Comprehensive Panel- 206 Genes

Test Description

The MolQ Comprehensive Panel includes 206 key solid tumor genes that are well characterized in the published literature and associated with oncology drugs that are FDA approved, part of NCCN guidelines, or in clinical trials. The assay allows concurrent analysis of DNA and RNA in a single workflow involving detection of multiple types of variants, including hotspots, single nucleotide variants (SNVs), indels, CNVs and gene fusions.

Patient Demographic
Name: Mr. Gajendra Pandey
Sex: Male
Date of Birth/Age: 63.1 years
Disease: Ewing Sarcoma (Round Cell Sarcoma)

Clinician
Clinician Name: Dr Amit Verma
Medical Facility: Dr AV Institute of Personalized Therapy and Cancer Research (IPTCR)
Pathologist: Not Provided

Specimen
Booking ID: 012307070027
Sample Type: FFPE
Tumor Content Percentage: 100%
Date of Collection:07-07-2023
Date of Booking:07-07-2023

CLINICAL SYNOPSIS

Gajendra Pandey, is a known case of round cell carcinoma. He has been evaluated for pathogenic variations in the genes listed in Appendix 2.

RESULTS

EWSR1-ERG Fusion was detected in the specified specimen.

Gene (Fusion)	Tier	Diagnostic
EWSR1::ERG	1B	Yes

RELEVANT CANCER SPECIFIC FINDINGS

Gene	Findings (At DNA Level)	Gene	Findings (At RNA Level)	Gene	Findings (At RNA Level)
ERBB2	None detected	*PAX8*	None detected	*SS18*	None detected
KRAS	None detected	*ETV6*	None detected		
BRAF	None detected	*FUS*	None detected		
KIT	None detected	*STAT6*	None detected		
PDGFRA	None detected	*ALK*	None detected		
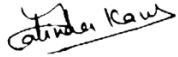
CLINICAL CORRELATION AND VARIANT INTERPRETATION

EWSR1-ERG   **Fusion**

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Variant description: The *EWSR1-ERG* fusion is known to be oncogenic. The *EWSR1-ERG* fusion encodes a chimeric protein with the N-terminal RNA-binding domain of *EWSR1* and the C-terminal DNA-binding domain of *ERG*. The *EWSR1* (Ewing sarcoma breakpoint region 1) gene encodes the EWS protein. *EWSR1-ERG* has been poorly studied as compared to the more prevalent and highly homologous *EWSR1-FLI1* fusion. Preclinical experiments have demonstrated that *EWSR1-FLI1* is associated with malignant transformation of mesenchymal stem cells. *EWSR1-FLI1* causes transcriptional dysregulation by binding to and opening GGAA repetitive elements in the chromatin to activate transcription and conversely, binding to canonical ETS binding GGAA sites and suppressing transcription at these sites. **The *EWSR1-ERG* fusion, t(21;22)(q22;q12), is the second most common fusion product in the Ewing Sarcoma family of tumors.**

RECOMMENDATIONS

- Genetic counselling is advised for interpretation on the consequences of the variant(s).

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Head, Molecular Biology & Genomics

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APPENDIX 1: TEST METHODOLOGY

Method

Massively Parallel Sequencing (Next Generation Sequencing): Tumor Nucleic acid from the submitted specimen was enriched for the coding regions of genes in the panel and splice site junctions of genes. DNA and RNA were extracted from samples using the Qiagen FFPE DNA and RNAeasy FFPE kit. Paired end sequencing was performed on Illumina platform (NovaSeq 6000/NextSeq2000) with a minimum depth of 500X. The assay allows concurrent analysis of DNA and RNA. Assay detect multiple types of variants, including hotspots, single nucleotide variants (SNVs), indels, CNVs, and gene fusions, in a single workflow**.** All positive variants are visualized on Integrative Genomics Viewer (IGV) and reported.

