VIA™ Software Annotation and Track Updates

Release Notes – February 2025

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G

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For Research Use Only. Not for use in diagnostic procedures.

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Revision History

REVISION	NOTES
A	February 2023 update
B	May 2023 update
C	September 2023 update; software name change to VIA Software
D	December 2023 update
E	March 2024 update
F	July 2024 update
G	February 2025 update

Changes to Tracks and Annotations

Major changes to tracks and annotation files used in VIA software that are provided and maintained by Bionano are outlined below. With each track update release, the VIA Admin will be prompted to download, install, and deploy the new tracks to all users. Those behind a firewall and not connected to the internet will require a manual update (by their Bionano support representative) and will not receive an alert through the software.

Any change to the track file including the following will prompt an update:

- Content change at the source site – this will be incorporated into the VIA track/annotation files.
- Changes to gene names/positions - even if there is no change to the content at the source site, there may be changes introduced to the regions/annotations files due to changes in RefSeq genes. If the position of a gene changes or the name changes, the change will be introduced into the region file as well.
- Changes to track meta data – information about the track (e.g., track description, linked URL, etc.)
- Changes to display of track elements – track elements may undergo a change in the color, label, or URL links.

As seen in **Figure 1**, tracks provided and updated by Bionano are housed in a folder called **BioDiscovery Provided Regions** within the **Regions** tab in the user interface (UI). User-created regions (tracks) are housed in a folder called **Custom Regions**.

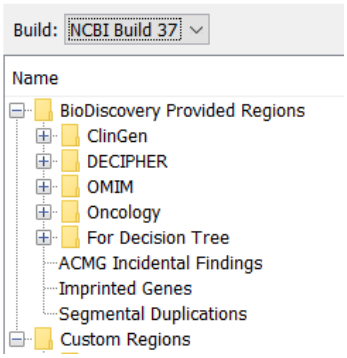

Figure 1. Organization of tracks

Software Version Compatibility

Annotation and Track updates are only compatible with software version 6.0 and newer.

NOTE: Bionano aggregates content retrieved from these external resources but there may be inconsistencies originating in the source content from these resources.

Changes to Annotation Files

These files are used internally within the software and include files for annotations, genes, and Human Phenotype Ontology (HPO) terms.

Green cells indicate changes to the file in this release

Annotation Files	hg19	hg38	T2T CHM13v2.0
Genes track			
DGV track			
HPO			
Canonical Transcripts			

Genes Track

Track data was obtained from UCSC Genome Browser on December 27, 2024.

Hg19: Source data version: NCBI Homo sapiens Updated Annotation Release NCBI RefSeq GCF_000001405.25-RS_2024_09 (2024-09-07)

Hg38: Source data version: NCBI Homo sapiens Updated Annotation Release NCBI RefSeq GCF_000001405.40-RS_2024_08 (2024-08-27)

T2TCHM13v2.0: Source data version: NCBI Homo sapiens Updated Annotation Release 110 (2022-04-12)

DGV TRACK

No changes to content. Source: 2020-02-25 release

HPO

Content was updated. Source: Release version 2024-12-12 https://hpo.jax.org/

CANONICAL TRANSCRIPTS

Content was updated.

Changes to Regions (Tracks)

Updates apply to hg19, hg38, and T2TCHM13v2.0, unless indicated otherwise. Green cells in the table depict changes to track content and/or meta data changes in this release; current versions of tracks are noted within the cells:

