Multiple Myeloma by FISH

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Multiple myeloma (MM) is a plasma cell dyscrasia that can evolve from a premalignant monoclonal gammopathy. Prognosis often depends on the presence or absence of particular genetic markers. Fluorescence in situ hybridization (FISH) testing for relevant markers should be performed upon diagnosis and in low-risk individuals at time of relapse to aid in risk stratification.[1]

Featured ARUP Testing

Multiple Myeloma Panel by FISH 3002063

Method: Fluorescence in situ Hybridization (FISH)

Detects genetic abnormalities predictive of outcome in individuals with MM

Test Description

Plasma cells are isolated from a bone marrow (BM) aspirate using CD138+ microbeads. CD138+ cells (plasma cells) are then analyzed by FISH using specific probes for the following:

- *CKS1B* (1q gain/amplification)
- *FGFR3/IGH* fusion t(4;14)
- *ASS1* (+9)
- *CCND1/IGH* fusion t(11;14) and/or (+11)
- *MAF/IGH* fusion t(14;16)
- *MAFB/IGH* fusion t(14;20)
- *TP53* (17p deletion)

Disease Overview

Incidence

1.8% of all cancers in the U.S.[2]

Age of Onset

Most frequently diagnosed between ages 65 and 74 years (median age 69 years)[2]

Symptoms

Presenting clinical features include symptoms of[1,2]:

- Hypercalcemia
- Impaired renal function
- Anemia
- Bone disease (lesions)

FISH Testing and Prognostic Issues

Abnormalities are detected by conventional cytogenetics in approximately 30% of MMs. FISH testing increases this number to >90%.[1] Cytogenetic abnormalities affect the prognosis of patients with MM. Because most genetic subtypes in MM are primary, ploidy state, *IGH* translocation, and genetic status need only be assessed once at diagnosis.[3] However, repeat testing is justified in cases of gain/amplification of *CKS1B* (1q21) and deletion of *TP53* (17p13), as these markers occur in disease progression and confer a worse prognosis.[1,3]

Genetic Markers and Resulting Prognostic Issues		
Markers	**Characteristics and Prognostic Value**	**Recurrent Testing[3]**
Primary Cytogenetic Abnormalities		
Hyperdiploidy Usually gains (trisomies) of three or more odd-numbered chromosomes (3, 5, 7, 9, 11, 15, 19, 21)	Presence: 40-60% of MM[1,4] Standard risk[1] Infrequently occurs with IGH translocations[1,4] Panel tests two of the most commonly gained chromosomes (9, 11)	Test only once
t(4;14)(p16;q32) *IGH-FGFR3/MMSET*	Presence: 5% of MM[1,3] High to intermediate risk[3,4] Detectable only by FISH (cytogenetically cryptic)	Test only once
t(11;14)(q13;q32) *IGH-CCND1*	Presence: 15% of MM[3] Standard risk[1,3]	Test only once
t(14;16)(q32;q23) *IGH-MAF*	Presence: 5% of MM[3] High risk[1,3]	Test only once
t(14;20)(q32;q12) *IGH-MAFB*	Presence: 1-2% of MM[3,4] High risk[1,3]	Test only once
Secondary Cytogenetic Abnormalities		
Gain/amplification of 1q21 (*CKS1B*)	Presence: 30-70% of MM[4,5] Presence higher in disease progression High risk May be observed in hypodiploid, hyperdiploid, and *IGH* translocation-positive MM Confers a poor prognosis in all subtypes	Repeat testing justified
Deletion 17p (*TP53*)	Presence: 5-10% of MM Presence higher in disease progression High risk[1,4] May be observed in hypodiploid, hyperdiploid, and *IGH* translocation-positive MM Confers a poor prognosis in all subtypes	Repeat testing justified

Test Interpretation

Analytic Sensitivity/Specificity

>95%

Results

- Abnormal: gain/loss/rearrangement/translocation detected; percentage of cells affected (out of 100 or 200) reported
- Normal: no evidence of gains, deletions, rearrangements, or translocations of loci tested

Limitations

Only detects aberrations specific to probes used

References

1. Swerdlow S, Campo E, Jaffe E, et al. *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues.* 4th ed. International Agency for Research on Cancer; 2017.

2. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Multiple myeloma. Version 2.2020. [Accessed: Mar 2020]

3. Fonseca R, Bergsagel PL, Drach J, et al. International Myeloma Working Group molecular classification of multiple myeloma: spotlight review. *Leukemia*. 2009;23(12):2210-2221.

4. Rajan AM, Rajkumar SV. Interpretation of cytogenetic results in multiple myeloma for clinical practice. *Blood Cancer J*. 2015;5(10):e365.

5. Hanamura I, Stewart JP, Huang Y, et al. Frequent gain of chromosome band 1q21 in plasma-cell dyscrasias detected by fluorescence in situ hybridization: incidence increases from MGUS to relapsed myeloma and is related to prognosis and disease progression following tandem stem-cell transplantation. *Blood*. 2006;108(5):1724-1732.

Related Information

Plasma Cell Dyscrasias
Plasma Cell Dyscrasias Testing Algorithm

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