Test Definition: UNIPD

Uniparental Disomy, Varies

Overview

Useful For

Evaluation of patients presenting with a personal or family history of Robertsonian chromosomal translocations

Evaluation of patients presenting with features of disorders known to be associated with uniparental disomy

Follow-up to chromosomal microarray results demonstrating regions of homozygosity or absence of heterozygosity

Evaluation of disease mechanism in individuals with rare autosomal recessive disease and only one carrier parent

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
CULFB	Fibroblast Culture for Genetic Test	Yes	No
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
MATCC	Maternal Cell Contamination, B	Yes	No

Genetics Test Information

Specimens from fetus or child and at least one parent are required for testing. Specimens from both parents are recommended for optimal interpretation of the results. Chromosome of interest **must be specified** on request form.

Testing Algorithm

Polymerase chain reaction amplification of microsatellite markers on the chromosome of interest are used to test DNA from the parents and the child for the presence of uniparental disomy.

For prenatal specimens:

If an amniotic fluid specimen or cultured amniocytes is received, amniotic fluid culture for genetic testing will be performed at an additional charge.

If a chorionic villus specimen or cultured chorionic villi is received, fibroblast culture for a genetic test will be performed at an additional charge.

For any prenatal specimen that is received, maternal cell contamination testing will be performed at an additional charge.

Cord blood:

For cord blood specimens that have an accompanying maternal blood specimen, maternal cell contamination studies will

be performed at an additional charge.

For more information see:
-Prader-Willi and Angelman Syndromes: Laboratory Approach to Diagnosis
-Beckwith-Wiedemann and Russell-Silver Syndromes: Laboratory Approach to Diagnosis

Special Instructions

- Informed Consent for Genetic Testing
- Prader-Willi and Angelman Syndromes: Laboratory Approach to Diagnosis
- Informed Consent for Genetic Testing (Spanish)
- Molecular Genetics: Uniparental Disomy Patient Information
- Beckwith-Wiedemann and Russell-Silver Syndromes: Laboratory Approach to Diagnosis

Method Name

Polymerase Chain Reaction (PCR)/Microsatellite markers

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

This test is only intended to rule out whole-chromosome uniparental disomy (UPD). If testing is desired to rule out UPD 11 for Beckwith-Wiedemann syndrome or Russell-Silver syndrome, the recommended test is BWRS / Beckwith-Wiedemann Syndrome/Russell-Silver Syndrome, Molecular Analysis, Varies, as it will also detect cases caused by segmental UPD.

Additional Testing Requirements

All prenatal specimens must be accompanied by a maternal blood specimen; order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on both the prenatal specimen and maternal specimen as separate orders.

Necessary Information

Molecular Genetics: Uniparental Disomy Patient Information is required. Testing will be delayed if this information is not provided.

Specimen Required

Specimens from both parents and the child or fetus are recommended for optimal interpretation of results. Each specimen must have a separate order for this test. Only the proband specimen will be charged.
Testing can be performed if only one parent specimen is submitted, however, biparental inheritance and some types of uniparental disomy (UPD) cannot be definitively established in the absence of one parent. Additionally, there is a higher likelihood for uninformative or inconclusive results.

If all required specimens are not received within one month of ordering, testing will be canceled.

Patient Preparation: A previous hematopoietic stem cell transplant from an allogenic donor will interfere with testing. For information about testing patients who have received a hematopoietic stem cell transplant, call 800-533-1710.

Submit only 1 of the following specimens:

Specimen Type: Whole blood
Container/Tube: Lavender top (EDTA) or yellow top (ACD)
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: Extracted DNA
Container/Tube:
Preferred: Screw Cap Micro Tube, 2mL with skirted conical base
Acceptable: Matrix tube, 1mL
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.

PRENATAL SPECIMENS
Due to its complexity, consultation with the laboratory is required for all prenatal testing; call 800-533-1710 to speak to a genetic counselor.

Specimen Type: Amniotic fluid
Container/Tube: Amniotic fluid container
Specimen Volume: 20 mL
Specimen Stability Information: Ambient (preferred) <24 hours/Refrigerated <24 hours
Additional Information: Specimen will only be tested after culture.

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 CULAF / Culture for Genetic Testing, Amniotic Fluid. An additional 2 to 3 weeks are required to culture amniotic fluid before genetic testing can occur.
3. **All prenatal specimens must be accompanied by a maternal blood specimen;** order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on the maternal specimen.

Specimen Type: Confluent cultured amniocytes
Container/Tube: T-25 flask
Specimen Volume: 2 Flasks
Collection Instructions: Submit confluent cultured amniocytes from another laboratory
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.
3. **All prenatal specimens must be accompanied by a maternal blood specimen;** order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on the maternal specimen.

Specimen Type: Chorionic villi
Container/Tube: 15-mL Tube containing 15 mL of transport media
Specimen Volume: 20 mg
Specimen Stability Information: Ambient (preferred) <24 hours/Refrigerated <24 hours
Additional Information: Specimen will only be tested after culture.
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.
3. **All prenatal specimens must be accompanied by a maternal blood specimen;** order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on the maternal specimen.

Specimen Type: Cultured chorionic villi
Container/Tube: T-25 flasks
Specimen Volume: 2 full flasks
Collection Instructions: Submit confluent cultured cells from another laboratory
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.
3. **All prenatal specimens must be accompanied by a maternal blood specimen;** order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on the maternal specimen.

