

Patient: John A. Doe



Case No: GS14-03755

DOB/Gender: xx/xx/xx (55 yrs) - Male

MRN/ID: xxxx

4 Science Park, 3rd Floor, New Haven, CT 06511
Phone: 203-787-7888 Fax: 203-901-1289
www.precipiodx.com

Collected: xx/xx/xx

Received: xx/xx/xx

Reported: xx/xx/xx

Provider: John Doe, M.D.

Account: Hematology Oncology Associates

Phone: 800-123-4567 Fax: 800-765-4321

Alert Status: Routine

Report Status: Final

Report Category: **Detected**

Clinical information: Colorectal cancer.

Received information: 1 Paraffin block, 1 H&E-stained slide Specimen analyzed: S-11-00123 Tests ordered: Omnia-50 panel



Professional Services Provided By
Yale SCHOOL OF MEDICINE

RESULT:

Solid tumors (#S-11-00123), 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: Demetrios Braddock, MD, PhD

INTERPRETATION:

Mutation(s):

| 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 sequence 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 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 R273H 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; 18081153].

Both APC R876* and R14509* mutations have been previously reported in colon cancer [PMID: 23085758; 20544848]. Although APC alterations are 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.

Variants classified as benign or likely benign based on the current knowledge of these genes are not reported but 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.L2888,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 | .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 Mutations Detected:

| | | | | | | | |
|--------|-------|---------|--------|--------|-------|--------|-------|
| ABL1 | AKT1 | ALK | ATM | BRAF | CDH1 | CDKN2A | CSF1R |
| CTNNB1 | EDGR | 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.