Package: SeqKat (via r-universe)

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Type Package

Title Detection of Kataegis

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Description Kataegis is a localized hypermutation occurring when a region is enriched in somatic SNVs. Kataegis can result from multiple cytosine deaminations catalyzed by the AID/APOBEC family of proteins. This package contains functions to detect kataegis from SNVs in BED format. This package reports two scores per kataegic event, a hypermutation score and an APOBEC mediated kataegic score. Yousif, F. et al.; The Origins and Consequences of Localized and Global Somatic Hypermutation; Biorxiv 2018 <doi:10.1101/287839>.

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LinkingTo Rcpp

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License GPL-2

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`combine.table` *Combine Table*

Description

Merges overlapped windows to identify genomic boundaries of kataegic events. This function also assigns hypermuation and kataegic score for combined windows

Usage

```
combine.table(test.table, somatic, mutdistance, segnum, output.name)
```

Arguments

`test.table`	Data frame of kataegis test scores
`somatic`	Data frame of somatic variants
`mutdistance`	The maximum intermutational distance allowed for SNVs to be grouped in the same kataegic event. Recommended value: 3.2
`segnum`	Minimum mutation count. The minimum number of mutations required within a cluster to be identified as kataegic. Recommended value: 4
`output.name`	Name of the generated output directory.

Author(s)

Fouad Yousif

Fan Fan

Examples

```
load(
 paste0(
  path.package("SeqKat"),
  "/extdata/test/somatic.rda"
  )
 );

load(
 paste0(
  path.package("SeqKat"),
  "/extdata/test/final.score.rda"
  )
 );

combine.table(
 final.score,
 somatic,
 3.2,
 4,
 tempdir()
 );
```

`final.score` *Final Score*

Description

Assigns hypermutation score (hm.score) and kataegic score (k.score)

Usage

```
final.score(test.table, cutoff, somatic, output.name)
```

Arguments

`test.table`	Data frame of kataegis test scores
`cutoff`	The minimum hypermutation score used to classify the windows in the sliding binomial test as significant windows. The score is calculated per window as follows: -log10(binomial test p-value). Recommended value: 5
`somatic`	Data frame of somatic variants
`output.name`	Name of the generated output directory.

Author(s)

Fan Fan

Fouad Yousif

Examples

```
load(
 paste0(
  path.package("SeqKat"),
  "/extdata/test/somatic.rda"
  )
 );

load(
 paste0(
  path.package("SeqKat"),
  "/extdata/test/test.table.rda"
  )
 );

final.score(
 test.table,
 5,
 somatic,
 tempdir()
 );
```

`get.context` *Get Context*

Description

Gets the 5' and 3' neighboring bases to the mutated base

Usage

```
get.context(file, start)
```

Arguments

`file`	Reference files directory
`start`	The position of the mutation gene

Value

The trinucleotide context.

Author(s)

Fouad Yousif

Fan Fan

Examples

```
example.ref.dir <- paste0(
 path.package("SeqKat"),
 "/extdata/test/ref/"
 );
get.context(file.path(example.ref.dir, 'chr4.fa'), c(1582933, 1611781))
```

`get.exprobntcx` *get.exprobntcx*

Description

Gets the expected probability for each trinucleotide and total number of tcx

Usage

```
get.exprobntcx(somatic, ref.dir, trinucleotide.count.file)
```

Arguments

`somatic`	Data frame of somatic variants
`ref.dir`	Path to a directory containing the reference genome.
`trinucleotide.count.file`	A tab seprarated file containing a count of all trinucleotides present in the reference genome. This can be generated with the get.trinucleotide.counts() function in this package.

Author(s)

Fan Fan

Fouad Yousif

Examples

```
load(
 paste0(
  path.package("SeqKat"),
  "/extdata/test/somatic.rda"
  )
 );

trinucleotide.count.file <- paste0(
 path.package("SeqKat"),
 "/extdata/tn_count.txt"
 );

example.ref.dir <- paste0(
 path.package("SeqKat"),
```

```
 "/extdata/test/ref/"
 );

get.exprobntcx(somatic, example.ref.dir, trinucleotide.count.file)
```

`get.nucleotide.chunk.counts` *Get Nucleotide Chunk Counts*

Description

Obtain counts for all possible trinucleotides within a specified genomic region

Usage

```
get.nucleotide.chunk.counts(key, chr, upstream = 1, downstream = 1,
  start = 1, end = -1)
```

Arguments

`key`	List of specify trinucleotides to count
`chr`	Chromosome
`upstream`	Length upstream to read
`downstream`	Length downstream to read
`start`	Starting position
`end`	Ending position

Author(s)

Fouad Yousif

Examples

```
example.ref.dir <- paste0(
 path.package("SeqKat"),
 "/extdata/test/ref/"
 );

bases.raw <- c('A','C','G','T','N');
tri.types.raw <- c(
 outer(
  c(outer(bases.raw, bases.raw, function(x, y) paste0(x,y))),
  bases.raw, function(x, y) paste0(x,y))
 );
tri.types.raw <- sort(tri.types.raw);
get.nucleotide.chunk.counts(
 tri.types.raw,
 file.path(example.ref.dir, 'chr4.fa'),
```

```
upstream = 1,
downstream = 1,
start = 1,
end = -1
);
```

`get.pair` *Get Pair*

Description

Generates the reverse compliment of a nucleotide sequence

Usage

```
get.pair(x)
```

Arguments

x	asdf

Details

Reverses and compliments the bases of the input string. Bases must be (A, C, G, T, or N).

