

Genomics, Bioinformatics & Medicine

<http://biochem158.stanford.edu/>

miRNA Regulatory Networks

<http://biochem158.stanford.edu/Gene%20Expression.html>



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Stanford University School of Medicine

Gene Regulatory Mechanisms

- Transcriptional Mechanisms
 - Type of promoters & RNA polymerase
 - Control of Transcription
 - Transcription Factors and TFBS
- RNA processing
 - 5' Capping & 3' poly-adenylation
 - RNA degradation rates
 - Splicing and Alternative Splicing
- Translational Mechanisms
 - Micro RNAs (miRNAs) control translation & degradation of mRNAs
 - Silencer RNAs (siRNAs or RNAi) catalyze degradation of mRNA
- Epigenetic Mechanisms
 - Chromatin remodeling
 - Histone acetylation
 - DNA methylation

The ENCODE Project

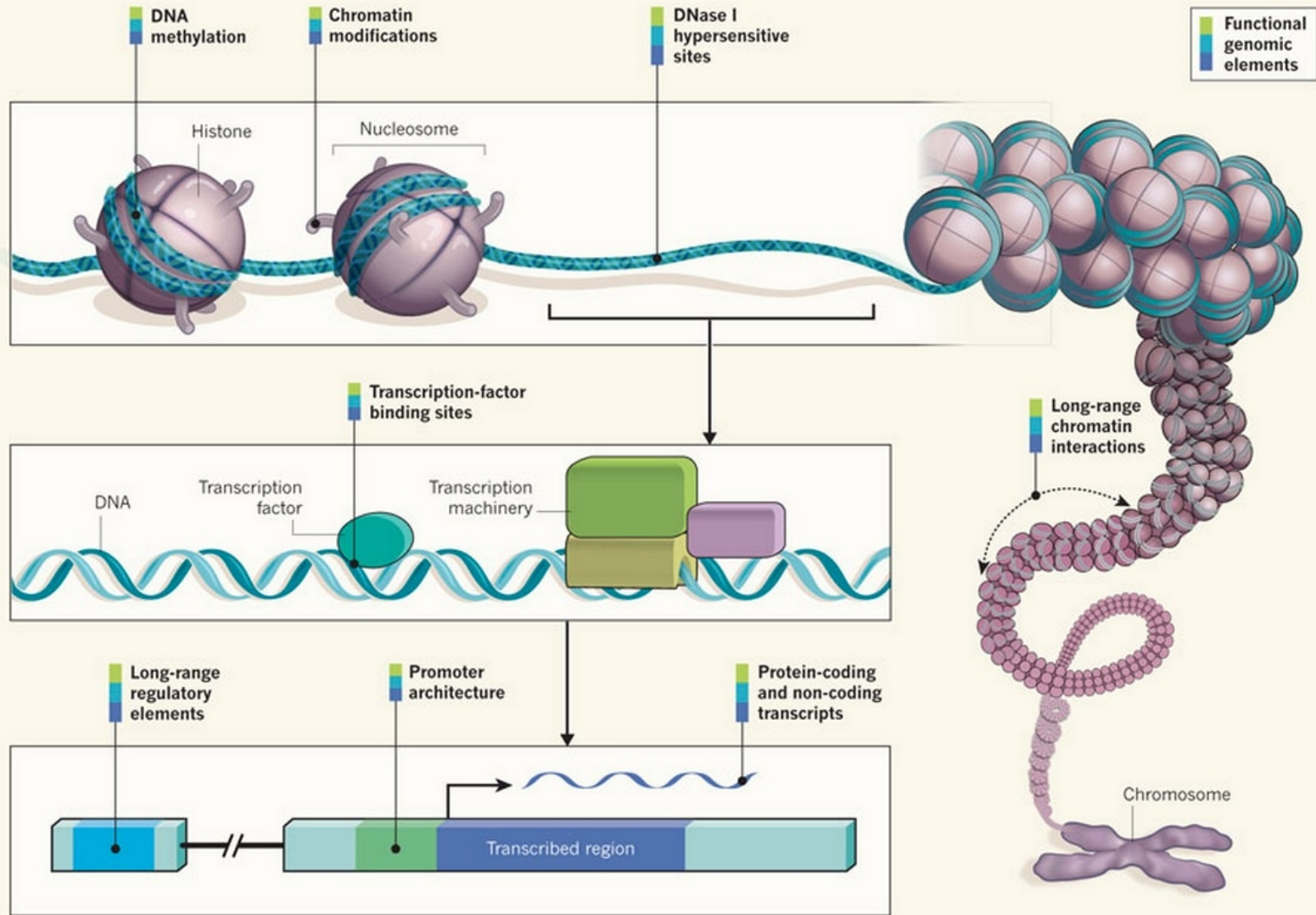
<http://www.nature.com/news/encode-the-human-encyclopaedia-1.11312>



- The ENCODE Project searches the human genome for:
 - Transcribed regions
 - Conserved regions
 - Transcription factor genes
 - Transcription factor and other protein binding sites
 - DNA methylated regions
 - Regions with “open” chromatin
 - lncRNA coding regions
 - Regions associated with modified histones (Chip-CHIP)
 - Regions associated with disease (GWAS)
- So far these functional or conserved regions comprise 80% of the human genome.

ENCODE Explained

<http://www.nature.com/nature/journal/v489/n7414/full/489052a.html>

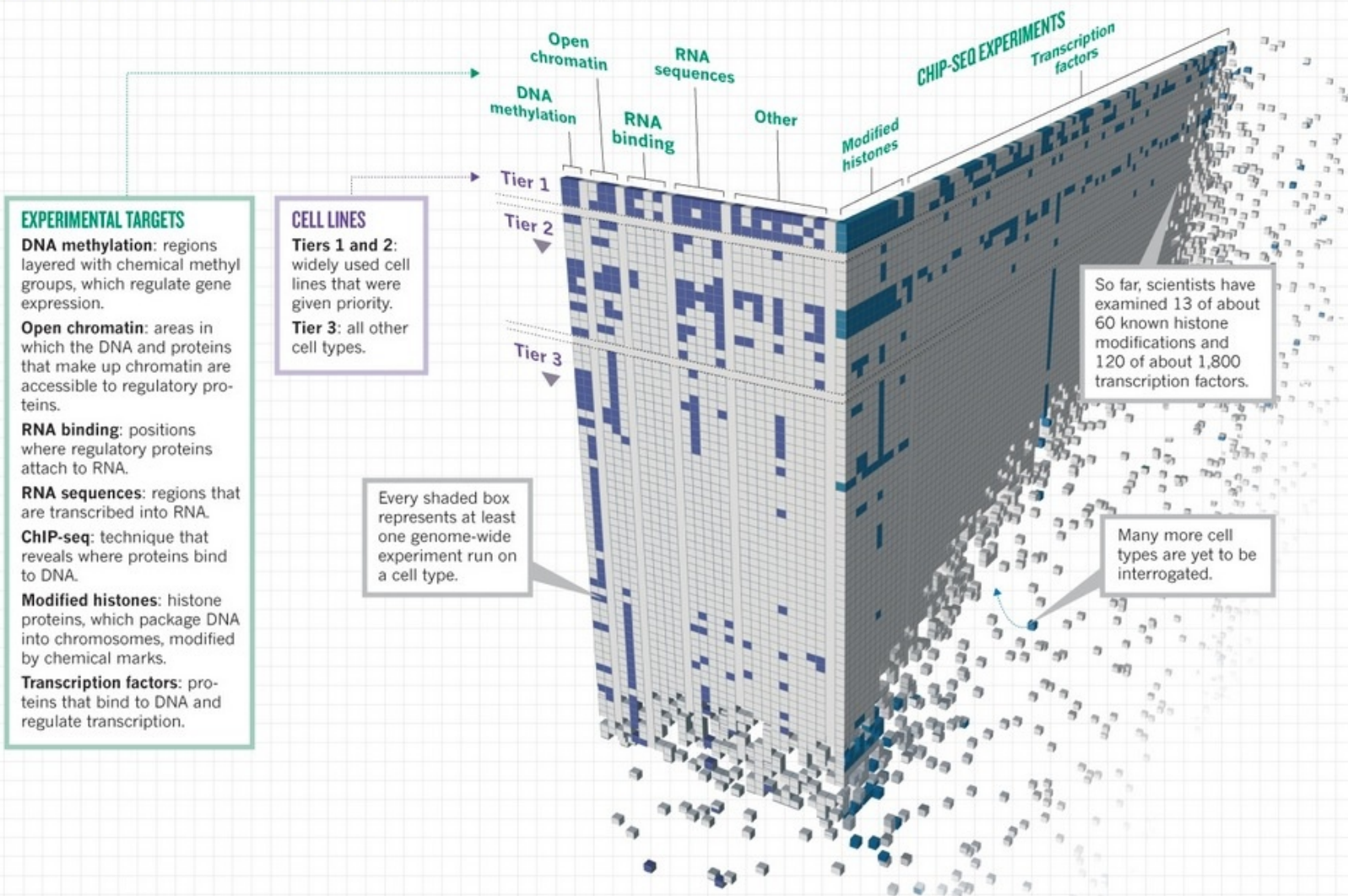


Making a Genome Manual

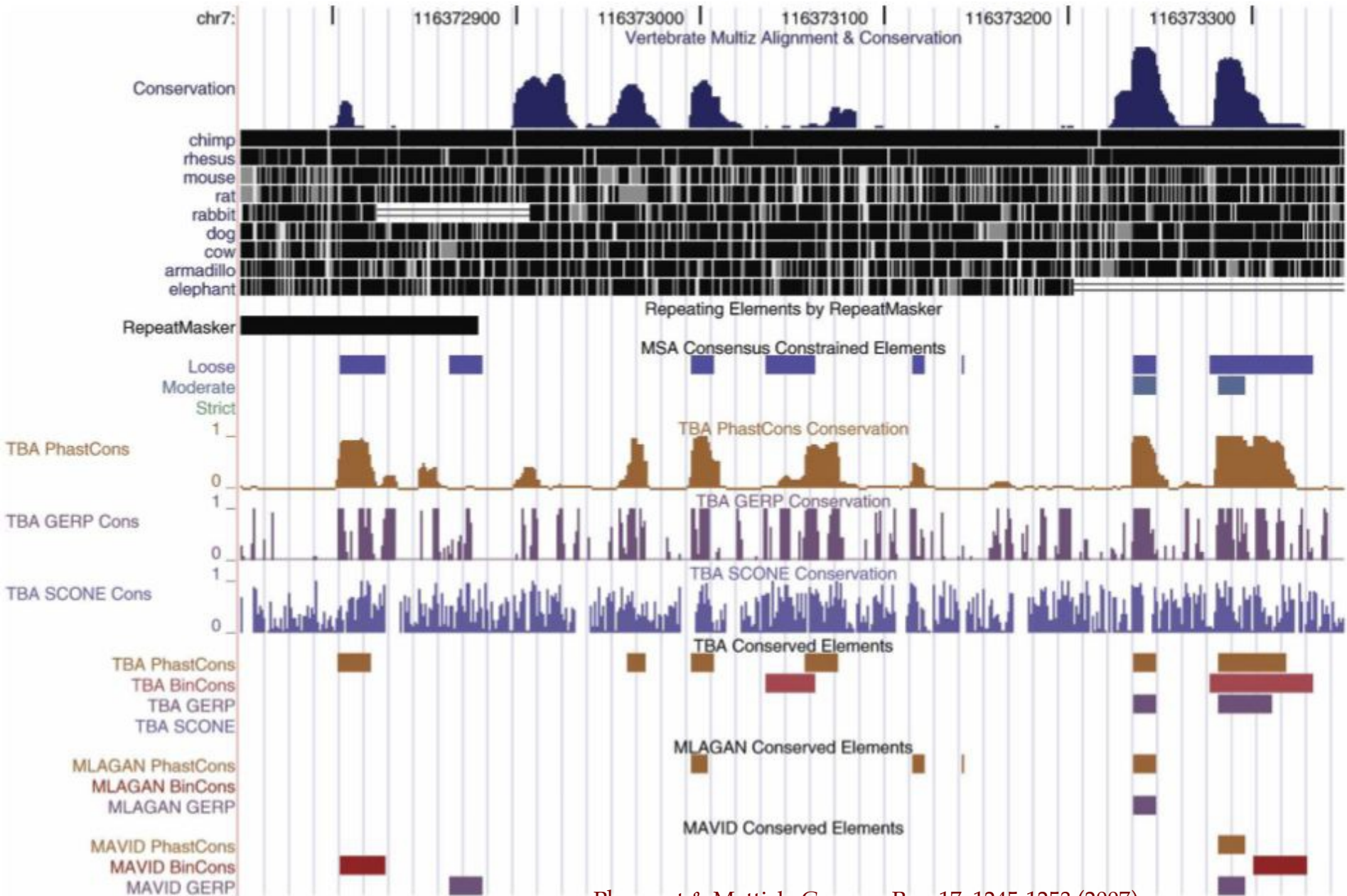
<http://www.nature.com/news/encode-the-human-encyclopaedia-1.11312#/manual>

MAKING A GENOME MANUAL

Scientists in the Encyclopedia of DNA Elements Consortium have applied 24 experiment types (across) to more than 150 cell lines (down) to assign functions to as many DNA regions as possible — but the project is still far from complete.



Conserved Regions in CFTR Intron



Epigenome Roadmap

<http://www.nature.com/collections/vbqgtr>

Epigenome Roadmap



Home | Research | Threads | News and Multimedia | Additional research | Sponsor



Welcome to the Epigenome Roadmap! Here, we have collected research papers describing the main findings of the NIH Roadmap Epigenomics Program, the aim of which was to systematically characterize epigenomic landscapes in primary human tissues and cells. The papers are complemented by eight threads each of which highlights a topic that runs through more than one paper. Threads are designed to help you explore the wealth of information collectively published across several Nature Publishing Group journals. Each thread consists of relevant paragraphs, figures and tables from across the papers, united around a specific theme.

Produced with exclusive support from:

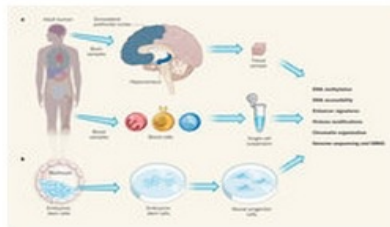
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We invite you to explore the research content, the News & Views,

the video and other associated material.

