

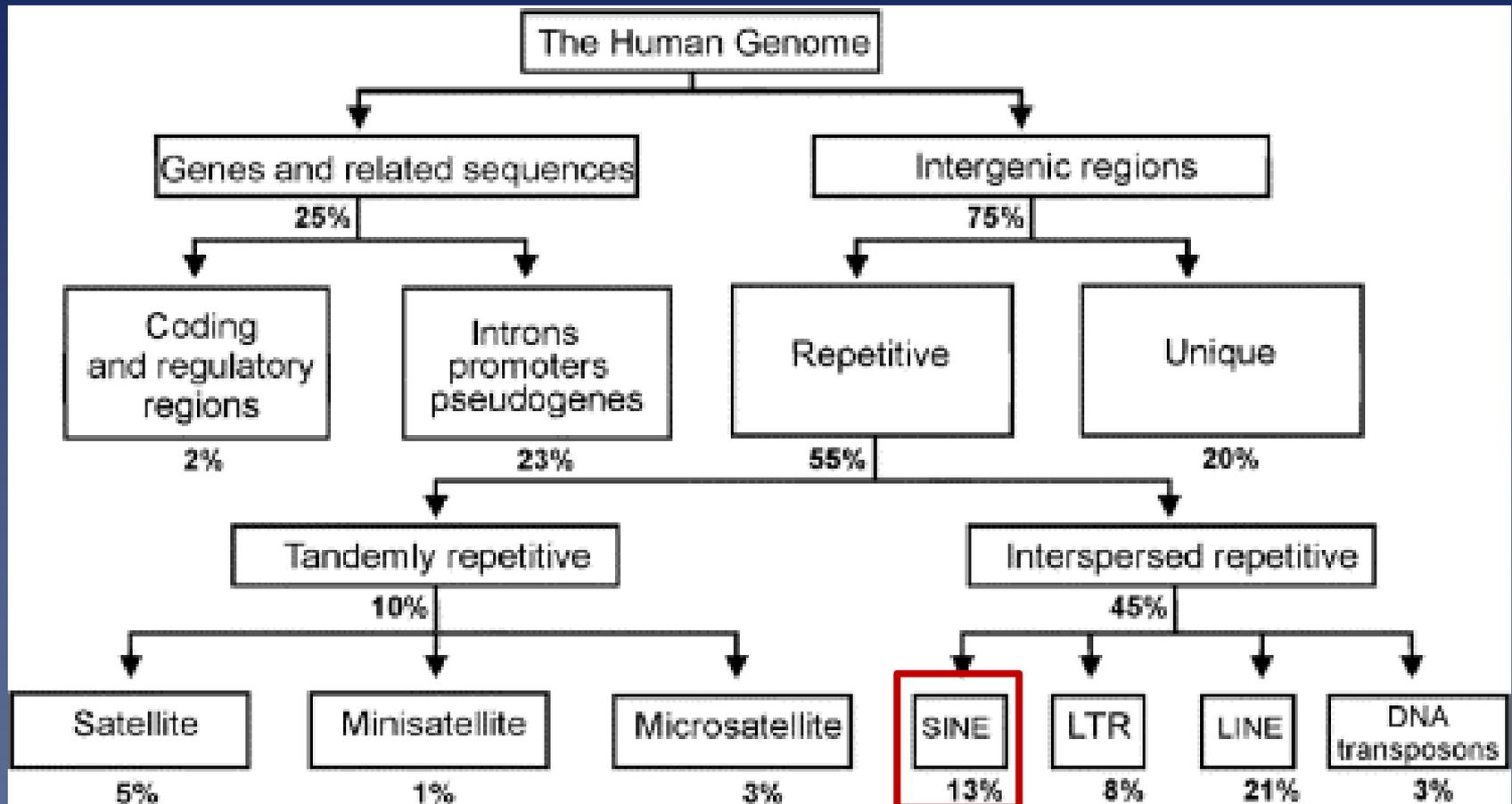
# Gene ontology analysis of protein-coding mRNAs with exonized ALU repeats and potential targets of ALU-derived microRNAs

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# Composition of the human genome

