RmiR.Hs.miRNA package vignette

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1 Introduction

RmiR.Hs.miRNA is an R package which includes various databases of miRNA targets:

- mirBase
- targetScan
- miRanda from microrna.org
- tarBase from Diana Labs
- mirTarget2 from mirDB
- picTar

With the package it is possible to evaluate or comapre different miRNA target database or also retrieve the targets or the miRNAs, given a list of miRNAs or a list of genes respectively.

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2 Querying and evaluating a miRNA target database

The miRNA targets databases are included in an SQLite object. We can browse and inspect them directly in an R environment:

```
> library(RmiR.Hs.miRNA)
> dbListTables(RmiR.Hs.miRNA_dbconn())

[1] "miranda"    "mirbase"    "mirtarget2" "pictar"     "tarbase"
[6] "targetscan"
```

We should make a SQL query to have the desired results only:

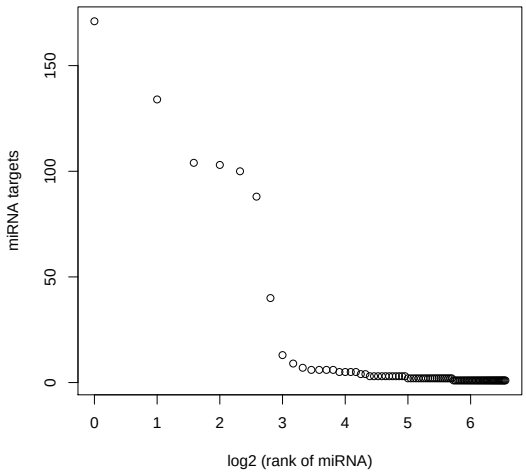
```
> dbGetQuery(RmiR.Hs.miRNA_dbconn(), "SELECT * FROM tarbase WHERE mature_miRNA='hsa-

  mature_miRNA gene_id     pmid
1   hsa-miR-21    7168 17363372
2   hsa-miR-21    7168 17363372
3   hsa-miR-21   27250 18270520
4   hsa-miR-21   27250 17968323
5   hsa-miR-21   27250 18372920
6   hsa-miR-21   27250 17991735
7   hsa-miR-21    5728 17681183
8   hsa-miR-21    5728 16762633
9   hsa-miR-21    5268 18270520
```

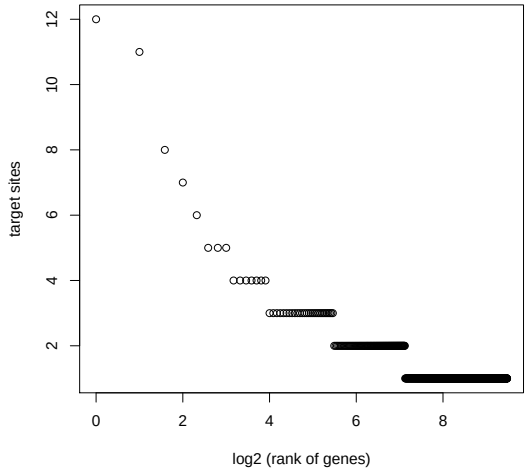
Every query gives a mature_miRNA column with the microRNA name and a gene_id column with the entrez gene id of the target. There could be also other additional columns useful for further investigation. These columns depend on the database. For example, in TarBase we have the PubMed ID of the article which proves the relation between the miRNA and its target, in TargetScan there are the start and the end point of the miRNA seed in the gene, and so on.

To evaluate the consistency of a database we can visualize two properties of the miRNA/Target relationship; the *multiplicity* and the *cooperativity* :

```
> tarbase <- dbReadTable(RmiR.Hs.miRNA_dbconn(), "tarbase")[, 1:2]
> tarb_mir <- sort(table(tarbase$mature_miRNA), decreasing = T)
> plot(x = log2(c(1:length(tarb_mir))), y = tarb_mir, ylab = "miRNA targets",
+     xlab = "log2 (rank of miRNA)")
> tarb_gene <- sort(table(tarbase$gene_id), decreasing = T)
> plot(x = log2(c(1:length(tarb_gene))), y = tarb_gene, ylab = "target sites",
+     xlab = "log2 (rank of genes)")
```

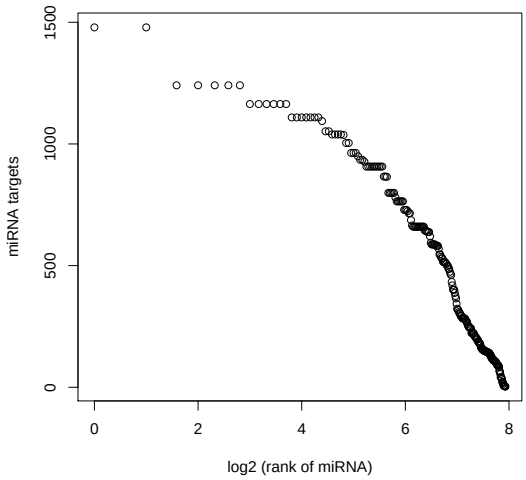


(a) Multiplicity of miRNA in TarBase.

