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,[1] gastrointestinal stromal tumors (GISTs),[2] hepatocellular carcinomas,[3] primary brain tumors,[4] colorectal,[5] bladder,[6] and thyroid cancer,[7] among others. Testing can be useful at initial diagnosis or in the presence of refractory disease.

Featured ARUP Testing

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.

Disease Overview

Diagnosis

- Genetic targets contained in the panel, including extended *RAS* targets,[5] 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
AKT1	NM_001014431.1	3, 4, 6
ALK	NM_004304.4	16-29
APC	NM_000038.5	16[a]
ATM	NM_000051.3	8, 9, 12, 17, 26, 34-36, 39, 50, 54-56, 59, 61, 63
BRAF	NM_004333.4	11,[b] 14, 15
CDH1	NM_004360.4	3, 8, 9
CDKN2A	NM_000077.4	2[b]
CTNNB1	NM_001904.3	3
DDR2	NM_001014796.1	18
EGFR	NM_005228.4	18-21
ERBB2	NM_004448.3	8, 17-22
ERBB4	NM_005235.2	3, 4, 6-9, 15, 23
EZH2	NM_004456.4	16, 18[b]
FBXW7	NM_033632.3	5, 8-11
FGFR1	NM_023110.2	4, 7
FGFR2	NM_000141.4	7, 9, 12
FGFR3	NM_000142.4	7, 9, 14, 16, 18

[a]c.2390-c.2879, c.3128-c.3497, c.3730-4932

[b]Exon known to contain known pseudogenes, homologous genomic regions, and/or low-mappability regions.

[c]c.374-c.743, c.815-c.1200+10

[d]c.7168-c.7657

[e]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
GNA11	NM_002067.4	5
GNAQ	NM_002072.4	5[b]
GNAS	NM_000516.5	8, 9
HRAS	NM_005343.3	2-4
IDH1	NM_005896.3	4
IDH2	NM_002168.3	4
KDR	NM_002253.2	6, 7, 11, 19, 21, 26, 27, 30
KIT	NM_000222.2	2, 9, 10, 11, 13, 14, 15, 17, 18
KRAS	NM_004985.4	2, 3, 4
MAP2K1	NM_002755.3	2,[b] 3, 6, 7,[b] 11[b]
MET	NM_001127500.2	2,[c] 11, 13, 14, 15, 16, 19
MTOR	NM_004958.3	27-58
NOTCH1	NM_017617.4	26, 27, 34[d]
NRAS	NM_002524.4	2-5
NTRK1	NM_002529.3	5-15, 17
PDGFRA	NM_006206.4	12, 14, 15, 18
PIK3CA	NM_006218.2	2, 5, 7, 8, 10,[b] 14,[b] 19, 21
PTEN	NM_000314.6	1,[b] 2,[b] 3, 4-9[b]

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[d]c.7168-c.7657

[e]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
RB1	NM_000321.2	4, 6, 10, 11, 14, 17, 18, 20, 21, 22
RET	NM_020975.4	6, 7, 8, 10-13, 15, 16
ROS1	NM_002944.2	7, 31-36, 38, 40, 41
SMAD4	NM_005359.5	3-12
SMO	NM_005631.4	3, 5, 6, 9-11
STK11	NM_000455.4	1, 4, 5, 6, 8
TERT Promoter	NM_198253.2.1	Selected promoter region variants[e]
TP53	NM_000546.5	2-11
VHL	NM_000551.3	1-3

[a]c.2390-c.2879, c.3128-c.3497, c.3730-4932

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[c]c.374-c.743, c.815-c.1200+10

[d]c.7168-c.7657

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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

[a]≤21 bp.

[b]22-60 bp.

[c]≥61 bp and ≤64 bp.

[d]≥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
Small insertions and duplications[a]	42	100	95.6-100.0
Medium insertions and duplications[b]	10	100	82.9-100.0
Large insertions[c]	1	100	22.9-100.0
Small deletions[a]	80	100	97.6-100.0
Medium deletions[b]	14	100	71.2-99.2
Large deletions[d]	22	64	42.9-81.1

[a]≤21 bp.

[b]22-60 bp.

[c]≥61 bp and ≤64 bp.

[d]≥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.

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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 (Colon) Cancer
Gastrointestinal Stromal Tumors (GISTs)
Lynch Syndrome - Hereditary Nonpolyposis Colorectal Cancer (HNPCC)
Non-Small Cell Lung Cancer - Non-Small Cell Lung Cancer Molecular Markers
Melanoma

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