MAYO CLINIC LABORATORIES

NEW TEST

Notification Date: March 25, 2025
Effective Date: March 25, 2025

LiquidHALLMARK ctDNA and ctRNA

Test ID: LUCHM

Useful for:

- As an alternative to invasive tissue biopsies to assist in tumor profiling for diagnosis, predicting prognosis, and identifying targeted therapies for the treatment and management of patients with a solid tumor
- This test is **not useful for** prenatal screening.

Genetics Information:

- This test uses amplicon-based next-generation sequencing (NGS) to determine single nucleotide variants (SNVs, including cis-trans), deletions and insertions (delins), copy number variations (CNVs), microsatellite instability (MSI) and fusions. Circulating tumor DNA (ctDNA) is used to detect sequence variants in 80 genes, fusions in 10 genes, and somatic mutations. Circulating tumor RNA (ctRNA) is used to analyze 10 ctRNA targets for actionable and emerging fusions. See LiquidHALLMARK Targets List for details regarding genes interrogated.
- Note: This test is performed to evaluate for somatic (ie, tumor-specific) mutations within the genes listed. Although germline (ie, inherited) alterations may be detected, this test cannot distinguish between germline variants and somatic mutations with absolute certainty.

Highlights:

- LiquidHALLMARK is a sensitive next-generation sequencing assay targeting both circulating tumor DNA and RNA to profile a patient's unique cancer. With a blood draw, LiquidHALLMARK provides important information for cancer care especially when tissue by invasive biopsy is insufficient or inaccessible.
- LiquidHALLMARK targets genes that are commonly associated with 15 cancers, including lung, breast and colon cancer.

Methods:

Amplicon-Based Next-Generation Sequencing

Reference Values:

An interpretive report will be provided

Specimen Requirements:

Specimen Type:	Whole blood
Supplies:	Strek Tan Top Tube Kit (T715)
Container/Tube:	Two 10-mL Streck cell-free DNA (cfDNA) blood collection tubes
Specimen Volume:	20 mL; 10 mL in two Streck tubes
Collection Instructions:	1. Invert several times to mix blood. 2. Send whole blood specimen in original tube. **Do not centrifuge or aliquot.**

Necessary Information:

1. Ask at order entry questions are required for testing to proceed.

If not ordering electronically, submit the following information with the specimen:

- **Original Diagnosis Date**
- **Diagnosis:** Lung, Breast, Colon, Prostate, Ovarian, Other, Not Specified
- **Subtype** If Applicable
- **Disease Stage:** Stage IIIB/IV-NSCLC, Stage III/IV, Other, Not Specified
- **Current Therapy and Response**
- **Disease Status:** Metastatic, Refractory, Progression, Recurrent, Relapse, Other, Not Specified
- **ICD-10 Codes**

2. A pathology report is **recommended**. Testing may proceed without this information; however, it aids in providing a more thorough and accurate interpretation of results. Ordering healthcare professionals are strongly encouraged to provide the information and send with the specimen.

Shipping Instructions:

Specimen must be received at Mayo Clinic Laboratories within 4 days of collection.

Specimen Stability Information:

Specimen Type	Temperature	Time	Special Container
WB Strek	Ambient	4 days	Strek Black/Tan top

Cautions:

- This report reflects the analysis of DNA and RNA from an extracted nucleic acid sample, and in very rare cases (for example, bone marrow transplant or recent blood transfusion), the analyzed DNA may not reflect the patient's genome, leading to possible false-negative or false-positive results. Nucleic acid studies do not constitute a definitive test for the selected conditions in all individuals.
- This circulating tumor (ct) DNA and ctRNA test is clinically validated for plasma specimens only. Other specimen types, including but not limited to pleural effusions, pericardial effusions, and cerebrospinal fluid, have not been validated.
- It should be realized that there are possible sources of error. Errors can result from trace contamination, rare technical errors, rare genetic variants that interfere with analysis, recent scientific developments, and alternative classification systems.

