Package 'antigen.garnish'

July 6, 2022

Title Tumor neoantigen prediction

Version 2.3.1

Description Ensemble tumor neoantigen prediction from complex variants. Immunogenicity filtering based on the Tumor Neoantigen Selection Alliance (TESLA).

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Imports Biostrings, data.table, magrittr, mclust, parallel, purrr, Rdpack, stats, stringr, testthat, tidyr, uuid, vcfR, zoo

RdMacros Rdpack

Encoding UTF-8

LazyData true

LazyLoad yes

RemoteUrl https://github.com/andrewrech/antigen.garnish

Roxygen list(markdown = TRUE)

RoxygenNote 7.2.0

R topics documented:

`antigen.garnish` **antigen.garnish**: *tumor neoantigen prediction*

Description

Github Documentation

See Also

`garnish_variants`

`garnish_affinity`

`garnish_antigens`

`dissimilarity_score` *Return dissimilarity (to reference proteome) values for a vector of peptides.*

Description

Return dissimilarity (to reference proteome) values for a vector of peptides.

Usage

```
dissimilarity_score(v, db, kval = 4.86936, aval = 32)
```

Arguments

`v`	Character. Vector of nmers.
`db`	Character. One of c("mouse", "human").
`kval`	Numeric. Steepness of sigmoidal curve at k. Default 4.86936, the value used in the analysis of Van Allen, Snyder, Rizvi, Riaz, and Hellmann datasets.
`aval`	Numeric. Optionally can be "mean" to use mean alignment for nmers passed. Horizontal displacement of partition function. Default is 32, based on max_SW of 75 million 8-15mers from the five clinical datasets against human, if using max_SW, use 52. This value may not be meaningful for murine alignment so use with care.

Value

Data table of nmers and corresponding dissimilarity values (to the non-mutated proteome).

`foreignness_score` *Return foreignness_scores for a vector of peptides.*

Description

Return foreignness_scores for a vector of peptides.

Usage

```
foreignness_score(v, db)
```

Arguments

v	Character. Vector of nmers.
db	Character. One of c("mouse", "human")

Value

Data table of nmers and corresponding foreignness_score values.

`garnish_affinity` *Perform neoantigen prediction.*

Description

Perform ensemble neoantigen prediction on a data table of missense mutations, insertions, or deletions using netMHC and mhcflurry.

Usage

```
garnish_affinity(
  dt = NULL,
  path = NULL,
  binding_cutoff = 500,
  counts = NULL,
  min_counts = 1,
  peptide_length = 15:8,
  blast = TRUE,
  save = TRUE,
  remove_wt = TRUE
)
```

Arguments

dt	Data table. Input data table from garnish_variants, or a data table in the correct form (see Github README).
path	Path to input csv or tsv file.
binding_cutoff	Numeric. Maximum consensus MHC-binding affinity that will be passed for IEDB and dissimilarity analysis. Default is 500 (nM). Note: If a peptide binds to any MHC allele in the table below this threshold, foreignness score and dissimilarity will be returned for all rows with that peptide.
counts	Optional. A file path to a csv or tsv RNA count matrix. The first column must contain Ensembl transcript ids. All samples in the input table must be present in the count matrix.
min_counts	Integer. The minimum number of estimated read counts for a transcript to be considered for neoantigen prediction. Default is 1.
peptide_length	Numeric vector. Length(s) of peptides to create.
blast	Logical. Run BLASTp to find wild-type peptide and known IEDB matches?
save	Logical. Save a copy of garnish_affinity output to the working directory as "ag_output.txt"? Default is TRUE.
remove_wt	Logical. Check all nmers generated against wt peptidome and remove matches? Default is TRUE. If investigating wild-type sequences, set this to FALSE.

Details

- see list_mhc for compatible MHC allele syntax, you may also use "all_human" or "all_mouse" in the MHC column to use all supported alleles

Parallel cores used can be set via environment variable AG_THREADS (default: all available).

