BaseSpace Variant Interpreter Release Notes

BaseSpace Variant Interpreter v.2.0 (1.0.19963)

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BaseSpace Variant Interpreter Software Release Notes
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v.2.0.0 (VI:1.0.109963, KN:0.11.15)
Release Date: August 2017
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INTRODUCTION

These Release Notes detail new features, known issues, and recently resolved issues for the BaseSpace Variant Interpreter software. For details on how to operate BaseSpace Variant Interpreter software, see the online help, which is available from the Help icon in the application.

For a full list of features in BaseSpace Variant Interpreter v2.0, see the Features List on page 7.

NEW FEATURES

Include Curations in Report

During Variant Interpretation for a case, users can now include SNV/InDel variant curations from the KnowledgeBase in the Report. When the Add to Interpretation checkbox for the curation is selected, the curation appears in the Included Curations section of the interpretation dialog for the corresponding variant being interpreted. These curations are included in the draft report as a summary table and in the PDF report under details of the specific variant being reported. Specific fields included from the curation include curation summaries and associated evidences for the curation.

Removing included curations can be done in any of the following ways:
- Uncheck the Add to Interpretation checkbox under the relevant curation
- Remove the curation from the Included Curations section on the interpretation dialog
- Removing the curation from the draft report Included Curations section

When a curation is included with a variant, the version number of the curation is stored in the system and is the same version that is migrated to the reports. If a new curation is available for a variant, remove the existing included curation and reimport the latest version.

Report Changes

The report format has been updated to take into account new features that permit the association and inclusion of curations from the KnowledgeBase to the report.

- **Draft Report**—Every reported variant now has an expandable section that contains a free text area to record variant comments and a section to display summary information for included curations. In addition, a new tab called Case Summary is provided on the draft report to include any general comments about the case.

- **PDF Report**—The PDF report has been reorganized to make it easier to find important information on the first page of the report. All reported variants are now listed first, separated by pathogenicity (for RUGD) or Association (Oncology). The next section displays any user-provided comments about the case. The subsequent pages of the report are split by variant category; each variant reported within the category includes variant comments (user-provided), curation summary, and details from each included curation associated with the variant in the report.

Phenotype deposition by identifiers

You can now also upload phenotypes using identifiers.
- **Manifest File**—You can provide phenotypes for a case via a manifest file upload. Provide comma-separated phenotypes under the relevant column in the manifest file using HPO (HP:0001258 for example) and SNOMED (numeric) Identifiers. Phenotype fields are validated after upload; successful entries are loaded for the relevant case as associated phenotypes.

- **User Interface**—You can provide phenotypes using HPO or SNOMED ontology identifiers (HP:NNNNNNN for HPO and NNNNNNNN for SNOMED). from the subject page for a case. Phenotype fields are validated on entry; successful entries are loaded as phenotypes associated with the case.

The maximum number of phenotypes that can be associated with a case, regardless of the method of phenotype entry, is 25.

Family-based QC Metrics

You can now view QC metrics for variant calls in related individuals. A pop-up in the metrics column displays variant call metrics information for any related individual in which that variant was called.

Association Column Redesign

The association content display has been redesigned to display content grouped by source.
- **Cases**—Content from interpretations made on other cases
- **MyKB**—Content within a private KnowledgeBase
- **BSKN**—Content from shared workgroups (if workgroup sharing is enabled) and public sources.

In Germline cases, association counts are grouped by pathogenicity. For Tumor cases, presence of associations is grouped by type (Predictive, Prognostic, Molecular Classification, and Clinical Trials). Predictive associations include a classification of On-Tumor or Off-Tumor, indicating the presence of any association matching the tumor type of the case. For small variants, associations are only shown for variants with at least one canonical transcript

Variant Grid Export

The variant grid export function now includes alt allele depth, total read depth, variant read frequency, paired read support, and split read support for SNV/Indel or SV variants.

Knowledge Network - Curation Portal

Bulk actions are now available for associations within a private workgroup for which the user has proper permission. All selected associations can be approved or rejected.
- Approved associations (for new or draft associations in progress) are enabled and added to a case report
- Rejected associations (either in progress or enabled) are disabled

Gene-level curation is provided for a specified transcript at a genomic coordinate that is mapped to a gene. When no gene is mapped, the transcript filtering is not utilized and all genes are returned.

