# Package 'consensusOV'

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**Type** Package

**Title** Gene expression-based subtype classification for high-grade serous ovarian cancer

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**Description** This package implements four major subtype classifiers for high-grade serous (HGS) ovarian cancer as described by Helland et al. (PLoS One, 2011), Bentink et al. (PLoS One, 2012), Verhaak et al. (J Clin Invest, 2013), and Konecny et al. (J Natl Cancer Inst, 2014). In addition, the package implements a consensus classifier, which consolidates and improves on the robustness of the proposed subtype classifiers, thereby providing reliable stratification of patients with HGS ovarian tumors of clearly defined subtype.

**License** Artistic-2.0

**Depends** R (>= 3.6)

**Imports** Biobase, GSVA (>= 1.50.0), gdata, genefu, limma, matrixStats, randomForest, stats, utils, methods, BiocParallel

**URL** http://www.pmgenomics.ca/bhklab/software/consensusOV

**Suggests** BiocStyle, ggplot2, knitr, rmarkdown, magick

**VignetteBuilder** knitr

**Encoding** UTF-8

**RoxygenNote** 7.3.1

**LazyData** true

**biocViews** Classification, Clustering, DifferentialExpression, GeneExpression, Microarray, Transcriptomics

**BugReports** https://github.com/bhklab/consensusOV/issues

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`dataset.merging` *Merging all individual esets and merging them into a big eset*

---

## Description

Merging all individual esets and merging them into a big eset

## Usage

```
dataset.merging(
  esets,
  method = c("union", "intersect"),
  standardization = c("quantile", "robust.scaling", "scaling", "none"),
  nthread = 1
)
```

## Arguments

| | |
|---|---|
| `esets` | The list containing all GSE file that need to be merged. |
| `method` | either "unique" or "intersect" is use to for selecting geneid |
| `standardization` | choose between "quantile", "robust.scaling", "scaling" or "none" |
| `nthread` | number of threads (1 by default) |

## Value

The merging eset

## get.bentink.subtypes *Get ovarian cancer subtypes as defined by Bentink et al., 2012*

### Description

Get ovarian cancer subtypes as defined by Bentink et al., 2012

### Usage

```
get.bentink.subtypes(expression.matrix, entrez.ids)
```

### Arguments

| | |
|---|---|
| expression.matrix | A matrix of gene expression values with rows as genes, columns as samples. |
| entrez.ids | A vector of Entrez Gene IDs, corresponding to the rows of expression.matrix |

### Value

A list with first value Bentink.subtypes containing a factor of subtype names; and second value angio containing the ouput of genefu::ovcAngiogenic

### References

Bentink et al. *Angiogenic mRNA and microRNA gene expression signature predicts a novel subtype of serous ovarian cancer.* PloS one (2012).

### Examples

```
library(Biobase)
library(genefu)
data(GSE14764.eset)
expression.matrix <- exprs(GSE14764.eset)
entrez.ids <- as.character(fData(GSE14764.eset)$EntrezGene.ID)
get.bentink.subtypes(expression.matrix, entrez.ids)
```

## get.consensus.subtypes *Get consensusOV ovarian cancer subtypes*

### Description

Get consensusOV ovarian cancer subtypes

## Usage

```
get.consensus.subtypes(
  expression.matrix,
  entrez.ids,
  concordant.tumors.only = TRUE,
  remove.using.cutoff = FALSE,
  percentage.dataset.removed = 0.75,
  .training.dataset = consensus.training.dataset.full,
  .dataset.names.to.keep = names(esets.rescaled.classified.filteredgenes)
)

margin(rf.probs)
```

