

TUTORIAL miRExplorer

This section provides a brief tutorial on the tools presented in this article. Each subsection includes a practical example to illustrate their functionalities and how they can be used in miRNA analysis.

Initial Screen and Selection of Diseases of Interest

By selecting "Disease" on the left sidebar under "Choose between:" a dropdown menu will open where we will select "inflammatory bowel disease", "Crohn's disease," and "ulcerative colitis".

miRExplorer

• Choose between:

☐ miRNA

☒ Disease

Select Disease:

inflammatory bowel disease

Crohn's disease

ulcerative colitis

• Upload miRNA-Disease Interaction File

Browse...

No file selected

• Select Database:

☒ Database MirCancer&HMDD

☐ Database DEMC

☐ Uploaded

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Context

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miRNA-Gene Interaction

Metabolic functions

Data

There are currently several biological databases containing information on miRNAs and their association with diseases (HMDD[1], MirCancer[2], dbDEMC[3]) or target genes (MirTarBase[4], TarBase[5]).

As these databases are often difficult to access, a user-friendly web application was developed to provide an overview of the role of miRNAs in the literature and their interactions with genes and diseases by merging information from the previously mentioned databases.

ABOUT miRNA-DISEASE INTERACTION:

DATABASE	ASSOCIATIONS	miRNAs	DISEASE	REFERENCES
HMDD	53530	1911	2360	37090
Mircancer	9080	1034	129	7271
dbDEMC	33610	2203	32	175

ABOUT miRNA-GENE INTERACTION:

DATABASE	ASSOCIATIONS	miRNAs	GENES	REFERENCES
miRTarBase	49158	757	10316	7619
TarBase	152760	396	17618	946

References

1. Cui C, Zhong B, Fan R, Cui Q. (2024). "HMDD v4.0: a database for experimentally supported human microRNA-disease associations". Nucleic Acids Research, 52(D1): D1327-D1332. doi:10.1093/nar/gkad717.

2. Xie B, Ding Q, Han H, Wu D. miRCancer: a microRNA-cancer association database constructed by text mining on literature. Bioinformatics. 2013 Mar 1;29(5):638-44. doi: 10.1093/bioinformatics/btt014. Epub 2013 Jan 16. PMID: 23325619.

3. Feng Xu, Yifan Wang, Yunchao Ling, Chenfen Zhou, Haizhou Wang, Andrew E Teschendorff, Yi Zhao, Haitao Zhao, Yungang He, Guoqing Zhang, Zhen Yang. dbDEMC 3.0: Functional exploration of differentially expressed miRNAs in cancers of human and model organisms. Genomics, Proteomics & Bioinformatics. 2022, 20(3):446-454. [doi: 10.1016/j.gpb.2022.04.0062022]

Exploring the Disease Context

The "Context" page displays a graphical representation of the relationships between the selected diseases and other related diseases.

