# Package 'miRNAtap'

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**Type** Package

**Title** miRNAtap: microRNA Targets - Aggregated Predictions

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**Description** The package facilitates implementation of workflows requiring miRNA predictions, it allows to integrate ranked miRNA target predictions from multiple sources available online and aggregate them with various methods which improves quality of predictions above any of the single sources. Currently predictions are available for Homo sapiens, Mus musculus and Rattus norvegicus (the last one through homology translation).

**License** GPL-2

**Depends** R (>= 3.3.0), AnnotationDbi

**Imports** DBI, RSQLite, stringr, sqldf, plyr, methods

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`aggregateRanks` *Aggreagate ranks from multiple sources with various methods*

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## Description

This function performs aggregation phase of target prediction for `getPredictedTargets`. Consensus ranking is derived from multiple individual rankings. Available methods include minimum, maximum and geometric mean with further tuning parameters which promote true positives at the top of the final ranking

## Usage

```
aggregateRanks(ranks, n_valid_srcs, min_src, method = "geom",
  promote = TRUE)
```

## Arguments

| | |
|---|---|
| `ranks` | `data.frame` with ordered scores |
| `n_valid_srcs` | number of valid sources in the dataset |
| `min_src` | minimum acceptable number fo sources |
| `method` | `'min'`,`'max'`, or `'geom'`, default `'geom'` |
| `promote` | add weights to improve accuracy of the method, default `TRUE` |

## Value

`data.frame` object with ranks per source and aggregate ranks

## Author(s)

Maciej Pajak <m.pajak@sms.ed.ac.uk>

## Examples

```
data = data.frame(GeneID=c("15364", "56520", "57781", "58180", "18035"),
                  source1scores=c(0.9,0.5,0.3,NA,NA),
                  source2scores=c(0.7,NA,0.8,0.6,0.5),
                  source3scores=c(0.5,NA,0.3,0.1,0.2))
data #dataframe with scores
aggregateRanks(data, n_valid_srcs=3, min_src=2, method='geom')
#note how gene 56520 is eliminated as it appeared in fewer than 2 sources
```

getPredictedTargets *Get aggregated ordered list of predicted targets for miRNA*

## Description

This method performs aggregation of target lists from multiple sources. Aggregated list is more accurate than any list from a single source. Multiple aggregation methods are available.Direct target data from five sources for Human and Mouse is supplied through `miRNAtap.db` package, for Rat targets are derived through homology translations whenever direct ones are not available.

## Usage

```
getPredictedTargets(mirna, sources = c("pictar", "diana",
"targetscan", "miranda","mirdb"), species = "mmu", min_src = 2,
method = "geom", promote = TRUE, synonyms = TRUE, both_strands = FALSE, ...)
```

## Arguments

| | |
|---|---|
| `mirna` | miRNA in a standard format |
| `sources` | a list of sources to use for aggregation, default is all five sources, i.e. `c('pictar','diana','targets` |
| `species` | species in a standard three-letter acronym, `'mmu'` and `'hsa'` available as direct targets, `'rno'` as homology translations, default `'mmu'` |
| `min_src` | minimum number of sources required for a target to be considered, default 2 |
| `method` | method of aggregation - choose from `'min'`, `'max'`, and `'geom'`; `'min'` is a minimum of ranks, `'max'` is a maximum of ranks, and default `'geom'` is based on geometric mean of the ranks which proves to be the most accurate method. |
| `promote` | add weights to improve accuracy of the method, default TRUE |
| `synonyms` | when searching for -3p miRNA automatically also searches for miRNA with the same name but ending with * (some databases list -3p miRNA this way) and other way around, similarly for -5p miRNA, default TRUE |
| `both_strands` | overrides `synonyms` and searches for targets of both -5p and -3p strands together |
| `...` | any optional arguments |

## Details

Tuning `min_src` parameter is an easy way of prioritising precision at the top of the list (high values) or total recall (low values). For the five default input sources, recommended values are 2, 3, or 4.

## Value

`data.frame` object where row names are entrez IDs of target genes, ranks from individual sources and aggregated rank are shown in columns. If no targets are found in any of the sources `NULL` and a warning are returned.

## Author(s)

Maciej Pajak <m.pajak@sms.ed.ac.uk>

## References

Agarwal V, Bell GW, Nam J, Bartel DP. Predicting effective microRNA target sites in mammalian mRNAs. eLife, 4:e05005, (2015).

Griffiths-Jones, S., Saini, H. K., van Dongen, S., and Enright, A. J. (2008). miRBase: tools for microRNA genomics. Nucleic acids research, 36(Database issue):D154-8.

Lall, S., Grun, D., Krek, A., Chen, K., Wang, Y.-L., Dewey, C. N., ... Rajewsky, N. (2006). A genome-wide map of conserved microRNA targets in C. elegans. Current biology : CB, 16(5):460-71.

Paraskevopoulou MD, Georgakilas G, Kostoulas N, Vlachos IS, Vergoulis T, Reczko M, Filippidis C, Dalamagas T, Hatzigeorgiou AG., "DIANA-microT web server v5.0: service integration into miRNA functional analysis workflows.", Nucleic Acids Res. 2013 Jul;41(Web Server issue):W169-73.

Wong N and Wang X (2015) miRDB: an online resource for microRNA target prediction and functional annotations. Nucleic Acids Research. 43(D1):D146-152.