News and Multimedia

Nature News | Editorial
Beyond the genome



Nature | News and Views

Epigenomics: Roadmap for regulation



Nature News | News

Epigenome: The symphony in your cells

Epigenome Roadmap

<http://www.nature.com/collections/vbqgtr>

Thread articles

Research papers

THREAD 1

1. Annotation of the non-coding genome

[Highlight referenced papers ▶](#)

THREAD 2

2. Relationship between different epigenomic marks: DNA accessibility and methylation, histone marks, and RNA

[Highlight referenced papers ▶](#)

THREAD 3

3. Epigenomic changes during differentiation and development

[Highlight referenced papers ▶](#)

THREAD 4

4. Regulatory models: networks, motifs, modules, sequence drivers and predictive models

[Highlight referenced papers ▶](#)

THREAD 5

5. Interpreting variation: GWAS, cancer, genotype, evolution and allelic

[Highlight referenced papers ▶](#)



Nature

Conserved epigenomic signals in mice and humans reveal immune basis of Alzheimer's disease

Elizabeta Gjoneska, Andreas R. Pfening, Hansruedi Mathys, Gerald Quon, Anshul Kundaje *et al.*

[◀ Highlight associated threads](#)



Nature Communications

The meta-epigenomic structure of purified human stem cell populations is defined at cis-regulatory sequences

N. Ari Wijetunga, Fabien Delahaye, Yong M. Zhao, Aaron Golden, Jessica C. Mar *et al.*

[◀ Highlight associated threads](#)



Nature

Genetic and epigenetic fine mapping of causal autoimmune disease variants

Kyle Kai-How Farh, Alexander Marson, Jiang Zhu, Markus Kleinewietfeld, William J. Housley *et al.*

[◀ Highlight associated threads](#)



Nature Communications

Epigenomic footprints across 111 reference epigenomes reveal tissue-specific epigenetic regulation of lincRNAs

Viren Amin, R. Alan Harris, Vitor Onuchic, Andrew R. Jackson, Tim Charnock *et al.*

[◀ Highlight associated threads](#)



Nature Communications

Intermediate DNA methylation is a conserved signature of genome regulation

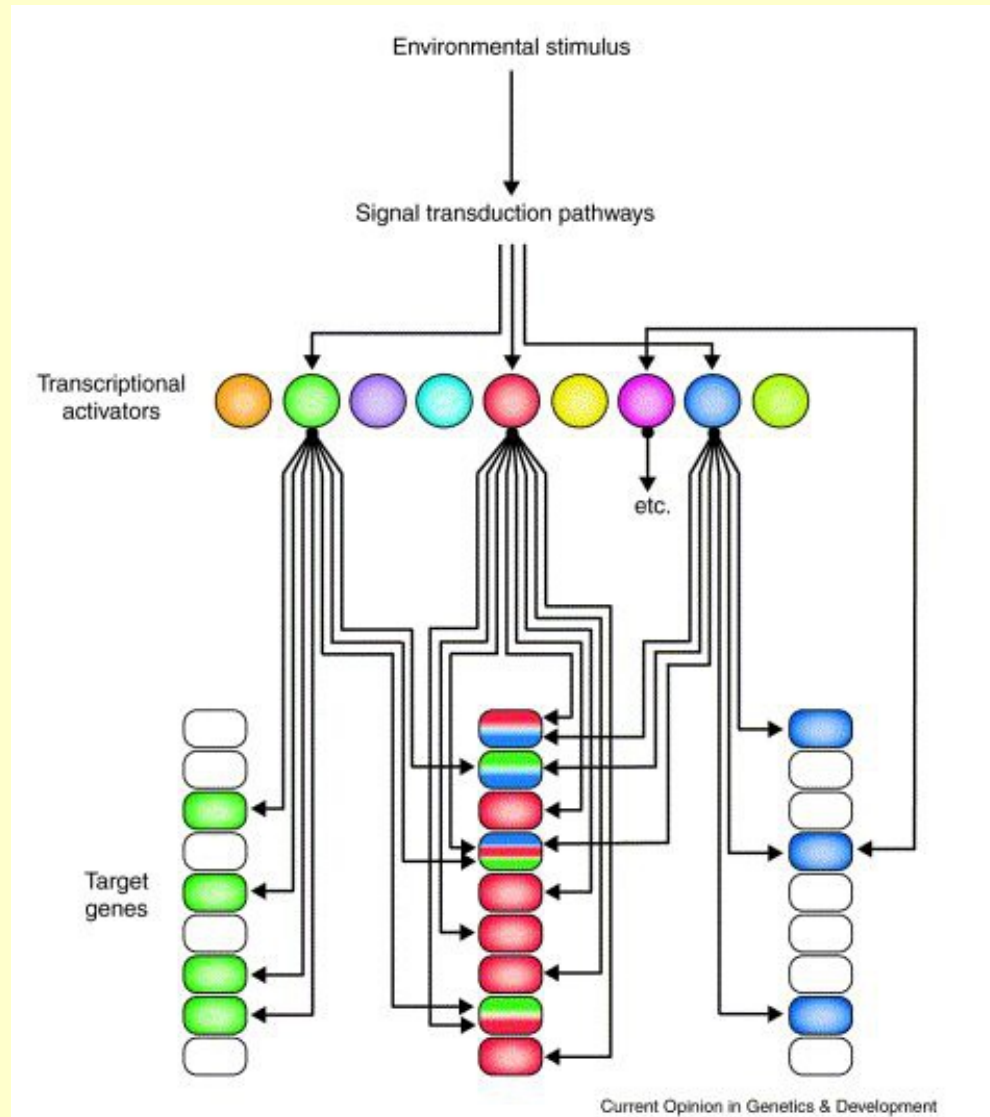
GiNell Elliott, Chibo Hong, Xiaoyun Xing, Xin Zhou, Daofeng Li *et al.*

Nature Biotechnology

Large-scale imputation of epigenomic datasets for systematic annotation of diverse human tissues