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```

graph BT
    disease((disease)) --> anatomical((disease of anatomical entity))
    anatomical --> gastrointestinal((gastrointestinal system disease))
    gastrointestinal --> intestinal((intestinal disease))
    intestinal --> inflammatory((inflammatory bowel disease))
    inflammatory --> gastroduodenal((gastroduodenal))
    gastroduodenal --> Crohn((Crohn's disease))
    Crohn --> jejunitis((jejunitis))
    Crohn --> ileitis((ileitis))
    Crohn --> CrohnColitis((Crohn's colitis))
    Crohn --> ulcerative((ulcerative colitis))
  
```

Select a Disease to View:

Crohn's disease
inflammatory bowel disease
Crohn's disease
ulcerative colitis

Analysis of miRNA-Disease Interactions

The "miRNA-Disease Interaction" page lists the interactions between miRNA and the selected diseases (in our case, IBD).

In the upper left corner, you can use the "Select Count Threshold" filter to set a minimum value for the number of times an interaction must be reported to be included in the table.

Documentation	Context	miRNA-Disease Interaction	miRNA-Gene Interaction	Metabolic functions
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Select Count Threshold

1

3

10

1

2

3

4

5

6

7

8

9

10

Table

Network

Total unique miRNA: 14

Show

10

entries

Search:

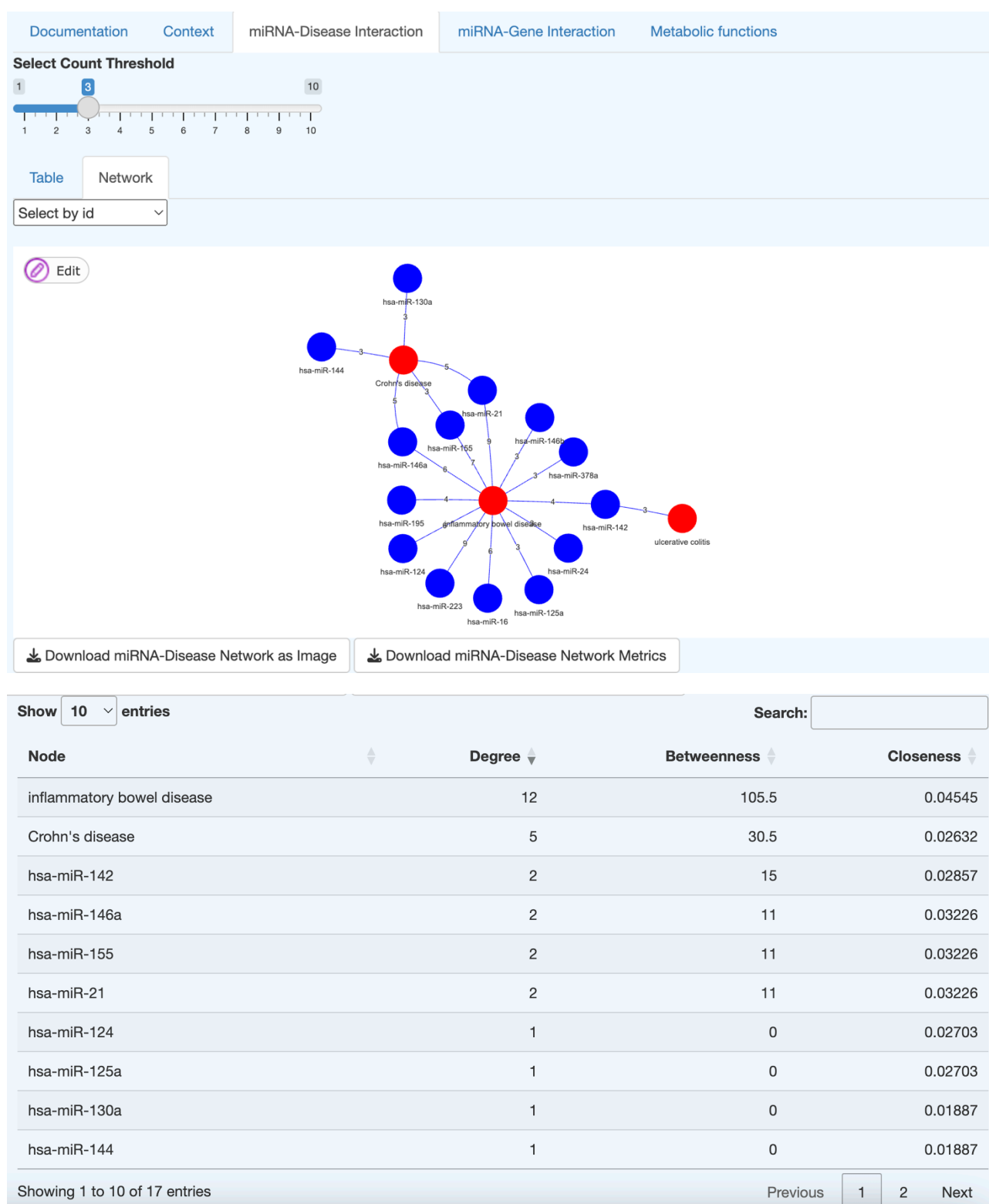
	miRNA	DOID	disease	Count	ID
14	hsa-miR-21	DOID:0050589	inflammatory bowel disease	9	33647883,32332611,32308936,32087719,33535181,32775420,30530166,32010260,3
16	hsa-miR-223	DOID:0050589	inflammatory bowel disease	9	35595039,35395459,34151668,31209454,36120988,33332758,32087719,32797879,3
