
TransVar Documentation

Release 2.4.1

Wanding Zhou

Aug 20, 2018

1	Download and Install	3
1.1	Install using pip	3
1.2	Download the program	3
1.3	Dependency	4
1.4	Install from source	4
2	Quick Start	5
3	Setup and Customize	7
3.1	Use environment variables	7
3.2	Install and specify reference genome assembly	7
3.3	Install and specify transcript annotations	8
3.4	Know Current configuration	9
3.5	Set default reference builds	9
3.6	Use Additional Resources	9
3.7	Control the length of reference sequence	10
4	Genomic level annotation	11
4.1	Short genomic regions	11
4.2	Long genomic regions	11
4.3	Genomic variant	13
4.4	Promoter region	17
4.5	Splice sites	18
4.6	UTR region	19
4.7	Non-coding RNA	20
4.8	Coding Start and Stop	21
4.9	Batch processing	22
5	Protein level annotation	25
5.1	Protein sites	25
5.2	Protein motif	25
5.3	Protein region	26
5.4	Protein variants	26
5.5	Whole transcript	30
5.6	Search alternative codon identifiers	31
6	cDNA level annotation	35

6.1	cDNA region	35
6.2	cDNA variant	35
7	Interpret consequence labels (CSQN)	43
7.1	General	43
7.2	Coding Start/Stop	43
7.3	Coding Insertion/Deletion	44
7.4	Intronic	44
7.5	Intergenic	44
7.6	Splice site	44
7.7	Others	44
8	Inspect variant sequences	45
8.1	Missense substitution	45
8.2	Deletion	46
8.3	Insertion	46
8.4	Block substitution	47
8.5	Frameshift sequence	48
9	FAQ	49
9.1	How to batch-process?	49
9.2	How to use VCF as input?	50
9.3	How to automatically decompose a haplotype into multiple mutations?	50
9.4	How to use 3-letter code instead of 1-letter code for protein?	51
9.5	How can I let TransVar output sequence context?	51
9.6	How to report results in one line for each query?	51
9.7	I got 'gene_not_recognized', what's wrong?	51
9.8	Does TransVar support alternative format for MNV such as c.508_509CC>TT?	52
9.9	Does TransVar support relaxed input without 'g.', 'c.' and 'p.'?	52
9.10	When I annotate a variant for protein identifier, why would I end up getting results in another variant type?	52
10	Features	53
11	License	55
12	Need Help	57
13	Indices and tables	59

Contents:

1.1 Install using pip

```
sudo pip install transvar
```

or locally

```
pip install --user transvar
```

to upgrade from a previous version

```
pip install -U transvar
```

1.2 Download the program

1.2.1 Current release

Latest release is available [here](#)

For all previous versions, see [here](#)

1.2.2 Other old stable releases

- stable 2.0.x version [v2.0.12.20150626](#)
- stable 1.x version [v1.40](#)

1.3 Dependency

The only requirement for building TransVar are Python 2.7 and a reasonably modern C compiler such as gcc.

1.4 Install from source

1.4.1 Local install

```
python setup.py install --prefix [folder]
```

The installation will create two subfolders: `[folder]/lib` (which would contain libraries) and `[folder]/bin` (which would contain transvar executable).

When you run transvar, make sure `[folder]/lib/python2.7/site-packages` is in your PYTHONPATH. In some occasions, you need to `mkdir -p [folder]/lib/python2.7/site-packages` to make sure it exists before you could run `setup.py`. You can add it by putting

```
export PYTHONPATH=$PYTHONPATH:[folder]/lib/python-2.7/site-packages/
```

to your `.bashrc` or `.profile` depending on your OS.

The installed executable is `[folder]/bin/transvar`.

1.4.2 System-wise install (need root)

```
sudo python setup.py install
```


Here we show how one can use TransVar on human hg19 (GRCh37).

```
# set up databases
transvar config --download_anno --refversion hg19

# in case you don't have a reference
transvar config --download_ref --refversion hg19

# in case you do have a reference to link
transvar config -k reference -v [path_to_hg19.fa] --refversion hg19
```

Test an input:

```
$ transvar panno -i 'PIK3CA:p.E545K' --ucsc --ccds
```

outputs show two hits from the two databases, i.e., UCSC and CCDS.

```
PIK3CA:p.E545K      NM_006218 (protein_coding)      PIK3CA  +
chr3:g.178936091G>A/c.1633G>A/p.E545K      inside_[cds_in_exon_10]
CSQN=Missense;reference_codon=GAG;candidate_codons=AAG,AAA;candidate_mnv_vari
ants=chr3:g.178936091_178936093delGAGinsAAA;dbsnp=rs104886003(chr3:178936091G
>A);source=UCSCRefGene
PIK3CA:p.E545K      CCDS43171 (protein_coding)      PIK3CA  +
chr3:g.178936091G>A/c.1633G>A/p.E545K      inside_[cds_in_exon_9]
CSQN=Missense;reference_codon=GAG;candidate_codons=AAG,AAA;candidate_mnv_vari
ants=chr3:g.178936091_178936093delGAGinsAAA;dbsnp=rs104886003(chr3:178936091G
>A);source=CCDS
```

One could provide input based on transcript ID, e.g **NM_006218.1:p.E545K** and TransVar would automatically restrict to the provided transcript.

```
$ transvar panno -i 'NM_006218.2:p.E545K' --ucsc --ccds
```

outputs

```
NM_006218.2:p.E545K NM_006218 (protein_coding) PIK3CA +  
chr3:g.178936091G>A/c.1633G>A/p.E545K inside_[cds_in_exon_10]  
CSQN=Missense;reference_codon=GAG;candidate_codons=AAG,AAA;candidate_mnv_vari  
ants=chr3:g.178936091_178936093delGAGinsAAA;dbsnp=rs104886003(chr3:178936091G  
>A);source=UCSCRefGene
```

3.1 Use environment variables

3.1.1 TRANSVAR_CFG

store the path to transvar.cfg

```
export TRANSVAR_CFG=path_to_transvar.cfg
```

If not specified, TransVar will use `[installdir]/lib/transvar/transvar.cfg` directory or your local `~/.transvar.cfg` if the installation directory is inaccessible.

3.1.2 TRANSVAR_DOWNLOAD_DIR

store the path to the directory where auto-download of annotation and reference go

```
export TRANSVAR_DOWNLOAD_DIR=path_to_transvar_download_directory
```

If not specified, TransVar will use `[installdir]/lib/transvar/transvar.download` directory or your local `~/.transvar.download` if the installation directory is inaccessible.

3.2 Install and specify reference genome assembly

3.2.1 Download from TransVar database

For some genome assembly (currently hg18, hg19, hg38, mm9 and mm10) we provide download via

```
transvar config --download_ref --refversion [reference name]
```

See `transvar config -h` for all choices of `[reference name]`.

3.2.2 Manual download and index

For other genome assemblies, one could manually download the genome as one file and index it manually by,

```
samtools faidx [fasta]
```

Once downloaded and indexed, the genome can be used through the “--reference” option followed by path to the genome:

```
transvar ganno -i "chr1:g.30000000_30000001" --gencode --reference path_to_hg19.fa
```

or “--refversion” followed by the short version id.

```
transvar ganno -i "chr1:g.30000000_30000001" --gencode --refversion hg19
```

One can store the location in *transvar.cfg* file. To set the default location of genome file for a reference version, say, to *path_to_hg19.fa*,

```
transvar config -k reference -v path_to_hg19.fa --refversion hg19
```

will create in *transvar.cfg* an entry

```
[hg19]
reference = hg19.fa
```

so that there is no need to specify the location of reference on subsequent usages.

3.3 Install and specify transcript annotations

3.3.1 Download from TransVar database

One could automatically download transcript annotations via E.g.,

```
transvar config --download_anno --refversion hg19
```

which download annotation from TransVar database to `[installdir]/lib/transvar/transvar.download` directory or your local `~/transvar.download` if the installation directory is inaccessible. See `transvar config -h` for all version names. These will also create default mappings under the corresponding reference version section of *transvar.cfg* like

```
[hg19]
ucsc = /home/wzhou1/download/hg19.ucsc.txt.gz
```

3.3.2 Index from GTF files

TransVar databases can be obtained from indexing a GTF file. For example,

```
transvar index --refseq hg38.refseq.gff.gz
```

The above will create a bunch of transvar database files with the suffix `hg38.refseq.gff.gz.transvardb*`.

3.3.3 Download from Ensembl ftp

One also has the option of downloading from Ensembl collection.

```
transvar config --download_ensembl --refversion mus_musculus
```

Without specifying the refversion, user will be prompted a collection of options to choose from.

3.4 Know Current configuration

To show the location and the content of currently used transvar.cfg, one may also run

```
transvar config
```

which returns information about the setup regarding to the current reference selection, including the location of the reference file and database file.

```
Current reference version: mm10
reference: /home/wzhou/genomes_link/mm10/mm10.fa
Available databases:
refseq: /home/wzhou/tools/transvar/transvar/transvar.download/mm10.refseq.gff.gz
ccds: /home/wzhou/tools/transvar/transvar/transvar.download/mm10.ccds.txt
ensembl: /home/wzhou/tools/transvar/transvar/transvar.download/mm10.ensembl.gtf.gz
```

specifying `--refversion` displays the information under that reference version (without changing the default reference version setup).

3.5 Set default reference builds

To switch reference build

```
transvar config --switch_build mm10
```

switches the default reference build to mm10. This is equivalent to

```
transvar config -k refversion -v mm10
```

which sets the refversion slot explicitly.

3.6 Use Additional Resources

TransVar uses optional additional resources for annotation.

3.6.1 dbSNP

For example, one could annotate SNP with dbSNP id by downloading the dbSNP files. This can be done by

```
transvar config --download_dbsnp
```

TransVar automatically download dbSNP file which corresponding to the current default reference version (as set in **transvar.cfg**). This also sets the entry in **transvar.cfg**. With dbSNP file downloaded, TransVar automatically looks for dbSNP id when performing annotation.

```
transvar panno -i 'A1CF:p.A309A' --ccds
```

```
A1CF:p.A309A CCDS7243 (protein_coding)      A1CF      -
chr10:g.52576004T>G/c.927A>C/p.A309A      inside_[cds_in_exon_7]
CSQN=Synonymous;reference_codon=GCA;candidate_codons=GCC,GCG,GCT;candidate_snv_variants=chr10:g.52576004T>C,chr10:g.52576004T>A;dbsnp=rs201831949(chr10:52576004T>G);source=CCDS
```

Note that in order to use dbSNP, one must download the dbSNP database through

```
transvar config --download_dbsnp
```

or by configure the dbsnp slot in the configure file via

```
transvar config -k dbsnp -v [path to dbSNP VCF]
```

Manually set path for dbSNP file must have the file tabix indexed.

3.7 Control the length of reference sequence

TransVar reduces the reference sequence in a deletion to its length when the deleted reference sequence is too long. For example

```
$ transvar ganno -i 'chr14:g.101347000_101347023del' --ensembl
```

outputs

```
chr14:g.101347000_101347023del      ENST00000534062 (protein_coding)      RTL1      -
chr14:g.101347000_101347023del24/c.4074+29_4074+52del24/. inside_[3-UTR;noncoding_
↳exon_1]
CSQN=3-UTRDeletion;left_align_gDNA=g.101347000_101347023del24;unaligned_gDNA=g.101347000_101347023del24;left_align_cDNA=c.4074+29_4074+52del24;unaligned_cDNA=c.4074+29_4074+52del24;aliases=ENSP00000435342;source=Ensembl
```

where the deletion sequence is reduced to its length (*del24*). The *-seqmax* option changes the length threshold (default:10) when this behavior occur. When *-seqmax* is negative, the threshold is lifted such that the reference sequence is always reported regardless of its length, i.e.,

```
$ transvar ganno -i 'chr14:g.101347000_101347023del' --ensembl --seqmax -1
```

outputs the full reference sequence:

```
chr14:g.101347000_101347023del      ENST00000534062 (protein_coding)      RTL1      -
chr14:g.101347000_101347023delTTGGGGTGAGAAATAGAGGGGACT/c.4074+29_
↳4074+52delAGTCCCCTCTATTCTCACCCCAA/.      inside_[3-UTR;noncoding_exon_1]
CSQN=3-UTRDeletion;left_align_gDNA=g.101347000_101347023delTTGGGGTGAGAAATAGAGGGGACT;unaligned_gDNA=g.101347000_101347023delTTGGGGTGAGAAATAGAGGGGACT;left_align_cDNA=c.4074+29_4074+52delAGTCCCCTCTATTCTCACCCCAA;unaligned_cDNA=c.4074+29_4074+52delAGTCCCCTCTATTCTCACCCCAA;aliases=ENSP00000435342;source=Ensembl
```

Genomic level annotation

Annotation from genomic level is handled by the *ganno* subcommand in TransVar.

4.1 Short genomic regions

To annotate a short genomic region in a gene,

```
$ transvar ganno --ccds -i 'chr3:g.178936091_178936192'
```

outputs

```
chr3:g.178936091_178936192    CCDS43171 (protein_coding)    PIK3CA  +
chr3:g.178936091_178936192/c.1633_1664+70/p.E545_R555    from_[cds_in_exon_9]_to_
↪[intron_between_exon_9_and_10]
C2=donor_splice_site_on_exon_9_at_chr3:178936123_included;start_codon=1789360
91-178936092-178936093;end_codon=178936121-178936122-178936984;source=CCDS
```

Results indicates the beginning position is at coding region while ending position is at intronic region (c.1633_1664+70). Note that there is no consequence label (*CSQN* tag) when performing a region annotation (instead of a variant).

For intergenic sites, TransVar also reports the identity and distance to the gene upstream and downstream. For example, *chr6:116991832* is simply annotated as intergenic in the original annotation. TransVar reveals that it is 1,875 bp downstream to ZUFSP and 10,518 bp upstream to KPNA5 showing a vicinity to the gene ZUFSP. There is no limit in the reported distance. If a site is at the end of the chromosome, TransVar is able to report the distance to the telomere.

4.2 Long genomic regions

```
$ transvar ganno -i 'chr19:g.41978629_41983350' --ensembl --refversion mm10
```

```

chr19:g.41978629_41983350   ENSMUST00000167927 (nonsense_mediated_decay),
↳ENSMUST00000026170 (protein_coding)           MMS19,UBTD1      -,+
chr19:g.41978629_41983350/./.   from_[intron_between_exon_1_and_2;MMS19]_to_
↳[intron_between_exon_1_and_2;UBTD1]
.
chr19:g.41978629_41983350   ENSMUST00000171561 (protein_coding),ENSMUST00000026170_
↳(protein_coding) MMS19,UBTD1      -,+
chr19:g.41978629_41983350/./.   from_[intron_between_exon_1_and_2;MMS19]_to_
↳[intron_between_exon_1_and_2;UBTD1]
.
chr19:g.41978629_41983350   ENSMUST00000163398 (nonsense_mediated_decay),
↳ENSMUST00000026170 (protein_coding)           MMS19,UBTD1      -,+
chr19:g.41978629_41983350/./.   from_[intron_between_exon_1_and_2;MMS19]_to_
↳[intron_between_exon_1_and_2;UBTD1]
.
chr19:g.41978629_41983350   ENSMUST00000164776 (nonsense_mediated_decay),
↳ENSMUST00000026170 (protein_coding)           MMS19,UBTD1      -,+
chr19:g.41978629_41983350/./.   from_[intron_between_exon_1_and_2;MMS19]_to_
↳[intron_between_exon_1_and_2;UBTD1]
.
chr19:g.41978629_41983350   ENSMUST00000026168 (protein_coding),ENSMUST00000026170_
↳(protein_coding) MMS19,UBTD1      -,+
chr19:g.41978629_41983350/./.   from_[intron_between_exon_1_and_2;MMS19]_to_
↳[intron_between_exon_1_and_2;UBTD1]
.
chr19:g.41978629_41983350   ENSMUST00000171755 (retained_intron),ENSMUST00000026170_
↳(protein_coding)           MMS19,UBTD1      -,+
chr19:g.41978629_41983350/./.   from_[intron_between_exon_1_and_2;MMS19]_to_
↳[intron_between_exon_1_and_2;UBTD1]
.
chr19:g.41978629_41983350   ENSMUST00000169775 (nonsense_mediated_decay),
↳ENSMUST00000026170 (protein_coding)           MMS19,UBTD1      -,+
chr19:g.41978629_41983350/./.   from_[intron_between_exon_1_and_2;MMS19]_to_
↳[intron_between_exon_1_and_2;UBTD1]
.
chr19:g.41978629_41983350   ENSMUST00000168484 (nonsense_mediated_decay),
↳ENSMUST00000026170 (protein_coding)           MMS19,UBTD1      -,+
chr19:g.41978629_41983350/./.   from_[intron_between_exon_1_and_2;MMS19]_to_
↳[intron_between_exon_1_and_2;UBTD1]
.

