MAYO CLINIC LABORATORIES

Test Definition: CMPRG

Family Member Comparator Specimen for Genome Sequencing, Varies

Overview

Useful For

Submitting a biological family member's specimen to be used as a comparator for affected patients (probands) undergoing whole genome sequencing

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
CULAF	Amniotic Fluid Culture/Genetic Test	Yes	No
_STR1	Comp Analysis using STR (Bill only)	No, (Bill only)	No
_STR2	Add'l comp analysis w/STR (Bill Only)	No, (Bill only)	No
CULFB	Fibroblast Culture for Genetic Test	Yes	No
MATCC	Maternal Cell Contamination, B	Yes	No

Genetics Test Information

This test is for the biological family members whose specimens are being submitted as comparators for patients undergoing WGSDX / Whole Genome Sequencing for Hereditary Disorders, Varies.

Special Instructions

- Muscle Biopsy Specimen Preparation Instructions
- Whole Genome Sequencing: Ordering Checklist
- Whole Exome and Genome Sequencing Information and Test Ordering Guide

Highlights

Additional information is available; see Whole Exome and Genome Sequencing Information and Test Ordering Guide.

Method Name

Next-Generation Sequencing (NGS) followed by Sanger Sequencing, Quantitative Polymerase Chain Reaction (qPCR), or other methods, as needed

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

This test is **not appropriate for** affected patients (probands) undergoing whole genome sequencing (WGS). This test is intended to be ordered for biological family member comparator specimens only. For WGS testing for the proband, order WGSDX / Whole Genome Sequencing for Hereditary Disorders, Varies. If this test is ordered on a proband, the test will be canceled and WGSDX will be performed as the appropriate test.

If this test is ordered on a family member comparator of a proband having WESDX / Whole Exome Sequencing for Hereditary Disorders, Varies; or WESMT / Whole Exome and Mitochondrial Genome Sequencing, Varies, this test will be canceled and CMPRE / Family Member Comparator Specimen for Exome Sequencing, Varies performed as the appropriate test.

Each specimen must be on a separate order.

Additional Testing Requirements

To order whole genome sequencing for the patient and the family member comparator specimens, see the following steps:

1. Order WGSDX / Whole Genome Sequencing for Hereditary Disorders, Varies on the patient (proband).
2. Order this test on all family members' specimens being submitted as comparators.
   a. When available, the patient's biological mother and biological father are the preferred family member comparators.
   b. If one or both of the patient's biological parents are not available for testing, specimens from other first-degree relatives (siblings or children) can be used as comparators. Testing typically includes up to 2 family member comparators. Contact the laboratory at 800-533-1710 for approval to send specimens from other relatives or to send the patient and 3 first-degree relatives (quad).
   c. The cost of analysis for family member comparator specimens is applied to the patient's (proband's) test. Family members will not be charged separately.
3. Collect patient (proband) and family member specimens. Label specimens with full name and birthdate. Do not label family members' specimens with the proband's name.
4. For each family, complete the following portions of the Whole Genome Sequencing: Ordering Checklist. **A separate form is not needed for each family member**.
   a. **Patient Information is required for all clients.**
   b. Informed Consent is **required for New York State clients.**
   c. **If the patient wishes to opt-out of receiving secondary findings or change the DNA storage selection**, select the appropriate boxes in the Informed Consent section.
5. Attach clinic notes from specialists relevant to patient's clinical features, if available.
6. Attach pedigree, if available.
7. Send paperwork to the laboratory along with the specimens. If not sent with the specimens, fax a copy of the paperwork to 507-284-1759, Attn: WGS Genetic Counselors.

For more information see Whole Exome and Genome Sequencing Information and Test Ordering Guide.

Necessary Information

Whole Genome Sequencing: Ordering Checklist is required for all clients, and Informed Consent is required for New

York clients. Fill out one form for the family and send with the specimens.

Specimen Required

Patient Preparation: A previous hematopoietic stem cell transplant from an allogenic donor will interfere with testing. Call 800-533-1710 for instructions for testing patients who have received a hematopoietic stem cell transplant.

Submit only 1 of the following specimens for each family member.