## Arguments

| | |
|---|---|
| `expression.matrix` | A matrix of gene expression values with rows as genes, columns as samples. |
| `entrez.ids` | A vector of Entrez Gene IDs, corresponding to the rows of `expression.matrix` |
| `concordant.tumors.only` | Logical. Should the classifier trained only on tumors that are concordantly classified by Helland, Konecny, and Verhaak? Defaults to TRUE. |
| `remove.using.cutoff` | Specify whether to classify NA for samples that do not meet a margin cutoff |
| `percentage.dataset.removed` | If remove.using.cutoff is TRUE, then classify this percentage of samples to NA based on margin values |
| `.training.dataset` | ExpressionSet containing the training data. Defaults to the pooled dataset across selected MetaGxOvarian datasets. |
| `.dataset.names.to.keep` | Names of MetaGxOvarian datasets to use for training |
| `rf.probs` | random forest probabilities for each subtype as returned by `get.consensus.subtypes` |

## Value

`get.consensus.subtypes` returns a list with first value `consensusOV.subtypes` containing a factor of subtype labels; and second value `rf.probs` containing a matrix of subtype probabilities.

`margin` returns a numeric vector containing the classification margin scores, i.e. the difference between the top two subtype scores for each tumor.

## Examples

```
library(Biobase)
data(GSE14764.eset)
expression.matrix <- exprs(GSE14764.eset)
entrez.ids <- as.character(fData(GSE14764.eset)$EntrezGene.ID)
sts <- get.consensus.subtypes(expression.matrix, entrez.ids)
margins <- margin(sts$rf.probs)
```

`get.hao.subtypes` *Get ovarian cancer subtypes as defined by Hao et al., 2017*

## Description

Get ovarian cancer subtypes as defined by Hao et al., 2017

## Usage

```
get.hao.subtypes(expression.matrix, entrez.ids)
```

## Arguments

| | |
|---|---|
| `expression.matrix` | A matrix of gene expression values with genes as rows, samples as columns. |
| `entrez.ids` | A vector of Entrez Gene IDs, corresponding to the rows of `expression.matrix`. |

## Details

Hao et al., 2017 derived a gene signature to predict the tissue of origin of ovarian tumors as either fallopian tube (FT) or ovarian surface epithelium (OSE).

The authors found that expression patterns of tissue-specific genes, prognostic genes, and molecular markers support a dualistic tissue origin of ovarian cancer, from either FT or OSE.

The subtype classifier considers 112 signature genes including 37 genes upregulated in FT and 75 genes upregulated in OSE. A score is computed that is designed to range from 0 to 1 for FT tumors, while OSE tumors have a score ranging from -1 to 0.

## Value

A list with first value `tissue` containing a factor of subtype names (tissue of origin); and second value `score` containing the tissue-of-origin score.

## Author(s)

Ludwig Geistlinger

## References

Hao et al. (2017) Integrated analysis reveals tubal- and ovarian-originated serous ovarian cancer and predicts differential therapeutic responses. Clinical Cancer Research, 23:7400-11.

## Examples

```
library(Biobase)
data(GSE14764.eset)
expression.matrix <- exprs(GSE14764.eset)
entrez.ids <- as.character(fData(GSE14764.eset)$EntrezGene.ID)
get.hao.subtypes(expression.matrix, entrez.ids)
```

## get.helland.subtypes *Get ovarian cancer subtypes as defined by Helland et al., 2011*

### Description

Get ovarian cancer subtypes as defined by Helland et al., 2011

### Usage

```
get.helland.subtypes(expression.matrix, entrez.ids)
```

### Arguments

| | |
|---|---|
| expression.matrix | A matrix of gene expression values with rows as genes, columns as samples. |
| entrez.ids | A vector of Entrez Gene IDs, corresponding to the rows of expression.matrix |

### Value

A list with first value Helland.subtypes containing a factor of subtype names; and second value subtype.scores containing a matrix of subtype scores

### References

Helland et al. *Deregulation of MYCN, LIN28B and LET7 in a molecular subtype of aggressive high-grade serous ovarian cancers.* PloS one (2011).