- Test sensitivity may be altered based on factors such as excessive cell lysis before processing, sampling during treatment, tissue heterogeneity, and the relative yield of circulating nucleic acids from sample. Lipemic plasma specimens may also result in reduced assay sensitivity or assay failure.
- Sensitivity of this test has been determined for the test methodology for a set of variants that do not necessarily include those identified in the report. Sensitivity and specificity data for all variants reported are not available. Where reported allele frequencies fall below 0.1% (single nucleotide variations/deletions-insertions) or 0.5% (DNA fusion), absolute number of variant reads supporting the call are considered, but specificity data is not available on this. Deletions or insertions involving more than 30 base pairs may not be reliably detected by the sequencing methodology. Although most of the intended targeted regions are sequenced in their entirety, some regions may be incompletely covered due to technical limitations. Therefore, absence of a detected variant in these regions and in regions not covered by this test does not exclude the presence of a disease-causing variant. Intronic variants and synonymous substitutions are not reported unless previously documented as clinically significant. Variants classified as benign or likely benign in ClinVar and/or variants with population allele frequency (in external or internal databases) of greater than 1% (non-founder mutations) are not reported.
- This test is not intended for and cannot confirm germline status in any manner. Variants detected may be of tumor-derived somatic, germline, or non-tumor somatic origins, including mosaicism, clonal hematopoiesis of indeterminate potential (CHIP). Genes with alterations that may be derived from CHIP include, but are not limited to, *ASXL1, ATM, CBL, DNMT3A, JAK2, MPL, MYD88, SF3B1, TET2, TP53,* and *U2AF1*. Clinical correlation is recommended. Genetic counseling may be considered if deemed appropriate clinically.
- For cases where no genomic alterations and no ctRNA findings are identified, the absence of plasma ctDNA alterations and ctRNA findings may correlate with low systemic disease volume or disease that is being effectively treated. It is also possible that there are genomic/ctRNA alterations in targets not included in the panel or others not detectable by this analysis due to inherent analytical limitations. Further clinical correlation is advised, with consideration of follow-up tissue or plasma testing.
- Results for fusions, splice and exon-skipping variants from ctDNA and ctRNA assay components may not be fully concordant due to differing test sensitivities and differing limits of detection for ctDNA and ctRNA assays, differing target gene coverage in each assay, and sample-specific variations in levels of fusion, splice and exon skipping variant RNA transcripts depending on transcription rates of DNA to RNA.
- For the ctRNA component, this test has been validated for fusions, splice and exon-skipping variants in *ALK*, *FGFR2*, *FGFR3*, *MET*, *NTRK1*, *NTRK2*, *RET*, *ROS1*, and *TMPRSS2*. The clinical significance of other findings presented in this section has not been established. These other findings are evaluated and reported as part of the standard workflow.
- This test should be one of many aspects used by the treating healthcare professional to help with a diagnosis and treatment plan, but it is not a diagnosis itself. Clinical diagnosis provided by the treating healthcare professional is used to determine the relevant indication for determining appropriate clinical actionability/evidence and matching clinical trials, presentation of which may be adversely affected in cases of incomplete or incorrect diagnosis information provided. Any mention of pharmacologic agents or their on-label or off-label use should not be considered as a recommendation or endorsement for therapeutic use. Approved indications for the listed therapies may have additional criteria of medical and treatment history and combination chemotherapy. Percentage map is for visualization purposes only and is not drawn to scale. Clinical correlation is advised. Past treatment or mutation history is not being considered for selection of clinical trials presented. Clinical correlation and suitability with specific trial's inclusion and exclusion criteria are advised. Drug and clinical trial information are obtained from curated databases including NCI thesaurus and ClinicalTrials.gov. Clinical trial curated database is updated with trials verified within the last month. Tiering of clinical actionability/evidence associated with a drug recommendation may be updated in source data but not reflected as at the time of the report. For latest information, refer to the

US Food and Drug Administration website and the respective source data websites for professional guidelines.

- Lucence does not warrant that the data from such third-party databases, websites, or guidelines are accurate, complete, or up to date and excludes all liability for any loss or damage howsoever arising as a result of any reliance on the accuracy of the data.

CPT Code:
81479

Day(s) Performed: Monday through Friday

Report Available: 8 to 12 days

Questions

Contact Michelle Raths, Laboratory Resource Coordinator at 800-533-1710.