Value

A data table of binding predictions including:

- **cDNA_seq**: mutant cDNA sequence
- **cDNA_locs**: starting index of mutant cDNA
- **cDNA_locl**: ending index of mutant cDNA
- **cDNA_type**: netMHC prediction tool output
- **frameshift**: frameshift variant?
- **coding**: wt cDNA sequence
- **coding_mut**: mutant cDNA sequence
- **pep_type**: type of peptide
- **pep_mut**: mutant peptide sequence
- **pep_wt**: wt peptide sequence
- **mismatch_s**: starting index of mutant peptide sequence
- **mismatch_l**: ending index of mutant peptide sequence

- **mutant_index**: index of mutant peptide
- **nmer**: nmer for prediction
- **nmer_i**: index of nmer in sliding window
- **_net**: netMHC prediction tool output
- **mhcflurry_**: mhcflurry_ prediction tool output
- **DAI**: Differential agretopicity index of missense and corresponding wild-type peptide. Differential agretopicty is the ratio of MHC binding afinity between mutant and corresponding normal peptide, with higher values indicating greater relative binding of the mutant peptide.
- **BLAST_A**: Ratio of consensus binding affinity of mutant peptide / closest single AA mismatch from blastp results. Returned only if `blast = TRUE`.

antigen.garnish quality analysis metric results:

- **Ensemble_score**: average value of MHC binding affinity from all prediction tools.
- **foreignness_score**: Neoantigen foreignness threshold. Value of 0 to 1 indicating the TCR recognition probability, calculated by summing alignments in IEDB immunogenic peptides, with 1 indicating greater homology to immunogenic peptides.
- **IEDB_anno**: The best alignment from the IEDB database queried for the sample if applicable.
- **min_DAI**: Minimum of value of BLAST_A or DAI values, to provide the most conservative proteome-wide estimate of differential binding between input and wildtype matches.
- **dissimilarity**: Value of 0 to 1 indicating alignment to the self-proteome, calculated in an analogous manner to neoanigen foreignness, with 1 indicating greater dissimilarity.

References

Richman LP, Vonderheide RH, and Rech AJ. Neoantigen dissimilarity to the self-proteome predicts immunogenicity and response to immune checkpoint blockade. Cell Systems. 2019. Duan, F., Duitama, J., Seesi, S.A., Ayres, C.M., Corcelli, S.A., Pawashe, A.P., Blanchard, T., McMahon, D., Sidney, J., Sette, A., et al. Genomic and bioinformatic profiling of mutational neoepitopes reveals new rules to predict anticancer immunogenicity. J Exp Med. 2014.

Luksza, M, Riaz, N, Makarov, V, Balachandran VP, et al. A neoepitope fitness model predicts tumour response to checkpoint blockade immunotherapy. Nature. 2017. Rech AJ, Balli D, Mantero A, Ishwaran H, Nathanson KL, Stanger BZ, Vonderheide RH. Tumor immunity and survival as a function of alternative neopeptides in human cancer. Clinical Cancer Research, 2018.

Wells DK, van Buuren MM, Dang KK, Hubbard-Lucey VM, Sheehan KCF, Campbell KM, Lamb A, Ward JP, Sidney J, Blazquez AB, Rech AJ, Zaretsky JM, Comin-Anduix B, Ng AHC, Chour W, Yu TV, Rizvi1 H, Chen JM, Manning P, Steiner GM, Doan XC, The TESLA Consortium, Merghoub T, Guinney J, Kolom A, Selinsky C, Ribas A, Hellmann MD, Hacohen N, Sette A, Heath JR, Bhardwaj N, Ramsdell F, Schreiber RD, Schumacher TN, Kvistborg P, Defranoux N. Key Parameters of Tumor Epitope Immunogenicity Revealed Through a Consortium Approach Improve Neoantigen Prediction. Cell. 2020.

See Also

`list_mhc`

`garnish_variants`

`garnish_antigens`

garnish_antigens *List top peptides using TESLA criteria for recognition features of immunogenic peptides.*

Description

The TESLA consortium identified recognition features of immunogenic peptides. This function filters peptides meeting any of these criteria.