Track category/name	hg19 Track Version	hg38 Track Version	T2T CHM13v2.0 Track Version
ACMG Incidental Findings	20250201	20250201	20240301
Imprinted Genes + tracks in the For Decision Tree folder	20250201	20250201	20250201
Segmental Duplications	20210331	20210331	20230415
CIViC Genes	20250201	20250201	20250201
CIViC Variants	20240701	20240701	20240701
RefSeq Exons	20250201	20250201	20240701
RefSeq Genes	20250201	20250201	20240701
RefSeq Coding Genes	20250201	20250201	20240701
RefSeq Non-Coding Genes	20250201	20250201	20240701
ClinGen Dosage Sensitive Map	20250201	20250201	20250201
ClinGen Dosage Sensitive Map - For Decision Tree	20250201	20250201	20250201
ClinGen Prenatal	20230201	20230201	20231201
ClinGen Prenatal - For Decision Tree	20230201	20230201	20231201
ClinGen Postnatal	20231201	20240301	20240301
ClinGen Postnatal - For Decision Tree	20231201	20240301	20240301
DECIPHER DDG2P	20250201	20250201	20250201
DECIPHER DDG2P - For Decision Tree	20250201	20250201	20250201
DECIPHER Syndromes	20230901	20230901	20230901
DECIPHER Syndromes - For Decision Tree	20230901	20230901	20240301
OMIM Genes	20250201	20250201	20250201
OMIM Morbid Phenotypes + Decision Tree	20250201	20250201	20250201
OMIM Morbid Phenotypes - For Decision Tree	20250201	20250201	20250201
OMIM Syndromes	20250201	20250201	20250201
OMIM Syndromes - For Decision Tree	20250201	20250201	20250201
Heme Guideline Regions	20230409	20230409	20230720
Heme Guideline Targets - For Decision Tree	20230409	20230409	20230720
Solve CNV Mask	20230409	20230409	20230720

ACMG INCIDENTAL FINDINGS TRACK

Source: ACMG SF v3.2. Source content has been updated.

CIViC TRACKS

Obtained from CIViC (https://civicdb.org/) on December 27, 2024. Content in the CIViC Genes tracks has changed as the source content is updated daily. CIViC Variants track has not been updated.

CLINGEN DOSAGE SENSITIVITY TRACKS

Downloaded on December 27, 2024, from clinicalgenome.org. Content has been updated.

CLINGEN PRENATAL TRACKS

Source: dbVar nstd75. There were no changes to the source content and therefore no changes to the track data.

CLINGEN POSTNATAL TRACKS

Source: dbVar nstd102. Downloaded on December 27, 2024. There were no changes to the source content since the last track and annotation update and therefore no changes to the track data.

CLINGEN PRENATAL AND POSTNATAL TRACKS

These tracks were retired at the end of 2022 and will no longer be updated via the track update process. Source content for the Postnatal tracks has changed where variant calls have been aggregated into one event, making it difficult to combine prenatal and postnatal datasets. The prenatal and postnatal tracks still exist separately so you can switch to using those if you have been using the ClinGen Prenatal and Postnatal track set. Please contact Support with any questions.

DDG2P TRACKS

Content has been updated and was downloaded on December 27, 2024, from the DDG2P database.

DECIPHER SYNDROMES TRACKS

Source: Database of Chromosomal Imbalance and Phenotype in Humans (DECIPHER) CNV Syndromes.

No change.

IMPRINTED GENES TRACKS

Source: geneimprint.com. Content has not been updated. Downloaded on December 27, 2024.

OMIM TRACKS

Data was obtained from the source on December 27, 2024, for all OMIM tracks.

REFSEQ TRACKS

Includes RefSeq Genes, RefSeq Exons, RefSeq Coding Genes, RefSeq Non-Coding Genes

OBTAINED FROM UCSC GENOME BROWSER ON DECEMBER 27, 2024. SEGMENTAL DUPLICATIONS TRACKS

Source: UCSC. No changes.

Tracks and Annotations Content

VIA software has annotations from many external databases integrated within the system for use in sample review and classification. A core set of these annotation files are available as internal annotation files and region files (region files are also referred to as tracks) within the initial VIA installation. Regions/tracks provided by Bionano are housed in a folder called **BioDiscovery Provided Regions** as seen in the **Regions** tab in the UI. Tracks in this folder are updated by Bionano and users (including Admins) cannot delete these tracks. Any user-added tracks will be housed in the **Custom Regions** folder. Review the section on "System Administration" in the *VIA Software User Guide* (CG-00043) for more information.