Author(s)

Fouad Yousif

Examples

```
get.pair("GATTACA")
```

`get.tn` *Get Trinucleotides*

Description

Count the frequencies of 32 trinucleotide in a region respectively

Usage

```
get.tn(chr, start.bp, end.bp, ref.dir)
```

Arguments

chr	Chromosome
start.bp	Starting position
end.bp	Ending position
ref.dir	Path to a directory containing the reference genome.

Author(s)

Fan Fan

Examples

```
example.ref.dir <- paste0(
 path.package("SeqKat"),
 "/extdata/test/ref/"
 );
get.tn(chr=4, start.bp=1, end.bp=-1, example.ref.dir)
```

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get.toptn *Get Top Trinucleotides*

Description

Generate a tri-nucleotide summary for each sliding window

Usage

```
get.toptn(somatic.subset, chr, start.bp, end.bp, ref.dir)
```

Arguments

somatic.subset	Data frame of somatic variants subset for a specific chromosome
chr	Chromosome
start.bp	Starting position
end.bp	Ending position
ref.dir	Path to a directory containing the reference genome.

Author(s)

Fan Fan

Fouad Yousif

Examples

```
## Not run:
get.toptn(somatic.subset, chr, start.bp, end.bp, ref.dir)

## End(Not run)
```

`get.trinucleotide.counts` *Get Trinucleotide Counts*

Description

Aggregates the total counts of each possible trinucleotide.

Usage

```
get.trinucleotide.counts(ref.dir, ref.name, output.dir)
```

Arguments

`ref.dir`	Path to a directory containing the reference genome.
`ref.name`	Name of the reference genome being used (i.e. hg19, GRCh38, etc)
`output.dir`	Path to a directory where output will be created.

Author(s)

Fan Fan

Fouad Yousif

Examples

```
## Not run:
get.trinucleotide.counts(ref.dir, "hg19", tempdir());

## End(Not run)
```

seqkat *SeqKat*

Description

Kataegis detection from SNV BED files

Usage

```
seqkat(sigcutoff = 5, mutdistance = 3.2, segnum = 4, ref.dir = NULL,
  bed.file = "./", output.dir = "./", chromosome = "all",
  chromosome.length.file = NULL, trinucleotide.count.file = NULL)
```

Arguments

sigcutoff	The minimum hypermutation score used to classify the windows in the sliding binomial test as significant windows. The score is calculated per window as follows: -log10(binomial test p-value). Recommended value: 5
mutdistance	The maximum intermutational distance allowed for SNVs to be grouped in the same kataegic event. Recommended value: 3.2
segnum	Minimum mutation count. The minimum number of mutations required within a cluster to be identified as kataegic. Recommended value: 4
ref.dir	Path to a directory containing the reference genome. Each chromosome should have its own .fa file and chromosomes X and Y are named as chr23 and chr24. The fasta files should contain no header
bed.file	Path to the SNV BED file. The BED file should contain the following information: Chromosome, Position, Reference allele, Alternate allele
output.dir	Path to a directory where output will be created.
chromosome	The chromosome to be analysed. This can be (1, 2, ..., 23, 24) or "all" to run sequentially on all chromosomes.
chromosome.length.file	A tab separated file containing the lengths of all chromosomes in the reference genome.
trinucleotide.count.file	A tab seprarated file containing a count of all trinucleotides present in the reference genome. This can be generated with the get.trinucleotide.counts() function in this package.

Details

The default paramters in SeqKat have been optimized using Alexanrov's "Signatures of mutational processes in human cancer" dataset. SeqKat accepts a BED file and outputs the results in TXT format. A file per chromosome is generated if a kataegic event is detected, otherwise no file is generated. SeqKat reports two scores per kataegic event, a hypermutation score and an APOBEC mediated kataegic score.

Author(s)

Fouad Yousif

Fan Fan

Christopher Lalansingh

Examples

```
example.bed.file <- paste0(
 path.package("SeqKat"),
 "/extdata/test/PD4120a-chr4-1-2000000_test_snvs.bed"
 );
example.ref.dir <- paste0(
 path.package("SeqKat"),
 "/extdata/test/ref/"
 );
example.chromosome.length.file <- paste0(
 path.package("SeqKat"),
 "/extdata/test/length_hg19_chr_test.txt"
 );
seqkat(
 5,
 3.2,
 2,
 bed.file = example.bed.file,
 output.dir = tempdir(),
 chromosome = "4",
 ref.dir = example.ref.dir,
 chromosome.length.file = example.chromosome.length.file
 );
```

`test.kataegis` *Test Kataegis*

Description

Performs exact binomial test to test the deviation of the 32 tri-nucleotides counts from expected

Usage

```
test.kataegis(chromosome.num, somatic, units, exprobntcx, output.name, ref.dir,
  chromosome.length.file)
```

Arguments

`chromosome.num`	Chromosome
`somatic`	Data frame of somatic variants
`units`	Base window size

exprobntcx	Expected probability for each trinucleotide and total number of tcx
output.name	Name of the generated output directory.
ref.dir	Path to a directory containing the reference genome.
chromosome.length.file	A tab separated file containing the lengths of all chromosomes in the reference genome.

Author(s)

Fouad Yousif

Examples

```
load(
 paste0(
  path.package("SeqKat"),
  "/extdata/test/somatic.rda"
  )
 );

load(
 paste0(
  path.package("SeqKat"),
  "/extdata/test/exprobntcx.rda"
  )
 );

example.chromosome.length.file <- paste0(
 path.package("SeqKat"),
 "/extdata/test/length_hg19_chr_test.txt"
 );

example.ref.dir <- paste0(
 path.package("SeqKat"),
 "/extdata/test/ref/"
 );

test.kataegis(
 4,
 somatic,
 2,
 exprobntcx,
 tempdir(),
 example.ref.dir,
 example.chromosome.length.file
 );
```

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