Test Definition: PDG14

PDGFRA exon 14, Mutation Analysis

Overview

Useful For

Diagnosis and management of patients with gastrointestinal stromal tumors or other tumors

Identification of a mutation in exon 14 of the *PDGFRA* gene

Additional Tests

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

Testing Algorithm

This test is performed in conjunction with SLIRV / Slide Review in MG. Additional testing may be performed after review by pathologist. Upon approval from the requesting clinician, PATHC / Pathology Consultation may be added, if determined to be appropriate.

Special Instructions

- Pathology/Cytology Information

Method Name

Polymerase Chain Reaction (PCR) and Sequencing

NY State Available

Yes

Specimen

Specimen Type

Varies

Advisory Information

Special stains performed outside Mayo Clinic Laboratories and included with the case may be repeated and charged at the reviewing pathologist's discretion. Testing requested by referring physician may not be performed if deemed unnecessary by Mayo Clinic pathologist.

Necessary Information

A pathology/diagnostic report including a brief history is required. If available, include KIT Immunostain results.

Specimen Required

A quality specimen is essential for evaluation. Submit only tissue containing tumor cells; **minimal tissue is required** for evaluation.

Supplies: Surgical Pathology Packaging Kit (T554) requested, but not required

Preferred:

Specimen Type: Formalin-fixed, paraffin-embedded (FFPE) tissue block with a minimum of 60% tumor cell population

Collection Instructions: Process all specimens into FFPE tissue blocks prior to submission.

Acceptable:

Specimen Type: Unstained slides with a minimum of 60% tumor population; slides may be stained and/or scraped

Slides: A minimum of ten, 4- to 5-micron thick, unstained slides are required.

Forms

1. Pathology/Cytology Information (T707) in Special Instructions

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

Reject Due To

Tissue	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

Occasional cases of gastrointestinal stromal tumors (GIST) can harbor mutations in *PDGFRA*, a gene structurally related to *KIT*. The frequency and type of mutations vary among these tumors and portent distinct clinical implications. The ordering physician is responsible for the diagnosis and management of disease and decisions based on the data provided.

Reference Values

An interpretative report will be provided.

Interpretation

Results are reported as positive, negative, or failed. A negative result does not rule out the presence of a mutation.

Cautions

Reliable results are dependent on adequate specimen collection and processing. This test has been validated on formalin-fixed, paraffin-embedded tissues; other types of fixatives are discouraged. Improper treatment of tissues, such as decalcification, may cause PCR failure. False-negative results may occur in heterozygous tumor specimens

when tumor cells comprise <60% of the cell population. Tumor cells are routinely enriched by macrodissection to avoid false-negative results.

PDGFRA mutations may be occasionally found in inflammatory fibroid polyps.(1)

Clinical diagnosis and therapy should not be based solely on this assay. The results should be considered in conjunction with clinical information, histologic evaluation, and additional diagnostic tests.

This test is unable to distinguish between a somatic and a germline *KIT* (or *PDGFRA*) mutation. Germline *KIT* (or *PDGFRA*) mutations are rare and their clinical relevance has been described in more detail in Clinical References 2 and 3. Testing of a peripheral blood specimen from this individual would be required to distinguish a germline from a somatic mutation. This test is not currently offered at Mayo Clinic.

Supportive Data

We studied a set of 75 formalin-fixed, paraffin-embedded specimens: 40 classic gastrointestinal stromal tumors (GIST), 10 unrelated tumors, 21 neuroendocrine tumors, and 4 other tumors (2 metastatic melanomas, 1 breast cancer, and 1 squamous cell carcinoma). The literature reports that approximately 80% of GISTs harbor a mutation in *KIT* gene, while 2% to 5% harbor mutations in *PDGFRA*. Overall, we found 83% of GISTs tested demonstrated mutations in *KIT* and/or *PDGFRA*, which is in accordance with the literature.

Clinical Reference

1. Schildhaus HU, Cavlar T, Binot E, et al: Inflammatory fibroid polyps harbour mutations in the platelet-derived growth factor receptor alpha (PDGFRA) gene. J Pathol 2008;216(2):176-182

2. Robson ME, Blogowski E, Sommer G, et al: Pleomorphic characteristics of a germ-line KIT mutation in a large kindred with gastrointestinal stromal tumors, hyperpigmentation, and dysphagia. Clin Cancer Res 2004;10:1250-1254

3. Li FP, Fletcher JA, Heinrich MC, et al: Familial gastrointestinal stromal tumor syndrome: phenotypic and molecular features in a kindred. J Clin Oncol 2005;23:2735-2743

4. Corless CL, Fletcher JA, Heinrich MC: Biology of gastrointestinal stromal tumors. J Clin Oncol 2004;22:3813-3825

5.Debiec-Rychter M, Raf Sciot R, Le Cesne A, et al: *KIT* mutations and dose selection for imatinib in patients with advanced gastrointestinal stromal tumors. Eur J Cancer 2006;42:1093-1103

6. Heinrich MC, Corless CL, Demetri GD, et al: Kinase mutations and imatinib response in patients with metastatic gastrointestinal stromal tumor. J Clin Onc 2003;21:4342-4349

7.Debiec-Rychter M, Dumez H, Judson I, et al: Use of c-*KIT*/*PDGFRA* mutational analysis to predict the clinical response to imatinib in patients with advanced gastrointestinal stromal tumors entered on phase I and II studies of the EORTC Soft Tissue and Bone Sarcoma Group. Eur J Cancer 2004;40:689-695

Performance

Method Description

The paraffin-embedded tissue is macroscopically examined and the tumor-rich portion is dissected, deparaffinized, lysed, and digested. Genomic DNA is extracted using either a phenol-chloroform method or the QIAamp DNA FFPE Tissue kit (Qiagen). The DNA is amplified via PCR. Primers specific for *PDGFRA* exon 14 are used. Controls are run with each specimen to assess possible contamination issues and overall test performance. The patient and control samples are sent for direct DNA sequencing. The sequencing chromatograms are analyzed by manual and software

methods and the presence or absence of a *PDGFRA* exon 14 mutation is determined. The results are interpreted and reported by a working group pathologist.(Instruction manual: Qiagen DNA FFPE Tissue Handbook; unpublished Mayo method)

PDF Report

No

Day(s) and Time(s) Test Performed

Monday through Friday; Varies

Analytic Time

14 days

Maximum Laboratory Time

20 days

Specimen Retention Time

Unused portions of blocks will be returned. Unused slides are stored indefinitely.

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 U.S. Food and Drug Administration.

CPT Code Information

81314-*PDGFRA (platelet-derived growth factor receptor alpha polypeptide)* (eg, gastrointestinal stromal tumor [GIST]), gene analysis, targeted sequence analysis (eg, exons 12, 18)

88381-Microdissection, manual

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
PDG14	PDGFRA exon 14, Mutation Analysis	In Process

Result ID	Test Result Name	Result LOINC Value
54844	Result Summary	50397-9
54845	Result	82939-0
54846	Interpretation	69047-9

Result ID	Test Result Name	Result LOINC Value
54847	Additional Information	48767-8
54848	Reason for Referral	42349-1
54849	Specimen	31208-2
54850	Source	31208-2
54851	Tissue ID	80398-1
54852	Released By	18771-6