MAYO CLINIC LABORATORIES

Test Definition: SARCP

Sarcoma Targeted Gene Fusion/Rearrangement Panel, Next-Generation Sequencing, Tumor

Overview

Useful For

Diagnosing specific soft tissue and bone tumors (sarcoma) based on the observed gene fusions (eg, *PAX3*/*FOXO1* gene fusion observed in alveolar rhabdomyosarcoma, *EWSR1-FLI1* gene fusion for Ewing sarcoma, *SS18-SSX1/2* gene fusion for synovial sarcoma)

Genetics Test Information

This test evaluates 138 gene targets for the presence of somatic gene fusions and also assesses for common *BCOR* internal tandem duplications. See Sarcoma Targeted Gene Fusion Panel and Common *BCOR* Tandem Duplications for details regarding the targeted gene regions identified by this test.

Targeted genes: *ACTB, AHRR, ALK, ASPSCR1, ATF1, ATIC, BCOR, BRD3, BRD4, CAMTA1, CARS, CCNB3, CDH11, CDX1, CD63, CEP128, CIC, CITED2, CLTC, CNBP, COL1A1, COL1A2, COL3A1, COL6A3, CREB1, CREB3L1, CREB3L2, CSF1, CXorf67, C11orf95, DDIT3, DUX4, DVL2, EML4, EPC1, EP400, ERG, ETV1, ETV4, ETV6, EWSR1, FEV, FGFR1, FLI1, FN1, FOSB, FOXO1, FOXO4, FUS, GLI1, HAS2, HEY1, HMGA2, IRF2BP2, JAZF1, KIRREL, KLF17, LAMTOR1, LPP, MAML3, MBTD, MEAF6, MED12, MIR143HG, MKL2, MYH9, NAB2, NCOA1, NCOA2, NFATC2, NFIB, NOTCH1, NOTCH2, NR4A3, NTRK1, NTRK3, NUMA1, NUTM1, NUTM2B, OMD, OPHN1, PATZ1, PAX3, PAX7, PBX1, PBX3, PDGFB, PDPN, PHF1, PLAG1, PLPP3, POU5F1, PPFIBP1, PRDM10, PRKCA, PRKCB, PRKCD, RAB2A,RAD51B, RANBP2, RNF213, RRAGB, SEC31A, SERPINE1, SETBP1, SFMBT1, SMARCA5, SP3, SQSTM1, SRF, SRSF3, SSX1, SSX2, SSX4, SS18, SS18L1, STAT6, SUZ12, S100A10, TAF15, TCF12, TEAD1, TFE3, TFG, THRAP3, TPM3, TPM4, TPR, USP6, VCL, VGLL2, WT1, WWTR1, YAP1, YWHAE, ZC3H7B, ZFP36,* and *ZNF444*.

Additional Tests

Test Id	Reporting Name	Available Separately	Always Performed
SLIRV	Slide Review in MG	No, (Bill Only)	Yes

Testing Algorithm

When this test is ordered, slide review will always be performed at an additional charge.

Special Instructions

- Tissue Requirements for Solid Tumor Next-Generation Sequencing
- Sarcoma Targeted Gene Fusion Panel
- Common BCOR Tandem Duplications

Method Name

Polymerase Chain Reaction (PCR)-based Next-Generation Sequencing (NGS)

NY State Available

Yes

Specimen

Specimen Type
Varies

Ordering Guidance
Multiple oncology (cancer) gene panels are available. For more information see Hematology, Oncology, and Hereditary Test Selection Guide.

