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Comparative Analysis of AmoyDx® NGS panels on GeneMind (Genolab M and FASTASeq300) and Illumina NextSeq 550 platforms

Abstract

This white paper presents comparative analysis of the representative AmoyDx® NGS panels (Table 1) across the major sequencing platforms: GeneMind (GenoLab M and FASTASeq 300) and Illumina NextSeq 550. Results demonstrate that GeneMind GenoLab M and FASTASeq 300 platforms deliver comparable sequencing data quality, supporting their suitability for reliable NGS testing in tumor mutation detection and research.

Table 1. AmoyDx® NGS panels used for performance assessment on GeneMind sequencers

Product	Technology	Panel Coverage	Sample Type	Variant Type	Sample Quantity
BRCA Pro	HANDLE	*BRCA1* and *BRCA2* genes	FFPE	SNV, InDel	27
			Whole Blood	SNV, InDel, LR	48
HRD Complete	HANDLE	20 HRR genes plus HRD	FFPE	SNV, InDel, HD, and HRD status (GSS)	88
Classic	HANDLE	40 genes plus MSI	FFPE	SNV, InDel, fusion, CNV, MSI	75
HRR Liquid	ddCAP	24 genes	Liquid biopsy	SNV, InDel, PTEN Loss	38

Note:

BRCA Pro: AmoyDx® BRCA Pro Panel

HRD Complete: AmoyDx® HRD Complete Panel

Classic: AmoyDx® HANDLE Classic NGS Panel

HRR Liquid: AmoyDx® HRR Liquid NGS Panel

Introduction

The AmoyDx® NGS Panels have 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® NGS Panels on the GeneMind Genolab M and FASTASeq 300 platforms. By comparing key performance metrics between the GeneMind and Illumina platforms, including sequencing quality and mutation detection consistency, this white paper explores the potential for expanding the use of AmoyDx® NGS Panels beyond the Illumina platform to the GeneMind GenoLab M and FASTASeq 300 platforms.

Methodology

1. Sample Collection

To validate the sequencing performance on GeneMind platforms, specimens with diverse sample types were collected to evaluate the agreement of the variant detection in accordance with the detection scope of each NGS panel.

1) BRCA Pro Panel:
A total of 48 whole blood samples and 27 FFPE samples were tested for performance evaluation of the GeneMind (GenoLab M and FASTASeq 300) and NextSeq 550. The sequencing quality and the concordance across different variant types, including single nucleotide variants (SNVs), insertions and deletions (InDels), and large rearrangements (LRs) were evaluated on both sequencing platforms.

2) HRD Complete Panel:

A total of 88 FFPE samples from ovarian cancer and prostate cancer were tested for performance evaluation of the GeneMind (GenoLab M and FASTASeq 300) and NextSeq 550. The sequencing quality and the concordance across different variant types, including SNVs, InDels, homozygous deletions (HDs), and HRD status were evaluated on both sequencing platforms.

3) Classic Panel:

A total of 75 FFPE samples from multiple cancer types were tested for performance evaluation of the GeneMind (GenoLab M and FASTASeq 300) and NextSeq 550. The sequencing quality and the concordance across different variant types, including SNVs, InDels, gene fusions, copy number amplifications (CNAs) and microsatellite instability (MSI) were evaluated on both sequencing platforms.

4) HRR Liquid Panel:

A total of 20 plasma cfDNA samples and 18 cell line-derived reference samples were tested for performance evaluation of the GeneMind (GenoLab M and FASTASeq 300) and NextSeq 550. The sequencing quality and the concordance across different variant types, including SNVs, InDels, and PTEN loss were evaluated on both sequencing platforms.

2. DNA/RNA Extraction, Library Preparation and Sequencing

The sample DNA (or RNA) was extracted using the AmoyDx extraction kits, following the manufacturer's instructions for the respective sample type. Library preparation was carried out in accordance with the manufacturer's instructions for each AmoyDx NGS panel. Sequencing was carried out for each library on both the GeneMind (Genolab M and FASTASeq 300) and NextSeq 550 platforms for comparative analysis.

