

DATE:	2022 June 27
TO:	All Pathologists, Hematologists and Oncologists
FROM:	Molecular Pathology Program, Alberta Precision Laboratories
RE:	New Myeloid NGS Panel

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Key Message

As of June 13, 2022, a new Myeloid NGS Panel ([Oncomine Myeloid Assay GX V2](#)) will be available in APL for diagnostic testing on blood and bone marrow samples. Testing will be available initially for Calgary and then expanded provincially at a later date.

Background

The Myeloid NGS Panel is validated to detect single nucleotide variants (SNVs), insertions/deletions (indels), and gene fusions in the following genes:

- Hotspot coverage only (28):** *ANKRD26, ABL1, BRAF, CBL, CSF3R, DDX41, DNMT3A, FLT3 (ITD, TKD), GATA2, HRAS, IDH1, IDH2, JAK2, KIT, KRAS, MPL, MYD88, NPM1, NRAS, PPM1D, PTPN11, SMC1A, SMC3, SETBP1, SF3B1, SRSF2, U2AF1, WT1*
- Full gene coverage (17):** *ASXL1**, *BCOR, CALR, CEBPA, ETV6, EZH2, IKZF1, NF1, PHF6, PRPF8, RB1, RUNX1, SH2B3, STAG2, TET2, TP53, ZRSR2*
- Fusion Driver Genes (30) Covering >700 Unique Fusions:** *ABL1, ALK, BCL2, BRAF, CCND1, CREBBP, EGFR, ETV6, FGFR1, FGFR2, FUS, HMGA2, JAK2, KMT2A PTDs, MECOM, MET, MLLT10, MLLT3, MYBL1, MYH11, NTRK3, NUP98, NUP214, PDGFRA, PDGFRB, RARA, RBM15, RUNX1, TCF3, TFE3*

*While the manufacturer claims full-gene coverage for *ASXL1*, internal evaluation shows some areas of inconsistent coverage. A negative result for *ASXL1* will be re-evaluated to ensure its validity by reflex sendout testing to a referral laboratory.

How this will impact you

- This panel provides a powerful diagnostic, prognostic and predictive tool for myeloid malignancies. The utility depends on the clinicopathologic context, and good stewardship entails rationing use of this panel to clinically relevant settings.
- Please see **Appendix A** for gene-disease associations and guideline recommendations.
- The test will be available to all Alberta Hematologists, Oncologists, and Pathologists.
 - In Calgary:** The test will be orderable through submitting the Bone Marrow requisition form or Calgary Molecular Hematology paper requisition.
- The target turnaround time of the Myeloid NGS Panel is 10 working days from specimen receipt in the Molecular Hematology laboratory. Molecular test results will be reported in Netcare and EPIC.



Action Required

- **Pathologists:** Order this panel on blood or bone marrow specimens when necessary for diagnostic purposes in the clinicopathologic context. When rush *PML/RARA* fusion testing with a turnaround time of less than 10 working days is clinically indicated, order rush FISH (South Sector) or RT-PCR (North Sector). In such scenarios, if additional genes on the Myeloid NGS Panel are clinically relevant, dual ordering above tests and NGS at the same time may be reasonable.
- **Hematologists / Oncologists:** Be aware that Myeloid NGS Panel results need to be integrated in the clinicopathologic context (similar to diagnostic PCR or FISH testing). Please reach out to the pathologist responsible for the specimen for clarification of the diagnostic significance of results when necessary.

Effective

- June 13, 2022 transition of all testing from Hematology Translational Lab (University of Calgary) for South Sector to APL Molecular Pathology Lab South

Questions/Concerns

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Approved by

- Imran Mirza, Provincial Medical Director, Molecular Pathology Program, Alberta Precision Laboratories
- Carolyn O'Hara, Chief Medical Laboratory Officer (Interim), Alberta Precision Laboratories



Appendix A: Gene-Disease Associations and Guideline Recommendations.

(AML, Acute Myeloid Leukemia; CML, Chronic Myeloid Leukemia; MDS, Myelodysplastic Syndrome; MPN, Myeloproliferative Neoplasm; NCCN, National Comprehensive Cancer Network; WHO, World Health Organization).

