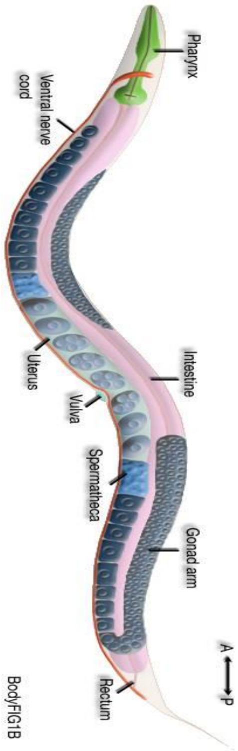
Bioinformatics Resources for microRNAs: Tools, Databases, and Platforms

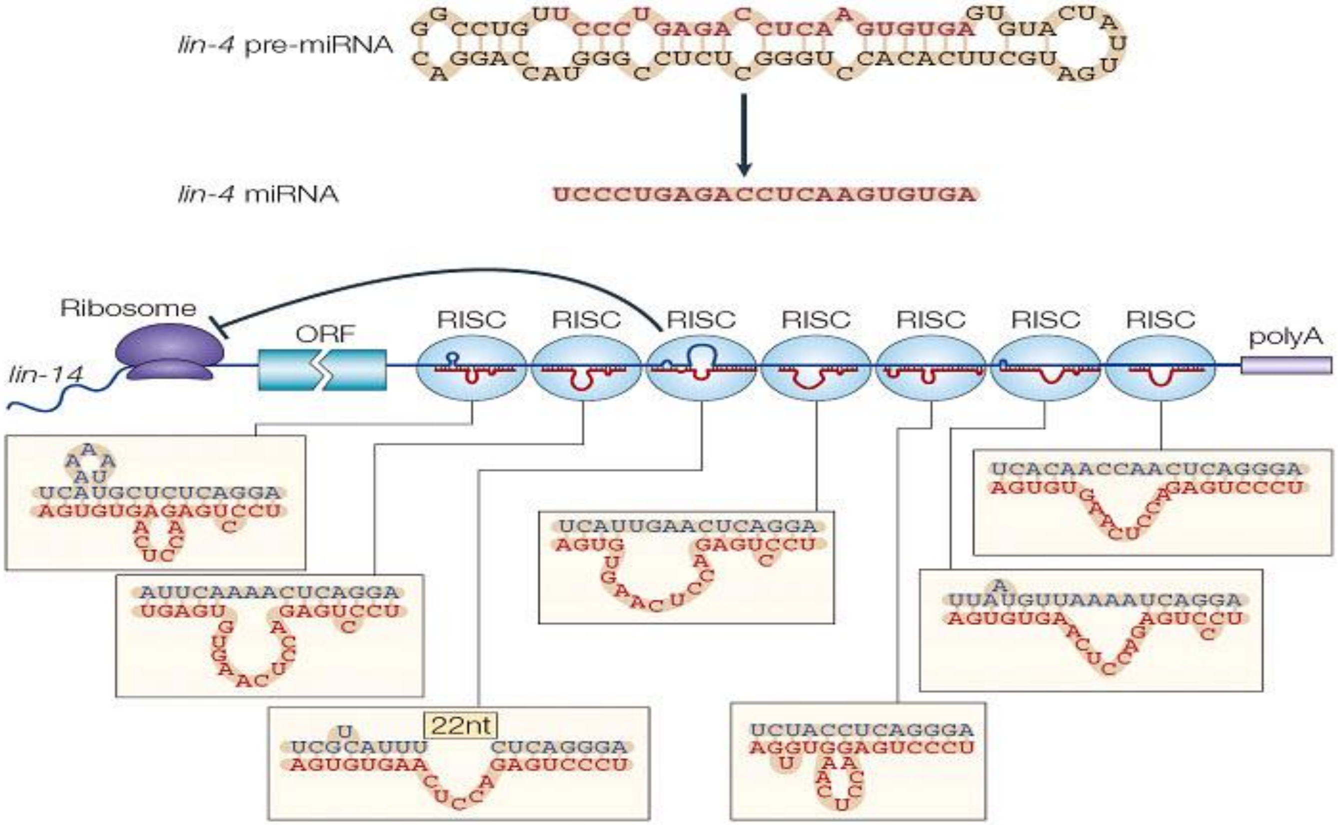
Prof. Hsien-Da Huang (黃憲達 教授) bryan@mail.nctu.edu.tw
Dr. Sheng-Da Hsu (許勝達 博士) Ken.sd.hsu@gmail.com
Chih-Hung Chou (周致宏) CHChou23@gmail.com
Integrative Systems Biology Laboratory,
Institute of Bioinformatics and Systems Biology,
Department of Biological Science and Technology,
National Chiao Tung University, Taiwan

Outline

- **Background**
  - What is microRNA?
  - miRNA functions
- **Databases for miRNAs and miRNA-target interactions**
  - miRBase
  - miRNAMap
  - miRTarBase
- **Tools for identifying miRNA-target interactions**
  - TargetScan
  - miRTar
  - microRNA.org
  - MicroCosm

The first discovered miRNA: *lin-4*

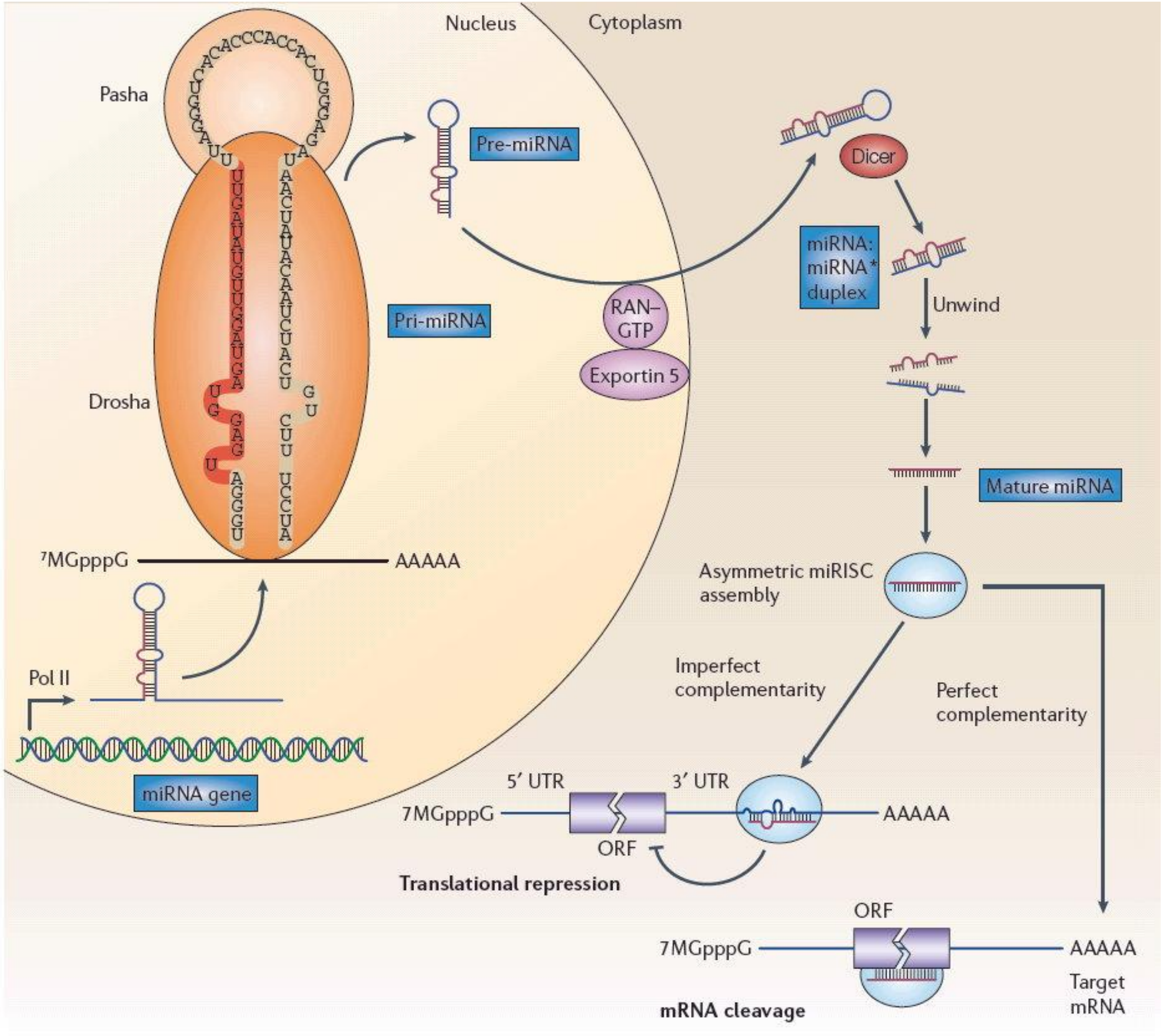




Ruvkun G, Wightman B, Ha I. The 20 years it took to recognize the importance of tiny RNAs. Cell. 2004 Jan 23;116 (2 Suppl):S93-6.

Lee R, Feinbaum R, Ambros V. A short history of a short RNA. Cell. 2004 Jan 23;116 (2 Suppl):S89-92

The biogenesis of microRNAs



(Esquela-Kerscher and Slack, 2006)

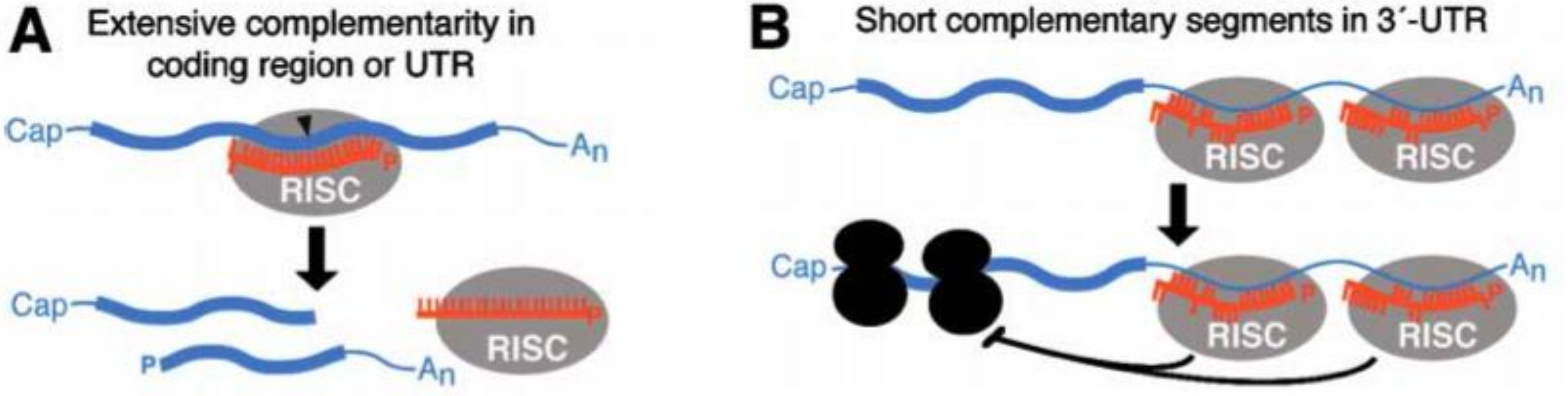
MicroRNAs:

Gene Regulation at the Post-transcriptional Level

MicroRNAs are small (17 to 25 nt.) RNA molecules which regulate gene expression by degrading mRNAs of certain genes or interfering with translational machinery of mRNAs.

mRNA Degradation

mRNA Suppression

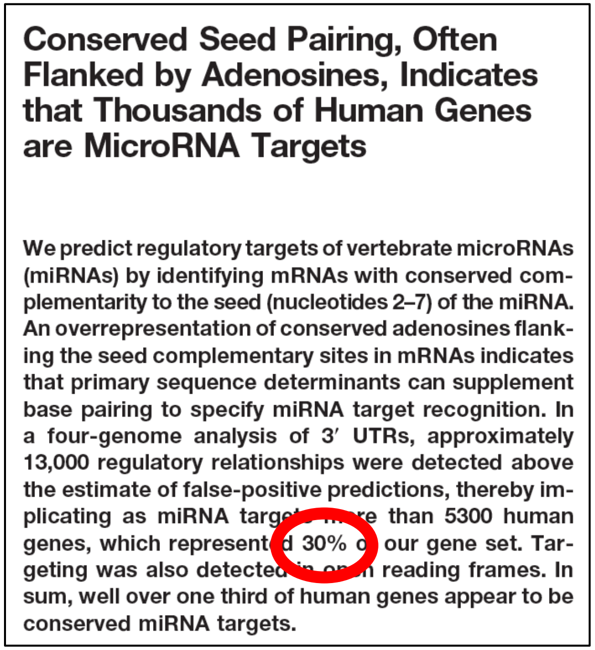


RISC - RNA induced silencing complex

UTR - untranslated region of an mRNA

Images from Bartel. (2004) Cell, Vol 116: 281-297

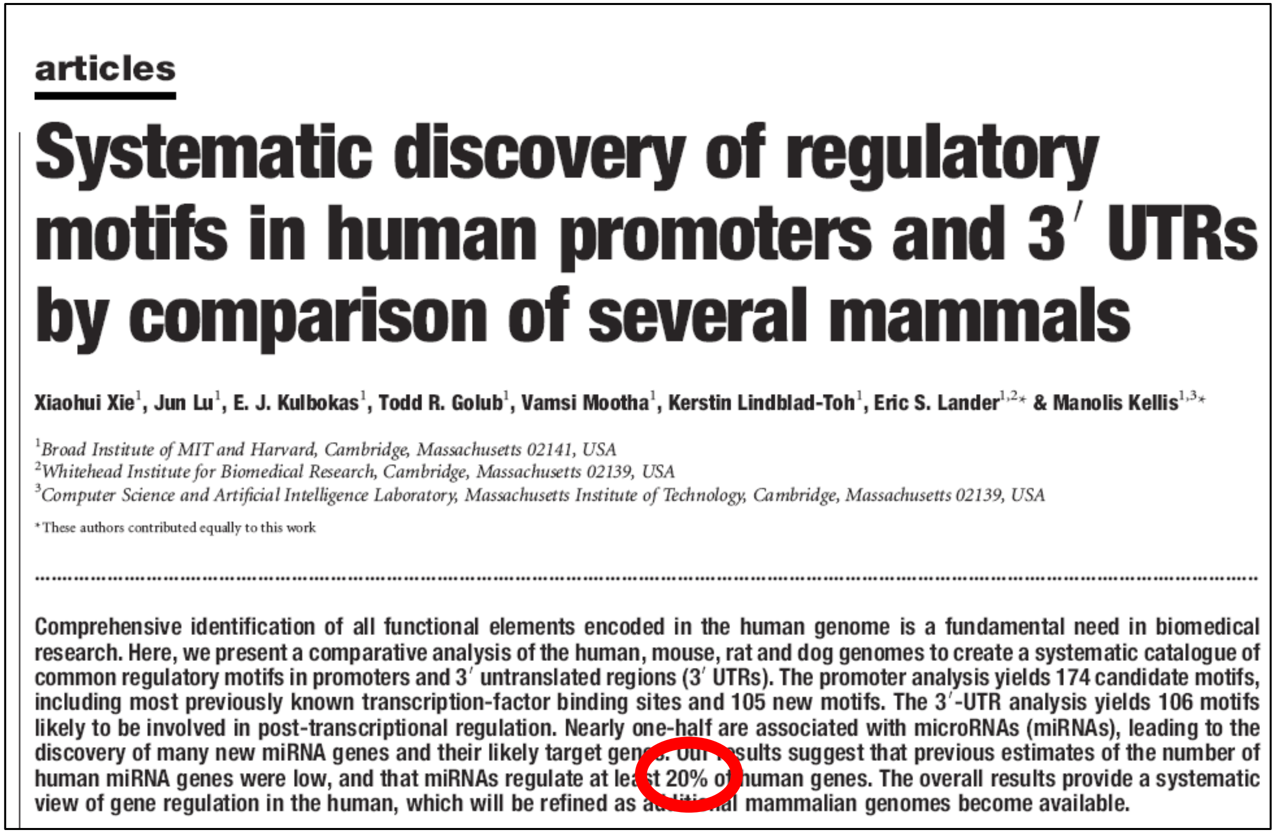
Are All RNAs Regulated by miRNAs?



Conserved Seed Pairing, Often Flanked by Adenosines, Indicates that Thousands of Human Genes are MicroRNA Targets

We predict regulatory targets of vertebrate microRNAs (miRNAs) by identifying mRNAs with conserved complementarity to the seed (nucleotides 2–7) of the miRNA. An overrepresentation of conserved adenosines flanking the seed complementary sites in mRNAs indicates that primary sequence determinants can supplement base pairing to specify miRNA target recognition. In a four-genome analysis of 3′ UTRs, approximately 13,000 regulatory relationships were detected above the estimate of false-positive predictions, thereby implicating as miRNA targets more than 5300 human genes, which represented 30% of our gene set. Targeting was also detected in open reading frames. In sum, well over one third of human genes appear to be conserved miRNA targets.

Adapter from Lewis BP et. al., ***Cell*** 2005.



articles

Systematic discovery of regulatory motifs in human promoters and 3′ UTRs by comparison of several mammals

Xiaohui Xie[1], Jun Lu[1], E. J. Kulbokas[1], Todd R. Golub[1], Vamsi Mootha[1], Kerstin Lindblad-Toh[1], Eric S. Lander[1,2]* & Manolis Kellis[1,3]*

[1] Broad Institute of MIT and Harvard, Cambridge, Massachusetts 02141, USA
[2] Whitehead Institute for Biomedical Research, Cambridge, Massachusetts 02139, USA
[3] Computer Science and Artificial Intelligence Laboratory, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, USA

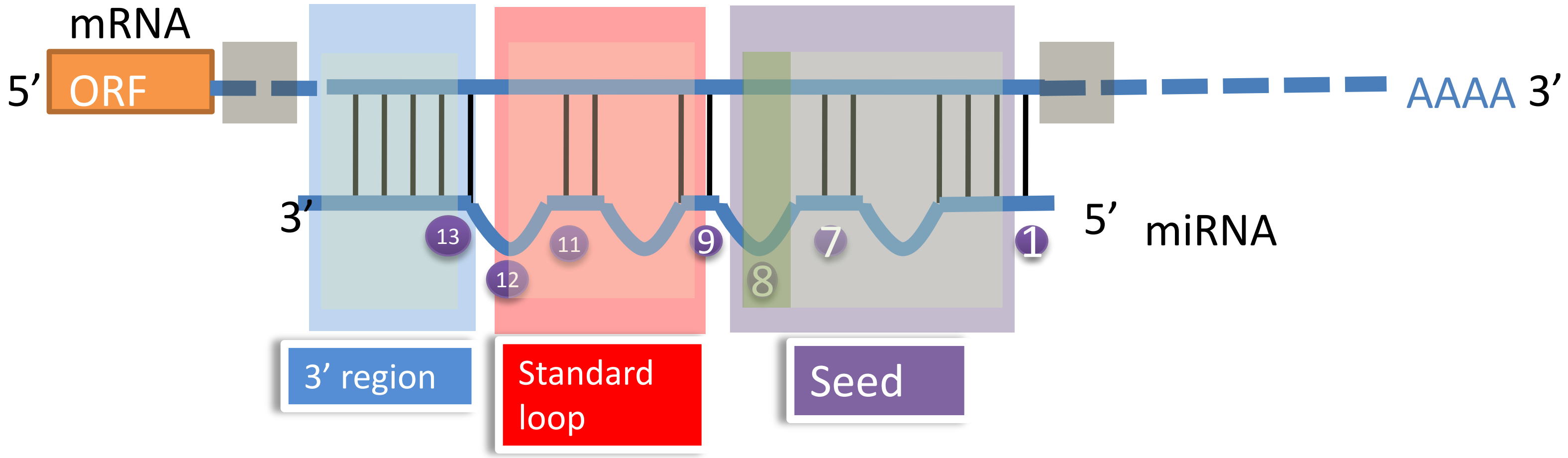
* These authors contributed equally to this work

……

Comprehensive identification of all functional elements encoded in the human genome is a fundamental need in biomedical research. Here, we present a comparative analysis of the human, mouse, rat and dog genomes to create a systematic catalogue of common regulatory motifs in promoters and 3′ untranslated regions (3′ UTRs). The promoter analysis yields 174 candidate motifs, including most previously known transcription-factor binding sites and 105 new motifs. The 3′-UTR analysis yields 106 motifs likely to be involved in post-transcriptional regulation. Nearly one-half are associated with microRNAs (miRNAs), leading to the discovery of many new miRNA genes and their likely target genes. Our results suggest that previous estimates of the number of human miRNA genes were low, and that miRNAs regulate at least 20% of human genes. The overall results provide a systematic view of gene regulation in the human, which will be refined as additional mammalian genomes become available.

Adapter from Xie X et. al., ***Nature*** 2005.

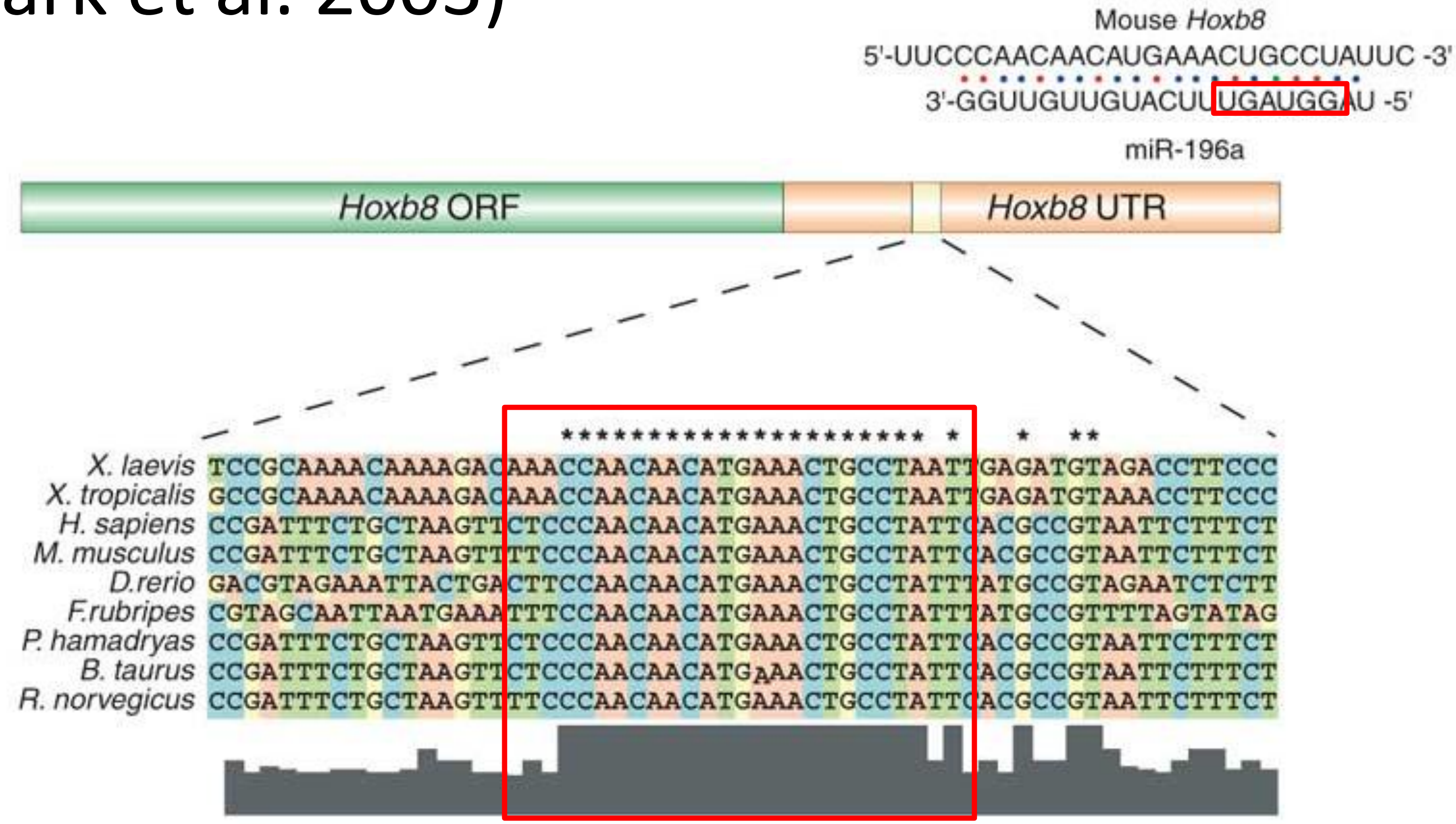
Target Prediction is often based on…



- Perfect pairing of miRNA-mRNA seed match
- Seed match conservation across different species
- Number of predicted sites for the same miRNA on a certain 3'UTR
- Thermodynamics of miRNA-target pair
- Target site accessibility

Cross Species Conserved Seed Match

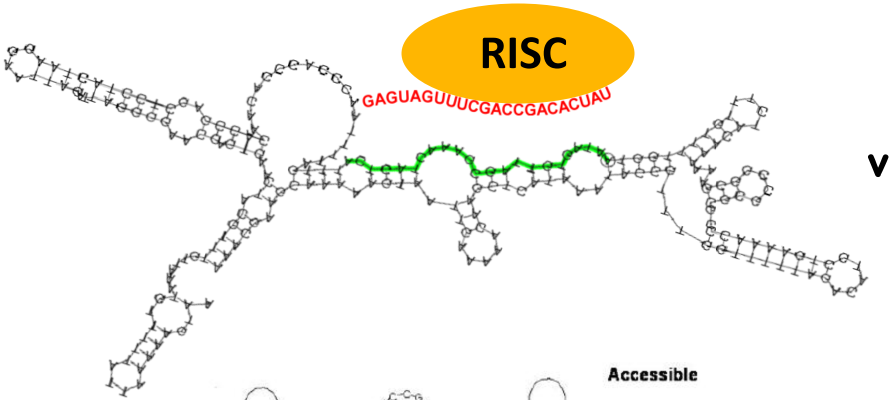
- MicroRNA targets conserve across species. (Stark et al. 2003)



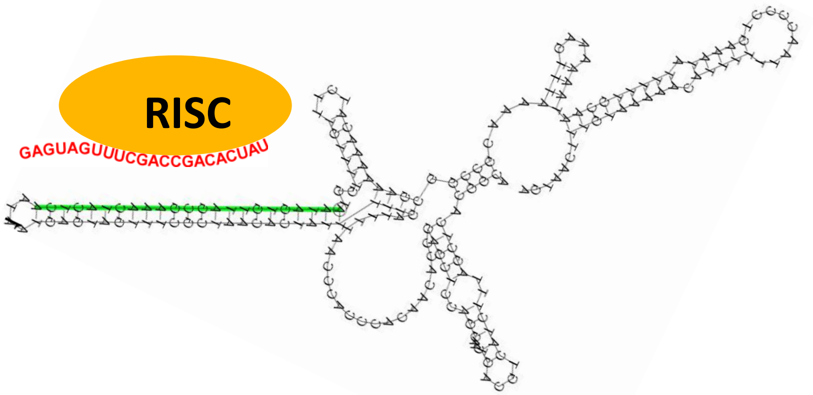
Mansfield, 2004, Nat Genet; MicroRNA-responsive 'sensor' transgenes uncover Hox-like and other developmentally regulated patterns of vertebrate microRNA expression.

