Data Sheet
Genomics

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Trusted Answers

Exome Enrichment using Agilent SureSelect Human All Exon V8 Panel and Agilent Alissa Clinical Informatics Platform

Key benefits of the Agilent integrated whole exome sequencing solution

- Powerful enrichment performance with SureSelect Exome Enrichment for efficient sequencing and confident results
- SureSelect Human All Exon V8 panel provides excellent uniformity of coverage for exon-level CNV detection without the need for reference samples
- Advanced variant classification and prioritization with Alissa Interpret for rapid interpretation and reporting

Agilent Integrated Whole Exome Sequencing Solutions

Many genetics laboratories have adopted exome sequencing as a first-tier response for individuals with suspected rare and inherited diseases. While identifying single nucleotide variants (SNVs) and small insertions/deletions (indels) from NGS data has become routine and well established, it is still quite a challenge to accurately detect germline copy-number variations (CNVs) from exome sequencing data as compared to the more conventional methodologies for CNV detection, including comparative genome hybridization (CGH) arrays.

Agilent now provides a whole exome sequencing solution for genetics labs that includes exome enrichment reagents and software for variant analysis and interpretation. This sequencing solution enables simultaneous detection of SNVs, indels, and CNVs, down to exonic resolution, and delivers a streamlined workflow with increased sensitivity to detect disease-causing mutations.

The SureSelect Human All Exon V8 panel provides comprehensive coverage of protein coding regions from RefSeq, CCDS, and GENCODE, as well as the TERT promoter region. The exome panel, powered by machine learning-based probe design and a new production process, delivers excellent enrichment performance, as well as efficient and cost-effective exome sequencing. It is also natively automated on the Agilent Magnis NGS Prep system and Bravo NGS workstation.

Users can readily examine sequencing data using the Agilent Alissa Clinical Informatics platform, an end-to-end exome sequencing solution for seamless and efficient variant analysis, interpretation, and reporting. Raw data can be analyzed with the Agilent Alissa Reporter software, an intuitive and streamlined cloud-based NGS software-as-a-service (SaaS) solution that simultaneously detects SNVs/indels and CNVs. Users can easily navigate data with integrated genome browsing, a built-in QC dashboard, and a seamless connection to the Agilent Alissa Interpret software for variant interpretation and reporting.

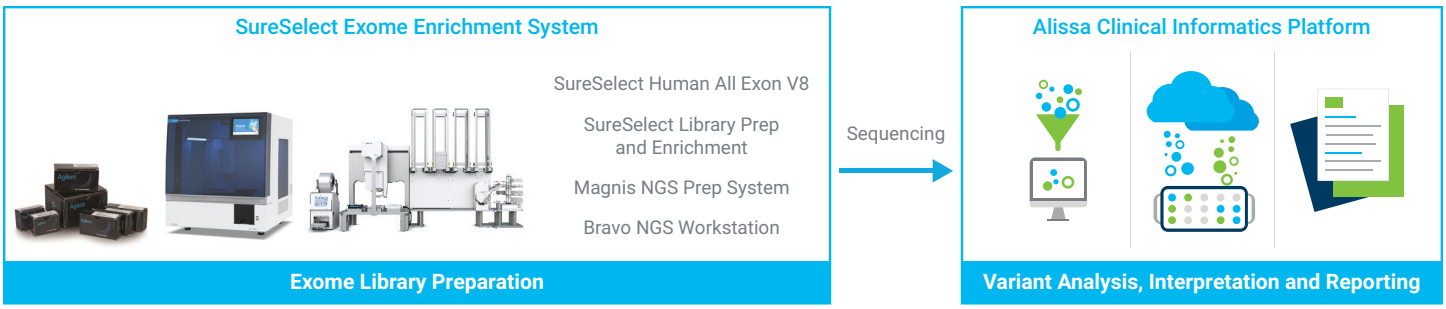

Figure 1. Agilent whole-exome sequencing solutions. The SureSelect Human All Exon V8 panel can be paired with Bravo NGS workstation and Magnis NGS Prep system automation and the Alissa Clinical Informatics platform to achieve operations efficiency. The exome is readily automated on the Bravo NGS workstation for high-throughput applications. The Magnis SureSelect Human All Exon V8 kit is pre-aliquoted for use on the Magnis NGS Prep system, which requires only 10 minutes of initial setup time and delivers eight exome-enriched libraries in less than nine hours without further operator intervention. The Alissa Clinical Informatics platform allows clinical workflow to be streamlined from variant analysis to variant annotation, enabling genetics and molecular medicine labs to efficiently triage, curate, and report genomic variants.

