Package 'Uniquorn'

September 16, 2024

Title Identification of cancer cell lines based on their weighted mutational/ variational fingerprint

Version 2.24.0

Description 'Uniquorn' enables users to identify cancer cell lines.
Cancer cell line misidentification and cross-
contamination reprents a significant challenge for cancer researchers.
The identification is vital and in the frame of this package based on the locations/ loci of somatic and germline mutations/ variations.
The input format is vcf/ vcf.gz and the files have to contain a single cancer cell line sample (i.e. a single member/genotype/gt column in the vcf file).

Imports stringr, R.utils, WriteXLS, stats, doParallel, foreach, GenomicRanges, IRanges, VariantAnnotation, data.table

Depends R (>= 3.5)

License Artistic-2.0

Type Package

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Contents

`add_custom_vcf_to_database` *add_custom_vcf_to_database This function adds the variants of parsed custom CCLs to a monet DB instance*

Description

add_custom_vcf_to_database This function adds the variants of parsed custom CCLs to a monet DB instance

Usage

```
add_custom_vcf_to_database(
    vcf_input_files,
    ref_gen = "GRCH37",
    library_name = "CUSTOM",
    n_threads = 1,
    test_mode = FALSE
)
```

Arguments

vcf_input_files	a character vector containing the input vcf files. This may be one or many vcf files.
ref_gen	a character string specifying the reference genome version. All training sets are associated with a reference genome version. Default is "GRCH37".
library_name	a character string giving the name of the library to add the cancer cell lines to. Default is "CUSTOM". Library name will be automatically added as a suffix to the identifier.
n_threads	an integer specifying the number of threads to be used.
test_mode	Is this a test? Just for internal use

Value

Message wheather the adding was successful

Examples

```
HT29_vcf_file = system.file("extdata/HT29_TEST.vcf", package = "Uniquorn");
add_custom_vcf_to_database(
    vcf_input_files = HT29_vcf_file,
    library_name = "CELLMINER",
    ref_gen = "GRCH37",
    n_threads = 1,
    test_mode = TRUE
)
```

---

add_missing_cls *add_missing_cls*

Description

add_missing_cls

Usage

```
add_missing_cls(res_table, dif_cls)
```

Arguments

res_table	Table that contains the identification results
dif_cls	Missing CLs

Value

Results table with added missing cls

add_penalty_statistics *add_penalty_statistics*

Description

Add penalty statistics to results

Usage

```
add_penalty_statistics(match_t, minimum_matching_mutations)
```

Arguments

match_t	object that contains the matching variants
minimum_matching_mutations	a numerical giving the minimum amount of mutations that has to match between query and training sample for a positive prediction

Value

The updated statistics

add_p_q_values_statistics *add_p_q_values_statistics*

Description

A hypergeometric distribution-assumption allows to calculate the p-values for a significant or non-significant overlap in this function

Usage

```
add_p_q_values_statistics(
  g_query,
  match_t,
  p_value,
  ref_gen,
  minimum_matching_mutations,
  top_hits_per_library
)
```

Arguments

g_query	IRanges object that contains the query variants
match_t	A table that contains the nubmber of matching variants
p_value	Threshold for the significance p-value
ref_gen	Reference genome version
minimum_matching_mutations	Manual lower amount of matching mutations require for a significant match between a query and a reference
top_hits_per_library	limits significant similarities to the first n hits

Details

add_p_q_values_statistics Calculates the p-values

Value

R table with a statistic

---

create_bed_file *create_bed_file*

Description

Creates BED files from the found and not found annotated mutations

Usage

```
create_bed_file(
match_t,
vcf_fingerprint,
output_file,
ref_gen,
manual_identifier

)
```

Arguments

match_t	R table which contains the mutations from the training database for the cancer cell lines
vcf_fingerprint	contains the mutations that are present in the query cancer cell line's vcf file
output_file	Path to output file
ref_gen	Reference genome version
manual_identifier	Manually enter a vector of CL name(s) whose bed files should be created, independently from them passing the detection threshold

Value

Returns a message which indicates if the BED file creation has succeeded

---

`identify_vcf_file` *identify_VCF_file*

Description

Identifies a cancer cell lines contained in a vcf file based on the pattern (start & length) of all contained mutations/ variations.