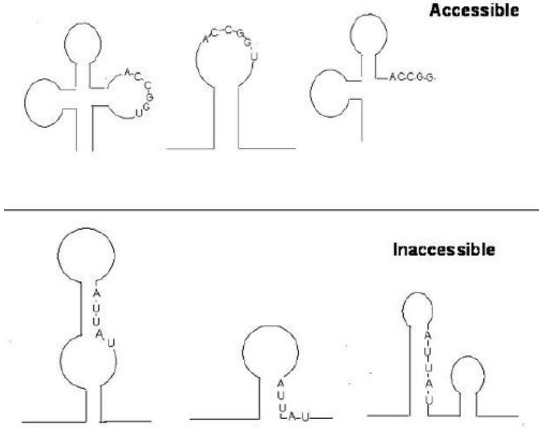
Accessibility: The Missing Component

What about target accessibility?



vs.





Incorporating mRNA UTR structure to predict microRNA targets (Robins et al. 2005)

- Make sure the predicted target "accessible".
- Not forming basing pairing its self.

What can we do with miRNAs?

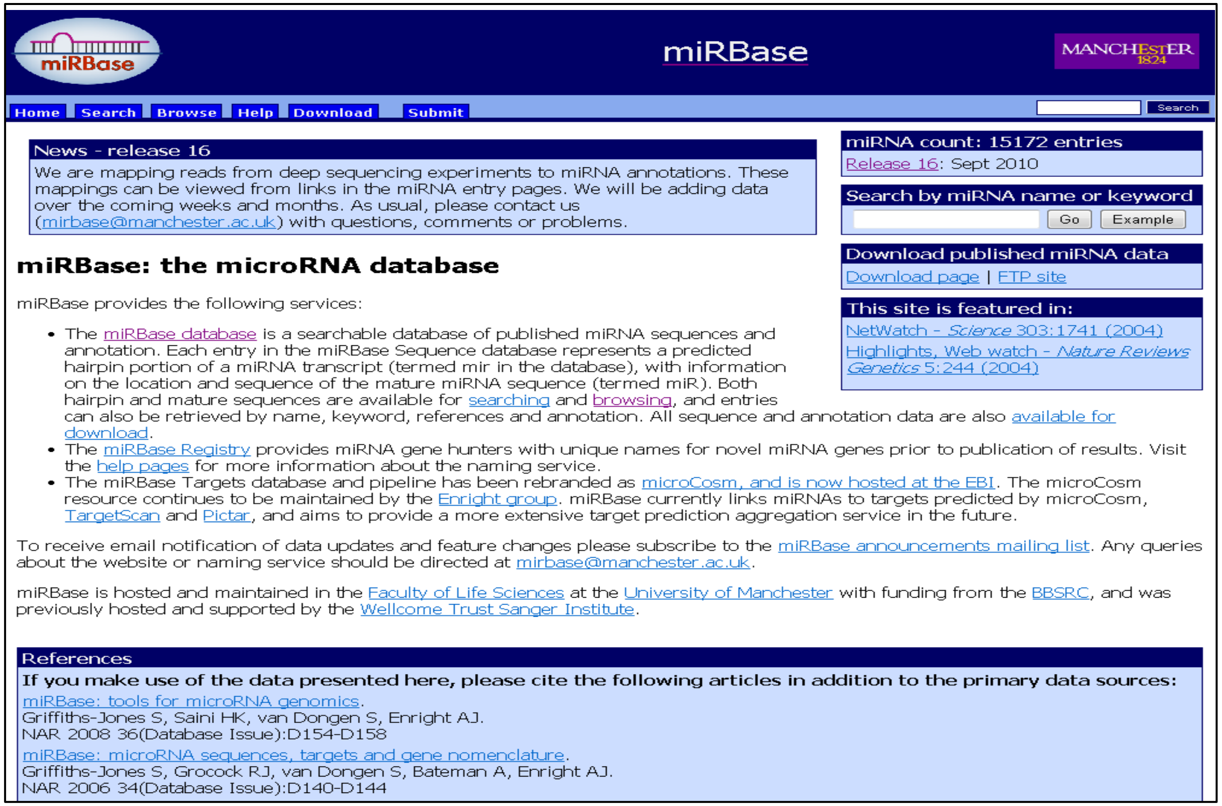
- We can look for microRNA genes
  - Is it a novel miRNA?
  - Where is my miRNA expressed?
- We can look for microRNA targets
  - Which miRNAs regulate my gene?
  - Which genes are regulated by my miRNAs?
  - Are there any common pathways affected by the same miRNA/combination of miRNAs?

Databases for miRNAs and miRNA-target interactions

- miRBase

- miRNAMap

- miRTarBase



News - release 16

We are mapping reads from deep sequencing experiments to miRNA annotations. These mappings can be viewed from links in the miRNA entry pages. We will be adding data over the coming weeks and months. As usual, please contact us (mirbase@manchester.ac.uk) with questions, comments or problems.

miRNA count: 15172 entries

Release 16: Sept 2010

Search by miRNA name or keyword

Download published miRNA data

Download page | FTP site

This site is featured in:

NetWatch - *Science* 303:1741 (2004)

Highlights, Web watch - *Nature Reviews Genetics* 5:244 (2004)

miRBase: the microRNA database

miRBase provides the following services:

- The miRBase database is a searchable database of published miRNA sequences and annotation. Each entry in the miRBase Sequence database represents a predicted hairpin portion of a miRNA transcript (termed mir in the database), with information on the location and sequence of the mature miRNA sequence (termed miR). Both hairpin and mature sequences are available for searching and browsing, and entries can also be retrieved by name, keyword, references and annotation. All sequence and annotation data are also available for download.
- The miRBase Registry provides miRNA gene hunters with unique names for novel miRNA genes prior to publication of results. Visit the help pages for more information about the naming service.
- The miRBase Targets database and pipeline has been rebranded as microCosm, and is now hosted at the EBI. The microCosm resource continues to be maintained by the Enright group. miRBase currently links miRNAs to targets predicted by microCosm, TargetScan and Pictar, and aims to provide a more extensive target prediction aggregation service in the future.

To receive email notification of data updates and feature changes please subscribe to the miRBase announcements mailing list. Any queries about the website or naming service should be directed at mirbase@manchester.ac.uk.

miRBase is hosted and maintained in the Faculty of Life Sciences at the University of Manchester with funding from the BBSRC, and was previously hosted and supported by the Wellcome Trust Sanger Institute.

References

If you make use of the data presented here, please cite the following articles in addition to the primary data sources:

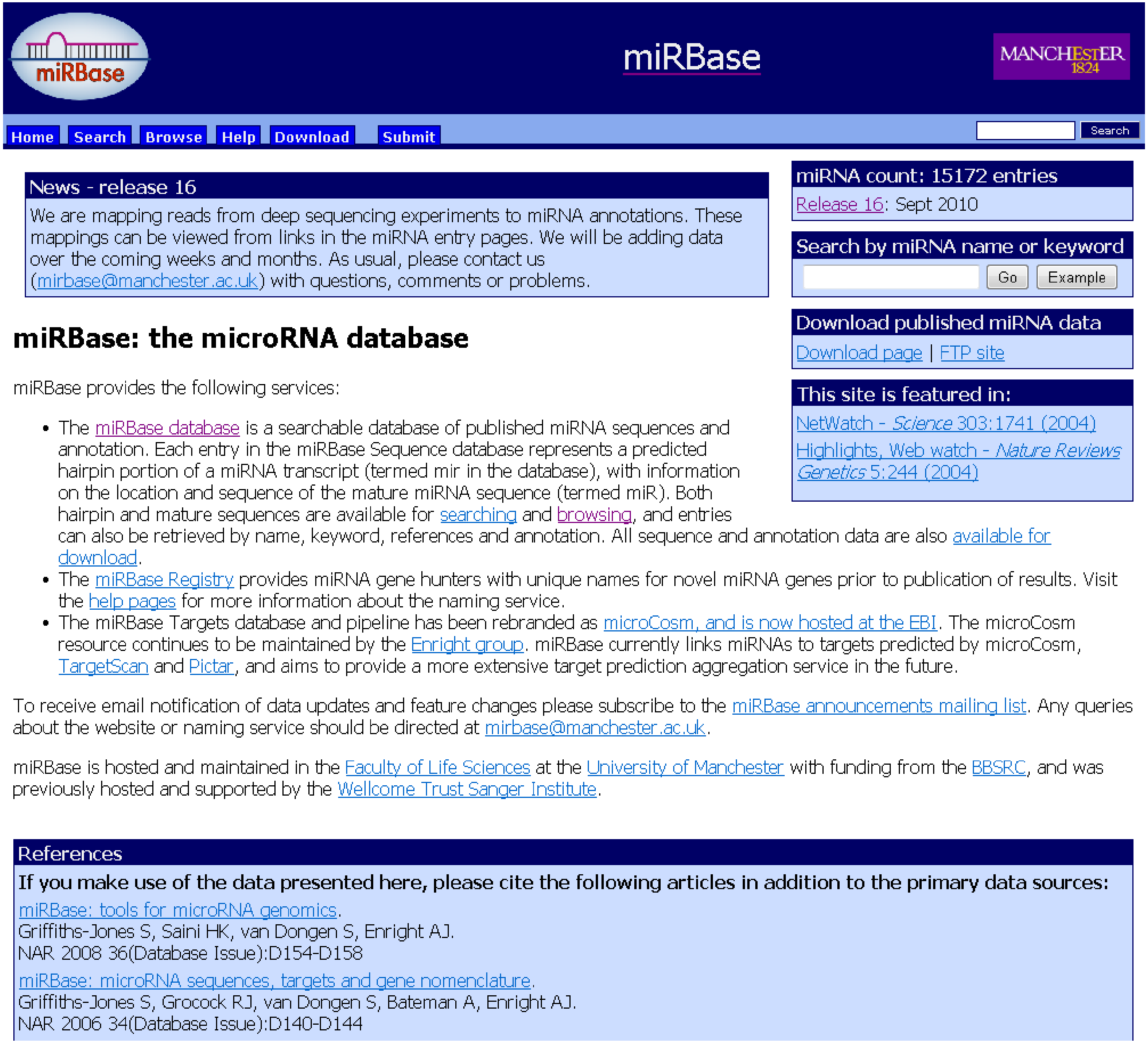
miRBase: tools for microRNA genomics.
Griffiths-Jones S, Saini HK, van Dongen S, Enright AJ.
NAR 2008 36(Database Issue):D154-D158

miRBase: microRNA sequences, targets and gene nomenclature.
Griffiths-Jones S, Grocock RJ, van Dongen S, Bateman A, Enright AJ.
NAR 2006 34(Database Issue):D140-D144

miRBase Database

The microRNA database

http://www.mirbase.org/



News - release 16

We are mapping reads from deep sequencing experiments to miRNA annotations. These mappings can be viewed from links in the miRNA entry pages. We will be adding data over the coming weeks and months. As usual, please contact us (mirbase@manchester.ac.uk) with questions, comments or problems.

miRNA count: 15172 entries

Release 16: Sept 2010

Search by miRNA name or keyword

Download published miRNA data

Download page | FTP site

This site is featured in:

NetWatch - *Science* 303:1741 (2004)

Highlights, Web watch - *Nature Reviews Genetics* 5:244 (2004)

miRBase: the microRNA database

miRBase provides the following services:

- The miRBase database is a searchable database of published miRNA sequences and annotation. Each entry in the miRBase Sequence database represents a predicted hairpin portion of a miRNA transcript (termed mir in the database), with information on the location and sequence of the mature miRNA sequence (termed miR). Both hairpin and mature sequences are available for searching and browsing, and entries can also be retrieved by name, keyword, references and annotation. All sequence and annotation data are also available for download.
- The miRBase Registry provides miRNA gene hunters with unique names for novel miRNA genes prior to publication of results. Visit the help pages for more information about the naming service.
- The miRBase Targets database and pipeline has been rebranded as microCosm, and is now hosted at the EBI. The microCosm resource continues to be maintained by the Enright group. miRBase currently links miRNAs to targets predicted by microCosm, TargetScan and Pictar, and aims to provide a more extensive target prediction aggregation service in the future.

To receive email notification of data updates and feature changes please subscribe to the miRBase announcements mailing list. Any queries about the website or naming service should be directed at mirbase@manchester.ac.uk.

miRBase is hosted and maintained in the Faculty of Life Sciences at the University of Manchester with funding from the BBSRC, and was previously hosted and supported by the Wellcome Trust Sanger Institute.

References

If you make use of the data presented here, please cite the following articles in addition to the primary data sources:

miRBase: tools for microRNA genomics.
Griffiths-Jones S, Saini HK, van Dongen S, Enright AJ.
NAR 2008 36(Database Issue):D154-D158

miRBase: microRNA sequences, targets and gene nomenclature.
Griffiths-Jones S, Grocock RJ, van Dongen S, Bateman A, Enright AJ.
NAR 2006 34(Database Issue):D140-D144

miRNA nomenclature

Pre-miRNA	Mature miRNA	Note
xxx-bantam	xxx-bantam	insect
xxx-lin-4	xxx-lin-4	nematode
xxx-mir-yyy	xxx-miR-yyy	
xxx-MIRyyy	xxx-miRyyy	Plant

xxx: abbreviations of species
yyy: three or four digital numbers and one alphabet

Pre-miRNA	Genomic location	Mature miRNA
rno-mir-103-1	chr10: 20695027-20695112 [+]	rno-miR-103, rno-miR-103-1*
rno-mir-103-2	chr3: 118996602-118996687 [+]	rno-miR-103, rno-miR-103-2*
has-let-7a-1	chr9: 96938239-96938318 [+]	hsa-let-7a-5p, hsa-let-7a-3p
hsa-let-7b	chr22: 46509566-46509648 [+]	hsa-let-7b-5p, hsa-let-7b-3p

Search page

Search miRBase

By miRNA identifier or keyword

Enter a miRNA accession, name or keyword:

By genomic location

Select organism, chromosome and start and end coordinates. Leave the start/end boxes blank to retrieve all miRNAs on the selected chromosome.

Choose species: Chr: Start: End:

For clusters

Select organism and the desired inter-miRNA distance.

Choose species: Inter-miRNA distance: 10000

By tissue expression

Select organism and tissue.

Choose species: Select tissue:

By sequence

Single sequence searches:

Paste a sequence here to search against miRNA sequences. You can choose to search against the intact precursor sequences or just the mature miRNAs. This search may take a few minutes. **(Max size 1000bp's)**

Or: Select the sequence file you wish to use

Search sequences: Mature miRNAs

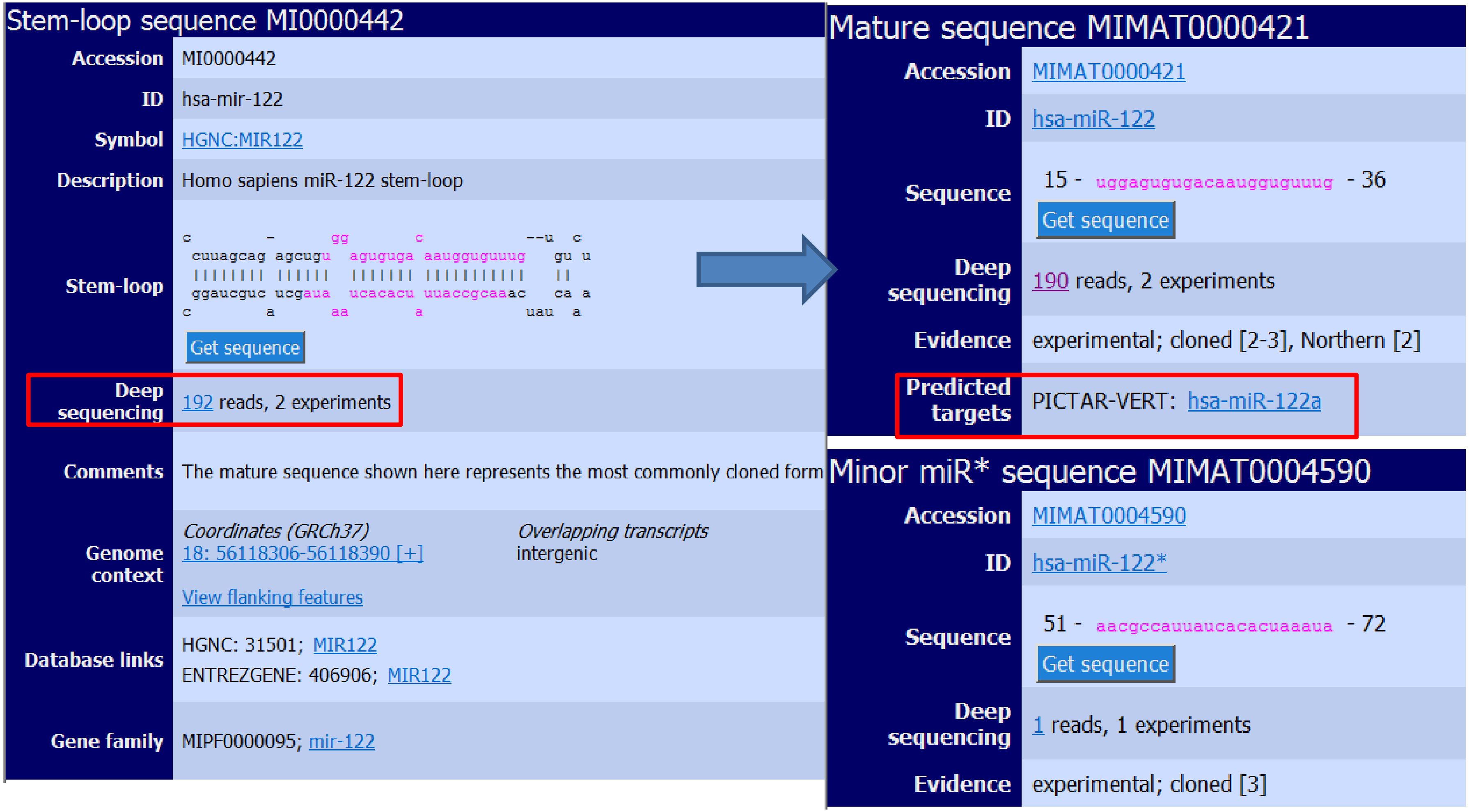
Search method: BLASTN

Choose BLASTN to search for a miRNA in a longer sequence. SSEARCH is useful for finding a short sequence within the library of miRNAs (for instance, find a short motif in a miRNA or precursor stem-loop, or find mature sequences that are related to your query).

E-value cutoff: 10

Maximum no. of hits: 100

hsa-mir-122



Stem-loop sequence MI0000442

Accession MI0000442

ID hsa-mir-122

Symbol HGNC:MIR122

Description Homo sapiens miR-122 stem-loop

Stem-loop

```
c        -      gg       c           --u  c
 cuuagcag agcugu  aguguga aaugguguuug   gu u
 |||||||| ||||||  ||||||| |||||||||||   ||
 ggaucguc ucgaua  ucacacu uuaccgcaaac   ca a
c        a      aa       a           uau  a
```

Deep sequencing 192 reads, 2 experiments

Comments The mature sequence shown here represents the most commonly cloned form

Genome context

Coordinates (GRCh37)	*Overlapping transcripts*
18: 56118306-56118390 [+]	intergenic

View flanking features

Database links

HGNC: 31501; MIR122

ENTREZGENE: 406906; MIR122

Gene family MIPF0000095; mir-122

Mature sequence MIMAT0000421

Accession MIMAT0000421

ID hsa-miR-122

Sequence 15 - uggagugugacaaugguguuug - 36

Deep sequencing 190 reads, 2 experiments

Evidence experimental; cloned [2-3], Northern [2]

Predicted targets PICTAR-VERT: hsa-miR-122a

Minor miR* sequence MIMAT0004590

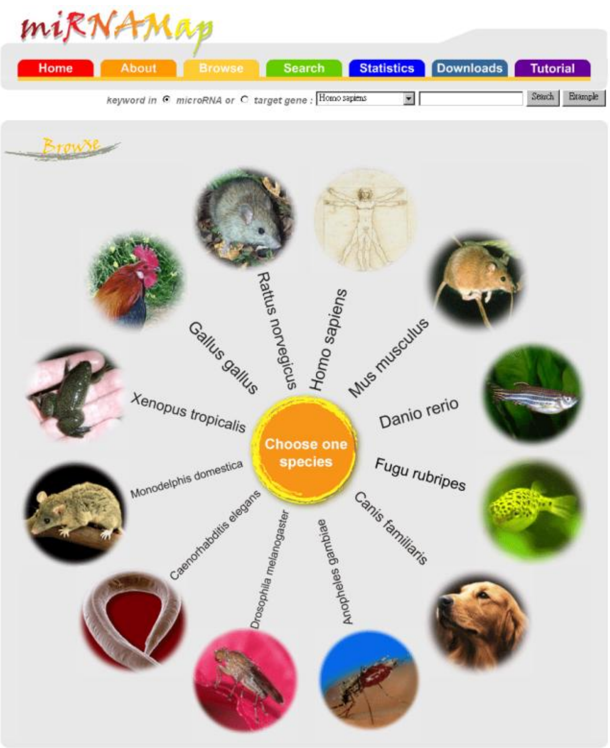
Accession MIMAT0004590

ID hsa-miR-122*

Sequence 51 - aacgccauuaucacacuaaaua - 72

Deep sequencing 1 reads, 1 experiments

Evidence experimental; cloned [3]



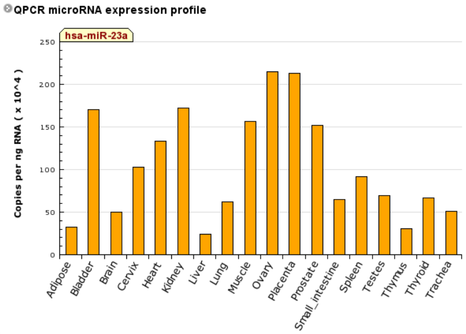
Known miRNAs

Known miRNA targets

Putative miRNA targets

miRNA expression profiles

Filtering criteria for putative miRNA targets



miRNAMap Database

Nucl Acids Res, Database Issue, 2006

Nucl Acids Res, Database Issue, 2008

An integrated resource to collect experimentally verified microRNAs and both known and putative miRNA target genes in human, mouse, rat and other metazoan genomes.

http://miRNAMap.mbc.nctu.edu.tw/

Homepage of miRNAMap 2.0

keyword in ● microRNA or ○ target gene : Homo sapiens

Welcome to miRNAMap!

What's new?

