Patient name_____ Test name_____

Informed consent for 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 or if other family members are at risk for the condition. (For more information on genetic concepts, please turn over the page)

Possible results

1. Positive – A variant was identified which explains your child's symptoms or condition.
2. Negative – No variants were identified which could explain the patient's condition. *A negative result does not always rule out a genetic basis for the patient's condition.*
3. Uncertain – A variant is classified as uncertain when there is insufficient evidence to determine if the variant is either disease causing (pathogenic) or has no effect (benign). *As more research is conducted, it is possible that uncertain variants may be reclassified as pathogenic or benign in the future.*
4. Unexpected results – In rare situations, it is possible that a genetic diagnosis, not directly related to your child's condition, is identified. These findings could have implications for the healthcare of your child.

Limitations

This genetic test cannot identify all types of genetic changes; therefore, it is possible that your physician will request additional tests in the future.

Genetic testing can reveal family relationships that may have not been previously known such as non-paternity or consanguinity.

The purpose of this testing is to determine if there is an underlying genetic basis for your child's condition. It can not determine all long term medical risks that your child may develop over time.

The purpose of this test is to identify the genetic basis for your child's condition. However, it is possible that this test could identify a genetic condition that is unrelated to you/ your child's current symptoms. This finding could have healthcare implications for your child or your family

It is recommended that you meet with a genetic counsellor, geneticist or other qualified healthcare provider before pursuing genetic testing. A genetic counsellor, geneticist or other qualified healthcare provider can help interpret genetic test results in the context of the patients family history to determine recurrence risks and risks to other family members.

I acknowledge, as the patient and/or his/her parent/legal guardian, that I have read the informed consent information and/or my physician or healthcare provider has discussed the benefits and limitations of genetic testing with me. I have been given an opportunity to ask any questions regarding this testing. I understand the purpose of this test and I consent to have my / my child's sample sent to Al Jalila Genomics Center for analysis.

☐ (WES ONLY) Check if I do NOT want to receive the 59 ACMG secondary findings

☐ Please check if you do NOT consent to having your/ your child's specimen and data de-identified and used for quality improvement and internal research. De-identified data may be used for population studies in collaboration with other institutions to understand normal genetic variation. Any unique identifiers such as your/ your child's name will not be used in any research study or publication.

Patient/Guardian name_____

Patient/Guardian signature:_____ Date:_____

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Our genetics can play an important part in our health. 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 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. Chromosomes are found within all of our cells.

What is a cell?

A cell is the smallest functional unit that our bodies are made of. Each part of our bodies are composed of different types of cells working together. The cells of our brain are different from the cells of our heart which are different from the cells of our skin and so on. However, every cell has a nucleus where our chromosomes are stored and every cell contains the same DNA.

What is genetic variation?

Changes within our DNA are common and that is what makes us unique. Even though we share the DNA we inherit from our parents with our siblings, there will still be genetic differences between family members. DNA changes within our genes are called “variants”. A change that does not disrupt the function of the gene is called a "benign variant". If a variant negatively impacts the gene and results in a syndrome or condition it is called a “pathogenic variant”. In the past, pathogenic variants were referred to as “mutations”. When there is insufficient evidence to determine if the change is pathogenic or benign it is called a “variant of uncertain significance”. Variants of uncertain significance are often reclassified as pathogenic or benign in the future when more research has been completed.

Genetic variation is not only single “letter” changes, but also includes larger segments of DNA. Segments of the chromosomes can be “duplicated” or “deleted”. These duplications and deletions are also called copy number variants. They can result in a genetic condition depending on the location and size of the duplication or deletion and the genes within the affected region.

Different types of genetic testing analyzes the DNA for different types of genetic variation.

Types of inheritance

Recessive inheritance - both copies of the same gene (one copy from each parent) need to have a variant for a person to be affected with a recessive condition. A variant in a single copy is insufficient to result in a condition. An individual who carries only one variant for a recessive condition is called a carrier for that condition and generally will be unaffected.

Dominant inheritance – Requires only one copy of the gene to have a variant to result in a condition or physical characteristic even if the other copy of the gene is normal. In general, if a condition is inherited in a

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dominant manner, and it is inherited from a parent, then the parent will also be affected. When a new variant is identified in an individual that is not present in the parents DNA, it is call *de novo* inheritance.

X-linked inheritance – this type of inheritance refers to variants that are inherited on the X chromosome. In general, males have XY chromosomes while females have XX chromosomes. It is more common for males to be affected by X-linked conditions compared to females as males have only one X chromosome. Since females have a second X chromosome, the presence of a second normal gene is generally sufficient to prevent disease.

Mitochondrial inheritance – Mitochondria are small structures (organelles) that are found within our cells. They have many important functions but the most important is energy production for our body. Mitochondria have their own DNA called mtDNA. Mitochondrial inheritance refers to inheritance of those genes that are located in the mtDNA. Mitochondria are only inherited from our mothers.

There can be as many as 1000-2000 mitochondria in a single cell. Not all mitochondria will have the exact same mtDNA. Some may contain pathogenic variants that can result in a mitochondrial disorder. When an individual has a mixture of normal mtDNA and mtDNA with a pathogenic variant, it is called heteroplasmy. The level of heteroplamsy can help determine the level of severity of a mitochondrial disorder. It is common for family members to have different levels of heteroplasmy and therefore very different presentations for the same mitochondrial disorder. It is not possible to determine the level of heteroplasmy that offspring will inherit from an affected mother.