

## Solid Tumor Mutation Panel, Sequencing

Individuals diagnosed with a solid tumor cancer may benefit from testing for genetic mutations and variants that can affect treatment options and prognosis. Solid tumor cancers that may benefit from this testing include melanoma,<sup>1</sup> gastrointestinal stromal tumors (GISTs),<sup>2</sup> hepatocellular carcinomas,<sup>3</sup> primary brain tumors,<sup>4</sup> colorectal,<sup>5</sup> bladder,<sup>6</sup> and thyroid cancer,<sup>7</sup> among others. Testing can be useful at initial diagnosis or in the presence of refractory disease.

### Disease Overview

#### Diagnosis

- Genetic targets contained in the panel, including extended *RAS* targets,<sup>5</sup> are relevant across the spectrum of solid tumors.
- Identification of one or more variants may aid in diagnostic subclassification.

#### Prognosis and Treatment

- Certain gene variants may have prognostic significance.
- Certain gene variants may confer sensitivity or resistance to available targeted therapies.

### Genetics

#### Genes

*AKT1, ALK, APC, ATM, BRAF, CDH1, CDKN2A, CTNNB1, DDR2, EGFR, ERBB2, ERBB4, EZH2, FBXW7, FGFR1, FGFR2, FGFR3, GNA11, GNAQ, GNAS, HRAS, IDH1, IDH2, KDR, KIT, KRAS, MAP2K1, MET, MTOR, NOTCH1, NRAS, NTRK1, PDGFRA, PIK3CA, PTEN, RB1, RET, ROS1, SMAD4, SMO, STK11, TERT* promoter, *TP53, VHL*

#### Variants Detected

- This test is intended to detect somatic mutations, but germline alterations may also be detected.
- The assay does not distinguish between somatic and germline findings.
- Consultation with a genetic counselor is advised if there is any clinical suspicion for a germline alteration.

**Solid Panel Targeted Regions**

Gene	Accession No.	Targeted Exons
<i>AKT1</i>	NM_001014431.1	3, 4, 6
<i>ALK</i>	NM_004304.4	16-29
<i>APC</i>	NM_000038.5	16 <sup>a</sup>
<i>ATM</i>	NM_000051.3	8, 9, 12, 17, 26, 34-36, 39, 50, 54-56, 59, 61, 63

<sup>a</sup>c.2390-c.2879, c.3128-c.3497, c.3730-4932

<sup>b</sup>Exon known to contain known pseudogenes, homologous genomic regions, and/or low-mappability regions.

<sup>c</sup>c.374-c.743, c.815-c.1200+10

<sup>d</sup>c.7168-c.7657

<sup>e</sup>Only c.-124C>T, c.-146C>T, c.-57 A>C, c.-125\_124delinsTT, and c.-139\_-138delinsTT hotspot promoter variants reported.

### Tests to Consider

#### Solid Tumor Mutation Panel, Sequencing 3004294

**Method:** Massively Parallel Sequencing

- Use to assess for targeted variants that are useful for prognosis and/or treatment of individuals with solid tumor cancers, including melanoma, GIST, colorectal, bladder, and hepatocellular carcinomas, at initial diagnosis or in the presence of refractory disease
- If the clinical indication is lung cancer, additional molecular genetic testing may be considered for detection of gene rearrangements and/or c-MET exon 14-skipping alterations.
- For evaluation of microsatellite instability, additional molecular testing should be considered.

See [Related Tests](#)

Gene	Accession No.	Targeted Exons
<i>BRAF</i>	NM_004333.4	11, <sup>b</sup> 14, 15
<i>CDH1</i>	NM_004360.4	3, 8, 9
<i>CDKN2A</i>	NM_000077.4	2 <sup>b</sup>
<i>CTNNB1</i>	NM_001904.3	3
<i>DDR2</i>	NM_001014796.1	18
<i>EGFR</i>	NM_005228.4	18-21
<i>ERBB2</i>	NM_004448.3	8, 17-22
<i>ERBB4</i>	NM_005235.2	3, 4, 6-9, 15, 23
<i>EZH2</i>	NM_004456.4	16, 18 <sup>b</sup>
<i>FBXW7</i>	NM_033632.3	5, 8-11
<i>FGFR1</i>	NM_023110.2	4, 7
<i>FGFR2</i>	NM_000141.4	7, 9, 12
<i>FGFR3</i>	NM_000142.4	7, 9, 14, 16, 18
<i>GNA11</i>	NM_002067.4	5
<i>GNAQ</i>	NM_002072.4	5 <sup>b</sup>
<i>GNAS</i>	NM_000516.5	8, 9
<i>HRAS</i>	NM_005343.3	2-4
<i>IDH1</i>	NM_005896.3	4
<i>IDH2</i>	NM_002168.3	4
<i>KDR</i>	NM_002253.2	6, 7, 11, 19, 21, 26, 27, 30
<i>KIT</i>	NM_000222.2	2, 9, 10, 11, 13, 14, 15, 17, 18
<i>KRAS</i>	NM_004985.4	2, 3, 4
<i>MAP2K1</i>	NM_002755.3	2, <sup>b</sup> 3, 6, 7, <sup>b</sup> 11 <sup>b</sup>
<i>MET</i>	NM_001127500.2	2, <sup>c</sup> 11, 13, 14, 15, 16, 19
<i>MTOR</i>	NM_004958.3	27-58

