BaseSpace Variant Interpreter Release Notes

BaseSpace Variant Interpreter v2.5.0

September 2018

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.

This release of BaseSpace Variant Interpreter can import single-sample (g)vcfs and analysis results from Whole Genome Sequencing v8. For a list of supported variant callers, see the online help.

NEW FEATURES

Data Import and Case Setup

- Improved warning messages for VCF parsing.
- Support for multitiered custom annotation.
- Support for hs37d5 as a synonym for GRCh37 in the reference line of VCFs.

Case Management

- Permissions
  - To maintain accountability, the ability to close and reopen cases is now restricted to privileged users.
  - Basic users are now able to create a report.

Case View

Gene List Management

- The number of genes supported in gene lists is increased to 5000.
- Gene lists are now sorted alphabetically in the filtering dialog and the settings page.
- Gene list creation now supports up to 50 phenotypes as inputs.
- Genomics England PanelApp is added to the gene list sources in the gene list manager.
- The PanelApp version is now displayed in the gene list manager.
- The gene list manager now provides a detailed view in addition to the default view.
- The number of genes in a gene list is displayed in the filtering dialog and the settings view.

Pedigree

- Zygosity and subject names within a pedigree are now included in the variant metrics display.
- Updated logic to derive total read depth and variant read frequency for associated family members when specific fields are missing from the VCF.

Filtering Enhancement

- New filters are added for the following:
  - Pathogenicity levels in MyKB and BSKN
  - Protein Altering consequence filter
  - MNVs by class
  - Structural Variants(SV) and Copy Number Variants (CNV) by length
  - Copy Number Variants by copy number
  - SV/CNVs by whether they have an OMIM gene
- MNV variants are now labeled on the variant grid.

- Redesigned filter pane supports complex filters.
- Complex filters can be chained together, saved. and applied individually or to multiple cases at one time.
- Filtering on exclusion criteria is now supported.

Reciprocal Overlap Improvements

- Reciprocal overlap threshold can be configured in the Settings menu.
- Only SV/CNV associations against DGV/1KG/BSKN with the minimum overlap are returned.
- Changing the threshold does not impact already ingested cases. Reimport or reanalyze cases to apply the threshold.
- Structural Variants in BSKN or MyKB are only displayed in the Associations grid if they achieve the minimum overlap.

Transcript Selection

- Transcripts for small variants can be selected on the variant grid, altering the transcript annotations shown on the variant grid.
- Transcript sources (Ensembl versus RefSeq) can be assigned by chromosome groups in the settings page.
- Per-gene preferred transcripts can be configured and applied across a workgroup.

External Links

- Links out to RefSeq or Ensembl are now annotation format-aware.

Select Multiple Associations for Reporting

- A variant can be linked to associations from multiple sources on the variant details page. Associations from the knowledge base can be included on a report and have many of the same properties as user provided associations.
- Only one association can be identified as primary, however multiple associations can be included in the final report in accordance with the laboratory protocol.

BaseSpace Knowledge Network (Variant Curation Portal)

Knowledge Network - Structural Variants (Position-level curation)

- Structural variants including tandem duplications, deletions, inversions, and insertions are now supported at the position level. These associations are genome build dependent.
- Cases with structural variants that meet a specific reciprocal overlap value are provided on the BSVI Variant Details page.
- Bulk upload and Variant Queue also support position-level structural variant associations.

Criteria Tag (ACMG) Calculator

- Criteria tags are available at the evidence level for all Mendelian associations. These tags can be added to either publication or miscellaneous evidence types.
- To support an ACMG criteria tag, new or edited evidence requires an updated support type (Pathogenic, Benign, or Not Selected).
- After a support type is selected, you can either directly select a criteria tag or include additional metadata that provides a criteria option.
- The ACMG calculator suggests a pathogenicity based on the evidence criteria tags supplied.

Case-level Variant Classification & Interpretation

Interpretation

- Associations for structural variants are now displayed.

RESOLVED ISSUES

Issue Key	Issue Category	Description
BSVI-35930	Ingestion	Infrequent, intermittent issue where some variants from an input .vcf file will not appear.
BSVI-32671	Curation	Codon-level curation cannot be added in VI.
BSVI-33413	Variant Details	Family member total read depth after family-based analysis (trio) is reported as -1
BSVI-32573	Filtering	OMIM filtering occasionally returns variants with no apparent OMIM gene.
BSVI-32600	Genome Browser	Reads with aberrant quality are marked by a colored frame that is incomplete when there is a gap in alignment.
BSVI-33578	Reporting	Basic user cannot create a draft report
BSKN-6173	Curation	The codon count is not updated when a codon-level curation is saved successfully.

KNOWN ISSUES

Issue Key	Issue Category	Description
BSVI-34480	Annotations	In rare circumstances in which Ensembl and RefSeq annotations differ significantly, variants may be incorrectly annotated as completely overlapping a gene
BSVI-30507	Audit Log	Date selection is not inclusive of the selected dates, which is unintuitive. Currently, to select a log for 01/15/2018, a user needs to select dates from 01/14/2018 to 01/16/2018.
BSVI-31340 **BSVI-26788**	Bulk Actions	Bulk actions drop-down does not display properly in Safari and IE11. Please use a different web browser.
BSVI-29665	Case Registry	If all cases are in "Action Required" status, pagination will not work. Please re-analyze one case to resolve.
BSVI-32574	Curation	New codon-level curations created in BaseSpace Knowledge Network do not show up in BSVI.
BSVI-36906	Filtering	When choosing ClinVar filters, user has the option to select both Position Specific and Allele Specific. Please only select one.
BSVI-36904	Filtering	Clearing a filter with variant length does not empty the value in the filters box on the right of the screen, however the filter is cleared and correctly applied. Returning to the variant grid will clear the box.

Issue Key	Issue Category	Description
BSVI-31659	Logging	Variant comments currently do not show up in the audit log.
BSVI-27730	Variant Details	Some variants that do not overlap known genes are nonetheless associated with gene associations.
BSVI-27938	Variant Details	In Germline cases, past cases do not show up if the variant is not mapped to a known gene.
BSVI-30418	Variant Details	Users are unable to submit higher order associations for a case.

Feature Request Updates & Issue Clarifications

BSVI-35930 was an issue that affected ingestion of a small number of samples into BaseSpace Variant Interpreter. The issue caused some variants from an input .vcf file to fail to appear in BSVI. The issue was intermittent and occurred unpredictably, but the root cause has been identified and resolved. Re-ingestion of affected samples (cases) will recover any variants that may have been affected.

Older feature request updates & issue clarifications are located in the BSVI v2.0.0 release notes.