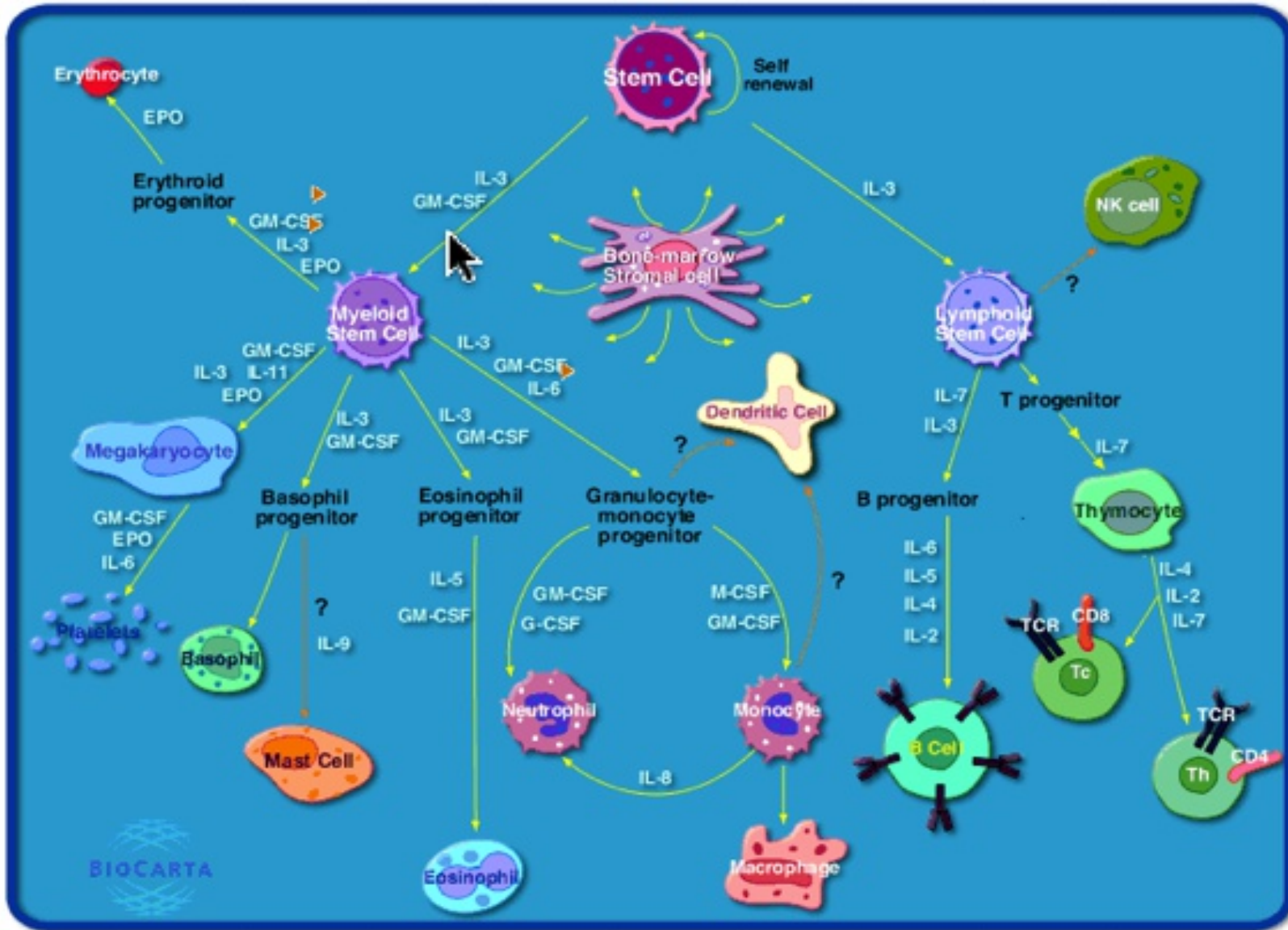
Jason Ernst, Manolis Kellis

Gene Expression Regulatory Network



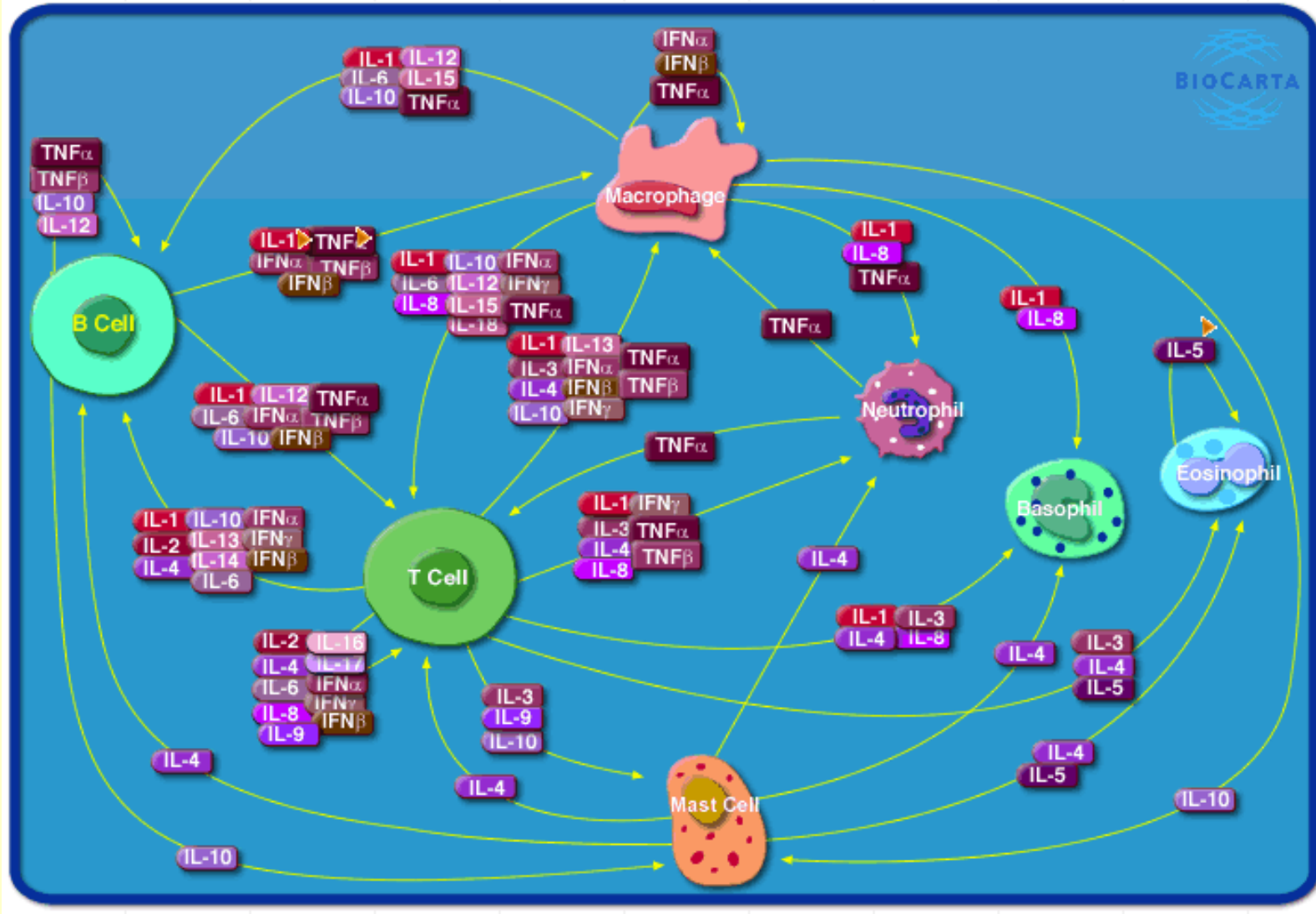
Hematopoiesis

http://www.biocarta.com/pathfiles/h_stemPathway.asp



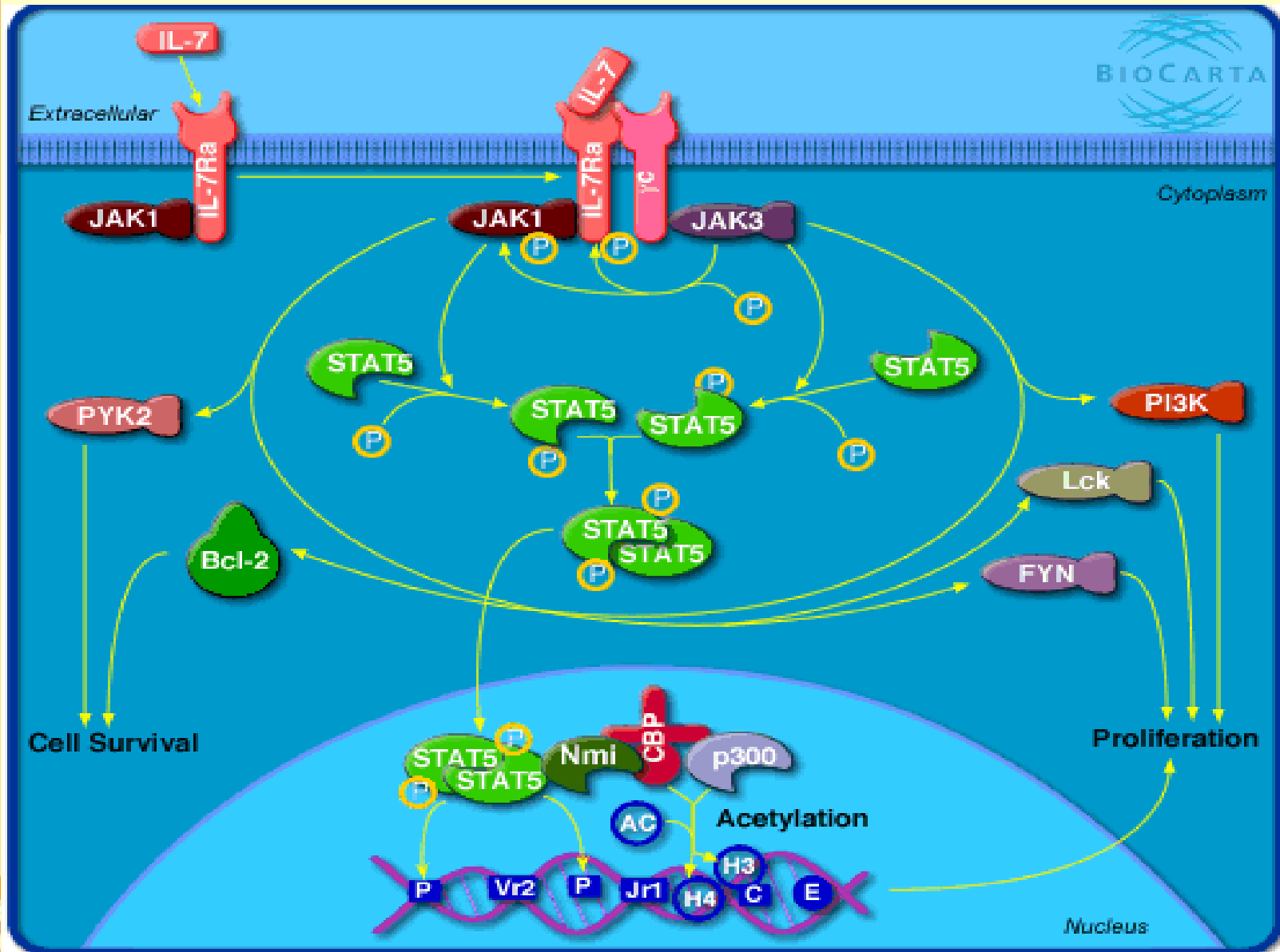
Cytokine Network

http://www.biocarta.com/pathfiles/h_cytokinePathway.asp

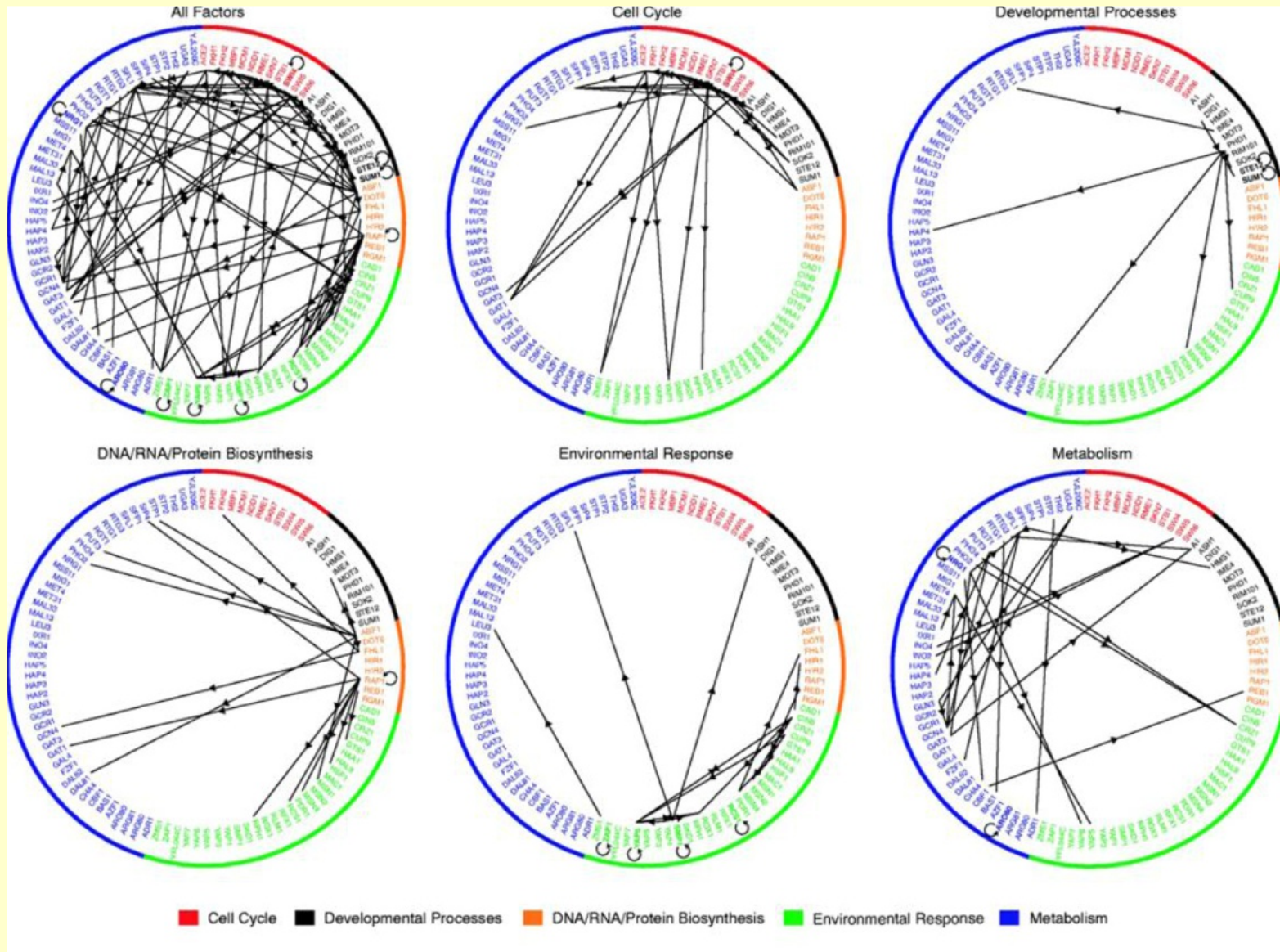


IL7 Regulatory Pathway

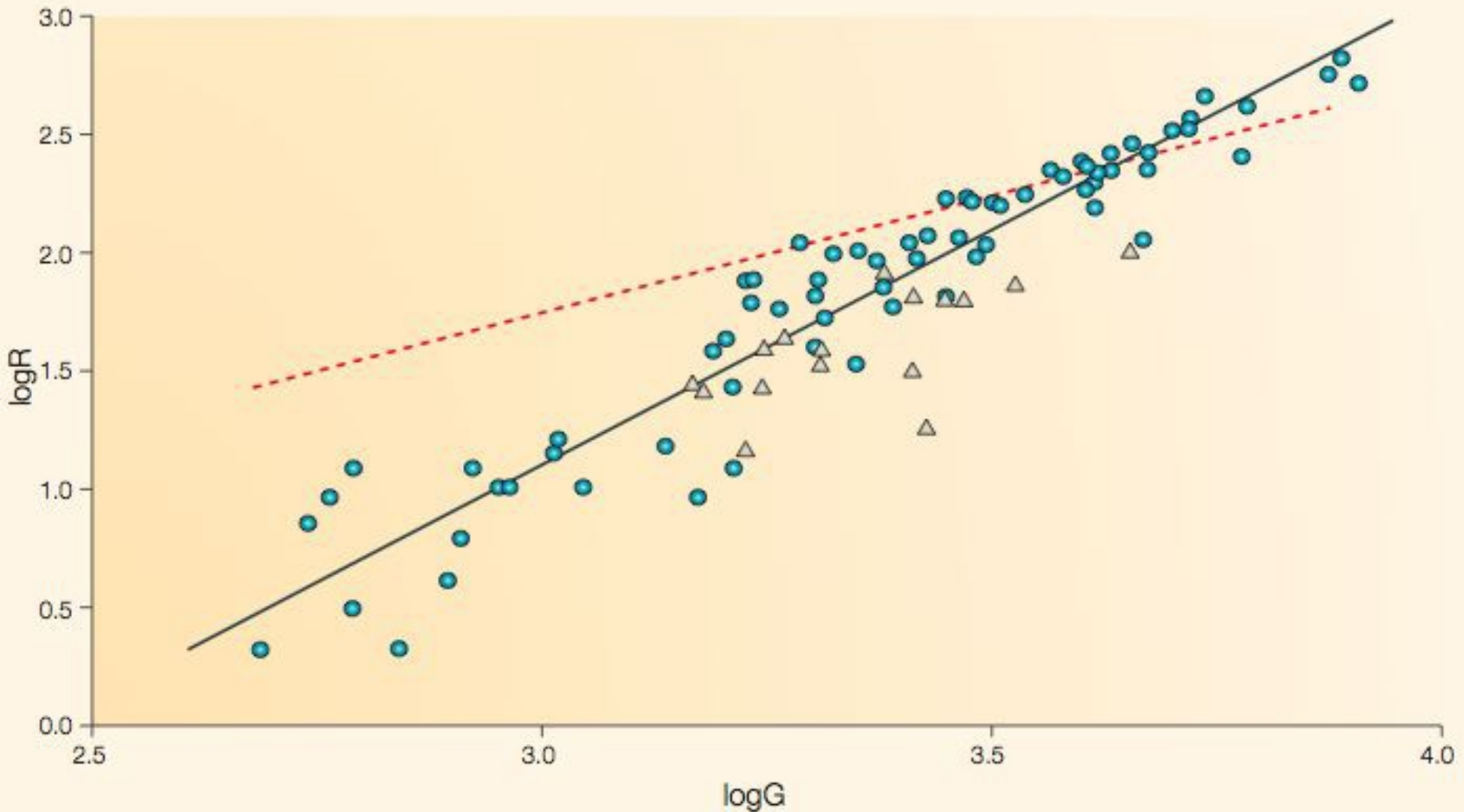
http://www.biocarta.com/pathfiles/h_il7Pathway.asp/



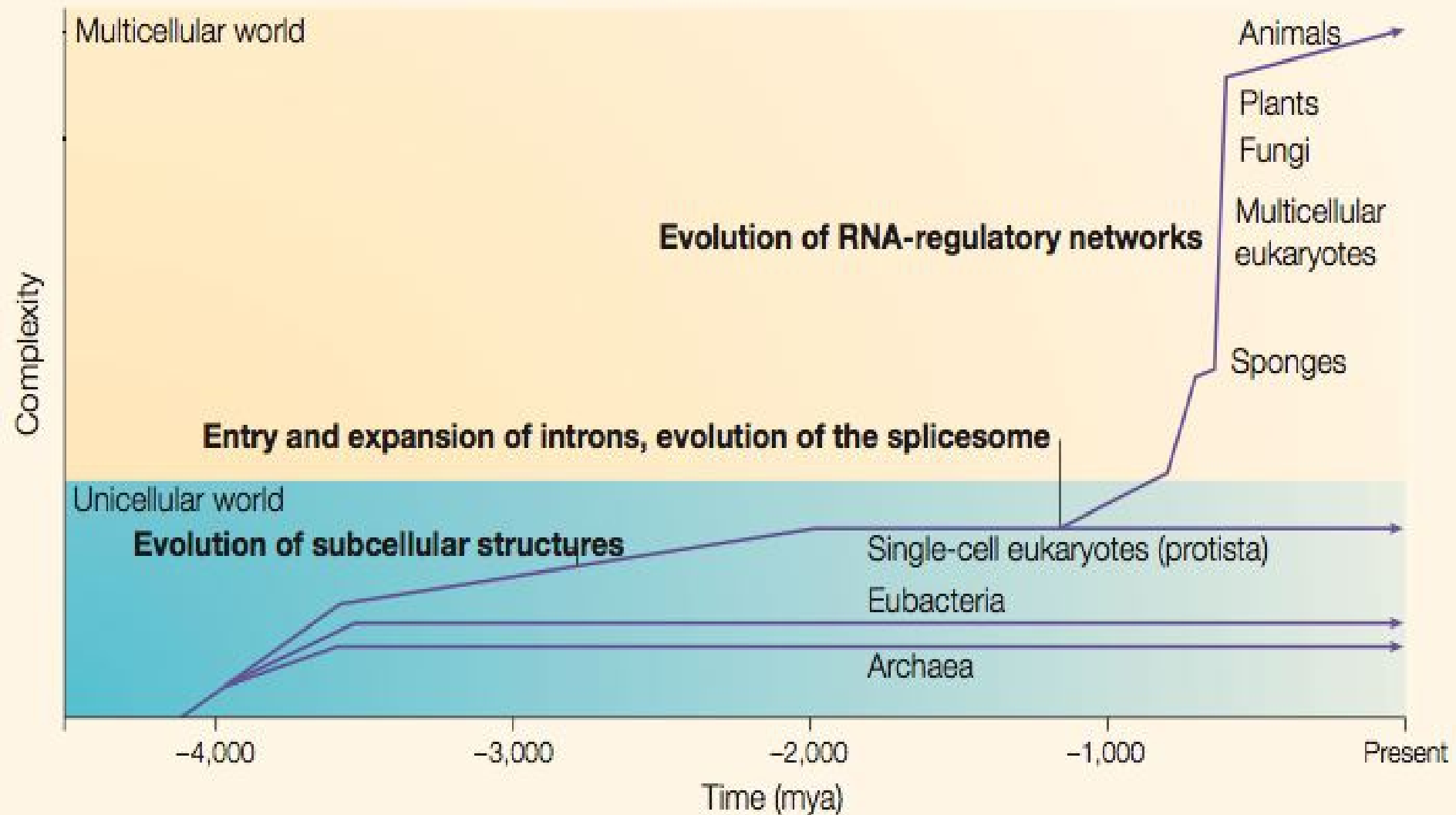
Yeast Transcription Factors



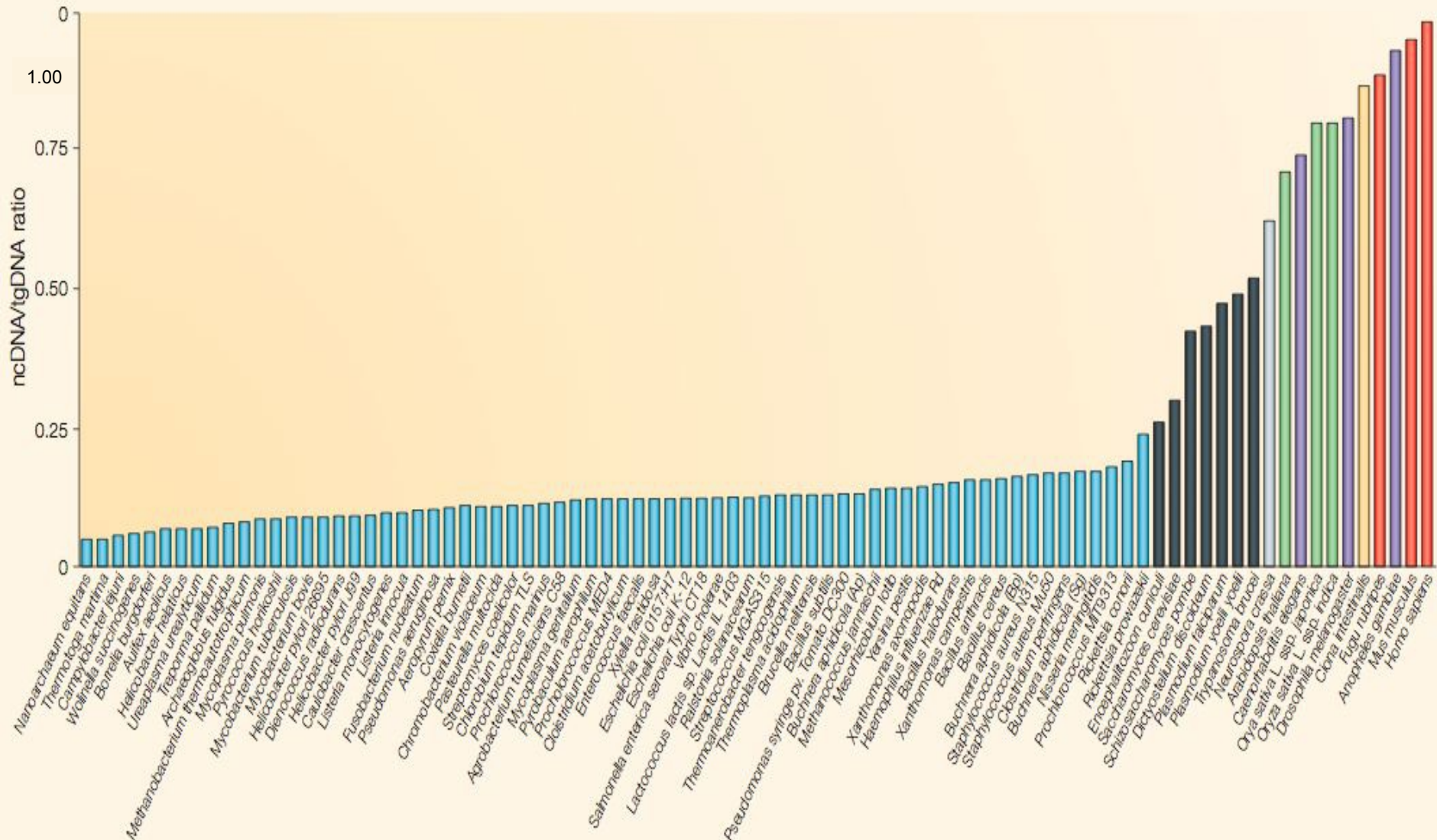
Prokaryotic Regulatory Genes Grow as the Square of the Total Number of Genes



