Package ‘oncoscanR’

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Type Package

Title Secondary analyses of CNV data (HRD and more)

Version 1.6.0

Description The software uses the copy number segments from a text file and identifies all chromosome arms that are globally altered and computes various genome-wide scores. The following HRD scores (characteristic of BRCA-mutated cancers) are included: LST, HR-LOH, nLST and gLOH. the package is tailored for the ThermoFisher Oncoscan assay analyzed with their Chromosome Alteration Suite (ChAS) but can be adapted to any input.

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oncoscanR-package

oncoscanR: an R package to perform secondary analysis of Copy Number Variation data.

Description

Allows computation of different homologous recombination deficiency (HRD) scores to identify PARP inhibitors responders. The package also allows for computation of the tandem duplication plus score (TDplus; hallmark of CDK12-mutated tumors) and the identification of arm-level alterations (e.g. gain of chromosome arm 1p).
Details

The package is tailored for the ThermoFisher Oncoscan assay analyzed with their Chromosome Alteration Suite (ChAS) but can be adapted to any input.

To learn more about oncoscanR, see the vignette using `browseVignettes(package = "oncoscanR")`.

Author(s)

Maintainer: Yann Christinat <yann.christinat@hcuge.ch>

Authors:

- Geneva University Hospitals [copyright holder]

See Also

Useful links:

- [https://github.com/yannchristinat/oncoscanR](https://github.com/yannchristinat/oncoscanR)
- Report bugs at [https://github.com/yannchristinat/oncoscanR/issues](https://github.com/yannchristinat/oncoscanR/issues)

---

**adjust_loh**

*Trim LOH segments with respect to loss segments.*

Description

Trim LOH segments with respect to loss segments.

Usage

`adjust_loh(segments)`

Arguments

- `segments` A GRanges object containing the segments, their copy number and copy number types.

Details

LOH segments completely contained within (or equal to) a copy loss segment are deleted. LOH segments partially overlapping (on one end only) with a copy loss segment are trimmed to remove the overlap or split into several segments.

Value

A GRanges object containing the cleaned segments, their copy number and copy number types.

Examples

```r
segs.adj <- adjust_loh(segs.chas_example)
```
armlevel_alt

Get all globally-altered chromosome arms.

Description
Get all globally-altered chromosome arms.

Usage
armlevel_alt(segments, kit.coverage, threshold = 0.9)

Arguments
segments A GRanges object containing the segments.
kit.coverage A GRanges object containing the regions covered on each chromosome arm.
threshold The minimum percentage of the arm to be considered as globally altered. Defaults to 80%.

Details
By default uses the sum of all alterations and set the arm as globally altered if >80% of the arm is altered. Does not account for alteration type and copy number. Will run the function trim_to_coverage on the segments.

Value
A list of globally-altered chromosome arms with the percentage of arm altered.

Examples
arms <- armlevel_alt(segs.chas_example, oncoscan_na33.cov, 0.9)

get_amp_segments
Return all segments with an amplification (5 or more copies).

Description
Return all segments with an amplification (5 or more copies).

Usage
get_amp_segments(segments)

Arguments
segments A GRanges object containing the segments, their copy number and copy number types.
get_gain_segments

Value

A GRanges object containing the selected segments, their copy number and copy number types.

Examples

```r
segs.amp <- get_amp_segments(segs.chas_example)
```

---

get_gain_segments

Return all segments with gain of copies.

Description

Return all segments with gain of copies.

Usage

```r
get_gain_segments(segments)
```

Arguments

- `segments`: A GRanges object containing the segments, their copy number and copy number types.

Value

A GRanges object containing the selected segments, their copy number and copy number types.

Examples

```r
segs.gain <- get_gain_segments(segs.chas_example)
```

---

get_hetloss_segments

Return all segments with heterozygous loss.

Description

Return all segments with heterozygous loss.

Usage

```r
get_hetloss_segments(segments)
```

Arguments

- `segments`: A GRanges object containing the segments, their copy number and copy number types.
get_loh_segments

Value
A GRanges object containing the selected segments, their copy number and copy number types.

Examples
```r
gens.hetloss <- get_hetloss_segments(segs.chas_example)
```

get_homloss_segments

Return all segments with homozygous loss.