Specimen Type: Whole blood
Container/Tube:
Preferred: Lavender top (EDTA) or yellow top (ACD)
Acceptable: Green top (Sodium heparin)
Specimen Volume: 3 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot**.
3. Whole blood collected postnatal from an umbilical cord is also acceptable. See Additional Information
Specimen Stability Information: Ambient (preferred) 4 days/Refrigerated 4 days/Frozen 4 days
Additional Information:
1. Specimens are preferred to be received within 4 days of collection. Extraction will be attempted for specimens received after 4 days, and DNA yield will be evaluated to determine if testing may proceed.
2. To ensure minimum volume and concentration of DNA are met, the requested volume must be submitted. Testing may be canceled if DNA requirements are inadequate.
3. For postnatal umbilical cord whole blood specimens, maternal cell contamination studies are recommended to ensure test results reflect that of the patient tested. A maternal blood specimen is required to complete maternal cell contamination studies. Order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on both the cord blood and maternal blood specimens under separate order numbers.

Specimen Type: Saliva
Patient Preparation: Patient should not eat, drink, smoke, or chew gum 30 minutes prior to collection.
Supplies:
DNA Saliva Kit High Yield (T1007)
Saliva Swab Collection Kit (T786)
Container/Tube:
Preferred: High-yield DNA saliva kit
Acceptable: Saliva swab
Specimen Volume: 1 Tube if using T1007 or 2 swabs if using T786
Collection Instructions: Collect and send specimen per kit instructions.
Specimen Stability Information: Ambient (preferred) 30 days/Refrigerated 30 days
Additional Information: Saliva specimens are acceptable but not recommended. Due to lower quantity/quality of DNA yielded from saliva, some aspects of the test may not perform as well as DNA extracted from a whole blood sample. When applicable, specific gene regions that were unable to be interrogated will be noted in the report. Alternatively, additional specimen may be required to complete testing.

Specimen Type: Cultured fibroblasts
Source: Skin
Container/Tube: T-25 flask

Specimen Volume: 2 Flasks
Collection Instructions: Submit confluent cultured fibroblast cells from a skin biopsy. Cultured cells from a prenatal specimen will not be accepted.
Specimen Stability Information: Ambient (preferred) <24 hours/Refrigerated <24 hours
Additional Information:
1. Specimens are preferred to be received within 24 hours of collection. Culture and/or extraction will be attempted for specimens received after 24 hours and will be evaluated to determine if testing may proceed.
2. A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks are required to culture fibroblasts before genetic testing can occur.

Specimen Type: Tissue biopsy
Supplies: Hank's Solution (T132)
Container/Tube: Sterile container with sterile Hank's balanced salt solution, Ringer's solution, or normal saline
Specimen Volume: 0.5 to 3 cm(3) or larger
Specimen Stability Information: Ambient (preferred) <24 hours/Refrigerated <24 hours
Additional Information:
1. Specimens are preferred to be received within 24 hours of collection. Culture and extraction will be attempted for specimens received after 24 hours and will be evaluated to determine if testing may proceed.
2. A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks are required to culture fibroblasts before genetic testing can occur.

Specimen Type: Muscle tissue biopsy
Supplies: Muscle Biopsy Kit (T541)
Specimen Volume: 20 to 80 mg
Collection Instructions: Prepare and transport specimen per instructions in Muscle Biopsy Specimen Preparation Instructions.
Specimen Stability Information: Frozen (preferred) <24 hours/Ambient <24 hours/Refrigerated <24 hours
Additional Information: Specimens are preferred to be received within 24 hours of collection. Extraction will be attempted for specimens received after 24 hours and will be evaluated to determine if testing may proceed.

Specimen Type: Extracted DNA
Container/Tube:
Preferred: Screw Cap Micro Tube, 2 mL with skirted conical base
Acceptable: Matrix tube, 1 mL
Collection Instructions:
1. The preferred volume is at least 100 mcL at a concentration of 75 ng/mcL.
2. Include concentration and volume on tube.
Specimen Stability Information: Frozen (preferred) 1 year/Ambient/Refrigerated
Additional Information: DNA must be extracted in a CLIA-certified laboratory, or equivalent, and must be extracted from a specimen type listed as acceptable for this test (including applicable anticoagulants). Our laboratory has experience with Chemagic, Puregene, Autopure, MagnaPure, and EZ1 extraction platforms and cannot guarantee that all extraction methods are compatible with this test. If testing fails, one repeat will be attempted, and if unsuccessful, the test will be reported as failed and a charge will be applied. If applicable, specific gene regions that were unable to be interrogated due to DNA quality will be noted in the report.

Forms

1. Whole Genome Sequencing: Ordering Checklist is required.

2. New York Clients-Informed consent is required, included in the above form. Document on the request form or electronic order that a copy is on file.

