

DATE: January 4th, 2017
TO: UCH Medical Staff, Housestaff, Patient Care Centers, and Outpatient Clinics,
University Chicago Comprehensive Cancer Center
FROM: Jeremy P. Segal, MD, PhD, Megan Mc Nerney, MD, PhD, Y. Lynn Wang, MD, PhD,
FCAP, and Carrie Fitzpatrick, PhD
RE: Update to UChicago OncoPlus Universal Cancer Mutation Analysis Panel

Announcement

The Clinical Genomics Laboratory in the Division of Genomic and Molecular Pathology is pleased to announce a significant update to our OncoPlus universal cancer mutation analysis panel. The OncoPlus panel is a targeted next generation sequencing (NGS) assay that is designed to interrogate 1,213 cancer-related genes for assessments of both solid tumors and hematological malignancies, with a subset clinically reported for personalized care. The previous version of the assay included 119 reportable genes and did not include detection of copy number changes or gene fusions.

Via this update, we are:

- 1) Increasing the number of reported genes by 28 to a total of 147 genes, including *CEBPA* (which was previously performed separately). The other new genes are: *CCND1*, *CCND2*, *CCND3*, *CHEK2*, *DDX41*, *ERBB3*, *ERCC3*, *FANCA*, *FH*, *HIST1H3B*, *HNFB1A*, *MLH1*, *MLH3*, *MRE11A*, *MSH2*, *MSH6*, *NBN*, *PALB2*, *PIK3CB*, *POLE*, *PTCH1*, *RAD51*, *SDHB*, *SDHC*, *SDHD*, *TSC1*, and *TSC2*.
- 2) Introducing detection and reporting of copy number variations (CNVs) for 136 genes.
- 3) Introducing detection and reporting of lung cancer-related gene fusions in *ALK*, *RET*, and *ROS1*.

This updated content will allow for examination of a broader array of tumor types and use of the panel as a pre-screening aid for any nucleic acid-based anomalies targeted via the MATCH trial. As before, sequencing data from the remaining non-reported 1,066 genes may be accessed for research purposes via the Division of Genomic and Molecular Pathology with appropriate IRB approval and patient consent, as appropriate.

Test information

Genes reported for mutations, insertions and deletions (147): *ABL1*, *AKT1*, *ALK*, *APC*, *ARID1A*, *ARID2*, *ASXL1*, *ATM*, *ATR*, *ATRX*, *AXL*, *B2M*, *BAP1*, *BCOR*, *BCORL1*, *BIRC3*, *BLM*, *BRAF*, *BRCA1*, *BRCA2*, *BTK*, *CALR*, *CBL*, *CBLB*, *CCND1*, *CCND2*, *CCND3*, *CDH1*, *CDKN2A*, *CEBPA*, *CHEK1*, *CHEK2*, *CSF1R*, *CSF3R*, *CTCF*, *CTNNA1*, *CTNNB1*, *CUX1*, *CXCR4*, *DAXX*, *DDR2*, *DDX3X*, *DDX41*, *DICER1*, *DNMT3A*, *EGFR*, *EP300*, *EPHA3*, *EPHA5*, *ERBB2*, *ERBB3*, *ERBB4*, *ERCC3*, *ESR1*, *ETV6*, *EZH2*, *FANCA*, *FAT3*, *FBXW7*, *FGFR1*, *FGFR2*, *FGFR3*, *FH*, *FLT3*, *FOXL2*, *GATA1*, *GATA2*, *GNA11*, *GNAQ*, *GNAS*, *GRIN2A*, *H3F3A*, *HIST1H3B*, *HIST1H3C*, *HNFB1A*, *HRAS*, *IDH1*, *IDH2*, *IKZF1*, *ITPKB*, *JAK2*, *KDM6A*, *KDR*, *KIT*, *KMT2A*, *KRAS*, *MAP2K1*, *MAPK1*, *MET*, *MLH1*, *MLH3*, *MPL*, *MRE11A*, *MSH2*, *MSH6*, *MTOR*, *MYD88*, *NBN*, *NF1*, *NF2*, *NFE2L2*, *NOTCH1*,

NOTCH2, NPM1, NRAS, PALB2, PBRM1, PDGFRA, PDGFRB, PHF6, PIK3CA, PIK3CB, PIK3R1, PLCG2, POLE, POT1, PPP2R1A, PTCH1, PTEN, PTPN11, RAD21, RAD51, RB1, RET, RUNX1, SDHB, SDHC, SDHD, SETBP1, SF3B1, SMAD4, SMARCB1, SMC1A, SMC3, SMO, SRSF2, STAG2, STK11, TERT, TET2, TP53, TSC1, TSC2, U2AF1, VHL, WT1, and ZRSR2.