Alissa Reporter: High-Performance Variant Detection

From a single genomic sample, researchers, can generate more valuable information than ever before. With Alissa Reporter's secondary analysis capabilities, you can detect single-nucleotide variants (SNVs), insertions and deletions (indels), and copy number variants (CNVs). As a fully transparent solution, Alissa Reporter includes confidence scores next to CNV calls.

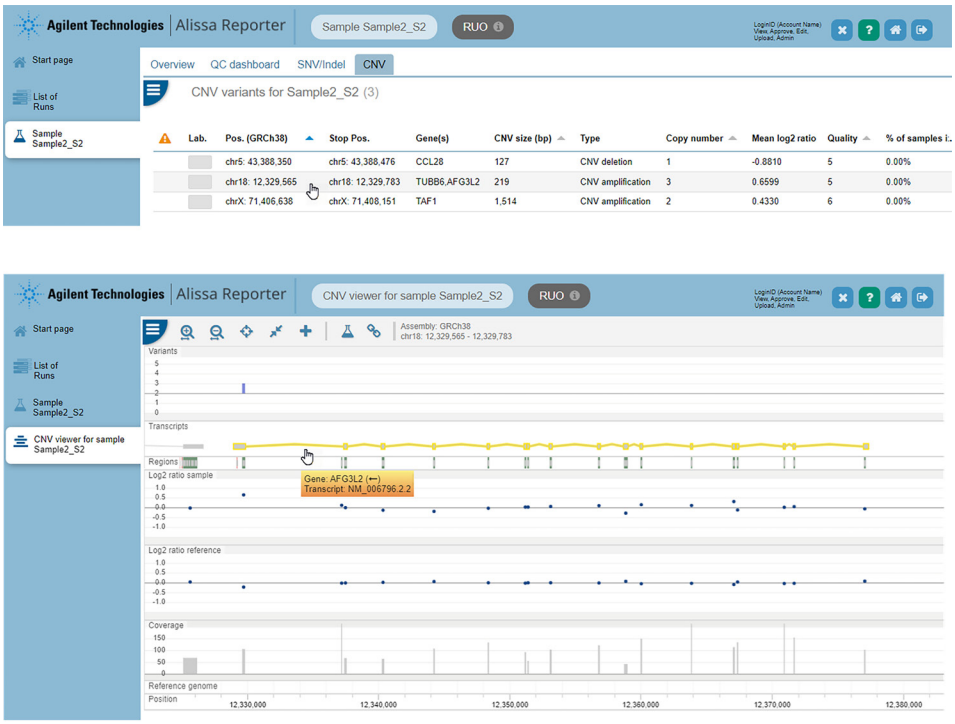

Figure 2. Alissa Reporter detects SNPs, indels, and CNVs from exome sequencing. The Alissa Reporter CNV detection module detects both CNV amplifications and deletions, down to the exon level. CNVs are visualized in a sortable and filterable table. A link to the detailed view is available from within the overview table, in which CNVs can visually be inspected using an integrated genome browser ("*CNV viewer*"). A single-exone CNV amplification in gene AFG3L2 is shown.

Built-In QC Dashboard for Operational Excellence

Alissa Reporter helps users quickly verify that an NGS assay is performing as planned. With the built-in QC dashboard, users can immediately assess whether key quality control metrics of individual samples (or the entire run) are within the anticipated range. Alissa Reporter flags problematic samples and shows users where the QC metric has deviated from recommended values.

