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BaseSpace® Variant Interpreter and BaseSpace Knowledge Network FAQs

Frequently asked questions (FAQs) about simplified variant interpretation with BaseSpace Variant Interpreter and BaseSpace Knowledge Network.

BaseSpace Variant Interpreter is a cloud-based interpretation and reporting platform designed to decrease the time and effort required to extract biological insight from genomic data while maximizing operational efficiency. The BaseSpace Knowledge Network curates variant information from numerous databases and organizes relevant literature associations into an easily accessible and readable interface. Together these products streamline prioritization, interpretation, and reporting of genomic variants in human samples. This document provides answers to some of the most frequently asked questions about BaseSpace Variant Interpreter and BaseSpace Knowledge Network.

Access to BaseSpace Variant Interpreter

How do I install and access BaseSpace Variant Interpreter?
BaseSpace Variant Interpreter is an independent software solution delivered as an online, cloud-based service accessed through a web browser; therefore, installation is not necessary. The minimum system standards are: Chrome version 49, Firefox version 45, Internet Explorer 11, or more recent versions.

How do I access BaseSpace Variant Interpreter through my company firewall?
BaseSpace Variant Interpreter is a web-based application. To access it through your company firewall, open port 443.

How do I allow BaseSpace Variant Interpreter to access my BaseSpace Sequence Hub account?
BaseSpace Variant Interpreter and BaseSpace Hub use the same login credentials for authentication, so logging in to one of the applications enables access to the other. After logging in to BaseSpace Interpreter, your account automatically links to your BaseSpace Sequence Hub account, allowing you to import and view any variant call files stored there.

Do I need to be a BaseSpace Sequence Hub user to access BaseSpace Variant Interpreter?
No, users are not required to have a BaseSpace Sequence Hub account to access BaseSpace Variant Interpreter. BaseSpace Variant Interpreter is an independent software solution delivered as an online, cloud-based service. Use of BaseSpace Variant Interpreter does not require a BaseSpace Sequence Hub account, although it integrates with your BaseSpace Sequence Hub account if it exists. If you have a MyIllumina account, you can use those credentials to log in to each application separately.

Is BaseSpace Variant Interpreter available as a command-line tool?
BaseSpace Variant Interpreter is not available as a command-line tool. BaseSpace Variant Interpreter is a software as a service (SaaS) (eg, online, cloud-based) solution with a graphical user interface that allows variant exploration, annotation, filtering, and reporting without bioinformatics expertise.

Does BaseSpace Variant Interpreter require an internet connection?
Yes, the software requires an internet connection. All software operations are conducted in the cloud.

Where is BaseSpace Variant Interpreter hosted? Where are the data stored?
BaseSpace Variant Interpreter is hosted on Amazon Web Services. Storage is account-specific and is also hosted on Amazon Web Services.

BaseSpace Variant Interpreter Workflow

What are the annotation sources for BaseSpace Variant Interpreter?
BaseSpace Variant Interpreter uses the following annotation sources: dbSNP, Catalogue of Somatic Mutations in Cancer (COSMIC), ClinVar, 1000 Genomes, Exome Variant Server (EVS), Exome Aggregation Consortium (ExAC), PolyPhen, and Sorting Tolerant From Intolerant (SIFT) algorithm. Database of Genomic Variants (DGV) and International Standards for Cytogenomic Arrays (ISCA) are also used for copy number variation and structured variant annotation. For more information on BaseSpace Variant Interpreter annotation sources, see the BaseSpace Variant Interpreter Data Sheet.

Can I import custom annotations?
Yes, users can import custom annotations in tab-delimited text (.TXT) file format into the software from the Custom Annotations tab in Settings. For more information, see the BaseSpace Variant Interpreter Online Help.

How am I notified when a new version of BaseSpace Variant Interpreter is released?
Users will receive an advanced notification via email ahead of any major release version changes to BaseSpace Variant Interpreter. Additionally, users will receive change notifications when they log in. Details of changes between versions are provided in the version release notes.

Can I save my filter settings as a template for use with other data sets?
Yes, any filter combination can be saved and applied to other data sets.

Does Illumina recommend filters or cutoffs to use for different scenarios?
No, Illumina does not provide recommended filters or cutoffs. Filtering parameters vary depending on the application and objective of the investigator.

Can I perform sample-to-sample comparisons?
No, BaseSpace Variant Interpreter does not currently support direct comparison of analysis results from two different samples.

Can I modify the classification categories in BaseSpace Variant Interpreter?
No, the software uses the following default classification schemes for tumor and germline samples:

- Tumor analysis—L1: National (eg, FDA) Guidance, L2: Professional Society Guidance, L3: Clinical Trial Available, and L4: Other Reportable Variant.
- Germline analysis—Pathogenic, Likely Pathogenic, Variant of Unknown Significance (VUS), Likely Benign, and Benign. These categories follow guidelines from the American College of Medical Genetics and Genomics (ACMG).

Does Illumina provide classified variants?
No, Illumina does not provide classified variants. With BaseSpace Variant Interpreter, users can upload classified variants from an external source or manually classify variants in samples that are being analyzed.