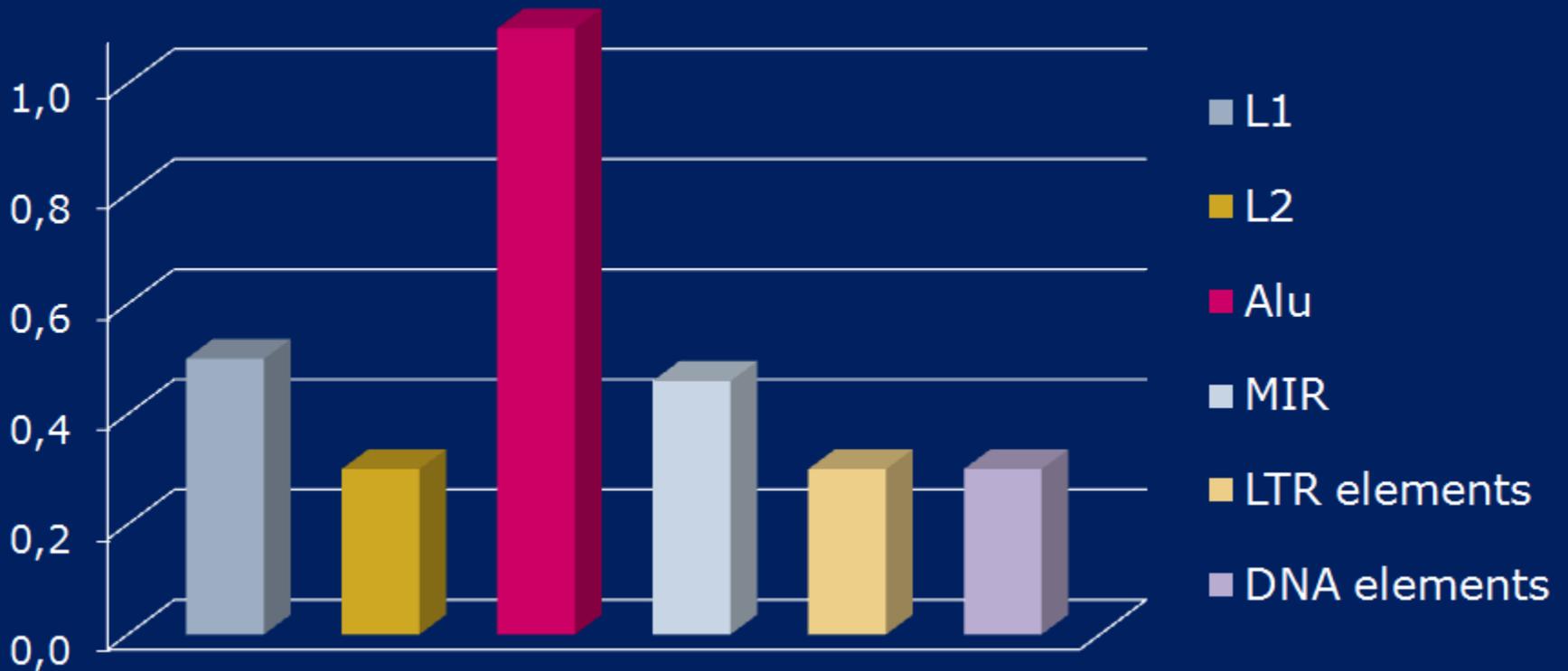


**Repetitive sequences that shape the human transcriptome.**

A Jasinska and WJ Krzyzosiak

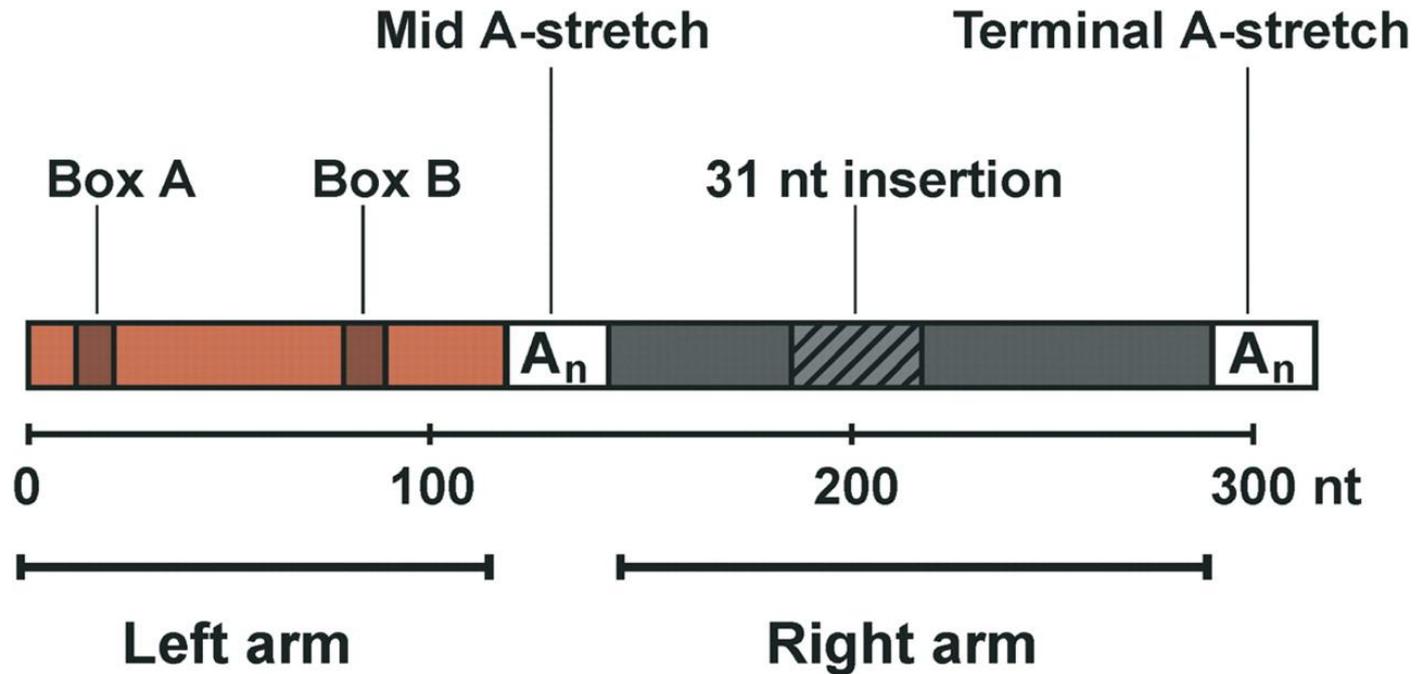
FEBS Lett, June 1, 2004; 567(1): 136-41

# Copy number of mobile elements in the human genome (millions)



By Deininger PL and Batzer MA Mammalian Retroelements // Genome Res., Oct 2002; 12: 1455 - 1465.

# Architecture of Alu elements



```

1 AluJ ..... 1 ..... 45
2 AluSx GGCCGGGCGCGGTGGCTCACGCCTGTAATCCCAGCACTTTGGGAG
3 AluSq .....
4 AluSp .....
5 AluSc .....
6 AluY .....
7 AluYa5 .....
8 AluYa8 .....
9 AluYb8 .....

1 AluJ ..... A ..... T ..... CC ..... 46 ..... 90
2 AluSx GCCGAGGCGGGCGGATCACCTGAGGTCAGGAGTTCGAGACCAGCC
3 AluSq ..... T .....
4 AluSp ..... G .....
5 AluSc ..... -- ..... A ..... A ..... T .....
6 AluY ..... -- ..... A ..... T .....
7 AluYa5 ..... -- ..... A ..... T .....
8 AluYa8 ..... -- ..... A ..... T .....
9 AluYb8 ..... T ..... T-- ..... A ..... T .....

1 AluJ ..... 91 ..... 135
2 AluSx ...G.....A.....A.....-TT
3 AluSq .....
4 AluSp ..A.....A.....-
5 AluSc .....
6 AluY ..... T ..... C ..... A .....
7 AluYa5 C...T..A.C.....A..
8 AluYa8 C...T..A.C.....C.....A-
9 AluYb8 ...T...A.....A.....

1 AluJ ..... 136 ..... 180
2 AluSx AGCCGGGCGTGGTGGCGCGCCTGTAATCCCAGCTACTCGGGAG
3 AluSq ..... G .....
4 AluSp ..... AT .....
5 AluSc ...T.....G.....
6 AluY ..... G ..... G .....
7 AluYa5 ..... A ..... G ..... G ..... T .....
8 AluYa8 ..... A ..... G ..... G ..... T ..... T .....
9 AluYb8 ..... C ..... G ..... G .....

