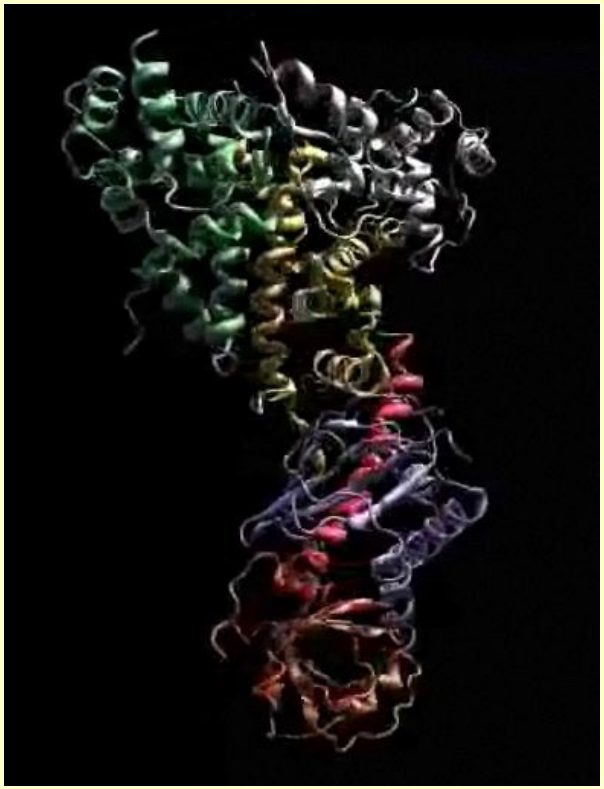
Computational Molecular Biology
Biochem 218 – BioMedical Informatics 231

http://biochem218.stanford.edu/

miRNA Regulatory Networks



Doug Brutlag
Professor Emeritus
Biochemistry & Medicine (by courtesy)

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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

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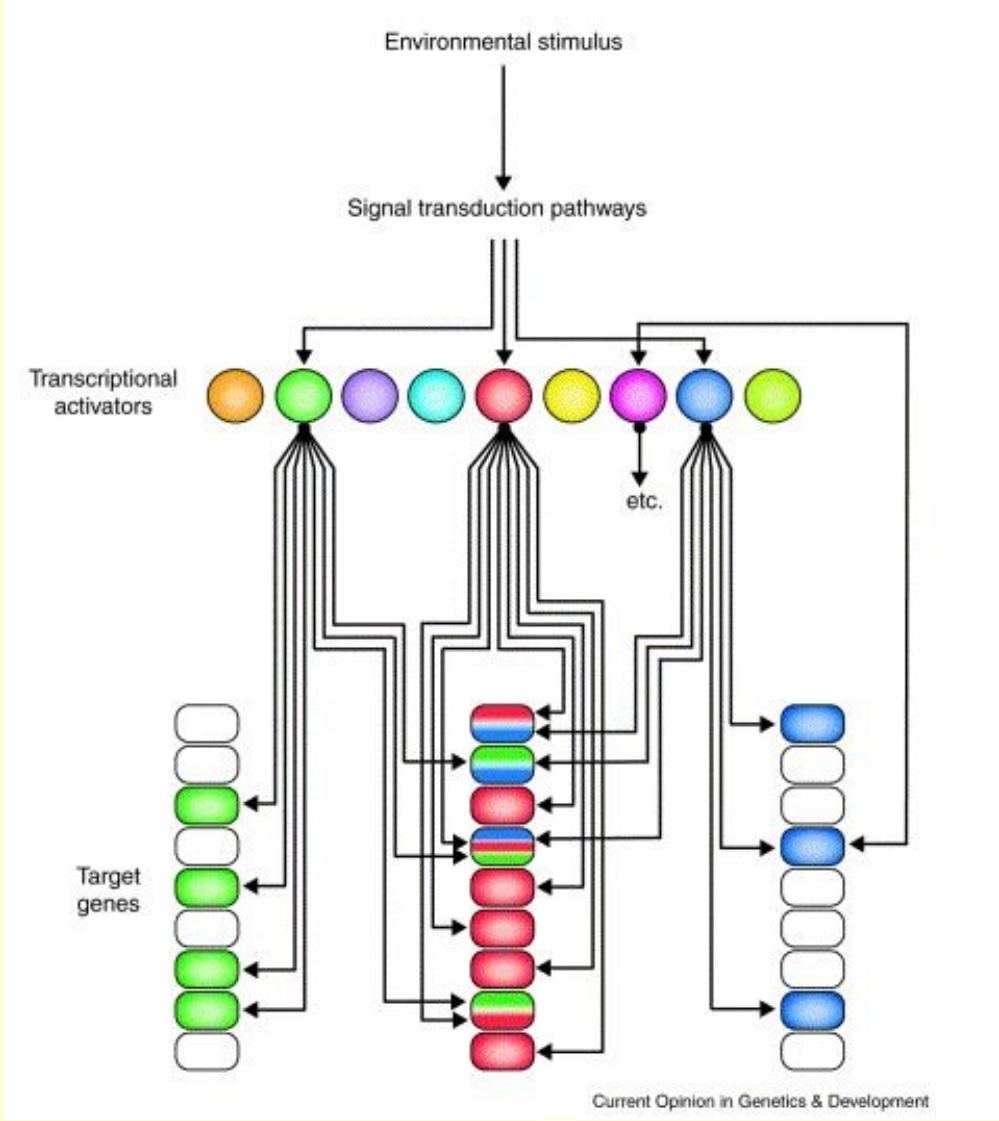
Gene Expression Regulatory Network



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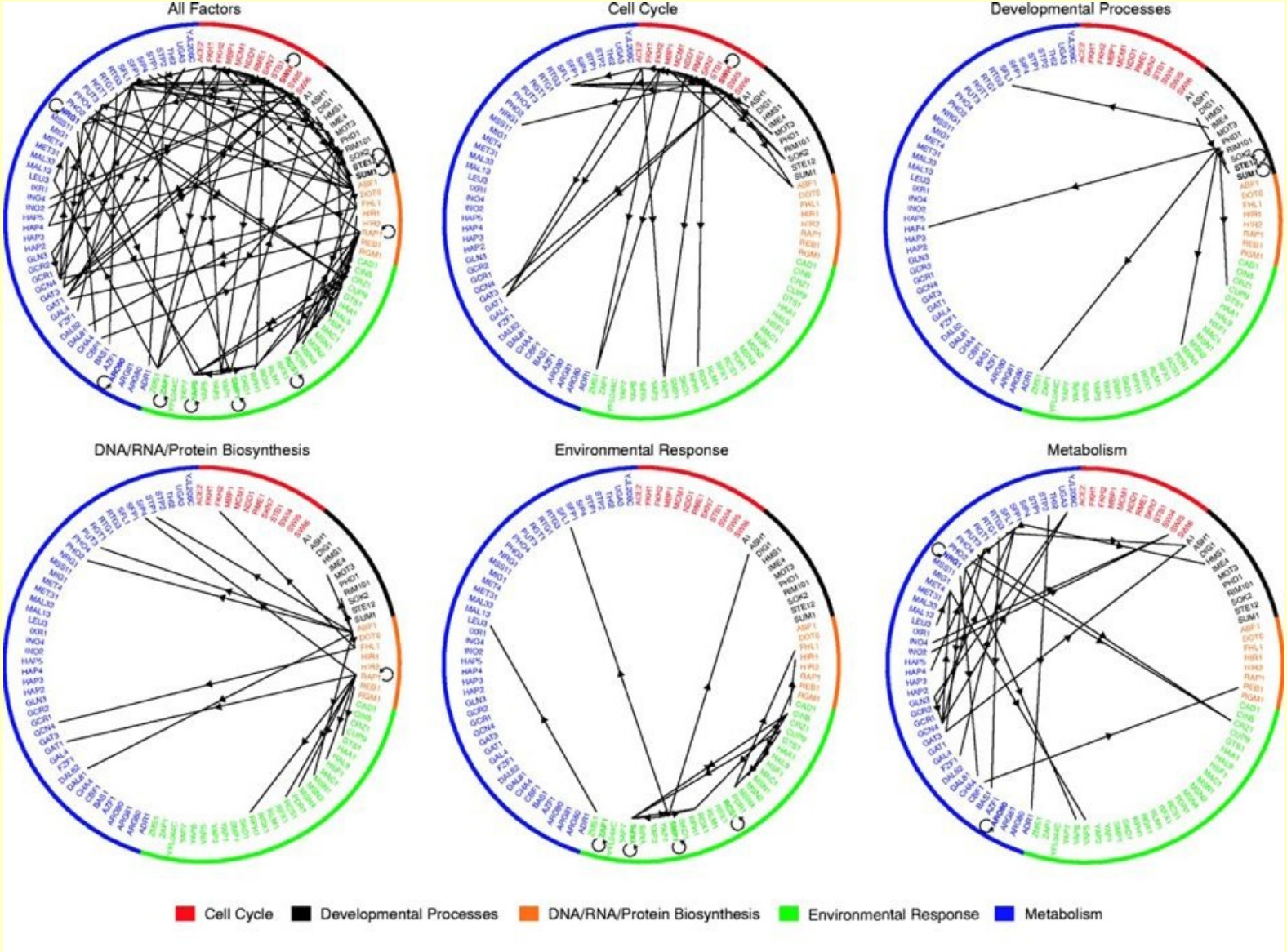
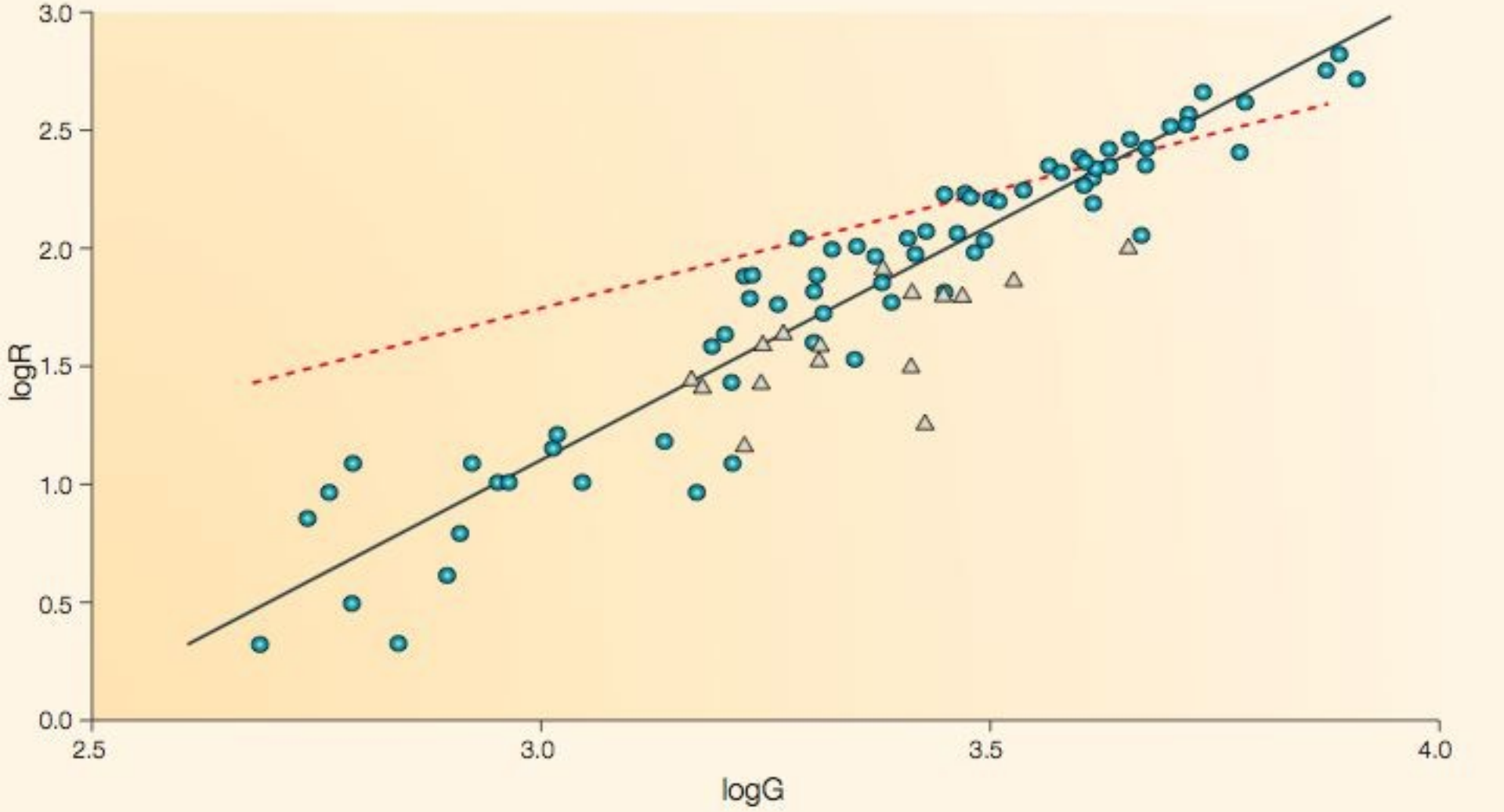
Yeast Regulatory Motifs



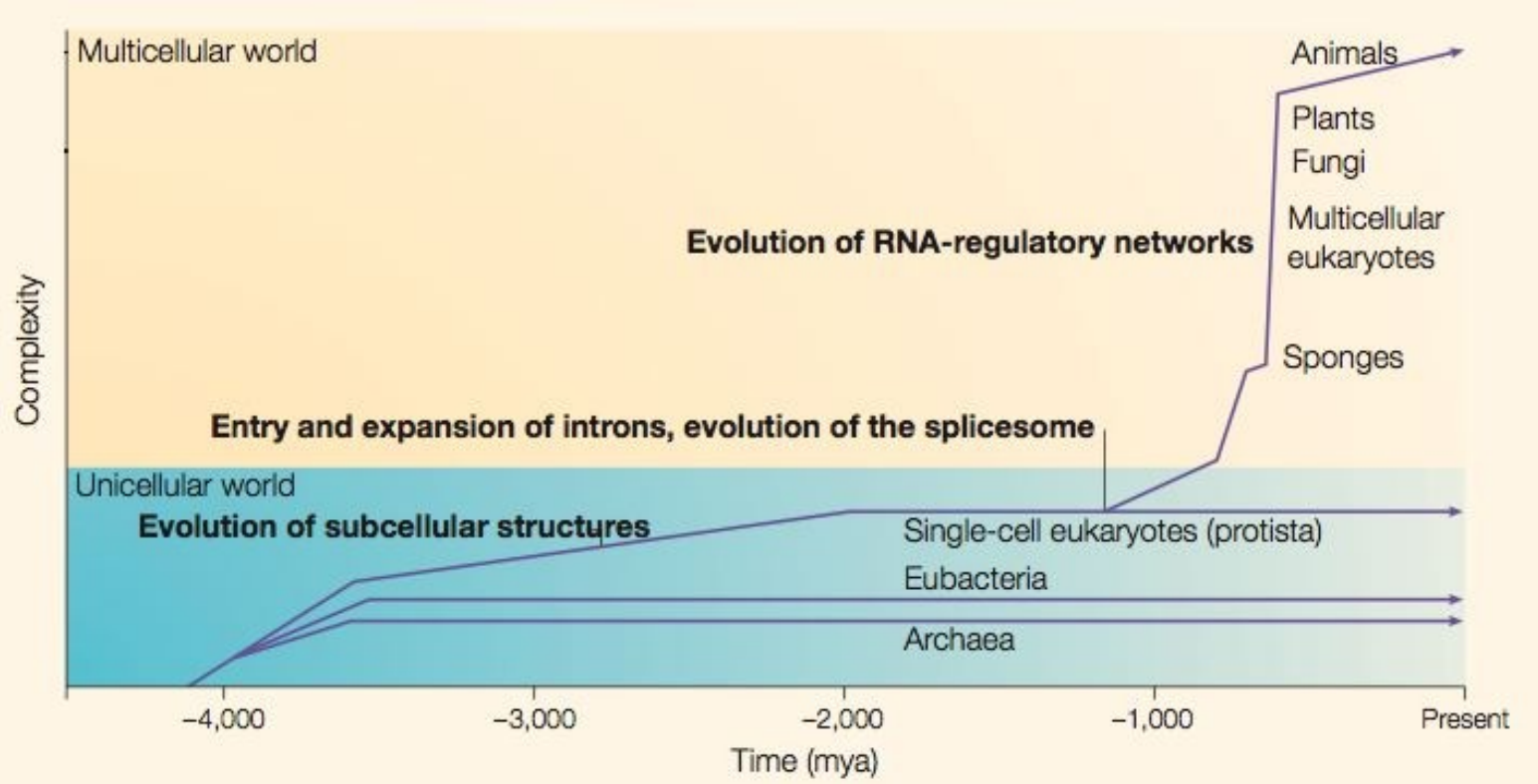
Lee et al. Science 298, 799-804 (2002)

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



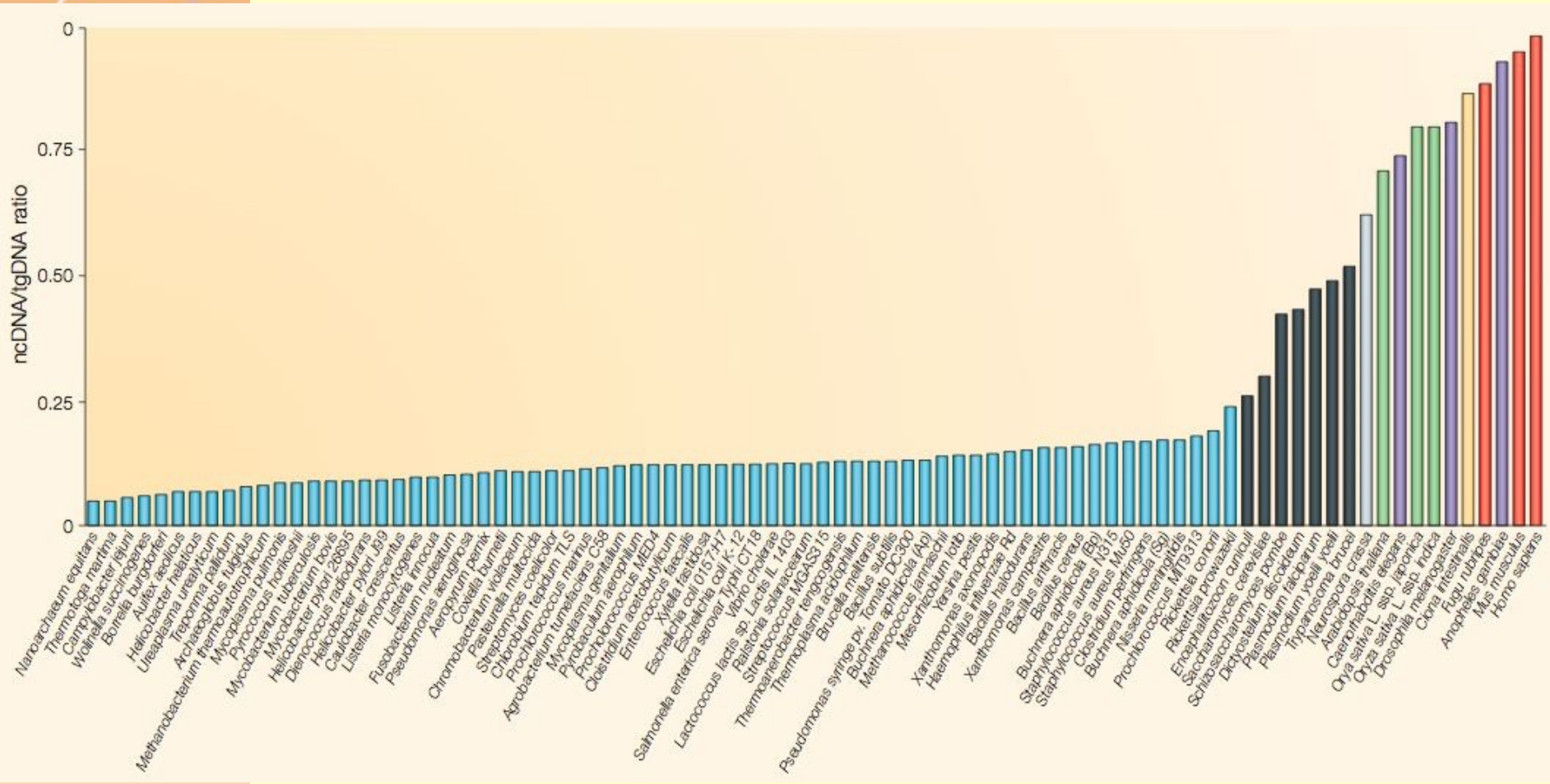
Mattick (2004) Nature Reviews Genetics 5: 316-323 .

