Homologous Recombination Deficiency (HRD) Test Report

Personal Information	Specimen Information	Test Information
Name: Jane Doe	Sample ID: 20200901-971-2105	Test reported: 2020-01-01
Date of Birth: 1984.01.01	Medical record No:	Ordering physician: Dr. Smith
Sex: Female	Date received: 2020-01-01	Institution: Hospital A

Cancer Type: High-grade serous ovarian cancer

SUMMARY

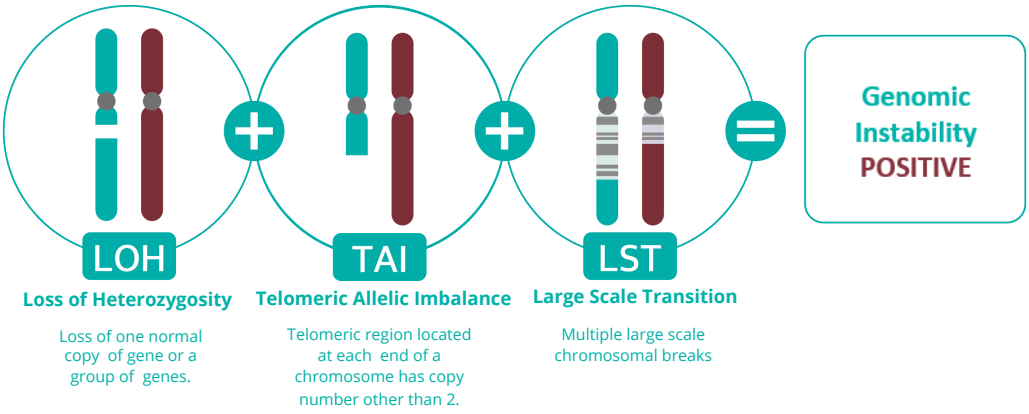
HRD	Positive	Genomic Instability	Positive
		BRCA Mutation	Positive

QC

DNA(SNV)	Pass	DNA(CNV)	Pass

TEST RESULT

Genomic Instability Status	Genomic Instability Score
Positive	66



INTERPRETATION

Analysis of 3 types of genomic scars caused by Homologous Recombination Deficiency in the patient showed Positive genomic instability status.

The 3 types of genomic scars are Loss of heterozygosity (LOH), Telomeric allelic imbalance (TAI), Large-scale transition (LST). If the combined score of each index exceeds score of 42, the genomic instability status is classified as positive.

Medical Technologist : M-K Lee M.T(20058) Lab Director(Medical Doctor) : Sae-Mi Lee M.D(1067)

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BRCA Mutation	Positive					
No	Gene	DNA	Protein	VAF(%)	Depth(X)	Class
1	BRCA1	c.3627dup	p.Glu1210ArgfsTer9	67	674	Deleterious

INTERPRETATION

The c.3627dup variant was found in the BRCA1 gene. This is a variant that the base at position 3627 is dupliacted, glutamic acid at position 1210 is substituted with arginine, and then the ninth amino acid to be changed to a stop codon. This variant has not been reported in the general population (gnomAD, KRGDB) and is classified as Pathogenic by Clinvar.

TEST INFORMATION

This assay uses the Next generation sequencing (NGS) technology to detect homologous recombination deficiency based on analysis of genomic instability and BRCA1/BRCA2 gene mutation.

1. What is HRD (Homologous recombination deficiency)?

Normally, when DNA damage occurs in a cell, the damage is repaired through a DNA repair process. However, in tumor cells, the DNA damage is not properly repaired and the cell continues to divide. A case in which DNA repair process does not occur due to problem in homologous recombination function or mutation in BRCA gene is referred to as Homologous Recombination Deficiency (HRD). Tumors with HRD are particularly susceptible to specific targeted cancer therapies such as the PARP inhibitors.

2. PARP inhibitor

PARP inhibitors are most notable anticancer drugs used in ovarian cancer. They suppress the activity of PARP protein, which is responsible for DNA repair process. In normal cells with proper DNA repair process, PARP inhibitor poses no lethality. But in tumor cells with non-functioning repair process, it poses lethal effects. PARP inhibitor shows unique effectiveness in tumors with homologous recombination deficiency such as BRCA1/BRCA2 mutation.

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3. LIMITATION

- This assay uses sequencing analysis to detects mutation and genomic instability of BRCA1 and BRCA2 genes, and cannot detect mutations in other genes or regions not covered by this test.
- The limit of detection (LOD) for SNV and small indel in BRCA1, BRCA2 genes is approximately 5%.
- Certain target regions may have lower coverage.
- This test does not distinguish between germline and somatic variants. If the variant allele frequency of the mutation is close to 50% or 100%, the possibility of germline variant cannot be eliminated
- Variants found in BRCA1 and BRCA2 genes are classified and reported as deleterious variant, suspected deleterious variant, and variant of uncertain significance (VUS), and mutations determined to be benign are excluded from reporting. If a deleterious variant or a suspected deleterious variant is detected, the BRCA variant is reported as positive.

4. REFERENCES

1. Br J Cancer. 2018 Nov;119(11):1401-1409.
2. Mol Cancer Res. 2018 Jul;16(7):1103-1111.
3. N Engl J Med. 2019 Dec 19;381(25):2391-2402.
4. N Engl J Med. 2019 Dec 19;381(25):2416-2428.

※ This test is a laboratory-developed test (LDT) developed by GC Genome, and it has been confirmed that it is suitable for clinical tests through appropriate evaluation.

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