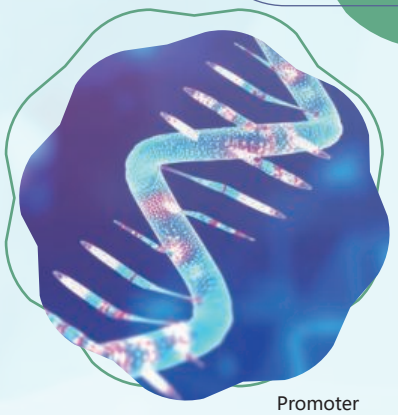
SpaceGen
飞朔生物

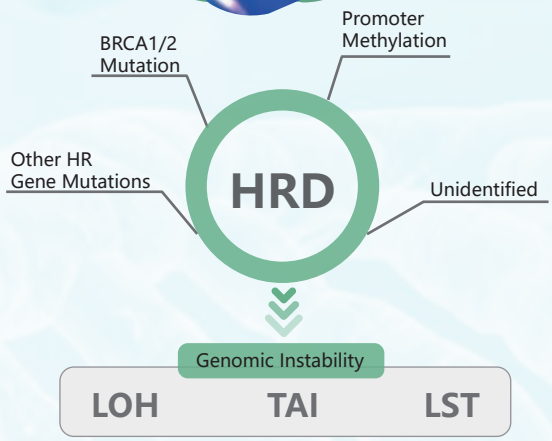
Homologous Recombination Deficiency (HRD) Panel (Next Generation Sequencing)



THE MECHANISM AND DETECTION METHOD OF HRD

Homologous Recombination Deficiency (HRD) typically refers to a cellular-level impairment in homologous recombination repair (HRR) functionality. This condition can result from various factors, including germline mutations in HRR-related genes, somatic mutations, and epigenetic inactivation [1]. TCGA studies suggest that approximately half of high-grade serous ovarian cancer (HGSOC) may exhibit HRD, but only about 20% of patients carry pathogenic BRCA1/2 mutations. HRD can also result from other factors such as BRCA1 methylation and mutations in other HRR genes [2].

HRD can lead to specific, quantifiable, and stable genomic alterations. Loss of Heterogeneity (LOH), Telomeric Allelic Imbalance (TAI), and Large-scale State Transitions (LST), are used as indicators of Genomic Scar. The unweighted sum of these markers is used as an HRD score [3]. Combining pathogenic mutations in BRCA1/2 with the HRD score can nearly double the population benefiting from testing compared to testing for BRCA1/2 gene mutations alone.



CAUSES AND MARKERS OF HRD

HRD STATUS INDICATES EFFICACY OF PARP INHIBITORS

Clinical testing for HRD has significant application value in predicting the efficacy of PARP inhibitors in the treatment of advanced ovarian cancer. It can stratify ovarian cancer patients, optimize treatment decisions, and maximize the clinical benefit of PARP inhibitors. Furthermore, in breast cancer, pancreatic cancer, and prostate cancer, HRD testing may also have potential guidance value for the clinical use of PARP inhibitors or platinum compounds [1].

FDA, EMA and NMPA have approved olaparib combined with bevacizumab for the maintenance treatment of ovarian cancer evaluated as CR / PR after first-line platinum-based chemotherapy[4]. While the indication for niraparib in the systemic treatment of heavily recurrent ovarian cancer has been withdrawn, the NCCN guidelines still maintain this recommendation [5]. Both of these treatment approaches rely on HRD as a biomarker. Additionally, HRD status plays an important reference role in the choice of maintenance therapy for patients with negative BRCA1/2 testing in tumors [6].

DETECTION CONTENT

Detection Project	Gene mutations, HRD score (LOH, LST and TAI)
Detection Gene	36 HRR genes, 5 MMR genes, 15 other common driver genes
Detection Range	The entire CDS region of common driver genes such as HRR gene, MMR gene and TP53, and the hotspot regions of some common genes such as BRAF and CTNNB1

[1] Expert consensus on clinical detection and application of homologous recombination repair defects (2021 version)
[2] Nature. 2011 Jun 29; 474(7353): 609-15.
[3] Clin Cancer Res. 2016 Aug 1;22(15):3764-73.
[4] FDA, EMA, NMPA database
[5] NCCN Ovarian Cancer, Fallopian Tube Cancer, and Primary Peritoneal Cancer Diagnosis and Treatment Guidelines 2023 v2
[6] Chinese expert consensus on detection of biomarkers related to PARP inhibitors in epithelial ovarian cancer

PRODUCT INFORMATION

Project	Core Technique	Pack Size	Instruments Validated	Sample type
Lucksen™ Homologous Recombination Deficiency (HRD) Panel	Probe Capture + Next Generation Sequencing	16 tests/kit 32 tests/kit	MGIseq Illumina	Tissue + whole blood

Capture probes should be used with SGPrep DNA library kit, SGPrep DNA library hybridization capture kit, Blockers and adapters.