A Simplified History of Life on Earth



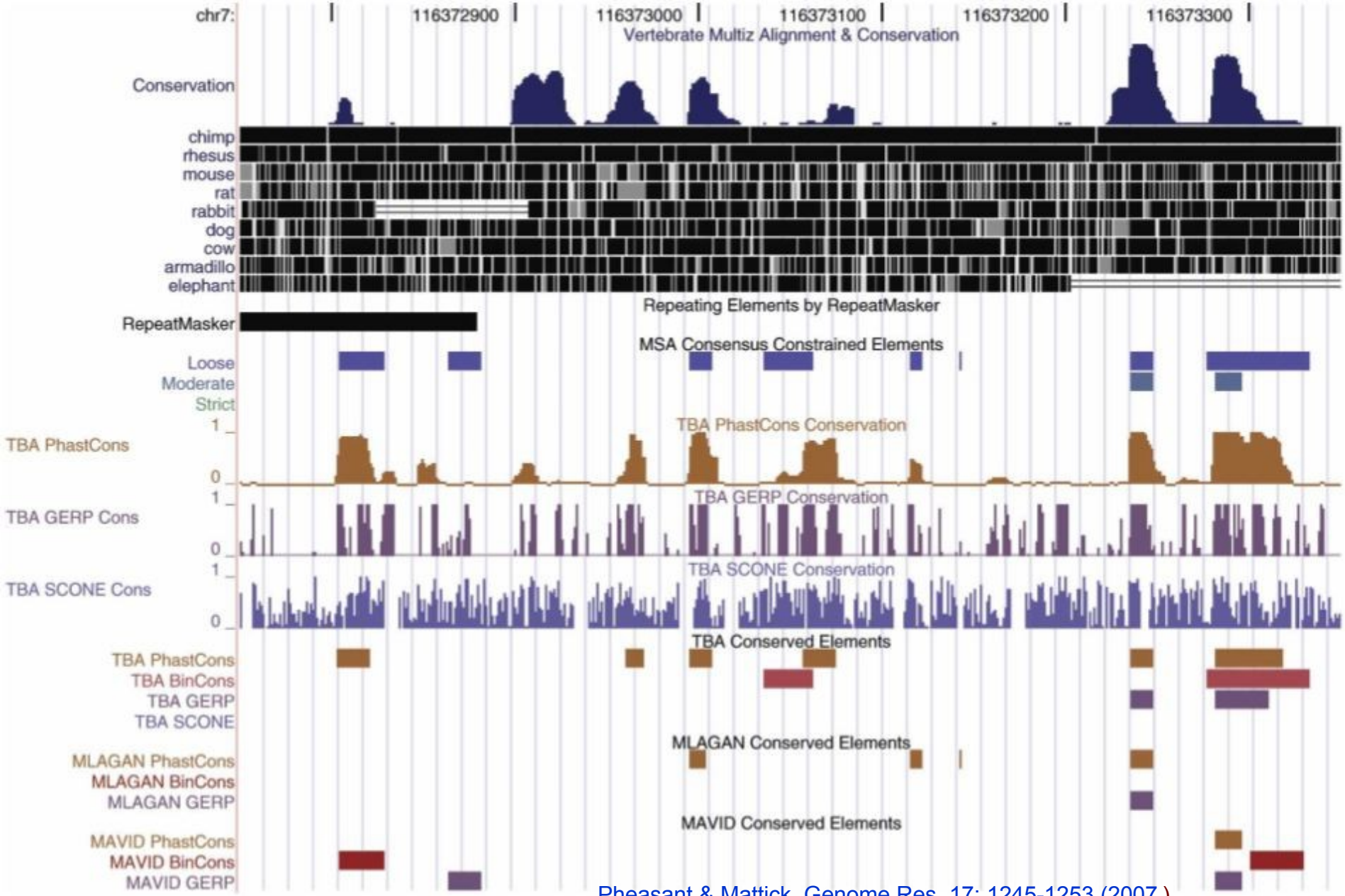
Mattick (2004) Nature Reviews Genetics 5: 316-323.

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



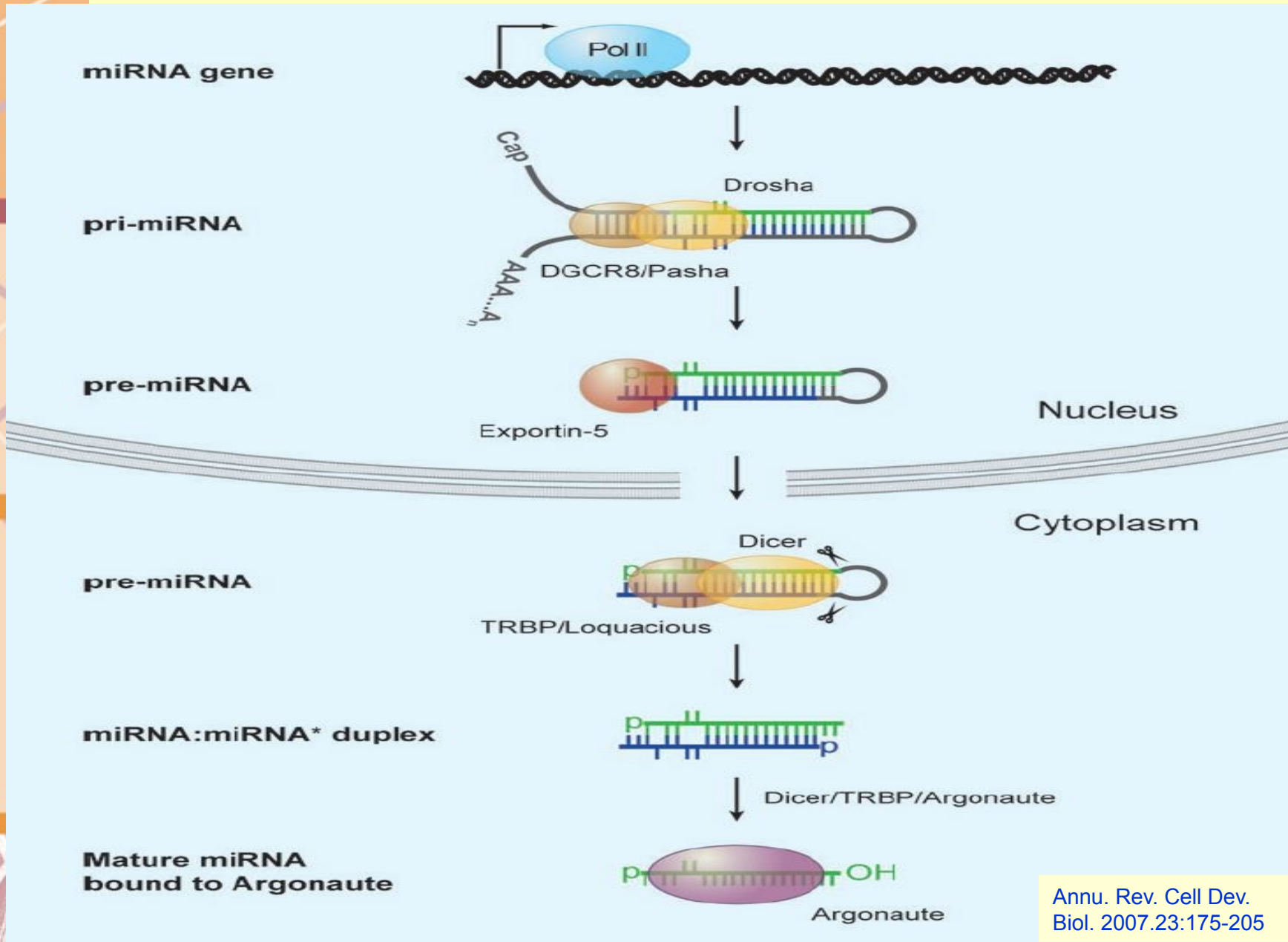
Mattick (2004) Nature Reviews Genetics 5: 316-323.

Conserved Regions in CFTR Intron



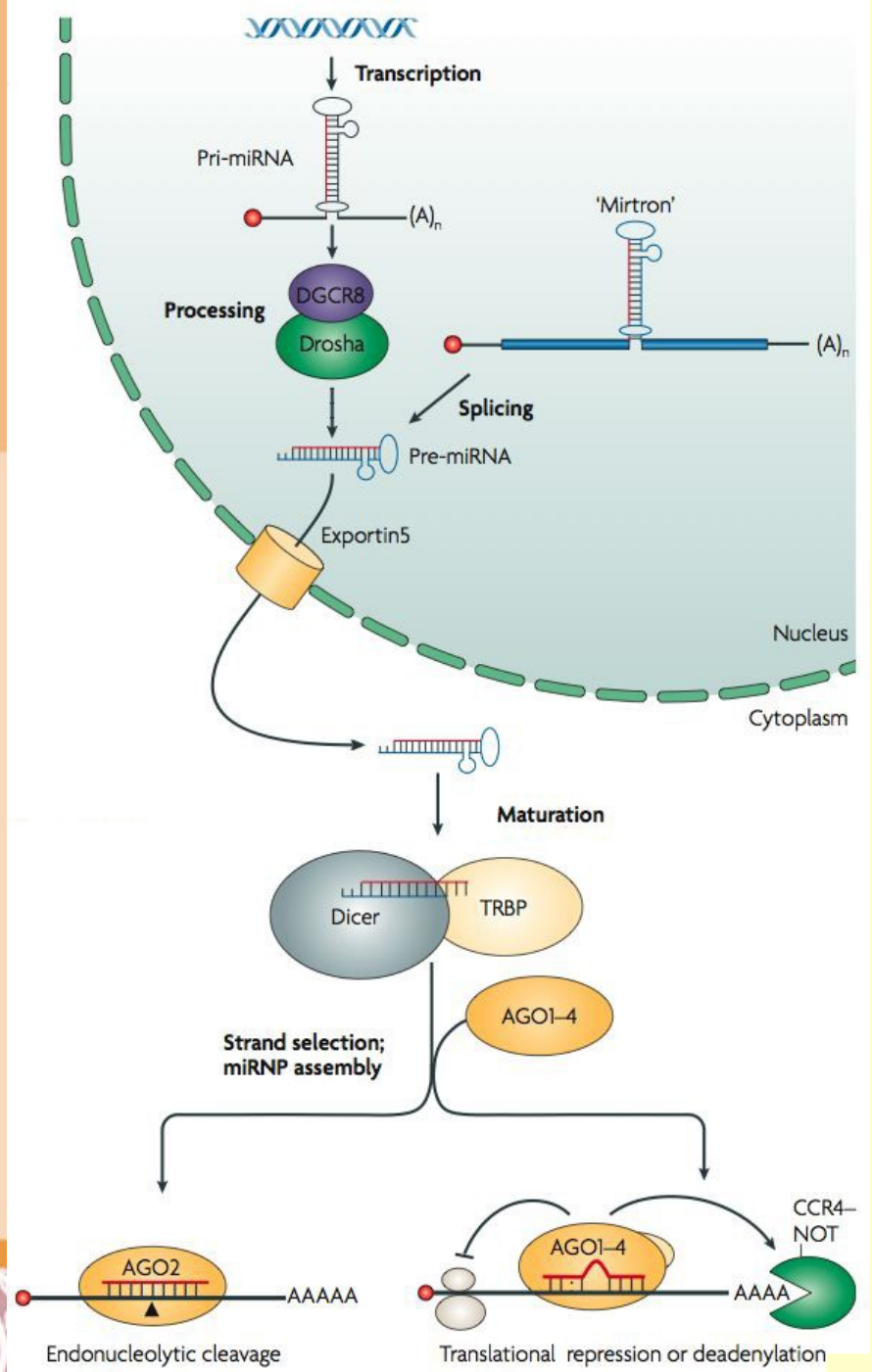
Pheasant & Mattick. Genome Res. 17: 1245-1253 (2007)

microRNA Biogenesis

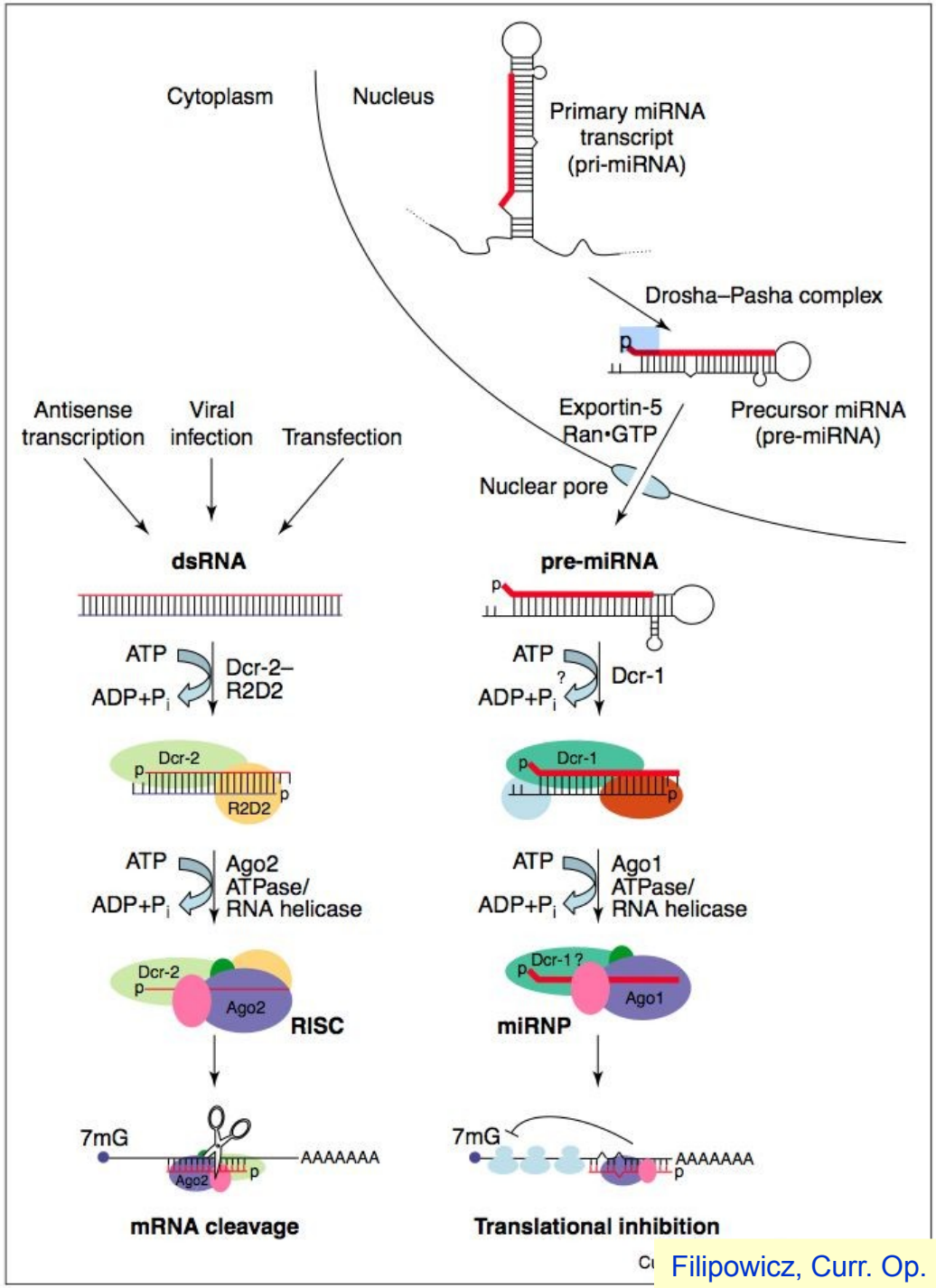


Annu. Rev. Cell Dev. Biol. 2007.23:175-205

Biogenesis of miRNA



Filipowicz (2008) Nature Review Genetics 9:102-112.



