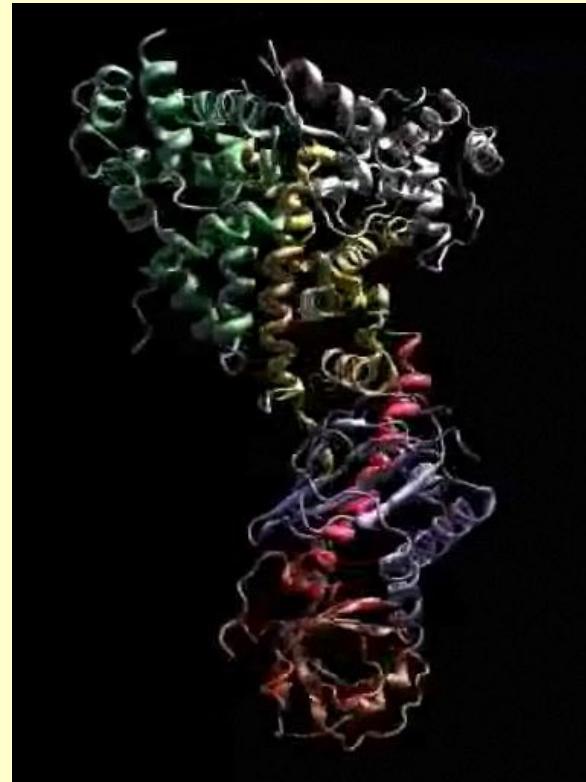


# Computational Molecular Biology Biochem 218 – BioMedical Informatics 231

<http://biochem218.stanford.edu/>

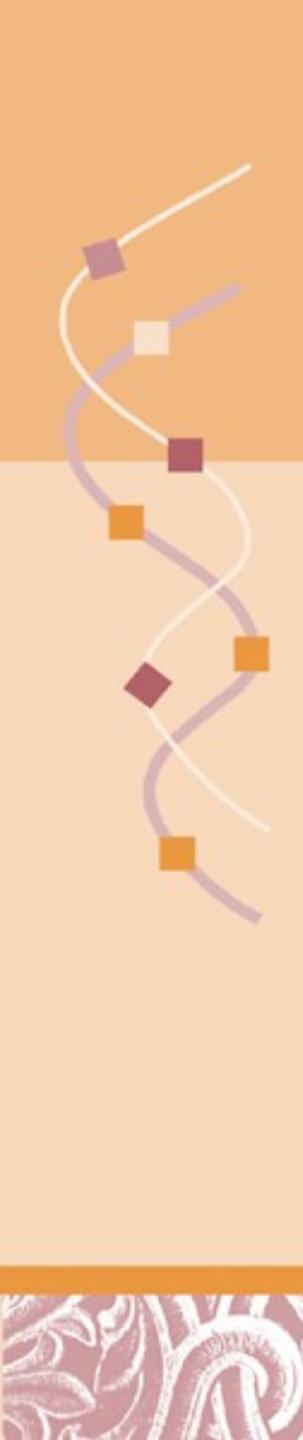
## miRNA Regulatory Networks



Doug Brutlag  
Professor Emeritus  
Biochemistry & Medicine (by courtesy)



Doug Brutlag 2010

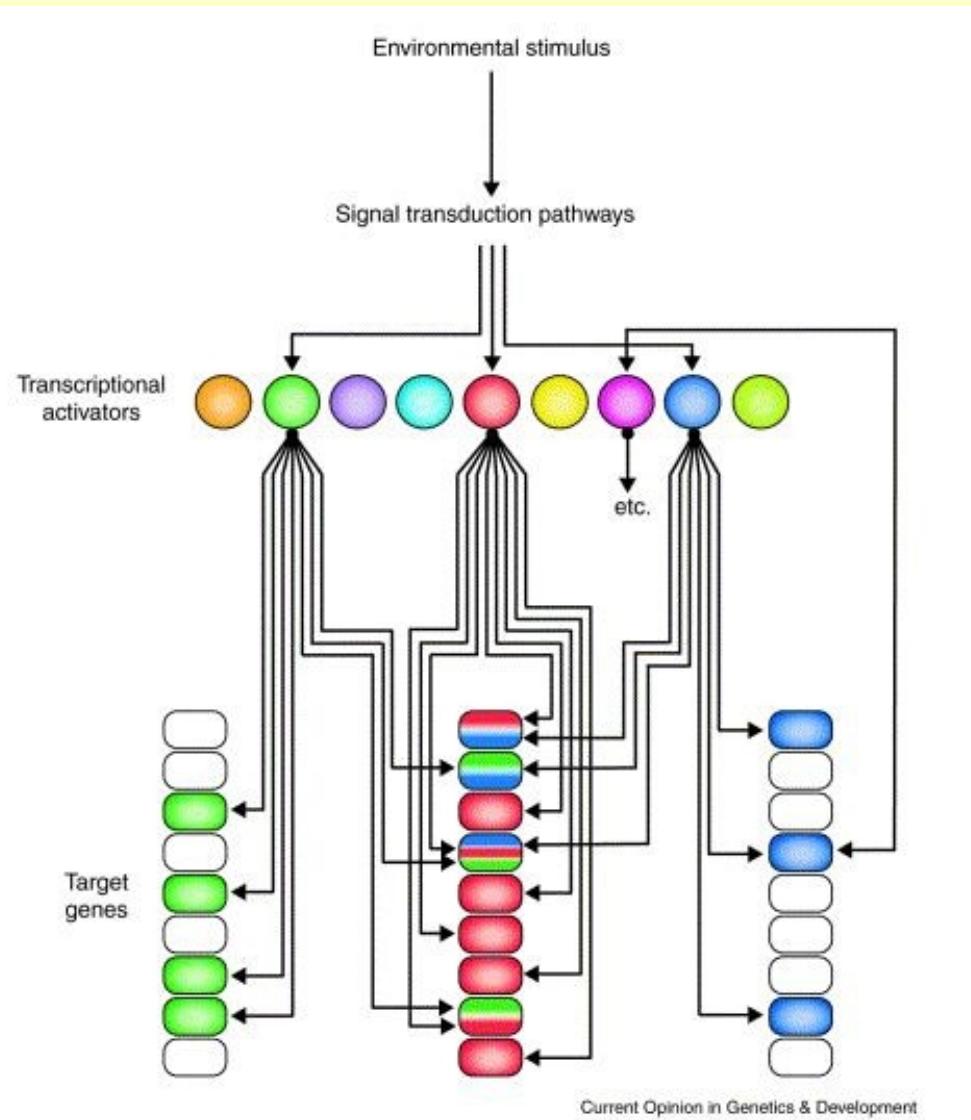


# Gene Regulatory Mechanisms

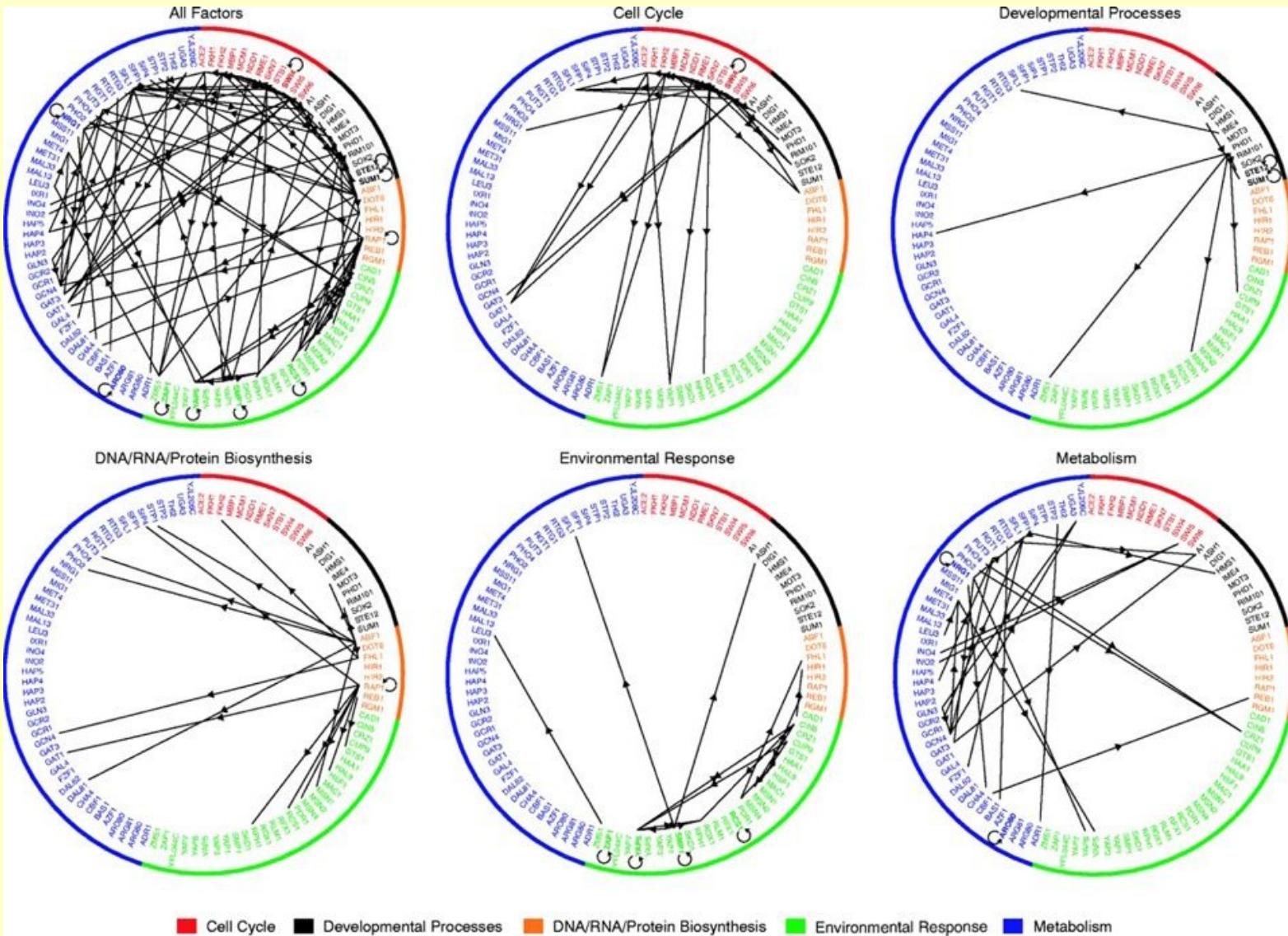
---

- Transcriptional Mechanisms
  - Type of promoters & RNA polymerase
  - Control of Transcription
    - Constitutive
    - Inducible
    - Repressible
  - Transcription Factors and TFBS
- Translational Mechanisms
  - Micro RNAs (miRNAs and RITS complexes)
    - Translational control
    - mRNA degradation
    - Promoter activation
  - Silencer RNAs (siRNAs & RISC complexes) degrading mRNA
- Epigenetic Mechanisms
  - Chromatin remodeling
  - Histone modifications (acetylation, phosphorylation, methylation ...)
  - DNA methylation

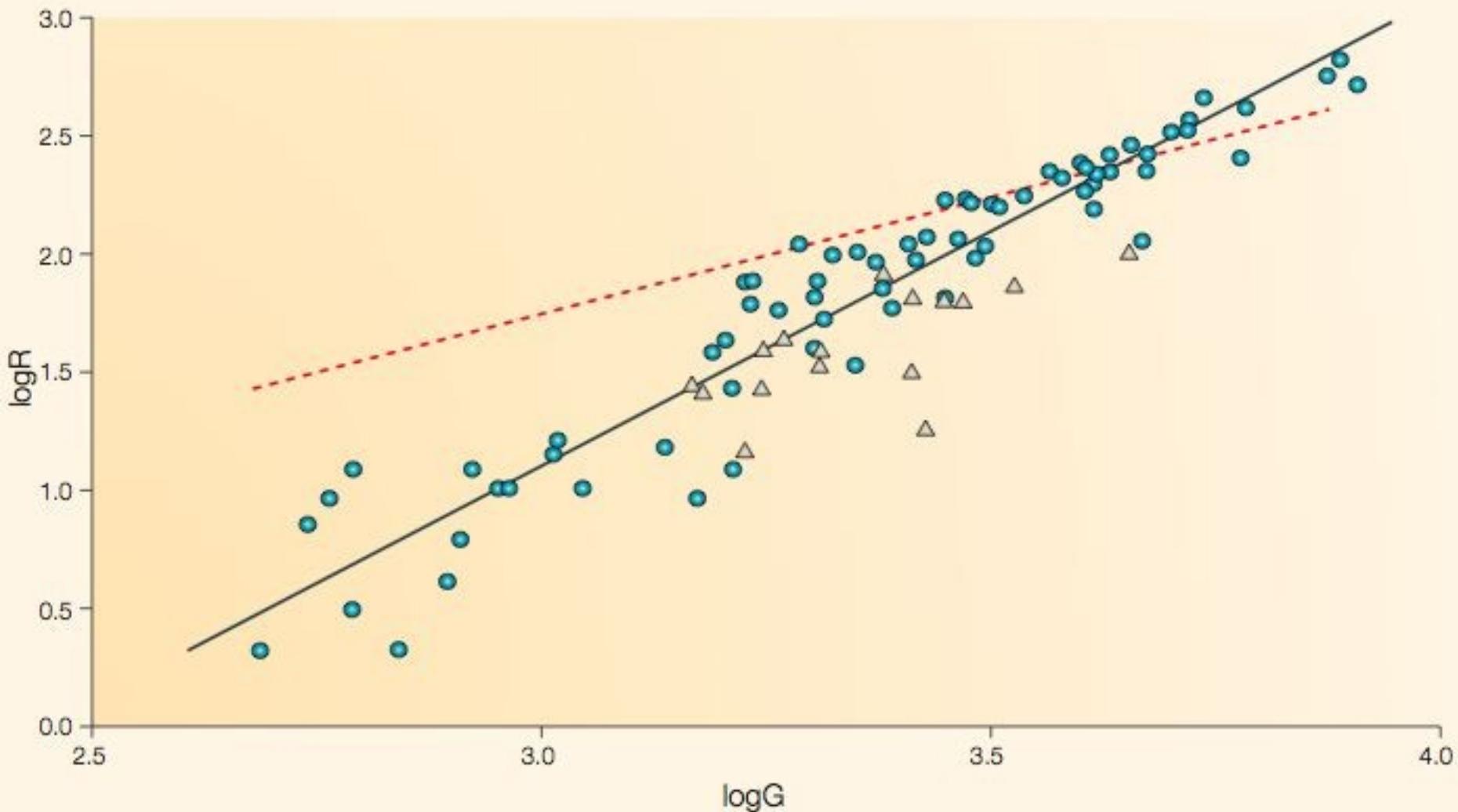
# Gene Expression Regulatory Network



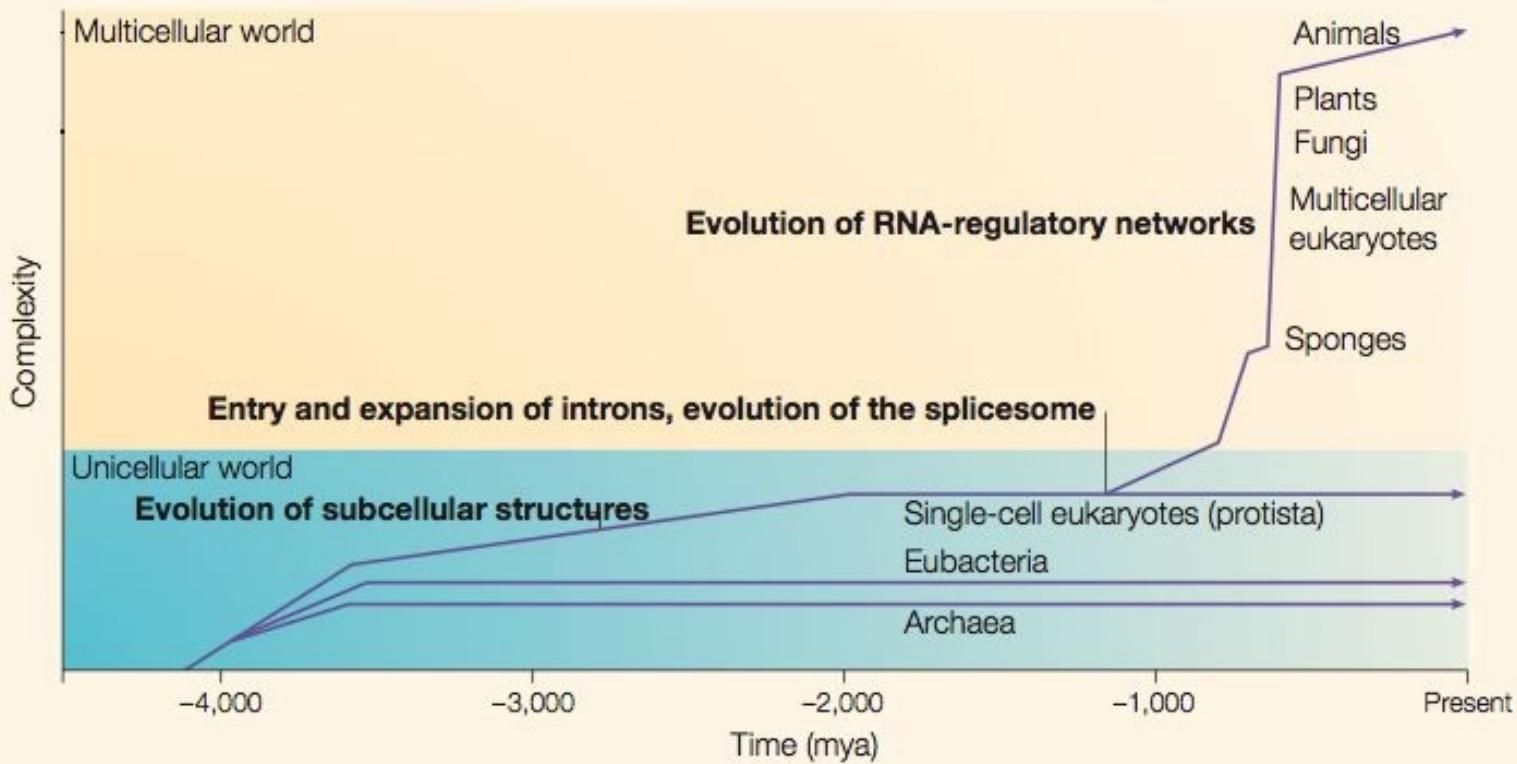
# Yeast Regulatory Motifs



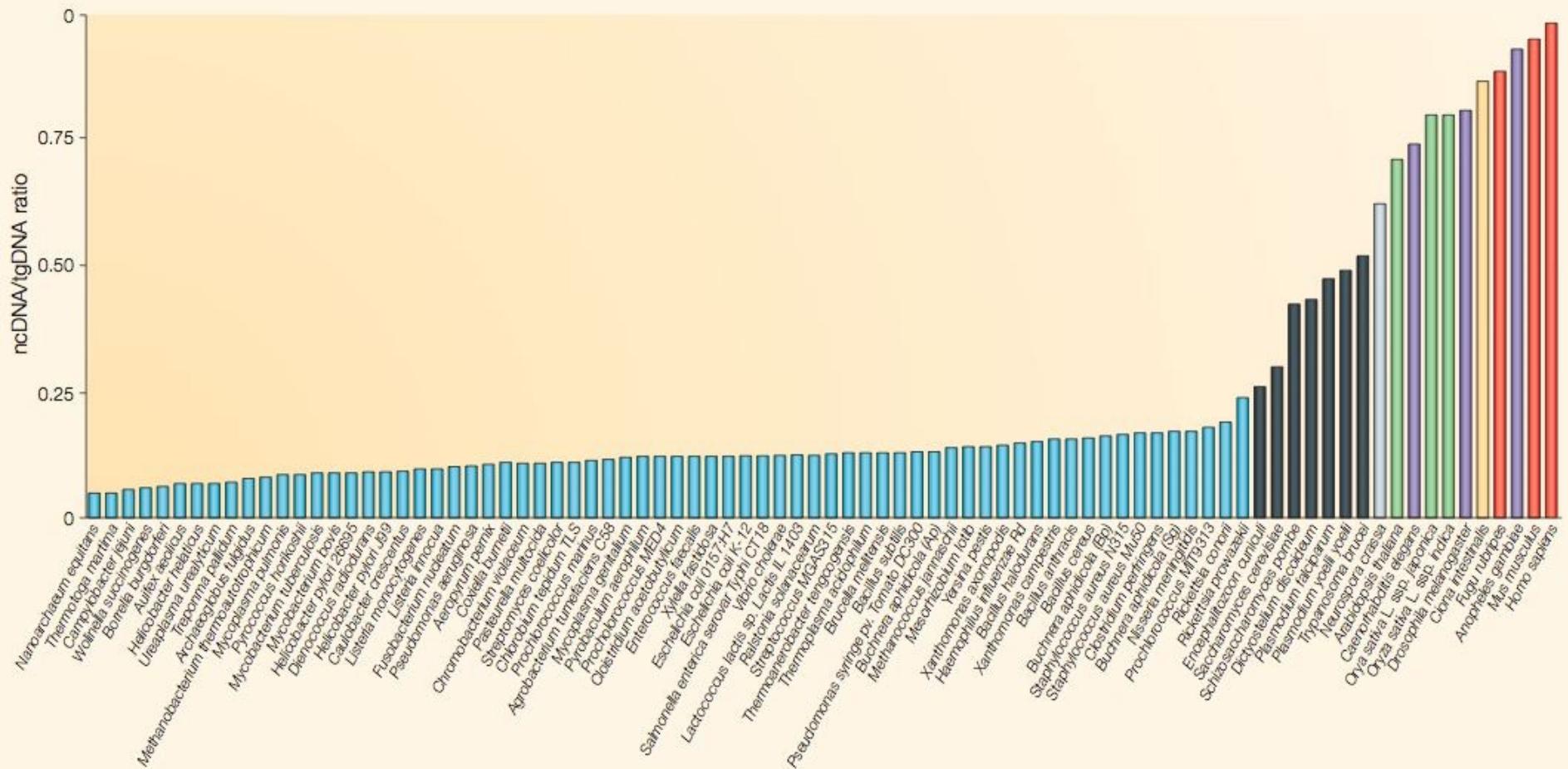
# Prokaryotic Regulatory Genes Grow as the Square of the Total Number of Genes