Alissa Reporter can track and display QC metrics longitudinally. By analyzing quality control data across runs, users can easily spot trends and deviations from expected performance parameters over time.

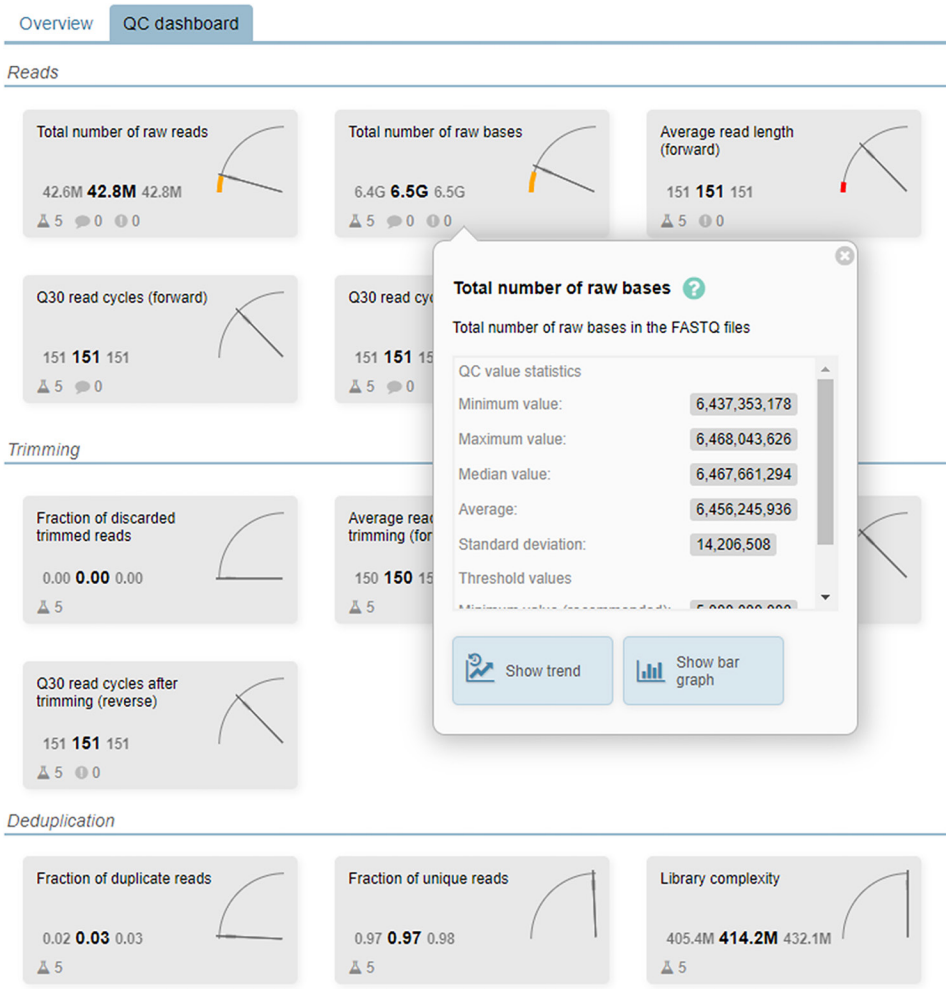

Figure 3. Alissa Reporter's QC dashboard helps you quickly find the metrics that matter most.

Virtual Gene and/or Regions Panels

If users are only interested in analyzing a subset of genes or regions, Alissa Reporter's in silico filter enables the creation of virtual gene panels.

Create targeted gene panels in advance based on your subpanels of interest or edit your selected panel on the fly. It is easy to manage in silico filters with Alissa Reporter's intuitive filtering functions. Simply select or upload the gene(s) and/or region(s) to be included, and Alissa Reporter will automatically filter the dataset based on this selection.