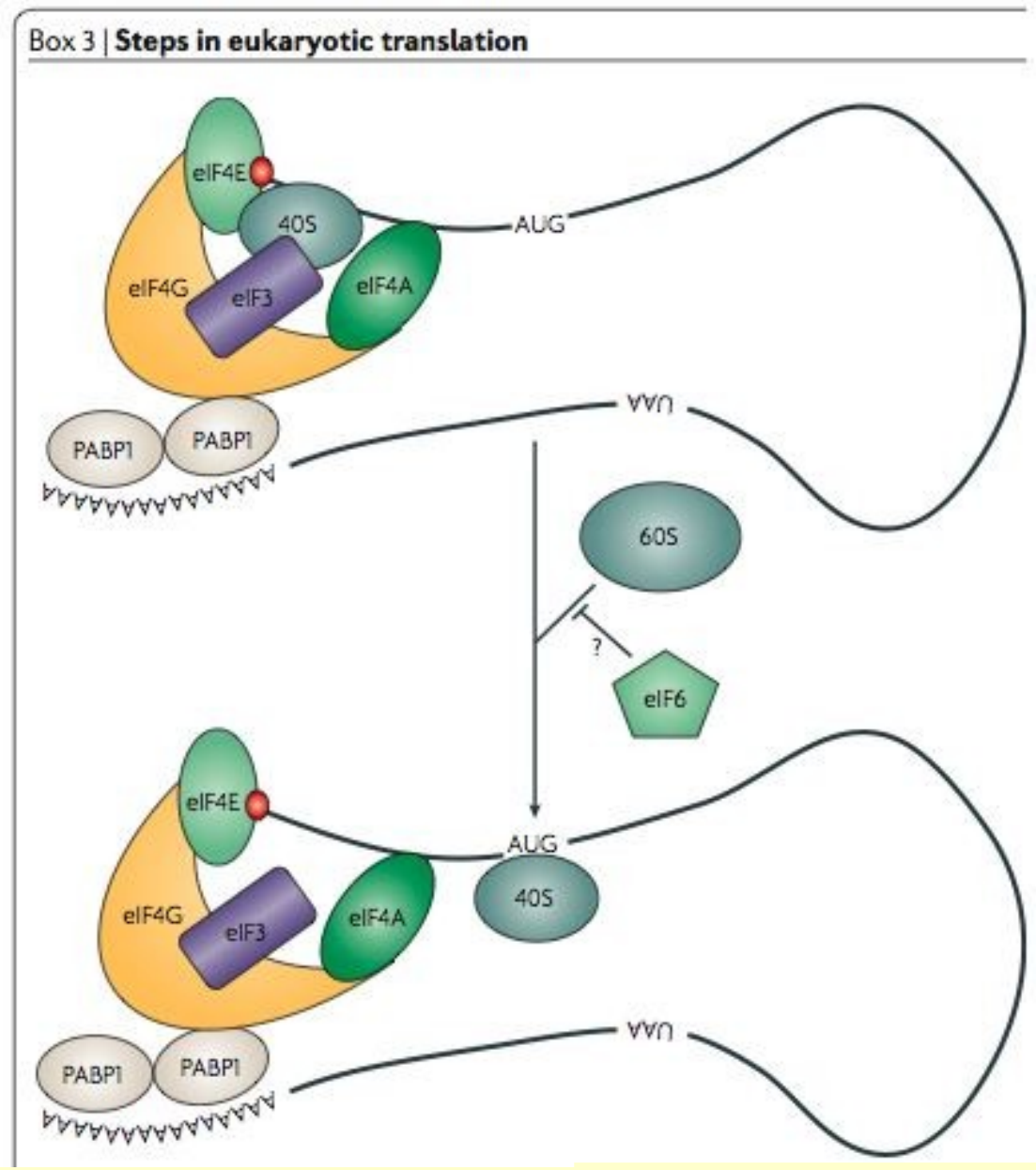
siRNA mediated degradation of mRNA

versus

miRNA mediated inhibition of mRNA translation

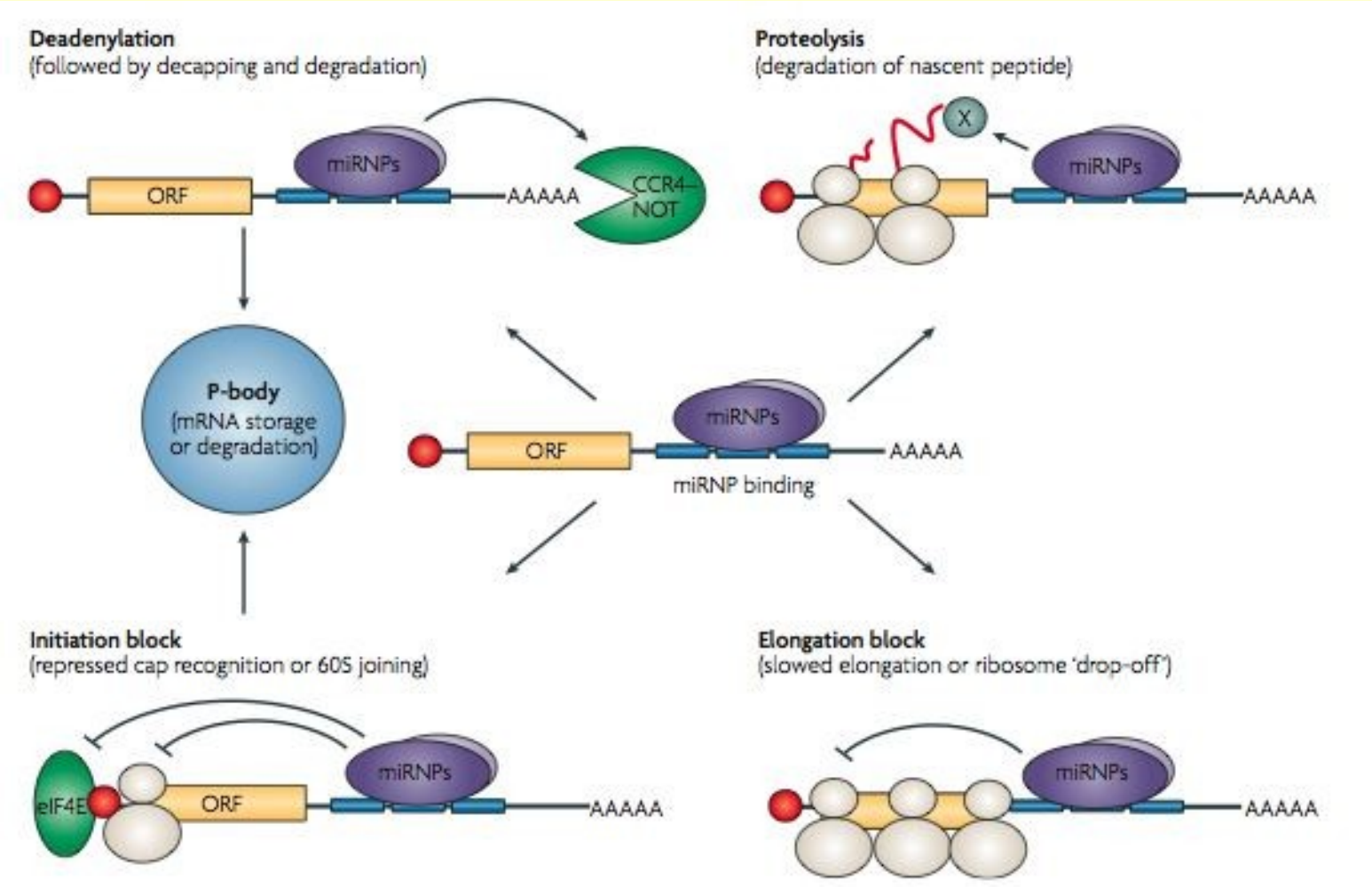
Filipowicz, Curr. Op. Structural Biology 15: 331-341 (2005)

Initiation of Translation



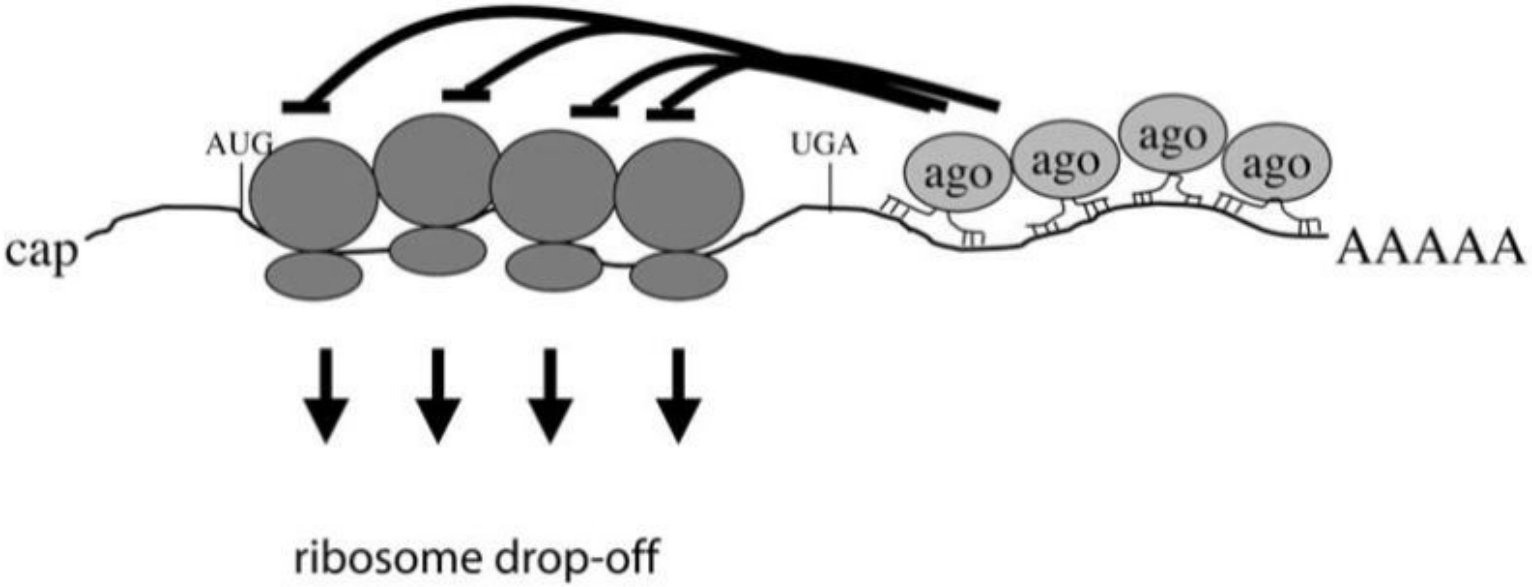
Filipowicz (2008) Nature Review Genetics 9:102-112.

Mechanisms of Translational Regulation by miRNP Complexes



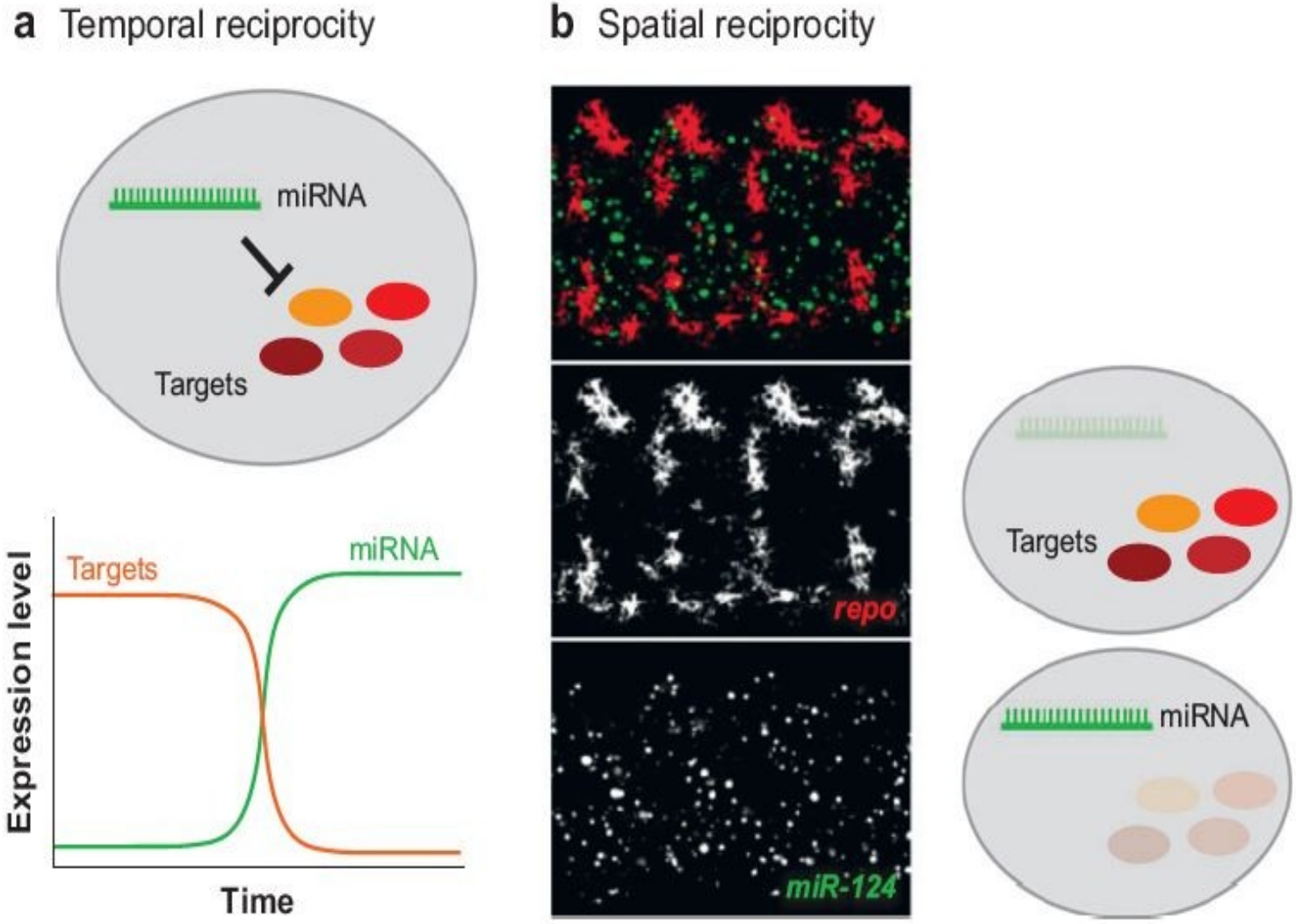
Filipowicz (2008) Nature Review Genetics 9:102-112.

miRNAs Inhibit Translation by Inducing Ribosome Drop-Off



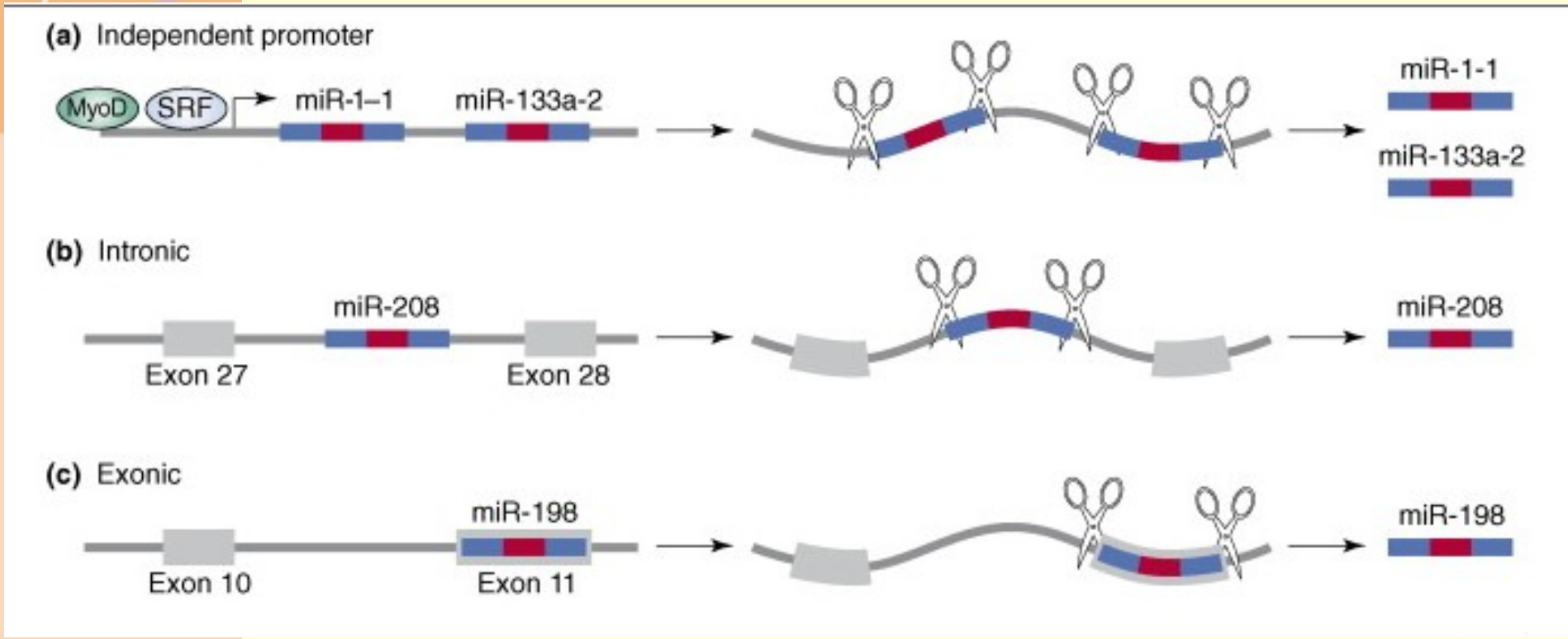
Petersen et al. (2006) Molecular Cell 21: 533-542.

miRNA Expression Results in Temporal and Spatial Reciprocity with Target Expression



