Package 'curatedOvarianData'

November 26, 2024

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| Type Package |
| Title Clinically Annotated Data for the Ovarian Cancer Transcriptome |
| Version 1.44.0 |
| Date 2023-10-31 |
| Author Benjamin F. Ganzfried, Markus Riester, Steve Skates, Victoria Wang, Thomas Risch, Benjamin Haibe-Kains, Svitlana Tyekucheva, Jie Ding, Ina Jazic, Michael Birrer, Giovanni Parmigiani, Curtis Huttenhower, Levi Waldron |
| Maintainer Levi Waldron < lwaldron.research@gmail.com> |
| Description The curatedOvarianData package provides data for gene expression analysis in patients with ovarian cancer. |
| Depends R ($>= 3.0.0$), Biobase |
| Imports BiocGenerics |
| Suggests survival, RUnit, metafor, genefilter, logging, sva, xtable, futile.logger, BiocStyle |
| License Artistic-2.0 |
| URL http://bcb.dfci.harvard.edu/ovariancancer |
| biocViews ExperimentData, RNASeqData, CancerData, OvarianCancerData, MicroarrayData |
| git_url https://git.bioconductor.org/packages/curatedOvarianData |
| git_branch RELEASE_3_20 |
| git_last_commit 7abb677 |
| git_last_commit_date 2024-10-29 |
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| Date/Publication 2024-11-26 |
| |
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| GSE51088_eset |
| GSE6008_eset |
| GSE6822_eset |
| GSE8842_eset |
| GSE9891_eset |
| PMID15897565_eset |
| PMID17290060_eset |
| PMID19318476_eset |
| TCGA.mirna.8x15kv2_eset |
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| |
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curatedOvarianData-package

Clinically Annotated Data for the Ovarian Cancer Transcriptome

Description

Index

The curatedOvarianData package provides manually curated clinical data, uniformly processed expression data, and convenience functions for gene expression analysis in patients with ovarian cancer

Details

Package: curatedOvarianData

Type: Package
Version: 1.44.0
Date: 2023-10-31
License: Artistic-2.0
Depends: R (>= 2.10.0), affy

Please see http://bcb.dfci.harvard.edu/ovariancancer for alterative versions of this package, differing in how redundant probe sets are dealt with. In the curatedOvarianData version, each gene is represented by the gene with maximum mean. In NormalizerVcuratedOvarianData, each gene is

represented by the mean of the probesets after removing "noisy" probesets (see the Normalizer function of the Sleipnir library for computational biology), and in FULLVcuratedOvarianData, no collapsing of probe sets is done, but a map is provided to allow the user to do so by their method of choice through featureData(eset).

In the "Available sample meta-data" sections of each dataset, please refer to the following key.

For "sample_type": tumor / metastatic / adjacentnormal / healthy / cellline: "healthy" should be only from individuals without cancer, "adjacentnormal" from individuals with cancer, "metastatic" for non-primary tumors.

For "histological_type": ser=serous / endo=endometrioid / clearcell / mucinous, undifferentiated / other / mix. Other includes sarcomatoid, adenocarcinoma, dysgerminoma.

For "primarysite" and for "arrayedsite": ovlftlother. ov=ovary;ft=fallopian tube

For "summarygrade": low = 1, 2, LMP. High= 3,4,23.

For "summarystage": early = 1,2, 12. late=3,4,23,34.

For "tumorstage": FIGO Stage (I-IV, but coded here as 1-4 to ensure correct ordering in factors). If multiple stages given (eg 34), use the highest.

For "substage": substage (abcd). For cases like ab, bc, use highest given.

For "grade": Grade (1-3): If multiple given, ie 12, 23, use highest given. Most ovarian cancer studies use FIGO grading, with a couple exceptions in this package (Yoshihara and Tothill).

For "pltx": (y/n): patient treated with platin.

For "tax": (y/n): patient treated with taxol.

For "neo": (y/n): patient treated with neoadjuvant treatment.

For "primary_therapy_outcome_success": completeresponselpartialresponselprogressivediseaselstabledisease: response to any kind of therapy (including radiation only).

For "days_to_tumor_recurrence": time to recurrence or last follow-up in days

For "recurrence_status": recurrence censoring variable (recurrence / norecurrence)

For "days_to_death": time to death or last follow-up in days

For "vital_status": Overall survival censoring variable (living / deceased)

For "os_binary": dichotomized overall survival variable as defined by study authors (short / long).

For "relapse_binary": dichotomized relapse variable as defined by study authors (short / long)

For "site_of_tumor_first_recurrence": (metastasis / locoregional / none / locoregional_plus_metastatic). none for no recurrence, na for unknown

For "primary_therapy_outcome_success": (completeresponse / partialresponse / progressivedisease / stabledisease) Response to any kind of therapy (including radiation only).

For "debulking": amount of residual disease (optimal = <1cm, suboptimal=>1cm).

For "percent_normal_cells": Estimated percentage of normal cells. An integer 0-100, or can be >70, <70, etc.

For "percent_stromal_cells": Estimated percentage of stromal cells. An integer 0-100, or can be >70, <70, etc.

For "percent_tumor_cells": Estimated percentage of tumor cells. An integer 0-100, or can be >70, <70, etc.

For "batch": batch variable when available. Hybridization date when Affymetrix CEL files are available.

For "uncurated_author_metadata": Original uncurated data, with each field separated by ///.

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Author(s)

Benjamin F. Ganzfried, Steve Skates, Markus Riester, Victoria Wang, Thomas Risch, Benjamin Haibe-Kains, Curtis Huttenhower, Svitlana Tyekucheva, Jie Ding, Ina Jazic, Michael Birrer, Giovanni Parmigiani, Levi Waldron

Department of Biostatistics and Computational Biology, Dana-Farber Cancer Institute, Harvard School of Public Health

Maintainer: Levi Waldron <levi@jimmy.harvard.edu>

Examples

```
##List all datasets:
data(package="curatedOvarianData")
##
##See the actual template used for syntax checking of clinical metadata:
template.file <- system.file("extdata/template_ov.csv", package = "curatedOvarianData")
template <- read.csv(template.file, as.is=TRUE)
head(template)</pre>
```

E.MTAB.386_eset

Angiogenic mRNA and microRNA gene expression signature predicts a novel subtype of serous ovarian cancer.

Description

Ovarian cancer is the fifth leading cause of cancer death for women in the U.S. and the seventh most fatal worldwide. Although ovarian cancer is notable for its initial sensitivity to platinum-based therapies, the vast majority of patients eventually develop recurrent cancer and succumb to increasingly platinum-resistant disease. Modern, targeted cancer drugs intervene in cell signaling, and identifying key disease mechanisms and pathways would greatly advance our treatment abilities. In order to shed light on the molecular diversity of ovarian cancer, we performed comprehensive transcriptional profiling on 129 advanced stage, high grade serous ovarian cancers. We implemented a, re-sampling based version of the ISIS class discovery algorithm (rISIS: robust ISIS) and applied it to the entire set of ovarian cancer transcriptional profiles. rISIS identified a previously undescribed patient stratification, further supported by micro-RNA expression profiles, and gene set enrichment analysis found strong biological support for the stratification by extracellular matrix, cell adhesion, and angiogenesis genes. The corresponding "angiogenesis signature" was validated in ten published independent ovarian cancer gene expression datasets and is significantly associated with overall survival. The subtypes we have defined are of potential translational interest as they may be relevant for identifying patients who may benefit from the addition of anti-angiogenic therapies that are now being tested in clinical trials.

Usage

```
data( E.MTAB.386_eset )
```

```
experimentData(eset):
Experiment data
Experimenter name: Bentink S, Haibe-Kains B, Risch T, Fan J-B, Hirsch MS, Holton K, Rubio R, April C
Laboratory: Bentink, Matulonis 2012
```

E.MTAB.386_eset 5

```
Contact information:
     Title: Angiogenic mRNA and microRNA gene expression signature predicts a novel subtype of serous ov
     URL:
     PMIDs: 22348002
     Abstract: A 212 word abstract is available. Use 'abstract' method.
     Information is available on: preprocessing
     notes:
      platform_title:
         Illumina humanRef-8 v2.0 expression beadchip
      platform_shorttitle:
         Illumina humanRef-8 v2.0
      platform_summary:
         illuminaHumanv2
      platform_manufacturer:
         Illumina
      platform_distribution:
         commercial
      platform_accession:
         GPL6104
      platform_technology:
         in situ oligonucleotide
   Preprocessing: default
   featureData(eset):
   An object of class 'AnnotatedDataFrame'
     featureNames: A2M A4GALT ... ZZEF1 (10357 total)
     varLabels: probeset gene
     varMetadata: labelDescription
Details
   assayData: 10357 features, 129 samples
   Platform type: illuminaHumanv2
   Overall survival time-to-event summary (in years):
   Call: survfit(formula = Surv(time, cens) ~ -1)
            n.max n.start events median 0.95LCL 0.95UCL
    129.00 129.00 129.00
                            73.00
                                      3.51
                                              2.68
                                                     4.13
    _____
   Available sample meta-data:
   unique_patient_ID:
      Length
              Class
                          Mode
         129 character character
   sample_type:
   tumor
```

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```
histological_type:
ser
129
primarysite:
ov
129
summarygrade:
high
129
summarystage:
early late
   1 128
tumorstage:
  2 3 4
  1 109 19
substage:
            c NA's
       b
      12
           93 19
{\tt age\_at\_initial\_pathologic\_diagnosis:}
  Min. 1st Qu. Median Mean 3rd Qu.
                                         Max.
  21.00 50.00 66.00
                         60.71 72.00
                                        95.00
days_to_death:
  Min. 1st Qu. Median
                        Mean 3rd Qu.
                                         Max.
   3.9 516.9 917.1 1007.0 1401.0 2724.0
vital_status:
deceased living
     73
              56
debulking:
   optimal suboptimal
                           NA's
       98
                  28
                              3
uncurated_author_metadata:
   Length
           Class
                       Mode
```

129 character character

GSE12418_eset

Expression analysis of stage III serous ovarian adenocarcinoma distinguishes a sub-group of survivors.

GSE12418_eset 7

Description

It is difficult to predict the clinical outcome for patients with ovarian cancer. However, the use of biomarkers as additional prognostic factors may improve the outcome for these patients. In order to find novel candidate biomarkers, differences in gene expressions were analysed in 54 stage III serous ovarian adenocarcinomas with oligonucleotide microarrays containing 27,000 unique probes. The microarray data was verified with quantitative real-time polymerase chain reaction for the genes TACC1, MUC5B and PRAME. Using hierarchical cluster analysis we detected a subgroup that included 60% of the survivors. The gene expressions in tumours from patients in this sub-group of survivors were compared with the remaining tumours, and 204 genes were found to be differently expressed. We conclude that the sub-group of survivors might represent patients with favourable tumour biology and sensitivity to treatment. A selection of the 204 genes might be used as a predictive model to distinguish patients within and outside of this group. Alternative chemotherapy strategies could then be offered as first-line treatment, which may lead to improvements in the clinical outcome for these patients.

Usage

```
data( GSE12418_eset )
```

```
experimentData(eset):
Experiment data
 Experimenter name: Partheen K, Levan K, Osterberg L, Horvath G.Expression analysis of stage III ser
 Laboratory: Partheen, Horvath 2006
 Contact information:
 Title: Expression analysis of stage III serous ovarian adenocarcinoma distinguishes a sub-group of
 URI:
 PMIDs: 16996261
 Abstract: A 177 word abstract is available. Use 'abstract' method.
  Information is available on: preprocessing
  notes:
   platform_title:
      SWEGENE H_v2.1.1_27k
   platform_shorttitle:
      SWEGENE H_v2.1.1_27k
   platform_summary:
      PartheenMetaData
   platform_manufacturer:
      other
   platform_distribution:
      non-commercial
   platform_accession:
      GPL5886
   platform_technology:
      spotted oligonucleotide
Preprocessing: default
featureData(eset):
An object of class 'AnnotatedDataFrame'
  featureNames: A1CF A2M ... ZZZ3 (12681 total)
```

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```
varLabels: probeset gene
varMetadata: labelDescription
```

```
assayData: 12681 features, 54 samples
Platform type: PartheenMetaData
Binary overall survival summary (definitions of long and short provided by study authors):
 long short
   20
        34
Available sample meta-data:
alt_sample_name:
   Length
          Class
                        Mode
       54 character character
sample_type:
tumor
   54
histological_type:
ser
 54
primarysite:
οv
54
summarystage:
late
  54
tumorstage:
 3
54
substage:
b c
19 35
age_at_initial_pathologic_diagnosis:
  Min. 1st Qu. Median Mean 3rd Qu.
                                          Max.
  35.00 51.25 59.50 59.56 69.75 84.00
pltx:
У
54
```

GSE12470_eset 9

```
os_binary:
long short
20 34

debulking:
optimal suboptimal
13 41

uncurated_author_metadata:
Length Class Mode
54 character character
```

GSE12470_eset

Gene expression profiling of advanced-stage serous ovarian cancers distinguishes novel subclasses and implicates ZEB2 in tumor progression and prognosis.

Description

To elucidate the mechanisms of rapid progression of serous ovarian cancer, gene expression profiles from 43 ovarian cancer tissues comprising eight early stage and 35 advanced stage tissues were carried out using oligonucleotide microarrays of 18,716 genes. By non-negative matrix factorization analysis using 178 genes, which were extracted as stage-specific genes, 35 advanced stage cases were classified into two subclasses with superior (n = 17) and poor (n = 18) outcome evaluated by progression-free survival (log rank test, P = 0.03). Of the 178 stage-specific genes, 112 genes were identified as showing different expression between the two subclasses. Of the 48 genes selected for biological function by gene ontology analysis or Ingenuity Pathway Analysis, five genes (ZEB2, CDH1, LTBP2, COL16A1, and ACTA2) were extracted as candidates for prognostic factors associated with progression-free survival. The relationship between high ZEB2 or low CDH1 expression and shorter progression-free survival was validated by real-time RT-PCR experiments of 37 independent advanced stage cancer samples. ZEB2 expression was negatively correlated with CDH1 expression in advanced stage samples, whereas ZEB2 knockdown in ovarian adenocarcinoma SKOV3 cells resulted in an increase in CDH1 expression. Multivariate analysis showed that high ZEB2 expression was independently associated with poor prognosis. Furthermore, the prognostic effect of E-cadherin encoded by CDH1 was verified using immunohistochemical analysis of an independent advanced stage cancer samples set (n = 74). These findings suggest that the expression of epithelial-mesenchymal transition-related genes such as ZEB2 and CDH1 may play important roles in the invasion process of advanced stage serous ovarian cancer.

