Release Notes

BaseSpace Variant Interpreter v2.7.0

August 2019

INTRODUCTION

These Release Notes detail the latest release of BaseSpace Variant Interpreter, including known issues.

BaseSpace Variant Interpreter provides an interface for users to annotate, curate, interpret and report on the results from the sequencing pipeline.

FEATURES

The following features are now available:

- The version of Nirvana (illumina's annotation engine) has been upgraded to v3.1.1. This refreshes many of the annotation sources and brings in new content including:
  - pLI scores; displayed in the Gene column. This is filterable.
  - GnomAD genome and exome; displayed in the population frequencies column. This content is filterable.
  - ExAC population frequencies are no longer shown as these are part of the GnomAD exome cohort.
  - If a case already has an active filter using ExAC, the user will be prompted to remove that filter.
  - For ClinVar, the most damaging pathogenicity is displayed.
  - The list of gene symbols has been updated.
  - The CNV consequence provided by Nirvana has changed. This means that all filters on CNV consequence based on Nirvana 1.6.2 are now obsolete. Users will be prompted to remove those filters on each case and can then apply fresh filters.
  - Saved filters containing the obsolete fields (Exac, CNV consequence) will no longer work and will need to be recreated.
  - **Gene symbols have been updated**. Gene lists containing deprecated gene symbols will not provide a filtering result. For reference, the gene lists visible in the Gene List Manager contain the original gene symbols that were submitted. These can be downloaded and resubmitted to update synonyms to the latest symbol. Gene lists that are no longer needed can also be deleted in the Gene List Manager.
  - Note that all cases will need to be reanalysed after release. The runtime for Nirvana may also longer than previous versions.
  - Annotation versions included in Nirvana 3.1.1:
    - VEP (91)
    - ClinVar (20190204)
    - COSMIC (84)
    - dbSNP (151)
    - gnomAD (2.0.1)
    - gnomAD_exome (2.0.1)
    - MITOMAP (20190225) (not displayed in BSVI 3.1)
    - 1000 Genomes Project (Phase 3 v3 plus)
    - TOPMed (freeze_5)
    - ClinGen (20160414)
    - DGV (20160515)
    - MITOMAP_SV (20190225) (not displayed in BSVI 3.1
    - OMIM (20190225)
    - ExAC (0.3.1)
    - phyloP (hg38)

Resolved Issues

- Removed low-level error messages.
- Arbitrary file uploads are now prevented.
- ClinVar data not shown for Tumor-Only samples. Enabled display of ClinVar data for all sample types, including Tumour-Normal. Note that ClinVar filtering is not available on tumour samples.
- Upload of manifest does not clear down previous error messages.
- Broken hyperlinks to OMIM from gene fusion popup box.
- Copy-neutral LOH CNVs on autosomes in germline samples are not displayed.

Known Issues

- VCFs containing nonstandard alternate alleles (*, NON_REF) may cause ingestion to fail. Variants with nonstandard alternate alleles may display the wrong genomic consequence.
- ClinVar filters applied to cases with sample type germline, will be invalid if the sample type is switched to tumour-only. To resolve this, users should switch the sample type back to germline and remove the ClinVar filter before enabling the sample type of tumour-only.
- Using tumour types with the ontology ILLUMINA-CUSTOM can prevent associations being saved. It is preferable to use SNOMED, HPO or OMIM to describe phenotypes and these are not affected by this issue.
- When adding an interpretation for a variant in a rare disease case, if a user selects the "Mode of Inheritance" as "Unknown", the interpretation cannot be saved. All other Modes of inheritance: autosomal recessive, de novo etc are unaffected.
- Mitochondrial genes coming from phenotype search are declined by Gene List Manager when saving.
- BSVI will fail to process manifest if the reference header in VCF is hg19 and Assembly column in manifest is GRCh37.
- User without BSKN Curator role can click approval button although approve will fail.
- Failed samples counter is not updated when VCF ingestion fails.
- Gene lists containing deprecated gene symbols will not return a result when filtering.
- Dragen VCFs not fully supported.
- Multi-sample germline VCFs are not supported.
- BSVI shows ClinVar status as "Enabled" for nested annotation.
- Count of Analysis Result is missing from Subjects list page.
- If filter results in 0 variants, count is shown as "0 of 0 variants".
- Variant grid is misaligned after removing an invalid filter.
- BSVI does not load small variants from manta.
- Gene List creator becomes unresponsive in workgroups with many custom annotation files.
- Case history is slow to load.
- Extend user session is not working.
- "Failed" counter is not updated when VCF ingestion fails.
- Partially overlapping genes are not displayed in order of pLI score (popup).