- More species
- More prediction tools
- Gene group search
- miRNA target accessibility
- faster and More comprehensive

Release 2.0 : July 2007

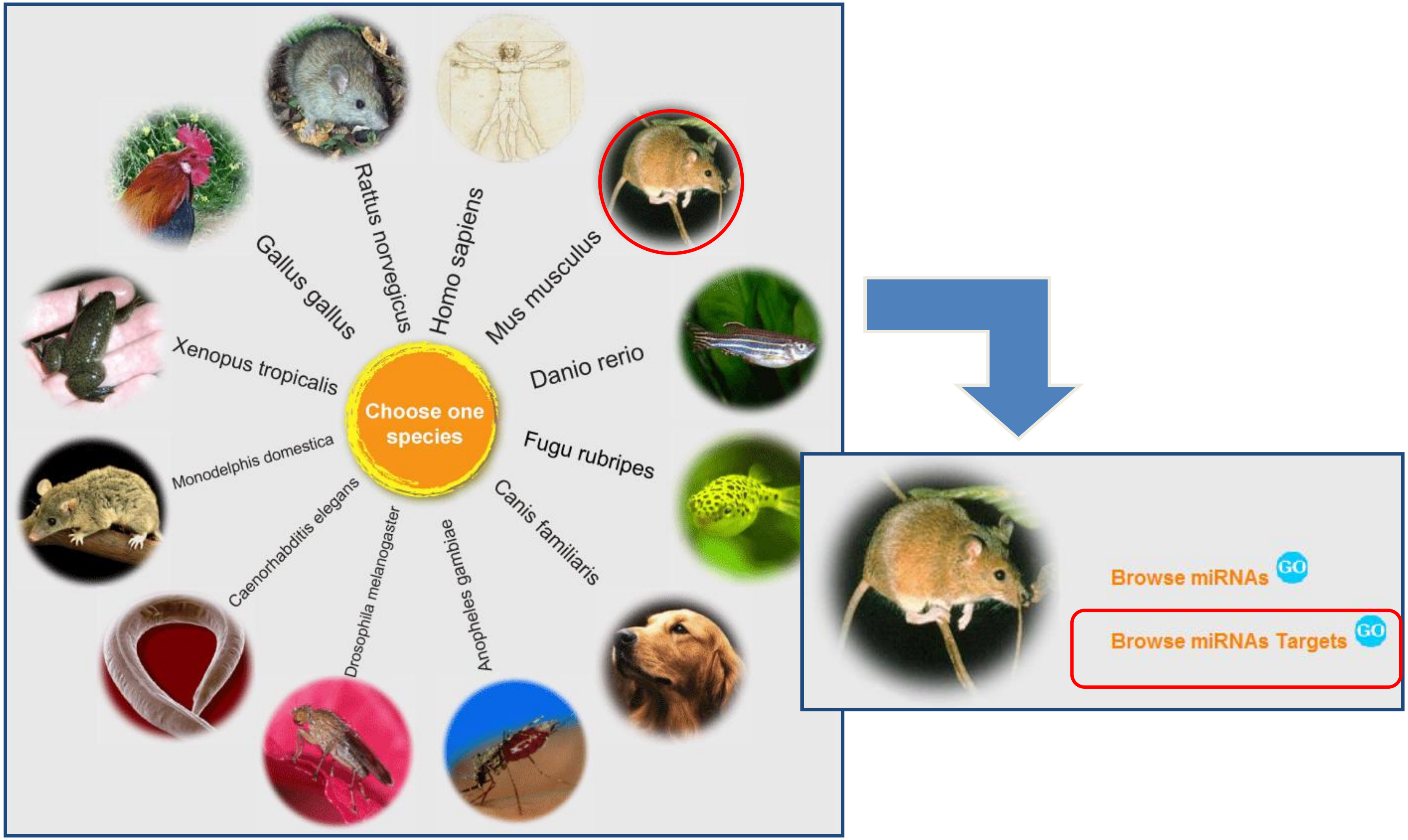
Previous version - miRNAMap 1.0

mature miRNA count:

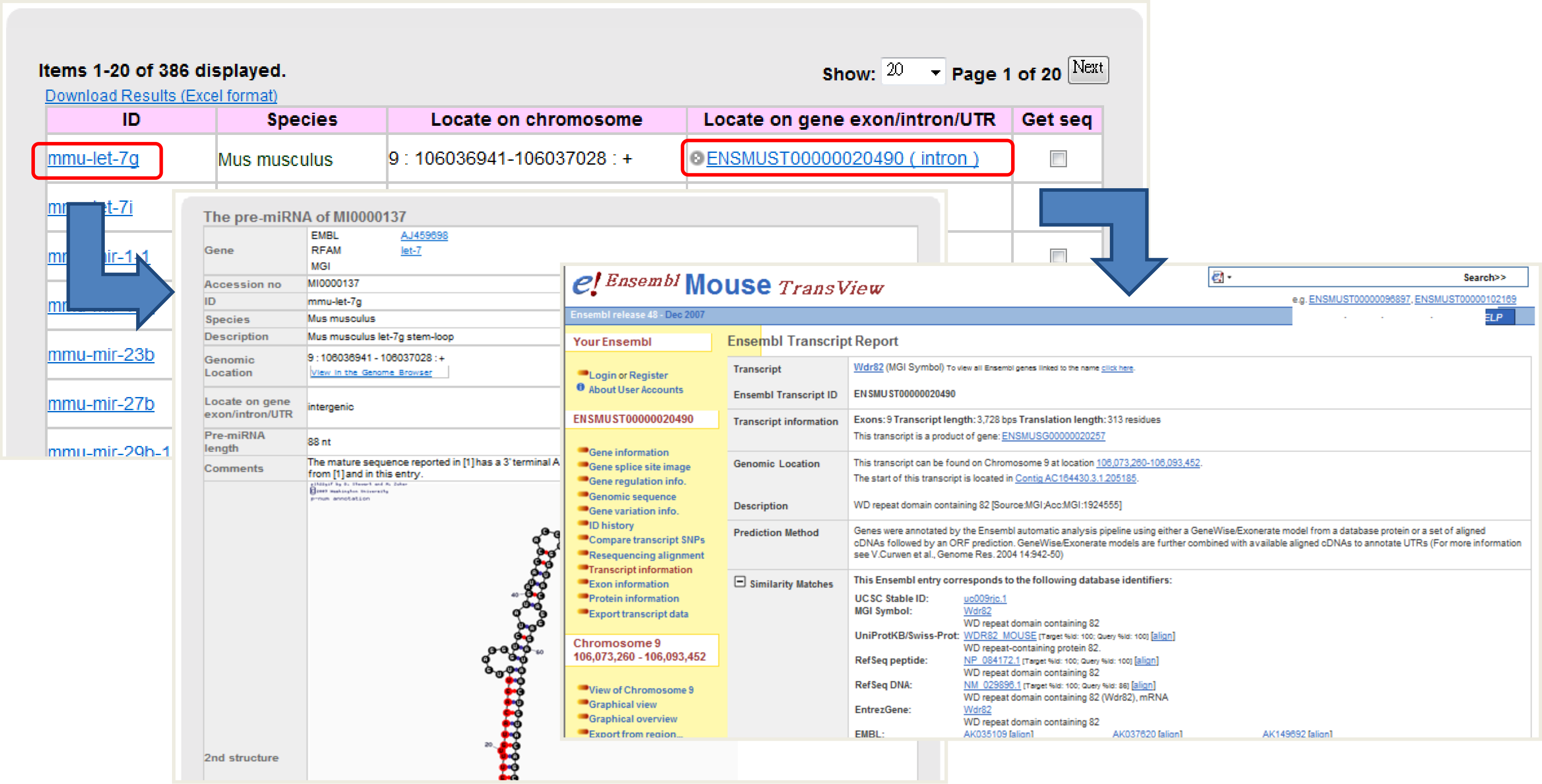
Homo sapiens	542
Mus musculus	424
Danio rerio	371
Rattus norvegicus	261
Xenopus tropicalis	196
Gallus gallus	162
Caenorhabditis elegans	135
Fugu rubripes	133
Monodelphis domestica	111
Drosophila melanogaster	85
Anopheles gambiae	38
Canis familiaris	6

Department of Biological Science and Technology,
Institute of Bioinformatics National Chiao Tung University, Hsinchu, Taiwan
Contact with: bryan@mail.NCTU.edu.tw

Web interface - Browse



Web interface - Browse



Items 1-20 of 386 displayed.

Download Results (Excel format)

ID	Species	Locate on chromosome	Locate on gene exon/intron/UTR	Get seq
mmu-let-7g	Mus musculus	9 : 106036941-106037028 : +	ENSMUST00000020490 (intron)	☐
mm t-7i				
mm ir-1-1				☐
mm				
mmu-mir-23b				
mmu-mir-27b				
mmu-mir-29b-1				

The pre-miRNA of MI0000137

Gene	EMBL AJ459698 RFAM let-7 MGI
Accession no	MI0000137
ID	mmu-let-7g
Species	Mus musculus
Description	Mus musculus let-7g stem-loop
Genomic Location	9 : 106036941 - 106037028 : + View in the Genome Browser
Locate on gene exon/intron/UTR	intergenic
Pre-miRNA length	88 nt
Comments	The mature sequence reported in [1] has a 3' terminal A from [1] and in this entry.
2nd structure	

Ensembl Mouse TransView

e.g. ENSMUST00000096897, ENSMUST00000102169

Your Ensembl

- Login or Register
- About User Accounts

ENSMUST00000020490

- Gene information
- Gene splice site image
- Gene regulation info.
- Genomic sequence
- Gene variation info.
- ID history
- Compare transcript SNPs
- Resequencing alignment
- Transcript information
- Exon information
- Protein information
- Export transcript data

Chromosome 9
106,073,260 - 106,093,452

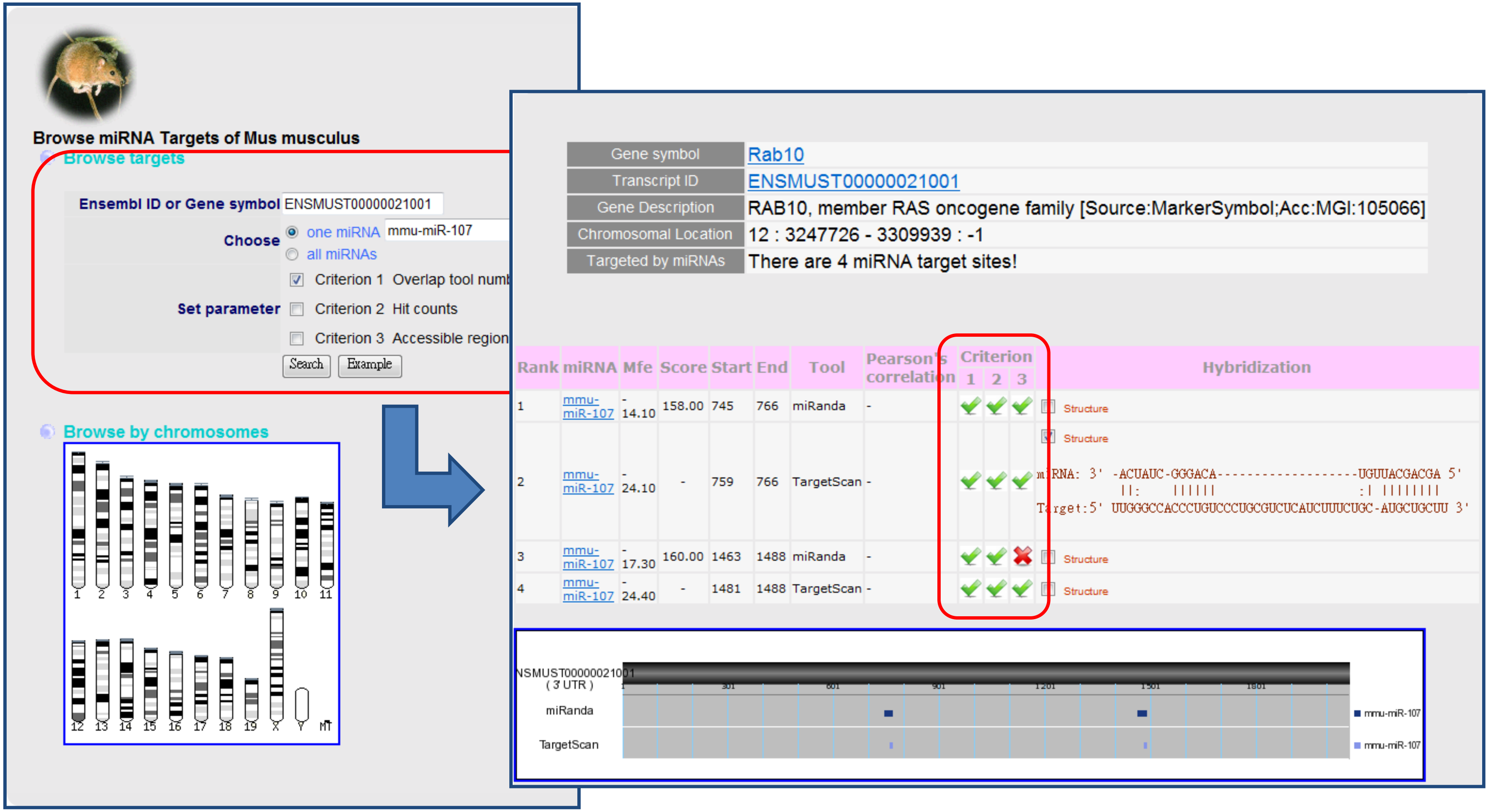
- View of Chromosome 9
- Graphical view
- Graphical overview
- Export from region...

Ensembl Transcript Report

Transcript	Wdr82 (MGI Symbol) To view all Ensembl genes linked to the name click here.
Ensembl Transcript ID	ENSMUST00000020490
Transcript information	**Exons:** 9 **Transcript length:** 3,728 bps **Translation length:** 313 residues This transcript is a product of gene: ENSMUSG00000020257
Genomic Location	This transcript can be found on Chromosome 9 at location 106,073,260-106,093,452. The start of this transcript is located in Contig AC164430.3.1.205185.
Description	WD repeat domain containing 82 [Source:MGI;Acc:MGI:1924555]
Prediction Method	Genes were annotated by the Ensembl automatic analysis pipeline using either a GeneWise/Exonerate model from a database protein or a set of aligned cDNAs followed by an ORF prediction. GeneWise/Exonerate models are further combined with available aligned cDNAs to annotate UTRs (For more information see V.Curwen et al., Genome Res. 2004 14:942-50)
⊟ Similarity Matches	**This Ensembl entry corresponds to the following database identifiers:**

UCSC Stable ID:	uc009rjc.1
MGI Symbol:	Wdr82 WD repeat domain containing 82
UniProtKB/Swiss-Prot:	WDR82_MOUSE [Target %id: 100; Query %id: 100] [align] WD repeat-containing protein 82.
RefSeq peptide:	NP_084172.1 [Target %id: 100; Query %id: 100] [align] WD repeat domain containing 82
RefSeq DNA:	NM_029896.1 [Target %id: 100; Query %id: 86] [align] WD repeat domain containing 82 (Wdr82), mRNA
EntrezGene:	Wdr82 WD repeat domain containing 82
EMBL:	AK035109 [align] AK037620 [align] AK149692 [align]

Web interface - Search



Browse miRNA Targets of Mus musculus

Browse targets

Ensembl ID or Gene symbol	ENSMUST00000021001
Choose	● one miRNA mmu-miR-107 ○ all miRNAs
Set parameter	☑ Criterion 1 Overlap tool numb ☐ Criterion 2 Hit counts ☐ Criterion 3 Accessible region

Browse by chromosomes

Gene symbol	Rab10
Transcript ID	ENSMUST00000021001
Gene Description	RAB10, member RAS oncogene family [Source:MarkerSymbol;Acc:MGI:105066]
Chromosomal Location	12 : 3247726 - 3309939 : -1
Targeted by miRNAs	There are 4 miRNA target sites!

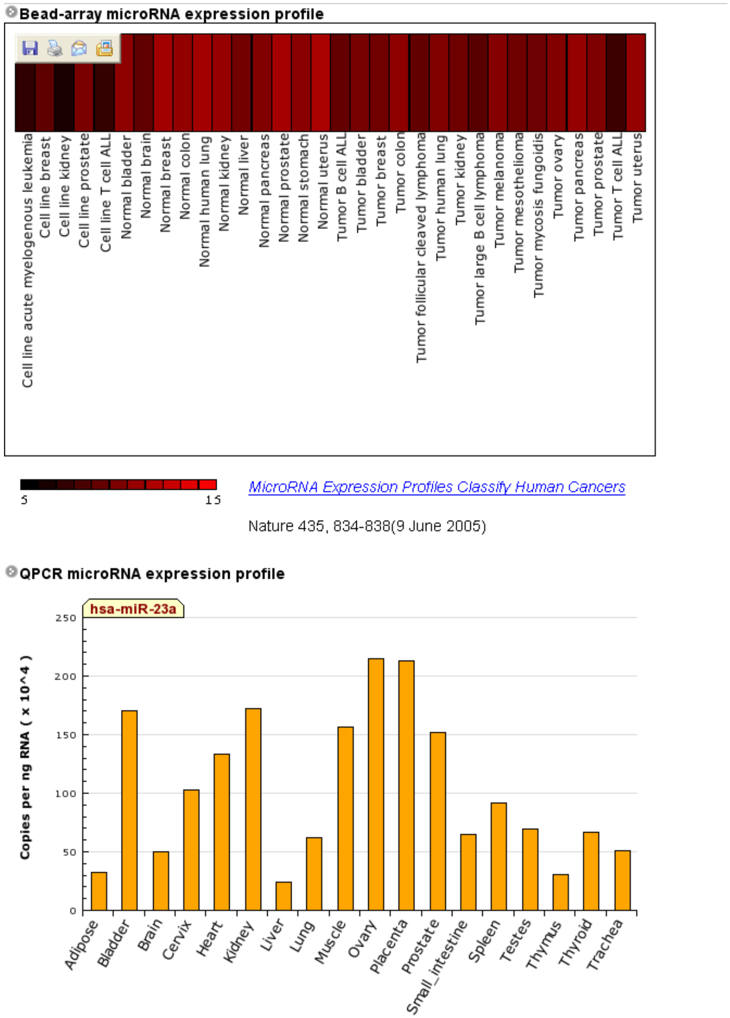
Rank	miRNA	Mfe	Score	Start	End	Tool	Pearson's correlation	Criterion 1	Criterion 2	Criterion 3	Hybridization
1	mmu-miR-107	-14.10	158.00	745	766	miRanda	-	✓	✓	✓	☐ Structure
2	mmu-miR-107	-24.10	-	759	766	TargetScan	-	✓	✓	✓	☑ Structure
3	mmu-miR-107	-17.30	160.00	1463	1488	miRanda	-	✓	✓	✗	☐ Structure
4	mmu-miR-107	-24.40	-	1481	1488	TargetScan	-	✓	✓	✓	☐ Structure

```
miRNA: 3' -ACUAUC-GGGACA-----------------UGUUACGACGA 5'
           ||:    ||||||                 :| ||||||||
Target:5' UUGGGCCACCCUGUCCCUGCGUCUCAUCUUUCUGC-AUGCUGCUU 3'
```

miRNA expression profiles

hsa-miR-23a

hsa-miR-122a (liver-specific miRNA)

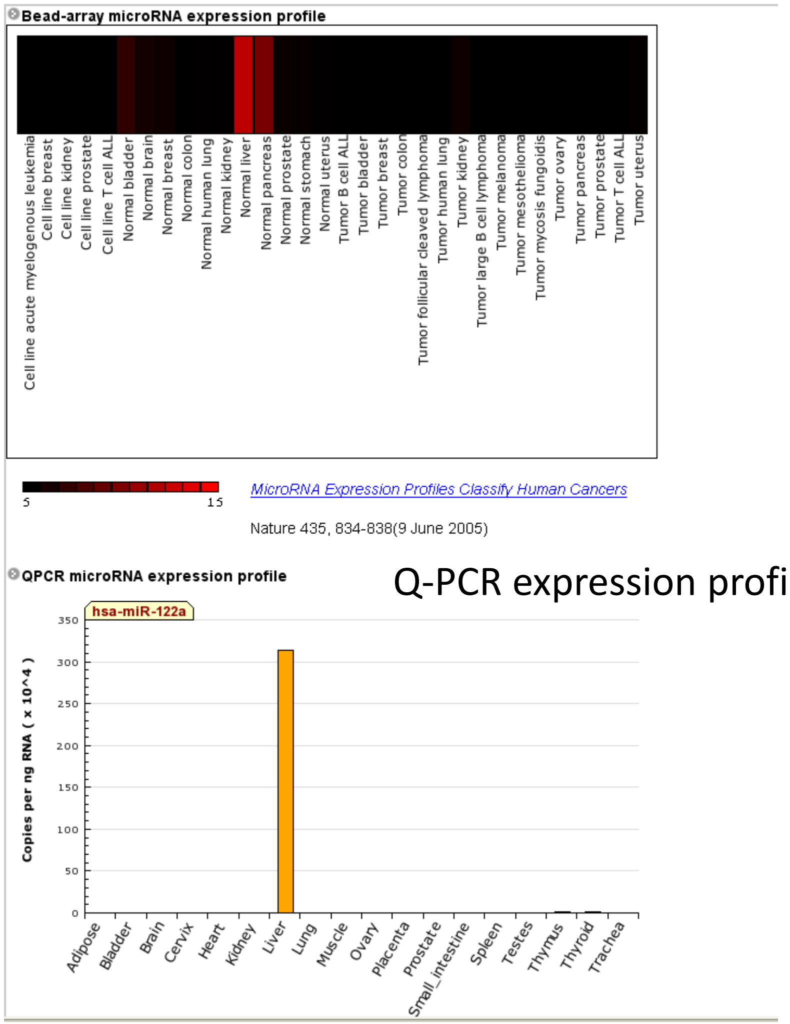


Bead-array microRNA expression profile

MicroRNA Expression Profiles Classify Human Cancers

Nature 435, 834-838(9 June 2005)

QPCR microRNA expression profile



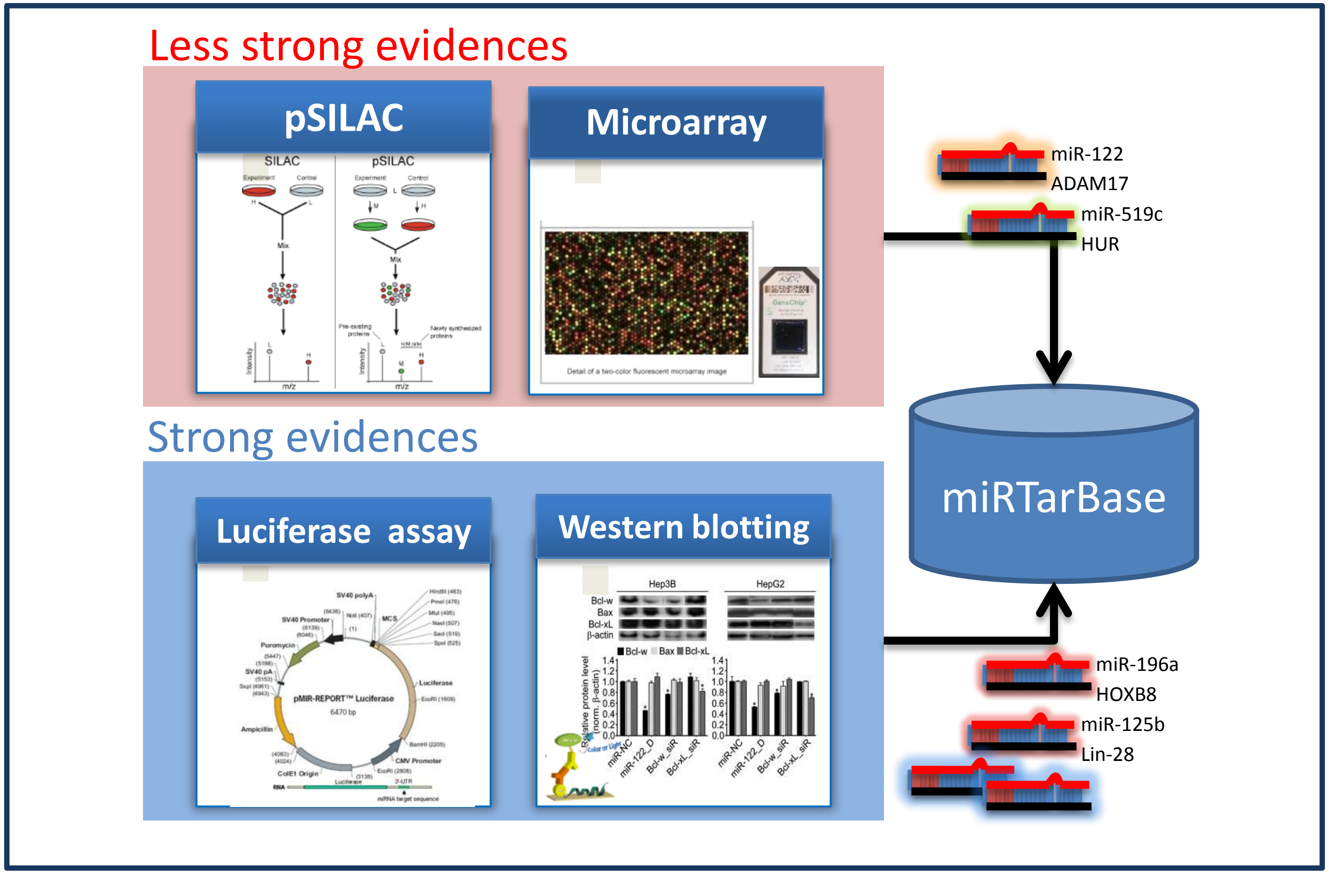
Bead-array microRNA expression profile

MicroRNA Expression Profiles Classify Human Cancers

Nature 435, 834-838(9 June 2005)

