MAYO CLINIC LABORATORIES

Test Definition: EGFRS

EGFR Gene, Targeted Mutation Analysis, 51 Mutation Panel, Tumor

Overview

Useful For

Identifying non-small cell lung cancers that may respond to epidermal growth factor receptor-targeted 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)

NY State Available

Yes

Specimen

Specimen Type

Varies

Necessary Information

Pathology report must accompany specimen for testing to be performed.

Specimen Required

Preferred: Submit 3, if available, or 2 of the following specimens.
Acceptable: Submit **at least one** of the following specimens.

Specimen Type: Tissue block
Collection Instructions: Submit a formalin-fixed, paraffin-embedded (FFPE) tissue block with acceptable amount of tumor tissue.

Specimen Type: Tissue slide
Source: FFPE tissue, cell block (prepared from fine-needle aspirate, or pleural fluid)
Slides: 1 Hematoxylin and eosin-stained and 5 unstained
Collection Instructions:
Submit the followings slides:

1 Slide stained with hematoxylin and eosin
AND
5 Unstained, nonbaked slides with 5-micron thick sections of the tumor tissue.
Additional Information:
1. Hematoxylin and eosin-stained and unstained slides will not be returned.
2. Broken or cracked unstained slides will be rejected. Stained slides that were broken and repaired (ie, double mounted) at the client site will not be rejected, as, in most cases, they can still be reviewed under the microscope. However, due to the double mounting, digital scanning cannot be performed.

Specimen Type: Cytology slide (direct smears; smears stained with Pap stain are not acceptable)
Slides: 2 Slides
Collection Instructions: Submit 2 slides stained with Diff Quik and coverslipped with a total of 5000 nucleated cells (preferred) or at least 3000 nucleated cells (minimum).
Note: Glass coverslips are preferred; plastic coverslips are acceptable but will result in longer turnaround times.
Additional Information:
1. Cytology slides will not be returned. An image of the slides will be stored per regulatory requirements.
2. Stained slides that were broken and repaired (ie, double mounted) at the client site will not be rejected, as, in most cases, they can still be reviewed under the microscope. However, due to the double mounting, digital scanning cannot be performed.

Forms

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

Specimen Minimum Volume

Formalin-fixed, paraffin-embedded tissue block or Slides: see Specimen Required
Cytology smear stained with Diff Quik: >1000 cells

Reject Due To

Broken or cracked unstained slides	Reject
Broken or cracked stained slides that cannot be repaired	Reject

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

Targeted cancer therapies are defined as antibody or small molecule drugs that block the growth and spread of cancer by interfering with specific cell molecules involved in tumor growth and progression. Multiple targeted therapies have been approved by the US Food and Drug Administration for treatment of specific cancers. Molecular genetic profiling is often needed to identify targets amenable to targeted therapies and to minimize treatment costs and therapy-associated risks.

Epidermal growth factor receptor (EGFR) protein 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 non-small cell lung cancer.

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

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

Cautions

A negative (wildtype) 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 (wildtype) result does not rule out the presence of other activating mutations in the *EGFR* gene.

Not all patients that have activating *EGFR* mutations detected by this assay respond to epidermal growth factor receptor-targeted therapies.

Rare genetic alterations (ie, polymorphisms) exist that could lead to false-negative or false-positive results.

Broken or cracked unstained slides are not compatible with the instrumentation used in our performing laboratories and will be rejected. Additional material may be requested.

Attempts will be made to repair broken or cracked stained slides; however, if they are unable to be repaired (ie, shattered in transit), they will be rejected and discarded due to safety concerns.

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. doi:10.1038/nrc2088
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. 2012;131(5):E822-829. doi:10.1002/ijc.27396
3. Mok TS. Personalized medicine in lung cancer: what we need to know. Nat Rev Clin Oncol. 2011;8(11):661-668. doi:10.1038/nrclinonc.2011.126
4. Lee CS, Sharma S, Miao E, Mensah C, Sullivan K, Seetharamu N. A comprehensive review of contemporary literature for epidermal growth factor receptor tyrosine kinase inhibitors in non-small cell lung cancer and their toxicity. Lung Cancer (Auckl). 2020;11:73-103. doi:10.2147/LCTT.S258444

Performance

Method Description

All specimens will undergo *EGFR* testing. The *EGFR* test is a qualitative polymerase chain reaction (PCR)-based assay employing fluorescently labeled probes that are used to detect exon 18 (G719A/C/S), exon 21 (L858R, L861Q), exon 20 (T790M, S768I) mutations, exon 19 deletions and exon 20 insertions of the *EGFR* gene.(Unpublished Mayo method)

