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

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 genetic discrimination by companies that sell long-term care, life and disability insurance. It also does not apply to individuals in the military. RCIGM will not share your identifiable genetic information with these industries – see Data Privacy section below.

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. 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.

Data Privacy

RCIGM acknowledges the confidentiality and privacy rights of the patient, parents and other family members tested. In accordance with its policies and applicable law, RCIGM will retain samples, the results of testing, associated data and reports. Identifiable samples and information will be kept confidential and accessible only to RCIGM clinical staff. Unless required or permitted by law, RCIGM will not disclose identifiable samples or information to any person or entity without your written authorization. For the limited purposes of treatment, payment, and healthcare operations and on a restricted need-to-know basis, RCIGM may share your samples and/or data with your provider(s).

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 your de-identified sample or de-identified testing data used for learning purposes, please let your child's doctor know before sample collection.

Resources

Genetic counseling is recommended before and after genetic testing.

Find Genetic Services in your area

National Society of Genetic Counseling (NSGC)
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
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

RCIGM-CGC Notice of Use and Disclosure of Samples & Information; Incidental Findings

Samples will be sent to RCIGM laboratories in California for testing. RCIGM acknowledges the confidentiality and privacy rights of the patient, parents and other family members tested. In accordance with its policies and applicable law, RCIGM will retain samples, the results of testing, associated data and reports. Identifiable samples and information will be kept confidential and accessible only to RCIGM clinical staff. Unless required or permitted by law, RCIGM will not disclose identifiable samples or information to any person or entity without your written authorization. For the limited purposes of treatment, payment, healthcare operations and on a restricted need-to-know basis, RCIGM may share your samples and/or data with your provider(s).

Additional Use of De-identified Information and/or Samples: RCIGM may use De-identified Information and Samples for research, scientific and technical development, and internal statistical and program operations analysis ("Additional Use"). De-identified data may be submitted to rare disease databases such as GeneMatcher to help identify new disease causing genes and aid in the ability to identify a genetic diagnosis in the individual. Additionally, samples may be sent de-identified to external clinical laboratories to resolve any analytical discrepancies that occur during testing at the discretion of RCIGM. Additional Use of De-identified Information and Samples for these purposes may improve identification and development of therapies for existing and new diseases now or in the future. At the time of placing an order and prior to testing, RCIGM offers patients/guardians and/or individuals tested the ability to prohibit RCIGM additional use of De-identified information and samples. No response will be treated as Opt-In (except for New York residents).

For New York Residents: If no selection is marked below, RCIGM laboratory will select Opt-Out by default. If Opt-In for additional use is not selected, New York law requires that no tests other than those authorized shall be performed on the biological sample and RCIGM is required to destroy samples no more than sixty (60) days after sample collection or at the end of the testing process. If Opt-In is selected for Additional Use, De-Identified samples may be stored and used longer than 60 days.

Data Release: RCIGM can provide the release of raw sequence data from WGS for patients and/or family members to the healthcare provider on record, upon request. Data will be provided as BAM and/or VCF files. For data release requests, the ordering provider can contact RCIGM_rWGS@rchsd.org.

Incidental Findings: In rare cases, RCIGM may also report an incidental finding during routine analysis. Incidental findings are pathogenic variants identified in genes not related to the patient's phenotype that are considered medically actionable and the results are significant for the health of the patient or family members tested.

What will be reported for relatives: The presence of any incidental findings reported for the proband may be provided for relatives included in this testing, unless they opt-out of receiving such results.

Limitations: Pathogenic variants that may be present in a relative, but not present in the proband, will not be identified or reported.

Please mark the appropriate boxes below to Opt-In or Opt-Out

If no selection is marked, RCIGM laboratory will select Opt-In by default (except for New York residents).

Use of De-identified Information and/or Samples		Incidental Findings		Proband and Family Member Names	
Opt-In	**Opt-Out**	**Opt-In**	**Opt-Out**	**Relationship**	**Print Name**
☐	☐	☐	☐	☐ Proband	
☐	☐	☐	☐	☐ Mother	
☐	☐	☐	☐	☐ Father	
☐	☐	☐	☐	☐ Sibling	
☐	☐	☐	☐	Other _____	

By signing below you are acknowledging that you have reviewed the WGS sequencing informational packet and authorize completion of the described test for the proband, minor sibling(s) and/or yourself. Your signature(s) confirm that you Opt-in or Opt-out of incidental findings and sharing of de-identified data for each participant as selected above. Print the name of the person signing. Parent/Guardian(s) must sign below for minors. Each adult (age 18 and older) must sign for themselves. If parent is under 18, parent guardian signature may be required.

Patient/Patient Guardian Name (Print)	Patient/Patient Guardian Signature	Date (MM/DD/YYYY)
Mother/Mother Guardian Name (Print)	Mother/Mother Guardian Signature	Date (MM/DD/YYYY)
Father/Father Guardian Name (Print)	Father/Father Guardian Signature	Date (MM/DD/YYYY)
Other Family Member Name (Print)	Other Family Member Signature	Date (MM/DD/YYYY)