Comparison of Illumina NovaSeq 6000 and MGISEQ-2000 in Profiling Xenograft Models

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INTRODUCTION

Comprehensive genomic profiling of tumor models, including patient-derived xenografts (PDX), cell lines and organoids, is an integral prerequisite for productive *in vivo* studies. There are now two leading sequencing platforms from Illumina and MGI Tech. In this study, we compared the performance of these two platforms in sequencing xenograft tumors, which contain both human tumor cells and mouse stromal cells.

METHODS

- Genomic profiling was performed on several xenograft tumors by MGI's MGISEQ-2000 (MGIseq) and Illumina's NovaSeq 6000 (NovaSeq), including RNA-Seq and whole-exome sequencing (WES) for three PDX samples, and whole-genome sequencing (WGS) for one PDX sample
- A comprehensive assessment was performed on sequencer performance using multiple criteria

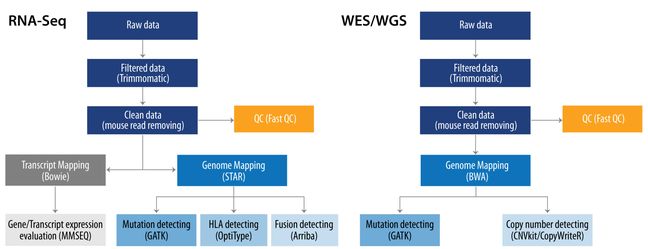
RESULTS

Mouse ratios from the two sequencers were very close in all RNA-Seq/WES/WGS datasets, indicating no, or similar, species bias for both platforms. RNA-Seq datasets showed high gene expression concordance, with Pearson correlation coefficients of 0.993, 0.992 and 0.993 for CR0588, GA0091 and LU0743 PDX models, respectively. WES datasets across these models also showed high mutation concordance, with mutation overlapping rates of 98.9%, 99.3% and 99.1%, and mutation ratio correlation coefficients of 0.971, 0.976 and 0.977, respectively. WGS data showed an overall overlapping rate of 95.5%, and mutation ratio correlation coefficient of 0.955, while for SNPs and INDELs, the overlapping rate was 97.1% and 86.1% for LU0743.

Table 1. Study design and sequencing kits

Sample	Sample Type	Sequencing Type	RNA-Seq Library	WES Capture Kit
CR0588P15	PDXO	RNA-Seq; WES	TrueSeq polyA non-stranded	Agilent V6
GA0091P26	PDXO	RNA-Seq; WES	TrueSeq polyA non-stranded	Agilent V6
LU0743P15	PDXO	RNA-Seq; WES; WGS	TrueSeq polyA non-stranded	Agilent V6

Fig 1. RNA-Seq and WES/WGS workflows



RESULTS

Table 2. RNA-Seq/WES/WGS data statistics

Sample	Data Type	# PE	# Base (Gb)	GC ratio(%)	Q30 ratio(%)	Q20 ratio (%)	Mouse read ratio (%)
CR0588P15 (MGIseq)	RNA-Seq	45.5 M	9.1	47.36	89.89	97.42	0.06
CR0588P15 (NovaSeq)	RNA-Seq	38.4 M	11.1	48.86	90.14	95.99	0.07
GA0091P26 (MGIseq)	RNA-Seq	54.6 M	10.9	47.37	90.13	97.49	0.97
GA0091P26 (NovaSeq)	RNA-Seq	37.1 M	10.8	49.92	89.92	95.91	0.78
LU0743P15 (MGIseq)	RNA-Seq	59.1 M	11.8	48.64	88.83	97.13	1.67
LU0743P15 (NovaSeq)	RNA-Seq	36.2 M	10.5	50.91	90.74	96.34	1.49
CR0588P15 (MGIseq)	WES	78.3 M	15.6	54.2	88.9	96.45	0.05
CR0588P15 (NovaSeq)	WES	50.3 M	15.1	52.98	93.33	97.25	0.15
GA0091P26 (MGIseq)	WES	77.1 M	15.4	53.59	88.76	96.38	0.05
GA0091P26 (NovaSeq)	WES	51.9 M	15.6	53.68	93.43	97.29	0.16
LU0743P15 (MGIseq)	WES	77 M	15.4	53.66	89.59	96.73	0.06
LU0743P15 (NovaSeq)	WES	51.7 M	15.5	53.31	92.98	97.09	0.15
LU0743P15 (MGIseq)	WGS	630.6 M	126	41.15	88.45	96.79	0.12%
LU0743P15 (NovaSeq)	WGS	334.8 M	100	40.94	91.19	96.51	0.32%

