

# miRNet



-- network-based visual analytics for microRNA  
functional analysis & systems biology

# Background

- MicroRNAs (miRNAs) regulate most cellular processes and are promising therapeutic candidates for cancer and other diseases.
- Understanding miRNA function is challenging due to the "many-to-many" relationships between miRNAs and their target genes.
- In addition, complex interplay exists between miRNAs and other functional elements, such as transcription factors, lncRNAs, etc.
- Network-based approach enables the integration of multiple data types and interpreting results at a systems level to allow the understanding of miRNA cooperative functions and regulatory mechanisms.

# Overall goal

To provide an easy-to-use web application to enable complex **miRNA-centric network analytics for systems-level interpretation** of miRNA functions and gene regulations

# From miRNet 1.0 to 2.0

**2016**

miRNet 1.0: miRNA – target gene network

- Added support for miRNA family mapping and enrichment analysis
- Added support for tissue and exosomal specific miRNA annotation
- Added support for more species based on user's feedback
- Added two modules to support xeno-miRNA targets exploration & visualization
- Added a new module to support miRNA-TF regulatory network
- Added a new module to support miR-SNP annotation and target interactions
- Added a new module to support integrating multiple types of molecules for systems-level visual analytics
- Added additional network layout algorithms, including bipartite/tripartite, concentric and backbone layout
- Significantly expanded miRNA interaction knowledgebase
- Revamped the web interface, optimized the workflow, and introduced microservices and web application programming interface (API)

