Illumina TruSight™ Software Suite Release Notes

v.2.0.0

November 2020

Introduction

TruSight™ Software Suite (TSS) is designed for translating genomic sequencing data in meaningful, interpretable results in rare disease cases. Highlights include:

Comprehensive, ultra-rapid variant calling

Use DRAGEN™ secondary analysis to call small variants, structural variants, mitochondrial variants, repeat expansions, runs of homozygosity, and SMN1/SMN2 variants.

Simplified, customizable case management

Manage cases from sample acquisition to report, assign cases to users, configure pipeline settings, and set quality control (QC) thresholds.

Intuitive, high-powered interpretation and reporting

Filter variants via gene lists, inheritance modes, custom annotations, and complex logic; flag, sort, and prioritize important variants; use customizable reporting templates.

Secure, compliant environment

TruSight Software Suite has been independently audited and certified for HIPAA compliance, ISO27001, and ISO13485. It is built to enable data privacy and compliance with the principles of GDPR.

These Release Notes detail the key features and changes to software components for the release of TruSight Software Suite v.2.0.0 For information on how to use the system, see the TruSight Software Suite Online Help. TruSight Software Suite is a comprehensive solution for alignment, variant calling, variant annotation, filtering, interpretation, curation, and reporting, including features such as:

- Automatic secondary analysis with DRAGEN™ and annotation of:
  - Small Variants, CNVs, SVs, Mitochondrial variants, ROH, STRs, SMA
- Support for whole genome and whole exome sequencing
- Sequencer and BaseSpace Sequence Hub Integration
- Case Dashboard and Test Management
- IGV Visualization
- Complex custom filters
- Custom flagging of variants
- Custom annotation
- SpliceAI & PrimateAI
- AI-based variant prioritization via Emedgene
- Gene lists from phenotypes
- Storage of variant curation
- Visualization of aggregate data for genes or variants

- Customized report generation
- Audit logging
- Command-line interface for uploading FASTQs
- API documentation

Release v.2.0.0 Highlights

- Exome (WES) support: ability to upload, analyze and report on exome data, in addition to whole genome data. Supports custom BED file upload, custom QC metric reporting, secondary analysis pipeline optimized for WES, and WES interpretation and reporting
- Sequencer Integration: seamless integration with sequencing instruments via BaseSpace Sequencer Hub for automating WGS and WES analysis. Enables rare disease workflow via an integrated, sample-to-report WGS solution, including Illumina DNA PCR-Free Prep, Tagmentation, the NovaSeq 6000 System, and TruSight Software Suite
- Emedgene Integration: a genomics artificial intelligence (AI) engine, powered by Emedgene, to rank variants and highlight the most-likely candidates. The engine generates a knowledge-graph showing supporting evidence for the variant prioritization, e.g., disease–gene relationships, generated by evaluating phenotypes, inheritance modes, splicing predictions, conservation, etc., and by the application of natural language processing (NLP) to various data sources

NEW FEATURES IN DETAIL

- System Level
    - Exome (WES) support: BED file upload, WES secondary analysis pipelines and WES reporting; maintains support for whole genome (WGS)
    - Sequencer Integration: seamless integration with sequencing instruments via BaseSpace Sequencer Hub for automating WGS and WES analysis
    - Link out to Support Page from TSS

- Test Management
    - Ability to export and import Test Definitions across workgroups and domains; supports creation of Test Definitions in one version and export to a new version
    - Allow text of the footer to be updated within the report template
    - Enable additional report summary sections for customized reporting
    - Support for multiple analysis pipeline versions (DRAGEN 3.5.7b, 3.7.5)

- Case Management
    - Ability to create additional Sample fields
        - Sample Name
        - Order Number (50 characters)
        - gDNA option to available Sample Types
    - Additional Subject Fields when creating a case
        - Define 'Other' as a relationship to the Proband
        - Expose External Subject ID
    - Ability to enter Additional Instructions for the Lab for the case
    - Ability to Filter on Case Sub-Status
    - Allow user to enter custom phenotypic information outside Ontology service
    - Display user who created the case in the Case List page
    - Ability to upload FASTQ files for sample ID prior to sample ID association to case.

- IGV
    - Update to IGV version 2.6.5
    - Updated IGV track names for better comprehension, toggle track selection by subject.
    - Sharing variant comment box in IGV
    - Support small variant VCF in custom IGV annotation track
    - Track item coloring by variant type and consequence.
    - Addition of aggregated population data tracks from 1K genomes samples for CNVs and SVs.