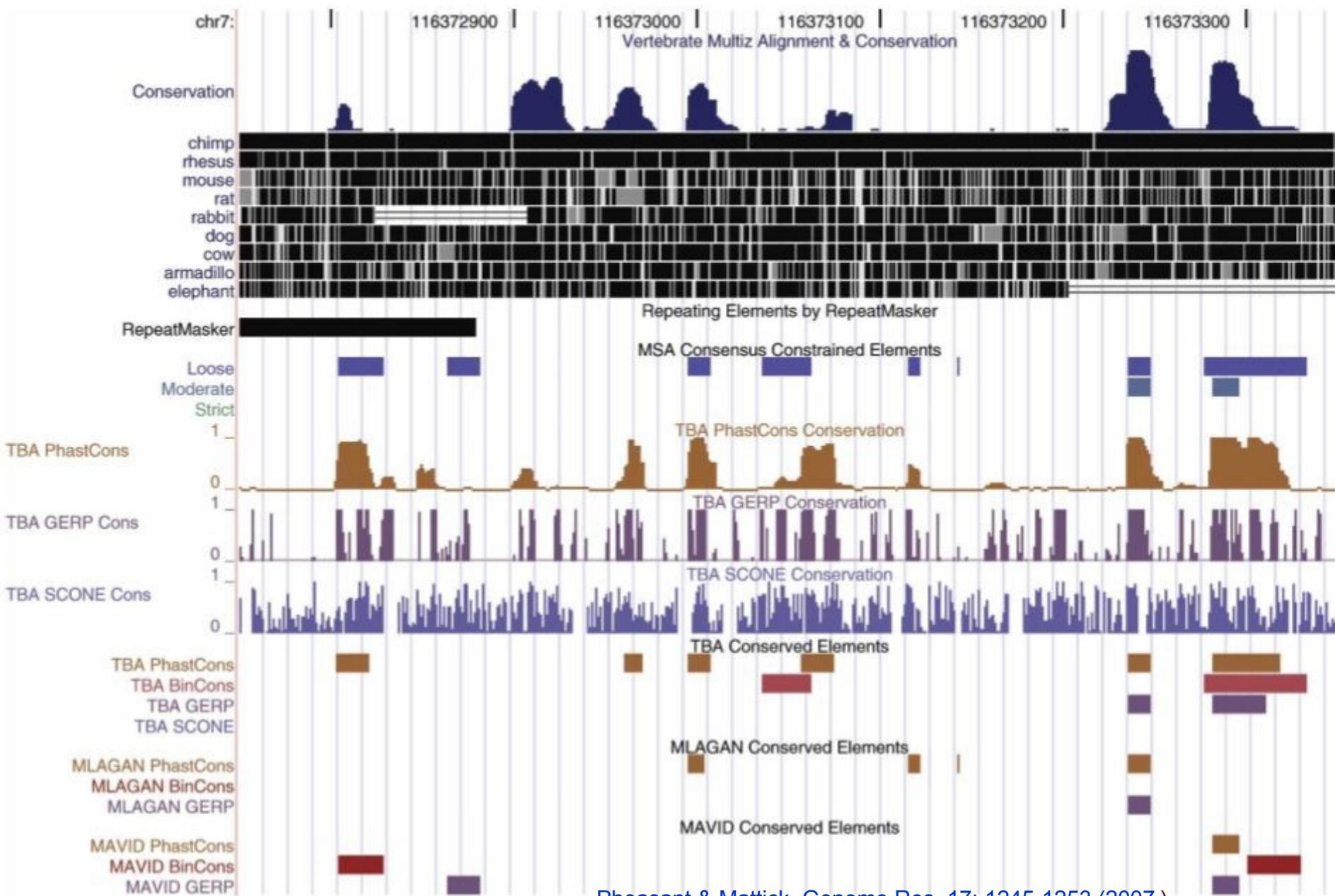
# A Simplified History of Life on Earth



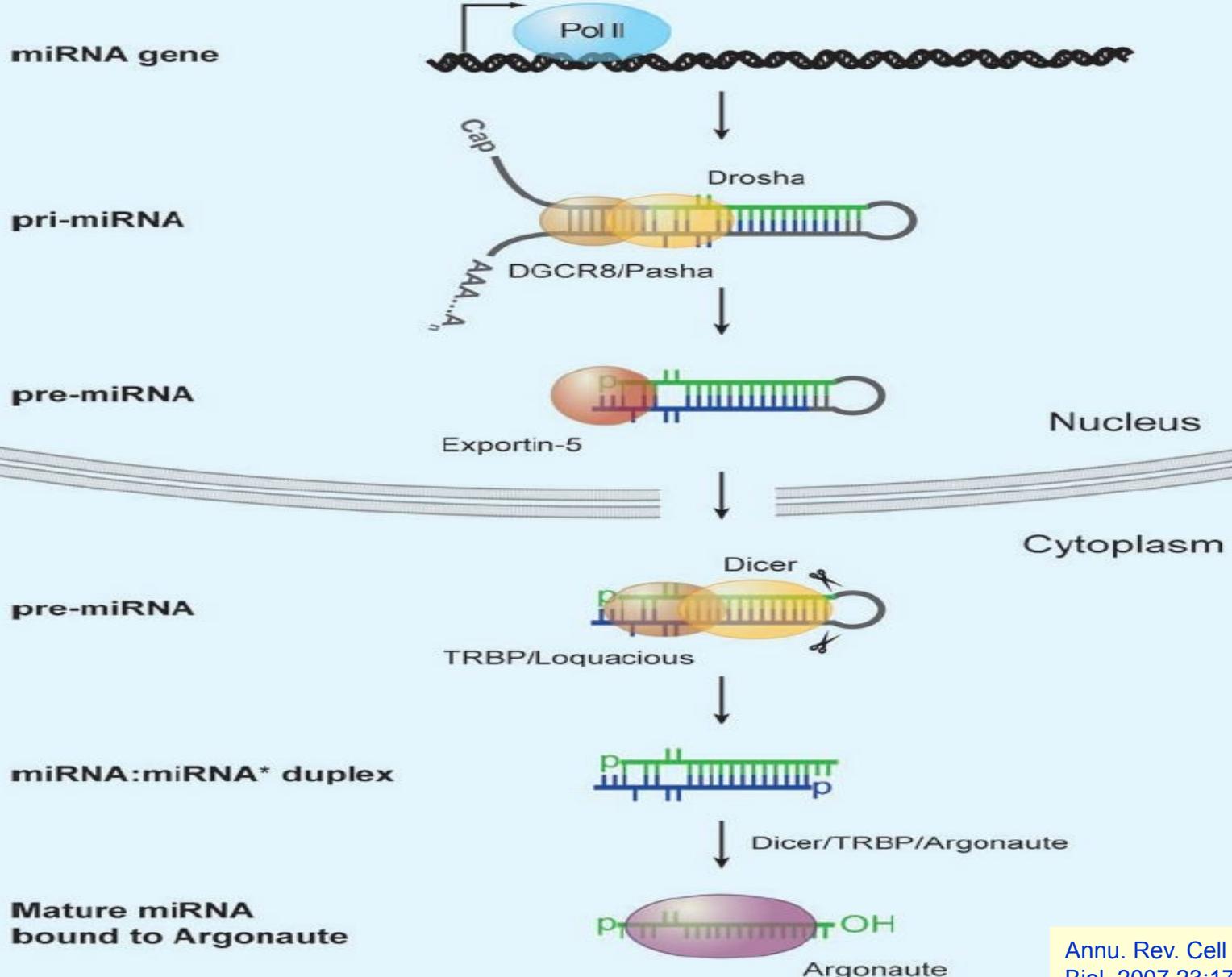
# Ratio of Non-Protein-Coding DNA to Protein-Coding DNA During Evolution