Description
Return all segments with homozygous loss.

Usage
```r
get_homloss_segments(segments)
```

Arguments
segments
A GRanges object containing the segments, their copy number and copy number types.

Value
A GRanges object containing the selected segments, their copy number and copy number types.

Examples
```r
get_homloss_segments <- get_homloss_segments(segs.chas_example)
```

get_loh_segments

Return all segments of type LOH, independently of the copy number.

Description
Return all segments of type LOH, independently of the copy number.

Usage
```r
get_loh_segments(segments)
```

Arguments
segments
A GRanges object containing the segments, their copy number and copy number types.
**get_loss_segments**

**Value**

A GRanges object containing the selected segments, their copy number and copy number types.

**Examples**

```r
segs.loh <- get_loh_segments(segs.chas_example)
```

---

**get_loss_segments**

Return all segments with loss of 1 or 2 copies.

**Description**

Return all segments with loss of 1 or 2 copies.

**Usage**

```r
get_loss_segments(segments)
```

**Arguments**

- `segments` A GRanges object containing the segments, their copy number and copy number types.

**Value**

A GRanges object containing the selected segments, their copy number and copy number types.

**Examples**

```r
segs.loh <- get_loh_segments(segs.chas_example)
```

---

**get_oncoscan_coverage_from_bed**

Load the oncoscan coverage BED file into a GenomicRanges object.

**Description**

Load the oncoscan coverage BED file into a GenomicRanges object.

**Usage**

```r
get_oncoscan_coverage_from_bed(filename)
```

**Arguments**

- `filename` Path to the coverage BED file.
load_ascat

Details

Expects the following columns from the BED file (no header): 1. Name of the chromosomal arm (e.g. "1p") 2. Start position of the arm 3. End position of the arm

Value

A GRanges object containing the regions covered on each chromosome arm.

Examples

```r
oncoscan_na33.cov <- get_oncoscan_coverage_from_bed(
  system.file('extdata', 'Oncoscan.na33.r2.cov.processed.bed',
  package = 'oncoscanR'))
```

load_ascat

Load am ASCAT text export file.

Description

Load am ASCAT text export file.

Usage

`load_ascat(filename, kit.coverage)`

Arguments

- `filename`: Path to the ASCAT file.
- `kit.coverage`: A GRanges object containing the regions covered on each chromosome arm by the kit.

Details

The ASCAT file is expected to have the following column names: 'chr' (chromosome number), 'startpos' (first position of CNV segment), 'endpos' (last position of CNV segment), 'nMajor' (Number of copies of the major allele) and 'nMinor' (Number of copies of the minor allele).

The segments are attributed to each chromosome arm and split if necessary.

Value

A GRanges object containing the segments, their copy number (field `cn`), their copy number types (field `cntype`). `cntype` contains either 'Gain', 'Loss' or 'LOH'. If the file contains twice the same segment or does not respect the format specifications, then an error is raised. NB. If the chromosome name is in the format '1' and not 'chr1' and will be transformed if needed.
load_chas

Examples

```r
segs.filename <- system.file('extdata', 'ascat_example.txt',
                            package = 'oncoscanR')
segs.ascat_example <- load_ascat(segs.filename, oncoscan_na33.cov)
```

Description

Load a ChAS text export file.

Usage

```r
load_chas(filename, kit.coverage)
```

Arguments

- `filename`: Path to the ChAS file.
- `kit.coverage`: A `GRanges` object containing the regions covered on each chromosome arm by the kit.

Details

The ChAS file is expected to have the following column names: 'CN State' (number or empty), 'Type' (expected value: 'Gain', 'Loss' or 'LOH') and 'Full Location' (in the format 'chr:start-end').

The segments are attributed to each chromosome arm and split if necessary.

Value

A `GRanges` object containing the segments, their copy number (field `cn`), their copy number types (field `cntype`). `cntype` contains either 'Gain', 'Loss' or 'LOH'. If the file contains twice the same segment or does not respect the format specifications, then an error is raised. NB. The chromosome name is in the format '1' and not 'chr1' and will be transformed if needed.

Examples

```r
segs.filename <- system.file('extdata', 'chas_example.txt',
                            package = 'oncoscanR')
segs.chas_example <- load_chas(segs.filename, oncoscan_na33.cov)
```
**merge_segments**

Merge segments with respect to the kit resolution and the copy number.

