MAYO CLINIC LABORATORIES

Test Definition: DD22F

22q11.2 Deletion/Duplication, FISH, Varies

Overview

Useful For

Establishing a diagnosis of 22q deletion/duplication syndromes

Detecting cryptic rearrangements involving 22q11.2 or 22q11.3 that are not demonstrated by conventional chromosome studies

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
_PBCT	Probe, +2	No, (Bill Only)	No
_PADD	Probe, +1	No, (Bill Only)	No
_PB02	Probe, +2	No, (Bill Only)	No
_PB03	Probe, +3	No, (Bill Only)	No
_ML10	Metaphases, 1-9	No, (Bill Only)	No
_M30	Metaphases, >=10	No, (Bill Only)	No
_IL25	Interphases, <25	No, (Bill Only)	No
_I099	Interphases, 25-99	No, (Bill Only)	No
_I300	Interphases, >=100	No, (Bill Only)	No

Testing Algorithm

This test includes a charge for application of the first probe set (2 fluorescence in situ hybridization (FISH) probes) and professional interpretation of results. Additional charges will be incurred for application of all reflex probes performed. Analysis charges will be incurred based on the number of cells analyzed per probe set. If no cells are available for analysis, no analysis charges will be incurred.

Special Instructions

- Final Disposition of Fetal/Stillborn Remains
- Informed Consent for Genetic Testing
- Informed Consent for Genetic Testing (Spanish)

Method Name

Fluorescence In Situ Hybridization (FISH)

NY State Available

Yes

Specimen

Specimen Type

Varies

Shipping Instructions

Advise Express Mail or equivalent if not on courier service.

Necessary Information

Provide a reason for testing with each specimen. The laboratory will not reject testing if this information is not provided, but appropriate testing and interpretation may be compromised or delayed.

Specimen Required

Submit only 1 of the following specimens:

Specimen Type: Amniotic fluid
Container/Tube: Amniotic fluid container
Specimen Volume: 20-25 mL
Collection Instructions:
1. Optimal timing for specimen collection is during 14 to 18 weeks of gestation, but specimens collected at other weeks of gestation are also accepted. Provide gestational age at the time of amniocentesis.
2. Discard the first 2 mL of amniotic fluid.
Additional Information:
1. Unavoidably, about 1% to 2% of mailed-in specimens are not viable.
2. Bloody specimens are undesirable.
3. If the specimen does not grow in culture, you will be notified within 7 days of receipt.
4. Results will be reported and also telephoned or faxed, if requested.

Specimen Type: Autopsy
Supplies: Hank's Solution (T132)
Container/Tube: Sterile container with sterile Hank's solution, Ringer's solution, or normal saline
Specimen Volume: 1 cm(3) biopsy specimen of muscle/fascia from the thigh
Collection Instructions:
1. Wash biopsy site with an antiseptic soap.
2. Thoroughly rinse area with sterile water.
3. **Do not** use alcohol or iodine preparations.
4. Biopsy specimens are best taken by punch biopsy to include full thickness of dermis.

Specimen Type: Blood
Container/Tube: Green top (sodium heparin)
Specimen Volume: 4 mL
Collection Instructions
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot**.
3. Other anticoagulants are not recommended and are harmful to the viability of the cells.

Specimen Type: Chorionic villi
Supplies: CVS Media (RPMI) and Small Dish (T095)

Container/Tube: 15-mL tube containing 15 mL of transport media
Specimen Volume: 20-25 mg
Collection Instructions:
1. Collect specimen by the transabdominal or transcervical method.
2. Transfer chorionic villi to a Petri dish containing transport medium (such as CVS Media (RPMI) and Small Dish).
3. Using a stereomicroscope and sterile forceps, assess the quality and quantity of the villi and remove any blood clots and maternal decidua.