### Examples

```
library(Biobase)
data(GSE14764.eset)
expression.matrix <- exprs(GSE14764.eset)
entrez.ids <- as.character(fData(GSE14764.eset)$EntrezGene.ID)
get.helland.subtypes(expression.matrix, entrez.ids)
```

## get.konecny.subtypes *Get ovarian cancer subtypes as defined by Konecny et al., 2014*

### Description

Get ovarian cancer subtypes as defined by Konecny et al., 2014

### Usage

```
get.konecny.subtypes(expression.matrix, entrez.ids)
```

### Arguments

| | |
|---|---|
| expression.matrix | A matrix of gene expression values with rows as genes, columns as samples. |
| entrez.ids | A vector of Entrez Gene IDs, corresponding to the rows of expression.matrix |

## Value

A list with first value `Konecny.subtypes` containing a factor of subtype names; and second value `spearman.cc.vals` containing the Spearman correlation values per subtype

## References

Konecny et al. *Prognostic and therapeutic relevance of molecular subtypes in high-grade serous ovarian cancer.* Journal of the National Cancer Institute (2014).

## Examples

```
library(Biobase)
data(GSE14764.eset)
expression.matrix <- exprs(GSE14764.eset)
entrez.ids <- as.character(fData(GSE14764.eset)$EntrezGene.ID)
get.konecny.subtypes(expression.matrix, entrez.ids)
```

---

`get.subtypes` *Get ovarian cancer subtypes*

---

## Description

Get ovarian cancer subtypes

## Usage

```
get.subtypes(
  expression.dataset,
  entrez.ids = NULL,
  method = c("consensusOV", "Helland", "Verhaak", "Konecny", "Bentink"),
  ...
)
```

## Arguments

| | |
|---|---|
| `expression.dataset` | Either a matrix of gene expression values with rows as genes, columns as samples; or a BioBase::ExpressionSet object from MetaGxOvarian. If `expression.dataset` is a matrix, then `entrez.ids` must have length equal to the number of rows of `expression.dataset`. |
| `entrez.ids` | A vector of Entrez Gene IDs, corresponding to the rows of `expression.dataset` |
| `method` | The subtyping method to use |
| `...` | Optional parameters to be passed to the low level function |

## Value

A list with first value `Konecny.subtypes` containing a factor of subtype names; and second value `spearman.cc.vals` containing the Spearman correlation values per subtype

## Examples

```
library(Biobase)
data(GSE14764.eset)
expression.matrix <- exprs(GSE14764.eset)
entrez.ids <- as.character(fData(GSE14764.eset)$EntrezGene.ID)
get.subtypes(expression.matrix, entrez.ids, method="Konecny")
```

---

# get.verhaak.subtypes *Get ovarian cancer subtypes as defined by Verhaak et al., 2013*

---

## Description

Get ovarian cancer subtypes as defined by Verhaak et al., 2013

## Usage

```
get.verhaak.subtypes(expression.matrix, entrez.ids)
```

## Arguments

| | |
|---|---|
| expression.matrix | A matrix of gene expression values with rows as genes, columns as samples. |
| entrez.ids | A vector of Entrez Gene IDs, corresponding to the rows of expression.matrix |

## Value

A list with first value Verhaak.subtypes containing a factor of subtype names; and second value gsva containing the GSVA subtype scores

## References

Verhaak et al. *Prognostically relevant gene signatures of high-grade serous ovarian carcinoma.* The Journal of Clinical Investigation (2013)

## Examples

```
library(Biobase)
data(GSE14764.eset)
expression.matrix <- exprs(GSE14764.eset)
entrez.ids <- as.character(fData(GSE14764.eset)$EntrezGene.ID)
get.konecny.subtypes(expression.matrix, entrez.ids)
```

GSE14764.eset *Sample ExpressionSet from MetaGxOvarian*

## Description

A Biobase::ExpressionSet from package MetaGxOvarian for the dataset GSE14764

## Usage

```
GSE14764.eset
```

## Format

A Biobase::ExpressionSet object

## Source

http://biorxiv.org/content/biorxiv/early/2016/05/12/052910.full.pdf

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