AMP/ASCO/CAP Classification

Tier I: Variants of Strong Clinical Significance	1A	Biomarkers that predict response or resistance to US FDA-approved therapies for a specific type of tumor or have been included in **professional guidelines** as **therapeutic, diagnostic, and/or prognostic biomarkers** for specific types of tumors.
	1B	Biomarkers that predict response or resistance to a therapy based on well-powered studies with consensus from experts in the field, or have diagnostic and/or prognostic significance of certain diseases based on **well- powered studies with expert consensus**.
Tier II: Variants of Potential Clinical Significance	2C	Biomarkers that predict response or resistance to therapies approved by FDA or professional **societies for a different tumor type (ie, off-label use of a drug)**, serve as inclusion criteria for clinical trials, or have diagnostic and/or prognostic significance based on the results of multiple small studies.
	2D	Biomarkers that show plausible therapeutic significance based on preclinical studies, or may assist disease diagnosis and/or prognosis themselves or along with other biomarkers based on **small studies or multiple case reports** with no consensus.
Tier III: Variants of Unknown Clinical Significance		Not observed at a significant allele frequency in the general or specific subpopulation databases, or pan-cancer or tumor-specific variant databases No convincing published evidence of cancer association.
Tier IV: Benign or Likely Benign Variants		Observed at significant allele frequency in the general or specific subpopulation databases.

DISCLAIMER

- Interpretation of variants in this report is performed to the best knowledge of the laboratory based on the information available at the time of reporting. The classification of variants can change over time and MolQ cannot be held responsible for this. Please feel free to contact MolQ Laboratory (contact@molq.in) in the future to determine if there have been any changes in the classification of any variations. Re-analysis of variants in previously issued reports in light of new evidence is not routinely performed, but may be considered upon request, provided the variant is covered in the current panel.
- Due to inherent technology limitations of the assay, not all bases of the exome can be covered by this test. Accordingly, variants in regions of insufficient coverage may not be identified and/or interpreted. Therefore, it is possible that certain variants are present in one or more of the genes analyzed, but have not been detected. The variants not detected by the assay that was performed may/ may not impact the phenotype.
- It is also possible that a pathogenic variant is present in a gene that was not selected for analysis and/or interpretation in cases where insufficient phenotypic information is available.
- Genes with pseudogenes, paralog genes and genes with low complexity may have decreased sensitivity and specificity of variant detection and interpretation due to inability of the data and analysis tools to unambiguously determine the origin of the sequence data in such regions.
- The mutations have not been validated/confirmed by Sanger sequencing.
- Incidental or secondary findings (if any) that meet the ACMG guidelines can be given upon request.
- The report shall be generated within turnaround time (TAT), however, such TAT may vary depending upon the complexity of test(s) requested. MolQ Laboratory under no circumstances will be liable for any delay beyond afore mentioned TAT.
- It is hereby clarified that the report(s) generated from the test(s) do not provide any diagnosis or opinion or recommends any cure in any manner. MolQ Laboratory hereby recommends the patient and/or the guardians of the patients, as the case may be, to take assistance of the clinician or a certified physician or doctor, to interpret the report(s) thus generated. MolQ Laboratory hereby disclaims all liability arising in connection with the report(s).

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- In a very few cases genetic test may not show the correct results, e.g. because of the quality of the material provided to MolQ Laboratory. In case where any test provided by MolQ Laboratory fails for unforeseeable or unknown reasons that cannot be influenced by MolQ Laboratory in advance, MolQ Laboratory shall not be responsible for the incomplete, potentially misleading or even wrong result of any testing if such could not be recognized by MolQ Laboratory in advance.
- This is a laboratory developed test and the development and the performance characteristics of this test was determined by reference laboratory.