Usage

```
identify_vcf_file(
    vcf_file,
    output_file,
    ref_gen,
    minimum_matching_mutations,
    mutational_weight_inclusion_threshold,
    write_xls,
    output_bed_file,
    top_hits_per_library,
    manual_identifier,
    verbose,
    p_value,
    confidence_score,
    n_threads,
    write_results
)
```

Arguments

`vcf_file`	Input vcf file. Only one sample column allowed.
`output_file`	Path of the output file. If blank, autogenerated as name of input file plus '_uniquorn_ident.tab' suffix.
`ref_gen`	Reference genome version. All training sets are associated with a reference genome version. Default: GRCH37
`minimum_matching_mutations`	The minimum amount of mutations that has to match between query and training sample for a positive prediction
`mutational_weight_inclusion_threshold`	Include only mutations with a weight of at least x. Range: 0.0 to 1.0. 1= unique to CL. ~0 = found in many CL samples.
`write_xls`	Create identification results additionally as xls file for easier reading

`output_bed_file`
: If BED files for IGV visualization should be created for the Cancer Cell lines that pass the threshold

`top_hits_per_library`
: Limit the number of significant similarities per library to n (default 3) many hits. Is particularrly used in contexts when heterogeneous query and reference CCLs are being compared.

`manual_identifier`
: Manually enter a vector of CL name(s) whose bed files should be created, independently from them passing the detection threshold

`verbose`
: Print additional information

`p_value`
: Required p-value for identification. Note that if you set the confidence score, the confidence score overrides the p-value

`confidence_score`
: Cutoff for positive prediction between 0 and 100. Calculated by transforming the p-value by -1 * log(p-value) Note that if you set the confidence score, the confidence score overrides the p-value

`n_threads`
: Number of threads to be used

`write_results`
: Write identification results to file

Details

`identify_vcf_file` parses the vcf file and predicts the identity of the sample

Value

R table with a statistic of the identification result

Examples

```
HT29_vcf_file = system.file("extdata/HT29.vcf", package = "Uniquorn");

identification = identify_vcf_file(
    vcf_file = HT29_vcf_file,
    verbose = FALSE,
    write_results = FALSE
)
```

`initiate_canonical_databases`
initiate_canonical_databases

Description

Parses data into r list variable

Usage

```
initiate_canonical_databases(
    cosmic_file = "CosmicCLP_MutantExport.tsv.gz",
    ccle_file = "CCLE_mutations.csv",
    ccle_sample_file = "sample_info.csv",
    ref_gen = "GRCH38"
)
```

Arguments

cosmic_file	The path to the Cosmic CLP file. The Cosmic file can be obtained from "https://cancer.sanger.ac.uk/cell_li and should be labeled "CosmicCLP_MutantExport.tsv.gz". Ensure that the right reference genome is used
ccle_file	The path to the ccle DNA genotype data file. It should be labeled "CCLE_mutations.csv". Ensure that the right reference genome is used
ccle_sample_file	The path to the CCLE sample file. It should be labeled "sample_info.csv" containing both the DepMap ID and corresponding cell line name.
ref_gen	Reference genome version

Value

Returns message if parsing process has succeeded

Examples

```
initiate_canonical_databases(
    cosmic_file = "CosmicCLP_MutantExport.tsv.gz",
    ccle_file = "CCLE_mutations.csv",
    ccle_sample_file = "sample_info.csv",
    ref_gen = "GRCH38"
)
```

---

init_and_load_identification

init_and_load_identification

Description

Initiate the analysis Output basic information

Usage

```
init_and_load_identification(
    verbose,
    ref_gen,
    vcf_file,
    output_dir
)
```

Arguments

verbose	Print additional information
ref_gen	Reference genome version. All training sets are associated with a reference genome version. Default: GRCH37
vcf_file	Path to vcf_file
output_dir	Output directory for identification results

Details

`init_and_load_identification` parses vcf file and output basic information

Value

Three file path instances and the fingerprint

`match_query_ccl_to_database` *match_query_ccl_to_database*

Description

Matches query ccl to the database

Usage

```
match_query_ccl_to_database(
  g_query,
  ref_gen = "GRCH37",
  library_name,
  mutational_weight_inclusion_threshold
)
```

Arguments

g_query	IRanges object that contains the variants
ref_gen	Reference genome version. All training sets are associated with a reference genome version. Default: GRCH37
library_name	a character string giving the name of the library
mutational_weight_inclusion_threshold	a numerical giving the lower bound for mutational weight to be included