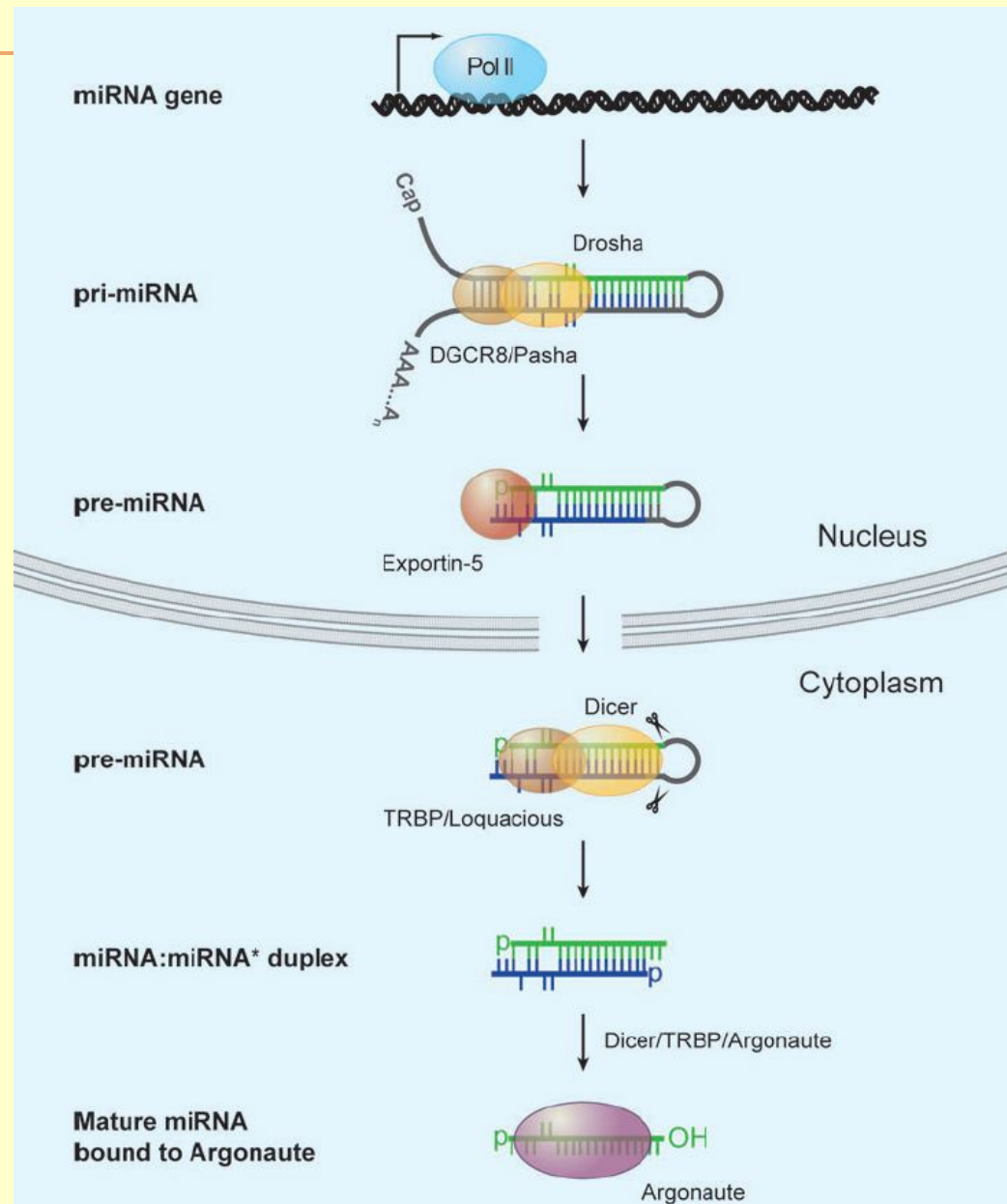
A Simplified History of Life on Earth

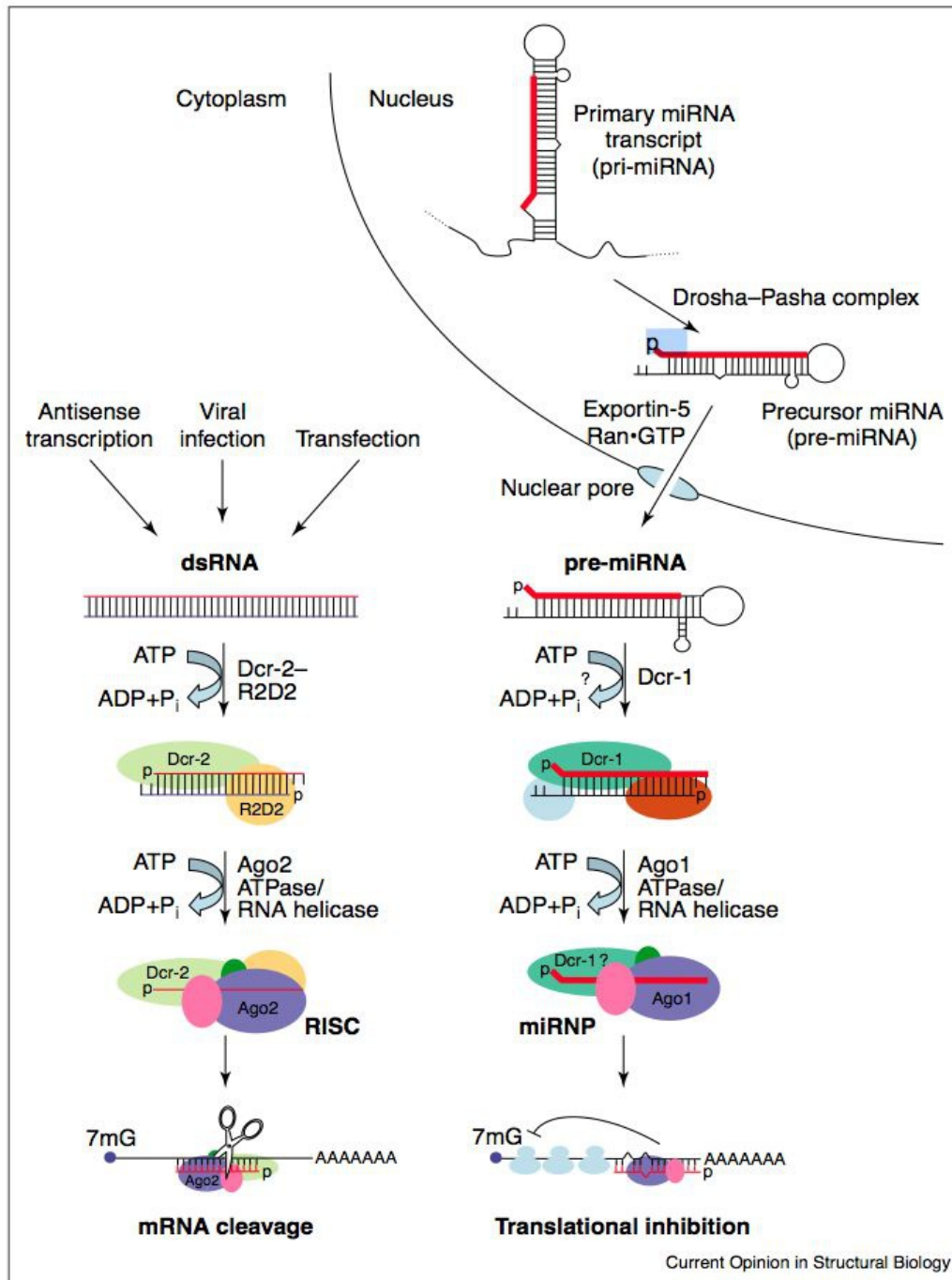


Fraction of Non-Protein-Coding DNA During Evolution



microRNA Biogenesis





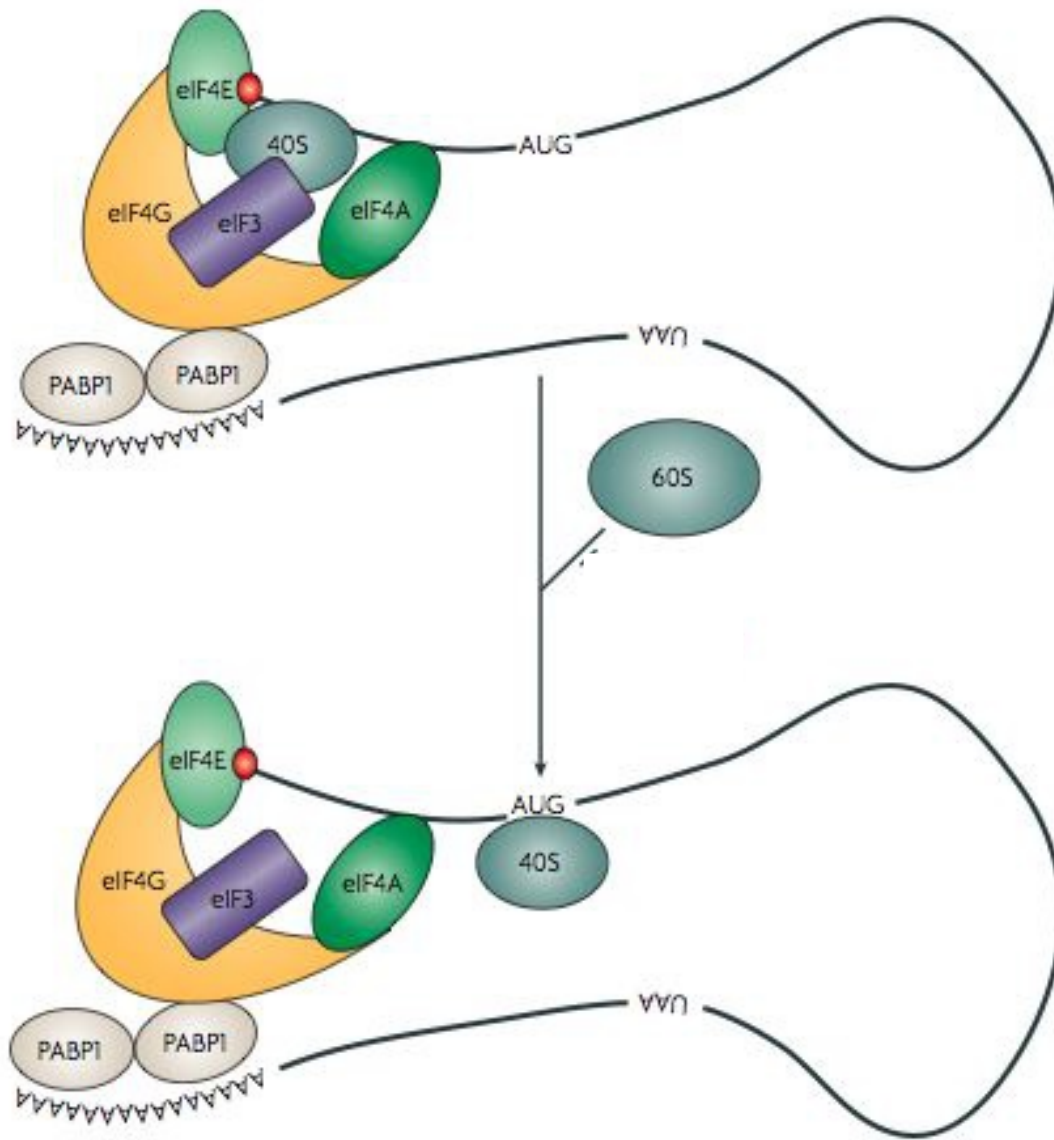
siRNA(or RNAi)
mediated
degradation of
mRNA

versus

miRNA
mediated
inhibition of
mRNA
translation

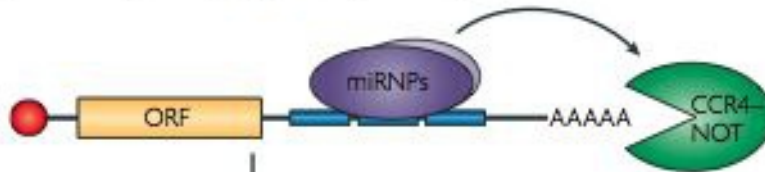
Initiation of Translation

Box 3 | Steps in eukaryotic translation

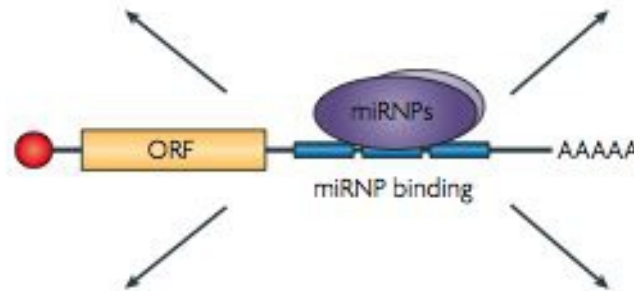
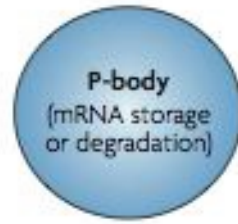
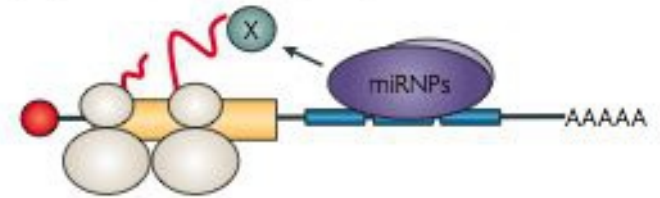


Mechanisms of Translational Regulation by miRNP Complexes

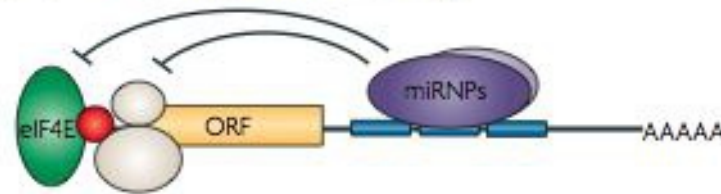
Deadenylation
(followed by decapping and degradation)



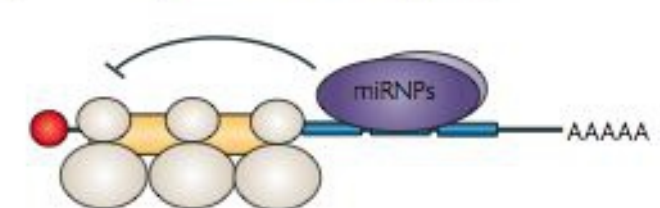
Proteolysis
(degradation of nascent peptide)



Initiation block
(repressed cap recognition or 60S joining)

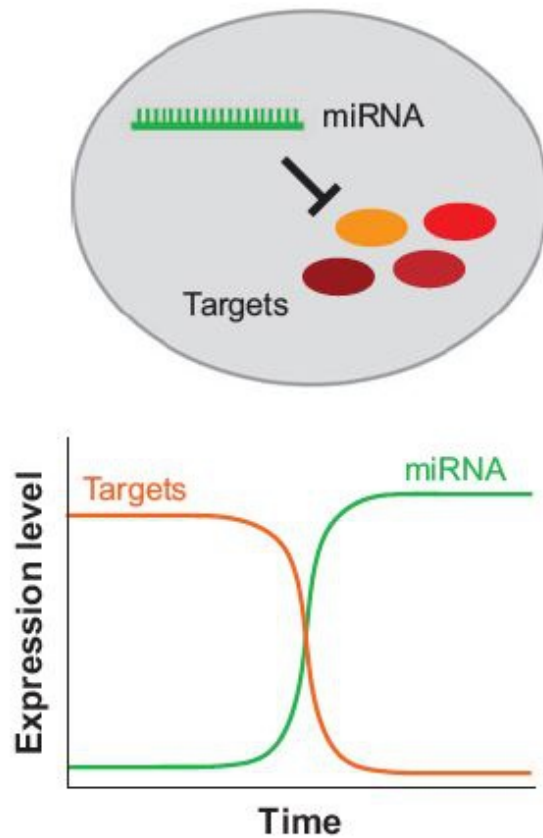


Elongation block
(slowed elongation or ribosome 'drop-off')

