About Rapid Whole Genome Sequencing

Why does my doctor want to order Whole Genome Sequencing (WGS)?

The purpose of Whole Genome Sequencing is to find genetic changes that are causing a child's health condition. The operating manual for the human body is found in our DNA which contains around 22,000 genes or "instructions". Whole Genome Sequencing is a genetic test that reads through the DNA to look for letter changes in the gene "spelling". Genes provide specific instructions to tell our bodies how to grow and develop. When a gene contains a spelling change, it may not work properly and can lead to health problems.

Benefits of Whole Genome Sequencing

Identifying the cause of a genetic disorder can:

1. Explain why a child is having health problems
2. Provide a diagnosis for a genetic condition
3. Help doctors take better care of a child
4. Let family members know if they are at risk of having the same genetic condition or if there is a chance of passing on the same genetic condition to future children.

Risks associated with genetic testing

There is a risk for genetic discrimination with all genetic tests, including Whole Genome Sequencing. Currently, there is a federal law in place called GINA (Genetic Information Nondiscrimination Act) which prevents health insurers, group health plans and employers, with 15 or more employees, from making decisions about an individual based on a genetic test result. However, this law does not protect from discrimination by companies that sell long-term care, life and disability insurance. It also does not apply to individuals in the military.

Genetic testing may also reveal information that may be unexpected or upsetting, such as biologic relationships that were previously unrecognized.

Genetic testing may also reveal that you or a family member has a genetic disorder. Lastly, Whole Genome Sequencing may not help a child.

What are possible results from this test?

POSITIVE: Genomic sequencing finds a genetic change that explains the health problems that a child is having. In some cases, a diagnosis may help guide medical care, but in other cases, it only provides a name or reason for a condition.

NEGATIVE: Genomic sequencing does NOT find a genetic change that explains a child's condition. This does not mean that a child does not have a genetic disorder *(see Limitations of Whole Genome Sequencing)*.

VARIANT OF UNCERTAIN SIGNIFICANCE SUSPICIOUS (VUSS): Genomic sequencing finds a genetic change possibly causing the health problem, but there is not enough scientific proof to know for certain. More tests may be needed to understand if the change is causing a problem.

INCIDENTAL FINDINGS: During analysis, a change is found in a gene that is NOT directly related to the child's symptoms but may cause a health problem in the future. Incidental findings will only be reported if the information could prompt a change in medical care. Some examples of incidental findings include genes related to increased future risk for cancers, heart or metabolic conditions. Knowing this can help a child's doctor check for the condition and may allow the doctor to better manage the child's care in the future. Some people may prefer not to learn this information.

NOTE: If you DO NOT want to receive information about incidental findings, please let your child's doctor know so it can be noted on the order form.

Why do you need parent samples?

DNA samples from biological parents can sometimes help us to find the answer faster and can tell us if a parent has the same genetic change as their child.

Limitations of Whole Genome Sequencing

This test is not able to detect all genetic changes. This is partly because scientists are still discovering new information about genes and the technology is continuing to improve. Also, a child may not have a disorder caused by a single genetic change. Instead the disorder may be caused by multiple genes, in combination with environmental factors, and therefore would not be detected by this test. It is also possible that a child's condition is not genetic.

There are different types of genetic tests. Some tests may be better at finding the cause of a specific genetic disorder than Whole Genome Sequencing, so your child's doctor may order additional testing.

Results that this test will not return

This test sequences a person's entire genome, but during analysis we focus on genes associated with the child's current health problems. Our testing does not look for or report carrier status for autosomal recessive diseases, in which a person carries only one copy of a nonfunctioning gene that does not affect his/her health. Also, our testing does not look for genetic changes that affect the way the body breaks down medications known as pharmacogenomic information. It also does not intentionally look for genetic changes in the 59 genes on the ACMG secondary findings list, but if a pathogenic variant is found in one of these genes, it will be reported as an incidental finding.

Use of de-identified data

When genetic testing is completed, standard procedure is for laboratories to remove all identifying information and keep the sample and testing data for possible future use to learn more about rare genetic disorders.

If you do not want de-identified sample or testing data retained, please let your child's doctor know.

Resources

Genetic counseling is recommended before and after genetic testing.

Find Genetic Services in your area

Rady Children's Hospital Genetics/ Dysmorphology
rchsd.org/programs-services/genetics-dysmorphology

National Society of Genetic Counseling (NSGC)
https://www.nsgc.org/findageneticcounselor

American College of Medical Genetics (ACMG)
acmg.net/ACMG/Genetic_Services_Directory_Search.aspx

Learn more

Genetic Information Nondiscrimination Act (GINA)
ginahelp.org/GINA_you.pdf

Genomic sequencing

Genetics Home Reference
ghr.nlm.nih.gov/primer/genomicresearch/sequencing

National Human Genome Research Institute
genome.gov

ACMG Secondary Findings
https://www.ncbi.nlm.nih.gov/clinvar/docs/acmg

Specific genetic conditions

Genetics Home Reference
ghr.nlm.nih.gov/

Online Mendelian Inheritance in Man (OMIM)
omim.org

GeneReviews
ncbi.nlm.nih.gov/books/NBK1116

Genetic Test Registry
ncbi.nlm.nih.gov/gtr