Knowledge Network – Public Content

Two new workgroups are available in curation portal for the public BaseSpace Knowledge Network.
- **BSKN Illumina Curated Content**—Contains manually curated content from Illumina
- **BSKN Illumina NLP Content**—Contains associations that were identified using natural language processing

Track-Level Genome Browser

TLGB now supports visualization of Tumor-Normal cases and Germline cases with related individuals. If users have existing Tumor-Normal cases, the existing case will need to be deleted and users will need to re-import the data from BaseSpace Sequence Hub.

RESOLVED ISSUES

Issue Key	Issue Category	Description
BSKN-3475	Associations	Importing associations from BSKN for retired ontology terms require users to select a current ontology term
BSVI-25693	Case Management	Users are unable to add a sibling where the sex of the sibling is set to unknown.
BSVI-25720	Case Registry	Checkbox selections do not clear when switching workgroups. When using bulk actions after a workgroup change, refresh the page before selecting new cases.
BSVI-22349	Case Registry	Some failed VCF uploads require reanalysis or reupload. Contact support if reuploading the VCF files is not successful.
BSVI-16048	Import	Uploading of multiple GRCh38 .vcf files occasionally results in an error. The error can be cleared by deleting the failed upload and retrying.
BSVI-23521	Variant Grid	If family members are removed from an original pedigree, the mode of inheritance calculation is occasionally inaccurate. Contact support if you encounter this or a similar issue.
BSVI-25609	Visualization	Visualization The karyotype for some chromosomes fails to render on GRCh38 samples on the track level genome browser.
BSVI-25613	Visualization	The track level genome browser fails to load BAMs for samples generated from the Tumor-Normal workflow.
BSVI-25249	Visualization	Some read pop-up content does not correspond to details for the selected read in the track level genome browser.
BSVI-26324	Workgroups	New users to Variant Interpreter cannot access the Workgroups Administration Console unless they are added to an existing workgroup.

FEATURE REQUEST UPDATES & ISSUE CLARIFICATIONS

Issue Key	Issue Category	Description
BSVI-24043	Case Management	Users can edit case status and owner via the status dropdown. However, data processing statuses (Action Required, Failed, etc.) are still be displayed on the Case Registry page. See help for more information.
ON-636	Gene Lookup	API should give back an appropriate error message when a given parameter value does not exist. This issue does not affect the end user of the software
ON-639	Gene Lookup	Gene autocomplete API: inconsistent sorting behavior for returned lists of matching genes. For the user, ordering of terms is not sorted, but does not impact results

Issue Key	Issue Category	Description
BSVI-12422	Import	If a user tries to upload a VCF file that is not properly formatted, the upload fails with an ambiguous error message. The file shows a status of fail, and the user can then delete it. Consequently, the variant grid does not appear. Note: If you experience a failed upload and reuploading the data does not resolve the issue, contact support
ON-345	Variant Grid	Autocomplete box shows results marked as 'obsolete' by nomenclature authority. This functionality is intended, Variant Interpreter does not support obsolete/legacy ontology terms.
ON-432	Variant Grid	Expansion to related phenotypes sometimes yields results that are too distant. When performing phenotype search, Variant Interpreter uses fuzzy matching, thus providing potentially related genes. This functionality does not omit any genes but does return additional genes.
ON-516	Variant Grid	Results in autocomplete pop-up might be sorted inconveniently (subjective). Contact support to give feedback if you would like this improved.
BSVI-21855	Variant Grid	VCF name truncation to analysis result name may not match expectation (subjective). For best results, maintain unique Analysis Result names in Variant Interpreter by keeping VCF file names unique up to the first period in the file. Contact support to give feedback if you would like this improved.
BSVI-24136	Visualization	The mutational signature plot is optimized for WGS, however a plot is not generated for any case with fewer than 200 SNVs. This functionality is intended, Variant Interpreter requires a minimum number of single nucleotide variants to generate a mutational signatures plot. Help documentation has been updated to reflect this.
BSVI-24137	Visualization	The dynamic visualization is located separate from the visualization panel, which can be misleading to users. This functionality is intended, static visualizations and dynamic visualizations are currently separate components within Variant Interpreter. Help documentation has been updated to reflect this.
WAC-767	Workgroups	Workgroup Administrators cannot revoke a pending invitation, however Workgroup Administrators can still remove members from the workgroup. If you would like to revoke an invitation to a workgroup and the user has not yet registered for BaseSpace Variant Interpreter, contact support for assistance.

