Agilent
Trusted Answers

High Performance Exome Built on Advanced and Proven Technology

Key Advantages

– Advanced technology that you can rely on

– Superior performance for confident results and efficient sequencing

– Comprehensive content for more complete coverage

– Native automation support for increased productivity

– Seamless integration with cloud-based informatics solutions for faster time-to-answers

Introduction

The SureSelect Human All Exon V8 provides up-to-date content and complete coverage* of protein coding regions from RefSeq, CCDS, and GENCODE. It also covers the *TERT* promoter and hard-to-capture exons that are omitted by other exomes on the market. Powered by machine learning-based probe design and a new production process, the SureSelect Human All Exon V8 spans a 35.1 Mb target region of the human genome with an efficient end-to-end design size of only 41.6 Mb. The panel delivers excellent enrichment performance, as well as efficient and cost-effective exome sequencing. In addition, the panel is manufactured in large scale to provide consistent results for many years.

The SureSelect Human All Exon V8 is compatible with the legacy SureSelectXT target enrichment system, as well as the streamlined SureSelectXT HS2, SureSelectXT HS, SureSelectXT Low Input, and SureSelectQXT library preparation and target enrichment systems, which feature a fast, 90-minute hybridization protocol and a single-day workflow. The V8 exome workflow is natively supported by the Bravo Automated Liquid Handling platform for high-throughput sample preparation, and the Magnis NGS Prep system for complete, walkaway automation. The sequencing data can be readily analyzed using Alissa Interpret for efficient variant interpretation and reporting, providing an end-to-end exome sequencing solution.

Built on More Than 10 Years of Exome Technology

Improved Manufacturing Process — Improved process and probe printing targeting both DNA strands

Powered by Machine Learning — Machine learning-based probe selection and placement

Excellent Enrichment Performance — Deeper and more uniform coverage across target regions

Small Design Footprint — Efficient probe design that is more economical to sequence

Comprehensive Exome — Up-to-date database coverage for CCDS, RefSeq, and GENCODE

Predesigned and Custom Content — UTRs / Clinical content / Custom content

Native Automation — High-throughput and walkaway automation with the Bravo and Magnis systems, respectively

Seamless Analysis Workflow — Variant calling, interpretation, and reporting with the Alissa Informatics Platform

Figure 1. Superior by design. The new Human All Exon V8 is built on more then ten years of SureSelect technology and is now powered by machine learning for improved coverage and efficiency.

Excellent Target Coverage and Uniform Distribution for Confident Results
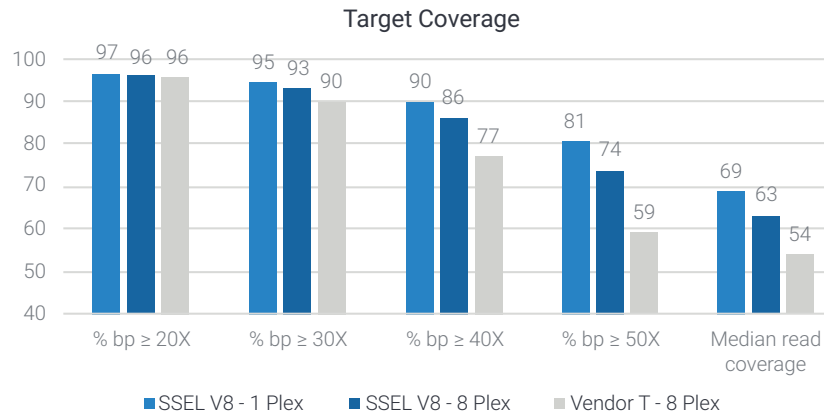

Target Coverage

Figure 2. The SureSelect Human All Exon V8 delivers broader target coverage across relevant depths and deeper median coverage for more confident variant detection. Exome-enriched libraries were generated following vendor protocols** and sequenced on an Illumina HiSeq 4000 instrument. All samples were downsampled to 5 Gb for analysis.
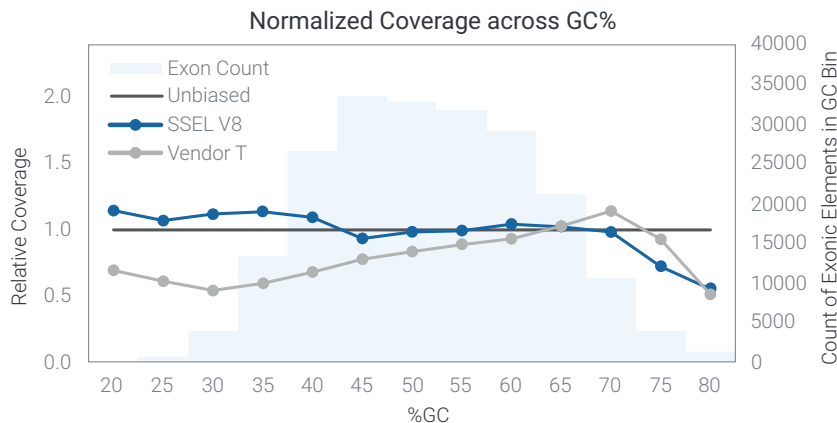