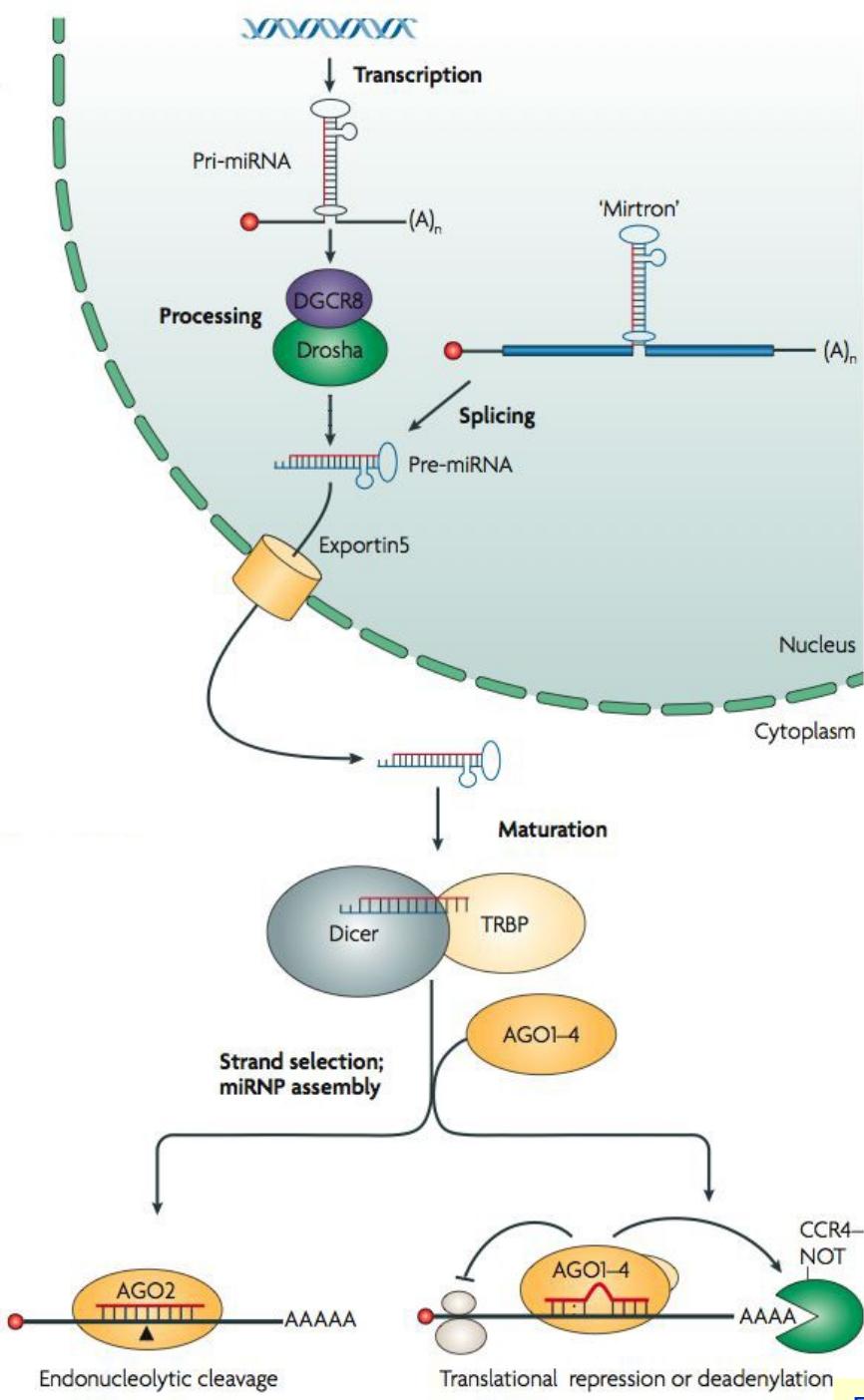
# Conserved Regions in CFTR Intron



# microRNA Biogenesis



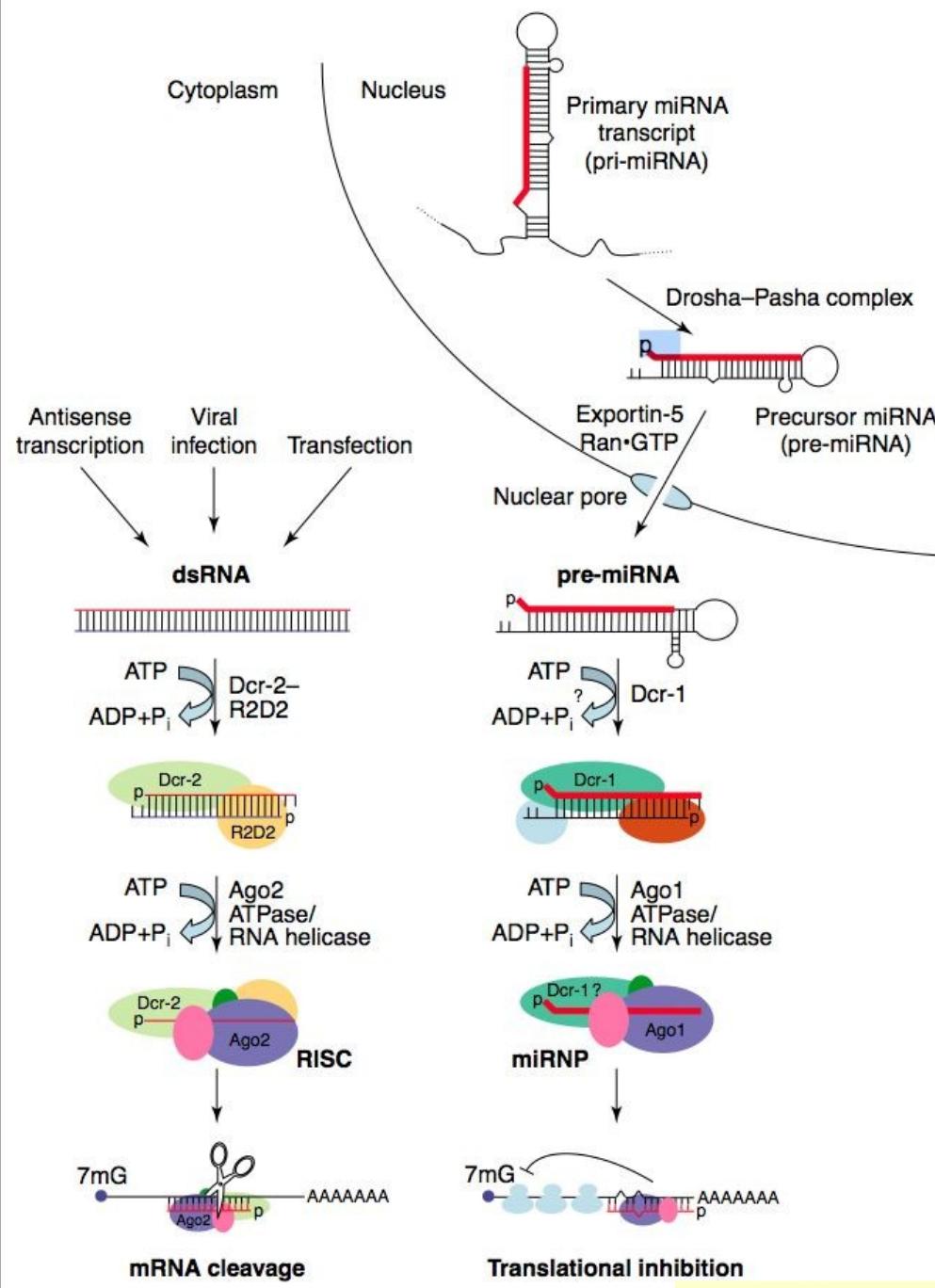
# Biogenesis of miRNA



# siRNA mediated degradation of mRNA

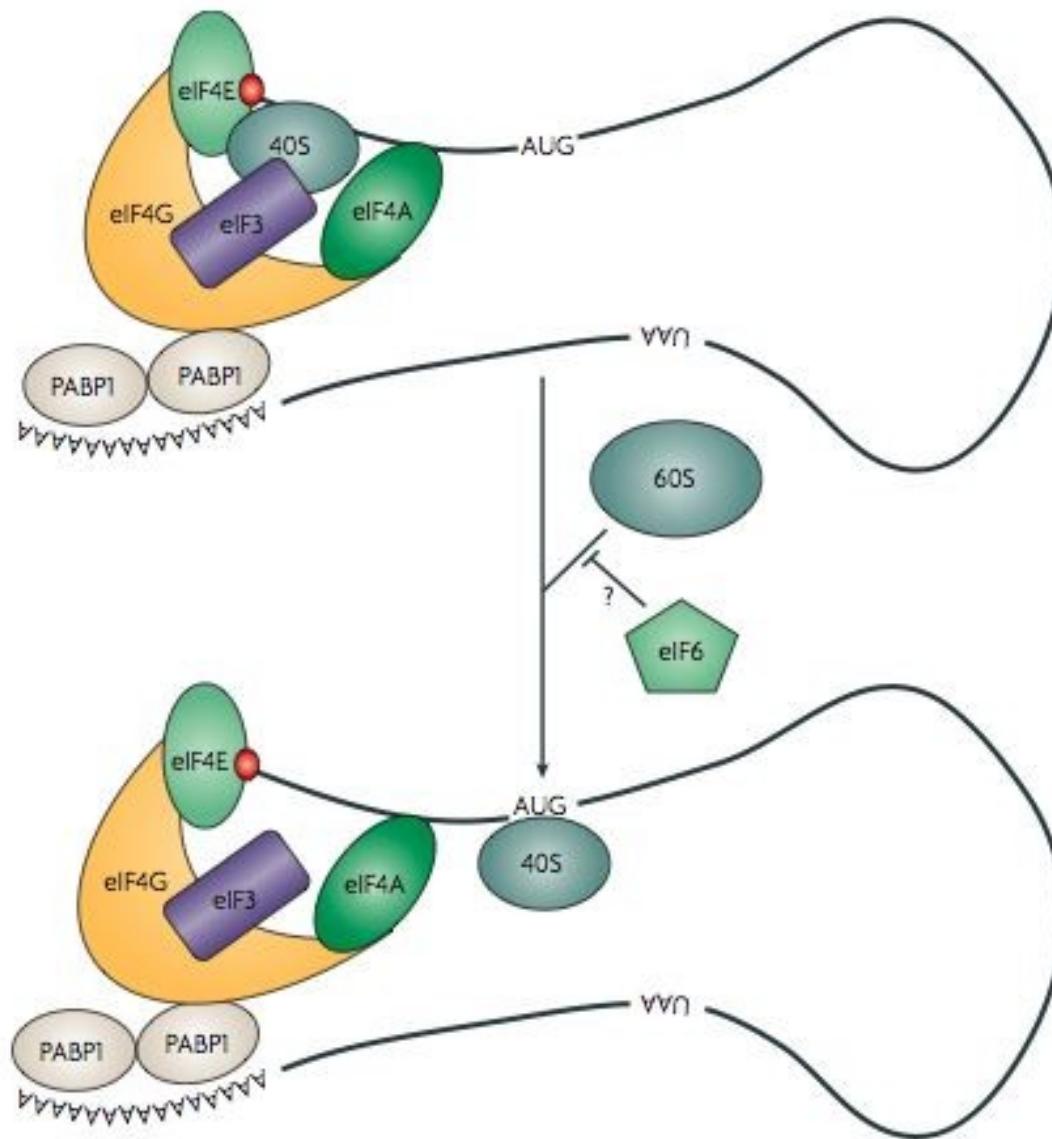
versus

# miRNA mediated inhibition of mRNA translation

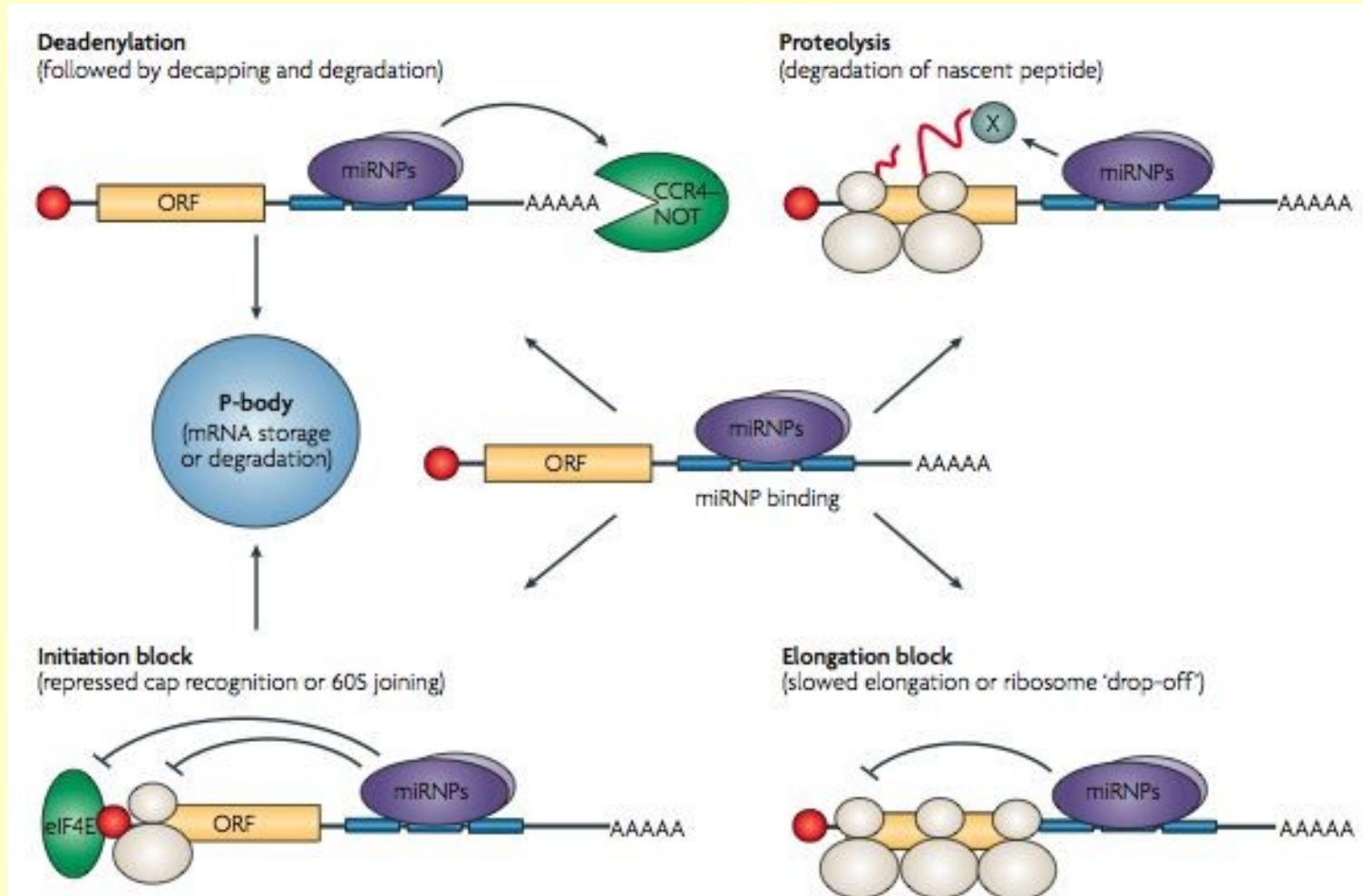


# Initiation of Translation

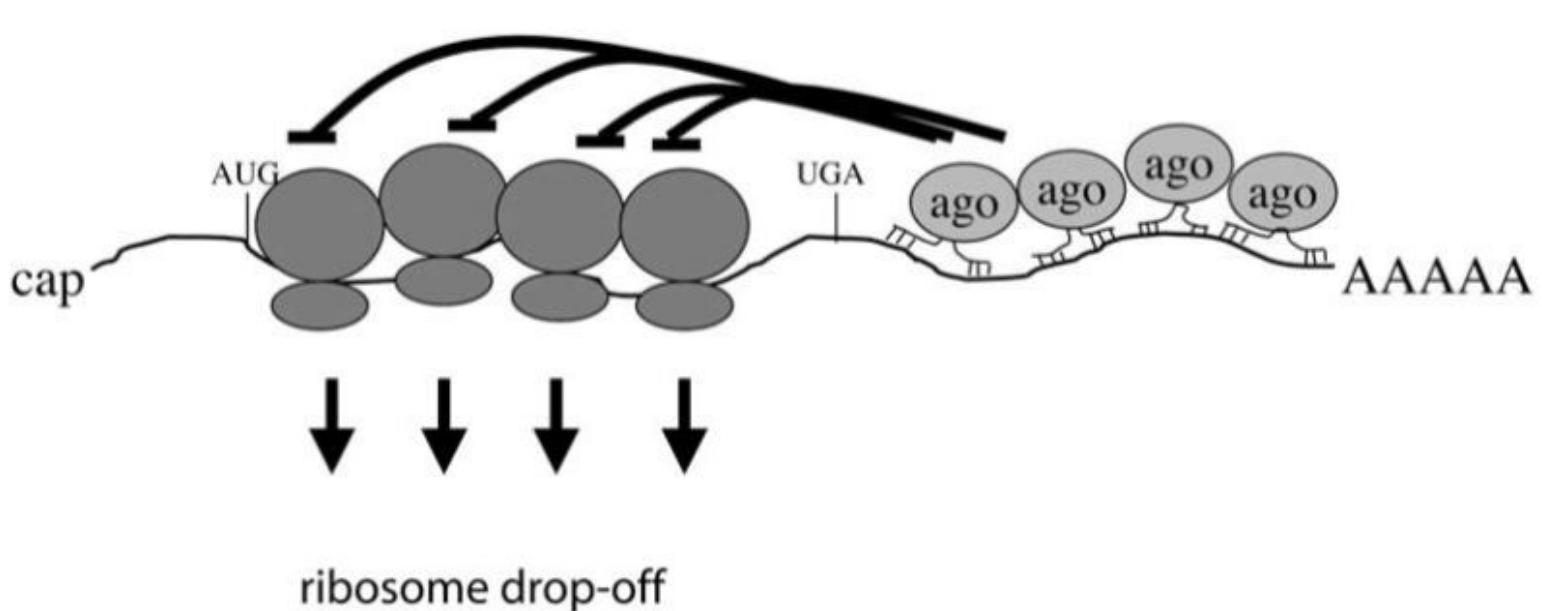
Box 3 | Steps in eukaryotic translation



# Mechanisms of Translational Regulation by miRNP Complexes

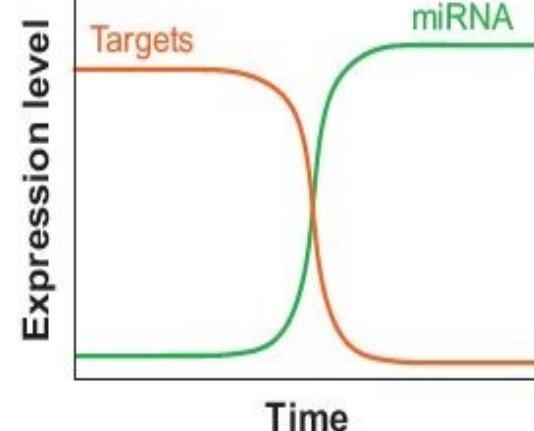
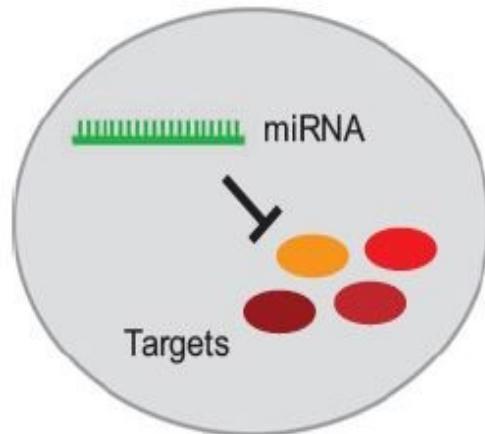


# miRNAs Inhibit Translation by Inducing Ribosome Drop-Off

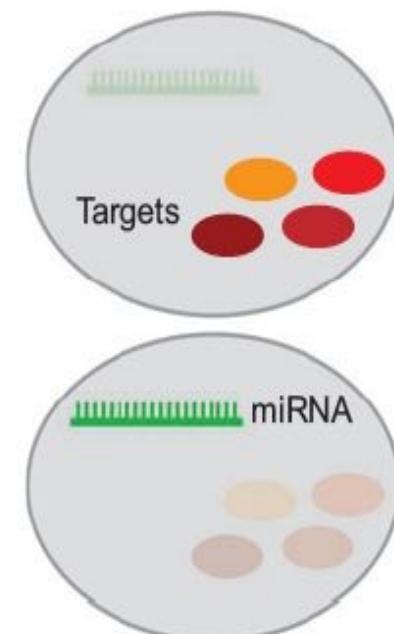
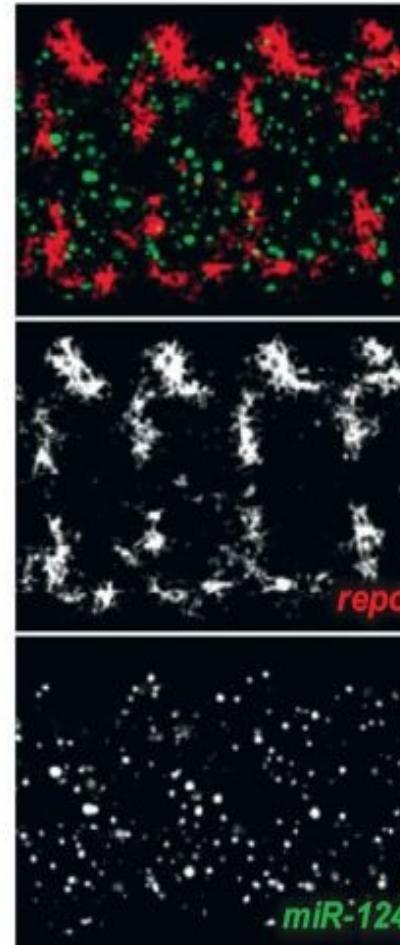


# miRNA Expression Results in Temporal and Spatial Reciprocity with Target Expression

a Temporal reciprocity

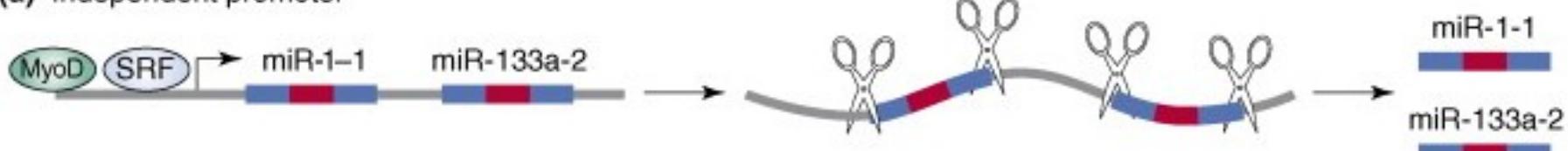


b Spatial reciprocity



# Genomic Organization of miRNA Genes

(a) Independent promoter



(b) Intronic



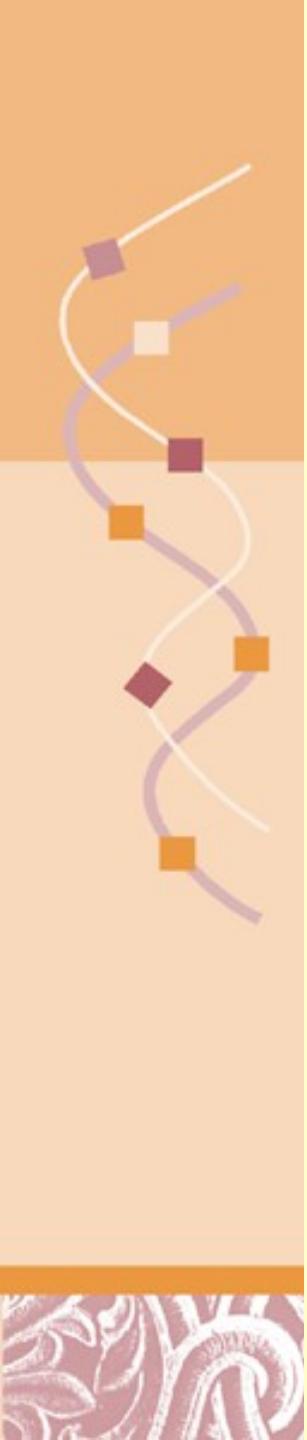
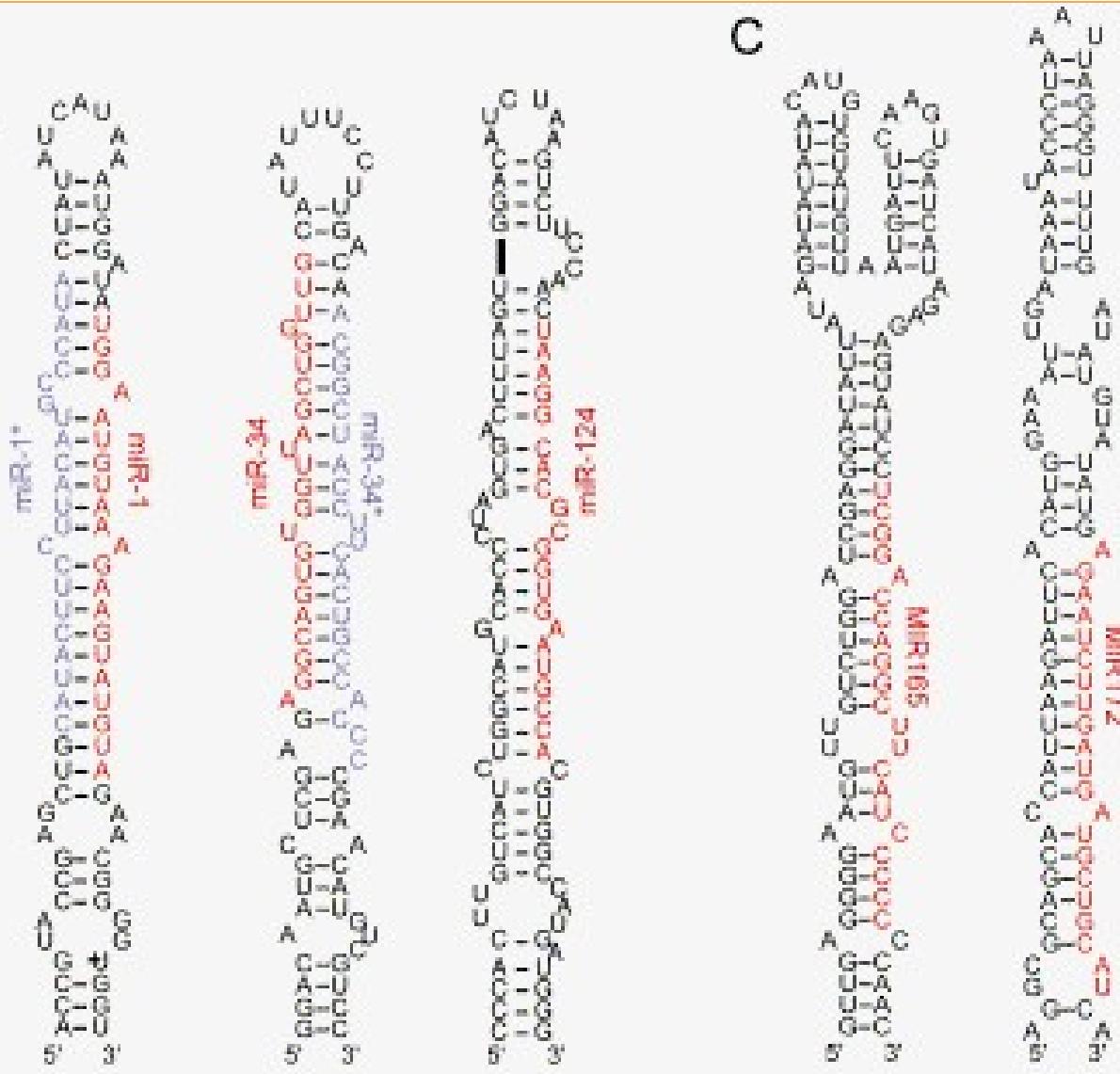
(c) Exonic



- Intrinsic miRNAs often in antisense direction, made from own promoter

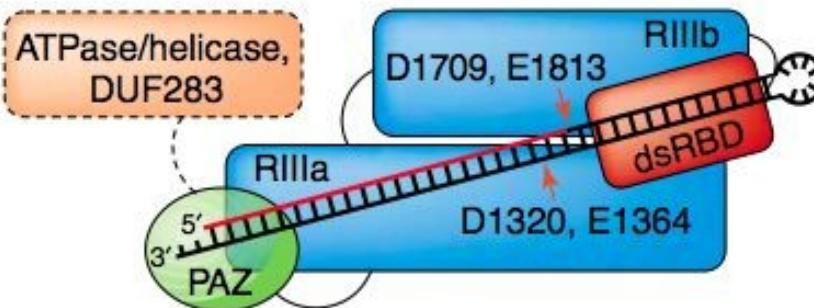
- Exonic miRNAs - non-coding (or in alternatively spliced exons)

# Precursor miRNA Products Form Stem Loop Structures



# Dicer Structure & Function

(a)



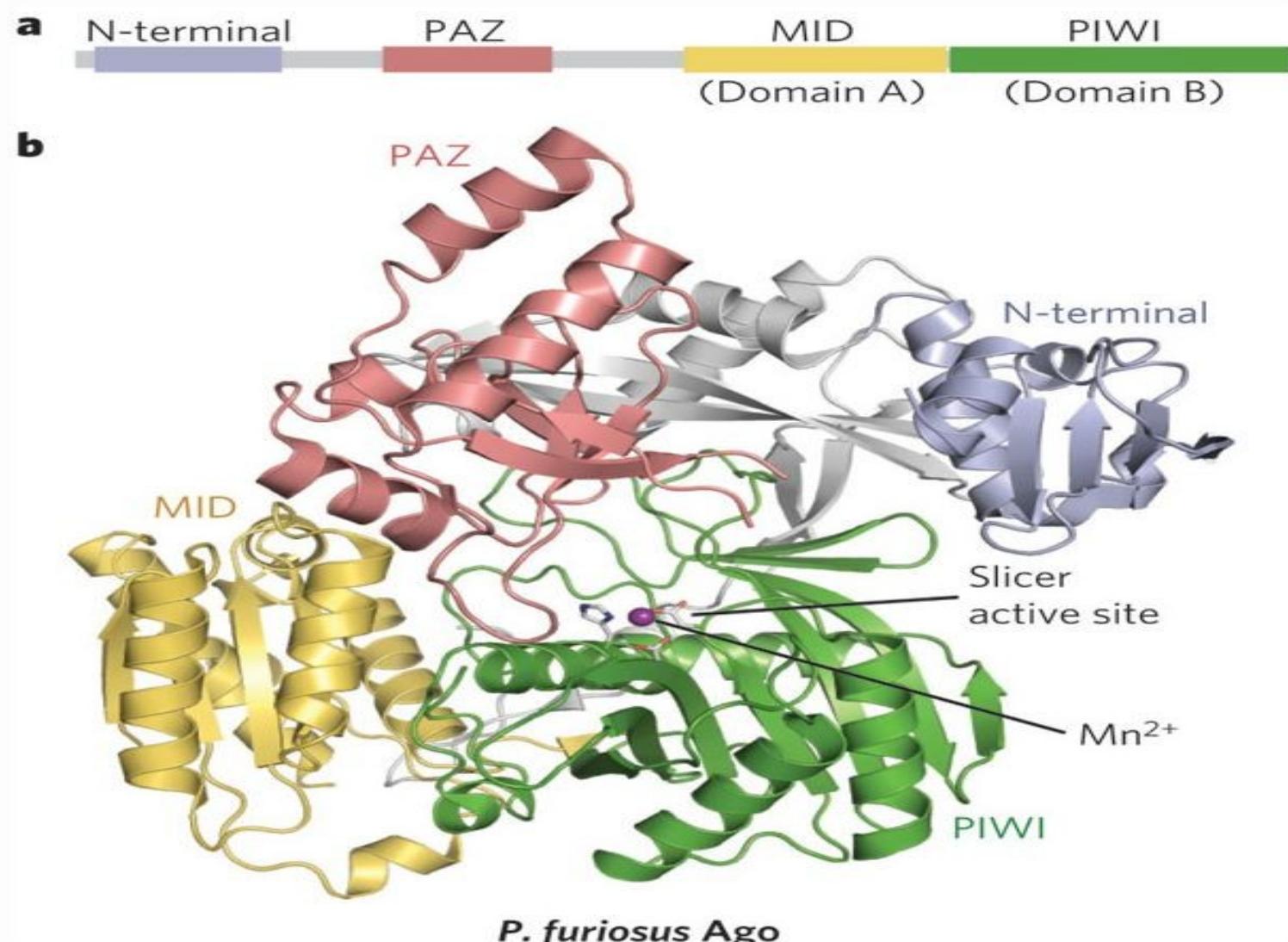
(b)



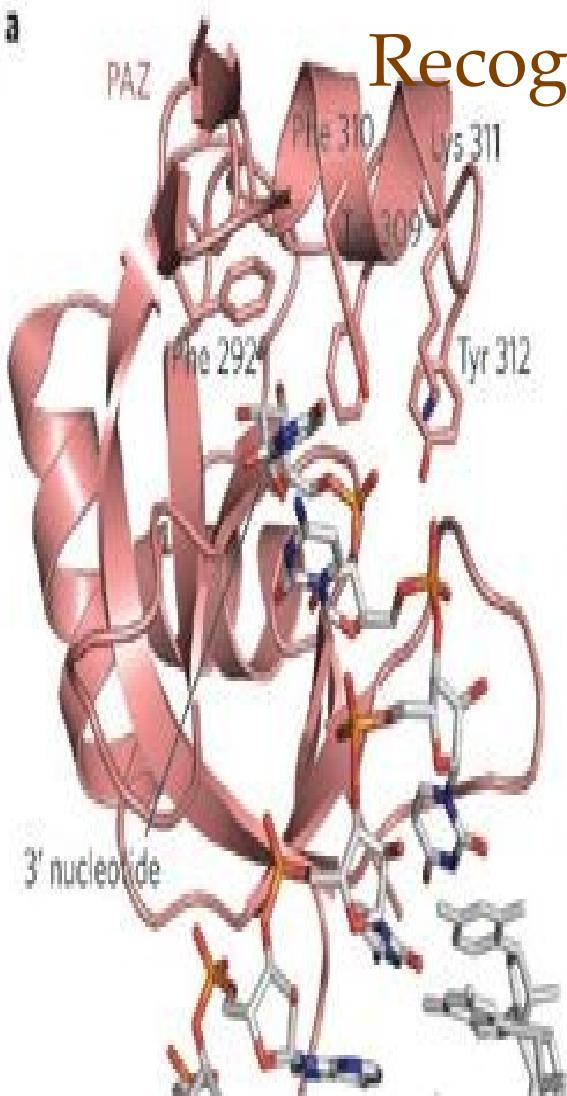
Current Opinion in Structural Biology

Dicer Movie

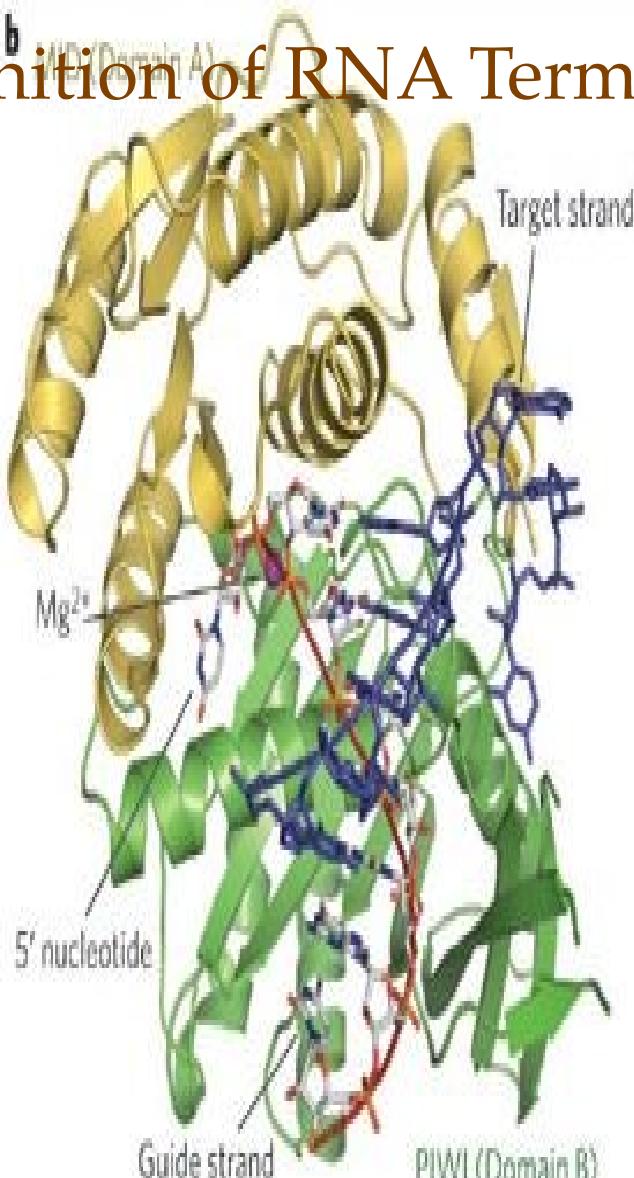
# Argonaute Structure and Function



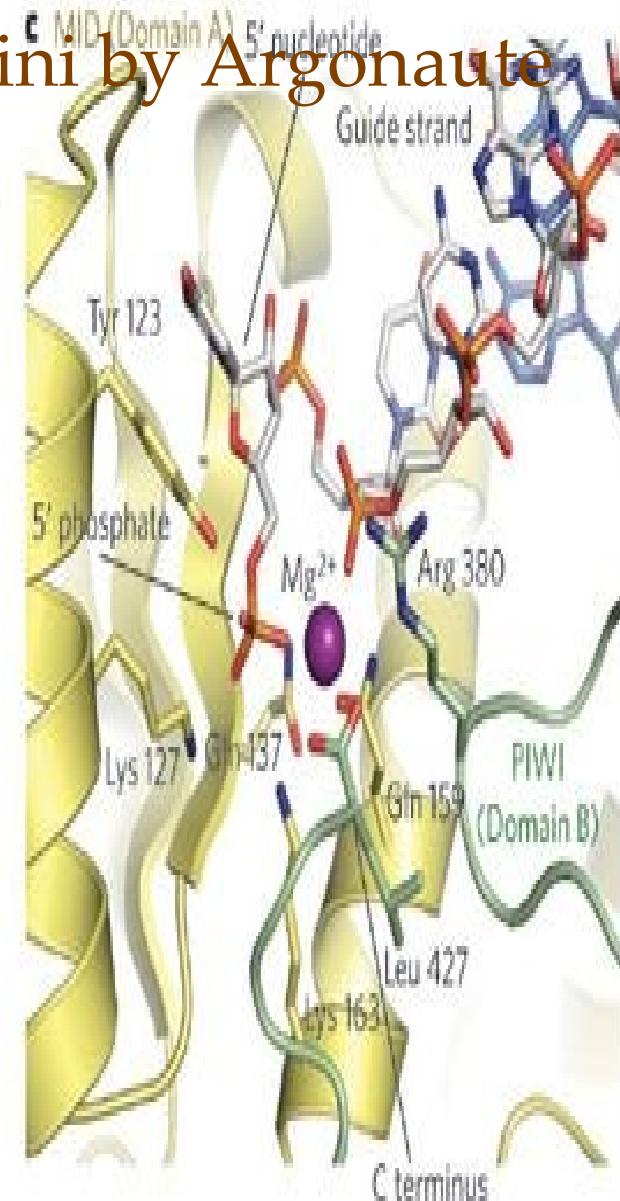
# Recognition of RNA Termini by Argonaute