```

```

181 ..... 225
1 AluJ .....G.....G.....TC....C.....
2 AluSx GCTGAGGCAGGAGAATCGCTTGAACCCGGGAGGCGGAGGTTGCAG
3 AluSq .....
4 AluSp ..... G .....
5 AluSc .....
6 AluY ..... G..G.....C.....
7 AluYa5 ..... G..G.....C.....
8 AluYa8 ..... G..G.....C.....
9 AluYb8 ..... G..G.....A.....C.....

226 ..... 263
1 AluJ .....T.....-----.....
2 AluSx TGAGCCGAGATCGCGCCACTGCACTCCA-----GCCTGGGCGA
3 AluSq .....-----.....A..
4 AluSp .....T.....-----.....A..
5 AluSc .....-----.....-
6 AluY .....-----.....
7 AluYa5 .....C.....-----.....
8 AluYa8 .....C.....-----.....
9 AluYb8 .....T.....G...GCAGTCCG.....

264 ..... 288
1 AluJ ..-.....C.T.....
2 AluSx CA-GAGCGAGACTCCGTCTCAAAAAA
3 AluSq ..A.....A.....
4 AluSp ..A.....A.....
5 AluSc ..-.....
6 AluY ..-.....
7 AluYa5 ..-.....
8 AluYa8 ..-.....
9 AluYb8 ..-.....

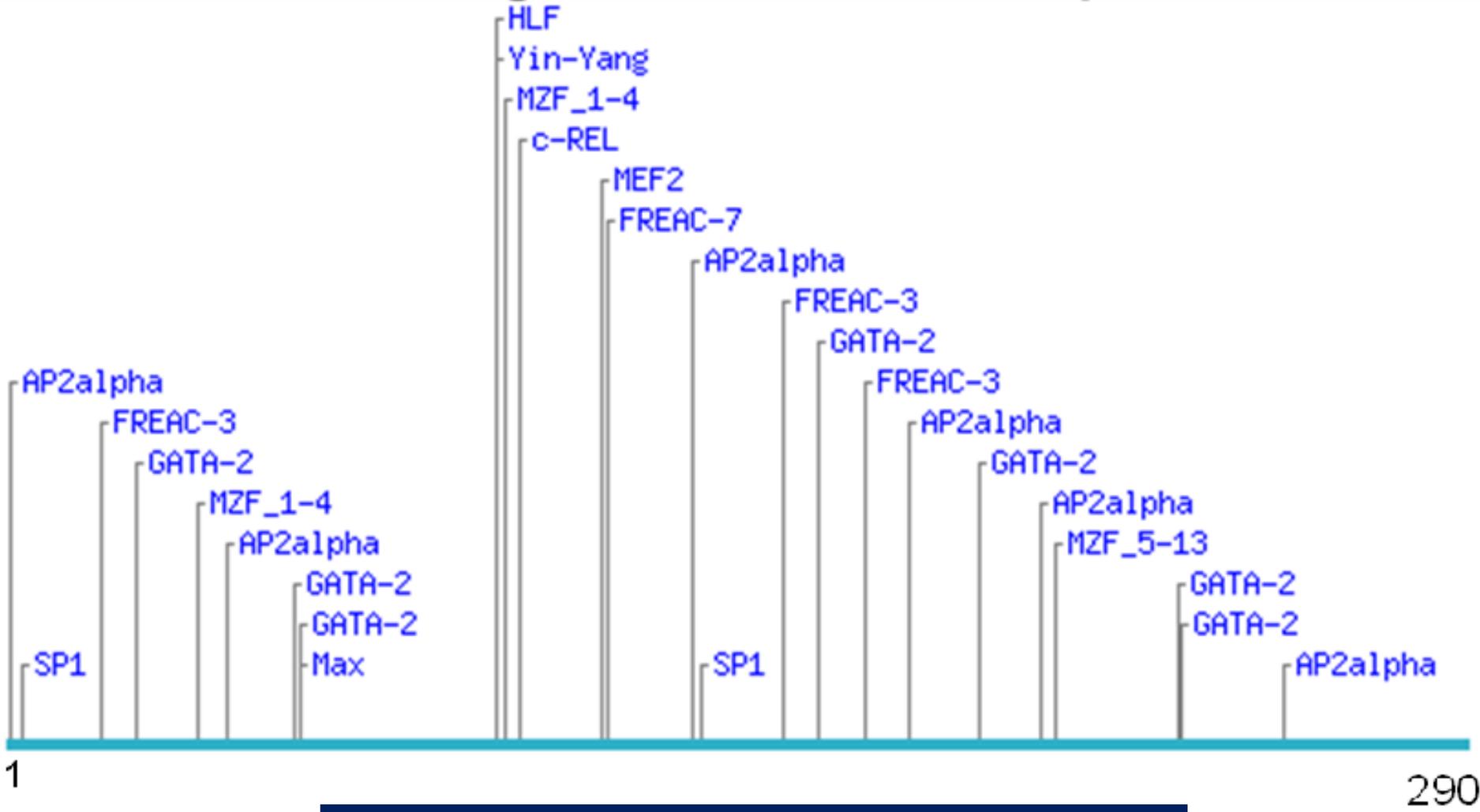
```

**Fig. 1.** Multiple alignment of Alu consensus subfamily sequences. Sequences from various Alu subfamilies are aligned beginning with the oldest (J) and proceeding downward with decreasing age to the youngest Alu subfamilies (Y). The *dots* below each consensus represent the same nucleotide. Mutations are denoted with the appropriate base while deletions are denoted by the *dashes*.

# Potential functional roles of ALUs in introns

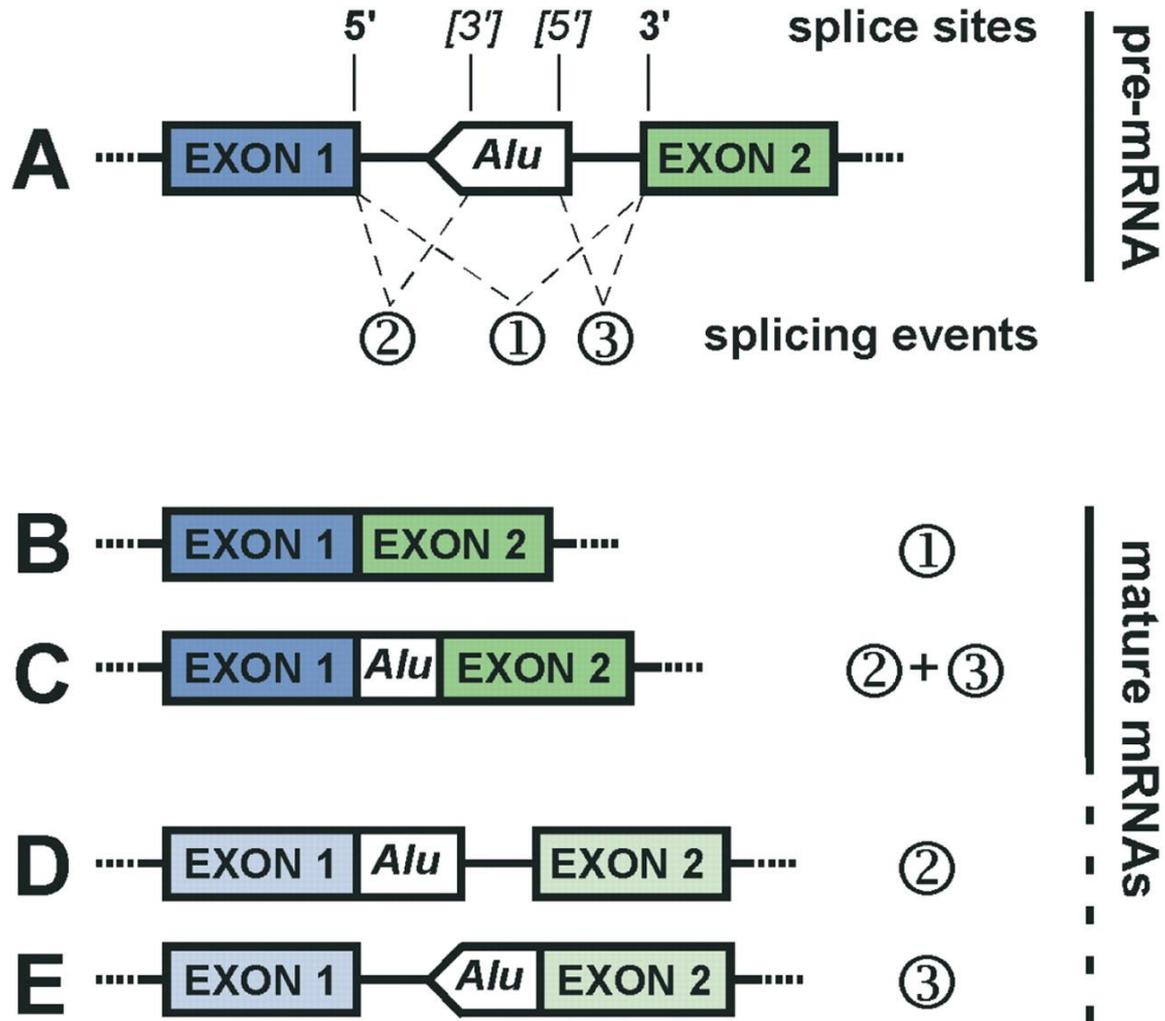
- ◆ Up to 33% of the total number of **CpG sites** in the genome are found within SINE. Alus have been reported to be **highly methylated** in most somatic tissues. Alus demethylation occurs in aging and cancer and is associated with gene reactivation and genomic instability [Rodriguez et al, 2008]
- ◆ Alus are carriers of **different TF binding sites** (nuclear factors, hormones, calcium nuclear factors and others) [by Polak, Domany, 2006]