Normalized Coverage across GC%

Figure 3. The SureSelect Human All Exon V8 provides more uniform distribution of coverage across the GC spectrum. Variants in GC-rich and GC-poor regions are better represented and less likely to be missed due to low coverage. Exome-enriched libraries were generated from 8-plex captures following vendor protocols** and sequenced on an Illumina HiSeq 4000 instrument. All samples were downsampled to 5 Gb for analysis.

Efficient Sequencing with High-Performance Enrichment

A Coverage Uniformity
Fold-80 Base Penalty

B Enrichment Specificity
% Reads on Target

C Sequencing Efficiency
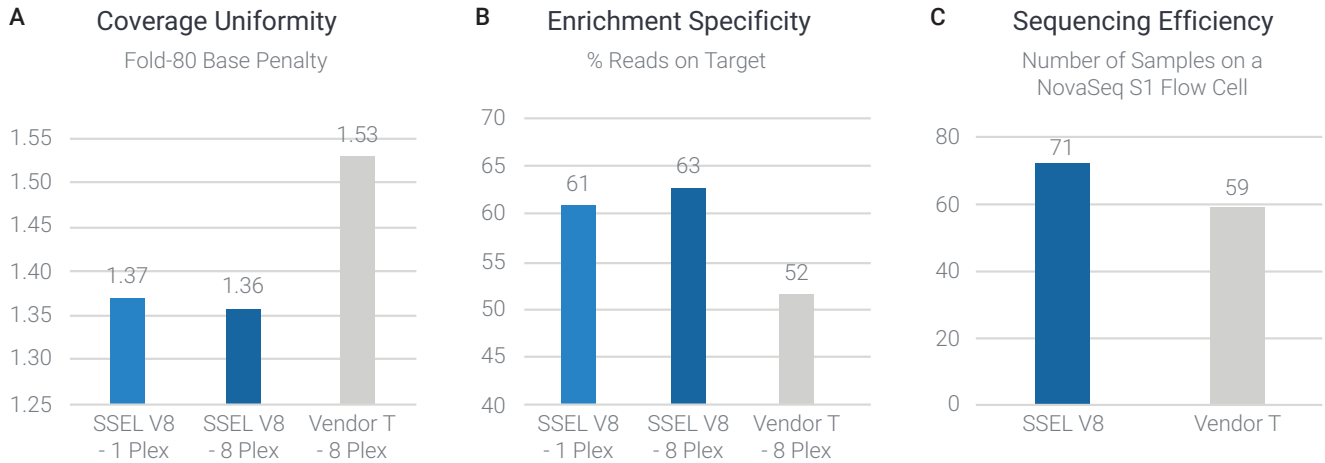Number of Samples on a
NovaSeq S1 Flow Cell

Figure 4. SureSelect Human All Exon V8 provides superior enrichment performance, resulting in lower sequencing costs. A) The SureSelect Human All Exon V8 delivers excellent coverage uniformity as measured by a lower fold-80 base penalty (lower is better). B) It also provides higher on-target rate, indicative of a highly specific enrichment of exonic sequences. C) SureSelect Human All Exon V8's high-performance exome enrichment, combined with an efficient design, reduces sequencing costs, allowing more samples to be sequenced together on a sequencing run. Exome-enriched libraries were generated from 8-plex captures following vendor protocols**, and the number of reads required to achieve a 30X coverage of 90% was calculated to determine the number of samples that can be sequenced together on a NovaSeq S1 flow cell.