3. Data Processing and Analysis

When the sequencing is finished, adopt AmoyDx ANDAS Data Analyzer to analyze the sequencing data. Select the appropriate analysis module according to the manufacturer's instructions for each AmoyDx NGS panel. Key metrics including sequencing depth, quality control parameters, and variant detection concordance were evaluated to assess the sequencing performance. The concordance of variant detection between different platforms, were investigated using overall/positive/negative percentage agreement (OPA/PPA/NPA).

Results

Sequencing and Data QC Performance Comparison

Table 2. Sequencing and data QC assessment for each product

Product	Metrics	GeneMind GenoLab M	GeneMind FASTASeq 300	Illumina NextSeq 550
BRCA Pro	Sequencing Quality (Q30)	≥75%	≥75%	≥75%
	Depth	FFPE ≥400×; Blood ≥50×	FFPE ≥400×; Blood ≥50×	FFPE ≥400×; Blood ≥50×
HRD Complete	Sequencing Quality (Q30)	≥75%	≥75%	≥75%
	Coverage (180×) BRCA	≥ 95%	≥ 95%	≥ 95%
	Coverage (180×) CDS	≥ 95%	≥ 95%	≥ 95%
	DepthNoise for GSS	≤0.35	≤0.35	≤0.35
	BRAFNoise for GSS	≤0.05	≤0.05	≤0.05
	CDSDepthNoise for HD	≤0.40	≤0.40	≤0.40
	CDSBRAFNoise for HD	≤0.05	≤0.05	≤0.05
Classic Panel	Sequencing Quality (Q30)	≥75%	≥75%	≥75%
	Depth	≥400×	≥400×	≥400×
	RNA-Control	≥20	≥20	≥20
HRR Liquid	Sequencing Quality (Q30)	≥75%	≥75%	≥75%
	CoverageRatioUNIQ1000	≥90%	≥90%	≥90%
	CNVNoise	≤0.20	≤0.20	≤0.20

BRCA Pro Panel Testing Results

Table 3. Testing result summary of BRCA Pro panel

Platform	Sample Type and Variant Type	Status	Illumina NextSeq 550		Concordance
			Positive	Negative	
GeneMind GenoLab M	Blood - Germline SNV/InDel	Positive	21	0	PPA = 100.00% NPA = 100.00% OPA = 100.00%
		Negative	0	27	
	Blood - Germline LR	Positive	19	0	PPA = 100.00% NPA = 100.00% OPA = 100.00%
		Negative	0	29	
	Tissue - SNV/InDel	Positive	11	0	PPA = 100.00% NPA = 100.00% OPA = 100.00%
		Negative	0	16	
GeneMind FASTASeq 300	Blood - Germline SNV/InDel	Positive	21	0	PPA = 100.00% NPA = 100.00% OPA = 100.00%
		Negative	0	27	
	Blood - Germline LR	Positive	19	0	PPA = 100.00% NPA = 100.00% OPA = 100.00%
		Negative	0	29	
	Tissue - SNV/InDel	Positive	11	0	PPA = 100.00% NPA = 100.00% OPA = 100.00%
		Negative	0	16	

HRD Complete Panel Testing Results

Table 4. Testing result summary of HRD Complete panel

Platform	Variant Type	Status	Illumina NextSeq 550		Concordance
			Positive	Negative	
GeneMind GenoLab M	SNV/InDel	Positive	46	0	PPA = 95.83% NPA = 100.00% OPA = 97.73%
		Negative	2	40	
	HD	Positive	6	0	PPA = 100.00% NPA = 100.00% OPA = 100.00%
		Negative	0	82	
	HRD Status	Positive	55	0	PPA = 96.49% NPA = 100.00% OPA = 97.73%
		Negative	2	31	
GeneMind FASTASeq 300	SNV/InDel	Positive	46	0	PPA = 95.83% NPA = 100.00% OPA = 97.73%
		Negative	2	40	
	HD	Positive	6	0	PPA = 100.00% NPA = 100.00% OPA = 100.00%
		Negative	0	82	
	HRD Status	Positive	55	0	PPA = 96.49% NPA = 100.00% OPA = 97.73%
		Negative	2	31	

Note: *A positive HRD status result is defined by either the presence of a pathogenic/likely pathogenic variant in BRCA1 and/or BRCA2 genes or a positive Genomic Scar Score (GSS).*