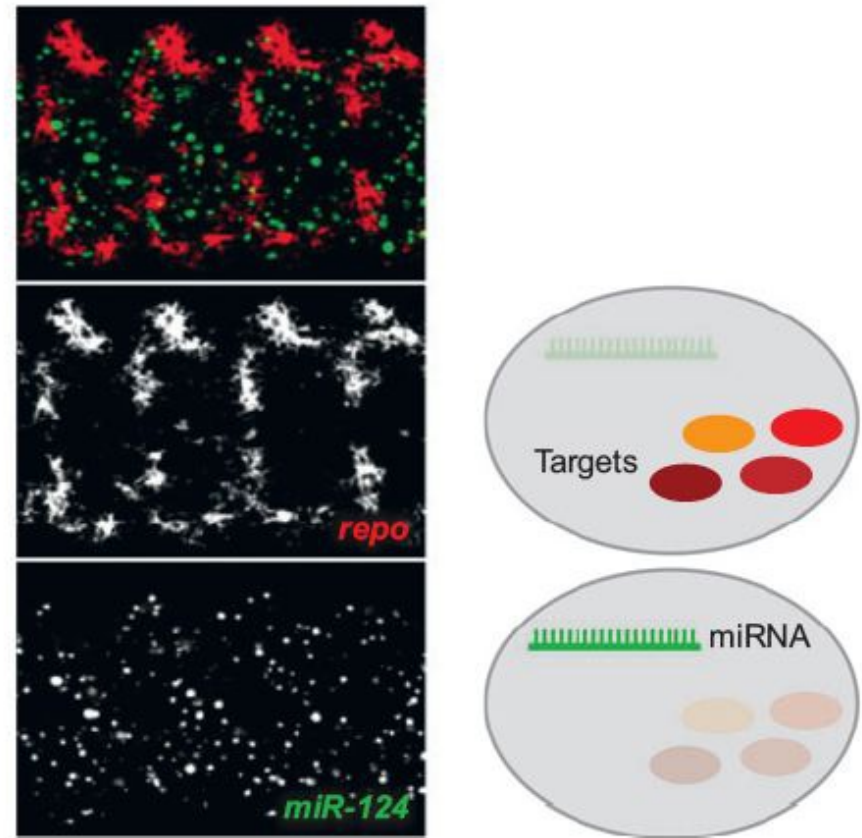


miRNA Expression Results in Temporal and Spatial Reciprocity with Target Expression

a Temporal reciprocity

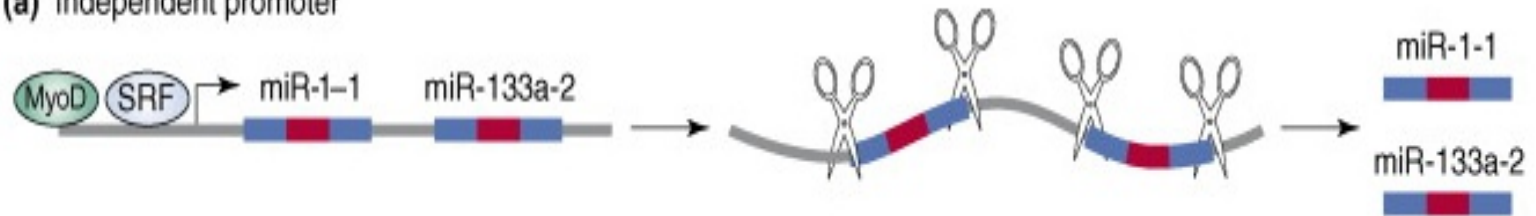


b Spatial reciprocity

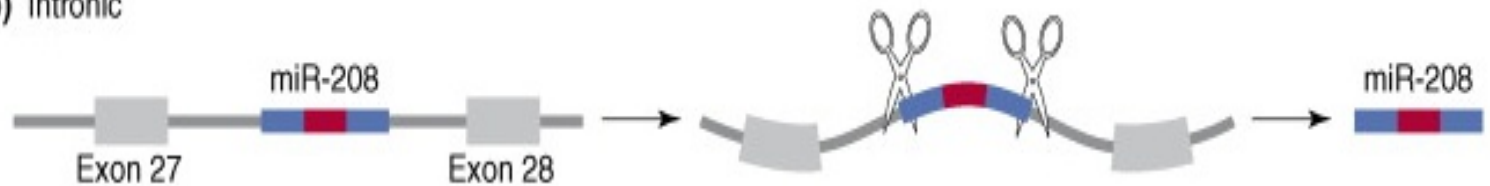


Genomic Organization of miRNA Genes

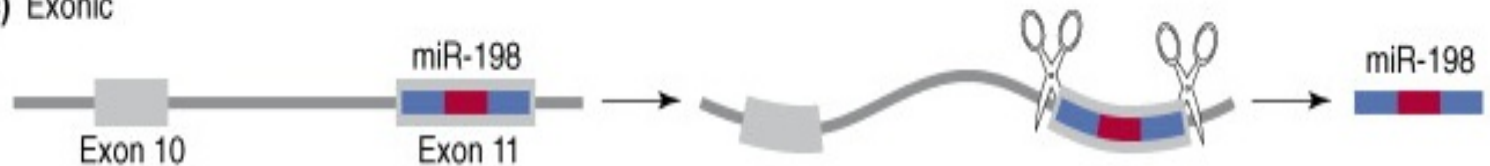
(a) Independent promoter



(b) Intronic

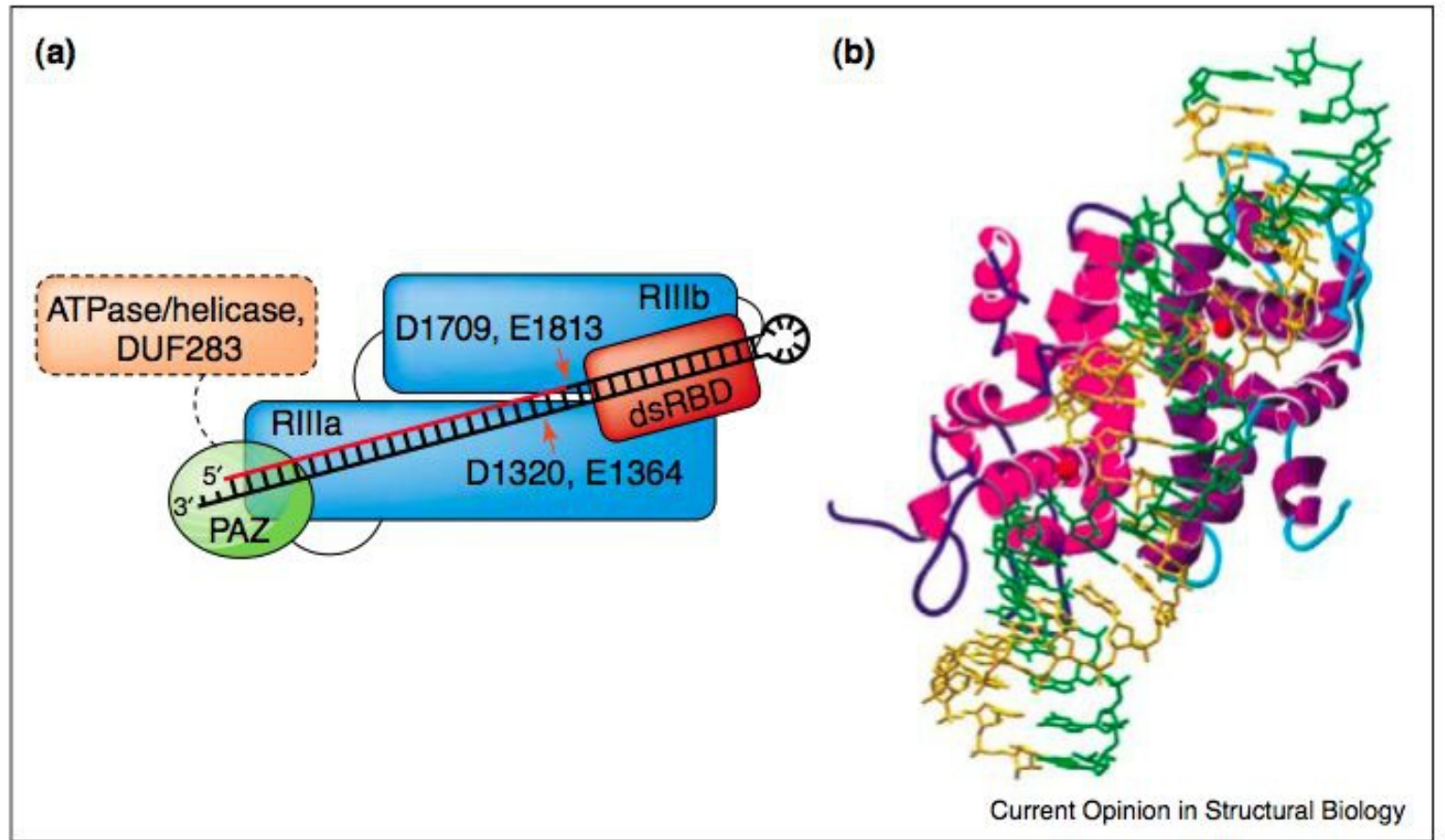


(c) Exonic



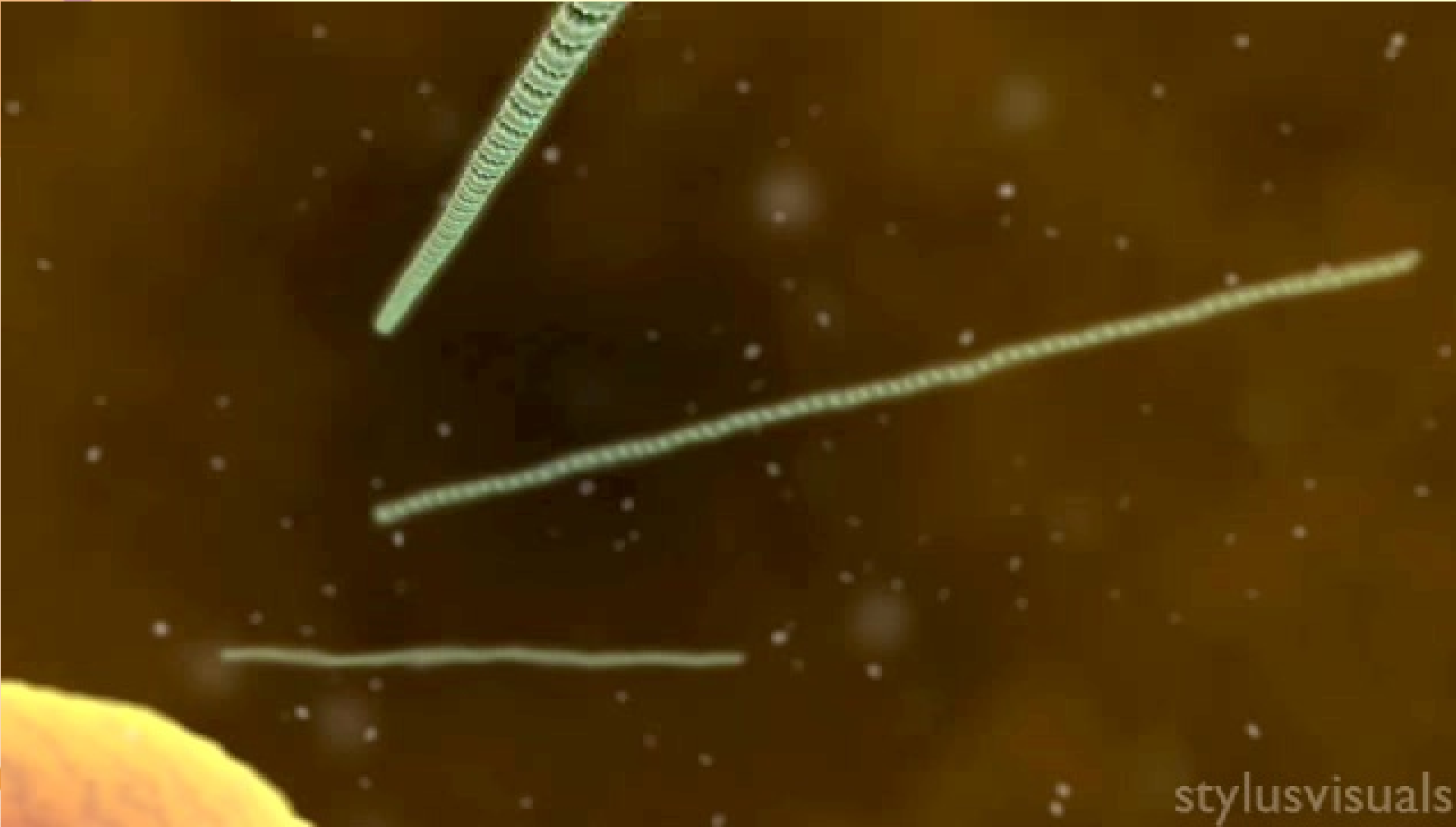
- Intronic miRNAs often in antisense direction, made from own promoter
- Exonic miRNAs - non-coding (or in alternatively spliced exons)

