Package 'clonotypeR'

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Type Package

Title High throughput analysis of T cell antigen receptor sequences

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Author Charles Plessy <plessy@riken.jp>

Maintainer Charles Plessy <plessy@riken.jp>

Description High throughput analysis of T cell antigen receptor sequences
The genes encoding T cell receptors are created by somatic recombination,generating an immense combination of V, (D) and J segments. Additional
processes during the recombination create extra sequence diversity between the
V an J segments. Collectively, this hyper-variable region is called the CDR3 loop.

The purpose of this package is to process and quantitatively analyse millions of
V-CDR3-J combination, called clonotypes, from multiple sequence libraries.

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Depends methods

Suggests BiocGenerics, edgeR, knitr, pvclust, RUnit, vegan

VignetteBuilder knitr

biocViews Bioinformatics, HighThroughputSequencing

R topics documented:

clonotype_table *Create a table count of clonotypes or other features.*

Description

Using a clonotype data frame loaded with read_clonotypes, clonotype_table will create a table counting how many times each clonotypes have been seen in each libraries. By default, the unproductive rearrangements are filtered out.

Usage

```
clonotype_table(libs, feats=c("V","pep","J"), data, filter=data$unproductive, minscore=0, minqual=1)
```

Arguments

libs	A character vector containing the name of one or many libraries. Same names must not appear twice. If no library names are provided, all the libraries present in the clonotypes data frame will be used.
feats	What to count. By default, it counts clonotypes, defined as c("V","pep","J"). But it can also count single features, such as the V or J segments.
data	Data frame as loaded by read_clonotypes.
filter	Logical vector to filter out clonotypes. By default it relies on the clonotypes data frame to provide a "unproductive" column, that indicates clonotypes with a stop codon or a frame shift.
minscore	Minimum alignment score. Clonotypes with an alignment score lower than this value are discarded.
minqual	Minimum mapping quality. Clonotypes with a mapping quality lower than this value are discarded.

Value

clonotype_table returns a data frame, where row names are features (clonotypes, segment names, ...), column names are libraries, and values are number of times each feature was found in each library.

Author(s)

Charles Plessy

See Also

read_clonotypes

Examples

```
# Read the packages example data
clonotypes <- read_clonotypes(system.file(extdata, clonotypes.txt.gz, package = "clonotypeR"))

# Inspect the alignment scores
hist(clonotypes$score)

# Count J segments
j <- clonotype_table(levels(clonotypes$lib), "J", data=clonotypes)

# Normalise counts in parts per million
J <- data.frame(prop.table(as.matrix(j),2) * 1000000)
```

`common_clonotypes` *Reports clonotypes common between samples.*

Description

When given one group of samples, lists the clonotypes that have been observed at least in one sample. The returned list can be used to subset a data frame produced by `clonotype_table`.

When given two groups of samples, lists the clonotypes that have been observed at least in one sample of each group. Groups can contain a single sample, in which case the returned list is simply the clonotypes found in both samples.

When given a table of clonotypes, produces a matrix in which each cell reports the number of clonotypes found in each pair of samples.

Usage

```
common_clonotypes(group1, group2, mode="groups", data)
```

Arguments

`group1`	A character vector containing clonotype library names
`group2`	A character vector containing clonotype library names
`mode`	By default, "groups" when "group1" or "group2" is provided, "matrix" mode otherwise.
`data`	A clonotype_table where the data is stored.

Value

In "groups" mode, a character vector of clonotype names. Their order follows the original row name order of the clonotype_table.

In "matrix" mode, a symmetric matrix of numbers, with the same row and column names as the row names of the clonotype_table used.

Author(s)

Charles Plessy

See Also

clonotype_table, unique_clonotypes

Examples

```
# Load example data
clonotypes.long <- read_clonotypes(system.file(extdata, clonotypes.txt.gz, package = "clonotypeR"))
clonotypes <- clonotype_table(levels(clonotypes.long$lib), data=clonotypes.long)
summary(clonotypes)

# List clonotypes found in library A, and B or C.
common_clonotypes(group1="A", group2=c("B","C"), data=clonotypes)

# Count clonotypes found in library A, and B or C.
length(common_clonotypes(group1="A", group2=c("B","C"), data=clonotypes))

# Matrix of numbers of common clonotypes
common_clonotypes(data=clonotypes)
```

---

extdata *Extra data used to calculate ID numbers in Yassai et al.'s nomenclature.*

Description

Data frame derived from Table 1 of Yassai et al., 2009, to construct clonotype names.

Details

`V_after_C`: sequence of the V segments after their conserved cystein.

`J_before_FGxG`: sequence of the J segments before their conserved FGxG motif.

`codon_ids`: data frame derived from Table 1 of Yassai et al., 2009, to construct clonotype names.

The V_after_C and J_before_FGxG tables are, generated from the mouse reference data with the command: `make refresh-data` in the source repository of clonotypeR.

Value

codon_ids:

`codon`	Nucleotide triplet.
`aminoacid`	Single-letter amino acid abbreviation ("O" for stop).
`id`	ID numbers assigned to the codons for each amino acids.

J_before_FGxG:

row name	J segment name, for instance "TRAJ61".
sequence	Sequence of the nucleic acids preceding the first codon of the conserved FGxG motif.

V_after_C:

row name	V segment name, for instance "TRAV1".
sequence	Sequence of the nucleic acids following the codon of the conserved cysteine.