Exon	Mutation	Protein change	Nucleotide change	Genotype
18	G719A	p.Gly719Ala	c.2156G>C	G719A/C/S
	G719C	p.Gly719Cys	c.2155G>T	
	G719C	p.Gly719Cys	c.2154_2155delinsTT	
	G719S	p.Gly719Ser	c.2155G>A	
19	Deletion 9	p.Leu747_Ala750delinsPro	c.2238_2248delinsGC	Exon 19 deletion
			c.2239_2248delinsC	
		p.Leu747_Ala750delinsSer	c.2240_2248del	
		p.Leu747_Glu749del	c.2239_2247del	
	Deletion 12	p.Leu747_Thr751delinsPro	c.2239_2251delinsC	
		p.Leu747_Thr751delinsSer	c.2240_2251del	
	Deletion 15	p.Glu746_Ala750del	c.2235_2249del	
			c.2236_2250del	
		p.Leu747_Thr751del	c.2239_2253del	
			c.2240_2254del	
			c.2238_2252del	
		p.Glu746_Thr751delinsAla	c.2237_2251del	
		p.Glu746_Thr751delinsIle	c.2235_2252delinsAAT	
		p.Glu746_Thr751delinsVal	c.2237_2252delinsT	
		p.Lys745_Ala750delinsThr	c.2234_2248del	
		p.Glu746_Thr751delinsLeu	c.2236_2253delinsCTA	
		p.Glu746_Thr751delinsVal	c.2237_2253delinsTA	
		p.Glu746_Thr751delinsAla	c.2235_2251delinsAG	

		p.Glu746_Thr751delinsGln	c.2236_2253delinsCAA	
		p.Ile744_Ala750delinsValLys	c.2230_2249delinsGTCAA	
	Deletion 18	p.Leu747_Pro753delinsSer	c.2240_2257del	
		p.Glu746_Ser752delinsVal	c.2237_2255delinsT	
		p.Leu747_Ser752del	c.2239_2256del	
		p.Glu746_Thr751del	c.2236_2253del	
		p.Leu747_Pro753delinsGln	c.2239_2258delinsCA	
		p.Glu746_Ser752delinsAla	c.2237_2254del	
		p.Glu746_Ser752delinsAsp	c.2238_2255del	
		p.Glu746_Pro753delinsValSer	c.2237_2257delinsTCT	
		p.Glu746_Ser752delinsIle	c.2236_2255delinsAT	
			c.2236_2256delinsATC	
		p.Glu746_Ser752delinsVal	c.2237_2256delinsTT	
			c.2237_2256delinsTC	
			c.2235_2255delinsGGT	
	Deletion 21	p.Leu747_Pro753del	c.2238_2258del	
		p.Glu746_Ser752del	c.2236_2256del	
	Deletion 24	p.Ser752_Ile759del	c.2253_2276del	
20	T790M	p.Thr790Met	c.2369C>T	T790M
	S768I**	p.Ser768Ile	c.2303G>T	S768I
	InsG	p.Asp770_Asn771insGly	c.2310_2311insGGT	Exon 20 insertion
	InsASV(9)	p.Val769_Asp770insAlaSerVal	c.2307_2308insGCCAGCGTG	
	InsASV(11)	p.Val769_Asp770insAlaSerVal	c.2309_2310delinsCCAGCGTGGAT	
	InsSVD	p.Asp770_Asn771insSerValAsp	c.2311_2312insGCGTGGACA	
	InsH	p.His773_Val774insHis	c.2319_2320insCAC	
21	L858R	p.Leu858Arg	c.2573T>G	L858R
			c.2573_2574delinsGT	
			c.2573_2574delinsGA	
	L861Q	p.Leu861Gln	c.2582T>A	L861Q

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
4 to 7 days

Specimen Retention Time

Tissue blocks: Unused portions of blocks will be returned; Tissue slides: Hematoxylin and eosin-stained and unstained slides will not be returned. Unused slides are stored for at least 5 years.

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

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)
88381-Microdissection, manual

LOINC® Information

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

Result ID	Test Result Name	Result LOINC® Value
616123	Result Summary	50397-9
616124	Result	21665-5
616125	Interpretation	69047-9
616126	Specimen	31208-2
616127	Source	31208-2
616128	Tissue ID	80398-1
616129	Released By	18771-6