Necessary Information
Pathology report (final or preliminary), at minimum containing the following information, **must** accompany specimen in order for testing to be performed:
1. Patient name
2. Block number-must be on all blocks, slides and paperwork (can be handwritten on the paperwork)
3. Tissue collection date
4. Source of the tissue

Specimen Required
This assay requires at least 10% tumor nuclei.
-Preferred amount of tumor area with sufficient percent tumor nuclei: tissue 144 mm(2)
-Minimum amount of tumor area: tissue 36 mm(2)
-These amounts are cumulative over up to 10 unstained slides and must have adequate percent tumor nuclei.
-Tissue fixation: 10% neutral buffered formalin, not decalcified
-For specimen preparation guidance, see Tissue Requirement for Solid Tumor Next-Generation Sequencing. In this document, the sizes are given as 4 mm x 4 mm x 10 slides as preferred: approximate/equivalent to 144 mm(2) and the minimum as 3 mm x 1 mm x 10 slides: approximate/equivalent to 36 mm(2).

Preferred:
Specimen Type: Formalin-fixed, paraffin-embedded (FFPE) tissue
Container/Tube: Tissue block
Collection Instructions: Submit a formalin-fixed, paraffin-embedded tissue block.

Acceptable:
Specimen Type: FFPE Tissue
Slides: 1 Stained and 10 unstained
Collection Instructions: Submit 1 slide stained with hematoxylin and eosin and 10 unstained, nonbaked slides with 5-micron thick sections of the tumor tissue.

Specimen Type: Cytology slide (direct smears or ThinPrep)
Slide: 1 to 3 slides

Collection Instructions: Submit 1 to 3 slides stained and coverslipped with a preferred total of 5000 nucleated cells or a minimum of at least 3000 nucleated cells.
Note: Glass coverslips are preferred; plastic coverslips are acceptable but will result in longer turnaround times.
Additional Information: Cytology slides will not be returned.

Forms

If not ordering electronically, complete, print, and send a Oncology Test Request (T729) with the specimen.

Specimen Minimum Volume

See Specimen Required

Reject Due To

Specimens that have been decalcified (all methods) Specimens that have not been formalin-fixed, paraffin-embedded Bone marrow in EDTA	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Ambient (preferred)		
	Refrigerated		
	Frozen		

Clinical & Interpretive

Clinical Information

Molecular analysis of biomarkers is increasingly being utilized in oncology practices to support and guide patient diagnosis, prognosis, and therapeutic management. Chromosomal translocations, interstitial deletions, and inversions that lead to gene fusions are common in various sarcomas, such as Ewing sarcoma and rhabdomyosarcoma. This next-generation sequencing assay is used to detect specific gene fusions to assist in the diagnosis of sarcomas. See Method Description for details regarding the targeted gene regions identified by this test.

Reference Values

An interpretive report will be provided.

Interpretation

The interpretation of molecular biomarker analysis includes an overview of the results and the associated diagnostic, prognostic, and therapeutic implications.

Cautions

This assay is not validated for the detection of point variations, deletions-insertions, copy number alterations, or gene expression.

This assay may detect gene fusions that are present at the RNA level, but not the DNA level, that result from cis splicing of adjacent genes or trans-splicing.(1)

This panel can detect in-frame and out-of-frame fusions. There may be lower sensitivity in detecting out-of-frame fusions such as exon-intron, intron-intron, or big insertions. This assay will only detect fusions involving at least one gene in the defined genes of interest list.

This assay will only detect fusions involving gene transcripts that have been defined in UCSC Genome Browser (March 2012 version) available from Illumina's iGenomes Project.(2)

Reliable results are dependent on adequate specimen collection and processing. This test has been validated on cytology slides and formalin-fixed, paraffin-embedded tissues; other types of fixatives are discouraged. Improper treatment of tissues, such as decalcification, may cause polymerase chain reaction failure.

A negative result does not rule out the presence of a gene fusion that may be present but below the limits of detection of this assay (tumor cells comprise <10% of the cell population; targeted fusion read coverage with <10 unique fusion molecules in a sample).

The limit of detection of this assay for specific gene fusions is dependent on several variables, including decreased sensitivity with decreased tumor percentage and decreased sensitivity with decreased level of expression of the gene fusion.

RNA is particularly labile and degrades quickly. Rapid preservation of the tumor sample after collection reduces the likelihood of degradation. Still, there can be biological factors, such as tumor necrosis, which interfere with obtaining a high-quality RNA specimen despite rapid preservation.

