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Comparative Analysis of BRCA Pro Data on MGI DNBSEQ-G50 and NextSeq 550

Abstract

This white paper presents comparative analysis of the AmoyDx® BRCA Pro Panel on two major sequencing platforms: MGI DNBSEQ-G50 (MGI G50) and Illumina NextSeq 550. The study analysed 229 clinical blood samples and 35 FFPE samples to assess sequencing quality, as well as SNV/InDel and CNV 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 BRCA mutation analysis in clinical diagnosis.

Introduction

Breast cancer is a leading cause of cancer-related mortality worldwide. The presence of germline *BRCA1* or *BRCA2* mutations significantly increase the risk of hereditary breast and ovarian cancers. Somatic *BRCA1* or *BRCA2* mutations also play an essential role in breast cancer development. Accurate detection of these mutations is crucial for the application of targeted therapies. The AmoyDx® BRCA Pro 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® BRCA Pro Panel on the MGI G50 platform. By comparing key performance metrics between the two platforms including sequencing quality, mutation detection and CNV consistency, this white paper explores the potential for expanding the use of AmoyDx® BRCA Pro Panel beyond Illumina systems to the MGI G50 platform.

Methodology

1. Sample Collection

Blood samples & FFPE samples used for performance testing of the MGI G50 & Nextseq 550 in this report as stated below:

a) Blood: 229 clinical blood samples
b) FFPE: including 10 positive reference,10 negative reference, 10 sensitivity reference and 5 precision reference samples.

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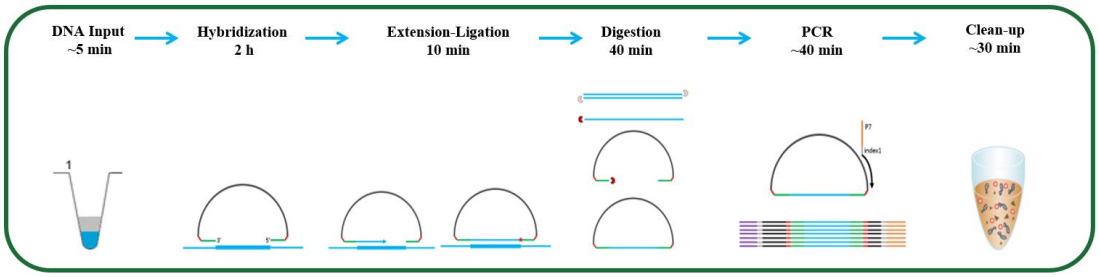
2. Extraction & Library Preparation

DNA extraction was conducted using the AmoyDx® Blood/Bone Marrow DNA Kit for blood samples and the AmoyDx FFPE DNA Kit for FFPE samples. Library preparation was performed according to the AmoyDx® BRCA Pro Panel protocol. Sequencing was carried out on both the MGI G50 and NextSeq 550 platforms for comparative analysis.



3. Data Processing and Analysis

Variant calling was conducted using the ADXHS_gBRCA-CNV module for germline mutations and the ADXHS_tBRCA module for somatic mutations. Key metrics including sequencing depth, quality control parameters, mutation detection efficiency and variant frequency were evaluated to assess performance.

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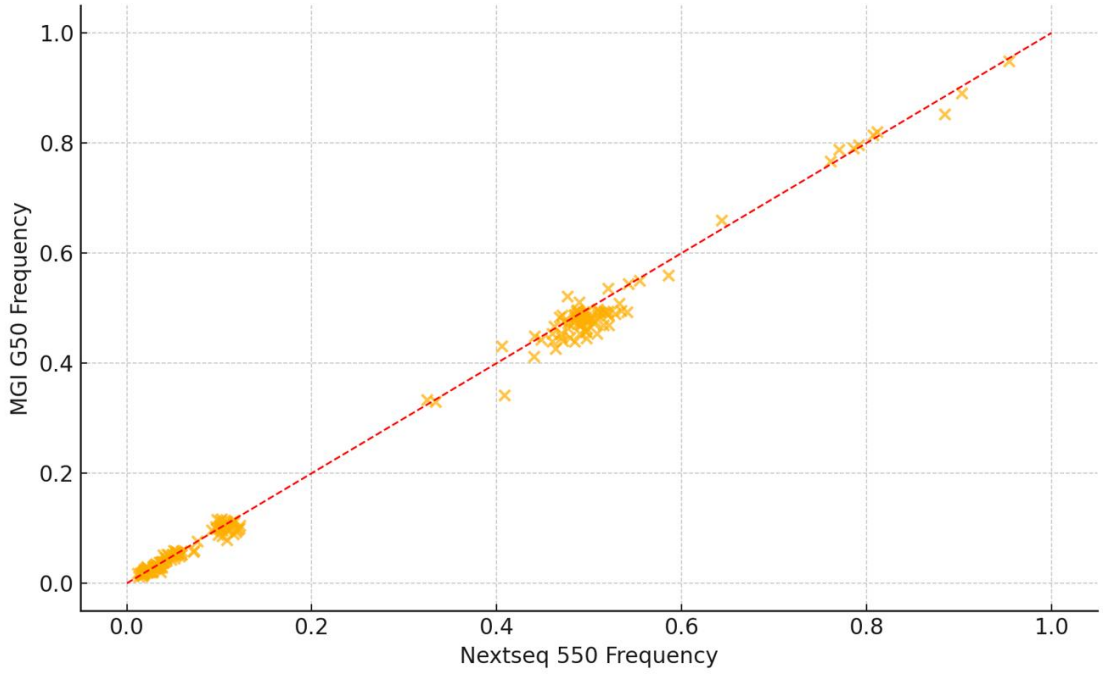
Results

