Patient: John A. Doe

DOB/Gender: xx/xx/xxxx (55 yrs) - Male
SSN: xxx-xx-xxxx
MRN/ID: xxxx

Provider: Jane Smith, M.D.
Account: Hematology Oncology Associates
Phone: 800-123-4567 **Fax:** 800-765-4321

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Case No: GS14-03755

Collected: xx/xx/xx
Received: xx/xx/xx
Reported: xx/xx/xx

Alert Status: Routine
Report Status: Final
Report Category: Detected

Clinical information: Colorectal cancer

Specimens received: 1 Paraffin block **Specimen analyzed:** X14-12345-B5 **Tests ordered:** NGS-50 Panel

SmartGen

Professional Services Provided By Yale SCHOOL OF MEDICINE

RESULT:

Solid tumors (#X14-12345-B5), colon adenocarcinoma:
APC c.2626C>T (p.R876*), c.4348C>T (p.R1450*), KRAS c.35G>A (p.G12D), and TP53 c.818G>A (p.R273H) mutations detected.

COMMENT:

The sequencing test reported above was performed and solely interpreted at Baylor College of Medicine, 2450 Holcombe Blvd., Houston, TX 77021 (Christine M. Eng, MD, Medical Director; CLIA # 45D0660090).

Electronically Signed By: S. David Hudnall, MD, FCAP

INTERPRETATION:

Gene	Type	Nucleotide Change	Amino Acid Change	Location	Reference(s) / Comment(s)
APC	Somatic	c.2626C>T	p.R876*	Exon 15	COSMIC ID 18852
APC	Somatic	c.4348C>T	p.R1450*	Exon 15	COSMIC ID 13127
KRAS	Somatic	c.35G>A	p.G12D	Exon 2	COSMIC ID 521
TP53	Somatic	c.818G>A	p.R273H	Exon 8	COSMIC ID 10660

BACKGROUND:
We were requested to perform next-generation sequencing analysis for a panel of 2,855 cancer-associated mutations in 50 key cancer genes on the tumor sample of this individual using the techniques described in the methodology section below.

Our next-generation sequencing analysis identified four mutations as listed above in the tumor sample from the patient.

The KRAS codon 12 mutation is commonly seen in advanced colorectal cancer and is an established negative predictor for anti-EGFR therapy in patients with colorectal cancer [PMID: 18946061].

The TP53 R175H mutation is a common mutation found in various cancer types including colon cancer [PMID: 21103049]. Mutations in TP53 gene are common in colon cancer and are associated with poor prognosis [PMID: 17060676].

Both APC R876* and R14509* mutations have been previously reported in colon cancer [PMID: 23085758]. Although APC alterations are a frequent event in colon cancer, the clinical significance of the APC somatic mutation remains to be delineated. Targeted sequencing on a normal sample, such as blood, is available to determine if one or both APC mutations are germline if clinical findings and family history indicate.

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Variants classified as benign or likely benign based on the current knowledge of these genes are not reported but are available upon request.

Target below 100X

Gene	Target(s)
APC	p.E1547,p.E1577,p.E1552,p.K1555,p.T1556,p.L1564
ATM	p.V410,p.T2666, p.I2888,p.L2890,p.T2947,
EGFR	p.A767,p.V765,p.S768,p.V769,p.D770,p.H773,p.V774,p.C775,p.R776,p.S784,p.G779,p.V786,p.T790,p.L792
ERBB4	p.T140
NOTCH1	p.L1601,p.V1579,p.L1575,p.R1599,p.L1597,p.V1577,p.L1594,p.F1593,p.L1586
PIK3CA	p.E418,p.C420,p.K111
PTEN	p.F56,p.L57,p.S59,p.K60,p.H61,p.N63,p.Y65,p.K66,p.Y68
RB1	p.C706,p.R320,p.L199,p.E137

No Mutation Detected

ABL1	AKT1	ALK	ATM	BRAF	CDH1	CDKN2A	CSF1R
CTNNB1	EGFR	ERBB2	ERBB4	EZH2	FBXW7	FGFR1	FGFR2
FGFR3	FLT3	GNA11	GNAS	GNAQ	HNF1A	HRAS	IDH1
IDH2	JAK2	JAK3	KDR	KIT	MET	MLH1	MPL
NOTCH1	NPM1	NRAS	PDGFRA	PIK3CA	PTEN	PTPN11	RB1
RET	SMAD4	SMARCB1	SMO	SRC	STK11	VHL	-

METHODOLOGY:

Genomic DNA extracted from this patient's sample was used for multiplex PCR amplification of 207 amplicons, which target 2855 mutations in 50 key cancer genes, with the Ion AmpliSeq Kit. Next generation sequencing was performed on the Ion Torrent Personal Genome Machine and analyzed with the Torrent Suite Software. Mutation details can be obtained from the Catalogue Of Somatic Mutations In Cancer (COSMIC) database with the corresponding COSMIC ID http://www.sanger.ac.uk/genetics/CGP/cosmic/. DNA sequences used as references for this panel of genes can be found at http://www.ncbi.nlm.nih.gov/refseq/rsg/. The mutation nomenclature is based on the convention recommended by the Human Genome Variation Society (http://www.hgvs.org/mutnomen/).

This mutation panel is designed to detect targeted mutations only. Other mutations in the 207 amplicons may not be detected. The 50 genes are not sequenced in their entirety. Mutations outside the 207 amplicons will not be detected. The limit of detection is 5% at 500X coverage and 10% at 200X coverage. This technology cannot reliably detect mutations at coverage below 100X. Confirmation of mutations is performed by castPCR, pyrosequencing, or Sanger sequencing.

Individuals being studied should understand that rare diagnostic errors may occur. Possible sources of diagnostic errors include sample mix-ups and genotyping errors. Genotyping errors can result from trace contamination of PCR, from rare genetic variants which interfere with analysis, from mosaicism at levels below standard detection, and from other sources.

DISCLAIMER: This test was developed and its performance characteristics determined by Baylor College of Medicine Medical Genetics Laboratories (CAP# 2109314/ CLIA# 45D0660090). It has not been cleared or approved by the FDA. The laboratory is regulated under CLIA as qualified to perform high-complexity testing. This test is used for clinical purposes. It should not be regarded as investigational or for research.

END OF REPORT

Medical Director: S. David Hudnall, MD, FCAP CLIA #: 07D2030009 CT state license #: CL-0679