**Description**

Merge segments with respect to the kit resolution and the copy number.

**Usage**

```r
merge_segments(segments, kit.resolution = 300)
```

**Arguments**

- `segments`: A `GRanges` object containing the segments, their copy number and copy number types.
- `kit.resolution`: Number >0 indicating the minimum segment size detectable by the technique (in kilobases). Defaults to the Oncoscan assay resolution outside of cancer genes: 300Kb.

**Details**

If two segments are at a distance smaller than the resolution, then the segments are merged if they share the same `cn` value. Note that the function does not look at the copy number type or subtype but only at the actual copy number to decide whether segments can be merged.

**Value**

A `GRanges` object containing the cleaned segments, their copy number and copy number types.

**Examples**

```r
segs.merged <- merge_segments(segs.chas_example)
segs.merged_50k <- merge_segments(segs.chas_example, 50)
```

---

**oncoscan_na33.cov**

GenomicRanges object of the chromosomal arms coverage for the oncoscan assay (based on file `extdata/Oncoscan.na33.r2.cov.processed.bed`).

**Description**

GenomicRanges object of the chromosomal arms coverage for the oncoscan assay (based on file `extdata/Oncoscan.na33.r2.cov.processed.bed`).

**Usage**

```r
oncoscan_na33.cov
```
prune_by_size

Format

A GRanges object containing the region covered on each chromosome arm.

Source

oncoscan_na33.cov <- get_oncoscan_coverage_from_bed(system.file('extdata', 'Oncoscan.na33.r2.cov.processed.bed'), package = 'oncoscanR')

---

prune_by_size | Remove segments smaller than the kit resolution.

Description

Remove segments smaller than the kit resolution.

Usage

prune_by_size(segments, threshold = 300)

Arguments

segments A GRanges object containing the segments, their copy number and copy number types.

threshold Number indicating the minimum segment size to be kept (in kilobases). Defaults to the Oncoscan assay resolution outside of cancer genes: 300Kb.

Value

A GRanges object containing the cleaned segments, their copy number and copy number types.

Examples

segs.300k <- prune_by_size(segs.chas_example)
segs.50k <- prune_by_size(segs.chas_example, 50)
score_avgcn  
Compute the average copy number variation across the genome.

Description

Compute the average copy number variation across the genome.

Usage

score_avgcn(segments, kit.coverage)

Arguments

segments  
A GRanges object containing the segments, their copy number and copy number types.

kit.coverage  
A GRanges object containing the regions covered on each chromosome arm.

Details

Compute the weighted average (by segment length) of the copy number variation. LOH segments and sexual chromosomes are excluded. Copy number variation is rounded to the next level (1.67 -> 1 but 2.33 -> 3).

Value

A decimal value

Examples

score_avgcn(segs.chas_example, oncoscan_na33.cov)

score_estwgd  
Estimates the number of whole-genome doubling events (WGD).

Description

Estimates the number of whole-genome doubling events (WGD).

Usage

score_estwgd(segments, kit.coverage)

Arguments

segments  
A GRanges object containing the segments, their copy number and copy number types.

kit.coverage  
A GRanges object containing the regions covered on each chromosome arm.
score_gloh

Details

Based on the publication from Carter et al. (Nature Biotechnology 2012; PubMed ID: 22544022). On a pan-cancer cohort, they observed that tumors that underwent one whole-genome doubling event had a ploidy (average copy number) between 2.2 and 3.4. This function relies on the function score_avgcn to compute the ploidy.

Value

A named list with two values: WGD (whole-genome doubling events) and avgCN (the average copy number). WGD values are 0 for no WGD event, 1 for one WGD event, 2 for several WGD events.

Examples

score_estwdg(segs.chas_example, oncoscan_na33.cov)

| score_gloh | Compute the genomic LOH score. |

Description

Compute the genomic LOH score.

Usage

score_gloh(segments, arms.loh, arms.hetloss, kit.coverage)

Arguments

segments A GRanges object containing the segments, their copy number and copy number types.
arms.loh A list of arms with global/arm-level LOH alteration.
arms.hetloss A list of arms with global/arm-level heterozygous loss.
kit.coverage A GRanges object containing the regions covered on each chromosome arm.

