**FLT3 Internal Tandem Duplication**
**for Prognosis of Acute Myeloid Leukemia**

*FLT3* internal tandem duplication confers a worse prognosis in acute myeloid leukemia (AML).

**Biology of the disease:** Approximately half of AMLs have in intermediate prognosis based on karyotype, yet at the molecular level there are often additional features influencing outcome. Internal tandem duplication (ITD) leading to activation of FLT3 tyrosine kinase, found in a third of adult AML and 13% of pediatric AML, is associated with a worse prognosis (except when there is coexisting 15;17 translocation). A positive result for FLT3 ITD in leukemic cells triggers consideration of allogeneic transplantation or experimental therapy. Results of FLT3 testing should be interpreted in the context of cytogenetics and other prognostic factors, such as mutation of NPM1, CEBPA or KIT that are components of the Myeloid Mutation Panel.

**Clinical Indications for FLT3 ITD test:** Testing is recommended in normal karyotype AML or intermediate prognosis AML when prognostic information impacts clinical management decisions.

**Laboratory test for FLT3 ITD:** The preferred sample is 1mL of marrow aspirate (EDTA-anticoagulated which may be refrigerated up to 24 hours before analysis. The specimen must contain at least 10% leukemic cells as a proportion of all nucleated cells. Other acceptable specimen types include blood, or fresh or frozen cells, or formalin-fixed paraffin embedded tissue (avoid acid decalcification) having at least 10% leukemic cells. This test is ordered reflexively as a component of the Myeloid Mutation Panel for AML.

DNA amplified using PCR primers targeting exons 14 and 15 of FLT3 is sized by capillary electrophoresis to detect an abnormally large amplicon implying ITD. The assay is sensitive to 1 in 10 cells and therefore is not suitable for minimal residual disease monitoring. Results are interpreted by a pathologist and are reported as positive or negative for FLT3 ITD.

**References:**

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. E-mail margaret_gulley@med.unc.edu