Genes reported for copy number gains and losses (136): *ABL1, AKT1, ALK, APC, ARID1A, ARID2, ASXL1, ATM, ATR, AXL, B2M, BAP1, BIRC3, BLM, BRAF, BRCA1, BRCA2, CALR, CBL, CBLB, CCND1, CCND2, CCND3, CDH1, CDKN2A, CEBPA, CHEK1, CHEK2, CSF1R, CSF3R, CTCF, CTNNA1, CTNNA1, CTNNB1, CUX1, CXCR4, DAXX, DDR2, DDX41, DICER1, DNMT3A, EGFR, EP300, EPHA3, EPHA5, ERBB2, ERBB3, ERBB4, ERCC3, ESRI, ETV6, EZH2, FANCA, FAT3, FBXW7, FGFR1, FGFR2, FGFR3, FH, FLT3, FOXL2, GATA2, GNA11, GNAQ, GNAS, GRIN2A, H3F3A, HIST1H3B, HIST1H3C, HNF1A, HRAS, IDH1, IDH2, IKZF1, ITPKB, JAK2, KDR, KIT, KMT2A, KRAS, MAP2K1, MAPK1, MET, MLH1, MLH3, MPL, MRE11A, MSH2, MSH6, MTOR, MYD88, NBN, NF1, NF2, NFE2L2, NOTCH1, NOTCH2, NPM1, NRAS, PALB2, PBRM1, PDGFRA, PDGFRB, PIK3CA, PIK3CB, PIK3R1, PLCG2, POLE, POT1, PPP2R1A, PTCH1, PTEN, PTPN11, RAD21, RAD51, RB1, RET, RUNX1, SDHB, SDHC, SDHD, SETBP1, SF3B1, SMAD4, SMARCB1, SMC3, SMO, SRSF2, STK11, TERT, TET2, TP53, TSC1, TSC2, U2AF1, VHL, and WT1.*

Genes reported for fusions/translocations: *ALK, RET, and ROS1.*

The test procedure involves DNA extraction and quantity/quality assessment, fragmentation and library preparation, followed by pooled capture targeting the desired genomic loci. Next generation sequencing (NGS) is performed on the HiSeq 2500 system (Illumina) and downstream analysis for quality control and detection of mutations is performed via custom-design bioinformatics pipelines on a HIPAA-compliant high performance computing system within the Center for Research Informatics (CRI). 147 genes will be reported for mutations and indels, 136 genes will be reported for copy number changes, and 3 genes will be reported for fusion events.

Specimen Requirements

Acceptable specimens include formalin-fixed, paraffin-embedded (FFPE) tissue or cytology (DiffQuick) aspirate smears for solid tumors, or blood/bone marrow aliquots for hematological malignancies (purple-top tubes). Specimens should contain >20% tumor cells and enough total cells to produce adequate DNA yield (typically >50,000 total cells). Specimens with less than 20% tumor cells may be tested at the discretion of the attending molecular pathologist.

Test ordering

The test can be ordered through Epic using the following codes:

a. LABAPNGPLSM for Bone Marrow

OncoPlus Large Tumor Panel by NextGen Sequencing, Bone Marrow ✓ Accept ✗ Cancel

Process Inst: This is a Next Generation Sequencing panel for the detection of point mutations and small insertions/deletions in 119 solid tumor and hematological malignancy related genes via analysis of Peripheral Blood, Bone Marrow and Formalin-Fixed Paraffin-Embedded specimens. Although 119 genes will clinically be reported, a large number of other genes are sequenced [Process Instructions] with results suppressed in lieu of IRB-approved access for the purpose of translational research. The genes clinically reported include:
ABL1, AKT1, ALK, APC, ARID1A, ARID2, ASXL1, ATM, ATR, ATRX, AXL, B2M, BAP1, BCOR, BCORL1, BIRC3, BRCA1, BRCA2, BRIP1, BRIP2, BRIP3, BRIP4, BRIP5, BRIP6, BRIP7, BRIP8, BRIP9, BRIP10, BRIP11, BRIP12, BRIP13, BRIP14, BRIP15, BRIP16, BRIP17, BRIP18, BRIP19, BRIP20, BRIP21, BRIP22, BRIP23, BRIP24, BRIP25, BRIP26, BRIP27, BRIP28, BRIP29, BRIP30, BRIP31, BRIP32, BRIP33, BRIP34, BRIP35, BRIP36, BRIP37, BRIP38, BRIP39, BRIP40, BRIP41, BRIP42, BRIP43, BRIP44, BRIP45, BRIP46, BRIP47, BRIP48, BRIP49, BRIP50, BRIP51, BRIP52, BRIP53, BRIP54, BRIP55, BRIP56, BRIP57, BRIP58, BRIP59, BRIP60, BRIP61, BRIP62, BRIP63, BRIP64, BRIP65, BRIP66, BRIP67, BRIP68, BRIP69, BRIP70, BRIP71, BRIP72, BRIP73, BRIP74, BRIP75, BRIP76, BRIP77, BRIP78, BRIP79, BRIP80, BRIP81, BRIP82, BRIP83, BRIP84, BRIP85, BRIP86, BRIP87, BRIP88, BRIP89, BRIP90, BRIP91, BRIP92, BRIP93, BRIP94, BRIP95, BRIP96, BRIP97, BRIP98, BRIP99, BRIP100, BRIP101, BRIP102, BRIP103, BRIP104, BRIP105, BRIP106, BRIP107, BRIP108, BRIP109, BRIP110, BRIP111, BRIP112, BRIP113, BRIP114, BRIP115, BRIP116, BRIP117, BRIP118, BRIP119