Human AGO1 PAZ-RNA complex



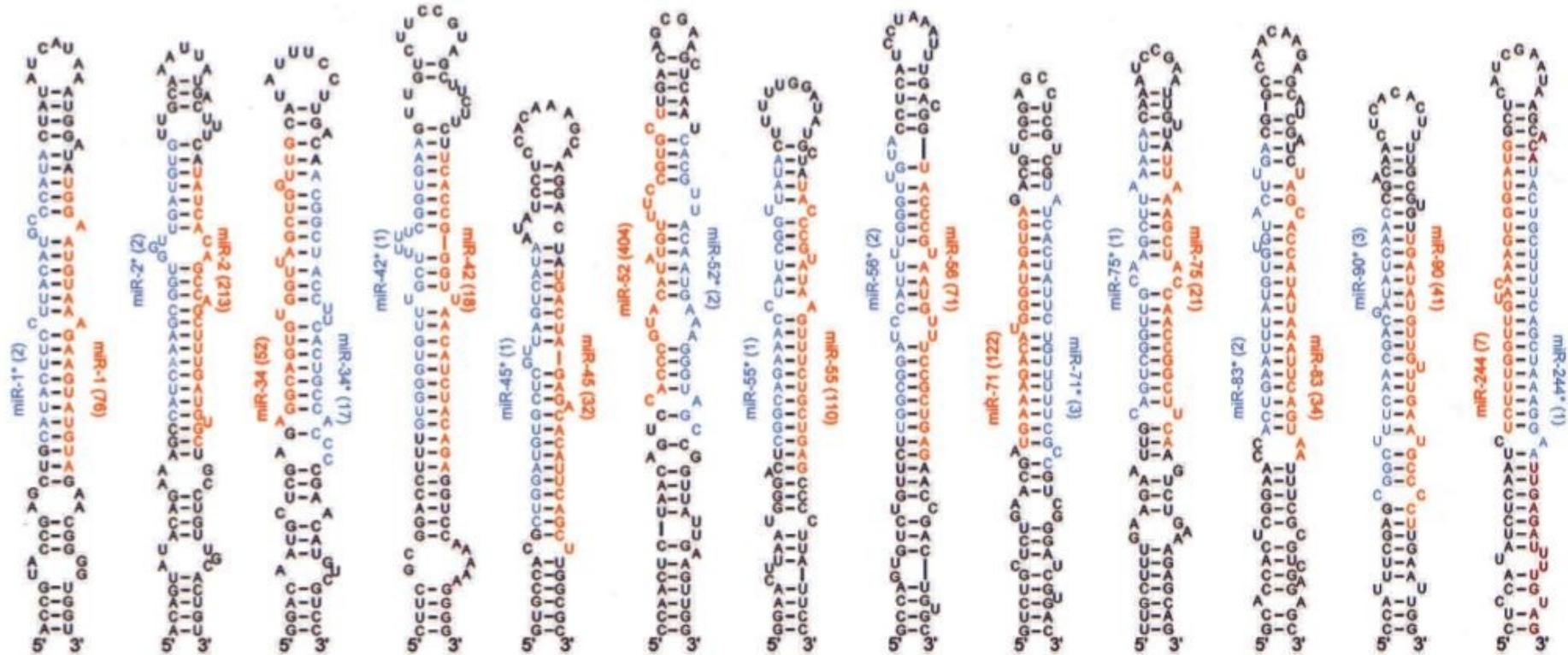
A. fulgidus Piwi-RNA complex

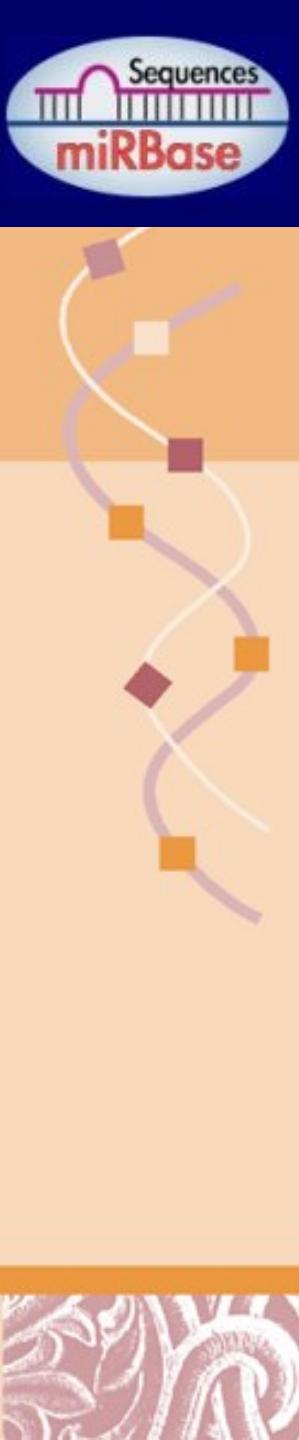


# Homology Between *C. elegans* and *Homo sapiens* miRNAs

<b><i>lin-4</i> family</b>	
UCCCUGAGA...CCCUAACUUGUGA	Hs miR-125b-1
UCCCUGAGA...CCCUAACUUGUGA	Hs miR-125b-2
UCCCUGAGA...CCUCAAQG...CUGA	Ce <i>lin-4</i>
UCCCUGAGAAUUCUCGAAACABCGUU	Ce miR-237
<b><i>let-7</i> family</b>	
AGAGGUAGUAGGGGUUCAUAGU...	Hs <i>let-7d</i>
UGAGGUAGUAGGGGUUCAUAGU...	Hs <i>let-7e</i>
UGAGGUAGUAGGGGUUCAUAGU...	Hs <i>let-7a-1</i>
UGAGGUAGUAGGGGUUCAUAGU...	Hs <i>let-7a-2</i>
UGAGGUAGUAGGGGUUCAUAGU...	Hs <i>let-7a-3</i>
UGAGGUAGUAGGGGUUCAUAGU...	Ce <i>let-7</i>
UGAGGUAGUAGGGGUUCAUAGU...	Hs <i>let-7f-1</i>
UGAGGUAGUAGGGGUUCAUAGU...	Hs <i>let-7f-2</i>
UGAGGUAGUAGGGGUUCAUAGU...	Hs <i>let-7g</i>
UGAGGUAGUAGGGGUUCAUAGU...	Ce <i>let-7i</i>
UGAGGUAGUAGGGGUUCAUAGU...	Hs <i>let-7j-1</i>
UGAGGUAGUAGGGGUUCAUAGU...	Hs <i>let-7j-2</i>
UGAGGUAGUAGGGGUUCAUAGU...	Hs <i>let-7j-3</i>
UGAGGUAGUAGGGGUUCAUAGU...	Hs <i>let-7k</i>
UGAGGUAGUAGGGGUUCAUAGU...	Hs <i>let-7l</i>
UGAGGUAGUAGGGGUUCAUAGU...	Hs <i>let-7m</i>
U...AGGUAGU...UUCAGUUGUUGG...	Hs miR-196-1
U...AGGUAGU...UUCAGUUGUUGG...	Hs miR-196-2
UGAGGUAGUAGGGGUUCAUAGU...	Ce miR-84
UGAGGUAGG...CUCAGUAGAUGCAGA...	Ce miR-48
UGAGGUAGG...UGC...G...AGAAAUGA...	Ce miR-241
<b><i>mir-1</i> family</b>	
UGGAAGUGUAAAAGAAGUAUGUA...	Hs miR-1b
UGGAAGUGUAAAAGAAGUAUGUA...	Hs miR-1d
UGGAAGUGUAAAAGAAGUAUGUA...	Ce miR-1
UGGAAGUGUAAAAGAAGUGUGG...	Hs miR-206
<b><i>mir-9</i> family</b>	
UCUUUUGGUUAU...CUAGCUG...UAUGA	Hs miR-9-1
UCUUUUGGUUAU...CUAGCUG...UAUGA	Hs miR-9-2
UCUUUUGGUUUGUACAAAGUGGUUAUG...	Ce miR-244
<b><i>mir-10</i> family</b>	
AACCC...GUAGAUCCGAACU...UGUG...	Hs miR-100-1
AACCC...GUAGAUCCGAACU...UGUG...	Hs miR-100-2
CACCC...GUAGAUCCGACCU...UGCG...	Hs miR-99b
UACCCUGUAGA...UCGAGCUGUGUGU	Ce miR-57
UACCCUGUAGA...UCGAGCUGUGUGU	Hs miR-10a
UACCCUGUAGA...UCGAGA...	Hs miR-10b
AACCC...GUAGAUCCGAACU...UGU...	Hs miR-99a
UACCC...GUAGCUCCUAAUCCAUGUU...	Ce miR-51
<b><i>mir-19</i> family</b>	
UGUGCAAAUUCUAU...GCAAAACUGA...	Hs miR-19a
UGUGCAAAUUCUAU...GCAAAACUGA...	Hs miR-19b-1
UGUGCAAAUUCUAU...GCAAAACUGA...	Hs miR-19b-2
...UGCAAAUUCUUCGGCG...ACUGUAGG	Ce miR-254
<b><i>mir-25</i> family</b>	
UAUUGCACUUGUC...CGGC...CUGU	Hs miR-92-1
UAUUGCACUUGUC...CGGCC...CUGU	Hs miR-92-2
UAUUGCACUCUC...CGGC...CUGA	Ce miR-235
CAUUGCACUUGUC...CGGU...CUGA	Hs miR-25-1
CAUUGCACUUGUC...CGGU...CUGA	Hs miR-25-2
UAUUGCACAUUA...CUGAU...UGC	Hs miR-32
<b><i>mir-29</i> family</b>	
UAGCACCACUUGAAAUCAGUGU...	Hs miR-29b-1
UAGCACCACUUGAAAUCAGUGU...	Hs miR-29b-2
UAGCACCACUUGAAAUCAGUGU...	Hs miR-29b-3
UAGCACCACUUGAAAUCAGUGU...	Hs miR-29c
UAGCACCACUUCAGAAAUCGGU...	Hs miR-29a-1
UAGCACCACUUCAGAAAUCGGU...	Hs miR-29a-2
UAGCACCACUUAUAAAUCAGUAA...	Ce miR-83
<b><i>mir-31</i> family</b>	
AGGCAGAAGUAGGUUGGCA...U...	Ce miR-72
AGGCAGAAGUAGGUUGGCA...U...	Hs miR-31
AGGCAGAAGUAGGUAGGCA...AGGU...	Ce miR-73
<b><i>mir-34</i> family</b>	
AGGCAGUGUGGUUUA...GCUGGUUG...	Ce miR-34
UGGCAGUGUC...UUA...GCUGGUUG...	Hs miR-34
UGG...AGUGUGACA...AUGGUUGUUG...	Hs miR-122a
<b><i>mir-50</i> family</b>	
UGAUAAUGUAUACU...AGCUUACAG...	Ce miR-62
UGAUAAUGUCUGGU...AUUCU...UGGU...	Ce miR-50
UGAUAAUGUUDGAG...AUAAA...GGU...	Hs miR-190
UGAUAAUGUUGUUU...GAUAGCCCG...	Ce miR-90
<b><i>mir-74</i> family</b>	
UGG...AGAGAA...AGGCAGUUC...	Hs miR-185
UGGCA...AGAAA...AUGGCAGU...CUACA	Ce miR-74
<b><i>mir-76</i> family</b>	
UCGU...UGUUGL...AU...GAAGCCUUGA	Ce miR-76
UCGUC...CUUUGUUGU...CAGCCG...	Hs miR-187
<b><i>mir-79</i> family</b>	
UAAAAGCUAGGUUACCAAGCU...	Ce miR-79
UAAAAGCUAGUAAACCGAAAGC...	Hs miR-131
UAAAAGCUAC...CAACCG...GCUUCA	Ce miR-75
<b><i>mir-80</i> family</b>	
UGAGAUCAUC...GU...GAAAGCAGU	Ce miR-81
UGAGAUCAUC...GU...GAAAGCAGU	Ce miR-82
UGAGAUCAUAGUGA...AAAGCCGA...	Ce miR-80
UGAGAUGAAGCACUGUA...GCUCA	Hs miR-143
<b><i>mir-105</i> family</b>	
UCAAUAGC...UCA...GACUCCUGU...	Hs miR-105-1
UCAAUAGC...UCA...GACUCCUGU...	Hs miR-105-2
UCAAUAGCAUCUUAACUGCGGUGA	Ce miR-232
<b><i>mir-124</i> family</b>	
UAAAAGGCACCGCG...GU...GAAUGCCA...	Hs miR-124a
UAAAAGGCACCGCG...GU...GAAUGCCA...	Hs miR-124a
UAAAAGGCACCGCG...GU...GAAUGCCA...	Hs miR-124a
UAAAAGGCACCGCG...GU...GAAUGCCA...	Ce miR-124
AAUUGCAC...UGCAU...GAAU...UCACCG	Ce miR-228
AAUUGCAC...UG...GUAGAAU...UCACUG	Hs miR-183
<b><i>mir-133</i> family</b>	
UUGGUCCCCUUCUCAACCAGCUGU	Hs miR-133a-1
UUGGUCCCCUUCUCAACCAGCUGU	Hs miR-133a-2
UUGGUCCCCUUCUCAACCAGCUGA	Hs miR-133b
AUGGUCCCCUUCUCAAGUAGCUC	Ce miR-245
<b><i>mir-137</i> family</b>	
UAUUGCCUCGAGAAAUACCCUU...	Ce miR-234
UAUUGCCUUAAGAAAUACCCGUAG	Hs miR-137
<b><i>mir-141</i> family</b>	
UAAUACUGUCACGGAAUAGACCCU	Ce miR-236
UACACUGUCACGGAAUAGACGG	Hs miR-141
<b><i>mir-193</i> family</b>	
UACUGGGCCCCCAA...UCUUCGCU	Ce miR-240
UACUGGGCCUACAAAUCCCAG...	Hs miR-193
<b><i>mir-220</i> family</b>	
CACACACCUCA...CUCACACUGAC	Ce miR-253
C...CACACCGUAAUCU...CACACUU	Hs miR-220

# Predicted miRNA Precursors





# miRBase

<http://www.mirbase.org/>

**miRBase**

MANCHESTER 1824

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miRBase has moved to <http://www.mirbase.org/> - please update your links.

**News - release 14**

The miRBase database has moved to a new location at <http://www.mirbase.org/>, hosted in the [Faculty of Life Sciences, University of Manchester](#). All pre-existing URLs should forward to their new locations. Please update your links, and note the new contact email address ([mirbase@manchester.ac.uk](mailto:mirbase@manchester.ac.uk)).

With release 14, the miRBase sequence database has broken through the 10000 entries barrier!

**miRNA count: 10883 entries**

Release 14: Sept 2009

**Search by miRNA name or keyword**

[Go](#) [Example](#)

**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](mailto: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](#).



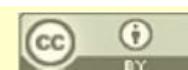
Doug Brutlag 2010

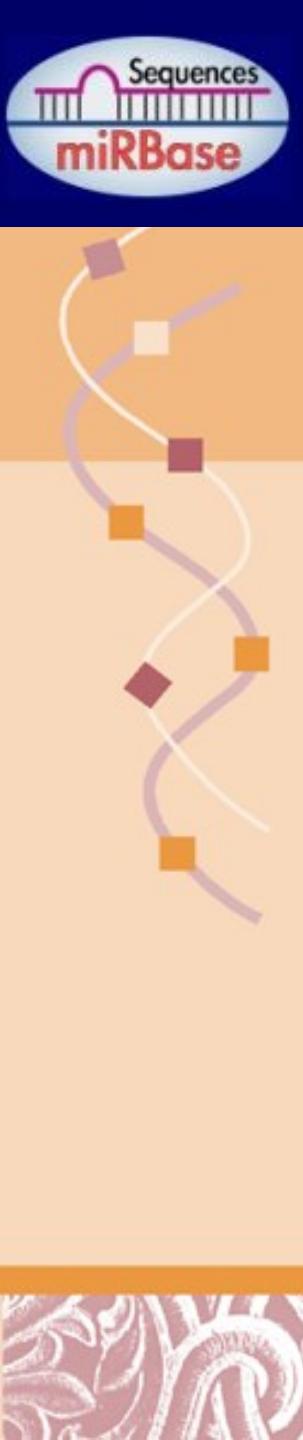


# miRBase Genome Browser

<http://www.mirbase.org/cgi-bin/browse.pl>

- +-- Carnivora
  - +-- [Canis familiaris](#) [CanFam2.0] (321)
- +-- Laurasiatheria
  - +-- [Equus caballus](#) [EquCab2] (346)
- +-- Metatheria
  - +-- [Monodelphis domestica](#) [MONDOM5] (157)
- +-- Primates
  - +-- Atelidae
    - +-- [Ateles geoffroyi](#) (60)
    - +-- [Lagothrix lagotricha](#) (48)
  - +-- Cebidae
    - +-- [Saguinus labiatus](#) (42)
  - +-- Cercopithecidae
    - +-- [Macaca mulatta](#) [MMUL1.0] (485)
    - +-- [Macaca nemestrina](#) (75)
    - +-- [Pygathrix bieti](#) (11)
  - +-- Hominidae
    - +-- [Gorilla gorilla](#) (86)
    - +-- [Homo sapiens](#) [GRCh37] (721)





# miRBase Human miRNAs

[http://www.mirbase.org/cgi-bin/mirna\\_summary.pl?org=hsa](http://www.mirbase.org/cgi-bin/mirna_summary.pl?org=hsa)

miRBase has moved to <http://www.mirbase.org/> - please update your links.

## Homo sapiens miRNAs (721 sequences)

ID	Accession	Chromosome	Start	End	Strand	Fetch
<a href="#">hsa-let-7a-1</a>	<a href="#">MI0000060</a>	9	96938239	96938318	+	<input type="checkbox"/>
<a href="#">hsa-let-7a-2</a>	<a href="#">MI0000061</a>	11	122017230	122017301	-	<input type="checkbox"/>
<a href="#">hsa-let-7a-3</a>	<a href="#">MI0000062</a>	22	46508629	46508702	+	<input type="checkbox"/>
<a href="#">hsa-let-7b</a>	<a href="#">MI0000063</a>	22	46509566	46509648	+	<input type="checkbox"/>
<a href="#">hsa-let-7c</a>	<a href="#">MI0000064</a>	21	17912148	17912231	+	<input type="checkbox"/>
<a href="#">hsa-let-7d</a>	<a href="#">MI0000065</a>	9	96941116	96941202	+	<input type="checkbox"/>
<a href="#">hsa-let-7e</a>	<a href="#">MI0000066</a>	19	52196039	52196117	+	<input type="checkbox"/>
<a href="#">hsa-let-7f-1</a>	<a href="#">MI0000067</a>	9	96938629	96938715	+	<input type="checkbox"/>
<a href="#">hsa-let-7f-2</a>	<a href="#">MI0000068</a>	X	53584153	53584235	-	<input type="checkbox"/>
<a href="#">hsa-let-7g</a>	<a href="#">MI0000433</a>	3	52302294	52302377	-	<input type="checkbox"/>
<a href="#">hsa-let-7i</a>	<a href="#">MI0000434</a>	12	62997466	62997549	+	<input type="checkbox"/>
<a href="#">hsa-mir-1-1</a>	<a href="#">MI0000651</a>	20	61151513	61151583	+	<input type="checkbox"/>
<a href="#">hsa-mir-1-2</a>	<a href="#">MI0000437</a>	18	19408965	19409049	-	<input type="checkbox"/>
<a href="#">hsa-mir-7-1</a>	<a href="#">MI0000263</a>	9	86584663	86584772	-	<input type="checkbox"/>
<a href="#">hsa-mir-7-2</a>	<a href="#">MI0000264</a>	15	89155056	89155165	+	<input type="checkbox"/>
<a href="#">hsa-mir-7-3</a>	<a href="#">MI0000265</a>	19	4770682	4770791	+	<input type="checkbox"/>
<a href="#">hsa-mir-9-1</a>	<a href="#">MI0000466</a>	1	156390133	156390221	-	<input type="checkbox"/>
<a href="#">hsa-mir-9-2</a>	<a href="#">MI0000467</a>	5	87962671	87962757	-	<input type="checkbox"/>
<a href="#">hsa-mir-9-3</a>	<a href="#">MI0000468</a>	15	89911248	89911337	+	<input type="checkbox"/>
<a href="#">hsa-mir-10a</a>	<a href="#">MI0000266</a>	17	46657200	46657309	-	<input type="checkbox"/>
<a href="#">hsa-mir-10b</a>	<a href="#">MI0000267</a>	2	177015031	177015140	+	<input type="checkbox"/>
<a href="#">hsa-mir-15a</a>	<a href="#">MI0000069</a>	13	50623255	50623337	-	<input type="checkbox"/>
<a href="#">hsa-mir-15b</a>	<a href="#">MI0000438</a>	3	160122376	160122473	+	<input type="checkbox"/>
<a href="#">hsa-mir-16-1</a>	<a href="#">MI0000070</a>	10	50623100	50623107	-	<input type="checkbox"/>





# miRBase Human let-7a-1

[http://www.mirbase.org/cgi-bin/mirna\\_entry.pl?acc=MI0000060](http://www.mirbase.org/cgi-bin/mirna_entry.pl?acc=MI0000060)

miRBase

Home Search Browse Genomics Help Download Submit hsa-let-7a-1

miRBase has moved to <http://www.mirbase.org/> - please update your links.

