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Laboratory Bulletin

DATE:	2022 March 21
TO:	All Pathologists and Oncologists
FROM:	Molecular Pathology Program, Alberta Precision Laboratories
RE:	**New Molecular Test for Diagnostic Fusions in Solid Tumors**

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Key Message

- As of April 4, 2022, a new custom Fusion RNA Panel (FusionPlex RNA NGS assay, ArcherDx Inc / Invitae) will be available in APL for pathologist-initiated diagnostic fusion testing in solid tumor FFPE samples. Testing is centralized in Calgary and is available for pan-provincial cases.

Background

- As the number of diagnostically relevant fusions in solid tumors continues to grow, it has become unsustainable to maintain a sufficient breadth of single-target fusion tests in APL.
- The APL Fusion RNA Panel for solid tumors is validated to detect fusions, oncogenic isoforms and/or selected single nucleotide variants (SNVs) and small insertions/deletions (indels) in the following 103 genes: *AKT1, AKT3, ALK, AR, ARHGAP26, BCOR* (including *BCOR* ITD)*, BRAF, BRD3, BRD4, CAMTA1, CCNB3, CIC, CSF1, CSF1R, CTNNB1, DNAJB1, EGF, EGFR, EPC1, ERBB2, ERBB4, ERG, ESR1, ETV1, ETV4, ETV5, ETV6, EWSR1, FGFR1, FGFR2, FGFR3, FOS, FOSB, FOXO1, FOXO4, FUS, GLI1, GLI2, GNAS, HMGA2, HRAS, IDH1, IDH2, JAZF1, KRAS, MAML2, MAP2K1, MEAF6, MET, MKL2, MN1, MSANTD3, MYB, MYBL1, MYOD1, NCOA1, NCOA2, NOTCH1, NOTCH2, NOTCH3, NR4A3, NRAS, NRG1, NTRK1, NTRK2, NTRK3, NUTM1, PAX3, PDGFB, PDGFRA, PDGFRB, PHF1, PLAG1, PPARG, PRDM10, PRKACA, PRKCA, PRKCB, PRKCD, PRKD1, PRKD2, PRKD3, RAF1, RELA, RET, ROS1, SRF, SS18, SS18L1, STAT6, TAF15, TCF12, TERT, TFCP2, TFE3, TFEB, THADA, THBS1, TMPRSS2, USP6, VGLL2, YAP1, YWHAE.*
- Note that while selected SNVs/indels can be detected on this panel, RNA is not an ideal analyte for detecting these mutations, and this test cannot exclude SNVs/indels when not detected. The panel is primarily indicated for detection of fusions and oncogenic isoforms.

How this will impact you

- This panel provides a powerful diagnostic tool for solid tumors in diverse organ systems (bone / soft tissue, central nervous system, salivary gland / head / neck, gynecologic and genitourinary organs, and others). **The utility depends on the clinicopathologic context, and good stewardship entails rationing use of this panel to clinically relevant settings (in a similar fashion as diagnostic FISH testing).**
- The test will be available to all Alberta pathologists.
    - **In Calgar**y: The test will be orderable through Millennium (electronic requisition), or by hand-labelling the Calgary Molecular Pathology paper requisition.
    - **In Edmonton:** The test will be ordered by indicating “Fusion RNA panel” in the “Other (specify)” field on the Edmonton Molecular Pathology Requisition, and submitting the request in the same fashion as other molecular test requests in the North zone.
- The target turnaround time of the Fusion RNA Panel is 10 working days from tissue receipt in the Molecular Pathology laboratory. Molecular test results will be reported in Netcare and EPIC.

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Action Required

- **Pathologists**: Order this fusion panel on FFPE specimens when necessary for diagnostic purposes in the clinicopathologic context. Order this panel instead of sendout fusion panel testing, and instead of FISH testing for *ETV6, FUS, MAML2, TFE3, FOXO1, EWSR1* and *SS18.* When rush *EWSR1* or *FOXO1* fusion testing with a turnaround time of less than 10 working days is clinically indicated, order rush FISH. In such scenarios, if the specific fusion partner is also of diagnostic importance, dual ordering FISH and RNA NGS at the same time may be reasonable (tissue permitting).
- **Oncologists:** Be aware that solid tumor Fusion RNA Panel results need to be integrated in the clinicopathologic context (similar to diagnostic FISH testing). Please reach out to the pathologist responsible for the specimen for clarification of the diagnostic significance of results when necessary.

Effective **April 4, 2022**

Questions/Concerns

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Approved by

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