10	hsa-miR-155	DOID:0050589	inflammatory bowel disease	7	35319228,33647883,32775420,34987126,30530166,33524272,33014211
1	hsa-miR-124	DOID:0050589	inflammatory bowel disease	6	36075249,36573890,32815642,36440907,33942299,32153570
7	hsa-miR-146a	DOID:0050589	inflammatory bowel disease	6	36075029,32826242,32793975,32775420,36160881,30915760
12	hsa-miR-16	DOID:0050589	inflammatory bowel disease	6	36111932,32361613,30978148,32087719,33535181,33182065

The "Network" section displays the interaction graph. The nodes in the graph represent both the miRNA (blue nodes) and the diseases (red nodes). The edges between the nodes represent the interactions between the miRNA and the diseases.

The numbers on the edges indicate the "Count," which refers to the number of times the interaction has been reported in the databases.

The graph is accompanied by a metrics table with the following columns:

- **Node:** The name of the node (miRNA or disease).
- **Degree:** The number of edges connecting the node to other nodes. A high "Degree" indicates that the node is highly connected.
- **Betweenness:** A measure of how frequently a node lies on the shortest paths between other nodes. A high "Betweenness" indicates that the node is crucial for the network's connectivity.
- **Closeness:** A measure of how "close" a node is to all other nodes in the network. A high "Closeness" indicates that the node is well-positioned to spread information or influence other nodes in the network.



Analysis of miRNA-Gene Interactions