Usage

```
data( GSE12470_eset )
```

```
experimentData(eset):
Experiment data
Experimenter name: Yoshihara K, Tajima A, Komata D, Yamamoto T, Kodama S, Fujiwara H, Suzuki M, Onis
Laboratory: Yoshihara, Tanaka 2009
Contact information:
```

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```
Title: Gene expression profiling of advanced-stage serous ovarian cancers distinguishes novel subc
  URL:
  PMIDs: 19486012
  Abstract: A 253 word abstract is available. Use 'abstract' method.
  Information is available on: preprocessing
  notes:
   platform_title:
      Agilent-012097 Human 1A Microarray (V2) G4110B (Feature Number version)
   platform_shorttitle:
      Agilent G4110B
   platform_summary:
      hgug4110b
   platform_manufacturer:
      Agilent
   platform_distribution:
      commercial
   platform_accession:
      GPL887
   platform_technology:
      in situ oligonucleotide
Preprocessing: default
featureData(eset):
An object of class 'AnnotatedDataFrame'
  featureNames: A1BG A1CF ... ZZZ3 (16889 total)
  varLabels: probeset gene
  varMetadata: labelDescription
```

```
assayData: 16889 features, 53 samples
Platform type: hgug4110b
-----
Available sample meta-data:
_____
alt_sample_name:
  Length Class
                   Mode
     53 character character
sample_type:
healthy tumor
    10
          43
histological_type:
ser NA's
 43 10
primarysite:
О۷
53
```

GSE13876_eset 11

GSE13876_eset

Survival-related profile, pathways, and transcription factors in ovarian cancer.

Description

Ovarian cancer has a poor prognosis due to advanced stage at presentation and either intrinsic or acquired resistance to classic cytotoxic drugs such as platinum and taxoids. Recent large clinical trials with different combinations and sequences of classic cytotoxic drugs indicate that further significant improvement in prognosis by this type of drugs is not to be expected. Currently a large number of drugs, targeting dysregulated molecular pathways in cancer cells have been developed and are introduced in the clinic. A major challenge is to identify those patients who will benefit from drugs targeting these specific dysregulated pathways. The aims of our study were (1) to develop a gene expression profile associated with overall survival in advanced stage serous ovarian cancer, (2) to assess the association of pathways and transcription factors with overall survival, and (3) to validate our identified profile and pathways/transcription factors in an independent set of ovarian cancers. According to a randomized design, profiling of 157 advanced stage serous ovarian cancers was performed in duplicate using approximately 35,000 70-mer oligonucleotide microarrays. A continuous predictor of overall survival was built taking into account well-known issues in microarray analysis, such as multiple testing and overfitting. A functional class scoring analysis was utilized to assess pathways/transcription factors for their association with overall survival. The prognostic value of genes that constitute our overall survival profile was validated on a fully independent, publicly available dataset of 118 well-defined primary serous ovarian cancers. Furthermore, functional class scoring analysis was also performed on this independent dataset to assess the similarities with results from our own dataset. An 86-gene overall survival profile discriminated between patients with unfavorable and favorable prognosis (median survival, 19 versus 41 mo, respectively; permutation p-value of log-rank statistic = 0.015) and maintained its independent prognostic value in multivariate analysis. Genes that composed the overall survival profile were also able to discriminate between the two risk groups in the independent dataset. In our dataset 17/167 pathways and 13/111 transcription factors were associated with overall survival, of which 16 and 12, respectively, were confirmed in the independent dataset. Our study provides new clues to genes, pathways, and transcription factors that contribute to the clinical outcome of serous ovarian cancer and might be exploited in designing new treatment strategies.

Usage

```
data( GSE13876_eset )
```

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Format

```
experimentData(eset):
Experiment data
 Experimenter name: Crijns AP, Fehrmann RS, de Jong S, Gerbens F, Meersma GJ, Klip HG, Hollema H, Hof
  Laboratory: Crijns, van der Zee 2009
  Contact information:
 Title: Survival-related profile, pathways, and transcription factors in ovarian cancer.
  URL:
  PMIDs: 19192944
  Abstract: A 371 word abstract is available. Use 'abstract' method.
  Information is available on: preprocessing
  notes:
   platform_title:
      Operon human v3 ~35K 70-mer two-color oligonucleotide microarrays
   platform_shorttitle:
      Operon v3 two-color
   platform_summary:
      OperonHumanV3
   platform_manufacturer:
   platform_distribution:
      non-commercial
   platform_accession:
      GPL7759
   platform_technology:
      spotted oligonucleotide
Preprocessing: default
featureData(eset):
An object of class 'AnnotatedDataFrame'
  featureNames: A1BG A1CF ... ZZZ3 (20577 total)
  varLabels: probeset gene
  varMetadata: labelDescription
```

GSE14764_eset 13

1 156 unique_patient_ID: Min. 1st Qu. Median Mean 3rd Qu. Max. 79 79 40 118 157 sample_type: tumor 157 histological_type: ser 157 primarysite: οv 157 summarygrade: high low NA's 85 59 13 summarystage: late 157 grade: 1 2 3 4 NA's 14 45 82 3 13 age_at_initial_pathologic_diagnosis: Min. 1st Qu. Median Mean 3rd Qu. Max. 21.00 50.00 60.00 57.95 67.00 84.00 days_to_death: Min. 1st Qu. Median Mean 3rd Qu. Max. 30 360 630 1100 1470 7020 vital_status: living deceased 113 44 uncurated_author_metadata: Length Class

GSE14764_eset

157 character character

A prognostic gene expression index in ovarian cancer - validation across different independent data sets.

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Description

Ovarian carcinoma has the highest mortality rate among gynaecological malignancies. In this project, we investigated the hypothesis that molecular markers are able to predict outcome of ovarian cancer independently of classical clinical predictors, and that these molecular markers can be validated using independent data sets. We applied a semi-supervised method for prediction of patient survival. Microarrays from a cohort of 80 ovarian carcinomas (TOC cohort) were used for the development of a predictive model, which was then evaluated in an entirely independent cohort of 118 carcinomas (Duke cohort). A 300-gene ovarian prognostic index (OPI) was generated and validated in a leave-one-out approach in the TOC cohort (Kaplan-Meier analysis, p = 0.0087). In a second validation step, the prognostic power of the OPI was confirmed in an independent data set (Duke cohort, p = 0.0063). In multivariate analysis, the OPI was independent of the post-operative residual tumour, the main clinico-pathological prognostic parameter with an adjusted hazard ratio of 6.4 (TOC cohort, CI 1.8-23.5, p = 0.0049) and 1.9 (Duke cohort, CI 1.2-3.0, p = 0.0068). We constructed a combined score of molecular data (OPI) and clinical parameters (residual tumour), which was able to define patient groups with highly significant differences in survival. The integrated analysis of gene expression data as well as residual tumour can be used for optimized assessment of the prognosis of platinum-taxol-treated ovarian cancer. As traditional treatment options are limited, this analysis may be able to optimize clinical management and to identify those patients who would be candidates for new therapeutic strategies.

Usage

```
data( GSE14764_eset )
```

```
experimentData(eset):
Experiment data
 Experimenter name: Denkert C, Budczies J, Darb-Esfahani S, Gy??rffy B et al. A prognostic gene expro
 Laboratory: Denkert, Lage 2009
  Contact information:
 Title: A prognostic gene expression index in ovarian cancer - validation across different independe
 URL:
  PMIDs: 19294737
 Abstract: A 254 word abstract is available. Use 'abstract' method.
  Information is available on: preprocessing
  notes:
   platform_title:
      [HG-U133A] Affymetrix Human Genome U133A Array
   platform_shorttitle:
      Affymetrix HG-U133A
   platform_summary:
      hgu133a
   platform_manufacturer:
      Affymetrix
   platform_distribution:
      commercial
   platform_accession:
      GPL96
   platform_technology:
      in situ oligonucleotide
```

GSE14764_eset 15

```
Preprocessing: frma
   featureData(eset):
   An object of class 'AnnotatedDataFrame'
     featureNames: A1CF A2M ... ZZZ3 (13104 total)
     varLabels: probeset gene
     varMetadata: labelDescription
Details
   assayData: 13104 features, 80 samples
   Platform type: hgu133a
   Overall survival time-to-event summary (in years):
   Call: survfit(formula = Surv(time, cens) ~ -1)
   records n.max n.start events median 0.95LCL 0.95UCL
     80.00 80.00 80.00 21.00 4.52 4.19
   Available sample meta-data:
   _____
   alt_sample_name:
     Min. 1st Qu. Median Mean 3rd Qu. Max.
      1.00 20.75 40.50 40.50 60.25 80.00
   sample_type:
   tumor
      80
   histological_type:
      Length
             Class
                        Mode
         80 character character
   primarysite:
   ον
   80
   summarygrade:
   high low
        26
     54
   summarystage:
   early late
      9 71
   tumorstage:
    1 2 3 4
    8 1 69 2
   substage:
               c NA's
     a b
```

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```
32
                  38
grade:
 1 2
       3
 3 23 54
recurrence_status:
norecurrence
                recurrence
                                    NA's
days_to_death:
   Min. 1st Qu.
                  Median
                             Mean 3rd Qu.
                                              Max.
    210
             660
                    1050
                             1011
                                     1328
                                              2190
vital_status:
deceased
            living
      21
                59
batch:
   Length
               Class
                           Mode
       80 character character
uncurated_author_metadata:
   Length
               Class
       80 character character
```

GSE17260_eset

Gene expression profile for predicting survival in advanced-stage serous ovarian cancer across two independent datasets.

Description

Advanced-stage ovarian cancer patients are generally treated with platinum/taxane-based chemotherapy after primary debulking surgery. However, there is a wide range of outcomes for individual patients. Therefore, the clinicopathological factors alone are insufficient for predicting prognosis. Our aim is to identify a progression-free survival (PFS)-related molecular profile for predicting survival of patients with advanced-stage serous ovarian cancer. Advanced-stage serous ovarian cancer tissues from 110 Japanese patients who underwent primary surgery and platinum/taxane-based chemotherapy were profiled using oligonucleotide microarrays. We selected 88 PFS-related genes by a univariate Cox model (p<0.01) and generated the prognostic index based on 88 PFS-related genes after adjustment of regression coefficients of the respective genes by ridge regression Cox model using 10-fold cross-validation. The prognostic index was independently associated with PFS time compared to other clinical factors in multivariate analysis [hazard ratio (HR), 3.72; 95% confidence interval (CI), 2.66-5.43; p<0.0001]. In an external dataset, multivariate analysis revealed that this prognostic index was significantly correlated with PFS time (HR, 1.54; 95% CI, 1.20-1.98; p = 0.0008). Furthermore, the correlation between the prognostic index and overall survival time was confirmed in the two independent external datasets (log rank test, p = 0.0010 and 0.0008). The prognostic ability of our index based on the 88-gene expression profile in ridge regression Cox hazard model was shown to be independent of other clinical factors in predicting cancer prognosis across two distinct datasets. Further study will be necessary to improve predictive accuracy of the

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prognostic index toward clinical application for evaluation of the risk of recurrence in patients with advanced-stage serous ovarian cancer.

Usage

```
data( GSE17260_eset )
```

Format

```
experimentData(eset):
Experiment data
 Experimenter name: Yoshihara K, Tajima A, Yahata T, Kodama S, Fujiwara H, Suzuki M, Onishi Y, Hatae
  Laboratory: Yoshihara, Tanaka 2010
  Contact information:
 Title: Gene expression profile for predicting survival in advanced-stage serous ovarian cancer acro
  URL:
  PMIDs: 20300634
  Abstract: A 257 word abstract is available. Use 'abstract' method.
  Information is available on: preprocessing
  notes:
   platform_title:
      Agilent-012391 Whole Human Genome Oligo Microarray G4112A
   platform_shorttitle:
      Agilent G4112A
   platform_summary:
      hgug4112a
   platform_manufacturer:
      Agilent
   platform_distribution:
      commercial
   platform_accession:
      GPL6848
   platform_technology:
      in situ oligonucleotide
Preprocessing: default
featureData(eset):
An object of class 'AnnotatedDataFrame'
  featureNames: A1BG A1BG-AS1 ... ZZZ3 (20106 total)
  varLabels: probeset gene
  varMetadata: labelDescription
```

```
assayData: 20106 features, 110 samples
Platform type: hgug4112a
Overall survival time-to-event summary (in years):
Call: survfit(formula = Surv(time, cens) ~ -1)
records n.max n.start events median 0.95LCL 0.95UCL
110.00 110.00 110.00 46.00 4.44 4.03 NA
```

18 GSE17260_eset

```
Available sample meta-data:
alt_sample_name:
  Length Class
                      Mode
     110 character character
sample_type:
tumor
 110
histological_type:
ser
110
primarysite:
ον
110
summarygrade:
high low
 43 67
summarystage:
late
110
tumorstage:
3 4
93 17
substage:
          c NA's
  a b
   6
     18 69 17
grade:
1 2 3
26 41 43
pltx:
 У
110
tax:
 У
110
days_to_tumor_recurrence:
  Min. 1st Qu. Median Mean 3rd Qu.
```

30.0 285.0 510.0 673.9 870.0 2250.0

GSE18520_eset 19

```
recurrence status:
norecurrence
               recurrence
                        76
          34
days_to_death:
   Min. 1st Qu.
                 Median
                            Mean 3rd Qu.
                                             Max.
            660
     30
                     915
                            1086
                                    1530
                                             2430
vital_status:
deceased
           living
      46
debulking:
   optimal suboptimal
        57
uncurated_author_metadata:
   Length
              Class
                          Mode
      110 character character
```

GSE18520_eset

A gene signature predictive for outcome in advanced ovarian cancer identifies a survival factor: microfibril-associated glycoprotein 2.

Description

Advanced stage papillary serous tumors of the ovary are responsible for the majority of ovarian cancer deaths, yet the molecular determinants modulating patient survival are poorly characterized. Here, we identify and validate a prognostic gene expression signature correlating with survival in a series of microdissected serous ovarian tumors. Independent evaluation confirmed the association of a prognostic gene microfibril-associated glycoprotein 2 (MAGP2) with poor prognosis, whereas in vitro mechanistic analyses demonstrated its ability to prolong tumor cell survival and stimulate endothelial cell motility and survival via the alpha(V)beta(3) integrin receptor. Increased MAGP2 expression correlated with microvessel density suggesting a proangiogenic role in vivo. Thus, MAGP2 may serve as a survival-associated target.

Usage

```
data( GSE18520_eset )
```

Format

```
experimentData(eset):
```

Experiment data

Experimenter name: Mok SC, Bonome T, Vathipadiekal V, Bell A, Johnson ME, Wong KK, Park DC, Hao K, Y: Laboratory: Mok, Birrer 2009

Contact information:

Title: A gene signature predictive for outcome in advanced ovarian cancer identifies a survival fac URL:

20 GSE18520_eset

```
PMIDs: 19962670
     Abstract: A 110 word abstract is available. Use 'abstract' method.
     Information is available on: preprocessing
     notes:
      platform_title:
         [HG-U133_Plus_2] Affymetrix Human Genome U133 Plus 2.0 Array
      platform_shorttitle:
         Affymetrix HG-U133Plus2
      platform_summary:
         hgu133plus2
      platform_manufacturer:
         Affymetrix
      platform_distribution:
         commercial
      platform_accession:
         GPL570
      platform_technology:
         in situ oligonucleotide
   Preprocessing: frma
   featureData(eset):
   An object of class 'AnnotatedDataFrame'
     featureNames: A1BG A1BG-AS1 ... ZZZ3 (19816 total)
     varLabels: probeset gene
     varMetadata: labelDescription
Details
   assayData: 19816 features, 63 samples
   Platform type: hgu133plus2
   Overall survival time-to-event summary (in years):
   Call: survfit(formula = Surv(time, cens) ~ -1)
      10 observations deleted due to missingness
   records n.max n.start events median 0.95LCL 0.95UCL
     53.00 53.00 53.00 41.00 2.05 1.48 3.70
   Available sample meta-data:
   _____
   alt_sample_name:
      Min. 1st Qu. Median Mean 3rd Qu.
                                             Max.
     312.0 395.0 694.0 893.3 1040.0 2237.0
   sample_type:
   healthy tumor
        10
   histological_type:
    ser NA's
```

GSE18520_eset 21

```
53 10
primarysite:
ον
63
summarygrade:
high NA's
 53 10
summarystage:
late NA's
 53 10
tumorstage:
  3 NA's
 53 10
grade:
  3 NA's
 53 10
days_to_death:
  Min. 1st Qu. Median Mean 3rd Qu.
                                               NA's
                                        Max.
   150 450
               630
                        1212 1440
                                        4500
                                               10
vital_status:
deceased living
                  NA's
     41
             12
                     10
debulking:
  optimal suboptimal
                          NA's
       28
percent_normal_cells:
63
percent_stromal_cells:
63
percent_tumor_cells:
100
63
batch:
  Length
           Class
                      Mode
      63 character character
uncurated_author_metadata:
  Length
          Class
                     Mode
```

63 character character

GSE19829.GPL570_eset

Gene expression profile of BRCAness that correlates with responsiveness to chemotherapy and with outcome in patients with epithelial ovarian cancer.