Specimen Type: Fixed cell pellet
Supplies: Hank's Solution (T132)
Container/Tube: Sterile container with a 3:1 fixative (methanol:glacial acetic acid)
Specimen Volume: Entire specimen

Specimen Type: Products of conception or stillbirth
Supplies: Hank's Solution (T132)
Container/Tube: Sterile container with sterile Hank's solution, Ringer's solution, sterile RPMI transport media, or normal saline
Specimen Volume: 1 cm(3) of placenta (including 20 mg of chorionic villi) **and** a 1-cm(3) biopsy specimen of muscle/fascia from the thigh
Collection Instructions If a fetus cannot be specifically identified, collect villus material or tissue that appears to be of fetal origin.
Additional Information: Do not send entire fetus.

Specimen Type: Skin biopsy
Supplies: Hank's Solution (T132)
Container/Tube: Sterile container with sterile Hank's solution, Ringer's solution, or normal saline
Specimen Volume: 1 cm(3) biopsy specimen of muscle/fascia from the thigh
Collection Instructions:
1. Wash biopsy site with an antiseptic soap.
2. Thoroughly rinse area with sterile water.
3. Do not use alcohol or iodine preparations.
4. A local anesthetic may be used.
5. Biopsy specimens are best taken by punch biopsy to include full thickness of dermis.

Forms

1. **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)
2. Final Disposition of Fetal/Stillborn Remains (if fetal specimen is sent) in Special Instructions (Only for products of conception or stillbirth specimen).
3. If not ordering electronically, complete, print, and send a Cardiovascular Test Request Form (T724) with the specimen.

Specimen Minimum Volume

Amniotic fluid: 5 mL
Autopsy, skin biopsy: 4 mm

Blood: 2 mL
Chorionic villi: 5 mg
Fixed cell pellet: 1 pellet
Products of conception: 1 cm(3)

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	Refrigerated (preferred)		
	Ambient		

Clinical & Interpretive

Clinical Information

The 22q deletion syndrome and 22q duplication syndrome have overlapping phenotypes. Deletions of 22q are associated with DiGeorge and velocardiofacial syndrome. These syndromes are manifested by the presence of growth deficiency, global developmental delay, heart defect, and hearing loss. The major birth defects include palatal clefting or insufficiency and thymus aplasia. Prominent facial features are widely spread eyes, superior placement of eyebrows, downward slanting palpebral fissures with or without ptosis (droopy upper eyelid), mild micrognathia (small jaw), and a long, narrow face.

Fluorescence in situ hybridization (FISH) studies are highly specific and do not exclude other chromosome abnormalities.

Reference Values

An interpretive report will be provided.

Interpretation

Any individual with a normal signal pattern in each metaphase is considered negative for this probe.

Any patient with a fluorescence in situ hybridization (FISH) signal pattern indicating loss of the critical region (1 signal) will be reported as having a deletion of the region tested by this probe. This is consistent with a diagnosis of 22q deletion syndrome.

Any patient with a FISH signal pattern indicating duplication of the critical region (3 signals) will be reported as having a duplication of the region tested by this probe. This is consistent with a diagnosis 22q duplication syndrome

Cautions

This test may fail to detect very small deletions within 22q11.2 or very distal deletions of chromosome 22 at 22q13.3.

Because this fluorescence in situ hybridization(FISH) test is not approved by the US Food and Drug Administration, it is important to confirm 22q deletion/duplication syndrome diagnoses by other established methods, such as clinical history or physical evaluation.

Interfering factors:
-Cell lysis caused by forcing the blood quickly through the needle
-Use of an improper anticoagulant or improperly mixing the blood with the anticoagulant
-Excessive transport time
-Inadequate amount of specimen may not permit adequate analysis
-Improper packaging may result in broken, leaky, and contaminated specimen during transport.
-Exposure of the specimen to temperature extremes (freezing or greater than 30 degrees C) may kill cells and interfere with attempts to culture cells.
-In prenatal specimens, a bloody specimen may interfere with attempts to culture cells and contamination by maternal cells may cause interpretive problems

Supportive Data

Fluorescence in situ hybridization (FISH) analysis was performed on a series of patients and results were compared to cytogenetic analyses and the patient's phenotype. Using a probe for the critical region locus (*HIRA*), FISH analysis of metaphase cells or interphase nuclei identified *HIRA* deletions or duplications in all patients with a phenotype consistent with 22q deletion or duplication syndromes. In a series of patient specimens with normal karyotypes, no deletions or duplications of the *HIRA* region were identified.

