

Package ‘ALDEx2’

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Type Package

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Description A differential abundance analysis for the comparison of two or more conditions. For example, single-organism and meta-RNA-seq high-throughput sequencing assays, or of selected and unselected values from in-vitro sequence selections. Uses a Dirichlet-multinomial model to infer abundance from counts, that has been optimized for three or more experimental replicates. Infers sampling variation and calculates the expected false discovery rate given the biological and sampling variation using the Wilcox rank test or Welches t-test (`aldex.ttest`) or the glm and Kruskal Wallis tests (`aldex.glm`). Reports both P and fdr values calculated by the Benjamini Hochberg correction.

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ALDEx2m-package	<i>Analysis of differential abundance taking sample variation into account</i>
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Description

A differential abundance analysis for the comparison of two or more conditions. For example, single-organism and meta-RNA-seq high-throughput sequencing assays, or of selected and unselected values from in-vitro sequence selections. Uses a Dirichlet-multinomial model to infer abundance from counts, that has been optimized for three or more experimental replicates. Infers sampling variation and calculates the expected false discovery rate given the biological and sampling variation using the Wilcox rank test or Welches t-test (`aldex.ttest`) or the glm and Kruskal Wallis tests (`aldex.glm`). Reports both P and fdr values calculated by the Benjamini Hochberg correction.

References

Please use the citation given by `citation(package="ALDEx")`.

See Also

[aldex.clr](#), [aldex.ttest](#), [aldex.glm](#), [aldex.effect](#), [selex](#)

Examples

```
# see examples for the aldex.clr, aldex.ttest, aldex.effect, aldex.glm functions
```

aldex	<i>Compute an aldex Object</i>
-------	--------------------------------

Description

Generate Monte Carlo samples of the Dirichlet distribution for each sample. Convert each instance using the centred log-ratio transform. Return two sample test values (Welch's t, Wilcoxon) or multi-sample test values (glm or Kruskal Wallace). Returns effect size values by default.

Usage

```
aldex(reads, conditions, mc.samples=128, test="t", effect=TRUE, include.sample.summary=FALSE, verbose)
```

Arguments

reads	a non-negative, integer-only containing data.frame that has unique names for all rows and columns, where each row is a different gene and each column represents a sequencing read-count. Rows with 0 reads in each sample are deleted prior to analysis
mc.samples	the number of Monte Carlo samples to use to estimate the underlying distributions; since we are estimating central tendencies, 128 is usually sufficient
conditions	a description of the data structure to be used for testing
test	which tests to perform: t = Welch's t and Wilcoxon, glm = Kruskal Wallace and glm
effect	calculate abundances and effect sizes
include.sample.summary	include median clr values for each sample, defaults to FALSE
verbose	Print diagnostic information while running. Useful only for debugging if fails on large datasets

Details

An explicit description of the input format for the reads object is shown under 'Examples', below. This is not intended to be the generic function. The system is intended to be used for demonstration or instructional purposes.

Value

returns a number of values that depends on the set of options. See the return values of `aldex.ttest`, `aldex.glm`, and `aldex.effect` for explanations and example

Author(s)

Greg Gloor, Andrew Fernandes and Matt Links contributed to this code

References

Please use the citation given by `citation(package="ALDEx")`.

See Also

[aldex.ttest](#), [aldex.glm](#), [aldex.effect](#), [aldex.corr](#), [selex](#)

Examples

```
# The reads data.frame should have row
# and column names that are unique, and
# looks like the following:
#
#           T1a T1b T2 T3 N1 N2 Nx
# Gene_00001  0  0  2  0  0  1  0
# Gene_00002 20  8 12  5 19 26 14
# Gene_00003  3  0  2  0  0  0  1
# Gene_00004 75 84 241 149 271 257 188
# Gene_00005 10 16  4  0  4  10 10
# Gene_00006 129 126 451 223 243 149 209
#           ... many more rows ...

data(selex)
conds <- c(rep("N", 7), rep("S",7))
x <- aldex(selex, conds, mc.samples = 2, test="t", effect=FALSE, verbose = FALSE)
```

aldex.clr

Compute an aldex.clr Object

Description

Generate Monte Carlo samples of the Dirichlet distribution for each sample. Convert each instance using the centred log-ratio transform This is the input for all further analyses.