Description

To define a gene expression profile of BRCAness that correlates with chemotherapy response and outcome in epithelial ovarian cancer (EOC). A publicly available microarray data set including 61 patients with EOC with either sporadic disease or BRCA(1/2) germline mutations was used for development of the BRCAness profile. Correlation with platinum responsiveness was assessed in platinum-sensitive and platinum-resistant tumor biopsy specimens from six patients with BRCA germline mutations. Association with poly-ADP ribose polymerase (PARP) inhibitor responsiveness and with radiation-induced RAD51 foci formation (a surrogate of homologous recombination) was assessed in Capan-1 cell line clones. The BRCAness profile was validated in 70 patients enriched for sporadic disease to assess its association with outcome. The BRCAness profile accurately predicted platinum responsiveness in eight out of 10 patient-derived tumor specimens, and between PARP-inhibitor sensitivity and resistance in four out of four Capan-1 clones. [corrected] When applied to the 70 patients with sporadic disease, patients with the BRCA-like (BL) profile had improved disease-free survival (34 months v 15 months; log-rank P = .013) and overall survival (72 months v 41 months; log-rank P = .006) compared with patients with a non-BRCA-like (NBL) profile, respectively. The BRCAness profile maintained independent prognostic value in multivariate analysis, which controlled for other known clinical prognostic factors. The BRCAness profile correlates with responsiveness to platinum and PARP inhibitors and identifies a subset of sporadic patients with improved outcome. Additional evaluation of this profile as a predictive tool in patients with sporadic EOC is warranted.

Usage

```
data( GSE19829.GPL570_eset )
```

platform_shorttitle:

```
experimentData(eset):
Experiment data
    Experimenter name: Konstantinopoulos PA, Spentzos D, Karlan BY, Taniguchi T et al. Gene expression
    Laboratory: Konstantinopoulos, Cannistra 2010 hgu133plus2
    Contact information:
    Title: Gene expression profile of BRCAness that correlates with responsiveness to chemotherapy and
    URL:
    PMIDs: 20547991

Abstract: A 241 word abstract is available. Use 'abstract' method.
    Information is available on: preprocessing
    notes:
        platform_title:
            [HG-U133_Plus_2] Affymetrix Human Genome U133 Plus 2.0 Array
```

```
Affymetrix HG-U133Plus2
      platform_summary:
         hgu133plus2
      platform_manufacturer:
         Affymetrix
      platform_distribution:
         commercial
      platform_accession:
         GPL570
      platform_technology:
         in situ oligonucleotide
   Preprocessing: frma
   featureData(eset):
   An object of class 'AnnotatedDataFrame'
     featureNames: A1BG A1BG-AS1 ... ZZZ3 (19816 total)
     varLabels: probeset gene
     varMetadata: labelDescription
Details
   assayData: 19816 features, 28 samples
   Platform type: hgu133plus2
   Overall survival time-to-event summary (in years):
   Call: survfit(formula = Surv(time, cens) ~ -1)
   records
           n.max n.start events median 0.95LCL 0.95UCL
           28.00 28.00 17.00 3.95 2.71
     28.00
   _____
   Available sample meta-data:
   alt_sample_name:
      Length
              Class Mode
          28 character character
   sample_type:
   tumor
      28
   primarysite:
   ΟV
   28
   days_to_death:
      Min. 1st Qu. Median Mean 3rd Qu.
                                            Max.
       150 540
                   1050
                            1291 1688
                                            3450
   vital_status:
   deceased living
         17
                 11
```

```
batch:
2009-08-14
28

uncurated_author_metadata:
Length Class Mode
28 character character
```

GSE19829.GPL8300_eset Gene expression profile of BRCAness that correlates with responsiveness to chemotherapy and with outcome in patients with epithelial ovarian cancer.

Description

To define a gene expression profile of BRCAness that correlates with chemotherapy response and outcome in epithelial ovarian cancer (EOC). A publicly available microarray data set including 61 patients with EOC with either sporadic disease or BRCA(1/2) germline mutations was used for development of the BRCAness profile. Correlation with platinum responsiveness was assessed in platinum-sensitive and platinum-resistant tumor biopsy specimens from six patients with BRCA germline mutations. Association with poly-ADP ribose polymerase (PARP) inhibitor responsiveness and with radiation-induced RAD51 foci formation (a surrogate of homologous recombination) was assessed in Capan-1 cell line clones. The BRCAness profile was validated in 70 patients enriched for sporadic disease to assess its association with outcome. The BRCAness profile accurately predicted platinum responsiveness in eight out of 10 patient-derived tumor specimens, and between PARP-inhibitor sensitivity and resistance in four out of four Capan-1 clones. [corrected] When applied to the 70 patients with sporadic disease, patients with the BRCA-like (BL) profile had improved disease-free survival (34 months v 15 months; log-rank P = .013) and overall survival (72 months v 41 months; log-rank P = .006) compared with patients with a non-BRCA-like (NBL) profile, respectively. The BRCAness profile maintained independent prognostic value in multivariate analysis, which controlled for other known clinical prognostic factors. The BRCAness profile correlates with responsiveness to platinum and PARP inhibitors and identifies a subset of sporadic patients with improved outcome. Additional evaluation of this profile as a predictive tool in patients with sporadic EOC is warranted.

Usage

```
data( GSE19829.GPL8300_eset )
```

Format

```
experimentData(eset):
Experiment data
Experimenter name: Konstantinopoulos PA, Spentzos D, Karlan BY, Taniguchi T et al. Gene expression
Laboratory: Konstantinopoulos, Cannistra 2010 hgu95
Contact information:
Title: Gene expression profile of BRCAness that correlates with responsiveness to chemotherapy and
```

PMIDs: 20547991

URL:

```
Abstract: A 241 word abstract is available. Use 'abstract' method.
     Information is available on: preprocessing
     notes:
      platform_title:
         [HG_U95Av2] Affymetrix Human Genome U95 Version 2 Array
      platform_shorttitle:
         Affymetrix HG_U95Av2
      platform_summary:
         hgu95av2
      platform_manufacturer:
         Affymetrix
      platform_distribution:
         commercial
      platform_accession:
         GPL8300
      platform_technology:
         in situ oligonucleotide
   Preprocessing: rma
   featureData(eset):
   An object of class 'AnnotatedDataFrame'
     featureNames: AADAC AAK1 ... ZZZ3 (8995 total)
     varLabels: probeset gene
     varMetadata: labelDescription
Details
   assayData: 8995 features, 42 samples
   Platform type: hgu95av2
   Overall survival time-to-event summary (in years):
   Call: survfit(formula = Surv(time, cens) ~ -1)
   records
             n.max n.start events median 0.95LCL 0.95UCL
     42.00 42.00 42.00 23.00
                                      3.78
                                              2.79
```

Available sample meta-data:
----alt_sample_name:
Length Class Mode
42 character character

sample_type:
tumor
 42
primarysite:

ov 42 26 GSE20565_eset

```
days_to_death:
  Min. 1st Ou.
                 Median
                           Mean 3rd Ou.
                                            Max.
        727.5 1155.0 1089.0 1485.0
   30 0
                                          2040.0
vital_status:
deceased
           living
      23
               19
batch:
2001-09-14 2001-12-14 2002-08-20 2003-09-09 2003-09-18
                    4
                              14
                                          13
uncurated_author_metadata:
   Length
              Class
       42 character character
```

GSE20565_eset

A genomic and transcriptomic approach for a differential diagnosis between primary and secondary ovarian carcinomas in patients with a previous history of breast cancer.

Description

The distinction between primary and secondary ovarian tumors may be challenging for pathologists. The purpose of the present work was to develop genomic and transcriptomic tools to further refine the pathological diagnosis of ovarian tumors after a previous history of breast cancer. Sixteen paired breast-ovary tumors from patients with a former diagnosis of breast cancer were collected. The genomic profiles of paired tumors were analyzed using the Affymetrix GeneChip Mapping 50 K Xba Array or Genome-Wide Human SNP Array 6.0 (for one pair), and the data were normalized with ITALICS (ITerative and Alternative normaLIzation and Copy number calling for affymetrix Snp arrays) algorithm or Partek Genomic Suite, respectively. The transcriptome of paired samples was analyzed using Affymetrix GeneChip Human Genome U133 Plus 2.0 Arrays, and the data were normalized with gc-Robust Multi-array Average (gcRMA) algorithm. A hierarchical clustering of these samples was performed, combined with a dataset of well-identified primary and secondary ovarian tumors. In 12 of the 16 paired tumors analyzed, the comparison of genomic profiles confirmed the pathological diagnosis of primary ovarian tumor (n = 5) or metastasis of breast cancer (n = 7). Among four cases with uncertain pathological diagnosis, genomic profiles were clearly distinct between the ovarian and breast tumors in two pairs, thus indicating primary ovarian carcinomas, and showed common patterns in the two others, indicating metastases from breast cancer. In all pairs, the result of the transcriptomic analysis was concordant with that of the genomic analysis. In patients with ovarian carcinoma and a previous history of breast cancer, SNP array analysis can be used to distinguish primary and secondary ovarian tumors. Transcriptomic analysis may be used when primary breast tissue specimen is not available.

Usage

```
data( GSE20565_eset )
```

GSE20565_eset 27

Format

```
experimentData(eset):
Experiment data
 Experimenter name: Meyniel JP, Cottu PH, Decraene C, Stern MH, Couturier J, Lebigot I, Nicolas A, We
  Laboratory: Meyniel, Sastre-Garau 2010
  Contact information:
 Title: A genomic and transcriptomic approach for a differential diagnosis between primary and secor
  URL:
  PMIDs: 20492709
  Abstract: A 277 word abstract is available. Use 'abstract' method.
  Information is available on: preprocessing
  notes:
   platform_title:
      [HG-U133_Plus_2] Affymetrix Human Genome U133 Plus 2.0 Array
   platform_shorttitle:
      Affymetrix HG-U133Plus2
   platform_summary:
      hgu133plus2
   platform_manufacturer:
      Affymetrix
   platform_distribution:
      commercial
   platform_accession:
      GPL570
   platform_technology:
      in situ oligonucleotide
Preprocessing: frma
featureData(eset):
An object of class 'AnnotatedDataFrame'
  featureNames: A1BG A1BG-AS1 ... ZZZ3 (19816 total)
  varLabels: probeset gene
  varMetadata: labelDescription
```

28 GSE2109_eset

```
histological_type:
  Length Class
                    Mode
     140 character character
primarysite:
other
       ٥v
  44
        96
summarygrade:
high low NA's
 63 33 44
summarystage:
early late NA's
  27
      67
             46
tumorstage:
          3
               4 NA's
  1
      2
 18
      9
         52 15 46
substage:
          c NA's
  а
     b
 14
     10
         55 61
grade:
          3 NA's
      2
  1
  6
     27
         63 44
batch:
         Class
  Length
                    Mode
     140 character character
uncurated_author_metadata:
  Length Class Mode
     140 character character
```

GSE2109_eset

IGC Expression Project for Oncology

Description

EXpression Project for Oncology, International Genomics Consortium, www.intgen.org

Usage

```
data( GSE2109_eset )
```

GSE2109_eset 29

Format

```
experimentData(eset):
Experiment data
 Experimenter name: EXpression Project for Oncology, International Genomics Consortium, www.intgen
  Laboratory: exp0, IGC 2005
  Contact information:
  Title: IGC EXpression Project for Oncology
  URL:
  PMIDs: PMID unknown
  Abstract: A 8 word abstract is available. Use 'abstract' method.
  Information is available on: preprocessing
  notes:
   platform_title:
      [HG-U133_Plus_2] Affymetrix Human Genome U133 Plus 2.0 Array
   platform_shorttitle:
      Affymetrix HG-U133Plus2
   platform_summary:
      hgu133plus2
   platform_manufacturer:
      Affymetrix
   platform_distribution:
      commercial
   platform_accession:
      GPL570
   platform_technology:
      in situ oligonucleotide
Preprocessing: frma
featureData(eset):
An object of class 'AnnotatedDataFrame'
  featureNames: A1BG A1BG-AS1 ... ZZZ3 (19816 total)
  varLabels: probeset gene
  varMetadata: labelDescription
```

30 GSE26193_eset

```
histological_type:
                         Mode
  Length
              Class
      204 character character
primarysite:
         ov NA's
other
        178
   23
summarygrade:
high low NA's
  91
       31
            82
summarystage:
early late NA's
   37
         87
               80
tumorstage:
   1
        2
             3
                  4 NA's
  20
       14
            58
                 18
                      94
substage:
        b
             c NA's
       22
            79
  17
                 86
grade:
        2
             3
                  4 NA's
   1
  11
       20
            83
                      82
                  8
{\tt age\_at\_initial\_pathologic\_diagnosis:}
  Min. 1st Qu. Median
                           Mean 3rd Qu.
                                            Max.
  25.00
        45.00
                 55.00
                           58.82
                                 65.00
                                           85.00
batch:
                         Mode
  Length
              Class
      204 character character
uncurated_author_metadata:
            Class
   Length
                         Mode
      204 character character
```

GSE26193_eset

miR-141 and miR-200a act on ovarian tumorigenesis by controlling oxidative stress response.

Description

Although there is evidence that redox regulation has an essential role in malignancies, its impact on tumor prognosis remains unclear. Here we show crosstalk between oxidative stress and the miR-200 family of microRNAs that affects tumorigenesis and chemosensitivity. miR-141 and miR-200a

GSE26193_eset 31

target p38?? and modulate the oxidative stress response. Enhanced expression of these microR-NAs mimics p38?? deficiency and increases tumor growth in mouse models, but it also improves the response to chemotherapeutic agents. High-grade human ovarian adenocarcinomas that accumulate miR-200a have low concentrations of p38?? and an associated oxidative stress signature. The miR200a-dependent stress signature correlates with improved survival of patients in response to treatment. Therefore, the role of miR-200a in stress could be a predictive marker for clinical outcome in ovarian cancer. In addition, although oxidative stress promotes tumor growth, it also sensitizes tumors to treatment, which could account for the limited success of antioxidants in clinical trials.