Gene	Disease Associations				Guidelines		Oncomine Myeloid Assay GX v2 Coverage
	AML	MPN	CML	MDS	NCCN	WHO	Coverage
ABL1	x	x	x		x	x	Hotspot, Fusion Driver
ALK	x	x					Fusion Driver
ANKRD26	x			x	x	x	Hotspot
ASXL1	x	x		x	x		Full Gene
BAALC	x						Expression Gene
BCL2			x				Fusion Driver
BCOR				x	x		Full Gene
BRAF				x			Hotspot, Fusion Driver
CALR		x		x	x		Full Gene
CBL	x	x		x	x		Hotspot
CCND1	x						Fusion Driver
CEBPA	x				x	x	Full Gene
CREBBP	x						Fusion Driver
CSF3R	x						Hotspot
DDX41				x	x	x	Hotspot
DNMT3A	x	x		x	x		Hotspot
EGFR	x						Fusion Driver
EIF2B1							Housekeeping gene (expression control)
ETV6	x			x	x	x	Full Gene, Fusion Driver
EZH2	x	x		x	x		Full Gene
FBXW2							Housekeeping gene (expression control)
FGFR1	x	x	x				Fusion Driver
FGFR2	x	x		x			Fusion Driver
FLT3	x			x	x		Hotspot
FUS	x						Fusion Driver
GATA2	x			x	x	x	Hotspot
HMGA2	x			x			Fusion Driver
HRAS	x			x			Hotspot
IDH1	x	x		x	x		Hotspot
IDH2	x	x		x	x		Hotspot
IKZF1	x	x					Full Gene
JAK2	x	x	x	x	x	x	Hotspot, Fusion Driver
KIT	x				x		Hotspot
KMT2A	x				x	x	Fusion Driver
KRAS	x	x		x	x		HotSpot



Gene	Disease Associations				Guidelines		Oncomine Myeloid Assay GX v2 Coverage
	AML	MPN	CML	MDS	NCCN	WHO	Coverage
MECOM	x				x	x	Fusion Driver, Expression Gene
MET	x						Fusion Driver
MLL10	x						Fusion Driver
MLLT3	x						Fusion Driver
MPL		x		x	x		Hotspot
MYBL1	x						Fusion Driver
MYC	x						Expression Gene
MYD88	x						Hotspot
MYH11	x				x	x	Fusion Driver
NF1				x	x		Full Gene
NPM1	x			x	x	x	Hotspot
NRAS	x	x		x	x		Hotspot
NTRK3	x						Fusion Driver
NUP214	x					x	Fusion Driver
NUP98	x		x	x			Fusion Driver
PDGFRA	x					x	Fusion Driver
PDGFRB	x					x	Fusion Driver
PHF6				x	x		Full Gene
PPM1D				x	x		Hotspot
PRPF8				x	x		Full Gene
PSMB2							Housekeeping gene (expression control)
PTPN11				x	x		Hotspot
PUM1							Housekeeping gene (expression control)
RARA	x				x	x	Fusion Driver
RB1	x			x			Full Gene
RBM15	x					x	Fusion Driver
RUNX1	x	x		x	x	x	Full Gene, Fusion Driver
SETBP1		x		x	x		Hotspot
SF3B1		x		x	x		Hotspot
SH2B3		x		x			Full Gene
SMC1A	x			x			Hotspot, Expression Gene
SMC3	x			x			Hotspot
SRSF2		x		x	x		Hotspot
STAG2				x	x		Full Gene
TCF3	x						Fusion Driver
TET2	x	x		x	x		Full Gene
TFE3	x						Fusion Driver
TP53	x	x		x	x		Full Gene



Gene	Disease Associations				Guidelines		Oncomine Myeloid Assay GX v2 Coverage
	AML	MPN	CML	MDS	NCCN	WHO	Coverage
TRIM27	x			x			Housekeeping gene (expression control)
U2AF1	x	x		x	x		Hotspot
WT1	x			x	x		Expression Gene, Hotspot
ZRSR2		x		x	x		Full Gene