Value

The R Table sim_list which contains the CoSMIC CLP fingerprints

---

parse_ccle_genotype_data

parse_ccle_genotype_data

Description

Parses ccle genotype data

Usage

```
parse_ccle_genotype_data(ccle_file, ccle_sample_file, ref_gen = "GRCH38")
```

Arguments

ccle_file	Path to CCLE file on hard disk
ccle_sample_file	Path to CCLE sample file
ref_gen	Reference genome version

Value

The R Table sim_list which contains the CCLE fingerprints

parse_cosmic_genotype_data *parse_cosmic_genotype_data*

Description

Parses cosmic genotype data

Usage

```
parse_cosmic_genotype_data(cosmic_file, ref_gen = "GRCH38")
```

Arguments

cosmic_file	Path to cosmic clp file in hard disk
ref_gen	Reference genome version

Value

The R Table sim_list which contains the CoSMIC CLP fingerprints

parse_vcf_file *Filter Parsed VCF Files*

Description

Intern utility function. Filters the parsed VCF file for all informations except for the start and length of variations/mutations.

Usage

```
parse_vcf_file(
    vcf_file,
    ref_gen,
    library_name
)
```

Arguments

vcf_file	character string giving the path to the vcf file on the operating system.
ref_gen	Reference genome version
library_name	Name of the reference library

Value

Loci-based DNA-mutational fingerprint of the cancer cell line as found in the input VCF file.

parse_vcf_query_into_db

parse_vcf_query_into_db This function adds the variants of parsed custom CCLs to a monet DB instance

Description

parse_vcf_query_into_db This function adds the variants of parsed custom CCLs to a monet DB instance

Usage

```
parse_vcf_query_into_db(
  g_query,
  ref_gen = "GRCH37",
  library_name,
  test_mode = FALSE
)
```

Arguments

g_query	a GenomicRanges object
ref_gen	a character string specifying the reference genome version. All training sets are associated with a reference genome version. Default is "GRCH37".
library_name	a character string giving the name of the library to add the cancer cell lines to. Default is "CUSTOM". Library name will be automatically added as a suffix to the identifier.
test_mode	Is this a test? Just for internal use

Value

Message wheather the adding was successful

read_library_names

Library Name Reader

Description

This function procides information on the reference library names

Usage

```
read_library_names(ref_gen)
```

Arguments

ref_gen	a character vector specifying the reference genome version. All training sets are associated with a reference genome version. Default is "GRCH37".

Value

Returns a character vector of the contained libraries

Examples

```
read_library_names(ref_gen = "GRCH37")
```

---

read_mutation_grange_objects *read_mutation_grange_objects*

Description

Read the GRange object for a specific library

Usage

```
read_mutation_grange_objects(
  library_name,
  mutational_weight_inclusion_threshold,
  ref_gen,
  test_mode
)
```

Arguments

library_name	a character string giving the name of the library
mutational_weight_inclusion_threshold	a numerical giving the lower bound for mutational weight to be included
ref_gen	Reference genome version. All training sets are associated with a reference genome version. Default: GRCH37
test_mode	Is this a test? Just for internal use

Value

The R Table sim_list which contains the CoSMIC CLP fingerprints

remove_ccls_from_database

Remove Cancer Cell Line

Description

This function removes a cancer cell line training fingerprint (VCF file) from the database. The names of all training sets can be seen by using the function show_contained_cls.

Usage

```
remove_ccls_from_database(ccl_names, ref_gen = "GRCH37",
    library_name, test_mode = FALSE)
```

Arguments

ccl_names	A character vector giving the names of the cancer cell line identifiers to be removed. Can be one or many
ref_gen	A character vector specifying the reference genome version. All training sets are associated with a reference genome version. Default is "GRCH37".
library_name	Name of the library from which ccls are to be removed
test_mode	Signifies if this is a test run

Value

Message that indicates whether the removal was succesful.

Examples

```
remove_ccls_from_database(
    ccl_names = "HT29",
    ref_gen = "GRCH37",
    library_name = "CELLMINER",
    test_mode = TRUE
)
```

remove_library_from_database

Remove entire Library from Database

Description

This function removes a entire library from the database by removing all associated cancer cell line fingerprints from the database.