References

A clonotype nomenclature for T cell receptors. Maryam B. Yassai, Yuri N. Naumov, Elena N. Naumova and Jack Gorski Immunogenetics, 2009, Volume 61, Number 7, Pages 493-502

See Also

yassai_identifier

Examples

```
V_after_C <- read.table(system.file(extdata, V_after_C.txt.gz, package = "clonotypeR"), stringsAsFactors=FALSE)

J_before_FGxG <- read.table(system.file(extdata, J_before_FGxG.txt.gz, package = "clonotypeR"), stringsAsFactors=

codon_ids <- read.table(system.file(extdata, codon_ids.txt.gz, package = "clonotypeR"), header=TRUE, row.names=1)
```

---

is_unproductive *Determines if clonotype sequences are productive.*

Description

ClonotypeR identifies V and J segments, isolates the DNA sequence between the conserved cystein and the FGxG motifs, and translates it. This functions verifies that this sequence is in frame and has no stop codon.

Usage

```
is_unproductive(data)
```

Arguments

data	Data frame of clonotype sequences, or character vector describing a single clonotype, where the DNA sequence is available under the name dQuote("dna") and its translation available under the name dQuote("pep").

Details

Clonotypes are marked unproductive if the length of their DNA sequence is not a multiple of 3, or if they contain a stop codon, as indicated by an asterisk in the translated sequence.

Value

Returns a logical vector, with one value per row in the original data.

Author(s)

Charles Plessy

See Also

read_clonotypes

Examples

```
clonotypes <- read_clonotypes(system.file(extdata, clonotypes.txt.gz, package = "clonotypeR"))
is_unproductive(clonotypes)
```

`read_clonotypes` *Reads a clonotype_table and returns a data frame.*

Description

Reads a clonotype_table in a TAB-separated or OSCT format, and returns a data frame that has eight columns, for library name, V and J segments names, sequence read identifier, DNA, sequence quality, aminoacid sequence of the CDR3 region, mark for unproductive recombinations.

Usage

```
read_clonotypes(filename, scores=TRUE, ...)
```

Arguments

`filename`	Path to the tabulation-delimited text file containing the extracted clonotypes.
`scores`	Set to false to load legacy data that did not contain “score” and “mapq” columns.
`...`	The rest of the arguments are passed to the `read.table()` function.

Value

lib	Library name (factor).
V	V segment name (factor).
J	J segment name (factor).
score	Alignment score (numeric).
mapq	Mapping quality (numeric). A sequence with a good alignment score will still have a low mapping quality if there are good alternative alignments to other V segments.
read	Sequence read identifier (character).
dna	DNA sequence of the CDR3 region (character).
qual	Quality values for the DNA sequence (character).
pep	Translation of the DNA sequence (character).
unproductive	Flag indicating stop codons or frame shifts (logical).

Author(s)

Charles Plessy

See Also

clonotype_table, is_unproductive, read.table, Order Switchable Column Table (OSCT, http://sourceforge.net/projects/osctf/)

Examples

```
clonotypes <- read_clonotypes(system.file(extdata, clonotypes.txt.gz, package = "clonotypeR"))
```

---

unique_clonotypes *Lists unique clonotypes in libraries.*

Description

Finds all the clonotypes expressed in one or more libraries, and returns a vector where they are listed once. This vector can be used to subset a clonotype_table.

Usage

```
unique_clonotypes(..., data)
```

Arguments

...	One or more character vectors contain clonotype library names
data	The name of the clonotype_table where the data is stored.

Details

Uses the table called "clonotypes" by default.

Value

Character vector of clonotype names. Their order follows the original row name order of the clonotype_table.

Author(s)

Charles Plessy

See Also

clonotype_table, common_clonotypes

Examples

```
# Load example data
clonotypes.long <- read_clonotypes(system.file(extdata, clonotypes.txt.gz, package = "clonotypeR"))
clonotypes <- clonotype_table(levels(clonotypes.long$lib), data=clonotypes.long)
summary(clonotypes)

# List clonotypes found in library A.
unique_clonotypes("A", data=clonotypes)

# List clonotypes found in library A or B.
unique_clonotypes("A","B", data=clonotypes)
```

---

yassai_identifier *TCR clonotype identifier (Yassai et al.).*

Description

The clonotype nomenclature defined by Yassai et al. in http://dx.doi.org/10.1007/s00251-009-0383-x.

Usage

```
yassai_identifier(data, V_after_C, J_before_FGxG)
```

Arguments

data	A data frame or a character vector containing a clonotype(s) with proper row or element names.
V_after_C	(optional) A data frame indicating the aminoacids following the conserved cystein for each V segment.
J_before_FGxG	(optional) A data frame indicating the aminoacids preceding the conserved FGxG motif for each V segment.

Details

By default, `yassai_identifier()` assume mouse sequences and will load the V_after_C and J_before_FGxG tables distributed in this package. It is possible to provide alternative tables either by passing them directly as argument, or by installing them as "./inst/extdata/V_after_C.txt.gz" and "./inst/extdata/J_before_FGxG.txt.gz".

Value

The name (for instance sIRSSy.1456B19S1B27L11) consists of five segments:

1. CDR3 amino acid identifier (ex. sIRSSy), followed by a dot ;
2. CDR3 nucleotide sequence identifier (ex. 1456) ;
3. variable (V) segment identifier (ex. BV19S1) ;
4. joining (J) segment identifier (ex. BJ2S7) ;
5. CDR3 length identifier (ex. L11).

Author(s)

Charles Plessy

See Also

`codon_ids`, `J_before_FGxG`, `V_after_C`

Examples

```
clonotypes <- read_clonotypes(system.file(extdata, clonotypes.txt.gz, package = "clonotypeR"))
head(yassai_identifier(clonotypes))
```

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