



Supplementary Figure 1. Genome structure of lnc-MGC. Genome organization shows that the mouse miR-379 megacluster is located within the largest miRNA cluster currently identified in the genome. It maps within the *DLK-DIO3* genomic region (mouse chr 12, human chr14), which is home to several miRNAs and lncRNAs. In the mouse genome, this locus is located at chr12qF1 (top). Several transcripts have been identified in this region, although all of these transcripts appear to be parts of a single long transcript. Because of rapid processing of this primary transcript, the complete large transcript could not be annotated and cloned by conventional approaches. However, partial fragments were cloned, and the figure depicts an assembled transcript from cloned and deposited sequences (in the database) which is shown along with the UCSC Genome browser. We named the longest noncoding RNA (lncRNA) as "lnc-MGC", the 3' region of which overlaps with Mirg and middle region with Gm2922, which are also other ncRNAs in this region. The 5' region, which starts from transcription start site (TSS) of lnc-MGC, was cloned by 5' RACE. miR-882 is located far-upstream of the miR-379 cluster and not covered by lnc-MGC.

а							
	copy/cell						
	SD	TGF	b	NG		HG	
	3.51081	2	3.94908	3.9	986743	5.3	39276
	3.65070)3 4	.357102	3.9	923746	5.	.06511
	3.77468	32 4	.666205	i 3.9	963863	4.7	76591
	3.6492	26 5	.486623	3.0	872292	4.4	72395
	3.65172	26 5	.451668	3	8.66281	4.4	51617
	3.73277	714	.955751	3.6	617369	4.7	44039



Supplementary Figure 2. Copy numbers of lnc-MGC in mouse mesangial cells. Copy numbers per cell of the upstream part (from initiator to just upstream of miR-379, INR-R2) of lncMGC were calculated by using the cloned fragment of INR-R2 (5' region of lncMGC) as standard (serial dilution of the fragment). Absolute numbers of INR-R2 molecules were calculated from absolute amount of INR-R2 fragments by real time qPCR. RNA was extracted from MMC (the numbers of cells were counted). Copy numbers of lncMGC per cell were calculated as absolute numbers of lncMGC molecules in sample RNAs divided by total cell number. Copy numbers of lncMGC were 3-4 copies per cell in control cells, and $4\sim6$ copies per cell in HG or TGF- β treated mesangial cells Data shows exact numbers in six cultures (a) and bar graph depiction (b).



Supplementary Figure 3. The host lnc-RNA (lnc-MGC) transcript of the megacluster of miRNAs (miR-379 cluster) and key component miRNAs are up-regulated in the glomeruli of C57BL/6 mice with longer duration of diabetes and significant renal dysfunction (22 weeks after onset of diabetes). (a) The expression of lnc-MGC and four cluster miRNAs in glomeruli from STZ diabetic mice (cortex and glomeruli) relative to controls (vehicle injected CTR). Five mice in each group. (b) Significant lower expression of potential targets of miR-379 cluster in kidney glomeruli from diabetic mice (STZ) than the non-diabetic control mice. Results are mean + SE. Five mice in each group. *, P<0.05.

a Potential targets

Supplementary Figure 4

RNA binding proteins

Translational regulators (CUGBP2, PUM2, TNRC6B, CPEB2/4, Rc3h1, HuR) RNA splicing factors (CUGBP2, Dxd3x, SFRS1, COX-2: VEGF alternative splicing)

Transcription factors

FOXP2, Arid2, NF1a/b,

Zinc-finger proteins (Zfx, Zfp148, Trps1, KLF12, KLF3)

Cofactors PHF21A (BHC 80 unmethylated histone biding protein in repressor complex)

ER stress-related EDEM3, ATF3

Others PTEN (Akt activation & protein synthesis)









Supplementary Figure 4. (a) IPA analysis on potential human gene targets of miR-379

cluster. The potential human gene targets containing at least 3 conserved binding sites for each miRNA in the cluster were predicted by seed-based algorithm¹ of TargetScan (http://www.targetscan.org/). All the target genes were then pooled to generate a target gene set. Ingenuity pathway analyses (IPA) were applied to this gene set to identify statistically-enriched biological functions and pathways at Benjamini-Hochberg (B-H) adjusted p values < 0.05 by right-tailed Fisher's exact tests. The significance level was presented in the y-axis as -log10 (B-H P value) in the barplots. (b-f) Human gene targets of the cluster miRNAs related to their molecular cellular functions (b), gene sets related to diseases (c), enriched canonical pathways (d), physiological development and function (e) and toxicity (f). For analyses with more than 10 categories identified, the top 10 significant ones were displayed.











Supplementary Figure 5. IPA analysis on potential mouse target genes of the miR-379

cluster as predicted by TargetScan mouse. Similar to the human target genes evaluated by seed-based algorithm¹ of TargetScan (http://www.targetscan.org/) in Supplementary Figure S4, the IPA analyses here included statistically-enriched molecular cellular functions (a), genesets related to diseases (b), enriched canonical pathways (c), physiological development and function (d) and toxicity (e). Please refer to the legend of Supplementary Figure S4 for further details.



Supplementary Figure 6. IPA network analysis on potential targets of miR-379 cluster. The network analysis depicted relationships of the potential target genes of the miRNA cluster to Akt (a) and Erk (b) kinases.

Human EDEM3 3'UTR			Supplementary Figure 7
k	1k 1	2k	3k
Position 552-558 of D	DEM3 3' UTR 5'	CUCAUUGCUUUCUCU	JGUUUCAU
hsa-miR-494	3'	CUCCAAAGGGCACAUA	ACAAAGU
Position 1277-1283	of EDEM3 3'UTR 5'.	cccuuuuuuuuuuuuuuuuuuuuuuuuuuuu	JGUUG
hsa-miR-495	3'	UU CUUCAC GUGGUA CAAA	ACAAA
Position 1975-198	31 of EDEM3 3' UTR 5'	UCGAUUACAGAAGCCUUA	UAUAC
hsa-miR-410	3'	UGUCCGGUAGACACAAU	AUAA
Position 2100-2	2106 of EDEM3 3' UTR	5'AAUGGCAUGAAGGA	UUGUGUGAC
hsa-miR-377		3' UGUUUUCAACGGA	 AACACUA
Position 22	76-2282 of EDEM3 3' U	TR 5'UACCCAGA	AGGAAUUAUACUCAA
hsa-miR-496		3' CUCUAACC	 GGUA CAUUAU GAGU
Position	2505-2512 of EDEM3 3	UTR 5'AAAGA	UUCAGGGGAUUCUAUGAA
hsa-miR-	376a	II 3' UGCACCU	
Positio	n 2535-2541 of EDEM3	3' UTR 5'AUUUAGA	AAACAUCUGGUCUACCU
<u>hsa-miR</u>	-379	3' GGAUG	 CAAGGUAUCAGAUGGU
Positi	on 2614-2620 of EDEM3	3'UTR 5'	.UUGUUUAAGAAAGAUUUAUAUAA
hsa-mi	R-410	3'	 UGUCCGGUA GACACA AUAUAA
Posi	tion 2821-2827 of EDE	M3 3' UTR 5'CC	CAUAAAGUUUUAAGUGUGAAA
hsa-	miR-377	3' 1	IIIIII IIIII UGUUUUCAACGGAAACACACUA
Po	sition 2866-2872 of H	DEM3 3' UTR 5'U	UUGGUAUGGGAUAUUUUGUUAG
h	sa-miR-495	3' U	IIIII IU CUUCAC GUGGUA CAAACAAA
_	Desition 2020-2024	ר אראשער אין אראשריים בי	
	hea-miD-404	SE EDENS S UIK S'	CHAMAGAGGGGAGAGGGGGGGGGGGGGGGGGGGGGGGGGG
	100 JUL 494	J	COCCHARGOUCACACACAAAGO

Supplementary Figure 7. The location of the binding sites of multiple cluster miRNAs in the 3'UTR of human *EDEM3* obtained from seed-based algorithm¹ of TargetScan (<u>http://www.targetscan.org/</u>) are shown.