Superior Coverage of the Exome

A RefSeq Exons with Coverage
≥20X

B RefSeq Genes with Coverage
≥20X

C Exons with Coverage ≥20X
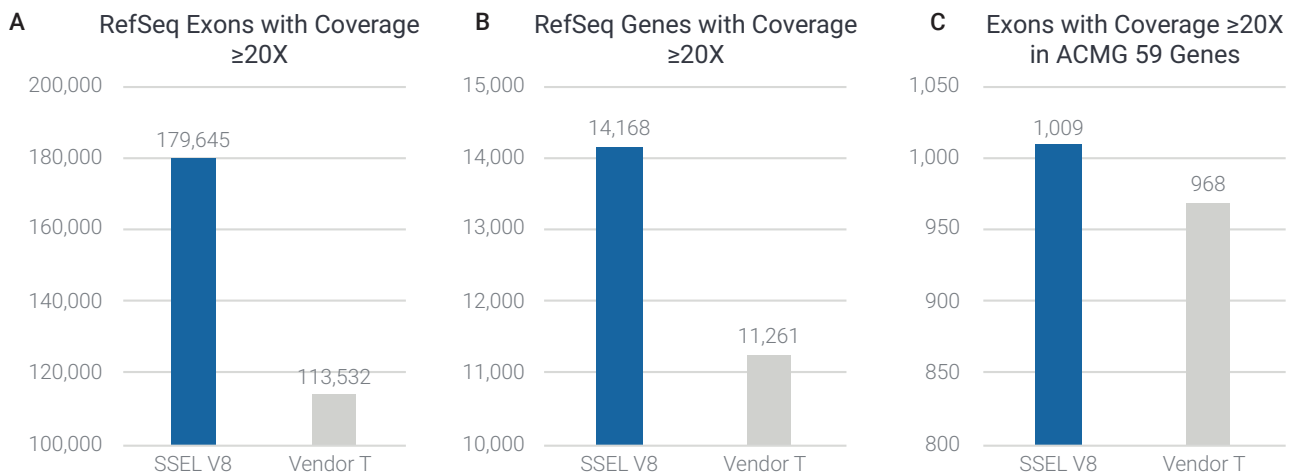in ACMG 59 Genes

Figure 5. The SureSelect Human All Exon V8 panel achieves better coverage of the exome. The SureSelect HumanAll Exon V8 panel provides 58% more RefSeq exons (A) and 26% more RefSeq genes (B) covered at a minimum depth of 20X. (C) In addition, within the clinically actionable ACMG 59 genes, the SureSelect Human All Exon V8 panel also provides more exons with a minimum depth of 20X. Exome-enriched libraries were generated from 8-plex captures following vendor protocols** and sequenced on an Illumina HiSeq 4000 instrument using 2x100bp reads. All samples were downsampled to 5 Gb for analysis.

More Complete Coverage of Genes Associated with Rare Diseases

A   Exons with Coverage ≥20X in Rare Disease Genes
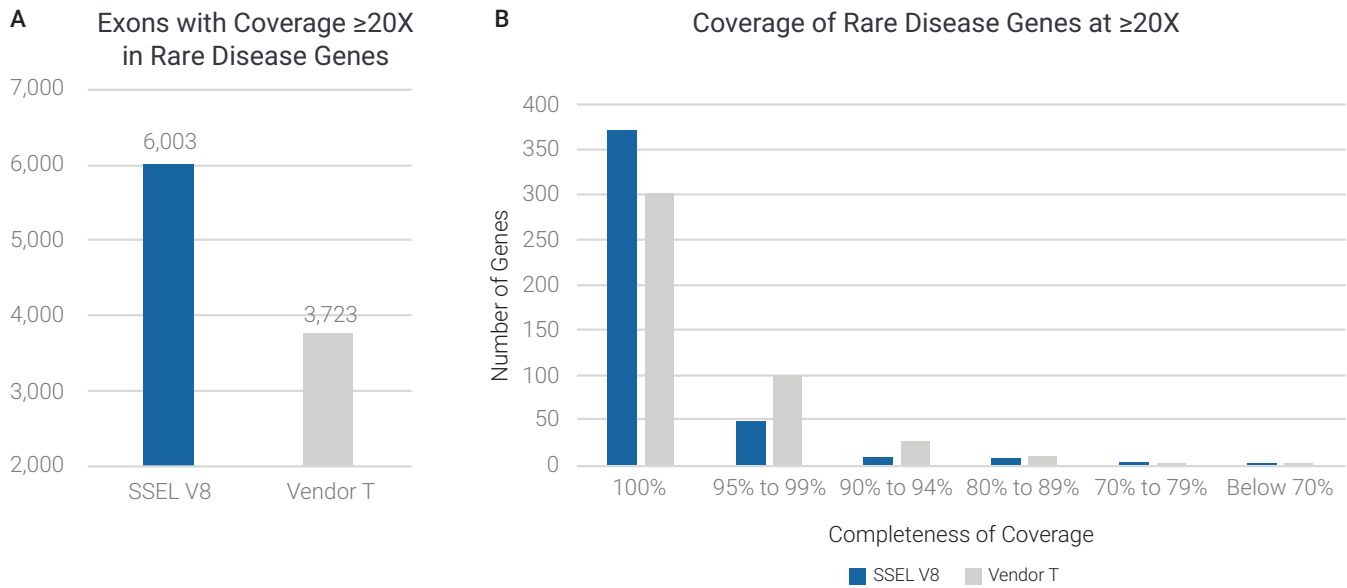
B   Coverage of Rare Disease Genes at ≥20X