An update system within VIA software will update tracks and annotations when new content is available. The local VIA Administrator is informed of any updates to these files and chooses if and when to install the updated files. Bionano aims to provide quarterly updates of these files.

Annotation Files

These files are used internally within the software and include files for annotations, genes, and HPO terms.

GENES TRACK

Source: NCBI RefSeq Genes (curated subset) from UCSC Genome Browser. The Genes track displays genes and transcripts obtained from RefSeq.

DGV TRACK

The DGV track in VIA uses data obtained from http://dgv.tcag.ca/. The DGV track is not a replicate of the downloaded DGV data; that data is curated by Bionano to create the VIA DGV track. VIA version 6.0 and later does not include the DGV Gold Standard tracks. The DGV track in VIA is filtered to provide a higher quality set of variants than what is provided in the source DGV data download. It is curated to include only high-quality results according to the following filtering criteria:

- exclude CNVs from any study that includes BAC results
- exclude all events less than 50bp (to filter out seq var changes from sequencing data, e.g., gnomAD-SV)

The DGV Gold Standard track can be accessed from http://dgv.tcag.ca/ and uploaded into VIA as a custom track if desired.

HPO (HUMAN PHENOTYPE ONTOLOGY)

HPO terms and gene to phenotype mapping are obtained from https://hpo.jax.org/.

CANONICAL TRANSCRIPTS

The canonical transcripts file is used to select the default transcript for display in the Genes track (see **Figure 2**).

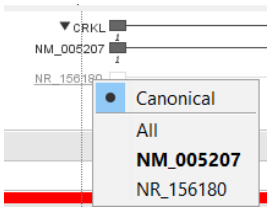

Figure 2. Canonical Transcripts file

For example, genes from the VIA genes track are matched to locate the canonical transcript from the data sources listed below. If the gene is not found, the next data source in the list is searched, and so on until all genes in the Genes track have been queried. There are a small number of genes that do not have canonical transcript listed in the sources below. In such cases, VIA will display the longest transcript in the Genes track.

Databases queried, in order, to obtain canonical transcripts:

Hg19:

1. RefSeq Select
2. VEP version 99

Hg38:

1. MANE Select v1.4
2. RefSeq Select
3. VEP version 99

Tracks/Region Files

VIA Regions (tracks) are composed of sets of tracks provided and maintained by Bionano as well as user-loaded tracks. Only the regions provided by Bionano are updated via the Bionano tracks and annotations update process.

The track description contains information of the source content, summary of track data, and the download date. Hover over the track name in the **Table and Track Preferences** to view these details.

ACMG Incidental Findings Track

This track contains the updated gene list of 78 genes (ACMG SF v3.2) published on June 22, 2023. ((https://www.gimjournal.org/article/S1098-3600(23)00879-1/fulltext). This is the minimal list of genes

recommended by the American College of Medical Genetics and Genomics (ACMG) to be reported as incidental or secondary findings. Entries were obtained from (https://www.ncbi.nlm.nih.gov/clinvar/docs/acmg/).

CIViC Tracks

Obtained from CIViC (https://civicdb.org/), these tracks contain cancer related variants from the CIViC knowledge base. Only variants records that have been accepted are included here.

NOTE: CIViC only provides hg19 coordinates. For the hg38 track, the coordinates were converted using the UCSC Liftover tool.

CIViC VARIANTS TRACK

This track contains variants from CIViC. The contents (variants in cancer genes with the event label in the track displaying the gene name and variant) are the same. The contents of this track comes from the **Variant Summaries** file downloaded from the CIViC website. The **Variant Summaries** file only contains variants with accepted variant records.

CIViC GENES TRACK

The CIViC Genes track now contains only genes implicated in cancer as found in the **Gene Summaries** file downloaded from the CIViC website. This track contains all genes from the CIViC website regardless of the status of variant records. Even if a gene does not have any accepted variant records, the gene is present in this file.