Dicer Structure & Function



Dicer Structure & Function

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



stylusvisuals

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

lin-4 family

```
UCCUGAGA . . . CCUAACUUGUGA Hs miR-125b-1
UCCUGAGA . . . CCUAACUUGUGA Hs miR-125b-2
UCCUGAGA . . . CCUAACUUGUGA Ce lin-4
UCCUGAGA AUUCUGAACAGCUU Ce miR-237
```

let-7 family

```
AGAGGUAGUAGGUUGCAUAGU . . . Hs let-7d
UGAGGUAGUAGGUUGUUAUAGU . . . Hs let-7e
UGAGGUAGUAGGUUGUUAUAGU . . . Hs let-7a-1
UGAGGUAGUAGGUUGUUAUAGU . . . Hs let-7a-2
UGAGGUAGUAGGUUGUUAUAGU . . . Hs let-7a-3
UGAGGUAGUAGGUUGUUAUAGU . . . Hs let-7a-4
UGAGGUAGUAGGUUGUUAUAGU . . . Ce let-7
UGAGGUAGUAGGUUGUUAUAGU . . . Hs let-7f-1
UGAGGUAGUAGGUUGUUAUAGU . . . Hs let-7f-2
UGAGGUAGUAGGUUGUUAUAGU . . . Hs miR-98
UGAGGUAGUAGGUUGUUAUAGU . . . Hs let-7g
UGAGGUAGUAGGUUGUUAUAGU . . . Hs let-7i
UGAGGUAGUAGGUUGUUAUAGU . . . Hs let-7b
UGAGGUAGUAGGUUGUUAUAGU . . . Hs let-7c
UAGGUAGU . . . UUCAUUGUUGGG Hs miR-196-1
UAGGUAGU . . . UUCAUUGUUGGG Hs miR-196-2
UGAGGUAGUAGGUUGUUAUAGU . . . Ce miR-84
UGAGGUAGG . . . CUCAGUAGUUGCA Ce miR-48
UGAGGUAGG . . . UGC . . . AGAAAUUGA Ce miR-241
```

mir-1 family

```
UGGAAUGUAAAAGAAUGUA A Hs miR-1b
UGGAAUGUAAAAGAAUGUA U Hs miR-1d
UGGAAUGUAAAAGAAUGUA . . . Ce miR-1
UGGAAUGUAAAAGAAUGUUGG Hs miR-206
```

mir-9 family

```
UCUUUGGUUUAU . . . CUGGUG . . . UAUUA Hs miR-9-1
UCUUUGGUUUAU . . . CUGGUG . . . UAUUA Hs miR-9-2
UCUUUGGUUUAU . . . CUGGUG . . . UAUUA Ce miR-244
```

mir-10 family

```
AACCC . . . GUAGAUCGAAACU . . . UUGG . . . Hs miR-100-1
AACCC . . . GUAGAUCGAAACU . . . UUGG . . . Hs miR-100-2
CAACC . . . GUAGAUCGAAACU . . . UUGG . . . Hs miR-99b
UACCCUGUAGA . . . UCGAGCUGUGUGU Ce miR-57
UACCCUGUAGAUCGAAACU . . . UUGG . . . Hs miR-10a
UACCCUGUAGAUCGAAACU . . . UUGG . . . Hs miR-10b
AACCC . . . GUAGAUCGAAACU . . . UUGG . . . Hs miR-99a
UACCC . . . GUAGUCCUAUCCAUUGU . . . Ce miR-51
```

mir-19 family

```
UGUGCAAUUC . . . UAU . . . GCAAAACUGA . . . Hs miR-19a
UGUGCAAUUC . . . UAU . . . GCAAAACUGA . . . Hs miR-19b-1
UGUGCAAUUC . . . UAU . . . GCAAAACUGA . . . Hs miR-19b-2
. . . UGCAAUUC . . . UAU . . . GCG . . . ACUGUAGG Ce miR-254
```

mir-25 family

```
UAUUGCACUUGUC . . . CGG . . . CUGU Hs miR-92-1
UAUUGCACUUGUC . . . CGG . . . CUGU Hs miR-92-2
UAUUGCACUUGUC . . . CGG . . . CUGU Ce miR-235
CAUUGCACUUGUC . . . CGG . . . CUGU Hs miR-25-1
CAUUGCACUUGUC . . . CGG . . . CUGU Hs miR-25-2
UAUUGCAC . . . UAU . . . UAGU . . . UGC Hs miR-32
```

mir-29 family

```
. . . UAGCACC . . . UUGAAAUCAGUGU Hs miR-29b-1
. . . UAGCACC . . . UUGAAAUCAGUGU Hs miR-29b-2
. . . UAGCACC . . . UUGAAAUCAGUGU Hs miR-29b-3
. . . UAGCACC . . . UUGAAAUCAGUGU Hs miR-29c
. . . UAGCACC . . . UUGAAAUCAGUGU Hs miR-29a-1
. . . UAGCACC . . . UUGAAAUCAGUGU Hs miR-29a-2
. . . UAGCACC . . . UUGAAAUCAGUGU Ce miR-83
```

mir-31 family

```
AGGCAAGAUGUUGGCA . . . U . . . AGC . . . Ce miR-72
. . . GGCAGAUGCUGGCA . . . U . . . AGCUG Hs miR-31
UGGCAAGAUGUUGGCA . . . U . . . AGC . . . Ce miR-73
```

mir-34 family

```
AGGCAGUGUGUUA . . . GCUGGUUG . . . Ce miR-34
UGGCAGUGUGUUA . . . GCUGGUUGU Hs miR-34
UGG . . . AGUCUC . . . ACAAU . . . GGUUGUUGGU Hs miR-122a
```

mir-50 family

```
UGAUUUGUAAUUC . . . AGCUUACAG . . . Ce miR-62
UGAUUUGUAAUUC . . . AGCUUACAGU Hs miR-50
UGAUUUGUAAUUC . . . AGCUUACAGU Hs miR-190
UGAUUUGUAAUUC . . . AGCUUACAGU Ce miR-90
```

mir-74 family

```
UGG . . . AGAGAA . . . AGGCAGUUC . . . Hs miR-185
UGGC . . . AGAAAU . . . AGGCAGU . . . CUACA Ce miR-74
```

mir-76 family

```
UCCGU . . . UGUUG . . . AU . . . GAAGCCUUGA Ce miR-76
UCCGU . . . UGUUG . . . AU . . . GAAGCCUUGA Hs miR-187
```

mir-79 family

```
A . . . AAAAGCUAGC . . . UACCAAAAGCU . . . Ce miR-79
. . . AAAAGCUAGC . . . UACCAAAAGCU . . . Hs miR-131
U . . . AAAAGCUAGC . . . UACCAAAAGCU . . . Ce miR-75
```

mir-80 family

```
UGAGAUCATC . . . GU . . . GAAAGCCUAGU Ce miR-81
UGAGAUCATC . . . GU . . . GAAAGCCUAGU Ce miR-82
UGAGAUCATC . . . GU . . . GAAAGCCUAGU Ce miR-80
UGAGAUCATC . . . GU . . . GAAAGCCUAGU Hs miR-143
```

mir-105 family

```
UCAAAUUC . . . UCA . . . GACUCCUUGU . . . Hs miR-105-1
UCAAAUUC . . . UCA . . . GACUCCUUGU . . . Hs miR-105-2
. . . UAAAUGCA . . . UGUUAAUUGCUGUGUA Ce miR-232
```

mir-124 family

```
U . . . AAGGCACGCG . . . GU . . . GAAUGCCA . . . Hs miR-124a
U . . . AAGGCACGCG . . . GU . . . GAAUGCCA . . . Hs miR-124a
U . . . AAGGCACGCG . . . GU . . . GAAUGCCA . . . Hs miR-124a
. . . U . . . AAGGCACGCG . . . GU . . . GAAUGCCA . . . Ce miR-124
. . . AAUGGCAC . . . UGCAU . . . GAAU . . . UCA . . . CGG Ce miR-228
. . . AAUGGCAC . . . UG . . . GUA . . . GAAU . . . UCA . . . CUG Hs miR-183
```

mir-133 family

```
. . . UUGGUCCCCU . . . UCAACCAGCUGU Hs miR-133a-1
. . . UUGGUCCCCU . . . UCAACCAGCUGU Hs miR-133a-2
. . . UUGGUCCCCU . . . UCAACCAGCUGU Hs miR-133b
A . . . UUGGUCCCCU . . . UCAACCAGCUGU Ce miR-245
```

mir-137 family

```
U . . . UAUUGCU . . . C . . . AGAAUACCCUU . . . Ce miR-234
. . . UAUUGCU . . . C . . . AGAAUACCCUU . . . Hs miR-137
```

mir-141 family

```
U . . . AAUACUGUC . . . AGGUAAU . . . GAC . . . GCU Ce miR-236
. . . AAUACUGUC . . . AGGUAAU . . . GAC . . . GCU Hs miR-141
```

mir-193 family

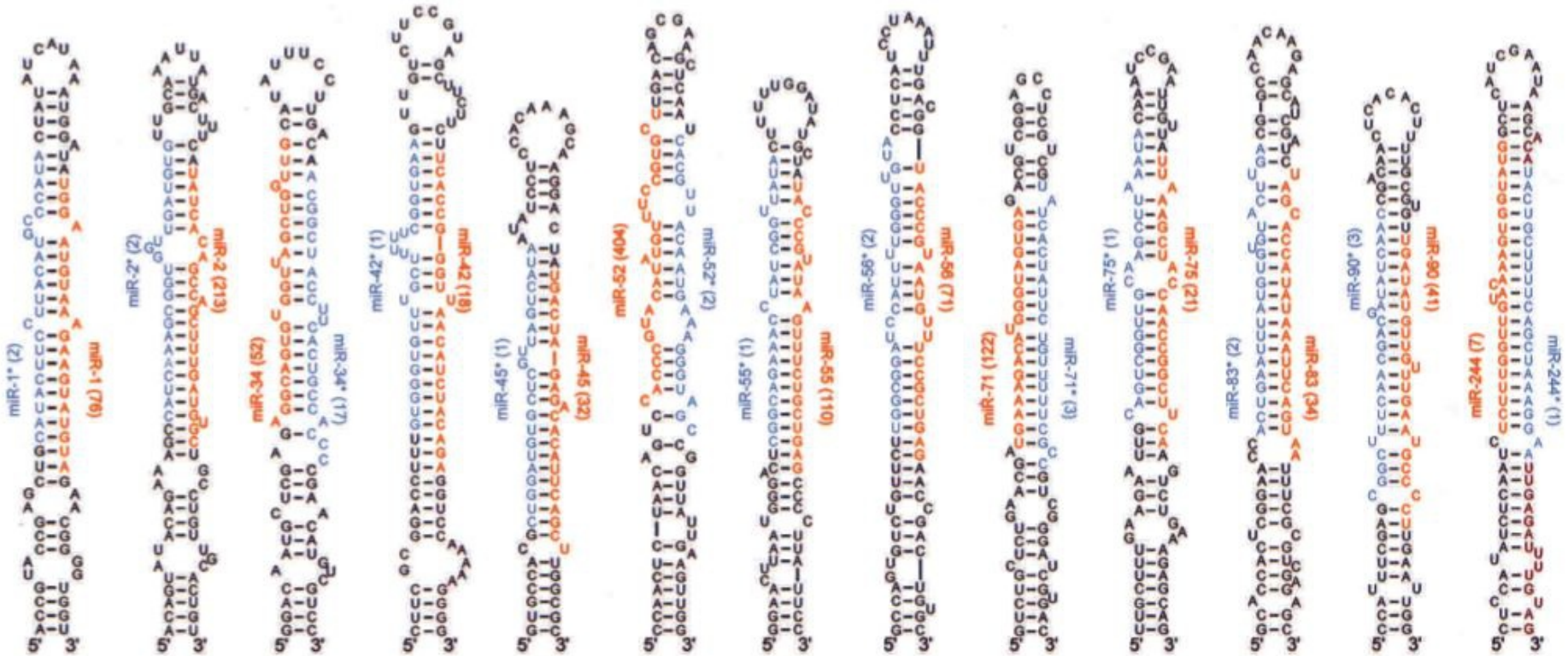
```
U . . . ACUGGCC . . . C . . . CAAA . . . UCUC . . . GCU Ce miR-240
A . . . ACUGGCC . . . C . . . CAAA . . . UCUC . . . GCU Hs miR-193
```

mir-220 family

```
. . . CACACAC . . . UCA . . . CUACACUGAC Ce miR-253
. . . CACACAC . . . UCA . . . CUACACUGAC Hs miR-220
```



Predicted miRNA Precursors





miRBase

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



miRBase

MANCHESTER
1824

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Latest miRBase blog posts

High confidence miRNA set available for miRBase 21

By [sam](#) (July 3, 2014)

As mentioned previously, we briefly held off from releasing the set of "high confidence" miRNAs for miRBase 21, because of a last-gasp bug. Those data are now available, tagged with the label "high confidence" on the entry pages, and for download on the FTP site. The total number of miRNAs labelled "high confidence" has increased [...]

miRBase 21 finally arrives

By [sam](#) (June 26, 2014)

Apologies for the longer-than-usual wait. miRBase 21 is now available on the website, and all data available for download on the FTP site. As usual, the release notes describe the major changes. Of particular note this time, the Genome Reference Consortium have released a new human genome assembly, GRCh38. We have therefore remapped the human [...]

miRNA count: 28645 entries

[Release 21](#): June 2014

Search by miRNA name or keyword

Download published miRNA data

[Download page](#) | [FTP site](#)

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.

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 managed by the [Griffiths-Jones lab](#) at the [Faculty of Life Sciences, University of Manchester](#) with funding from the [BBSRC](#). miRBase was previously hosted and supported by the [Wellcome Trust Sanger Institute](#).

Tweets

[Follow](#)

 **miRBase**
@mirbase 9 Dec

.@JungeAlexander FTP site works for me. Firewall/passive FTP incompatibilities have caused issues for some users. Shout if still have probs.

 **Naomi Attar**
@naomiattar 12 Nov

Anton Petrov talking thru @RNAcentral, which brings together likes of @mirbase, ENA, IncRNAdb etc - with more to be added soon #compRNA

↻ Retweeted by miRBase

Expand

Tweet to @mirbase



Kozomara and Griffiths-Jones. miRBase: integrating microRNA annotation and deep-sequencing data. *Nucleic Acids Res.* (2010) Vol 39, pages D152-D157.

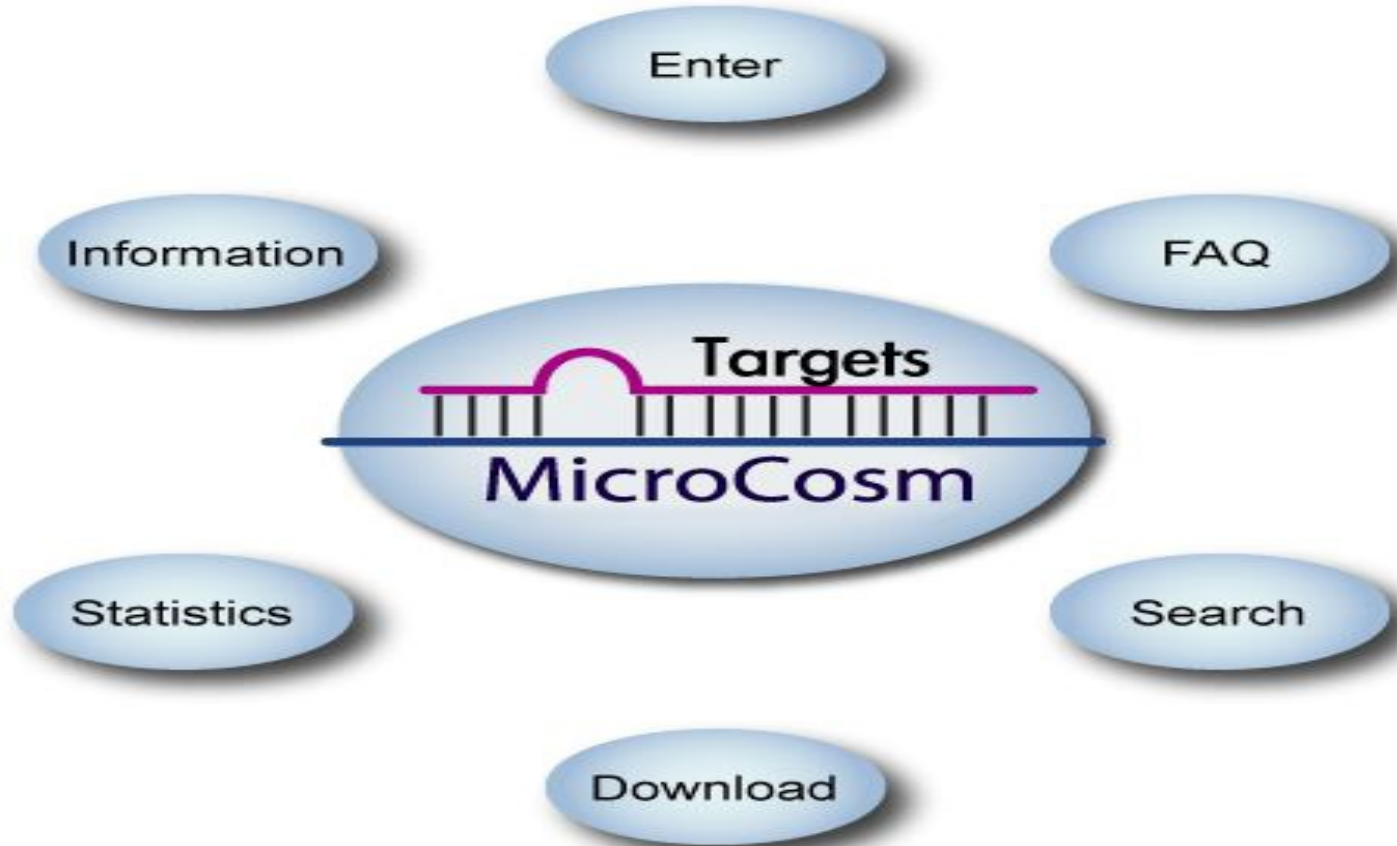
© Doug Brutlag 2015

miRBase::MicroCosm miRNA Targets

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

MicroCosm Targets Version 5

Email microcosm@ebi.ac.uk with queries or problems.