Figure 6. The SureSelect Human All Exon V8 panel provides more complete coverage of genes associated with rare diseases to ensure better detection of disease-causing variants. The coverage of a panel of 438 genes responsible for 448 childhood recessive diseases[1] is analyzed at both the exon and gene level. A) The SureSelect Human All Exon V8 panel delivers superior coverage at the exon level across the 448 genes, providing 60% more exons that have a minimum coverage of 20X. B) The SureSelect Human All Exon V8 panel also provides 24% more genes that are completely covered, such that 100% of bases have a coverage greater than 20X. Exome-enriched libraries were generated from 8-plex captures following vendor protocols** and sequenced on an Illumina HiSeq 4000 instrument using 2x100bp reads. All samples were downsampled to 5 Gb for analysis.

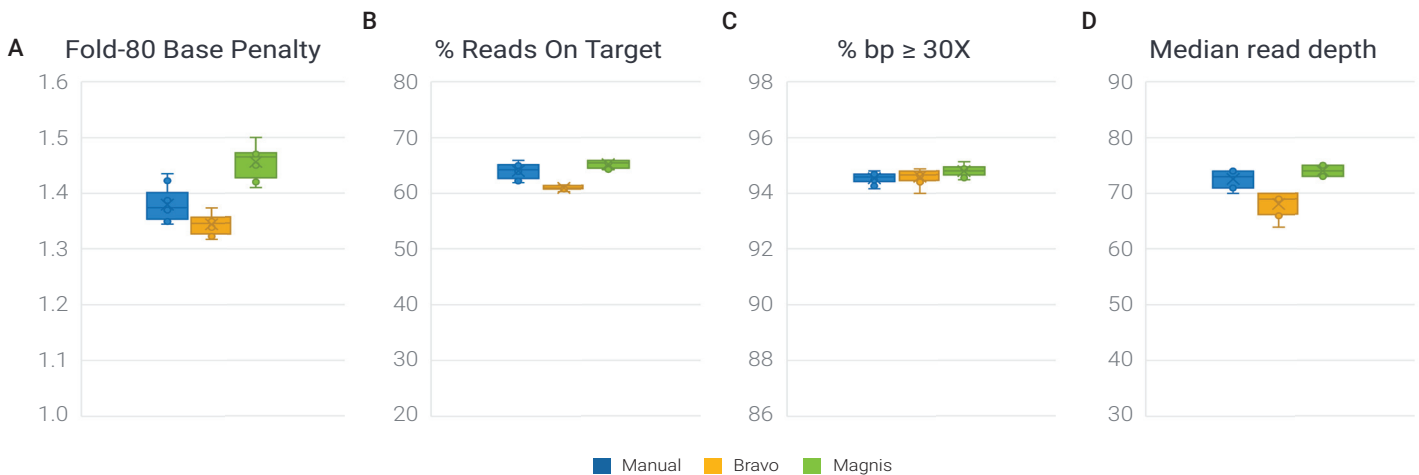# Consistent Performance Across Manual and Automated Workflows

A Fold-80 Base Penalty   **B** % Reads On Target   **C** % bp ≥ 30X   **D** Median read depth