**2020**

miRNet 2.0: miRNA-centric complex networks & functions

# miRNet & its knowledgebase

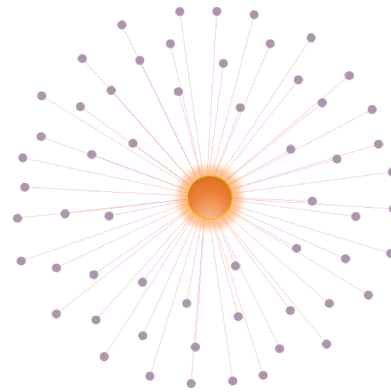


TAM 2.0



PhenomiR

SNP2TFBS



SM2miR

TransmiR

ADmiRE

PolymiRTS

miR2Disease

miRNet 2.0

HMDD

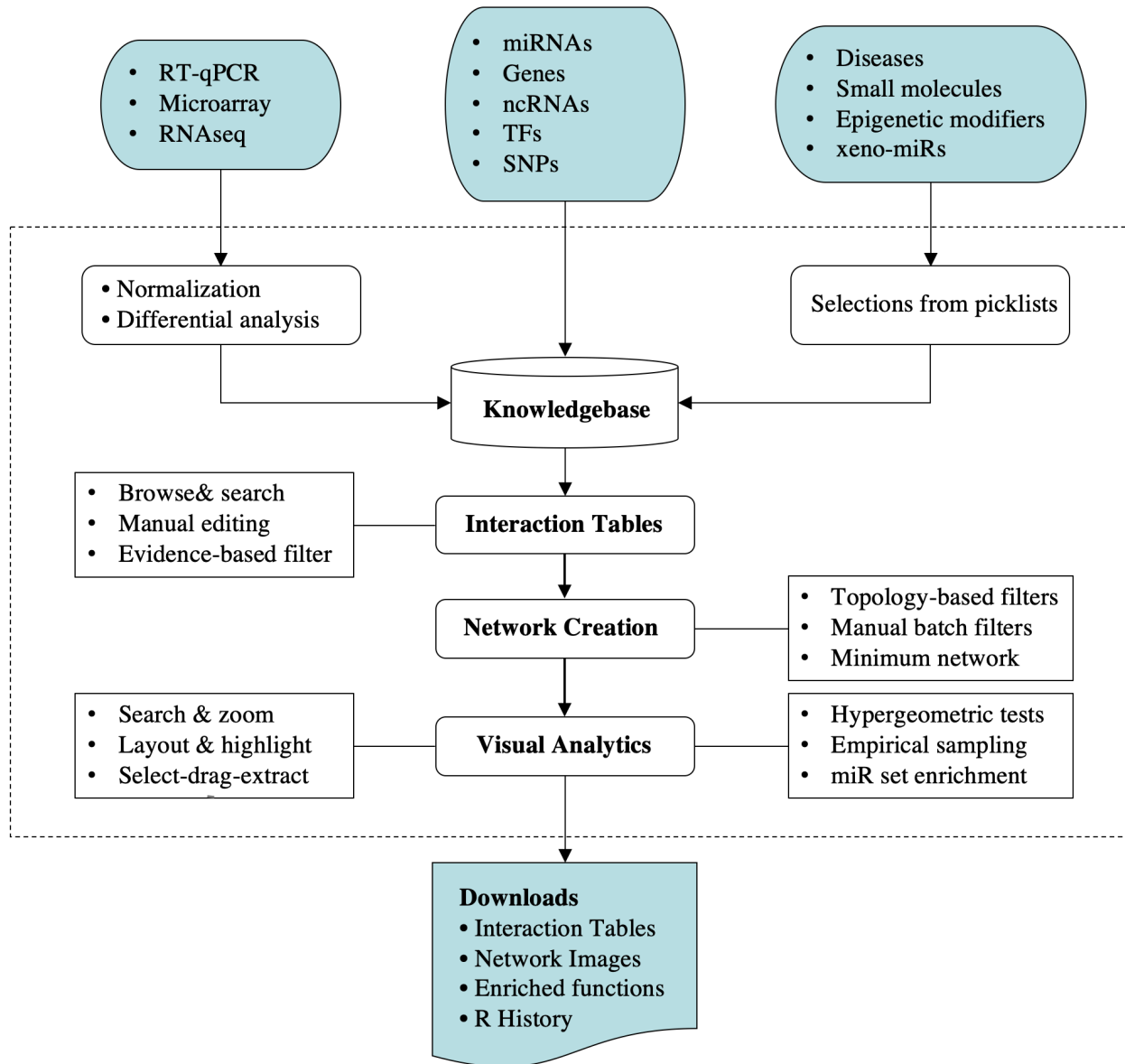


PharmacomiR

miRearBase TarBase

miRecords

# Workflow



# Network Analysis

The screenshot displays a network analysis software interface with a central network graph and several tool panels. The network graph shows a complex web of nodes (colored red, yellow, and cyan) and edges. Callout boxes point to various features:

- Viewer Tool:** Points to the central network graph.
- Function Explorer:** Points to the right-hand panel showing a table of gene functions.
- Module Explorer:** Points to the bottom-right panel showing a table of modules.