QPCR microRNA expression profile

Q-PCR expression profiles


Less strong evidences

pSILAC

Microarray

Strong evidences

Luciferase assay

Western blotting

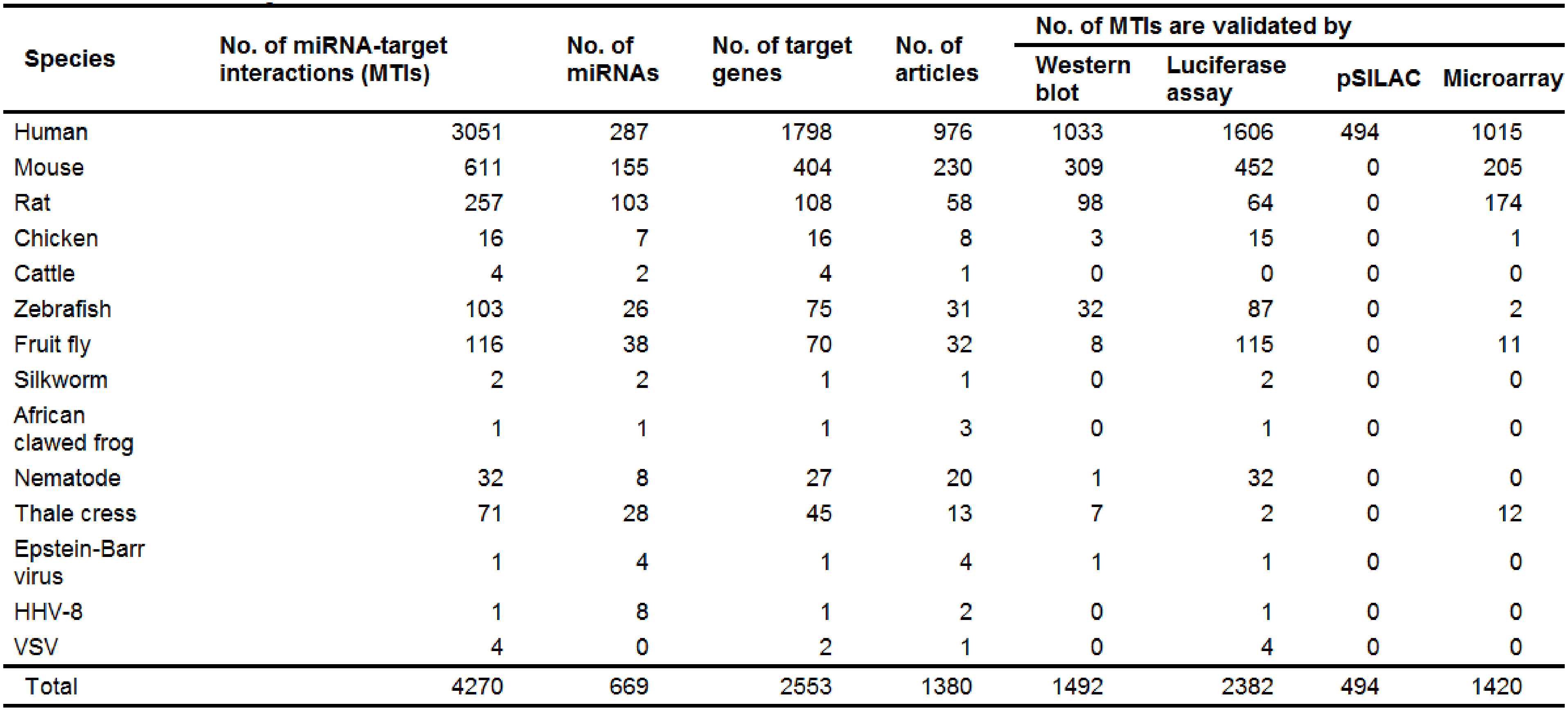
miRTarBase

miRTarBase

A database curates experimentally validated microRNA-target interactions

http://miRTarBase.mbc.nctu.edu.tw/

The statistics of miRTarBase

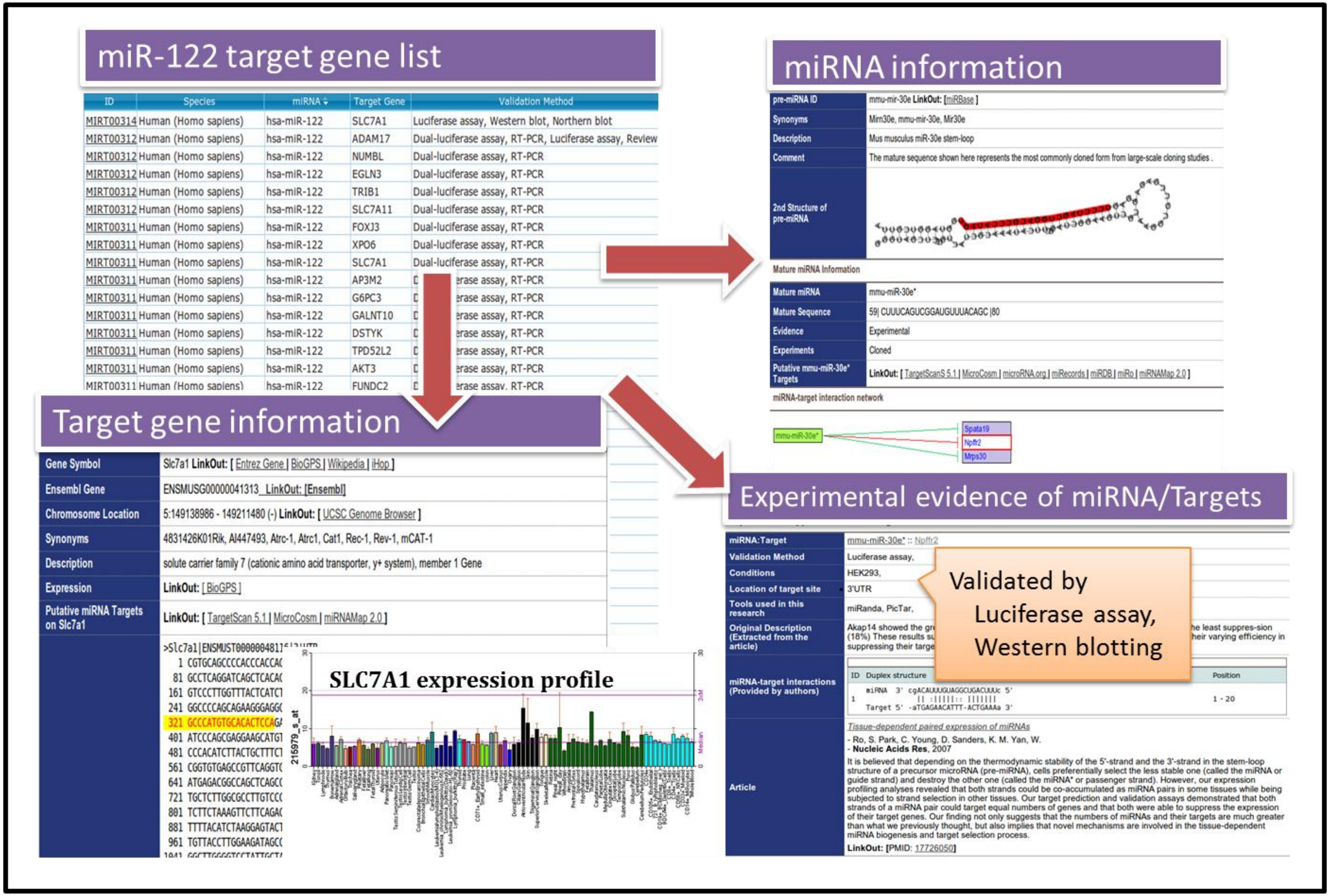


Species	No. of miRNA-target interactions (MTIs)	No. of miRNAs	No. of target genes	No. of articles	No. of MTIs are validated by			
					Western blot	Luciferase assay	pSILAC	Microarray
Human	3051	287	1798	976	1033	1606	494	1015
Mouse	611	155	404	230	309	452	0	205
Rat	257	103	108	58	98	64	0	174
Chicken	16	7	16	8	3	15	0	1
Cattle	4	2	4	1	0	0	0	0
Zebrafish	103	26	75	31	32	87	0	2
Fruit fly	116	38	70	32	8	115	0	11
Silkworm	2	2	1	1	0	2	0	0
African clawed frog	1	1	1	3	0	1	0	0
Nematode	32	8	27	20	1	32	0	0
Thale cress	71	28	45	13	7	2	0	12
Epstein-Barr virus	1	4	1	4	1	1	0	0
HHV-8	1	8	1	2	0	1	0	0
VSV	4	0	2	1	0	4	0	0
Total	4270	669	2553	1380	1492	2382	494	1420

Comparison of miRTarBase with other MTI databases

	TarBase	**miRecords**	**miR2Disease**	**miRTarBase**	**Number of records added**
Publications	RNA (2006), Nucleic Acids Res. Database Issue (2009)	Nucleic Acids Res. Database Issue (2009)	Nucleic Acids Res. Database Issue (2009)	NAR Database Issue (2011)	
Release version	V5	V1			
Last update	2008/6	2010/5/5	2010/06/02	2011/10/15	
Support species	Metazoa x 6 Viridiplantae Viruses	Metazoa x 11 Viruses x 2	Human	Metazoa x 8 Viridiplantae x 3 Viruses x 4	
Number of miRNAs	223	381*	179	657	+ 276
Number of target genes	1028	1058*	394	2297	+ 1240
Number of **articles**	155	410	430*	985	+ 564
Number of **miRNA-target interactions**	1264	1513*	635	3576	+ 2063
No. of miRNA-target interactions validated by "Luciferase reporter assay"	305*	256	0	2017	+ 1345
No. of miRNA-target interactions validated by "Western blotting"	27	290*	0	901	+ 606
No. of miRNA-target interactions validated by "Luciferase reporter assay AND Western blotting"	25	123	0	711	+ 588
No. of miRNA-target interactions validated by "Luciferase reporter assay or Western blotting"	307	636*	635	2207	+ 1460
No. of miRNA-target interactions validated by "pSILAC experiments"	455	0	0	455	+ 0
No. of miRNA-target interactions validated by "Microarray experiments"	343	380*	0	861	+ 481

Experimentally verified miR-122 targets



miR-122 target gene list

ID	Species	miRNA	Target Gene	Validation Method
MIRT00314	Human (Homo sapiens)	hsa-miR-122	SLC7A1	Luciferase assay, Western blot, Northern blot
MIRT00312	Human (Homo sapiens)	hsa-miR-122	ADAM17	Dual-luciferase assay, RT-PCR, Luciferase assay, Review
MIRT00312	Human (Homo sapiens)	hsa-miR-122	NUMBL	Dual-luciferase assay, RT-PCR
MIRT00312	Human (Homo sapiens)	hsa-miR-122	EGLN3	Dual-luciferase assay, RT-PCR
MIRT00312	Human (Homo sapiens)	hsa-miR-122	TRIB1	Dual-luciferase assay, RT-PCR
MIRT00312	Human (Homo sapiens)	hsa-miR-122	SLC7A11	Dual-luciferase assay, RT-PCR
MIRT00311	Human (Homo sapiens)	hsa-miR-122	FOXJ3	Dual-luciferase assay, RT-PCR
MIRT00311	Human (Homo sapiens)	hsa-miR-122	XPO6	Dual-luciferase assay, RT-PCR
MIRT00311	Human (Homo sapiens)	hsa-miR-122	SLC7A1	Dual-luciferase assay, RT-PCR
MIRT00311	Human (Homo sapiens)	hsa-miR-122	AP3M2	D erase assay, RT-PCR
MIRT00311	Human (Homo sapiens)	hsa-miR-122	G6PC3	D erase assay, RT-PCR
MIRT00311	Human (Homo sapiens)	hsa-miR-122	GALNT10	D erase assay, RT-PCR
MIRT00311	Human (Homo sapiens)	hsa-miR-122	DSTYK	D erase assay, RT-PCR
MIRT00311	Human (Homo sapiens)	hsa-miR-122	TPD52L2	D erase assay, RT-PCR
MIRT00311	Human (Homo sapiens)	hsa-miR-122	AKT3	D erase assay, RT-PCR
MIRT00311	Human (Homo sapiens)	hsa-miR-122	FUNDC2	D erase assay, RT-PCR

miRNA information

pre-miRNA ID	mmu-mir-30e **LinkOut:** [miRBase]
Synonyms	Mirn30e, mmu-mir-30e, Mir30e
Description	Mus musculus miR-30e stem-loop
Comment	The mature sequence shown here represents the most commonly cloned form from large-scale cloning studies .
2nd Structure of pre-miRNA	

Mature miRNA Information

Mature miRNA	mmu-miR-30e*
Mature Sequence	59| CUUUCAGUCGGAUGUUUACAGC |80
Evidence	Experimental
Experiments	Cloned
Putative mmu-miR-30e* Targets	**LinkOut:** [TargetScanS 5.1 | MicroCosm | microRNA.org | miRecords | miRDB | miRo | miRNAMap 2.0]

miRNA-target interaction network

Target gene information

Gene Symbol	Slc7a1 **LinkOut:** [Entrez Gene | BioGPS | Wikipedia | iHop]
Ensembl Gene	ENSMUSG00000041313 **LinkOut: [Ensembl]**
Chromosome Location	5:149138986 - 149211480 (-) **LinkOut:** [UCSC Genome Browser]
Synonyms	4831426K01Rik, AI447493, Atrc-1, Atrc1, Cat1, Rec-1, Rev-1, mCAT-1
Description	solute carrier family 7 (cationic amino acid transporter, y+ system), member 1 Gene
Expression	**LinkOut:** [BioGPS]
Putative miRNA Targets on Slc7a1	**LinkOut:** [TargetScan 5.1 | MicroCosm | miRNAMap 2.0]

```
>Slc7a1|ENSMUST00000048115
   1 CGTGCAGCCCCACCCACCAC
  81 GCCTCAGGATCAGCTCACAC
 161 GTCCCTTGGTTTACTCATCT
 241 GGCCCCAGCAGAAGGGAGGC
 321 GCCCATGTGCACACTCCAGA
 401 ATCCCAGCGAGGAAGCATGT
 481 CCCACATCTTACTGCTTTCT
 561 CGGTGTGAGCCGTTCAGGTC
 641 ATGAGACGGCCAGCTCAGCC
 721 TGCTCTTGGCGCCTTGTCCC
 801 TCTTCTAAAGTTCTTCAGAC
 881 TTTTACATCTAAGGAGTACT
 961 TGTTACCTTGGAAGATAGCC
```

SLC7A1 expression profile

Experimental evidence of miRNA/Targets

miRNA:Target	mmu-miR-30e* :: Npffr2
Validation Method	Luciferase assay,
Conditions	HEK293,
Location of target site	3'UTR
Tools used in this research	miRanda, PicTar,
Original Description (Extracted from the article)	Akap14 showed the gr he least suppres-sion (18%) These results su heir varying efficiency in suppressing their targe
miRNA-target interactions (Provided by authors)	ID: 1 Duplex structure: miRNA 3' cgACAUUUGUAGGCUGACUUUc 5' / || :|||||:: ||||||| / Target 5' -aTGAGAACATTT-ACTGAAAa 3' Position: 1 - 20
Article	*Tissue-dependent paired expression of miRNAs* - Ro, S. Park, C. Young, D. Sanders, K. M. Yan, W. - **Nucleic Acids Res**, 2007 It is believed that depending on the thermodynamic stability of the 5'-strand and the 3'-strand in the stem-loop structure of a precursor microRNA (pre-miRNA), cells preferentially select the less stable one (called the miRNA or guide strand) and destroy the other one (called the miRNA* or passenger strand). However, our expression profiling analyses revealed that both strands could be co-accumulated as miRNA pairs in some tissues while being subjected to strand selection in other tissues. Our target prediction and validation assays demonstrated that both strands of a miRNA pair could target equal numbers of genes and that both were able to suppress the expression of their target genes. Our finding not only suggests that the numbers of miRNAs and their targets are much greater than what we previously thought, but also implies that novel mechanisms are involved in the tissue-dependent miRNA biogenesis and target selection process. **LinkOut:** [PMID: 17726050]

Validated by
Luciferase assay,
Western blotting

Tools for identifying miRNA-target interactions

-TargetScan
-miRTar
-microRNA.org
-MicroCosm

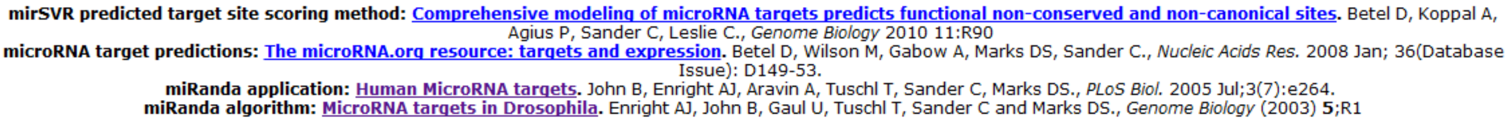
Tools for miRNA-Target Prediction

Total cited

miRanda (microRNA.org)

cited

1378



mirSVR predicted target site scoring method: Comprehensive modeling of microRNA targets predicts functional non-conserved and non-canonical sites. Betel D, Koppal A, Agius P, Sander C, Leslie C., *Genome Biology* 2010 11:R90

microRNA target predictions: The microRNA.org resource: targets and expression. Betel D, Wilson M, Gabow A, Marks DS, Sander C., *Nucleic Acids Res.* 2008 Jan; 36(Database Issue): D149-53.

miRanda application: Human MicroRNA targets. John B, Enright AJ, Aravin A, Tuschl T, Sander C, Marks DS., *PLoS Biol.* 2005 Jul;3(7):e264.

miRanda algorithm: MicroRNA targets in Drosophila. Enright AJ, John B, Gaul U, Tuschl T, Sander C and Marks DS., *Genome Biology* (2003) **5**;R1

35

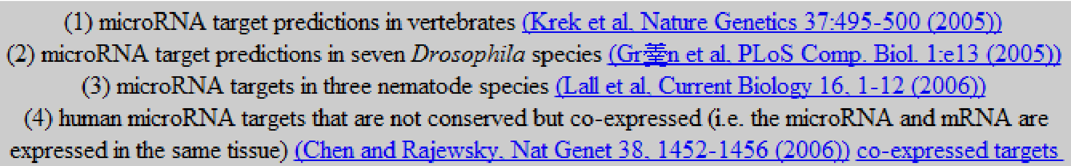
260

721

362

PicTar

1881



(1) microRNA target predictions in vertebrates (Krek et al. Nature Genetics 37:495-500 (2005))

(2) microRNA target predictions in seven *Drosophila* species (Gr菫n et al. PLoS Comp. Biol. 1:e13 (2005))

(3) microRNA targets in three nematode species (Lall et al. Current Biology 16, 1-12 (2006))

(4) human microRNA targets that are not conserved but co-expressed (i.e. the microRNA and mRNA are expressed in the same tissue) (Chen and Rajewsky, Nat Genet 38, 1452-1456 (2006)) co-expressed targets

1371

186

175

149

TargetScan

4178

References:

1) Conserved Seed Pairing, Often Flanked by Adenosines, Indicates that Thousands of Human Genes are MicroRNA Targets
Benjamin P Lewis, Christopher B Burge, David P Bartel. ***Cell***, 120:15-20 (2005).

2) Most Mammalian mRNAs Are Conserved Targets of MicroRNAs
Robin C Friedman, Kyle Kai-How Farh, Christopher B Burge, David P Bartel. ***Genome Research***, 19:92-105 (2009).

3) MicroRNA Targeting Specificity in Mammals: Determinants beyond Seed Pairing
Andrew Grimson, Kyle Kai-How Farh, Wendy K Johnston, Philip Garrett-Engele, Lee P Lim, David P Bartel. ***Molecular Cell***, 27:91-105 (2007).

4) Weak Seed-Pairing Stability and High Target-Site Abundance Decrease the Proficiency of lsy-6 and Other miRNAs
David M García, Daehyun Baek, Chanseok Shin, George W Bell, Andrew Grimson, David P Bartel ***Nat Struct Mol Biol.***, 18:1139-1146 (2011).

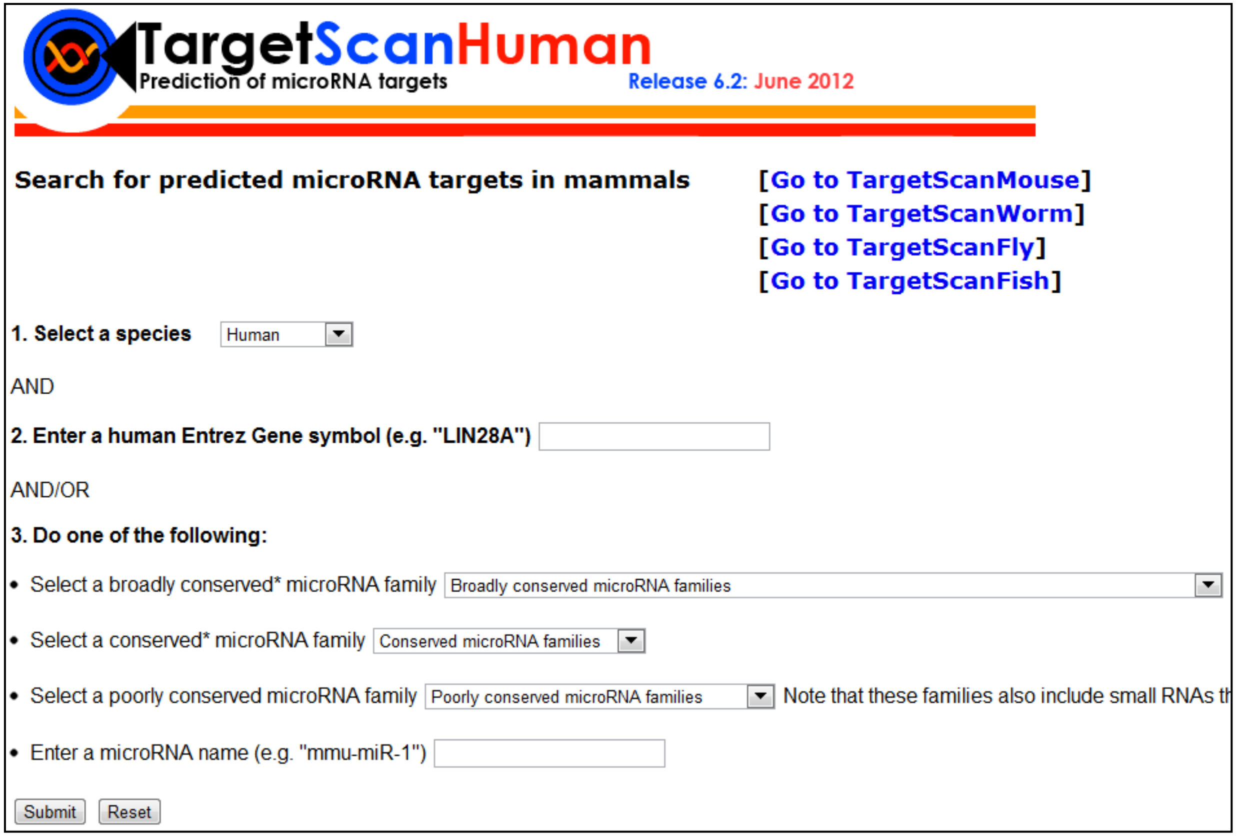
2627

693

865

2

Statistic from ***Web of Science***, 2012.6



TargetScanHuman

Prediction of microRNA targets

Release 6.2: June 2012

Search for predicted microRNA targets in mammals

[Go to TargetScanMouse]
[Go to TargetScanWorm]
[Go to TargetScanFly]
[Go to TargetScanFish]

1. Select a species Human ▼

AND

2. Enter a human Entrez Gene symbol (e.g. "LIN28A")

AND/OR

3. Do one of the following:

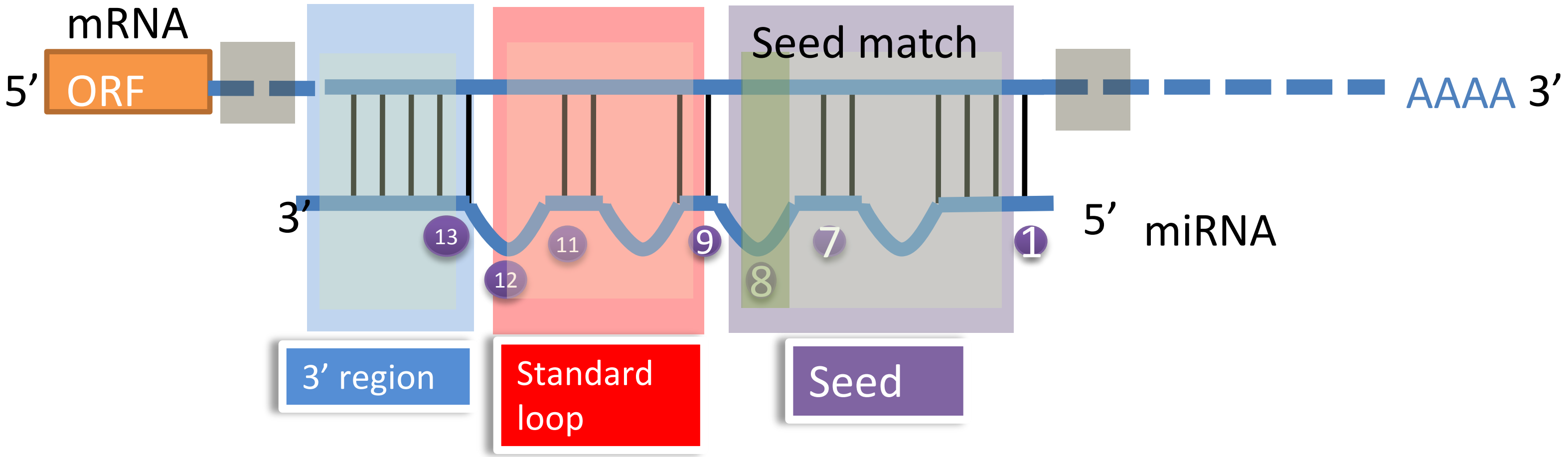
- Select a broadly conserved* microRNA family Broadly conserved microRNA families ▼
- Select a conserved* microRNA family Conserved microRNA families ▼
- Select a poorly conserved microRNA family Poorly conserved microRNA families ▼ Note that these families also include small RNAs t
- Enter a microRNA name (e.g. "mmu-miR-1")

TargetScan

Prediction of microRNA targets

http://www.targetscan.org/

MicroRNA Target Prediction



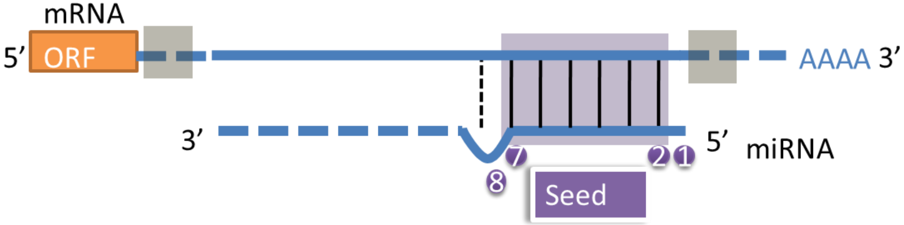
- Perfect pairing of miRNA-mRNA seed match (2-8mer).
- Thermodynamic stability of miRNA::mRNA regulation element duplex.
- Conserved miRNA targets.
- Target site accessibility.
- Order of target proficiency in different mRNA region is that:
  - 3'UTR > ORF >> 5'UTR.

