University of Nebraska Medical Center
REGIONAL PATHOLOGY SERVICES

# Lab Alert: New Solid Tumor Molecular Assays Assessing Biomarker Targets for FDA-Approved Therapies

Date: February 18, 2022

Dear Regional Pathology Services Clients,

We are very excited to announce two new molecular gene panels as added tools in the field of personalized medicine! These two gene panels are available effective today.

*****These new tumor panels will either require prior-authorization or a signed ABN. *****

## I. Solid Tumor Precision Panel

**Test Name:** Solid Tumor Precision Panel

**Test code:** STPP

**Specimen Type:** FFPE tissue block, or 5 Unstained slides- 5-10µm thick at least 5mm X 5mm tumor tissue, preferably 10mm X 10mm tumor tissue, with accompanying H&E if possible

**Unacceptable specimens:** Paraffin blocks with low tumor percentage. Tissue fixed in heavy metal fixative or decalcified tissue.

**CPT Code:** 81445

**TAT:** 5 -10 business days

The Solid Tumor Precision Panel is for assessment of molecular genetic biomarker targets for FDA-approved therapies in solid tumors. This gene panel will assess 49 genes (see below) for somatically-derived, selected hotspot mutations including single nucleotide variants (SNVs), small insertions or deletions (indels), copy number variations (CNV) and structural variants (inter-genetic and intra-genetic fusions).

| SNVs and Indels (DNA) | | | | | | CNVs (DNA) | Fusions (RNA) | | |
|---|---|---|---|---|---|---|---|---|---|
| AKT1 | CDKN2A | FGFR1 | HRAS | MTOR | RAF1 | CDKN2A del | ALK | MET | RSPO2 |
| AKT2 | CHEK2 | FGFR2 | IDH1 | NRAS | RET | PTEN del | AR | NRG1 | RSPO3 |
| AKT3 | CTNNB1 | FGFR3 | IDH2 | NTRK1 | ROS1 | EGFR amp | BRAF | NTRK1 | |
| ALK | EGFR | FGFR4 | KIT | NTRK2 | SMO | ERBB2 amp | EGFR | NTRK2 | |
| AR | ERBB2 | FLT3 | KRAS | NTRK3 | TP53 | FGFR1 amp | ESR1 | NTRK3 | |
| ARAF | ERBB3 | GNA11 | MAP2K1 | PDGFRA | | MET amp | FGFR1 | NUTM1 | |
| BRAF | ERBB4 | GNAQ | MAP2K2 | PIK3CA | | | FGFR2 | RET | |
| CDK4 | ESR1 | GNAS | MET | PTEN | | | FGFR3 | ROS1 | |

*Note: This assay is designed to identify well-characterized Tier 1 and Tier 2 hotspot variants [CAP/ASCO/AMP Guidelines; Li, M. et .al. JMD 2017 19(1):4-23] and does not assess full genes. For specific gene panel coverage information, please contact the laboratory.*

This new gene panel is especially recommended for the subpanel tumor types (Lung, Colorectal, Melanoma, Gastrointestinal stromal tumors-GIST). Other panel testing may be indicated for certain solid tumors (e.g. ovarian, endometrial, breast, prostate), depending on therapeutic considerations (e.g. PARP inhibitors, etc).

| Variant Type | Limit of Detection |
|---|---|
| Single Nucleotide Variants | 5% variant allele fraction (20% tumor cellularity preferred) |
| Small Indels (≤15 base pairs) | 5-10% variant allele fraction (20% tumor cellularity) |
| Large Indels (>15 base pairs) | Limit of Detection has not been established |
| Copy Number Amplifications | 15% tumor cellularity |
| Copy Number Losses (CDKN2A and PTEN genes | 70% tumor cellularity |
| Inter-genetic and Intra-genetic Fusions | 30% tumor cellularity |

## II. Tumor Mutational Burden (TMB) Assay

**Test Name:** Tumor Mutational Burden

**Test code:** TMBO

**Specimen Type**: FFPE tissue block, or 5 Unstained slides- 5-10µm thick at least 5mm X 5mm tumor tissue, preferably 10mm X 10mm tumor tissue, with accompanying H&E if possible

**Unacceptable specimens:** Paraffin blocks with low tumor percentage. Tissue fixed in heavy metal fixative or decalcified tissue.

**CPT Code:** 81479

**TAT:** 5 -10 business days

The Tumor Mutation Load (TML) Assay is a targeted next-generation sequencing assay that is designed for providing an accurate assessment of TMB (mutations/Mb). Studies have shown that tumors that have a high tumor mutation burden/load (TML or TMB) potentially have a better response to immunotherapy.

