Test Definition: XL2

FOXL2 Mutation Analysis, Tumor

Overview

Useful For

Assisting in the clinical diagnosis of adult granulosa cell tumor (GCT) by assessing gene targets with in the *FOXL2* gene

This test is **not useful for** hematological malignancies.

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

Method Name

Polymerase Chain Reaction (PCR)-Based Next-Generation Sequencing

NY State Available

Yes

Specimen

Specimen Type

Varies

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 20% tumor nuclei.

-Preferred amount of tumor area with sufficient percent tumor nuclei: tissue144 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 Special Instructions. In this document, the sizes are given as 4mm x 4mm x 10 slides as preferred: approximate/equivalent to 144 mm(2) and the minimum as 3mm x 1mm x 10 slides: approximate/equivalent to 36mm(2).

Preferred:

Specimen Type: Tissue block

Collection Instructions: Submit a formalin-fixed, paraffin-embedded tissue block with acceptable amount of tumor tissue.

Acceptable:

Specimen Type: Tissue slide

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.

Note: The total amount of required tumor nuclei can be obtained by scraping up to 10 slides from the same block.

Specimen Type: Cytology slide (direct smears or ThinPrep)

Slides: 1 to 3 slides

Collection Instructions: Submit 1 to 3 slides stained and cover slipped 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 an Oncology Test Request (T729) with the specimen.

Specimen Minimum Volume

See Specimen Required

Reject Due To

Other	Specimens that have been decalcified (all methods) Specimens that have not been formalin-fixed, paraffin-embedded

Specimen Stability Information

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

Clinical and Interpretive

Clinical Information

Granulosa cell tumor (GCT) represents approximately 5% to 10% of all ovarian malignancies and is the most common type of malignant ovarian sex-cord stromal tumor. The majority of patients with GCT (95%) are adults and 5% are juveniles. The histopathological diagnosis of GCT is challenging. Forkhead box L2 (*FOXL2*) gene is involved in ovarian development and function. The *FOXL2* gene point mutation 402C->G in exon 1 (C134W) was reported in the majority of adult GCT (>90%), 5% to 10% of thecomas (tumors closely related to GCT) and less than 10% of juvenile GCT cases, but not in other ovarian tumors. Detection of *FOXL2* mutation aids in the clinical diagnosis of adult GCT.

Next-generation sequencing has recently emerged as an accurate, cost-effective method to identify alterations across numerous genes. This test uses formalin-fixed paraffin-embedded tissue or cytology slides to assess for common somatic mutations in the *FOXL2* gene known to be associated with adult GCT. The results of this test can be useful for supporting a diagnosis of adult GCT.

Reference Values

An interpretative report will be provided.

Interpretation

An interpretive report will be provided.

Cautions

This test cannot differentiate between somatic and germline alterations. Additional testing may be necessary to clarify the significance of results if there is a potential hereditary risk.

DNA variants of uncertain significance may be identified.

A negative (wild-type) result does not rule out the presence of a mutation that may be present but below the limits of detection of this assay.

Point mutations and small insertion and deletion mutations will be detected with in the *FOXL2* gene only. This test does not detect large single or multiexon deletions, or duplications or genomic copy number variants.

Rare polymorphisms may be present that could lead to false-negative or false-positive results. Test results should be interpreted in the context of clinical findings, tumor sampling and other laboratory data. If results obtained do not

match other clinical or laboratory findings, please contact the laboratory for updated interpretation. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

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 PCR failure.

Supportive Data

This next-generation sequencing assay detects somatic mutations that can be used to assist in the diagnosis of granulosa cell tumor (GCT).

This assay has been shown to be very reproducible, having a 100% concordance for intra- and interassay reproducibility experiments. All somatic mutations that had been previously identified by various other molecular methods were detected by this assay during accuracy studies. No pathogenic variants were detected in known mutation-negative samples.

Clinical Reference

1. Shah SP, Kobel M, Senz J, et al: Mutation of *FOXL2* in granulosa-cell tumors of the ovary. N Engl J Med 2009;360:2719-2729

2. Kim MS, Hur SY, Yoo NJ, et al: Mutational analysis of *FOXL2* codon 134 in granulosa cell tumour of ovary and other human cancers. J Pathol 2010;221:147-152

3. Schrader KA, Gorbatcheva B, Senz J, et al: The specificity of the *FOXL2* c.402C->G somatic mutation: a survey of solid tumors. PLoS One 2009 Nov 24;4(11):e7988

4. Benayoun BA, Kalfa N, Sultan C, et al: The forkhead factor *FOXL2*: a novel tumor suppressor? Biochim Biophys Acta 2010;1805:1-5

Performance

Method Description

Next-generation sequencing is performed to test for the presence of a mutation in targeted regions of the *FOXL2* gene, including exon 1 codons 92-148. (Unpublished Mayo method).

Gene	GenBank Accession Number	Nucleotide Start	Nucleotide End	Chromosome	Exon	Codons
FOXL2	NM_023067	138665124	138665246	Chromosome 3	Exon 1	107-147

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

12 to 20 days

Performing Laboratory Location

Rochester

Fees and 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 Regional Manager. 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. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

81479

88381

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
XL2	FOXL2 Mutation Analysis, Tumor	95785-2

Result ID	Test Result Name	Result LOINC Value
92373	Result Summary	50397-9
92374	Result	82939-0
92375	Interpretation	69047-9
92376	Additional Information	48767-8
92377	Specimen	31208-2
92378	Source	31208-2
92379	Tissue ID	80398-1
92380	Released By	18771-6