TargetScan: Context+ scores

- Seed-type contribution
  - 8mer >> 7mer-m8 > 7mer-A1 >> 6mer > no site.
- 3' pairing contribution
  - additional Watson-Crick pairing at nucleotides 12–17 enhances miRNA targeting.
- Local AU contribution
  - Out of seed region is prefect AU rich sequence.
- Position contribution
  - two ends of long UTRs generally were more effective than those near the center.
- TA and SPS contribution
  - TA: **t**arget-site **a**bundance ↓
  - SPS: **s**eed-**p**airing **s**tability (Nearest-neighbor method) ↑
- Context+ score is sum of these contribution.

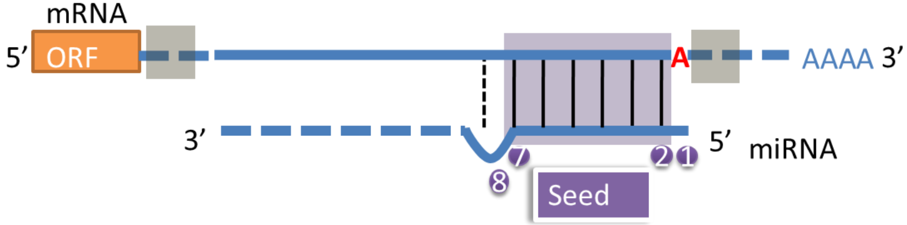
Seed-type contribution

6mer



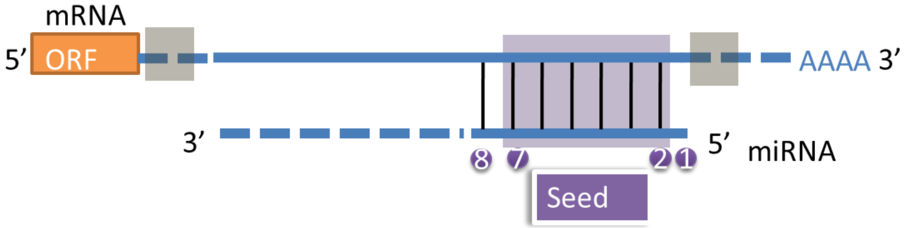
2 to 7 mer perfect match

7mer-A1



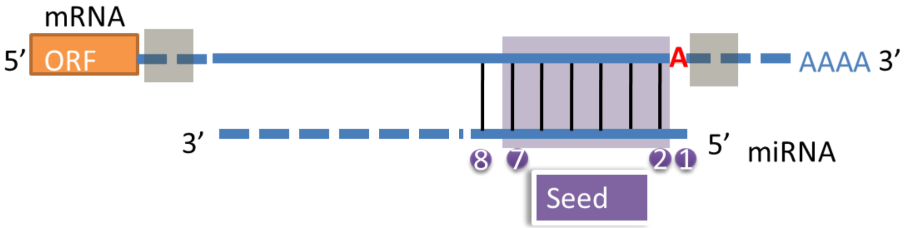
2 to 7 mer perfect match and position 1 in mRNA must be nucleotide A

7mer-m8



2 to 8 mer perfect match

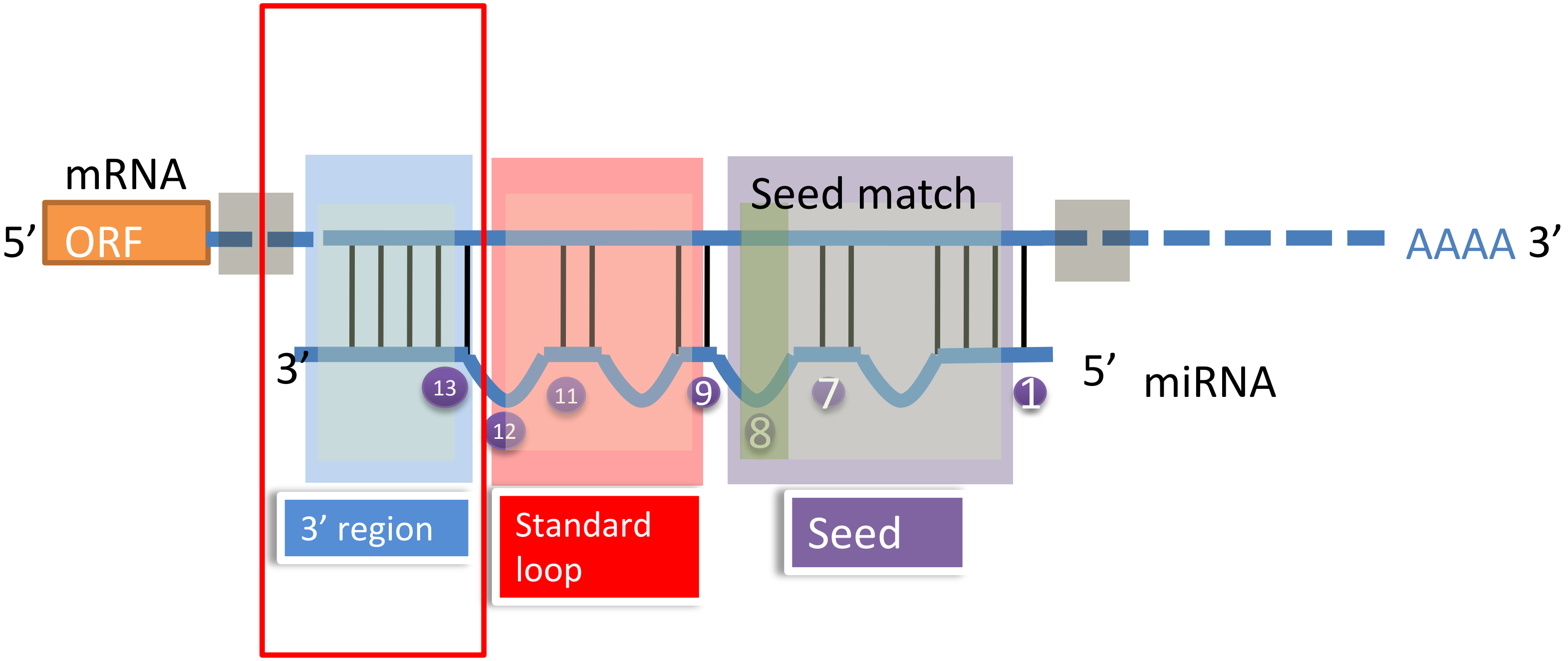
8mer



2 to 8 mer perfect match and position 1 in mRNA must be nucleotide A

8mer >> 7mer-m8 > 7mer-A1 >> 6mer > no site.

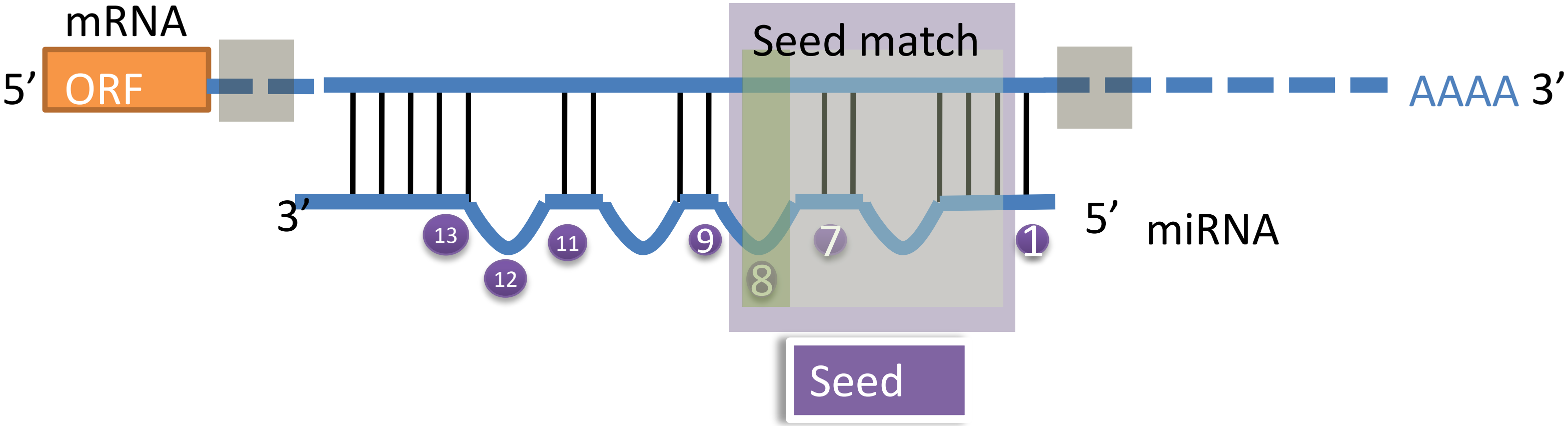
3' pairing contribution



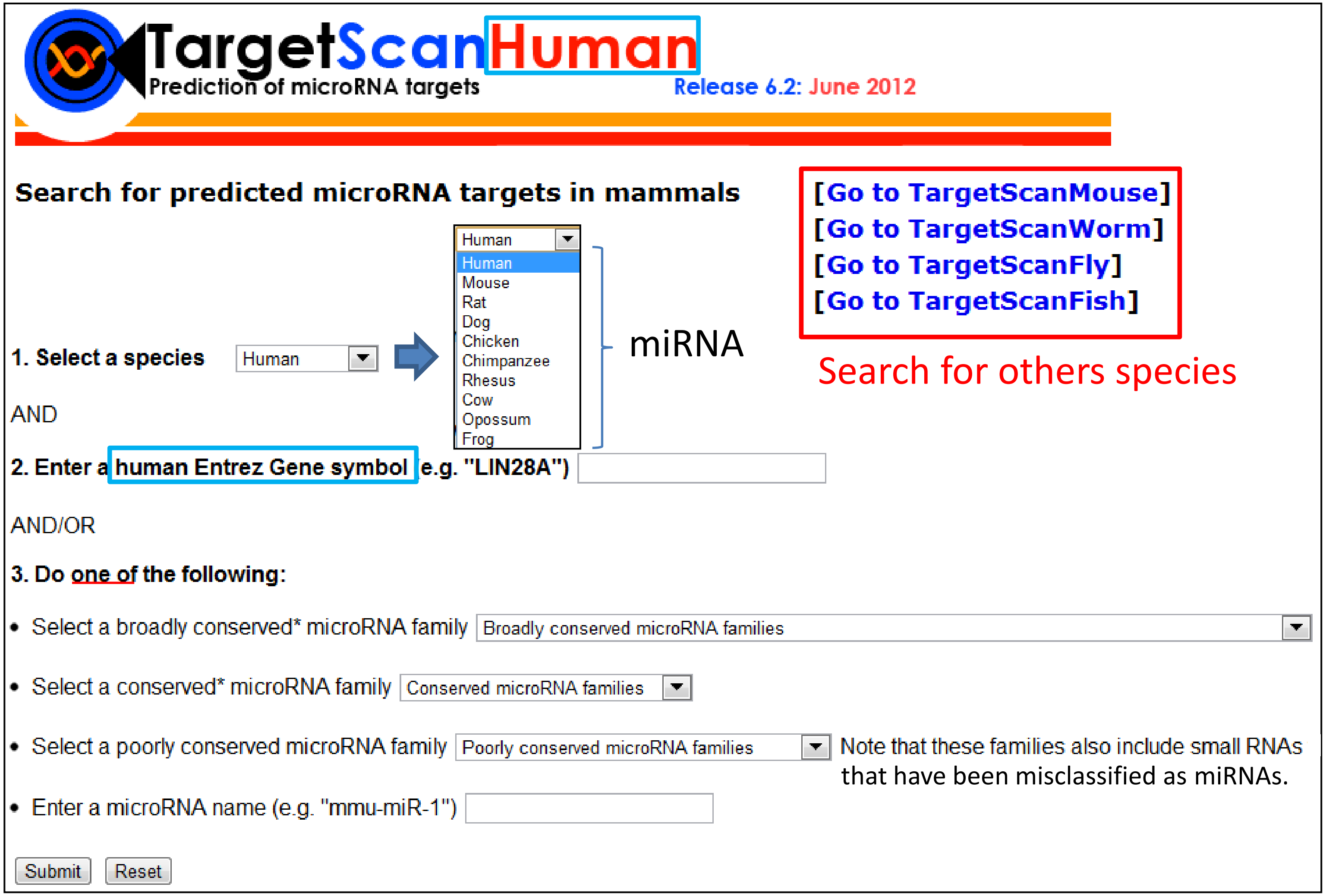
additional Watson-Crick pairing at nucleotides 12–17 enhances miRNA targeting

Local AU & Position contribution

- Local AU contribution
  - Out of seed region is prefer AU rich sequence.
- Position contribution
  - Two ends of long UTRs generally were more effective than those near the center.



TargetScan web interface



TargetScanHuman
Prediction of microRNA targets
Release 6.2: June 2012

Search for predicted microRNA targets in mammals

[Go to TargetScanMouse]
[Go to TargetScanWorm]
[Go to TargetScanFly]
[Go to TargetScanFish]

Search for others species

1. Select a species: Human

miRNA

AND

2. Enter a human Entrez Gene symbol (e.g. "LIN28A")

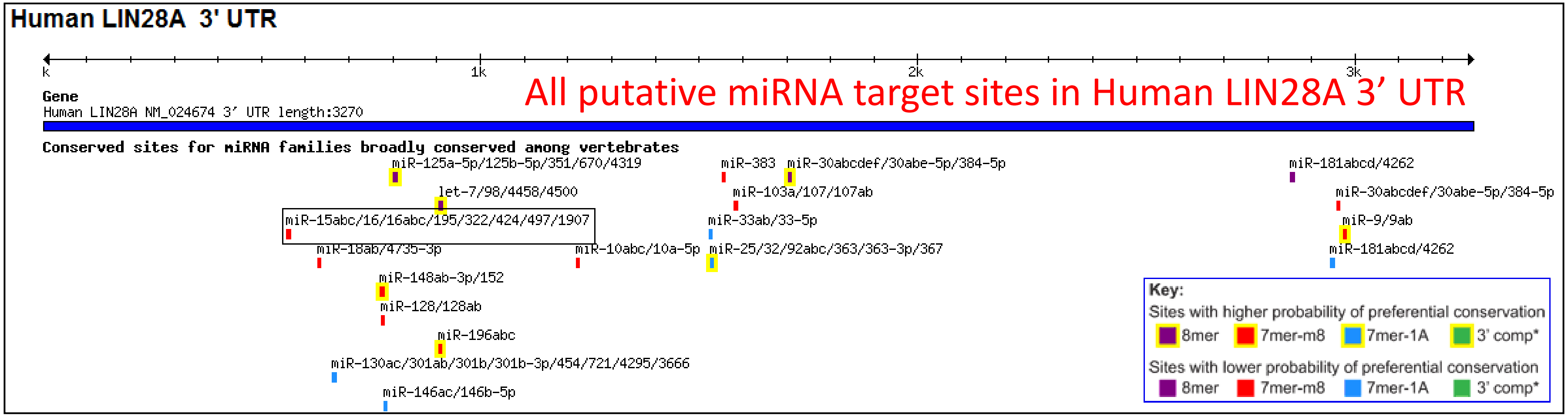
AND/OR

3. Do one of the following:

- Select a broadly conserved* microRNA family: Broadly conserved microRNA families
- Select a conserved* microRNA family: Conserved microRNA families
- Select a poorly conserved microRNA family: Poorly conserved microRNA families. Note that these families also include small RNAs that have been misclassified as miRNAs.
- Enter a microRNA name (e.g. "mmu-miR-1")

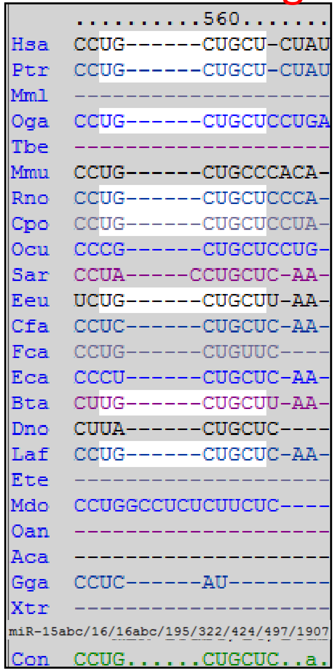
broadly conserved = conserved across most vertebrates, usually to zebrafish.
conserved = conserved across most mammals, but usually not beyond placental mammals.

TargetScan search results



All putative miRNA target sites in Human LIN28A 3’ UTR

Conserved Target sites in different species

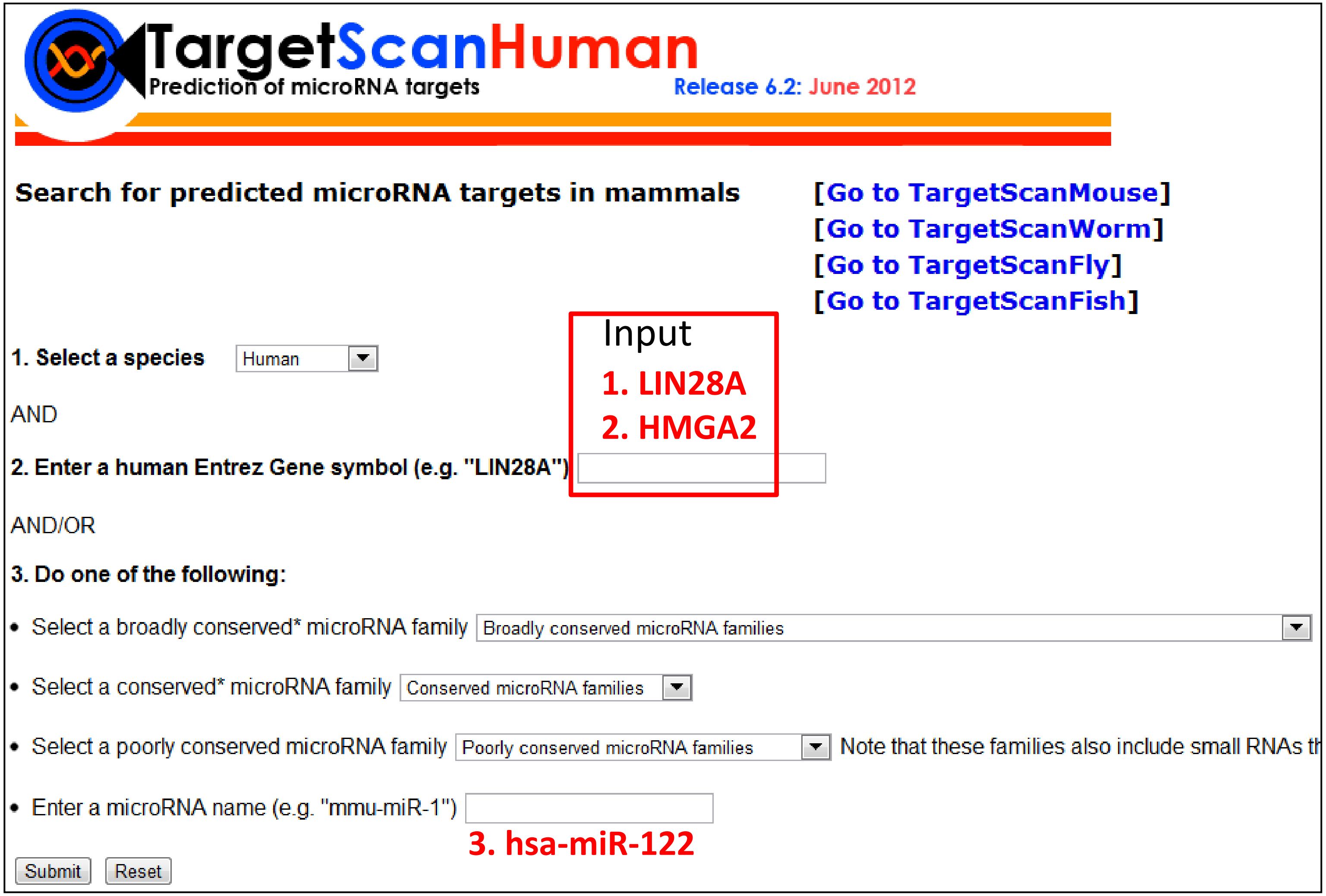


```
          ..........560.......
Hsa   CCUG------CUGCU-CUAU
Ptr   CCUG------CUGCU-CUAU
Mml   --------------------
Oga   CCUG------CUGCUCCUGA
Tbe   --------------------
Mmu   CCUG------CUGCCCACA-
Rno   CCUG------CUGCUCCCA-
Cpo   CCUG------CUGCUCCUA-
Ocu   CCCG------CUGCUCCUG-
Sar   CCUA-----CCUGCUC-AA-
Eeu   UCUG------CUGCUU-AA-
Cfa   CCUC------CUGCUC-AA-
Fca   CCUG------CUGUUC----
Eca   CCCU------CUGCUC-AA-
Bta   CUUG------CUGCUU-AA-
Dno   CUUA------CUGCUC----
Laf   CCUG------CUGCUC-AA-
Ete   --------------------
Mdo   CCUGGCCUCUCUUCUC----
Oan   --------------------
Aca   --------------------
Gga   CCUC------AU--------
Xtr   --------------------
miR-15abc/16/16abc/195/322/424/497/1907
Con   CCUG......CUGCUC..a.
```

Target prediction rank and others parameter

	predicted consequential pairing of target region (top) and miRNA (bottom)	seed match	site-type contri-bution	3' pairing contri-bution	local AU contri-bution	position contri-bution	TA contribution	SPS contribution	context+ score	context+ score percentile	conserved branch length	PCT
Position 558-564 of LIN28A 3' UTR hsa-miR-424	5' ...GAACAGCUGCAGACCUGCUGCUC... ||||||| 3' AAGUUUUGUACUUAACGACGAC	7mer-m8	-0.120	0.003	0.075	0.017	0.019	-0.048	-0.05	28	1.324	0.46
Position 558-564 of LIN28A 3' UTR hsa-miR-497	5' ...GAACAGCUGCAGACCUGCUGCUC... ||||||| 3' UGUUUGGUGUCACACGACGAC	7mer-m8	-0.120	0.003	0.075	0.017	0.019	-0.048	-0.05	27	1.324	0.46
Position 558-564 of LIN28A 3' UTR hsa-miR-15b	5' ...GAACAGCUGCAGACCUGCUGCUC... ||||||| 3' ACAUUUGGUACUACACGACGAU	7mer-m8	-0.120	0.003	0.075	0.017	0.019	-0.048	-0.05	27	1.324	0.46
Position 558-564 of LIN28A 3' UTR hsa-miR-15a	5' ...GAACAGCUGCAGACCUGCUGCUC... ||||||| 3' GUGUUUGGUAAUACACGACGAU	7mer-m8	-0.120	0.003	0.075	0.017	0.019	-0.048	-0.05	27	1.324	0.46
Position 558-564 of LIN28A 3' UTR hsa-miR-195	5' ...GAACAGCUGCAGACCUGCUGCUC... ||||||| 3' CGGUUAUAAAGACACGACGAU	7mer-m8	-0.120	0.021	0.075	0.017	0.019	-0.048	-0.04	22	1.324	0.46
Position 558-564 of LIN28A 3' UTR hsa-miR-16	5' ...GAACAGCUGCAGACCUGCUGCUC... ||||||| 3' GCGGUUAUAAAUGCACGACGAU	7mer-m8	-0.120	0.021	0.075	0.017	0.019	-0.048	-0.04	22	1.324	0.46

TargetScan Practice



Search for predicted microRNA targets in mammals

[Go to TargetScanMouse]
[Go to TargetScanWorm]
[Go to TargetScanFly]
[Go to TargetScanFish]

1. Select a species Human

AND

2. Enter a human Entrez Gene symbol (e.g. "LIN28A")

AND/OR

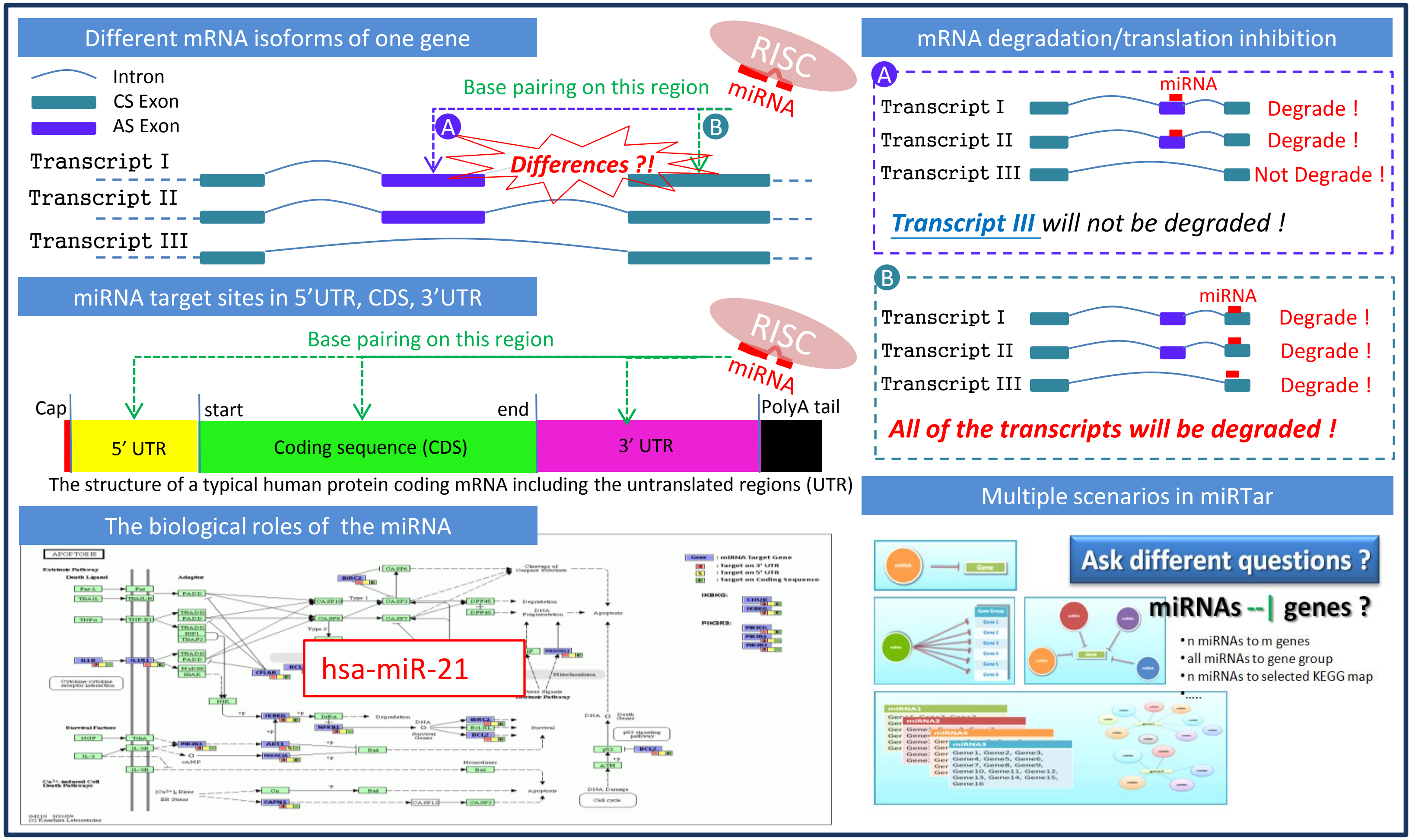
3. Do one of the following:

- Select a broadly conserved* microRNA family: Broadly conserved microRNA families
- Select a conserved* microRNA family: Conserved microRNA families
- Select a poorly conserved microRNA family: Poorly conserved microRNA families. Note that these families also include small RNAs th
- Enter a microRNA name (e.g. "mmu-miR-1")

Input

1. LIN28A
2. HMGA2
3. hsa-miR-122

http://www.targetscan.org/



The structure of a typical human protein coding mRNA including the untranslated regions (UTR)

Transcript III will not be degraded !