3k Position 999-1005 of EDEM3 3' UTR 5' ... AAAUCAUGGGUUUAGGUUUGUUU... 1111111 UU CUUCAC GUGGUA CAAACAAA mmu-miR-495 31 Position 1022-1028 of EDEM3 3' UTR 5' ... UGUUUUGUUUUAACAAAUACUCC... 1111111 mmu-miR-496 31 CUCUAACC GGUACAUUAUGAGU Position 2035-2042 of EDEM3 3' UTR 5' ... CUAACUAGAAGGAAUAAUACUCA... 1111111 mmu-miR-496 31 CUCUAACCGGUACAUUAUGAGU Position 2218-2225 of EDEM3 3' UTR 5' ... UUCAUUGUUGUUGAUGUUUGUUA... 1111111 UUCUUCACGUGGUACAAACAAA mmu-miR-495 3' Position 2301-2307 of EDEM3 3' UTR 5' ...GUUUAGAAACAUCUGGUCUACCU... 1111111 **GGAUG CAAGGUAUCAGAUGGU** 31 mmu-miR-379 Position 2384-2390 of EDEM3 3' UTR 51 ...UUGACUAAGAAAGAUUUAUAUAA... 111111 UGUCCGGUAGACACAAUAUAA mmu-miR-410 31 Position 2633-2639 of EDEM3 3' UTR 5' ... UUUUGGGUGGGGUAUUUUGUUAA... | | | | | | mmu-miR-495 31 UUCUUCAC GUGGUA CAAACAAA Position 2871-2877 of EDEM3 3' UTR 5' ... UUAUACAAAGCCAGCGUUUGUUC... 1111111 mmu-miR-495 31 UUCUUCA CGUGGUACAAACAAA Position 2944-2950 of EDEM3 3' UTR 5' ... AUUCAAAUAGUGCUUACAACUUU... 1111111 GCUUAG GUGGUG CUUGUU GAAG mmu-miR-382 3' Position 2977-2983 of EDEM3 3' UTR 5' ... AGGUAGCAUUCAGUCAAUACUCC... 1111111 CUCUAACC GGUACAUUAUGA GU mmu-miR-496 31 Position 3262-3269 of EDEM3 3' UTR 5' ... AAAAUGUAUAUAUCCUUGUAUA... 1111111 mmu-miR-381 31 UGUCUCUC GAACGG GAACAUAU

Supplementary Figure 8. The location of the binding sites of multiple cluster miRNAs in the 3'UTR of mouse *Edem3* obtained from seed-based algorithm¹ of TargetScan (<u>http://www.targetscan.org/</u>) are shown.

Human ATF3 3' UTR Supplementary Figure 9 1.2k 1.3 1.4 1.5k 1.1k 1.6k 0.1k 0.2k 0.3k 1k 0.4k 0.5k 0.9k 0.6k 0.7k 0.8k Position 150-156 of ATF3 3' UTR 5' ... AGCUUGAUGAGCCCCGGUGUGUC... 1111111 hsa-miR-329-3p 31 UUUCUCCAAUUGGUCCACACAA Position 272-278 of ATF3 3' UTR 5' ...CGGAGAAGCUGGAAAGUGUGAAU... 111111 UGUUUUCAACGGAAACACACUA hsa-miR-377-3p 31 ...GAUGGCCCCCAGCUGGUGUCCUG... Position 724-730 of ATF3 3' UTR 5' 1111111 hsa-miR-1197 31 UCUUC AUCUGGUACACAGGAU Position 1165-1171 of ATF3 3' UTR 5' ... CAAAAUCCAUGGGCA-GUAUGAUG... 1111111 31 hsa-miR-487a-3p UUGACCUACAGGGACAUACUAA Position 1203-1209 of ATF3 3' UTR 5' ...CAAACUCAGUUCCAAAGUCACAG... 111111 hsa-miR-134-5p 31 GGG GAGACC AGUUGG UCAGUGU Position 1532-1538 of ATF3 3' UTR 5' ... UCUAUUAAAAUUCUGAUGUUUCU... 1111111 hsa-miR-494-3p 31 CUCCAAAGGGCACAUACAAAGU

Supplementary Figure 9. The location of the binding sites of multiple cluster miRNAs in the 3'UTR of human *ATF3* obtained from seed-based algorithm¹ of TargetScan (<u>http://www.targetscan.org/</u>) are shown.

1k 1.1k 1.2k 1.3k 1.4k 0.1k 0.2k 0.9k 0.3k 0.4k 0.5k 0.6k 0.7k 0.8k ...CAGAGAAACUGGAGAGUGUGAAU... Position 121-127 of ATF3 3' UTR 5' 111111 UGUUUUCAACGGAAACACACUA 31 mmu-miR-377-3p Position 624-630 of ATF3 3' UTR 51 ... GAUUC AGGCAGAAGUGUCUACCU... 1111111 GGAUGCAAGGUAUCA GAUGGU mmu-miR-379-5p 31 Position 624-630 of ATF3 3' UTR 5' ... GAUUCAGGCAGAAGUGUCUACCU... 1111111 ACAUGC AGUGGC CAGAUG GU mmu-miR-1193-5p 3' Position 834-840 of ATF3 3' UTR 5' ...GAUGUUUGUCUUGCACAACAUUG... 1111111 mmu-miR-409-3p 3' UCCCCAAGUGGCUCGUUGUAAG Position 1140-1146 of ATF3 3' UTR ...AGGGUGUAGGACUCCAUACUCAG... 5' 111111 mmu-miR-496a-3p.1 31 CUCUAAC CGGUAC AUUAUG AGU Position 1146-1152 of ATF3 3' UTR 5' ... UAGGACUCCAUACUCAGUGACAG... 111111 3' CCAUCACCCGGCUCGGCUCACUGU mmu-miR-668-3p Position 1350-1356 of ATF3 3' UTR 5' ... ACUGUUAAAAUC CUGAUGUUUCU... | | | | | | | | mmu-miR-494-3p 31 CUCCAAAGGGCACAUACAAAGU

Supplementary Figure 10. The location of the binding sites of multiple cluster miRNAs in the 3'UTR of mouse *Atf3* obtained from seed-based algorithm¹ of TargetScan (<u>http://www.targetscan.org/</u>) are shown.