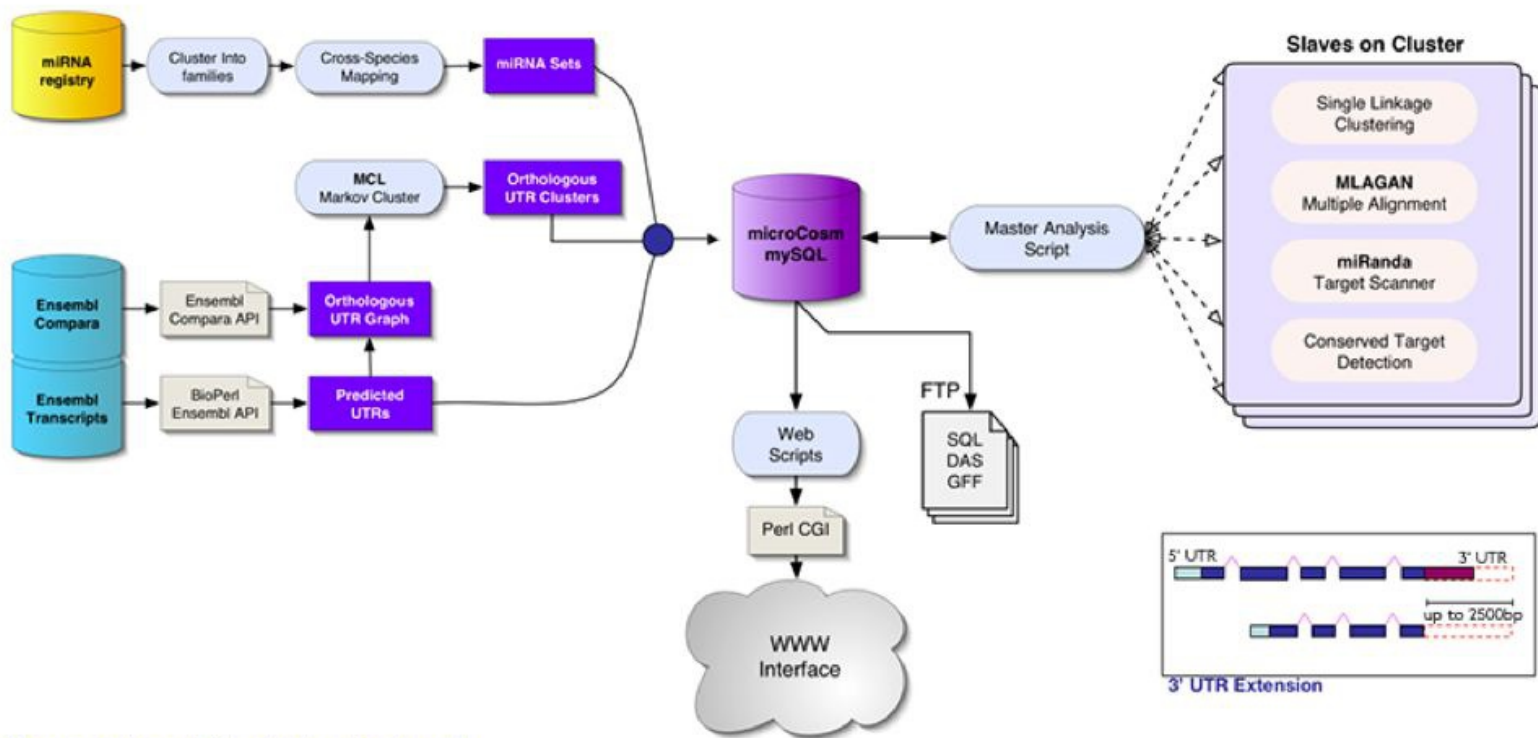


miRBase Targets Release Version v5

MicroCosm miRNA Targets Prediction

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

Computational Protocol



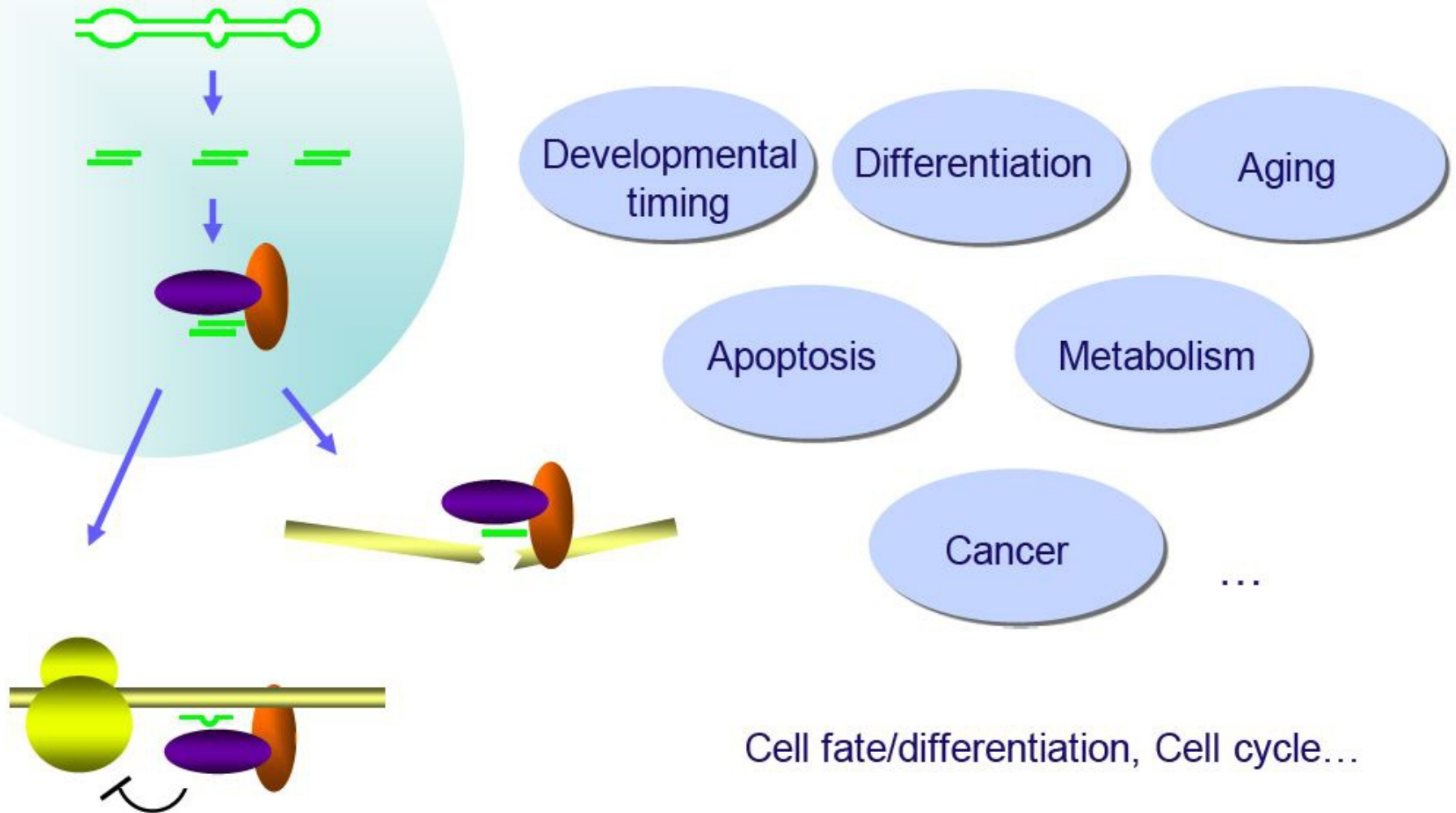
Computational Prediction Protocol

Human miRNAs (March 4, 2014)

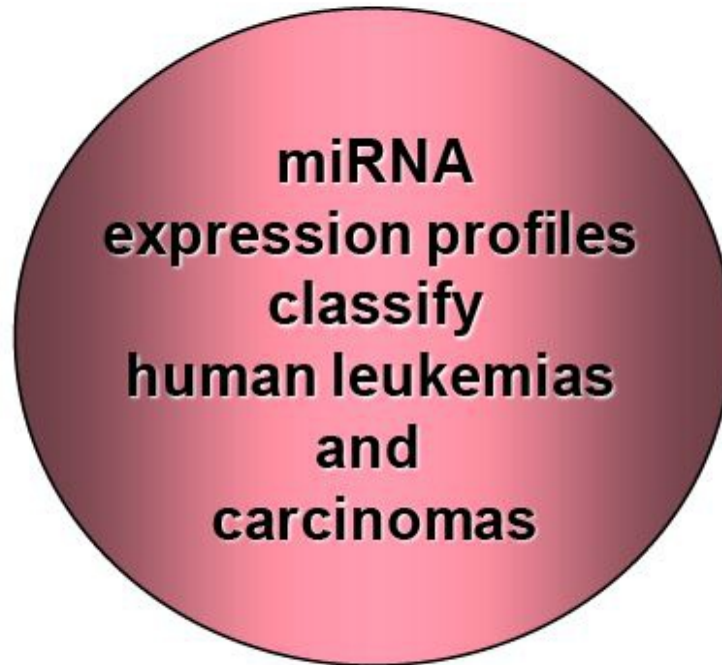
- Total number of miRNAs known 24,521
 - Number human miRNAs identified 2,652
 - Number of human mRNA targets 34,788
-