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<sup>b</sup>Exon known to contain known pseudogenes, homologous genomic regions, and/or low-mappability regions.

<sup>c</sup>c.374-c.743, c.815-c.1200+10

<sup>d</sup>c.7168-c.7657

<sup>e</sup>Only c.-124C>T, c.-146C>T, c.-57 A>C, c.-125\_124delinsTT, and c.-139\_-138delinsTT hotspot promoter variants reported.

Gene	Accession No.	Targeted Exons
<i>NOTCH1</i>	NM_017617.4	26, 27, 34 <sup>d</sup>
<i>NRAS</i>	NM_002524.4	2-5
<i>NTRK1</i>	NM_002529.3	5-15, 17
<i>PDGFRA</i>	NM_006206.4	12, 14, 15, 18
<i>PIK3CA</i>	NM_006218.2	2, 5, 7, 8, 10, <sup>b</sup> 14, <sup>b</sup> 19, 21
<i>PTEN</i>	NM_000314.6	1, <sup>b</sup> 2, <sup>b</sup> 3, 4-9 <sup>b</sup>
<i>RB1</i>	NM_000321.2	4, 6, 10, 11, 14, 17, 18, 20, 21, 22
<i>RET</i>	NM_020975.4	6, 7, 8, 10-13, 15, 16
<i>ROS1</i>	NM_002944.2	7, 31-36, 38, 40, 41
<i>SMAD4</i>	NM_005359.5	3-12
<i>SMO</i>	NM_005631.4	3, 5, 6, 9-11
<i>STK11</i>	NM_000455.4	1, 4, 5, 6, 8
<i>TERT</i> Promoter	NM_198253.2.1	Selected promoter region variants <sup>e</sup>
<i>TP53</i>	NM_000546.5	2-11
<i>VHL</i>	NM_000551.3	1-3

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## Test Interpretation

### Analytic Sensitivity

Variant Class	No. of Variants Tested	PPA (%)	PPA (%), 95% Tolerance at 95% Reliability
SNVs	177	99	97.4-99.9
MNVs	42	93	82.2-98.0
Small insertions and duplications <sup>a</sup>	42	100	95.6-100.0

<sup>a</sup>≤21 bp.

<sup>b</sup>22-60 bp.

<sup>c</sup>≥61 bp and ≤64 bp.

<sup>d</sup>≥61 bp and ≤13547 bp.

bp, base pairs; MNV, multinucleotide variant; PPA, positive percent agreement; SNV, single nucleotide variant

Variant Class	No. of Variants Tested	PPA (%)	PPA (%), 95% Tolerance at 95% Reliability
Medium insertions and duplications <sup>b</sup>	10	100	82.9-100.0
Large insertions <sup>c</sup>	1	100	22.9-100.0
Small deletions <sup>a</sup>	80	100	97.6-100.0
Medium deletions <sup>b</sup>	14	100	71.2-99.2
Large deletions <sup>d</sup>	22	64	42.9-81.1

<sup>a</sup>≤21 bp.

<sup>b</sup>22-60 bp.

<sup>c</sup>≥61 bp and ≤64 bp.

<sup>d</sup>≥61 bp and ≤13547 bp.

bp, base pairs; MNV, multinucleotide variant; PPA, positive percent agreement; SNV, single nucleotide variant

## Results

Results	Variants Detected	Interpretation
Positive	Variants in ≥1 of the 44 genes were detected	Clinical relevance (diagnosis, prognosis, or therapy) will be correlated, if known
Negative	No pathogenic variants were detected	n/a

n/a, not available

## Limitations

- Does not detect copy number alterations, translocations, microsatellite instability (MSI), gene rearrangements, and tumor mutational burden
- Variants in areas outside the targeted genomic regions or below the limit of detection (LOD) of 5% variant allele frequency for SNVs or small- to medium-sized MNVs (<60 bp) will not be detected.
- 10 ng input DNA from extracted tissue sample is minimally required, but 50 ng input DNA is recommended for optimal results.
- Large variants (>60 bp) may not be detected.
- Variants in known pseudogenes, homologous genomic regions, and/or low-mappability regions may not be detected (see the [Solid Panel Targeted Regions](#) table).
- Not intended to detect minimal residual disease
- Does not distinguish between somatic and germline variants