```

Results indicates a 4721 bp region spanning the promoters of two closely located, opposite-oriented genes MMS19 and UBTD1. The starting point and ending point are situated in the first introns of the two genes.

```
$ transvar ganno -i '9:g.133750356_137990357' --ccds
```

outputs

```

9:g.133750356_137990357   CCDS35165 (protein_coding),CCDS6986 (protein_coding)
↳ABL1,OLFM1      +,+
chr9:g.133750356_137990357/./.   from_[cds_in_exon_7;ABL1]_to_[intron_between_
↳exon_4_and_5;OLFM1]_spanning_[51_genes]
.
9:g.133750356_137990357   CCDS35166 (protein_coding),CCDS6986 (protein_coding)
↳ABL1,OLFM1      +,+
chr9:g.133750356_137990357/./.   from_[cds_in_exon_7;ABL1]_to_[intron_between_
↳exon_4_and_5;OLFM1]_spanning_[51_genes]
.

```


The result indicates that the region span 53 genes. The beginning of the region resides in the coding sequence of ABL1, c.1187A and the ending region resides in the intronic region of OLFM1, c.622+6C. 2 different usage of transcripts in annotating the starting position is represented in two lines, each line corresponding to a combination of transcript usage. This annotation not only shows the coverage of the region, also reveals the fine structure of the boundary.

In another example, where the ending position exceeds the length of the chromosome, TransVar truncates the region and outputs upstream and downstream information of the ending position.

```
$ transvar ganno -i '9:g.133750356_1337503570' --ccds
```

outputs

```
9:g.133750356_1337503570    CCDS35165 (protein_coding),    ABL1,    +
  chr9:g.133750356_141213431/./.    from_[cds_in_exon_7;ABL1]_to_[intergenic_between_
  ↪EHMT1(484,026_bp_downstream)_and_3'-telomere(0_bp)]_spanning_[136_genes]
.
9:g.133750356_1337503570    CCDS35166 (protein_coding),    ABL1,    +
  chr9:g.133750356_141213431/./.    from_[cds_in_exon_7;ABL1]_to_[intergenic_between_
  ↪EHMT1(484,026_bp_downstream)_and_3'-telomere(0_bp)]_spanning_[136_genes]
.
```

4.3 Genomic variant

4.3.1 Single nucleotide variation (SNV)

This is the forward annotation

```
$ transvar ganno --ccds -i 'chr3:g.178936091G>A'
```

outputs

```
chr3:g.178936091G>A    CCDS43171 (protein_coding)    PIK3CA    +
  chr3:g.178936091G>A/c.1633G>A/p.E545K    inside_[cds_in_exon_9]
  CSQN=Missense;dbsnp=rs104886003 (chr3:178936091G>A);codon_pos=178936091-178936
  092-178936093;ref_codon_seq=GAG;source=CCDS
```

Another example:

```
$ transvar ganno -i "chr9:g.135782704C>G" --ccds
```

outputs

```
chr9:g.135782704C>G    CCDS6956 (protein_coding)    TSC1    -
  chr9:g.135782704C>G/c.1317G>C/p.L439L    inside_[cds_in_exon_11]
  CSQN=Synonymous;dbsnp=rs770692313 (chr9:135782704C>G);codon_pos=135782704-1357
  82705-135782706;ref_codon_seq=CTG;source=CCDS
chr9:g.135782704C>G    CCDS55350 (protein_coding)    TSC1    -
  chr9:g.135782704C>G/c.1164G>C/p.L388L    inside_[cds_in_exon_10]
  CSQN=Synonymous;dbsnp=rs770692313 (chr9:135782704C>G);codon_pos=135782704-1357
  82705-135782706;ref_codon_seq=CTG;source=CCDS
```

and a nonsense mutation:

```
$ transvar ganno -i 'chr1:g.115256530G>A' --ensembl
```

outputs

```
chr1:g.115256530G>A ENST00000369535 (protein_coding) NRAS -
chr1:g.115256530G>A/c.181C>T/p.Q61* inside_[cds_in_exon_3]
CSQN=Nonsense;codon_pos=115256528-115256529-115256530;ref_codon_seq=CAA;alias
es=ENSP00000358548;source=Ensembl
```

CSQN fields indicates a nonsense mutation.

4.3.2 Deletions

A frameshift deletion

```
$ transvar ganno -i "chr2:g.234183368_234183380del" --ccds
```

outputs

```
chr2:g.234183368_234183380del CCDS2502 (protein_coding) ATG16L1 +
chr2:g.234183368_234183380del13/c.841_853del13/p.T281Lfs*5 inside_[cds_in_
↳exon_8]
CSQN=Frameshift;left_align_gDNA=g.234183367_234183379del13;unaligned_gDNA=g.2
34183368_234183380del13;left_align_cDNA=c.840_852del13;unalign_cDNA=c.841_853
del13;source=CCDS
chr2:g.234183368_234183380del CCDS2503 (protein_coding) ATG16L1 +
chr2:g.234183368_234183380del13/c.898_910del13/p.T300Lfs*5 inside_[cds_in_
↳exon_9]
CSQN=Frameshift;left_align_gDNA=g.234183367_234183379del13;unaligned_gDNA=g.2
34183368_234183380del13;left_align_cDNA=c.897_909del13;unalign_cDNA=c.898_910
del13;source=CCDS
chr2:g.234183368_234183380del CCDS54438 (protein_coding) ATG16L1 +
chr2:g.234183368_234183380del13/c.409_421del13/p.T137Lfs*5 inside_[cds_in_
↳exon_5]
CSQN=Frameshift;left_align_gDNA=g.234183367_234183379del13;unaligned_gDNA=g.2
34183368_234183380del13;left_align_cDNA=c.408_420del13;unalign_cDNA=c.409_421
del13;source=CCDS
```

Note the difference between left-aligned identifier and the right aligned identifier.

An in-frame deletion

```
$ transvar ganno -i "chr2:g.234183368_234183379del" --ccds
```

outputs

```
chr2:g.234183368_234183379del CCDS2502 (protein_coding) ATG16L1 +
chr2:g.234183368_234183379del12/c.841_852del12/p.T281_G284delTHPG inside_[cds_in_
↳exon_8]
CSQN=InFrameDeletion;left_align_gDNA=g.234183367_234183378del12;unaligned_gDN
A=g.234183368_234183379del12;left_align_cDNA=c.840_851del12;unalign_cDNA=c.84
1_852del12;left_align_protein=p.T281_G284delTHPG;unalign_protein=p.T281_G284d
elTHPG;source=CCDS
chr2:g.234183368_234183379del CCDS2503 (protein_coding) ATG16L1 +
chr2:g.234183368_234183379del12/c.898_909del12/p.T300_G303delTHPG inside_[cds_in_
↳exon_9]
CSQN=InFrameDeletion;left_align_gDNA=g.234183367_234183378del12;unaligned_gDN
A=g.234183368_234183379del12;left_align_cDNA=c.897_908del12;unalign_cDNA=c.89
8_909del12;left_align_protein=p.T300_G303delTHPG;unalign_protein=p.T300_G303d
```

(continues on next page)

(continued from previous page)

```

elTHPG;source=CCDS
chr2:g.234183368_234183379del      CCDS54438 (protein_coding)      ATG16L1 +
chr2:g.234183368_234183379del12/c.409_420del12/p.T137_G140delTHPG inside_[cds_in_
↔exon_5]
CSQN=InFrameDeletion;left_align_gDNA=g.234183367_234183378del12;unaligned_gDN
A=g.234183368_234183379del12;left_align_cDNA=c.408_419del12;unalign_cDNA=c.40
9_420del12;left_align_protein=p.T137_G140delTHPG;unalign_protein=p.T137_G140d
elTHPG;source=CCDS

```

Another example

```
$ transversanno --ccds -i 'chr12:g.53703425_53703427del'
```

outputs

```

chr12:g.53703425_53703427del CCDS8856 (protein_coding)      AAAS      -
chr12:g.53703427_53703429delCCC/c.769_771delGGG/p.G257delG      inside_[cds_in_
↔exon_8]
CSQN=InFrameDeletion;left_align_gDNA=g.53703424_53703426delCCC;unaligned_gDNA
=g.53703425_53703427delCCC;left_align_cDNA=c.766_768delGGG;unalign_cDNA=c.768
_770delGGG;left_align_protein=p.G256delG;unalign_protein=p.G256delG;source=CC
DS
chr12:g.53703425_53703427del CCDS53797 (protein_coding)      AAAS      -
chr12:g.53703427_53703429delCCC/c.670_672delGGG/p.G224delG      inside_[cds_in_
↔exon_7]
CSQN=InFrameDeletion;left_align_gDNA=g.53703424_53703426delCCC;unaligned_gDNA
=g.53703425_53703427delCCC;left_align_cDNA=c.667_669delGGG;unalign_cDNA=c.669
_671delGGG;left_align_protein=p.G223delG;unalign_protein=p.G223delG;source=CC
DS

```

Note the difference between left and right-aligned identifiers on both protein level and cDNA level.

An in-frame out-of-phase deletion

```
$ transversanno -i "chr2:g.234183372_234183383del" --ccds
```

outputs

```

chr2:g.234183372_234183383del      CCDS2502 (protein_coding)      ATG16L1 +
chr2:g.234183372_234183383del12/c.845_856del12/p.H282_G286delinsR inside_[cds_in_
↔exon_8]
CSQN=MultiAAMissense;left_align_gDNA=g.234183372_234183383del12;unaligned_gDN
A=g.234183372_234183383del12;left_align_cDNA=c.845_856del12;unalign_cDNA=c.84
5_856del12;source=CCDS
chr2:g.234183372_234183383del      CCDS2503 (protein_coding)      ATG16L1 +
chr2:g.234183372_234183383del12/c.902_913del12/p.H301_G305delinsR inside_[cds_in_
↔exon_9]
CSQN=MultiAAMissense;left_align_gDNA=g.234183372_234183383del12;unaligned_gDN
A=g.234183372_234183383del12;left_align_cDNA=c.902_913del12;unalign_cDNA=c.90
2_913del12;source=CCDS
chr2:g.234183372_234183383del      CCDS54438 (protein_coding)      ATG16L1 +
chr2:g.234183372_234183383del12/c.413_424del12/p.H138_G142delinsR inside_[cds_in_
↔exon_5]
CSQN=MultiAAMissense;left_align_gDNA=g.234183372_234183383del12;unaligned_gDN
A=g.234183372_234183383del12;left_align_cDNA=c.413_424del12;unalign_cDNA=c.41
3_424del12;source=CCDS

```

4.3.3 Insertions

An in-frame insertion of three nucleotides

```
$ transvar ganno -i 'chr2:g.69741762_69741763insTGC' --ccds
```

outputs

```
chr2:g.69741762_69741763insTGC      CCDS1893 (protein_coding)      AAK1      -
chr2:g.69741780_69741782dupCTG/c.1614_1616dupGCA/p.Q546dupQ      inside_[cds_in_
↳exon_12]
CSQN=InFrameInsertion;left_align_gDNA=g.69741762_69741763insTGC;unalign_gDNA=
g.69741762_69741763insTGC;left_align_cDNA=c.1596_1597insCAG;unalign_cDNA=c.16
14_1616dupGCA;left_align_protein=p.Y532_Q533insQ;unalign_protein=p.Q539dupQ;p
hase=2;source=CCDS
```

Note the proper right-alignment of protein level insertion Q. The left-aligned identifier is also given in the *LEFTALN* field.

A frame-shift insertion of two nucleotides

```
$ transvar ganno -i 'chr7:g.121753754_121753755insCA' --ccds
```

outputs

```
chr7:g.121753754_121753755insCA      CCDS5783 (protein_coding)      AASS      -
chr7:g.121753754_121753755insCA/c.1064_1065insGT/p.I355Mfs*10      inside_[cds_in_
↳exon_9]
CSQN=Frameshift;left_align_gDNA=g.121753753_121753754insAC;unalign_gDNA=g.121
753754_121753755insCA;left_align_cDNA=c.1063_1064insTG;unalign_cDNA=c.1063_10
64insTG;source=CCDS
```

```
$ transvar ganno -i 'chr17:g.79093270_79093271insGGGCGT' --ccds
```

outputs

```
chr17:g.79093270_79093271insGGGCGT      CCDS45807 (protein_coding)      AATK      -
chr17:g.79093282_79093287dupTGGGCG/c.3988_3993dupACGCC/p.T1330_P1331dupTP      ↳
↳inside_[cds_in_exon_13]
CSQN=InFrameInsertion;left_align_gDNA=g.79093270_79093271insGGGCGT;unalign_gD
NA=g.79093270_79093271insGGGCGT;left_align_cDNA=c.3976_3977insCGCCCA;unalign_
cDNA=c.3988_3993dupACGCC;left_align_protein=p.A1326_P1327insPT;unalign_prote
in=p.T1330_P1331dupTP;phase=0;source=CCDS
```

Notice the difference in the inserted sequence when left-alignment and right-alignment conventions are followed.

A frame-shift insertion of one nucleotides in a homopolymer

```
$ transvar ganno -i 'chr7:g.117230474_117230475insA' --ccds
```

outputs

```
chr7:g.117230474_117230475insA      CCDS5773 (protein_coding)      CFTR      +
chr7:g.117230479dupA/c.1752dupA/p.E585Rfs*4      inside_[cds_in_exon_13]
CSQN=Frameshift;left_align_gDNA=g.117230474_117230475insA;unalign_gDNA=g.1172
30474_117230475insA;left_align_cDNA=c.1747_1748insA;unalign_cDNA=c.1747_1748i
nsA;source=CCDS
```

Notice the right alignment of cDNA level insertion and the left alignment reported as additional information.

A in-frame, in-phase insertion

```
$ transvar ganno -i 'chr12:g.109702119_109702120insACC' --ccds
```

```
chr12:g.109702119_109702120insACC    CCDS31898 (protein_coding)    ACACB    +
chr12:g.109702119_109702120insACC/c.6870_6871insACC/p.Y2290_H2291insT    inside_
↪[cds_in_exon_49]
CSQN=InFrameInsertion;left_align_gDNA=g.109702118_109702119insCAC;unalign_gDN
A=g.109702119_109702120insACC;left_align_cDNA=c.6869_6870insCAC;unalign_cDNA=
c.6870_6871insACC;left_align_protein=p.Y2290_H2291insT;unalign_protein=p.Y229
0_H2291insT;phase=0;source=CCDS
```

4.3.4 Block substitutions

A block-substitution that results in a frameshift.

```
$ transvar ganno -i 'chr10:g.27329002_27329002delinsAT' --ccds
```

```
chr10:g.27329002_27329002delinsAT    CCDS41499 (protein_coding)    ANKRD26 -
chr10:g.27329009dupT/c.2266dupA/p.M756Nfs*6    inside_[cds_in_exon_21]
CSQN=Frameshift;left_align_gDNA=g.27329002_27329003insT;unalign_gDNA=g.273290
02_27329003insT;left_align_cDNA=c.2259_2260insA;unalign_cDNA=c.2266dupA;sourc
e=CCDS
```

A block-substitution that is in-frame,

```
$ transvar ganno -i 'chr10:g.52595929_52595930delinsAA' --ccds
```

```
chr10:g.52595929_52595930delinsAA    CCDS7243 (protein_coding)    A1CF    -
chr10:g.52595929_52595930delinsAA/c.532_533delinsTT/p.P178L    inside_[cds_in_
↪exon_4]
CSQN=Missense;codon_cDNA=532-533-534;source=CCDS
chr10:g.52595929_52595930delinsAA    CCDS7241 (protein_coding)    A1CF    -
chr10:g.52595929_52595930delinsAA/c.508_509delinsTT/p.P170L    inside_[cds_in_
↪exon_4]
CSQN=Missense;codon_cDNA=508-509-510;source=CCDS
chr10:g.52595929_52595930delinsAA    CCDS7242 (protein_coding)    A1CF    -
chr10:g.52595929_52595930delinsAA/c.508_509delinsTT/p.P170L    inside_[cds_in_
↪exon_4]
CSQN=Missense;codon_cDNA=508-509-510;source=CCDS
```