In this section, you can filter miRNA-gene interactions based on the types of experiments used to identify them. ShinyMir classifies the experiments into "Select Strong Assays" (strong experiments) and "Select Weak Assays" (weak experiments). By default, the "Luciferase reporter assay" is always selected.

This section allows you to explore three different tables: miRNA with the suffix -3p, miRNA with the suffix -5p, and miRNA without a suffix.

Above the table, there is information indicating the total number of unique target genes identified for the selected miRNA.

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Select All

Deselect All

Select Strong Assays:

☐ In Situ Hybridization

☒ Luciferase reporter assay

☐ qPCR

☐ Reporter assay

Select Weak Assays:

☐ ChIP

☐ ChIP-seq

☐ ELISA

☐ Flow Cytometry

☐ Immunocytochemistry

☐ Immunofluorescence

☐ Immunohistochemistry

☐ Immunoprecipitation

☐ Microarray

☐ Northern Blot

☐ Proteomics

☐ Sequencing

☐ Western Blot

Choose miRNA type:

miRNA-5p

miRNA-5p

miRNA-3p

Other

Table

Network

Enrichment

Choose miRNA type:

miRNA-5p

Total unique target genes: 224

Min. Count for Interaction:

1

2

10

Show

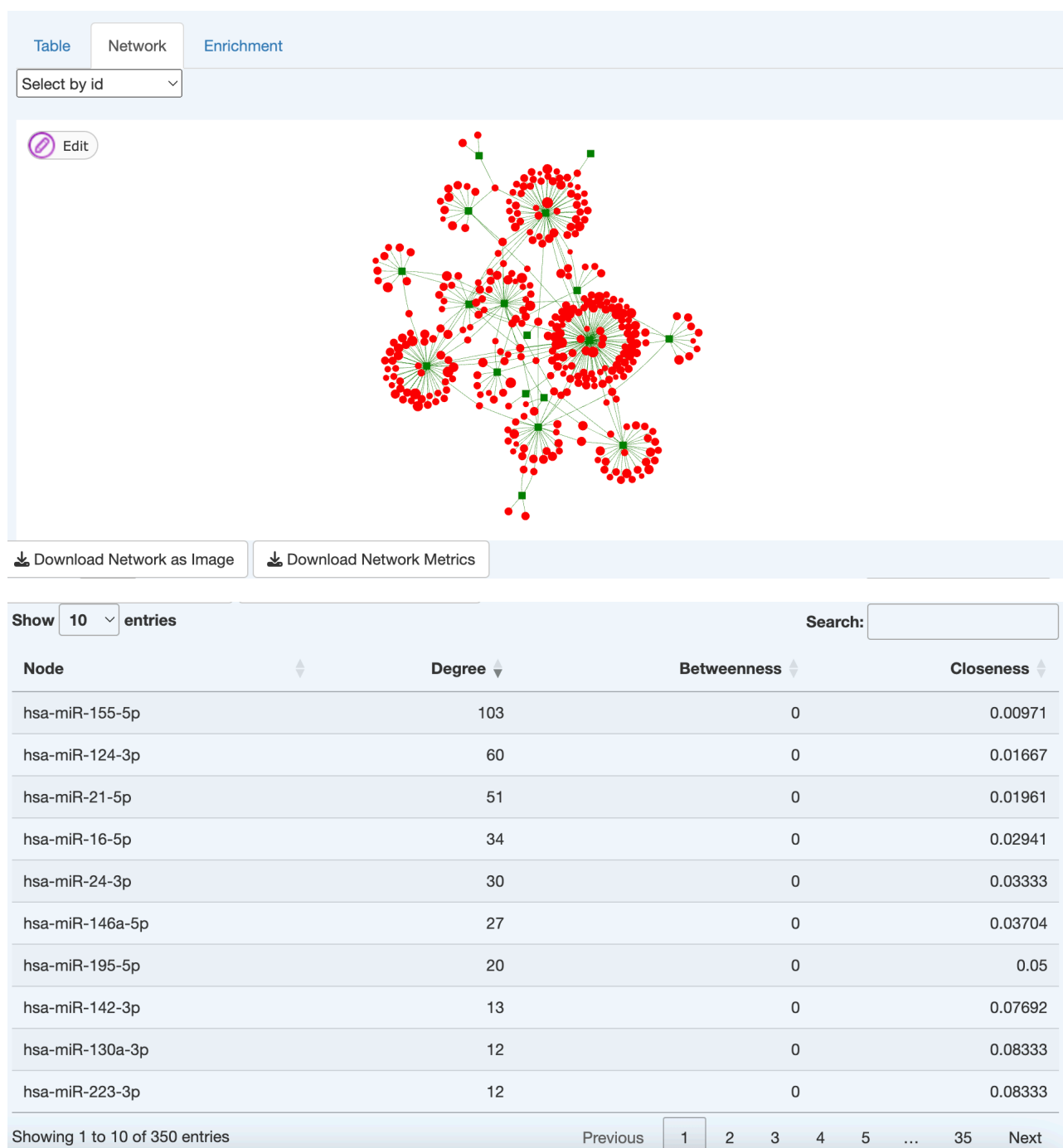
10

entries

Search:

The "Network" section shows a graphical representation of the interactions between miRNA and their target genes.

The nodes in the graph represent both the miRNA and the target genes, while the edges represent the interactions between the miRNA and the genes.



The "Enrichment" section shows the enrichment analysis results of the target genes for the selected miRNA.

