Medgenome Labs Ltd
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DNA TEST REPORT

Full Name	**Christopher Kalinski**	Order ID/Sample ID	**1228078/9018634**
Age/Gender	**74 Years/Male**	Sample Type	**FFPE**
Referring Clinician	**Dr. Senaka Kandegedara Aegle Omics Private Limited (Colombo)**	Block No & Tumor content	**RP3326 (A4) / 65%**
		Date & time of Sample Receipt	**13-03-2025, 11:15:00**
		Date & time of Report	**17-03-2025, 18:02:27**
Collection Center/ Partner Lab			
Test Requested	**EGFR gene analysis (Hot Spot) - 4 exons (18, 19, 20, 21) [MGM190]**		

CLINICAL DIAGNOSIS / SYMPTOMS / HISTORY

Biopsy of lung - Squamous cell carcinoma of lung

RESULTS

No mutation is detected in Exons 18, 19, 20 and 21 of the EGFR gene

Sl. No.	*Mutation Tested in EGFR	Exon No.	Mutation status	Sensitive to TKIs
1	Ex-19 Deletion	19	Negative	NA
2	L858R	21	Negative	NA
3	T790M	20	Negative	NA
4	Ex-20 Insertions	20	Negative	NA
5	G719X	18	Negative	NA
6	S7681	20	Negative	NA
7	L861Q	21	Negative	NA

***HGVS annotation details shared in Appendix I**

CLINICAL CORRELATION AND INTERPRETATION

No Missense mutations, Insertions and Deletions are detected in Exons 18, 19, 20 and 21 of the EGFR gene.

TEST DETAILS

Epidermal Growth Factor Receptor (EGFR) is a cellular transmembrane receptor protein. The activation of EGFR plays an important role in cellular tumor growth proliferation and metastasis. EGFR tyrosine kinase (TK) gene mutations have been identified in non-small cell lung cancer (NSCLC) patients. NSCLC patients with EGFR mutation are known to respond to TK inhibitor therapy [eg. Gefitinib (Iressa) or Erlotinib (Tarceva)]. Also, during the course of treatment, some patients develop T790M resistance mutation in EGFR kinase domain and no longer respond to TK inhibitors. As per the clinical guidelines (NCCN version 3.2018 / ESMO 2022), detection of this mutation recommends change of first and second generation TKI to third generation TKI Osimertinib (Tagrisso), and it has been demonstrated to have improvement in progression free survival in NSCLC. Presence of Exon 20 insertions mutations in the tumor confers decreased sensitivity to first and second-generation EGFR tyrosine kinase inhibitors. Recently FDA has approved JNJ-6372, an EGFR-MET bispecific antibody (dual targeting) for treatment of NSCLC patients with EGFR Exon 20 Insertions mutation, whose disease has progressed on or after platinum-based chemotherapy. The scope of this test is to screen for 29 somatic mutations in the kinase domain (Exons - 18, 19, 20, 21) of EGFR gene by ARMS real-time PCR technology. It includes the good responder, poor responder and the resistance mutation T790M in Exon 20 for EGFR TKIs..

METHODOLOGY

FFPE tumor tissue sections are deparaffinized and DNA is extracted from the sample is tested for the presence of indicated hotspot mutations (Exon 19 deletions, Exon 20 insertions and substitution mutations G719X, S768I, T790M, L858R and L861Q in exons 18, 20 and 21 of the EGFR gene) using ARMS real-time PCR QuantStudio version 5. The target exons are amplified with mutation specific primers. Mutations are reported according to HGVS guidelines for mutation nomenclature (www.hgvs.org) and according to the reference sequence NM_005228.3.

LIMITATIONS

This test is performed using a CE, IVD marked commercial kit. However, there may be limitations imposed by the sensitivity and the specificity of the assay and should be interpreted in conjunction with clinical presentation and other related investigations. Results of the test could be affected by contamination during specimen collection, inappropriate specimen storage and transport.

DISCLAIMER

The analytical sensitivity of the test allows detection of the mutation when the mutant clone comprises at least 1% of the total genomic DNA. Real-time PCR is a highly sensitive technique; reasons for apparently contradictory results may be due to improper quality control during sample collection and fixation, intrinsic heterogeneity of the sample, tumor depletion, high degree of necrosis, mucin content and/or presence of PCR inhibitors.

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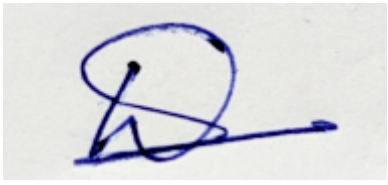

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APPENDIX I - EGFR MUTATIONS DETECTED BY THE KIT

SlNo.	EGFR mutation	Exon	Mutation	Base change	Cosmic ID
1	Exon 19 Deletions	19	E746_A750del (1)	2235_2249del15	6223
			E746_A750del (2)	2236_2250del15	6225
			L747_P753>S	2240_2257del18	12370
			E746_T751>I>	2235_2252>AAT(complex)	13551
			E746_T751del	2236_2253del18	12728
			E746_T751>A	2237_2251del15	12678
			E746_S752>A	2237_2254del18	12367
			E746_S752>V	2237_2255>T(complex)	12384
			E746_S752>D	2238_2255del18	6220
			L747_A750>P	2238_2248>GC(complex)	12422
			L747_T751>Q	2238_2252>GCA(complex)	12419
			L747_E749del	2239_2247del9	6218
			L747_T751del	2239_2253del15	6254
			L747_S752del	2239_2256del18	6255
			L747_A750>P	2239_2248TTAAGAGAAG>C(complex)	12382
			L747_P753>Q	2239_2258>CA(complex)	12387
			L747_T751>S	2240_2251del12	6210
			L747_T751del	2240_2254del15	12369
			L747_T751>P	2239_2251>C(complex)	12383
2	L858R	21	L858R	2573T>G	6224
3	T790M	20	T790M	2369C>T	6240
4	Insertions	20	H773_V774insH	2319_2320insCAC	12377
			D770_N771insG	2310_2311insGGT	12378
			V769_D770insASV	2307_2308insgccagcgtg	12376
5	G719X	18	G719A	2156G>C	6239
			G719S	2155G>A	6252
			G719C	2155G>T	6253
6	S768I	20	S768I	2303G>T	6241
7	L861Q	21	L861Q	2582T>A	6213