Usage

```
data( GSE26193_eset )
```

```
experimentData(eset):
Experiment data
 Experimenter name: Mateescu B, Batista L, Mariani O, Meyniel J, Cottu PH, Sastre-Garau X, Mechta-Gr
  Laboratory: Mateescu, Mechta-Grigoriou 2011
  Contact information:
 Title: miR-141 and miR-200a act on ovarian tumorigenesis by controlling oxidative stress response.
  URL:
  PMIDs: 22101765
  Abstract: A 149 word abstract is available. Use 'abstract' method.
  Information is available on: preprocessing
   platform_title:
      [HG-U133_Plus_2] Affymetrix Human Genome U133 Plus 2.0 Array
   platform_shorttitle:
      Affymetrix HG-U133Plus2
   platform_summary:
      hgu133plus2
   platform_manufacturer:
      Affymetrix
   platform_distribution:
      commercial
   platform_accession:
      GPL570
   platform_technology:
      in situ oligonucleotide
Preprocessing: frma
featureData(eset):
An object of class 'AnnotatedDataFrame'
  featureNames: A1BG A1BG-AS1 ... ZZZ3 (19816 total)
  varLabels: probeset gene
  varMetadata: labelDescription
```

32 GSE26193_eset

```
assayData: 19816 features, 107 samples
Platform type: hgu133plus2
Overall survival time-to-event summary (in years):
Call: survfit(formula = Surv(time, cens) ~ -1)
records n.max n.start events median 0.95LCL 0.95UCL
107.00 107.00 107.00 76.00
                              3.05
                                      2.50 4.56
_____
Available sample meta-data:
alt_sample_name:
  Length
         Class
     107 character character
sample_type:
tumor
 107
histological_type:
clearcell
         endo mucinous
                              other
                                        ser
             8 8
                                         79
      6
                                6
summarygrade:
high low
 67 40
summarystage:
early late
  31
      76
tumorstage:
1 2 3 4
20 11 59 17
substage:
          c NA's
  a b
 16 12 62 17
grade:
1 2 3
7 33 67
days_to_tumor_recurrence:
  Min. 1st Qu. Median
                      Mean 3rd Qu.
                                      Max.
   3.0 340.5 584.0 1108.0 1525.0 7386.0
recurrence_status:
norecurrence recurrence
               80
        27
```

GSE26712_eset 33

```
days_to_death:
   Min. 1st Qu.
                            Mean 3rd Qu.
                 Median
                                             Max
      3
            668
                   1096
                            1520
                                    2220
                                             7386
vital_status:
deceased
           living
      76
batch:
                          Mode
   Length
              Class
      107 character character
uncurated_author_metadata:
              Class
   Length
                          Mode
      107 character character
```

GSE26712_eset

A gene signature predicting for survival in suboptimally debulked patients with ovarian cancer.

Description

Despite the existence of morphologically indistinguishable disease, patients with advanced ovarian tumors display a broad range of survival end points. We hypothesize that gene expression profiling can identify a prognostic signature accounting for these distinct clinical outcomes. To resolve survival-associated loci, gene expression profiling was completed for an extensive set of 185 (90 optimal/95 suboptimal) primary ovarian tumors using the Affymetrix human U133A microarray. Cox regression analysis identified probe sets associated with survival in optimally and suboptimally debulked tumor sets at a P value of <0.01. Leave-one-out cross-validation was applied to each tumor cohort and confirmed by a permutation test. External validation was conducted by applying the gene signature to a publicly available array database of expression profiles of advanced stage suboptimally debulked tumors. The prognostic signature successfully classified the tumors according to survival for suboptimally (P = 0.0179) but not optimally debulked (P = 0.144) patients. The suboptimal gene signature was validated using the independent set of tumors (odds ratio, 8.75; P = 0.0146). To elucidate signaling events amenable to the rapeutic intervention in suboptimally debulked patients, pathway analysis was completed for the top 57 survival-associated probe sets. For suboptimally debulked patients, confirmation of the predictive gene signature supports the existence of a clinically relevant predictor, as well as the possibility of novel therapeutic opportunities. Ultimately, the prognostic classifier defined for suboptimally debulked tumors may aid in the classification and enhancement of patient outcome for this high-risk population.

Usage

```
data( GSE26712_eset )
```

```
experimentData(eset):
Experiment data
```

34 *GSE26712_eset*

```
Experimenter name: Bonome T, Levine DA, Shih J, Randonovich M, Pise-Masison CA, Bogomolniy F, Ozbun
     Laboratory: Bonome, Birrer 2008
     Contact information:
     Title: A gene signature predicting for survival in suboptimally debulked patients with ovarian cand
     URL:
     PMIDs: 18593951
     Abstract: A 238 word abstract is available. Use 'abstract' method.
     Information is available on: preprocessing
     notes:
      platform_title:
         [HG-U133A] Affymetrix Human Genome U133A Array
      platform_shorttitle:
         Affymetrix HG-U133A
      platform_summary:
         hgu133a
      platform_manufacturer:
         Affymetrix
      platform_distribution:
         commercial
      platform_accession:
         GPL96
      platform_technology:
         in situ oligonucleotide
   Preprocessing: frma
   featureData(eset):
   An object of class 'AnnotatedDataFrame'
     featureNames: A1CF A2M ... ZZZ3 (13104 total)
     varLabels: probeset gene
     varMetadata: labelDescription
Details
   assayData: 13104 features, 195 samples
   Platform type: hgu133a
   Overall survival time-to-event summary (in years):
   Call: survfit(formula = Surv(time, cens) ~ -1)
      10 observations deleted due to missingness
   records n.max n.start events median 0.95LCL 0.95UCL
    185.00 185.00 185.00 129.00
                                      3.83
                                              3.24
                                                     4.83
   Available sample meta-data:
    _____
   alt_sample_name:
      Length
              Class
         195 character character
```

sample_type:

GSE26712_eset 35

healthy tumor

```
10
        185
histological_type:
ser NA's
185 10
primarysite:
ov
195
summarygrade:
high NA's
185 10
summarystage:
late NA's
185 10
tumorstage:
  3 4 NA's
146 36 13
substage:
  b c NA's
  9 137 49
age_at_initial_pathologic_diagnosis:
  Min. 1st Qu. Median Mean 3rd Qu. Max.
                                              NA's
 26.00 52.00 63.00 61.54 70.00 84.00
                                               13
recurrence_status:
norecurrence recurrence
        42
              153
days_to_death:
  Min. 1st Qu. Median Mean 3rd Qu.
                                              NA's
                                       Max.
  21.9 660.6 1164.0 1429.0 1880.0 4982.0
                                               10
vital_status:
{\tt deceased \  \  living \  \  \, NA's}
    129
          56
                  10
debulking:
  optimal suboptimal
                        NA's
       90
                 95
                          10
percent_normal_cells:
20-
195
percent_stromal_cells:
```

36 GSE30009_eset

```
20-
195

percent_tumor_cells:
80+
195

batch:
    Length Class Mode
    195 character character

uncurated_author_metadata:
    Length Class Mode
    195 character character
```

GSE30009_eset

Multidrug resistance-linked gene signature predicts overall survival of patients with primary ovarian serous carcinoma.

Description

This study assesses the ability of multidrug resistance (MDR)-associated gene expression patterns to predict survival in patients with newly diagnosed carcinoma of the ovary. The scope of this research differs substantially from that of previous reports, as a very large set of genes was evaluated whose expression has been shown to affect response to chemotherapy. We applied a customized TaqMan low density array, a highly sensitive and specific assay, to study the expression profiles of 380 MDR-linked genes in 80 tumor specimens collected at initial surgery to debulk primary serous carcinoma. The RNA expression profiles of these drug resistance genes were correlated with clinical outcomes.Leave-one-out cross-validation was used to estimate the ability of MDR gene expression to predict survival. Although gene expression alone does not predict overall survival (OS; P = 0.06), four covariates (age, stage, CA125 level, and surgical debulking) do (P = 0.03). When gene expression was added to the covariates, we found an 11-gene signature that provides a major improvement in OS prediction (log-rank statistic P < 0.003). The predictive power of this 11-gene signature was confirmed by dividing high- and low-risk patient groups, as defined by their clinical covariates, into four specific risk groups on the basis of expression levels. This study reveals an 11-gene signature that allows a more precise prognosis for patients with serous cancer of the ovary treated with carboplatin- and paclitaxel-based therapy. These 11 new targets offer opportunities for new therapies to improve clinical outcome in ovarian cancer.

Usage

```
data( GSE30009_eset )
```

```
experimentData(eset):
Experiment data
Experimenter name: Gillet JP, Calcagno AM, Varma S, Davidson B et al. Multidrug resistance-linked g
Laboratory: Gillet, Gottesman 2012
Contact information:
```

GSE30009_eset 37

```
Title: Multidrug resistance-linked gene signature predicts overall survival of patients with prima
     URL:
     PMIDs: 22492981
     Abstract: A 244 word abstract is available. Use 'abstract' method.
     Information is available on: preprocessing
     notes:
      platform_title:
         TaqMan qRT-PCR Homo sapiens Low-Density Array 380
      platform_shorttitle:
         TaqMan qRT-PCR
      platform_summary:
      platform_manufacturer:
         TaqMan
      platform_distribution:
         custom
      platform_accession:
         GPL13728
      platform_technology:
         qRT-PCR
   Preprocessing: default
   featureData(eset):
   An object of class 'AnnotatedDataFrame'
     featureNames: ABCA1 ABCA10 ... XRCC6 (359 total)
     varLabels: probeset gene
     varMetadata: labelDescription
Details
   assayData: 359 features, 103 samples
   Platform type: NA
   Overall survival time-to-event summary (in years):
   Call: survfit(formula = Surv(time, cens) ~ -1)
   records n.max n.start events median 0.95LCL 0.95UCL
    103.00 103.00 103.00 57.00
                                     3.42
                                            2.92
                                                  5.34
   _____
   Available sample meta-data:
   _____
   alt_sample_name:
      Length
              Class
                         Mode
         103 character character
   sample_type:
   borderline
                  tumor
            1
                    102
   histological_type:
```

38 GSE30161_eset

```
clearcell
                ser
                102
summarygrade:
high low NA's
  92
             2
summarystage:
late
 103
tumorstage:
 3 4
82 21
substage:
  b
        c NA's
   2
       60
            41
grade:
        2
             3 NA's
   1
        5
            92
                  2
age_at_initial_pathologic_diagnosis:
  Min. 1st Qu. Median
                          Mean 3rd Qu.
                                           Max.
  30.00
          56.00
                 61.00
                          62.45
                                 71.50
                                          87.00
days_to_death:
   Min. 1st Qu. Median
                           Mean 3rd Qu.
                                           Max.
     24
            598
                   1053
                           1156
                                            4748
                                   1568
vital_status:
deceased
          living
      57
               46
debulking:
   optimal suboptimal
        81
uncurated_author_metadata:
  Length
            Class
                         Mode
      103 character character
```

GSE30161_eset

Multi-gene expression predictors of single drug responses to adjuvant chemotherapy in ovarian carcinoma: predicting platinum resistance.

Description

Despite advances in radical surgery and chemotherapy delivery, ovarian cancer is the most lethal gynecologic malignancy. Standard therapy includes treatment with platinum-based combination

GSE30161_eset 39

chemotherapies yet there is no biomarker model to predict their responses to these agents. We here have developed and independently tested our multi-gene molecular predictors for forecasting patients' responses to individual drugs on a cohort of 55 ovarian cancer patients. To independently validate these molecular predictors, we performed microarray profiling on FFPE tumor samples of 55 ovarian cancer patients (UVA-55) treated with platinum-based adjuvant chemotherapy. Genomewide chemosensitivity biomarkers were initially discovered from the in vitro drug activities and genomic expression data for carboplatin and paclitaxel, respectively. Multivariate predictors were trained with the cell line data and then evaluated with a historical patient cohort. For the UVA-55 cohort, the carboplatin, taxol, and combination predictors significantly stratified responder patients and non-responder patients (p = 0.019, 0.04, 0.014) with sensitivity = 91%, 96%, 93 and NPV = 57%, 67%, 67% in pathologic clinical response. The combination predictor also demonstrated a significant survival difference between predicted responders and non-responders with a median survival of 55.4 months vs. 32.1 months. Thus, COXEN single- and combination-drug predictors successfully stratified platinum resistance and taxane response in an independent cohort of ovarian cancer patients based on their FFPE tumor samples.

Usage

```
data( GSE30161_eset )
```

```
experimentData(eset):
Experiment data
 Experimenter name: Ferriss JS, Kim Y, Duska L, Birrer M, Levine DA, Moskaluk C, Theodorescu D, Lee Jk
  Laboratory: Ferriss, Lee 2012
  Contact information:
 Title: Multi-gene expression predictors of single drug responses to adjuvant chemotherapy in ovaria
  URI:
  PMIDs: 22348014
  Abstract: A 215 word abstract is available. Use 'abstract' method.
  Information is available on: preprocessing
  notes:
   platform_title:
      [HG-U133_Plus_2] Affymetrix Human Genome U133 Plus 2.0 Array
   platform_shorttitle:
      Affymetrix HG-U133Plus2
   platform_summary:
      hgu133plus2
   platform_manufacturer:
      Affymetrix
   platform_distribution:
      commercial
   platform_accession:
      GPL570
   platform_technology:
      in situ oligonucleotide
Preprocessing: frma
featureData(eset):
An object of class 'AnnotatedDataFrame'
  featureNames: A1BG A1BG-AS1 ... ZZZ3 (19816 total)
```

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varLabels: probeset gene
varMetadata: labelDescription

Details

```
assayData: 19816 features, 58 samples
Platform type: hgu133plus2
Overall survival time-to-event summary (in years):
Call: survfit(formula = Surv(time, cens) ~ -1)
records n.max n.start events median 0.95LCL 0.95UCL
 58.00 58.00 58.00 36.00 4.19 2.70 6.17
_____
Available sample meta-data:
alt_sample_name:
  Length Class
                      Mode
      58 character character
sample_type:
tumor
  58
histological_type:
  Length
         Class
                      Mode
      58 character character
summarygrade:
high low NA's
 33 21
summarystage:
late
 58
tumorstage:
3 4
53 5
substage:
a b c
9 11 38
grade:
  1
       2
          3 NA's
      19
           33
{\tt age\_at\_initial\_pathologic\_diagnosis:}
  Min. 1st Qu. Median Mean 3rd Qu.
                                       Max.
 38.00 53.50 62.00 62.57 72.00 85.00
```

```
pltx:
У
58
tax:
n y
4 54
neo:
n
58
days_to_tumor_recurrence:
  Min. 1st Qu. Median
                       Mean 3rd Qu.
                                       Max.
               386.0 742.1 768.2 4208.0
  12.0
       255.2
recurrence_status:
                              NA's
norecurrence recurrence
          6
              48
                                 4
days_to_death:
  Min. 1st Qu. Median
                        Mean 3rd Qu.
                                       Max.
  49.0 585.2 1010.0 1375.0 2131.0 4208.0
vital_status:
deceased
         living
     36
             22
debulking:
  optimal suboptimal
                         NA's
          30
                            2
batch:
2009-10-07 2009-10-08 2009-10-09 2009-10-20
          18
                      8
uncurated\_author\_metadata:
  Length Class
      58 character character
```

GSE32062.GPL6480_eset High-risk ovarian cancer based on 126-gene expression signature is uniquely characterized by downregulation of antigen presentation pathway.