DETECTION SIGNIFICANCE

1. Combining pathogenic mutations in BRCA1/2 with HRD score can be used to assess the HRD status of tumors, which suggests the efficacy of PARP inhibitors in patients with ovarian cancer and other patients.
2. Testing for mutations in 36 HRR genes provides comprehensive guidance on the use of PARP inhibitors in patients with prostate cancer and metastatic breast cancer.
3. Testing for mutations in 15 common driver genes offers insights into cross-cancer therapy efficacy and targeted treatment efficacy for rare ovarian cancer subtypes like low-grade serous ovarian carcinoma (LGSOC).
4.Testing for germline mutations in HRR and MMR genes can indicate the risk of hereditary cancer syndromes such as Hereditary Breast and Ovarian Cancer (HBOC) and Lynch syndrome.

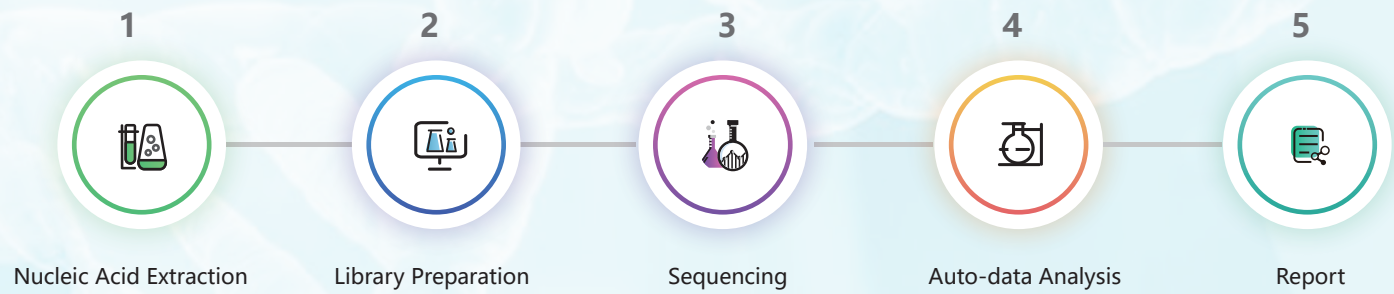
APPLICABLE SITUATIONS

HRD status may serve as a biomarker for efficacy of PARP inhibitors in the following indications:
1. Maintenance therapy for ovarian cancer evaluated as CR/PR after first-line platinum-containing chemotherapy;
2. Maintenance treatment of platinum-sensitive recurrent ovarian cancer;
3. Systemic treatment of multiple lines of recurrent ovarian cancer;
4. Adjuvant treatment after neoadjuvant/adjuvant chemotherapy for HER2-negative early-stage high-risk breast cancer;
5. Salvage treatment of HER2-negative metastatic breast cancer;
6. Systemic treatment for metastatic castration-resistant prostate cancer after failure of androgen receptor therapy;
7. Maintenance treatment of metastatic pancreatic cancer that has not progressed after first-line platinum-containing chemotherapy.

FEATURES & ADVANTAGES

Clever Design: The specific heterozygous SNP loci were used to cover the entire human genome, covering the entire human genome, to analyze the three Genomic Scar markers - LOH, TAI, and LST.
Comprehensive Testing: Testing 36 HRR genes, 5 MMR genes, and 15 common driver genes, offering comprehensive insights into the efficacy of various targeted therapies.
Cost-Effective: Testing paired samples from both tissue and peripheral blood, assisting in the diagnosis of hereditary tumors while providing information on drug efficacy.
Stringent Quality Control: Implementing rigorous quality control standards at various stages, including sample collection, nucleic acid extraction, library preparation, and data analysis.

DETECTION PROCESS



For Research Use Only

T e l ：+86-592-7578317
Email： spacegen@ispacegen.com
www.sspacegen.com
XIAMEN SPACEGEN CO.,LTD
XIAMEN SPACESEQ MEDLAB CO.,LTD
A d d ： NO.2041,XizhouRoad,Xike Town, Tong'an District,Xiamen City, Fujian Province, China
SUZHOU SPACESEQ MEDLAB CO.,LTD
4th Floor, Building 1, No. 777 Kangyuan Road, Chengyang Street, Suzhou City 213000