Usage

```
aldex.clr(reads, mc.samples = 128, verbose = FALSE, useMC=FALSE)
```

Arguments

<code>reads</code>	a non-negative, integer-only containing <code>data.frame</code> or <code>SummarizedExperiment</code> that has unique names for all rows and columns, where each row is a different gene and each column represents a sequencing read-count. Rows with 0 reads in each sample are deleted prior to analysis
<code>mc.samples</code>	the number of Monte Carlo samples to use to estimate the underlying distributions; since we are estimating central tendencies, 128 is usually sufficient

verbose	Print diagnostic information while running. Useful only for debugging if fails on large datasets
useMC	use multicore by default (FALSE). Multi core processing will be attempted with the BiocParallel package, then the parallel package. If neither are installed, serial processing will be used.

Details

An explicit description of the input format for the reads object is shown under ‘Examples’, below.

Value

The object produced by the clr function contains the clr transformed values for each Monte-Carlo Dirichlet instance, which can be accessed through getMonteCarloInstances(x), where x is the clr function output. Each list element is named by the sample ID. getFeatures(x) returns the features, getSampleIDs(x) returns sample IDs, and getFeatureNames(x) returns the feature names.

Author(s)

Greg Gloor, Ruth Grace Wond, Andrew Fernandes and Matt Links contributed to this code

References

Please use the citation given by citation(package="ALDEx").

See Also

[aldex.ttest](#), [aldex.glm](#), [aldex.effect](#), [selex](#)

Examples

```
# The reads data.frame or
# SummarizedExperiment object should have
# row and column names that are unique,
# and looks like the following:
#
#           T1a T1b T2 T3 N1 N2 Nx
# Gene_00001  0  0  2  0  0  1  0
# Gene_00002 20  8 12  5 19 26 14
# Gene_00003  3  0  2  0  0  0  1
# Gene_00004 75 84 241 149 271 257 188
# Gene_00005 10 16  4  0  4 10 10
# Gene_00006 129 126 451 223 243 149 209
# ... many more rows ...

data(selex)
x <- aldex.clr(selex, mc.samples = 2, verbose = FALSE)
```

aldex.clr-class *The aldex.clr class*

Description

The aldex.clr S4 class is a class which stores the data generated by the aldex.clr method.

Details

An aldex.clr object contains the Monte Carlo Dirichlet instances derived from estimating the technical variance of the raw read count data. It is created by the aldex.clr function, which is invoked by the aldex.clr method. It consists of four attributes: the sample names, the feature names, the conditions vector (assigns each sample to a condition), and the Monte Carlo Dirichlet instances themselves. These can be accessed, along with information about the length of some attributes. A single Monte Carlo instance can also be retrieved.

Value

The aldex.clr object contains the clr transformed values for each Monte-Carlo Dirichlet instance, which can be accessed through getMonteCarloInstances(x), where x is the clr function output. Each list element is named by the sample ID. getFeatures(x) returns the features, getSampleIDs(x) returns sample IDs, and getFeatureNames(x) returns the feature names.

Methods

In the code below, x is an aldex.clr object, and i is a numeric whole number.

getMonteCarloInstances(x): Returns x's Monte Carlo Dirichlet instances.

getSampleIDs(x): Returns the names of the samples. These can be used to access the original reads, as in reads[sampleID] (if the reads are a data frame).

getFeatures(x): Returns the names of the features as a vector.

numFeatures(x): Returns the number of features associated with the data.

numMCInstances(x): Returns the names of the keys that can be used to subset the data rows. The keys values are the rsid's.

getFeatureNames(x): Returns the names of the keys that can be used to subset the data rows. The keys values are the rsid's.

getReads(x): Returns the names of the keys that can be used to subset the data rows. The keys values are the rsid's.

numConditions(x): Returns the names of the keys that can be used to subset the data rows. The keys values are the rsid's.

getMonteCarloReplicate(x, i): Returns the names of the keys that can be used to subset the data rows. The keys values are the rsid's.

Author(s)

Greg Gloor, Ruth Grace Wong, Andrew Fernandes and Matt Links contributed to this code

References

Please use the citation given by `citation(package="ALDEx")`.