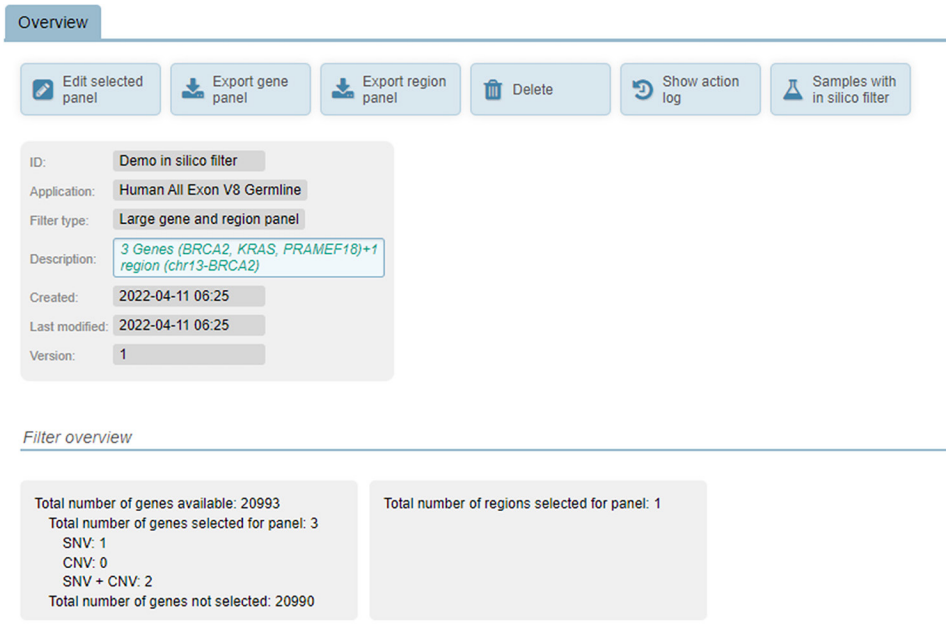

Figure 4. Use the virtual gene panel option and filter based on your genes and/or regions of interest.

Alissa Interpret, A Genomic Data Interpretation and Reporting Solution

Alissa Interpret enables clinical genetics labs to efficiently triage, curate and report genomic variants. Alissa Interpret combines SNPs, indels, CNVs and translocations in a single integrated workflow and can help you reduce turnaround time and increase diagnostic yield through:

Advanced decision tree-based filtration system

Automate your lab's variant assessment workflow in configurable, versioned pipelines. Slice and dice to quickly drill down to your variants of interest for further manual review. Store and version your pipelines to support increasing volumes and scale your sample throughput with ease (Figure 5).

Phenotype-driven variant prioritization

Alissa Interpret provides a variant prioritization feature using patient phenotypical traits, phenotype-genotype association data and other variant annotations to propose a set of potentially relevant variants to the user, ranked by estimated relevance for the analysis at hand.

Direct access to up-to-date clinical findings

Collaboratively curate your internal knowledge base while also tapping into an expansive array of public databases, including variant adaptations and effect annotations, frequency databases, clinically relevant peer reviewed findings, and classification according to ACMG guidelines (Figure 6 and 7).

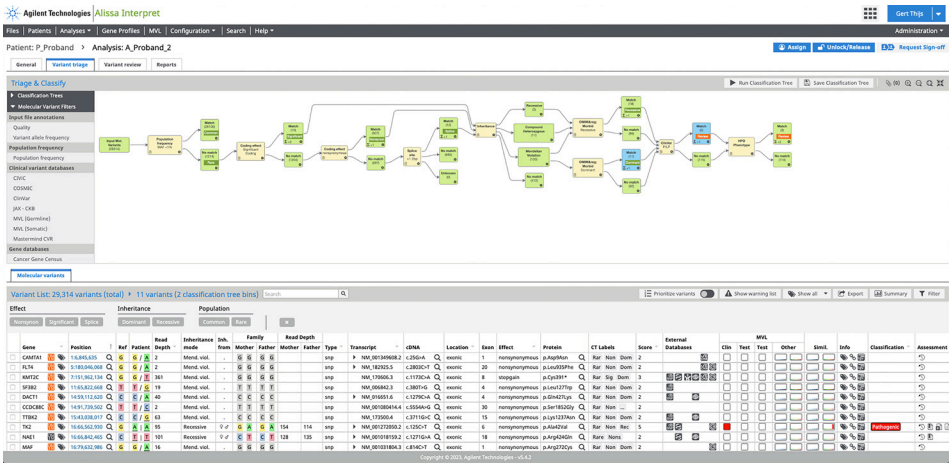

Figure 5. Flexible classification trees for rapid, transparent variant filtration.

