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Comparative Analysis of HRD Complete Data on MGI DNBSEQ-G50 and NextSeq 550

Abstract

This white paper presents comparative analysis of the AmoyDx® HRD Complete Panel on two major sequencing platforms: MGI DNBSEQ-G50 (MGI G50) and Illumina NextSeq 550. The study analysed 79 samples including reference materials and clinical FFPE samples from ovarian, breast, or prostate cancer patients to assess sequencing quality, HRD (GSS) status assessment, as well as SNV/InDel and HD detection performance. The findings confirm that the MGI G50 platform demonstrates accuracy and reliability comparable to the NextSeq 550, making it an alternative sequencer for HRD status assessment and variant detection.

Introduction

Ovarian cancer patients of advanced stages are typically advised to assess their HRD (homologous recombination deficiency) status, which aids in identifying those who may benefit from PARP inhibitor therapy. Breast cancer patients shall be screened for the presence of BRCA mutations which not only inform treatment options but may also provide valuable insights for risk assessment and prevention strategies. In prostate cancer, evaluating HRR (homologous recombination repair) gene mutations is crucial for guiding targeted therapies, including PARP inhibitors and other emerging treatments. The AmoyDx® HRD Complete Panel enables the assessment of HRD status, as well as the detection of SNVs/InDels and HDs (homozygous deletions) for 20 HRR genes, including *BRCA1* and *BRCA2*. The AmoyDx® HRD Complete Panel has been optimized for use on the Illumina NextSeq 550 platform. With the growing demand for more flexible and efficient sequencing options, this study aims to validate the performance of AmoyDx® HRD Complete Panel on the MGI G50 platform. By comparing key performance metrics between the two platforms including sequencing quality, mutation detection and HRD status consistency, this white paper explores the potential for expanding the use of AmoyDx® HRD Complete Panel beyond Illumina systems to the MGI G50 platform.

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Methodology

1. Sample Collection

A total of 79 samples were used for performance testing of the MGI G50 & Nextseq 550 in this report as stated below:

a) SNV/InDel-positive samples: A total of 42 samples with known SNV/InDel variants were used, including 30 cell line-derived reference materials, 4 ovarian cancer FFPE samples, 4 breast cancer FFPE samples, and 4 prostate cancer FFPE samples.

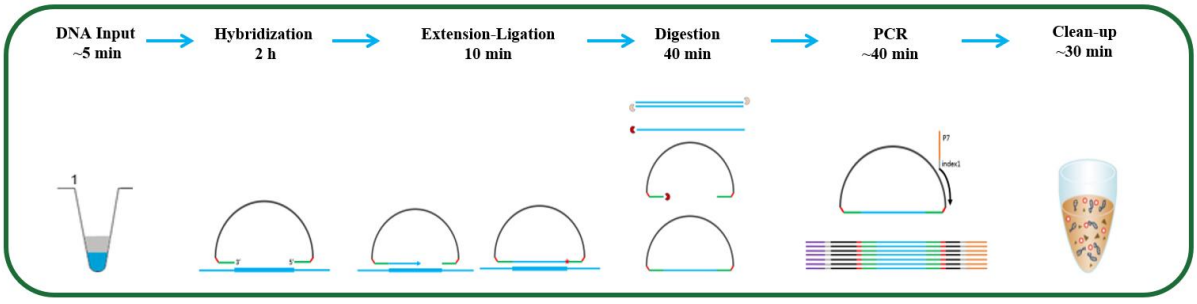
b) HD-positive samples: A total of 9 samples with known HD variants were used, including 6 cell line-derived reference materials, and 3 prostate cancer FFPE samples.

c) GSS (genomic scar score)-positive samples: A total of 13 samples which are HRD (GSS) positive, including 8 cell line-derived reference materials, 3 ovarian cancer FFPE samples, and 2 breast cancer FFPE samples.

d) Negative samples: A total of 19 samples which are HRD negative and have no pathogenic or likely-pathogenic SNV/InDel or HD variants within the panel's scope of detection were used, including 4 cell line-derived reference materials, 5 ovarian cancer FFPE samples, 5 breast cancer FFPE samples, and 5 prostate cancer FFPE samples.