# Putative transcription factor binding sites found along *Alu-consensus* sequence



TF score cutoff =85%  
<http://asp.ii.uib.no:8090/cgi-bin/CONSITE/consite>

# Exonization of intronic Alu elements



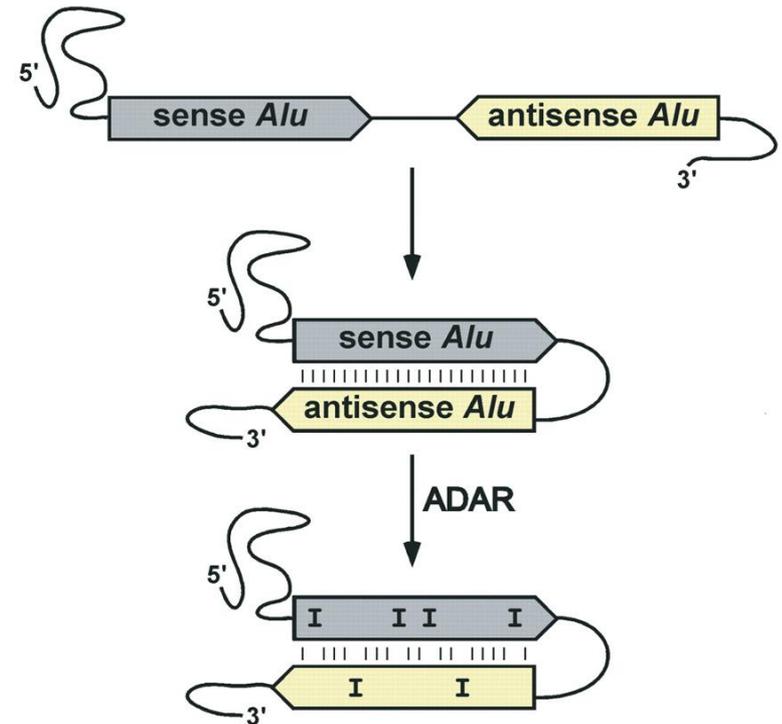
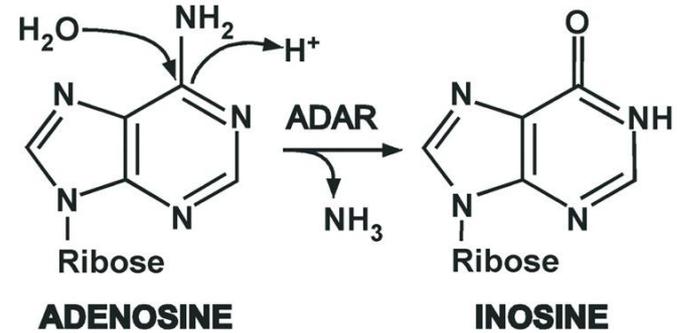
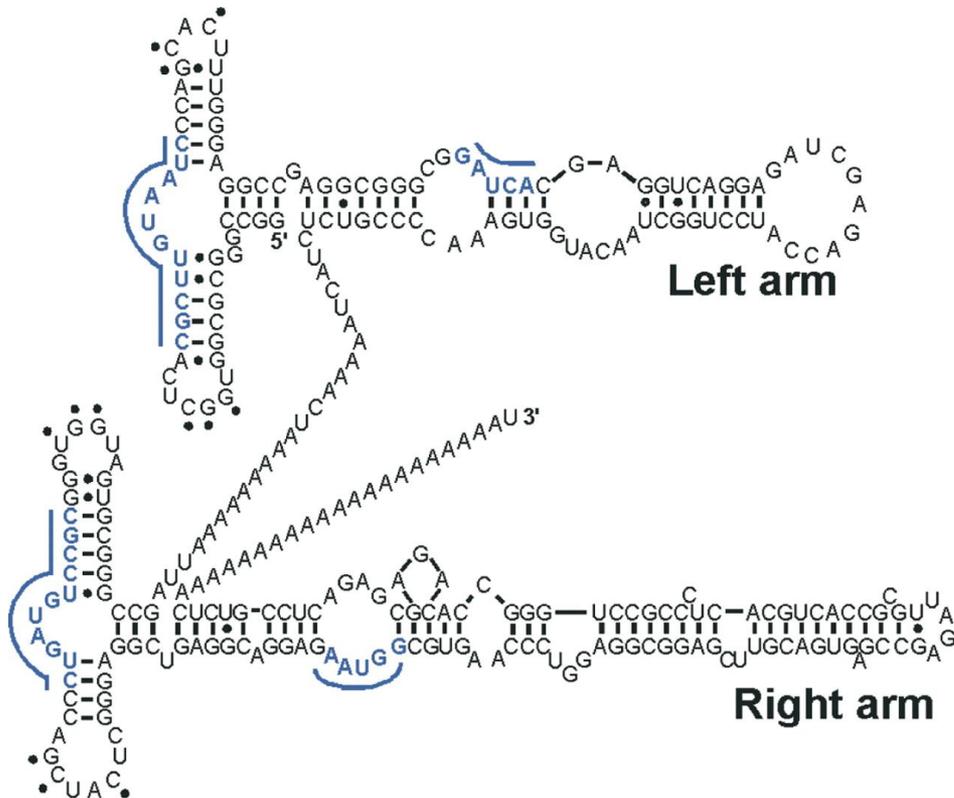
# Potential functional roles of exonized ALUs

