SCHOOL OF MEDICINE
INDIANA UNIVERSITY

FISH Panel for MyelodysplasticSyndrome (MDS)

5q, 7q, 8 Centromere/20q, KMT2A/MLL)

Clinical Background

- Leukemias are clonal proliferations of malignant leukocytes that arise initially in the bone marrow prior to disseminating to the peripheral blood, lymph nodes and other organs.
- They are broadly classified by the type of blood cell giving rise to the clonal proliferation (lymphoid or myeloid), as well as the clinical course (acute or chronic).
- Myelodysplastic syndromes (MDS) are clonal hematopoietic malignancies occurring mainly in the older adults and characterized by ineffective hematopoiesis, a hyper-cellular bone marrow and low peripheral blood counts with significant morbidity and mortality.
- MDS eventually progresses to either bone marrow failure or transformation to acute myeloid leukemia (AML).
- MDS may be primary/de novo or secondary/therapy-related.

Epidemiology

- 4/100,000 in the general population
- >20/100,000 in the older population (>70 years)
- Median age at diagnosis is 65-70 years.

Genetics

Abnormality	**Gene(s) Involved**
del(5q)	*EGR1* and multiple genes
-7/del(7q)	Multiple genes
8 Centromere/20q	D8Z2/D20S108/Multiple genes
t(11q23)	*KMT2A/MLL*

Indications for Ordering

- Detection of a neoplastic clone that is associated with any common chromosome abnormality seen in patients with MDS
- Evaluate specimens in which standard cytogenetic analysis has been unsuccessful
- Identify and track chromosome abnormalities in patients with MDS and for follow-up of patients to evaluate response to therapy

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- This test can ordered as a panel (4 probes) or each probe can be ordered on an individual probe basis.

Interpretation

- **Negative:**

No evidence of translocation, rearrangement, gain or loss from the probes sets that were tested according to our laboratory standards. The total number of cells analyzed and standard FISH nomenclature are detailed. These results are considered normal.**Limitations:** The probes in this FISH panel detect only specific aberrations. Chromosomal alterations present outside the regions targeted by the probes may not be detected**.**

- **Positive:**

Translocation, rearrangement, gain or loss detected for the probe sets that were tested.
A description of the abnormality, the number of cells and percentage of cells that demonstrate the abnormality, and standard FISH nomenclature are detailed. These results are considered abnormal.

Methodology

- Fluorescence *in situ* hybridization (FISH) is a molecular cytogenetic method that detects fluorescently-labeled DNA/RNA or oligonucleotide probes hybridized to metaphase or interphase cells. Fluorescent signals are detected with a fluorescence microscope. In general, two hundred interphase cells are analyzed per probe by two readers (100 cells/reader).
- FISH serves as an adjunct to conventionalkaryotype analysis for the detection of cytogenetic abnormalities. FISH studies often provide clarification of G-banded abnormalities or identify cryptic abnormalities not observed by conventional karyotype analysis. However, dividing cells are not required for FISH analysis.
- The high sensitivity and specificity, rapid turnaround time, capacity to analyze large numbers of cells, and ability to obtain adequate data from samples with a low mitotic index or terminally differentiated cells are the main advantages of FISH. This method is most useful when the analysis is targeted toward those abnormalities that are known to be associated with a particular disease.

References

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3. Bernasconi P, Klersy C, Boni M, et al: World Health Organization classification in combination with cytogenetic markers improves the prognostic stratification of patients with de novo primary myelodysplastic syndromes. Br J Haematol 2007 May;137(3):193-205
4. Swerdlow SH, Campo C, Harris NL, et al. WHO classification of tumours of haematopoietic and lymphoid tissues, 4th ed. Lyon: IARC, 2008.