# Test Definition: IN16Q

CBFB::MYH11 Inversion(16), Quantitative Detection and Minimal Disease Risk Monitoring, qRT-PCR, Varies

## Overview

### Useful For

Detection of *CBFB::MYH11* gene fusion in patients recently diagnosed with acute myeloid leukemia (AML)

Minimal residual disease monitoring during the clinical and therapeutic course of patients with AML

### Highlights

This test is a highly sensitive quantitative assay for the detection of inv(16)(p13.1q22) or t(16;16)(p13.1;q22) *CBFB::MYH11* gene fusion. This detection is useful for patients with acute myeloid leukemia at the time of diagnosis as well as for minimal residual disease monitoring during the clinical and therapeutic course of these patients.

### Method Name

Quantitative Real-Time Reverse Transcription Polymerase Chain Reaction (qRT-PCR)

### NY State Available

Yes

## Specimen

### Specimen Type

Varies

### Shipping Instructions

**1. Refrigerated specimens must arrive within 5 days of collection, and ambient specimens must arrive within 3 days of collection.**

2. Collect and package specimen as close to shipping time as possible.

### Necessary Information

**The following information is required:**

1. Pertinent clinical history
2. Date of collection
3. Specimen source (blood or bone marrow)

### Specimen Required

**Submit only 1 of the following specimens:**

**Specimen Type:** Blood

**Container/Tube:** Lavender top (EDTA) or yellow top (ACD-B)

**Specimen Volume:** 10 mL
**Collection Instructions:**
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot**.
3. Label specimen as blood.

**Specimen Type:** Bone marrow
**Container/Tube:** Lavender top (EDTA) or yellow top (ACD-B)
**Specimen Volume:** 4 mL
**Collection Instructions:**
1. Invert several times to mix bone marrow.
2. Send bone marrow specimen in original tube. **Do not aliquot**.
3. Label specimen as bone marrow.

## Forms

1. Hematopathology Patient Information (T676)
2. If not ordering electronically, complete, print, and send an Hematopathology/Cytogenetics Test Request (T726) with the specimen.

## Specimen Minimum Volume

Blood: 8 mL; Bone marrow: 2 mL

## Reject Due To

| | |
|---|---|
| Gross hemolysis | Reject |
| Bone marrow core biopsies<br>Paraffin-embedded bone marrow clots<br>Slides<br>Paraffin shavings<br>Moderately to severely clotted | Reject |

## Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---|---|---|---|
| Varies | Refrigerated (preferred) | 5 days | |
| | Ambient | 72 hours | |

## Clinical & Interpretive

### Clinical Information

*CBFB::MYH11* minimal residual disease (MRD) monitoring in patients with acute myeloid leukemia (AML) with inv(16) or t(16;16) is useful for evaluating disease response after therapy and identifying individuals with increased risk of relapse. Quantitative real-time reverse transcription polymerase chain reaction testing in neoplasms with known clonal genetic markers can achieve highly sensitive detection of neoplastic cells in peripheral blood or bone marrow specimens. It is one of the most mature technologies available for this purpose. In this assay, inversion or translocation of chromosome 16 resulting in fusion of two genes, *CBFB* and *MYH11*, will be evaluated. Quantitative results will provide physicians with an accurate and precise measurement of disease burden to guide patient intervention decisions. This assay can be used for post-therapy MRD monitoring as well as detection of *CBFB::MYH11* fusion in AML patients at the time of diagnosis.

### Reference Values

An interpretive report will be provided.

### Interpretation

The assay is reported in the form of a normalized ratio of *CBFB::MYH11* fusion transcript to the control gene *ABL1* expressed as a percentage, which is an estimate of the level of *CBFB::MYH11* fusion RNA present in the specimen, expressed in relation to the level of RNA from an internal control gene (*ABL1*). The normalized ratio has no units but is directly related to the level of *CBFB::MYH11* detected (ie, larger numbers indicate higher relative levels of *CBFB::MYH11*, and smaller numbers indicate lower levels). A relative expression value minimizes variability in the RNA levels and cell numbers measured in separate specimens tested at different times.