Sequencing Performance Comparison

Metric	MGI G50	NextSeq 550
Sequencing Quality (Q30)	≥75%	≥75%
Blood Sample Depth (minAmp)	≥50×	≥50×
FFPE Sample Depth (effectiveDepth)	≥400×	≥400×

Allele Frequency (Blood & FFPE) Comparison Illumina Nextseq 550 vs MGI G50



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Comparison of Illumina NextSeq 550 and MGI G50 for CNV Results in Blood Samples

MGI G50	Illumina NextSeq 550		Total
	Positive	Negative	
Positive	38	0	38
Negative	0	191	191
Total	38	191	229

Comparison and Statistical Analysis of Illumina NextSeq 550 and MGI G50 Platforms for SNV/INDEL Detection in Blood and FFPE Samples

MGI G50	Illumina NextSeq 550		Total	Positive percent agreement (PPA) (95%CI)	Negative percent agreement (NPA) (95%CI)	Overall percent agreement (OPA) (95%CI)	Kappa
	Positive	Negative					
Positive	239	0	239	98.76% (96.42%-99.58%)	100% (97.49%-100%)	99.23% (97.77%-99.74%)	0.9838
Negative	3	149	152				
Total	242	149	391				

Discussion

The comparative analysis highlights several key findings:

Sequencing Quality:

Both platforms demonstrated high sequencing quality, with Q30 values exceeding 75%. This indicates that both the MGI G50 and NextSeq 550 can generate accurate sequencing data suitable for clinical analysis. The consistency in Q30 values between the platforms suggests comparable base-calling accuracy, reinforcing the reliability of the MGI G50 for BRCA mutation detection.

Depth of Coverage:

Sequencing depth for both blood and FFPE samples was consistent across platforms. Blood samples on both the MGI G50 and NextSeq 550 achieved minimum amplicon depth greater than 50× ensuring sufficient coverage for reliable mutation detection. Similarly, FFPE samples showed an effective sequencing depth exceeding 400× on both platforms, providing adequate sensitivity for detecting low-frequency mutations. The consistent depth of coverage across platforms highlights the capability of the MGI G50 to match the performance of the NextSeq 550 in terms of coverage and sensitivity.

Detection Performance of germline and somatic SNVs/InDels:

Both platforms achieved a 100% detection rate for single nucleotide variants (SNVs) and insertions/deletions (InDels) in both blood and FFPE samples. The overall percent agreement (OPA) was 99.23%, with a positive percent agreement (PPA) of 98.76%, a negative percent agreement (NPA) of 100%, and a kappa value of 0.9838. The frequencies of detected variants were comparable between different platforms. These data confirm the high accuracy and consistency of the MGI G50 platform in mutation detection positioning it as a reliable alternative to the NextSeq 550.

Detection Performance of germline CNVs:

Copy number variation (CNV) detection rates were identical across both platforms with a 100% detection rate. The copy numbers of detected CNVs were comparable between different platforms. These data suggest that the MGI platform can reliably detect CNVs with precision comparable to the NextSeq 550.

Conclusion

The study confirms that the AmoyDx® BRCA Pro Panel performs exceptionally well on both MGI G50 and NextSeq 550 platforms. The MGI G50 demonstrated superior sequencing quality and depth while maintaining comparable accuracy, mutation frequency detection, and detection performance. These findings validate MGI G50 as a robust and reliable platform for BRCA mutation screening in both clinical and research applications.