## References

1. Seth R, Messersmith H, Kaur V, et al. [Systemic therapy for melanoma: ASCO guideline](#). *J Clin Oncol*. 2020;38(33):3947-3970.
2. von Mehren M, Joensuu H. [Gastrointestinal stromal tumors](#). *J Clin Oncol*. 2018;36(2):136-143.
3. Cancer Genome Atlas Research Network. [Comprehensive and integrative genomic characterization of hepatocellular carcinoma](#). *Cell*. 2017;169(7):1327-1341.e23.
4. Kristensen BW, Priesterbach-Ackley LP, Petersen JK, et al. [Molecular pathology of tumors of the central nervous system](#). *Ann Oncol*. 2019;30(8):1265-1278.
5. Sepulveda AR, Hamilton SR, Allegra CJ, et al. [Molecular biomarkers for the evaluation of colorectal cancer: guideline from the American Society for Clinical Pathology, College of American Pathologists, Association for Molecular Pathology, and the American Society of Clinical Oncology](#). *J Clin Oncol*. 2017;35(13):1453-1486.
6. Loriot Y, Necchi A, Park SH, et al. [Erdafitinib in locally advanced or metastatic urothelial carcinoma](#). *N Engl J Med*. 2019;381(4):338-348.
7. Nikiforov YE. [Role of molecular markers in thyroid nodule management: then and now](#) [published correction appears in *Endocr Pract*. 2017;23(11):1362]. *Endocr Pract*. 2017;23(8):979-988.

## Related Information

[Colorectal Cancer](#)  
[Gastrointestinal Stromal Tumors \(GISTs\)](#)  
[Hepatocellular Carcinoma - HCC](#)  
[Lynch Syndrome - Hereditary Nonpolyposis Colorectal Cancer \(HNPCC\)](#)  
[Non-Small Cell Lung Cancer - Non-Small Cell Lung Cancer Molecular Markers](#)  
[Melanoma](#)

## Related Tests

[ALK \(D5F3\) by Immunohistochemistry with Reflex to ALK Gene Rearrangements by FISH 2011431](#)

**Method:** Immunohistochemistry/Fluorescence in situ Hybridization

[ALK \(D5F3\) with Interpretation by Immunohistochemistry 2007324](#)

**Method:** Immunohistochemistry

[ALK Gene Rearrangements by FISH, Lung 3001302](#)

**Method:** Fluorescence in situ Hybridization (FISH)

[BRAF Codon 600 Mutation Detection by Pyrosequencing 2002498](#)

**Method:** Polymerase Chain Reaction/Pyrosequencing

[BRAF V600E Mutation Detection in Circulating Cell-Free DNA by Digital Droplet PCR 2013921](#)

**Method:** Polymerase Chain Reaction

[EGFR Mutation Detection by Pyrosequencing 2002440](#)

**Method:** Polymerase Chain Reaction/Pyrosequencing

[EGFR T790M Mutation Detection in Circulating Tumor DNA by Digital Droplet PCR 2012868](#)

**Method:** Polymerase Chain Reaction

[Gastrointestinal Stromal Tumor Mutations 3004279](#)

**Method:** Massively Parallel Sequencing

[IDH1 and IDH2 Mutation Analysis, exon 4 2006444](#)

**Method:** Polymerase Chain Reaction/Sequencing

[KIT Mutations Melanoma 3004283](#)

**Method:** Massively Parallel Sequencing

[KRAS Mutation Detection 0040248](#)

**Method:** Polymerase Chain Reaction/Pyrosequencing

[MET Gene Amplification by FISH 3001313](#)

**Method:** Fluorescence in situ Hybridization (FISH)

[Microsatellite Instability \(MSI\) HNPCC/Lynch Syndrome by PCR 3004277](#)

**Method:** Capillary Electrophoresis

[Mismatch Repair by Immunohistochemistry 0049302](#)

**Method:** Qualitative Immunohistochemistry

[NRAS Mutation Detection by Pyrosequencing 2003123](#)

**Method:** Polymerase Chain Reaction/Pyrosequencing

[RET Gene Rearrangements by FISH 3001312](#)

**Method:** Fluorescence in situ Hybridization (FISH)

[ROS1 by FISH 3001308](#)

**Method:** Fluorescence in situ Hybridization (FISH)

[ROS1 with Interpretation by Immunohistochemistry with Reflex to FISH if Equivocal or Positive 2008414](#)

**Method:** Immunohistochemistry