Fig 2. Gene coverage randomness. (A) MGIseq; **(B)** NovaSeq

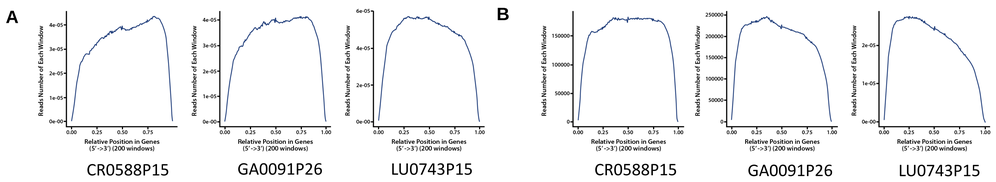


Fig 3. Gene expression correlation between two platforms in three PDX tumors

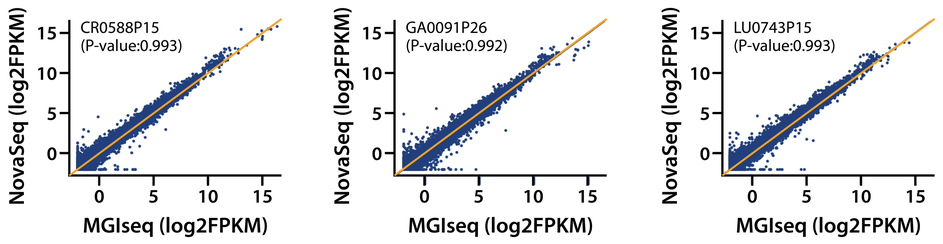


Fig 4. Accumulative depth distribution of WES and WGS data

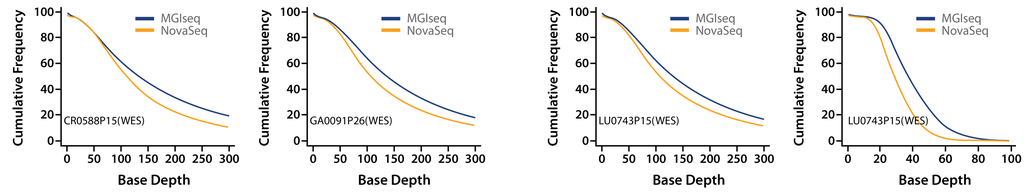
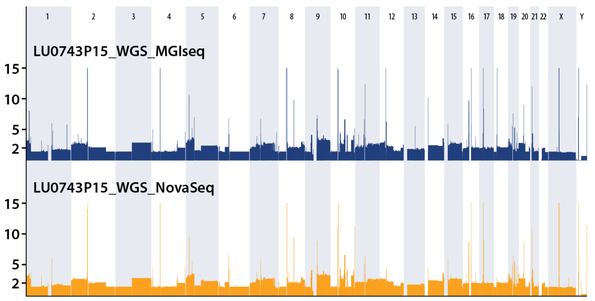


Table 3. Comparison of variant detection result between two platforms

Sample	Data Type	Mutation Frequency correlation	# detected on both platforms	# detected on MGIseq	# detected on NovaSeq	Concordance (%)
CR0588P15	WES	0.971	10663	59	58	98.9
GA0091P26	WES	0.976	8485	23	34	99.3
LU0743P15	WES	0.977	10284	58	39	99.1
LU0743P15	WGS	0.955	3788129	107846	70683	95.5

Fig 5. Comparison of DNA copy number detected by WGS data. The copy number result is highly concordant



SUMMARY

- High consistency between the MGIseq and NovaSeq platforms was observed on the RNA-Seq data sets, including GC ratio, Q20/Q30 ratio, mapping ratio and randomness
- A high correlation in gene expression was detected across the two platforms
- The consistency between the MGIseq and NovaSeq platforms on WES/WGS data sets (including GC ratio, Q20/Q30 ratio, mapping ratio) is high
- The mutation frequency, mutation concordance and DNA copy number status detected by the two platforms are consistent

CONCLUSION

Our study demonstrates that the MGISEQ and Illumina sequencers have comparable performance in sequencing xenograft tumor samples.