Description

High-grade serous ovarian cancers are heterogeneous not only in terms of clinical outcome but also at the molecular level. Our aim was to establish a novel risk classification system based on

a gene expression signature for predicting overall survival, leading to suggesting novel therapeutic strategies for high-risk patients. In this large-scale cross-platform study of six microarray data sets consisting of 1,054 ovarian cancer patients, we developed a gene expression signature for predicting overall survival by applying elastic net and 10-fold cross-validation to a Japanese data set A (n = 260) and evaluated the signature in five other data sets. Subsequently, we investigated differences in the biological characteristics between high- and low-risk ovarian cancer groups. An elastic net analysis identified a 126-gene expression signature for predicting overall survival in patients with ovarian cancer using the Japanese data set A (multivariate analysis, P = 4 ?? 10(-20)). We validated its predictive ability with five other data sets using multivariate analysis (Tothill's data set, P = 1 ?? 10(-5); Bonome's data set, P = 0.0033; Dressman's data set, P = 0.0016; TCGA data set, P = 0.0027; Japanese data set B, P = 0.021). Through gene ontology and pathway analyses, we identified a significant reduction in expression of immune-response-related genes, especially on the antigen presentation pathway, in high-risk ovarian cancer patients. This risk classification based on the 126-gene expression signature is an accurate predictor of clinical outcome in patients with advanced stage high-grade serous ovarian cancer and has the potential to develop new therapeutic strategies for high-grade serous ovarian cancer patients.

Usage

```
data( GSE32062.GPL6480_eset )
```

```
experimentData(eset):
Experiment data
 Experimenter name: Yoshihara K, Tsunoda T, Shigemizu D, Fujiwara H et al. High-risk ovarian cancer I
  Laboratory: Yoshihara, Tanaka 2012
  Contact information:
 Title: High-risk ovarian cancer based on 126-gene expression signature is uniquely characterized by
  URL:
  PMIDs: 22241791
  Abstract: A 255 word abstract is available. Use 'abstract' method.
  Information is available on: preprocessing
  notes:
   platform_title:
      Agilent-014850 Whole Human Genome Microarray 4x44K G4112F (Probe Name vers
   platform_shorttitle:
      Agilent G4112F
   platform_summary:
      hgug4112a
   platform_manufacturer:
      Agilent
   platform_distribution:
      commercial
   platform accession:
      GPI 6480
   platform_technology:
      in situ oligonucleotide
Preprocessing: default
featureData(eset):
```

pltx:

An object of class 'AnnotatedDataFrame'

featureNames: A1BG A1BG-AS1 ... ZZZ3 (20106 total)

```
varLabels: probeset gene
     varMetadata: labelDescription
Details
   assayData: 20106 features, 260 samples
   Platform type: hgug4112a
   Overall survival time-to-event summary (in years):
   Call: survfit(formula = Surv(time, cens) ~ -1)
   records n.max n.start events median 0.95LCL 0.95UCL
    260.00 260.00 260.00 121.00 4.93
                                            4.11 6.58
   Available sample meta-data:
   alt\_sample\_name:
      Length Class
                           Mode
         260 character character
   sample_type:
   tumor
     260
   histological_type:
   260
   summarygrade:
   high low
    129 131
   summarystage:
   late
    260
   tumorstage:
     3 4
   204 56
   substage:
     a b c NA's
      4 20 180 56
   grade:
     2 3
   131 129
```

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```
У
260
tax:
 ٧
260
days_to_death:
   Min. 1st Qu.
                  Median
                             Mean 3rd Qu.
                                              Max.
     30
             810
                    1245
                             1344
                                     1710
                                              3840
vital_status:
deceased
           living
     121
               139
debulking:
   optimal suboptimal
       103
uncurated_author_metadata:
   Length
               Class
      260 character character
```

GSE32063_eset

High-risk ovarian cancer based on 126-gene expression signature is uniquely characterized by downregulation of antigen presentation pathway.

Description

High-grade serous ovarian cancers are heterogeneous not only in terms of clinical outcome but also at the molecular level. Our aim was to establish a novel risk classification system based on a gene expression signature for predicting overall survival, leading to suggesting novel therapeutic strategies for high-risk patients. In this large-scale cross-platform study of six microarray data sets consisting of 1,054 ovarian cancer patients, we developed a gene expression signature for predicting overall survival by applying elastic net and 10-fold cross-validation to a Japanese data set A (n = 260) and evaluated the signature in five other data sets. Subsequently, we investigated differences in the biological characteristics between high- and low-risk ovarian cancer groups. An elastic net analysis identified a 126-gene expression signature for predicting overall survival in patients with ovarian cancer using the Japanese data set A (multivariate analysis, P = 4 ?? 10(-20)). We validated its predictive ability with five other data sets using multivariate analysis (Tothill's data set, P = 1 ?? 10(-5); Bonome's data set, P = 0.0033; Dressman's data set, P = 0.0016; TCGA data set, P = 0.0027; Japanese data set B, P = 0.021). Through gene ontology and pathway analyses, we identified a significant reduction in expression of immune-response-related genes, especially on the antigen presentation pathway, in high-risk ovarian cancer patients. This risk classification based on the 126-gene expression signature is an accurate predictor of clinical outcome in patients with advanced stage high-grade serous ovarian cancer and has the potential to develop new therapeutic strategies for high-grade serous ovarian cancer patients.

GSE32063_eset 45

Usage

```
data( GSE32063_eset )
```

Format

```
experimentData(eset):
Experiment data
 Experimenter name: Yoshihara K, Tsunoda T, Shigemizu D, Fujiwara H et al. High-risk ovarian cancer I
  Laboratory: Yoshihara, Tanaka 2012
  Contact information:
 Title: High-risk ovarian cancer based on 126-gene expression signature is uniquely characterized by
  URL:
  PMIDs: 22241791
  Abstract: A 255 word abstract is available. Use 'abstract' method.
  Information is available on: preprocessing
  notes:
   platform_title:
     Agilent-014850 Whole Human Genome Microarray 4x44K G4112F (Probe Name vers
ion)
   platform_shorttitle:
      Agilent G4112F
   platform_summary:
      hgug4112a
   platform_manufacturer:
      Agilent
   platform_distribution:
      commercial
   platform_accession:
      GPL6480
   platform_technology:
      in situ oligonucleotide
Preprocessing: default
featureData(eset):
An object of class 'AnnotatedDataFrame'
  featureNames: A1BG A1BG-AS1 ... ZZZ3 (20106 total)
  varLabels: probeset gene
  varMetadata: labelDescription
```

Details

```
assayData: 20106 features, 40 samples
Platform type: hgug4112a
Overall survival time-to-event summary (in years):
Call: survfit(formula = Surv(time, cens) ~ -1)
records n.max n.start events median 0.95LCL 0.95UCL
40.00 40.00 40.00 22.00 4.44 3.29 NA
```

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```
Available sample meta-data:
alt_sample_name:
  Length Class
     40 character character
sample_type:
tumor
  40
histological_type:
40
summarygrade:
high low
17 23
summarystage:
late
 40
tumorstage:
3 4
31 9
substage:
  b c NA's
  3 28 9
grade:
2 3
23 17
pltx:
У
40
tax:
У
40
days_to_death:
  Min. 1st Qu. Median Mean 3rd Qu.
                                      Max.
   210 705 1155 1346 1792
                                      3330
vital_status:
deceased living
     22
          18
```

debulking:

GSE44104_eset 47

```
optimal suboptimal
uncurated_author_metadata:
   Length
              Class
       40 character character
```

GSE44104_eset

COL11A1 promotes tumor progression and predicts poor clinical outcome in ovarian cancer.

Description

Biomarkers that predict disease progression might assist the development of better therapeutic strategies for aggressive cancers, such as ovarian cancer. Here, we investigated the role of collagen type XI alpha 1 (COL11A1) in cell invasiveness and tumor formation and the prognostic impact of COL11A1 expression in ovarian cancer. Microarray analysis suggested that COL11A1 is a disease progression-associated gene that is linked to ovarian cancer recurrence and poor survival. Small interference RNA-mediated specific reduction in COL11A1 protein levels suppressed the invasive ability and oncogenic potential of ovarian cancer cells and decreased tumor formation and lung colonization in mouse xenografts. A combination of experimental approaches, including realtime RT-PCR, casein zymography and chromatin immunoprecipitation (ChIP) assays, showed that COL11A1 knockdown attenuated MMP3 expression and suppressed binding of Ets-1 to its putative MMP3 promoter-binding site, suggesting that the Ets-1-MMP3 axis is upregulated by COL11A1. Transforming growth factor (TGF)-beta (TGF-??1) treatment triggers the activation of smad2 signaling cascades, leading to activation of COL11A1 and MMP3. Pharmacological inhibition of MMP3 abrogated the TGF-??1-triggered, COL11A1-dependent cell invasiveness. Furthermore, the NF-YA-binding site on the COL11A1 promoter was identified as the major determinant of TGF-??1-dependent COL11A1 activation. Analysis of 88 ovarian cancer patients indicated that high COL11A1 mRNA levels are associated with advanced disease stage. The 5-year recurrence-free and overall survival rates were significantly lower (P=0.006 and P=0.018, respectively) among patients with high expression levels of tissue COL11A1 mRNA compared with those with low expression. We conclude that COL11A1 may promote tumor aggressiveness via the TGF-??1-MMP3 axis and that COL11A1 expression can predict clinical outcome in ovarian cancer patients.

Usage

```
data( GSE44104_eset )
```

Format

```
experimentData(eset):
Experiment data
  Experimenter name: Wu Y, Chang T, Huang Y, Huang H, Chou C
 Laboratory: Wu, Chou 2013
 Contact information:
 Title: COL11A1 promotes tumor progression and predicts poor clinical outcome in ovarian cancer.
 URL:
```

PMIDs: 23934190

48 *GSE44104_eset*

```
Abstract: A 260 word abstract is available. Use 'abstract' method.
     Information is available on: preprocessing
     notes:
      platform_title:
         [HG-U133_Plus_2] Affymetrix Human Genome U133 Plus 2.0 Array
      platform_shorttitle:
         Affymetrix HG-U133Plus2
      platform_summary:
         hgu133plus2
      platform_manufacturer:
         Affymetrix
      platform_distribution:
         commercial
      platform_accession:
         GPL570
      platform_technology:
         in situ oligonucleotide
   Preprocessing: frma
   featureData(eset):
   An object of class 'AnnotatedDataFrame'
     featureNames: A1BG A1BG-AS1 ... ZZZ3 (19816 total)
     varLabels: probeset gene
     varMetadata: labelDescription
Details
   assayData: 19816 features, 60 samples
   Platform type: hgu133plus2
   Binary overall survival summary (definitions of long and short provided by study authors):
    long short
      44 16
   Available sample meta-data:
    _____
   alt_sample_name:
      Length Class
                          Mode
          60 character character
   sample_type:
   tumor
      60
   histological_type:
   clearcell endo mucinous
                                       ser
          12
                  11
                                       28
   summarystage:
   early late
```

GSE49997_eset 49

```
25
         35
tumorstage:
    2 3
 1
         4
17
   8 30 5
recurrence_status:
norecurrence
               recurrence
os_binary:
 long short
   44
         16
relapse_binary:
 long short
   40
         20
batch:
2010-09-07 2010-09-08 2010-10-14 2010-12-10 2010-12-14
                     2
                                           16
uncurated_author_metadata:
   Length
              Class
       60 character character
```

GSE49997_eset

Validating the impact of a molecular subtype in ovarian cancer on outcomes: a study of the OVCAD Consortium.

Description

Most patients with epithelial ovarian cancer (EOC) are diagnosed at advanced stage and have a poor prognosis. However, a small proportion of these patients will survive, whereas others will die very quickly. Clinicopathological factors do not allow precise identification of these subgroups. Thus, we have validated a molecular subclassification as new prognostic factor in EOC. One hundred and ninety-four patients with Stage II-IV EOC were characterized by whole-genome expression profiling of tumor tissues and were classified using a published 112 gene set, derived from an International Federation of Gynecology and Obstetrics (FIGO) stage-directed supervised classification approach. The 194 tumor samples were classified into two subclasses comprising 95 (Subclass 1) and 99 (Subclass 2) tumors. All nine FIGO II tumors were grouped in Subclass 1 (P = 0.001). Subclass 2 (54% of advanced-stage tumors) was significantly correlated with peritoneal carcinomatosis and non-optimal debulking. Patients with Subclass 2 tumors had a worse overall survival for both serous and non-serous histological subtypes, as revealed by univariate analysis (hazard ratios [HR] of 3.17 and 17.11, respectively; P??? 0.001) and in models corrected for relevant clinicopathologic parameters (HR 2.87 and 12.42, respectively; P ??? 0.023). Significance analysis of microarrays revealed 2082 genes that were differentially expressed in advanced-grade serous tumors of both subclasses and the focal adhesion pathway as the most deregulated pathway. In the present validation study, we have shown that, in advanced-stage serous ovarian cancer, two approximately equally large molecular subtypes exist, independent of classical clinocopathological parameters and 50 GSE49997_eset

presenting with highly different whole-genome expression profiles and a markedly different overall survival. Similar results were obtained in a small cohort of patients with non-serous tumors.?? 2012 Japanese Cancer Association.

Usage

```
data( GSE49997_eset )
```

Format

```
experimentData(eset):
Experiment data
 Experimenter name: Pils D1, Hager G, Tong D, Aust S, Heinze G, Kohl M, Schuster E, Wolf A, Sehouli J,
  Laboratory: Pils, Zeilinger 2012
  Contact information:
 Title: Validating the impact of a molecular subtype in ovarian cancer on outcomes: a study of the OV
  URL:
  PMIDs: 22497737
  Abstract: A 276 word abstract is available. Use 'abstract' method.
  Information is available on: preprocessing
  notes:
   platform title:
      ABI Human Genome Survey Microarray Version 2
   platform_shorttitle:
      ABI Human Genome
   platform_summary:
   platform_manufacturer:
      Applied Biosystems
   platform_distribution:
      commercial
   platform_accession:
      GPL2986
   platform_technology:
      in situ oligonucleotide
Preprocessing: default
featureData(eset):
An object of class 'AnnotatedDataFrame'
  featureNames: A1BG A1CF ... ZZZ3 (16048 total)
  varLabels: probeset gene
  varMetadata: labelDescription
```

Details

```
assayData: 16048 features, 204 samples
Platform type:
Overall survival time-to-event summary (in years):
Call: survfit(formula = Surv(time, cens) ~ -1)

10 observations deleted due to missingness
```

GSE49997_eset 51

records n.max n.start events median 0.95LCL 0.95UCL 194.00 194.00 194.00 57.00 3.67 Available sample meta-data: ----alt_sample_name: Length Class 204 character character sample_type: tumor 204 histological_type: other ser NA's 171 10 23 summarygrade: high low NA's 143 50 11 summarystage: early late NA's 9 185 10 tumorstage: 2 3 4 NA's 9 154 31 10 grade: 2 3 NA's 50 143 11 age_at_initial_pathologic_diagnosis: Min. 1st Qu. Median Mean 3rd Qu. Max. NA's 26.00 50.00 57.00 57.66 67.00 85.00 10 days_to_tumor_recurrence: Min. 1st Qu. Median Mean 3rd Qu. NA's Max. 30.0 335.0 487.0 580.1 722.5 1461.0 10 recurrence_status: NA's norecurrence recurrence 70 124 10 days_to_death: Min. 1st Qu. Median Mean 3rd Qu. NA's Max.