Classic Panel Testing Results

Table 5. Testing result summary of Classic panel

Platform	Variant Type	Status	Illumina NextSeq 550		Concordance
			Positive	Negative	
GeneMind GenoLab M	SNV/InDel	Positive	51	0	PPA = 96.23% NPA = 100.00% OPA = 97.33%
		Negative	2	22	
	Fusion	Positive	18	0	PPA = 94.74% NPA = 100.00% OPA = 98.67%
		Negative	1	56	
	CNV	Positive	14	1	PPA = 87.50% NPA = 98.31% OPA = 96.00%
		Negative	2	58	
	MSI	Positive	8	0	PPA = 100.00% NPA = 100.00% OPA = 100.00%
		Negative	0	67	
GeneMind FASTASeq 300	SNV/InDel	Positive	52	0	PPA = 98.11% NPA = 100.00% OPA = 98.67%
		Negative	1	22	
	Fusion	Positive	18	2	PPA = 100.00% NPA = 96.49% OPA = 97.33%
		Negative	0	55	
	CNV	Positive	15	0	PPA = 88.24% NPA = 100.00% OPA = 97.33%
		Negative	2	58	
	MSI	Positive	8	0	PPA = 100.00% NPA = 100.00% OPA = 100.00%
		Negative	0	67	

HRR Liquid Panel Testing Results

Table 6. Testing result summary of HRR Liquid panel

Platform	Variant Type	Status	Illumina NextSeq 550		Concordance
			Positive	Negative	
GeneMind GenoLab M	SNV/InDel	Positive	7	0	PPA = 100.00% NPA = 100.00% OPA = 100.00%
		Negative	0	31	
	PTEN Loss	Positive	14	0	PPA = 100.00% NPA = 100.00% OPA = 100.00%
		Negative	0	24	
GeneMind FASTASeq 300	SNV/InDel	Positive	7	0	PPA = 100.00% NPA = 100.00% OPA = 100.00%
		Negative	0	31	
	PTEN Loss	Positive	14	0	PPA = 100.00% NPA = 100.00% OPA = 100.00%
		Negative	0	24	

Discussion

The comparative analysis highlights several key findings:

Sequencing Quality and Data QC Performance:

The GeneMind GenoLab M and FASTASeq 300 sequencing platforms have been evaluated and exhibit high Q30 value and data quality comparable to the Illumina NextSeq 550 platform, indicating high sequencing accuracy and data quality, which supports their compatibility for downstream biomarker assessment and data analysis.

Detection Performance:

Both platforms demonstrated high accuracy and specificity across multiple variant types, including SNVs/InDels, CNVs, homozygous deletions, HRD status, and MSI status.

For the BRCA Pro panel, all the biomarkers investigated demonstrated 100% consistency across both the GeneMind GenoLab M and FASTASeq 300 sequencing platforms.

For the HRD Complete panel, all the biomarkers investigated demonstrated over 95% consistency across both the GeneMind GenoLab M and FASTASeq 300 sequencing platforms. The discrepancies observed in BRCA variants or HRD status were caused by the variant frequency or the GSS value being near the cut-off of the assay.

For the Classic panel, all the biomarkers investigated demonstrated over 95% consistency across both the GeneMind GenoLab M and FASTASeq 300 sequencing platforms. The minor discrepancies observed were caused by variants being filtered out due to the frequency/copy number below the cut-off of the assay.

For the HRR Liquid panel, all the biomarkers investigated demonstrated 100% consistency across both the GeneMind GenoLab M and FASTASeq 300 sequencing platforms.

In summary, these data confirm the high accuracy and consistency of the GeneMind GenoLab M and FASTASeq 300 platform in variant detection and biomarker analysis performance at both DNA and RNA levels, positioning them as reliable alternatives to the NextSeq 550 system.

Conclusion

The study confirms that the AmoyDx® NGS Panels demonstrate exceptional performance on both the GeneMind GenoLab M and FASTASeq 300 platforms. These platforms have demonstrated superior performance in sequencing quality and variant detection, comparable to the capabilities of Illumina platforms. These findings validate GeneMind GenoLab M and FASTASeq 300 as robust and reliable platforms for reliable NGS testing in tumor mutation detection and research.

Disclaimer:

The results presented in this document are for informational purposes only and should not be considered as definitive medical conclusions. These results are based on the analysis of genetic data and are intended to support, not replace, professional medical evaluation, diagnosis, or treatment.

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