second normal copy of the gene and is why they are less affected than males.

The FMR1 mutation is a result of a DNA “expansion” within the gene causing it become longer and prevent it from functioning. The expansion is caused by repetition of a triplet of DNA bases – CGG. A repetition of this triplet within the gene is what can result in fragile X syndrome. An expansion of the repeat can occur between generations.

Other disorders associated with FMR1 include fragile X-associated ataxia syndrome and primary ovarian insufficiency.

Why pursue testing?

Your physician or genetics specialist may recommend fragile X testing if your child's clinical presentation is suggestive of fragile X syndrome. Accurately identifying the cause of your child's symptoms and finding a diagnosis can help determine the best course of treatment and what to expect in the future.

Accurate diagnosis can help determine the risk of recurrence for future pregnancies.

How is testing performed?

Fragile X testing requires a blood sample DNA is extracted from the sample and is analysed for the number of triplet repeats within the FMR1 gene.

How long before the results are ready?

The results of a fragile X syndrome analysis are generally ready in 2 - 3 weeks. Depending on what you have agreed with you healthcare provider, results may be delivered over the phone or in person.

Possible results –

The number of triplet repeats within the gene can be divided into four categories

1. Normal: 5 - 44 CGG repeats. An individual with this range of repeats within the FMR1 gene will be unaffected and their children will be unaffected
2. Intermediate: 45 - 54 CGG repeats.An individual with this range of repeats within the FMR1 gene will be unaffected and their children will be unaffected. However, there is a small chance that this repeat number will expand and will result in a "premutation" in the offspring
3. Premutation: 55 - 200 CGG repeats. An individual with this range of repeats will not have fragile X syndrome but will be at an increased risk for fragile X-associated ataxia syndrome and primary ovarian insufficiency. Offspring of individuals with a premutation have a risk of inheriting a full mutation
4. Full mutation: >200 CGG repeats. An individual with this range of repeats will have fragile X syndrom

Limitations of Fragile X syndrome analysis

Fragile X syndrome analysis cannot detect all types of genetic changes. It is possible that your healthcare provider will suggest additional genetic testing.

A negative result will rule out a diagnosis of fragile X syndrome but it does not rule out the possibility of a genetic basis for your child's condition.

It is important to follow up with your physician, a medical geneticist or a genetic counsellor to discuss the results of your genetic testing.