All of the transcripts will be degraded !

- n miRNAs to m genes
- all miRNAs to gene group
- n miRNAs to selected KEGG map
- .....

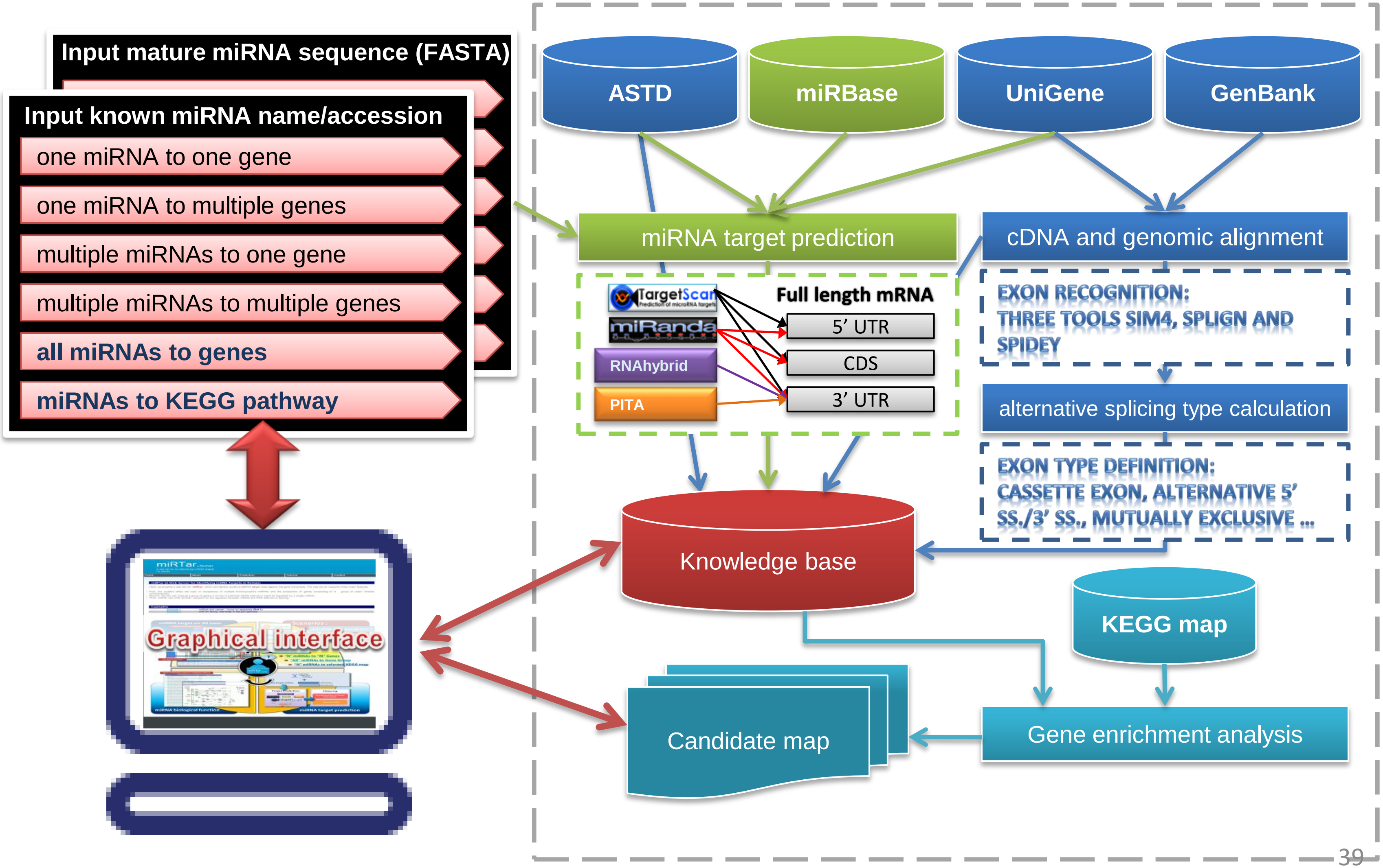
miRTar

A web server for identifying miRNA targets for human

http://mirtar.mbc.nctu.edu.tw

BMC Bioinformatics, 2011

The system flow of miRTar



Input mature miRNA sequence (FASTA)

Input known miRNA name/accession

- one miRNA to one gene
- one miRNA to multiple genes
- multiple miRNAs to one gene
- multiple miRNAs to multiple genes
- **all miRNAs to genes**
- **miRNAs to KEGG pathway**

Graphical interface

ASTD

miRBase

UniGene

GenBank

miRNA target prediction

TargetScan

miRanda

RNAhybrid

PITA

Full length mRNA

5' UTR

CDS

3' UTR

cDNA and genomic alignment

EXON RECOGNITION:
THREE TOOLS SIM4, SPLIGN AND SPIDEY

alternative splicing type calculation

EXON TYPE DEFINITION:
CASSETTE EXON, ALTERNATIVE 5' SS./3' SS., MUTUALLY EXCLUSIVE ...

Knowledge base

KEGG map

Gene enrichment analysis

Candidate map

Multiple scenarios of miRTar

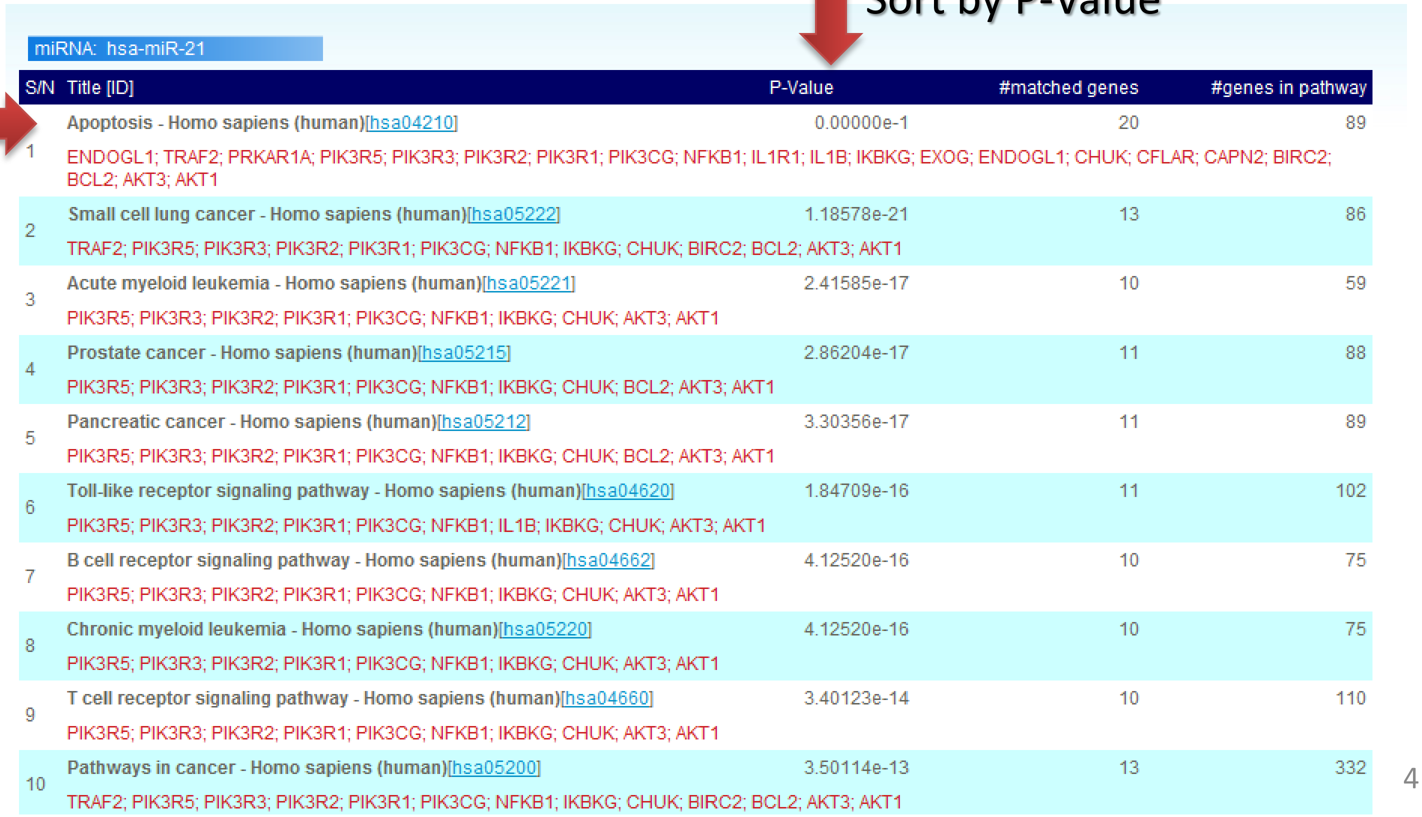
- Single miRNA to single gene (1:1)
- Single miRNA to multiple genes (1:N)
- Multiple miRNAs to single gene (N:1)
- Multiple miRNAs to multiple genes (N:M)
  - The miRNAs in one of the pathway
  - All miRNAs to one/multiple genes

The biological roles of miRNA in metabolic pathway

- An interesting gene group will be targeted by a single miRNA
- These genes will be involved in different metabolic pathway
- Using gene enrichment analysis of metabolic pathway

Sort by P-Value

Metabolic Pathway



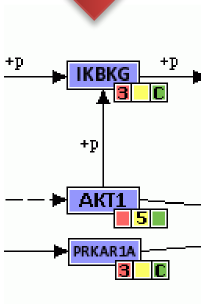
miRNA: hsa-miR-21

S/N	Title [ID]	P-Value	#matched genes	#genes in pathway
1	Apoptosis - Homo sapiens (human)[hsa04210] ENDOGL1; TRAF2; PRKAR1A; PIK3R5; PIK3R3; PIK3R2; PIK3R1; PIK3CG; NFKB1; IL1R1; IL1B; IKBKG; EXOG; ENDOGL1; CHUK; CFLAR; CAPN2; BIRC2; BCL2; AKT3; AKT1	0.00000e-1	20	89
2	Small cell lung cancer - Homo sapiens (human)[hsa05222] TRAF2; PIK3R5; PIK3R3; PIK3R2; PIK3R1; PIK3CG; NFKB1; IKBKG; CHUK; BIRC2; BCL2; AKT3; AKT1	1.18578e-21	13	86
3	Acute myeloid leukemia - Homo sapiens (human)[hsa05221] PIK3R5; PIK3R3; PIK3R2; PIK3R1; PIK3CG; NFKB1; IKBKG; CHUK; AKT3; AKT1	2.41585e-17	10	59
4	Prostate cancer - Homo sapiens (human)[hsa05215] PIK3R5; PIK3R3; PIK3R2; PIK3R1; PIK3CG; NFKB1; IKBKG; CHUK; BCL2; AKT3; AKT1	2.86204e-17	11	88
5	Pancreatic cancer - Homo sapiens (human)[hsa05212] PIK3R5; PIK3R3; PIK3R2; PIK3R1; PIK3CG; NFKB1; IKBKG; CHUK; BCL2; AKT3; AKT1	3.30356e-17	11	89
6	Toll-like receptor signaling pathway - Homo sapiens (human)[hsa04620] PIK3R5; PIK3R3; PIK3R2; PIK3R1; PIK3CG; NFKB1; IL1B; IKBKG; CHUK; AKT3; AKT1	1.84709e-16	11	102
7	B cell receptor signaling pathway - Homo sapiens (human)[hsa04662] PIK3R5; PIK3R3; PIK3R2; PIK3R1; PIK3CG; NFKB1; IKBKG; CHUK; AKT3; AKT1	4.12520e-16	10	75
8	Chronic myeloid leukemia - Homo sapiens (human)[hsa05220] PIK3R5; PIK3R3; PIK3R2; PIK3R1; PIK3CG; NFKB1; IKBKG; CHUK; AKT3; AKT1	4.12520e-16	10	75
9	T cell receptor signaling pathway - Homo sapiens (human)[hsa04660] PIK3R5; PIK3R3; PIK3R2; PIK3R1; PIK3CG; NFKB1; IKBKG; CHUK; AKT3; AKT1	3.40123e-14	10	110
10	Pathways in cancer - Homo sapiens (human)[hsa05200] TRAF2; PIK3R5; PIK3R3; PIK3R2; PIK3R1; PIK3CG; NFKB1; IKBKG; CHUK; BIRC2; BCL2; AKT3; AKT1	3.50114e-13	13	332

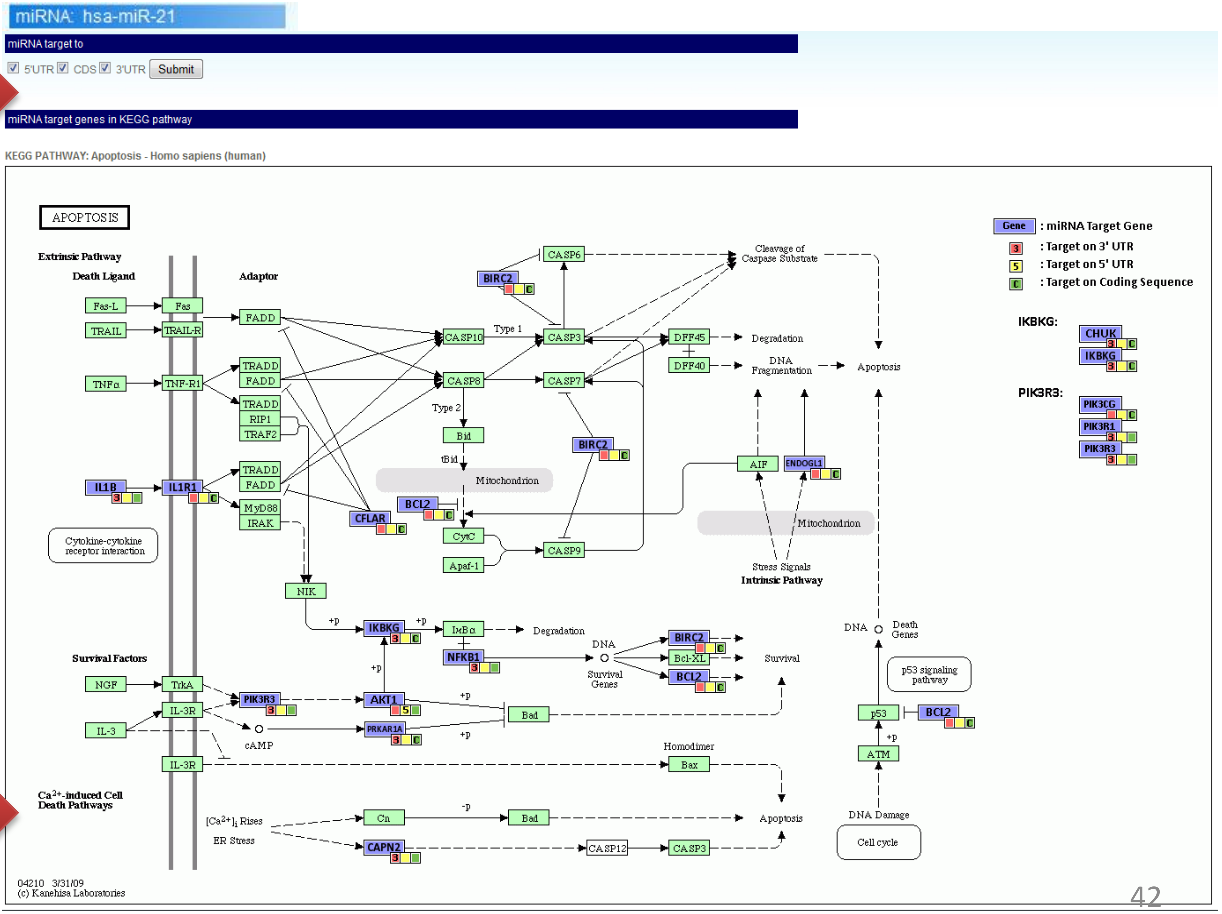
The biological roles of miR-21 in metabolic pathway

- hsa-miR-21 might target in 5’UTR, CDS or 3’UTR of genes’ transcripts.

Focus on different target region of the transcripts



hsa-miR-21 target genes in KEGG Map


miRNA: hsa-miR-21

miRNA target to

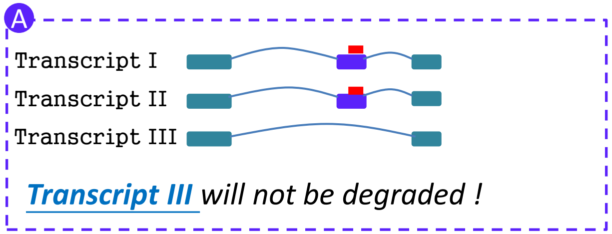
☑ 5'UTR ☑ CDS ☑ 3'UTR Submit

miRNA target genes in KEGG pathway

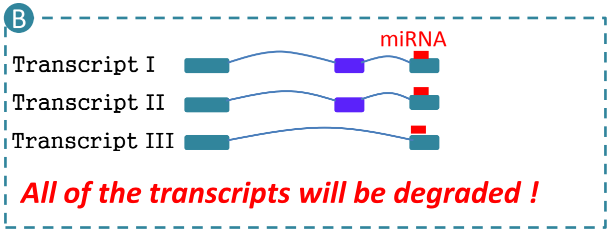
KEGG PATHWAY: Apoptosis - Homo sapiens (human)

miRNA target on alternatively spliced exons

Assumption: one gene has three different transcripts

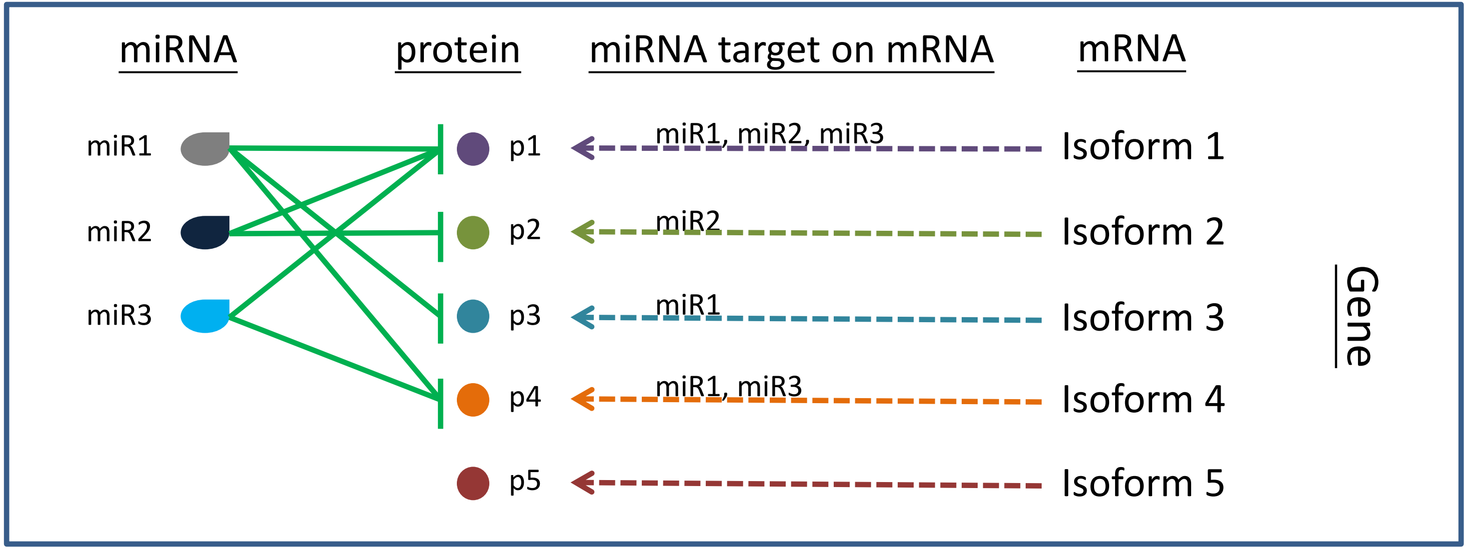


Transcript III *will not be degraded !*



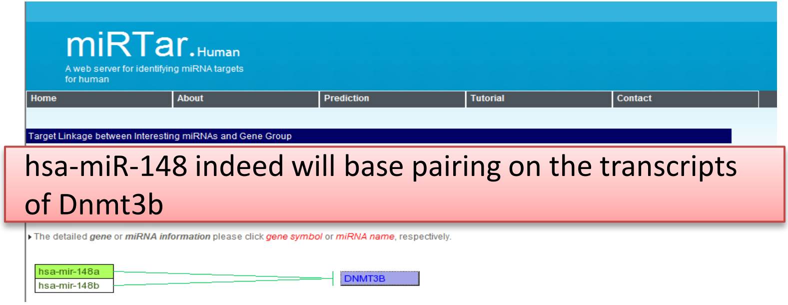
All of the transcripts will be degraded !