ClinGen Dosage Sensitivity Tracks

Data is obtained from ClinicalGenome.org. Dosage Sensitivity Map genes and regions for which evidence was collected either supporting or refuting haploinsufficiency or triplosensitivity. Evidence in the ClinGen Dosage Sensitivity curation process is evaluated on a continual basis by the ClinGen Structural Variation Working Group as described in Riggs et al. 2012 (http://www.ncbi.nlm.nih.gov/pubmed/22097934). The results are compiled into the ClinGen Genome Dosage Map Resource.

Main tracks:

- ClinGen Dosage Sensitive Map All
- ClinGen Dosage Sensitive Map Benign
- ClinGen Dosage Sensitive Map Likely Pathogenic
- ClinGen Dosage Sensitive Map Pathogenic

Decision Tree tracks with folder hierarchy:

- Gains
  - Genes
    - ClinGen Dosage Sensitive Map Triplosensitivity Benign Genes
    - ClinGen Dosage Sensitive Map Triplosensitivity Likely Pathogenic Genes
    - ClinGen Dosage Sensitive Map Triplosensitivity Pathogenic Genes

    - Regions
        - ClinGen Dosage Sensitive Map Triplosensitivity Benign Regions
        - ClinGen Dosage Sensitive Map Triplosensitivity Likely Pathogenic Regions
        - ClinGen Dosage Sensitive Map Triplosensitivity Pathogenic Regions
- Losses
    - Genes
        - ClinGen Dosage Sensitive Map Haploinsufficiency Benign Genes
        - ClinGen Dosage Sensitive Map Haploinsufficiency Canonical Transcript
        - ClinGen Dosage Sensitive Map Haploinsufficiency Gene Components
        - ClinGen Dosage Sensitive Map Haploinsufficiency Likely Pathogenic Genes
        - ClinGen Dosage Sensitive Map Haploinsufficiency Pathogenic Genes
    - Regions
        - ClinGen Dosage Sensitive Map Haploinsufficiency Benign Regions
        - ClinGen Dosage Sensitive Map Haploinsufficiency Likely Pathogenic Regions
        - ClinGen Dosage Sensitive Map Haploinsufficiency Pathogenic Regions

CLINGEN DOSAGE CURATION SCORING:

- 3: Sufficient evidence suggesting dosage sensitivity is associated with clinical phenotype
- 2: Emerging evidence suggesting dosage sensitivity is associated with clinical phenotype
- 1: Little evidence suggesting dosage sensitivity is associated with clinical phenotype
- 0: No evidence to suggest that dosage sensitivity is associated with clinical phenotype
- 40: Dosage sensitivity unlikely
- 30: Gene associated with autosomal recessive phenotype

Clinical classification is extrapolated from the scores. Segmented tracks are created for benign, likely pathogenic, and pathogenic based on the scores above: 3=pathogenic; 1, 2=likely pathogenic; 40=benign. 0 and 30 are ignored and not included in the default Decision Tree tracks. The tracks below are used by the ACMG Scoreboard feature:

- ClinGen Dosage Sensitive Map Haploinsufficiency Canonical Transcript
- ClinGen Dosage Sensitive Map Haploinsufficiency Gene Components

Coloring for track events:

- Loss events -> red
- Gain events -> blue

ClinGen Prenatal Tracks

Source: dbVar nstd75. Contains CNVs in the prenatal array dataset from Wapner et. al. 2012 (http://www.ncbi.nlm.nih.gov/pubmed/23215555), also known as nstd 75 (ClinGen Prenatal).