### Stem-loop sequence MI0000060

<b>Accession</b>	MI0000060
<b>ID</b>	hsa-let-7a-1
<b>Symbol</b>	<a href="#">HGNC:MIRLET7A1</a>
<b>Description</b>	Homo sapiens let-7a-1 stem-loop
<b>Stem-loop</b>	<p>Get sequence</p>
<b>Comments</b>	let-7a* cloned in [6] has a 1 nt 3' extension (U), which is incompatible with the genome sequence.
<b>Genome context</b>	<i>Coordinates (GRCh37)</i> 9: 96938239-96938318 [+] <a href="#">View flanking features</a> <i>Overlapping transcripts</i> intergenic
<b>Clustered miRNAs</b>	< 10kb from hsa-let-7a-1 hsa-let-7a-1 <a href="#">9: 96938239-96938318 [+]</a> hsa-let-7f-1 <a href="#">9: 96938629-96938715 [+]</a> hsa-let-7d <a href="#">9: 96941116-96941202 [+]</a>
<b>Database links</b>	EMBL: <a href="#">AJ421724</a> RFAM: RF00027; <a href="#">let-7</a> HGNC: 31476; <a href="#">MIRLET7A1</a>



# miRBase Human let-7a-1 Page 2

[http://www.mirbase.org/cgi-bin/mirna\\_entry.pl?acc=MI0000060](http://www.mirbase.org/cgi-bin/mirna_entry.pl?acc=MI0000060)



## Mature sequence MIMAT0000062

<b>Accession</b>	MIMAT0000062
<b>ID</b>	hsa-let-7a
<b>Sequence</b>	6 - <i>ugagguaguagguuguauuu</i> - 27
	<a href="#">Get sequence</a>
<b>Evidence</b>	experimental; cloned [1-3,5-8], Northern [1]
<b>Predicted targets</b>	MICROCOSM: <a href="#">hsa-let-7a</a> TARGETSCAN: <a href="#">hsa-let-7a</a> PICTAR-VERT: <a href="#">hsa-let-7a</a>

## Minor miR\* sequence MIMAT0004481

<b>Accession</b>	MIMAT0004481
<b>ID</b>	hsa-let-7a*
<b>Sequence</b>	57 - <i>cuauacaaucuacugucuuuc</i> - 77
	<a href="#">Get sequence</a>
<b>Evidence</b>	experimental; cloned [6]
<b>Predicted targets</b>	MICROCOSM: <a href="#">hsa-let-7a*</a> TARGETSCAN: <a href="#">hsa-let-7a*</a>

## References

- 1** "Identification of novel genes coding for small expressed RNAs"  
Lagos-Quintana M, Rauhut R, Lendeckel W, Tuschl T  
Science. 294:853-858(2001).
- 2** "Human embryonic stem cells express a unique set of microRNAs"  
Suh MR, Lee Y, Kim JY, Kim SK, Moon SH, Lee JY, Cha KY, Chung HM, Yoon HS, Moon SY, Kim VN, Kim KS  
Dev Biol. 270:488-498(2004).

## 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-let-7a

1046 hits found.

Page 1 of 21

[1](#) [2](#) [3](#) [4](#) [5](#) [6](#) [7](#) [8](#) [9](#) [10](#) [11](#) .. [21](#) [next>>](#)

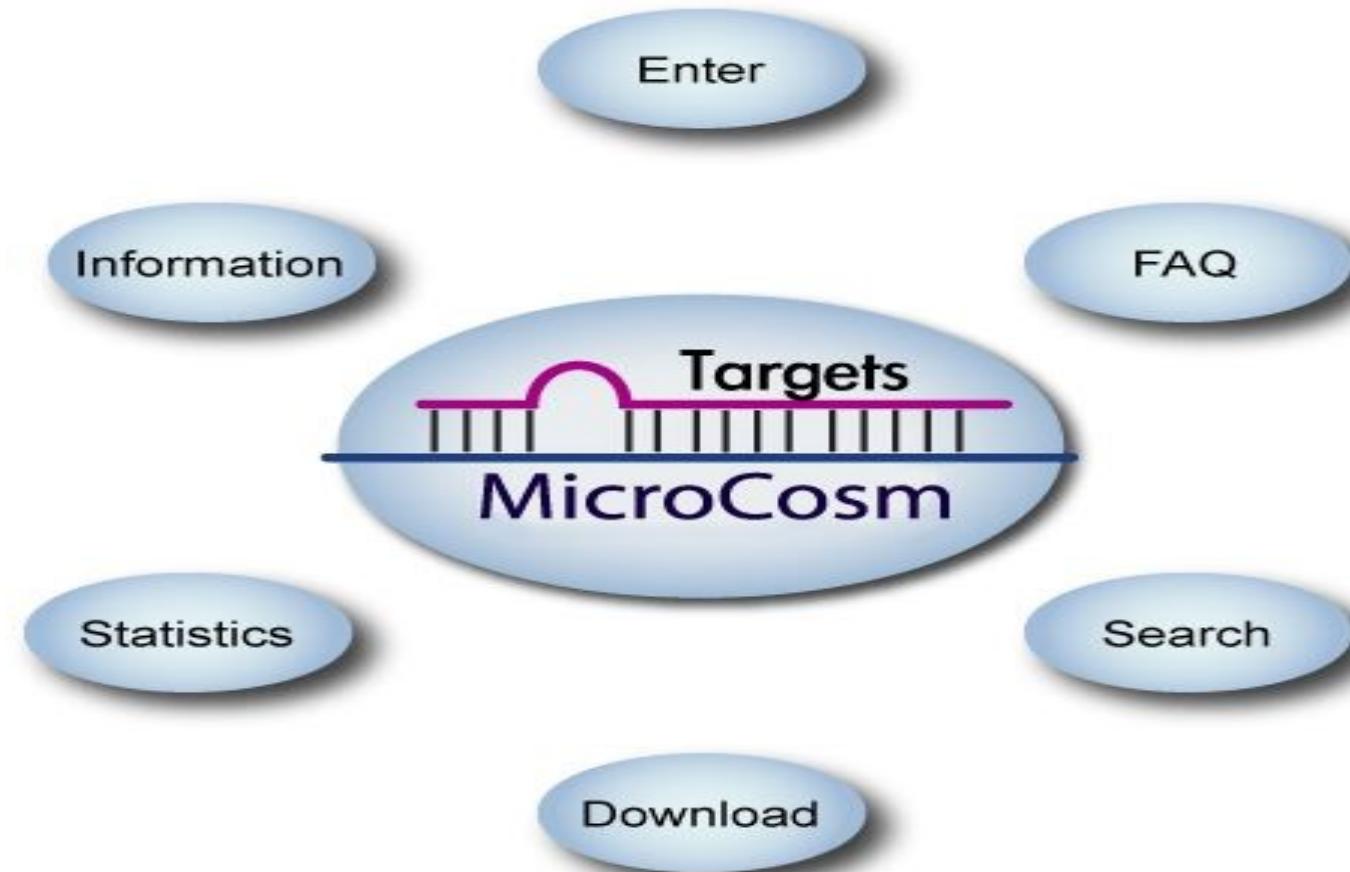
Species	Gene Name	Transcript	Description	GO Terms	Score	Energy	P-value	Length	Total Sites	No. Cons Species	No. miRNAs	
Homo sapiens	TRIM71	<a href="#">ENST00000383763</a>	Tripartite motif-containing protein 71 (Lin-41 homolog). [Source:Uniprot/SWISSPROT;Acc:Q2Q1W2]		16.4005	-18.93	1.11674e-10	1000	20	7	32 [+]	<a href="#">View</a>
Homo sapiens	Q5FWF1_HUMAN	<a href="#">ENST00000257359</a>	ADAMTS8 protein (Fragment). [Source:Uniprot/SPTREMBL;Acc:Q5FWF1]		16.062	-15.06	5.55098e-10	633	21	9	38 [+]	<a href="#">View</a>
Homo sapiens	GALE	<a href="#">ENST00000313298</a>	UDP-glucose 4-epimerase (EC 5.1.3.2) (Galactowaldenase) (UDP-galactose 4-epimerase). [Source:Uniprot/SWISSPROT;Acc:Q14376]		16.7617	-18.05	2.13152e-08	350	16	6	53 [+]	<a href="#">View</a>
Homo sapiens	SEMA4C	<a href="#">ENST00000305476</a>	Semaphorin-4C precursor. [Source:Uniprot/SWISSPROT;Acc:Q9C0C4]		16.1569	-19.34	2.94605e-08	884	25	9	39 [+]	<a href="#">View</a>
Homo sapiens	PIAS4	<a href="#">ENST00000262971</a>	E3 SUMO-protein ligase PIAS4 (Protein inhibitor of activated STAT protein 4) (Protein inhibitor of activated STAT protein gamma) (PIAS- gamma) (PIASy). [Source:Uniprot/SWISSPROT;Acc:Q8N2W9]		16.9125	-20.67	5.95665e-08	1510	21	3	23 [+]	<a href="#">View</a>
Homo sapiens	MYC	<a href="#">ENST00000377970</a>	Myc proto-oncogene protein (c-Myc) (Transcription factor p64). [Source:Uniprot/SWISSPROT;Acc:P01106]		17.2032	-15.97	7.34567e-08	467	16	13	40 [+]	<a href="#">View</a>
Homo sapiens	RNF20	<a href="#">ENST00000374819</a>	E3 ubiquitin-protein ligase BRE1A (EC 6.3.2.-) (BRE1-A) (hBRE1) (RING finger protein 20). [Source:Uniprot/SWISSPROT;Acc:Q5VTR2]		16.3346	-19.63	8.72291e-08	922	26	7	30 [+]	<a href="#">View</a>
Homo sapiens	UHRF2	<a href="#">ENST00000276893</a>	E3 ubiquitin-protein ligase UHRF2 (EC 6.3.2.-) (Ubiquitin-like PHD and RING finger domain-containing protein 2) (Ubiquitin-like-containing PHD and RING finger domains protein 2) (Np95/CBP90-like RING finger protein) (Np95-like RING finger protein) (Nucleic acid binding protein 2). [Source:Uniprot/SWISSPROT;Acc:Q96PU4]		15.9349	-16.89	8.91282e-08	872	19	9	33 [+]	<a href="#">View</a>
Homo sapiens	TARBP2	<a href="#">ENST00000266987</a>	TAR RNA-binding protein 2 (Trans-activation-responsive RNA-binding protein). [Source:Uniprot/SWISSPROT;Acc:Q15633]		17.7377	-18.41	9.98851e-08	281	16	8	74 [+]	<a href="#">View</a>
Homo sapiens	CDC34	<a href="#">ENST00000215574</a>	Ubiquitin-conjugating enzyme E2 R1 (EC 6.3.2.19) (Ubiquitin-protein ligase R1). Ubiquitin-conjugating enzyme E2-32 kDa complementing) (E2- CDC34).		18.6812	-25.43	2.25526e-07	532	23	5	50 [+]	<a href="#">View</a>

# miRBase::MicroCosm miRNA Targets

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

## MicroCosm Targets Version 5

Email [microcosm@ebi.ac.uk](mailto:microcosm@ebi.ac.uk) with queries or problems.



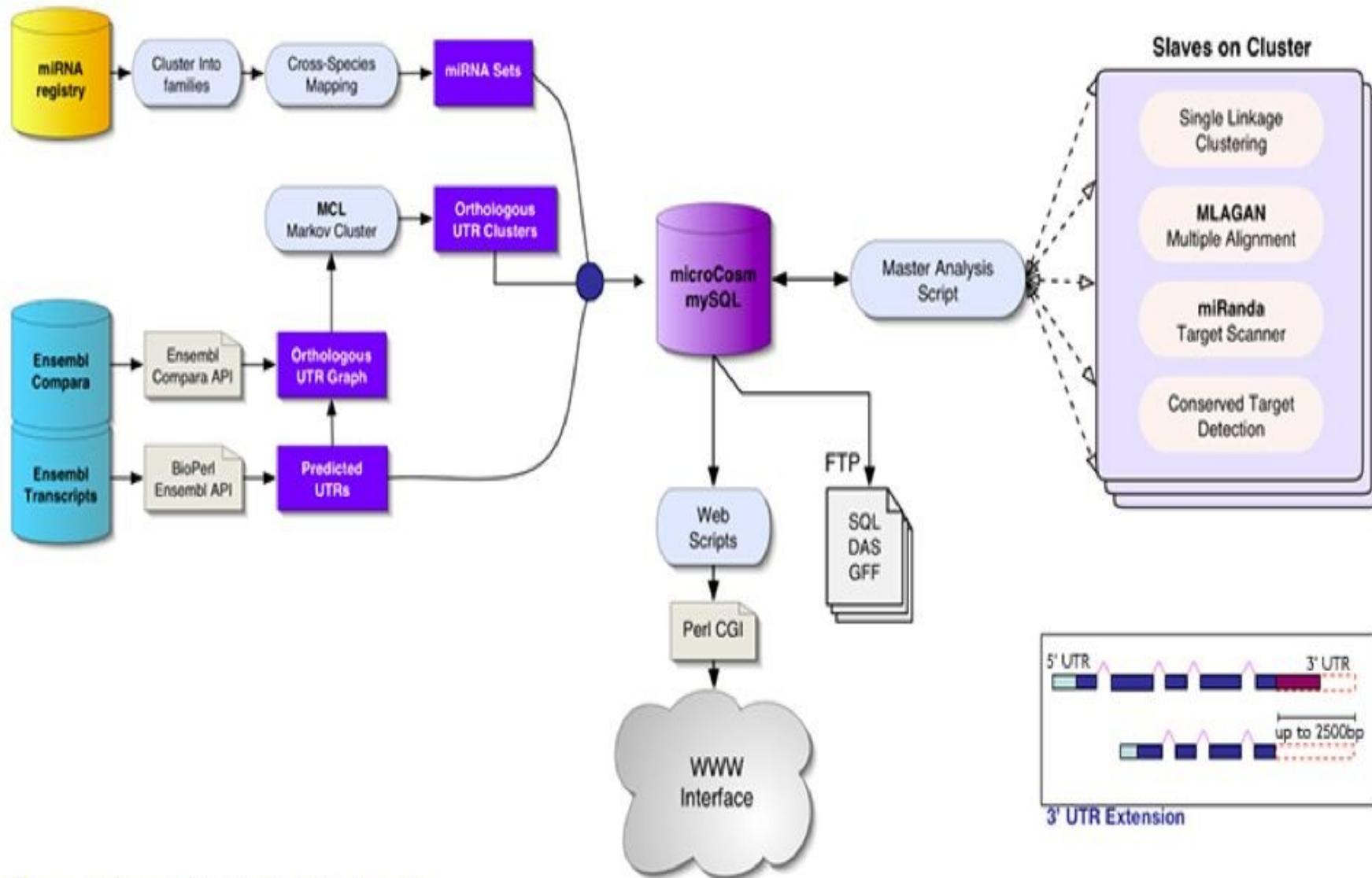
miRBase Targets Release Version v5



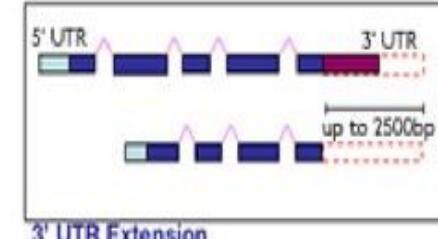
Doug Brutlag 2010

# MicroCosm miRNA Targets Prediction

## Computational Protocol



Computational Prediction Protocol



# miRViewer

<http://people.csail.mit.edu/akiezun/miRviewer>

# miRviewer

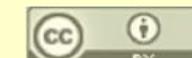
miRviewer presents a global view of homologous miRNA genes in many species. miRviewer exhibits a comprehensive set of miRNA genes both from [miRbase](#) and candidate homologs identified using [miRNAMiner](#). miRviewer table shows conservation of miRNA genes, grouped by name, in addition to other information (see [Help](#)).

The table shows conservation of miRNA genes, grouped by name. Click on group name to see conservation for each miRNA and genomic location. Point cursor on miRNA to see summary of origin information. Symbols • indicate miRNAs present in [miRbase](#) (other miRNAs are newly discovered by [miRNAMiner](#).) Blank box indicates that the miRNA was not identified in this genome, under stringent parameters. Zoom out to see the full table by pressing Ctr- (or Mac-) a few times.

Initial loading of table might take a few moments (for best performance use [Firefox](#)).  
For questions, comments and credits see contact information at the bottom of page.

[Help](#)

conservation	1.0	0.97	0.94	0.91	0.88	0.85	0.82	0.79	0.76	0.73	0.7	0.67	0.64	0.61	0.58	0.55	0.52	0.49	0.46	0.43	0.4															
miRNA	hsa	ptr	ppy	mmi	mim	oga	cpo	mmu	ocu	opr	rno	sar	str	bta	cfa	dno	eca	eeu	ete	fca	laf	tbe	mlu	mdo	oan	gga	dre	gac	ola	tni	tru	xtr	cin	aae	aga	dme
mir-92 (8)	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•				
let-7 (28)	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•				
mir-124 (13)	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•				
mir-34 (8)	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•				
mir-7 (8)	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•				
mir-10 (9)	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•				
mir-125 (9)	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•				
mir-133 (7)	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•				
mir-190 (3)	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•				
mir-9 (13)	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•				
mir-1 (9)	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•				
mir-33 (5)	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•				
mir-101 (7)	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•				
mir-181 (9)	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•				
mir-216 (7)	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•				



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# miRViewer: mir-10 family

[http://people.csail.mit.edu/akiezun/miRviewer/mir-10\\_index.html](http://people.csail.mit.edu/akiezun/miRviewer/mir-10_index.html)

# miRviewer

The table shows conservation of mir-10 homologs identified by miRviewer. Click on miRNA name to see additional information such as conservation, alignment, mismatches, genomic location and orientation. Symbols • in table cells indicate miRNAs present in miRbase. Blank box indicates that the miRNA was not identified in this genome, under stringent parameters.

[Help](#)

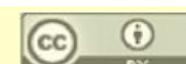
conservation	1.0	0.97	0.94	0.91	0.88	0.85	0.82	0.79	0.76	0.73	0.7	0.67	0.64	0.61	0.58	0.55	0.52	0.49	0.46	0.43	0.4
--------------	-----	------	------	------	------	------	------	------	------	------	-----	------	------	------	------	------	------	------	------	------	-----



Questions:[mirnaminer@gmail.com](mailto:mirnaminer@gmail.com)

miRViewer is developed by [Adam Kiezun \(MIT\)](#), [Shay Artzi \(MIT\)](#), and [Noam Shomron \(Tel Aviv\)](#).

