Lung Cancer Mutation Panel

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Molecular analysis may be used in lung cancer diagnosis to identify actionable targets and guide subsequent therapy selection.[1] This test uses targeted massively parallel sequencing (MPS; next generation sequencing [NGS]) to identify hotspot variants in genes critical for the diagnostic, prognostic, and therapeutic assessment of non-small cell lung cancer.

Featured ARUP Testing

Lung Cancer Mutation Panel 3017230

Method: Massively Parallel Sequencing

Recommended test to detect mutations in *BRAF*, *EGFR*, *ERBB2*, *KRAS*, and *MET* in non-small cell lung cancer.

Disease Overview

Lung cancer is a leading cause of cancer-related mortality in the United States. Diagnosis typically involves a combination of imaging studies, cytologic or histopathologic specimen evaluation, and subsequent immunohistochemistry (IHC) and genetic analysis.[1]

Most lung cancer cases are classified as non-small cell lung cancers (NSCLCs), of which adenocarcinomas are the most common. Adenocarcinoma is characterized by a prevalence of oncogenic driver genetic alterations that may influence prognosis and predict response to targeted therapies if present.

Test Interpretation

Clinically significant single nucleotide variants (SNVs), multiple nucleotide variants (MNVs), and small insertions and deletions (1-25 base pairs [bp]) and variants of uncertain significance within the preferred transcripts of the genes below are reported.

Genes Tested

Gene	Transcript (NM)	Covered Exon(s)[a]	Covered Regions
BRAF	NM_004333.4	15[a]	chr7:140453100-140453172
EGFR	NM_005228.4	18, 19, 20, 21	chr7:55241604-55241746, chr7:55242415-55242523, chr7:55248976-55249181, chr7:55259402-55259577
ERBB2	NM_004448.3	8[a], 19, 20[a]	chr17:37868171-37868259, chr17:378801560-37880273, chr17:37880969-37881085
KRAS	NM_004985.4	2[a], 3[a], 4[a]	chr12:25398230-25398318, chr12:25380261-25380349, chr12:25378541-25378683
MET	NM_001127500.2	14, 15[a], intron 14 (partial coverage)	chr7:116411806-116412053, chr7:116414925-116414978

[a]Indicated exons are partially covered for hotspots only and not reported in full.

Limitations

- This test does not detect variants in areas outside the targeted genomic regions or below the limit of detection. Additional clinical evaluation should be considered for complete genetic analysis, including detection of translocations or gene rearrangements. Interrogation of the many variants known to cause METex14 skipping is largely limited to canonical variants. For comprehensive evaluation of variants resulting in METex14 skipping, RNA-based assays should be considered.
- Copy number alterations (losses or amplifications), translocations, microsatellite instability, tumor mutational burden, deep intronic variants, insertions/deletions larger than 25 bp, and RNA variants are not detected.
- This test evaluates for variants in tumor tissue only and cannot distinguish between somatic and germline variants. If a hereditary/familial cancer is of clinical concern, additional clinical evaluation and genetic counseling should be considered before additional testing.
- In some cases, variants may not be identified due to technical limitations related to the presence of known pseudogenes, GC-rich regions, repetitive or homologous regions, low mappability regions, and/or variants located in regions overlapping amplicon primers.
- Tissue samples yielding between 1 ng and 5 ng total DNA input may yield suboptimal results and will be accepted for testing with a client-approved disclaimer.
- Benign or likely benign variants in the preferred transcript are not reported.
- Variant allele frequency (VAF) is not reported.
- Results of this test must always be interpreted within the context of clinical findings and other relevant data and should not be used alone for a diagnosis of malignancy, determination of prognosis, or recommendation of therapy.
- This test is not intended to detect minimal residual disease (MRD).

Limit of Detection (LOD)

10% VAF for all variant classes detected by the assay. For variants near the assay LOD, positive percent agreement (PPA) was found to be greater than 90% for all variant classes.

Analytic Accuracy/Sensitivity (PPA)

The PPA estimates for the respective variant classes (with 95% credibility region) are listed below.

Variant Class	Analytic Sensitivity (PPA)[a] Estimate (%)	Analytic Sensitivity (PPA)[a] 95% Credibility Region (%)
SNVs	98.4	95.1-99.7
Deletions (1-25 bp)	96.8	90.2-99.3
Insertions/duplications (1-25 bp)	96.8	90.2-99.3
MNVs	98.2	91.8-99.8

[a]Genes included on this test are a subset of a larger methods-based validation from which the PPA values are derived.

References

1. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: non-small cell lung cancer. Version 5.2022. Updated Sep 2022; accessed Oct 2020.