See Also

[aldex.clr.function](#)

Examples

```
# The reads data.frame or
# SummarizedExperiment object should have
# row and column names that are unique,
# and looks like the following:
#
#           T1a T1b T2 T3 N1 N2 Nx
# Gene_00001  0  0  2  0  0  1  0
# Gene_00002 20  8 12  5 19 26 14
# Gene_00003  3  0  2  0  0  0  1
# Gene_00004 75 84 241 149 271 257 188
# Gene_00005 10 16  4  0  4 10 10
# Gene_00006 129 126 451 223 243 149 209
#           ... many more rows ...

data(selex)

# x is an object of type aldex.clr
x <- aldex.clr(selex, mc.samples = 2, verbose = FALSE)

# get all of the Monte Carlo Dirichlet instances
monteCarloInstances <- getMonteCarloInstances(x)

# get sample names
sampleIDs <- getSampleIDs(x)

# get features
features <- getFeatures(x)

# get number of features
numFeatures <- numFeatures(x)

# get number of Monte Carlo Dirichlet instances
numInstances <- numMCInstances(x)

# get names of features
featureNames <- getFeatureNames(x)

# get number of conditions
conditions <- numConditions(x)

# get number of conditions
reads <- getReads(x)
```

```
# retrieve the first Monte Carlo Dirichlet instance.
monteCarloInstance <- getMonteCarloReplicate(x,1)
```

aldex.corr	<i>calculate Pearson's Product moment and Spearman's rank correlations</i>
------------	--

Description

calculates expected values of Pearson's Product moment and Spearman's rank correlations on the data returned by `clr_function.r`

Usage

```
aldex.corr(clr, covar)
```

Arguments

<code>clr</code>	<code>clr</code> is the data output of the <code>aldex.clr</code> function
<code>covar</code>	a per-sample continuous variable to be correlated with the <code>clr</code> values

Details

An explicit example for two conditions is shown in the 'Examples' below.

Value

Outputs a dataframe with the following information:

<code>pearson.ecor</code>	a vector containing the expected Pearson's Product moment value for each feature
<code>pearson.ep</code>	a vector containing the expected P value of the Pearson Product moment value for each feature
<code>pearson.eBH</code>	a vector containing the expected Benjamini-Hochberg corrected P value of the Pearson Product moment value for each feature
<code>spearman.erho</code>	a vector containing the expected Spearman's rank correlation value for each feature
<code>spearman.ep</code>	a vector containing the expected P value of Spearman's rank correlation value for each feature
<code>spearman.eBH</code>	a vector containing the expected Benjamini-Hochberg corrected P value of Spearman's rank correlation value for each feature

Author(s)

Arianne Albert

References

Please use the citation given by `citation(package="ALDEx")`.

See Also

[aldex.clr](#), [aldex.glm](#), [aldex.effect](#), [selex](#)

Examples

```
# x is the output of the \code{x <- aldex.clr(data, mc.samples)} function
# conditions is a description of the data
# aldex.ttest(clr, covar)
```

<code>aldex.effect</code>	<i>calculate effect sizes and differences between conditions</i>
---------------------------	--

Description

determines the median clr abundance of the feature in all samples and in groups determines the median difference between the two groups determines the median variation within each two group determines the effect size, which is the median of the ratio of the between group difference and the larger of the variance within groups

Usage

```
aldex.effect(clr, conditions, verbose = TRUE, include.sample.summary = FALSE, useMC=FALSE)
```

Arguments

<code>clr</code>	<code>clr</code> is the data output of <code>aldex.clr</code>
<code>conditions</code>	a description of the data structure to be used for testing
<code>verbose</code>	Print diagnostic information while running. Useful only for debugging if fails on large datasets
<code>include.sample.summary</code>	include median clr values for each sample, defaults to FALSE
<code>useMC</code>	use multicore by default (FALSE)

Details

An explicit example for two conditions is shown in the ‘Examples’ below.

Value

returns a dataframe with the following information:

rab.all	a vector containing the median clr value for each feature
rab.win.conditionA	a vector containing the median clr value for each feature in condition A
rab.win.conditionB	a vector containing the median clr value for each feature in condition B
diff.btw	a vector containing the per-feature median difference between condition A and B
diff.btw	a vector containing the per-feature maximum median difference between Dirichlet instances within conditions
effect	a vector containing the per-feature effect size
overlap	a vector containing the per-feature proportion of effect size that is 0 or less

Author(s)

Greg Gloor, Andrew Fernandes, Matt Links

References

Please use the citation given by `citation(package="ALDEx")`.