A tumor mutation burden will be reported as a Mutation Load (Mutations/Mb). The exact level of TML that should be used to predict response has not been definitively determined and may differ among tumor types. Pembrolizumab has been approved by the FDA for solid tumors with a TMB ≥ 10 mut/Mb in children and adults.

- The assay detects low frequency somatic variants (SNPs and INDELs) from 409 genes, spanning ~1.7 Megabases (Mb) of genomic space, encompassing 1.2 Mb of exonic sequence.
- The limit of detection for the TMB Assay is 20% Tumor Cellularity.
- This assay can be ordered in conjunction with the Solid Tumor Precision Panel or as a stand-alone test.

| **New test build information:** | | | | |
|---|---|---|---|---|
| **OrderCode** | **OrderName** | **ResultCode** | **ResultName** | **CPT** |
| STPP | Solid Tumor Precision Panel | STPPR | Solid Tumor Precision Panel | 81445 |
| TMBO | Tumor Mutational Burden | TMB | Tumor Mutational Burden | 81479 |

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**The Solid Tumor Precision panel will replace the individual gene tumor panels listed below. Please deactivate the following:**

| **OrderCode** | **OrderName** | **ResultCode** | **ResultName** | **CPT** |
|---|---|---|---|---|
| 50GCP | 50 Gene Cancer Panel | 50GCP | 50 Gene Cancer Panel | 81445 |
| 50GCPO | 50 GENE CANCER PANEL/OTHER | 50GCPO | 50 GENE CANCER PANEL/OTHER | 81450 |
| CCMP | COLON CANCER MUTATION PANEL | CCMP | COLON CANCER MUTATION PANEL | 81445 |
| EGFR | EGFR Mutations | EGFR | EGFR Mutations | 81235 |
| GIST | Gastrointestinal Stromal Tumor (GIST) Panel byNGS | GIST | Gastrointestinal Stromal Tumor (GIST) Panel by NGS | 81210 |
| KITPB | Kit Mutation detection/Blood (D816V) | KITPB | Kit Mutation detection/Blood (D816V) | 81273 |
| KRASM | KRAS Mutation Detection | KRASM | KRAS Mutation Detection | 81275, 81403 |
| LCMP | Lung Cancer Mutation Panel | LCMP | Lung Cancer Mutation Panel | 81445 |
| MMP | Melanoma Mutation Panel by Next Generation Sequencing | MMP | Melanoma Mutation Panel by Next Generation Sequencing | 81445 |
| PIK3CA | PIK3CA Mutation Detection | PIK3CA | PIK3CA Mutation Detection | 81309 |
| TP53P | TP53 Mutation Detection/Paraffin | TP53P | TP53 Mutation Detection/Paraffin | 81405 |

| **Update the order and results descriptions for the following tests (these tests can only be ordered on fresh specimens with a blast count >40%):** | | | | |
|---|---|---|---|---|
| **OrderCode** | **OrderName** | **ResultCode** | **ResultName** | **CPT** |
| IDH12 | IDH1 and IDH2 mutation detection | IDH12 | IDH1 and IDH2 mutation detection | 81403 |
| IDH12B | IDH1 and IDH2 mutation dection/blood | IDH12B | IDH1 and IDH2 mutation dection/blood | 81403 |

**Additional Resources:**

1. Hellmann MD, *et al*. Nivolumab plus Ipilimumab in Lung Cancer with a High Tumor Mutational Burden. N Engl J Med. 2018 May 31;378(22):2093-2104.

2. Marabelle A, *et al*. Association of tumour mutational burden with outcomes in patients with advanced solid tumours treated with pembrolizumab: prospective biomarker analysis of the multicohort, open-label, phase 2 KEYNOTE-158 study. Lancet Oncol. 2020 Oct;21(10):1353-1365.

3. Palmeri M, *et al*. Real-world application of tumor mutational burden-high (TMB-high) and microsatellite instability (MSI) confirms their utility as immunotherapy biomarkers, ESMO Open, Volume 7, Issue 1,2022.

4. Strickler JH, Hanks BA, Khasraw M. Tumor Mutational Burden as a Predictor of Immunotherapy Response: Is More Always Better? Clin Cancer Res. 2021 Mar 1;27(5):1236-1241.

**5.** https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-pembrolizumab-adults-and-children-tmb-h-solid-tumors

**If you have any questions about these new assays please contact your account manager at:** https://www.reglab.org/contact-us/