Main tracks:

- ClinGen Prenatal All
- ClinGen Prenatal Benign
- ClinGen Prenatal Likely Benign
- ClinGen Prenatal Likely Pathogenic
- ClinGen Prenatal Pathogenic
- ClinGen Prenatal Uncertain Significance

Decision Tree tracks:

- ClinGen Prenatal Gains Benign
- ClinGen Prenatal Gains Likely Benign
- ClinGen Prenatal Gains Likely Pathogenic
- ClinGen Prenatal Gains Pathogenic
- ClinGen Prenatal Gains Uncertain Significance
- ClinGen Prenatal Losses Benign
- ClinGen Prenatal Losses Likely Benign
- ClinGen Prenatal Losses Likely Pathogenic
- ClinGen Prenatal Losses Pathogenic
- ClinGen Prenatal Losses Uncertain Significance

Coloring for track events:

- Loss events -> red
- Gain events -> blue

ClinGen Postnatal Tracks

Source: dbVar nstd102. Track contains CNVs designated as benign, likely benign, pathogenic, likely pathogenic, conflicting, and regions of uncertain significance in clinical structural variants submitted to ClinVar. It replaces and supplements clinical variants from several studies that were originally submitted to dbVar (e.g., nstd37, nstd101).

HOW VARIANT CALLS ARE REPRESENTED IN THE NSTD102 STUDY AND OUR TRACKS

- Variant calls in the study are aggregated into one entry per call type. If all classifications match, then there will be a single top-level aggregate classification. If they do not match, the classification will be “Conflicting.” For example, if there were five cases with the following:
  - Gain-benign
  - Gain-benign
  - Gain-benign
  - Loss-Pathogenic

- Loss-Benign

The nstd102 study consolidates these into the following two entries:

- Gain-benign
- Loss-Conflicting interpretations of pathogenicity

In addition to segmented tracks based on clinical interpretation (Pathogenic, Likely Pathogenic, Uncertain Significance, Likely Benign, and Benign**)**, there is an additional segment called Conflicting. The Conflicting tracks contain events in nstd102 with interpretation values that do not fall into one of the segments listed above. Values such as the following would be segmented into the Conflicting track:
  - Conflicting data from submitters
  - Conflicting interpretations of pathogenicity
- If there is more than one clinical interpretation in an entry classification, the entry will be segmented into each individual clinical interpretation track.
  - e.g., **Benign/Likely benign**: **See cases** will be segmented into the Benign track and Likely benign track.
  - e.g., **Uncertain significance, Pathogenic/Likely pathogenic: See cases** will be segmented into the Uncertain significance track, Pathogenic track, and Likely pathogenic track.
- Call types **copy number gain** and **duplication** in the study = **gain** in our tracks
- Call types **copy number loss** and **deletion** in the study = **loss** in our tracks
- The label displays clinical significance in addition to the subject phenotype, for example, Pathogenic: Developmental Delay
- The **Subject Phenotype** field contains values such as **See Cases** or **not provided** for most of the events, therefore many entries may have labels such as **Pathogenic: See Cases**.

Coloring for track events:

- Loss events -> red
- Gain events -> blue

DDG2P Tracks

Source: DDG2P database. A curated list of genes reported to be associated with developmental disorders in the Decipher Developmental Disorders Gene2Phenotype database (DDG2P).

Includes all DDG2P related tracks in VIA software. **NOTE**: DECIPHER has moved to hg38 (Dec. 2020). Both hg19 and hg38 track coordinates are obtained via DECIPHER.

Table 1 shows how the events are segmented into respective For Decision Tree tracks based on DDD category**,** Confidence and Allelic requirement labels in the source data.

Table 1. DDG2P segmented tracks in For Decision Tree folder

NxC Track name contains	Confidence category	D2P Allelic Requirement
Biallelic Confirmed	Definitive	biallelic_autosomal biallelic_PAR
Monoallelic Confirmed	Definitive	monoallelic_autosomal monoallelic_X_hem monoallelic_Y_hem monoallelic_X_het monoallelic_PAR
Biallelic Unconfirmed	Strong Limited Moderate Both RD and IF	biallelic_autosomal biallelic_PAR
Monoallelic Unconfirmed	Strong Limited Moderate Both RD and IF	monoallelic_autosomal monoallelic_X_hem monoallelic_Y_hem monoallelic_X_het monoallelic_PAR
Recessive	Definitive Strong Limited Moderate Both RD and IF	biallelic_autosomal biallelic_PAR
Dominant	Definitive Strong Limited Moderate Both RD and IF	monoallelic_autosomal monoallelic_X_hem monoallelic_Y_hem monoallelic_X_het monoallelic_PAR