- Batch Selection:** Points to the bottom-right panel showing a table of modules.
- Path Finder:** Points to the bottom-right panel showing a table of modules.
- Node Explorer:** Points to the left-hand panel showing a table of node properties.

**Node Explorer Table:**

ID	Degree	Betweenness	Status
hsa-mir-101-3p	393	645476.5	*
hsa-mir-361-5p	160	224782.8	*
hsa-mir-147a	149	211709.8	*
hsa-mir-510-5p	149	206372.5	*
TP53	127	126331.9	*
hsa-mir-3140-3p	124	175439.3	*
DDX3X	118	186629.9	*
E2F1	106	170537.9	*
E2F3	93	70266.92	*
hsa-mir-133b	90	160798.3	*
CEBPA	84	55382.53	*
OLR1	81	120253.4	*
EPAS1	79	47258.78	*
NFIA	79	46210.86	*
SRF	71	102955.2	*
HIF1A	63	50169.48	*
RNF6	40	38513.9	*
E2F2	38	9943.58	*
HAPLN1	18	60908.43	*
MEF2A	12	7178.699	*
hsa-mir-21-5p	11	204653.5	*
ELOVL4	11	14759.7	*
MYOD1	10	553.3538	*
MEGF9	9	11477.1	*
MYOCD	8	1804.333	*
ZEB1	7	49458.82	*