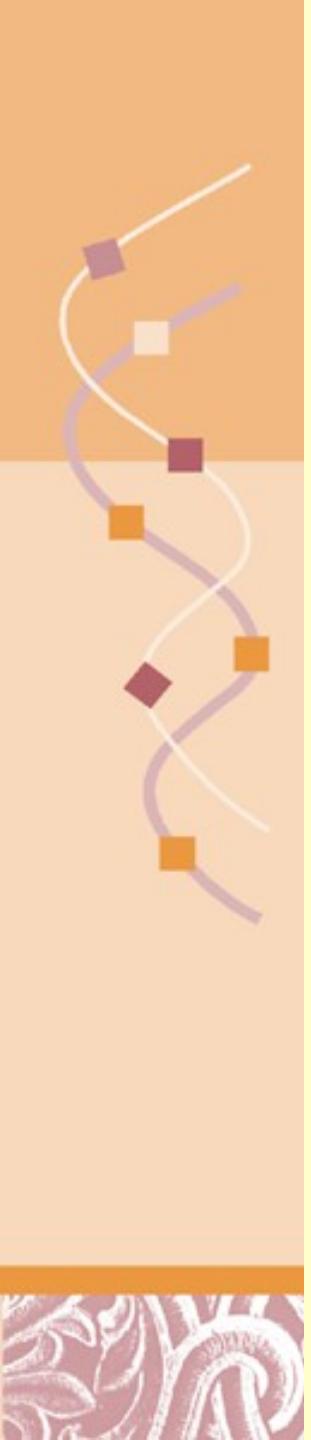
Last update Nov 9, 2008



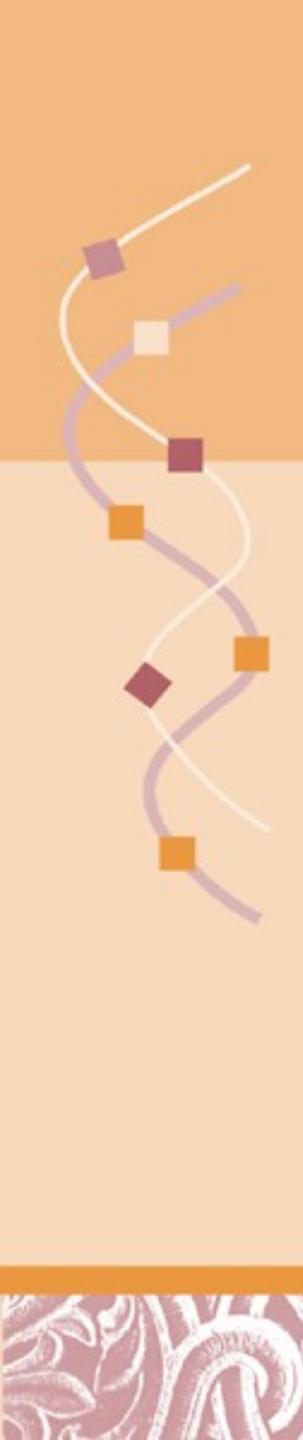
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# miRViewer: mir-10 Alignment

<http://people.csail.mit.edu/akiezun/miRviewer/mir-10a-align.html>



hsa	-----GAUCUGUCUGUCUUCUGUAUAUACCCUGUAGAUCCGAAUUUGUGU-AAGG--AAUUUUGUGGUCAAAAUU-CGUAUCUAGGGAAUAUGUAGUUGACAUAAACACUCGG
ptr	-----AUCUGUCUGUCUUCUGUAUAUACCCUGUAGAUCCGAAUUUGUGU-AAGG--AAUUUUGUGGUACAAAAAUU-CGUAUCUAGGGAAUAUGUAGUUGACAUAAACACUCGG
ppy	-----GAUCUGUCUGUCUUCUGUAUAUACCCCGUAGAUCCGAAUUUGUGU-AAGG--AAUUUUGUGGUACAAAAAUU-CGUAUCUAGGGAAUAUGUAGUUGACAUAAACACUCGG
mml	-----GAUCUGUCUGUCUUCUGUAUAUACCCUGUAGAUCCGAAUUUGUGU-AAGG--AAUUUUGUGGUACAAAAAUU-CGUAUCUAGGGAAUAUGUAGUUGACAUAAACACUCGG
mim	-----GAUCUGUCUGUCUUCUGUAUAUACCCUGUAGAUCCGAAUUUGUGU-AAGG--AAUUUUGUGGUACAAAAAUU-CGUAUCUAGGGAAUAUGUAGUUGACAUAAACACUCGG
oga	-----GAUCUGUCUGUCUUCUGUAUAUACCCUGUAGAUCCGAAUUUGUGU-AAGG--AAUUUUGUGGUACAAAAAUU-CGUAUCUAGGGAAUAUGUAGUUGACAUAAACACUCGG
cpo	-----GAUCUGUCUGUCUUCUGUAUAUACCCUGUAGGUCCGAAUUUGUGU-AAGG--AAUUUUAGGUACAAAAAUU-CGUAUCUAGGGAAUAUGUAGUUGACAUAAACACUCGG
mmu	-----GACCUGUCUGUCUUCUGUAUAUACCCUGUAGAUCCGAAUUUGUGU-AAGG--AAUUUUGUGGUCAAAAUU-CGUAUCUAGGGAAUAUGUAGUUGACAUAAACACUCGG
oci	-----GAUCUGUCUGUCUUCUGUAUAUACCCUGUAGAUCCGAAUUUGUGU-AAGG--AAUUUUGUGGUACAAAAAUUUCGUAUCUAGGGAAUAUGUAGUUGACAUAAACACUCGG
opr	-----GAUCUGUCUGUCUUCUGUAUAUACCCUGUAGAUCCGAAUUUGUGU-AAGG--AAUUUUGUGGUACAAAAAUU-CGUAUCUAGGGAAUAUGUAGUUGACAUAAACACUCGG
rno	-----GACCUGUCUGUCUUCUGUAUAUACCCUGUAGAUCCGAAUUUGUGU-AAGG--AAUUUUGUGGUCAAAAUU-CGUAUCUAGGGAAUAUGUAGUUGACAUAAACACUCGG
sar	-----
str	-----
bta	-----GAUCUGUCUGUCUUCUGUAUAUACCCUGUAGAUCCGAAUUUGUGU-AAGG--AAUUUJUGAUCACAAAAAUU-CGUAUCUAGGGAAUAUGUAGUUGACAUAAACACUCGG
cfa	-----
dno	-----GAUCUGUCUGUCUUCUGUAUAUACCCUGUAGAUCCGAAUUUGUGU-AAGG--AAUUUUGUGGUACAAAAAUU-CGUAUCUAGGGAAUAUGUAGUUGACAUAAACACUCGG
eca	-----GAUUCUGUCUUCUGUAUAUACCCUGUAGAUCCGAAUUUGUGU-AAGG--AAUUUUGUGGUACAAAAAUU-CGUAUCUAGGGAAUAUGUAGUUGACAUAAACACUCGG
eeu	-----GAUCUGUCUGUCUUCUGUAUAUACCCUGUAGAUCCGAAUUUGUGUAAGA-AAUUUUGUGGUACAAAAAUU-CGUAUCUAGGGAAUAUGUAGUUGACAUAAACACUCGG
ete	-----GAUCUGUCUGUCUUCUGUAUAUACCCUGUAGAUCCGAAUUUGUGU-AAGG--AGUUUJUGAUCACAAAAAUU-CGUAUCUAGGGAAUAUGUAGUUGACAUAAACACUCGG
fca	-----GAUCUGUCUGUCUUCUGUAUAUACCCUGUAGAUCCGAAUUUGUGU-AAGG--AAUUUUGUGGUACAAAAAUU-CGUAUCUAGGGAAUAUGUAGUUGACAUAAACACUCGG
laf	-----GAUCUGUCUGUCUUCUGUAUAUACCCUGUAGAUCCGAAUUUGUGU-AAGG--AAUUUJUGAUCACAAAAAUU-CGUAUCUAGGGAAUAUGUAGUUGACAUAAACACUCGG
tbe	-----GAUCUGUCUGUCUUCUGUAUAUACCCUGUAGAUCCGAAUUUGUGU-AAGG--AAUUUUGUGGUACAAAAAUU-CGUAUCUAGGGAAUAUGUAGUUGACAUAAACACUCGG
mlu	-----
mdo	-----CUGCUUCUGUAUAUACCCUGUAGAUCCGAAUUUGUGU-AAGG--AAUUUUGUGGUACAAAAAUU-CGUAUCUAGGGAAUAUGUAGUUGACAUAAACACUCGG
oan	-----AAAGAAGAU AUGUCUGUCUUCUGUAUAUACCCUGUAGAUCCGAAUUUGUGU-AAGG--AGUUUCGUUGGUCAAAAUU-CGUAUCUAGGGAAUAUGUAGUUGACAUAAACACUCGG
gga	-----CUAUAGUACCCUGUAGAUCCGAAUUUGUGUAAGG-AAGUUG-GGUACAAAAAUU-CGUAUCUAGGGAAUAUGUAG
dre	-----UGUCUGUCAUCUAUAUAUACCCUGUAGAUCCGAAUUUGUGU-----GAUUAACAGUCGCAAUUU-CGUGUCUUGGGAAUAUGUAGUUGACAUAAACACACACGG
gac	-----
ola	-----UGUCUUUCUAUAUCUACCCUGUAGAUCCGAAUUUGUGUGACGGUCGAUAAAACAACAAUCACAAAAAUU-CGCCUUCUAGGGGAUAUUAUGU
tni	-----
tru	-----GCCACUGUCUUCUAUAUCUACCCUGUAGAUCCGAAUUUGUGAAAUAUCAUAAAACCAAUCACAAAAAUU-CGCCUUCUAGGGGAUAUUAUGUG
xtr	-----GAUUUGCCUGUCCUCUGUAUAGUACCCUGUAGAUCCGAAUUUGUGUGAGCG-CAAUCA-UAUCACAAAAAUU-CGUGUCUGGGGGGAUAUGCAGUUGACACAAACG
cin	-----
aae	-----
aga	-----
dme	-----



# Human miRNAs ( February 22, 2010)

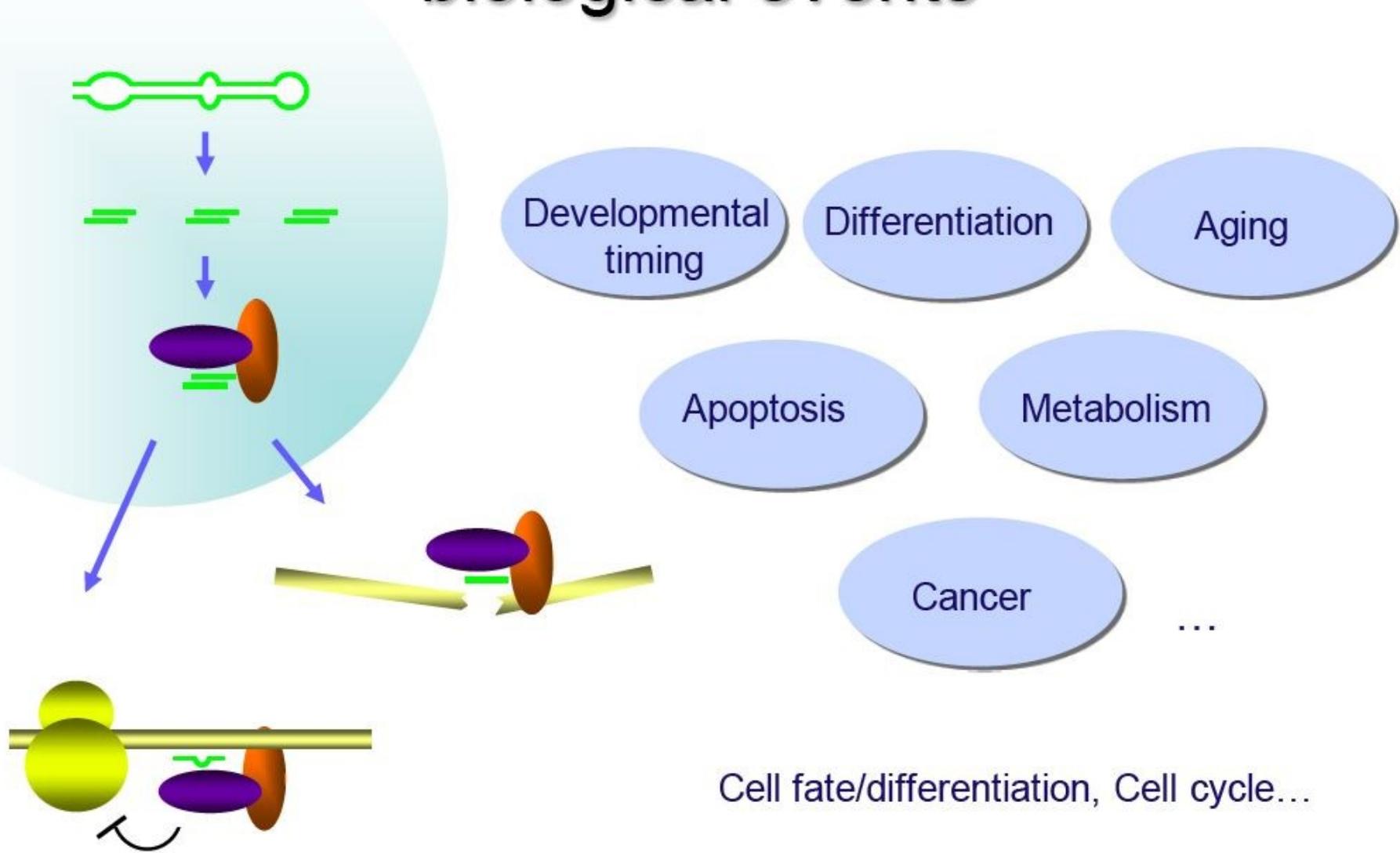
---

- Total miRNA genes in 115 species 10,882
  - Total number of miRNAs known 1,580
  - Number human miRNAs identified 851
  - Number of human mRNA targets 34,788
- 

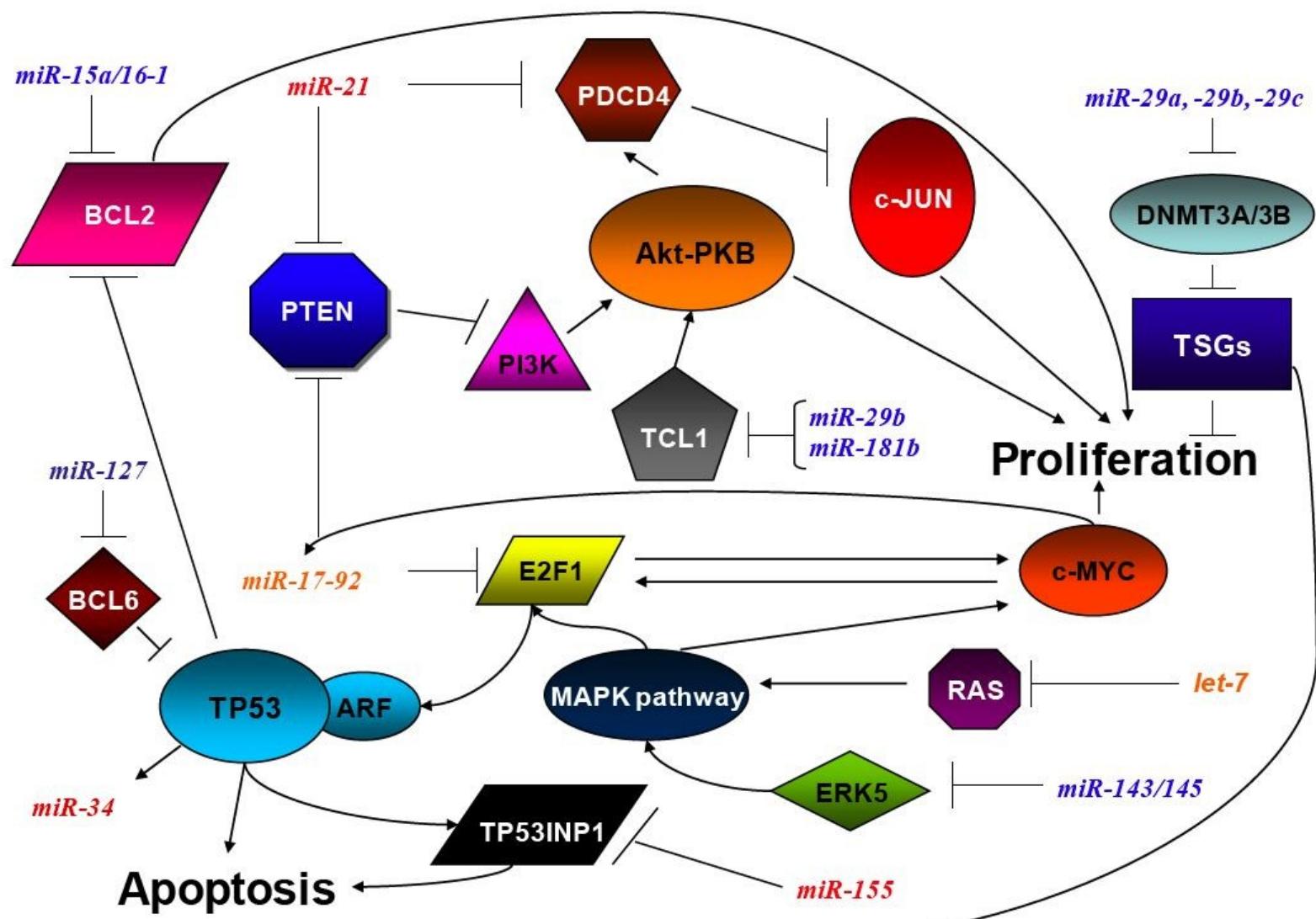
- miRNAs can have multiple targets
- Target mRNAs can have multiple miRNA binding sites



# Thousands of microRNAs act in multiple biological events

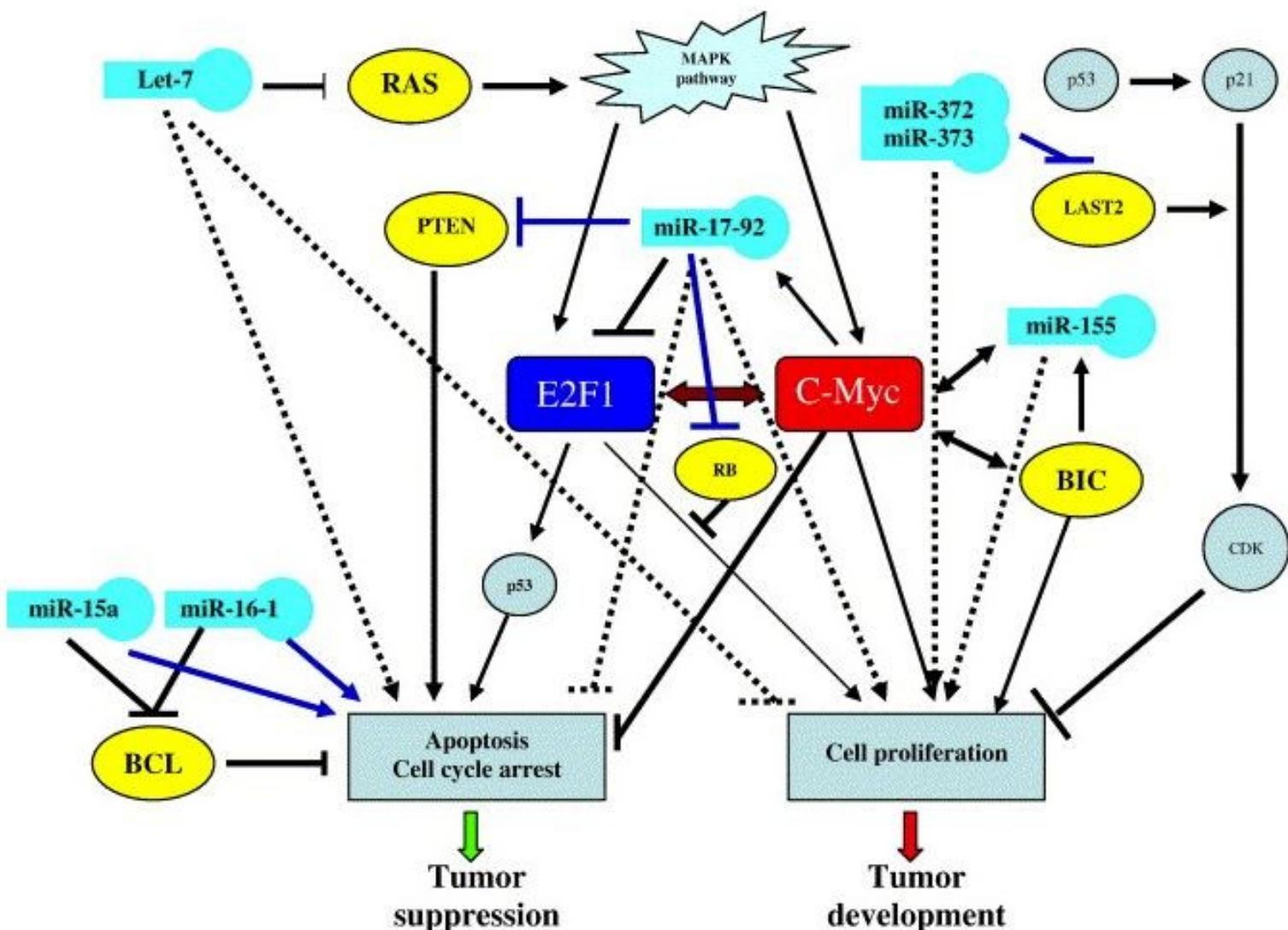


# Micro RNAs Regulate Cell Growth and Death

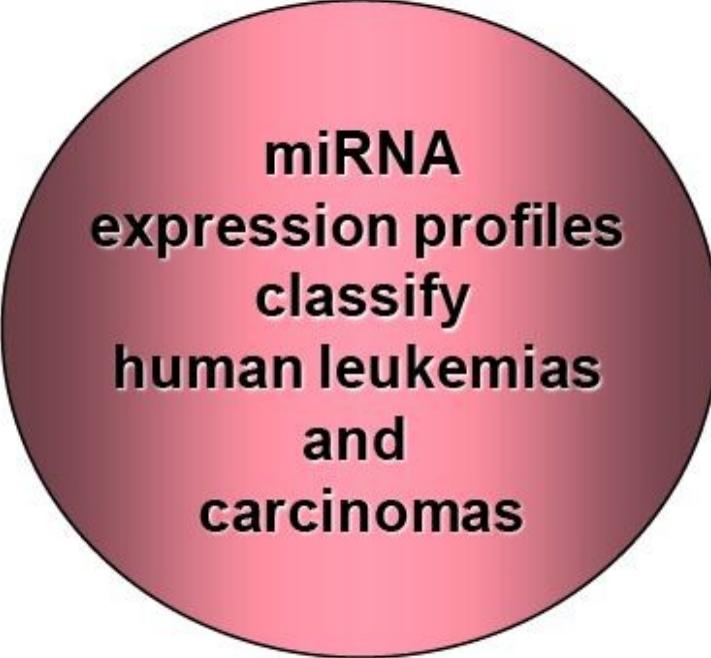


# miRNAs as Oncogenes and Tumor Suppressors

Zhang et al Dev Biol. 2007 Feb 1;302(1):1-12



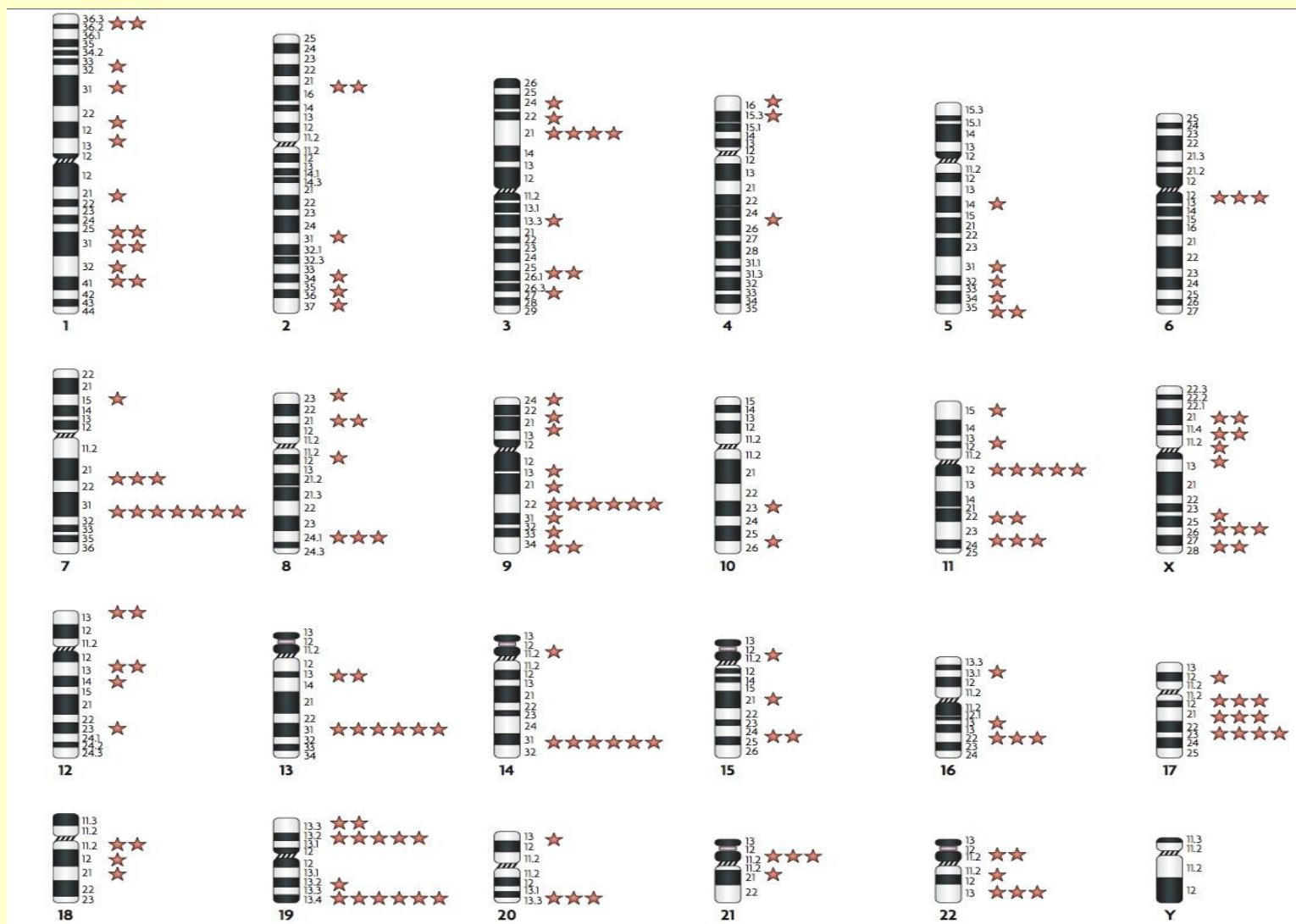
# ***ALTERATIONS OF MICRORNAs ARE FOUND IN EVERY TYPE OF HUMAN CANCER***



**miRNA  
expression profiles  
classify  
human leukemias  
and  
carcinomas**

# miRNAs Involved in Human Cancer

(Croce Nat Rev Genet. 2009 Oct;10(10):704-14.)