Human TNRC6B 3' UTR

Supplementary Figure 11

k 1k	2k	3k	4k	5k	6k	7k	8k	9k	10k	11k	12k
Position	353-359 of	TNRC6B 3	UTR	5'	t	UUCACUUU	UUUCAUGU	JUAUAUG.	•		
hsa-miR-4	10			3'		UGUCCGG	UAGACACA	AUAUAA			
Position	442-449 of	E TNRC6B	3' UTR	5'U	GUUUCC	GUCCUUAG(GUCUACCA				
hsa-miR-	379			3'	G GAUG	CAAGGUAU	CAGAUGGU				
Position	423-429 of	E TNRC6B	3' UTR	5'.	ACUU	UGUUUGCA(CUGGGUGU 	GUU 			
hsa-miR-	329			3'	ບບບບບ	CCAAUUGGI	UCCACA	CAA			
Position	512-518 o	f TNRC6B	3'UTR	5'	GG	GAAGACUU	GAC GGAGC	CUCAC			
hsa-miR-	485-5p			3'	cu	UAAGUAGU	GCCGGUCG	III GAGA			
Positi	on 1431-143	7 of TNRC	6B 3' UT	TR 5'	AA	ACGUUUAC	UUAACGAA				
hsa-mil	R-543			3'	υ	UCUUCACG	UGGC GCUU	IIII JACAAA			
Positi	on 1447-14.	53 of TNR	С6В 3' О	JTR 5	'AA	UGUUCUUA	AACCAGUG	GUGUAC			
hsa-mi	.R-329			3	י ש	UCUCCAAU	UGGUCCAC	CACAA			
	Position 34	481-3488 (of TNRC6	в з' UT.	R .	5't	JUGGAUUG	CUGAGAAU	CUAUGUA.		
	hsa-miR-376	5 <u>c</u>			:	3'	UGCAC CI	UUAAAGGA	GAUACAA		
	Positi	on 4447-4	454 of T	NRC6B 3	' UTR	5'	.UUUGGCA	AGAGCCAU	GUCUACUA		
	hsa-mil	R-411				3'	GCAUG	C GAUAUG C	CAGAUGAU	T	
	Posit	ion 4511-	4517 of	TNRC6B	3' UTR	5'.	AGUGCC	υυς υυς υς	UUCUACCA	.C	
	hsa-m	iR-379				3'	GGAUGC	AAG GUAUC	-AGAUGGU	г	
		Position	9935-994	41 of T1	WRC6B 3	' UTR	5'UG	GUGAAACO	CCGUCUCU	ACUAA	
		hsa-miR-4	11				3' G	CAUGCGAU	AUGCCAGA	UGAU	
		Position	n 12141-1	12147 o:	f TNRC6	5B 3' UTR	5'	ААААА	CAAACAAU	AAAAUGUUA.	A
		hsa-miR-	-543				3'	ໜດໜ	CACGUGGCO	GCUUACAAA	
		Positi	ion 1215)	1-12157	of TNF	С6В 3' U	TTR	5'	AUAAAAU	GUUAA ACUCI	JACUAA
		hsa-mi	IR-411				:	3'	GCAUGC G	AUAUGCCAG	AUGAU

Supplementary Figure 11. The location of the binding sites of multiple cluster miRNAs in the 3'UTR of human *TNRC6B* obtained from seed-based algorithm¹ of TargetScan (<u>http://www.targetscan.org/</u>) are shown.

Mouse Tnrc6b 3' UTR

Supplementary Figure 12

4								
k 1k 2k Position 351-357 of TM	3k 4k IRC6B 3' UTR	5' ^{5k}	WUCAC	υυυυυδοαυ	GUUAUAUG	9k	10k	11k
mmu-miR-410		3'	UGUC	CGGUAGACA	CAAUAUAA	7		
Position 419-425 of	TNRC6B 3' UTR	5'A	сипленнов	ACUGGGUGU	IGUU			
mmu-miR-329		3' UU	UUUCCAAUCO	ACCCACA	CAA			
Position 438-445 of	TNRC6B 3' UTR	5'	UGUUUCCGU	CCUUAGGUC	UACCA			
mmu-miR-379		3'	GGAUGCA	AGGUAUCAG.	AUGGU			
Position 508-514 of	TNRC6B 3' UTR	5'	GGGAAG	A CUUGAC GG.	AGCCUCAC			
mmu-miR-485		3'	CUUAAG	UAGUGCC GGI	UCGGAGA			
Position 1306-13	12 of TNRC6B 3'	UTR 5'	ACA	GUAAGUUAU	IGAGCAGCCUC	c		
mmu-miR-485		3'	ст	JUAA GUAGUG	CCGGUCGGAG	A		
Position 1435-1	441 of TNRC6B 3	UTR 5	5'AAA	CGUUUACUU	AACGAAUGUUC			
mmu-miR-543		з	טט יו	CUUCACGUG	GC GCUUAC AAA	L		
Position 1451–	-1457 of TNRC6B	3' UTR	5'AAU	GUUCUUAAA	CCAGUGUGUAC			
mmu-miR-329			3' UUU	UUCCAAUCG.	ACCCACACAA			
Positio	n 4611-4617 of	TNRC6B 3'	UTR 5'	GCUUGCT	JAGUCACCAUU	AUAUAG		
mmu-miR	-410		3'	UGUCC	II GGUAGACACAA	UAUAA		
	Position 10987-	10993 of	TNRC6B 3'	UTR 5'	UUCA	CUUAAAAA	ACAAAUGUU	AA
	mmu-miR-543			3'	ໜະຫ	UCACGUGGO	GCUUACAA	¥.
	Position 10997-	11003 of	TNRC6B 3'	UTR 5'	AAACA	AAUGUUAA	ACUCUACUA	A
	mmu-miR-411			3'	GCAU	IGC GAUAUG	CCAGAUGAU	í
	Position 110	91-11097	of TNRC6B	3' UTR	5'GA1	UUUCAAAAA	AUAUUAAAAU	4UAU
	mmu-miR-410				3' U	GUCCGGUAG	GACACAAUAU	JAA

Supplementary Figure 12. The location of the binding sites of multiple cluster miRNAs in the 3'UTR of mouse *Tnrc6b* obtained from seed-based algorithm¹ of TargetScan (<u>http://www.targetscan.org/</u>) are shown.

Human CELF2 3' UTR (CUGBP2)