- miRNA base pairing on the purple exon
  - Transcript I and II will degradation/translation inhibition
  - Transcript III will produce the protein product
- miRNA base pairing on the green exon
  - None protein products will produce from the gene

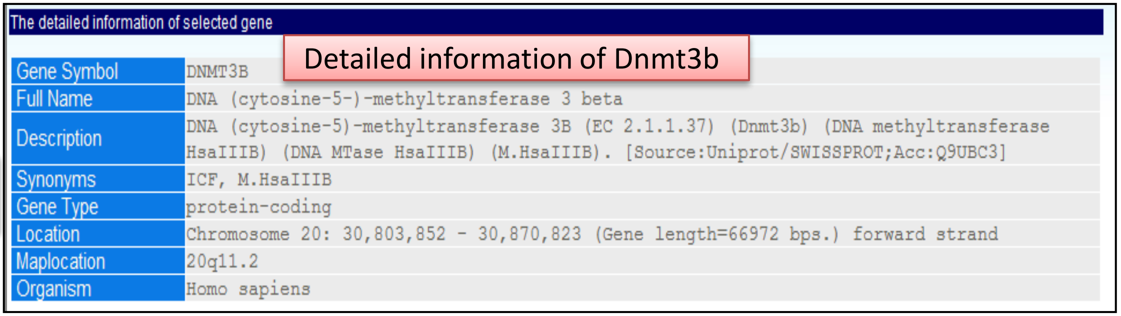


Case study of miRNA:target duplex on alternatively spliced exon

Dnmt3b will be regulated by hsa-miR-148a



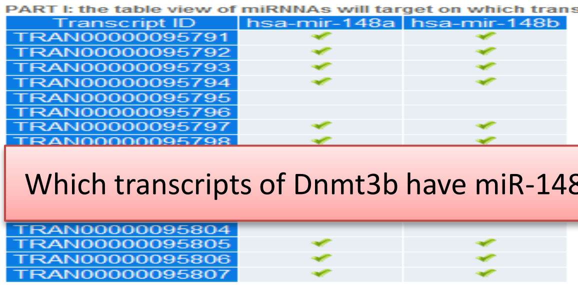
hsa-miR-148 indeed will base pairing on the transcripts of Dnmt3b



The detailed information of selected gene

Gene Symbol	DNMT3B
Full Name	DNA (cytosine-5-)-methyltransferase 3 beta
Description	DNA (cytosine-5)-methyltransferase 3B (EC 2.1.1.37) (Dnmt3b) (DNA methyltransferase HsaIIIB) (DNA MTase HsaIIIB) (M.HsaIIIB). [Source:Uniprot/SWISSPROT;Acc:Q9UBC3]
Synonyms	ICF, M.HsaIIIB
Gene Type	protein-coding
Location	Chromosome 20: 30,803,852 - 30,870,823 (Gene length=66972 bps.) forward strand
Maplocation	20q11.2
Organism	Homo sapiens

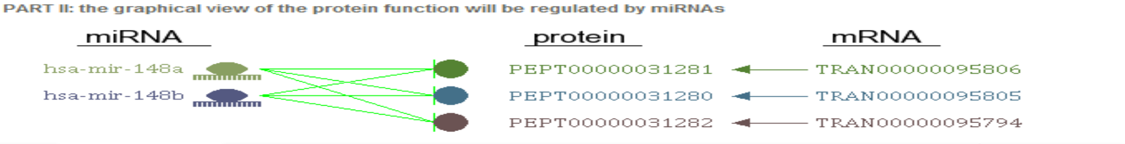
Detailed information of Dnmt3b



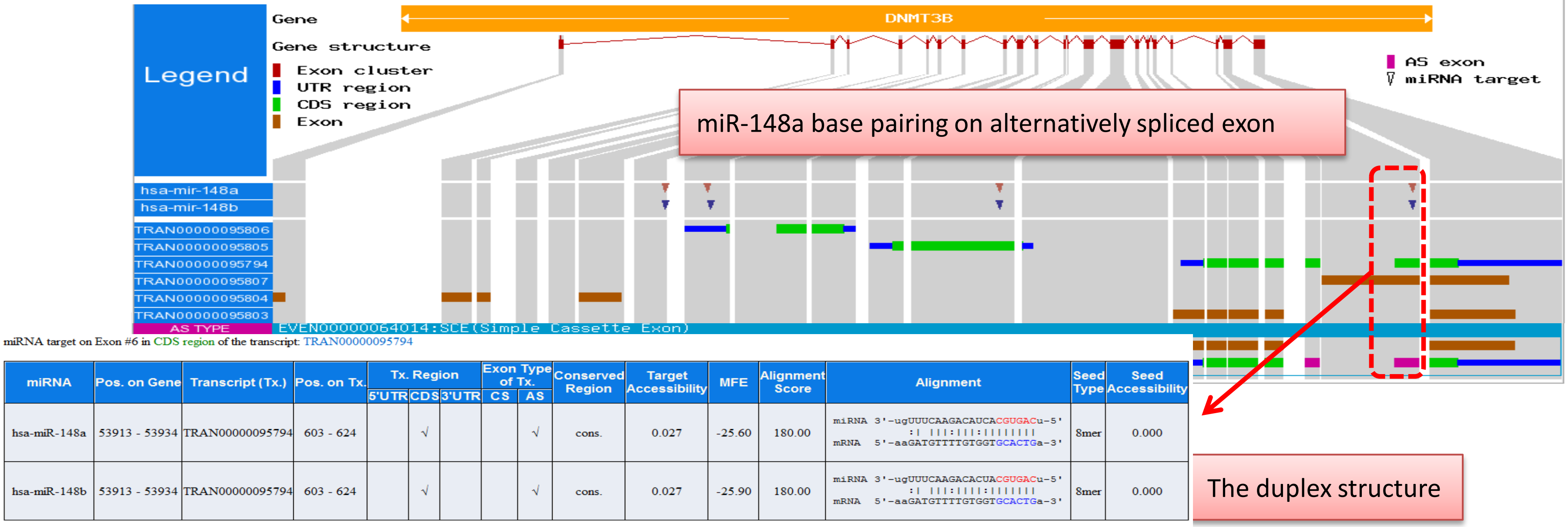
PART I: the table view of miRNNAs will target on which transcripts

Transcript ID	hsa-mir-148a	hsa-mir-148b
TRAN00000095791	✓	✓
TRAN00000095792	✓	✓
TRAN00000095793	✓	✓
TRAN00000095794	✓	✓
TRAN00000095795		
TRAN00000095796		
TRAN00000095797	✓	✓
TRAN00000095798	✓	✓
TRAN00000095804		
TRAN00000095805	✓	✓
TRAN00000095806	✓	✓
TRAN00000095807	✓	✓

Which transcripts of Dnmt3b have miR-148 target sites


PART II: the graphical view of the protein function will be regulated by miRNAs

Which protein function of Dnmt3b might be regulated by miR-148



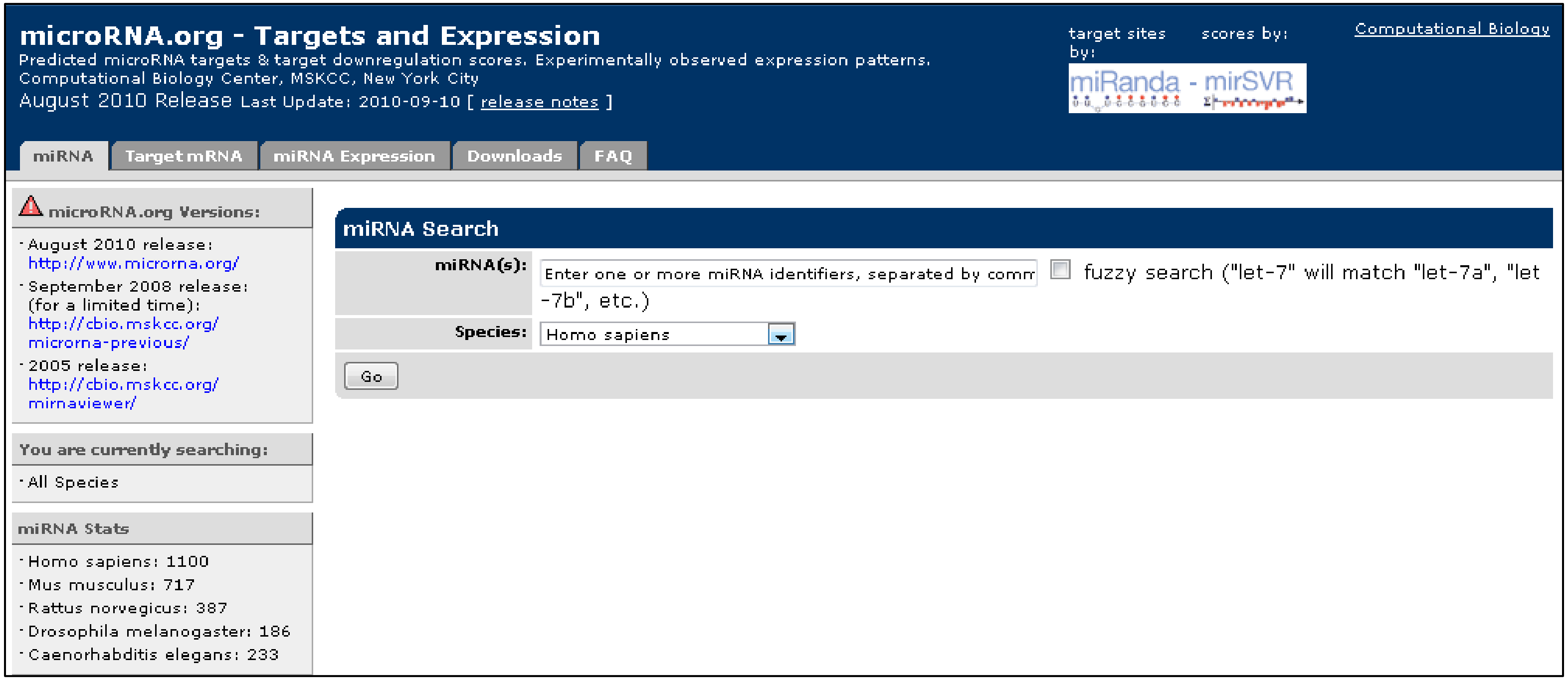
miR-148a base pairing on alternatively spliced exon

miRNA target on Exon #6 in CDS region of the transcript: TRAN00000095794

miRNA	Pos. on Gene	Transcript (Tx.)	Pos. on Tx.	Tx. Region			Exon Type of Tx.		Conserved Region	Target Accessibility	MFE	Alignment Score	Alignment	Seed Type	Seed Accessibility
				5'UTR	CDS	3'UTR	CS	AS							
hsa-miR-148a	53913 - 53934	TRAN00000095794	603 - 624		√			√	cons.	0.027	-25.60	180.00	miRNA 3'-ugUUUCAAGACAUCACGUGACu-5' :| |||:|||:|||||||| mRNA 5'-aaGATGTTTTGTGGTGCACTGa-3'	8mer	0.000
hsa-miR-148b	53913 - 53934	TRAN00000095794	603 - 624		√			√	cons.	0.027	-25.90	180.00	miRNA 3'-ugUUUCAAGACACUACGUGACu-5' :| |||:||||:||||||| mRNA 5'-aaGATGTTTTGTGGTGCACTGa-3'	8mer	0.000

The duplex structure

http://mirtar.mbc.nctu.edu.tw



microRNA.org - Targets and Expression

Predicted microRNA targets & target downregulation scores. Experimentally observed expression patterns.
Computational Biology Center, MSKCC, New York City
August 2010 Release Last Update: 2010-09-10 [release notes]

microRNA.org Versions:

- August 2010 release: http://www.microrna.org/
- September 2008 release: (for a limited time): http://cbio.mskcc.org/microrna-previous/
- 2005 release: http://cbio.mskcc.org/mirnaviewer/

You are currently searching:

- All Species

miRNA Stats

- Homo sapiens: 1100
- Mus musculus: 717
- Rattus norvegicus: 387
- Drosophila melanogaster: 186
- Caenorhabditis elegans: 233

miRNA Search

miRNA(s): Enter one or more miRNA identifiers, separated by comm ☐ fuzzy search ("let-7" will match "let-7a", "let-7b", etc.)

Species: Homo sapiens

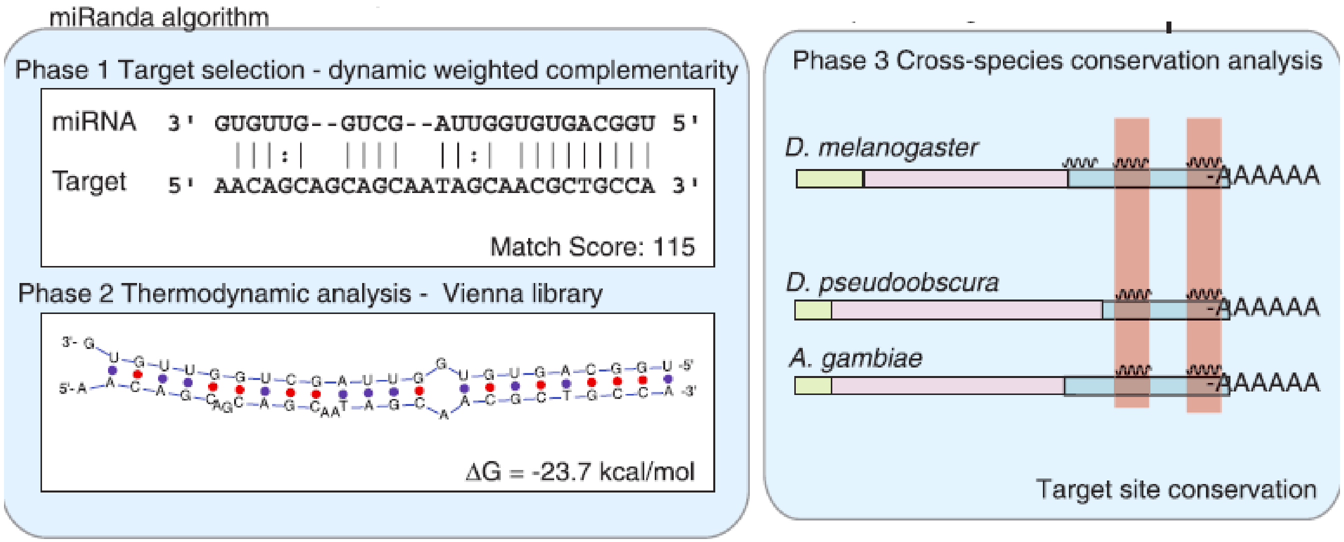
microRNA.org

microRNA targets and expression

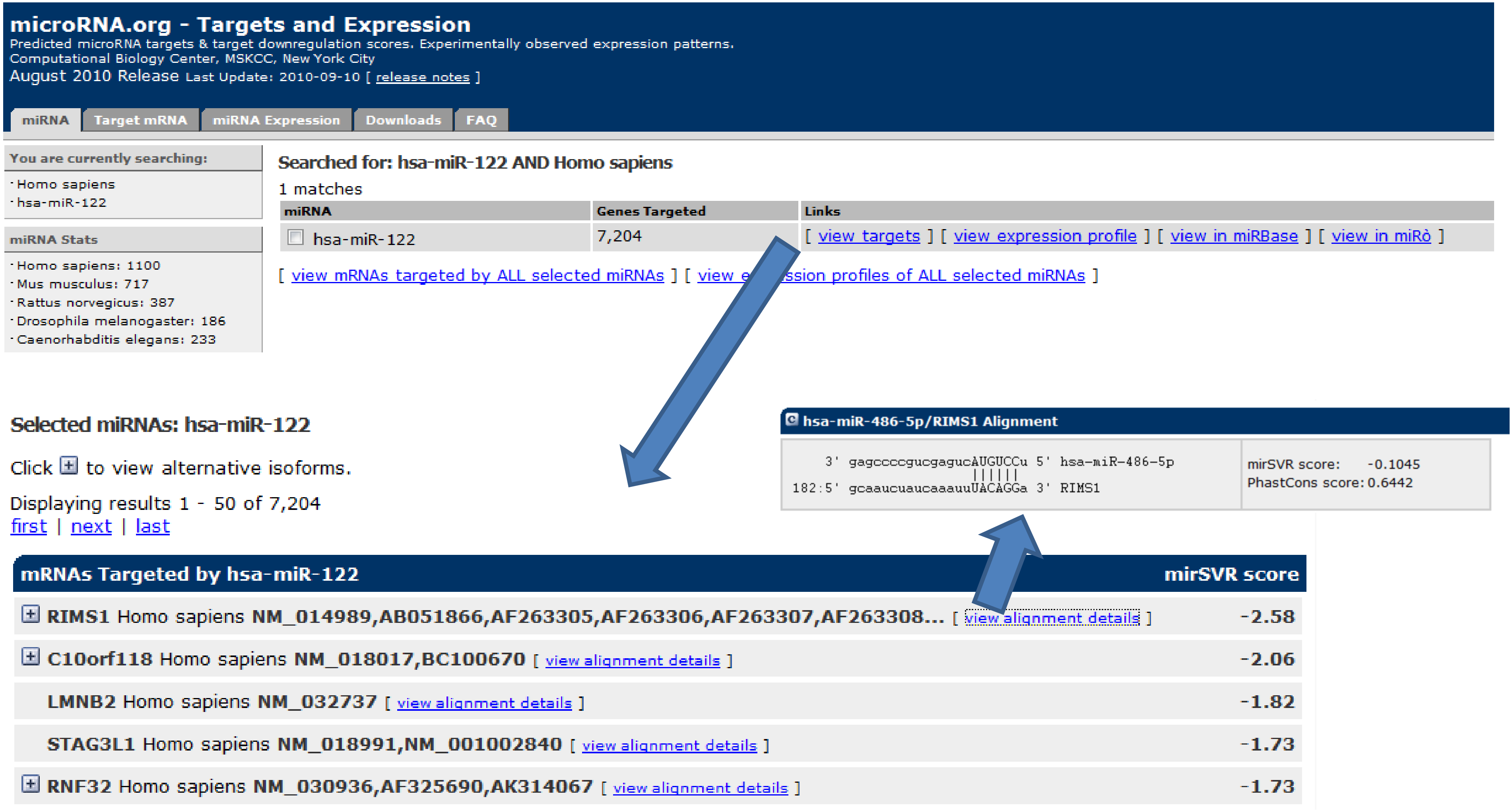
http://www.microrna.org/microrna/home.do

miRanda

- Target prediction:
  - miRNA-target complementarity (strong in 5’, weaker in 3’)
  - Refinement with binding free energy scores
  - Use conservation to increase signal to noise



hsa-miR-122



microRNA.org - Targets and Expression
Predicted microRNA targets & target downregulation scores. Experimentally observed expression patterns.
Computational Biology Center, MSKCC, New York City
August 2010 Release Last Update: 2010-09-10 [release notes]

You are currently searching:
- Homo sapiens
- hsa-miR-122

miRNA Stats
- Homo sapiens: 1100
- Mus musculus: 717
- Rattus norvegicus: 387
- Drosophila melanogaster: 186
- Caenorhabditis elegans: 233

Searched for: hsa-miR-122 AND Homo sapiens

1 matches

miRNA	Genes Targeted	Links
☐ hsa-miR-122	7,204	[view targets] [view expression profile] [view in miRBase] [view in miRò]

[view mRNAs targeted by ALL selected miRNAs] [view expression profiles of ALL selected miRNAs]

Selected miRNAs: hsa-miR-122

Click ⊞ to view alternative isoforms.

Displaying results 1 - 50 of 7,204
first | next | last

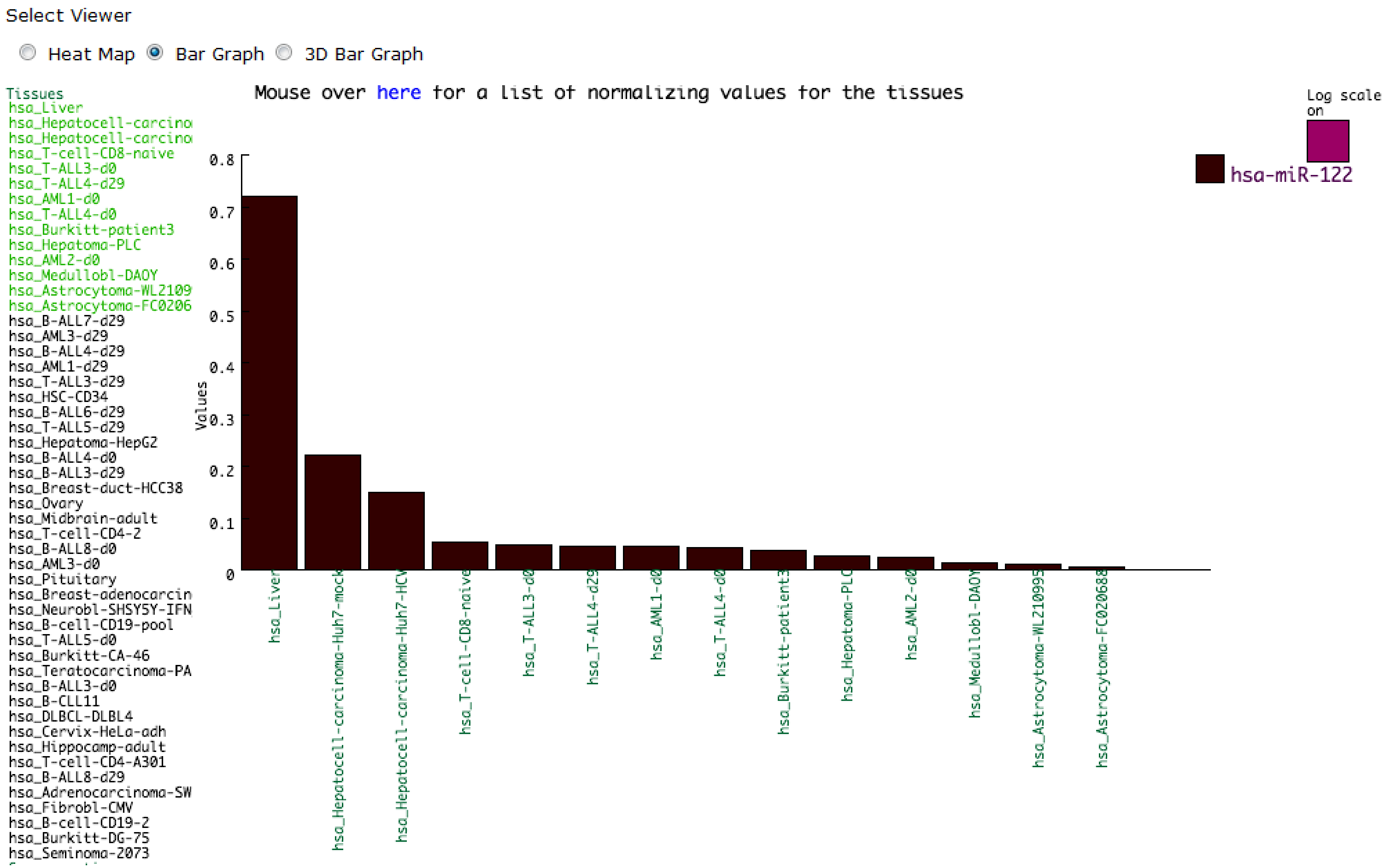
mRNAs Targeted by hsa-miR-122	mirSVR score
⊞ **RIMS1** Homo sapiens **NM_014989,AB051866,AF263305,AF263306,AF263307,AF263308...** [view alignment details]	-2.58
⊞ **C10orf118** Homo sapiens **NM_018017,BC100670** [view alignment details]	-2.06
LMNB2 Homo sapiens **NM_032737** [view alignment details]	-1.82
STAG3L1 Homo sapiens **NM_018991,NM_001002840** [view alignment details]	-1.73
⊞ **RNF32** Homo sapiens **NM_030936,AF325690,AK314067** [view alignment details]	-1.73

hsa-miR-486-5p/RIMS1 Alignment

```
    3' gagccccgucgagucAUGUCCu 5' hsa-miR-486-5p
                      |||||||
182:5' gcaaucuaucaaauuUACAGGa 3' RIMS1
```

mirSVR score: -0.1045
PhastCons score: 0.6442

Expression profile - hsa-miR-122

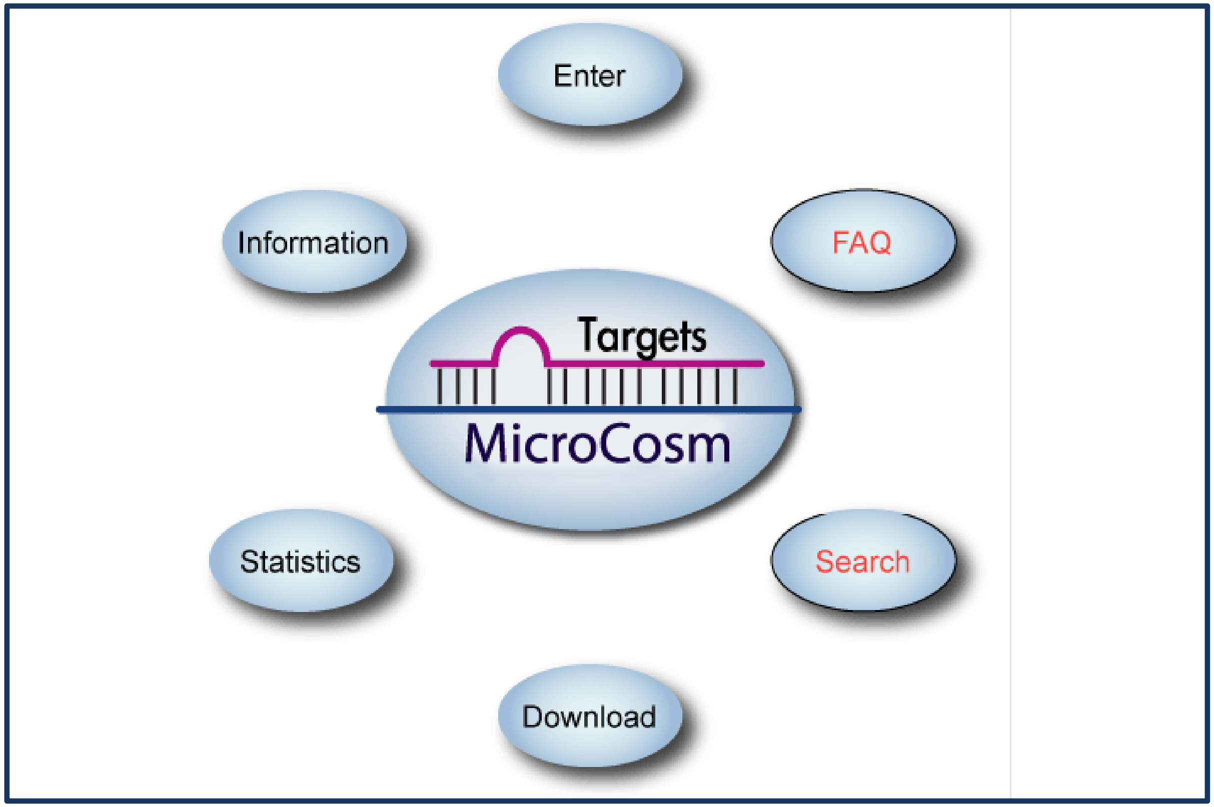


Select Viewer

○ Heat Map ● Bar Graph ○ 3D Bar Graph

Tissues
hsa_Liver
hsa_Hepatocell-carcino
hsa_Hepatocell-carcino
hsa_T-cell-CD8-naive
hsa_T-ALL3-d0
hsa_T-ALL4-d29
hsa_AML1-d0
hsa_T-ALL4-d0
hsa_Burkitt-patient3
hsa_Hepatoma-PLC
hsa_AML2-d0
hsa_Medullobl-DAOY
hsa_Astrocytoma-WL2109
hsa_Astrocytoma-FC0206
hsa_B-ALL7-d29
hsa_AML3-d29
hsa_B-ALL4-d29
hsa_AML1-d29
hsa_T-ALL3-d29
hsa_HSC-CD34
hsa_B-ALL6-d29
hsa_T-ALL5-d29
hsa_Hepatoma-HepG2
hsa_B-ALL4-d0
hsa_B-ALL3-d29
hsa_Breast-duct-HCC38
hsa_Ovary
hsa_Midbrain-adult
hsa_T-cell-CD4-2
hsa_B-ALL8-d0
hsa_AML3-d0
hsa_Pituitary
hsa_Breast-adenocarcin
hsa_Neurobl-SHSY5Y-IFN
hsa_B-cell-CD19-pool
hsa_T-ALL5-d0
hsa_Burkitt-CA-46
hsa_Teratocarcinoma-PA
hsa_B-ALL3-d0
hsa_B-CLL11
hsa_DLBCL-DLBL4
hsa_Cervix-HeLa-adh
hsa_Hippocamp-adult
hsa_T-cell-CD4-A301
hsa_B-ALL8-d29
hsa_Adrenocarcinoma-SW
hsa_Fibrobl-CMV
hsa_B-cell-CD19-2
hsa_Burkitt-DG-75
hsa_Seminoma-2073