Annu. Rev. Cell Dev. Biol. 2007.23:175-205

Genomic Organization of miRNA Genes

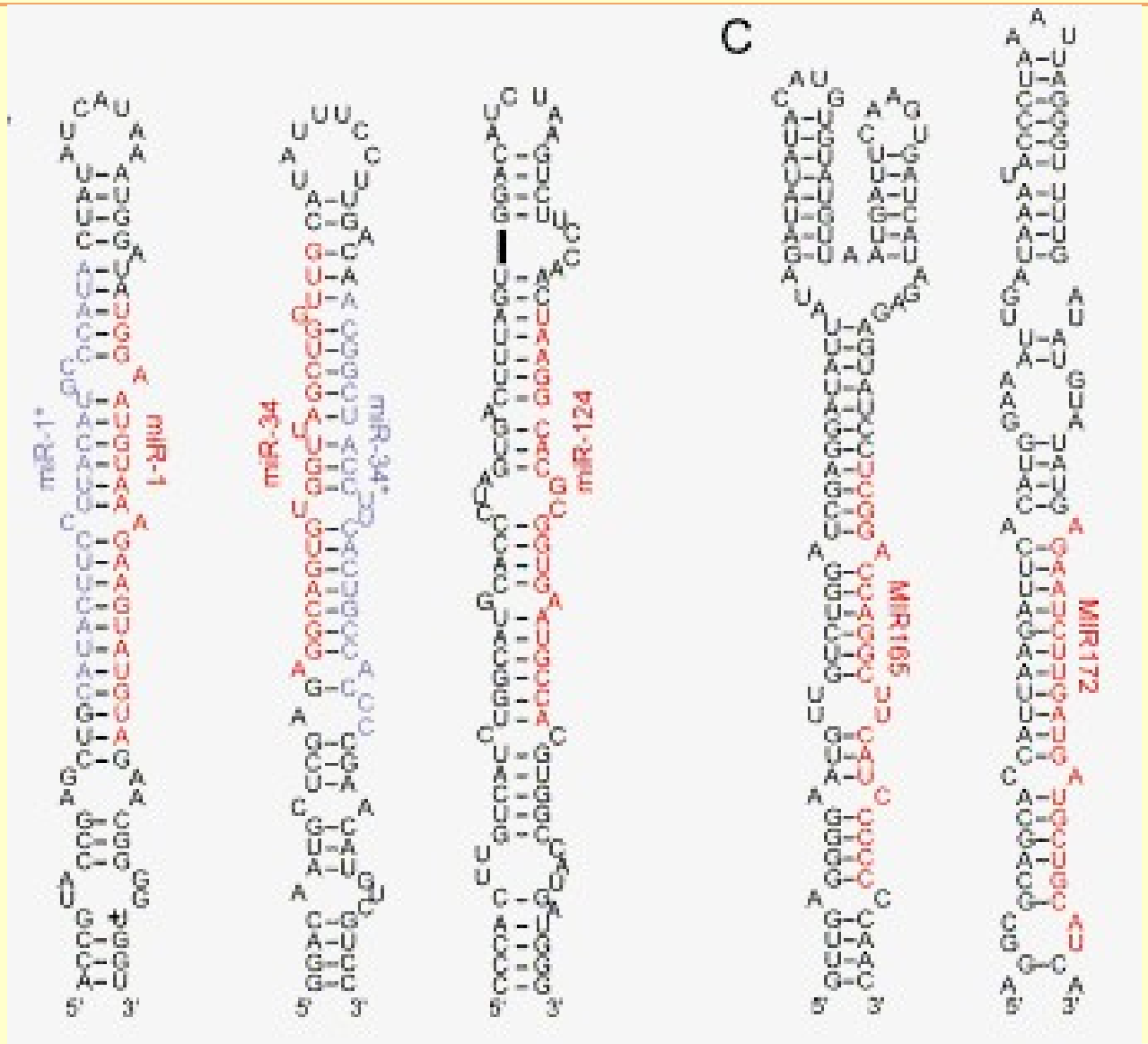


- Intronic miRNAs often in antisense direction, made from own promoter

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

Zhao Y, Srivastava D, TIBS 32:189,2007

Precursor miRNA Products Form Stem Loop Structures



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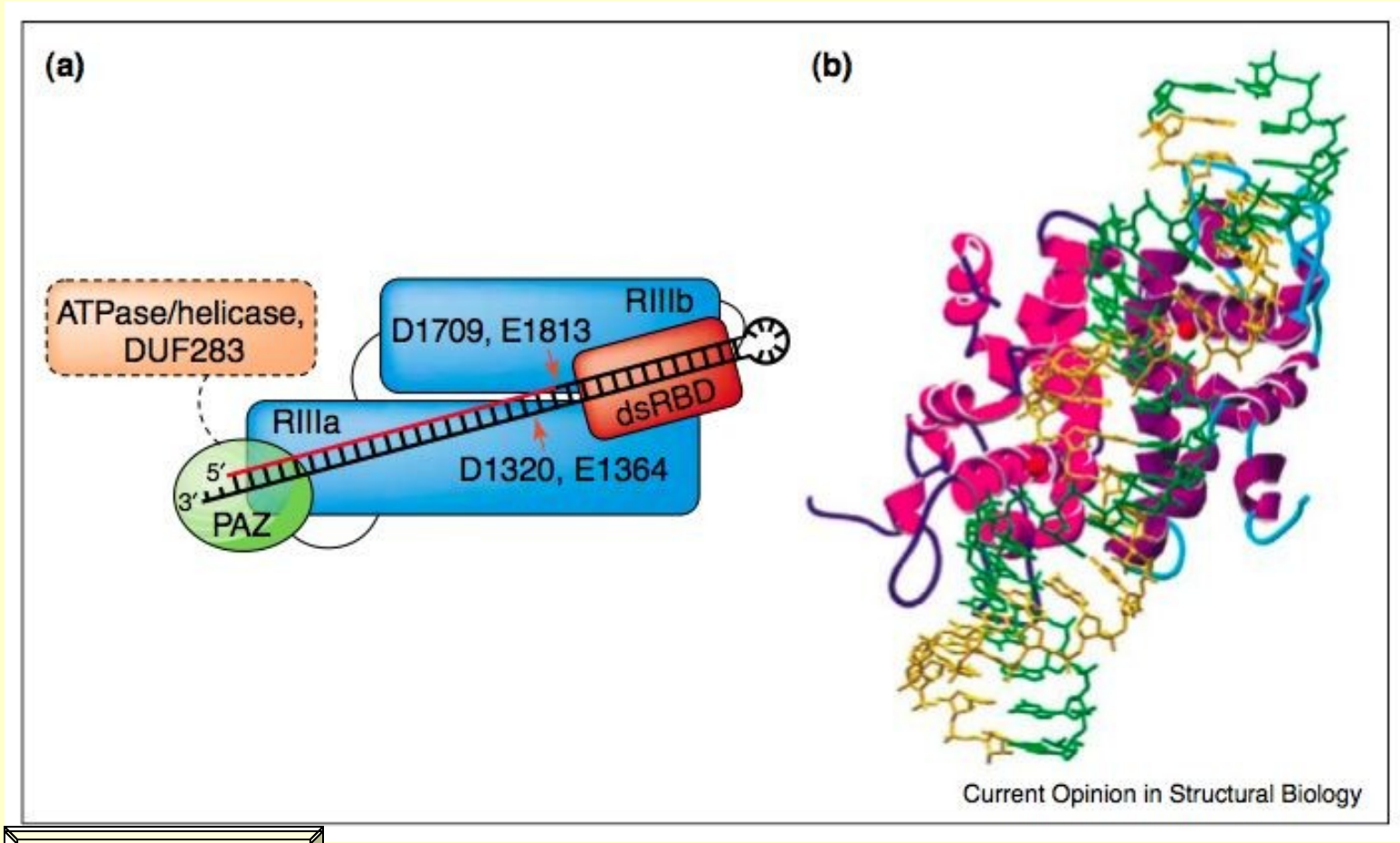
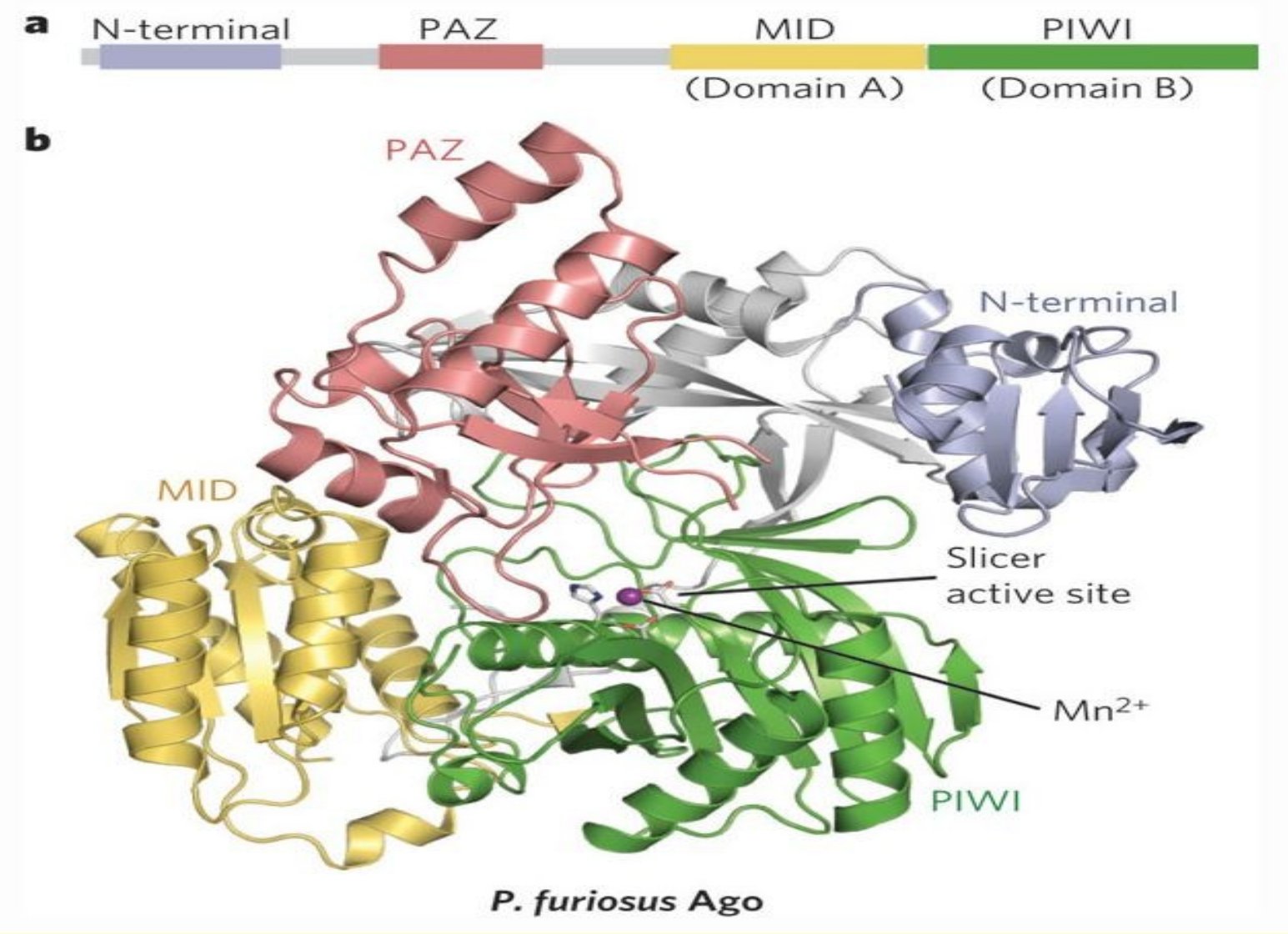
Dicer Structure & Function



Dicer Movie

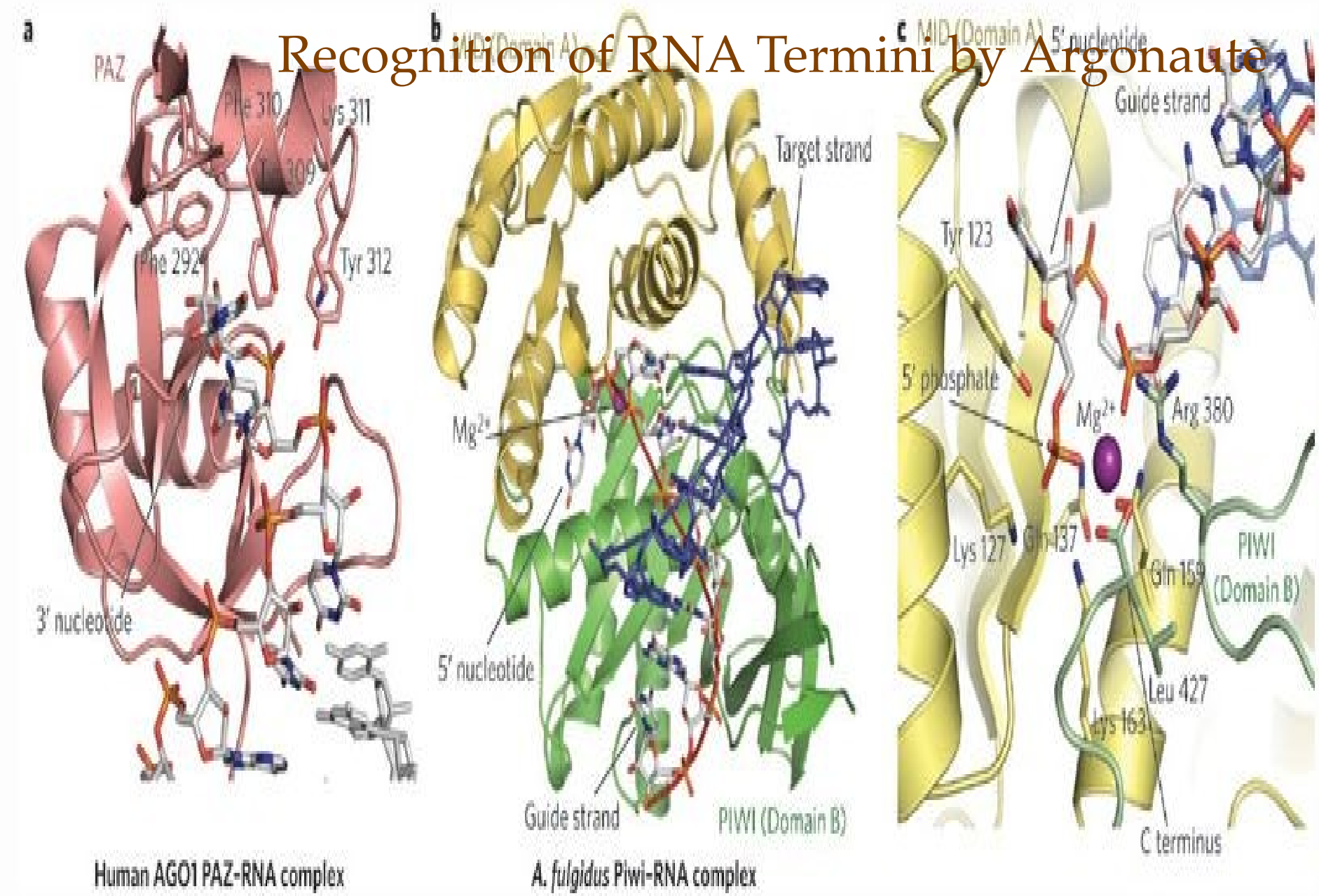
Filipowicz, Curr. Op. Structural Biology 15: 331-341 (2005)