There is a slider, "Pathway size: Min.", which allows you to set a minimum value for the size of the biological pathways to consider in the analysis.

Additionally, you can upload your ontology file to customize the enrichment analysis.

The supporting graphs for the enrichment analysis are the barplot and the heatmap.

In the barplot, the x-axis represents the q-value, and the y-axis represents the pathways (you can choose how many to display using the "Number of Categories to Show in Barplot" slider). The color scale is set based on the Fold Enrichment value (darker colors represent a low Fold Enrichment value and vice versa).

In the heatmap, the x-axis represents the miRNA, and the y-axis represents the pathways. Again, the

color scale is based on the Fold Enrichment value (lighter colors represent a low Fold Enrichment value and vice versa).

Select View

Table

Pathway size: Min.

2

20

Upload Reactome Ontology File

Browse...

No file selected

Show 10 entries

Search:

miRNA	name	p_value	q_value	coverage	Fold_enrichment	
1	hsa-miR-195-5p, hsa-miR-142-3p, hsa-miR-223-3p, hsa-miR-16-5p, hsa-miR-124-3p, hsa-miR-155-5p	2-LTR circle formation	0.02300174690369304	0.0998202794201536	2/13	8.366543
2	hsa-miR-142-5p, hsa-miR-155-5p, hsa-miR-24-3p, hsa-miR-130a-3p, hsa-miR-195-5p, hsa-miR-21-5p, hsa-miR-16-5p, hsa-miR-124-3p, hsa-miR-146a-5p, hsa-miR-223-3p	AKT phosphorylates targets in the cytosol	0.001929325771470236	0.01380149859231857	3/14	11.653399
3	hsa-miR-124-3p, hsa-miR-130a-3p, hsa-miR-223-3p, hsa-miR-146a-5p, hsa-miR-155-5p, hsa-miR-21-5p	AKT phosphorylates targets in the nucleus	0.000671756745619036	0.005848990262810333	3/10	16.314759