**Function Explorer Table:**

Name	Hits	Pval	Color
Pathways in cancer	79	3.69e-22	
Prostate cancer	30	2.23e-11	
Chronic myeloid leukemia	26	2.73e-10	
Pancreatic cancer	25	3.48e-10	
Renal cell carcinoma	21	3.05e-8	
Colorectal cancer	18	1.78e-7	
Melanoma	19	0.000008	
Acute myeloid leukemia	17	0.000012	
Small cell lung cancer	20	0.000024	
Transcriptional misregulation in	9	0.000069	
MAPK signaling pathway	41	0.000083	
TGF-beta signaling pathway	19	0.000157	
Focal adhesion	33	0.000157	
Adherens junction	17	0.000157	
Cell cycle	24	0.000163	
Glioma	16	0.000208	
HTLV-1 infection	32	0.000297	
Bladder cancer	10	0.000329	
Non-small cell lung cancer	13	0.000937	

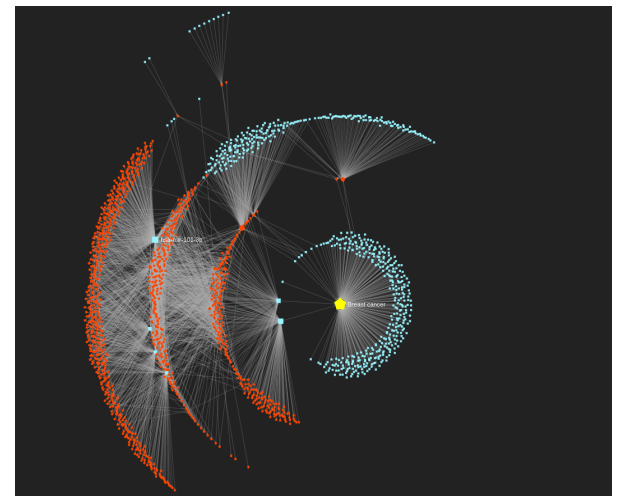
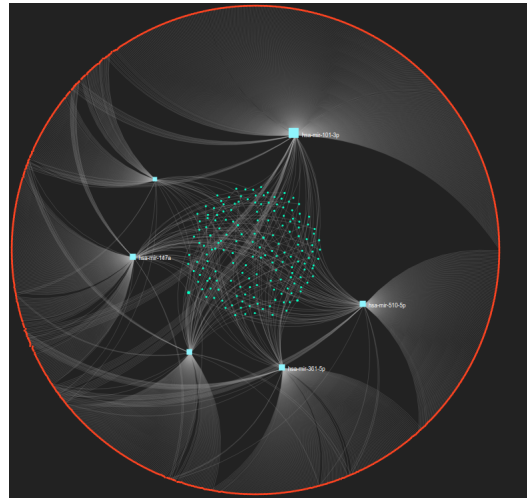
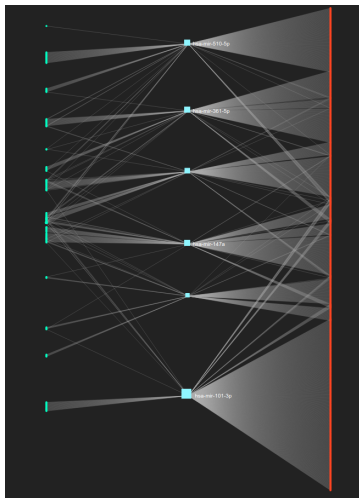
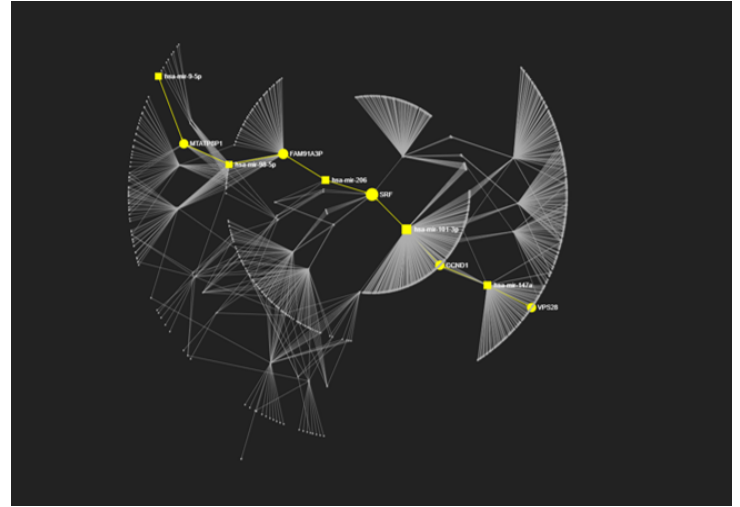
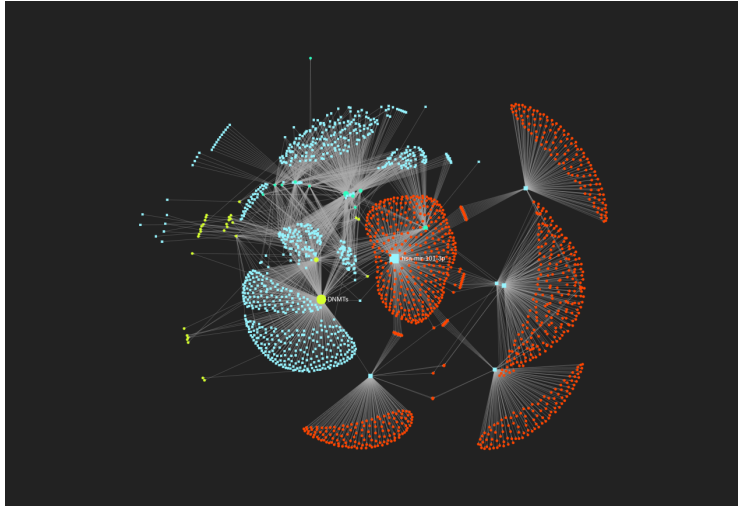
**Module Explorer Table:**