Forms

1. Molecular Genetics: Uniparental Disomy Patient Information **is required**.
2. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing-Spanish (T826)

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

Uniparental disomy (UPD) occurs when a child inherits 2 copies of a chromosome from only one parent and no copies of that chromosome from the other parent. This is typically due to an error in cell division during the formation of egg or sperm cells (meiosis). When an error causing UPD occurs during meiosis I, both chromosome homologs from a single parent are transmitted, resulting in uniparental heterodisomy. When the error causing UPD occurs during meiosis II or as a postzygotic event, and a single parental homolog is transmitted to offspring in duplicate, isodisomy results. Meiotic recombination events within the context of UPD often result in a mixture of regions of heterodisomy and isodisomy.

When UPD occurs, the imbalance of maternal versus paternal genetic information for the involved chromosome can be associated with clinical symptoms in the affected child. However, UPD does not always impart an abnormal clinical phenotype. While isodisomy can result in disease due to a recessive allele, heterodisomy is not expected to result in an abnormal clinical phenotype unless the involved chromosome or chromosomal segment includes imprinted genes. Imprinted genes demonstrate differential expression depending on parent of origin. Disorders that result from UPD of imprinted genes are not due to a defect in the imprinting mechanism itself, but rather they are due to an unbalanced parental contribution of normally imprinted alleles that results in altered expression of imprinted genes. For example, when maternal UPD 15 occurs (2 copies of the maternal chromosome 15 instead of 1 maternal and 1 paternal copy of chromosome 15), it causes Prader-Willi syndrome due to the lack of paternally expressed genes at the imprinted site.

Uniparental disomy has been described for many but not all chromosomes. In addition to the rare cases of autosomal recessive disease that result from isodisomy, clinical syndromes associated with UPD have been described for only a few chromosomes, including chromosomes 6, 7, 11, 14, 15 and 20.

Uniparental disomy cannot be identified by gross cytogenetic analysis and requires molecular DNA-based analysis using multiple polymorphic markers spanning the chromosome of interest.

For optimal interpretation of results, specimens from both parents and the child or fetus are recommended. If only one parent specimen is submitted, testing can be performed; however, biparental inheritance and some types of UPD cannot be definitively established. Additionally, the likelihood for uninformative or inconclusive results is higher.

Reference Values

An interpretive report will be provided.

Interpretation

Microsatellite markers are compared between the proband and parental samples for the chromosome of interest. The pattern of the microsatellite markers will be classified as demonstrating uniparental disomy or biparental inheritance when sufficient informative markers are identified.

Cautions

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Errors in the interpretation of results may occur if the information given is inaccurate or incomplete.

This test will detect nonpaternity.

Uniparental disomy (UPD) may not be detected by this assay in cases where there is low-level mosaicism for a particular chromosome.

This test only rules out whole-chromosome UPD and cannot reliably detect cases of segmental UPD. If testing is desired to rule out UPD 11 for Beckwith-Wiedemann syndrome or Russell-Silver syndrome, BWRS / Beckwith-Wiedemann Syndrome/Russell-Silver Syndrome, Molecular Analysis, Varies is the recommended test as it will also detect cases caused by segmental UPD.

Although UPD testing is available for all chromosomes, prenatal testing for UPD for chromosomes other than those associated with known phenotypes should be done only after genetic counseling involving adequate discussion of risks, benefits, and limitations of testing.

Clinical Reference

1. Del Gaudio D, Shinawi M, Astbury C, et al. Diagnostic testing for uniparental disomy: a points to consider statement from the American College of Medical Genetics and Genomics (ACMG). Genet Med. 2020;22(7):1133-1141. doi:10.1038/s41436-020-0782-9
2. Kotzot D, Utermann G. Uniparental disomy (UPD) other than 15: phenotypes and bibliography updated. Am J Med Genet. 2005;136(3):287-305. doi:10.1002/ajmg.a.30483
3. Kotzot D. Prenatal testing for uniparental disomy: indications and clinical relevance. Ultrasound Obstet Gynecol. 2008:31(1):100-105. doi: 10.1002/uog.5133
4. Engel E. A fascination with chromosome rescue in uniparental disomy: Mendelian recessive outlaws and imprinting copyrights infringements. Eur J Hum Genet. 2006;14(11):1158-1169. doi:10.1038/sj.ejhg.5201619
5. Kearney HM, Kearney JB, Conlin LK. Diagnostic implications of excessive homozygosity detected by SNP-based microarrays: consanguinity, uniparental disomy, and recessive single-gene mutations. Clin Lab Med. 2011;31(4):595-ix. doi:10.1016/j.cll.2011.08.003

Performance

Method Description

A polymerase chain reaction-based assay, using multiple microsatellite markers (dinucleotide repeats) for the specific chromosome being tested, is used to test DNA from parents and child for the presence of uniparental disomy.(Vnencak-Jones CL. Molecular testing for inherited diseases. Am J Clin Pathol. 1999;112[1 Suppl 1]:S19-S32)

PDF Report
No

Day(s) Performed
Monday and Wednesday

Report Available
5 to 21 days

Specimen Retention Time
Whole blood: 28 days (if available); 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.

CPT Code Information
81402 – proband
81402 (if appropriate for parental specimen)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
UNIPD	Uniparental Disomy	36917-3

Result ID	Test Result Name	Result LOINC® Value
53356	Result Summary	50397-9
53357	Result	36917-3
53358	Interpretation	69047-9
53359	Reason for Referral	42349-1
53360	Specimen	31208-2
53361	Source	31208-2
53362	Method	85069-3

53363	Released By	18771-6