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

Thousands of microRNAs act in multiple biological events



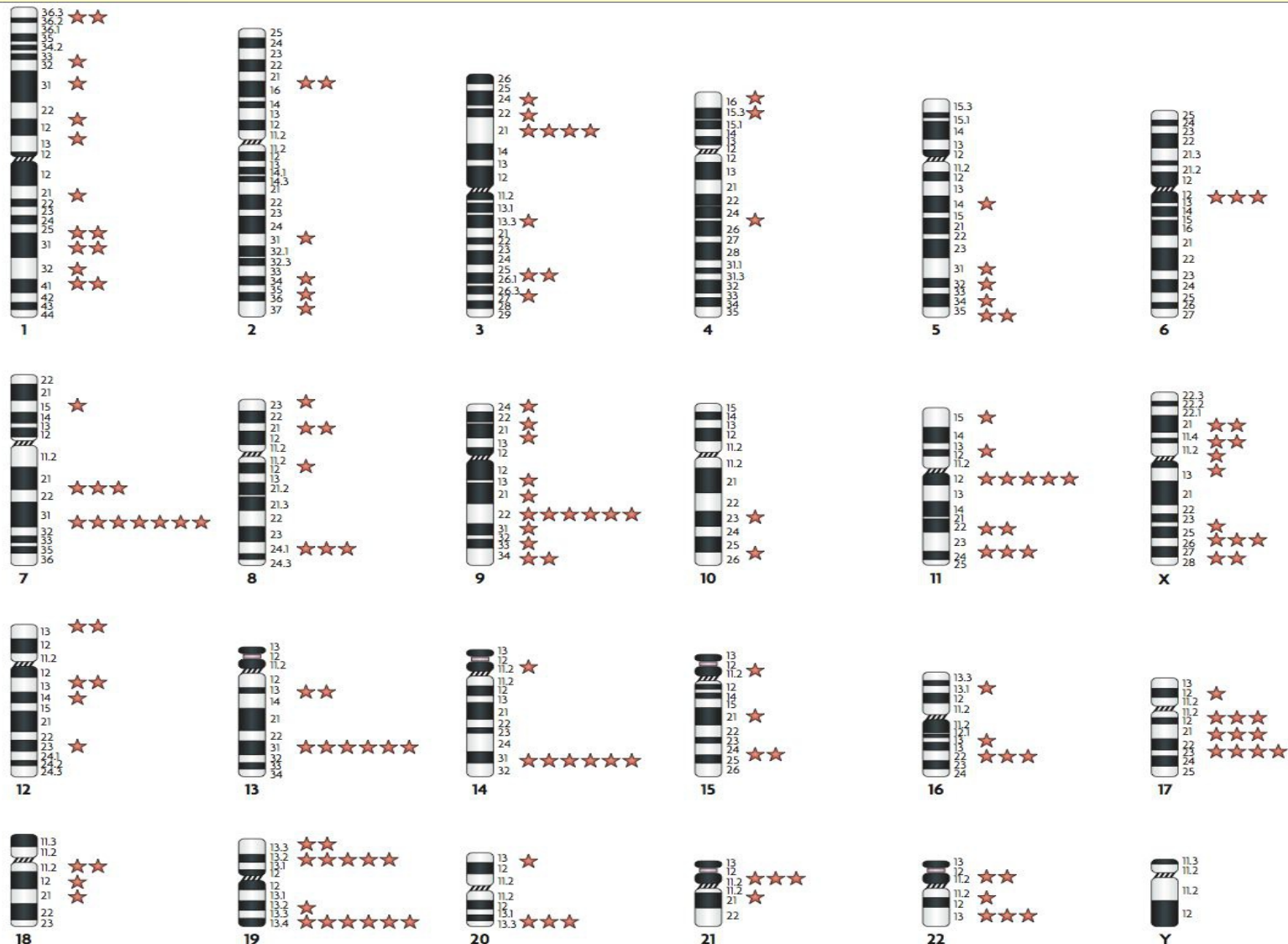
***ALTERATIONS OF MICRORNAS ARE FOUND IN EVERY
TYPE OF HUMAN CANCER***



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

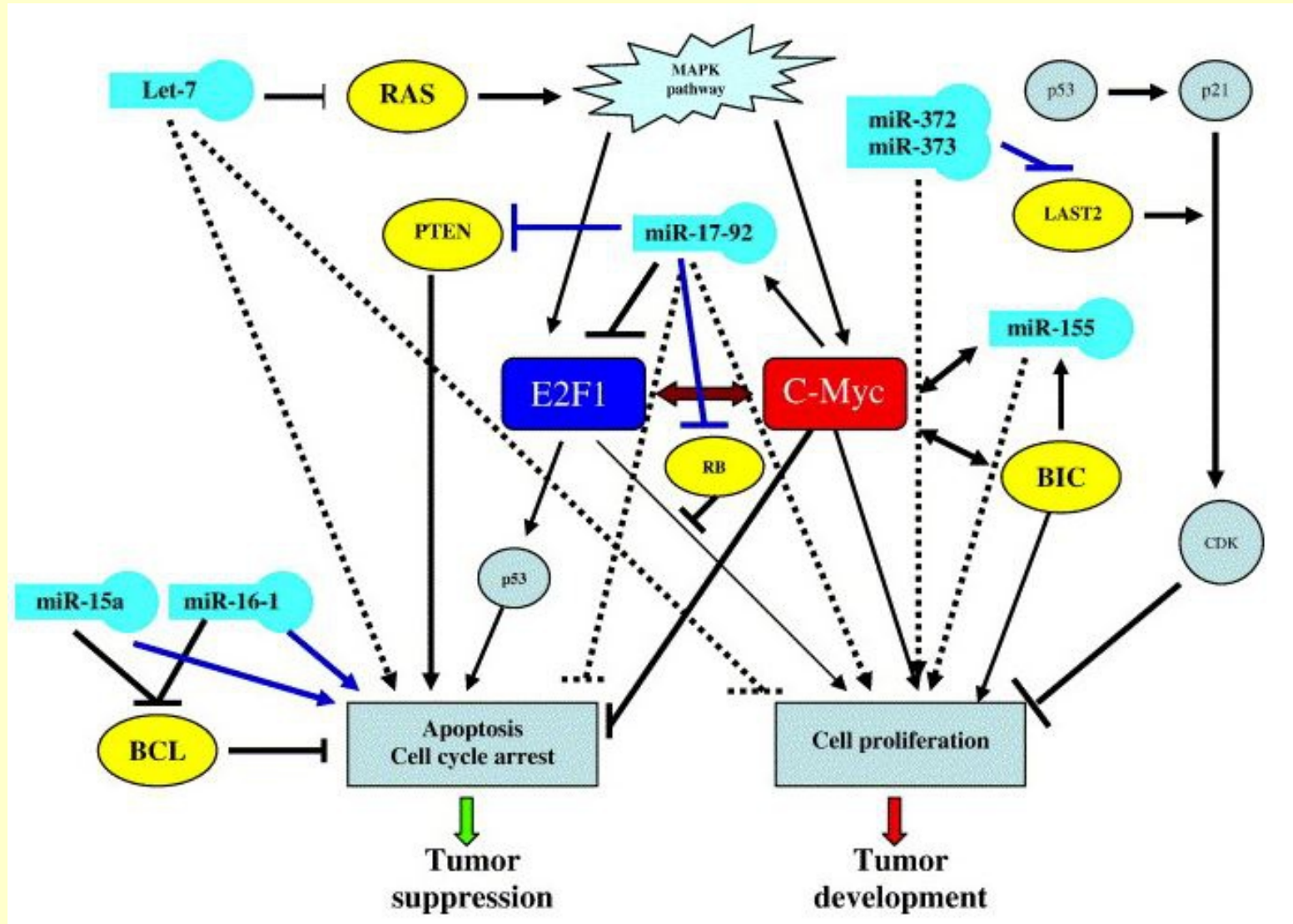
miRNAs Involved in Human Cancer

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



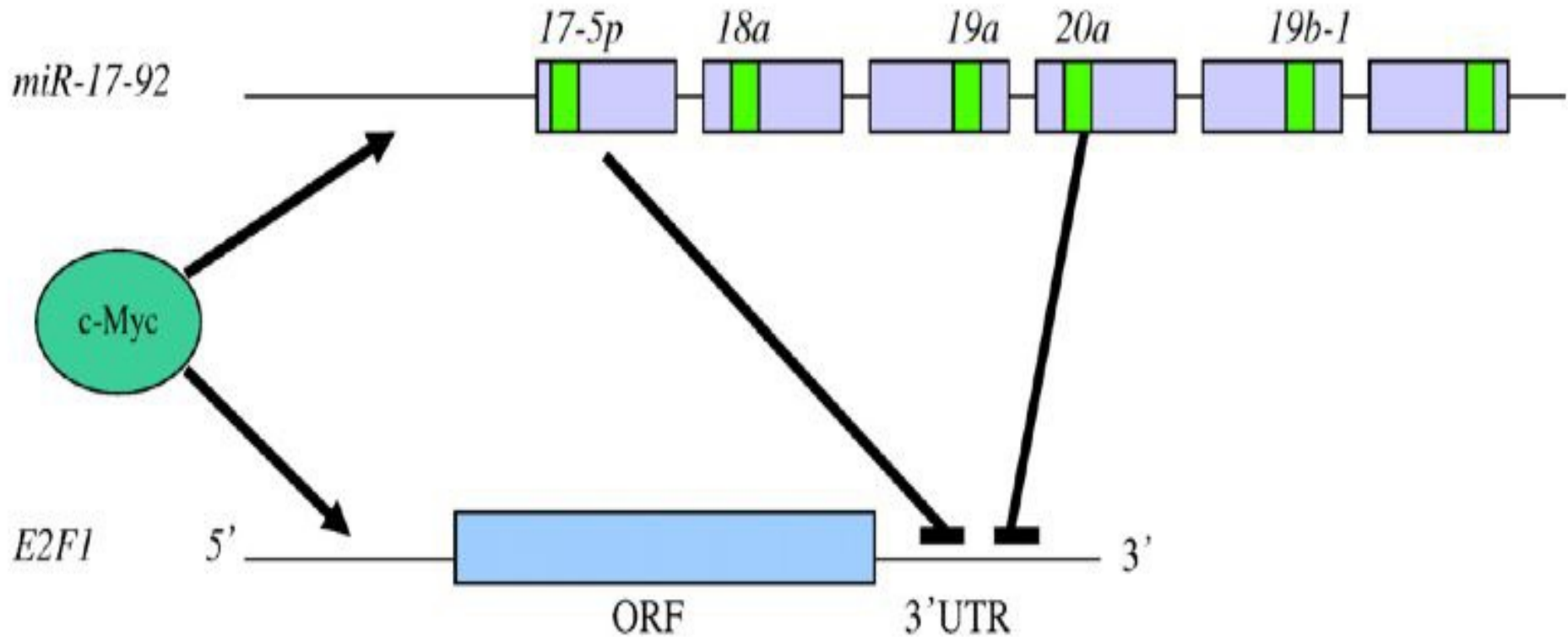
miRNAs as Oncogenes and Tumor Suppressors

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

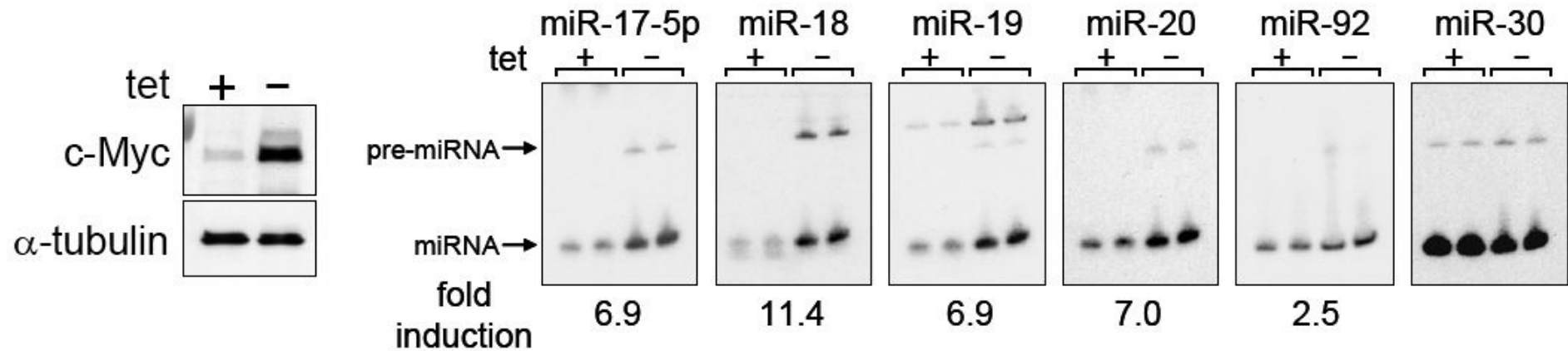
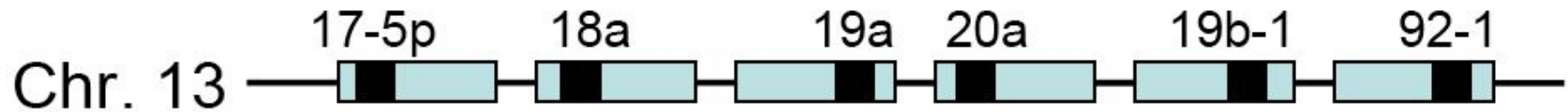


cMyc & miRNAs Regulate E2F1 Cell Cycle TF

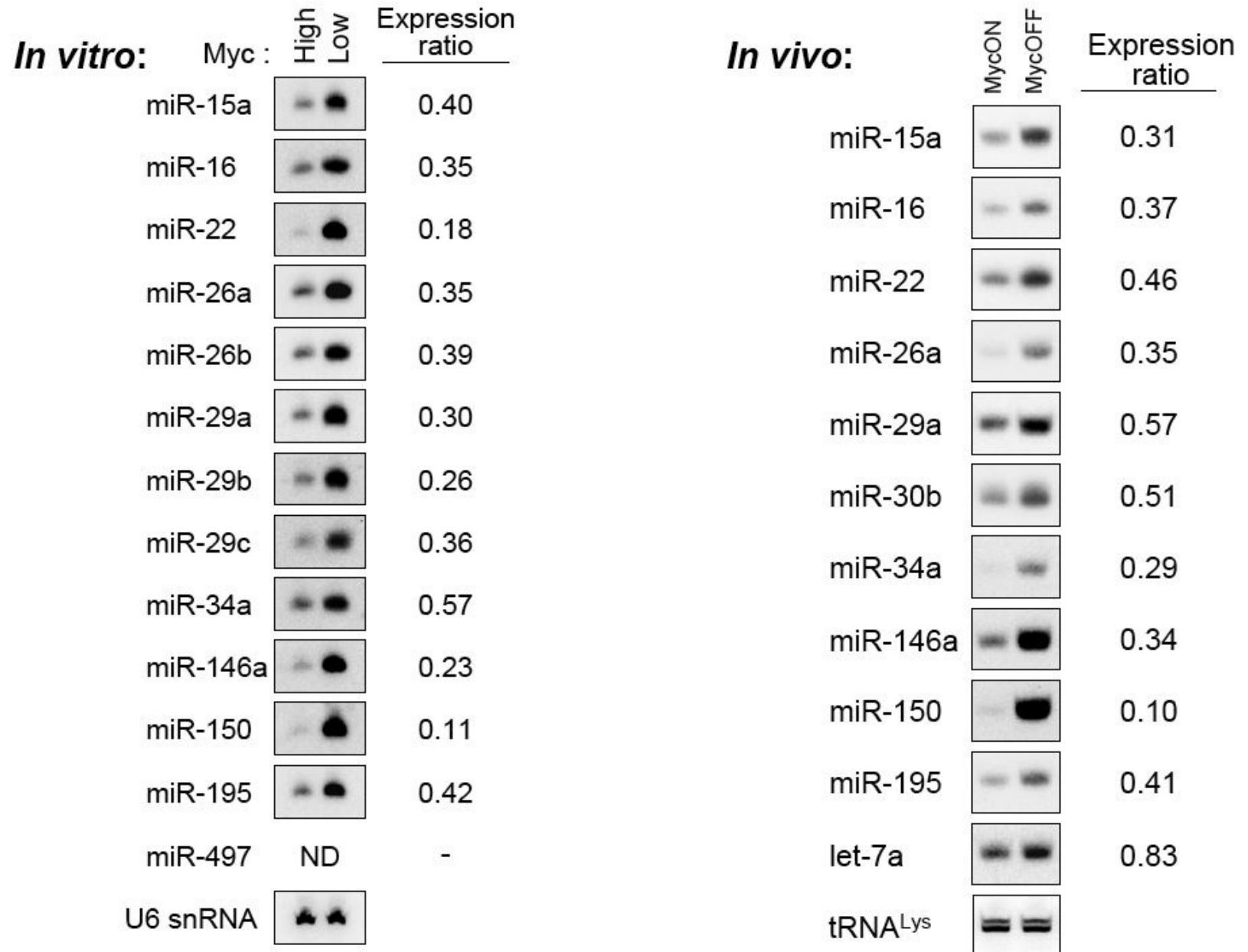
Zhang et al Dev Biol. 2007 Feb 1;302(1):1-12



The miR-17-92 cluster is activated by Myc



Myc represses the expression of many miRNAs



miRNA Oncogenes or Tumor Suppressor Genes (Croce Nat Rev Genet. 2009 Oct;10(10):704-14.)

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</i> 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
<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.

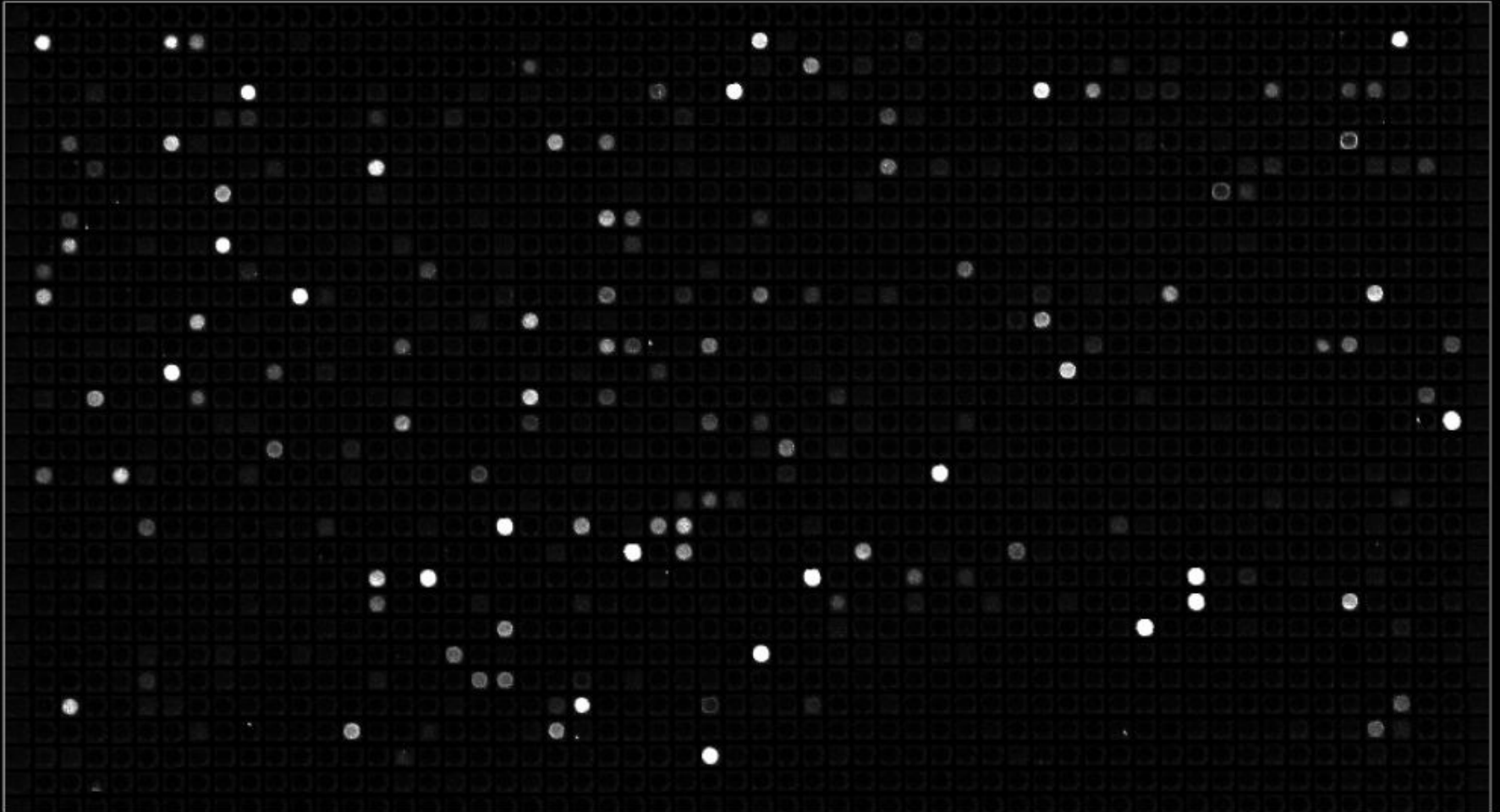
MIRNA PROFILING AS A NEW DIAGNOSTIC & PROGNOSTIC TOOL FOR CANCER PATIENTS



**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

- 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.

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- The microRNAs of *Caenorhabditis elegans*. [Lim Genes Dev. 2003 Apr 15;17\(8\):991-1008.](#)
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[Jinek Nature. 2009 Jan 22;457\(7228\):405-12.](#)
- 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

- 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/>
- TargetRank: <http://hollywood.mit.edu/targetrank>
- TargetScanS: <http://www.targetscan.org/>