**Figure 1 | MicroRNA genes map to chromosomal regions that are involved in alterations in human cancer.**

Croce Nat Rev Genet. 2009 Oct;10(10):704-14

# miRNA Oncogenes or Tumor Suppressor Genes

Table 1 | MicroRNAs that function as oncogenes or tumour suppressor genes in human cancers

MicroRNA	Dysregulation	Function	Validated targets	Oncogene (ONC) or tumour suppressor (TS)	Refs
<i>miR-15a</i> and <i>miR-16-1</i>	Loss in CLL, prostate cancer and multiple myeloma	Induces apoptosis and inhibits tumorigenesis	BCL2, WT1 RAB9B and MAGE83	TS	15,20,23, 30,52,69
<i>let-7 (a, b, c, d, e, f, g and i)</i>	Loss in lung and breast cancer and in various solid and haematopoietic malignancies	Induces apoptosis and inhibits tumorigenesis	RAS, MYC and HMGA2	TS	22,26, 42,70
<i>miR-29 (a, b and c)</i>	Loss in aggressive CLL, AML (11q23), MDS lung and breast cancers and cholangiocarcinoma	Induces apoptosis and inhibits tumorigenicity. Reactivates silenced tumour suppressor genes	TCL1, MCL1 and DNMTs	TS	30,64, 71,72
<i>miR-34</i>	Loss in pancreatic, colon, breast and liver cancers	Induces apoptosis	CDK4, CDK6, cyclin E2, EZF3 and MET	TS	56–58
<i>miR-145</i>	Loss in breast cancer	Inhibits proliferation and induces apoptosis of breast cancer cells	ERG	TS	31
<i>miR-221</i> and <i>miR-222</i>	Loss in erythroblastic leukaemia	Inhibits proliferation in erythroblasts	KIT	TS	30
<i>miR-221</i> and <i>miR-222</i>	Overexpression in aggressive CLL, thyroid carcinoma and hepatocellular carcinoma	Promotes cell proliferation and inhibits apoptosis in various solid malignancies	p27, p57, PTEN and TIMP3	ONC	43,51,73
<i>miR-155</i>	Upregulated in aggressive CLL, Burkitt's lymphoma and lung, breast and colon cancers	Induces cell proliferation and leukaemia or lymphoma in mice	MAF and SHIP1	ONC	32–34, 36,37
<i>miR-17–92 cluster</i>	Upregulated in lymphomas and in breast, lung, colon, stomach and pancreatic cancers	Induces proliferation	E2F1, BIM and PTEN	ONC	19,34,35, 40,41
<i>miR-21</i>	Upregulated in glioblastomas, AML (11q23), aggressive CLL and breast, colon, pancreatic, lung, prostate, liver and stomach cancers	Inhibits apoptosis and increases tumorigenicity	PTEN, PDCD4, TPM1 and TIMP3	ONC	31,37–39, 44–50
<i>miR-372</i> and <i>miR-373</i>	Upregulated in testicular tumours	Promotes tumorigenicity in cooperation with RAS	LATS2	ONC	74

AML, acute myeloid leukaemia; BCL2, B cell leukaemia/lymphoma 2; BIM, Bcl2-interacting mediator of cell death; CLL, chronic lymphocytic leukaemia; DNMT, DNA methyltransferase; HMGA2, high mobility group AT-hook 2; LATS2, large tumour suppressor homologue 2; MCL1, myeloid cell leukaemia sequence 1; MDS, myelodysplastic syndrome; PDCD4, programmed cell death 4; PTEN, phosphatase and tensin homologue; SHIP1, SH2 domain-containing inositol-5'-phosphatase 1; TCL1, T cell lymphoma breakpoint 1; TIMP3, tissue inhibitor of metalloproteinases 3; TPM1, tropomyosin 1; WT1, Wilms tumour 1.

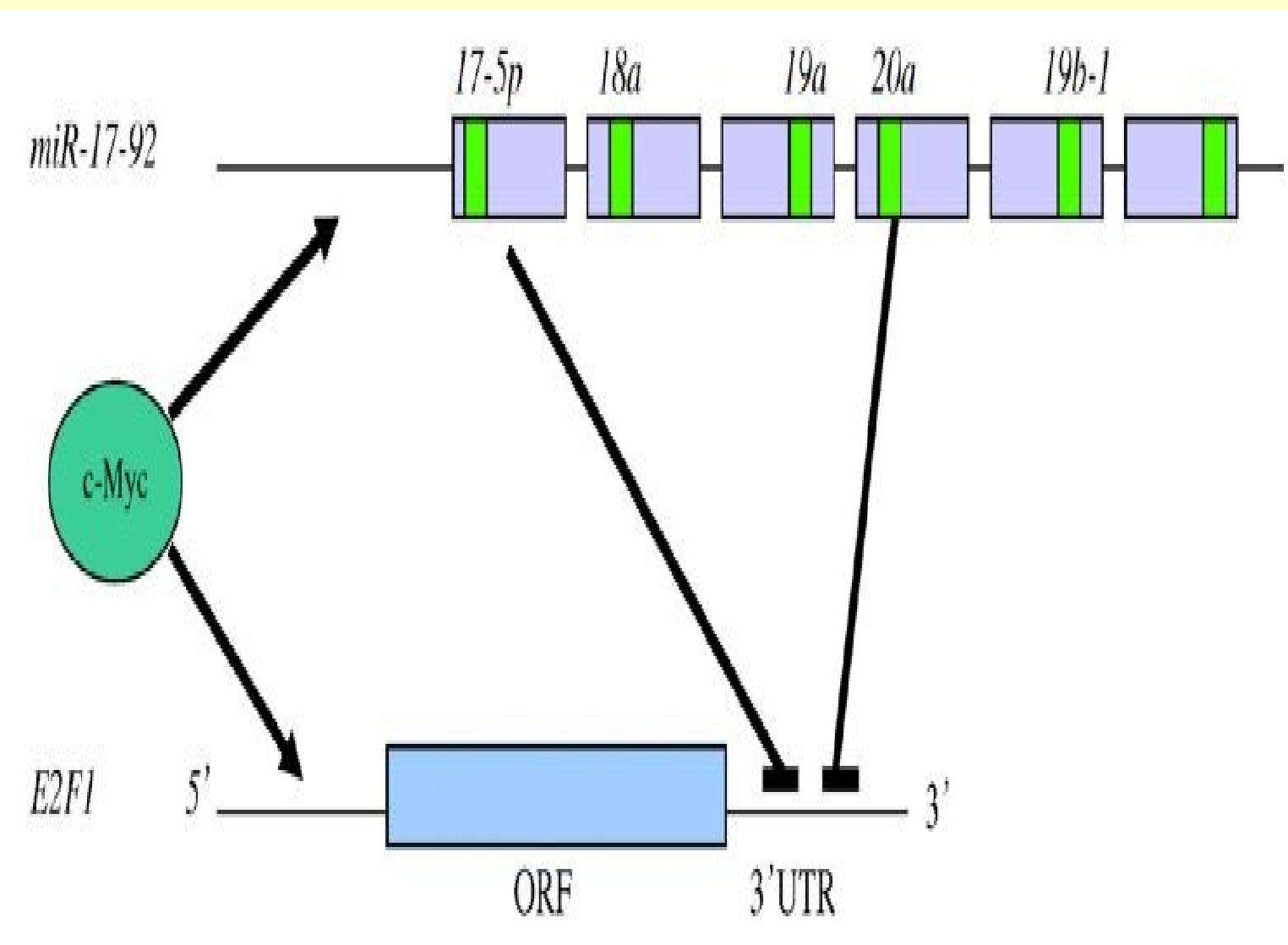
**Table 2 | Consequences of microRNA dysregulation in human cancers**  
 (Croce Nat Rev Genet. 2009 Oct;10(10):704-14.)

MicroRNA dysregulation	Targets	Consequences
MicroRNA overexpression	Tumour suppressors	Downregulation of tumour suppressors—for example, PTEN, p22, p57, TIMP3 and PDCD4
MicroRNA loss	Oncogenes	Upregulation of oncogenes—for example, BCL2, MCL1, RAS, HMGA2, MYC and MET
MicroRNA loss	DNA methyltransferases	Downregulation of tumour suppressors—for example, p16, FHIT and WWOX
MicroRNA loss	Chromatin silencers	Downregulation of tumour suppressors

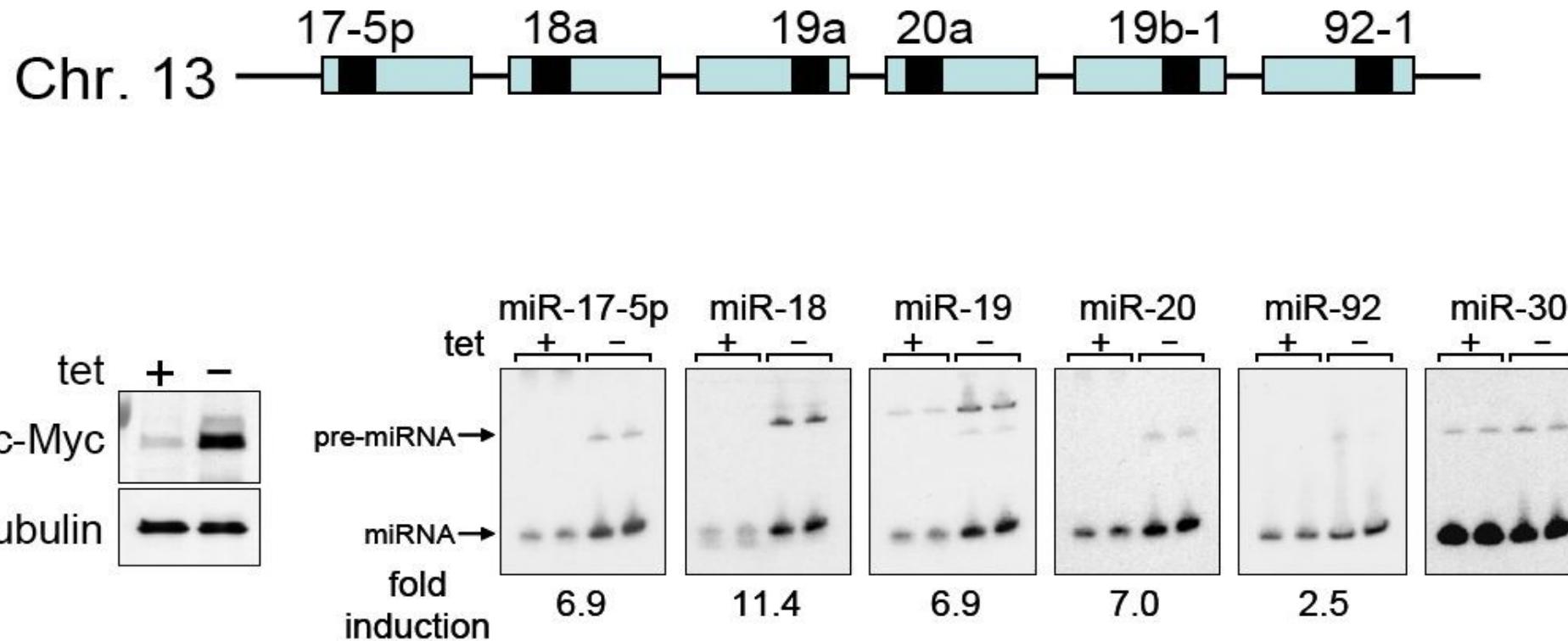
BCL2, B cell leukaemia/lymphoma 2; FHIT, fragile histidine triad protein; HMGA2, high mobility group AT-hook 2; MCL1, myeloid cell leukaemia sequence 1; PDCD4, programmed cell death 4; PTEN, phosphatase and tensin homologue; TIMP3, tissue inhibitor of metalloproteinases 3; WWOX, WW domain-containing oxidoreductase.

# cMyc & miRNAs Regulate E2F1 Cell Cycle TF

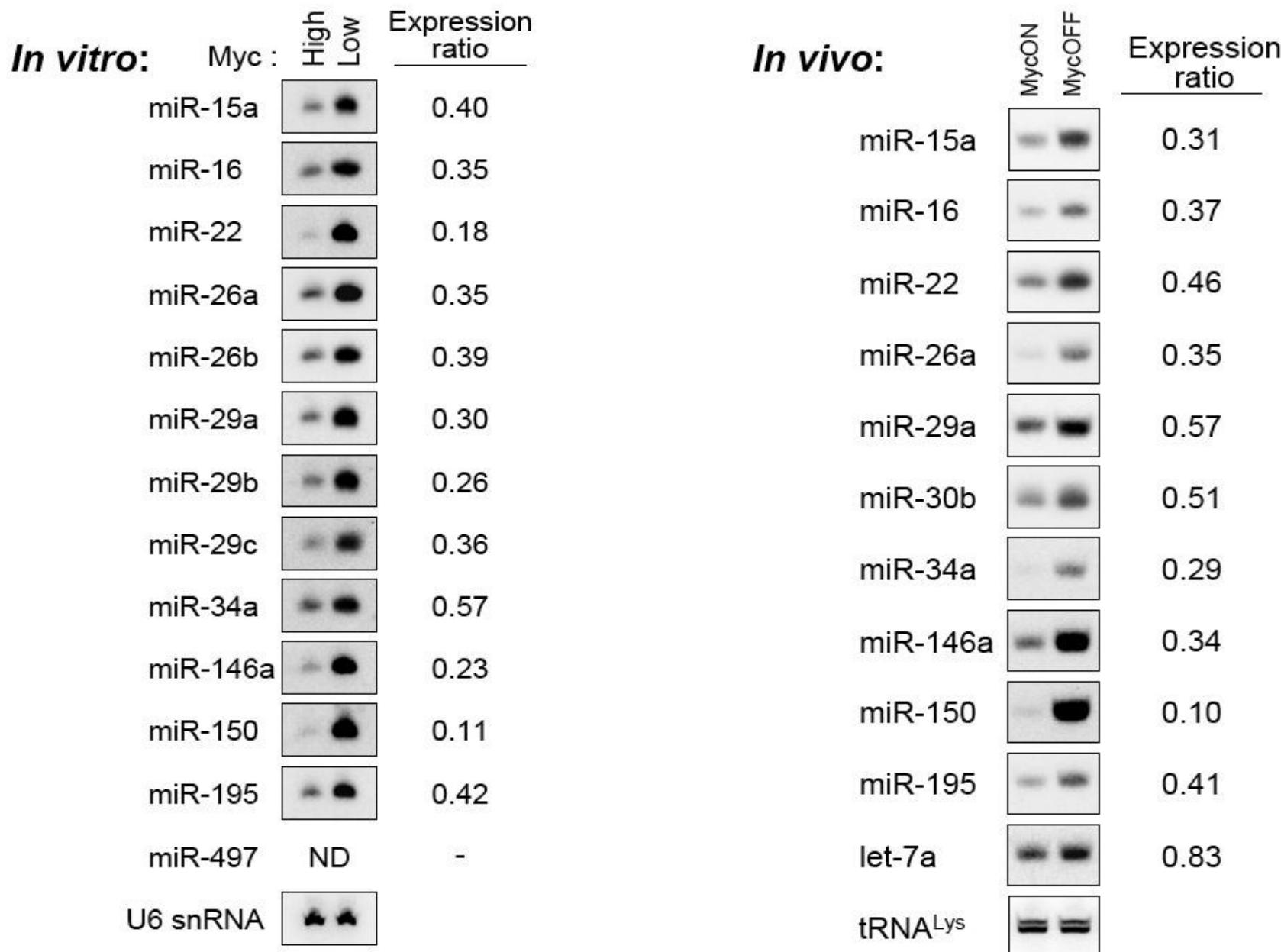
Zhang et al Dev Biol. 2007 Feb 1;302(1):1-12



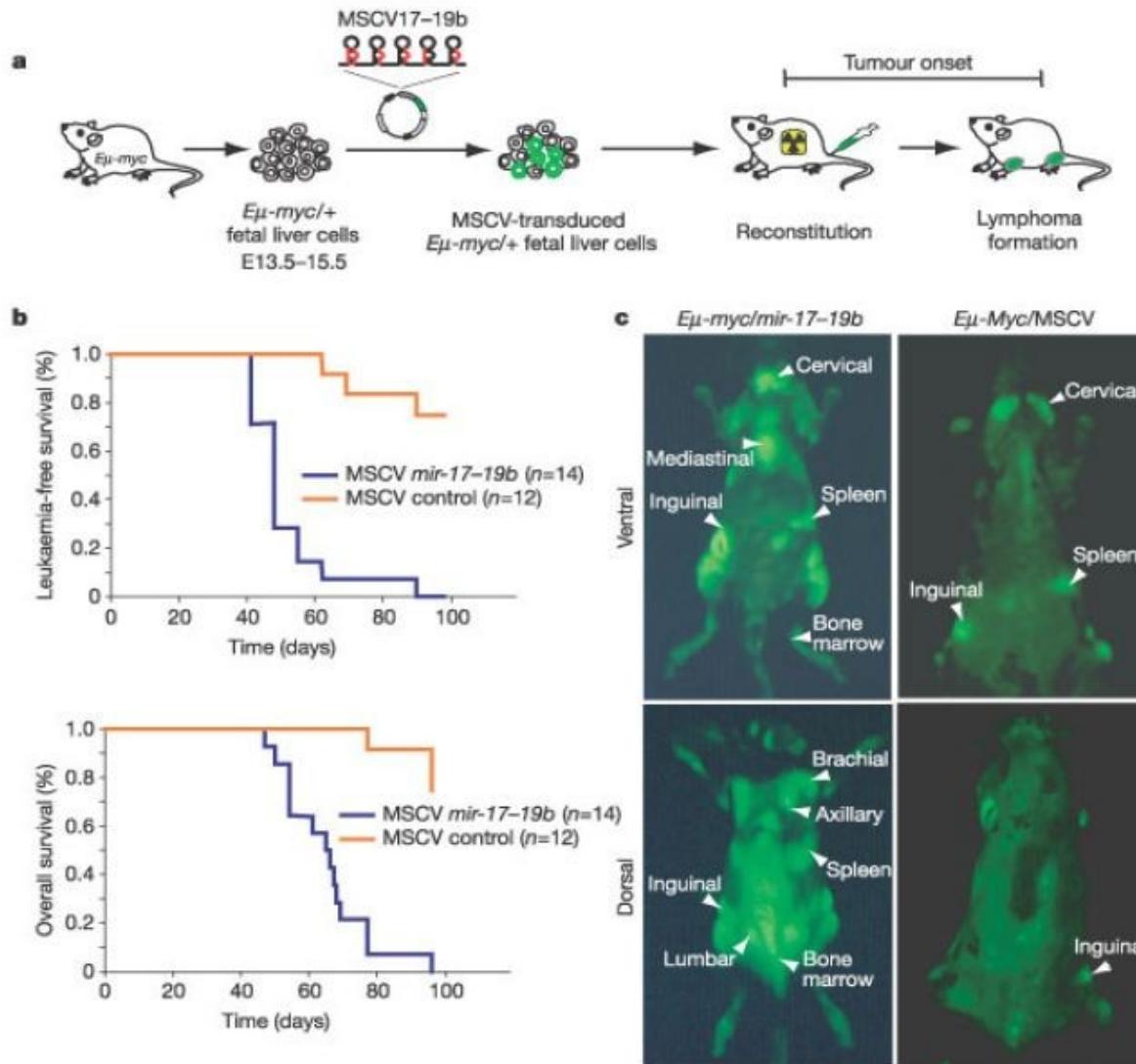
# The miR-17-92 cluster is activated by Myc



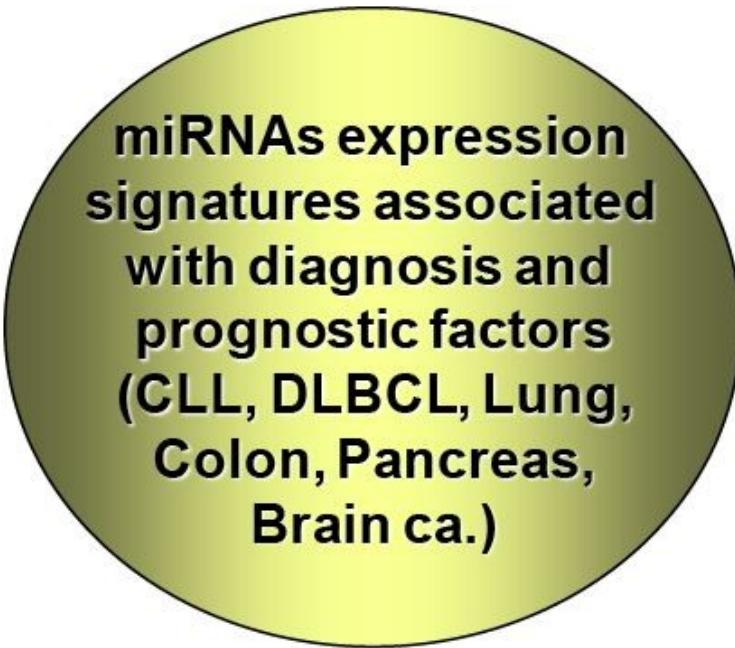
# Myc represses the expression of many miRNAs