Supplementary Figure 13

€ + + + + + + + + + + + + + + + + + + +	-++++++++++ 2k	 3k	++++++++++++++++++++++++++++++++++++++	++++++++++++++++++++++++++++++++++++++	++++++++++++++++++++++++++++++++++++++	-+++++++++++++++++++++++++++++++++++++
Position 754-760 of CE	LF2 3' UTR	5'GA	GUGAAAAUACU	UGAUGUUUCU		
hsa-miR-494		3' 0	UCCAAAGGGCA	IIIIII CAUACAAAGU		
Position 1579-1585 c	of CELF2 3'	UTR 5'	UGUGACCU	CAUCUAGCUAUGA	AU	
<u>hsa-miR-376b</u> Position 1934-194	0 of CELF2 3	3' 3' UTR 5'	UUGUACCU	AAAAGGAGAUACU UGGCUCACUUUCU	VA JCAU	
hsa-miR-539		3'	UGUGUGO	UUCCUAUUAAAGA	AGG	
Position 2097-2	103 of CELF2	2 3' UTR	5'ACC	UAUAUUUUUAUACU	GUUUCAA	
hsa-miR-494			з' сис	I CAAAGGGCACAUA	LILLI CAAAGU	
Position 2531	-2537 of CE	LF2 3' UTR	5'	AUUUUAUUAUGUG	GUUUUGUAUAA	
hsa-miR-300			31	UCUCUCUCAGACO	IIIII GGAACAIIAII	
Position 2531	L-2537 of CE	LF2 3' UTR	5'	. AUUUUAUUAUGU	GUUUUGUAUAA	
hsa-miR-381			3'	UGUCUCUC GAAC	GGGAACAUAU	
Position 25	85-2592 of	CELF2 3' Մ	TR 5'	. A A A A A A A G GUUA	CAAAGUUUGUUA	
hsa-miR-495	<u>i</u>		3'	UUCUUCACGU	GUACAAACAAA	
Position 2	632-2639 of	CELF2 3' U	JTR ⁵ '	CCUGAAAUUGUUA	AUUGUUUGUUA	
hsa-miR-49	5		3'	UUCUUCACGUG	JUACAAACAAA	
Positio	on 2639-2645	of CELF2	3'UTR 5'	UUGUUAUUGI	JUUGUUAUUUCUCU.	
hsa-miF	R-539		3'	UGUGUGGUI	JCCUAUUAAAGAGG	
Posit	ion 2667-267	73 of CELF2	23'UTR 5	'GUUUUUU	UAAGACAUUGUAUAA	A
hsa-m	iR-300		3	UCUCUCUC	AGACGGGAACAUAU	
Positi	ion 2667-267	3 of CELF2	3' UTR	5'G	UUUUUUGUAAGACAU I	UGUAUAA
hsa-mi	<u>iR-381</u>			3' U	GUCUCUCGAACGGGA	ACAUAU
	Position 51	02-5108 of	CELF2 3' U	ΓR 5'	AGAUUUAGAAGUACI	JCAGUCACU
	hsa-miR-134	L		3'	GGGGAGACCAGUU	GGUCAGUGU
	Position	5253-5259	of CELF2 3'	UTR 5'	UGUAAUGUAU	GUUAUUGUGUGAU
	hsa-miR-3	77		3'	UGUUUUCAA	IIIIII CGGAAACACACUA
	Posit	ion 5376-5:	382 of CELF	2 3' UTR 5'	AUCUGCACAC	CUCACUGUUUCAC
	hsa-1	niR-494		3'	CUCCAAAGGG	CACAUACAAAGU

Supplementary Figure 13. The location of the binding sites of multiple cluster miRNAs in the 3'UTR of human *CUGBP2* obtained from seed-based algorithm¹ of TargetScan (<u>http://www.targetscan.org/</u>) are shown.

Supplementary Figure 14 Mouse Celf2 3' UTR (Cuqbp2) 3 -1k Ŵ Δk Position 756-762 of CELF2 3' UTR ...GAGUGAAAAUACUUGAUGUUUCU... 5' 1111111 mmu-miR-494 31 CUCCAAAGGGCACAUACAAAGU Position 1574-1580 of CELF2 3' UTR 51 ...UGUGACCUCAUCUAGCUAUGAAU... 111111 UUCACCUACAAGGAGAUACUA 31 mmu-miR-376b ...AAACCUGUGGCAAAAAUGUUUCU... Position 1670-1676 of CELF2 3' UTR -51 1111111 mmu-miR-494 31 CUCCAAAGGGCACAUACAAAGU Position 1931-1937 of CELF2 3' UTR 5' ... UUUUUAGGUGGCUCACUUUCUCAU... 111111 UGUGUGGUUCCUAUUAAAGAGG mmu-miR-539-5p 31 Position 2558-2564 of CELF2 3' UTR 51 ...AUUUUAUUAUGUGUUUUGUAUAA... 111111 UGUCUCUC GAACGG GAACAUAU mmu-miR-381 31 ... AUUUUAUUAUGUGUUUUGUAUAA... Position 2558-2564 of CELF2 3' UTR 51 ||||||111111 mmu-miR-539-3p 31 UUUUUUUUUAAUAGG---AACAUAC Position 2611-2618 of CELF2 3' UTR 51 ...AAAAAAGGUUACAAAGUUUGUUA... 1111111 mmu-miR-495 31 UUCUUC ACGUGGUACAAA CAAA Position 2658-2665 of CELF2 3' UTR 5' ...CCUGAAAUUGUUAUUGUUUGUUA... 1111111 UUCUUCACGUGGUACAAACAAA mmu-miR-495 3' Position 2665-2671 of CELF2 3' UTR 5' ... UUGUUAUUGUUUGUUAUUUCUCU... 1111111 mmu-miR-539-5p 31 UGUGUGGUUCCUAUUAAAGAGG Position 2693-2699 of CELF2 3' UTR ... GUUUUUUGUAA GACAUU GUAUAA... 51 111111 mmu-miR-381 31 UGUCU CUCGAA CGGGAA CAUAU ... GUUUUUUGUAAGA CAUUGUAUAA... Position 2693-2699 of CELF2 3' UTR 51 111111 UUUUUCUUUAAUA GGAACAUAC mmu-miR-539-3p 31 5' ... AUUUGAUUUAAUGUGUGUGUGAA... Position 3576-3583 of CELF2 3' UTR 1111111 UGUUUUCAACGGAAACACACUA 31 mmu-miR-377 Position 4081-4088 of CELF2 3' UTR 51 ... AGGGCUUGGUUUUGCAUGUUUCA... 111111 CUCCAAAGGGCACAUACAAAGU mmu-miR-494 31 Position 4977-4983 of CELF2 3' UTR 5' ...AGAUUUAGAAGUACUCAGUCACU... 1111111 mmu-miR-134 3' GGGGAGACCAGUUGGUCAGUGU Position 5128-5134 of CELF2 3' UTR 51 ... UGUAAUGUAUGUUAUUGUGUGAU... 1111111 mmu-miR-377 3' UGUUUUCAACGGAAACACACUA

Supplementary Figure 14. The location of the binding sites of multiple cluster miRNAs in the 3'UTR of mouse *Cugbp2* obtained from seed-based algorithm¹ of TargetScan (<u>http://www.targetscan.org/</u>) are shown.