Usage

```
garnish_antigens(
  dt,
  affinity_threshold = 34,
  differential_agretopcity_threshold = 10,
  dissimilarity_threshold = 0,
  foreignness_threshold = 1e-15
)
```

Arguments

dt	An output data table from garnish_affinity, either a data table object or path to a file.
affinity_threshold	Numeric. Neoantigen affinity threshold, nanomolar (nM) scale.
differential_agretopcity_threshold	Numeric. Neoantigen differential agretopcity threshold. Differential agretopicty is the proteome-wide ratio of MHC binding afinity between mutant and closest normal peptide, with higher values indicating greater relative binding of the mutant peptide.
dissimilarity_threshold	Numeric. Neoantigen dissimilarity threshold. Value of 0 to 1 indicating alignment to the self-proteome, calculated in an analogous manner to neoanigen foreignness, with 1 indicating greater dissimilarity.
foreignness_threshold	Numeric. Neoantigen foreignness threshold. Value of 0 to 1 indicating the TCR recognition probability, calculated by summing alignments in IEDB immunogenic peptides, with 1 indicating greater homology to immunogenic peptides.

Value

A data table with ranked and annotated peptides.

References

Richman LP, Vonderheide RH, and Rech AJ. Neoantigen dissimilarity to the self-proteome predicts immunogenicity and response to immune checkpoint blockade. Cell Systems. 2019. Duan, F., Duitama, J., Seesi, S.A., Ayres, C.M., Corcelli, S.A., Pawashe, A.P., Blanchard, T., McMahon, D., Sidney, J., Sette, A., et al. Genomic and bioinformatic profiling of mutational neoepitopes reveals new rules to predict anticancer immunogenicity. J Exp Med. 2014.

Luksza, M, Riaz, N, Makarov, V, Balachandran VP, et al. A neoepitope fitness model predicts tumour response to checkpoint blockade immunotherapy. Nature. 2017. Rech AJ, Balli D, Mantero A, Ishwaran H, Nathanson KL, Stanger BZ, Vonderheide RH. Tumor immunity and survival as a function of alternative neopeptides in human cancer. Clinical Cancer Research, 2018.

Wells DK, van Buuren MM, Dang KK, Hubbard-Lucey VM, Sheehan KCF, Campbell KM, Lamb A, Ward JP, Sidney J, Blazquez AB, Rech AJ, Zaretsky JM, Comin-Anduix B, Ng AHC, Chour W, Yu TV, Rizvi1 H, Chen JM, Manning P, Steiner GM, Doan XC, The TESLA Consortium, Merghoub T, Guinney J, Kolom A, Selinsky C, Ribas A, Hellmann MD, Hacohen N, Sette A, Heath JR, Bhardwaj N, Ramsdell F, Schreiber RD, Schumacher TN, Kvistborg P, Defranoux N. Key Parameters of Tumor Epitope Immunogenicity Revealed Through a Consortium Approach Improve Neoantigen Prediction. Cell. 2020.

See Also

`garnish_variants`

`garnish_affinity`

`garnish_variants` *Process VCF variants and return a data table for epitope prediction.*

Description

Process paired tumor-normal VCF variants annotated with SnpEff for neoantigen prediction using `garnish_affinity`. All versioned Ensembl transcript IDs (e.g. ENST00000311936.8) from any GRCh38 or GRCm38 release are supported. Parsing will fall back to using RefSeq IDs, but RefSeq IDs are not preferred.

Usage

```
garnish_variants(vcfs, tumor_sample_name = "TUMOR")
```

Arguments

`vcfs`	Paths to one or more VFC files to import. See details below.
`tumor_sample_name`	Character, name of column in vcf of tumor sample.

Value

A data table with one unique SnpEff variant annotation per row, including:

- **sample_id**: sample identifier constructed from input `.vcf` file names
- **ANN**: SnpEff annotation
- **effect_type**: SnpEff effect type
- **transcript_id**: transcript effected
- **cDNA_change**: cDNA change in HGVS format

See Also

`garnish_affinity`

`garnish_antigens`

`list_mhc` *Return a data table of available MHC types for all prediction tools.*

Description

Return a data table of available MHC types for all prediction tools.

Usage

```
list_mhc()
```