4.4 Promoter region

One can define the promoter boundary through the `-prombeg` and `-promend` option. Default promoter region is defined from 1000bp upstream of the transcription start site to the transcription start site. One could customize this setting to e.g., [-1000bp, 2000bp] by

```
$ transvar ganno -i 'chr19:g.41978629_41980350' --ensembl --prombeg 2000 --promend_
↪1000 --refversion mm10
```

```

chr19:g.41978629_41980350   ENSMUST00000167927 (nonsense_mediated_decay)  MMS19 -
chr19:g.41978629_41980350/c.115+649_115+2370/.   inside_[intron_between_exon_1_
↔and_2]
  promoter_region_of_[MMS19]_overlapping_237_bp(13.76%);aliases=ENSMUSP000001324
  83;source=Ensembl
chr19:g.41978629_41980350   ENSMUST00000171561 (protein_coding)      MMS19 -
chr19:g.41978629_41980350/c.115+649_115+2370/.   inside_[intron_between_exon_1_
↔and_2]
  promoter_region_of_[MMS19]_overlapping_194_bp(11.27%);aliases=ENSMUSP000001309
  00;source=Ensembl
chr19:g.41978629_41980350   ENSMUST00000163398 (nonsense_mediated_decay)  MMS19 -
chr19:g.41978629_41980350/c.115+649_115+2370/.   inside_[intron_between_exon_1_
↔and_2]
  promoter_region_of_[MMS19]_overlapping_234_bp(13.59%);aliases=ENSMUSP000001268
  64;source=Ensembl
chr19:g.41978629_41980350   ENSMUST00000164776 (nonsense_mediated_decay)  MMS19 -
chr19:g.41978629_41980350/c.115+649_115+2370/.   inside_[intron_between_exon_1_
↔and_2]
  promoter_region_of_[MMS19]_overlapping_215_bp(12.49%);aliases=ENSMUSP000001294
  78;source=Ensembl
chr19:g.41978629_41980350   ENSMUST00000026168 (protein_coding)      MMS19 -
chr19:g.41978629_41980350/c.115+649_115+2370/.   inside_[intron_between_exon_1_
↔and_2]
  promoter_region_of_[MMS19]_overlapping_219_bp(12.72%);aliases=ENSMUSP000000261
  68;source=Ensembl
chr19:g.41978629_41980350   ENSMUST00000171755 (retained_intron)      MMS19 -
chr19:g.41978629_41980350/c.141+649_141+2370/.   inside_[intron_between_exon_1_
↔and_2]
  promoter_region_of_[MMS19]_overlapping_212_bp(12.31%);source=Ensembl
chr19:g.41978629_41980350   ENSMUST00000169775 (nonsense_mediated_decay)  MMS19 -
chr19:g.41978629_41980350/c.115+649_115+2370/.   inside_[intron_between_exon_1_
↔and_2]
  promoter_region_of_[MMS19]_overlapping_214_bp(12.43%);aliases=ENSMUSP000001282
  34;source=Ensembl
chr19:g.41978629_41980350   ENSMUST00000168484 (nonsense_mediated_decay)  MMS19 -
chr19:g.41978629_41980350/c.115+649_115+2370/.   inside_[intron_between_exon_1_
↔and_2]
  promoter_region_of_[MMS19]_overlapping_221_bp(12.83%);aliases=ENSMUSP000001268
  81;source=Ensembl

```

The last result shows that 12-13% of the target region is inside the promoter region. The overlap is as long as ~200 base pairs.

4.5 Splice sites

Consider a splice donor site chr7:5568790_5568791 (a donor site, intron side by definition, reverse strand, chr7:5568792- is the exon),

The 1st exonic nucleotide before donor splice site:

```
$ transvar ganno -i 'chr7:5568792C>G' --ccds
```

output a exonic variation and a missense variation

```
chr7:5568792C>G      CCDS5341 (protein_coding)      ACTB      -
chr7:g.5568792C>G/c.363G>C/p.Q121H      inside_[cds_in_exon_2]
CSQN=Missense;C2=NextToSpliceDonorOfExon2_At_chr7:5568791;codon_pos=5568792-5
568793-5568794;ref_codon_seq=CAG;source=CCDS
```

The 1st nucleotide in the canonical donor splice site (intron side, this is commonly regarded as the splice site location):

```
$ transvar ganno -i 'chr7:5568791C>G' --ccds
```

output a splice variation

```
chr7:5568791C>G      CCDS5341 (protein_coding)      ACTB      -
chr7:g.5568791C>G/c.363+1G>C/.      inside_[intron_between_exon_2_and_3]
CSQN=SpliceDonorSNV;C2=SpliceDonorOfExon2_At_chr7:5568791;source=CCDS
```

The 2nd nucleotide in the canonical donor splice site (2nd on the intron side, still considered part of the splice site):

```
$ transvar ganno -i 'chr7:5568790A>G' --ccds
```

output a splice variation

```
chr7:5568790A>G      CCDS5341 (protein_coding)      ACTB      -
chr7:g.5568790A>G/c.363+2T>C/.      inside_[intron_between_exon_2_and_3]
CSQN=SpliceDonorSNV;C2=SpliceDonorOfExon2_At_chr7:5568791;source=CCDS
```

The 1st nucleotide downstream next to the canonical donor splice site (3rd nucleotide in the intron side, not part of the splice site):

```
$ transvar ganno -i 'chr7:5568789C>G' --ccds
```

output a pure intronic variation

```
chr7:5568789C>G      CCDS5341 (protein_coding)      ACTB      -
chr7:g.5568789C>G/c.363+3G>C/.      inside_[intron_between_exon_2_and_3]
CSQN=IntronicSNV;source=CCDS
```

4.6 UTR region

```
$ transvar ganno -i 'chr2:25564781G>T' --refseq
```

results in a UTR-containing CSQN field

```
chr2:25564781G>T      NM_022552 (protein_coding)      DNMT3A      -
chr2:g.25564781G>T/c.1-27928C>A/.      inside_[5-UTR;noncoding_exon_1]
CSQN=5-UTRSNV;dbxref=GeneID:1788,HGNC:2978,HPRD:04141,MIM:602769;aliases=NP_0
72046;source=RefSeq
chr2:25564781G>T      NM_175629 (protein_coding)      DNMT3A      -
chr2:g.25564781G>T/c.1-27928C>A/.      inside_[5-UTR;intron_between_exon_1_and_2]
CSQN=IntronicSNV;dbxref=GeneID:1788,HGNC:2978,HPRD:04141,MIM:602769;aliases=N
P_783328;source=RefSeq
chr2:25564781G>T      NM_175630 (protein_coding)      DNMT3A      -
chr2:g.25564781G>T/c.1-27928C>A/.      inside_[5-UTR;intron_between_exon_1_and_2]
CSQN=IntronicSNV;dbxref=GeneID:1788,HGNC:2978,HPRD:04141,MIM:602769;aliases=N
P_783329;source=RefSeq
```

4.7 Non-coding RNA

Given Ensembl, GENCODE or RefSeq database, one could annotate non-coding transcripts such as lincRNA. E.g.,

```
$ transvar ganno --gencode -i 'chr1:g.3985200_3985300' --refversion mm10
```

results in

```
chr1:g.3985200_3985300    ENSMUST00000194643 (lincRNA)    RP23-333I7.1    -
  chr1:g.3985200_3985300/c.121_221/.    inside_[noncoding_exon_2]
  source=GENCODE
chr1:g.3985200_3985300    ENSMUST00000192427 (lincRNA)    RP23-333I7.1    -
  chr1:g.3985200_3985300/c.685_785/.    inside_[noncoding_exon_1]
  source=GENCODE
```

or

```
$ transvar ganno --refseq -i 'chr14:g.20568338_20569581' --refversion mm10
```

results in

```
chr14:g.20568338_20569581    NR_033571 (lincRNA)    1810062O18RIK    +
  chr14:g.20568338_20569581/c.260-1532_260-289/.    inside_[intron_between_exon_4_
  ↪and_5]
  dbxref=GeneID:75602,MGI:MGI:1922852;source=RefSeq
chr14:g.20568338_20569581    XM_011245228 (protein_coding)    USP54    -
  chr14:g.20568338_20569581/c.1357+667_1357+1910/.    inside_[intron_between_exon_6_
  ↪and_7]
  dbxref=GeneID:78787,MGI:MGI:1926037;aliases=XP_011243530;source=RefSeq
chr14:g.20568338_20569581    XM_011245226 (protein_coding)    USP54    -
  chr14:g.20568338_20569581/c.1972+667_1972+1910/.    inside_[intron_between_exon_13_
  ↪and_14]
  dbxref=GeneID:78787,MGI:MGI:1926037;aliases=XP_011243528;source=RefSeq
chr14:g.20568338_20569581    NM_030180 (protein_coding)    USP54    -
  chr14:g.20568338_20569581/c.2188+667_2188+1910/.    inside_[intron_between_exon_15_
  ↪and_16]
  dbxref=GeneID:78787,MGI:MGI:1926037;aliases=NP_084456;source=RefSeq
chr14:g.20568338_20569581    XM_011245225 (protein_coding)    USP54    -
  chr14:g.20568338_20569581/c.2359+667_2359+1910/.    inside_[intron_between_exon_16_
  ↪and_17]
  dbxref=GeneID:78787,MGI:MGI:1926037;aliases=XP_011243527;source=RefSeq
chr14:g.20568338_20569581    XM_006519705 (protein_coding)    USP54    -
  chr14:g.20568338_20569581/c.2188+667_2188+1910/.    inside_[intron_between_exon_15_
  ↪and_16]
  dbxref=GeneID:78787,MGI:MGI:1926037;aliases=XP_006519768;source=RefSeq
chr14:g.20568338_20569581    XM_006519703 (protein_coding)    USP54    -
  chr14:g.20568338_20569581/c.2359+667_2359+1910/.    inside_[intron_between_exon_16_
  ↪and_17]
  dbxref=GeneID:78787,MGI:MGI:1926037;aliases=XP_006519766;source=RefSeq
chr14:g.20568338_20569581    XM_011245227 (protein_coding)    USP54    -
  chr14:g.20568338_20569581/c.2359+667_2359+1910/.    inside_[intron_between_exon_16_
  ↪and_17]
  dbxref=GeneID:78787,MGI:MGI:1926037;aliases=XP_011243529;source=RefSeq
chr14:g.20568338_20569581    XM_006519709 (protein_coding)    USP54    -
  chr14:g.20568338_20569581/c.2359+667_2359+1910/.    inside_[intron_between_exon_16_
  ↪and_17]
  dbxref=GeneID:78787,MGI:MGI:1926037;aliases=XP_006519772;source=RefSeq
```

(continues on next page)

(continued from previous page)

```
chr14:g.20568338_20569581 XM_006519708 (protein_coding) USP54 -
chr14:g.20568338_20569581/c.2359+667_2359+1910/. inside_[intron_between_exon_16_
↳and_17]
dbxref=GeneID:78787,MGI:MGI:1926037;aliases=XP_006519771;source=RefSeq
```

or using Ensembl

```
$ transvar ganno --ensembl -i 'chr1:g.29560_29570'
```

results in

```
chr1:g.29560_29570 ENST00000488147 (unprocessed_pseudogene) WASH7P -
chr1:g.29560_29570/c.1_11/. inside_[noncoding_exon_1]
promoter_region_of_[WASH7P]_overlapping_1_bp(9.09%);source=Ensembl
chr1:g.29560_29570 ENST00000538476 (unprocessed_pseudogene) WASH7P -
chr1:g.29560_29570/c.237_247/. inside_[noncoding_exon_1]
source=Ensembl
chr1:g.29560_29570 ENST00000473358 (lincRNA) MIR1302-10 +
chr1:g.29560_29570/c.7_17/. inside_[noncoding_exon_1]
source=Ensembl
```

4.8 Coding Start and Stop

The following illustrates deletion of a coding start.

```
$ transvar ganno -i "chr7:g.5569279_5569288del" --ccds
```

results in

```
chr7:g.5569279_5569288del CCDS5341 (protein_coding) ACTB -
chr7:g.5569279_5569288delCATCATCCAT/c.3_12delGGATGATGAT/. inside_[cds_in_exon_1]
CSQN=CdsStartDeletion;left_align_gDNA=g.5569277_5569286delATCATCATCC;unaligned_gDNA=g.5569279_5569288delCATCATCCAT;left_align_cDNA=c.1_10delATGGATGATG;unaligned_cDNA=c.1_10delATGGATGATG;cds_start_at_chr7:5569288_lost;source=CCDS
```

Deletion of a coding stop

```
$ transvar ganno -i "chr7:g.5567379_5567380del" --ccds
```

results in

Coding start loss due to SNP

```
$ transvar ganno -i "chr7:g.5568911T>A" --refseq
```

results in

```
chr7:g.5568911T>A XM_005249819 (protein_coding) ACTB -
chr7:g.5568911T>A/c.1A>T/. inside_[cds_in_exon_2]
CSQN=CdsStartSNV;C2=cds_start_at_chr7:5568911;dbxref=GeneID:60,HGNC:132,HPRD:00032,MIM:102630;aliases=XP_005249876;source=RefSeq
chr7:g.5568911T>A NM_001101 (protein_coding) ACTB -
chr7:g.5568911T>A/c.244A>T/p.M82L inside_[cds_in_exon_3]
CSQN=Missense;codon_pos=5568909-5568910-5568911;ref_codon_seq=ATG;dbxref=Gene
```

(continues on next page)

(continued from previous page)

```
ID:60,HGNC:132,HPRD:00032,MIM:102630;aliases=NP_001092;source=RefSeq
chr7:g.5568911T>A XM_005249820 (protein_coding) ACTB -
chr7:g.5568911T>A/c.1-564A>T/. inside_[5-UTR;noncoding_exon_3]
CSQN=5-UTRSNV;dbxref=GeneID:60,HGNC:132,HPRD:00032,MIM:102630;aliases=XP_005249877;source=RefSeq
chr7:g.5568911T>A XM_005249818 (protein_coding) ACTB -
chr7:g.5568911T>A/c.244A>T/p.M82L inside_[cds_in_exon_3]
CSQN=Missense;codon_pos=5568909-5568910-5568911;ref_codon_seq=ATG;dbxref=GeneID:60,HGNC:132,HPRD:00032,MIM:102630;aliases=XP_005249875;source=RefSeq
```

Coding stop loss due to SNP

```
$ transvers ganno -i "chr7:g.5567379C>A" --refseq
```

results in

```
chr7:g.5567379C>A XM_005249819 (protein_coding) ACTB -
chr7:g.5567379C>A/c.885G>T/. inside_[cds_in_exon_5]
CSQN=CdsStopSNV;C2=cds_end_at_chr7:5567379;dbxref=GeneID:60,HGNC:132,HPRD:00032,MIM:102630;aliases=XP_005249876;source=RefSeq
chr7:g.5567379C>A NM_001101 (protein_coding) ACTB -
chr7:g.5567379C>A/c.1128G>T/. inside_[cds_in_exon_6]
CSQN=CdsStopSNV;C2=cds_end_at_chr7:5567379;dbxref=GeneID:60,HGNC:132,HPRD:00032,MIM:102630;aliases=NP_001092;source=RefSeq
chr7:g.5567379C>A XM_005249820 (protein_coding) ACTB -
chr7:g.5567379C>A/c.762G>T/. inside_[cds_in_exon_7]
CSQN=CdsStopSNV;C2=cds_end_at_chr7:5567379;dbxref=GeneID:60,HGNC:132,HPRD:00032,MIM:102630;aliases=XP_005249877;source=RefSeq
chr7:g.5567379C>A XM_005249818 (protein_coding) ACTB -
chr7:g.5567379C>A/c.1128G>T/. inside_[cds_in_exon_6]
CSQN=CdsStopSNV;C2=cds_end_at_chr7:5567379;dbxref=GeneID:60,HGNC:132,HPRD:00032,MIM:102630;aliases=XP_005249875;source=RefSeq
```

4.9 Batch processing

To illustrate batch processing with the following small batch input

```
$ cat data/small_batch_input
```

```
chr3 178936091 G A CCDS43171
chr9 135782704 C G CCDS6956
```

```
$ transvers ganno -l data/small_batch_input -g 1 -n 2 -r 3 -a 4 -t 5 --ccds
```

```
chr3|178936091|G|A|CCDS43171 CCDS43171 (protein_coding) PIK3CA +
chr3:g.178936091G>A/c.1633G>A/p.E545K inside_[cds_in_exon_9]
CSQN=Missense;dbSNP=rs104886003(chr3:178936091G>A);codon_pos=178936091-178936092-178936093;ref_codon_seq=GAG;source=CCDS
chr9|135782704|C|G|CCDS6956 CCDS6956 (protein_coding) TSC1 -
chr9:g.135782704C>G/c.1317G>C/p.L439L inside_[cds_in_exon_11]
CSQN=Synonymous;dbSNP=rs770692313(chr9:135782704C>G);codon_pos=135782704-135782705-135782706;ref_codon_seq=CTG;source=CCDS
```

One can also make a HGVS-like input and call

```
$ cat data/small_batch_hgvs
```

```
CCDS43171   chr3:g.178936091G>A
CCDS6956   chr9:g.135782704C>G
```

```
$ transvar ganno -l data/small_batch_hgvs -m 2 -t 1 --ccds
```

```
CCDS43171|chr3:g.178936091G>A      CCDS43171 (protein_coding)      PIK3CA  +
chr3:g.178936091G>A/c.1633G>A/p.E545K      inside_[cds_in_exon_9]
CSQN=Missense;dbsnp=rs104886003 (chr3:178936091G>A);codon_pos=178936091-178936
092-178936093;ref_codon_seq=GAG;source=CCDS
CCDS6956|chr9:g.135782704C>G      CCDS6956 (protein_coding)      TSC1    -
chr9:g.135782704C>G/c.1317G>C/p.L439L      inside_[cds_in_exon_11]
CSQN=Synonymous;dbsnp=rs770692313 (chr9:135782704C>G);codon_pos=135782704-1357
82705-135782706;ref_codon_seq=CTG;source=CCDS
```

The first column for transcript ID restriction is optional.