## → **Transcriptome diversity and versatility**

- ◆ All Alu-derived exons were found to be **alternatively spliced** [Sorek et al, 2002]. Alus are present in one or several (but not all) splice isoforms.
- ◆ Alternative mRNAs **polyadenylation** within exonized Alus lead to the expression of transcripts with different UTR in different tissues [Chen et al, 2009].
- ◆ Transcripts with Alus undergo adenosine-to-inosine (A-to-I) **RNA editing** in multiple sites [Barak et al, 2009].

# A-to-I editing in Alu elements

## AluRNA secondary structure

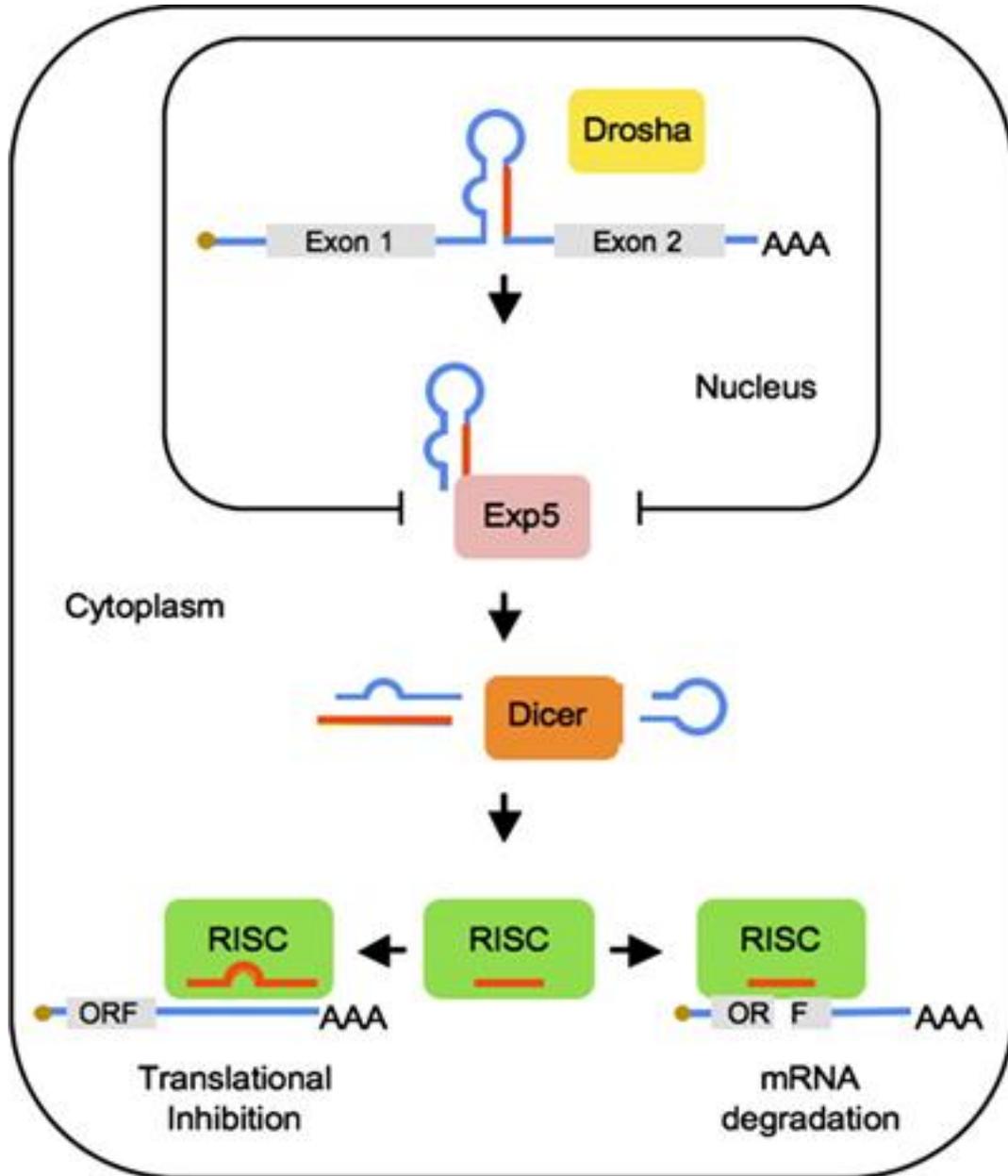


# Potential functional roles of exonized ALUs

## → **Antisense-mediated control of gene expression (miRNA targets)**

- ◆ The majority of the Alus in **3'UTRs** of analyzed human genes were found to carry strong potential **target sites for different miRNAs** [Smallheiser, 2006], [Daskalova et al, 2006].
- ◆ Alus contributed to growth of cluster of **miRNAs** that are predicted to **target free Alu transcripts** and to prevent catastrophic or self-destructive intensities of Alu retroposition. So co-evolution between Human MicroRNAs and Alu-Repeats could occur [Lehnert, 2009]

# Schematic outline of miRNA biogenesis



- transcription of miRNAs genes → *pri*-miRNAs
- *pri*-miRNAs processing by Drosha → *pre*-miRNAs
- *pre*-miRNA export from nucleus
- *pre*-miRNA processing by Dicer → mature miRNA (~22 nt)
- miRNA integration as single strand in RNA-induced silencing complex (RISC).
- Targeting RISC by miRNAs to specific mRNAs by partial or full complementary binding
- Translation arrest

Umbach J L , Cullen B R  
Genes Dev. 2009;23:1151-1164

# Study design

**Search for genes with exonized  
ALUs by BLAST of Alu-  
consensus vis Refseq with  
certain search options**



**Set of genes with exonized  
ALUs**



**Search for ALU-derived  
miRNAs by TranspoMicrogene**



**Prediction of miRNAs targets  
by selected tools**



**Set of predicted miRNAs targets**



**Gene ontology analysis of each gene set,  
comparison of gene sets**

# BLAST (NCBI) search

<http://blast.ncbi.nlm.nih.gov/Blast.cgi>

>Alu-consensus/Jurka-1988

```
GGCCGGGCGCGGTGGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCCGAGGCGGGCGGA
TCACCTGAGGTCAGGAGTTTCGAGACCAGCCTGGCCAACATGGTGAAACCCCGTCTCTACT
AAAATACAAAAATTAGCCGGGCGTGGTGGCGCGCGCCTGTAATCCCAGCTACTCGGGAG
GCTGAGGCAGGAGAATCGCTTGAACCCGGGAGGCGGAGGTTGCAGTGAGCCGAGATCGCG
CCTACTGCACTCCAGCCTGGGCGACAGAGCGAGACTCCGTCTCAAAAAAAAA
```