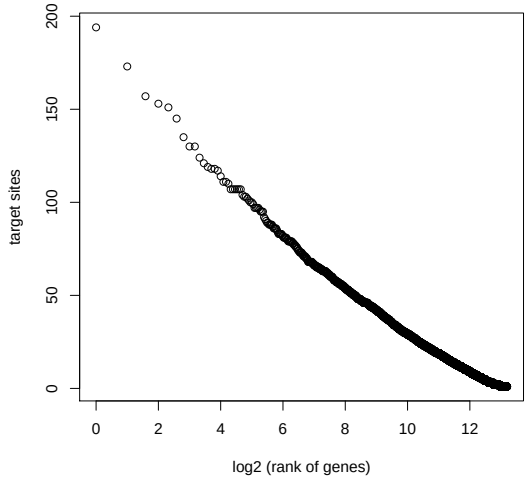


(b) Cooperativity of miRNA in TarBase.

Figure 1: Plot of the multiplicity and cooperativity generated with the TarBase database.



(a) Multiplicity of miRNA in TargetScan.



(b) Cooperativity of miRNA in TargetScan.

Figure 2: Plot of the multiplicity and cooperativity generated with the TargetScan database.

```
> targetscan <- dbReadTable(RmiR.Hs.miRNA_dbconn(), "targetscan")[,
+     1:2]
> targ_mir <- sort(table(targetscan$mature_miRNA), decreasing = T)
> plot(x = log2(c(1:length(targ_mir))), y = targ_mir, ylab = "miRNA targets",
+     xlab = "log2 (rank of miRNA)")
> targ_gene <- sort(table(targetscan$gene_id), decreasing = T)
> plot(x = log2(c(1:length(targ_gene))), y = targ_gene, ylab = "target sites",
+     xlab = "log2 (rank of genes)")
```

From the graphs we can see that for some miRNAs the number of predicted targets is huge (Fig. 2(a)) compared with the number of experimentally validated targets (Fig. 1(a)).

For a predicted database we note how miRNA have a cooperative control for a lot of gene targets (Fig. 2(b)), when in the TarBase database many gene targets do not have more than four target sites (Fig. 1(b)).

2.1 Find a list of miRNAs or targets

In general the result of an analysis is a list of genes or microRNAs. A nice continuation it is to look for interesting miRNAs or gene targets matching the results.

```
> mirna <- c("hsa-miR-148b", "hsa-miR-27b", "hsa-miR-25", "hsa-miR-181a",
+     "hsa-miR-27a", "hsa-miR-7", "hsa-miR-32", "hsa-miR-32", "hsa-miR-7")
> genes <- c("A_23_P171258", "A_23_P150053", "A_23_P150053", "A_23_P150053",
+     "A_23_P202435", "A_24_P90097", "A_23_P127948")
```

We have created a list of miRNA and a list of genes, we use the table of `targetscan` we created in the previous example, to look for the information we need:

```
> mirs <- targetscan[targetscan$mature_miRNA %in% mirna, ]
> nrow(mirs)

[1] 5479

> mirs[1:10, ]

      mature_miRNA gene_id
36870 hsa-miR-148b   57419
36873 hsa-miR-148b   22870
36876 hsa-miR-148b   11176
36879 hsa-miR-148b    8065
36882 hsa-miR-148b    7471
36885 hsa-miR-148b  285527
36888 hsa-miR-148b   79718
```

```
36891 hsa-miR-148b      93
36894 hsa-miR-148b   85461
36897 hsa-miR-148b    8556
```

```
> library(hgug4112a.db)
> targs <- targetscan[targetscan$gene_id %in% mget(genes, hgug4112aENTREZID),
+     ]
> nrow(targs)
```

```
[1] 34
```

```
> targs[1:10, ]
```

```
      mature_miRNA gene_id
24852  hsa-miR-128      59
35204  hsa-miR-143     120
36449  hsa-miR-145     120
36550  hsa-miR-145     120
38093  hsa-miR-152      22
38094 hsa-miR-148b      22
38095 hsa-miR-148a      22
54948 hsa-miR-181d     133
54949 hsa-miR-181c     133
54950 hsa-miR-181b     133
```