Human CPEB4 3' UTR

Supplementary Figure 15

(+ + + + + + + + + + + + + + + + + + +	
k 1k 2k	3k 4k
Position 954-961 of CPEB4 3' UTR 5'AUAUCCUAAUUUACUAAUA	ACUCA
hsa-miR-496 3' CUCUAACCGGUACAUUAL	JGAGU
Position 2127-2133 of CPEB4 3' UTR 5'UGCACAN	UAAUGUAUAUUUGUUAU
hsa-miR-495 3' UUCUUCA	ACGUGGUACAAACAAA
Position 2144-2150 of CPEB4 3' UTR 5'UGUUAUGCACU	ACUUUUGUAUAU
hsa-miR-300 3' UCUCUCUCAGA	CGGGAACAUAU
Position 2144-2150 of CPEB4 3' UTR 5'UGUUAUGCAC	UACUUUUGUAUAU
hsa-miR-381 3' UGUCUCUCGA	ACGGGAACAUAU
Position 2488-2495 of CPEB4 3' UTR 5' UAAUUUAA	GAAAUAG-UCUAUGUA
hsa-miR-376c 3' UGCAC	III IIIII CUUAAAGGAGAUACAA
Position 2772-2779 of CPEB4 3' UTR 5'GCCUG	GCCUUGGGACAGGUGUGUA
hsa-miR-329 3' UUUU	CUCCAAUUGGUCCACACAA
Position 2816-2822 of CPEB4 3' UTR 5'GUA	AGAAAUUGUUAUUCUACUAA
hsa-miR-411 3' GC	AUGCGAUAUGC CAGAUGAU
Position 2838-2844 of CPEB4 3' UTR 5'AUAUUU	ACUUGUGAUUGUGUGAC
hsa-miR-377 3' UGUUU	UCAACGGAAACACACUA
Position 3146-3153 of CPEB4 3' UTR 5'UGU	JUUCUGAUUAUUUUCUAUGUA
hsa-miR-376c 3'	UGCAC CUUAAA GGAGAU ACAA
Position 3228-3234 of CPEB4 3' UTR 5'	CCAUACACAGACCUCUGCAGAAU
hsa-miR-544 3'	CUUGAAC GAUUUUUACGUCUUA
Position 3544-3550 of CPEB4 3' UTR 5'	UCAGAAAUCAAUCUUUCUACUAA
<u>hsa-miR-411</u> 3'	G CAUGC GAUAUGC CAGAUGAU
Position 3738-3744 of CPEB4 3' UTR	5'AAUUUUCAUCAGAUUUUUGUUAU
hsa-miR-495	3' UU CUUCAC GUGGUA CAAACAAA
Position 3741-3747 of CPEB4 3' UTR	5' UUU CAUCAGAUUUUU GUUAUAUU
hsa-miR-410	 3' UGUCCGGUAGACACAAUAUAA
Position 4011-4018 of CPEB4 3' UTR	5'AUGUUCUACUCUUAAGUUAUAUA
hsa-miR-410	 3' UGUCCGGUAGACACAAUAUAA

Supplementary Figure 15. The location of the binding sites of multiple cluster miRNAs in the 3'UTR of human *CPEB4* obtained from seed-based algorithm¹ of TargetScan (<u>http://www.targetscan.org/</u>) are shown.

Mouse Cpeb4 3'UTR Supplementary Figure 16 2 Position 2052-2058 of CPEB4 3' UTR 5' ... UGCACAUGAUGUACAUUUGUUAU... 11111 mmu-miR-495 31 UUCUUCACGUGGUACAAACAAA Position 2069-2075 of CPEB4 3' UTR 51 ... UGUUAUGCACUACUUUUGUAUAC... 111111 mmu-miR-381 31 UGUCUCUC GAACGG GAACAUAU Position 2069-2075 of CPEB4 3' UTR 5' ... UGUUAUGCACUACUUUUGUAUAC... 111111 31 UUUUUUUUUAAUAGGAACAUAC mmu-miR-539-3p Position 2413-2420 of CPEB4 3' UTR 5' ... UAAUUUAAGAAAUAG--UCUAUGUA... 11111 1111111 31 UGCACUUUAAA GGAGAUACAA mmu-miR-376c Position 2588-2594 of CPEB4 3' UTR 5' ...GCA GACAUUUUGGGU GAAUGUUU... 1111111 31 UUCUUCAC GUGGCGCUUACAAA mmu-miR-543 Position 2704-2710 of CPEB4 3' UTR 51 ... A CAGGAC AGGUUU GUAAUGUUAG... 111111 31 UUCUUCA CGUGGC GCUUAC AAA mmu-miR-543 Position 2763-2769 of CPEB4 3' UTR 5' ...AUAUUUACUUGUGAUUGUGUGAC... 1111111 111 31 mmu-miR-377 UGUUUUCAACGGAAACACACUA Position 3070-3077 of CPEB4 3' UTR 5' ... UGUUUCUGAUUAUUU--UCUAUGUA... 1111 111111 mmu-miR-376c 31 UGCACUUUAAAGGAGAUACAA Position 3148-3154 of CPEB4 3' UTR 51 ...CCAUACACAGACCUCUGCAGAAU... 1111111 CUCGAACGAUUUUUAC GUCUUA mmu-miR-544-3p 31 Position 3463-3469 of CPEB4 3' UTR ... UCAGAAAUCAAUCUUUCUACUAA... 51 111111 mmu-miR-411 31 GCAUGCGAUAUGC CAGAUGAU Position 3661-3667 of CPEB4 3' UTR 51 ... UA AUUUCA UCAGAU UUUUGU UAU... 111111 mmu-miR-495 31 UU CUUCAC GUGGUA CAAACAAA Position 3664-3670 of CPEB4 3' UTR 5' ... UUU CAUCAGAUUUUU GUUAUAUU... 1111111 mmu-miR-410 **UGUCCGGUAGACACAAUAUAA** 31 Position 3932-3939 of CPEB4 3' UTR 5' ... AUGUUCUACUCUUAAGUUAUAUA... 1111111 mmu-miR-410 31 UGUCCGGUAGACACAAUAUAA Position 3992-3998 of CPEB4 3' UTR 5' ... UGC UAGUGGAAAAUU AAUGUUAU... 1111 111111 UUCUUCACGUGGCGCUUACAAA mmu-miR-543 31

Supplementary Figure 16. The location of the binding sites of multiple cluster miRNAs in the 3'UTR of mouse *Cpeb4* obtained from seed-based algorithm¹ of TargetScan (<u>http://www.targetscan.org/</u>) are shown.

Human PHF21A 3' UTR

Supplementary Figure 17

4 • • • • • • • • • • • • • • • • • • •			
k 1k	24.	3K	4k
Position 93-99 of PHF21A 3' UTR	5'CGGAUUUCUGO	AAAGUGCAGAAU	
hsa-miR-544	3' CUUGAACGAU	TUUUUACGUCUUA	
Position 184-190 of PHF21A 3' UTR	5'GAUCCUUCUU	AUUCU-GUGUGUAC	
hsa-miR-329	3' UUUCUCCAA	UUGGUCCACACAA	
Position 309-315 of PHF21A 3' UTR	5'AG	UGUGUGCCUGCAGCAGCCUC	с
hsa-miR-485-5p	3' C1	UUAA GUAGUG C C GGUC GGAG.	A
Position 330-336 of PHF21A 3'	UTR 5'CC	ACAGCCACGAUGGGUUUGUU	σ
hsa-miR-495	3' U	UCUUCACGUGGUACAAACAA	LÀ.
Position 410-416 of PHF21A 3'	UTR 5'CUUA	CUUGC CGAGCC GUUUGUUU.	
hsa-miR-495	זי טטכע	UCACGUGGUA-CAAACAAA	
Position 940-946 of PHF21A	3'UTR 5'	GCAGCACGC GACCCAGGUGU	JGUG
hsa-miR-329	3'	UUUCUCCAAUUGGUCCACA	ACAA
Position 944-951 of PHF2	21A 3'UTR 5'	CACGCGACCCAGGUGU	GUGUGAA
hsa-miR-377	3'	I UGUUUUCAACGGAAA	CACACUA
Position 4502-4508	of PHF21A 3' UTR	5' UUCAGUC	CUUGGUAGACUUGUAUU
hsa-miR-300		3' UCUCUCUCAG	GACGGGAACAUAU
Position 4502-4508	of PHF21A 3' UTF	5'UUCAGUCI	JUGGUAGACUUGUAUU
hsa-miR-381		3' UGUCUCI	JCGAAC GGGAAC AUAU
Position 45	41-4547 of PHF21#	3'UTR 5'AAA	
hsa-miR-495		3' UU	ICUUCACGUGGUACAAACAAA

Supplementary Figure 17. The location of the binding sites of multiple cluster miRNAs in the 3'UTR of human *PHF21A(BHC80)* obtained from seed-based algorithm¹ of TargetScan (<u>http://www.targetscan.org/</u>) are shown.