Details

The percentage genomic LOH score is computed as described in the FoundationFocus CDx BRCA LOH assay; i.e. the percentage of bases covered by the Oncoscan that display a loss of heterozygosity independently of the number of copies, excluding chromosomal arms that have a global LOH (>=90 arm length). To compute with the armlevel_alt function on LOH segments only). This score was linked to BRCA1/2-deficient tumors.

Value

An integer representing the percentage of LOH bases.
score_loh

Examples
armlevel.loh <- armlevel_alt(get_loh_segments(segs.chas_example),
  kit.coverage = oncoscan_na33.cov)
armlevel.hetloss <- armlevel_alt(get_hetloss_segments(segs.chas_example),
  kit.coverage = oncoscan_na33.cov)
score_gloh(segs.chas_example, names(armlevel.loh), names(armlevel.hetloss),
  oncoscan_na33.cov)

score_loh

Compute the number HR deficiency-associated LOH regions.

Description
Compute the number HR deficiency-associated LOH regions.

Usage
score_loh(segments, arms.loh, arms.hetloss, kit.coverage)

Arguments
segments A GRanges object containing the segments, their copy number and copy number
types.
arms.loh A list of arms with global/arm-level LOH alteration.
arms.hetloss A list of arms with global/arm-level heterozygous losses.
kit.coverage A GRanges object containing the regions covered on each chromosome arm.

Details
Procedure based on the paper from Abkevich et al., Br J Cancer 2012 (PMID: 23047548). All LOH
segments larger than 15Mb but excluding chromosome with a global LOH alteration (to compute
with the armlevel_alt function on LOH segments only). This score was linked to BRCA1/2-
deficient tumors. Note that the function will merge overlapping or neighbor LOH segments (at a
distance of 1bp).

Value
An integer representing the number of HRD-LOH regions.

Examples
armlevel.loh <- armlevel_alt(get_loh_segments(segs.chas_example),
  kit.coverage = oncoscan_na33.cov)
armlevel.hetloss <- armlevel_alt(get_hetloss_segments(segs.chas_example),
  kit.coverage = oncoscan_na33.cov)
score_loh(segs.chas_example, names(armlevel.loh), names(armlevel.hetloss),
  oncoscan_na33.cov)
**score_lst**

*Compute the number of Large-scale State Transitions (LSTs).*

**Description**

Compute the number of Large-scale State Transitions (LSTs).

**Usage**

```r
score_lst(segments, kit.coverage)
```

**Arguments**

- `segments` A GRanges object containing the segments, their copy number and copy number types.
- `kit.coverage` A GRanges object containing the regions covered on each chromosome arm.

**Details**

Procedure based on the paper from Popova et al, Can. Res. 2012 (PMID: 22933060). First segments smaller than 3Mb are removed, then segments are smoothed with respect to copy number at a distance of 3Mb. The number of LSTs is the number of breakpoints (breakpoints closer than 3Mb are merged) that have a segment larger or equal to 10Mb on each side. This score was linked to BRCA1/2-deficient tumors.

**Value**

An integer representing the number of LSTs.

**Examples**

```r
score_lst(segs.chas_example, oncoscan_na33.cov)
```

---

**score_mbalt**

*Computes the total number of Mbp altered.*

**Description**

Computes the total number of Mbp altered.

**Usage**

```r
score_mbalt(segments, kit.coverage, loh.rm = TRUE)
```
score_nlst

Compute the number of LSTs, normalized by the number of WGD events.

**Arguments**

- `segments` A GRanges object containing the segments, their copy number and copy number types.
- `n.wgd` Number of whole-genome doubling events (0 if diploid).
- `kit.coverage` A GRanges object containing the regions covered on each chromosome arm.
- `threshold` A number above which the test is returned positive (>=).

**Details**

Compute the number of LSTs in non-LOH segments using the score_lst function and subtract the extra noise induced by WGD events: \( nLST = LST - 7*W/2 \) where \( W \) is the number of WGD events. A sample is HRD positive (deficient in HR pathway) if \( nLST \) is greater or equal to the threshold (15 by default). This score was linked to BRCA1/2-deficient tumors.