See Also

[aldex.clr](#), [aldex.ttest](#), [aldex.glm](#), [selex](#)

Examples

```
# x is the output of the \code{x <- clr(data, mc.samples)} function
# conditions is a description of the data
# for the selex dataset, conditions <- c(rep("N", 7), rep("S", 7))
data(selex)
x <- aldex.clr(selex, mc.samples=2)
conditions <- c(rep("N", 7), rep("S", 7))
effect.test <- aldex.effect(x, conditions)
```

aldex.glm

calculate glm and Kruskal Wallis test statistics

Description

calculates expected values of the glm and Kruskal Wallis functions on the data returned by `clr_function.r`

Usage

```
aldex.glm(clr, conditions, useMC=FALSE)
```

Arguments

clr	clr is the data output of <code>aldex.clr</code>
conditions	a description of the data structure to be used for testing
useMC	use multicore by default (FALSE)

Details

An explicit example for two conditions is shown in the ‘Examples’ below.

Value

Outputs a dataframe with the following information:

kw.ep	a vector containing the expected P value of the Kruskal Wallis test for each feature
kw.eBH	a vector containing the expected value of the Benjamini Hochberg corrected P value for each feature
glm.ep	a vector containing the expected P value of the glm test for each feature
glm.eBH	a vector containing the expected value of the Benjamini Hochberg corrected P value for each feature

Author(s)

Arianne Albert

References

Please use the citation given by `citation(package="ALDEx")`.

See Also

[aldex.clr](#), [aldex.ttest](#), [aldex.effect](#), [selex](#)

Examples

```
# x is the output of the x <- aldex.clr(data, mc.samples) function
# conditions is a description of the data
# for the selex dataset, conditions <- c(rep("N", 7), rep("S", 7))
data(selex)
x <- aldex.clr(selex, mc.samples=1)
conditions <- c(rep("N", 7), rep("S", 7))
glm.test <- aldex.glm(x, conditions)
```

aldex.plot

*Plot an aldex Object***Description**

Create 'MW'- or 'MA'-type plots from the given aldex object.

Usage

```
## S3 method for class plot
aldex( x, ..., type=c("MW","MA"),
       xlab=NULL, ylab=NULL, xlim=NULL, ylim=NULL,
       all.col=rgb(0,0,0,0.2), all.pch=19, all.cex=0.4,
       called.col=red, called.pch=20, called.cex=0.6,
       thres.line.col=darkgrey, thres.lwd=1.5,
       test=welch, cutoff=0.1, rare.col=black, rare=0,
       rare.pch=20, rare.cex=0.2 )
```

Arguments

x	an object of class aldex produced by the aldex function
...	optional, unused arguments included for compatibility with the S3 method signature
type	which type of plot is to be produced. MA is a Bland-Altman style plot; MW is a difference between to a variance within plot as described in the paper
test	the method of calculating significance, one of: welch = welch's t test; wilcox = wilcox rank test; glm = glm; kruskal = Kruskal-Wallis test
cutoff	the Benjamini-Hochberg fdr cutoff, default 0.1
xlab	the x-label for the plot, as per the parent plot function
ylab	the y-label for the plot, as per the parent plot function
xlim	the x-limits for the plot, as per the parent plot function
ylim	the y-limits for the plot, as per the parent plot function
all.col	the default colour of the plotted points
all.pch	the default plotting symbol
all.cex	the default symbol size
called.col	the colour of points with false discovery rate, $q \leq 0.1$
called.pch	the symbol of points with false discovery rate, $q \leq 0.1$
called.cex	the character expansion of points with false discovery rate, $q \leq 0.1$
thres.line.col	the colour of the threshold line where within and between group variation is equivalent
thres.lwd	the width of the threshold line where within and between group variation is equivalent

rare	relative abundance cutoff for rare features, default 0 or the mean abundance
rare.col	color for rare features, default black
rare.pch	the default symbol of rare features
rare.cex	the default symbol size of rare points

Details

This particular specialization of the `plot` function is relatively simple and provided for convenience. For more advanced control of the plot is is best to use the values returned by `summary(x)`.

Value

None.

References

Please use the citation given by `citation(package="ALDEx")`.