30.0 517.0 745.5 782.9 1027.0 1491.0

vital_status:

10

52 GSE51088_eset

```
deceased living NA's
57 137 10

debulking:
optimal suboptimal NA's
137 57 10

uncurated_author_metadata:
Length Class Mode
204 character character
```

GSE51088_eset

POSTN/TGFBI-associated stromal signature predicts poor prognosis in serous epithelial ovarian cancer.

Description

To identify molecular prognosticators and therapeutic targets for high-grade serous epithelial ovarian cancers (EOCs) using genetic analyses driven by biologic features of EOC pathogenesis. Ovarian tissue samples (n = 172; 122 serous EOCs, 30 other EOCs, 20 normal/benign) collected prospectively from sequential patients undergoing gynecologic surgery were analyzed using RNA expression microarrays. Samples were classified based on expression of genes with potential relevance in ovarian cancer. Gene sets were defined using Rosetta Similarity Search Tool (ROAST) and analysis of variance (ANOVA). Gene copy number variations were identified by array comparative genomic hybridization. No distinct subgroups of EOC could be identified by unsupervised clustering, however, analyses based on genes correlated with periostin (POSTN) and estrogen receptoralpha (ESR1) yielded distinct subgroups. When 95 high-grade serous EOCs were grouped by genes based on ANOVA comparing ESR1/WT1 and POSTN/TGFBI samples, overall survival (OS) was significantly shorter for 43 patients with tumors expressing genes associated with POSTN/TGFBI compared to 52 patients with tumors expressing genes associated with ESR1/WT1 (median 30 versus 49 months, respectively; P = 0.022). Several targets with therapeutic potential were identified within each subgroup. BRCA germline mutations were more frequent in the ESR1/WT1 subgroup. Proliferation-associated genes and TP53 status (mutated or wild-type) did not correlate with survival. Findings were validated using independent ovarian cancer datasets. Two distinct molecular subgroups of high-grade serous EOCs based on POSTN/TGFBI and ESR1/WT1 expressions were identified with significantly different OS. Specific differentially expressed genes between these subgroups provide potential prognostic and therapeutic targets. Copyright ?? 2013 Elsevier Inc. All rights reserved.

Usage

```
data( GSE51088_eset )
```

```
experimentData(eset):
Experiment data
Experimenter name: Karlan BY, Dering J, Walsh C, Orsulic S, Lester J, Anderson LA, Ginther CL, Fejzo Laboratory: Karlan, Slamon 2014
Contact information:
```

GSE51088_eset 53

```
Title: POSTN/TGFBI-associated stromal signature predicts poor prognosis in serous epithelial ovari
     URL:
     PMIDs: 24368280
     Abstract: A 250 word abstract is available. Use 'abstract' method.
     Information is available on: preprocessing
     notes:
      platform_title:
         Agilent-012097 Human 1A Microarray (V2) G4110B (Probe Name version)
      platform_shorttitle:
         Agilent G4110B
      platform_summary:
         hgug4110b
      platform_manufacturer:
         Agilent
      platform_distribution:
         commercial
      platform_accession:
         GPL7264
      platform_technology:
         in situ oligonucleotide
   Preprocessing: default
   featureData(eset):
   An object of class 'AnnotatedDataFrame'
     featureNames: A1CF A2M ... ZZZ3 (8211 total)
     varLabels: probeset gene
     varMetadata: labelDescription
Details
   assayData: 8211 features, 172 samples
   Platform type: hgug4110b
   Overall survival time-to-event summary (in years):
   Call: survfit(formula = Surv(time, cens) ~ -1)
      20 observations deleted due to missingness
   records n.max n.start events median 0.95LCL 0.95UCL
    152.00 152.00 152.00 112.00
                                     4.13
                                             3.50
                                                    4.92
   _____
   Available sample meta-data:
   alt_sample_name:
      Length
               Class
                          Mode
         172 character character
   sample_type:
                           healthy metastatic
       benign borderline
                                                   tumor
            5
                 12
                            15
                                      17
                                                     123
```

54 *GSE51088_eset*

Mode

histological_type: Length Class

```
172 character character
summarygrade:
high low NA's
119 30 23
summarystage:
early late NA's
  31 120 21
tumorstage:
 1 2 3 4 NA's
     9 103 17 21
 22
substage:
         c NA's
  a b
 17
     22
         94 39
grade:
      1
         2 3 NA's
  0
         14 119 23
  8
      8
{\tt age\_at\_initial\_pathologic\_diagnosis:}
  Min. 1st Qu. Median Mean 3rd Qu.
                                    Max.
  26.0 49.0 57.5 58.6 68.0
                                    91.0
neo:
 n
172
recurrence_status:
norecurrence recurrence NA's
        36
             111
                             25
days_to_death:
  Min. 1st Qu. Median Mean 3rd Qu.
                                    Max. NA's
    30 791 1491
                      1835 2344
                                    7001
                                             20
vital_status:
deceased living NA's
    112
            40
                   20
percent_normal_cells:
30- NA's
140 32
{\tt percent\_stromal\_cells:}
30- NA's
140 32
```

GSE6008_eset 55

```
percent_tumor_cells:
  70+ NA's
  140    32

uncurated_author_metadata:
  Length    Class    Mode
         172 character character
```

GSE6008_eset

Lysophosphatidic acid-induced transcriptional profile represents serous epithelial ovarian carcinoma and worsened prognosis.

Description

Lysophosphatidic acid (LPA) governs a number of physiologic and pathophysiological processes. Malignant ascites fluid is rich in LPA, and LPA receptors are aberrantly expressed by ovarian cancer cells, implicating LPA in the initiation and progression of ovarian cancer. However, there is an absence of systematic data critically analyzing the transcriptional changes induced by LPA in ovarian cancer.In this study, gene expression profiling was used to examine LPA-mediated transcription by exogenously adding LPA to human epithelial ovarian cancer cells for 24 h to mimic long-term stimulation in the tumor microenvironment. The resultant transcriptional profile comprised a 39-gene signature that closely correlated to serous epithelial ovarian carcinoma. Hierarchical clustering of ovarian cancer patient specimens demonstrated that the signature is associated with worsened prognosis. Patients with LPA-signature-positive ovarian tumors have reduced disease-specific and progression-free survival times. They have a higher frequency of stage IIIc serous carcinoma and a greater proportion is deceased. Among the 39-gene signature, a group of seven genes associated with cell adhesion recapitulated the results. Out of those seven, claudin-1, an adhesion molecule and phenotypic epithelial marker, is the only independent biomarker of serous epithelial ovarian carcinoma. Knockdown of claudin-1 expression in ovarian cancer cells reduces LPA-mediated cellular adhesion, enhances suspended cells and reduces LPA-mediated migration. The data suggest that transcriptional events mediated by LPA in the tumor microenvironment influence tumor progression through modulation of cell adhesion molecules like claudin-1 and, for the first time, report an LPA-mediated expression signature in ovarian cancer that predicts a worse prognosis.

Usage

```
data( GSE6008_eset )
```

PMIDs: 19440550

Format

```
experimentData(eset):
Experiment data
Experimenter name: Murph MM, Liu W, Yu S, Lu Y, Hall H, Hennessy BT, Lahad J, Schaner M, Helland A, K
Laboratory: Murph, Mills 2009
Contact information:
Title: Lysophosphatidic acid-induced transcriptional profile represents serous epithelial ovarian
URL:
```

Abstract: A 247 word abstract is available. Use 'abstract' method.

56 GSE6008_eset

```
notes:
      platform_title:
         [HG-U133A] Affymetrix Human Genome U133A Array
      platform_shorttitle:
        Affymetrix HG-U133A
      platform_summary:
        hgu133a
      platform_manufacturer:
         Affymetrix
      platform_distribution:
         commercial
      platform_accession:
         GPL96
      platform_technology:
         in situ oligonucleotide
   Preprocessing: frma
   featureData(eset):
   An object of class 'AnnotatedDataFrame'
     featureNames: A1CF A2M ... ZZZ3 (13104 total)
     varLabels: probeset gene
     varMetadata: labelDescription
Details
   assayData: 13104 features, 103 samples
   Platform type: hgu133a
   _____
   Available sample meta-data:
   alt_sample_name:
      Length Class
        103 character character
   sample_type:
   healthy tumor
        4
              99
   histological_type:
                                ser
   clearcell endo mucinous
                                             NA's
          8
                 37 13
                                     41
   primarysite:
    ٥v
   103
   summarygrade:
   high low NA's
     38 36 29
```

Information is available on: preprocessing

GSE6822_eset 57

```
summarystage:
early late NA's
   42
         53
tumorstage:
             3
                   4 NA's
   1
        2
  35
       11
            44
substage:
        b
                   d NA's
   а
             С
  19
        2
            54
                       27
grade:
        2
   1
             3 NA's
  19
       17
            38
                 29
batch:
   Length
                          Mode
              Class
      103 character character
uncurated_author_metadata:
   Length
              Class
                          Mode
      103 character character
```

GSE6822_eset

Classification of ovarian tumor samples

Description

Ouellet V, Provencher DM, Maugard CM, Le Page C, Ren F, Lussier C, Novak J, Ge B, Hudson TJ, Tonin PN, Mes-Masson A-M: Discrimination between serous low malignant potential and invasive epithelial ovarian tumors using molecular profiling. Oncogene 2005, 24:4672-4687.

Usage

```
data( GSE6822_eset )
```

```
experimentData(eset):
Experiment data
Experimenter name: Ouellet V, Provencher DM, Maugard CM, Le Page C, Ren F, Lussier C, Novak J, Ge B, Laboratory: Ouellet, Mes-Masson 2005
Contact information:
Title: Classification of ovarian tumor samples
URL:
PMIDs: PMID unknown

Abstract: A 40 word abstract is available. Use 'abstract' method.
Information is available on: preprocessing
```

58 GSE6822_eset

```
notes:
   platform_title:
      [Hu6800] Affymetrix Human Full Length HuGeneFL Array
   platform_shorttitle:
     Affymetrix Hu6800
  platform_summary:
     hu6800
   platform_manufacturer:
     Affymetrix
   platform_distribution:
     commercial
  platform_accession:
     GPL80
   platform_technology:
      in situ oligonucleotide
Preprocessing: rma
featureData(eset):
An object of class 'AnnotatedDataFrame'
  featureNames: A2M AADAC ... ZYX (5251 total)
 varLabels: probeset gene
 varMetadata: labelDescription
assayData: 5251 features, 66 samples
Platform type: hu6800
Available sample meta-data:
-----
```

Details

```
alt_sample_name:
  Length Class Mode
      66 character character
sample_type:
borderline cellline
                         tumor
        6
                           58
                 2
histological_type:
  Length Class
      66 character character
primarysite:
ον
66
summarygrade:
high low NA's
     15 11
grade:
```

GSE8842_eset 59

```
1 2 3 NA's
1 14 40 11

batch:
Length Class Mode
66 character character

uncurated_author_metadata:
Length Class Mode
66 character character
```

GSE8842_eset

Analysis of gene expression in early-stage ovarian cancer.

Description

Gene expression profile was analyzed in 68 stage I and 15 borderline ovarian cancers to determine if different clinical features of stage I ovarian cancer such as histotype, grade, and survival are related to differential gene expression. Tumors were obtained directly at surgery and immediately frozen in liquid nitrogen until analysis. Glass arrays containing 16,000 genes were used in a dualcolor assay labeling protocol. Unsupervised analysis identified eight major patient partitions, one of which was statistically associated to overall survival, grading, and histotype and another with grading and histotype. Supervised analysis allowed detection of gene profiles clearly associated to histotype or to degree of differentiation. No difference was found between borderline and grade 1 tumors. As to recurrence, a subset of genes able to differentiate relapsers from nonrelapsers was identified. Among these, cyclin E and minichromosome maintenance protein 5 were found particularly relevant, as their expression was inversely correlated to progression-free survival (P = 0.00033 and 0.017, respectively). Specific molecular signatures define different histotypes and prognosis of stage I ovarian cancer. Mucinous and clear cells histotypes can be distinguished from the others regardless of tumor grade. Cyclin E and minichromosome maintenance protein 5, whose expression was found previously to be related to a bad prognosis of advanced ovarian cancer, appear to be potential prognostic markers in stage I ovarian cancer too, independent of other pathologic and clinical variables.

Abstract: A 225 word abstract is available. Use 'abstract' method.

Usage

```
data( GSE8842_eset )
```

```
experimentData(eset):
Experiment data
Experimenter name: Marchini S, Mariani P, Chiorino G, Marrazzo E, Bonomi R, Fruscio R, Clivio L, Gar Laboratory: Marchini, D'Incalci 2008
Contact information:
Title: Analysis of gene expression in early-stage ovarian cancer.
URL:
PMIDs: 19047114
```

60 GSE8842_eset

```
Information is available on: preprocessing
     notes:
      platform_title:
         Agilent Human 1 cDNA Microarray (G4100A)
      platform_shorttitle:
         Agilent G4100A cDNA
      platform_summary:
         hgug4100a
      platform_manufacturer:
         Agilent
      platform_distribution:
         custom-commerical
      platform_accession:
         GPL5689
      platform_technology:
         spotted DNA/cDNA
   Preprocessing: default
   featureData(eset):
   An object of class 'AnnotatedDataFrame'
     featureNames: A2M AADAC ... ZYX (6536 total)
     varLabels: probeset gene
     varMetadata: labelDescription
Details
   assayData: 6536 features, 83 samples
   Platform type: hgug4100a
   Overall survival time-to-event summary (in years):
   Call: survfit(formula = Surv(time, cens) ~ -1)
   records
            n.max n.start events median 0.95LCL 0.95UCL
              83 83
                           15
                                            12
        83
                                     NA
   Available sample meta-data:
   _____
   alt_sample_name:
      Length Class
                          Mode
          83 character character
   sample_type:
   borderline
                 tumor
          15
                     68
   histological_type:
      Length Class
                           Mode
          83 character character
   primarysite:
```

```
83
summarygrade:
high low NA's
 35
     33
          15
summarystage:
early
  83
tumorstage:
1
83
substage:
a b c
25 5 53
grade:
  1
       2
            3 NA's
  13
      20
           35 15
age_at_initial_pathologic_diagnosis:
  Min. 1st Qu. Median Mean 3rd Qu.
                                         Max.
  21.00 43.00
                50.00 51.25 61.00
                                        87.00
recurrence_status:
norecurrence recurrence
         62
                      21
days_to_death:
  Min. 1st Qu. Median
                          Mean 3rd Qu.
                                         Max.
          1192
                  2248
                          2273 3048
                                         5824
vital_status:
deceased
          living
     15
              68
uncurated_author_metadata:
  Length Class
      83 character character
```

GSE9891_eset

Novel molecular subtypes of serous and endometrioid ovarian cancer linked to clinical outcome.

