Title: BaseSpace Variant Interpreter v2.16 Release Notes

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

- There are several security updates with this release.
- BSVI has been updated to use Nirvana 3.15
    - Update annotation sources: OMIM, ClinVar, dbSNP and 1000 Genomes Project. ExAC has been deprecated
    - pLI score now comes from gnomAD rather than ExAC
    - Note that all cases will need to be reanalysed

Resolved Issues

- The version of Illumina's Annotation Engine (Nirvana 3.6.2) used in BSVI versions 2.10 to 2.15 contains an issue. This affects a small number of RefSeq transcripts, which contain 'RNA-edits'. In these cases, the wrong HGVS c-dot and/or p-dot position number may be shown for insertions or deletions. The sequence change will be displayed correctly. It is worth noting that VEP91 also has the same issue. Ensembl transcripts are not affected. Nirvana 3.15 reduces the number of these errors significantly, although in a few cases, the wrong c-dot or p-dot notation may still be shown. Please contact illumina's technical support if you require additional information on this topic: techsupport@illumina.com
- The genome visualization plot is now displayed for DRAGEN Somatic (tumour-normal) 3.7, 3.8 and 3.9
- Fixed the display of potential gene fusions where the gene name contained a hyphen
- Fixed an issue where the static genome visualization plot is lost after reanalysing DRAGEN analysis.

Known Issues

- Pressing Save multiple times when saving a comment may result in the comment being listed multiple times. Any additional entries can be deleted by the user.
- Closed cases that are also Inactive appear in the default registry grid, showing their status as Inactive.
- It is possible to use the URL of a case to access it directly. However, if the name of the case contains special characters such as # or %, the hyperlink will not load the case.
- DRAGEN Amplicon data cannot be imported directly into BSVI from BaseSpace Sequence Hub. DNA Amplicon data can be imported.
- The Past Cases component of the Associations grid will include the existing case when looking for cases in the workgroup with interpretations on the same variant. This behaviour is seen after the case

is reanalysed. The Past Cases section of the Variant Details is not affected and does not refer to the existing case.
- Bulk re-analyse does not update the case ‘last modified date’.
- Occasionally bulk re-analyse will fail in the case registry. Enter an individual case to reanalyse it.
- Gene names in the export file: the gene name is not provided in the export file unless the variant overlaps with the canonical transcript
- 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.
- Other DRAGEN workflows, versions and VCFs are not fully supported.
- 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
- 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.
- 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