

SureSelect Target Enrichment Solutions on DNBSEQ Platform from MGI

Introduction

MGI, as a subsidiary of the BGI Group, is a pioneering company in the NGS industry, offering multiple sequencer models (including the DNBSEQ-G50, DNBSEQ-G400, and DNBSEQ-T7) that use their proprietary DNBSEQ method. This proprietary technology leverages DNA nanoballs (DNB) and rolling-circle amplification (RCA) to provide high-sensitivity sequencing with lower error rates and reduced sequencing cost. MGI's DNBSEQ platform has shown excellent performance in terms of cost, data quality, and flexibility, and their sequencers have been widely used in laboratories and institutes for both research and clinical applications.

The MGIEasy exome universal library prep set is specifically designed for preparing exome libraries to sequence on the MGI DNBSEQ platform. This set is compatible with the Agilent SureSelect target enrichment system, the market leading hybrid capture-based platform which uses RNA-based probes to selectively capture genomic regions of interest. MGI and Agilent now provide an end-to-end solution for converting genomic DNA into single-stranded circularized DNA libraries for sequencing on DNBSEQ platforms, resulting in outstanding coverage and performance.

Here, DNA libraries were prepared from HapMap reference gDNA NA12878 using either the MGIEasy exome universal library prep set or the MGIEasy library prep set with the MGIEasy exome capture accessory kit. Sample barcodes were added through the adapter ligation step. Target enrichment was performed using the SureSelect Human All Exon V6 or V7 and the SureSelect target enrichment hybridization module. Final libraries were sequenced on the DNBSEQ-G400 system using 150 bp paired-end reads (refer to the Appendix for more details on protocols used for library preparation and target enrichment). Data was normalized to 100X sequencing depth and analyzed using MegaBOLT, a field-programmable gate array (FPGA)-boosted data analysis platform that is capable of fast, accurate, cost-effective analysis of whole-genome and whole-exome sequencing data.

Consistent depth accumulation

Using identical input quantities of PCR products, samples were processed with either the SureSelect All Exon V6 or SureSelect All Exon V7. The V6 sample underwent the SureSelect XT target enrichment protocol with an overnight hybridization, while the V7 sample was processed with the SureSelect XT HS target enrichment protocol (which uses a 90 minute fast hybridization). Both samples showed comparable performance with greater than 65 % on-target rates, more than 95% similar coverage above 20X, and duplication rates less than 10%.

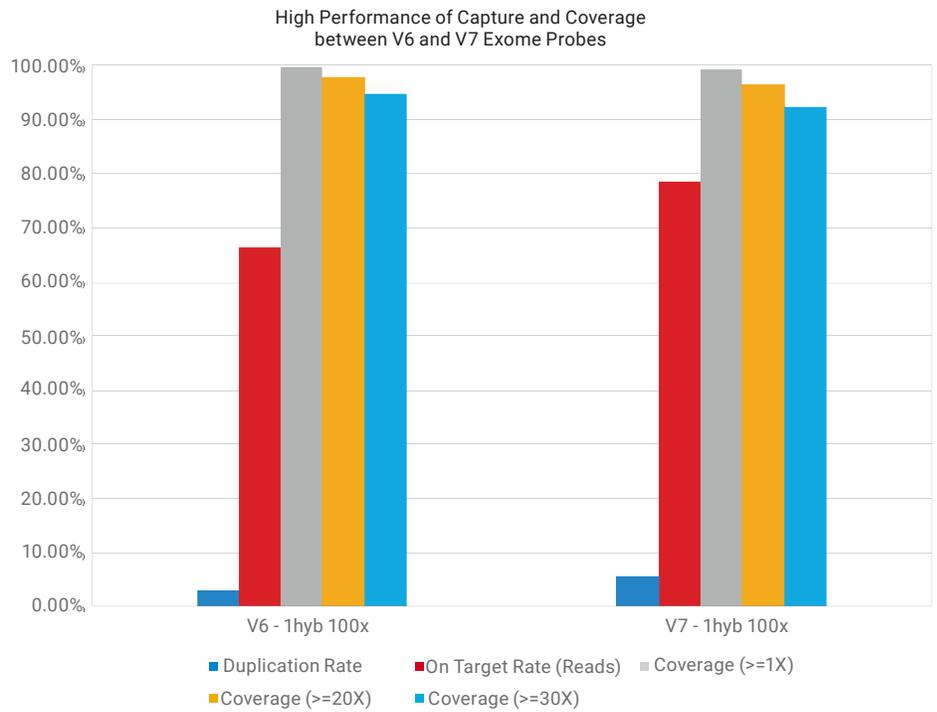


Figure 1. Performance of different hybrid capture probes.