See Also

[aldex](#), [aldex.effect](#), [aldex.ttest](#), [aldex.glm](#)

Examples

```
# See the examples for aldex.
```

aldex.ttest	<i>calculate Welch's t-test and Wilcoxon test statistics</i>
-------------	--

Description

calculates expected values of the Welch's t-test and Wilcoxon rank test on the data returned by `clr_function.r`

Usage

```
aldex.ttest(clr, conditions, paired.test = FALSE, hist.plot=FALSE)
```

Arguments

clr	clr is the data output of the <code>aldex.clr</code> function
conditions	a description of the data structure to be used for testing
paired.test	whether the Welch's test should be paired or not
hist.plot	whether to plot a histogram of P values for an individual Dirichlet Monte-Carlo instance. Plot is output to the standard R plotting device.

Details

An explicit example for two conditions is shown in the ‘Examples’ below.

Value

Outputs a dataframe with the following information:

<code>we.ep</code>	a vector containing the expected P value of the Welch’s t-test for each feature
<code>we.eBH</code>	a vector containing the expected value of the Benjamini Hochberg corrected P value for each feature
<code>wi.ep</code>	a vector containing the expected P value of the Wilcoxon test for each feature
<code>wi.eBH</code>	a vector containing the expected value of the Benjamini Hochberg corrected P value for each feature

Author(s)

Greg Gloor

References

Please use the citation given by `citation(package="ALDEx")`.

See Also

[aldex.clr](#), [aldex.glm](#), [aldex.effect](#), [selex](#)

Examples

```
# x is the output of the \code{x <- aldex.clr(data, mc.samples)} function
# conditions is a description of the data
# for the selex dataset, conditions <- c(rep("N", 7), rep("S", 7))
data(selex)
x <- aldex.clr(selex, mc.samples=2)
conditions <- c(rep("N", 7), rep("S", 7))
ttest.test <- aldex.ttest(x, conditions)
```

getFeatureNames

getFeatureNames

Description

Returns the names of the features as a vector, for an `aldex.clr` object.

Usage

```
getFeatureNames(.object)
```

Arguments

`.object` A `aldex.clr` object containing the Monte Carlo Dirichlet instances derived from estimating the technical variance of the raw read count data, along with sample and feature information.

Details

Returns the names of the keys that can be used to subset the data rows. The keys values are the `rsid`'s.

Value

A vector of feature names.

See Also

`aldex.clr`

Examples

```
data(selex)
x <- aldex.clr(selex, mc.samples = 2, verbose = FALSE)
featureNames <- getFeatureNames(x)
```

`getFeatures`

getFeatures

Description

Returns the features as a vector, for an `aldex.clr` object.

Usage

```
getFeatures(.object)
```

Arguments

`.object` A `aldex.clr` object containing the Monte Carlo Dirichlet instances derived from estimating the technical variance of the raw read count data, along with sample and feature information.

Details

Returns the features as a vector, for an `aldex.clr` object.

Value

A vector of features.

See Also`aldex.clr`**Examples**

```
data(selex)
x <- aldex.clr(selex, mc.samples = 2, verbose = FALSE)
features <- getFeatures(x)
```

`getMonteCarloInstances`*getMonteCarloInstances*

Description

Returns the Monte Carlo Dirichlet instances used to create an `aldex.clr` object.

Usage

```
getMonteCarloInstances(.object)
```

Arguments

<code>.object</code>	A <code>aldex.clr</code> object containing the Monte Carlo Dirichlet instances derived from estimating the technical variance of the raw read count data, along with sample and feature information.
----------------------	--

Details

Returns the Monte Carlo Dirichlet instances used to create an `aldex.clr` object.

Value

A list of data frames of Monte Carlo Dirichlet instances derived from estimating the technical variance of the raw read count data.

See Also`aldex.clr`**Examples**

```
data(selex)
x <- aldex.clr(selex, mc.samples = 2, verbose = FALSE)
monteCarloInstances <- getMonteCarloInstances(x)
```

getMonteCarloReplicate
getMonteCarloReplicate

Description

Returns the designated Monte Carlo Dirichlet replicate generated from analysis, for an `aldex.clr` object.

Usage

```
getMonteCarloReplicate(.object, i)
```

Arguments

<code>.object</code>	A <code>aldex.clr</code> object containing the Monte Carlo Dirichlet instances derived from estimating the technical variance of the raw read count data, along with sample and feature information.
<code>i</code>	The numeric index of the desired replicate.

