

**Date:** October 27, 2016

**To:** All Zones  
Physicians, Nurses, Laboratory Directors and Managers

**From:** AHS Laboratory Services – Genetic Laboratory Services (GLS)  
Molecular Pathology Laboratory – University of Alberta Hospital

**Re:** *FLT3/NPM1* Mutation Detection Assay

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### Key Messages:

On Monday, October 31, 2016, the GLS Molecular Pathology Laboratory located at the University of Alberta Hospital will begin to offer a *FLT3/NPM1* mutation detection assay.

### Why this is important:

The *FLT3* gene codes for a transmembrane tyrosine kinase receptor that is involved in hematopoietic stem cell survival and proliferation as well as inhibition of cell death through apoptosis. This gene is mutated in about 1/3 of AML cases and most commonly involves internal tandem duplications (ITD) in the juxtamembrane domain of the receptor. An ITD in exons 14 and 15 of *FLT3* is an independent prognostic factor for poor outcome in both pediatric and adult normal karyotype AML but also in other non-APL acute myeloid leukemia patients. Prognostic significance of *FLT3* ITD may be modified by the allelic ratio (ratio of mutant to wildtype).

The nucleophosmin 1 (*NPM1*) gene codes for a shuttling protein that moves between the nucleus and cytoplasm. It is also involved in the binding of nucleic acids, centrosome duplication and ribosomal function. Mutations in exon 12 of the *NPM1* gene have been found in approximately 35% of AML patients and are so far found to be a 4 base pair insertion leading to a frame shift and an elongated protein that resides in the cytoplasm. *NPM1* mutation in the absence of *FLT3* ITD is associated with better event free survival and overall survival.

Thus the identification of both the *FLT3*-ITD and *NPM1* mutations in AML patients is clinically beneficial for prognostic and treatment purposes. Performing the assay in Edmonton, will also allow a more rapid turnaround time (TAT) that permits prompt institution of efficacious therapy.

### Action Required:

Please refer to the AHS Central and Edmonton Zone Test Directory for additional test information at:  
<http://www.albertahealthservices.ca/3217.asp>

**Standard Turnaround Time:** One week from receipt of sample to reporting of results.

### Inquiries and feedback may be directed to:

Dr. Iyare Izevbye, Lab Head, Molecular Pathology Laboratory, GLS, (780) 407-8025

### This bulletin has been reviewed and approved by:

Dr. Martin Somerville, Medical/Scientific Director, Genetic Laboratory Services  
Dr. Carolyn O'Hara, Interim Medical Director, AHS Laboratory Services