Coloring for DDG2P track events:

- Dominant/monoallelic events -> green
- Recessive/biallelic events -> orange

DECIPHER Syndromes Tracks

Source: DECIPHER CNV Syndromes. DECIPHER CNV Syndromes is a list of expert-curated microdeletion and microduplication syndromes involved in developmental disorders.

NOTE: On the source site, a few events do not have coordinates in build 37 because DECIPHER moved to display of coordinates in hg38 (end of 2020); coordinates were lifted over to hg38. For some events, manual annotation was required either because events could not be lifted over automatically or there was an issue with the lifted over coordinates. DECIPHER does not provide hg19 coordinates for these events since the events were not lifted over automatically. For these handful of events, Bionano has used the build 37 coordinates provided by DECIPHER prior to their change to display of events in hg38.

Coloring for track events is as follows:

- deletion syndrome -> red
- duplication syndrome -> blue

Heme Guideline Regions (All SV Types)

Source: Bionano

Located in the **Oncology** folder, this resource contains aggregate summaries of professional society guidelines from the US, NHS, and WHO societies for the assessment of cytogenomic aberrations across hematological malignancies, including aneusomies, deletions, duplications, translocations, fusions, inversions, and rearrangements. Starting with VIA 7.0, these heme resources are used as part of the analysis workflow for hematological diseases with OGM data. Content is organized into disease specific tracks, which are also amalgamated into a Pan Heme Guideline Regions track.

Disease Specific Tracks:

- ALL Guideline Regions
- AML Guideline Regions
- CLL Guideline Regions
- Lymphoma Guideline Regions
- MDS Guideline Regions
- MM Guideline Regions
- MPN Guideline Regions
- Pan Heme Guideline Regions

The Heme Guideline Region lists are further segmented into multiple tracks per disease condition based on the variant type and size for more effective use with the Decision Tree. Variants that are gene level or smaller than a cytoband can be categorized as Small Variant tracks. Aneusomies and other variants larger than a cytoband can be categorized as Large Variant tracks. These segmented tracks are stored in the **For Decision Tree** folder hierarchy. The disease specific small and large guideline panels provided by Bionano represent the composite of the relevant target tracks listed in **Table 2**.

Table 2: Heme Guideline Target Tracks

Small Variant Guideline Tracks	Large Variant Guideline Tracks
ALL Deletion Small	ALL Trisomy
ALL Duplication Small	AML Deletion Large
ALL Rearrangements Small	AML Monosomy
ALL Translocation Interchr	AML Trisomy
AML Deletion Small	CLL Deletion Large
AML Duplication Small	CLL Monosomy
AML Rearrangements Small	CLL Trisomy
AML Translocation Interchr	Lymphoma Deletion Large
AML Translocation Intrachr	Lymphoma Duplication Large
CLL Deletion Small	Lymphoma Monosomy
CLL Rearrangements Small	Lymphoma Rearrangements Large
Lymphoma Deletion Small	Lymphoma Trisomy
Lymphoma Duplication Small	MDS Deletion Large
Lymphoma Rearrangements Small	MDS Duplication Large
Lymphoma Translocation Interchr	MDS Monosomy
Lymphoma Translocation Intrachr	MDS Rearrangements Large
MDS Deletion Small	MDS Trisomy
MDS Rearrangements Small	MM Deletion Large
MDS Translocation Intrachr	MM Duplication Large
MM Deletion Small	MM Monosomy
MM Duplication Small	MM Trisomy
MM Rearrangements Small	MPN Deletion Large
MM Translocation Interchr	MPN Duplication Large
MPN Deletion Small	MPN Monosomy
MPN Duplication Small	MPN Rearrangements Large
MPN Inversion Small	MPN Trisomy
MPN Rearrangements Small	Pan Heme Deletion Large
MPN Translocation Interchr	Pan Heme Duplication Large
MPN Translocation Intrachr	Pan Heme Monosomy
Pan Heme Deletion Small	Pan Heme Rearrangements Large
Pan Heme Duplication Small	Pan Heme Trisomy
Pan Heme Inversion Small	
Pan Heme Rearrangements Small	
Pan Heme Translocation Interchr	
Pan Heme Translocation Intrachr	