Protein level annotation

Protein level inputs are handled by the *panno* subcommand.

5.1 Protein sites

To use uniprot id as protein name, one must first download the uniprot id map by

```
transvar config --download_idmap
```

Then one could use protein id instead of gene name by applying the *-uniprot* option to TransVar. For example,

```
$ transvar panno --ccds -i 'Q5VUM1:47' --uniprot
```

```
Q5VUM1:47    CCDS4972 (protein_coding)    C6ORF57 +
chr6:g.71289191_71289193/c.139_141/p.47S    inside_[cds_in_exon_2]
protein_sequence=S;cDNA_sequence=TCC;gDNA_sequence=TCC;source=CCDS
```

TransVar use a keyword extension *ref* in *Q5VUM1:p.47refS* to differentiate from the synonymous mutation *Q5VUM1:p.47S*. The former notation specifies that the reference protein sequence is *S* while the later specifies the target protein sequence is *S*.

5.2 Protein motif

For example, one can find the genomic location of a DRY motif in protein P28222 by issuing the following command,

```
$ transvar panno -i 'P28222:p.146_148refDRY' --uniprot --ccds
```

```
P28222:p.146_148refDRY    CCDS4986 (protein_coding)    HTR1B -
chr6:g.78172677_78172685/c.436_444/p.D146_Y148    inside_[cds_in_exon_1]
```

(continues on next page)

(continued from previous page)

```
protein_sequence=DRY;cDNA_sequence=GACCGCTAC;gDNA_sequence=GTAGCGGTC;source=C
CDS
```

One can also use wildcard *x* (lowercase) in the motif.

```
$ transvar panno -i 'HTR1B:p.365_369refNPxxY' --ccds --seqmax 30
```

```
HTR1B:p.365_369refNPxxY      CCDS4986 (protein_coding)      HTR1B  -
chr6:g.78172014_78172028/c.1093_1107/p.N365_Y369  inside_[cds_in_exon_1]
protein_sequence=NPIIY;cDNA_sequence=AACCCATAATCTAT;gDNA_sequence=ATAGATTATG
GGGTT;source=CCDS
```

5.3 Protein region

```
$ transvar panno --ccds -i 'ABCB11:p.200_400'
```

outputs

```
ABCB11:p.200_400      CCDS46444 (protein_coding)      ABCB11  -
chr2:g.169833195_169851872/c.598_1200/p.T200_K400  inside_[cds_in_exons_[6,7,8,9,10,
↪11]]
protein_sequence=TRF..DRK;cDNA_sequence=ACA..AAA;gDNA_sequence=TTT..TGT;sourc
e=CCDS
```

5.4 Protein variants

5.4.1 Single amino acid substitution

Mutation formats acceptable in TransVar are ``PIK3CA:p.E545K`` or without reference or alternative amino acid identity, e.g., ``PIK3CA:p.545K`` or ``PIK3CA:p.E545``. TransVar takes native HGVS format inputs and outputs. The reference amino acid is used to narrow the search scope of candidate transcripts. The alternative amino acid is used to infer nucleotide change which results in the amino acid.

```
$ transvar panno -i PIK3CA:p.E545K --ensembl
```

outputs

```
PIK3CA:p.E545K      ENST00000263967 (protein_coding)      PIK3CA  +
chr3:g.178936091G>A/c.1633G>A/p.E545K      inside_[cds_in_exon_10]
CSQN=Missense;reference_codon=GAG;candidate_codons=AAG,AAA;candidate_mnv_vari
ants=chr3:g.178936091_178936093delGAGinsAAA;dbsnp=rs104886003(chr3:178936091G
>A);aliases=ENSP00000263967;source=Ensembl
```

One may encounter **ambiguous cases** where the multiple substitutions exist in explaining the amino acid change. For example,

```
$ transvar panno -i ACSL4:p.R133R --ccds
```

outputs

```
ACSL4:p.R133R      CCDS14548 (protein_coding)      ACSL4      -
chrX:g.108926078G>T/c.399C>A/p.R133R      inside_[cds_in_exon_2]
CSQN=Synonymous;reference_codon=CGC;candidate_codons=AGG,AGA,CGA,CGG,CGT;cand
idate_snv_variants=chrX:g.108926078G>C,chrX:g.108926078G>A;candidate_mnv_vari
ants=chrX:g.108926078_108926080delGCGinsCCT,chrX:g.108926078_108926080delGCGi
nsTCT;source=CCDS
```

In those cases, TransVar prioritizes all the candidate base changes by minimizing the edit distance between the reference codon sequence and the target codon sequence. One of the optimal base changes is arbitrarily chosen as the default and all the candidates are included in the appended *CddMuts* entry.

Ambiguous amino acid code

TransVar instantiates input of ambiguous amino acid code such as ('B', for "Asx", which stands for "Asp" or "Asn") to more specific amino acid. Even if the reference amino acid is a subset of the ambiguous alternative amino acid, TransVar assume a mutation on the nucleotide level (can still deduce synonymous mutations):

```
$ transvar panno -i 'APC:p.D326B' --ccds
```

```
APC:p.D326B      CCDS4107 (protein_coding)      APC      +
chr5:g.112154705G>A/c.976G>A/p.D326N      inside_[cds_in_exon_9]
CSQN=Missense;reference_codon=GAT;candidate_codons=AAC,AAT,GAC;candidate_snv_
variants=chr5:g.112154707T>C;candidate_mnv_variants=chr5:g.112154705_11215470
7delGATinsAAC;source=CCDS
```

Here input alternative amino acids is B (D or N). After TransVar processing, a 'N' is derived (though a D is equally likely, as shown in the candidates).

5.4.2 Insertion

```
$ transvar panno --ccds -i 'AATK:p.P1331_A1332insTP'
```

```
AATK:p.P1331_A1332insTP      CCDS45807 (protein_coding)      AATK      -
chr17:g.79093270_79093271insAGGTGT/c.3993_3994insACACCT/p.T1330_P1331dupTP
↳inside_[cds_in_exon_13]
CSQN=InFrameInsertion;left_align_protein=p.A1326_P1327insPT;unaligned_protein=p
.T1330_P1331dupTP;left_align_gDNA=g.79093270_79093271insAGGTGT;unaligned_gDNA=g
.79093270_79093271insAGGTGT;left_align_cDNA=c.3993_3994insACACCT;unaligned_cDNA
=c.3993_3994insACACCT;16_CandidatesOmitted;source=CCDS
```

5.4.3 Deletion

```
$ transvar panno --ccds -i 'AADACL4:p.W263_I267delWRDAI'
```

```
AADACL4:p.W263_I267delWRDAI      CCDS30590 (protein_coding)      AADACL4      +
chr1:g.12726310_12726324del15/c.788_802del15/p.W263_I267delWRDAI      inside_[cds_in_
↳exon_4]
CSQN=InFrameDeletion;left_align_gDNA=g.12726308_12726322del15;unaligned_gDNA=
g.12726309_12726323del15;left_align_cDNA=c.786_800del15;unaligned_cDNA=c.787_80
1del15;left_align_protein=p.W263_I267delWRDAI;unaligned_protein=p.W263_I267delW
RDAI;imprecise;source=CCDS
```

5.4.4 Block substitution

```
$ transversar panno --ccds -i 'ABCC3:p.Y556_V557delinsRRR'
```

```
ABCC3:p.Y556_V557delinsRRR    CCDS32681 (protein_coding)    ABCC3    +
chr17:g.48745254_48745259delinsAGGAGGAGG/c.1666_1671delinsAGGAGGAGG/p.Y556_
↔V557delinsRRR    inside_[cds_in_exon_13]
CSQN=MultiAAMissense;216_CandidatesOmitted;source=CCDS
```

Sometimes block substitution comes from in-frame deletion on the nucleotide level.

```
$ transversar panno -i 'MAP2K1:p.F53_Q58delinsL' --ensembl
```

```
MAP2K1:p.F53_Q58delinsL    ENST00000307102 (protein_coding)    MAP2K1    +
chr15:g.66727443_66727457del15/c.159_173del15/p.F53_Q58delinsL    inside_[cds_in_
↔exon_2]
CSQN=MultiAAMissense;left_align_gDNA=g.66727443_66727457del15;unaligned_gDNA=
g.66727443_66727457del15;left_align_cDNA=c.159_173del15;unaligned_cDNA=c.159_17
3del15;candidate_alternative_sequence=CTT/CTG/CTA/CTC/TTA/TTG;aliases=ENSP000
00302486;source=Ensembl
```

5.4.5 Frame-shift variants

Frame-shift variants can be results of either insertion or deletion. In the cases where both are plausible the variants are prioritized by the length of the insertion/deletion. Mutations of smallest variants are given as the most likely inference. Other candidates are in given in the *candidates* field.

```
$ transversar panno --refseq -i 'PTEN:p.T319fs*1' --max-candidates 2
```

```
PTEN:p.T319fs*1    NM_000314 (protein_coding)    PTEN    +
chr10:g.89720803_89720804insTA/c.954_955insTA/p.T319fs*1    inside_[cds_in_exon_8]
CSQN=Frameshift;left_align_cDNA=c.954_955insTA;left_align_gDNA=g.89720803_897
20804insTA;candidates=g.89720803_89720804insTG/c.954_955insTG/g.89720803_8972
0804insTG/c.954_955insTG,g.89720804_89720807delACTT/c.955_958delACTT/g.897207
99_89720802delTACT/c.950_953delTACT;1_CandidatesOmitted;dbxref=GeneID:5728,HG
NC:9588,MIM:601728;aliases=NP_000305;source=RefSeq
```

In this example, both deletion *c.950_953delTACT* and insertion *c.954_955insTA* are possible. Both insertion involves fewer nucleotides and is chosen as the most likely inference. Deletion is given in the *candidates* tag.

The *candidates* field shows the right-aligned genomic, right-aligned cDNA, left-aligned genomic and left-aligned cDNA identifiers separated by /.

```
$ transversar panno --ccds -i 'A1BG:p.G132fs*2' --max-candidates 1
```

```
A1BG:p.G132fs*2    CCDS12976 (protein_coding)    A1BG    -
chr19:g.58863868delC/c.395delG/p.G132fs*2    inside_[cds_in_exon_4]
CSQN=Frameshift;left_align_cDNA=c.394delG;left_align_gDNA=g.58863867delC;cand
idates=g.58863873delG/c.393delC/g.58863869delG/c.389delC;13_CandidatesOmitted
;source=CCDS
```

Frameshift variants can be difficult since there might be too many valid underlying nucleotide variants. Suppose we have a relatively long insertion,


```
$ transvar ganno -i 'chr11:g.32417908_32417909insACCGTACA' --ccds
```

```
chr11:g.32417908_32417909insACCGTACA CCDS55750 (protein_coding) WT1 -
chr11:g.32417908_32417909insACCGTACA/c.456_457insTGTACGGT/p.A153Cfs*70 inside_
↔[cds_in_exon_6]
CSQN=Frameshift;left_align_gDNA=g.32417908_32417909insACCGTACA;unalign_gDNA=g
.32417908_32417909insACCGTACA;left_align_cDNA=c.456_457insTGTACGGT;unalign_cD
NA=c.456_457insTGTACGGT;source=CCDS
chr11:g.32417908_32417909insACCGTACA CCDS55751 (protein_coding) WT1 -
chr11:g.32417908_32417909insACCGTACA/c.507_508insTGTACGGT/p.A170Cfs*70 inside_
↔[cds_in_exon_7]
CSQN=Frameshift;left_align_gDNA=g.32417908_32417909insACCGTACA;unalign_gDNA=g
.32417908_32417909insACCGTACA;left_align_cDNA=c.507_508insTGTACGGT;unalign_cD
NA=c.507_508insTGTACGGT;source=CCDS
chr11:g.32417908_32417909insACCGTACA CCDS7878 (protein_coding) WT1 -
chr11:g.32417908_32417909insACCGTACA/c.1143_1144insTGTACGGT/p.A382Cfs*70 inside_
↔[cds_in_exon_7]
CSQN=Frameshift;left_align_gDNA=g.32417908_32417909insACCGTACA;unalign_gDNA=g
.32417908_32417909insACCGTACA;left_align_cDNA=c.1143_1144insTGTACGGT;unalign_
cDNA=c.1143_1144insTGTACGGT;source=CCDS
chr11:g.32417908_32417909insACCGTACA CCDS44561 (protein_coding) WT1 -
chr11:g.32417908_32417909insACCGTACA/c.1092_1093insTGTACGGT/p.A365Cfs*70 inside_
↔[cds_in_exon_6]
CSQN=Frameshift;left_align_gDNA=g.32417908_32417909insACCGTACA;unalign_gDNA=g
.32417908_32417909insACCGTACA;left_align_cDNA=c.1092_1093insTGTACGGT;unalign_
cDNA=c.1092_1093insTGTACGGT;source=CCDS
chr11:g.32417908_32417909insACCGTACA CCDS44562 (protein_coding) WT1 -
chr11:g.32417908_32417909insACCGTACA/c.1143_1144insTGTACGGT/p.A382Cfs*70 inside_
↔[cds_in_exon_7]
CSQN=Frameshift;left_align_gDNA=g.32417908_32417909insACCGTACA;unalign_gDNA=g
.32417908_32417909insACCGTACA;left_align_cDNA=c.1143_1144insTGTACGGT;unalign_
cDNA=c.1143_1144insTGTACGGT;source=CCDS
```

But now suppose we only know its protein identifier and forget about the original identifier. Using *panno*, we can get roughly how the original identifier look like:

```
$ transvar panno -i 'WT1:p.A170Cfs*70' --ccds --max-candidates 2
```

would return more than 80 underlying variants. In this case the argument *-max-candidates* (default to 10) controls the maximum number of candidates output.

```
WT1:p.A170Cfs*70 CCDS55751 (protein_coding) WT1 -
chr11:g.32417908_32417909insTTGGGGCA/c.507_508insTGCCCCAA/p.A170Cfs*70 inside_
↔[cds_in_exons_[7,8,9]]
CSQN=Frameshift;left_align_cDNA=c.507_508insTGCCCCAA;left_align_gDNA=g.324179
08_32417909insTTGGGGCA;candidates=g.32417908_32417909insTTGNNNCA/c.507_508ins
TGNNNCAA/g.32417908_32417909insTTGNNNCA/c.507_508insTGNNNCAA,g.32417908_32417
909insGTGNNNCA/c.507_508insTGNNNCA/g.32417908_32417909insGTGNNNCA/c.507_508i
nsTGNNNCA;80_CandidatesOmitted;source=CCDS
```

Sometimes the alternative amino acid can be missing

```
$ transvar panno -i ADAMTSL1:p.I396fs*30 --ccds --max-candidates 2
```

```
ADAMTSL1:p.I396fs*30 CCDS6485 (protein_coding) ADAMTSL1 +
chr9:g.18680360_18680361insG/c.1187_1188insG/p.I396fs*30 inside_[cds_in_exon_11]
```

(continues on next page)

(continued from previous page)

```

CSQN=Frameshift;left_align_cDNA=c.1187_1188insG;left_align_gDNA=g.18680360_18
680361insG;candidates=g.18680359dupA/c.1186dupA/g.18680358_18680359insA/c.118
5_1186insA,g.18680359_18680360insC/c.1186_1187insC/g.18680359_18680360insC/c.
1186_1187insC;11_CandidatesOmitted;source=CCDS
ADAMTSL1:p.I396fs*30 CCDS47954 (protein_coding)      ADAMTSL1      +
chr9:g.18680360_18680361insG/c.1187_1188insG/p.I396fs*30  inside_[cds_in_exon_11]
CSQN=Frameshift;left_align_cDNA=c.1187_1188insG;left_align_gDNA=g.18680360_18
680361insG;candidates=g.18680359dupA/c.1186dupA/g.18680358_18680359insA/c.118
5_1186insA,g.18680359_18680360insC/c.1186_1187insC/g.18680359_18680360insC/c.
1186_1187insC;11_CandidatesOmitted;source=CCDS

```

TransVar can also take protein identifiers such as as input. For example,

```
$ transvar panno --refseq -i 'NP_006266.2:p.G240Afs*50'
```

```

NP_006266.2:p.G240Afs*50      NM_006275 (protein_coding)      SRSF6      +
chr20:g.42089387delG/c.719delG/p.G240Afs*50      inside_[cds_in_exon_6]
CSQN=Frameshift;left_align_cDNA=c.718delG;left_align_gDNA=g.42089386delG;cand
idates=g.42089385delA/c.717delA/g.42089382delA/c.714delA;dbxref=GeneID:6431,H
GNC:10788,HPRD:09054,MIM:601944;aliases=NP_006266;source=RefSeq

```

The output gives the exact details of the mutation on the DNA levels, properly right-aligned. The *candidates* fields also include other equally-likely mutation identifiers. *candidates* have the format *[right-align-gDNA]/[right-align-cDNA]/[left-align-gDNA]/[left-align-cDNA]* for each hit and , separation between hits.

