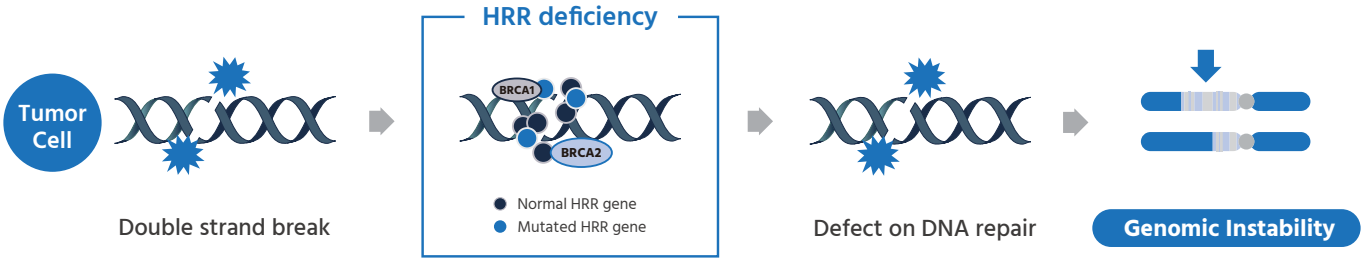
New Paradigm & Essential test
for target therapy application in ovarian caner patients

HRD

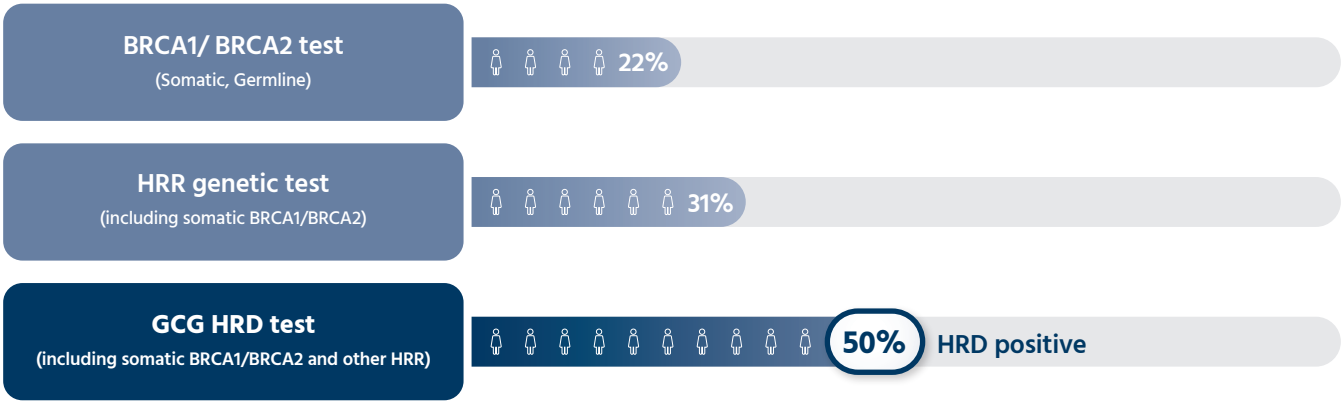
Homologous Recombination Deficiency Test

What is the HRD?

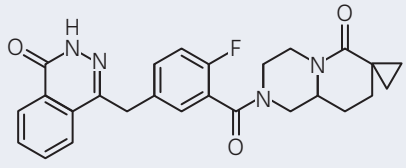


Normally, when DNA damage occurs in a cell, the damage is repaired through a DNA repair process. However, in tumor cells, the DNA damage is not properly repaired and the cell continues to divide.
A case in which DNA repair process does not occur due to problem in homologous recombination function or 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.**

Why is the HRD test important?[1]



50% of the high-grade serous epithelial ovarian cancer patient is HRD positive, which is a target for PARP inhibitors. However, only 20-30% of patient can be screened through conventional test.
Using PARP inhibitors has shown a benefit in progression-free survival for HRD-positive patients, both with and without BRCA mutations.



PARP inhibitor

Following ovarian cancer patients may be benefit from PARP inhibitors

- Patients who relapsed within 6 months of platinum-based chemotherapy
- Patients with g/s BRCA 1/2 mutation or problems with Genomic instability
- Patients without experience of PARP inhibitors

1 Konstantinopoulos PA, Ceccaldi R, Shapiro GI, D'Andrea AD. Homologous Recombination Deficiency: Exploiting the Fundamental Vulnerability of Ovarian Cancer. Cancer Discov. 2015 Nov;5(11):1137-54. doi: 10.1158/2159-8290.CD-15-0714. Epub 2015 Oct 13. PMID: 26463832; PMCID: PMC4631624.

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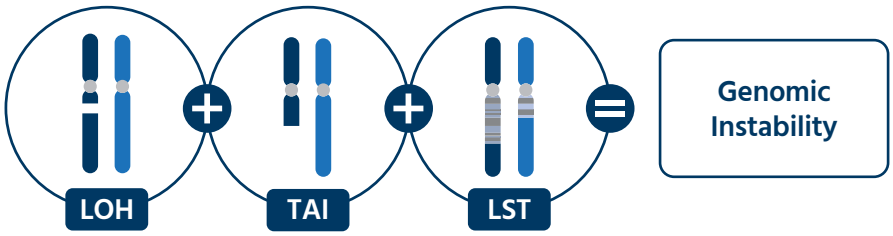
What can we know from HRD test?

1) GIS (Genomic Instability Score)



Loss of Heterozygosity (LOH) Loss of one normal copy of gene or a group of genes

Telomeric Allelic Imbalance (TAI) Telomeric region located at each end of a chromosome has copy number other than 2.

Large Scale Transition (LST) Multiple large scale chromosomal breaks

2) 28 HRR(Homologous Recombination Repair) genes

ATM, BARD1, BRIP1, BRCA1, BRCA2, CDK12, CHEK1, CHEK2, FANCC, FANCD2, FANCE, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, MRE11, NBN, PALB2, PP2R2A, RAD50, RAD51, RAD51B, RAD51C, RAD51D, RAD52, RAD54L, XRCC2

Service features

Test	HRD	**Code**	ON140
Specimen	[Formalin-fixed, paraffin-embedded (FFPE) slide] – 10 unstained sections from one block (10 µm x 10 sections) & H&E 1 slide – tissue size : 4 mm x 4 mm	**TAT**	14 days
Method	NGS (Next Generation Sequencing)	**Sample Storage**	Room temperature (Refrigerated is recommended.)
Test description	A case in which DNA repair does not occur due to a problem in the function of homologous recombination such as a BRCA gene abnormality during the DNA repair process is called homologous recombination deficiency (HRD). Tumors caused by homologous recombination deficiency are characterized by good therapeutic effects using specific drugs such as PARP inhibitors.		
Caution & 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 20%. • 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.		

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