

# Myelodysplastic Syndrome (MDS) Panel by FISH

## *DETECTION OF SPECIFIC RECURRENT GENOMIC ABERRATIONS IN MYELODYSPLASTIC SYNDROME (MDS) BY FLUORESCENCE IN SITU HYBRIDIZATION (FISH)*

### Test Highlights

- This test provides significant prognostic information for MDS and is suitable for widespread use.
- Hematopoietic neoplasms that can be detected using this test include:
  - Refractory cytopenias [refractory anemia (RA), refractory neutropenia (RN), and refractory thrombocytopenia (RT)]
  - Refractory anemia with ringed sideroblasts (RARS)
  - Refractory cytopenia with multilineage dysplasia (RCMD)
  - Refractory anemia with excess blasts-1 (RAEB-1)
  - Refractory anemia with excess blasts-2 (RAEB-2)
  - Myelodysplastic syndrome, unclassifiable (MDS-U)
  - Myelodysplastic syndrome with isolated deletion of 5q (5q-)
- Acute myeloid leukemia may also include abnormalities detectable by this FISH panel.
- FISH may detect specific genomic aberrations that are not detected by cytogenetics.
- This test aids in monitoring response to therapy or progression of disease.

### Clinical Background

- Myelodysplastic disorders are clonal hematopoietic malignancies characterized by ineffective hematopoiesis, cytopenia, unilineage or multilineage dysplasia, and susceptibility to leukemia. They are most common in adults, particularly in the elderly population, and the incidence in males is twice that in females. 10–15 percent of MDS occurs following treatment with chemotherapy and radiation (therapy-related MDS, t-MDS). A separate category of disease, myelodysplastic/myeloproliferative neoplasm, unclassifiable, includes myeloid disorders with features intermediate between MPD and MDS.
- Classification of MDS is based on bone marrow histology, cytochemical and immunophenotypic features, and cytogenetic findings. Genetic studies are required at diagnosis not only for identifying specific genetic abnormalities but also for monitoring disease progression.
- Recurrent cytogenetic abnormalities observed in MDS include deletions in the long arm of chromosome 5 (5q-); monosomy 7 or deletions in the long arm of chromosome 7 (7q-); trisomy 8; and deletions in the long arm of chromosome 20 (20q-).
- The International Prognostic Scoring System (IPSS) was developed by the Myelodysplastic Syndrome Working Group to predict survival in patients with MDS. This system combines information on bone marrow blast percentage, cytogenetic abnormalities, and type(s) of cytopenia into low, intermediate-1, intermediate-2, and high-risk disease. The IPSS scoring system is also useful in predicting the outcome of allogeneic stem cell transplantation in patients with MDS. In this system, cytogenetic abnormalities are classified as follows:

- Good risk: normal karyotype, isolated del(5q), isolated del(20q), and -Y
- Poor risk: abnormalities of chromosome 7 or complex karyotype with three or more abnormalities
- Intermediate risk: all other abnormalities
- Standard chromosome analysis using metaphase cells requires dividing cells and remains the gold standard for the detection of cytogenetic abnormalities. However, cytogenetically visible rearrangements can sometimes be missed due to suboptimal chromosome morphology, lack of dividing neoplastic cells, or preferential growth of normal cells in culture.
- In a diagnostic cytogenetics laboratory, FISH analysis has several advantages over chromosome studies. It has a rapid turnaround time, detects small numbers of abnormal cells, and can also be performed on non-dividing (interphase) cells. In addition, FISH can detect cryptic or subtle rearrangements that might be difficult to detect by routine karyotyping.

### Indications for Ordering

- Myeloid dysplasia, cytopenias.
- FISH testing is indicated at the time of diagnosis for proper classification. However, it may be also used for follow-up studies, either to monitor response to therapy or progression of the disease.

### Additional Ordering Notes

- A sodium-heparin (green-top) tube with 3–4 mL of bone marrow is required.
- Samples should be stored at room temperature and transported to the laboratory within 24 hours of draw.

## Methodology

- Bone marrow cells on unstimulated cultures either from direct harvest or 24-hour culture are analyzed by FISH using a set of commercially available FISH probes.
- Each probe can be run as a part of the panel or individually.
- The FISH probes for del(5q), del(q)/monosomy 7, trisomy 8, and del(20q) are set up separately for each patient.
- Hybridization and detection of hybridization signals are performed according to the manufacturer's protocols.
- At least two technologists score each case.
- 200 nuclei are evaluated for each probe.
- Bone marrow samples from 20 individuals without apparent hematological diseases and with normal karyotype are used as controls for each probe to determine the cutoff value for normal variation of the probe-signal patterns.

## Limitations

- This probe panel only detects specific aberrations in the chromosomes of interest for diagnosis and prognosis.
- Chromosome alterations outside the regions complementary to these FISH probes will not be detected.

## Tests Available

FISH panel for myelodysplastic syndrome:

	CHROMOSOME ABNORMALITIES	PROBE NAMES (GENES INVOLVED)	PROBE TYPE
1.	Deletion 5q	D5S23, D5S721 as control(EGR1)	Dual color
2.	Deletion 7q/monosomy 7	D7Z1/D7S486	Dual color
3.	Trisomy 8	CEP8	Single color
4.	Deletion 20q	D20S108	Single color

## References

1. Myelodysplastic syndromes. In *Cancer Cytogenetics*, 3rd ed. Heim S and Mitelman F, eds. 2009; Hoboken, NJ: Wiley-Blackwell.
2. Swerdlow SH, et al. 2008. *WHO classification of tumours of haematopoietic and lymphoid tissues*, 4th ed. Lyon, France: International Agency for Research on Cancer.

## Test Information

**2002709**

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For specific collection, transport, and testing information, refer to the ARUP Web site at [www.aruplab.com](http://www.aruplab.com).

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at [www.arupconsult.com](http://www.arupconsult.com).