Similar applies when the underlying mutation is an insertion. TransVar can infer insertion sequence of under 3 base pairs long. For example,

```
$ transvar panno -i 'AASS:p.I355Mfs*10' --ccds --max-candidates 1
```

```

AASS:p.I355Mfs*10      CCDS5783 (protein_coding)      AASS      -
chr7:g.121753753_121753754insTC/c.1064_1065insGA/p.I355Mfs*10      inside_[cds_in_
↪exon_9]
CSQN=Frameshift;left_align_cDNA=c.1064_1065insGA;left_align_gDNA=g.121753753_
121753754insTC;candidates=g.121753753_121753754insGC/c.1064_1065insGC/g.12175
3753_121753754insGC/c.1064_1065insGC;3_CandidatesOmitted;source=CCDS

```

When the alternative becomes a stop codon, frameshift mutation becomes a nonsense mutation:

```
$ transvar panno -i 'APC:p.I1557*fs*3' --ccds
```

returns a nonsense mutation

```

APC:p.I1557*fs*3      CCDS4107 (protein_coding)      APC      +
chr5:g.112175960_112175962delATTinsTAA/c.4669_4671delATTinsTAA/p.I1557*      inside_
↪[cds_in_exon_15]
CSQN=Nonsense;reference_codon=ATT;candidate_codons=TAA, TAG, TGA;candidate_mnv_
variants=chr5:g.112175960_112175962delATTinsTAG, chr5:g.112175960_112175962del
ATTinsTGA;source=CCDS

```

5.5 Whole transcript

TransVar provides an easy way to investigate a whole transcript by supplying the gene id.

```
$ transvar panno -i 'Dnmt3a' --refseq
```

outputs the basic information of transcripts of the protein, in an intuitive way,

```
Dnmt3a      XM_005264176 (protein_coding)  DNMT3A  -
chr2:g.25451421_25537541/c.1_2739/p.M1_*913  whole_transcript
promoter=chr2:25537541_25538541;#exons=23;cds=chr2:25457148_25536853
Dnmt3a      XM_005264175 (protein_coding)  DNMT3A  -
chr2:g.25451421_25537354/c.1_2739/p.M1_*913  whole_transcript
promoter=chr2:25537354_25538354;#exons=23;cds=chr2:25457148_25536853
Dnmt3a      XM_005264177 (protein_coding)  DNMT3A  -
chr2:g.25451421_25475145/c.1_2070/p.M1_*690  whole_transcript
promoter=chr2:25475145_25476145;#exons=18;cds=chr2:25457148_25471091
Dnmt3a      NM_175629 (protein_coding)  DNMT3A  -
chr2:g.25455830_25565459/c.1_2739/p.M1_*913  whole_transcript
promoter=chr2:25565459_25566459;#exons=23;cds=chr2:25457148_25536853
Dnmt3a      NM_022552 (protein_coding)  DNMT3A  -
chr2:g.25455830_25564784/c.1_2739/p.M1_*913  whole_transcript
promoter=chr2:25564784_25565784;#exons=23;cds=chr2:25457148_25536853
Dnmt3a      NM_153759 (protein_coding)  DNMT3A  -
chr2:g.25455830_25475184/c.1_2172/p.M1_*724  whole_transcript
promoter=chr2:25475184_25476184;#exons=19;cds=chr2:25457148_25475066
Dnmt3a      NM_175630 (protein_coding)  DNMT3A  -
chr2:g.25504321_25565459/c.1_501/p.M1_*167   whole_transcript
promoter=chr2:25565459_25566459;#exons=4;cds=chr2:25505257_25536853
```

5.6 Search alternative codon identifiers

An identifier is regarded as an alternative if the underlying codon overlap with the one from the original identifier. Example: to search alternative identifiers of CDKN2A.p.58 (without knowing reference allele),

```
$ transvar codonsearch --ccds -i CDKN2A:p.58
```

```
origin_id  alt_id  chrm  codon1  codon2  transcripts_choice
CDKN2A:p.58  CDKN2A.p.73  chr9  21971184-21971185-21971186
      21971182-21971183-21971184  CCDS6510 [CCDS] / CCDS6511 [CCDS] , CCDS56565 [CCDS] /
↳ CCDS6511 [CCDS]
CDKN2A:p.58  CDKN2A.p.72  chr9  21971184-21971185-21971186
      21971185-21971186-21971187  CCDS6510 [CCDS] / CCDS6511 [CCDS] , CCDS56565 [CCDS] /
↳ CCDS6511 [CCDS]
```

The pair of transcript id listed corresponds to the transcripts based on which, the original and alternative identifiers are defined. Multiple pairs of transcript definitions are appended following a ,.

Example: to search alternative identifiers of DHODH:G152R (knowing reference allele G, alternative allele here will be ignored),

```
$ transvar codonsearch -i DHODH:G152R --refseq
```

outputs

```
origin_id  alt_id  chrm  codon1  codon2  transcripts_choice
DHODH:G152R  DHODH.p.G124  chr16  72050942-72050943-72050944
      72050942-72050943-72050944  NM_001361 [RefSeq] / XM_005255827 [RefSeq]
```

(continues on next page)

(continued from previous page)

DHODH:G152R	DHODH.p.G16	chr16	72050942-72050943-72050944	
			72050942-72050943-72050944	NM_001361 [RefSeq] / XM_005255828 [RefSeq]
DHODH:G152R	DHODH.p.G9	chr16	72050942-72050943-72050944	
			72050942-72050943-72050944	NM_001361 [RefSeq] / XM_005255829 [RefSeq]

TransVar outputs genomic positions of codons based on original transcript (4th column in the output) and alternative transcript (5th column in the output). The potential transcript usages are also appended.

Example: to run *transvar codonsearch* to **batch process** a list of mutation identifiers.

```
$ transvar codonsearch -l example/input_table2 --ccds -m 1 -o 1
```

Example input table

origin_id	alt_id	chr	codon1	codon2	transcripts_choice
CDKN2A:p.61	CDKN2A.p.76	chr9	21971173-21971174-21971175	21971175-21971176-21971177	CCDS6510 [CCDS] / CCDS6511 [CCDS], CCDS56565 [CCDS] / ↪CCDS6511 [CCDS]
CDKN2A:p.61	CDKN2A.p.75	chr9	21971176-21971177-21971178	21971175-21971176-21971177	CCDS6510 [CCDS] / CCDS6511 [CCDS], CCDS56565 [CCDS] / ↪CCDS6511 [CCDS]
CDKN2A:p.69	CDKN2A.p.84	chr9	21971149-21971150-21971151	21971151-21971152-21971153	CCDS6510 [CCDS] / CCDS6511 [CCDS], CCDS56565 [CCDS] / ↪CCDS6511 [CCDS]
CDKN2A:p.69	CDKN2A.p.83	chr9	21971152-21971153-21971154	21971151-21971152-21971153	CCDS6510 [CCDS] / CCDS6511 [CCDS], CCDS56565 [CCDS] / ↪CCDS6511 [CCDS]
CDKN2A:p.69	CDKN2A.p.55	chr9	21971193-21971194-21971195	21971194-21971195-21971196	CCDS6511 [CCDS] / CCDS6510 [CCDS], CCDS6511 [CCDS] / ↪CCDS56565 [CCDS]
CDKN2A:p.69	CDKN2A.p.54	chr9	21971196-21971197-21971198	21971194-21971195-21971196	CCDS6511 [CCDS] / CCDS6510 [CCDS], CCDS6511 [CCDS] / ↪CCDS56565 [CCDS]
ERBB2:p.755	ERBB2.p.725	chr17	37880219-37880220-37880221	37880219-37880220-37880221	CCDS32642 [CCDS] / CCDS45667 [CCDS]
ERBB2:p.755	ERBB2.p.785	chr17	37881024-37881025-37881026	37881024-37881025-37881026	CCDS45667 [CCDS] / CCDS32642 [CCDS]

outputs

origin_id	alt_id	chr	codon1	codon2	transcripts_choice
CDKN2A:p.61	CDKN2A.p.76	chr9	21971173-21971174-21971175	21971175-21971176-21971177	CCDS6510 [CCDS] / CCDS6511 [CCDS], CCDS56565 [CCDS] / ↪CCDS6511 [CCDS]
CDKN2A:p.61	CDKN2A.p.75	chr9	21971176-21971177-21971178	21971175-21971176-21971177	CCDS6510 [CCDS] / CCDS6511 [CCDS], CCDS56565 [CCDS] / ↪CCDS6511 [CCDS]
CDKN2A:p.69	CDKN2A.p.54	chr9	21971196-21971197-21971198	21971194-21971195-21971196	CCDS6511 [CCDS] / CCDS6510 [CCDS], CCDS6511 [CCDS] / ↪CCDS56565 [CCDS]
CDKN2A:p.69	CDKN2A.p.55	chr9	21971193-21971194-21971195	21971194-21971195-21971196	CCDS6511 [CCDS] / CCDS6510 [CCDS], CCDS6511 [CCDS] / ↪CCDS56565 [CCDS]
CDKN2A:p.69	CDKN2A.p.83	chr9	21971152-21971153-21971154	21971151-21971152-21971153	CCDS6510 [CCDS] / CCDS6511 [CCDS], CCDS56565 [CCDS] / ↪CCDS6511 [CCDS]

(continues on next page)

(continued from previous page)

CDKN2A:p.69	CDKN2A.p.84	chr9	21971151-21971152-21971153 21971149-21971150-21971151 ↔CCDS6511 [CCDS]	21971151-21971152-21971153 CCDS6510 [CCDS] / CCDS6511 [CCDS], CCDS56565 [CCDS] /
ERBB2:p.755	ERBB2.p.785	chr17	37881024-37881025-37881026 37881024-37881025-37881026	37881024-37881025-37881026 CCDS45667 [CCDS] / CCDS32642 [CCDS]
ERBB2:p.755	ERBB2.p.725	chr17	37880219-37880220-37880221 37880219-37880220-37880221	37880219-37880220-37880221 CCDS32642 [CCDS] / CCDS45667 [CCDS]

The third column indicates the potential transcript usage for the alternative identifier. Each transcript usage is denoted by <listing transcript>/<actual transcript>. Different potential choices are separated by ‘,’.

5.6.1 Infer potential codon identity

Example: to check if MET.p1010 and MET.p992 may be referring to one mutation due to different usage of transcripts,

```
$ transvar codonsearch --refseq -i MET:p.1010
```

gives

origin_id	alt_id	chr	codon1	codon2	transcripts_choice
MET:p.1010	MET.p.991	chr7	116411932-116411933-116411934	116411932-116411933-116411934	XM_005250353 [RefSeq] / NM_001127500 [RefSeq]
MET:p.1010	MET.p.973	chr7	116411932-116411933-116411934	116411932-116411933-116411934	XM_005250353 [RefSeq] / NM_000245 [RefSeq]
MET:p.1010	MET.p.543	chr7	116411932-116411933-116411934	116411932-116411933-116411934	XM_005250353 [RefSeq] / XM_005250354 [RefSeq]
MET:p.1010	MET.p.1029	chr7	116411989-116411990-116411991	116411989-116411990-116411991	NM_001127500 [RefSeq] / XM_005250353 [RefSeq]
MET:p.1010	MET.p.992	chr7	116411989-116411990-116411991	116411989-116411990-116411991	NM_001127500 [RefSeq] / NM_000245 [RefSeq]
MET:p.1010	MET.p.562	chr7	116411989-116411990-116411991	116411989-116411990-116411991	NM_001127500 [RefSeq] / XM_005250354 [RefSeq]
MET:p.1010	MET.p.1047	chr7	116412043-116414935-116414936	116412043-116414935-116414936	NM_000245 [RefSeq] / XM_005250353 [RefSeq]
MET:p.1010	MET.p.1028	chr7	116412043-116414935-116414936	116412043-116414935-116414936	NM_000245 [RefSeq] / NM_001127500 [RefSeq]
MET:p.1010	MET.p.580	chr7	116412043-116414935-116414936	116412043-116414935-116414936	NM_000245 [RefSeq] / XM_005250354 [RefSeq]

Since MET.p.992 is in the list, the two identifiers might be due to the same genomic mutation.

cDNA level annotation

Annotation from cDNA level is handled by the *canno* subcommand.

6.1 cDNA region

```
$ transvar canno --ccds -i 'ABCB11:c.1198-8_1202'
```

outputs

```
ABCB11:c.1198-8_1202 CCDS46444 (protein_coding)      ABCB11  -
chr2:g.169833193_169833205GGTTTCTGGAGTG/c.1198-8_1202CACTCCAGAAACC/p.400_401KP
↔from_[cds_in_exon_11]_to_[intron_between_exon_10_and_11]
C2=acceptor_splice_site_on_exon_11_at_chr2:169833198_included;source=CCDS
```

6.2 cDNA variant

6.2.1 Single Nucleotide Variation (SNV)

TransVar infers nucleotide mutation through `PIK3CA:c.1633G>A`. Note that nucleotide identity follows the natural sequence, i.e., if transcript is interpreted on the reverse-complementary strand, the base at the site needs to be reverse-complemented too.

```
$ transvar canno --ccds -i 'PIK3CA:c.1633G>A'
```

outputs

```
PIK3CA:c.1633G>A      CCDS43171 (protein_coding)      PIK3CA  +
chr3:g.178936091G>A/c.1633G>A/p.E545K      inside_[cds_in_exon_9]
CSQN=Missense;dbsnp=rs104886003 (chr3:178936091G>A);reference_codon=GAG;altern
ative_codon=AAG;source=CCDS
```

The SNV can be in the intronic region, e.g.,

```
$ transvar canno --ccds -i 'ABCB11:c.1198-8C>A'
```

outputs

```
ABCB11:c.1198-8C>A  CCDS46444 (protein_coding)  ABCB11  -
chr2:g.169833205G>T/c.1198-8C>A/.  inside_[intron_between_exon_10_and_11]
CSQN=IntronicSNV;source=CCDS
```

Or in the 5'-UTR region, e.g.,

```
$ transvar canno -i 'KCNJ11:c.-134G>T' --ensembl
```

```
KCNJ11:c.-134G>T  ENST00000339994 (protein_coding)  KCNJ11  -
chr11:g.17409772C>A/c.1-134G>T/.  inside_[5-UTR;noncoding_exon_1]
CSQN=5-UTRSNV;dbsnp=rs387906398 (chr11:17409772C>A);aliases=ENSP00000345708;source=Ensembl
```

Or in the 3'-UTR region, e.g.,

```
$ transvar canno -i 'MSH2:c.*95C>T' --refseq
```

```
MSH2:c.*95C>T  NM_000251 (protein_coding)  MSH2  +
chr2:g.47710183C>T/c.*95C>T/.  inside_[3-UTR;noncoding_exon_16]
CSQN=3-UTRSNV;dbsnp=rs587779062 (chr2:47710183C>T);dbxref=GeneID:4436,HGNC:7325,HPRD:00389,MIM:609309;aliases=NP_000242;source=RefSeq
MSH2:c.*95C>T  NM_001258281 (protein_coding)  MSH2  +
chr2:g.47710183C>T/c.*95C>T/.  inside_[3-UTR;noncoding_exon_17]
CSQN=3-UTRSNV;dbsnp=rs587779062 (chr2:47710183C>T);dbxref=GeneID:4436,HGNC:7325,HPRD:00389,MIM:609309;aliases=NP_001245210;source=RefSeq
MSH2:c.*95C>T  XM_005264333 (protein_coding)  MSH2  +
chr2:g.47710183C>T/c.*95C>T/.  inside_[3-UTR;noncoding_exon_15]
CSQN=3-UTRSNV;dbsnp=rs587779062 (chr2:47710183C>T);dbxref=GeneID:4436,HGNC:7325,HPRD:00389,MIM:609309;aliases=XP_005264390;source=RefSeq
```

6.2.2 insertion

An insertion may result in: 1) a pure insertion of amino acids; 2) a block substitution of amino acids, when insertion occur after 1st or 2nd base in a codon; or 3) a frame-shift. Following HGVS nomenclature, TransVar labels the first different amino acid and the length of the peptide until stop codon, assuming no change in the splicing.