Mouse over here for a list of normalizing values for the tissues

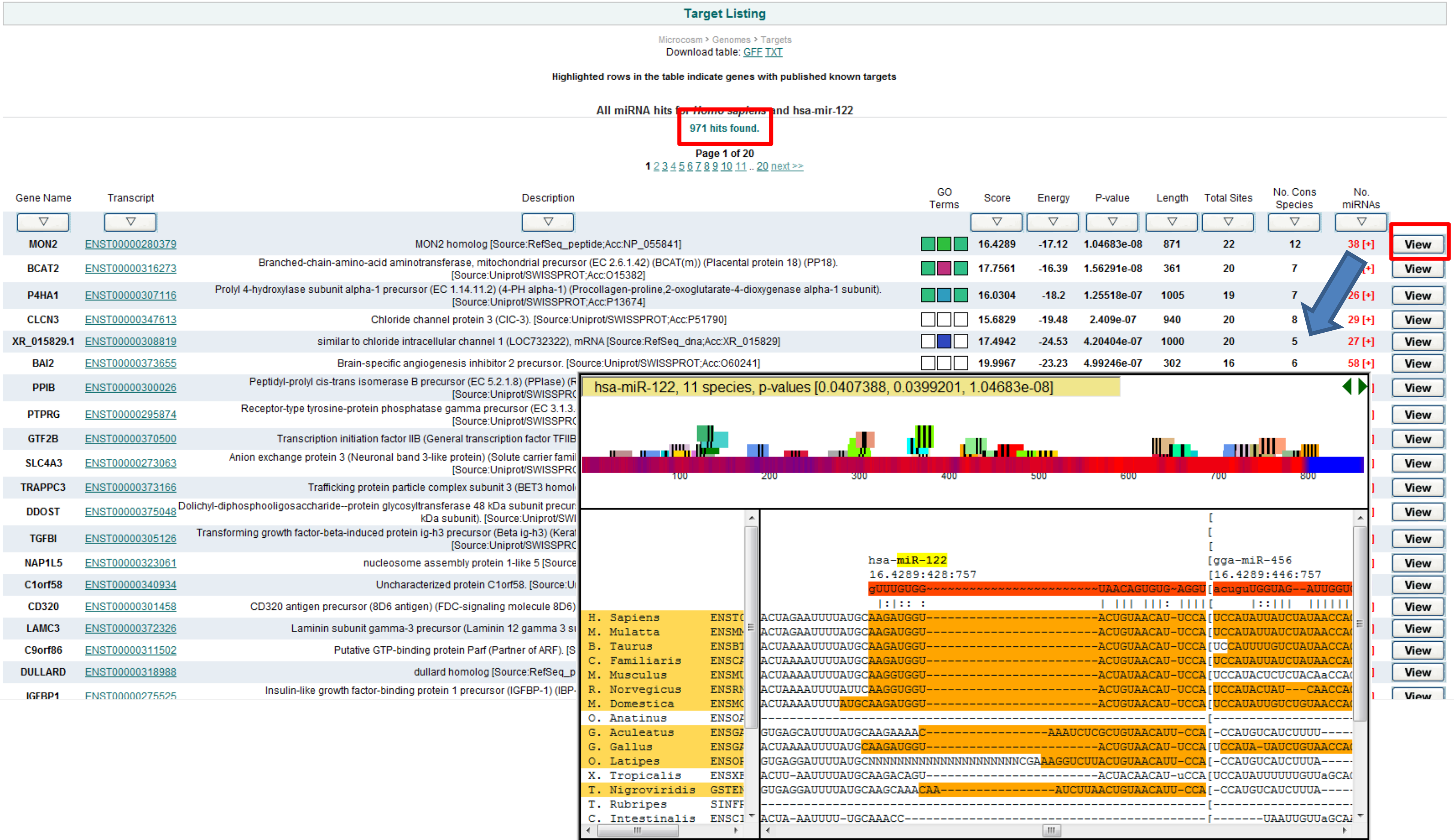


MicroCosm

Containing computationally predicted targets for microRNAs across many species

http://www.ebi.ac.uk/enright-srv/microcosm/htdocs/targets/v5/

hsa-miR-122



Target Listing

Microcosm > Genomes > Targets

Download table: GFF TXT

Highlighted rows in the table indicate genes with published known targets

All miRNA hits for *Homo sapiens* and hsa-mir-122

971 hits found.

Page 1 of 20

1 2 3 4 5 6 7 8 9 10 11 .. 20 next >>

Gene Name	Transcript	Description	GO Terms	Score	Energy	P-value	Length	Total Sites	No. Cons Species	No. miRNAs	
▽	▽	▽		▽	▽	▽	▽	▽	▽	▽	
MON2	ENST00000280379	MON2 homolog [Source:RefSeq_peptide;Acc:NP_055841]	🟩🟩🟩	**16.4289**	**-17.12**	**1.04683e-08**	**871**	**22**	**12**	38 [+]	View
BCAT2	ENST00000316273	Branched-chain-amino-acid aminotransferase, mitochondrial precursor (EC 2.6.1.42) (BCAT(m)) (Placental protein 18) (PP18). [Source:Uniprot/SWISSPROT;Acc:O15382]	🟩🟪🟩	**17.7561**	**-16.39**	**1.56291e-08**	**361**	**20**	**7**	+]	View
P4HA1	ENST00000307116	Prolyl 4-hydroxylase subunit alpha-1 precursor (EC 1.14.11.2) (4-PH alpha-1) (Procollagen-proline,2-oxoglutarate-4-dioxygenase alpha-1 subunit). [Source:Uniprot/SWISSPROT;Acc:P13674]	🟩🟦🟩	**16.0304**	**-18.2**	**1.25518e-07**	**1005**	**19**	**7**	26 [+]	View
CLCN3	ENST00000347613	Chloride channel protein 3 (ClC-3). [Source:Uniprot/SWISSPROT;Acc:P51790]	☐☐☐	**15.6829**	**-19.48**	**2.409e-07**	**940**	**20**	**8**	29 [+]	View
XR_015829.1	ENST00000308819	similar to chloride intracellular channel 1 (LOC732322), mRNA [Source:RefSeq_dna;Acc:XR_015829]	☐🟦☐	**17.4942**	**-24.53**	**4.20404e-07**	**1000**	**20**	**5**	27 [+]	View
BAI2	ENST00000373655	Brain-specific angiogenesis inhibitor 2 precursor. [Source:Uniprot/SWISSPROT;Acc:O60241]	☐☐☐	**19.9967**	**-23.23**	**4.99246e-07**	**302**	**16**	**6**	58 [+]	View
PPIB	ENST00000300026	Peptidyl-prolyl cis-trans isomerase B precursor (EC 5.2.1.8) (PPIase) (F [Source:Uniprot/SWISSPR								]	View
PTPRG	ENST00000295874	Receptor-type tyrosine-protein phosphatase gamma precursor (EC 3.1.3. [Source:Uniprot/SWISSPR								]	View
GTF2B	ENST00000370500	Transcription initiation factor IIB (General transcription factor TFIIB								]	View
SLC4A3	ENST00000273063	Anion exchange protein 3 (Neuronal band 3-like protein) (Solute carrier fami [Source:Uniprot/SWISSPR								]	View
TRAPPC3	ENST00000373166	Trafficking protein particle complex subunit 3 (BET3 homol								]	View
DDOST	ENST00000375048	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase 48 kDa subunit precur kDa subunit). [Source:Uniprot/SWI								]	View
TGFBI	ENST00000305126	Transforming growth factor-beta-induced protein ig-h3 precursor (Beta ig-h3) (Kera [Source:Uniprot/SWISSPR								]	View
NAP1L5	ENST00000323061	nucleosome assembly protein 1-like 5 [Source								]	View
C1orf58	ENST00000340934	Uncharacterized protein C1orf58. [Source:U								]	View
CD320	ENST00000301458	CD320 antigen precursor (8D6 antigen) (FDC-signaling molecule 8D6)								]	View
LAMC3	ENST00000372326	Laminin subunit gamma-3 precursor (Laminin 12 gamma 3 su								]	View
C9orf86	ENST00000311502	Putative GTP-binding protein Parf (Partner of ARF). [S								]	View
DULLARD	ENST00000318988	dullard homolog [Source:RefSeq_p								]	View
IGFBP1	ENST00000275525	Insulin-like growth factor-binding protein 1 precursor (IGFBP-1) (IBP-								]	View

hsa-miR-122, 11 species, p-values [0.0407388, 0.0399201, 1.04683e-08]

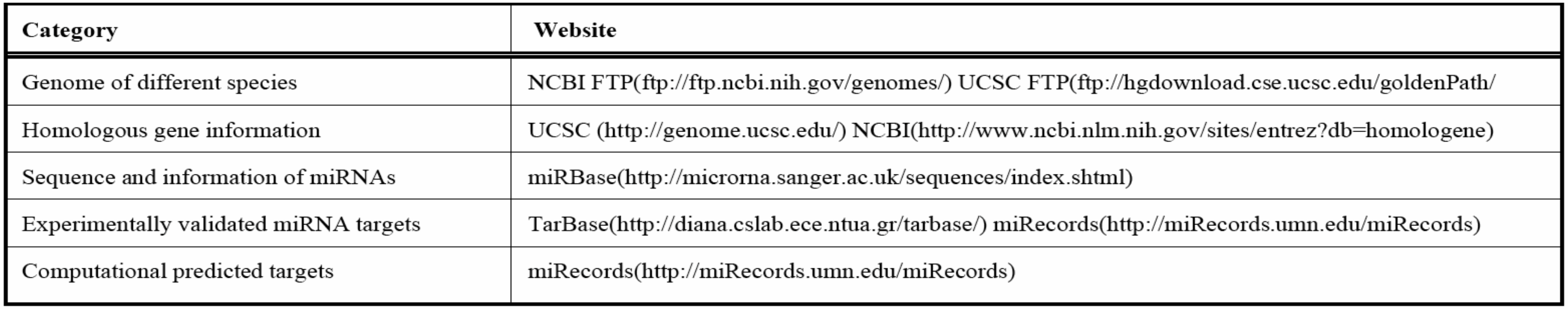
```
                                                                                    [
                                                                                    [
                                                                                    [
                                     hsa-miR-122                                    [gga-miR-456
                                     16.4289:428:757                                [16.4289:446:757
                                     gUUUGUGG~~~~~~~~~~~~~~~~~~~~~~~~UAACAGUGUG~AGGU[acuguUGGUAG--AUUGGU
                                      |:|:: :                        | ||| |||: ||||[     |::|||  ||||||
H. Sapiens          ENST  ACUAGAAUUUUAUGCAAGAUGGU------------------------ACUGUAACAU-UCCA[UCCAUAUUAUCUAUAACCA
M. Mulatta          ENSM  ACUAGAAUUUUAUGCAAGAUGGU------------------------ACUGUAACAU-UCCA[UCCAUAUUAUCUAUAACCA
B. Taurus           ENSB  ACUAAAAUUUUAUGCAAGAUGGU------------------------ACUGUAACAU-UCCA[UCCAUUUUGUCUAUAACCA
C. Familiaris       ENSC  ACUAAAAUUUUAUGCAAGAUGGU------------------------ACUGUAACAU-UCCA[UCCAUAUUAUCUAUAACCA
M. Musculus         ENSM  ACUAAAAUUUUAUGCAAGGUGGU------------------------ACUAUAACAU-UCCA[UCCAUACUCUCUACAaCCA
R. Norvegicus       ENSR  ACUAAAAUUUUAUUCAAGGUGGU------------------------ACUGUAACAU-UCCA[UCCAUACUAU---CAACCA
M. Domestica        ENSM  ACUAAAAUUUUAUGCAAGAUGGU------------------------ACUGUAACAU-UCCA[UCCAUAUUGUCUGUAACCA
O. Anatinus         ENSO  --------------------------------------------------------------[-------------------
G. Aculeatus        ENSG  GUGAGCAUUUUAUGCAAGAAAAC-----------------AAAUCUCGCUGUAACAUU-CCA[-CCAUGUCAUCUUUU----
G. Gallus           ENSG  ACUAAAAUUUUAUGCAAGAUGGU------------------------ACUGUAACAU-UCCA[UCCAUA-UAUCUGUAACCA
O. Latipes          ENSO  GUGAGGAUUUUAUGCNNNNNNNNNNNNNNNNNNNNNCGAAAGGUCUUACUGUAACAUU-CCA[-CCAUGUCAUCUUUA----
X. Tropicalis       ENSX  ACUU-AAUUUUAUGCAAGACAGU------------------------ACUACAACAU-uCCA[UCCAUAUUUUUGUUaGCA
T. Nigroviridis     GSTE  GUGAGGAUUUUAUGCAAGCAAACAA----------------AUCUUAACUGUAACAUU-CCA[-CCAUGUCAUCUUUA----
T. Rubripes         SINF  --------------------------------------------------------------[-------------------
C. Intestinalis     ENSC  ACUA-AAUUUU-UGCAAACC------------------------------------------[-------UAAUUGUUaGCA
```

Compare the miRTar with other tools

Features		miRTar	DIANA microT/miRPath	EIMMO	miRU	RNAhybrid	STarMir	RNA22	MMIA
Species		Human	Human and mouse	Vertebrates, nematode, fly	Plants	Human, nematodes, flies	-	Vertebrates, nematode, fly	Human
Possible relation between miRNA and gene group	* 1 to 1	+	+	+	-	+	+	+	-
	* 1 to N	+	1 to All genes	+	-	+	+	-	+
	* N to 1	+	-	+	-	+	+	-	-
	* N to M	+	-	+	-	+	+	-	+
	* All to M	+	All miRNAs to 1	+	-	-	-	-	-
	* 1 to KEGG	+	+	-	-	-	-	-	-
miRNA targets on alternatively splicing exon		+	-	-	-	-	-	-	-
miRNA targets from mRNA		Full length	3'UTR	3'UTR	Full length	3'UTR	Full length	Full length	3'UTR
Known miRNAs		miRBase V15	-	miRBase V12	-	-	-	-	-
Accessibility of target site		+	-	-	-	-	Sfold	-	-
Conservation of target site		+	+	+	+	-	-	-	-
Expression profile of	miRNA	-	-	-	-	-	-	-	+
	Target	-	-	+	-	-	-	-	+

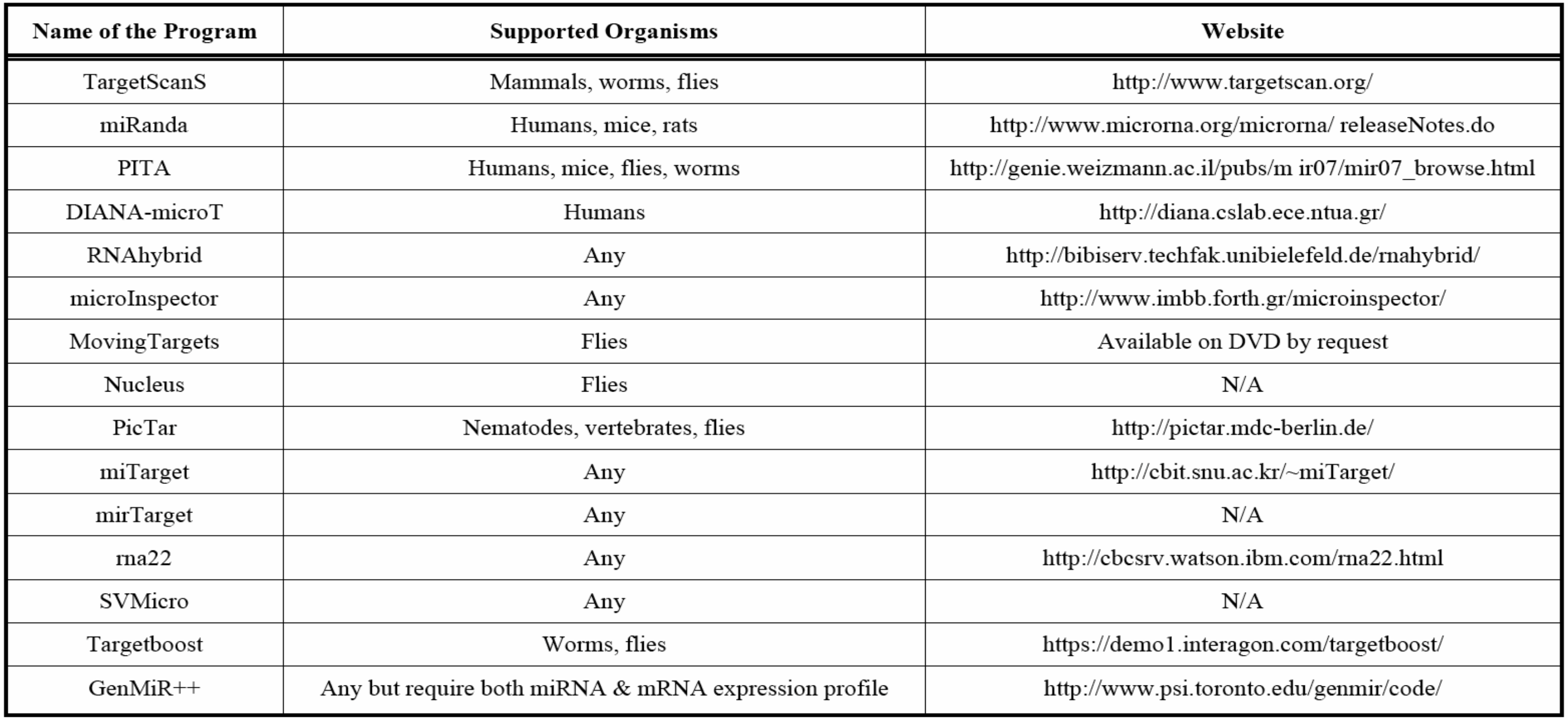
Appendix: other miRNA resources

Table 1. Online Resource for miRNA Target Prediction



Category	Website
Genome of different species	NCBI FTP(ftp://ftp.ncbi.nih.gov/genomes/) UCSC FTP(ftp://hgdownload.cse.ucsc.edu/goldenPath/
Homologous gene information	UCSC (http://genome.ucsc.edu/) NCBI(http://www.ncbi.nlm.nih.gov/sites/entrez?db=homologene)
Sequence and information of miRNAs	miRBase(http://microrna.sanger.ac.uk/sequences/index.shtml)
Experimentally validated miRNA targets	TarBase(http://diana.cslab.ece.ntua.gr/tarbase/) miRecords(http://miRecords.umn.edu/miRecords)
Computational predicted targets	miRecords(http://miRecords.umn.edu/miRecords)

Table 2. Support Organisms and Websites of miRNA Target Prediction Algorithms



Name of the Program	Supported Organisms	Website
TargetScanS	Mammals, worms, flies	http://www.targetscan.org/
miRanda	Humans, mice, rats	http://www.microrna.org/microrna/ releaseNotes.do
PITA	Humans, mice, flies, worms	http://genie.weizmann.ac.il/pubs/m ir07/mir07_browse.html
DIANA-microT	Humans	http://diana.cslab.ece.ntua.gr/
RNAhybrid	Any	http://bibiserv.techfak.unibielefeld.de/rnahybrid/
microInspector	Any	http://www.imbb.forth.gr/microinspector/
MovingTargets	Flies	Available on DVD by request
Nucleus	Flies	N/A
PicTar	Nematodes, vertebrates, flies	http://pictar.mdc-berlin.de/
miTarget	Any	http://cbit.snu.ac.kr/~miTarget/
mirTarget	Any	N/A
rna22	Any	http://cbcsrv.watson.ibm.com/rna22.html
SVMicro	Any	N/A
Targetboost	Worms, flies	https://demo1.interagon.com/targetboost/
GenMiR++	Any but require both miRNA & mRNA expression profile	http://www.psi.toronto.edu/genmir/code/

What can we do with miRNAs?

- We can look for microRNA genes
  - Is it a novel miRNA or known miRNA? miRBase
  - Where is my miRNA expressed? microRNA.org
- We can look for microRNA targets
  - Which miRNAs regulate my gene OR genes are regulated by my miRNAs?
    - Known: miRTarBase
    - Predicted: miRNAMap, microRNA.org, MicroCosm, miRTar,and TargetScan
  - Are there any common pathways affected by the same miRNA? miRTar

Thanks for your attention

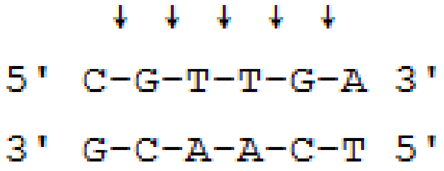
Useful resource for miRNA research

miRNA database	
miRBase	http://www.mirbase.org/
miRNAMap	http://miRNAMap.mbc.nctu.edu.tw/
miRTarBase	http://miRTarBase.mbc.nctu.edu.tw/
miRNA target prediction tools	
TargetScan	http://www.targetscan.org/
miRTar	http://mirtar.mbc.nctu.edu.tw
microRNA.org	http://www.microrna.org/microrna/home.do
Microcosm	http://www.ebi.ac.uk/enright-srv/microcosm/htdocs/targets/v5/
RNA secondary structure folding tools	
mfold	http://mfold.rna.albany.edu/?q=mfold/RNA-Folding-Form
RNAfold	http://rna.tbi.univie.ac.at/cgi-bin/RNAfold.cgi
Example of this class	
Example	http://mirtarbase.mbc.nctu.edu.tw/example.txt

Nearest-neighbor method

- nearest-neighbor model treats a DNA helix as a string of interactions between 'neighboring' base pairs.

SPS:

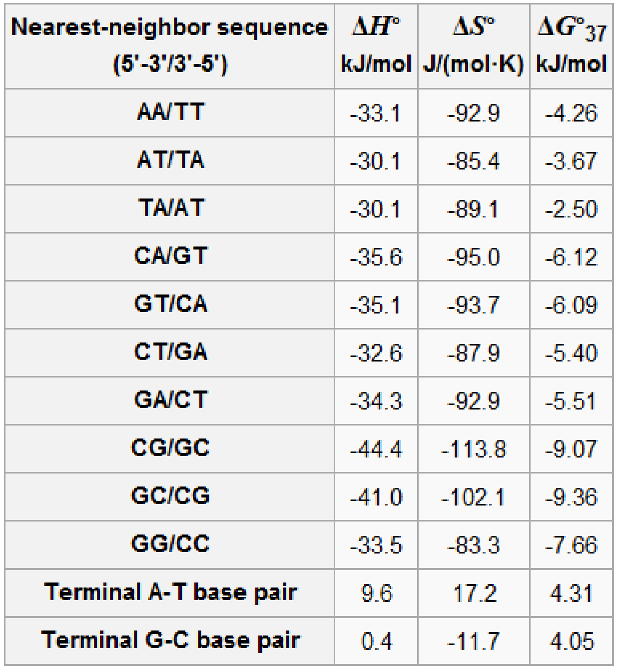


5' C-G-T-T-G-A 3'

3' G-C-A-A-C-T 5'

ΔG˚37(predicted) = ΔG˚37(CG initiation) + ΔG˚37(CG/GC) + ΔG˚37(GT/CA) + ΔG˚37(TT/AA) + ΔG˚37(TG/AC) + ΔG˚37(GA/CT) + ΔG˚37(AT initiation)

Nearest-neighbor parameters for DNA/DNA duplexes in 1 M NaCl.



Nearest-neighbor sequence (5'-3'/3'-5')	ΔH° kJ/mol	ΔS° J/(mol·K)	$\Delta G^\circ{}_{37}$ kJ/mol
AA/TT	-33.1	-92.9	-4.26
AT/TA	-30.1	-85.4	-3.67
TA/AT	-30.1	-89.1	-2.50
CA/GT	-35.6	-95.0	-6.12
GT/CA	-35.1	-93.7	-6.09
CT/GA	-32.6	-87.9	-5.40
GA/CT	-34.3	-92.9	-5.51
CG/GC	-44.4	-113.8	-9.07
GC/CG	-41.0	-102.1	-9.36
GG/CC	-33.5	-83.3	-7.66
Terminal A-T base pair	9.6	17.2	4.31
Terminal G-C base pair	0.4	-11.7	4.05