Description

The study aim to identify novel molecular subtypes of ovarian cancer by gene expression profiling with linkage to clinical and pathologic features. Microarray gene expression profiling was done

on 285 serous and endometrioid tumors of the ovary, peritoneum, and fallopian tube. K-means clustering was applied to identify robust molecular subtypes. Statistical analysis identified differentially expressed genes, pathways, and gene ontologies. Laser capture microdissection, pathology review, and immunohistochemistry validated the array-based findings. Patient survival within kmeans groups was evaluated using Cox proportional hazards models. Class prediction validated k-means groups in an independent dataset. A semisupervised survival analysis of the array data was used to compare against unsupervised clustering results. Optimal clustering of array data identified six molecular subtypes. Two subtypes represented predominantly serous low malignant potential and low-grade endometrioid subtypes, respectively. The remaining four subtypes represented higher grade and advanced stage cancers of serous and endometrioid morphology. A novel subtype of high-grade serous cancers reflected a mesenchymal cell type, characterized by overexpression of N-cadherin and P-cadherin and low expression of differentiation markers, including CA125 and MUC1. A poor prognosis subtype was defined by a reactive stroma gene expression signature, correlating with extensive desmoplasia in such samples. A similar poor prognosis signature could be found using a semisupervised analysis. Each subtype displayed distinct levels and patterns of immune cell infiltration. Class prediction identified similar subtypes in an independent ovarian dataset with similar prognostic trends. Gene expression profiling identified molecular subtypes of ovarian cancer of biological and clinical importance.

Usage

```
data( GSE9891_eset )
```

Preprocessing: frma

```
experimentData(eset):
Experiment data
 Experimenter name: Tothill RW, Tinker AV, George J, Brown R, Fox SB, Lade S, Johnson DS, Trivett MK,
 Laboratory: Tothill, Bowtell 2008
 Contact information:
 Title: Novel molecular subtypes of serous and endometrioid ovarian cancer linked to clinical outcom
 URL:
 PMIDs: 18698038
  Abstract: A 243 word abstract is available. Use 'abstract' method.
  Information is available on: preprocessing
  notes:
   platform_title:
      [HG-U133_Plus_2] Affymetrix Human Genome U133 Plus 2.0 Array
   platform_shorttitle:
      Affymetrix HG-U133Plus2
   platform_summary:
      hgu133plus2
   platform_manufacturer:
      Affymetrix
   platform_distribution:
      commercial
   platform_accession:
      GPL570
   platform_technology:
      in situ oligonucleotide
```

```
featureData(eset):
   An object of class 'AnnotatedDataFrame'
     featureNames: A1BG A1BG-AS1 ... ZZZ3 (19816 total)
     varLabels: probeset gene
     varMetadata: labelDescription
Details
   assayData: 19816 features, 285 samples
   Platform type: hgu133plus2
   Overall survival time-to-event summary (in years):
   Call: survfit(formula = Surv(time, cens) ~ -1)
      7 observations deleted due to missingness
           n.max n.start events median 0.95LCL 0.95UCL
    278.00 278.00 278.00 113.00
                                     3.95
                                            3.53
                                                    5.01
   Available sample meta-data:
   alt_sample_name:
      Length Class
         285 character character
   sample_type:
   borderline
                tumor
          18
                    267
   histological_type:
    endo other
                ser
      20
           1
                264
   primarysite:
      ft other
                 ΟV
       8
            34
                243
   arrayedsite:
      ft other
                 ΟV
            83
                200
       2
   summarygrade:
   high low NA's
    163 116 6
   summarystage:
   early late NA's
         240
                3
      42
   tumorstage:
                    4 NA's
      1
          2
               3
     24
         18 218 22 3
```

```
substage:
    a    b    c NA's
 grade:
 1 2 3 NA's
 19 97 163 6
age_at_initial_pathologic_diagnosis:
 Min. 1st Qu. Median Mean 3rd Qu. Max. NA's
 22.00 53.00 59.00 59.62 68.00 80.00 3
pltx:
 n y NA's
 39 243 3
tax:
 n y NA's
 87 195 3
neo:
n y NA's
264 18 3
days_to_tumor_recurrence:
  Min. 1st Qu. Median Mean 3rd Qu. Max. NA's
   0.0 300.0 450.0 618.9 810.0 4980.0 10
recurrence_status:
norecurrence recurrence NA's
   94 188
                         3
days_to_death:
  Min. 1st Qu. Median Mean 3rd Qu. Max. NA's
  0.0 547.5 855.0 955.1 1252.0 6420.0 7
vital_status:
deceased living NA's 113 169 3
debulking:
  optimal suboptimal NA's
    160 88
                     37
batch:
  Length Class Mode
    285 character character
uncurated_author_metadata:
  Length Class Mode
    285 character character
```

PMID15897565_eset 65

PMID15897565_eset

Patterns of gene expression that characterize long-term survival in advanced stage serous ovarian cancers.

Description

A better understanding of the underlying biology of invasive serous ovarian cancer is critical for the development of early detection strategies and new therapeutics. The objective of this study was to define gene expression patterns associated with favorable survival.RNA from 65 serous ovarian cancers was analyzed using Affymetrix U133A microarrays. This included 54 stage III/IV cases (30 short-term survivors who lived <3 years and 24 long-term survivors who lived >7 years) and 11 stage I/II cases. Genes were screened on the basis of their level of and variability in expression, leaving 7,821 for use in developing a predictive model for survival. A composite predictive model was developed that combines Bayesian classification tree and multivariate discriminant models. Leave-one-out cross-validation was used to select and evaluate models.Patterns of genes were identified that distinguish short-term and long-term ovarian cancer survivors. The expression model developed for advanced stage disease classified all 11 early-stage ovarian cancers as long-term survivors. The MAL gene, which has been shown to confer resistance to cancer therapy, was most highly overexpressed in short-term survivors (3-fold compared with long-term survivors, and 29fold compared with early-stage cases). These results suggest that gene expression patterns underlie differences in outcome, and an examination of the genes that provide this discrimination reveals that many are implicated in processes that define the malignant phenotype. Differences in survival of advanced ovarian cancers are reflected by distinct patterns of gene expression. This biological distinction is further emphasized by the finding that early-stage cancers share expression patterns with the advanced stage long-term survivors, suggesting a shared favorable biology.

Usage

```
data( PMID15897565_eset )
```

```
experimentData(eset):
Experiment data
 Experimenter name: Berchuck A, Iversen ES, Lancaster JM, Pittman J, Luo J, Lee P, Murphy S, Dressmar
 Laboratory: Berchuck, Marks 2005
 Contact information:
 Title: Patterns of gene expression that characterize long-term survival in advanced stage serous ov
  URL:
 PMIDs: 15897565
  Abstract: A 258 word abstract is available. Use 'abstract' method.
  Information is available on: preprocessing
  notes:
   platform_title:
      [HG-U133A] Affymetrix Human Genome U133A Array
  platform_shorttitle:
      Affymetrix HG-U133A
   platform_summary:
```

66 PMID15897565_eset

hgu133a

```
platform_manufacturer:
         Affymetrix
      platform_distribution:
         commercial
      platform_accession:
         GPL96
      platform_technology:
         in situ oligonucleotide
      warnings:
         These samples are a subset of PMID17290060.
   Preprocessing: frma
   featureData(eset):
   An object of class 'AnnotatedDataFrame'
     featureNames: A1CF A2M ... ZZZ3 (13104 total)
     varLabels: probeset gene
     varMetadata: labelDescription
Details
   assayData: 13104 features, 63 samples
   Platform type: hgu133a
   Binary overall survival summary (definitions of long and short provided by study authors):
    long short NA's
      24
           28 11
   ______
   Available sample meta-data:
   alt_sample_name:
      Min. 1st Qu. Median
                             Mean 3rd Qu.
                                             Max.
      1761 1828 1907
                                     2032
                             2001
                                             2536
   sample_type:
   tumor
      63
   histological_type:
   ser
    63
   primarysite:
   οv
   63
   summarygrade:
   high low NA's
     25 37 1
```

PMID17290060_eset 67

```
summarystage:
early late
         52
   11
tumorstage:
1
   2
       3 4
   4 48 4
grade:
        2
             3
                   4 NA's
   1
   2
       35
            24
age_at_initial_pathologic_diagnosis:
   Min. 1st Qu. Median
                            Mean 3rd Qu.
                                             Max.
  33.00
          52.50
                  59.00
                           59.21
                                   67.00
                                            79.00
os_binary:
long short NA's
   24
         28
               11
debulking:
   optimal suboptimal
                             NA's
        24
                    28
                               11
batch:
   Length
              Class
                          Mode
       63 character character
uncurated_author_metadata:
   Length
              Class
                          Mode
       63 character character
```

PMID17290060_eset

An integrated genomic-based approach to individualized treatment of patients with advanced-stage ovarian cancer.

Description

The purpose of this study was to develop an integrated genomic-based approach to personalized treatment of patients with advanced-stage ovarian cancer. We have used gene expression profiles to identify patients likely to be resistant to primary platinum-based chemotherapy and also to identify alternate targeted therapeutic options for patients with de novo platinum-resistant disease. A gene expression model that predicts response to platinum-based therapy was developed using a training set of 83 advanced-stage serous ovarian cancers and tested on a 36-sample external validation set. In parallel, expression signatures that define the status of oncogenic signaling pathways were evaluated in 119 primary ovarian cancers and 12 ovarian cancer cell lines. In an effort to increase chemotherapy sensitivity, pathways shown to be activated in platinum-resistant cancers were subject to targeted therapy in ovarian cancer cell lines. Gene expression profiles identified patients with ovarian cancer likely to be resistant to primary platinum-based chemotherapy with greater than 80% accuracy. In patients with platinum-resistant disease, we identified expression signatures consistent

68 PMID17290060_eset

with activation of Src and Rb/E2F pathways, components of which were successfully targeted to increase response in ovarian cancer cell lines. We have defined a strategy for treatment of patients with advanced-stage ovarian cancer that uses therapeutic stratification based on predictions of response to chemotherapy, coupled with prediction of oncogenic pathway deregulation, as a method to direct the use of targeted agents.

Usage

```
data( PMID17290060_eset )
```

Format

```
experimentData(eset):
Experiment data
 Experimenter name: Dressman HK, Berchuck A, Chan G, Zhai J, Bild A, Sayer R, Cragun J, Clarke J, Whi
  Laboratory: Dressman, Lancaster 2007
  Contact information:
 Title: An integrated genomic-based approach to individualized treatment of patients with advanced-
  URL:
  PMIDs: 17290060
  Abstract: A 223 word abstract is available. Use 'abstract' method.
  Information is available on: preprocessing
  notes:
   platform_title:
      [HG-U133A] Affymetrix Human Genome U133A Array
   platform_shorttitle:
      Affymetrix HG-U133A
   platform_summary:
      hgu133a
   platform_manufacturer:
      Affymetrix
   platform_distribution:
      commercial
   platform_accession:
      GPL96
   platform_technology:
      in situ oligonucleotide
   warnings:
      This paper has been retracted.
Preprocessing: frma
featureData(eset):
An object of class 'AnnotatedDataFrame'
  featureNames: A1CF A2M ... ZZZ3 (13104 total)
  varLabels: probeset gene
  varMetadata: labelDescription
```

Details

assayData: 13104 features, 117 samples Platform type: hgu133a

69

```
Overall survival time-to-event summary (in years):
Call: survfit(formula = Surv(time, cens) ~ -1)
records n.max n.start events median 0.95LCL 0.95UCL
117.00 117.00 117.00 67.00 5.26 2.79 7.48
Available sample meta-data:
_____
alt_sample_name:
  Length Class
                    Mode
     117 character character
sample_type:
tumor
 117
histological_type:
117
primarysite:
ον
117
summarygrade:
high low NA's
 57 57
summarystage:
early late NA's
  1 115 1
tumorstage:
  2 3 4 NA's
  1 98 17 1
grade:
      2
  1
          3
              4 NA's
  4 53
          56
               1 3
days_to_death:
  Min. 1st Qu. Median Mean 3rd Qu.
                                     Max.
    30 510
               1020
                       1496
                              2220
                                     5550
vital_status:
deceased living
     67
             50
primary_therapy_outcome_success:
 completeresponse progressivedisease
```

70 PMID19318476_eset

debulking:
 optimal suboptimal
 63 54

batch:
 Length Class Mode
 117 character character

uncurated_author_metadata:
 Length Class Mode
 117 character character

PMID19318476_eset

Microarray analysis of early stage serous ovarian cancers shows profiles predictive of favorable outcome.

Description

Although few women with advanced serous ovarian cancer are cured, detection of the disease at an early stage is associated with a much higher likelihood of survival. We previously used gene expression array analysis to distinguish subsets of advanced cancers based on disease outcome. In the present study, we report on gene expression of early-stage cancers and validate our prognostic model for advanced-stage cancers. Frozen specimens from 39 stage I/II, 42 stage III/IV, and 20 low malignant potential cancers were obtained from four different sites. A linear discriminant model was used to predict survival based upon array data. We validated the late-stage survival model and show that three of the most differentially expressed genes continue to be predictive of outcome. Most early-stage cancers (38 of 39 invasive, 15 of 20 low malignant potential) were classified as long-term survivors (median probabilities 0.97 and 0.86). MAL, the most differentially expressed gene, was further validated at the protein level and found to be an independent predictor of poor survival in an unselected group of advanced serous cancers (P = 0.0004). These data suggest that serous ovarian cancers detected at an early stage generally have a favorable underlying biology similar to advanced-stage cases that are long-term survivors. Conversely, most late-stage ovarian cancers seem to have a more virulent biology. This insight suggests that if screening approaches are to succeed it will be necessary to develop approaches that are able to detect these virulent cancers at an early stage.

Usage

```
data( PMID19318476_eset )
```

Format

```
experimentData(eset):
Experiment data
```

Experimenter name: Berchuck A, Iversen ES, Luo J, Clarke JP, Horne H, Levine DA, Boyd J, Alonso MA, S. Laboratory: Berchuck, Lancaster 2009

Contact information:

Title: Microarray analysis of early stage serous ovarian cancers shows profiles predictive of favor

```
URL:
     PMIDs: 19318476
     Abstract: A 241 word abstract is available. Use 'abstract' method.
     Information is available on: preprocessing
     notes:
      platform_title:
         [HG-U133A] Affymetrix Human Genome U133A Array
      platform_shorttitle:
         Affymetrix HG-U133A
      platform_summary:
         hgu133a
      platform_manufacturer:
         Affymetrix
      platform_distribution:
         commercial
      platform_accession:
         GPL96
      platform_technology:
         in situ oligonucleotide
      warnings:
         These samples are a subset of PMID17290060.
   Preprocessing: frma
   featureData(eset):
   An object of class 'AnnotatedDataFrame'
     featureNames: A1CF A2M ... ZZZ3 (13104 total)
     varLabels: probeset gene
     varMetadata: labelDescription
Details
   assayData: 13104 features, 42 samples
   Platform type: hgu133a
   Overall survival time-to-event summary (in years):
   Call: survfit(formula = Surv(time, cens) ~ -1)
            n.max n.start events median 0.95LCL 0.95UCL
   records
     42.00
            42.00 42.00
                           22.00
                                     2.79
                                             2.30
    _____
   Available sample meta-data:
   alt_sample_name:
               Class Mode
      Length
          42 character character
   sample_type:
   tumor
      42
```

72 PMID19318476_eset

histological_type:

```
ser
42
summarygrade:
high low NA's
24 17 1
summarystage:
early late NA's
 2 39 1
tumorstage:
 1 2 3 4 NA's
 1 1 29 10 1
substage:
  a b c NA's
  1 1 29 11
grade:
  1 2 3 NA's
  2 15 24 1
age_at_initial_pathologic_diagnosis:
  Min. 1st Qu. Median Mean 3rd Qu. Max. NA's
 33.00 55.00 62.00 61.46 70.00 81.00 1
recurrence_status:
norecurrence recurrence
       6
            36
days_to_death:
  Min. 1st Qu. Median Mean 3rd Qu. Max.
  30.0 367.5 825.0 1105.0 1050.0 3420.0
vital_status:
deceased living
   22 20
debulking:
  optimal suboptimal NA's 20 21 1
batch:
  Length Class Mode
     42 character character
uncurated_author_metadata:
  Length Class Mode
     42 character character
```

TCGA.mirna.8x15kv2_eset

Integrated genomic analyses of ovarian carcinoma.