Example: to annotate an **in-frame, in-phase insertion**,

```
$ transvar canno --ccds -i 'ACIN1:c.1932_1933insATTAC'
```

```
ACIN1:c.1932_1933insATTAC  CCDS9587 (protein_coding)  ACIN1  -
chr14:g.23548785_23548786insGTGAAT/c.1932_1933insATTAC/p.R644_S645insIH  inside_
↪[cds_in_exon_6]
CSQN=InFrameInsertion;left_align_gDNA=g.23548785_23548786insGTGAAT;unalign_gDNA=g.23548785_23548786insGTGAAT;left_align_cDNA=c.1932_1933insATTAC;unalign_cDNA=c.1932_1933insATTAC;left_align_protein=p.R644_S645insIH;unalign_protein=p.R644_S645insIH;phase=0;source=CCDS
ACIN1:c.1932_1933insATTAC  CCDS53889 (protein_coding)  ACIN1  -
chr14:g.23548157_23548158insGTGAAT/c.1932_1933insATTAC/p.P644_V645insIH  inside_
↪[cds_in_exon_6]
```

(continues on next page)

(continued from previous page)

```

CSQN=InFrameInsertion;left_align_gDNA=g.23548157_23548158insGTGAAT;unalign_gDNA=g.23548157_23548158insGTGAAT;left_align_cDNA=c.1932_1933insATTACAC;unalign_cDNA=c.1932_1933insATTACAC;left_align_protein=p.P644_V645insIH;unalign_protein=p.P644_V645insIH;phase=0;source=CCDS
ACIN1:c.1932_1933insATTACAC  CCDS55905 (protein_coding)      ACIN1  -
chr14:g.23548785_23548786insGTGAAT/c.1932_1933insATTACAC/p.R644_S645insIH  inside_
↳[cds_in_exon_6]
CSQN=InFrameInsertion;left_align_gDNA=g.23548785_23548786insGTGAAT;unalign_gDNA=g.23548785_23548786insGTGAAT;left_align_cDNA=c.1932_1933insATTACAC;unalign_cDNA=c.1932_1933insATTACAC;left_align_protein=p.R644_S645insIH;unalign_protein=p.R644_S645insIH;phase=0;source=CCDS

```

Phase = 0, 1, 2 indicates whether the insertion happen after the 3rd, 1st or 2nd base of a codon, respectively. An insertion *in phase* refers to one with Phase=0.

Example: to annotate an **out-of-phase, in-frame insertion**,

```
$ transvar canno --ccds -i 'ACIN1:c.1930_1931insATTACAC'
```

```

ACIN1:c.1930_1931insATTACAC  CCDS9587 (protein_coding)      ACIN1  -
chr14:g.23548792_23548793insGTGAA/c.1930_1931insATTACAC/p.S643_R644insHS  inside_
↳[cds_in_exon_6]
CSQN=InFrameInsertion;left_align_gDNA=g.23548787_23548788insGTGAAT;unalign_gDNA=g.23548787_23548788insGTGAAT;left_align_cDNA=c.1925_1926insTTCACA;unalign_cDNA=c.1930_1931insATTACAC;left_align_protein=p.R642_S643insSH;unalign_protein=p.S643_R644insHS;phase=1;source=CCDS
ACIN1:c.1930_1931insATTACAC  CCDS53889 (protein_coding)      ACIN1  -
chr14:g.23548162_23548163insAATGTG/c.1930_1931insATTACAC/p.P643_P644insHS  inside_
↳[cds_in_exon_6]
CSQN=InFrameInsertion;left_align_gDNA=g.23548159_23548160insGTGAAT;unalign_gDNA=g.23548159_23548160insGTGAAT;left_align_cDNA=c.1927_1928insCACATT;unalign_cDNA=c.1930_1931insATTACAC;left_align_protein=p.P643_P644insHS;unalign_protein=p.P643_P644insHS;phase=1;source=CCDS
ACIN1:c.1930_1931insATTACAC  CCDS55905 (protein_coding)      ACIN1  -
chr14:g.23548792_23548793insGTGAA/c.1930_1931insATTACAC/p.S643_R644insHS  inside_
↳[cds_in_exon_6]
CSQN=InFrameInsertion;left_align_gDNA=g.23548787_23548788insGTGAAT;unalign_gDNA=g.23548787_23548788insGTGAAT;left_align_cDNA=c.1925_1926insTTCACA;unalign_cDNA=c.1930_1931insATTACAC;left_align_protein=p.R642_S643insSH;unalign_protein=p.S643_R644insHS;phase=1;source=CCDS

```

Reverse annotation can result in different identifiers after left/right alignments, e.g.,

```
$ transvar canno --ccds -i 'AATK:c.3976_3977insCGCCCA'
```

results in

```

AATK:c.3976_3977insCGCCCA  CCDS45807 (protein_coding)      AATK  -
chr17:g.79093282_79093287dupTGGGCG/c.3988_3993dupACGCCC/p.T1330_P1331dupTP
↳inside_[cds_in_exon_13]
CSQN=InFrameInsertion;left_align_gDNA=g.79093270_79093271insGGGCGT;unalign_gDNA=g.79093282_79093287dupTGGGCG;left_align_cDNA=c.3976_3977insCGCCCA;unalign_cDNA=c.3976_3977insCGCCCA;left_align_protein=p.A1326_P1327insPT;unalign_protein=p.A1326_P1327insPT;phase=1;source=CCDS

```

Note how insertion switch to duplication when 5' flanking is identical. This conforms to HGVS recommendation to replace insertion notation with duplication when possible.

Example: to annotate a **frame-shift insertion**, frameshift mutations have not alternative alignments. Hence only cDNA and gDNA have left alignment and unalignment reports.

```
$ transvar canno --ccds -i 'AAAS:c.1225_1226insG'
```

results in

```
AAAS:c.1225_1226insG CCDS8856 (protein_coding) AAAS -
chr12:g.53702093dupC/c.1225dupG/p.E409Gfs*17 inside_[cds_in_exon_13]
CSQN=Frameshift;left_align_gDNA=g.53702089_53702090insC;unalign_gDNA=g.537020
89_53702090insC;left_align_cDNA=c.1221_1222insG;unalign_cDNA=c.1225dupG;sourc
e=CCDS
AAAS:c.1225_1226insG CCDS53797 (protein_coding) AAAS -
chr12:g.53701842_53701843insC/c.1225_1226insG/p.L409Rfs*54 inside_[cds_in_
↪exon_13]
CSQN=Frameshift;left_align_gDNA=g.53701842_53701843insC;unalign_gDNA=g.537018
42_53701843insC;left_align_cDNA=c.1225_1226insG;unalign_cDNA=c.1225_1226insG;
source=CCDS
```

Example: to annotate an **intronic insertion**,

```
$ transvar canno --ccds -i 'ADAM33:c.991-3_991-2insC'
```

outputs

```
ADAM33:c.991-3_991-2insC CCDS13058 (protein_coding) ADAM33 -
chr20:g.3654151dupG/c.991-3dupC/. inside_[intron_between_exon_10_and_11]
CSQN=IntronicInsertion;left_align_gDNA=g.3654145_3654146insG;unalign_gDNA=g.3
654145_3654146insG;left_align_cDNA=c.991-9_991-8insC;unalign_cDNA=c.991-3dupC
;source=CCDS
```

In the case of intronic insertions, amino acid identifier is not applicable, represented in a .. But cDNA and gDNA identifier are right-aligned according to their natural order, respecting HGVS nomenclature.

Insertion could occur to *splice sites*. TransVar identifies such cases and report splice site and repress translation of protein change.

```
$ transvar canno --ccds -i 'ADAM33:c.991_992insC'
```

results in

```
ADAM33:c.991_992insC CCDS13058 (protein_coding) ADAM33 -
chr20:g.3654142_3654143insG/c.991_992insC/. inside_[cds_in_exon_11]
CSQN=SpliceAcceptorInsertion;left_align_gDNA=g.3654142_3654143insG;unalign_gD
NA=g.3654142_3654143insG;left_align_cDNA=c.991_992insC;unalign_cDNA=c.991_992
insC;C2=acceptor_splice_site_on_exon_11_at_chr20:3654144_affected;source=CCDS
```

6.2.3 deletion

Similar to insertions, deletion can be in-frame or frame-shift. The consequence of deletion to amino acid sequence may appear a simple deletion or a block substitution (in the case where in-frame deletion is out of phase, i.e., partially delete codons).

Example: to annotate an **in-frame deletion**,

```
$ transvar canno --ccds -i 'A4GNT:c.694_696delTTG'
```

```
A4GNT:c.694_696delTTG      CCDS3097 (protein_coding)      A4GNT      -
chr3:g.137843435_137843437delACA/c.694_696delTTG/p.L232delL      inside_[cds_in_
↳exon_2]
CSQN=InFrameDeletion;left_align_gDNA=g.137843433_137843435delCAA;unaligned_gDNA
NA=g.137843433_137843435delCAA;left_align_cDNA=c.692_694delTGT;unaligned_cDNA=c
.694_696delTTG;left_align_protein=p.L232delL;unaligned_protein=p.L232delL;source
=CCDS
```

Example: to annotate a **in-frame, out-of-phase deletion**,

```
$ transvar canno --ccds -i 'ABHD15:c.431_433delGTG'
```

```
ABHD15:c.431_433delGTG      CCDS32602 (protein_coding)      ABHD15      -
chr17:g.27893552_27893554delCAC/c.431_433delGTG/p.C144_V145delinsF      inside_
↳[cds_in_exon_1]
CSQN=MultiAAMissense;left_align_gDNA=g.27893552_27893554delCAC;unaligned_gDNA
=g.27893552_27893554delCAC;left_align_cDNA=c.431_433delGTG;unaligned_cDNA=c.431
_433delGTG;source=CCDS
```

Example: to annotate a **frame-shift deletion**,

```
$ transvar canno --ccds -i 'AADACL3:c.374delG'
```

```
AADACL3:c.374delG      CCDS41252 (protein_coding)      AADACL3      +
chr1:g.12785494delG/c.374delG/p.C125Ffs*17      inside_[cds_in_exon_3]
CSQN=Frameshift;left_align_gDNA=g.12785494delG;unaligned_gDNA=g.12785494delG;
left_align_cDNA=c.374delG;unaligned_cDNA=c.374delG;source=CCDS
```

Example: to annotate a **deletion that span from intronic to coding region**, protein prediction is suppressed due to loss of splice site.

```
$ transvar canno --ccds -i 'ABCB11:c.1198-8_1199delcactccagAA'
```

```
ABCB11:c.1198-8_1199delcactccagAA      CCDS46444 (protein_coding)      ABCB11      -
chr2:g.169833196_169833205delTTCTGGAGTG/c.1198-8_1199delCACTCCAGAA/.      from_
↳[cds_in_exon_11]_to_[intron_between_exon_10_and_11]
CSQN=SpliceAcceptorDeletion;left_align_gDNA=g.169833196_169833205delTTCTGGAGT
G;unaligned_gDNA=g.169833196_169833205delTTCTGGAGTG;left_align_cDNA=c.1198-8_
1199delCACTCCAGAA;unaligned_cDNA=c.1198-8_1199delCACTCCAGAA;C2=acceptor_splice_
site_on_exon_11_at_chr2:169833198_lost;source=CCDS
```

6.2.4 block substitution

Example: to annotate a block substitution in **coding region**,

```
$ transvar canno --ccds -i 'A1CF:c.508_509delinsTT'
```

```
A1CF:c.508_509delinsTT      CCDS7241 (protein_coding)      A1CF      -
chr10:g.52595929_52595930delinsAA/c.508_509delinsTT/p.P170L      inside_[cds_in_
↳exon_4]
CSQN=Missense;codon_cDNA=508-509-510;source=CCDS
A1CF:c.508_509delinsTT      CCDS7242 (protein_coding)      A1CF      -
chr10:g.52595929_52595930delinsAA/c.508_509delinsTT/p.P170L      inside_[cds_in_
↳exon_4]
```

(continues on next page)

(continued from previous page)

```
CSQN=Missense;codon_cDNA=508-509-510;source=CCDS
A1CF:c.508_509delinsTT      CCDS7243 (protein_coding)      A1CF      -
chr10:g.52595953_52595954delinsAA/c.508_509delinsTT/p.G170F      inside_[cds_in_
↔exon_4]
CSQN=Missense;codon_cDNA=508-509-510;source=CCDS
```

Block substitution does not necessarily results in block substitution in amino acid. For example, the following substitution results in a deletion, where protein alternative alignment should be reported.

```
$ transvar canno --ccds -i 'CSRNP1:c.1212_1224delinsGGAGGAGGAA'
```

```
CSRNP1:c.1212_1224delinsGGAGGAGGAA  CCDS2682 (protein_coding)      CSRNP1  -
chr3:g.39185092_39185104delinsTTCTCTCTCC/c.1212_1224delinsGGAGGAGGAA/p.E411delE  ↪
↔inside_[cds_in_exon_4]
CSQN=InFrameDeletion;begin_codon_cDNA=1210-1211-1212;end_codon_cDNA=1222-1223
-1224;left_align_protein=p.E405delE;unalign_protein=p.E408delE;source=CCDS
```

Likewise, block substitution could occur to **intronic region**,

```
$ transvar canno --ccds -i 'A1CF:c.1460+2_1460+3delinsCC'
```

```
A1CF:c.1460+2_1460+3delinsCC  CCDS7241 (protein_coding)      A1CF      -
chr10:g.52570797_52570798delinsGG/c.1460+2_1460+3delinsCC/.      inside_[intron_
↔between_exon_9_and_10]
CSQN=IntronicBlockSubstitution;source=CCDS
```

When block substitution occurs **across splice site**, TransVar put a tag in the info fields and does not predict amino acid change.

```
$ transvar canno --ccds -i 'A1CF:c.1459_1460+3delinsCC'
```

```
A1CF:c.1459_1460+3delinsCC  CCDS7241 (protein_coding)      A1CF      -
chr10:g.52570797_52570801delinsGG/c.1459_1460+3delinsCC/.  from_[intron_between_
↔exon_9_and_10]_to_[cds_in_exon_9]
CSQN=SpliceDonorBlockSubstitution;C2=donor_splice_site_on_exon_9_at_chr10:525
70799_lost;source=CCDS
```

6.2.5 duplication

Duplication can be thought of as special insertion where the inserted sequence is identical to the sequence flanking the breakpoint. Similar to insertion, the annotation of duplication may possess alternative alignment.

Example: to annotate a duplication coding region,

```
$ transvar canno --ccds -i 'CHD7:c.1669_1674dup'
```

```
CHD7:c.1669_1674dup  CCDS47865 (protein_coding)      CHD7      +
chr8:g.61693564_61693569dupCCCGTC/c.1669_1674dup/p.P558_S559dupPS  inside_[cds_in_
↔exon_2]
CSQN=InFrameInsertion;left_align_gDNA=g.61693561_61693562insTCCCCG;unalign_gD
NA=g.61693562_61693567dupTCCCCG;left_align_cDNA=c.1668_1669insTCCCCG;unalign_
cDNA=c.1669_1674dupTCCCCG;left_align_protein=p.H556_S557insSP;unalign_protein
=p.S557_P558dupSP;phase=0;source=CCDS
```

Example: a duplication on the nucleotide level may lead to frame-shift or block substitution on the amino acid level,

```
$ transvar canno --ccds -i 'CHD7:c.1668_1669dup'
```

```
CHD7:c.1668_1669dup  CCDS47865 (protein_coding)      CHD7      +
chr8:g.61693561_61693562dupTT/c.1668_1669dup/p.S557Ffs*8  inside_[cds_in_exon_2]
CSQN=Frameshift;left_align_gDNA=g.61693560_61693561insTT;unalign_gDNA=g.61693
561_61693562dupTT;left_align_cDNA=c.1667_1668insTT;unalign_cDNA=c.1668_1669du
pTT;source=CCDS
```

Example: to annotate a duplication in intronic region,

```
$ transvar canno --ccds -i 'CHD7:c.1666-5_1666-3dup'
```

```
CHD7:c.1666-5_1666-3dup  CCDS47865 (protein_coding)      CHD7      +
chr8:g.61693554_61693556dupCTC/c.1666-5_1666-3dup/.      inside_[intron_between_
↔exon_1_and_2]
CSQN=IntronicInsertion;left_align_gDNA=g.61693553_61693554insCTC;unalign_gDNA
=g.61693554_61693556dupCTC;left_align_cDNA=c.1666-6_1666-5insCTC;unalign_cDNA
=c.1666-5_1666-3dupCTC;source=CCDS
```

Interpret consequence labels (CSQN)

For each genetic variant, TransVar assigns a consequence label with *CSQN* tag. The consequence label sometimes explains the behaviour of the output, e.g., the missing of protein level representation due to the loss of splice site.

