NPM1 mutation to Monitor Acute Myeloid Leukemia

The UNC Hospitals Molecular Genetics Laboratory measures NPM1 mutant transcripts as a marker of tumor burden in serial blood specimens of leukemia patients.

NPM1 Mutation as a Marker of Acute Myeloid Leukemia

Acute myeloid leukemia (AML) management increasingly relies on molecular test results that add value for monitoring tumor burden in serial samples collected over time. NPM1 mutation is the most prevalent of the commonly tested molecular events in AML, occurring in approximately 50% of affected adults, and has been shown to be a molecularly stable event which allows for use as a clinical marker of relapse and to monitor minimal residual disease.

A somatic, frameshift mutation in exon 12 of NPM1 confers a more favorable prognosis in AML that is otherwise intermediate prognosis. Many variants of mutant NPM1 have been described, typically 4-base insertions, yet the majority (~80%) are characterized as mutation type A (956 ins tctg). This particular common variant is measurable using quantitative rtPCR, and levels reflect tumor burden and may serve as harbingers of relapse.

Laboratory Measurement of NPM1 type A mutation by Q-rtpCR:

Specimens must be delivered promptly to the laboratory to minimize RNA degradation. The preferred sample is EDTA blood (3mL purple-top), although EDTA marrow is also acceptable (0.5mL). RNA is extracted and converted to cDNA that is PCR-amplified using primers flanking the insertion hotspot, and a fluorescent probe permits detection of PCR products in real time. A separate control assay targeting ABL1 cDNA normalizes for the amount of amplifiable cDNA in the sample. Results relative to internal and external calibrators are reported as the number of “mutant NPM1 transcripts per 10,000 cell equivalents”. Analytic sensitivity is 1 in 10^4 (one tumor cell in 10,000 normal cells). In serial specimens, changes of 10-fold (one log) are considered to be significant.

References:
9. NCCN Clinical Practice Guidelines in Oncology, Acute Myeloid Leukemia.

To consult a pathologist about indications for testing or the significance of a result, call the Molecular Genetics Lab at (984) 974-1825 or Dr. Gulley at (919) 843-4595. Email: margaret_gulley@med.unc.edu


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