Consistent depth accumulation

The sample repeats give high stability in depth accumulation.

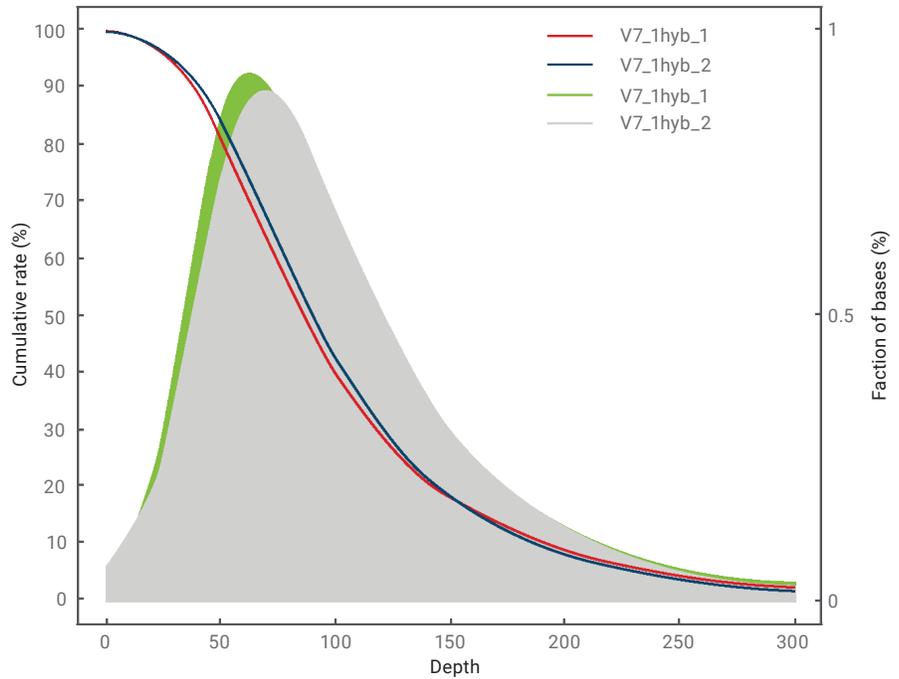


Figure 2. Accumulated depth curve from single capture library repeats of SureSelect All Exon V7.

Identical sample replicates with the All Exon V7 kit were run, demonstrating excellent uniformity as evidenced by consistent performance in both cumulative rate and fraction of bases across the analyzed depths.

High consistency of variants detection

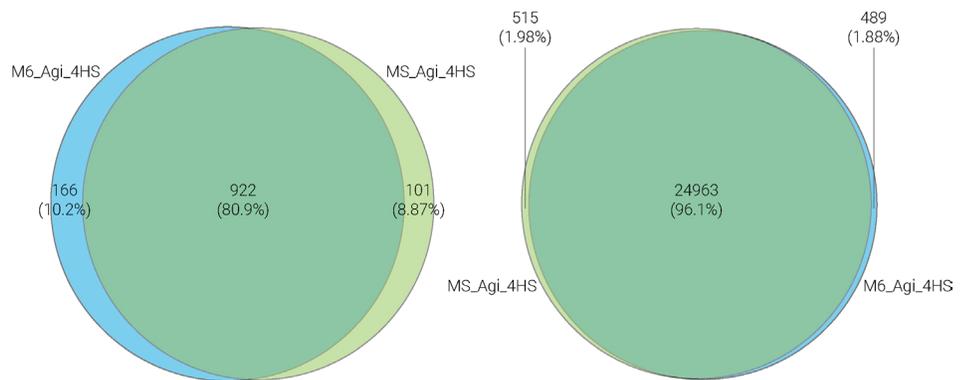


Figure 3. Consistency of SNP and indel detection across two identical samples prepared with the SureSelect All Exon V7 kit.

Technical replicates prepared using the V7 kit demonstrated high consistency, resulting in >95 % SNPs and >80 % of indels being detected between two technical replicates.

