Release Notes

BaseSpace Variant Interpreter v2.10.1

June 2020

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.

Note that all cases will have to be reanalyzed before they can be accessed after this release.

FEATURES

Support for DRAGEN Somatic v3.5.7 output:

- BSVI now supports the loading of output from DRAGEN Somatic v3.5.7 by import from BaseSpace Sequence Hub (BSSH) or by manifest. Variants from all three variant callers provided by DRAGEN are displayed in the variant grid (single nucleotide variants/indels, structural variants, copy number variants).
- For an analysis result to load all types of variants into one case, the small variant VCF must be present in the DRAGEN output files. Users are advised to use the “hard-filtered” VCF for ingestion.
- The SQ (somatic quality) value from the small variant VCF is displayed as the variant calling metric “Somatic Q Score”.
- For a somatic DRAGEN case that has been loaded from BSSH, if the alignment was also performed on BSSH using DRAGEN, the reads supporting a variant will be visible when using “ViewInIGV”.
- Purity and ploidy are extracted from the cnv.vcf header and displayed in the Case Panel.
- The Dragen variant caller version is extracted from the VCF header and displayed in the Case Panel.
- Static and dynamic genome visualisations are available if the tumor.target.counts.gc-corrected and baf.bedgraph.gz files are present in the same BSSH folder as the VCFs. These are only produced if copy number calling was run as part of the DRAGEN analysis.
- Earlier versions of the DRAGEN Somatic workflow are not fully supported.

Annotation update to Nirvana 3.6.2:

- This includes updates to the following annotation sources: OMIM to v20191004; gnomAD to v2.1
- GnomAD data sources (genomes and exomes) have been merged into a single annotation source with the name of gnomAD. Any filters that use GnomAD exome will no longer filter out variants on this basis. The GnomAD exome panel within the population frequency popup will not show any data.
- BSVI will provide a pathogenicity prediction if there is no BSKN (BaseSpace Knowledge Network), ClinVar or OMIM entry for a variant. The population frequency is part of this prediction. As GnomAD exome has been deprecated, the overall GnomAD population frequency is used instead.
- The RefSeq predicted “XM_” and “XR_” transcripts are no longer provided as annotation.
- The UTR (untranscribed region) of the gene is now also considered when annotating potential gene fusion events.
- This release of Nirvana brings in support for RNA editing and may result in some changes in HGVS variant consequences.

- In some situations, Nirvana's variant recomposition would crash. This has been resolved in Nirvana 3.6.1. However, for some VCF types, eg pisces, BSVI still turns off Nirvana's variant recomposition feature (BSVI 2.8 release).
- Support for platypus VCFs has been deprecated. The read depth and variant read frequency fields are no longer available for platypus data.
- Variants aligning to the HLA contigs are not annotated.

Resolved Issues

- When importing an analysis result from BSSH, if the SV.vcf in a folder did not contain any valid variants, ingestion would fail, regardless of any valid variants in the small variant VCF. Now in the situation where there are small variants, but there are no valid variants in the SV.vcf, the small variants will be ingested. At least one valid variant must exist in the small variant VCF for ingestion to succeed.
- Copy Number Variants (CNVs) called by DRAGEN are now correctly displayed as CNVs, rather than SVs (Structural Variants).
- Static genome plot y-axis has been scaled to ensure that plottable data is not hidden behind the chart label.
- An issue with users being unable to delete cases with very short names has been resolved.

Known Issues

- When importing from BSSH, users are advised not to add information to the Project column of the manifest as this may result in a duplicated view of the case in the registry. The case itself is not duplicated.
- Copy number variants with LOH (loss of heterozygosity) will have two near-identical entries in the variant grid, one representing the "deletion" part of this event and another for the "duplication"
- Importing associations from BSKN may fail if they were created using an ILLUMINA-CUSTOM tumour type
- Other Dragen workflows, versions and VCFs are not fully supported.
- Hyperlinks to variants within cases will take the user to that variant only if they are already logged in and in the appropriate workgroup. Otherwise, following a hyperlink to a variant will take the user to the Case Registry of their current workgroup, if logged in, or to the BSVI login page, if not logged in.
- During an import from BaseSpace Sequence Hub, the Last Updated date is unavailable, and the case will appear at the bottom of the last page in the Case Registry. This is because the default sort of the Case Registry is on the Last Updated date. Cases that fail ingestion and result in a Failed state also have no Last Updated date, so will appear at the end of the Case Registry listing.
- ClinVar filters applied to cases with sample type germline become invalid if the sample type is switched to tumour-only. To resolve this, change the sample type back to germline and remove the ClinVar filter before enabling the tumour-only sample type.
- Using tumour types with the ontology ILLUMINA-CUSTOM can prevent associations being saved. Use SNOMED, HPO, or OMIM to describe phenotypes, as these are not affected by this issue.
- When adding an interpretation for a variant in a rare disease case, the interpretation is not saved if the Mode of Inheritance selection is Unknown. All other Modes of inheritance: autosomal recessive, de novo etc are saved correctly.
- Mitochondrial genes coming from phenotype search are declined by Gene List Manager when saving.

- BaseSpace Variant Interpreter fails to process manifests if the reference header in VCF is hg19 and the Assembly column in the manifest file is GRCh37.
- Users who do not have BSKN Curator permissions can select the approval button although approve will fail.
- Gene lists containing deprecated gene symbols do not return a result when filtering.
- Multi-sample germline VCFs are not supported.
- BaseSpace Variant Interpreter 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".
- BaseSpace Variant Interpreter does not load small variants from the structural variant caller manta.
- Case history is slow to load.
- Extend user session is not working.
- Partially overlapping genes are not displayed in order of pLI score (popup).
- The case registry displays the owner as “Unassigned” for inactive cases.
- In the registry, a case owner cannot be assigned to inactive cases
- After reanalysis, there is a lag before the case owner and status is displayed