Test Definition: EGFRT

EGFR Gene, Mutation Analysis, Tumor

Overview

Useful For

Identifying non-small cell lung cancers that may respond to epidermal growth factor receptor-tyrosine kinase inhibitor therapies

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.

Method Name

Polymerase Chain Reaction (PCR) Analysis

NY State Available

Yes

Specimen

Specimen Type

Varies

Specimen Required

Pathology report**must** accompany specimen in order for testing to be performed.

Preferred:

Specimen Type: Tissue

Container/Tube: Tissue block

Collection Instructions: Submit a formalin-fixed, paraffin-embedded tissue block.

Acceptable:

Specimen Type: Tissue

Container/Tube: Slides

Specimen Volume: 1 stained and 5 unstained

Collection Instructions: Submit 1 slide stained with hematoxylin and eosin and5 unstained, non-baked slides with

5-micron thick sections of the tumor tissue.

Forms

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

Specimen Minimum Volume

Formalin-fixed, paraffin-embedded (FFPE) tissue block (preferred) or 1 slide stained with hematoxylin and eosin and 5 unstained, nonbaked slides with 5-microns thick sections of the tumor tissue.

Reject Due To

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

Specimen Stability Information

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

Clinical and Interpretive

Clinical Information

Lung cancer is the leading cause of cancer-related deaths in the world. Non-small cell lung cancer (NSCLC) represents 70% to 85% of all lung cancer diagnoses. Small molecular agents that target the tyrosine kinase domain of the epidermal growth factor receptor (EGFR) protein are approved for the treatment of locally advanced or metastatic NSCLC as a second- or third-line regimen. Subsequently, randomized trials have suggested that targeted agents alone or combined with chemotherapy may be beneficial in maintenance and first-line settings. Because the combination of targeted therapy and standard chemotherapy leads to an increase in toxicity and cost, strategies that help to identify the individuals most likely to benefit from targeted therapies are desirable.

EGFR is a growth factor receptor that is activated by the binding of specific ligands, resulting in activation of the RAS/MAPK pathway. Activation of this pathway induces a signaling cascade ultimately leading to cell proliferation. Dysregulation of the RAS/MAPK pathway is a key factor in tumor progression for many solid tumors. Targeted therapies directed to tumors harboring activating mutations within the *EGFR* tyrosine kinase domain (exons 18-21) have demonstrated some success in treating a subset of patients with NSCLC by preventing adenosine 5'-triphosphate (ATP)-binding at the active site. Gefitinib and erlotinib have been approved by the FDA for use in treating patients with NSCLC who previously failed to respond to the traditional platinum-based doublet chemotherapy. These 2 drugs have also recently been shown to increase progression-free and overall survival in patients who receive EGFR-tyrosine kinase inhibitor therapy as a first-line therapy for the treatment of NSCLC.

Agents such as gefitinib and erlotinib, which prevent ATP binding to EGFR kinase, do not appear to have any meaningful inhibitor activity on tumors that demonstrate the presence of the specific drug-resistant *EGFR* mutation T790M. Therefore, current data suggest that the efficacy of EGFR-targeted therapies in NSCLC is confined to patients with tumors demonstrating the presence of *EGFR*- activating mutations such as L858R, L861Q, G719A/S/C, S768I or small deletions within exon 19 **and** the absence of the drug-resistant mutation T790M. As a result, the

mutation status of *EGFR* can be a useful marker by which patients are selected for EGFR-targeted therapy.

Reference Values

An interpretive report will be provided.

Interpretation

An interpretive report will be provided.

Cautions

A negative (wild type) result does not rule out the presence of a mutation that may be present but below the limits of detection for this assay (approximately 10%).

A negative (wild type) result does not rule out the presence of other activating mutations in the epidermal growth factor receptor (*EGFR*) gene.

The predictive value of epidermal growth factor receptor (EGFR) testing applies to EGFR--tyrosine kinase inhibitors (TKI) therapies, not to other therapeutic agents.

Not all patients that have activating *EGFR* mutations detected by this assay respond to EGFR-TKI therapies.

Rare polymorphisms exist that could lead to false-negative or false-positive results.

Clinical Reference

1. Sharma SV, Bell DW, Settleman J, Haber DA: Epidermal growth factor receptor mutations in lung cancer. Nat Rev Cancer 2007;7(3):169-181

2. Gao G, Ren S, Li A, et al: Epidermal growth factor receptor-tyrosine kinase inhibitor therapy is effective as first-line treatment of advanced non-small-cell lung cancer with mutated EGFR: a meta-analysis from six phase III randomized controlled trials. Int J Cancer 2011;131(5):E822-829

3. Mok TS: Personalized medicine in lung cancer: what we need to know. Nat Rev Clin Oncol 2011;8:661-668

Performance

Method Description

A PCR-based assay employing Scorpions real-time PCR and allele-specific PCR technologies is used to test for 29 mutations within exons 18 through 21 of the *EGFR* gene:

G719A	2239_2256del8
G719S	2239_2248TTAAGAGAAG->C
G719C	2239_2258->CA
2235_2249del15	2240_2251del12
2235_2252->AAT	2240_2257del8
2236_2253del18	2240_2254del15
2237_2251del15	2239_2251->C
2237_2254del18	2307_2308ins9

2237_2255->T	2310_2311insGGT
2236_2250del15,	2319_2320insCAC
2238_2255del18,	S768I
2238_2248->GC	T790M
2238_2252->GCA	L858R
2239_2247del9	L861Q
2239_2253del15	

A pathology review and macro dissection to enrich for tumor cells is performed prior to DNA extraction.(Package insert: EGFR RGQ PCR Kit, Qiagen, Valencia, CA, 2011)

PDF Report

No

Day(s) and Time(s) Test Performed

Monday through Friday; 10 a.m.

Analytic Time

5 days

Maximum Laboratory Time

7 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 has been modified from the manufacturer's instructions. Its performance characteristics were 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

EGFR Gene, Mutation Analysis, 29 Mutation Panel, Tumor

81235-*EGFR* (epidermal growth factor receptor) (eg, non-small cell lung cancer) gene analysis, common variants (eg, exon 19 LREA deletion, L858R, T790M, G719A, G719S, L861Q)

Slide Review

88381-Microdissection, manual

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
EGFRT	EGFR Gene, Mutation Analysis, Tumor	21665-5

Result ID	Test Result Name	Result LOINC Value
53246	Result Summary	50397-9
53247	Result	21665-5
53248	Interpretation	69047-9
53249	Specimen	31208-2
53250	Source	31208-2
54442	Tissue ID	80398-1
53251	Released By	18771-6