Argonaute Structure and Function



Martin Jinek & Jennifer A. Doudna *Nature 457, 405-412(22 January 2009)*

Recognition of RNA Termini by Argonaute

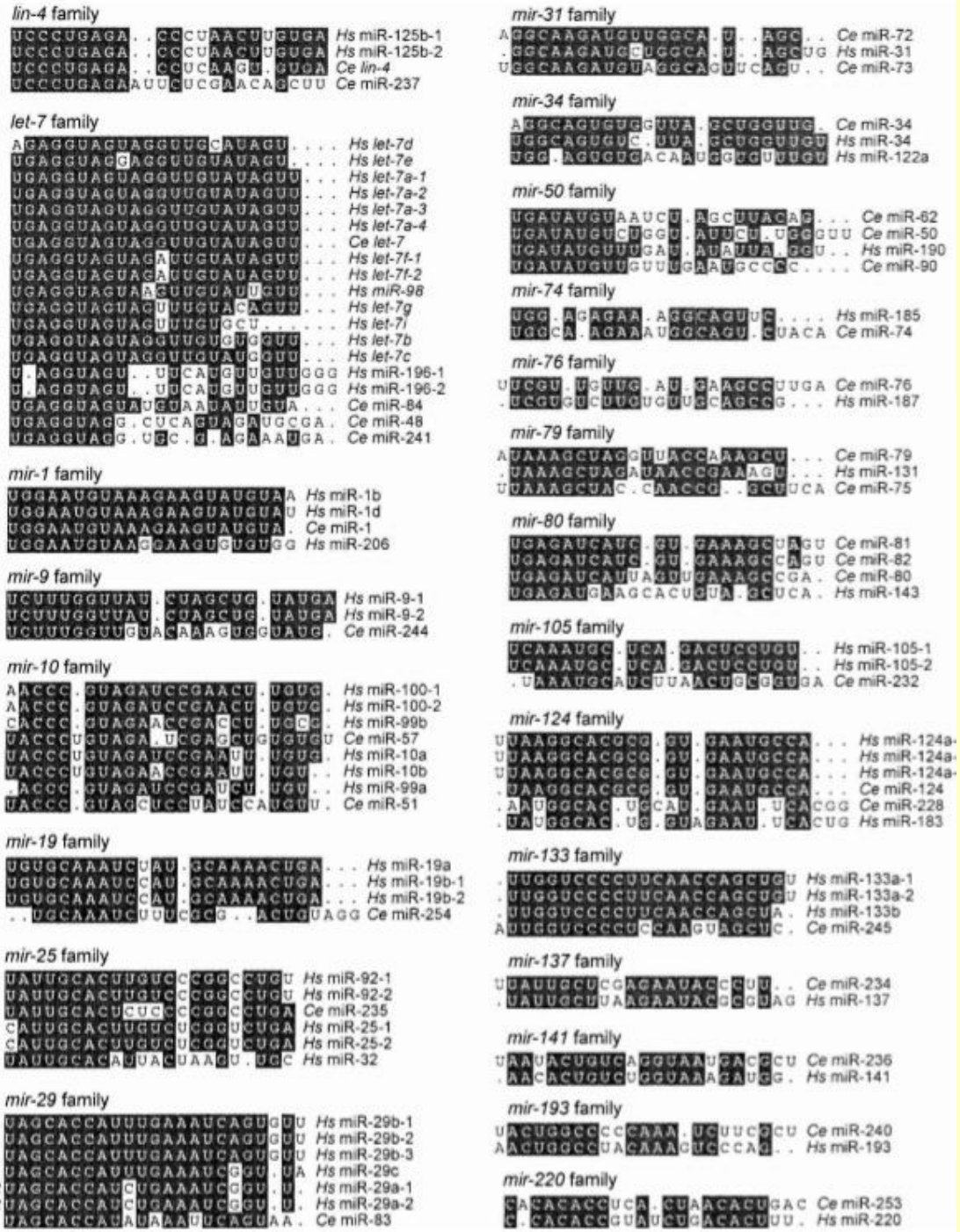


Human AGO1 PAZ-RNA complex

A. fulgidus Piwi-RNA complex

Martin Jinek & Jennifer A. Doudna *Nature 457, 405-412(22 January 2009)*

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



Lim (2003) Genes & Dev. 17: 99

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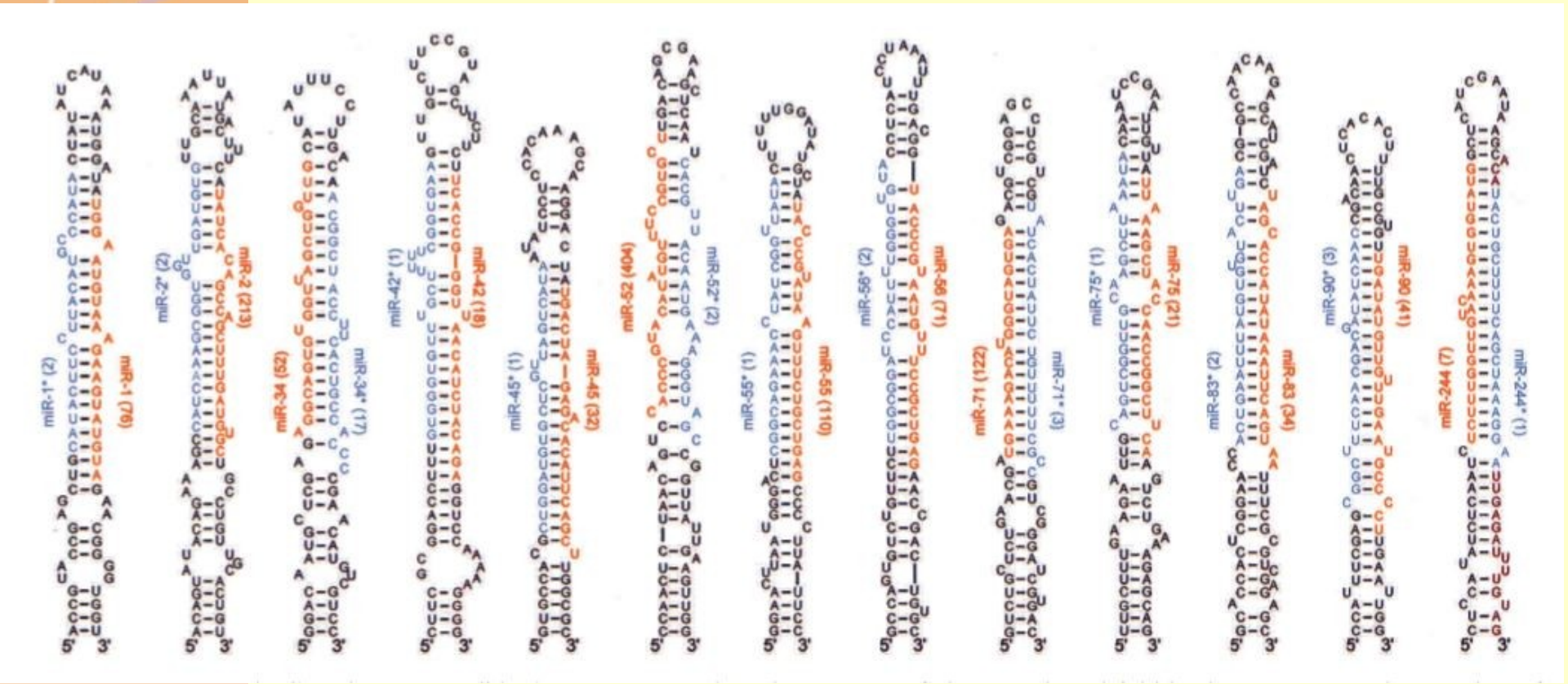
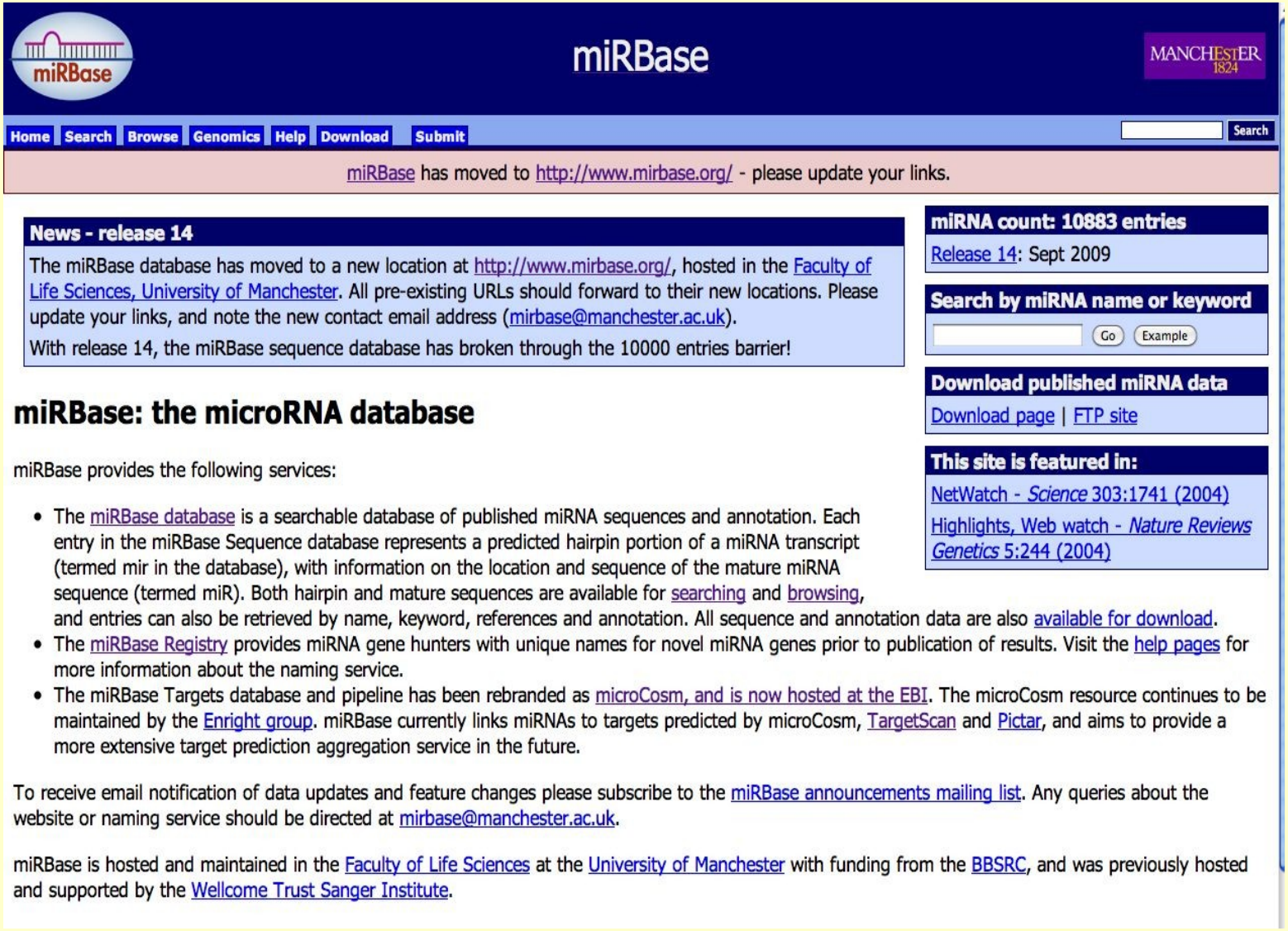
Predicted miRNA Precursors



Lim (2003) Genes & Dev. 17: 991-1008

miRBase

http://www.mirbase.org/



miRBase

MANCHESTER 1824

Home | Search | Browse | Genomics | Help | Download | Submit

Search

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).

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.

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.

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miRBase Genome Browser

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

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miRBase Human miRNAs

http://www.mirbase.org/cgi-bin/mirna_summary.pl?org=hsa

miRBase

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

Homo sapiens miRNAs (721 sequences)

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

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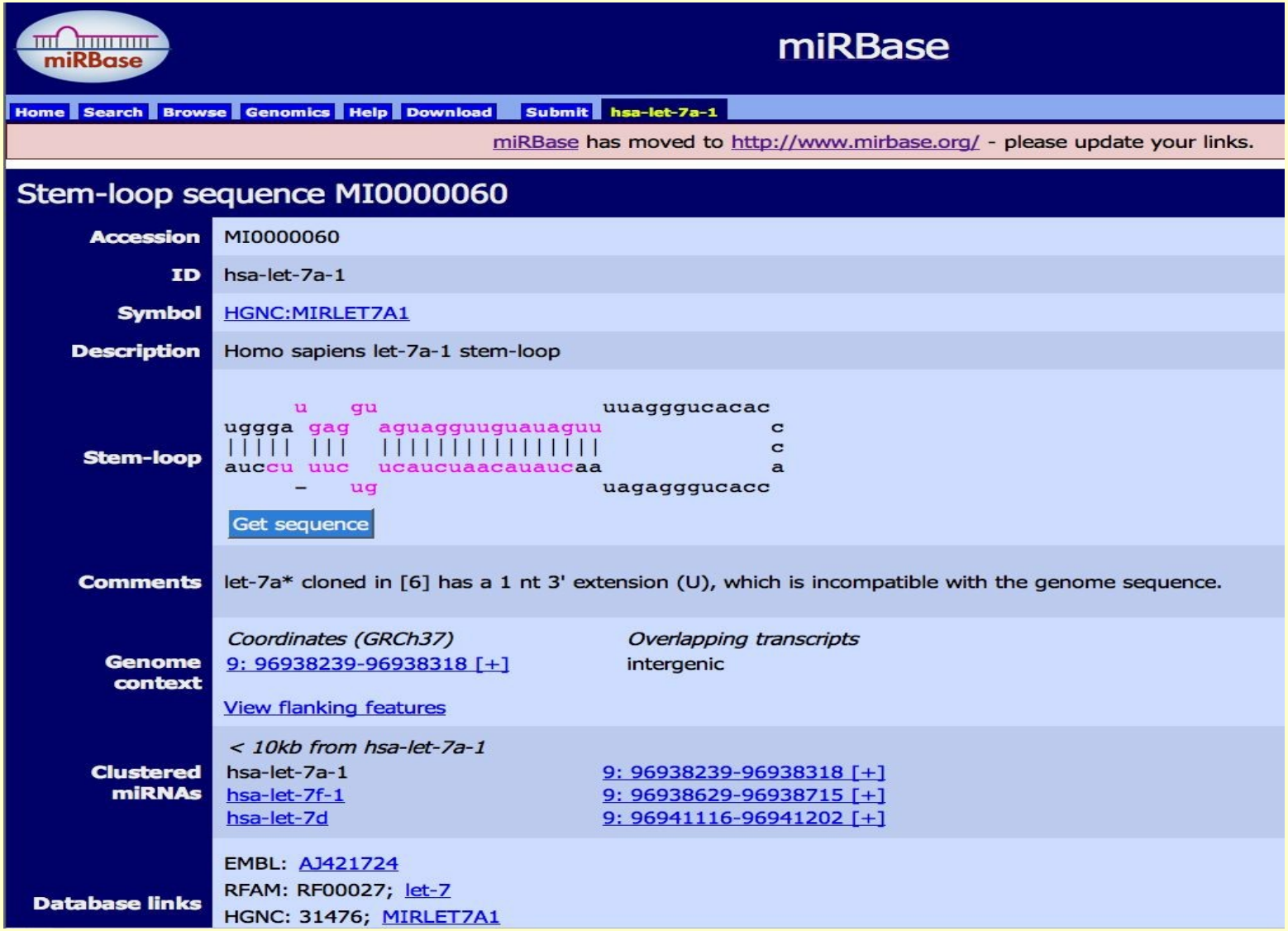
miRBase Human let-7a-1

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

Accession	MI0000060
ID	hsa-let-7a-1
Symbol	HGNC:MIRLET7A1
Description	Homo sapiens let-7a-1 stem-loop
Stem-loop	u gu uuagggucacac uggga gag aguagguuguauaguu c ||||| ||| |||||||||||||| c auccu uuc ucaucuaacauaucaa a – ug uagagggucacc Get sequence
Comments	let-7a* cloned in [6] has a 1 nt 3' extension (U), which is incompatible with the genome sequence.
Genome context	*Coordinates (GRCh37)*: 9: 96938239-96938318 [+] *Overlapping transcripts*: intergenic View flanking features
Clustered miRNAs	*< 10kb from hsa-let-7a-1* hsa-let-7a-1 — 9: 96938239-96938318 [+] hsa-let-7f-1 — 9: 96938629-96938715 [+] hsa-let-7d — 9: 96941116-96941202 [+]
Database links	EMBL: AJ421724 RFAM: RF00027; let-7 HGNC: 31476; MIRLET7A1

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miRBase Human let-7a-1 Page 2

http://www.mirbase.org/cgi-bin/mirna_entry.pl?acc=MI0000060

Mature sequence MIMAT0000062

Accession	MIMAT0000062
ID	hsa-let-7a
Sequence	6 - ugagguaguagguuguauaguu - 27 Get sequence
Evidence	experimental; cloned [1-3,5-8], Northern [1]
Predicted targets	MICROCOSM: hsa-let-7a TARGETSCAN: hsa-let-7a PICTAR-VERT: hsa-let-7a

Minor miR* sequence MIMAT0004481

Accession	MIMAT0004481
ID	hsa-let-7a*
Sequence	57 - cuauacaaucuacugucuuuc - 77 Get sequence
Evidence	experimental; cloned [6]
Predicted targets	MICROCOSM: hsa-let-7a* TARGETSCAN: hsa-let-7a*

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).

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miRBase::MicroCosm miRNA Targets

- EMBL-EBI
- Enright Lab
- Services
  - MicroCosm Targets
  - MapMi
  - Sylamer
- MicroCosm Targets
  - Home
  - Genomes
  - miRNAs

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

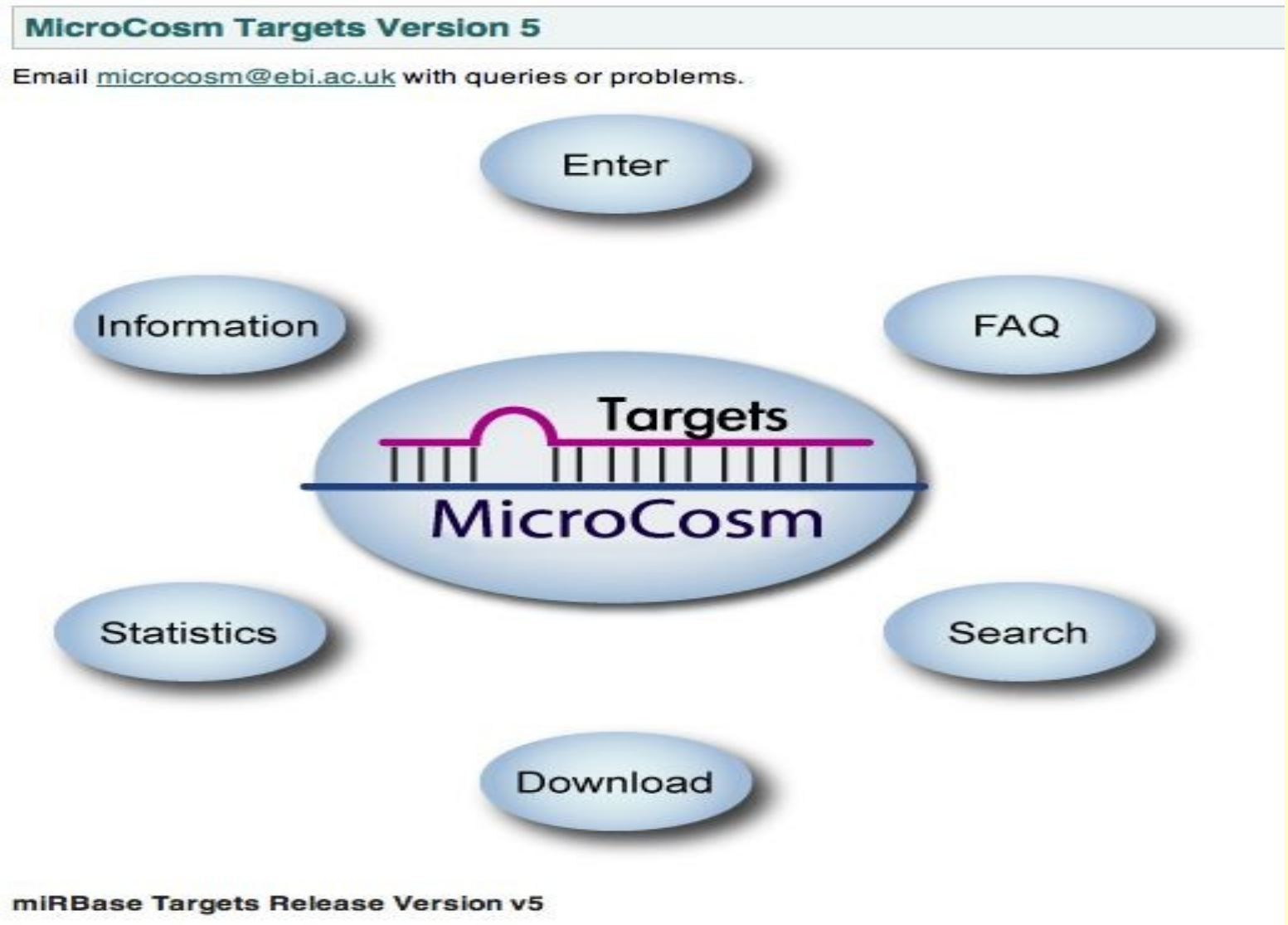
1046 hits found.

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**	ENST00000383763	Tripartite motif-containing protein 71 (Lin-41 homolog). [Source:Uniprot/SWISSPROT;Acc:Q2Q1W2]		16.4005	-18.93	1.11674e-10	1000	20	7	32 [+]	View
Homo sapiens	**Q5FWF1_HUMAN**	ENST00000257359	ADAMTS8 protein (Fragment). [Source:Uniprot/SPTREMBL;Acc:Q5FWF1]		16.062	-15.06	5.55098e-10	633	21	9	38 [+]	View
Homo sapiens	**GALE**	ENST00000313298	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 [+]	View
Homo sapiens	**SEMA4C**	ENST00000305476	Semaphorin-4C precursor. [Source:Uniprot/SWISSPROT;Acc:Q9C0C4]		16.1569	-19.34	2.94605e-08	884	25	9	39 [+]	View
Homo sapiens	**PIAS4**	ENST00000262971	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 [+]	View
Homo sapiens	**MYC**	ENST00000377970	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 [+]	View
Homo sapiens	**RNF20**	ENST00000374819	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 [+]	View
Homo sapiens	**UHRF2**	ENST00000276893	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/ICBP90-like RING finger protein) (Np95-like RING finger protein) (Nucle [Source:Uniprot/SWISSPROT;Acc:Q96PU4]		15.9349	-16.89	8.91282e-08	872	19	9	33 [+]	View
Homo sapiens	**TARBP2**	ENST00000266987	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 [+]	View
Homo sapiens	**CDC34**	ENST00000215574	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 [+]	View