The consequence label is in the following alphabet:

7.1 General

label	interpretation
Synonymous	Variation in protein-coding sequence results in the same protein sequence
Missense	Single or multiple amino acid substitution to coding gene (1-1)
MultiAAMissense	In-frame multiple amino acid replacement (m to n, either m>1 or n>1)
Nonsense	Introduction of stop codon by single, multiple amino acid substitution or in-frame insertions/deletions

7.2 Coding Start/Stop

label	interpretation
CdsStartSNV	SNV at coding start
CdsStopSNV	SNV at coding stop
CdsStartDeletion	deletion of coding start
CdsStopDeletion	deletion of coding stop

7.3 Coding Insertion/Deletion

label	interpretation
Frameshift	Frameshift mutation to a coding gene
InFrameDeletion	In-frame deletion to a coding gene
InFrameInsertion	In-frame insertion to a coding gene

7.4 Intronic

label	interpretation
IntronicSNV	Intronic single nucleotide variation
IntronicDeletion	Intronic deletion
IntronicInsertion	Intronic insertion
IntronicBlockSubstitutio	Intronic block substitution

7.5 Intergenic

label	interpretation
IntergenicSNV	Intergenic single nucleotide variation
IntergenicDeletion	Intergenic deletion
IntergenicInsertion	Intergenic insertion
IntergenicBlockSubstitution	Intergenic block substitution

7.6 Splice site

label	interpretation
SpliceDonorDeletion	Deletion occurs to splice donor
SpliceAcceptorDeletion	Deletion occurs to splice acceptor
SpliceDonorSNV	Genetic variation at splice donor
SpliceAcceptorSNV	Genetic variation at splice acceptor
SpliceDonorBlockSubstitution	Block substitution occurs at splice donor
SpliceAcceptorBlockSubstitution	Block substitution occurs at splice acceptor
SpliceDonorInsertion	Insertion at splice donor
SpliceAcceptorInsertion	Insertion at splice acceptor

7.7 Others

label	interpretation
Unclassified	Unclassified

Inspect variant sequences

The `--print-protein` and `--print-protein-pretty` options displays the full variant protein sequence in the `variant_protein_seq` field of the info when the genomic variant hits a protein-coding transcript.

8.1 Missense substitution

```
$ transvar ganno -i 'chr1:g.115256530G>A' --ensembl --print-protein
```

```
chr1:g.115256530G>A ENST00000369535 (protein_coding) NRAS -
chr1:g.115256530G>A/c.181C>T/p.Q61* inside_[cds_in_exon_3]
CSQN=Nonsense;variant_protein_seq=MTEYKLVVVGAGGVGKSALTIQLIQNHFVDEYDPTIEDSYRKQ
VVIDGETCLLDILDITAG*;codon_pos=115256528-115256529-115256530;ref_codon_seq=CAA;
aliases=ENSP00000358548;source=Ensembl
```

`--print-protein-pretty` output is more human-readable and highlight the mutation in brackets.

```
$ transvar ganno --ccds -i 'chr3:g.178936091G>A' --print-protein-pretty
```

```
chr3:g.178936091G>A CCDS43171 (protein_coding) PIK3CA +
chr3:g.178936091G>A/c.1633G>A/p.E545K inside_[cds_in_exon_9]
CSQN=Missense;dbsnp=rs104886003 (chr3:178936091G>A);variant_protein_seq=MPPRPS
SGELWGIHLMPPRILVECLLPNGMIVTLECLREATLITIKHELKFEARKYPLHQLLQDESSYIFVSVTQEAEREFF
DETRRLCDLRLFPFLKVIIEPVGNREEKILNREIGFAIGMPVCEFDVMKDPFVQDFRRNILNVCKEAVDLRDLNSPH
SRAMYVYPPNVESSPELPHKHIYNKLDKGQIIIVVIWVIVSPNNDKQKYTLKINHDCVPEQVIAEAIRKTRSMLLSSE
QLKLCVLEYQGYILKVCDCDEYFLEKYPLSQYKIRSCIMLGRMPNLMLMAKESLYSQLPMDCFMTPSYSRRISTA
TPYMNGETSTKSLWVINSALRIKILCATYVNVNIRDIDKIYVRTGIYHGGEPLCDNVNTQVRVPCSNRPNWNLNYDI
YIPDLPRAARLCLCSVKGGRKGAKEEHCP LAWGNINLFDYDTLTVSGKMALNLWVPHGLEDLLNP IGVTGSNPNK
ETPCLELEFDWFSVVKFPDMSVIEEHANWSVSREAGFSYSHAGLSNRLARDNELRENDKEQLKAISTRDPLSEIT_
_[E>K]__QEKDFLWSHRHYCVTIPEIILPKLLLSVKWNSRDEVAQMYCLVKDWPP IKPEQAMELLDCNYPDPMVRGF
AVRCLEKYLTDKLSQYLIQLVQVLKYEQYLDNLLVRFLLKALTNQRI GHFFFVHLKSEMHNKTVSQRFGLLLESY
CRACGMYLKHLNRQVEAMEKLINLTDILKQEKKDETQKVQMKFLVEQMRPDMFMDALQGF LSP LNP AHQLGNLRLEE
CRIMSSAKRPLWLNWENPDIMSELLFQNEE I FKNQDGLRQDMLTLQIIRIMENIWQNQGLDLRMLPYGCLSIGDCV
```

(continues on next page)

(continued from previous page)

```
GLIEVVRNSHTIMQIQCKGGLKALQFNSHTLHQWLKDKNKGEIYDAAIDLFRSCAGYCVATFILGIGDRHNSNIM
VKDDGQLFHIDFGHFLDHKKKFKFYKRERVPFVLTQDFLIVISKGAQECTKTREPERFERQEMCYKAYLAIRQHANLFI
NLFSMMLGSGMPELQSFDDIAYIRKTLALDKTEQEALEYFMKQMNDAHHGGWTTKMDWIFHTIKQHALN*; codon_
pos=178936091-178936092-178936093; ref_codon_seq=GAG; source=CCDS
```

The alphabet transformation option **-aa3** applies here as well.

```
$ transvar ganno -i 'chr1:g.115256530G>A' --ensembl --print-protein-pretty --aa3
```

```
chr1:g.115256530G>A ENST00000369535 (protein_coding) NRAS -
chr1:g.115256530G>A/c.181C>T/p.Gln61X inside_[cds_in_exon_3]
CSQN=Missense; variant_protein_seq=MetThrGluTyrLysLeuValValValGlyAlaGlyGlyValG
lyLysSerAlaLeuThrIleGlnLeuIleGlnAsnHisPheValAspGluTyrAspProThrIleGluAspSerTyr
ArgLysGlnValValIleAspGlyGluThrCysLeuLeuAspIleLeuAspThrAlaGly__[GluGluTyrSerAl
aMetArgAspGlnTyrMetArgThrGlyGluGlyPheLeuCysValPheAlaIleAsnAsnSerLysSerPheAlaA
spIleAsnLeuTyrArgGluGlnIleLysArgValLysAspSerAspAspValProMetValLeuValGlyAsnLys
CysAspLeuProThrArgThrValAspThrLysGlnAlaHisGluLeuAlaLysSerTyrGlyIleProPheIleGl
uThrSerAlaLysThrArgGlnGlyValGluAspAlaPheTyrThrLeuValArgGluIleArgGlnTyrArgMetL
ysLysLeuAsnSerSerAspAspGlyThrGlnGlyCysMetGlyLeuProCysValValMet>X]; codon_pos=1
15256528-115256529-115256530; ref_codon_seq=CAA; aliases=ENSP00000358548; source
=Ensembl
```

8.2 Deletion

```
$ transvar canno --ccds -i 'CCDS8856:c.769_771delGGG' --print-protein-pretty
```

```
CCDS8856:c.769_771delGGG CCDS8856 (protein_coding) AAAS -
chr12:g.53703427_53703429delCCC/c.769_771delGGG/p.G257delG inside_[cds_in_
↪exon_8]
CSQN=InFrameDeletion; left_align_gDNA=g.53703424_53703426delCCC; unaligned_gDNA
=g.53703424_53703426delCCC; left_align_cDNA=c.766_768delGGG; unalign_cDNA=c.769
_771delGGG; left_align_protein=p.G256delG; unalign_protein=p.G257delG; variant_p
rotein_seq=MCSLGLFPFPPRQVTLTYEHNNELVGTSSYESPPDFRGQWINLPVLQLTKDPLKTPGRDLHGTR
TAFIHHREQVWKRCINIWDRVGLFVGLNEIANSEEEVFEWVKTAGWALALCRWASSLHGSLFPHLSLRSEDLIAEF
AQVTNWSSCCLRVFAWHPHNTKFAVALDDSVRVYNASSTIVPSLKHRLQRNVASLAWKPLSASVLAVACQSCILIW
TLDPTSLSTRPSSGCAQVLSHPGHTPVTSLAWAPSG__[G_deletion]__RLLSASPVDAAIRVWDVSTETCVPL
PWFRRGGVNTNLLWSPDGSKILATTPSAVFRVWEAQMWTCERWPTLSGRCQTGCWSPDGSRLFTVLGEPLIYLSLFP
ERCGEKGKCVGGAKSATIVADLSETTIQTPDGEERLGGEAHSMVWDPSGERLAVLMKGPVQDGKPVILLFRTRNS
PVFELLPCGIIQGEPGAQPQLITFHPSFNKGALLSVGWSTGRIAHIPLYFVNAQFPRFSPVLGRAQEPAPAGGGSIH
DLPLFTETSPSAPWDPLPGPPPVLPHSPHSHL*; source=CCDS
```

8.3 Insertion

```
$ transvar ganno -i 'chr2:g.69741762_69741763insTGC' --ccds --print-protein-pretty
```

```
chr2:g.69741762_69741763insTGC CCDS1893 (protein_coding) AAK1 -
chr2:g.69741780_69741782dupCTG/c.1614_1616dupGCA/p.Q546dupQ inside_[cds_in_
↪exon_12]
CSQN=InFrameInsertion; left_align_gDNA=g.69741762_69741763insTGC; unalign_gDNA=
g.69741762_69741763insTGC; left_align_cDNA=c.1596_1597insCAG; unalign_cDNA=c.16
```

(continues on next page)

(continued from previous page)

```

14_1616dupGCA;left_align_protein=p.Y532_Q533insQ;unalign_protein=p.Q539dupQ;v
ariant_protein_seq=MKKFFDSRREQGGSGLSGSSGGGGSTSLGSGYIGRVFGIGRQQVTVEVLAEGGFA
IVFLVRTSNGMKCALKRMFVNNEHDLQVCKREIQIMRDLSGHKNIVGYIDSSINNVSSGDVWEVLILMDFCRGGQVV
NLMNQRLQTGFTENEVLQIFCDTCEAVARLHQCKTPIIHRDLKVENILLHDRGHYVLCDFGSATNKFQNPQTEGVNA
VEDEIKKYTTLSYRAPEMVNLYSGKIIITKADIWALGCLLYKLCYFTLPPFGESQVAICDGNFTIPDNSRYSDMHCL
IRYMLEPDPDKRPDIYQVSYFSFKLLKKECPIPNVQNSPIPAKLPEPVKASEAAAKKTQPKARLTDPIPTTETSIAP
RQRPKAGQTQPNPILPIQPALTPRKRATVQPPPQAAGSSNQPGLLASVPPQPKPQAPPSPLPQTQAKQPQAPPPTPQ
QTPSTQAQGLPAQAQATPQHQQQLFLKQQQQQQQPPPAQQQPAGTFYQQQQAQTTQQFQAVHPATQKPAIAQFPVVSQ
GGSQQQLMQNFYQQQQQQQQQQQQQ__[insert_Q]__LATALHQQQLMTQQAALQQKPTMAAGQQPQPQAAAAP
QPAPAQEPAPVQPKVQTTTPPAVQGGQKVGSLTPPSSPKTQRAGHRRILSDVTHSAVFGVPAKSTQLLQAAA
AEASLNKSKSATTPSGSPRTSQQNVYNPSEGSTWNPFDNDFSKLTAEEELNKNDFAKLGEKHKPEKLGSSAESLIP
GFQSTQGDFAFATTSFSAGTAEKRKGGQTVDSGLPLLSVDFPIPLQVPDAPEKLIIEGLKSPDTSLLLPDLLPMTDPF
GSTSDAVIEKADVAVESLIPGLEPPVPQRLPSQTESVTSNRDTSLTGEDSLLDCSLLSNPTDLEEFAPTAISAPV
HKAADSNIISGFDVPEGSDKVAEDEFDPIPVLITKNPQGGHSRNSGSSSESLPNLARSLLLVDQLIDL*;phase
=2;source=CCDS

```

8.4 Block substitution

```
$ transvar ganno -i "chr2:g.234183372_234183383del" --ccds --print-protein-pretty
```

```

chr2:g.234183372_234183383del      CCDS2502 (protein_coding)      ATG16L1 +
chr2:g.234183372_234183383del12/c.845_856del12/p.H282_G286delinsR inside_[cds_in_
↪exon_8]
CSQN=MultiAAMissense;left_align_gDNA=g.234183372_234183383del12;unaligned_gDN
A=g.234183372_234183383del12;left_align_cDNA=c.845_856del12;unalign_cDNA=c.84
5_856del12;variant_protein_seq=MSSGLRAADFPRWKRHISEQLRRRDRLQRQAFEEIILQYNKLEKS
DLHSVLAQKLQAEKHDVFNRIEISPGHDGTWNDNQLQEMAQLRIKHQEELTELHKKRGELAQLVIDLNNQMQRKDRE
MQMNEAKIAECLQITISDLETECLDLRKLCDLERANQTLKDEYDALQITFTALEGKLRKTEENQELVTRWMAEKAQ
EANRLNAENEKDSRRRQARLQKELAEAAKEPLVEQDDDIIEVIVDETSDHTEETSPVRAISRAATRRSVSFPVPQD
NVDT__[HPGSG>R]__KEVRVPATALCVFDAQHDGEVNAVQFSPGSRLLATGGMDRRVKLWEVFGKCEFEKGLSLSGS
NAGITSIEFDSAGSYLLAASNDFASRIWTVDDYRLRHTLTGHSGKVLSAKFLLDNARIVSGSHDRTLKLDLRSKVC
IKTVFAGSSCNDIVCTEQCVMSGHFDKKIRFWDIRSESVIREMELLGKITALDLNPERTELLSCSRDDLKVIDLRT
NAIKQTF SAPGFKCGSDWTRVVFSPDGSYVAAGSAEGSLYIWSVLTGKVEKVLKQHSINAVAWSPSGSHVVSVD
KGCKAVLWAQY*;source=CCDS
chr2:g.234183372_234183383del      CCDS2503 (protein_coding)      ATG16L1 +
chr2:g.234183372_234183383del12/c.902_913del12/p.H301_G305delinsR inside_[cds_in_
↪exon_9]
CSQN=MultiAAMissense;left_align_gDNA=g.234183372_234183383del12;unaligned_gDN
A=g.234183372_234183383del12;left_align_cDNA=c.902_913del12;unalign_cDNA=c.90
2_913del12;variant_protein_seq=MSSGLRAADFPRWKRHISEQLRRRDRLQRQAFEEIILQYNKLEKS
DLHSVLAQKLQAEKHDVFNRIEISPGHDGTWNDNQLQEMAQLRIKHQEELTELHKKRGELAQLVIDLNNQMQRKDRE
MQMNEAKIAECLQITISDLETECLDLRKLCDLERANQTLKDEYDALQITFTALEGKLRKTEENQELVTRWMAEKAQ
EANRLNAENEKDSRRRQARLQKELAEAAKEPLVEQDDDIIEVIVDETSDHTEETSPVRAISRAATKRLSQPAGGLLD
SITNIFGRRSVSFPVPQDNVDT__[HPGSG>R]__KEVRVPATALCVFDAQHDGEVNAVQFSPGSRLLATGGMDRRV
KLWEVFGKCEFEKGLSLSGSNAGITSIEFDSAGSYLLAASNDFASRIWTVDDYRLRHTLTGHSGKVLSAKFLLDNARI
VSGSHDRTLKLDLRSKVCIKTVFAGSSCNDIVCTEQCVMSGHFDKKIRFWDIRSESVIREMELLGKITALDLNPER
TELLSCSRDDLKVIDLRTNAIKQTF SAPGFKCGSDWTRVVFSPDGSYVAAGSAEGSLYIWSVLTGKVEKVLKQHS
SSINAVAWSPSGSHVVSVDKGCKAVLWAQY*;source=CCDS
chr2:g.234183372_234183383del      CCDS54438 (protein_coding)      ATG16L1 +
chr2:g.234183372_234183383del12/c.413_424del12/p.H138_G142delinsR inside_[cds_in_
↪exon_5]
CSQN=MultiAAMissense;left_align_gDNA=g.234183372_234183383del12;unaligned_gDN
A=g.234183372_234183383del12;left_align_cDNA=c.413_424del12;unalign_cDNA=c.41