Figure 7. SureSelect Human All Exon V8 provides consistent enrichment performance using both manual and automated library preparation. Both the Bravo automated liquid handling platform and the Magnis NGS Prep system generated libraries with reproducible and comparable performance as those prepared using a manual workflow by experienced operators. For all workflows, 200 ng of HapMap genomic DNA from the Coriell Institute (Camden, New Jersey) was Covaris-sheared and used as input material. For manual (4 operators, total of 10 samples) and Bravo (8 samples) workflows, libraries were constructed using the SureSelectXT Low Input Reagent kit and enriched as 1-plex captures using a 90 min hybridization. For the Magnis (4 runs, total of 10 samples) workflow, libraries were generated using the Agilent Magnis SureSelectXT HS Human All Exon V8. Rev B Kit, which is supplied as pre-aliquoted reagents in plates. Samples were sequenced on an Illumina HiSeq 2500 instrument (manual and Bravo) or HiSeq 4000 instrument (Magnis) using 2x100bp reads and downsampled to 50 million reads or 5 Gb of data for analysis.

Increased Productivity with Automated Library Preparation and Variant Assessment
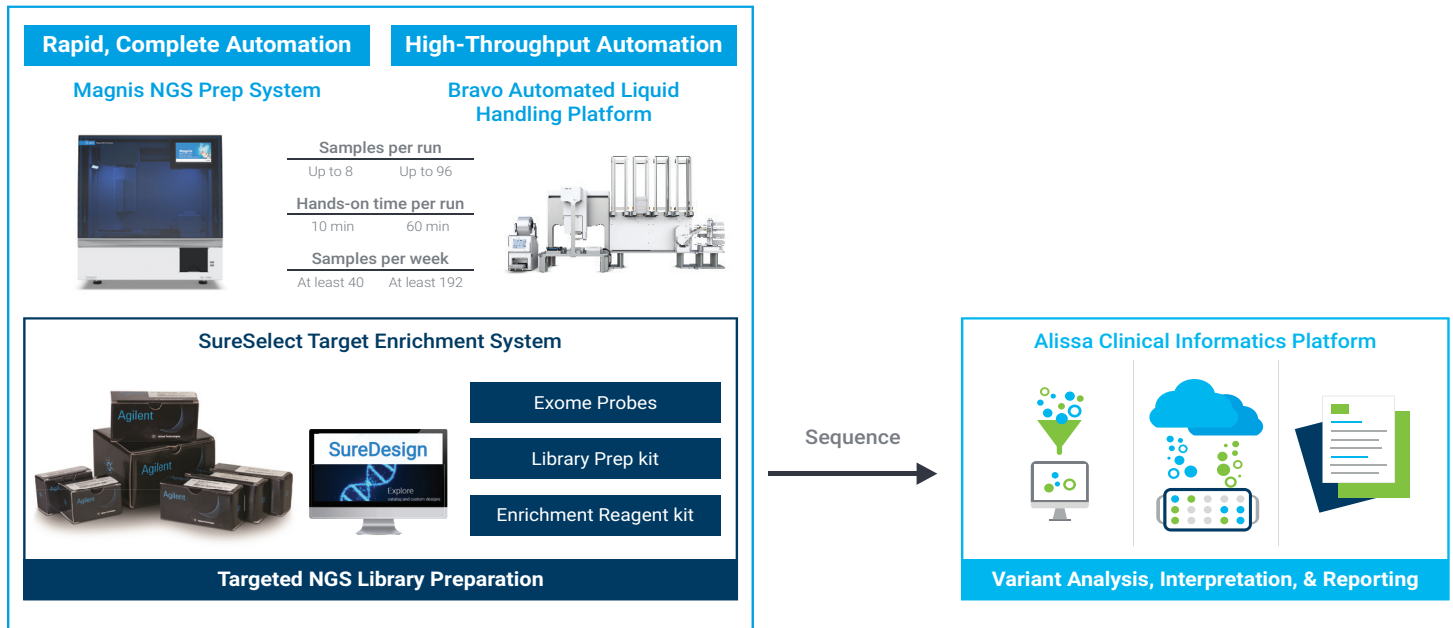

Figure 8. Agilent whole-exome sequencing solutions. The SureSelect Human All Exon V8 panel can be easily supplemented with additional targets required for exome sequencing using the Agilent SureDesign web-based application. The V8 exome panel can be paired with Bravo and Magnis automation and the Alissa Clinical Informatics platform to achieve greater operational efficiency. The exome is readily automated on the Bravo automated liquid handling platform for high-throughput applications, requiring only 60 min of hands-on time to process up to 96 samples. The Agilent Magnis SureSelect Human All Exon V8 kit is pre-aliquoted for use on the Magnis NGS Prep system. Only 10 minutes of hands-on time is needed to set up the instrument run and load reagents and consumables onto the instrument's deck. From there, the Magnis system delivers 8 exome-enriched libraries in less than 9 hours without further operator intervention. The Alissa Clinical Informatics platform allows clinical workflow to be automated from variant filtration and annotation, through curation and classification, enabling clinical genetics and molecular pathology labs to efficiently triage, curate, and report genomic variants.