## Examples

```
targets <- getPredictedTargets('let-7a',species='hsa', method = 'min')
head(targets) #top of the list with minimum aggregation
targets2 <- getPredictedTargets('let-7a',species='hsa', method='geom')
head(targets2) #top of the list with geometric mean aggregation
```

---

# getTargetsFromSource *Get target list from a single source*

---

## Description

This function queries precompiled annotation SQLite database which contains miRNA - target gene associations with their respective scores.

## Usage

```
getTargetsFromSource(mirna, species = "mmu", source = "diana",
  synonyms = TRUE, both_strands = FALSE)
```

## Arguments

| | |
|---|---|
| mirna | miRNA in a standard format |
| species | species in a standard three-letter acronym, default 'mmu' |
| source | a source target prediction algorithm table to query, default 'diana', other possible values are 'miranda', 'targetscan', and 'pictar'. |
| synonyms | when searching for -3p miRNA automatically also searches for miRNA with the same name but ending with * (some databases list -3p miRNA this way) and other way around, similarly for -5p miRNA, default TRUE |
| both_strands | overrides synonyms and searches for targets of both -5p and -3p strands together |

## Value

data.frame object with entrez IDs of target genes and their scores, if there are no targets found for a given miRNA in a given table then an empty

## Author(s)

Maciej Pajak <m.pajak@sms.ed.ac.uk>

## References

Friedman, R. C., Farh, K. K.-H., Burge, C. B., and Bartel, D. P. (2009). Most mammalian mRNAs are conserved targets of microRNAs. Genome research, 19(1):92-105.

Griffiths-Jones, S., Saini, H. K., van Dongen, S., and Enright, A. J. (2008). miRBase: tools for microRNA genomics. Nucleic acids research, 36(Database issue):D154-8.

Lall, S., Grun, D., Krek, A., Chen, K., Wang, Y.-L., Dewey, C. N., ... Rajewsky, N. (2006). A genome-wide map of conserved microRNA targets in C. elegans. Current biology : CB, 16(5):460-71.

Maragkakis, M., Vergoulis, T., Alexiou, P., Reczko, M., Plomaritou, K., Gousis, M., ... Hatzigeorgiou, A. G. (2011). DIANA-microT Web server upgrade supports Fly and Worm miRNA target prediction and bibliographic miRNA to disease association. Nucleic Acids Research, 39(Web Server issue), W145-8.

## Examples

```
targets <- getTargetsFromSource('let-7a', species='hsa', source='targetscan')
head(targets)
#top of the listof human targets of let-7a from TargetScan only
```

---

# MirnaDb-class *Database class*

---

## Description

object of MirnaDb class holds the sqlite database connection, and extends AnnotationDb class from AnnotationDbi package. columns, keys, keytypes and select methods allow access to database tables and retrieval of miRNA target information.

select is the most important method, allows querying the database for predictions from a specific source and species for a given miRNA

## Usage

```
columns(x)
keytypes(x)
keys(x, keytype, ...)
select(x, keys, columns, keytype, ...)

## S4 method for signature 'MirnaDb'
columns(x)

## S4 method for signature 'MirnaDb'
keytypes(x)

## S4 method for signature 'MirnaDb'
keys(x, keytype, ...)

## S4 method for signature 'MirnaDb'
select(x, keys, columns, keytype, ...)
```

### Arguments

| | |
|---|---|
| x | the MirnaDb object |
| keytype | the keytype that matches the keys used; the table in which the search should be performed. |
| ... | any optional arguments |
| keys | the key to select records for from the database - miRNA name; all possible keys (miRNAs) are returned by using the keys method. |
| columns | in this case same as keytype, the table in which the search should be performed, this value specifies the source of predictions as well as species; as with keys, all possible columns are returned by using the columns method. |

### Value

string vectors, for select a data.frame with target genes and scores

### Author(s)

Maciej Pajak <m.pajak@sms.ed.ac.uk>

### Examples

```
#first load the annotations
require(miRNAtap.db)
#see all available tables
keytypes(miRNAtap.db)
```

---

## miRNAtap *miRNAtap: microRNA Targets - Aggregated Predictions.*

---

### Description

It is a package with tools to facilitate implementation of workflows requiring miRNA prediction through access to multiple prediction results (DIANA, Targetscan, PicTar, Miranda, and miRDB) and their aggregation. Three aggregation methods are available: minimum, maximum and geometric mean, additional parameters provide further tuning of the results. Predictions are available for Homo sapiens, Mus musculus and Rattus norvegicus (the last one through homology translation).

### Author(s)

Maciej Pajak <m.pajak@sms.ed.ac.uk>, Ian Simpson

### Examples

```
#direct targets in mouse aggregated from all sources:
targets_mouse <- getPredictedTargets('let-7a',species='mmu', method='geom')
#homology-translated targets in rat aggregated from all sources
targets_rat <- getPredictedTargets('let-7a',species='rno', method='geom')
```

translate *Homology transfer for miRNAtap*

## Description

This function maps gene entrez ID between species using homology information from Homologene.

## Usage

```
translate(entrezes, from = "mmu", to = "rno", ...)
```

## Arguments

| | |
|---|---|
| entrezes | data.frame with entrez Gene IDs and their scores |
| from | origin species, default 'mmu', Mus musculus |
| to | target species, default |
| ... | any optional arguments |

## Value

data.frame object with orthologous genes' entrez IDs and corresponding scores

## Author(s)

Maciej Pajak <m.pajak@sms.ed.ac.uk>

## Examples

```
mouse_genes <- data.frame(GeneID =
        c("15364", "56520", "57781", "58180", "18035", "239857"))
translate(mouse_genes, from='mmu', to='rno')
```

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