MAYO CLINIC LABORATORIES

Test Definition: MFCDF

Myeloma, High Risk with Reflex Probes, Diagnostic FISH Evaluation, Fixed Cell Pellet

Overview

Useful For

Aiding in the diagnosis of new cases of multiple myeloma or other plasma cell proliferative disorders using a fixed cell pellet derived from bone marrow

Identifying prognostic markers based on the abnormalities found

This test **should not be used** to track the progression of disease.

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
MFCDB	Probe, Each Additional (MFCDF)	No, (Bill Only)	No

Testing Algorithm

This test includes a charge for the probe application, analysis, and professional interpretation of results for 3 probe sets (6 individual fluorescence in situ hybridization [FISH] probes). Additional charges will be incurred for all reflex or additional probe sets performed.

This test is designed for diagnostic bone marrow specimens from patients with multiple myeloma or other plasma cell proliferative disorders. Best results are obtained when the bone marrow demonstrates at least 20% involvement by a plasma cell proliferative disorder.

The FISH panel includes testing for the following abnormalities using the FISH probes listed:

For **diagnostic** samples, the following probes will be evaluated:
17p-, TP53/D17Z1
1q gain, TP73/1q22
14q32 rearrangement, IGH break-apart
Based on the results from the initial panel, reflex testing may be performed to identify the following abnormalities using the probes listed:
t(11;14)(q13;q32), CCND1/IGH fusion
t(14;16)(q32;q23), IGH/MAF fusion
t(4;14)(p16.3;q32), FGFR3/IGH fusion
t(14;20)(q32;q12), IGH/MAFB fusion

For **follow-up** samples, the following probes will be evaluated if sufficient plasma cells are identified:
If a previous diagnostic sample was uninformative for a probe set, attempts may be made to achieve results for the missing probe on a subsequent sample.
17p-, TP53/D17Z1

1q gain, TP73/1q22
8q24.1 rearrangement, MYC break-apart

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.

Method Name
Fluorescence In Situ Hybridization (FISH)

NY State Available
Yes

Specimen

Specimen Type
Fixed Cell Pellet Bone Marrow

Ordering Guidance
For the most complete genetic evaluation on fresh bone marrow specimens, order MPCDS / mSMART, Plasma Cell Proliferative Disorder, FISH, Bone Marrow.
For evaluation of high-risk abnormalities plus CCND1/IGH fusion on fresh bone marrow specimens, order PCPDS / Plasma Cell Proliferative Disorder, High Risk with Reflex Probes, Diagnostic FISH Evaluation, Bone Marrow.

For testing paraffin-embedded tissue samples from patients with a plasma cell disorder, order PLASF / Plasma Cell Proliferative Disorder, FISH, Tissue.

Testing will be changed to the appropriate test if this test is ordered on paraffin or a fresh bone marrow specimen.

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

Necessary Information
A reason for testing and a flow cytometry and/or a bone marrow pathology report should be sent 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. If this information is not provided, an appropriate indication for testing may be entered by Mayo Clinic Laboratories.

Specimen Required
Container/Tube: Sterile container
Specimen Volume: 1 Fixed cell pellet
Collection Instructions: Place specimen in a sterile container with a 3:1 methanol:glacial acetic acid (or similar) fixative.

Forms

If not ordering electronically, complete, print, and send a Hematopathology/Cytogenetics Test Request (T726) with the specimen.

Reject Due To

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

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Fixed Cell Pellet Bone Marrow	Ambient (preferred)		
	Refrigerated		

Clinical & Interpretive

Clinical Information

Multiple myeloma is a hematologic neoplasm that generally originates in the bone marrow and develops from malignant plasma cells. There are 4 main categories of plasma cell proliferative disorders: monoclonal gammopathy of undetermined significance (MGUS), monoclonal immunoglobulin deposition diseases (amyloidosis), plasmacytoma, and multiple myeloma. MGUS, which occurs in 3% to 4% of individuals over 50 years of age, represents the identification of an asymptomatic monoclonal protein, yet approximately 1% per year will progress to multiple myeloma. Amyloidosis represents a rare group of deposition disorders including primary amyloidosis vs. light chain and heavy chain disease. Plasmacytomas represent isolated collections of bone or extramedullary plasma cells with a risk for development of multiple myeloma. Generalized bone pain, anemia, limb numbness, or weakness, symptoms of hypercalcemia, and recurrent infections are all symptoms that may indicate multiple myeloma.