Module	Size	P-value	Col
Pathways in cancer			
CEBPA			
E2F1			
E2F2			

**Current Selections:**

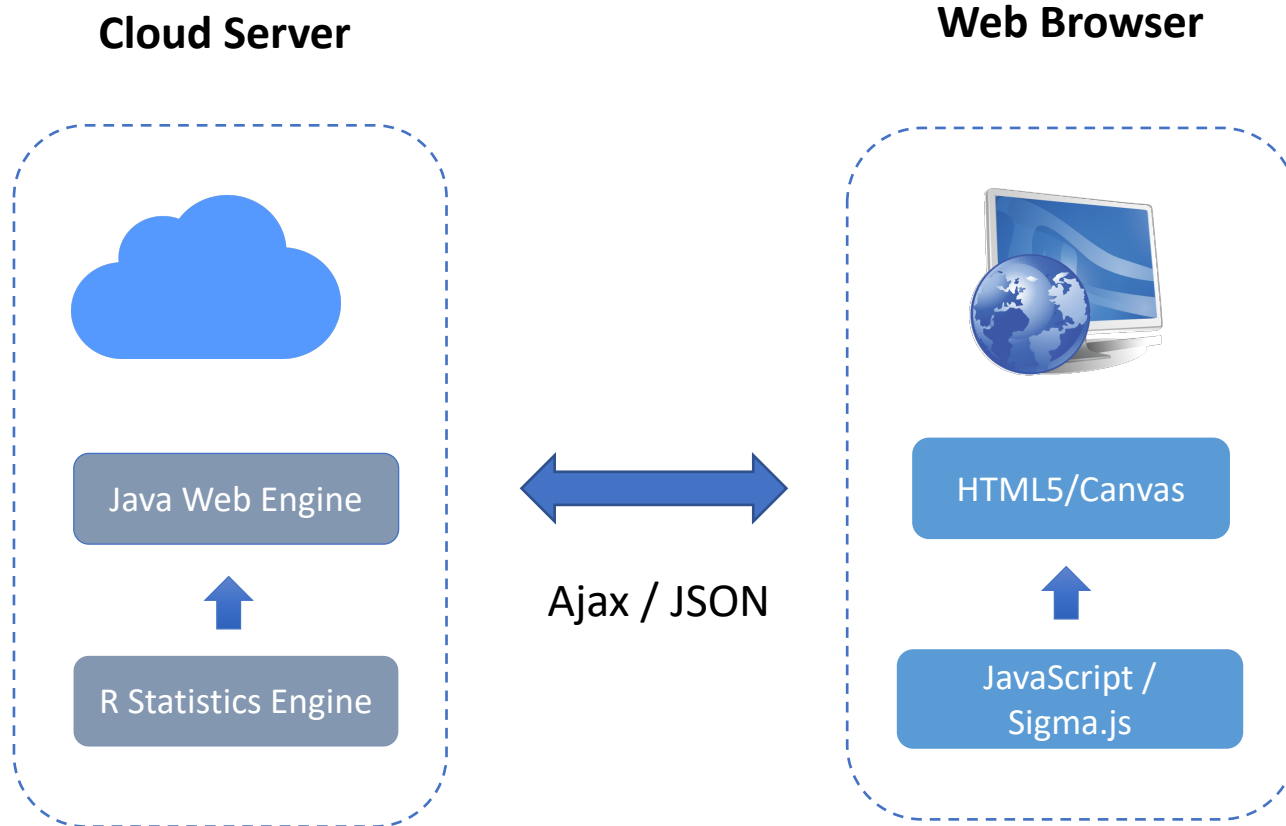
- Pathways in cancer
- CEBPA
- E2F1
- E2F2

# Network Customization





# Implementations



# Comparison with other tools

Tool name	miRNet		miRTargetLink	MIENTURNET	Arena- Idb	starBase
	2.0	1.0				
<b>Data input and processing</b>						
Species #	11	8	1	6	1	23
<b>Target genes</b>						
Experimental	+++	++	++	+	++	+++
Predicted	√	√	√	√	√	√
<b>Other targets &amp; associations</b>						
miR-SNP	√	-	-	-	-	-
TF	√	-	-	-	-	-
ncRNA	+++	+	-	-	+	++++
xeno-miRNA	√	-	-	-	-	-
Disease	+++	++	-	-	++	++
Epigenetic modifier	√	√	-	-	-	-
Small molecule	√	√	-	-	-	-
Expression profiling	√	√	-	-	-	-
<b>Enrichment analysis</b>						
Hypergeometric tests	√	√	√	√	-	√
Empirical sampling	√	√	-	-	-	-
miR-set enrichment	√	-	-	-	-	-
<b>Network visual analytics</b>						
Multiple query types	√	-	-	-	-	-
Integration with PPI network	√	-	-	-	-	-
Multipartite network visualization	√	-	-	-	-	-
Subnetwork extraction	√	-	-	-	-	-

miRTargetLink: <https://ccb-web.cs.uni-saarland.de/mirtargetlink/>  
 Arena-Idb: <http://ncrnadb.scienze.univr.it/sites/arenaidb/>

MIENTURNET: <http://userver.bio.uniroma1.it/apps/mienturnet/>  
 starBase: <http://starbase.sysu.edu.cn/index.php>

==END==