SAMPLE REPORT

GC Genome

Breast & Ovarian

GCG Women's Cancer Panel

Test Report

Name	Jane Doe		
DOB / Gender	1970-01-01 / Female	**Sample ID**	20220101-971-2101
MRN	M0000000	**Collection Date**	2022-01-01
Institution	Hospital A	**Received Date**	2022-01-05
Ordering Physician	Dr. Smith	**Reporting Date**	2022-01-19

Tested by : Myeong-Keun Lee M.T(20058) Confirmed by : Sae-Mi, Lee M.D(1067) Cho,EunHae M.D(690)

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COLLEGE of AMERICAN PATHOLOGISTS

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Summary

Positive

Variant of uncertain significance in the PALB2 gene was found.
Additionally, likely pathogenic variant in the SDHB gene was found.

Results

Gene	DNA Change	AA Change	Zygosity	OMIM Disease	Inherit	Class
PALB2	DNA c.1054G>C	p.Glu352Gln	Het	BCs	AD	VUS
SDHB	c.406del	p.Ile136Ter	Het	GIST	AD	LPV

· Reference sequence : NM_024675.3(PALB2);NM_003000.2(SDHB)
· Abbreviations: Het=Heterozygote; BCs=Susceptibility to breast cancer; AD=Autosomal dominant; VUS=Variant of uncertain
· significance; GIST= Gastrointestinal stromal tumor; LPV= Likely pathogenic variant;

Interpretation

A Heterozygous variant (c.1054G>C;p.Glu352Gln) in the PALB2 gene was detected. This variant has been classified as a Likely benign(2);Uncertain significance(3) in Clinvar and as a possible pathological mutation in HGMD. This variant has not been reported in the South Asian population database, while minor allele frequency (MAF) of the variant was estimated to be 0.000061 (gnomAD_all). Taken together, this PALB2 variant can be classified as VUS. Pathogenic variants in PALB2 are known to cause Breast cancer, Fanconi anemia, Pancreatic cancer, etc.

As further analysis, a Heterozygous variant (c.406del;p.Ile136Ter) in the SDHB gene was detected. This variant has been classified as a deleterious mutation in HGMD and this variant has not been reported in the population database (gnomAD). Taken together, this SDHB variant can be classified as Likely pathogenic. Pathogenic variants in SDHB are known to cause Gastrointestinal stromal tumor, Paraganglioma and gastric stromal sarcoma, Paragangliomas 4, Pheochromocytoma, etc.

This test analyzes the coding exons and adjacent intron areas of the genes included in the panel and cannot detect exon deletions/duplications, and copy number variants including genomic rearrangements etc. For more information on the technical limitations of a test, see the limits of the test below.

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The result details and related diseases

Gene	Key Areas Where Hereditary Cancer occurs	RESULTS
ATM	BREAST CANCER, OVARIAN CANCER	Not Detected
BARD1	BREAST CANCER	Not Detected
BRCA1	BREAST CANCER, OVARIAN CANCER	Not Detected
BRCA2	BREAST CANCER, OVARIAN CANCER	Not Detected
BRIP1	OVARIAN CANCER	Not Detected
CDH1	BREAST CANCER	Not Detected
CHEK2	BREAST CANCER	Not Detected
NBN	BREAST CANCER	Not Detected
NF1	BREAST CANCER	Not Detected
PALB2	BREAST CANCER	**Detected**
PPM1D	BREAST CANCER, OVARIAN CANCER	Not Detected
PTEN	BREAST CANCER	Not Detected
RAD51C	OVARIAN CANCER	Not Detected
STK11	BREAST CANCER, OVARIAN CANCER	Not Detected
TP53	BREAST CANCER	Not Detected

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Relevant Disease Information

Hereditary Breast and Ovarian Cancer

Disease Information

For breast cancer, 5% to 20% of cases are caused by a genetic variation which one has since birth. The major cause of most hereditary breast cancers are pathogenic variants of the BRCA1 and BRCA2 genes.
When there is a pathogenic variant of these genes, a maximum of 80% of those women have breast cancer and a maximum of 40% of those women have ovarian cancer.

Genetic features

Most hereditary breast cancers are autosomal dominant and associated with pathogenic mutations of the BRCA1 and BRCA2 genes. BRCA1 and BRCA2, identified in 1994 and 1995, respectively, are considered to be one of the important factors for the pathogenesis of breast cancers because the incidence risk is high with pathogenic mutations of BRCA1 and BRCA2. BRCA1 and BRCA2 are located on the long arm of chromosome 17 and chromosome 13, respectively.
In case of DNA damage, these genes, reacting with other proteins, play a role in repairing the damaged double strand DNA. If BRCA1 or BRCA2 is damaged, the DNA repair process is not properly performed, and therefore, the risk of cancer increases. Pathogenic mutations of the BRCA genes are autosomal dominant and the same genetic disorders have a 50% probability of occurring in the patient's children and other family members.
Therefore, when a pathogenic variant is found in a person, the person's children and family members in a direct line are recommended to have genetic testing.

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Test Information

Method

- Target Region:
- Target enrichment method: Hybridization with oligonucleotide probes
- Massively parallel sequencing: MiseqDX (150 bp x 2 paired-ends)
- Reference genome: GRCh37/hg19
- Bioinformatic pipeline:

Coverage

- Mean depth of coverage: 300x
- % of Target Bases ≥ 10X: 99X

Gene List

ATM, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, NBN, NF1, PALB2, PPM1D, PTEN, RAD51C, STK11, TP53

Limitation

This test is performed by NGS technique. The genes included in the test include the entire exon, but in some areas sequencing may not be sufficiently covered. In addition, if a highly homologous sequence exists, the sequencing of the base may not be accurate, and exonic deletion/duplication, regulatory or deep intronic region, repeat expansion, imprinting defect etc. may be difficult to detect. Genetic variation is divided into five categories, pathogenic variant (PV), likely pathogenic variant (LPV), variant of unknown significance (VUS), likely benign variant (LBV), and benign variant (BV), according to 2015 ACMG/AMP (Genet Med 2015;17:405-24). Likely benign variant (LBV) and Benign variant (BV) are not reported. However, the interpretation of the variation could be changed as additional evidence builds up after the results are reported.

Reference

1. Breast Cancer Information Core (http://research.nhgri.nih.gov/bic)
2. The Human Gene Mutation Database (http://www.hgmd.cf.ac.uk)
3. Gene Reviews (http://geneclinics.org)

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