The presence or absence of a fusion may not be predictive of response to therapy or prognosis in all patients.

Fusions of uncertain significance may be identified.

Supportive Data

In a verification study, this next-generation sequencing (NGS) assay was performed in 111 sarcoma formalin-fixed, paraffin-embedded and cytology samples (86 fusion positive and 25 fusion negative). The NGS assay results were

confirmed by reverse transcription-polymerase chain reaction and fluorescence in situ hybridization tests. The overall accuracy of the NGS assay was 95.5% (106/111). No targeted gene fusions were detected in 20 negative control samples (100% specificity).

Clinical Reference

1. Jia Y, Xie Z, Li H. Intergenically spliced chimeric RNAs in cancer. Trends Cancer. 2016;2(9):475-484. doi:10.1016/j.trecan.2016.07.006
2. Jo VY, Fletcher CD. WHO classification of soft tissue tumours: an update based on the 2013 (fourth) edition. Pathology. 2014;46(2):95-104. doi:10.1097/PAT.0000000000000050
3. Fletcher CD. The evolving classification of soft tissue tumours - an update based on the new 2013 WHO classification. Histopathology. 2014;64(1):2-11. doi:10.1111/his.12267
4. Quesada J, Amato R. The molecular biology of soft-tissue sarcomas and current trends in therapy. Sarcoma. 2012;2012(3):849456. doi:10.1155/2012/849456
5. Podnar J, Deiderick H, Huerta G, Hunicke-Smith S. Next-generation sequencing RNA-seq library construction. Curr Protoc Mol Biol. 2014;106:4.21.1-4.21.19
6. Mertens F, Tayebwa J. Evolving techniques for gene fusion detection in soft tissue tumours. Histopathology. 2014;64(1):151-162. doi:10.1111/his.12272
7. AI-Zaid T, Wang WL, Somaiah N, Lazar AJ. Molecular profiling of sarcomas: new vistas for precision medicine. Virchows Arch. 2017;471(2):243-255
8. Gao Q, Liang WW, Foltz SM, et al. Driver fusions and their implications in the development and treatment of human cancers. Cell Rep. 2018;23(1):227-238. doi:10.1016/j.celrep.2018.03.050
9. Lam SW, Cleton-Jansen AM, Cleven AHG, et al. Molecular analysis of gene fusions in bone and soft tissue tumors by anchored multiplex PCR-based targeted next-generation sequencing. J Mol Diagn. 2018 Sep;20(5):653-663. doi:10.1016/j.jmoldx.2018.05.007
10. Roy A, Kumar V, Zorman B, et al. Recurrent internal tandem duplications of BCOR in clear cell sarcoma of the kidney. Nat Commun. 2015;6:8891. doi:10.1038/ncomms9891
11. Marino-Enriquez A, Lauria A, Przybyl J, et al. BCOR Internal tandem duplication in high-grade uterine sarcomas. Am J Surg Pathol. 2018;42(3):335-341. doi:10.1097/PAS.0000000000000993

Performance

Method Description

RNA-based next-generation sequencing is performed to test for the presence of rearrangements involving targeted regions of 138 fusion genes. See Sarcoma Targeted Gene Fusion Panel and Common *BCOR* Tandem Duplications for details regarding the targeted gene regions identified by this test.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Varies

Report Available
10 to 14 days

Specimen Retention Time
FFPE tissue block: Unused portions of FPPE blocks will be returned; Unused, unstained slides: 5 years; Stained slides: Indefinitely

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
81456
88381

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
SARCP	Sarcoma Targeted Gene Fusion Panel	95124-4

Result ID	Test Result Name	Result LOINC® Value
606430	Result Summary	50397-9
606431	Result	95123-6
606432	Interpretation	69047-9
606433	Additional Information	48767-8
606434	Method	85069-3
606435	Disclaimer	62364-5
606436	Specimen	31208-2
606437	Source	39111-0
606452	Tissue ID	80398-1

606438	Released By	18771-6