Select View

Barplot

Pathway size: Min.

2

20

Upload Reactome Ontology File

Browse...

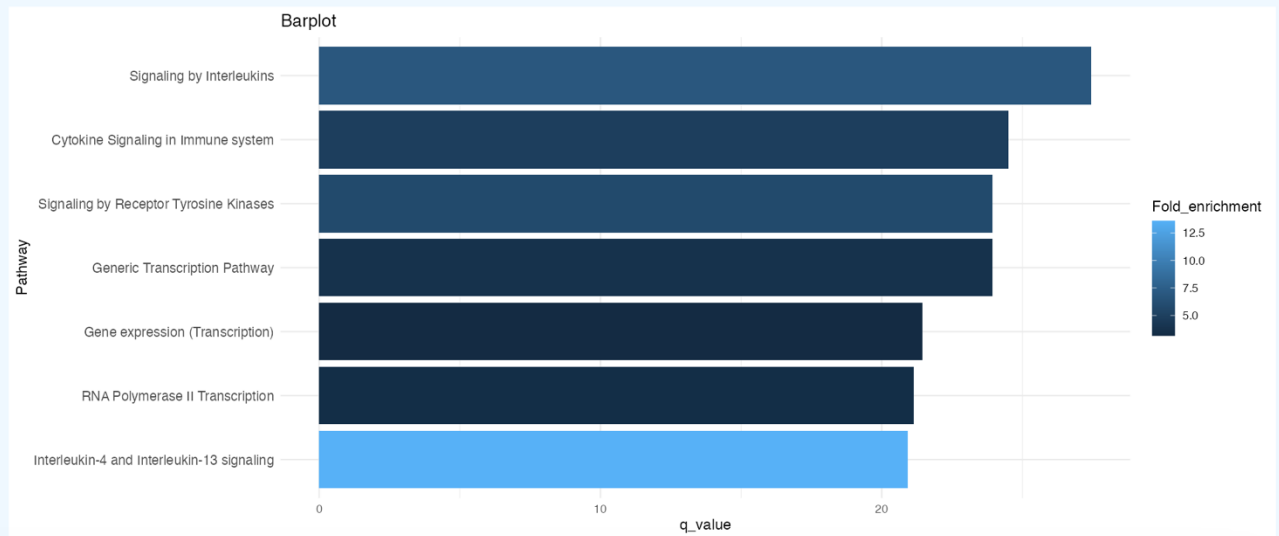
No file selected

Number of Categories to Show in Barplot

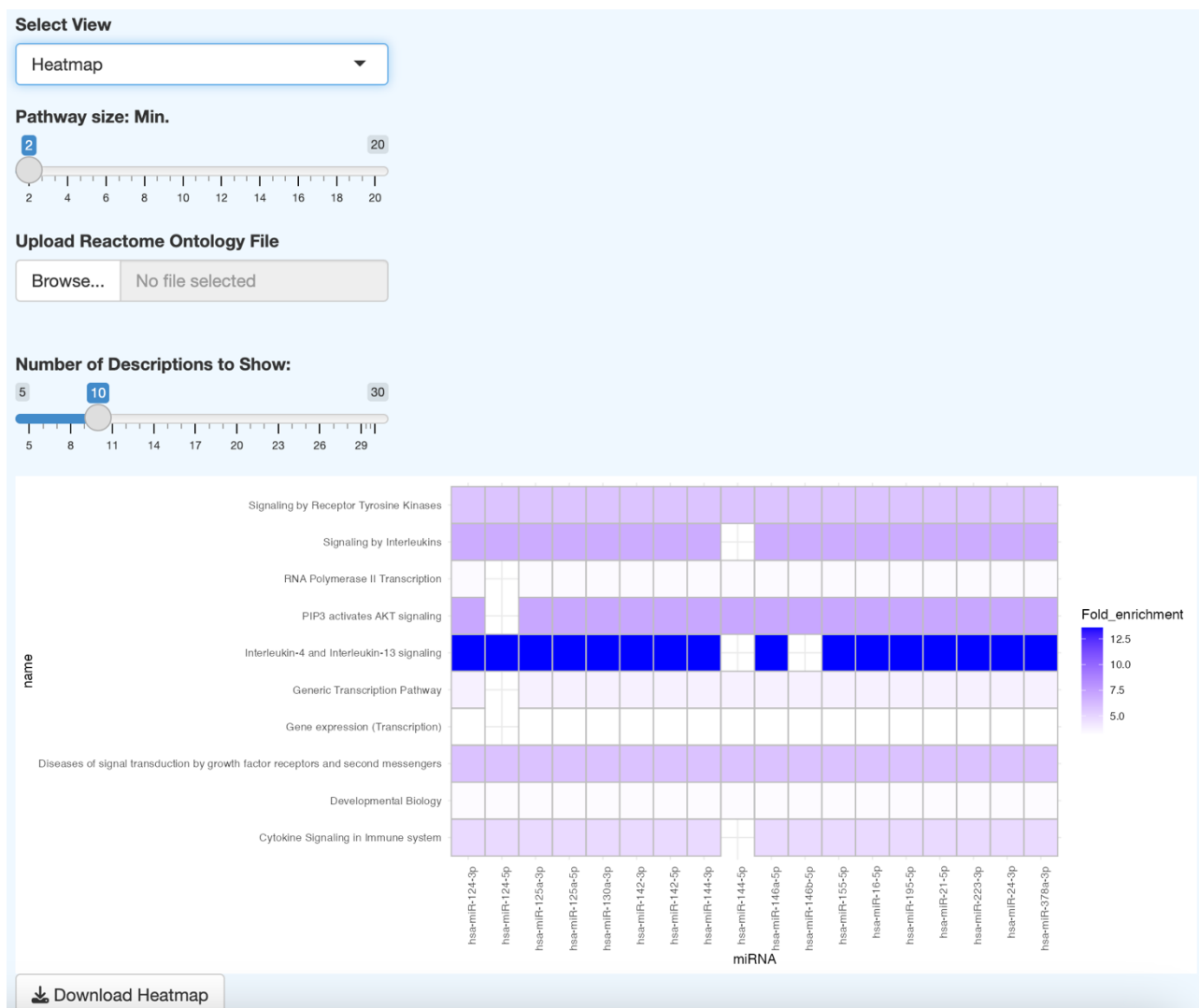
5

7

30



Download Barplot



Analysis of Metabolic Functions

The "Metabolic functions" section shows the interactions between the miRNA and the genes involved in metabolism.

The "Show Metabolic Genes" checkbox allows you to view the complete list of metabolic genes considered in the analysis.

The "Total unique genes" information indicates the total number of unique metabolic genes identified.

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☒ Show Metabolic Genes

Total unique genes: 78 Metabolic genes are: SLC16A1, CDS2, DHFR, B4GALT1, NDST1, GATM, INPP5D, MTAP, NOS3, PTGS2, PTEN, PIK3R1, RDH10, SGPL1, SPHK1, PPARA, TRIB3, CTGF, FAS, SMYD3, EZH2, SIRT1, MET, PDGFRA, IGF1R, NTRK3, ERBB2, EGFR, INSR, ERBB4, ERBB3, CSF1R, FGFR1, PTPRF, PTPN14, CDC25A, PTPN9, PARP9, TRIM32, RNF123, TOPORS, UHRF1, PPIF, CLOCK, PCMT1, DDAH1, AKT2, CDK6, TGFBR1, RPS6KB1, PRKAR1A, MAPK14, CSNK1A1, MASTL, ACVR2A, CDK2, PAK4, MAP3K10, RAF1, ROCK2, CDK4, ACVR1B, PIM1, IKBKE, CHEK1, TGFB2, WEE1, MAPK7, PRKCE, PAK2, IRAK1, BMPR2, CHUK, MAP3K9, PKN2, ROCK1, MAPK1, CTDSP1

Table

Network

☐ Show GPR column

Show

10

 entries

Search:

	MIRNA	gene	Reaction	Formula	Gruppi	group	essentiality
1	hsa-miR-124-3p, hsa-miR-130a-3p, hsa-miR-142-3p, hsa-miR-142-5p	SLC16A1	2-Hydroxybutyrate Symport with Proton	2hb[e] + h[e] <=> 2hb[c] + h[c]	Transport, extracellular	SLC16A1	YES