# The miR-17-92 cluster accelerates Myc-induced lymphomagenesis



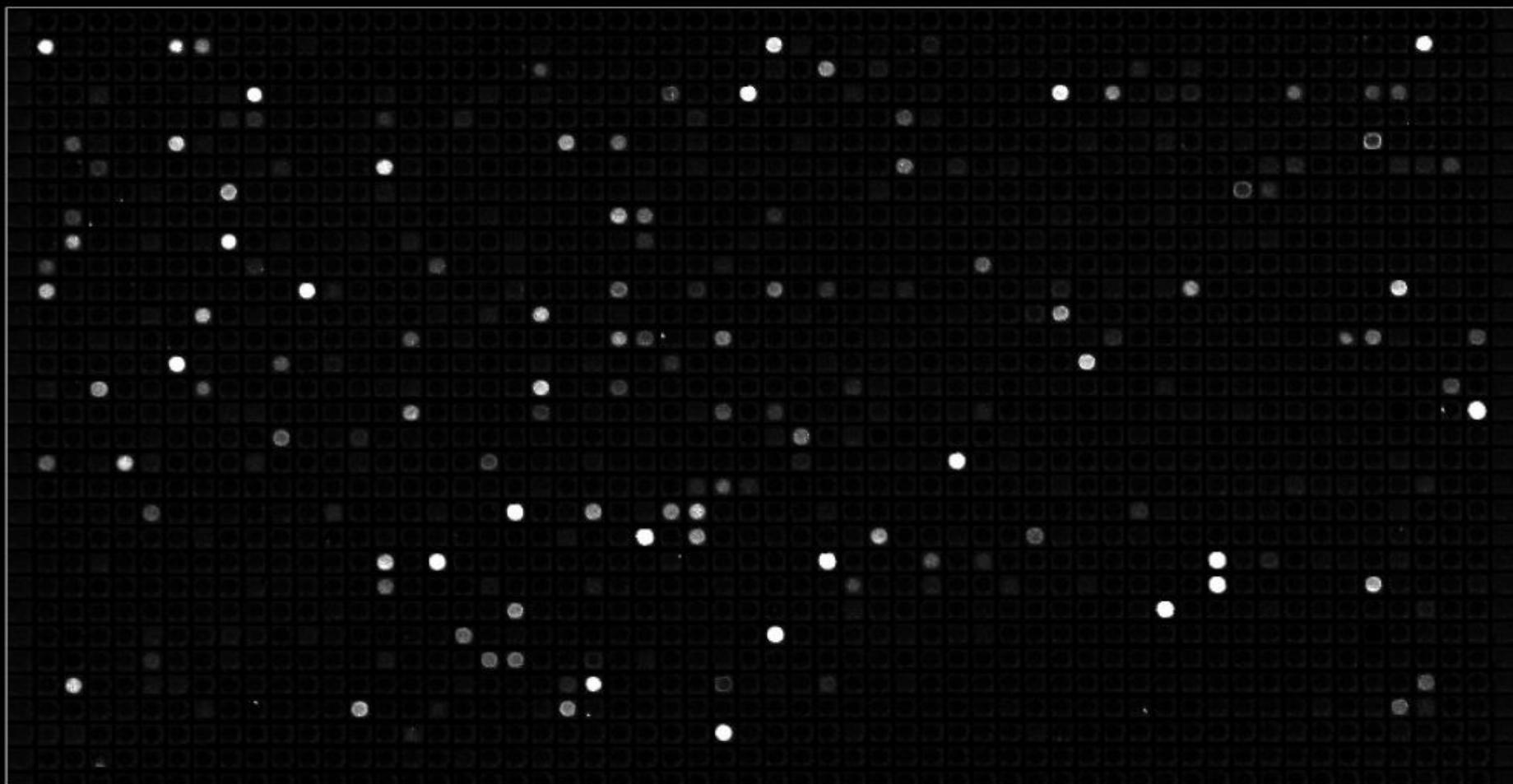
# **MIRNA PROFILING AS A NEW DIAGNOSTIC & PROGNOSTIC TOOL FOR CANCER PATIENTS**

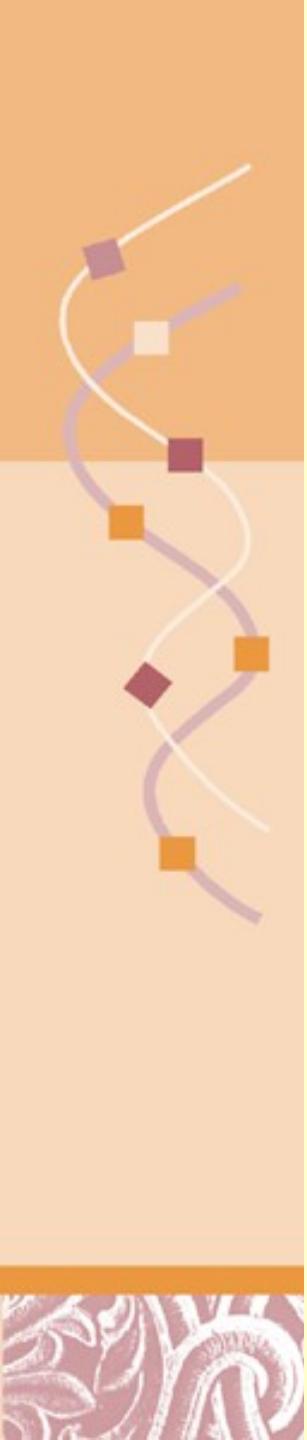


**miRNAs expression  
signatures associated  
with diagnosis and  
prognostic factors  
(CLL, DLBCL, Lung,  
Colon, Pancreas,  
Brain ca.)**

(Michael et al, Molec Cancer Res 2003; Lu et al, Nature, 2005; Eis et al, PNAS, 2005  
Lui et al, Cancer Res 2007, Bloomston et al, JAMA 2007; Mi et al, PNAS, 2007; Garzon et al, Blood in press 2008)

# Profiling miRNA expression using custom microarrays



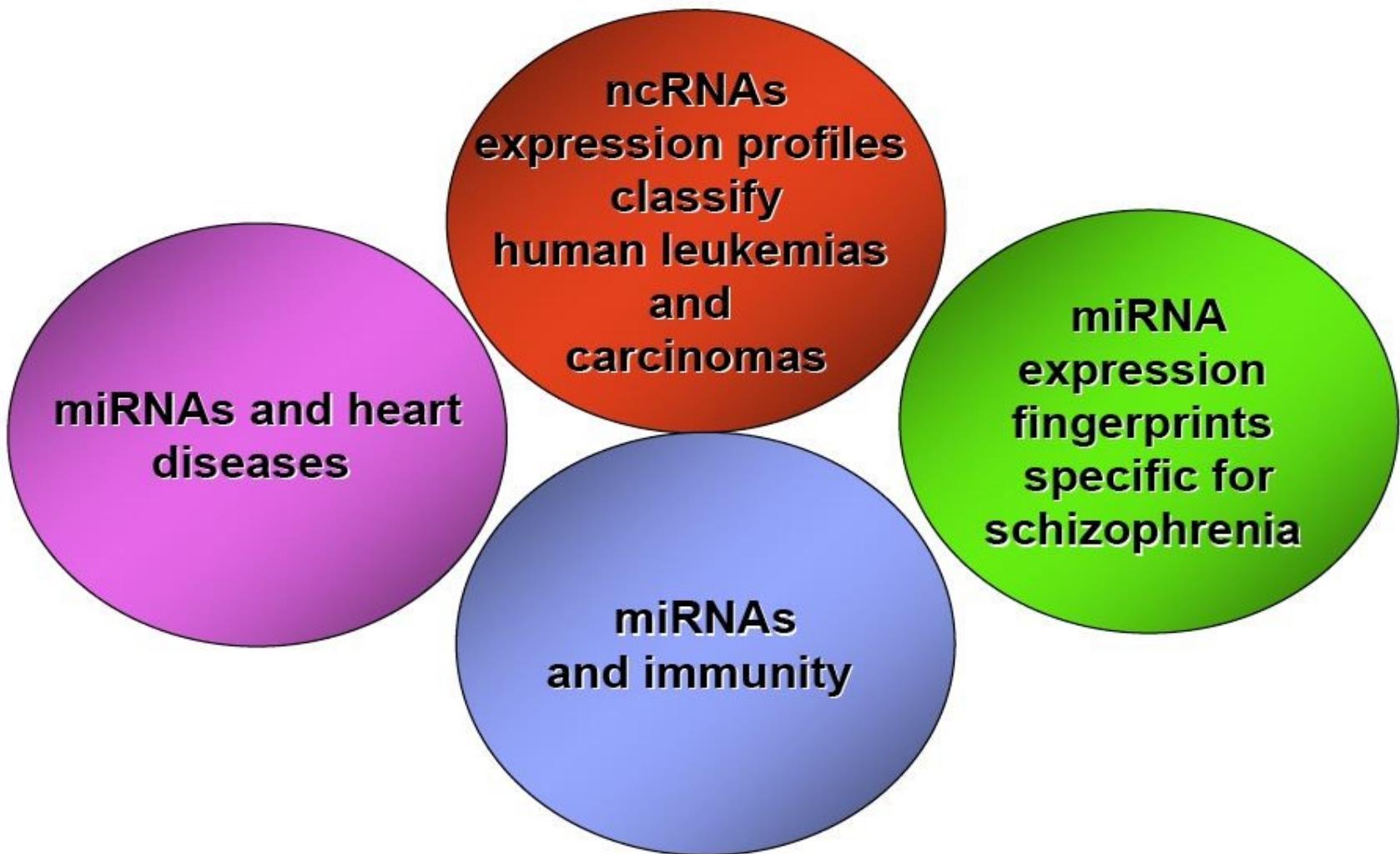


# miRNAs and Cancer – A Summary

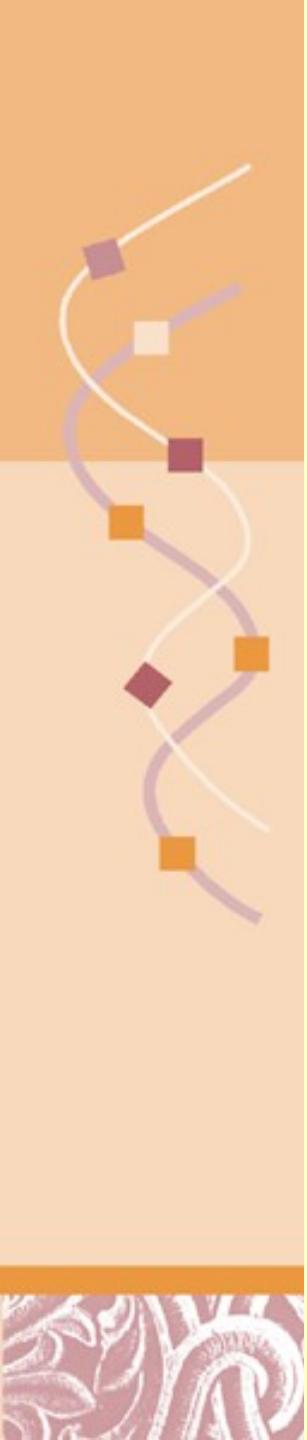
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- miRNAs control cell cycle, cell differentiation and apoptosis by regulating oncogenes and tumor suppressor genes
- •miRNAs are misexpressed in cancer and are therefore excellent diagnostic/ prognostic markers in cancer
- •Some miRNAs e.g. *mir-155*, *can cause cancer and oncogenic miRNAs may be therapeutic targets in cancer*
- •Other miRNAs like *let-7*, *may prevent cancer and may be therapeutic molecules themselves.*
- •MicroRNAs could augment current cancer therapies.

# **ALTERATIONS OF NONCODING RNAs ARE FOUND IN EVERY TYPE OF HUMAN DISEASE**



(Calin et al, PNAS 2002; Lu et al, Nature, 2005; Landgraf et al, Cell 2007; Perkins et al Genome Biol 2007; Hansen et al PLoS ONE, 2007; Beveridge et al, Hum Molec Genet 2008, Baltimore D, Nat Immunol 2008; van Rooij, Trends Genet, 2008 )

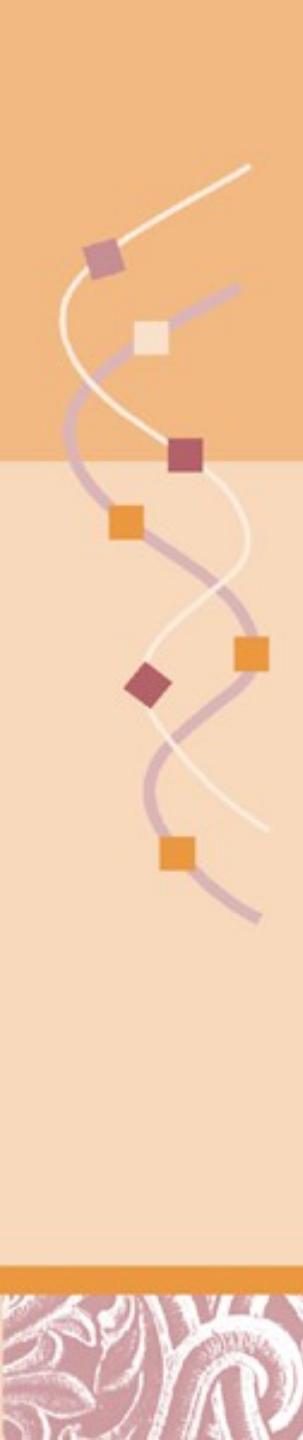


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[Croce Nat Rev Genet. 2009 Oct;10\(10\):704-14.](#)
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- Transcriptional regulatory networks in *Saccharomyces cerevisiae*. [Lee Science. 2002 Oct 25;298\(5594\):799-804.](#)
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[Filipowicz Curr Opin Struct Biol. 2005 Jun;15\(3\):331-41 .](#)
- The microRNAs of *Caenorhabditis elegans*. [Lim Genes Dev. 2003 Apr 15;17\(8\):991-1008.](#)
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- miRNAs and Cancer AAAI Science Webinars February 20 with George Calin, Brank Slack and Scott Hammond
- Short RNAs repress translation after initiation in mammalian cells. [Petersen Mol Cell. 2006 Feb 17;21\(4\):533-42.](#)
- Raising the estimate of functional human sequence . [Pheasant Genome Res. 2007 Sep;17\(9\):1245-53.](#)
- A developmental view of microRNA function. [Zhao Trends Biochem Sci. 2007 Apr;32\(4\):189-97.](#)
- c-Myc-regulated microRNAs modulate E2F1 expression  
[O'Donnell Nature. 2005 Jun 9;435\(7043\):839-43.](#)





# Important Micro RNA Web Sites

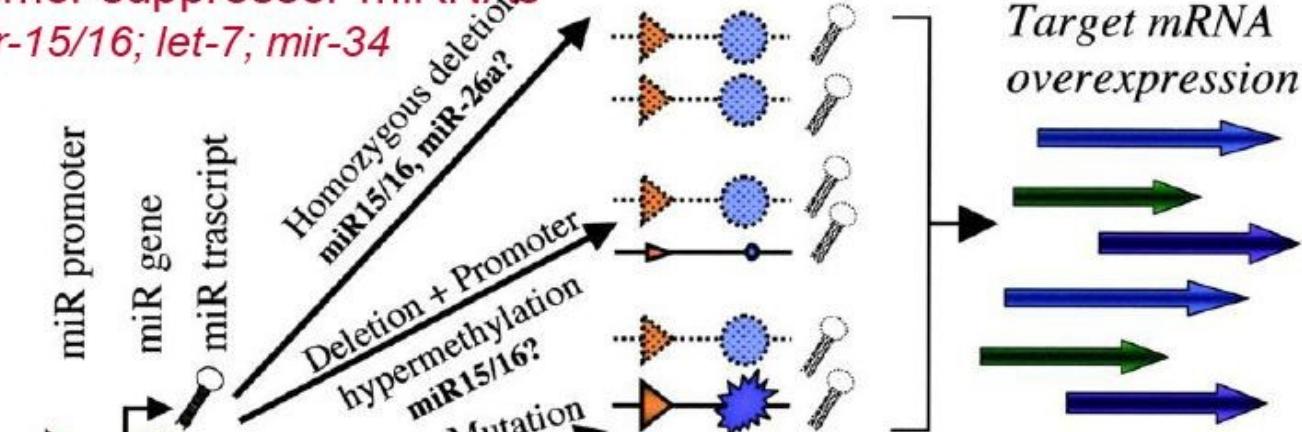
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- Diana Lab: <http://diana.cslab.ece.ntua.gr/>
- miRBase: <http://microrna.sanger.ac.uk/>
- miRBase: <http://www.mirbase.org/>
- MicroCosm: <http://www.ebi.ac.uk/enright-srv/microcosm/>
- miRNAMiner: <http://groups.csail.mit.edu/pag/mirnaminer>
- miRviewer: <http://people.csail.mit.edu/akiezun/miRviewer>
- Patrocles: <http://www.patrocles.org/>
- PicTar: <http://pictar.mdc-berlin.de/>
- TargetRank: <http://hollywood.mit.edu/targetrank>
- TargetScanS: <http://www.targetscan.org/>

# Oncomirs - miRNAs and cancer

## Tumor suppressor miRNAs

*mir-15/16; let-7; mir-34*



*Target mRNA  
overexpression*

## Oncogenes

*RAS; MYC  
BCL2; MET*



Proliferation

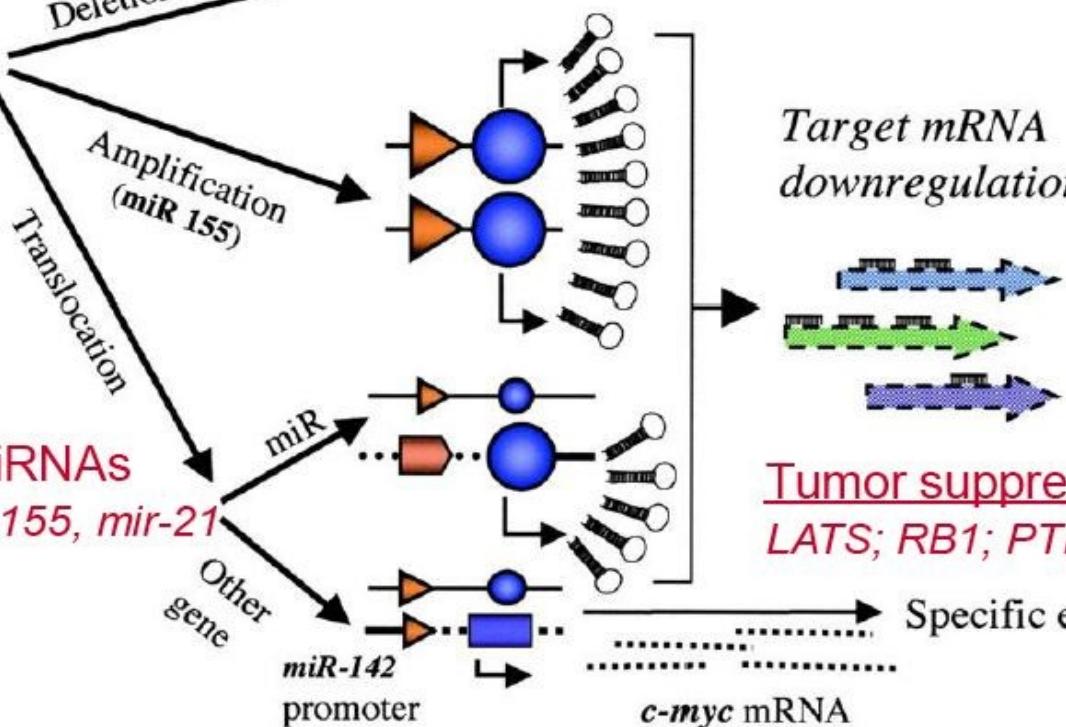
Apoptosis

Invasion

Angiogenesis

## Oncogene miRNAs

*mir-17-92; mir-155, mir-21*



*Target mRNA  
downregulation*

## Tumor suppressor genes

*LATS; RB1; PTEN*

Specific effects



# MicroRNAs Commonly Associated with Human Cancer

miRNA	Gene Loci	Cancer association	Function*	References
miR15, miR-16	chromosome 13q14	Frequently deleted/downregulated in B-cell chronic lymphocytic leukemia. Negatively regulates the anti-apoptotic gene, BCL2.	TS	Calin, 2002 Cimmino, 2005
miR-143, miR-145	chromosome 5q3233	Decreased abundance in colorectal cancer. Down-regulated in breast, prostate, cervical, and lymphoid cancer celllines. miR-145 decreased in breast cancer.	TS	Michael, 2003 Iorio, 2005
miR-21	chromosome 17q23.2	Antiapoptotic factor. Upregulated in glioblastomas and breast cancer.	OG	Chan, 2005 Ciaffre, 2005 Iorio, 2005
let-7	multiple loci	Negatively regulates the Ras oncogene. Directs cell proliferation, differentiation. Decreased abundance in lung cancer.	TS	Johnson, 2005 Takamizawa, 2004
miR-142	chromosome 17q22	t(8,17) translocation that places the MYC oncogene downstream of the <i>mir-142</i> hairpin resulting in an aggressive B cell leukemia due to MYC over-expression.	N/A	Lagos-Quintana, 2002
BIC/miR-155	chromosome 21q21	Upregulated in pediatric Burkitt's lymphomas, Hodgkins, primary mediastinal and diffuse large B cell lymphomas. Upregulated in human breast cancer.	OG	Eis, 2005 Kluiver, 2005 van den Berg, 2003 Metzler, 2003 Iorio, 2005
miR-17-19b cluster	chromosome 13q3132	Upregulated by the c-Myc oncogene Negatively modulates E2F1 oncogene.  Loss-of-heterozygosity of cluster in hepatocellular carcinoma. Over-expressed in B cell lymphomas.	TS/ OG	He, 2005 O'Donnell, 2005

\*Abbreviations: TS, tumor-suppressor gene; OGoncogene; N/A, not applicable