2. Extraction & Library Preparation

DNA extraction was conducted using AmoyDx® Magnetic FFPE DNA Extraction Kit. Library preparation was performed according to the AmoyDx® HRD Complete Panel protocol. Library preparation for each sample was repeated 3 times across 3 different reagent lots. Sequencing was carried out for each replication of libraries on both the MGI G50 and NextSeq 550 platforms for comparative analysis.



3. Data Processing and Analysis

Data analysis was conducted using the ADXHS-tHRD-Complete module. Key metrics including sequencing depth, quality control parameters, mutation detection efficiency and variant frequency were evaluated to assess performance.

Results

Sequencing and Data QC Performance Comparison

Metric	MGI G50	NextSeq 550
Sequencing Quality (CleanQ30)	≥75%	≥75%
Coverage(180×)_BRCA	≥95%	≥95%
Coverage(180x)_CDS	≥95%	≥95%
BAFNoise	≤0.05	≤0.05
DepthNoise	≤0.35	≤0.35
CDSBAFNoise	≤0.05	≤0.05
CDSDepthNoise	≤0.40	≤0.40

Comparison of Illumina NextSeq 550 and MGI G50 for SNV/InDel Detection

MGI G50	Illumina NextSeq 550		Total	Agreement
	Positive	Negative		
Positive	126	0	126	PPA = 100% NPA = 100% OPA = 100%
Negative	0	57	57	
Total	126	57	183	

Comparison of Illumina NextSeq 550 and MGI G50 for GSS Assessment

MGI G50	Illumina NextSeq 550		Total	Agreement
	Positive	Negative		
Positive	39	0	39	PPA = 100% NPA = 100% OPA = 100%
Negative	0	57	57	
Total	39	57	96	

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Comparison of Illumina NextSeq 550 and MGI G50 for HD Detection

MGI G50	Illumina NextSeq 550		Total	Agreement
	Positive	Negative		
Positive	27	0	27	PPA = 100% NPA = 100% OPA = 100%
Negative	0	57	20	
Total	27	57	77	

Discussion

The comparative analysis highlights several key findings:

Sequencing Quality and Data QC Performance:

Both sequencing platforms demonstrated high sequencing quality and data QC performance.
The CleanQ30 values exceeded 75% for both platforms. This indicates that both the MGI G50 and NextSeq 550 can generate accurate sequencing data suitable for downstream biomarker assessment and clinical analysis.

The quality control (QC) data for each variant type (SNVs/InDels, HDs, and HRD status) on both MGI G50 and NextSeq 550 platforms met all QC criteria, showing high concordance between the two sequencing platforms. This demonstrates the capability and reliability of the MGI G50 to match the performance of the NextSeq 550 in detecting SNVs/InDels, HDs, and HRD status.

The consistency in sequencing quality and data QC values between the platforms suggests comparable base-calling accuracy and data QC performance, reinforcing the reliability of the MGI G50 for the analysis of SNVs/InDels, HDs, and HRD status.

Detection Performance:

Both platforms demonstrated 100% accuracy in detecting SNVs/InDels, HDs and HRD status, and showed complete concordance with each other. These data confirm the high accuracy and consistency of the MGI G50 platform in SNVs/InDels, HDs and HRD status detection, positioning it as a reliable alternative to the NextSeq 550.

Conclusion

The study confirms that the AmoyDx® HRD Complete Panel performs exceptionally well on both MGI G50 and NextSeq 550 platforms. The MGI G50 demonstrated superior sequencing quality and data QC performance while maintaining comparable accuracy in SNVs/InDels and HDs detection as well as HRD (GSS) assessment. These findings validate MGI G50 as a robust and reliable platform for HRR gene

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mutation screening and HRD (GSS) status analysis.