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Issue Key	Issue Category	Description
BSVI-24655	Zygosity	Zygosity text for variants on sex chromosomes does not account for pseudoautosomal regions. This functionality is intended, Variant Interpreter does not yet support PAR regions. Help documentation has been updated to reflect this.
BSVI-24656	Zygosity	Pedigree diagrams reflect familial inheritance only for PASS variants This functionality is intended, Variant Interpreter does not yet support display of non-PASS variants in the pedigree diagram. Help documentation has been updated to reflect this.

VARIANT INTERPRETER 2.0 FEATURES LIST

Variant Interpreter provides the following features to aid in Variant Interpretation for targeted, whole exome, and whole genome analysis.

Data Import and Case Setup

- Local VCF/gVCF upload:
    - Local individual import and metadata.
    - Batch upload.
    - Metadata sheet (eg manifest).
    - Annotations are applied to human genomes aligned to genome assemblies hg19, GRC37, hg38, and GRCh38. Variants identified on chromosome M for hg19 and hg38 are not supported and are not displayed.
- Direct VCF import from BaseSpace Sequence Hub projects. BAM files in BaseSpace Sequence Hub can be visualized in the Track-Level Genome Browser (IGV).

Case Management

- Case status management for lab managers and general users.
    - Assign owners
    - Update case status, close cases (generate PDF report), or reopen cases on the case page or in the Case Registry
- Bulk actions on multiple cases
    - Assign owners
    - Apply filters (applied to the first applicable tab in each case or to a new tab)
    - Reanalyze
    - Delete (Privileged Users only)

Case View

- Case Metadata allows input of details related to the analysis result, sample, and subject
- Case-level visualizations
    - Static Genome Plot
    - Static Mutational Signature
    - Dynamic Genome Plot
- Inspect reads supporting variant calls using IGV
- Variant Grid
    - Variant Annotation
        - Supports the annotation and display of SNV (including MNV), Indel, CNV, and SV variant types using multiple sources
        - External links to sources (eg OMIM)
        - Autoclassification of pathogenicity
    - Variant Association
        - Content grouped by source
        - Import, layer, and filter custom annotations

- Variant Filtering.
  - Apply filters specific to sample type (tumor analysis vs germline)
  - Filter variants by:
    - Genomic Regions or Gene
    - Variant Consequences
    - Associations and Population Frequency
    - Variant Caller QC Metrics
    - Family
      - Family pedigree
      - Inheritance mode filtering
    - Custom Annotations
  - Gene List Manager
- Bookmarking key variants of interest for later review and collaboration

BaseSpace Knowledge Network (Variant Curation Portal)

knowledgenetwork.kn.basespace.illumina.com/bskn

- Import Associations from Knowledge Network to a private database.
- Higher-Order Curation—BaseSpace Knowledge Network supports biomarkers at five curation levels
  - **Nucleotide** curation provides a specific alteration, which is frequently observed in the disease condition or mentioned in the evidence.

  - **Amino Acid** curation enables biomarker content at the protein level. These alterations, frequently referred to in publications and observed in disease conditions, can support a wide range of nucleotide changes.

  - **Codon** curation provides an opportunity to add content from public sources on cohort analysis, grouping clinical observations at a specific protein location.

  - **Exon** curation, in combination with mutation classes, provides robust content, which matches functional protein alterations.

  - **Gene** curation, in combination with mutation class to refine the association to match the evidence.

- Genome Equivalence
- Bulk actions can be performed for associations within a private workgroup (for limited user roles
- Links to PubMed and clinical trials (clinicaltrials.gov)
- You can complete the full workflow (add/edit/enable/disable) for external associations on the Association Summary page

Case-level Variant Classification & Interpretation

- Enhanced Interpretation
- Precisely select the appropriate transcript for a variant instead of the default canonical transcript
- Optional fields capture penetrance information, validation status, variant contribution in Germline cases, and association type in Oncology cases
- View Past Cases

Report Generation and Data Export

- Add comments to reports
- Create and modify report templates
- Export up to 1000 variants to a tab-separated value (TSV) file. This includes some details provided by the variant caller and annotation engine.

User Management, Auditing, and Security

- Workgroups
  - Workgroup administrators can modify access to BaseSpace Variant interpreter, BaseSpace Sequence Hub, and BaseSpace Knowledge Network all in one place
  - Workgroup administrators can be added without being granted permission to access data within the workgroup in Variant Interpreter
- Audit Log

  - Full audit log
  - Tracks access and changes to case data
  - Data also includes IP Address and Workgroup fields
  - Workgroup owners can export workgroup-level audit logs