Clinical Reference

1. Ensenauer RE, Adeyinka A, Flynn HC, et al: Microduplication 22q11.2 an emerging syndrome: clinical, cytogenetic and molecular analysis of thirteen patients. Am J Hum Genet. 2003;73:1027-1040
2. Yobb TM, Sommerville MJ, Willatt L, et al: Microduplication and triplication of 22q11.2: a highly variable syndrome. Am J Hum Genet. 2005;76:865-876
3. Bassett AS, Chow EWC, Husted J, et al: Clinical features of 78 adults with 22q11 deletion syndrome. Am J Med Genet. 2005;138A:307-313
4. Manji A, Roberson JR, Wiktor A, et al: Prenatal diagnosis of 22q11.2 deletion when ultrasound examination reveals a heart defect. Genet Med. 2001;3:65-66
5. McDonald-McGinn DM, Emanuel BS, Zackai EH: 22q11.2 Deletion Syndrome. GeneReviews. Updated February 27,2020. Accessed April 28, 2023. Available at www.ncbi.nlm.nih.gov/books/NBK1523/

Performance

Method Description

Identification of 22q deletions and duplications is based on fluorescence in situ hybridization analysis of the critical region locus (*HIRA*) on the long arm of chromosome 22 (22q11.2). Metaphase cells are examined for the presence of *HIRA* at 22q11.2 (orange signal) and the control probe arylsulfatase-A at 22q13.3 (green signal). In metaphase cells with a deletion, the abnormal (deleted) chromosome 22 will exhibit only a control probe signal, while signals for both the critical region and control probes will be present on the normal chromosome 22 homolog. Since direct 22q duplications of *HIRA* may be difficult to detect on metaphase cells, interphase nuclei are scored to identify duplications that would be represented by the observation of 3 orange signals.(Crifasi PA, Michels VV, Discoll DJ, et al: DNA fluorescent probes for diagnosis of velocardiofacial and related syndromes. Mayo Clin Proc 1995;195[70]:1148-1153)

PDF Report

No

Day(s) Performed
Monday through Friday

Report Available
2 to 10 days

Specimen Retention Time
Amniotic fluid. (remaining supernatant/whole fluid aliquots): Discarded 14 days after report. Blood: 4 weeks. Products of conception (identifiable fetal tissue): Cremated quarterly after results reported. All other specimens: Discarded when results reported.

Performing Laboratory Location
Rochester

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 using an analyte specific reagent. Its performance characteristics were determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
88271 x 2, 88291-DNA probe, each (first probe set), Interpretation and report
88271 x 2-DNA probe, each; each additional probe set (if appropriate)
88271 x 1-DNA probe, each; coverage for sets containing 3 probes (if appropriate)
88271 x 2-DNA probe, each; coverage for sets containing 4 probes (if appropriate)
88271 x 3-DNA probe, each; coverage for sets containing 5 probes (if appropriate)
88273 w/modifier 52-Chromosomal in situ hybridization, less than 10 cells (if appropriate)
88273-Chromosomal in situ hybridization, 10-30 cells (if appropriate)
88274 w/modifier 52-Interphase in situ hybridization, <25 cells, each probe set (if appropriate)
88274-Interphase in situ hybridization, 25 to 99 cells, each probe set (if appropriate)
88275-Interphase in situ hybridization, 100 to 300 cells, each probe set (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
DD22F	22q11.2 Deletion/Duplication, FISH	82246-0

Test Definition: DD22F

22q11.2 Deletion/Duplication, FISH, Varies

Result ID	Test Result Name	Result LOINC® Value
51851	Result Summary	50397-9
51853	Interpretation	69965-2
54538	Result	62356-1
CG669	Reason For Referral	42349-1
CG670	Specimen	31208-2
51854	Source	31208-2
51855	Method	85069-3
51852	Additional Information	48767-8
51856	Released By	18771-6
53875	Disclaimer	62364-5