## ◆ Search parameters:

ALU-consensus (query length 290) vis RefSeq (mRNA)  
in human genome

E<1e-50; program: megablast

search is **limited** to records matching entrez query:

mRNA NOT 'open reading frame' NOT predicted NOT

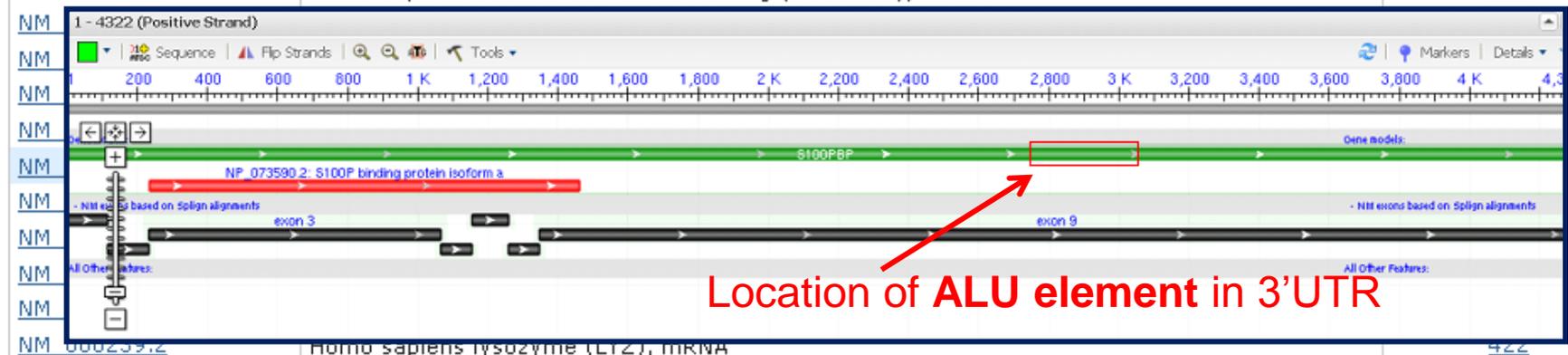
kiaa NOT clone NOT non-coding AND txid9606

[ORGN].

# BLAST results: 2103 hits (2103 transcripts of 1416 protein-coding and 1 RNA-coding genes with known GO annotation)

## Sequences producing significant alignments:

Accession	Description	Max score
<a href="#">NM_001037165.1</a>	Homo sapiens forkhead box K1 (FO XK1), mRNA	<a href="#">457</a>
<a href="#">NM_002985.2</a>	Homo sapiens chemokine (C-C motif) ligand 5 (CCL5), mRNA	<a href="#">448</a>
<a href="#">NM_000202.5</a>	Homo sapiens iduronate 2-sulfatase (IDS), transcript variant 1, mRNA	<a href="#">444</a>
<a href="#">NM_001146214.1</a>	Homo sapiens TBC1 domain family, member 15 (TBC1D15), transcript variant 2, mRNA	<a href="#">440</a>
<a href="#">NM_001146213.1</a>	Homo sapiens TBC1 domain family, member 15 (TBC1D15), transcript variant 3, mRNA	<a href="#">440</a>
<a href="#">NM_022771.4</a>	Homo sapiens TBC1 domain family, member 15 (TBC1D15), transcript variant 1, mRNA	<a href="#">440</a>
<a href="#">NM_001080480.1</a>	Homo sapiens membrane bound O-acyltransferase domain containing 1 (MBOAT1), mRNA	<a href="#">440</a>
<a href="#">NM_001171661.1</a>	Homo sapiens cytochrome b5 reductase 3 (CYB5R3), transcript variant 4, mRNA	<a href="#">433</a>
<a href="#">NM_001171660.1</a>	Homo sapiens cytochrome b5 reductase 3 (CYB5R3), transcript variant 5, mRNA	<a href="#">433</a>
<a href="#">NM_000398.6</a>	Homo sapiens cytochrome b5 reductase 3 (CYB5R3), transcript variant 1, mRNA	<a href="#">433</a>
<a href="#">NM_007326.4</a>	Homo sapiens cytochrome b5 reductase 3 (CYB5R3), transcript variant 2, mRNA	<a href="#">433</a>
<a href="#">NM_001129819.2</a>	Homo sapiens cytochrome b5 reductase 3 (CYB5R3), transcript variant 3, mRNA	<a href="#">433</a>
<a href="#">NM_002898.3</a>	Homo sapiens RNA binding motif, single stranded interacting protein 2 (RBMS2), mRNA	<a href="#">433</a>
<a href="#">NM_020728.2</a>	Homo sapiens extended synaptotagmin-like protein 2 (ESYT2), mRNA	<a href="#">431</a>
<a href="#">NM_015035.3</a>	Homo sapiens zinc fingers and homeoboxes 3 (ZHX3), mRNA	<a href="#">431</a>
<a href="#">NM_032043.2</a>	Homo sapiens BRCA1 interacting protein C-terminal helicase 1 (BRIP1), mRNA	<a href="#">429</a>
<a href="#">NM_181708.2</a>	Homo sapiens BCDIN3 domain containing (BCDIN3D), mRNA	<a href="#">429</a>



# Pre-microRNA structurally derived from ALUs

(by microTransposgene database:

<http://transposgene.tau.ac.il/cgi-bin/tg/alugene/microTransposgene.pl>)

Pre-microRNA positions	Strand	Pre-microRNA	TE
chr3:50185763-50185856	+	hsa-mir-566	AluSg (Class SINE, <b>Alu family</b> )
chr12:107754813-107754911	-	hsa-mir-619	L1MC4 (LINE, L1 family), AluSx (Class SINE, <b>Alu family</b> )
chr22:19718465-19718561	-	hsa-mir-649	L1M4 (LINE, L1 family), MER8 (DNA, MER2_type family), AluSx (Class SINE, <b>Alu family</b> )

[http://www.mirbase.org/  
search.shtml](http://www.mirbase.org/search.shtml)

hsa-mir-566

[HGNC:MIR566](#)

Homo sapiens miR-566 stem-loop

```
-----gcuagg u gg --c ga a a u
      cg ggu cggggcg cugu uccca cu c c
      || ||| ||||| |||| ||||| || |
      gc cca guucgc gacg ggggu gg g a
cgagugacguuggaagcggagg - -a uaa ac c a g
```

hsa-mir-619

[HGNC:MIR619](#)

Homo sapiens miR-619 stem-loop

```
-c cc -cu ccucccaaaa au ag cugc ga
gc ac cag ugcuggg uacaggcaug cca gguc c
|| || ||| ||||| ||||| ||| |||
cg ug guc augaccg guguuuguac ggu ccag c
ga uu acu ----- -- -a ---- ua
```

hsa-mir-649

[HGNC:MIR649](#)

Homo sapiens miR-649 stem-loop

```
ggcc c u -- u uu gaaa c
uagc aaauac gu auuuuuga cgacau gguu aaauu u
|||| ||||| || ||||| ||||| ||| |||||
gucg uuugug ca ugagaacu guugug ccaa uuaug a
---- u u cc u -u auga u
```

"The colorectal microRNAome"  
Cummins JM et al.  
Proc Natl Acad Sci  
103:3687-3692 (2006).

