MAYO CLINIC LABORATORIES

Test Definition: WS7F

Williams Syn, 7q11.23 Del, FISH

Overview

Useful For

Establishing a diagnosis of Williams syndrome

Detecting cryptic rearrangements involving 7q11.23 that are not demonstrated by conventional chromosome studies

Testing Algorithm

This test includes a charge for application of the first probe set (2 FISH probes) and professional interpretation of results. Additional charges will be incurred for 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

- Informed Consent for Genetic Testing
- Informed Consent for Genetic Testing (Spanish)

Reflex Tests

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

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 referral 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

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Advise Express Mail or equivalent if not on courier service.

Submit only 1 of the following specimens:

Preferred:

Specimen Type: Blood

Container/Tube: Green top (sodium heparin)

Specimen Volume: 5 mL

Collection Instructions:

1. Invert several times to mix blood.
2. Other anticoagulants are not recommended and are harmful to the viability of the cells.

Acceptable:

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. Place the tubes in a Styrofoamcontainer (T329).
2. Fill remaining space with packing material.
3. Unavoidably, about 1% to 2% of mailed-in specimens are not viable.
4. Bloody specimens are undesirable.
5. If the specimen does not grow in culture, you will be notified within 7 days of receipt.
6. Results will be reported and also telephoned or faxed, if requested.

Specimen Type: Chorionic villi

Container/Tube: 15-mL tube containing 15 mL of transport medium

Specimen Volume: 20-30 mg

Collection Instructions:

1. Collect specimen by the transabdominal or transcervical method.
2. Transfer chorionic villi to Petri dish containing transport medium (T095).
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: Skin biopsy

Container/Tube: Sterile container with sterile Hank's balanced salt solution (T132), Ringer's solution, or normal saline

Specimen Volume: 4 mm diameter

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

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 in Special Instructions:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing-Spanish (T826)

Reject Due To

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

Specimen Minimum Volume

Amniotic Fluid: 5 mL/Blood: 2 mL/Chorionic Villi: 5 mg

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Refrigerated (preferred)		
	Ambient		

Clinical & Interpretive

Clinical Information

Williams syndrome (WS) is a genetic disorder that occurs in 1/20,000 to 1/50,000 live births. Although WS is typically a sporadic disorder, familial cases have been reported.
WS is characterized by a variable combination of cardiovascular abnormalities, connective tissue abnormalities, distinct facial features, infantile hypercalcemia, mental retardation, and characteristic social interactions such as extreme friendliness and attention-deficit hyperactivity disorder.
Isolated congenital narrowing of the ascending aorta is common in WS patients and results in a separate syndrome called supravalvular aortic stenosis (SVAS).
WS is a contiguous gene deletion syndrome, caused by deletion of several genes on chromosome 7q. One gene that often is deleted in WS is the elastin gene, which causes SVAS and other cardiovascular disease in these patients. This association was described by Ewart et al (1993) who identified hemizygosity of the elastin gene in WS and SVAS.
The elastin gene, *ELN*, has been mapped to 7q11.23 (Williams syndrome chromosome region, and is reportedly hemizygous in up to 96% of patients with WS). The deletion of an elastin gene locus cannot be detected by conventional high-resolution chromosome analysis in the vast majority of cases due to the small size of this deletion. Nickerson et al used molecular methods to detect a deletion of the elastin gene in 91% (39/43) of WS patients.
In up to 1% of patients, WS is caused by a gene mutation within or near the elastin gene. These mutations would not be detected by this FISH test. FISH testing involves a DNA probe that detects only large deletions including this entire gene and the DNA probe, small deletions or mutations may give normal results by FISH.
Patients with a deletion outside of the elastin gene could display normal development of connective tissue, including the heart, but have other features of WS.

Reference Values

An interpretive report will be provided.

Interpretation

The use of high-resolution chromosome studies and FISH for Williams syndrome chromosome region should diagnose about 96% of Williams syndrome patients and, at the same time, identify any other chromosome anomalies.

Cautions

Because this FISH test is not approved by the US Food and Drug Administration it is important to confirm Williams syndrome (WS) by other established methods, such as clinical history or physical evaluation.
Chromosomal microarray (CMACB / Chromosomal Microarray, Congenital, Blood or CMAP / Chromosomal Microarray, Prenatal) 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 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 >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. Morris CA: Williams Syndrome. In GeneReviews, Accessed 05/22/2013. Available at: www.ncbi.nlm.nih.gov/books/NBK1249/
2. American Academy of Pediatrics: Health care supervision for children with Williams syndrome. Pediatrics 2001;107:1192-204

Performance

Method Description

This test is performed using commercially available probe for the elastin Williams syndrome (WS) chromosome region (*ELN*) at 7q11.23. Metaphase cells are examined for the presence *ELN*.(Unpublished Mayo method)

PDF Report

No

Specimen Retention Time

Amniotic Fl. (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

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

88271x2, 88291-DNA probe, each (first probe set), Interpretation and report
88271x2-DNA probe, each; each additional probe set (if appropriate)
88271x1-DNA probe, each; coverage for sets containing 3 probes (if appropriate)
88271x2-DNA probe, each; coverage for sets containing 4 probes (if appropriate)
88271x3-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)