ALBERTA PRECISION LABORATORIES
Leaders in Laboratory Medicine

Laboratory Bulletin

DATE:	1 December 2022
TO:	All Pathologists and Hematologists/Oncologists in Alberta
FROM:	Molecular Pathology Program, Alberta Precision Laboratories
RE:	**Sendout Testing for Fusions in Solid Tumors**

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Key Message

- All fusion panel RNA next generation sequencing (NGS) requests on solid tumors received on or after November 29, 2022, that would normally be tested in Calgary, will be sent out for external testing until further notice. This includes all indications for Pan-Solid Tumor Fusion Panel and Lung Fusion Panel (Kinase Fusion Panel). Selected test requests received prior to November 29 will also be sent out, and a list of impacted cases will be sent to the ordering pathologists / clinicians for awareness.

Background

- There is a critical shortage of reagents needed to perform Archer FusionPlex RNA NGS testing, impacting the Pan-Solid Tumor Fusion Panel and Lung Fusion Panel (Kinase Fusion Panel) that are performed in Calgary for provincial testing. As per communication with the distributor, new reagents are anticipated to arrive in January 2023.
- These are custom panels designed to cover a broad range of test indications. On a review of available sendout options, no single direct substitute exists that can cover the full breadth of testing with adequate turnaround time and sufficient throughput for the volume of Alberta cases. Therefore, multiple different sendout assays will be utilized on a case-by-case basis depending on the clinicopathologic context.

How this will impact you

- Sendout test strategies include the following:
  - **Lung adenocarcinoma, predictive fusions:** MayoComplete Lung Rearrangements, Rapid, Tumor (MCLNR) – Mayo Clinic Laboratories (turnaround time (TAT): 4 to 8 days)
    - https://www.mayocliniclabs.com/test-catalog/Overview/616488
  - **Bone/soft tissue tumor / gynecologic mesenchymal tumors, diagnostic fusions:** Sarcoma Targeted Gene Fusion/Rearrangement Panel, Next-Generation Sequencing, Tumor (SARCP) – Mayo Clinic Laboratories (TAT: 14 to 21 days)
    - https://www.mayocliniclabs.com/test-catalog/overview/606427
    - See Appendix A for panel content comparison
  - **Central nervous system tumor, diagnostic fusions:** Neuro-Oncology Expanded Gene Panel with Rearrangement, Tumor (NONCP) – Mayo Clinic Laboratories (TAT: 12 to 20 days)
    - https://www.mayocliniclabs.com/test-catalog/overview/603047
    - See Appendix B for panel content comparison
  - **Melanocytic lesion, diagnostic fusions:** FusionPlex® Solid Tumor Panel – University of Washington Laboratory for Precision Diagnostics (TAT: 7-14 days)
    - http://uwcpdx.org/fusionplex-solid-tumor-panel/
  - **Thyroid carcinoma, predictive fusions:** FusionPlex® Solid Tumor Panel – University of Washington Laboratory for Precision Diagnostics (TAT: 7-14 days)
    - http://uwcpdx.org/fusionplex-solid-tumor-panel/
  - ***NTRK* fusions (FastTRK program):** Oncomine Focus Assay performed in Edmonton.

- **Salivary gland, head/neck, kidney, and other tumors, diagnostic fusions:** In-house options include MAML2 FISH and TFE3 FISH in the Calgary Cancer Cytogenetics Laboratory. The above listed sendout options are also available if they are of utility on a case-by-case basis.

Action Required

- **Pathologists:** Please continue to submit requests in the same way. Incoming test requests will be reviewed by the molecular pathologist on service in the North / South sectors, who will assess and initiate the appropriate sendout strategy as per the above list. Please feel free to discuss the test strategy with the molecular pathologist on service, who can also aid in considering other sendout options if needed for unusual cases. Test results will be received by the molecular pathology laboratories and transcribed into your local EMR.
- **Oncologists:** Please continue to submit requests in the same way. Predictive fusion testing (lung adenocarcinoma, thyroid carcinoma, FastTRK program) will be arranged by the molecular pathology laboratory. Look for transcribed results from sendout testing in your local EMR.