# Target prediction for ALUs derived miRNAs

<b>Tool</b>	<b>Update</b>	<b>Algorithms</b>
<b>microRNA.org</b>	2008	1 (miRanda)
<b>Targetscan</b>	2009	1 (Targetscan)
<b>PicTar</b>	2007	1 (PicTar)
<b>Magia</b>	2010	3 (PITA, Target-scan, miRanda)
<b>miRror</b>	2010	12 (в т.ч PITA, Targetscan, miRanda)
<b>DIANA microT v3.0</b>	2010	12
<b>miRWalk</b>	2010	8 (в т.ч. PITA, Targetscan, Diana, miRanda, Pictar)
<b>RSSF/miRNA target search</b>	2009	Perfect seed match (at least 7nt)
<b>ncRNAppi</b>	2008	1 (Jaccard index)
<b>EIMMo3</b>	2009	1 EIMMo

# http://www.ma.uni-heidelberg.de/apps/zmf/mirwalk/mirnapredictedtarget.php

## MicroRNAs Predicted Targets in mRNA 3' UTR Region Produced by miRWalk and Other Programs

Note : The below table displays all putative miRNA sites produced by both miRWalk and other programs. It contains all the putative targets of other programs (3rd party algorithms).

[See Complete Table](#)
[Paging View](#)
[Download Table](#)

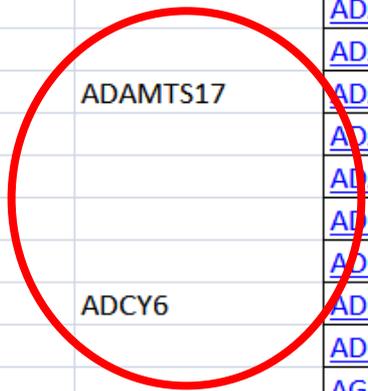
MicroRNA	Gene	DIANAmT	miRanda	miRDB	miRWalk	PICTAR4	PICTAR5	PITA	RNA22	RNAhybrid	Targetscan	SUM
<a href="#">hsa-miR-619</a>	<a href="#">GLCCI1</a>	0	1	1	1	0	0	1	0	1	1	6
<a href="#">hsa-miR-649</a>	<a href="#">JAG1</a>	0	1	1	1	0	0	1	0	1	1	6
<a href="#">hsa-miR-649</a>	<a href="#">KIN</a>	0	1	1	1	0	0	1	0	1	1	6
<a href="#">hsa-miR-649</a>	<a href="#">RAB6IP1</a>	0	1	1	1	0	0	1	0	1	1	6
<a href="#">hsa-miR-649</a>	<a href="#">HEY2</a>	0	1	1	1	0	0	1	0	1	1	6

2907	<a href="#">hsa-miR-619</a>	<a href="#">AMMECR1</a>	0	0	0	1	0	0	1	0	0	1	3
2908	<a href="#">hsa-miR-649</a>	<a href="#">USP15</a>	0	1	0	0	0	0	1	0	0	1	3
2909	<a href="#">hsa-miR-619</a>	<a href="#">SLC23A2</a>	0	0	0	1	0	0	1	0	0	1	3
2910	<a href="#">hsa-miR-566</a>	<a href="#">THRAP3</a>	0	0	0	1	0	0	1	0	1	0	3
2911	<a href="#">hsa-miR-649</a>	<a href="#">MED13</a>	0	1	0	1	0	0	1	0	0	0	3
2912	<a href="#">hsa-miR-619</a>	<a href="#">CDC34</a>	0	0	0	1	0	0	1	0	0	1	3
2913	<a href="#">hsa-miR-649</a>	<a href="#">SLC12A6</a>	0	1	0	0	0	0	1	0	0	1	3
2914	<a href="#">hsa-miR-619</a>	<a href="#">ROD1</a>	0	1	0	1	0	0	1	0	0	0	3
2915	<a href="#">hsa-miR-566</a>	<a href="#">ADA</a>	0	0	0	1	0	0	0	0	1	0	2
2916	<a href="#">hsa-miR-649</a>	<a href="#">CDH2</a>	0	0	0	0	0	0	1	0	1	0	2
2917	<a href="#">hsa-miR-619</a>	<a href="#">AKT3</a>	0	0	0	1	0	0	1	0	0	0	2
2918	<a href="#">hsa-miR-566</a>	<a href="#">MED6</a>	0	0	0	1	0	0	1	0	0	0	2
2919	<a href="#">hsa-miR-619</a>	<a href="#">NR2E3</a>	0	0	0	0	0	0	1	0	0	1	2
2920	<a href="#">hsa-miR-649</a>	<a href="#">GNPDA1</a>	0	0	0	1	0	0	1	0	0	0	2
2921	<a href="#">hsa-miR-649</a>	<a href="#">KCNE3</a>	0	0	0	0	0	0	1	0	0	1	2

# Gene sets comparison by Visual Basic macros for Excel (Find\_Matches)

	A	B	C	D
1	A2ML1		<a href="#">A4GALT</a>	
2	AAK1		<a href="#">ABCC4</a>	
3	AARSD1		<a href="#">ABHD14B</a>	
4	AASS		<a href="#">ABHD2</a>	
5	ABCB5		<a href="#">ABHD8</a>	
6	ABHD1		<a href="#">ABRA</a>	
7	ABHD11		<a href="#">ACAD9</a>	
8	ABHD15		<a href="#">ACBD3</a>	
9	ABL2		<a href="#">ACCN1</a>	
10	ACACB		<a href="#">ACSBG1</a>	
11	ACBD4		<a href="#">ACSF3</a>	
12	ACBD7		<a href="#">ACSS2</a>	
13	ACOT13		<a href="#">ADAM11</a>	
14	ACOX1		<a href="#">ADAM8</a>	
15	ACTR10		<a href="#">ADAMDEC1</a>	
16	ADAMTS17	ADAMTS17	<a href="#">ADAMTS1</a>	
17	ADAMTS2		<a href="#">ADAMTS17</a>	
18	ADAMTS4		<a href="#">ADAMTS19</a>	
19	ADAT1		<a href="#">ADCY6</a>	
20	ADCY1		<a href="#">ADM</a>	
21	ADCY6	ADCY6	<a href="#">ADM2</a>	
22	ADIPOQ		<a href="#">ADPRHL2</a>	
23	ADRA1A		<a href="#">AGBL2</a>	
24	ADRBK2		<a href="#">AGTRAP</a>	
25	AFMID		<a href="#">AHCY</a>	

identities	
	ADAMTS17
	ADCY6
	AKAP5
	ANGEL2
	ARFIP2
	ASB6
	ASB6
	ATP1B4
	ATP1B4
	ATXN3
	BDH1
	C1QTNF3
	CA5B
	CBFA2T2
	CC2D1B
	CCDC113
	CCL22
	CCRN4L
	CDKN2AIPNL
	CHP