As myeloma progresses, the malignant plasma cells interfere with normal blood product formation in the bone marrow resulting in anemia and leukopenia. Myeloma also causes an overstimulation of osteoclasts, causing excessive breakdown of bone tissue without the normal corresponding bone formation. These bone lesions are seen in approximately 66% of myeloma patients. In advanced disease, bone loss may reach a degree where the patient suffers fractures easily.

Multiple myeloma is increasingly recognized as a disease characterized by marked cytogenetic, molecular, and proliferative heterogeneity. This heterogeneity is manifested clinically by varying degrees of disease aggressiveness. Multiple myeloma patients with more aggressive disease experience suboptimal responses to some therapeutic approaches; therefore, identifying these patients is critically important for selecting appropriate treatment options.

Reference Values

An interpretive report will be provided.

Interpretation

A neoplastic clone is detected when the percent of cells with an abnormality exceeds the normal reference range for any given probe.

The absence of an abnormal clone does not rule out the presence of neoplastic disorder.

Cautions

This test is not approved by the US Food and Drug Administration, and it is best used as an adjunct to existing clinical and pathologic information.

Supportive Data

Each probe was independently tested and verified on unstimulated peripheral blood and bone marrow specimens. Normal cutoffs were calculated based on the results of 25 normal specimens. Each probe set was evaluated to confirm the probe set detected the abnormality it was designed to detect.

Clinical Reference

1. Swerdlow S, Campo E, Harris NL, et al, eds: WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. IARC Press; 2017
2. Kumar SK, Rajkumar SV: The multiple myelomas-current concepts in cytogenetic classification and therapy. Nat Rev Clin Oncol. 2018;15(7):409-421. doi: 10.1038/s41571-018-0018-y
3. Rajkumar SV, Landgren O, Mateos MV: Smoldering multiple myeloma. Blood. 2015 May 14;125(20):3069-3075. doi: 10.1182/blood-2014-09-568899
4. Muchtar E, Dispenzieri A, Kumar S, et al: Interphase fluorescence in situ hybridization in untreated AL amyloidosis has an independent prognostic impact by abnormality type and treatment category. Leukemia. 2017 Jul;31(7);1562-1569. doi: 10.1038/leu.2016.369
5. Lakshman A, Paul S, Rajkumar SV, et al: Prognostic significance of interphase FISH in monoclonal gammopathy of undetermined significance. Leukemia. 2018 Aug;32(8);1811-1815. doi: 10.1038/s41375-018-0030-3
6. Bochtler T, Hegenbart U, Kunz C, et al: Prognostic impact of cytogenetic aberrations in AL amyloidosis patients after high-dose melphalan: a long-term follow-up study. Blood. 2016 Jul 28;128(4):594-602. doi: 10.1182/blood-2015-10-7
7. Treatment guidelines: multiple myeloma. mSMART 3.0. Accessed 01/16/2020. Available at www.msmart.org/mm-treatment-guidelines

Performance

Method Description

This test is performed using commercially available and laboratory-developed probes. Deletion or monosomy of chromosome 17 and copy number gain of 1q are detected using enumeration strategy probes. Translocations involving *IGH* are detected using dual-color, dual-fusion fluorescence in situ hybridization strategy probes. Rearrangement of *IGH* and *MYC* are detected using a break-apart strategy probe. For each probe set, 50 plasma cells (if possible) are scored and the result for each probe is reported.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Friday

Test Definition: MFCDF

Myeloma, High Risk with Reflex Probes,
Diagnostic FISH Evaluation, Fixed Cell Pellet

Report Available
7 to 10 days

Specimen Retention Time
4 weeks

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
88271x6, 88275x3, 88291 x1-FISH Probe, Analysis, Interpretation; 3 probe sets
88271x2, 88275x1-FISH Probe, Analysis; each additional probe set (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
MFCDF	Myeloma Fixed Cell, High Risk, FISH	In Process

Result ID	Test Result Name	Result LOINC® Value
614300	Result Summary	50397-9
614301	Interpretation	69965-2
614302	Result Table	93356-4
614303	Result	62356-1
GC128	Reason for Referral	42349-1
614304	Specimen	31208-2
614306	Method	85069-3
614307	Additional Information	48767-8
614308	Disclaimer	62364-5
614309	Released By	18771-6
614305	Source	31208-2