Does BaseSpace Variant Interpreter automatically assign variant classification?
For germline variants, the software uses a simple rule set to predict the classification:

- Variants are automatically ranked and prioritized based on their annotations, predicted consequence (loss of function, missense, or noncoding) and population allele frequency (using the highest frequency from ExAC, 1000 Genomes, and EVS).
- Variants are typically assigned the ClinVar pathogenicity unless the variant is greater than 5% population frequency, in which case they are assigned Benign per ACMG guidelines.
- Variants without ClinVar entries that are common (over 1% population frequency) are assigned Likely Benign.
- Variants without ClinVar entries that are uncommon (less than 1% population allele frequency) are assigned Likely Pathogenic if loss-of-function (frameshift, stop-gained or essential splice), VUS if a missense or near-splice, and Likely Benign if noncoding.
- Variants with public associations are assigned the pathogenicity with the most pathogenic public association.
- Variants with an association in a private knowledgebase are assigned the pathogenicity with the most pathogenic private association and takes priority over public associations.
- Variants with past cases are assigned the most pathogenic between two options: 1) pathogenicity based on past cases or 2) pathogenicity calculated using previous steps.

Can I perform family-based genetic disease analysis in BaseSpace Variant Interpreter?
BaseSpace Variant Interpreter supports family-based analysis for singletons (proband only), duo (proband plus one parent), trios (proband plus both parents), and extended pedigree (proband, both parents, and up to five siblings).

How does BaseSpace Variant Interpreter handle tri-allelic sites?
When both alleles of a heterozygous position are different from the reference, as in a tri-allelic position, the variants are split into two lines and both variants are annotated.

Can I import sample information (metadata) instead of entering it manually?
Yes, metadata can be added to a sample at any point, with options to add it when importing the .VCF files (recommended). After importing .VCF files, sample metadata can still be added or edited using the software interface or a sample metadata sheet. Metadata

autopopulates the appropriate section of the report with either entry method.

Can I perform comparisons across large groups of samples for cohort or population analysis?
No, BaseSpace Variant Interpreter does not support comparisons of two or more groups of samples. Use BaseSpace Cohort Analyzer for cohort or population analysis.

BaseSpace Variant Interpreter File Formats and Compatibility

Does BaseSpace Variant Interpreter support the genome VCF (.gVCF) variant call file format?
Yes, the software supports .VCF and .gVCF file formats.

What are the requirements for importing whole genome data or large .gVCF files?
Batch uploads from a network or local directory are limited to 100 files or 10 GB, whichever is greater.

Which export formats are available from BaseSpace Variant Interpreter?
You can export reports in .PDF and tab separated values (.TSV) file formats.

Can I import .VCF files produced by non-Illumina software products into BaseSpace Variant Interpreter?
Yes, the software accepts .VCF files produced by the Genome Analysis Toolkit (GATK) v1.6.

Can BaseSpace Variant Interpreter be used for applications other than whole-genome sequencing?
Yes, BaseSpace Variant Interpreter can be used to interpret DNA sequencing data from whole-exome sequencing and small targeted panels.

BaseSpace Variant Interpreter Validation

Is the BaseSpace Variant Interpreter software validated?
BaseSpace Variant Interpreter has undergone the standard software development and testing requirements that are applied to all Illumina software tools developed for research use only. Illumina has not submitted the software for regulatory approval and it is not a medical device. It is important that laboratories follow procedures for validating the software per institution, local, state, and federal guidelines.

BaseSpace Knowledge Network

What qualifies as a content entry in the BaseSpace Knowledge Network?
A knowledge base content entry in BaseSpace Knowledge Network is defined as an association between a genetic biomarker (such as a variant) and phenotypic content (such as a disease). Each association can contain multiple pieces of evidence (such as a publication, clinical trial, or statistical measure) used to support the association.

Does BaseSpace Knowledge Network provide clinical diagnostic variant interpretations?
No, BaseSpace Knowledge Network provides content for research use only focused on expediting interpretation of variants.

How up to date is the variant interpretation content in BaseSpace Knowledge Network?
Each curated entry in BaseSpace Knowledge Network is stamped with an entry date parameter.

How often is content in the BaseSpace Knowledge Network updated?
The content available in BaseSpace Knowledge Network is regularly evaluated, but Illumina does not provide a specific schedule for content updates.

Can I add my own entries to BaseSpace Knowledge Network?
Yes, users can add new entries to BaseSpace Knowledge Network via the Add Curation workflow in BaseSpace Variant Interpreter as well as through the BaseSpace Knowledge Network portal. These entries are stored in your private knowledge base where members of your workgroup can review them upon encountering a matching variant in a new sample.

Can I add previously generated content entries to the BaseSpace Knowledge Network?
Yes, users can add new content to their private knowledge base through either the Add Curation workflow in BaseSpace Variant Interpreter or through the BaseSpace Knowledge Network portal.

Learn More

To learn more about BaseSpace Variant Interpreter, see the BaseSpace Variant Interpreter Data Sheet and BaseSpace Variant Interpreter Online Help.

For more on BaseSpace Knowledge Network, download the BaseSpace Knowledge Network Data Sheet.

To learn more about BaseSpace Cohort Analyzer, visit the BaseSpace Cohort Analyzer web page.

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