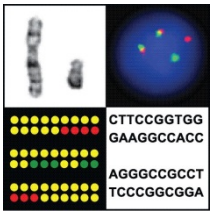

UW Cytogenetic Services Bulletin

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Contents:

Test Menu Update: AML Mutation Panel

The UW Cytogenetics and Molecular Laboratory is now offering an AML mutation panel that includes:

1. *FLT3*-ITD and *FLT3*-TKD (D835) analysis
2. *NPM1* exon 12 variant analysis
3. *CEBPA* variant analysis

These tests can be ordered as a panel or as individual tests.

Background

Acute myeloid leukemia (AML) is a neoplasm seen primarily in older adults, but can been seen in childhood, and results in the accumulation of immature myeloid blasts in the bone marrow. Cytogenetic abnormalities can be observed in the majority of cases of AML and aid in diagnosis and prognostic risk stratification. A subset of patients with AML, however, have no observable cytogenetic abnormalities and are consequently classified as intermediate risk. Within this patient group, several molecular markers of prognostic significance have been identified.

***FLT3* -ITD and *FLT3*-TKD (D835)**

FLT3 (FMS Related Tyrosine Kinase 3) is a receptor tyrosine kinase that helps to regulate hematopoiesis. Internal tandem duplications (ITD) in exons 14 and 15 of *FLT3* are detected in up to a third of cytogenetically normal AML cases. *FLT3*-ITD mutations are associated with a worse prognosis. Another functionally important *FLT3* variant, a missense mutation at the aspartic acid residue at position 835 (D835) in the tyrosine kinase domain (TKD), also appears to be associated with a worse prognosis.

NPM1

NPM1 (Nucleophosmin) is a nucleolar protein that moves between the nucleus and the cytoplasm and is involved in several cell processes. Variants in exon 12 can be found in a large percentage of cytogenetically normal adult AML cases and a smaller percentage of childhood AML cases. In adults, *NPM1*-mutated AML is strongly associated with acute myelomonocytic and acute monocytic leukemias. It is also, in the absence of a coexisting *FLT3*-ITD, associated with a favorable prognosis in patients with normal cytogenetics and other intermediate risk karyotypes.

CEBPA

CEBPA (CCAAT/Enhancer Binding Protein Alpha) is a transcription factor containing a basic leucine zipper that recognizes the CCAAT motif in the promoters of target genes. Variants in *CEBPA* are found in almost one fifth of cytogenetically normal AML cases and are associated with a favorable prognosis.

Specimen requirements and collection instructions for the AML mutation panel can be found on our website.

***KIT* Exons 8 and 17 Variant Analysis**

Core binding factor acute myeloid leukemias (CBF-AMLs) are defined by the presence of the recurrent translocations t(8;21)(q22;q22) or inv(16)(p13.1;q22)/t(16;16)(p13.1;q22). While CBF-AMLs are classified as having favorable prognoses, genetic heterogeneity among cases often contributes to relapse and mortality. *KIT* (KIT Proto-Oncogene Receptor Tyrosine Kinase) variants, often found in exons 8 and 17, appear to be associated with adverse outcomes. In addition to the AML Mutation Panel above, the UW Cytogenetics and Molecular Laboratory is offering *KIT* exons 8 and 17 Variant Analysis. Please see our website for specimen requirements and collection instructions: www.slh.wisc.edu/clinical/cytogenetics

Disease Spotlight: Turner Syndrome

What is Turner syndrome?

Turner syndrome is a chromosomal disorder that affects approximately 1/2500 liveborn females. The most notable feature in girls with Turner syndrome is short stature. Other common features include:

· Ovarian failure
· Webbing of the neck
· Edema of the hands and feet
· Cardiac defects
· Renal anomalies
· Broad chest.

Girls with Turner syndrome usually have normal intelligence, but can have some learning disabilities.

Most cases are caused by a loss of a sex chromosome, resulting in only one copy of the X chromosome being present instead of the normal two copies. Thus, this condition is also referred to as monosomy X. Some girls with Turner syndrome do still have two X chromosomes, but one is structurally abnormal – either there is a deletion (partial loss of chromosome material) or a rearrangement of an X chromosome. This is often referred to as a Turner variant.

Is Turner syndrome inherited?

Turner syndrome is usually *de novo*, meaning new, not inherited. It usually results from a random loss of an X (sex) chromosome either during the formation of the egg or sperm cells or the embryo.

How is Turner syndrome diagnosed?

Usually a physician suspects Turner syndrome based on clinical features. Turner syndrome may be suspected prenatally if there is an increased nuchal translucency or cystic hygroma. At birth, girls with Turner syndrome may have a webbed neck, cardiac defect, renal anomaly, or puffy hands and/or feet. Older children may present with short stature or primary amenorrhea. Chromosome analysis can confirm a suspicion of Turner syndrome. This test analyzes the number and general structure of the chromosomes, which can identify monosomy X, Turner variants, and even mosaicism.