Mouse Phf21a 3'UTR

Supplementary Figure 18

k		***************************************	4k.
Position 172-178 of PHF21A 3' UTR 5'	GAUUCUU	UGUUAUUCU-GUGUGUAC	
<u>mmu-miR-329</u> 3'	ບບບບບ	IIII IIIII CCAAUCGAC CCACACAA	
Position 296-302 of PHF21A 3' UTR	5'	AGUGUGUGCCUGCAGCAGCCUCC	
mmu-miR-485	3'	 CUUAA GUAGUG CCGGUC GGAGA	
Position 395-401 of PHF21A 3' UTR	5'U	JCCUUACUGGGAGCCGUUUGUUU	
mmu-miR-495	3'	 UU CUUCAC GUGGUA CAAACAAA	
Position 858-864 of PHF21A 3' U	TR 5'	. GAG CAGCAC GACCCA GGUGUGUG	
mmu-miR-329	3'	UUUUUCCAAUCGACCCACACAA	
Position 862-869 of PHF21A 3' U	TR 5'	.AGCACGACCCAGGUGUGUGUGAA	
mmu-miR-377	3'	UGUUUUCAACGGAAACACACUA	
Position 1151-1157 of PHF21A	3' UTR	5' UCAGGC ACUGUU CUGGUU UGUUU	
mmu-miR-495		3' UUCUUCACGUGGUACAAACAAA	
Position 1155-1161 of PHF21A	3' UTR	5'GCACUGUUCUGGUUUGUUUGUUU	
mmu-miR-495		3' UUCUUCACGUGGUACAAACAAA	
Position 1251-1257 of PHF	21A 3' UTR	5' UUGUAC CUGGGGAAAACAACUUU	
mmu-miR-382		31 GCUUA GGUGGU GCUUGUUGAAG	

Supplementary Figure 18. The location of the binding sites of multiple cluster miRNAs in the 3'UTR of mouse *Phf21a* (*Bhc80*) obtained from seed-based algorithm¹ of TargetScan (<u>http://www.targetscan.org/</u>) are shown.

Human PUM2 3' UTR

€ k

Supplementary Figure 19

k 1k 2k
Position 55-62 of PUM2 3' UTR 5' AAAAGAAUUUUUUUUGUGUGUGAA
hsa-miR-377 3' UGUUUUCAACGGAAACACACUA
Position 82-88 of PUM2 3' UTR 5' CAAAACACAACUCAACUAUGAAU
hsa-miR-376b 3' UUGUAC CUAAAA GGAGAU ACUA
Position 322-329 of PUM2 3' UTR 5' UUUUUUACCUUGUAAAGUCACAAA
hsa-miR-758 3' CCAAUCACCUGGUCCAGUGUUU
Position 545-551 of PUM2 3' UTR 5'UUGUAUUUUGAUAAUUCACAAAC
hsa-miR-758 3' CCAAUCAC CUGGUC CAGUGUUU
Position 684-690 of PUM2 3' UTR 5'CAAUGUACAGAAAUAUUGUAUAU
hsa-miR-300 3' UCUCUCUCAGACGGGAACAUAU
Position 684-690 of PUM2 3' UTR 5'CAAUGUACAGAAAUAUUGUAUAU
hsa-miR-381 3' UGUCUCUCGAACGGGAACAUAU
Position 1020-1026 of PUM2 3' UTR 5'AAAUAUAUGCAUUGUGUGUGUGUGAG
hsa-miR-329 3' UUUCUCCAAUUGGUCCACAAA
Position 1063-1069 of PUM2 3' UTR 5'UUUGAAAGGAAAUCUUGUUUCAA
hsa-miR-494 3' CUCCAAAGGGCACAUACAAAGU
Position 1240-1246 of PUM2 3' UTR 5'CCUGGCAAUAUAGUGUUGUAUAA
 bsa-miR-300 3' UCUCUCUCAGACGGGAACAUAU
Position 1240-1246 of PUM2 3' UTR 5'CCUGGCAAUAUAGUGUUGUAUAA
Position 1257-1263 of PUM2 3' UTR 5'GUAUAAUUUAUUUUUUUUUUUUU.
<u>hsa-mik-539</u> 3' UGUGUGGUULLUAUUAAAGAGG Desition 1725-1731 of PHM2 3' HTP 5' HHHHHAAHCCHHHGCCHAUGAAA
hsa-miR-376b 3' UUGUACCUAAAAGGAGAUACUA
Position 1815-1821 of POMZ 3' UIR 5'GUUGAAGUUAGUAUUUUGUAUAA
hsa-miR-300 3' UCUCUCUCAGACGGG-AACAUAU
Position 1815-1821 of PUM2 3' UTR 5'GUUGAAGUCAGUAUUUUGUAUAA
hsa-miR-381 3' UGUCUCUCGAACGGGAACAUAU
Position 2180-2186 of PUM2 3' UTR 5'GCAGCAACGCCUUGUGUUUGUUU
hsa-miR-495 3' UUCUUCAC GUGGUA CAAACAAA
Position 2183-2189 of PUM2 3' UTR 5'GCAACGCCUUGUGUUUGUUUCAU
 hsa-miR-494 3' CUCCAAAGGGCACAUACAAAGU
Position 2789-2795 of PUM2 3' UTR 5'GUUAACUUCACUUCUUUGUAUAU
hsa-miR-381 3' UGUCUCUCGAACGGGAACAUAU
POSITION 2789-2795 OF PUM2 3' UTR 5'GUUAACUUCACUUCUUUGUAUAU
hsa-miR-300 3' UCUCUCUCAGACGGGAACAUAU
Position 2822-2829 of PUM2 3' UTR 5'UUAGAAAAUGAAAAUGUGUGUAA
hsa-miR-377 3' UGUUUUCAACGGAAACACACUA

Supplementary Figure 19. The location of the binding sites of multiple cluster miRNAs in the 3'UTR of human *PUM2* obtained from seed-based algorithm¹ of TargetScan (<u>http://www.targetscan.org/</u>) are shown.