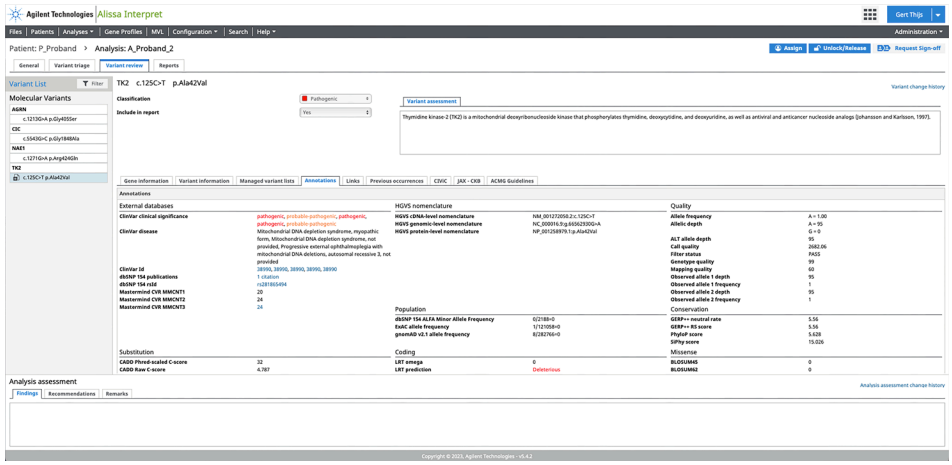

Figure 6. Integrates with industry standard and best-in-class annotation sources for inherited disease. Provides access to frequently updated annotation sources, including expert-curated databases and builds the lab's internal knowledge base.

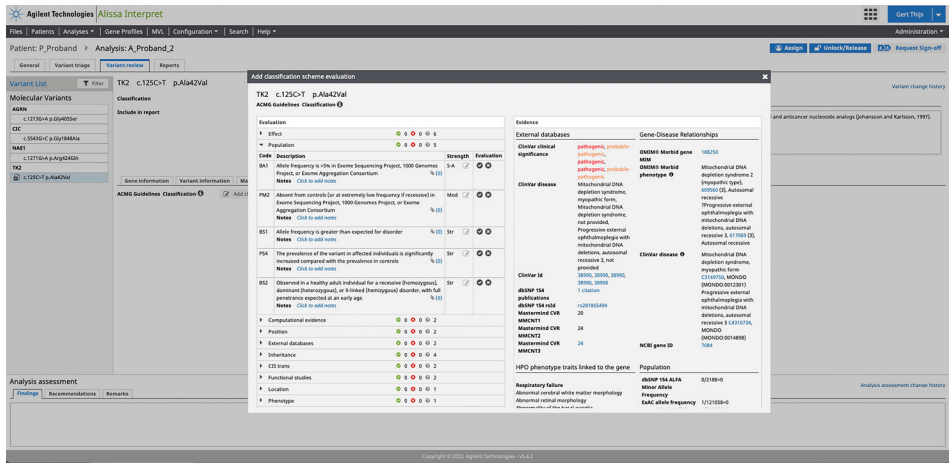

Figure 7. Variant curation using the ACMG guidelines made easy, with all relevant evidence at your fingertips. In this example the '*Evidence*' section includes the relevant computation evidence for the detected TK2 gene mutation.

An End-to-End Automated NGS Software Workflow

Alissa Reporter turns raw NGS FASTQ files into variant call format (VCF) files for key files for Agilent SureSelect Human All Exon V7 and V8 germline and for custom germline applications. As part of the Agilent Clinical Informatics platform, Alissa Reporter seamlessly transfers data to the Alissa Interpret tertiary analysis solution for a fully integrated end-to-end NGS software workflow.

