Predicine

PrediSeq Hereditary Cancer Test Result

CONFIDENTIAL

Barcode

RECEIVING PHYSICIAN
Test HCP, MD
Test Medical Center
3555 Arden Rd
Hayward, CA 94545

SPECIMEN
Specimen Type: **Blood**
Collection Date: **Dec 20, 2017**
Receipt Date: **Dec 21, 2017**
Report Date: **May 31, 2018**

PATIENT
Name:
Date of Birth:
Patient ID:
Gender:
Requisition #:

ORDERING PHYSICIAN: **Test HCP, MD**

Test Results and Interpretation

POSITIVE - CLINICALLY SIGNIFICANT MUTATION IDENTIFIED

DETAILS ABOUT TEST RESULTS

GENE	MUTATION	ZYGOSITY	FUNCTIONAL CLASSIFICATION	CLINICAL SIGNIFICANCE
BRCA1	c.4327C>T (p.Arg1443Ter)	Heterozygous	**Pathogenic**	**High Cancer Risk** This variant is associated with Hereditary Breast and Ovarian Cancer syndrome (HBOC)

Note about Clinically Significant Variants: All individuals carry DNA changes (i.e., variants), and most variants do not increase an individual's risk of cancer or other diseases. When identified, only pathogenic and likely pathogenic results are considered as 'clinically significant variants' and hereby reported. Variants of uncertain significance, likely benign, and benign variants are not reported. Present evidence does not suggest using these non-clinically significant variants to modify patient medical management unless indicated by the personal and family history and other clinical findings. An amended report will be made available to the healthcare provider when new evidence about a variant is determined to result in clinical significance.

THE PATIENT'S GENE-RELATED CANCER RISKS

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION	RELATED TO
FEMALE BREAST	To age 70	46-87%	7.1%	*BRCA1*
OVARIAN	To age 70	39-63%	0.7%	*BRCA1*
PANCREATIC	To age 70	Elevated risk	1%	*BRCA1*

Note: "High Risk" for a cancer type is described if all of the following conditions are met: the absolute risk of cancer is approximately 5% or higher, the increase in risk over the general population is approximately 3-fold or higher, and there is significant data from multiple studies supporting the cancer risk estimate. A gene is described as "Elevated Risk" for a cancer type if there is sufficient data to support an increase in cancer risk over the general population risk, but not all criteria for "High Risk" are met.

References:

- PMID: 16484695, 23628597, 7907678, 7825587, 16484695, 23628597, 15796958.
- A PMID is a unique identifier referring to a published scientific paper. Search by PMID at http://www.ncbi.nlm.nih.gov/pubmed
- NCCN is National Comprehensive Cancer Network, which develops the NCCN Clinical Practice Guidelines in Oncology. http://www.nccn.org/

Additional Information

Genes Analyzed *ARID1A, ATM, ATR, BARD1, BRCA1, BRCA2, BRIP1, CHEK2, EPCAM*, ERCC1, ERCC2, ERCC4, FANCC, FANCD2, MLH1, MSH2, MSH6, NBN, PALB2, PMS2, POLE*, PTEN, RAD51C, RAD51D, TP53*

**selective exonic regions only: EPCAM: exon 8-9; POLE: exon 9-14, 34-36*

About the assay

This assay is a clinically validated Laboratory Developed Test for detection of germline mutations in genes associated with a predisposition to various hereditary cancer syndromes. Patients with Likely Pathogenic and/or Pathogenic results may submit their samples for confirmatory test at the physician's discretion. If variant and interpretation is confirmed, genetic counseling and testing of close relatives is recommended.

Methods

Genomic DNA obtained from the submitted sample is enriched for targeted regions using a hybridization-based protocol, and sequenced using Illumina technology. Unless otherwise indicated, unique median sequence depth is >50 and >90% targeted regions are sequenced with ≥30 unique depth. Enrichment and analysis focus on coding exonic regions of the above genes, and their flanking intronic regions that typically do not extend more than 20 base pairs (bp) proximal to the 5' end and 10 bp distal to the 3' end of each exon. For some genes, only selected exonic loci are analyzed as described above.

Sequence Reads are aligned to a reference sequence (GRCh37), and sequence changes are identified by an in-house developed pipeline, reviewed according to ACMG standards, and interpreted based on data in internal curated database at that time. Only variants with allele frequencies between 30% (for single nucleotide variants and short insertions and deletions) or 20% (for long insertion/deletions larger than 10bp) and 70% are reported and called heterozygous and those above 70% are called homozygous.

The absence of a Pathogenic or Likely Pathogenic result does not mean that the individual has zero-risk of developing cancer over his or her lifetime. Cancer is a multifactorial disease and exposure to environmental factors, ultra-violet light, and other lifestyle factors impacts risk.

Limitations

This assay achieves >99% sensitivity and specificity for single nucleotide variants and insertions/deletions less than 10bp, based on validation study results. Sensitivity at underperforming target regions as specified below and sensitivity to detect insertions and deletions larger than 10bp may be reduced. Sequence changes in promoter regions, untranslated regions, and other non-coding regions will not be detected by this assay unless specified. This methodology may not detect low-level mosaicism. This report reflects the analysis of an extracted DNA sample. In very rare cases, (circulating hematolymphoid neoplasm, bone marrow transplant, recent blood transfusion), the analyzed DNA may not represent the patient's constitutional genome.

Underperforming assay target regions: NONE

Disclaimer

This test was developed and its performance characteristics were determined by Predicine laboratory (CLIA# 05D2148483). It has not been cleared or approved by the FDA, the FDA has determined no clearance is necessary. 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.

This report has been reviewed and approved by:

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Signature Date