Usage

```
remove_library_from_database(library, ref_gen = "GRCH37", test_mode = FALSE)
```

Arguments

library	a character vector giving the names of the library to be removed.
ref_gen	a character vector specifying the reference genome version. All training sets are associated with a reference genome version. Default is "GRCH37".
test_mode	is this a test? Just for internal use.

Value

Message that indicates whether the removal was succesful.

Examples

```
remove_library_from_database(library = "CELLMINER",
                                ref_gen = "GRCH37",
                                test_mode = TRUE)
```

---

show_contained_ccls *show_contained_ccls*

Description

This function displays the names, amount of mutations and the overall weight of the mutations of all contained cancer cell line fingerprints for a chosen reference genome and optional library.

Usage

```
show_contained_ccls(ref_gen, verbose)
```

Arguments

ref_gen	a character vector specifying the reference genome version. All training sets are associated with a reference genome version. Default is "GRCH37".
verbose	Should DB informations be printed?

Value

R table which contains identifiers of all cancer cell line samples which match the specified parameters (reference genome and library).

Examples

```
## Show all contained cancer cell lines for reference GRCH37:
show_contained_ccls(ref_gen = "GRCH37", verbose = TRUE)
```

show_contained_variants_for_ccl *Variants In Cancer Cell Line*

Description

This function shows all mutations present in the database for a selected cancer cell line and reference genome.

Usage

```
show_contained_variants_for_ccl(
    name_ccl,
    ref_gen,
    library_name,
    mutational_weight_inclusion_threshold
)
```

Arguments

name_ccl	a character vector giving the identifier of the cancer cell line for which mutations will be shown.
ref_gen	a character vector specifying the reference genome version. All training sets are associated with a reference genome version. Default is "GRCH37".
library_name	Name of the reference library
mutational_weight_inclusion_threshold	Include only mutations with a weight of at least x. Range: 0.0 to 1.0. 1= unique to CL. ~0 = found in many CCL samples.

Value

GenomicRanges object that contains the ccl's variants

Examples

```
## Show all mutations for Cancer Cell Line 'SK_OV_3'
show_contained_variants_for_ccl(
    name_ccl = "SK_OV_3",
    ref_gen = "GRCH37",
    library_name = "CELLMINER",
    mutational_weight_inclusion_threshold = 0
)
```

show_contained_variants_in_library
All variants contained in reference library

Description

This function shows all variants contained in a reference library for a given inclusion weight. Default inclusion weight is 0 (all variants).

Usage

```
show_contained_variants_in_library(
    ref_gen,
    library_name,
    mutational_weight_inclusion_threshold
)
```

Arguments

ref_gen	a character vector specifying the reference genome version. All training sets are associated with a reference genome version. Default is "GRCH37".
library_name	Name of the reference library.
mutational_weight_inclusion_threshold	Include only mutations with a weight of at least x. Range: 0.0 to 1.0. 1 = unique to CL. ~0 = found in many CL samples.

Value

Returns a GenomicRanges object that contains the variants

Examples

```
## Show all variants contained in reference library CELLMINER
show_contained_variants_in_library(
    ref_gen = "GRCH37",
    library_name = "CELLMINER",
    mutational_weight_inclusion_threshold = 0
)
```

`show_which_ccls_contain_variant` *Cancer cell lines with specific variant*

Description

This function displays all cancer cell lines in the database which contain a specified variant. Utilizes closed interval coordinates.

Usage

```
show_which_ccls_contain_variant(
    start,
    end,
    chromosome,
    ref_gen,
    library_name,
    mutational_weight_inclusion_threshold
)
```

Arguments

`start`	Start coordinate
`end`	Stop coordinate
`chromosome`	Chromosome, 'chr' prefixes are ignored
`ref_gen`	a character vector specifying the reference genome version. All training sets are associated with a reference genome version. Default is `"GRCH37"`.
`library_name`	Name of the reference library
`mutational_weight_inclusion_threshold`	Include only mutations with a weight of at least x. Range: 0.0 to 1.0. 1= unique to CL. ~0 = found in many CCL samples.

Value

Returns a GenomicRanges object that contains the variant if present. Member ccls can be found in the $Member_ccl vector

Examples

```
show_which_ccls_contain_variant(
    start = 92030762,
    end = 92030762,
    chromosome = 8,
    ref_gen = "GRCH37",
    library_name = "CELLMINER",
    mutational_weight_inclusion_threshold = 0
)
```

Index