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 the probe application, analysis, and professional interpretation of results for one probe set (2 individual fluorescence in situ hybridization probes). 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.

Appropriate ancillary probes may be performed at consultant discretion to render comprehensive assessment. Any additional probes will have the results included within the final report and will be performed at an additional charge.

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

Ordering Guidance
This test does not detect other chromosomal or structural anomalies and is intended to be ordered in conjunction with chromosomal microarray or chromosome analysis.

For detection of unbalanced translocations, deletions, or duplications, chromosomal microarray may be the more appropriate test; order CMACB / Chromosomal Microarray, Congenital, Blood; or CMAP / Chromosomal Microarray, Prenatal, Amniotic Fluid/Chorionic Villus Sampling.

Additional Testing Requirements
Normal fluorescence in situ hybridization (FISH) results will not exclude the majority of cytogenetically detectable abnormalities. As FISH testing is not a substitute for complete cytogenetic analysis, additional cytogenetic testing should be performed in conjunction with this test; order CMACB / Chromosomal Microarray, Congenital, Blood; or CHRCB / Chromosome Analysis, Congenital Disorders, Blood

Shipping Instructions
Advise Express Mail or equivalent if not on courier service.

Necessary Information
A reason for testing must be provided. The laboratory will not reject testing if this information is not provided however an applicable indication for testing may be entered by Mayo Clinic Laboratories. Appropriate testing and interpretation may be compromised or delayed.

Specimen Required
Submit only 1 of the following specimens:

Preferred:
Specimen Type: Whole blood
Container/Tube:
Preferred: Green top (sodium heparin)
Acceptable: Lavender top (EDTA) or yellow top (ACD)
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.
4. Cord blood is acceptable
Additional Information:
1. If the specimen does not grow in culture, you will be notified within 7 days of receipt.
2. Specimen cannot be frozen.

Acceptable:
Specimen Type: Fixed cell pellet
Container/Tube: Sterile container with a 3:1 fixative (methanol:glacial acetic acid)
Specimen Volume: Entire specimen

Specimen Type: Amniotic fluid
Container/Tube: Amniotic fluid container
Specimen Volume: 20 to 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.
3. If ordering with CMAP / Chromosomal Microarray, Prenatal, Amniotic Fluid/Chorionic Villus Sampling, submit a minimum of 12 mL.
4. If ordering with CHRAF / Chromosome Analysis, Amniotic Fluid, submit a minimum of 12 mL.
5. If ordering with both CMAP and CHRAF, submit a minimum of 26 mL.
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. Specimen cannot be frozen.

Specimen Type: Chorionic villi
Container/Tube: 15-mL tube containing 15 mL of transport media
Specimen Volume: 20 to 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 (T095).
3. Using a stereomicroscope and sterile forceps, assess the quality and quantity of the villi and remove any blood clots and maternal decidua.
4. If ordering with CMAP / Chromosomal Microarray, Prenatal, Amniotic Fluid/Chorionic Villus Sampling, submit a minimum of 12 mg.
5. If ordering with CHRCV / Chromosome Analysis, Chorionic Villus Sampling, submit a minimum of 12 mg.
6. If ordering with both CMAP and CHRCV, then submit a minimum of 26 mg.
Additional Information:
1. Label each container with the specimen type, patient's name, and laboratory control number.
2. Specimen cannot be frozen.

Specimen Type: Products of conception or stillbirth
Supplies: Hank's Solution (T132)
Container/Tube: Sterile container with sterile Hank's balanced salt 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:

1. Do not handle specimen with hands.
2. If a fetus cannot be specifically identified, collect 50-mg villus material or tissue that appears to be of fetal origin.

Additional Information:

1. **Do not** send the entire fetus.
2. If a fetus is sent, please provide a parental release form or complete the Final Disposition of Fetal/Stillborn Remains form and send it with the fetus. (A copy of this form can be found in Special Instructions.) Please note that completion of the form requires a parent's signature.

3. Specimen cannot be frozen.

4. While fresher specimens prepared as described above are preferred, we can attempt analysis on specimens that have been in less-than-ideal conditions.
5. Label each container with the specimen type, patient's name, and laboratory control number.

Specimen Type: Autopsy
Supplies: Hank's Solution (T132)
Container/Tube: Sterile container with sterile Hank's balanced salt solution, Ringer's solution, sterile RPMI transport media, 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.

Additional Information:

1. Label each container with the specimen type, patient's name, and laboratory control number.

2. Specimen cannot be frozen.

Specimen Type: Skin biopsy
Supplies: Hank's Solution (T132)
Container/Tube: Sterile container with sterile Hank's balanced salt solution, Ringer's solution, sterile RPMI transport media, 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.

Additional Information:

1. Label each container with the specimen type, patient's name, and laboratory control number.

2. Specimen cannot be frozen.

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) 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; Whole 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 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 q13.3.

This test is not approved by the US Food and Drug Administration, and it is best used as an adjunct with other established methods to a confirm 22q deletion/duplication syndrome diagnoses, such as existing clinical history or physical evaluation.

This test is not designed to detect low-level mosaicism.

Chromosomal microarray (CMACB / Chromosomal Microarray, Congenital, Blood or CMAP / Chromosomal Microarray, Prenatal, Amniotic Fluid/Chorionic Villus Sampling) may be the more appropriate test to detect unbalanced translocations, deletions or duplications.

Interfering factors:
-Cell lysis caused by forcing the blood quickly through the needle
-Use of an improper anticoagulant (sodium heparin is best) 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 (either freezing or >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

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(5):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(5):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;138(4):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(1):65-66
5. McDonald-McGinn DM, Emanuel BS, Zackai EH: 22q11.2 Deletion Syndrome. GeneReviews. Updated May 9, 2024. Accessed June 13, 2024. Available at www.ncbi.nlm.nih.gov/books/NBK1523/

Performance

Method Description

This test is performed using a commercially available enumeration strategy probe set including the critical region locus (*HIRA*) on the long arm of chromosome 22 (22q11.2) and the control probe arylsulfatase-A at 22q13.3. Ten metaphase cells are examined for deletion or duplication of the HIRA fluorescence in situ hybridization probe. Since 22q duplications of *HIRA* may be difficult to detect on metaphase cells, 200 interphase nuclei are scored to identify duplications.(Crifasi PA, Michels VV, Driscoll DJ, Jalal SM, Dewald GW. DNA fluorescent probes for diagnosis of velocardiofacial and related syndromes. Mayo Clin Proc. 1995;70(12):1148-1153)

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
7 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 (eg, placenta, chorionic villus): Discarded when results reported.

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 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