After the variant of interest has been identified in Alissa Interpret, users can easily link back to Alissa Reporter to visualize read pileups in Alissa Reporter's highly responsive, integrated genome browser.

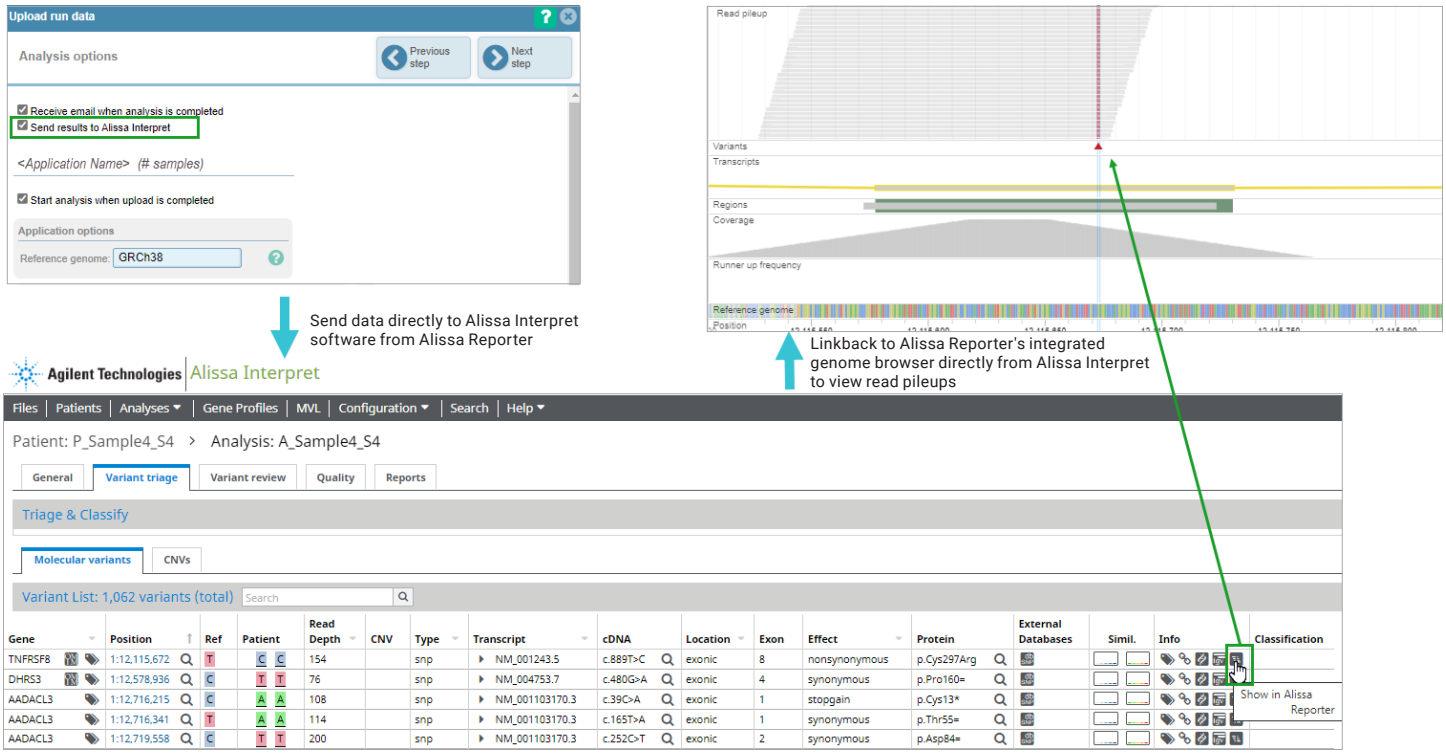

Figure 8. Fully optimized and integrated software solution. Users can send data directly from Alissa Reporter to Alissa Interpret for a streamlined NGS data analysis experience. Data is linked back to Alissa Reporter, allowing users to view read pileups for the variant of interest.

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Published in the USA, May 15, 2023
5994-4249EN

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