- Variant Grid / Filters
    - Emedgene integration: AI-based variant prioritization. Variants tagged as "candidate" or "most-likely" in new variant grid column
    - Update default transcript logic to display gene with greatest phenotypic overlap
    - Improve modes of inheritance tags to display those that are beneficial to the user
    - Support exclusion logic for gene and transcript filters
        - Allow gene criteria to be added as part of the OR clauses
    - Retain tab sort order within given filter view
    - Allow user to maximize/minimize the filter grid headers to view more variants

  - Improved column usability –move columns dynamically and pin them
  - Custom Annotation updates
    - User can annotate small variants by position or allelic matches
    - User can specify multiple columns with labels and allow filtering for them
    - User can specify whether annotation label should match using reciprocal overlap (best for similarity of two events are to be compared) or annotation overlap (best for qualitative properties for a given region)
  - Improve Variant Length Filter
    - Enable configuring units (bp, kbp, Mbp) when filtering by length
    - Update the grid to specify 'BP' as units for the Length Column and add commas for readability

- Variant Details
  - Support 0bp insertion match for large variants
  - Support dynamic aggregate plots for mitochondrial variants
  - Provide annotated data – such as percentile data for each sample – for mitochondrial variants
  - Default transcript logic now selects the gene with the greatest phenotypic overlap
  - Allow user to copy a list of genes when two or more genes are affiliated with the variant
  - Ability to update ACMG Criteria and Evidences in Variant Detail
  - Daily updates of literature search capability for up-to-date publications
  - Ability to copy OMIM description into Gene Information
  - Auto-import OMIM Related Diseases information when creating a gene-level association

- Knowledge Network
  - Group variants under curation level (Position, Gene)
  - Support search for Gene, Chromosomal position (with or without overlap threshold), HGVS annotation, Cytoband, Variant Type, Disease, Mode of Inheritance and Classification
  - Hide non-Mendelian association types that are not currently supported
  - Show additional columns in the variant landing page
  - Support size and updated date sorting in the variant landing page
  - Support bulk download variants in ClinVar submission ready format

  - Support ClinVar Accession number update
  - Bulk upload improvement to support STR and adding evidences to gene information
  - Save chromosomal start and stop in addition to position for small variants to improve search accuracy
  - Save cytoband information for all variants
  - Route to original page after timeout/forced log out

- Annotation
  - Support for gnomAD 3.0 INDELs

- CaseLog
  - Supports case deletion via API

- Release versions
  - TruSight Software Suite v.2.0.0 runs multiple DRAGEN versions for secondary analysis:
    - Whole genome v.3.5.7b
    - Whole genome v.3.7.5
    - Whole exome v.3.7.5
  - TSS v.2.0.0 uses Nirvana v.3.12 for annotation
  - TSS v.2.0.0 uses KNS-API v.0.12.0 and KNS-UI v.0.2.0- for curation

RESOLVED ISSUES

Defect repairs (bug fixes) from v1.5.1 release:

- (AUS instance only) When creating a virtual variant in the IGV view and then clicking back to the Interpretation page, the user is stuck in the processing page.
- When filtering with OMIM, gnomAD and ClinGen filters, the "exclude consequences" filter does not return correct results.
- Whitespaces are not allowed when filtering tabs.
- In a Test with multiple customer annotation files, user is unable to see the row names in the 'All Population' modal.
- For ROH variants, the partial overlap symbol does not work correctly, and is applied to all ROH variants regardless of overlap.
- In certain SVs, false positive de novo calls are seen. This issue has been fixed in a subsequent DRAGEN release.
- If a variant spans >2400 genes, the transcript tab fails to upload correctly.
- When adding InDels to a report, the variant ID may get cutoff in the report modal instead of wrapping around.
- Confusing error message when editing a variant association that has a draft variant association present
- When a user with API Access role accesses interpretation page directly, user is redirected to a broken page.
- While working in the literature search section, idle timeout may occur.
- When removing a variant from a report and then re-adding it back into the report, an error message is seen.
- If a gene list name contains (_) underscore in it, the gene list autocomplete is unable to find it. Workaround is to create gene lists without (_).
- Selecting a gene list in test management will close the entire Gene List modal, not just the gene list dropdown menu.
- In locked filter tabs, number of genes selected for filtering can exceed 7500.
- Gene list dropdown does not appear until user clicks out and back in after first selection.
- Long variant notes will not be fully displayed in IGV when editing.

KNOWN ISSUES

- Annotation will fail if custom annotation files contain duplicate keys/labels. Workaround is to name each custom annotation file with a unique name.
- For cases added to CaseLog, variants in some samples are missing.

- In IGV, the RefSeq gene track has ENSEMBL annotations
- In exome samples, sex ploidy check has been removed since it was incorrect.
- For variants with result "no interpretation for the single variant" from ClinVar, Emedgene calculation cannot be run and the case will not be processed. Workaround is to run this case without Emedgene functionality with tech support.
- The User needs to provide Address and Recipient information while creating the Client though the UI shows the fields as not required.
- In variants that overlap 2 or more genes, Ontology terms are not seen in the Overlap modal for some variants.
- Associations created for STR variants are only perfectly matched, so STRs at the same position but a different length will not show as a variant association match.

Open known issues from previous releases can be found in TruSight Software Suite Release Notes v.1.5.1:

https://support.illumina.com/content/dam/illumina-support/documents/documentation/software_documentation/trusight/trusight-software-suite/trusight-software-suite-v1.5.1-release-notes-1000000132277-00.pdf