miRBase::MicroCosm miRNA Targets

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



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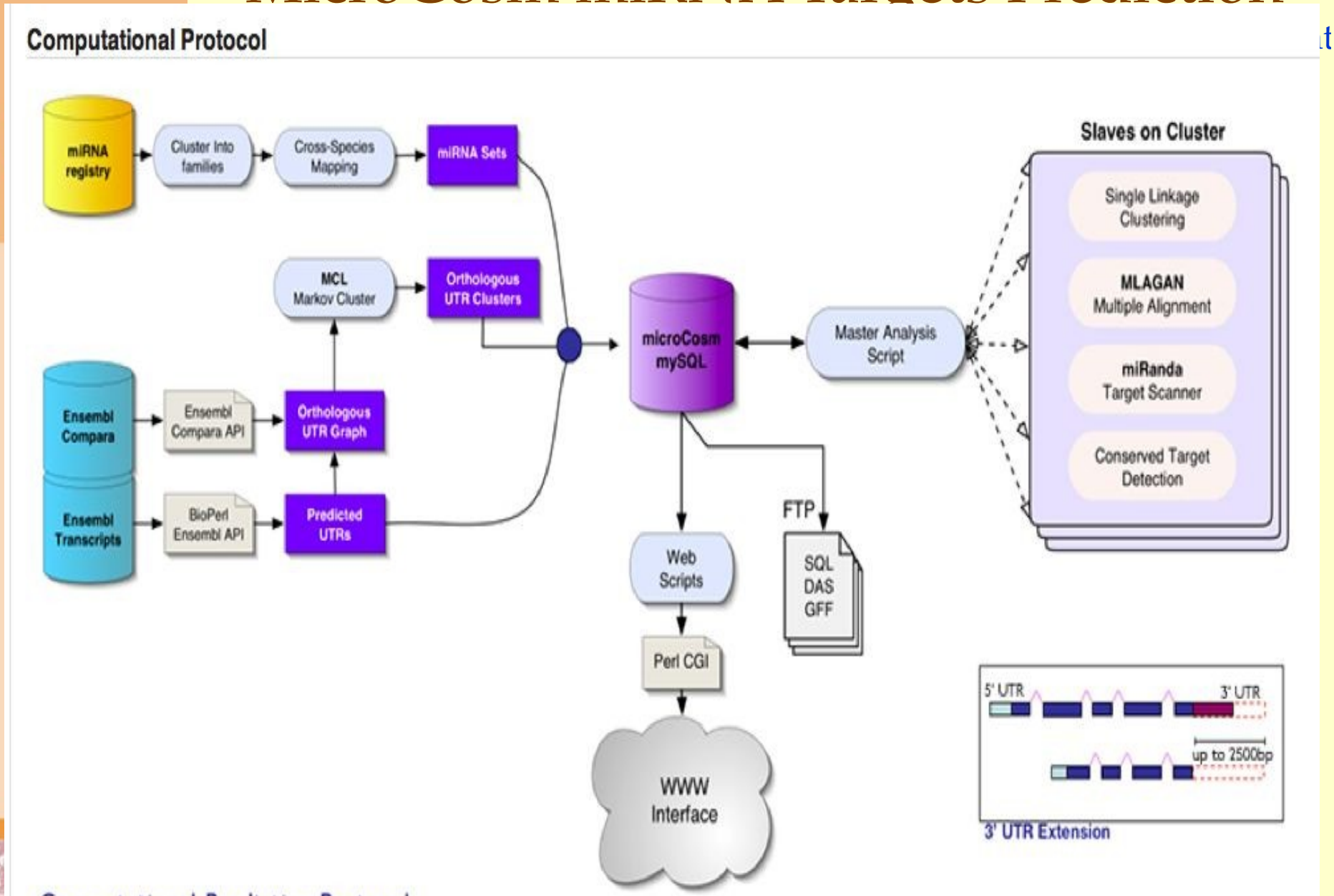
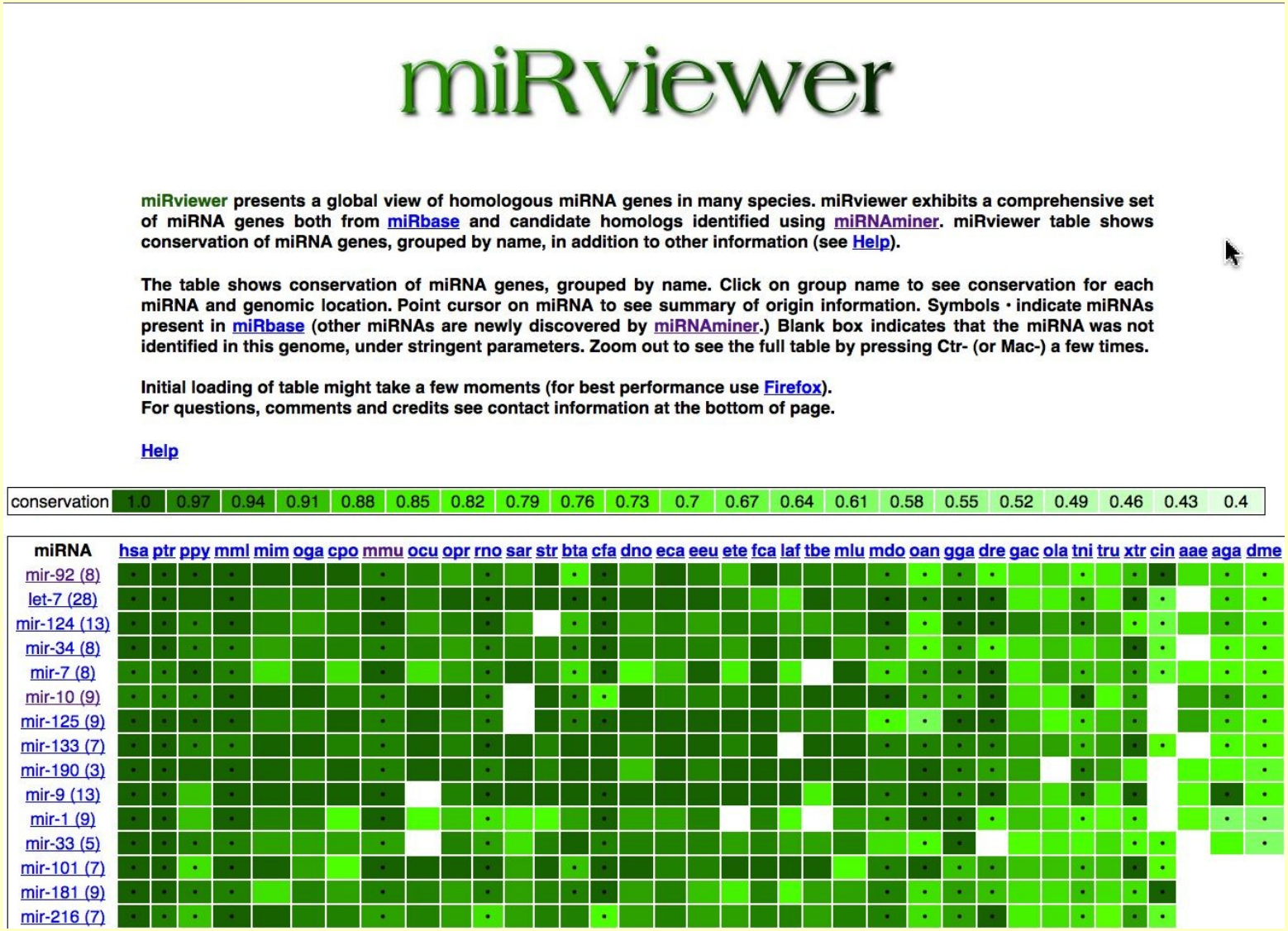
MicroCosm miRNA Targets Prediction



Computational Prediction Protocol

miRViewer

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



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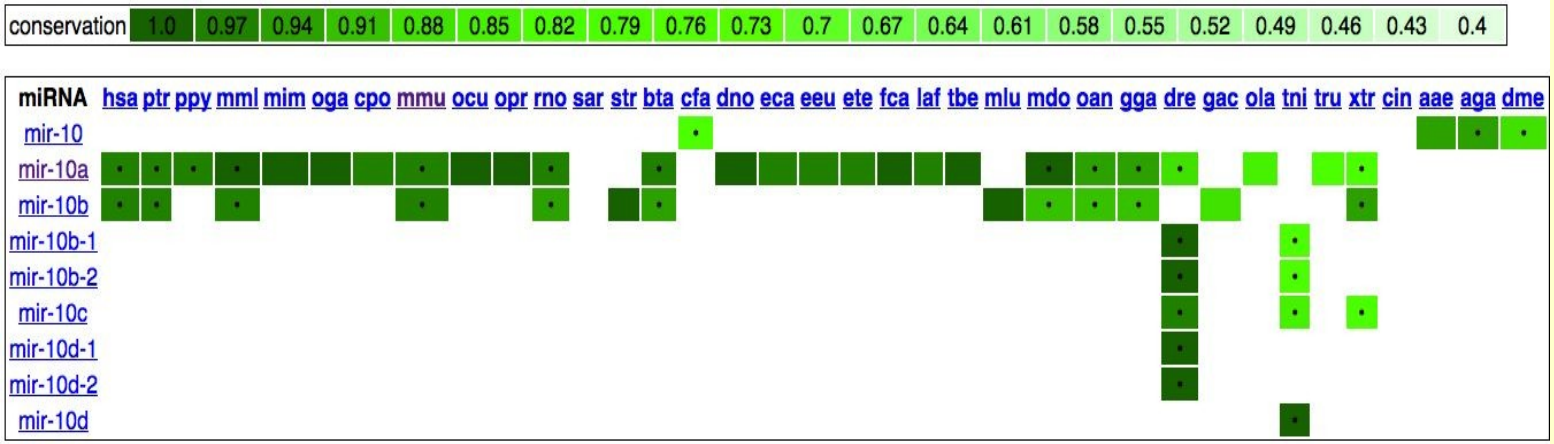
miRViewer: mir-10 family

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



Questions: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

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

miRBase @ http://www.mirbase.org/
MicroCosm @ http://www.ebi.ac.uk/enright-srv/microcosm/

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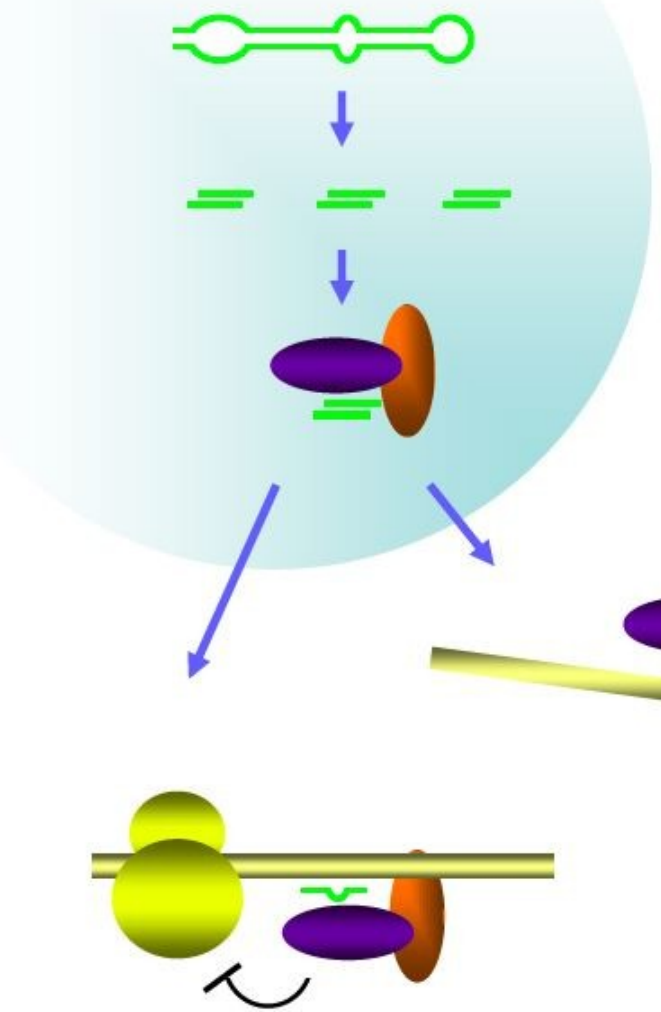
Thousands of microRNAs act in multiple biological events



Developmental timing

Differentiation

Aging

Apoptosis

Metabolism

Cancer

…

Cell fate/differentiation, Cell cycle…

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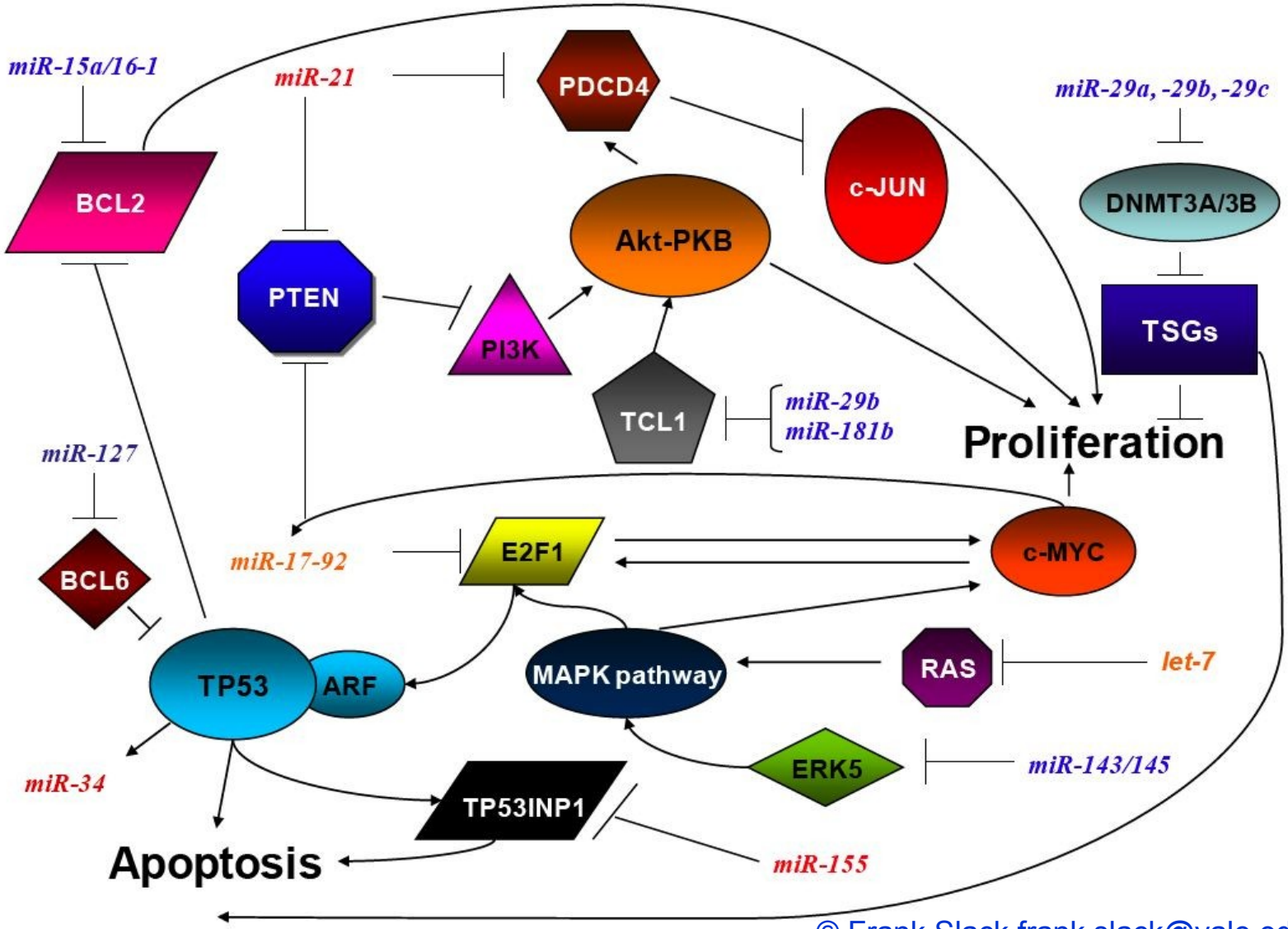
Micro RNAs Regulate Cell Growth and Death



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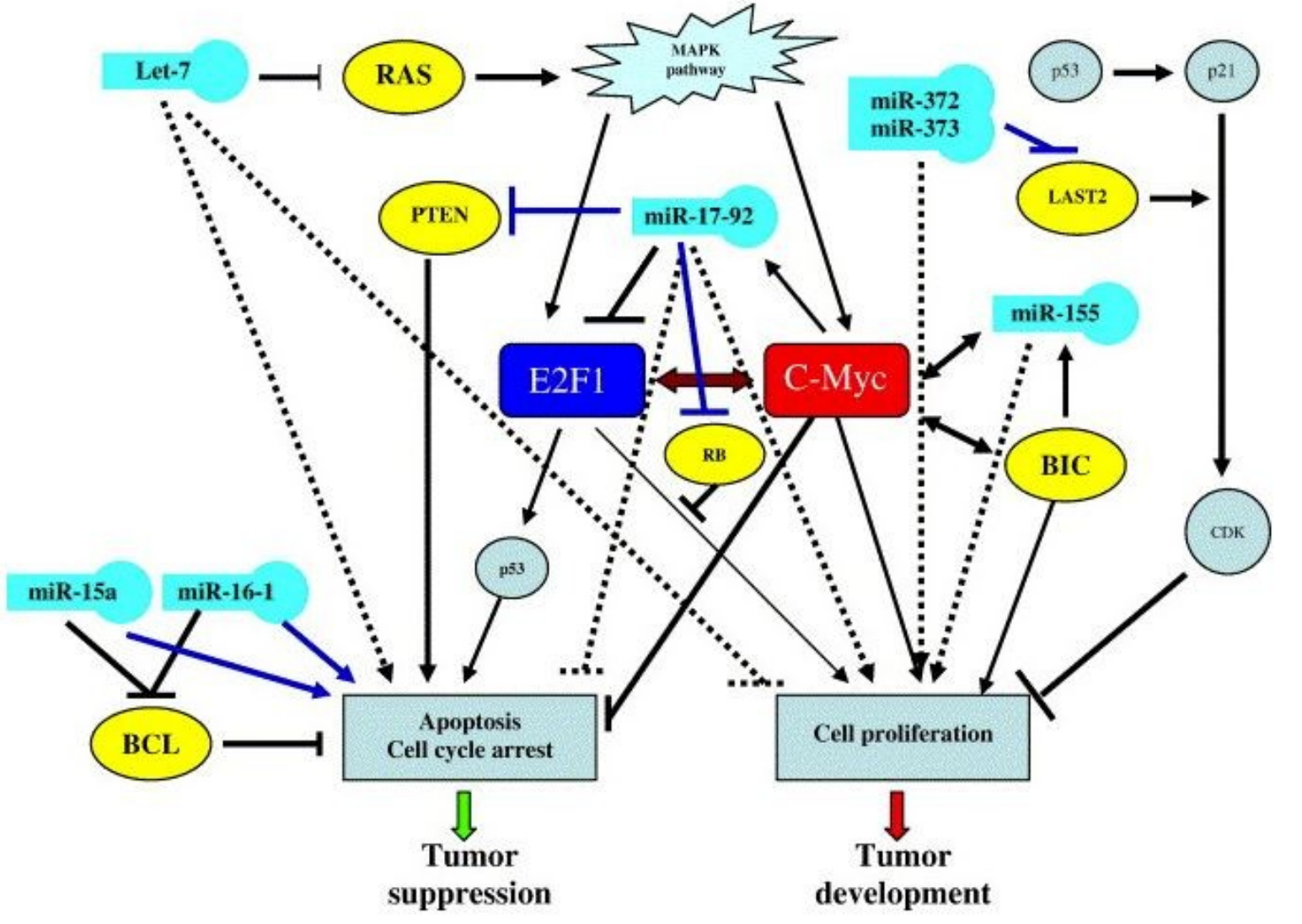
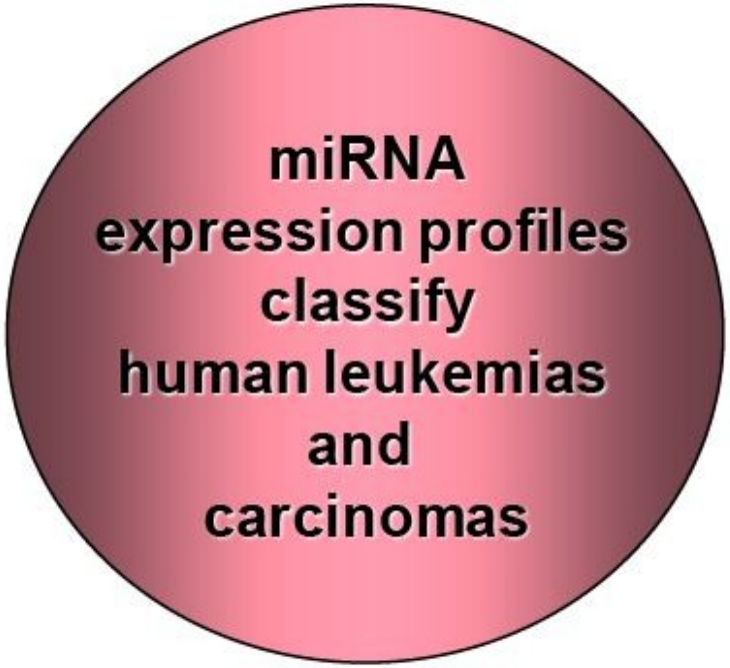
miRNAs as Oncogenes and Tumor Supressors
Zhang et al Dev Biol. 2007 Feb 1;302(1):1-12