```

(continues on next page)

(continued from previous page)

```
3_424del12;variant_protein_seq=MSSGLRAADFPRWKRHISEQLRRRDRLQRQAFEEIILQYNKLLLEKS
DLHSVLAQKLQAEKHDVPNRHEIRRRQARLQKELAEAAKEPLVEQDDDDIEVIVDETS DHTEETSPVRAISRATR
SVSSFPVPQDNVD__ [HPGSG>R]__KEVRVPATALCVFDAHDGEVNAVQFSPGSRLLATGGMDRRVKLWEVFGEK
CEFKGSLSGSNAGITSIEFDSAGSYLLAASNDFFASRIWTVDDYRLRHTLTGHSGKVLAKFLLDNARIVSGSHDRTL
KLWDLRSKVCIKTVFAGSSCNDIVCTEQCVMSGHFDKKIRFWDIRSESVREME LLGKITALDLNPERTELLSCSRD
DLLKVIDLRINA IKQTF SAPGFKCGSDWTRVVFSPDGSYVAAGSAEGSLYIWSVLTGKVEKVL SKQHSSSINAVAWS
PSGSHVVSVDKGCKAVLWAQY*;source=CCDS
```

8.5 Frameshift sequence

```
$ transvar canno --ccds -i 'CCDS8856:c.769_770delGG' --print-protein-pretty
```

```
CCDS8856:c.769_770delGG      CCDS8856 (protein_coding)      AAAS      -
chr12:g.53703428_53703429delCC/c.770_771delGG/p.G257Afs*65      inside_[cds_in_
↳exon_8]
CSQN=Frameshift;left_align_gDNA=g.53703424_53703425delCC;unaligned_gDNA=g.537
03425_53703426delCC;left_align_cDNA=c.766_767delGG;unaligned_cDNA=c.769_770delG
G;variant_protein_seq=MCSLGLFPPPPRQVTLYEHNNELV TGSSYESPPPDFRGQWINLPVLQTKDPL
KTPGRLDHGTRTAFIHHREQVWKRCINIW RDVGLFGLVNEIANSEEEVFEWVKTAGWALALCRWASSLHGS LFP HL
SLRSEDLIAEFAQVTNWSSCCLRVFAWHPHNTKFAVALDDSVRVYNASSTIVPSLKHRLQRNVASLAWKPLSASVL
AVACQSCILIWTLDP TSLSTRPSSGCAQVLSHPGHTPV TSLAWAPSG__ [frameshift_GRLLSASPVDAAIRVW
DVSTETCVPLPWFRGGGVNLLWSPDGSKILATTPSAVFRVWEAQMWTCERWPTLSGRCQTGCWSPDGSRL LFTV LG
EPLIYLSLSPERCGEGKGCVGAKSATIVADLSETTIQTPDGEERLGGEAHSMVWDP SGERLAVLMKGP RVQDGKP
VILLFRTRNSPVFELLPCGI IQGEPGAQPQLITFHPSFNKGALLSVGWSTGRIAHIPLYFVNAQFPRFSPVLGRAQE
PPAGGGGSIHDLPLFTETSP TSAPWDPLPGPPPVLPHSPHSHL*>AAALS FTRGCCYPGMGCLNRDLCPPSLVPRRW
GDQPALVPRRQQNPGYHSF SCLSSLGGPDVDL*];source=CCDS
```

```
$ transvar canno -i 'CCDS54438:c.409_421del' --ccds --print-protein-pretty
```

```
CCDS54438:c.409_421del      CCDS54438 (protein_coding)      ATG16L1 +
chr2:g.234183368_234183380del113/c.409_421del113/p.T137Lfs*5      inside_[cds_in_
↳exon_5]
CSQN=Frameshift;left_align_gDNA=g.234183367_234183379del113;unaligned_gDNA=g.2
34183368_234183380del113;left_align_cDNA=c.408_420del113;unaligned_cDNA=c.409_421
del113;variant_protein_seq=MSSGLRAADFPRWKRHISEQLRRRDRLQRQAFEEIILQYNKLLLEKSDLHSV
LAQKLQAEKHDVPNRHEIRRRQARLQKELAEAAKEPLVEQDDDDIEVIVDETS DHTEETSPVRAISRATR SVSSF
PVPQDNVD__ [frameshift_THPGSGKEVRVPATALCVFDAHDGEVNAVQFSPGSRLLATGGMDRRVKLWEVFGE
KCEFKGSLSGSNAGITSIEFDSAGSYLLAASNDFFASRIWTVDDYRLRHTLTGHSGKVLAKFLLDNARIVSGSHDRT
LKLWDLRSKVCIKTVFAGSSCNDIVCTEQCVMSGHFDKKIRFWDIRSESVREME LLGKITALDLNPERTELLSCSR
DDLLKVIDLRINA IKQTF SAPGFKCGSDWTRVVFSPDGSYVAAGSAEGSLYIWSVLTGKVEKVL SKQHSSSINAVAW
SPSGSHVVSVDKGCKAVLWAQY*>LVKK*];source=CCDS
```

9.1 How to batch-process?

For all mutation types, one can batch process a list of mutation identifiers with optional transcript id to constraint the search. Take SNV for example,

```
transvar panno -l example/input_table -g 1 -m 5 -t 2 --ensembl -o 2,3,4
```

As suggested by the command, TransVar takes as input the 1st column as gene and 4th column as identifier. The 2nd column will be used as the transcript id from Ensembl to constrain the alternative identifier search. The 2nd, 3rd and 5th columns are chosen to be output as a validation of TransVar's performance.

Input:

ADAMTSL3	ENST00000286744	15:84442328	c.243G>A	p.W81*	Nonsense
ADAMTSL3	ENST00000286744	15:84442326	c.241T>C	p.W81R	Missense
ADAMTSL4	ENST00000369038	1:150530513	c.2270G>A	p.G757D	Missense
ADCY2	ENST00000338316	5:7802364	c.2662G>A	p.V888I	Missense
ADCY2	ENST00000338316	5:7802365	c.2663T>C	p.V888A	Missense

Output:

```
ENST00000286744|15:84442328|c.243G>A ENST00000286744 (protein_coding) ADAMTSL3_
↪ +
chr15:g.84442327G>A/c.242G>A/p.W81* cds_in_exon_4
reference_codon=TGG;candidate_codons=TAA, TAG, TGA;candidate_snv_variants=chr15
:g.84442328G>A;candidate_mnv_variants=chr15:g.84442327_84442328delGGinsAA;mis
sense;aliases=ENSP00000286744;source=Ensembl
ENST00000286744|15:84442326|c.241T>C ENST00000286744 (protein_coding) ADAMTSL3_
↪ +
chr15:g.84442326T>A/c.241T>A/p.W81R cds_in_exon_4
reference_codon=TGG;candidate_codons=AGG, AGA, CGA, CGC, CGG, CGT;candidate_snv_va
riants=chr15:g.84442326T>C;candidate_mnv_variants=chr15:g.84442326_84442328de
lTGGinsAGA, chr15:g.84442326_84442328delTGGinsCGA, chr15:g.84442326_84442328del
```

(continues on next page)

(continued from previous page)

```

TGGinsCGC, chr15:g.84442326_84442328delTGGinsCGT;missense;aliases=ENSP00000286
744;source=Ensembl
ENST00000369038|1:150530513|c.2270G>A      ENST00000369038 (protein_coding)
↪ADAMTSL4      +
chr1:g.150530513G>A/c.2270G>A/p.G757D      cds_in_exon_12
reference_codon=GGT;candidate_codons=GAC,GAT;candidate_mnv_variants=chr1:g.15
0530513_150530514delGTinsAC;missense;aliases=ENSP00000358034;source=Ensembl
ENST00000338316|5:7802364|c.2662G>A      ENST00000338316 (protein_coding)      ADCY2      +
chr5:g.7802364G>A/c.2662G>A/p.V888I      cds_in_exon_21
reference_codon=GTC;candidate_codons=ATC,ATA,ATT;candidate_mnv_variants=chr5:
g.7802364_7802366delGTCinsATA,chr5:g.7802364_7802366delGTCinsATT;missense;ali
ases=ENSP00000342952;source=Ensembl
ENST00000338316|5:7802365|c.2663T>C      ENST00000338316 (protein_coding)      ADCY2      +
chr5:g.7802365T>C/c.2663T>C/p.V888A      cds_in_exon_21
reference_codon=GTC;candidate_codons=GCA,GCC,GCG,GCT;candidate_mnv_variants=c
hr5:g.7802365_7802366delTCinsCA,chr5:g.7802365_7802366delTCinsCG,chr5:g.78023
65_7802366delTCinsCT;missense;aliases=ENSP00000342952;source=Ensembl

```

9.2 How to use VCF as input?

TransVar can take VCF as input when annotating from genomic level.

```

transvar ganno --vcf ALL.wgs.phase1_release_v3.20101123.snps_indel_sv.sites.vcf.gz --
↪ccds
# or
transvar ganno --vcf demo.1kg.vcf --ccds

```

9.3 How to automatically decompose a haplotype into multiple mutations?

TransVar performs local alignment to allow long haplotype to be decomposed into multiple mutations.

```
$ transvar ganno --ccds -i 'chr20:g.645097_645111delinsGTGCGATACCCAGGAG' --haplotype
```

leads to 2 snv and one insertion

```

chr20:g.645097_645111delinsGTGCGATACCCAGGAG      CCDS13006 (protein_coding)      SCRT2      -
chr20:g.645098G>T/c.141C>A/p.A47A      inside_[cds_in_exon_2]
CSQN=Synonymous;codon_pos=645098-645099-645100;ref_codon_seq=GCC;source=CCDS
chr20:g.645097_645111delinsGTGCGATACCCAGGAG      CCDS13006 (protein_coding)      SCRT2      -
chr20:g.645101_645102insA/c.137_138insT/p.A47Rfs*350      inside_[cds_in_exon_2]
CSQN=Frameshift;left_align_gDNA=g.645101_645102insA;unalign_gDNA=g.645101_645
102insA;left_align_cDNA=c.137_138insT;unalign_cDNA=c.137_138insT;source=CCDS
chr20:g.645097_645111delinsGTGCGATACCCAGGAG      CCDS13006 (protein_coding)      SCRT2      -
chr20:g.645107T>A/c.134-2A>T/.      inside_[intron_between_exon_1_and_2]
CSQN=SpliceAcceptorSNV;C2=SpliceAcceptorOfExon1_At_chr20:645106;source=CCDS

```

9.4 How to use 3-letter code instead of 1-letter code for protein?

TransVar automatically infer whether the input is a 3-letter code or 1-letter code. The output is default to 1-letter code. But can be switched to 3-letter code through the `--aa3` option. For example,

```
$ transvar panno --ccds -i 'PIK3CA:p.Glu545Lys' --aa3
```

```
PIK3CA:p.Glu545Lys  CCDS43171 (protein_coding)  PIK3CA  +
chr3:g.178936091G>A/c.1633G>A/p.Glu545Lys  inside_[cds_in_exon_9]
CSQN=Missense;reference_codon=GAG;candidate_codons=AAG,AAA;candidate_mnv_vari
ants=chr3:g.178936091_178936093delGAGinsAAA;dbsnp=rs104886003(chr3:178936091G
>A);source=CCDS
```

9.5 How can I let TransVar output sequence context?

The option `--aacontext 5` output +/- 5bp protein sequence context.

```
$ transvar ganno -i 'chr17:7577124' --ccds --aacontext 5
```

```
chr17:7577124  CCDS11118 (protein_coding)  TP53  -
chr17:g.7577124C>/c.814G>/p.V272  inside_[cds_in_exon_7]
is_gene_body;aacontext=RNSFE[V]RVCAC;codon_pos=7577122-7577123-7577124;source
=CCDS
chr17:7577124  CCDS45605 (protein_coding)  TP53  -
chr17:g.7577124C>/c.814G>/p.V272  inside_[cds_in_exon_7]
is_gene_body;aacontext=RNSFE[V]RVCAC;codon_pos=7577122-7577123-7577124;source
=CCDS
chr17:7577124  CCDS45606 (protein_coding)  TP53  -
chr17:g.7577124C>/c.814G>/p.V272  inside_[cds_in_exon_7]
is_gene_body;aacontext=RNSFE[V]RVCAC;codon_pos=7577122-7577123-7577124;source
=CCDS
```

shows the protein sequence context in the `aacontext` tag.

9.6 How to report results in one line for each query?

Use `--oneline` option. This separates the outputs from each transcript by '|||'.

9.7 I got 'gene_not_recognized', what's wrong?

Most likely you forgot to specify a transcript definition such as `--ccds` or `--ensembl`. Sometimes there are non-canonical names for genes, this can be fixed through the `--alias` option and specify an alias table. TransVar comes with alias table from UCSC knownGene.

9.8 Does TransVar support alternative format for MNV such as c.508_509CC>TT?

Yes, but only in input. For example, **c.508_509CC>TT**

```
$ transvar canno --ccds -i 'A1CF:c.508_509CC>TT'
```

```
A1CF:c.508_509CC>TT CCDS7241 (protein_coding) A1CF -  
chr10:g.52595929_52595930delinsAA/c.508_509delinsTT/p.P170L inside_[cds_in_  
↪exon_4]  
CSQN=Missense;codon_cDNA=508-509-510;source=CCDS  
A1CF:c.508_509CC>TT CCDS7242 (protein_coding) A1CF -  
chr10:g.52595929_52595930delinsAA/c.508_509delinsTT/p.P170L inside_[cds_in_  
↪exon_4]  
CSQN=Missense;codon_cDNA=508-509-510;source=CCDS
```

9.9 Does TransVar support relaxed input without 'g.', 'c.' and 'p.'?

Yes, the 'g.', 'c.' and 'p.' are optional in the input. For example, 12:109702119insACC is equally acceptable as chr12:g.109702119_109702120insACC. TransVar also accepts '>' in denoting MNV. E.g., c.113G>TACTAGC can be used in place of c.113delGinsTACTAGC. This is common in some database such as COSMIC.

9.10 When I annotate a variant for protein identifier, why would I end up getting results in another variant type?

TransVar follows in full the HGVS nomenclature while annotating protein level mutation identifiers. For example, a out-of-phase, in frame insertion, ACIN1:c.1930_1931insATTAC will be annotated with p.S643_R644insHS rather than R644delinsHSR. Protein level mutation will be generated as if no nucleotide mutation information exists.

CHAPTER 10

Features

- supports HGVS nomenclature
- supports input from gene name, transcript ID, protein ID, UniProt ID and other aliases
- supports both left-alignment and right-alignment convention in reporting indels and duplications
- supports annotation of a region based on a transcript-dependent characterization
- supports mutations at both coding region and intronic/UTR regions
- supports noncoding RNA annotation
- supports VCF inputs
- supports long haplotype decomposition
- supports single nucleotide variation (SNV), insertions and deletions (indels) and block substitutions
- supports transcript annotation from commonly-used databases such as Ensembl, NCBI RefSeq and GENCODE etc.
- supports GRCh36, 37, 38 (human), GRCm38 (mouse), NCBIM37 (mouse)
- supports >60 other genomes available from Ensembl
- functionality of forward annotation.

The MIT License (MIT)

Copyright (c) 2015,2016

The University of Texas MD Anderson Cancer Center

Wanding Zhou, Tenghui Chen, Ken Chen

Permission is hereby granted, free of charge, to any person obtaining a copy of this software and associated documentation files (the “Software”), to deal in the Software without restriction, including without limitation the rights to use, copy, modify, merge, publish, distribute, sublicense, and/or sell copies of the Software, and to permit persons to whom the Software is furnished to do so, subject to the following conditions:

The above copyright notice and this permission notice shall be included in all copies or substantial portions of the Software.

THE SOFTWARE IS PROVIDED “AS IS”, WITHOUT WARRANTY OF ANY KIND, EXPRESS OR IMPLIED, INCLUDING BUT NOT LIMITED TO THE WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE AND NONINFRINGEMENT. IN NO EVENT SHALL THE AUTHORS OR COPYRIGHT HOLDERS BE LIABLE FOR ANY CLAIM, DAMAGES OR OTHER LIABILITY, WHETHER IN AN ACTION OF CONTRACT, TORT OR OTHERWISE, ARISING FROM, OUT OF OR IN CONNECTION WITH THE SOFTWARE OR THE USE OR OTHER DEALINGS IN THE SOFTWARE.

CHAPTER 12

Need Help

If you have trouble using TransVar, please email zhouwanding@gmail.com. Bug reports are also welcomed at the [issue tracker](#).

If you use TransVar in your work please cite [Zhou et al. Nature Methods 12, 1002-1003 \(2015\)](#). Thank you.

CHAPTER 13

Indices and tables

- `genindex`
- `modindex`
- `search`