* SureSelect Human All Exon V8 covers 100% of the protein coding sequences from CCDS release 22, GENCODE release 31, and RefSeq release 95, accessed in August 2019.

** For both vendors, the respective protocol was followed without modification using NA12878 genomic DNA from the Coriell Institute (Camden, New Jersey). The starting DNA amount was 200 ng for samples prepared with the SureSelect Human All Exon V8 and 50 ng for Vendor T, as specified in Vendor T's protocol. For samples prepared with the SureSelect Human All Exon V8, libraries were constructed from Covaris-sheared DNA using the SureSelectXT Low Input Reagent kit and enriched as 1-plex or 8-plex captures, using 90-min hybridization. For Vendor T, DNA was enzymatically fragmented and libraries were generated and captured in 8-plex, using overnight hybridization. All samples were sequenced on an Illumina HiSeq 4000 instrument using 2x100bp reads and downsampled to 50 million reads or 5 Gb of data. Analysis was carried out using vendor provided target BED files. Fold-80 base penalty was reported from analysis with Picard HsMetrics (Broad Institute). The percentage of on-target reads was calculated as the total number of reads with at least 50% overlap with any base of the target, divided by the number of uniquely mapped reads.

References

1. Kingsmore, S. Comprehensive Carrier Screening and Molecular Diagnostic Testing for Recessive Childhood Diseases. PLoS Curr. 2012, 4, e4f9877ab8ffa9.

Ordering Information

Compatible with Fast Hybridization

Product Description	16 Rxns	96 Rxns	96 Rxns Auto
SureSelect XT HS Human All Exon V8	5191-6873	5191-6874	5191-6875
SureSelect XT HS Human All Exon V8+UTR	5191-7401	5191-7402	5191-7403
SureSelect XT HS Human All Exon V8+NCV	5191-7407	5191-7408	5191-7409
Product Description	**2 Hybs**	**12 Hybs**	**12 Hybs Auto**
SureSelect XT HS PreCap Human All Exon V8	5191-6876	5191-6877	5191-6878
SureSelect XT HS PreCap Human All Exon V8+UTR	5191-7404	5191-7405	5191-7406
SureSelect XT HS PreCap Human All Exon V8+NCV	5191-7410	5191-7411	5191-7412

Compatible with Overnight Hybridization

Product Description	16 Rxns	96 Rxns	96 Rxns Auto
SureSelect XT Human All Exon V8	5191-6879	5191-6891	5191-6892
SureSelect XT Human All Exon V8+UTR		Contact Sales	
SureSelect XT Human All Exon V8+NCV		Contact Sales	
Product Description	**2 Hybs**	**12 Hybs**	**12 Hybs Auto**
SureSelect XT PreCap Human All Exon V8	5280-0032	5280-0033	5280-0034
SureSelect XT PreCap Human All Exon V8+UTR		Contact Sales	
SureSelect XT PreCap Human All Exon V8+NCV		Contact Sales	

Compatible with Magnis NGS Prep System

Product Description	32 Rxns	96 Rxns
Magnis SSEL XT HS Human All Exon V8, Rev B	G9772C	G9772D
Magnis SSEL XT HS2 Human All Exon V8, Rev B	G9774A	G9774B
Magnis SSEL XT HS2 Human All Exon V8+UTR	G9779A	G9779B
Magnis SSEL XT HS2 Human All Exon V8+NCV	G9778A	G9778B

Other Configurations

Product Description	
SureSelect Human All Exon V8+Pan-Cancer	Contact Sales
SureSelect Human All Exon V8+Mitochondrial Genome	Contact Sales
SureSelect Human All Exon V8+OneSeq CNV Backbone	Contact Sales

Automation and Software

Product Description	
Magnis NGS Prep System	Contact Sales
Bravo NGS (Option A)	Contact Sales
Bravo NGS Workstation (Option B)	Contact Sales
Alissa Reporter	Contact Sales
Alissa Interpret	Contact Sales

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