① Status: **Future** Expected: Approx. Expires:

Class: **Unit Collect**

① Ordering Physician pager number:

① Clinical Information/Reason for Test:

① Institution where specimen was obtained? **University of Chicago**

① Pathology case number or sample date:

Additional physician comments:

Lab: Resulting Agency: Collection Date: Collection Time:

Comments (F6) [Click to add text](#)

Sched Inst.: [Click to add text](#)

Performing Dept:

ANESTHESIA | PAIN CLINIC | IV THERAPY | ELECTROPHYSIOLOGY | UROLOGY | PEDS SPEC. PROC. AREA
STUDENT CARE CENTER | SOUTH SHORE SENIOR CTR | CLINICAL RESEARCH CNTR
BSD EH PERS HLTH & PRV

▶ Additional Order Details

① Next Required ✓ Accept ✗ Cancel

b. LABAPNGPLB for Peripheral Blood

OncoPlus Large Tumor Panel by NextGen Sequencing, Peripheral Blood ✓ Accept ✗ Cancel

Process Inst: This is a Next Generation Sequencing panel for the detection of point mutations and small insertions/deletions in 119 solid tumor and hematological malignancy related genes via analysis of Peripheral Blood, Bone Marrow and Formalin-Fixed Paraffin-Embedded specimens. Although 119 genes will clinically be reported, a large number of other genes are sequenced simultaneously, with results suppressed in lieu of IRB-approved access for the purpose of translational research. The genes clinically reported include:
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Class: **Lab Collect**

① Type of Draw: **Central Line**

① Ordering Physician pager number:

① Clinical Information/Reason for Test:

① Institution where specimen was obtained? **University of Chicago**

① Pathology case number or sample date:

Additional physician comments:

Lab: Resulting Agency: Collection Date: Collection Time:

Comments (F6)

Sched Inst.: [Click to add text](#)

Performing Dept:

ANESTHESIA | PAIN CLINIC | IV THERAPY | ELECTROPHYSIOLOGY | UROLOGY
PEDS SPEC. PROC. AREA | STUDENT CARE CENTER | SOUTH SHORE SENIOR CTR
CLINICAL RESEARCH CNTR | BSD EH PERS HLTH & PRV

① Next Required ✓ Accept ✗ Cancel

c. LABAPNGPLF for FFPE:

OncoPlus Large Tumor Panel by NextGen Sequencing, FFPE ✓ Accept ✗ Cancel

Process Inst: This is a Next Generation Sequencing panel for the detection of point mutations and small insertions/deletions in 119 solid tumor and hematological malignancy related genes via analysis of Peripheral Blood, Bone Marrow and Formalin-Fixed Paraffin-Embedded specimens. Although 119 genes will clinically be reported, a large number of other genes are sequenced simultaneously, with results suppressed in lieu of IRB-approved access for the purpose of translational research. The genes clinically reported include:
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Status:

Class:

Ordering Physician pager number:

Clinical Information/Reason for Test:

Institution where specimen was obtained?

Pathology case number or sample date:

Additional physician comments:

Lab: Resulting Agency: Collection Date: Collection Time:

Comments (F6): [Click to add text](#)

Sched Inst.: [Click to add text](#)

Performing Dept:

Additional Order Details

✗ Next Required ✓ Accept ✗ Cancel

Reporting and Test limitations

The basic report format will remain similar to our current OncoPlus format, with mutations (and now copy numbers and fusions) listed according to interpreted pathogenicity, along with interpretative summaries. This test is intended for the detection of single-nucleotide mutations and insertions/deletions up to 60 bp in size. Internal tandem duplications of the FLT3 gene are detected at larger sizes (largest size tested = 102 bp). Copy number changes will be reported at levels greater than 2X or less than 0.6X. The assay is intended for performance on specimens with >20% tumor cells and adequate overall tissue. Mutational assay sensitivity is 10% mutant allelic fraction (MAF). False-negative results of all types may occur when there is a lower than adequate tumor cell burden.

Testing Frequency and Turnaround Time

Testing will be performed at least once weekly, Monday through Friday during day shifts only. Expected turnaround time is 12-18 business days following receipt of adequate specimens.

Additional Questions

Additional questions may be directed to the Division of Genomic and Molecular Pathology at 773-702-4946 or Dr. Jeremy Segal at 773-702-3674.