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Comparative Analysis of Classic NGS Panel Data on MGI DNBSEQ-G50 and NextSeq 550

Abstract

This white paper presents comparative analysis of the AmoyDx® HANDLE Classic NGS Panel on two major sequencing platforms: MGI DNBSEQ-G50 (MGI G50) and Illumina NextSeq 550. The study analyzed 68 pairs of DNA and RNA standard reference samples to assess sequencing quality, as well as SNV/InDel, gene fusion, CNV and MSI 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 the HANDLE Classic NGS Panel mutation analysis in clinical diagnosis.

Introduction

Lung cancer, primarily non-small cell lung cancer (NSCLC), frequently harbors driver mutations, including EGFR (10-35%), KRAS (5-30%), and ALK fusions (3-7%). These genetic alterations guide targeted therapy, such as EGFR-TKIs for EGFR mutations and ALK inhibitors for ALK fusions. Similarly, colorectal cancer (CRC) commonly carries KRAS (20-50%) and BRAF (8-15%) mutations, which impact anti-EGFR therapy response. Advancements in NGS have enabled precision oncology by identifying biomarkers like NTRK fusions, which respond well to TRK inhibitors.

The AmoyDx® HANDLE Classic NGS Panel is designed for qualitative detection of common mutations in 40 solid tumor genes and microsatellite instability (MSI), and has been optimized for use on the Illumina sequencing platforms including NextSeq 550. With the growing demand for more flexible and efficient sequencing options, this study aims to validate the performance of AmoyDx® HANDLE Classic NGS 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® HANDLE Classic NGS Panel beyond Illumina systems to the MGI G50 platform.

Methodology

1. Sample Collection

In total 120 Clinical FFPE samples and 75 standard reference samples were used for performance testing of the MGI G50 & Nextseq 550 in this report.

2. Extraction & Library Preparation

DNA and RNA extraction was conducted using the AmoyDx® FFPE DNA/RNA Kit for FFPE samples. Library preparation was performed according to the AmoyDx® HANDLE Classic NGS Panel protocol. Sequencing was carried out on both the MGI G50 and NextSeq 550 platforms for comparative analysis.

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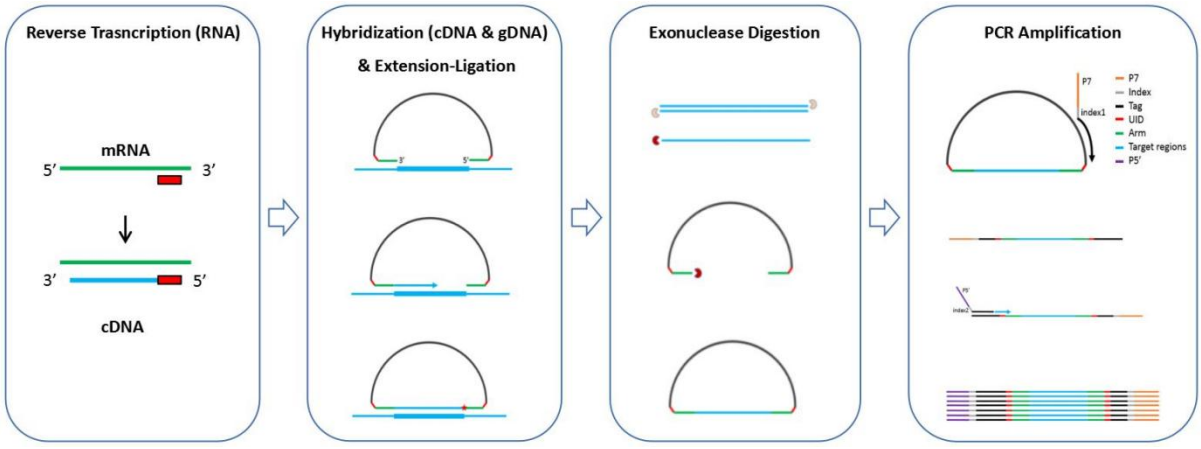

3. Data Processing and Analysis

Variant calling was conducted using the ADXHS-Classic module. Key metrics including quality control parameters, sequencing depth, inner RNA-Control and variant frequency were evaluated to assess performance.

4. Results

Sequencing Performance Comparison

Metric	MGI G50	NextSeq 550
Sequencing Quality (Q30)	≥75%	≥75%
FFPE Sample Depth (effectiveDepth)	≥400×	≥400×
Variant Depth (Depth)	≥30×	≥30×
RNA-Control (Copies)	≥20 Copies	≥20 Copies

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

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	62	0	62	100%	100%	100%	100%
Negative	0	133	133				
Total	62	133	195				

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Comparison and Statistical Analysis of Illumina NextSeq 550 and MGI G50 Platforms for Gene Fusion and MET Skipping Detection

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	37	0	37	100%	100%	100%	100%
Negative	0	158	158				
Total	37	158	195				

Comparison of Illumina NextSeq 550 and MGI G50 for Platforms for CNA Detection

MGI G50	Illumina NextSeq 550		Total
	Positive	Negative	
Positive	13	0	13
Negative	0	182	182
Total	13	182	195

Comparison of Illumina NextSeq 550 and MGI G50 for Platforms for MSI Detection

MGI G50	Illumina NextSeq 550		Total
	MSI-H	MSS	
MSI-H	14	0	14
MSS	0	181	181
Total	14	181	195

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 mutation detection within the target region of the 40 key solid tumor genes from the AmoyDx® HANDLE Classic NGS Panel.

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Depth of Coverage:

Sequencing depth for the samples was consistent across platforms. Both the MGI G50 and NextSeq 550 achieved minimum effective Depth exceeding 400× on both platforms, meanwhile, the RNA control from both platforms exceeded 1000× which is providing excellent coverage for reliable mutation detection. 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.

Detection Performance:

Both platforms achieved a 100% detection rate for single nucleotide variants (SNVs) and insertions/deletions (InDels), gene fusions, MET skippings, copy number amplifications (CNAs), and MSI. The overall percent agreement (OPA) was 100%, with a positive percent agreement (PPA) of 100%, a negative percent agreement (NPA) of 100%. These data confirm the high accuracy and consistency of the MGI G50 platform in mutation detection and MSI detection positioning it as a reliable alternative to the NextSeq 550.

Conclusion:

The study confirms that the AmoyDx® HANDLE Classic NGS 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 detecting the target region of the 40 key solid tumor genes from the panel in both clinical and research applications.