Details

Returns the designated Monte Carlo Dirichlet replicate generated from analysis.

Value

A data frame representing the designated Monte Carlo Dirichlet replicate generated from analysis.

See Also

`aldex.clr`

Examples

```
data(selex)
x <- aldex.clr(selex, mc.samples = 2, verbose = FALSE)
monteCarloInstance <- getMonteCarloReplicate(x,1)
```

<code>getReads</code>	<i>getReads</i>
-----------------------	-----------------

Description

Returns the count table used as input for analysis, for an `aldex.clr` object.

Usage

```
getReads(.object)
```

Arguments

<code>.object</code>	A <code>aldex.clr</code> object containing the Monte Carlo Dirichlet instances derived from estimating the technical variance of the raw read count data, along with sample and feature information.
----------------------	--

Details

Returns the count table.

Value

A data frame representing the count table used as input for analysis.

See Also

`aldex.clr`

Examples

```
data(selex)
x <- aldex.clr(selex, mc.samples = 2, verbose = FALSE)
reads <- getReads(x)
```

<code>getSampleIDs</code>	<i>getSampleIDs</i>
---------------------------	---------------------

Description

Returns the names of the samples for an `aldex.clr` object. These can be used to access the original reads, as in `reads$sampleID` (if the reads are a data frame).

Usage

```
getSampleIDs(.object)
```

Arguments

`.object` A `aldex.clr` object containing the Monte Carlo Dirichlet instances derived from estimating the technical variance of the raw read count data, along with sample and feature information.

Details

Returns the names of the samples. These can be used to access the original reads, as in `reads$sampleID` (if the reads are a data frame).

Value

A vector of sample names.

See Also

`aldex.clr`

Examples

```
data(selex)
x <- aldex.clr(selex, mc.samples = 2, verbose = FALSE)
sampleIDs <- getSampleIDs(x)
```

`numConditions`

numConditions

Description

Returns the number of conditions compared for analysis, for an `aldex.clr` object.

Usage

```
numConditions(.object)
```

Arguments

`.object` A `aldex.clr` object containing the Monte Carlo Dirichlet instances derived from estimating the technical variance of the raw read count data, along with sample and feature information.

Details

Returns the number of conditions compared.

Value

A numeric representing the number of conditions compared.

See Also

aldex.clr

Examples

```
data(selex)
x <- aldex.clr(selex, mc.samples = 2, verbose = FALSE)
conditions <- numConditions(x)
```

numFeatures

numFeatures

Description

Returns the number of features associated with the data, for an `aldex.clr` object.

Usage

```
numFeatures(.object)
```

Arguments

`.object` A `aldex.clr` object containing the Monte Carlo Dirichlet instances derived from estimating the technical variance of the raw read count data, along with sample and feature information.

Details

Returns the number of features associated with the data.

Value

A numeric representing the number of features associated with the data.

See Also

aldex.clr

Examples

```
data(selex)
x <- aldex.clr(selex, mc.samples = 2, verbose = FALSE)
numFeatures <- numFeatures(x)
```

numMCInstances	<i>numMCInstances</i>
----------------	-----------------------

Description

Returns the number of Monte Carlo Dirichlet instances generated for analysis, for an `aldex.clr` object.

Usage

```
numMCInstances(.object)
```

Arguments

`.object` A `aldex.clr` object containing the Monte Carlo Dirichlet instances derived from estimating the technical variance of the raw read count data, along with sample and feature information.

Details

Returns the number of Monte Carlo Dirichlet instances generated for analysis.

Value

A numeric representing the number of Monte Carlo Dirichlet instances generated for analysis.

See Also

`aldex.clr`

Examples

```
data(selex)
x <- aldex.clr(selex, mc.samples = 2, verbose = FALSE)
numInstances <- numMCInstances(x)
```

selex	<i>Selection-based differential sequence variant abundance dataset</i>
-------	--

Description

This data set gives the differential abundance of 1600 enzyme variants grown under selective (NS) and selective (S) conditions

Usage

```
selex
```

Format

A dataframe of 1600 features and 14 samples. The first 7 samples are non-selected, the last 7 are selected.

Source

McMurrough et al (2014) PNAS doi:10.1073/pnas.1322352111

References

McMurrough et al, submitted

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