Imprinted Genes Tracks

Source: geneimprint.com. A curated list of gene names, status (predicted, imprinted, etc.) and the expressed allele (maternal, paternal, isoform dependent, unknown, etc.) in the imprinted gene database (Gene Imprint). This track excludes all entries with status=Not Imprinted.

The Imprinted Genes track includes all events from the Gene Imprint db except those labeled as Not_Imprinted. The default link from this track is to OMIM. If the gene is not in OMIM at the time of track generation, then the entry links out to NCBI.

Coloring for track events is as follows:

- paternally expressed -> blue
- maternally expressed -> pink
- all others -> gray

OMIM Tracks

Source: omim.org. Includes all genes represented in OMIM (Online Mendelian Inheritance in Man), an online catalog of human genes and genetic disorders. Includes all OMIM related tracks in VIA. The OMIM API is used to obtain data and only hg38 genomic coordinates are provided by OMIM. Locations for build 37 tracks are obtained from RefSeq Genes, curated subset by mapping gene names. For genes in OMIM data that are not in RefSeq curated, the positions are obtained from UCSC Genes. For build 37 OMIM Syndromes, the provided cytoband location is used and the corresponding hg19 coordinates for the cytoband are displayed. OMIM Syndromes in build 38 uses the OMIM provided genomic coordinates therefore variations may be seen between hg19 and hg38 where hg38 may have more precise coordinates than hg19.

OMIM Genes - All genes represented in OMIM.

OMIM Morbid Phenotypes - Cytogenomic locations of the genes associated with disorders (OMIM Morbid Map) as well as phenotypes and mode of inheritance (where available) from OMIM.

Event coloring for OMIM tracks (excluding Syndromes tracks):

- Dominant events -> green
- Recessive events -> orange
- Morbid genes -> black
- All other events -> gray

OMIM Syndromes - Cytogenomic locations of deletion and duplication syndromes represented in OMIM.

OMIM Syndromes includes syndromes not labeled as deletion or duplication syndromes. These additional entries are not represented in the OMIM Morbid Phenotypes Deletion Syndromes or OMIM Morbid Phenotypes Duplication Syndromes tracks.

For build 37 OMIM Syndromes, the provided cytoband location is used and the corresponding hg19 coordinates for the cytoband are displayed. OMIM Syndromes in build 38 uses the OMIM provided genomic coordinates therefore variations may be seen between hg19 and hg38 where hg38 may have more precise coordinates than hg19.

OMIM Syndromes coloring:

- Duplication syndromes -> blue
- Deletion syndromes -> red
- Syndromes not labeled as deletion or duplication -> black

RefSeq Tracks

Includes RefSeq Genes, RefSeq Exons, RefSeq Coding Genes, RefSeq Non-Coding Genes and Mitochondrial Genes. Source: NCBI RefSeq Genes (curated subset) from the UCSC Genome Browser and GENCODE project in V46 (Ensembl 112) release. These are the same sources as those for the Genes track.

RefSeq Genes - Locations of official RefSeq genes (NCBI RefSeq genes, curated subset).

RefSeq Exons - Locations of exons of the RefSeq genes (NCBI RefSeq genes, curated subset).