Mouse Pum2 3' UTR

Supplementary Figure 20,

Mouse Pum2 3 01R Supplementary Figure 20,
k Position 74-80 of PUM2 3' UTR ^{1k} 5'CAAAACACAAUUCAACUAUGAAU ^{2k}
Position 343-350 of PUM2 3' UTR 5' UUUAUACCUUGUAAAGUCACAAA
mmu-miR-758 3' AUCACCUGGUCCAGUGUUU
Position 478-485 of PUM2 3' UTR 5'CUUAUUUUUUUCCUUUGUGUGAA
<u>mmu-miR-377</u> 3' UGUUUUCAACGGAAACACACUA
Position 566-572 of PUM2 3' UTR 5' UUGUAUUUUGGUAAUUCACAAAC
Position 696-702 of PUM2 3' UTR 5'UGACAAUGUACAGAAUUGUAUAU
mmu-miR-381 3' UGUCUCUCGAACGGGAACAUAU
Position 696-702 of PUM2 3' UTR 5'UGACAAUGUACAGAAUUGUAUAU
mmu-miR-539-3p 3' UUUUUCUUUAAUAGGAACAUAC
Position 881-887 of PUM2 3' UTR 5'GUUGAGGAAGUGUUGGUUUGUUC
Position 1072-1078 of PUM2 3' UTR 5'UUUGAAAGCAAAUCUUGUUUCAG
mmu-miR-494 3' CUCCAAAGGGCACAUACAAAGU
Position 1081-1088 of PUM2 3' UTR 5'AAAUCUUGUUUCAGUGUUUGUUA
mmu-miR-495 3' UUCUUCAC GUGGUA CAAACAAA
Position 1262-1268 of PUM2 3' UTR 5'GUAUAAUGUAAAUUUAUUUCUCC
mmu-miB-520-5m 21 HEHEHEEHHEEHHEAACACC
Position 1245-1251 of PHM2 3' HTR 5' CCHGGCAAHAHAGHGHHHHAA
mmu-miR-381 3' UGUCUCUCGAACGGGAACAUAU
Position 1245-1251 of PUM2 3' UTR 5'CCUGGCAAUAUAGUGUUGUAUAA
mmu-miR-539-3p 3' UUUUUCUUUAAUAGG-AACAUAC
Position 1765-1771 of PUM2 3' UTR 5'UUGGAAAAAAUUGCUUUGUAUAU
mmu-miR-381 3' UGUCUCUCGAACGGGAACAUAU
Position 1765-1771 of PUM2 3' UTR 5'UUGGAAAAAAUUGCU-UUGUAUAU
mmu-miR-539-3p 3' UUUUUCUUUAAUAGGAACAUAC
Position 1737-1743 of PUM2 3' UTR 5'UUUUUUAAUCCUUUGCCUAUGAAA
mmu-miR-376b 3' UUCACCUACAAGGAGAUACUA
Position 2109-2116 of PUM2 3' UTR 5'CCACUAAGUCUGGCCAUGUUUCA
mmu-miR-494 3' CUCCAAAGGGCACAUACAAAGU
Position 2754-2760 of PUM2 3' UTR 5'AAUGUUAUCUUCACUUUGUAUAU
mmu-miR-381 3' UGUCUCUCGAACGGGAACAUAU
Position 2754-2760 of PUM2 3' UTR 5'AAUGUUAUCUUCACUUUGUAUAU
mmu-miR-539-3p 3' UUUUUUUUAAUAGGAACAUAC
mmu-miR-377 3' UGUUUUCAACGGAAACACACUA

Supplementary Figure 20. The location of the binding sites of multiple cluster miRNAs in the 3'UTR of mouse *Pum2* obtained from seed-based algorithm¹ of TargetScan (http://www.targetscan.org/) are shown.





Supplementary Figure 21. Regulatory role of Smad, CHOP and E-box regulators (USF1, Tfe3 and Zeb1). (a-d) TGF- β 1 increased the enrichment of Smad2/3 (a) at potential Smad binding elements (CAGA repeats), E-box activators USF1(b) and Tfe3 (c) but decreased E-box repressor Zeb1 (d) at the CHOP binding element and E-box region in MMC. (e-i) Effects of *Chop* siRNA on the expression of miR-379 (e), miR-495 (f), miR-377 (g), lnc-MGC (h) and Mirg (i). *Chop* siRNA inhibited the induction of these RNAs in MMC treated with TGF- β 1 or HG but did not affect basal levels. Respective control treatments are NG and mannitol for HG, and SD for TGF- β 1. Results are mean + SE in triplicate PCRs of three independent culture experiments. *, P<0.05.



Supplementary Figure 22. Effects of *Chop* siRNA on the expression of potential targets of the cluster miRNAs in MMC treated with TGF- β 1 or HG. (a) *Chop* siRNA reverses the inhibition of *Tnrc6* expression in MMC treated with TGF- β 1 or HG. NC refers to negative control siRNA (b-g) Effects of *Chop* siRNA on the expression of candidate pro-fibrotic genes. *Chop* siRNA significantly inhibited the induction of *Col1a2* (b), *Col4a1* (c), *Tgf-\beta1* (d), *PAI1* (e) but not *FN1* (f) or *Ctgf* (g) in MMC treated with TGF- β 1. SD is serum-depleted control. No significant effect of *Chop* siRNA on basal expression of these profibrotic genes was detected. Results are mean + SE in triplicate PCRs of three independent culture experiments. *, P<0.05.



Supplementary Figure 23. Inc-MGC, miR-379 cluster miRNAs and potential targets in MMC treated with TGF- β 1 and in MMC from *Chop* -KO mice. (a) Induction of lnc-MGC and candidate miR-379 cluster miRNAs in MMC treated with TGF- β 1 was attenuated in MMC from *Chop* -KO mice. (b) Decrease of potential targets of miR-379 cluster in MMC treated with TGF- β 1 was attenuated in MMC from *Chop* -KO mice (except *Cugbp2*). (c) Induction of profibrotic genes in MMC from WT mice treated with TGF- β 1 was attenuated in MMC from *Chop* - KO mice. Results are mean + SE in triplicate PCRs of three-four independent culture experiments. *, P<0.05. (d) TGF- β 1 induced cellular hypertrophy is ameliorated in MMC from WT mice treated with TGF- β 1 relative to SD control, no change was observed in MMC from *Chop* - KO mice. For TGF- β 1 treatment, MMC were serum-depleted (SD) and treated with or without 10 ng/ml TGF- β 1 for 24 hours. Results are mean + SE in three independent experiments. *, P<0.05.



Supplementary Figure 24. Inc-MGC, miR-379 cluster miRNAs and potential targets in MMC treated with HG and in MMC from *Chop* -KO mice. (a) Induction of lnc-MGC and miR-379 cluster miRNAs in MMC treated with HG was attenuated in MMC from *Chop* -KO mice. (b) Decrease of potential targets of miR-379 cluster in MMC treated with HG was attenuated in MMC from *Chop* -KO mice. (c) Induction of pro-fibrotic genes in MMC from WT mice treated with HG was attenuated in MMC from *Chop* -KO mice. (c) Induction of pro-fibrotic genes in MMC from WT mice treated with HG was attenuated in MMC from *Chop* -KO mice. For HG treatment, MMC were cultured in medium containing HG (25mM) and serum for 72 hours while control cells were cultured for the same time period in NG (5.5 mM). (d-i) The effects of miR-379 overexpression (with mimics) on the expression of targets and profibrotic genes in *Chop*-KO MMC. Significant increase of miR-379 was confirmed after transfection on MMC with miR-379 mimics relative to NTC (d). Significant decrease of targets, *Edem3* and *Tnrc6b* (e & f) and significant increase of profibrotic genes, *Col1a2* (g), *Col4a1* (h) and *Tgf-β1* (i) were detected in *Chop*-KO MMC transfected with miR-379 mimic. Results are mean + SE in triplicate PCRs of three independent culture experiments. *, P<0.05.