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

ALTERATIONS OF MICRORNAS ARE FOUND IN EVERY TYPE OF HUMAN CANCER



(Calin et al, PNAS 2002; Lu et al, Nature, 2005; Volinia & Calin et al, PNAS 2006; Landgraf et al, Cell 2007)

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miRNAs Involved in Human Cancer

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

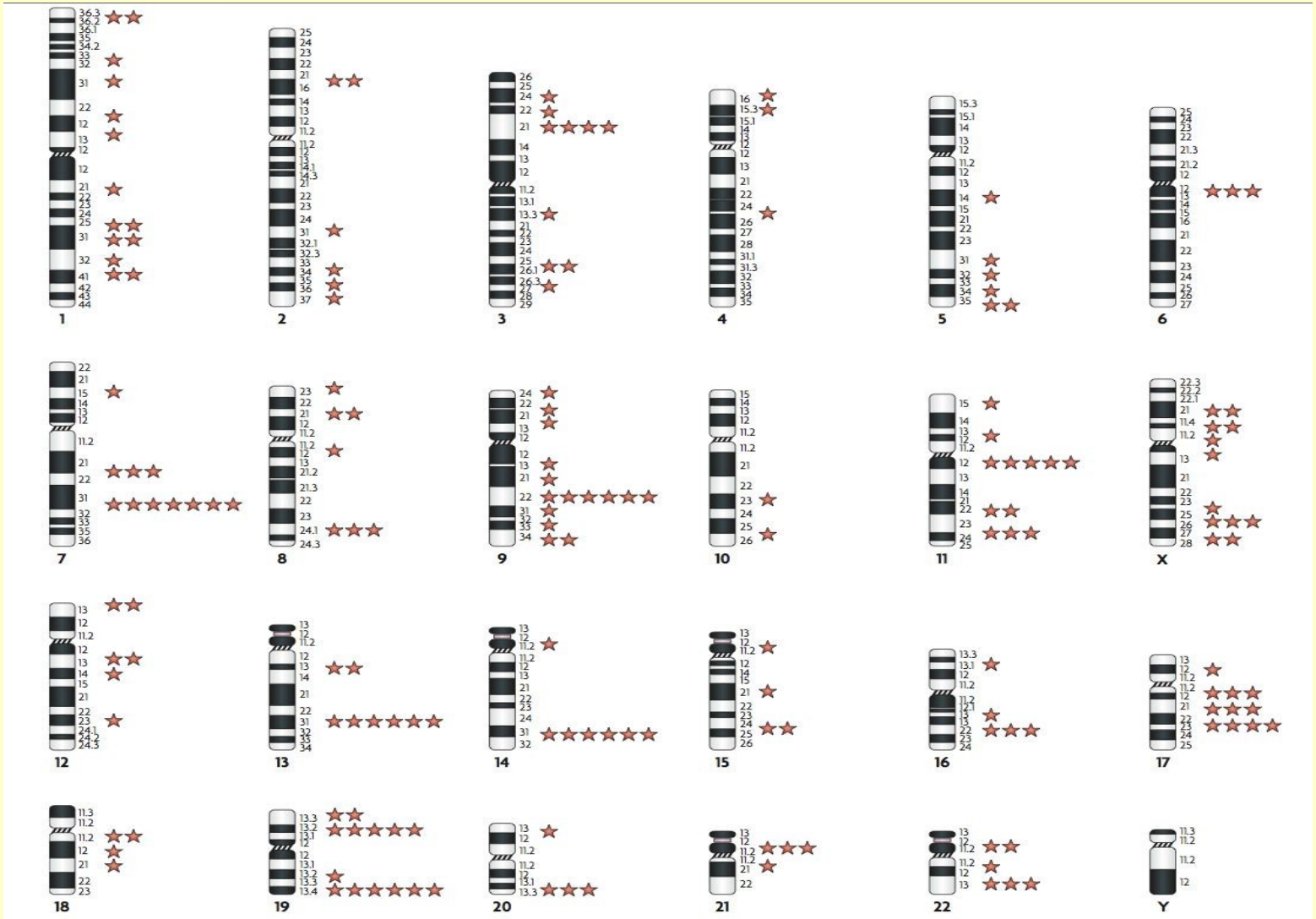


Figure 1 | **MicroRNA genes map to chromosomal regions that are involved in alterations in human cancer.**

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
miR-15a and *miR-16-1*	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
let-7 (*a*, *b*, *c*, *d*, *e*, *f*, *g* and *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
miR-29 (*a*, *b* and *c*)	Loss in aggressive CLL, AML (11q23), MDS lung and breast cancers and cholangocarcinoma	Induces apoptosis and inhibits tumorigenicity. Reactivates silenced tumour suppressor genes	TCL1, MCL1 and DNMTs	TS	30,64, 71,72
miR-34	Loss in pancreatic, colon, breast and liver cancers	Induces apoptosis	CDK4, CDK6, cyclin E2, EZF3 and MET	TS	56–58
miR-145	Loss in breast cancer	Inhibits proliferation and induces apoptosis of breast cancer cells	ERG	TS	31
miR-221 and *miR-222*	Loss in erythroblastic leukaemia	Inhibits proliferation in erythroblasts	KIT	TS	30
miR-221 and *miR-222*	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
miR-155	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
miR-17–92 cluster	Upregulated in lymphomas and in breast, lung, colon, stomach and pancreatic cancers	Induces proliferation	E2F1, BIM and PTEN	ONC	19,34,35, 40,41
miR-21	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
miR-372 and *miR-373*	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.

miRNA Dysregulation in Human Cancers

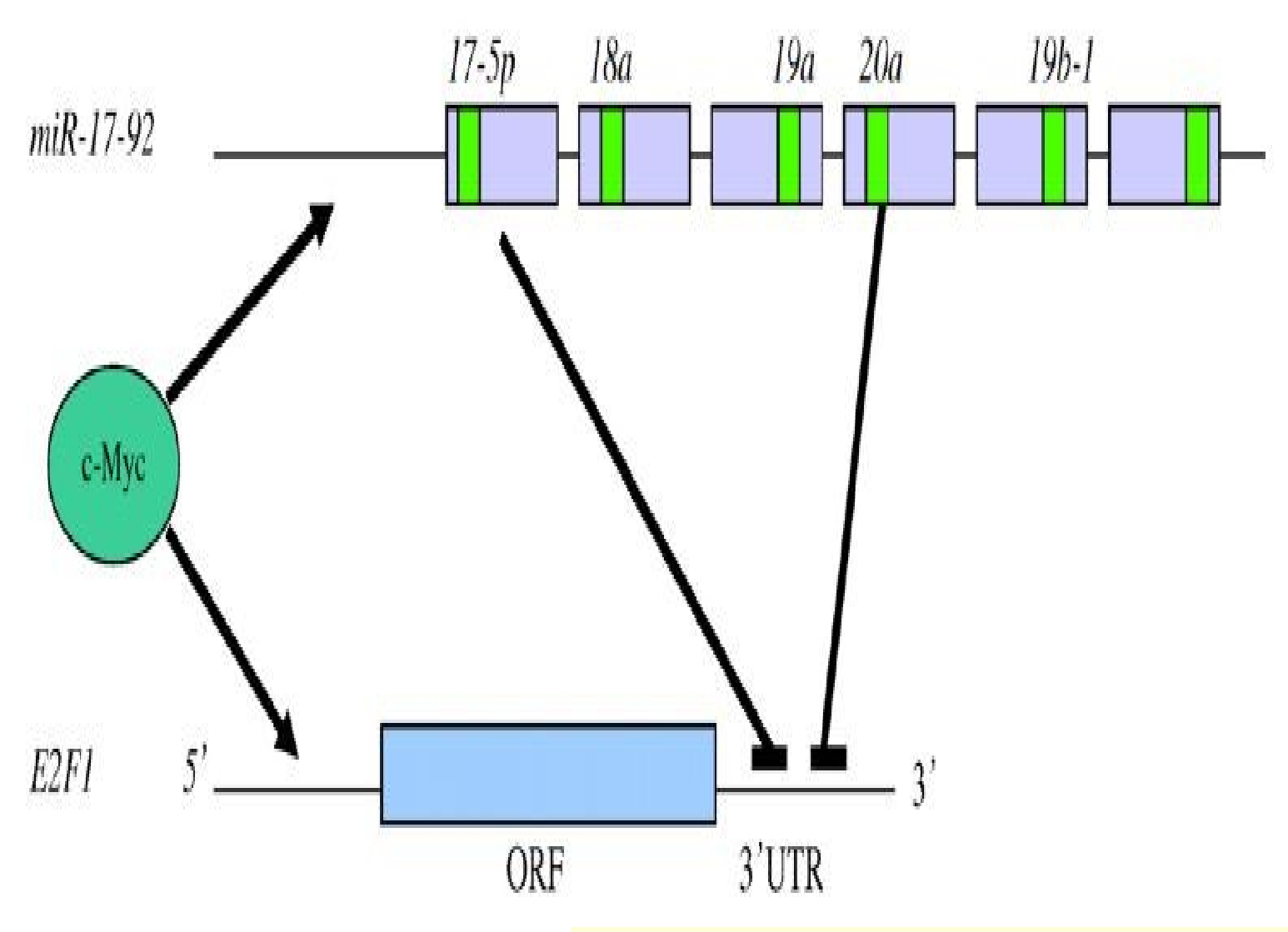
(Croce Nat Rev Genet. 2009 Oct;10(10):704-14.)

Table 2 | Consequences of microRNA dysregulation in human cancers

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

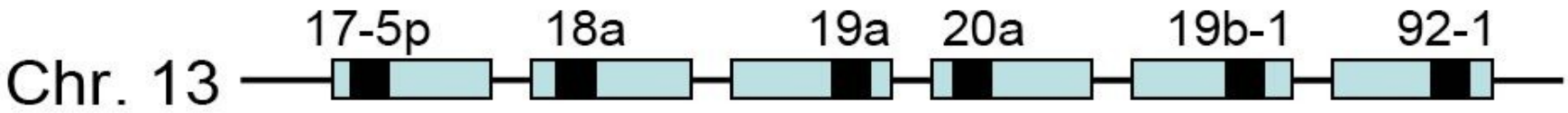
BCL2, B cell leukaemia/lymphoma 2; FHIT, fragile histidine triad protein; *HMGA2*, high mobility group AT-hook 2; *MCL1*, myeloid cell leukaemia sequence 1; PDCD4, programmed cell death 4; PTEN, phosphatase and tensin homologue; TIMP3, tissue inhibitor of metalloproteinases 3; WWOX, WW domain-containing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

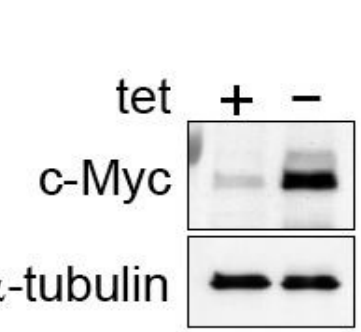
cMyc & miRNAs Regulate E2F1 Cell Cycle TF
Zhang et al Dev Biol. 2007 Feb 1;302(1):1-12