3. If not ordering electronically, complete, print, and send a Neurology Specialty Testing Client Test Request (T732) with the specimen.

Specimen Minimum Volume

See Specimen Required

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical & Interpretive

Clinical Information

Note: Where applicable, verbiage refers to sex assigned at birth.

This test uses next-generation sequencing technology to assess the genome of patients with suspected underlying genetic disorders. This information is used to assist in the interpretation of the patient's (proband's) whole genome sequencing results (WGSDX / Whole Genome Sequencing for Hereditary Disorders, Varies). Ordering this test on biological family members of the affected proband can help determine the inheritance of genetic variants that are identified and if the variants segregate with a phenotype in the family. Submitting comparator samples from biological family members increases the chance of identifying a diagnosis in the proband. Whole genome sequencing is most informative when samples from both biological parents are used as comparators. Therefore, it is highly recommended that samples are also submitted from the patient's biological mother and biological father.

If more than 2 biological family member comparator specimens are submitted, the additional comparator specimens may not be fully sequenced but rather used for confirmatory presence or absence of identified variants of interest after initial variant calling and review.

Reference Values

An interpretive report will be provided.

Interpretation

Interpretive information will only be provided on the proband's whole genome sequencing report (WGSDX / Whole Genome Sequencing for Hereditary Disorders, Varies). The presence of a variant in family member comparator samples is stated on the proband's report. Variants that are present in family member comparator samples but absent from the

proband sample are not evaluated or reported.

Secondary Findings:
Patients are evaluated for medically actionable secondary findings and these findings are reported in accordance with the American College of Medical Genetics and Genomics recommendations.(1) The presence of a secondary finding in family member comparator samples is stated on the patient's (proband's) report unless family members opt-out of secondary findings. If the proband opts out, secondary findings will not be evaluated or reported in any family member comparators. Secondary findings that are present in family member comparators but absent from the patient (proband) are not evaluated or reported.

The absence of a reportable secondary finding does not guarantee that there are no disease-causing or likely disease-causing variants in these genes, as review is limited to known or highly suspected pathogenic findings, and not all regions of these genes are adequately evaluated by this technology.

Cautions

This testing is intended to be used for biological family members whose specimens are being submitted as comparators for affected patients (probands) undergoing whole genome sequencing. Although test results will only be provided in the context of the proband, it is possible for family members serving as comparators to learn unexpected genetic information about themselves. For example, it is possible for individuals to learn that they carry certain genetic variants that are being reported in the proband, or that biological relationships are not as described.

It is not guaranteed that patient data will be stored indefinitely.

If the patient has had an allogeneic hematopoietic stem cell transplant or a recent blood transfusion, results may be inaccurate due to the presence of donor DNA. Call Mayo Clinic Laboratories at 800-533-1710 for instructions for testing patients who have received a bone marrow transplant.

A genetic consultation is recommended for patients undergoing this test, both prior to testing and after results are available.

Clinical Reference

1. Miller DT, Lee K, Gordon AS, et al. Recommendations for reporting of secondary findings in clinical exome and genome sequencing, 2021 update: a policy statement of the American College of Medical Genetics and Genomics (ACMG). Genet Med. 2021;23(8):1391-1398

Performance

Method Description

Polymerase chain-reaction-free next-generation sequencing is performed on DNA extracted from the patient (proband) and all applicable comparator samples to test for the presence of variants. The human genome reference GRCh38/hg38 build is used for sequence read alignment. Variants are called using an optimized bioinformatics package. The average genomic coverage is at or above a read depth of 32X. Sensitivity is estimated at above 99% for single nucleotide variants,

above 94% for deletion-insertions (delins) less than 50 base pairs (bp). This assay also detects greater than 99% copy number variants (deletions/duplications) at least 1000 bp in size. Confirmation of select reportable variants in the proband and submitted comparator samples may be performed by alternate methodologies based on internal laboratory criteria.

There may be regions of genes that cannot be effectively evaluated by sequencing as a result of technical limitations of the assay, including regions of homology, variable depth of coverage, and repetitive sequences.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Varies

Report Available
70 to 84 days

Specimen Retention Time
Whole blood: 28 days (if available);; Saliva (if available): 30 days; Extracted DNA: 3 months

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CMPRG	Family Member Comparator for Genome	86206-0

Result ID	Test Result Name	Result LOINC® Value
614930	Interpretation	69047-9

614931	Specimen	31208-2
614932	Source	31208-2
614941	Released By	18771-6