# GO enrichments analysis

GO-enrichment tool	URL	Ref/Update
<b>GORilla</b>	<a href="http://cbl-gorilla.cs.technion.ac.il/">http://cbl-gorilla.cs.technion.ac.il/</a>	2009
<b>Genecodis</b>	<a href="http://genecodis.dacya.ucm.es/analysis/">http://genecodis.dacya.ucm.es/analysis/</a>	2009
<b>GOTree machine</b> (WebGestalt2)	<a href="http://bioinfo.vanderbilt.edu/webgestalt/option.php">http://bioinfo.vanderbilt.edu/webgestalt/option.php</a>	2010
<b>GOToolBox</b>	<a href="http://genome.crg.es/GOToolBox/">http://genome.crg.es/GOToolBox/</a>	2009
<b>GOSTat</b>	<a href="http://gostat.wehi.edu.au/cgi-bin/goStat.pl">http://gostat.wehi.edu.au/cgi-bin/goStat.pl</a>	2009

# Gorilla

mRNAs with ALUs in UTR	Targets of hsa-miR-566, hsa-miR-619, hsa-miR-649	133 identical matches
<p>ATP biosynthetic process</p> <p>DNA catabolic process</p> <p><b>ribonucleotide biosynthetic process</b></p> <p>heterocycle metabolic process</p> <p>multicellular organismal process</p> <p>oxidation reduction</p> <p>proton transport</p> <p><b>signal transduction</b></p> <p>cell morphogenesis</p> <p><b>hydrolase activity</b></p> <p>receptor binding</p> <p><b>transmembrane transporter activity</b></p> <p>cytokine activity</p> <p>extracellular region</p> <p><b>plasma membrane</b></p>	<p><b>ATP biosynthetic process</b></p> <p>ATP metabolic process</p> <p><b>integrin-mediated signaling pathway</b></p> <p><b>proteolysis</b></p> <p>developmental process</p> <p>plasma membrane organization</p> <p><b>metalloendopeptidase activity</b></p> <p>ATPase activity, coupled to transmembrane movement of ions</p> <p><b>hydrolase activity</b></p> <p>ligase activity, forming carbon-sulfur bonds</p> <p>intrinsic to membrane</p> <p><b>plasma membrane</b></p>	<p><b>regulation of cyclic nucleotide biosynthetic process</b></p> <p>regulation of cAMP biosynthetic process</p> <p>regulation of cAMP metabolic process</p> <p>No enrichment in function and component</p>

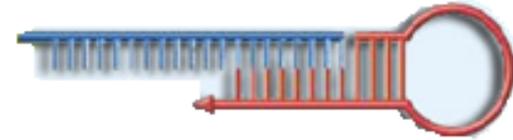
# Genecodis

mRNAs with ALUs in UTR (1417)	Targets of hsa-miR-566, hsa-miR-619, hsa-miR-649 (1205)	133 identical matches
<p><b>regulation of transcription, DNA-dependent (BP)</b></p> <p>protein amino acid phosphorylation (BP)</p> <p>transmembrane transport (BP)</p> <p><b>metal ion binding (MF)</b></p> <p>zinc ion binding (MF)</p> <p><b>protein binding (MF)</b></p> <p>DNA binding (MF)</p> <p>hydrolase activity (MF)</p> <p><b>nucleus (CC)</b></p> <p><b>membrane (CC)</b></p> <p>endosome membrane (CC)</p> <p><b>Golgi apparatus (CC)</b></p>	<p><b>protein binding (MF)</b></p> <p><b>nucleus (CC)</b></p> <p>cytoplasm (CC)</p> <p><b>membrane (CC)</b></p> <p><b>metal ion binding (MF)</b></p> <p>nervous system development (BP)</p> <p>nucleotide binding (MF)</p> <p><b>regulation of transcription, DNA-dependent (BP)</b></p> <p><b>Golgi apparatus (CC)</b></p> <p><b>mitochondrion (CC)</b></p>	<p>No enrichment for process</p> <p>Function:</p> <p><b>protein binding (MF)</b></p> <p>Cellular component:</p> <p>intracellular (CC)</p> <p><b>mitochondrial inner membrane (CC)</b></p> <p><b>nucleus (CC)</b></p> <p><b>Golgi apparatus (CC)</b></p> <p>membrane raft (CC)</p>

# GOStat

mRNAs with ALUs in UTR	Targets of hsa-miR-566, hsa-miR-619, hsa-miR-649	133 identical matches
<p><b>Intracellular membrane-bound organelle</b></p> <p>Nucleus</p> <p><b>Protein binding</b></p> <p>Biological regulation</p> <p>Membrane</p> <p><b>Golgi apparatus</b></p> <p><b>Developmental process</b></p> <p>Metal ion binding</p> <p><b>Cell differentiation</b></p> <p>Endosomes</p>	<p>Cytoplasm</p> <p><b>Protein binding</b></p> <p>Membrane part</p> <p><b>Developmental process</b></p> <p><b>Cell differentiation</b></p> <p>Plasma membrane</p>	<p><b>Intracellular membrane-bound organelle</b></p> <p>Mitochondrial membrane</p> <p><b>Developmental process</b></p> <p><b>Golgi apparatus</b></p> <p>Regulation of cellular process</p> <p>Signal transduction</p>

# Conclusions



- ❑ Both miRNAs targets prediction and GO enrichment analysis are highly dependent on bioinformatics tool selected.
- ❑ Rather low number of identical matches within 2 gene sets (about 10%) was revealed. So ALU-derived miRNAs binding can't be considered the main regulatory mechanism for genes with exonized ALUs.
- ❑ All 3 set of genes investigated are associated with signal transduction, regulation of developmental processes, protein binding, nucleus and Golgi apparatus location.
- ❑ Genes with exonized ALUs are specifically linked with phosphorylation and hydrolysis metabolic reactions; metal ion binding, exocytosis and intracellular membrane location of encoded proteins.
- ❑ Genes that are targets for ALUs-derived miRNAs are specifically GO enriched for proteolysis and peptidase activity, cytoplasm and plasma membrane.