

# Package ‘Uniquorn’

November 21, 2024

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

**Version** 2.27.0

**Description** 'Uniquorn' enables users to identify cancer cell lines.

Cancer cell line misidentification and cross-contamination represents 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 . . . . .         | 2  |
| add_missing_cls . . . . .                    | 3  |
| add_penalty_statistics . . . . .             | 4  |
| add_p_q_values_statistics . . . . .          | 4  |
| create_bed_file . . . . .                    | 5  |
| identify_vcf_file . . . . .                  | 6  |
| initiate_canonical_databases . . . . .       | 7  |
| init_and_load_identification . . . . .       | 8  |
| match_query_ccl_to_database . . . . .        | 9  |
| parse_ccl_genotype_data . . . . .            | 10 |
| parse_cosmic_genotype_data . . . . .         | 11 |
| parse_vcf_file . . . . .                     | 11 |
| parse_vcf_query_into_db . . . . .            | 12 |
| read_library_names . . . . .                 | 12 |
| read_mutation_grange_objects . . . . .       | 13 |
| remove_ccls_from_database . . . . .          | 14 |
| remove_library_from_database . . . . .       | 14 |
| show_contained_ccls . . . . .                | 15 |
| show_contained_variants_for_ccl . . . . .    | 16 |
| show_contained_variants_in_library . . . . . | 17 |
| show_which_ccls_contain_variant . . . . .    | 18 |

|              |           |
|--------------|-----------|
| <b>Index</b> | <b>19</b> |
|--------------|-----------|

---

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 | <i>add_missing_cls</i> |
|-----------------|------------------------|

---

**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 | <i>create_bed_file</i> |
|-----------------|------------------------|

---

**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 | <i>identify_VCF_file</i> |
|-------------------|--------------------------|

---

**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 particularly 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 $-1 * \log(\text{p-value})$ 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**

|                               |   |
|-------------------------------|---|
| <code>cosmic_file</code>      | 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 |
| <code>ccle_file</code>        | The path to the ccle DNA genotype data file. It should be labeled "CCLE_mutations.csv". Ensure that the right reference genome is used  |
| <code>ccle_sample_file</code> | The path to the CCLE sample file. It should be labeled "sample_info.csv" containing both the DepMap ID and corresponding cell line name.  |
| <code>ref_gen</code>          | 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**

|  |   |
|--|---|
| <code>g_query</code>                               | IRanges object that contains the variants   |
| <code>ref_gen</code>                               | Reference genome version. All training sets are associated with a reference genome version. Default: GRCH37 |
| <code>library_name</code>                          | a character string giving the name of the library   |
| <code>mutational_weight_inclusion_threshold</code> | 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**

|                               |                                |
|-------------------------------|--------------------------------|
| <code>ccle_file</code>        | Path to CCLE file on hard disk |
| <code>ccle_sample_file</code> | Path to CCLE sample file       |
| <code>ref_gen</code>          | 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_ccls`.

### Usage

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

### Arguments

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

### Value

Message that indicates whether the removal was successful.

### 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 an 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

## \* internal

- [parse\\_ccle\\_genotype\\_data, 10](#)
- [parse\\_cosmic\\_genotype\\_data, 11](#)
  
- [add\\_custom\\_vcf\\_to\\_database, 2](#)
- [add\\_missing\\_cls, 3](#)
- [add\\_p\\_q\\_values\\_statistics, 4](#)
- [add\\_penalty\\_statistics, 4](#)
  
- [create\\_bed\\_file, 5](#)
  
- [identify\\_vcf\\_file, 6](#)
- [init\\_and\\_load\\_identification, 8](#)
- [initiate\\_canonical\\_databases, 7](#)
  
- [match\\_query\\_ccl\\_to\\_database, 9](#)
  
- [parse\\_ccle\\_genotype\\_data, 10](#)
- [parse\\_cosmic\\_genotype\\_data, 11](#)
- [parse\\_vcf\\_file, 11](#)
- [parse\\_vcf\\_query\\_into\\_db, 12](#)
  
- [read\\_library\\_names, 12](#)
- [read\\_mutation\\_grange\\_objects, 13](#)
- [remove\\_ccls\\_from\\_database, 14](#)
- [remove\\_library\\_from\\_database, 14](#)
  
- [show\\_contained\\_ccls, 15](#)
- [show\\_contained\\_variants\\_for\\_ccl, 16](#)
- [show\\_contained\\_variants\\_in\\_library, 17](#)
- [show\\_which\\_ccls\\_contain\\_variant, 18](#)