LIMITATIONS

- Testing has been performed assuming that the sample received belongs to the above-named individual(s) and any stated relationships between individuals are accepted as true.
- 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. The analytical sensitivity of this assay is 5%. Sequencing is performed at a depth of 500x
- This test does not differentiate between somatic and germline alterations. Additional testing may be necessary to clarify the significance of results if there is a potential hereditary risk.
- Due to inherent technology limitations, coverage is not uniform across all regions. Hence pathogenic variants present in areas of insufficient coverage may not be analyzed/ reported.
- The classification and interpretation of all the variants in this assay reflects the current state of scientific understanding at the time this report was issued. In some instances, the classification and interpretation of such variants may change as new scientific information comes to light.
- Test results should be interpreted in context of clinical findings, tumor sampling, histopathology, and other laboratory data.
- If results obtained do not match other clinical laboratory findings, please contact the laboratory for possible. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.
- Genetic testing is highly accurate. Rarely, inaccurate results may occur for various reasons. These reasons include, but are not limited to mislabelled samples, inaccurate reporting of clinical/medical information, rare technical errors or unusual circumstances such as bone marrow transplantation, blood transfusion; or the presence of change(s) in such a small percentage of cells that may not be detectable by the test (mosaicism).

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APPENDIX 2: GENE LIST

Gene	Gene	Gene	Gene	Gene	Gene	Gene
ABL1	CD274	EWSR1	HRAS	MYCN	POLE	SMARCA4
ACVR1	CD74	EZHIP	IDH1	MYH7	PPARG	SMARCB1
AKT1	CDH1	FANCA	IDH2	NAB2	PPP2R2A	SMARCE1
AKT2	CDK12	FANCI	JAG1	NBN	PRDM6	SMO
AKT3	CDK4	FANCL	JAZF1	NCOA2	PRKCA	SS18
ALK	CDK6	FBXW7	KDM6A	NF1	PTCH1	SSX1
APC	CDKN1B	FEV	KDR	NF2	PTEN	SSX2
AR	CDKN2A	FGFR1	KIF5B	NOTCH1	QKI	SSX2B
ARAF	CDKN2B	FGFR2	KIT	NOTCH2	RAD51	STAT6
ARID1A	CHEK1	FGFR3	KLF4	NRAS	RAD51B	STK11
ASPSCR1	CHEK2	FGFR4	KMT2A	NRG1	RAD51C	SUFU
ATF1	CREB3L1	FH	KRAS	NTRK1	RAD51D	SUZ12
ATM	CTNNB1	FLCN	MAML2	NTRK2	RAD54L	TERT
ATP7B	CYSLTR2	FLI1	MAP2K1	NTRK3	RAF1	TEX12
ATR	DDIT3	FLT1	MAP2K2	NUTM1	RARA	TFE3
ATRX	DDR2	FLT3	MDM2	PALB2	RB1	TFEB
BAP1	DDX3X	FLT4	MDM4	PAX3	RELA	TMPRSS2
BARD1	DICER1	FOXL2	MEN1	PAX7	RET	TOE1
BCL2	DNAJB1	FOXO1	MET	PAX8	RHEB	TP53
BCL6	DPYD	FOXR2	MGMT	PDGFB	RICTOR	TPM3
BCOR	EGFR	FUS	MLH1	PDGFRA	ROS1	TRAF7
BCR	EML4	GLI2	MN1	PDGFRB	SDC4	TSC1
BRAF	EP300	GNA11	MRE11	PGR	SDCCAG8	TSC2
BRCA1	EPCAM	GNAQ	MSH2	PIK3CA	SDHA	VHL
BRCA2	ERBB2	GNAS	MSH6	PIK3R1	SDHB	WT1
BRIP1	ERBB3	H3-3A	MTOR	PKD1	SDHC	YAP1
CCND1	ERCC2	H3C2	MUTYH	PKHD1	SDHD	YWHAE
CCND2	ERG	H3C3	MYB	PLCB4	SF3B1	
CCND3	ESR1	HEY1	MYC	PMS2	SLC34A2	
CCNE1	ETV6	HFE	MYCL	POLD1	SMAD4	