2	hsa-miR-124-3p, hsa-miR-130a-3p, hsa-miR-142-3p, hsa-miR-142-5p	SLC16A1	Acetoacetate Mitochondrial Transport via H+ Symport	acac[c] + h[c] <=> acac[m] + h[m]	Transport, mitochondrial	SLC16A1	YES
3	hsa-miR-124-3p, hsa-miR-130a-3p, hsa-miR-142-3p, hsa-miR-142-5p	SLC16A1	Acetone Transport via Proton Symport	acetone[e] + h[e] <=> acetone[c] + h[c]	Transport, extracellular	SLC16A1	YES

The "Network" section displays a graphical representation of the interactions between the miRNA and the genes involved in metabolism.

The nodes in the graph represent both the reactions and the metabolic genes, while the edges represent the interactions between the miRNA and the metabolic genes.

[Documentation](#)[Context](#)[miRNA-Disease Interaction](#)[miRNA-Gene Interaction](#)[Metabolic functions](#)

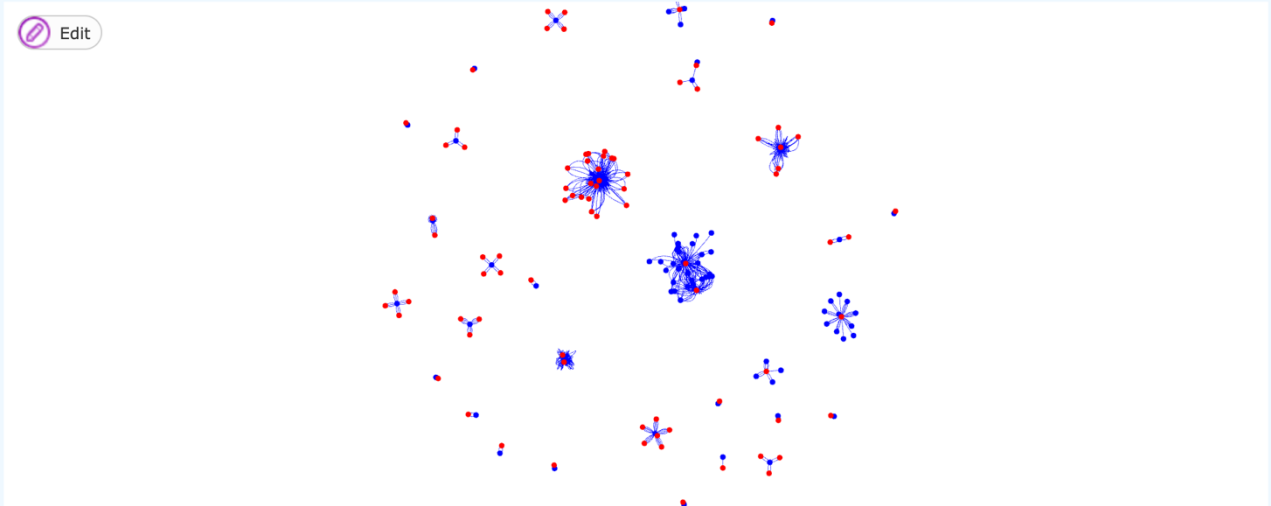
☐ Show Metabolic Genes

Table

Network

Select by id

Edit



Download Metabolic Network as Image

Download Metabolic Network Metrics

Show

10

 entries

Search:

Node	Degree	Betweenness	Closeness
SLC16A1	312	231	0.04545
Major Facilitator (Mfs) Tcdb:2.A.1.13.1	224	0	0.02326
B4GALT1	125	15	0.16667
Non-Specific Serine/Threonine Protein Kinase	123	436.5	0.0303
Beta-N-Acetylglucosaminylglycopeptide Beta-1, 4-Galactosyltransferase, Golgi	100	0	0.09091
PTGS2	95	1	0.5
Prostaglandin-Endoperoxide Synthase	85	0	0.33333
ATP:Protamine O-Phosphotransferase	59	45.5	0.01493
Receptor Protein-Tyrosine Kinase	37	55	0.09091
DHFR	30	15	0.16667

Showing 1 to 10 of 161 entries

Previous

1

2

3

4

5

...

17

Next