RefSeq Coding Genes and **RefSeq Non-Coding Genes** - Genes that are annotated as coding genes or non-coding genes, respectively, by the GENCODE project in V46 (Ensembl 112) release. The gene position is the same as that in the Genes track (NCBI RefSeq curated subset obtained from UCSC Annotation Downloads). GENCODE is used only to label genes as coding/non-coding. The GENCODE Genes show high-quality manual annotations merged with evidence-based automated annotations across the entire human genome generated by the GENCODE project. The annotation was conducted on genome assembly GRCh38.

Segmental Duplications Tracks

Source: UCSC.

A summary of large genomic duplications (>1kb, >90% similar) in the genome. Detailed track description at https://genome.ucsc.edu/cgi-bin/hgTables. For a region to be included in the track, at least 1 Kb of the total sequence (containing at least 500bp of non-RepeatMasked sequence) had to align and a sequence identity of at least 90% was required.

Solve CNV Mask

Source: Bionano

Mask Generated from Control Database samples for CNV masking. Used to mask regions of unreliable and common CNV calls. The CNV mask is applicable to samples processed on Solve version 3.8.3.

Region File Update Procedure

Bionano routinely provides updated files to VIA Administrators and checks external database sites for any updates. If there are updates to the database, Bionano obtains the files and processes them for use within VIA and assesses and validates the files before uploading onto the update server. The VIA system checks this server on a regular basis for any updates; if updates are available, the VIA Administrator is alerted when they log into VIA.

If there are no updates to the external databases, Bionano does not post new files to the update server and hence no alert goes out to the VIA Administrator. If a region file in VIA has not been updated in a while, it is because the external database has not been updated as Bionano checks regularly for any updates.

Region files have two main components to which changes may occur:

- Actual content (genes, locations, classifications, etc.) in the source database
- Meta properties which are the meta data for the region file (Bionano version for the region file, description of the content in the file, download date, etc.)

Sometimes there may be changes to the meta properties of the region files resulting in an available update even though no clinical/genomic content has changed within the source files.

Update Process for Region Files

1. Bionano checks the external database to see if there are any updates.
2. If there are updates:
    a) Bionano obtains the files and processes them for use within VIA.
    b) A version number is assigned to each region file for tracking and auditing.
    c) The region properties file is updated to indicate:
        i. the date the files were downloaded by Bionano from the external database
        ii. the date the external database itself was last updated
    a) Bionano validates the new region files:
        i. Reviews to make sure the source file retrieval and resulting file creations worked correctly and performs spot checking of a few genes/regions in the region/annotation files.
        ii. Tests the new region/annotation files in VIA
        iii. Tests the update system with the new files

b) Customers are notified about upcoming annotation and track updates via email. Sites connected to the internet will also get a notification within VIA.

1. If the external database has not been updated since Bionano last obtained the files, region files will have no content changes but may have an update available depending on changes to the meta properties of the region file.

   a) If the meta properties (description/version) are not updated, no update for that region file will be available. Meta properties include source database version and download date or date checked for new content; but these are not updated each time to prevent triggering unnecessary region file updates.

   b) If meta properties are updated, the region file will have an update available.

   c) Roughly once a year for each region file the meta properties will be updated to reflect that the source database was checked and there was no updated content available.

Update Process for Internal Annotation Files

Internal annotation files are integral to the system and are provided with each VIA installation. These include RefSeq genes, genome assembly, DGV, and HPO terms. The same procedure as that for region files is followed for updating these files.

Technical Assistance

For technical assistance, contact Bionano Technical Support.

You can retrieve documentation on Bionano products, SDS's, certificates of analysis, frequently asked questions, and other related documents from the Support website or by request through e-mail and telephone.

TYPE	CONTACT
Email	support@bionano.com
Phone	Hours of Operation: Monday through Friday, 9:00 a.m. to 5:00 p.m., PST US: +1 (858) 888-7663 Monday through Friday, 9:00 a.m. to 5:00 p.m., CET UK: +44 115 654 8660 France: +33 5 37 10 00 77 Belgium: +32 10 39 71 00
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