

Patient: John A. Doe



Case No: GS11-00044

DOB/Gender: xx/xx/xxxx (54 yrs) - Male

4 Science Park, 3<sup>rd</sup> 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: Jane Smith, M.D.

Account: Oncology Associates

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

Alert Status: Routine

Report Status: Final

Report Category: Detected

Clinical information: Known CA colon with metastasis to liver and lungs. Had several chemotherapy. Now no longer responsive.

Received information: 1 Paraffin block

Specimen analyzed: S11-123-A1

Tests ordered: NGS-20 Panel



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Yale SCHOOL OF MEDICINE

**RESULT:**  
Solid tumors (#S11-123-A1), left lower lung nodules, wedge resection:  
A missense mutation in TP53 at amino acid 175 converting the wild type residue, Arginine, to Histidine in 682 reads out of a total 2071 sequence reads for an allele frequency of 32.93% (Transcript ID NM\_001126112)

**DISEASE ASSOCIATED MUTATIONS (see interpretation and comments):**

Gene	Protein Change	cDNA Change
TP53	p.R175H	c.524G>A

**COMMENT:**

The NGS-20 sequencing test reported above was performed and solely interpreted at Center for Personalized Diagnostics, Perelman School of Medicine at the University of Pennsylvania, 3020 Market Street, Philadelphia, PA 19104, by Dr. Jennifer J.D. Morrisette (Scientific Director and Clinical Director: Jennifer J.D. Morrisette, Ph.D., FACMG; CLIA #39D2060198).

Electronically Signed By: Demetrios Braddock, MD, PhD

**INTERPRETATION:**

**GENE INFORMATION:**

TP53: The tumor protein p53 gene (TP53) is located on chromosome 17p13.1 and functions as a tumor suppressor by regulating cellular division.

Mutations in TP53 have been reported in a variety of cancers. The types of mutations in TP53 include whole gene or partial gene deletions, nonsense mutations and missense changes that result in a loss of function. These changes can occur throughout the entire coding sequence and result in uncontrolled cell proliferation.

Solid Tumor Sequencing Panel: Sequence analysis of 20 genes (AKT1, ALK, BRAF, CS1R, EGFR, ERBB2, HRAS, IDH1, IDH2, KIT, KRAS, MAP2K1, MET, NOTCH1, NRAS, PDGRR, PIK3CA, PTEN, RET, TP53).

The design of the panel was based on the literature at the time of development and the most frequently mutated genes observed in solid tumors. Either the full length gene or the mutational hot spots of a gene are targeted. For a complete listing of genomic coordinates covered in this panel please contact the laboratory.

**DISCLAIMERS:**

This report has been created based on various scientific manuscripts, references and publically available databases that describe correlations between certain genetic mutations and disease. This information which comes from numerous sources is subject to change over time in response to future scientific and medical findings and correlations. The University Of Pennsylvania Health System (UPHS) makes no representation or warranty of any kind regarding the accuracy of information provided or contained in these manuscripts, references or other sources of information. If any of the information provided by or contained in the referenced material is later deemed to be inaccurate, this may impact the accuracy of this report and interpretation of the findings. UPHS is not obligated to notify you of any impact that additional or modified information, or future scientific or medical research may have on this report.

This report must always be interpreted and considered within the clinical context, and the treating physician(s) should always consider other pertinent information and data that a physician would prudently consider, in addition to the mutations identified in this report. The results in this report are not based on diagnostic or prognostic test, and therefore should be carefully considered within the context of clinical and other laboratory data. The genes tested in this assay have been found to be altered in the manifestation of many diseases. The manifestation of disease is commonly caused by many genes, in addition to other variables not addressed in this report, including but not limited to modifier genes, epigenetic factors, environmental factors, and factors that are not known at this time. This report is relevant only in its interpretation based on the context of the patient's clinical manifestations.

This report is provided on an "AS IS" basis. UPHS makes no representation or warranty of any kind, expressed or implied, regarding this report. In no event will UPHS be liable for any actual damages, indirect damages, and/or special or consequential damages arising out of or in any way connected with your use of this report.

This test was developed and its performance characteristics determined by the University of Pennsylvania Center for Personalized Diagnostics Laboratory as required by the CLIA 1988 regulations. It has not been cleared or approved for specific uses by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes. Pursuant to the requirements of CLIA 1988, this laboratory has established and verified the test's accuracy and precision.

**METHODOLOGY:**

Genomic DNA was extracted from the submitted specimen according to manufacturer's instructions (Qiagen, Inc.). Targeted analysis for mutations in the regions specified in this testing panel was achieved by enrichment 77 amplicons covering 20 genes enriched for hotspots and tumor suppressor coverage. Sequencing of PCR-enriched libraries was performed on the Illumina MiSeq platform using multiplexed, paired end reads with Version 3 chemistry. Analysis and interpretation utilized a customized bioinformatics process. All variants listed are with reference to the hg19 Genome build. Variants are reported according to HGVS nomenclature and classified into 3 categories: Pathogenic, Variants of uncertain significance and Benign. Categorization of variants was dependent upon literature review, variant existence in a variety of publically available databases including dbSNP, COSMIC, and the 1000 genome project. Variants classified as Benign are not listed in this report.

This assay will detect single nucleotide variants and small insertions or deletions (indels). Large or complex indels, inversions, translocations, gene amplifications, copy number changes or other complex genomic mutations may not be detected by this assay. Variants existing outside the target regions will not be detected. Only variants in the exonic regions of the gene panel will be reported. This assay does not determine variant causality, or whether a variant is inherited or somatically acquired. This assay will detect variants representing at least 10% of the total sequence reads at a given genomic position. Note that it is possible that pathogenic variants present in the sample will not be detected by one of more of the informatics processing tools because of the parameters used. During test validation the choice of parameters was optimized to maximize sensitivity and specificity.

This assay cannot guarantee all regions will meet variant calling criteria due to the possibility of underlining genomic changes. Genomic regions not meeting criteria for variant calling include the genomic loci for which the depth of coverage did not meet our minimum criteria of 250 reads at all positions within that locus. Since the sensitivity and specificity of our assay was determined by achieving a minimum depth of coverage of 250 reads, regions not meeting this criterion cannot be guaranteed to be mutation negative. The depth of coverage is dependent upon the starting amount of DNA for a given region which could be affected by underlying chromosomal copy number changes. Since the genomic loci targeted in this assay are enriched using loci specific primers, patient variants existing within those primer sequences may also cause a region to fail enrichment and therefore not achieve 250xcoverage.

**REFERENCES:**

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- The NGS-20 Precision Panel test was performed in the Department of Pathology and Lab Medicine at the Penn Clinical CytoGenomics Lab 3020 Market Street, Philadelphia, PA 19104.