The precision of the quantitative assay is excellent, but interassay variability can occur such that result changes should not be considered significant if 2 single measurements differ by less than 0.5 log. More critical results, such as a change in the status of positivity or greater or equal to 1 log increase between 2 positive samples should be repeated on a separate specimen with appropriate time interval to verify the result.

### Cautions

This assay will only detect the 3 major types of exon fusions of *CBFB::MYH11* (> or =95%) and will not detect messenger RNA from rare fusion of *CBFB::MYH11* (<5%).

### Clinical Reference

1. Krauter J1, Hoellge W, Wattjes MP, et al. Detection and quantification of *CBFB/MYH11* fusion transcripts in patients with inv(16)-positive acute myeloblastic leukemia by real-time RT-PCR. Genes Chromosomes Cancer. 2001;30(4):342-348. doi:10.1002/gcc.1100
2. Dohner H, Estey E, Grimwade D, et al. Diagnosis and management of AML in adults: 2017 ELN recommendations from an international expert panel. Blood. 2017;129(4):424-447. doi:10.1182/blood-2016-08-733196
3. O'Donnell MR, Tallman MS, Abboud CN, et al. Acute Myeloid Leukemia, Version 3.2017, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2017;15(7):926-957. doi:10.6004/jnccn.2017.0116
4. Schuurhuis GJ, Heuser M, Freeman S, et al. Minimal/measurable residual disease in AML: a consensus document from the European Leukemia Net MRD Working Party. Blood. 2018;131(12):1275-1291. doi:10.1182/blood-2017-09-801498

5. Jourdan E, Boissel N, Chevret S, et al. Prospective evaluation of gene mutations and minimal residual disease in patients with core binding factor acute myeloid leukemia. Blood. 2013;121(12):2213-2223. doi:10.1182/blood-2012-10-462879
6. Lane S, Saal R, Mollee P, et al. A > or =1 log rise in RQ-PCR transcript levels defines molecular relapse in core binding factor acute myeloid leukemia and predicts subsequent morphologic relapse. Leuk Lymphoma. 2008;49(3):517-523. doi:10.1080/10428190701817266
7. Yin JA, O'Brien MA, Hills RK, Daly SB, Wheatley K, Burnett AK. Minimal residual disease monitoring by quantitative RT-PCR in core binding factor AML allows risk stratification and predicts relapse: results of the United Kingdom MRC AML-15 trial. Blood. 2012;120(14):2826-2835. doi:10.1182/blood-2012-06-435669
8. Corbacioglu A, Scholl C, Schlenk RF, et al. Prognostic impact of minimal residual disease in CBFB-MYH11-positive acute myeloid leukemia. J Clin Oncol. 2010;28(23):3724-3729. doi: 10.1200/JCO.2010.28.6468

## Performance

### Method Description

Total RNA is extracted from blood or bone marrow and reverse transcribed to generate complementary DNA. Quantitative real-time reverse transcription polymerase chain reaction is performed using the LightCycler instrument platform, and the data analyzed using the dedicated software for relative quantification with calibrator normalization. Results are provided as a normalized relative value of *CBFB::MYH11::ABL1* messenger RNA transcripts with a reproducible analytical sensitivity of 0.01%.(Unpublished Mayo method)
The normalized ratio is a relative quantification calculation as follows:

$$\text{Normalized ratio} = \frac{\textit{CBFB::MYH11} \text{ (sample)}/\textit{ABL1} \text{ (sample)}}{\textit{CBFB::MYH11} \text{ (run calibrator)}/\textit{ABL1} \text{ (run calibrator)}}$$

### PDF Report

Supplemental

### Day(s) Performed

Monday through Saturday

### Report Available

4 to 8 days

### Specimen Retention Time

Blood/Bone marrow: 2 weeks; Extracted RNA: 3 months

### Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

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## 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

81401-*CBFB-MYH11*

### LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---|---|---|
| IN16Q | Inv(16); CBFB-MYH11, Quant, V | 101377-0 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|
| MP057 | Specimen Type | 31208-2 |
| 610267 | Interpretation | 59465-5 |
| 614375 | Signing Pathologist | 19139-5 |