**Value**

A named list with the number of nLSTs and the corresponding label ('Positive', 'Negative').
score_td

Examples

w <- score_estwd(segs.chas_example, oncoscan_na33.cov)
score_nlst(segs.chas_example, w["WGD"], oncoscan_na33.cov)

score_td

Compute the number of large tandem duplication (TDplus).

Description

Compute the number of large tandem duplication (TDplus).

Usage

score_td(segments)

Arguments

segments A GRanges object containing the segments, their copy number and copy number
types.

Details

Procedure based on the paper from Popova et al., Cancer Res 2016 (PMID: 26787835). The TDplus
score is defined as the number of regions larger than 1Mb but smaller or equal to 10Mb with a gain
of one or two copies. This score was linked to CDK12-deficient tumors. They also identified as
second category of tandem duplication whose size is smaller or equal than 1Mb and around 300Kb
but could not link it to a phenotype. Note that due to its resolution the Oncoscan assay will most
likely miss this second category. Nonetheless it is reported by the function.

Value

A list of integer containing the TDplus score ("TDplus") and the small TD score ("TD").

Examples

score_td(segs.chas_example)
segs.chas_example  
*Expected segments from loading the ChAS file ‘chas_example.txt’.*

**Description**

Expected segments from loading the ChAS file ‘chas_example.txt’.

**Usage**

`segs.chas_example`

**Format**

A GRanges object containing the segments, their copy number (field `cn`) and their copy number types (field `cn.type`).

**Source**

```r
segs.filename <- system.file('extdata', 'chas_example.txt', package = 'oncoscanR')
mykit.cov <- get_oncoscan_coverage_from_probes() segs.chas_example <- load_chas(segs.filename, kit.coverage = mykit.cov)
```

trim_to_coverage  
*Trim segments with respect to the kit’s coverage.*

**Description**

Trim segments with respect to the kit’s coverage.

**Usage**

`trim_to_coverage(segments, kit.coverage)`

**Arguments**

- `segments`  
  A GRanges object containing the segments, their copy number and copy number types.

- `kit.coverage`  
  A GRanges object containing the regions covered on each chromosome arm.

**Details**

All segments that are not entirely contained within the kit coverage will be trimmed to the coverage’s limits.

**Value**

A GRanges object containing the cleaned segments, their copy number and copy number types.
Examples

segs.trimmed <- trim_to_coverage(segs.chas_example, oncoscan_na33.cov)

---

Run the standard workflow for ASCAT files (from oncoscan data).

Description

Run the standard workflow for ASCAT files (from oncoscan data).

Usage

workflow_oncoscan.ascat(ascat.fn)

Arguments

ascat.fn Path to the text-export ASCAT file

Details

Identifies the globally altered arms (>90% of arm altered), computes the HRD and TD+ scores. The amplification is defined as a CN>=5. An arm is gained if of CN type cntype.gain unless the arm is amplified.

Value

A list of lists with the following elements: armlevel = list(AMP= list of arms, GAIN= list of arms, LOSS= list of arms, LOH= list of arms), scores = list(LST= number, LOH= number, TDplus= number, TD= number), file = path of the ChAS file as given by the parameter)

Examples

segs.filename <- system.file('extdata', 'ascat_example.txt', package = 'oncoscanR')
workflow_oncoscan.ascat(segs.filename)
Run the standard workflow for Oncoscan ChAS files.

Description

Run the standard workflow for Oncoscan ChAS files.

Usage

workflow_oncoscan.chas(chas.fn)

Arguments

chas.fn Path to the text-export ChAS file

Details

Identifies the globally altered arms (>90% of arm altered), computes the HRD and TD+ scores. The amplification is defined as a CN subtype cnctype.weakamp or cnctype.strongamp. An arm is gained if of CN type cnctype.gain unless the arm is amplified.

Value

A list of lists with the following elements: armlevel = list(AMP= list of arms, GAIN= list of arms, LOSS= list of arms, LOH= list of arms), scores = list(LST= number, LOH= number, TDplus= number, TD= number), file = path of the ChAS file as given by the parameter)

Examples

segs.filename <- system.file('extdata', 'chas_example.txt',
package = 'oncoscanR')
workflow_oncoscan.chas(segs.filename)
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