Ordering information

XT HS/Low input, quick hybridization

| Procedure | Vendor | Kit | Catalog Number |
|---------------------|---------|---|---|
| Library preparation | MGI | MGIEasy universal DNA library prep set | 1000006985 (16rxn) |
| | | MGIEasy exome capture accessory kit | 1000007743 (16rxn) |
| | | Or | |
| | | MGIEasy exome universal library prep set V2.0 | 1000009657 (16rxn) |
| Target enrichment | Agilent | SureSelect XT HS Target Enrichment kit, ILM Hyb Module (Post PCR), 16-Rxn | G9916B |
| | | SureSelect XT HS and XT Low Input Human All Exon V7 | 5191-4028 (16 rxn) 5191-4028 (96 rxn) |
| | | SureSelect XT HS and XT Low Input Human All Exon V7 Plus 1 | 5191-4031 (16 rxn) 5191-4032 (96 rxn) |
| | | SureSelect XT HS and XT Low Input Human All Exon V7 Plus 2 | 5191-4034 (16 rxn) 5191-4035 (96 rxn) |
| | | SureSelect custom and catalog panels | Various visit www.agilent.com |
| Sequencing | MGI | Genetic sequencers DNBSEQ-G400RS | 900-000170-00 |
| | | DNBSEQ-G400RS High-throughput sequencing set (FCL PE150) | 1000016952 |
| Analysis | MGI | MegaBOLT bio informatics analysis accelerator | 510-000307-00 |

XT-overnight hybridization

| Procedure | Vendor | Kit | Catalog Number |
|---------------------|---------|--|---|
| Library preparation | MGI | MGIEasy universal DNA library prep set | 1000006985 (16rxn) |
| | | MGIEasy exome capture accessory kit | 1000007743 (16rxn) |
| | | Or | |
| | | MGIEasy exome universal library prep set V2.0 | 1000009657 (16rxn) |
| Target enrichment | Agilent | Custom SSEL XT enrichment only HSQ | 930671 (16rxn); 930672 (96rxn) |
| | | SureSelect custom and catalog panels | Various visit www.agilent.com |
| Sequencing | MGI | Genetic sequencers DNBSEQ-G400RS | 900-000170-00 |
| | | DNBSEQ-G400RS High-throughput sequencing set (FCL PE150) | 1000016952 |
| Analysis | MGI | MegaBOLT bio-informatics analysis accelerator | 510-000307-00 |

Appendix

Library preparation, post-capture PCR and DNA single strand circularization

Refer to the MGIEasy Exome Universal Library Prep Set User Manual version A2 (SOP-013-B02-144).

Target enrichment and capture

For SureSelectXT refer to the SureSelect XT Target Enrichment for Illumina Paired-End Multiplex Sequencing Library protocol version C3 (G7530-90000), Pg 61-70.

For SureSelectXT HS refer to the SureSelect XT HS Target Enrichment for Illumina Paired-End Multiplex Sequencing Library protocol version C2 (G9702-90000), Pg 45-55.

Preparation of blocker mix

| For XT protocol | |
|--|------------------|
| Reagent | Volume for 1 rxn |
| SureSelect Indexing Block 1 (green cap) | 2.5 μ L |
| SureSelect Block 2 (blue cap) | 2.5 μ L |
| Block 3 (MGIEasy Exome Capture Accessory Kit) | 1 μ L |
| Block 4 (MGIEasy Exome Capture Accessory Kit) | 10 μ L |
| For XT HS protocol | |
| Reagent | Volume for 1 rxn |
| SureSelect XT HS and XT Low Input Blocker Mix (blue cap) | 5 μ L |
| Block 3 (MGIEasy Exome Capture Accessory Kit) | 1 μ L |
| Block 4 (MGIEasy Exome Capture Accessory Kit) | 10 μ L |

For the SureSelectXT protocol, concentrate blocker mix to 5.6 μ L/rxn using a speed vacuum before proceeding to Step 6.

For the SureSelextXT HS protocol, concentrate blocker mix to 5 μ L/rxn using a speed vacuum prior to adding to the DNA sample in Step 3.

Sequencing

Refer to the DNBSEQ-G400RS High-throughput Sequencing Set User manual version A1.

www.agilent.com

For Research Use Only. Not for use in diagnostic procedures.

This information is subject to change without notice.

PR7000-2558
© Agilent Technologies, Inc. 2020
Printed in the USA, May 1, 2020
5994-1888EN