Effective **November 30, 2022**

Questions/Concerns

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Approved by

- Adrian Box, Medical/Scientific Director, Molecular Pathology Program
- Mark Douesnard, Operations Director, Molecular Pathology Program

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Appendix A: List of genes **pertinent to BST tumors / gynecologic mesenchymal tumors** covered on APL Pan-Solid Tumor Fusion Panel that are **not covered on Mayo Clinic Laboratories SARCP panel**

Gene	Relevant Bone/Soft Tissue Tumors	Covered Mutation Types on APL Pan-Solid Tumor Fusion Panel
BRAF	Infantile fibrosarcoma, spindle cell sarcomas with kinase fusions	fusions, V600E, kinase domain duplications, BRAFΔ2-10, BRAFΔ4-10, BRAFΔ2-8, BRAFΔ3-8, BRAFΔ4-8
CTNNB1	desmoid type fibromatosis	SNVs/indels
EGF	lipofibromatosis, calcifying aponeurotic fibroma	fusions
EGFR	Tyrosine kinase-altered spindle cell neoplasms with EGFR internal tandem duplication	fusions, EGFRvIII (exon 2-7 skipping), kinase domain duplication, SNVs/indels
FOS	epithelioid hemangioma	fusions
GLI2	sclerosing stromal tumor of the ovary	fusions
GNAS	fibrous dysplasia	SNVs/indels
IDH1	chondrocytic neoplasms	SNVs/indels
IDH2	chondrocytic neoplasms	SNVs/indels
MET	spindle cell sarcoma with kinase fusion	fusions, exon 14 skipping
MYOD1	spindle cell / sclerosing rhabdomyosarcoma	point mutation (p.L122R)
NOTCH3	myofibroma, myofibromatosis	p.L1519P
NTRK2	spindle cell sarcoma with kinase fusion	fusions, SNVs/indels
PDGFRB	myofibroma, myofibromatosis	fusions, SNVs/indels
RAF1	spindle cell sarcoma with kinase fusion	fusions
RET	spindle cell sarcoma with kinase fusion	fusions, SNVs/indels
ROS1	spindle cell sarcoma with kinase fusion	fusions, SNVs/indels
TFCP2	TFCP2-rearranged rhabdomyosarcoma	fusions
THBS1	acral fibrochondromyxoid tumor	fusions

Full list of genes covered on APL Pan-Solid Tumor Fusion Panel not covered on SARCP: *AKT1 AKT3 AR ARHGAP26 BRAF CSF1R CTNNB1 DNAJB1 EGF EGFR ERBB2 ERBB4 ESR1 ETV5 FGFR2 FGFR3 FOS GLI2 GNAS HRAS IDH1 IDH2 KRAS MAML2 MAP2K1 MET MN1 MSANTD3 MYB MYBL1 MYOD1 NOTCH3 NRAS NRG1 NTRK2 PDGFRA PDGFRB PPARG PRKACA PRKD1 PRKD2 PRKD3 RAF1 RELA RET ROS1 TERT TFCP2 TFEB THADA THBS1 TMPRSS2)*

Appendix B: List of genes **pertinent to CNS tumors** covered for fusions on APL Pan-Solid Tumor Fusion Panel, that are **not covered on the fusion (RNA) component of Mayo Clinic Laboratories NONCP panel**

Gene	Relevant Solid Tumors	Covered Mutation Types on APL Pan-Solid Tumor Fusion Panel
AKT3	glioma	fusions
ALK	rarely in pediatric high grade glioma	fusions, internal deletion (ALKΔ2-17, ALKΔ2-3), ATI, SNVs/indels
BCOR	CNS tumor with BCOR ITD (BCOR fusions also rarely reported)	fusions, ITD
MAML2	low grade glioma, DNET (MYB-MAML2)	fusions
ROS1	pediatric high grade glioma	fusions, SNVs/indels

Full list of genes covered **for fusions** on APL Pan-Solid Tumor Fusion Panel not covered on NONCP:
AKT1 AKT3 ALK AR ARHGAP26 BCOR BRD3 BRD4 CAMTA1 CCNB3 CIC CSF1 CSF1R DNAJB1 EGF EPC1 ERBB2 ERBB4 ERG ETV1 ETV4 ETV5 FGFR2 FOS FOSB FOXO1 FOXO4 FUS GLI2 HMGA2 JAZF1 MAML2 MEAF6 MKL2 MSANTD3 NCOA1 NCOA2 NOTCH1 NOTCH2 NR4A3 NRG1 NUTM1 PAX3 PDGFB PDGFRB PHF1 PLAG1 PPARG PRDM10 PRKACA PRKCB PRKCD PRKD1 PRKD2 PRKD3 RET ROS1 SRF SS18 SS18L1 TAF15 TCF12 TERT TFCP2 TFE3 TFEB THADA THBS1 TMPRSS2 USP6 VGLL2 YWHAE