Description

A catalogue of molecular aberrations that cause ovarian cancer is critical for developing and deploying therapies that will improve patients' lives. The Cancer Genome Atlas project has analysed messenger RNA expression, microRNA expression, promoter methylation and DNA copy number in 489 high-grade serous ovarian adenocarcinomas and the DNA sequences of exons from coding genes in 316 of these tumours. Here we report that high-grade serous ovarian cancer is characterized by TP53 mutations in almost all tumours (96%); low prevalence but statistically recurrent somatic mutations in nine further genes including NF1, BRCA1, BRCA2, RB1 and CDK12; 113 significant focal DNA copy number aberrations; and promoter methylation events involving 168 genes. Analyses delineated four ovarian cancer transcriptional subtypes, three microRNA subtypes, four promoter methylation subtypes and a transcriptional signature associated with survival duration, and shed new light on the impact that tumours with BRCA1/2 (BRCA1 or BRCA2) and CCNE1 aberrations have on survival. Pathway analyses suggested that homologous recombination is defective in about half of the tumours analysed, and that NOTCH and FOXM1 signalling are involved in serous ovarian cancer pathophysiology.

Usage

```
data( TCGA.mirna.8x15kv2_eset )
```

Format

```
experimentData(eset):
Experiment data
 Experimenter name: Integrated genomic analyses of ovarian carcinoma. Nature 2011, 474:609-615.
 Laboratory: Cancer Genome Atlas Research Network 2011
  Contact information:
  Title: Integrated genomic analyses of ovarian carcinoma.
  URL:
  PMIDs: 21720365
 Abstract: A 179 word abstract is available. Use 'abstract' method.
  Information is available on: preprocessing
  notes:
   platform_title:
      [miRNA-8x15k2] Agilent Human miRNA G4470B
   platform_shorttitle:
      Agilent miRNA-8x15k2 G4470B
   platform_summary:
      NA
   platform_manufacturer:
      Agilent
   platform_distribution:
      commercial
   platform_accession:
      NA
```

platform_technology:

summarystage:
early late NA's

```
in situ oligonucleotide
   Preprocessing: default
   featureData(eset):
   An object of class 'AnnotatedDataFrame'
     featureNames: ebv-miR-BART10 ebv-miR-BART10* ... kshv-miR-K12-9* (799
       total)
     varLabels: probeset gene
     varMetadata: labelDescription
Details
   assayData: 799 features, 554 samples
   Platform type: NA
   Overall survival time-to-event summary (in years):
   Call: survfit(formula = Surv(time, cens) ~ -1)
      10 observations deleted due to missingness
   records n.max n.start events median 0.95LCL 0.95UCL
    544.00 544.00 544.00 286.00 3.71 3.42 4.03
   _____
   Available sample meta-data:
   ______
   alt_sample_name:
      Length Class
                         Mode
        554 character character
   unique_patient_ID:
      Length
             Class
                          Mode
        554 character character
   sample_type:
   tumor
     554
   histological_type:
   ser
   554
   primarysite:
   other
          ٥v
          550
      4
   summarygrade:
   high low NA's
    474 68 12
```

```
39 511 4
tumorstage:
 1 2 3 4 NA's
 16 23 426 85 4
substage:
 b c NA's
 31 434 89
grade:
 1 2 3 4 NA's
  6 62 473 1 12
age_at_initial_pathologic_diagnosis:
  Min. 1st Qu. Median Mean 3rd Qu. Max.
 26.00 51.00 59.00 59.81 69.00 89.00
pltx:
  n y NA's
 19 478 57
tax:
 n y NA's
 43 454 57
neo:
  n NA's
497 57
days_to_tumor_recurrence:
  Min. 1st Qu. Median Mean 3rd Qu. Max. NA's 8.0 235.2 436.0 618.7 797.0 5480.0 44
recurrence_status:
norecurrence recurrence
        268
                286
days_to_death:
  Min. 1st Qu. Median Mean 3rd Qu. Max. NA's 8.0 346.0 867.5 997.7 1446.0 5480.0 10
vital_status:
deceased living NA's
    286
          261 7
site_of_tumor_first_recurrence:
              locoregional locoregional_plus_metastatic
                      145
```

metastasis 138 NA's

268

```
primary_therapy_outcome_success:
  completeresponse
                       partialresponse progressivedisease
                                                                 stabledisease
                308
                                     63
                                                                             30
              NA's
                112
debulking:
                             NA's
   optimal suboptimal
       359
                               58
percent_normal_cells:
   Min. 1st Qu. Median
                            Mean 3rd Qu.
                                             Max.
                                                      NA's
  0.000
          0.000
                   0.000
                                    0.000
                                           55.000
                           2.375
                                                        10
percent_stromal_cells:
                                                      NA's
   Min. 1st Qu. Median
                            Mean 3rd Qu.
                                             Max.
   0.00
           5.00
                  10.00
                                    19.00
                           12.78
                                            70.00
                                                        16
percent_tumor_cells:
   Min. 1st Qu.
                 Median
                            Mean 3rd Qu.
                                                      NA's
                                             Max.
   0.00
          75.00
                   85.00
                           80.72
                                    90.00
                                           100.00
                                                        13
uncurated_author_metadata:
   Length
              Class
      554 character character
```

TCGA.RNASeqV2_eset

Integrated genomic analyses of ovarian carcinoma.

Description

A catalogue of molecular aberrations that cause ovarian cancer is critical for developing and deploying therapies that will improve patients' lives. The Cancer Genome Atlas project has analysed messenger RNA expression, microRNA expression, promoter methylation and DNA copy number in 489 high-grade serous ovarian adenocarcinomas and the DNA sequences of exons from coding genes in 316 of these tumours. Here we report that high-grade serous ovarian cancer is characterized by TP53 mutations in almost all tumours (96%); low prevalence but statistically recurrent somatic mutations in nine further genes including NF1, BRCA1, BRCA2, RB1 and CDK12; 113 significant focal DNA copy number aberrations; and promoter methylation events involving 168 genes. Analyses delineated four ovarian cancer transcriptional subtypes, three microRNA subtypes, four promoter methylation subtypes and a transcriptional signature associated with survival duration, and shed new light on the impact that tumours with BRCA1/2 (BRCA1 or BRCA2) and CCNE1 aberrations have on survival. Pathway analyses suggested that homologous recombination is defective in about half of the tumours analysed, and that NOTCH and FOXM1 signalling are involved in serous ovarian cancer pathophysiology.

Usage

```
data( TCGA.RNASeqV2_eset )
```

Format

```
experimentData(eset):
Experiment data
 Experimenter name: Integrated genomic analyses of ovarian carcinoma. Nature 2011, 474:609-615.
  Laboratory: Cancer Genome Atlas Research Network 2011
  Contact information:
  Title: Integrated genomic analyses of ovarian carcinoma.
  URL:
  PMIDs: 21720365
  Abstract: A 179 word abstract is available. Use 'abstract' method.
  Information is available on: preprocessing
  notes:
   platform_title:
      [RNASeqV2] Illumina HiSeq RNA sequencing
   platform_shorttitle:
      Illumina HiSeq RNA sequencing
   platform_summary:
   platform_manufacturer:
      Illumina
   platform_distribution:
      sequencing
   platform_accession:
   platform_technology:
      RNA sequencing
Preprocessing: default
featureData(eset):
An object of class 'AnnotatedDataFrame'
  featureNames: ? A1BG ... ZZZ3 (20502 total)
  varLabels: probeset gene
  varMetadata: labelDescription
```

Details

```
Length Class Mode
     261 character character
unique_patient_ID:
  Length Class
     261 character character
sample_type:
tumor
 261
histological_type:
261
primarysite:
other ov
1 260
summarygrade:
high low NA's
226 29 6
summarystage:
early late NA's
  18 242 1
tumorstage:
  2 3 4 NA's
 18 209 33 1
substage:
 b c NA's
16 211 34
grade:
  1 2 3 4 NA's
  1 28 225 1 6
age_at_initial_pathologic_diagnosis:
 Min. 1st Qu. Median Mean 3rd Qu. Max. 34.00 51.00 58.00 58.84 66.00 87.00
pltx:
  n y NA's
 17 215 29
tax:
 n y NA's
 17 215 29
neo:
```

n NA's 232 29

days_to_tumor_recurrence:

Min. 1st Qu. Median Mean 3rd Qu. Max. NA's 9.0 225.0 426.5 585.3 755.0 5480.0 19

recurrence_status:

norecurrence recurrence 123 138

days_to_death:

Min. 1st Qu. Median Mean 3rd Qu. Max. NA's 9.0 341.8 878.0 1018.0 1446.0 5480.0 5

vital_status:

deceased living NA's 143 114 4

site_of_tumor_first_recurrence:

locoregional metastasis NA's 82 56 123

primary_therapy_outcome_success:

completeresponse partialresponse progressivedisease stabledisease
147 30 15 15
NA's
54

debulking:

optimal suboptimal NA's 171 60 30

percent_normal_cells:

Min. 1st Qu. Median Mean 3rd Qu. Max. NA's 0.000 0.000 0.000 2.066 0.000 55.000 5

percent_stromal_cells:

Min. 1st Qu. Median Mean 3rd Qu. Max. NA's 0.00 5.00 10.00 11.43 15.00 70.00 4

percent_tumor_cells:

Min. 1st Qu. Median Mean 3rd Qu. Max. NA's 0.00 77.00 85.00 82.07 90.00 100.00 4

 $uncurated_author_metadata:$

Length Class Mode 261 character character

Description

A catalogue of molecular aberrations that cause ovarian cancer is critical for developing and deploying therapies that will improve patients' lives. The Cancer Genome Atlas project has analysed messenger RNA expression, microRNA expression, promoter methylation and DNA copy number in 489 high-grade serous ovarian adenocarcinomas and the DNA sequences of exons from coding genes in 316 of these tumours. Here we report that high-grade serous ovarian cancer is characterized by TP53 mutations in almost all tumours (96%); low prevalence but statistically recurrent somatic mutations in nine further genes including NF1, BRCA1, BRCA2, RB1 and CDK12; 113 significant focal DNA copy number aberrations; and promoter methylation events involving 168 genes. Analyses delineated four ovarian cancer transcriptional subtypes, three microRNA subtypes, four promoter methylation subtypes and a transcriptional signature associated with survival duration, and shed new light on the impact that tumours with BRCA1/2 (BRCA1 or BRCA2) and CCNE1 aberrations have on survival. Pathway analyses suggested that homologous recombination is defective in about half of the tumours analysed, and that NOTCH and FOXM1 signalling are involved in serous ovarian cancer pathophysiology.

Usage

```
data( TCGA_eset )
```

Format

```
experimentData(eset):
Experiment data
 Experimenter name: Integrated genomic analyses of ovarian carcinoma. Nature 2011, 474:609-615.
  Laboratory: Cancer Genome Atlas Research Network 2011
  Contact information:
  Title: Integrated genomic analyses of ovarian carcinoma.
  URL:
  PMIDs: 21720365
  Abstract: A 179 word abstract is available. Use 'abstract' method.
  Information is available on: preprocessing
  notes:
   platform_title:
      [HT_HG-U133A] Affymetrix HT Human Genome U133A Array
   platform_shorttitle:
      Affymetrix HT_HG-U133A
   platform_summary:
      hthgu133a
   platform_manufacturer:
      Affymetrix
   platform_distribution:
      commercial
   platform_accession:
      GPL3921
   platform_technology:
      in situ oligonucleotide
   warnings:
      The following samples are likely from specimens also used in GSE26712: TCG
A.13.0725, TCGA.13.0885, TCGA.13.0887, TCGA.13.0890, TCGA.13.0886, TCGA.13
.0714, TCGA.13.0727, TCGA.13.1817, TCGA.13.1499, TCGA.13.0883
```

Preprocessing: rma

```
featureData(eset):
   An object of class 'AnnotatedDataFrame'
     featureNames: A1CF A2M ... ZZZ3 (13104 total)
     varLabels: probeset gene
     varMetadata: labelDescription
Details
   assayData: 13104 features, 578 samples
   Platform type: hthgu133a
   Overall survival time-to-event summary (in years):
   Call: survfit(formula = Surv(time, cens) ~ -1)
      21 observations deleted due to missingness
   records n.max n.start events median 0.95LCL 0.95UCL
    557.00 557.00 557.00 290.00
                                   3.73
                                           3.45
   Available sample meta-data:
   -----
   alt_sample_name:
      Length Class
                         Mode
         578 character character
   unique_patient_ID:
      Length
             Class
                          Mode
         578 character character
   sample_type:
   healthy tumor
              570
   histological_type:
    ser NA's
    568
        10
   primarysite:
   other ov NA's
          564 10
   summarygrade:
   high low NA's
    480
        75 23
   summarystage:
   early late NA's
         520
               15
   tumorstage:
```

```
1 2 3 4 NA's
 16 27 436
             84 15
substage:
  b c NA's
 31 448 99
grade:
         3
      2
  1
               4 NA's
  6 69 479
               1 23
age_at_initial_pathologic_diagnosis:
  Min. 1st Qu. Median Mean 3rd Qu.
                                    Max.
                                           NA's
 26.00 51.00 59.00 59.70 68.25 89.00
                                            10
pltx:
  n y NA's
 19 492 67
tax:
  n y NA's
 43 468 67
neo:
  n NA's
511 67
days_to_tumor_recurrence:
                     Mean 3rd Qu. Max.
  Min. 1st Qu. Median
                                           NA's
   8.0 238.2 443.5 623.7 812.0 5480.0
                                            56
recurrence_status:
norecurrence recurrence
             299
       279
days_to_death:
  Min. 1st Qu. Median Mean 3rd Qu.
                                           NA's
                                     Max.
    8 349 881 1010 1446
                                     5480
                                            21
vital_status:
deceased living NA's
    290
          270
site_of_tumor_first_recurrence:
             locoregional locoregional_plus_metastatic
                     153
                                             NA's
               metastasis
                                              279
primary_therapy_outcome_success:
 completeresponse partialresponse progressivedisease
                                                     stabledisease
             318
                              65
```

NA's 124

debulking:

optimal suboptimal NA's 367 140 71

percent_normal_cells:

Min. 1st Qu. Median Mean 3rd Qu. Max. NA's 0.000 0.000 0.000 2.385 0.000 55.000 19

percent_stromal_cells:

Min. 1st Qu. Median Mean 3rd Qu. Max. NA's 0.00 5.00 10.00 12.85 20.00 70.00 25

percent_tumor_cells:

Min. 1st Qu. Median Mean 3rd Qu. Max. NA's 0.00 75.00 85.00 80.64 90.00 100.00 22

batch:

Min. 1st Qu. Median Mean 3rd Qu. Max. NA's 9.00 13.00 17.00 18.55 22.00 40.00 1

uncurated_author_metadata:

Length Class Mode 578 character character

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