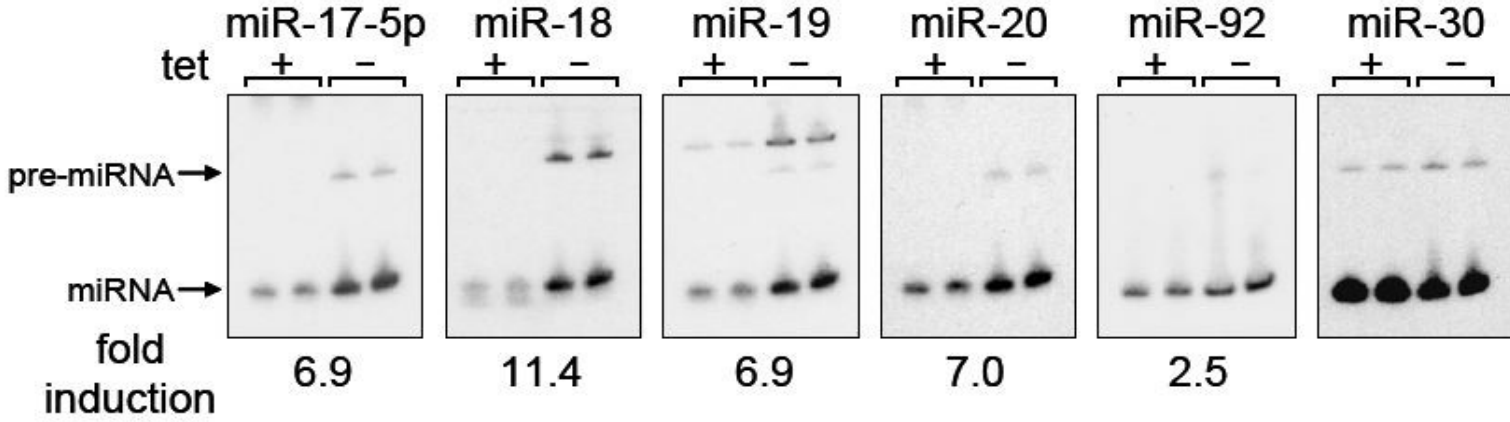


Zhang et al Dev Biol. 2007 Feb 1;302(1):1-12

The miR-17-92 cluster is activated by Myc

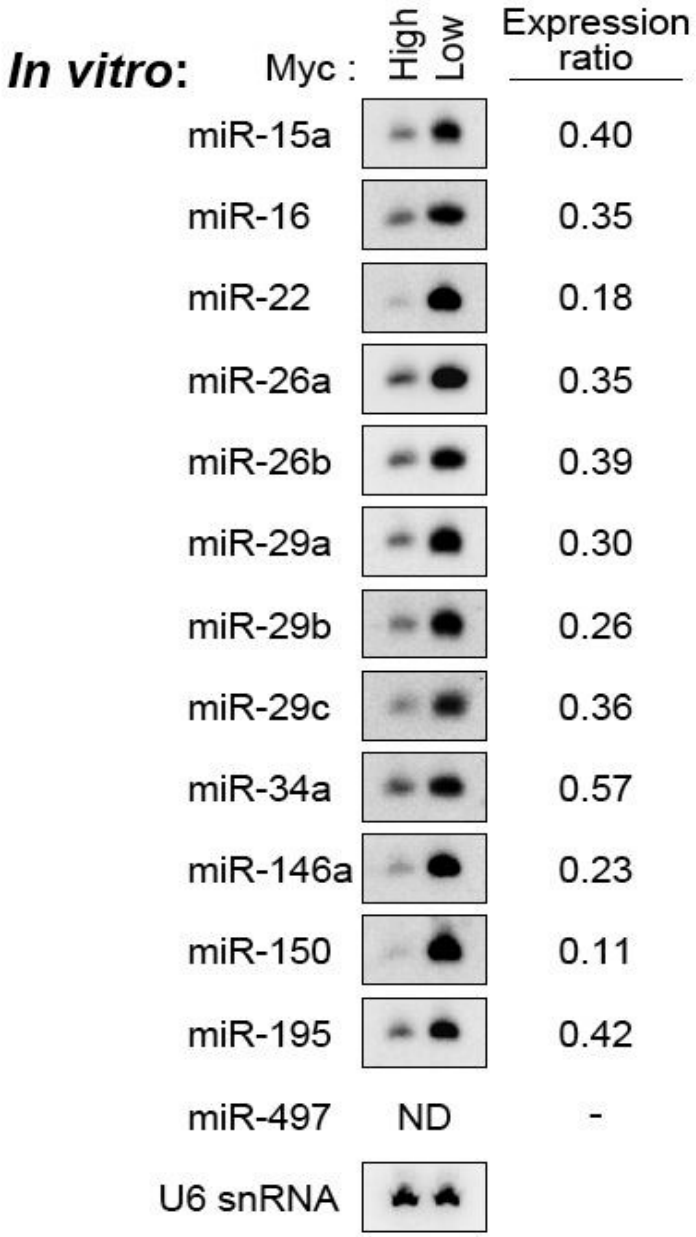


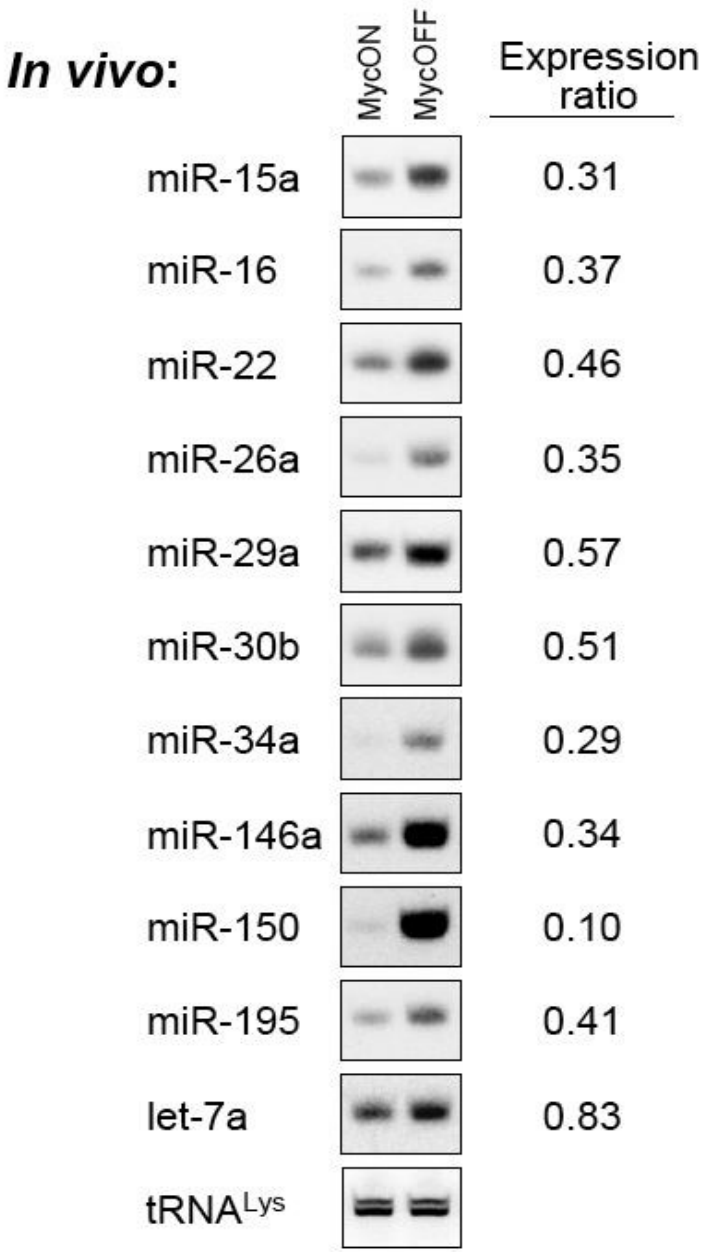




O'Donnell et al. Nature 2005 435, 839-843

Myc represses the expression of many miRNAs





hang *et al. Nature Genetics*, 2008

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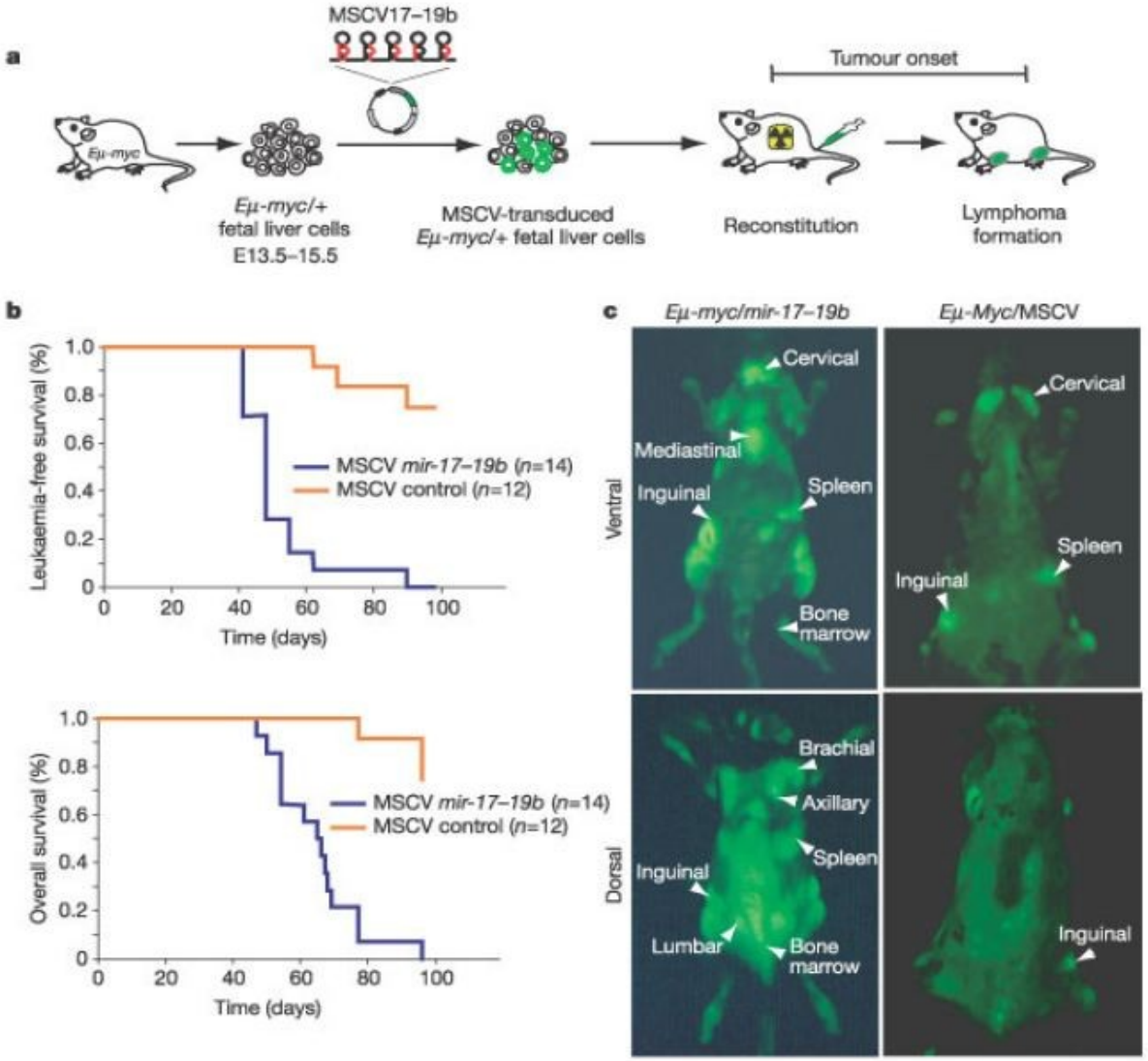
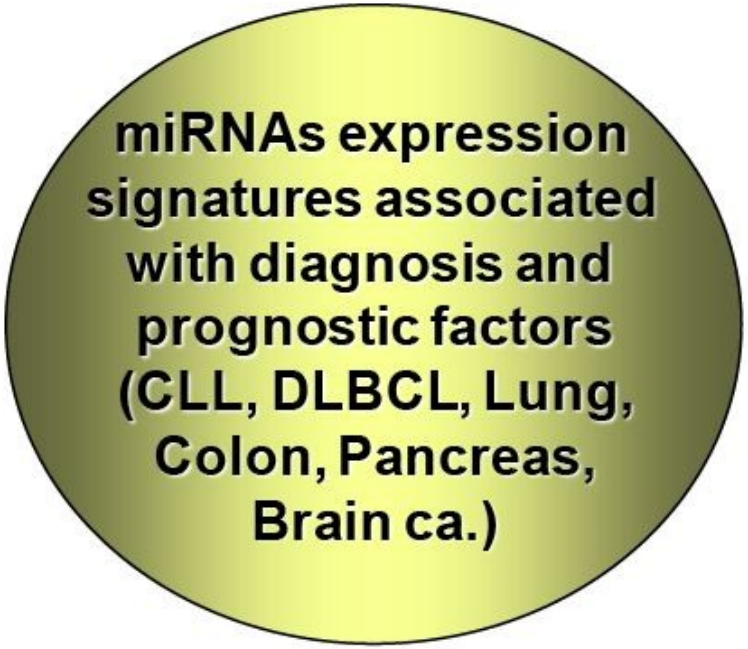
The miR-17-92 cluster accelerates Myc-induced lymphomagenesis



He *et al. Nature* 2005

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



(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)

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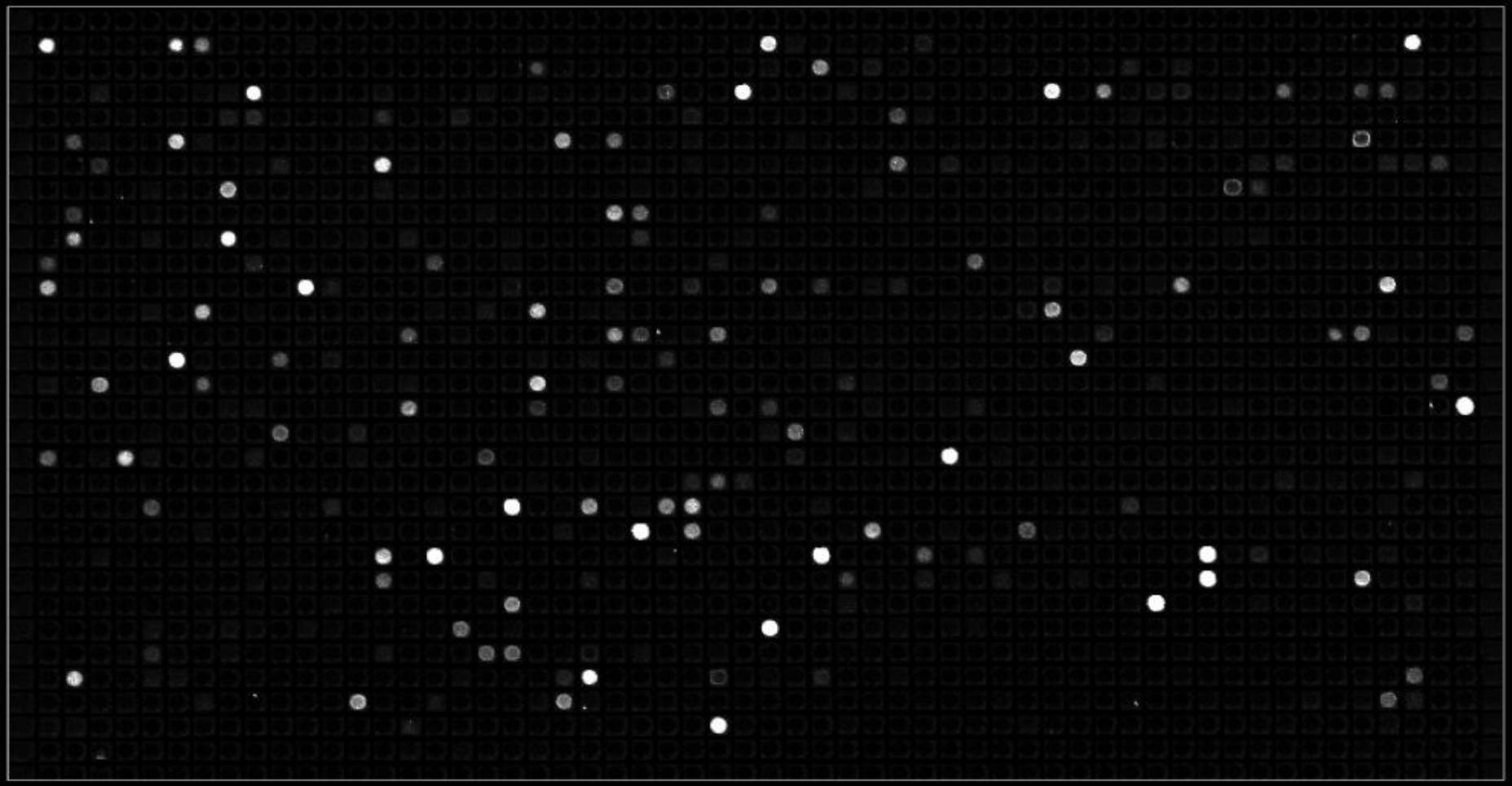
Profiling miRNA expression using custom microarrays



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miRNAs and Cancer – A Summary

- miRNAs control cell cycle, cell differentiation and apoptosis by regulating oncogenes and tumor supressor 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.

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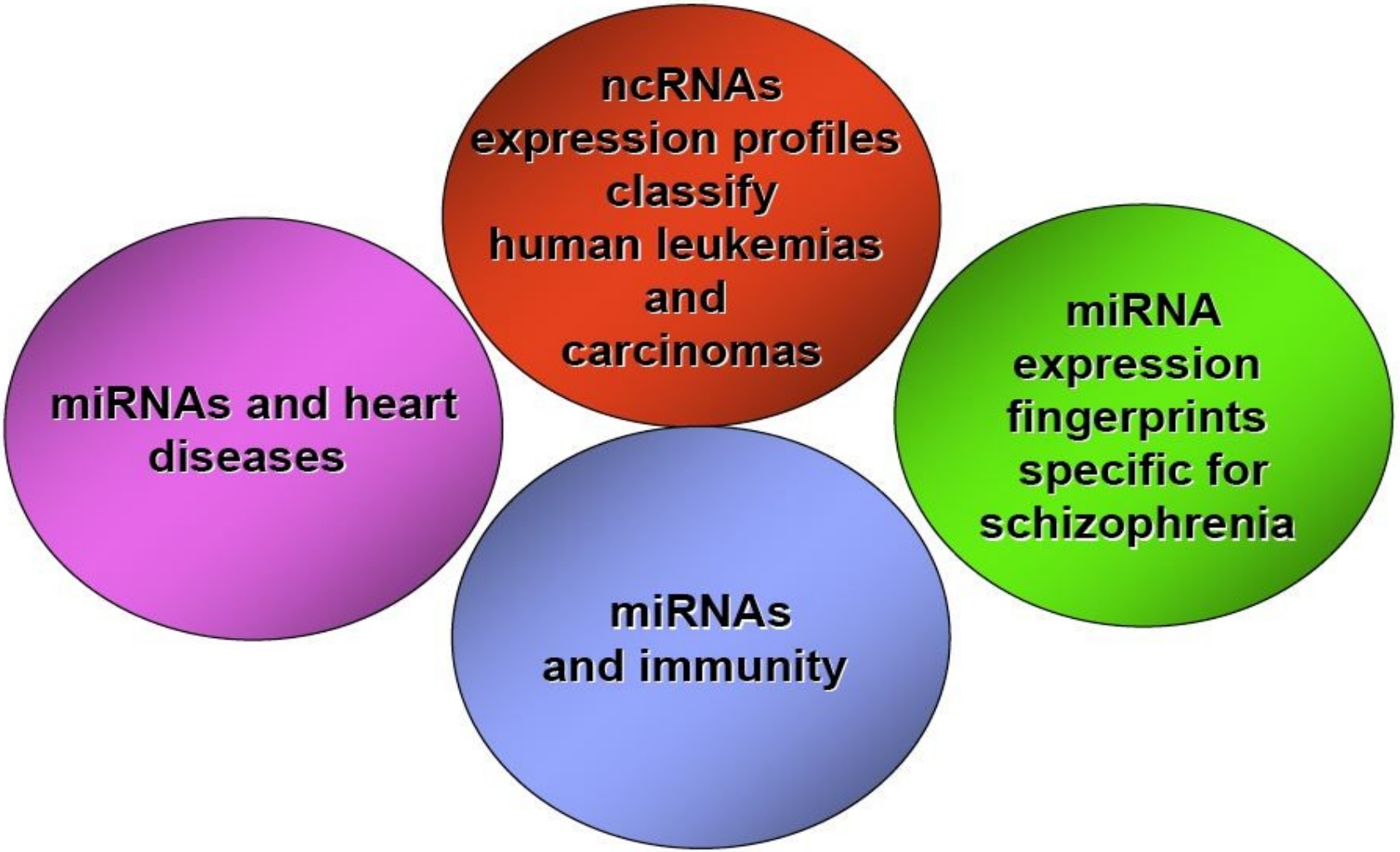
ALTERATIONS OF NONCODING RNAS ARE FOUND IN EVERY TYPE OF HUMAN DISEASE



(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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Important Micro RNA Web Sites

- 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/

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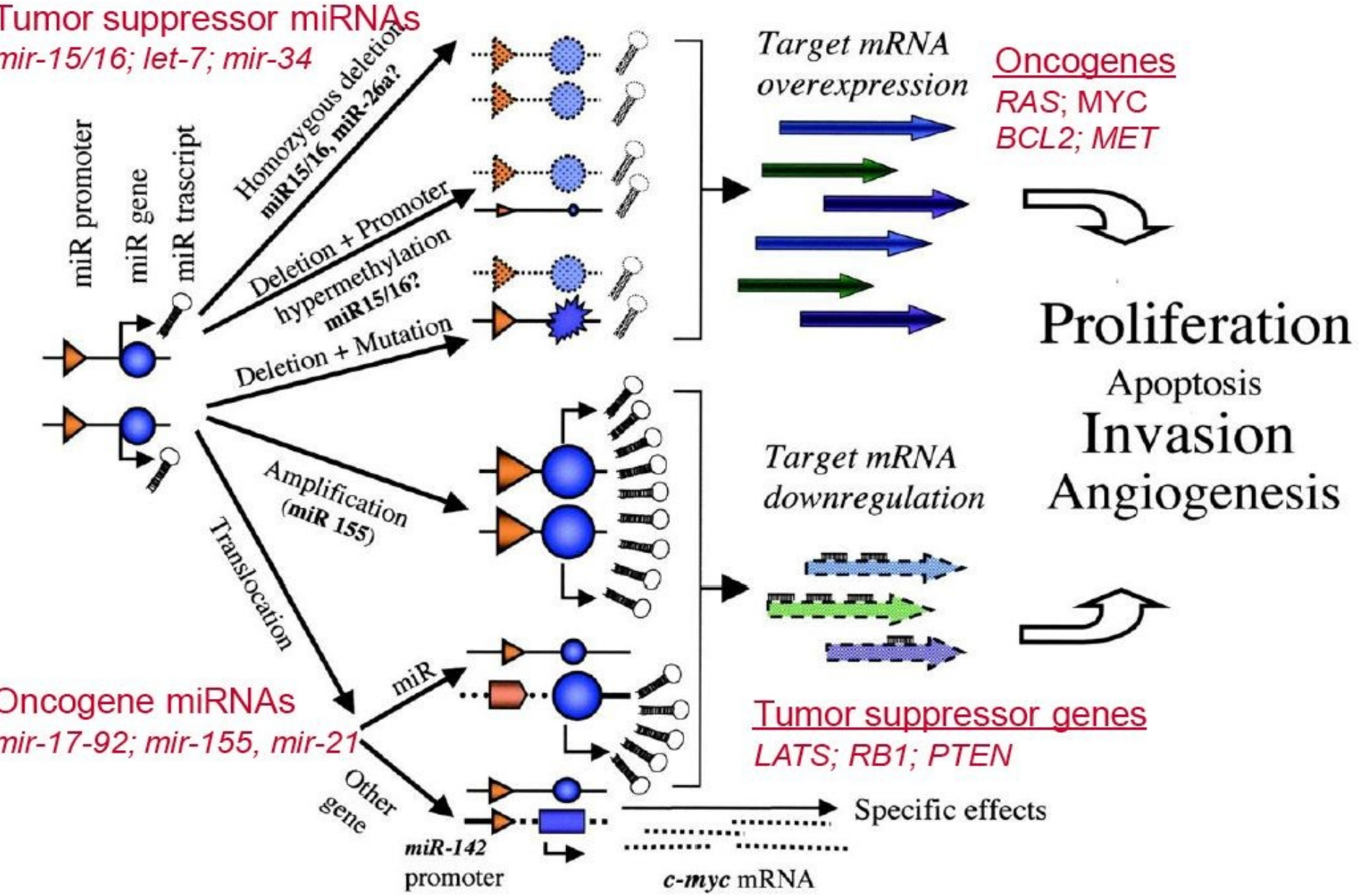
Oncomirs - miRNAs and cancer



Calin et al. (2004) Proc. Natl. Acad. Sci. USA 101, 2999-3004

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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 Ciafre, 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 *mir-142* 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; OG, oncogene; N/A, not applicable

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