Supplementary Figure 25. Tunicamycin (TM) induces the expression of miRNAs in the miR-379 cluster in MMC. (a) To optimize TM treatment conditions in MMC to induce ER stress, HSPA5 was used as indicator of ER stress in response to several doses of TM. 50 ng/ml was the minimum dose required to induce significant expression of HSPA5 in MMC. (b&c) The same dose 50 mg/ml was optimal for induction of *Chop* mRNA (b) and protein (uncropped scans are shown in Supplementary Figure 38) (c) in MMC. Wider (uncropped) scans of blots are shown in Supplementary Figure 38. (d-i) The expression of lnc-MGC (d, 5'; f, middle; i, 3') and miRNAs, miR-379 (e), miR-495 (g) and miR-377 (h) in the cluster were increased by TM (~50ng/ml). Results are mean + SE in triplicate PCRs of three independent culture experiments. *, P<0.05.



Supplementary Figure 26. Tunicamycin (TM) reduces targets of miRNA cluster in MMC. (a) A target of miR-379, *Edem3* mRNA was decreased by TM. (b-g) Five other indicated targets of the miR-379 cluster were also down regulated by TM in MMC (mRNA and protein). Results are mean + SE in triplicate PCRs of three independent culture experiments. *, P<0.05. (g) Western blots showing the decrease of Edem3, Bhc60, Cpeb4 proteins by TM in MMC. Faster migrating isoform of Edem3 protein was detected in TM-treated cells by western blot while no such isoform was detected in MMC treated with TGF- β 1 (h) or transfected with miR-379 mimic relative to control oligo (i). Wider (uncropped) scans of blots are shown in Supplementary Figure 38 and 39.



Supplementary Figure 27. The expression of pro-fibrotic genes in MMC treated with TM and *Xbp1* splicing in MMC treated with TM, HG or TGF- β 1. (a-d) The expression of pro-fibrotic genes, *Tgf-\beta1* (a), *Col1a2* (b), *Col4a1* (c) and *Fn* (d) was also increased by TM in MMC. Results are mean + SE in triplicate PCRs of three independent culture experiments. *, P<0.05. (e-h) *Xbp1* splicing was monitored by PCR. ER stress-induced spliced form (shorter form) was detected in MMC treated with TM in a dose-dependent manner (e), with HG (25mM) for 72 hours (f) and with 10ng/ml TGF- β 1 for 6 and 24 hours (g).



Supplementary Figure 28. *Edem3* 3'UTR is a *bonafide* target of miR-379 (and miR-200b). (a) Schematic structures of the luciferase reporter of *Edem3* 3'UTR. Potential miR-200b/c target site was also found in the 3'UTR of *Edem3*. Deletion mutants (delta-up, delta-middle and down) were constructed. Full and delta-up include miR-379 and miR-200b/c sites but these sites are deleted in delta-middle and down. (b) MMC was transfected with reporter plasmids with 3'UTR of *Edem3* and miR-379 or miR-200b mimic. Full length reporter responded (significant decrease of luciferase activity) to TGF- β 1 and also to miR-379 and miR-200b. (c). Full and delta-up (including miR-379 and miR-200b/c sites) significantly responded to miR-379 and miR-200b but others (Delta-middle and down without miR-379 and miR-200b/c sites) did not. Results are mean + SE from triplicate reads of four independent cultures. *, P<0.05.



Supplementary Figure 29. siRNAs against lnc-MGC inhibited expression of miR-379 cluster miRNAs. (a) Three siRNAs were designed to target the upstream region of lnc-MGC. (b) The mixture of these siRNAs inhibited TGF- β 1-induced increase in the expression of not only linc-MGC but also miR-379, miR-495 and miR-377 in MMC compared to negative control siRNA (NC). Results are mean + SE in triplicate PCRs of three independent culture experiments. *, P<0.05.



b

Mouse miR-379 upstream

Py Py A N T/A Py Py (INR) TATAGTCAGCACAGTGGTTCATTTTTCTGAGTTA GTGTGGCCTTCATCTGGTAA TGTACTACCTGA GGGGGGG GGTGCCG CCTCTCTTTCAGCACCGTGCAACCATTCAAGGAGGGTGTGTTGTTCACCACATCTG<mark>CTTCCCACTGCCAAAT</mark>CAGGCCTCA GAAAAGCTTTCTGGAAGTGACGCCAGCTTCAGGGACAAGGCCCAAGTTTCTAGGGGTCAACACC-miR-379---

Mouse target CTTCCCACTGCCAAAT

MGC10 (ATTTGGCAGTGGGAAG) LNA & full PS







Supplementary Figure 30. Design and Efficacy of GapmeRs targeting lnc-MGC. LNAmodified GapmeR inhibits lnc-MGC in MMC in vitro. (a) Four GapmeRs (MGC 1,5, 8 and 10) were designed to target the upstream sequence of lnc-MGC. (b) Location of mouse lnc-MGC target sequence (red font) and chemistry of MGC10 (the best design based on the effects on expression of lnc-MGC in MMC in vitro). First and last three bases were replaced with LNA (green font) and others were DNA. The backbone was fully phosphorothioated. The Control GapmeR oligo had similar chemistry (modification) as MGC10, (our specific lncRNA targeting GapmeR), and also with no homology to any known mRNA, miRNA, or lncRNA in mouse, rat and human. (c&d) Out of the four oligos tested, MGC10 was the most effective and consistent inhibited the expression of lnc-MGC even after treatment of TGF- β 1 in MMC. Results are mean + SE in triplicate PCRs of three independent culture experiments. *, P<0.05.



Supplementary Figure 31. LNA-modified GapmeR targeting lnc-MGC inhibits candidate miRNAs in the miR-379 cluster in MMC in vitro compared to control oligo (Ctr). (a-c) miR-379 cluster miRNAs, miR-379 (a), miR-495 (b) and miR-377 (c) were significantly downregulated by MGC10. (d-g) Several target genes of key cluster miRNAs, *Edem3* (d), *Trnc6b* (e), *Cpeb4* (f) and *Bhc80* (g) were upregulated by MGC10 as related to reduction of the miR-379 cluster miRNAs. Results are mean + SE in triplicate PCRs of three independent culture experiments. *, P<0.05.



Supplementary Figure 32. MGC10 inhibits miR-379 cluster miRNAs in the mouse kidney in vivo. (a-f) Subcutaneous injection of 5mg/kg MGC10 consistently inhibited the expression of lnc-MGC in kidney cortex of normal mice at 24-72 hours after injection. Three mice in each group. The expression of lnc-MGC (b) and miRNAs in the miR-379 cluster, miR-379 (c), miR-495 (d), miR-377 (e) were inhibited by subcutaneous injection of 5mg/kg MGC10, while miR-882 outside of the cluster was not (f). Three mice were injected for each condition and each time point. Gene expression quantified in cortical samples. Results are mean + SE in triplicate PCRs from each mouse, *, P<0.05.

Possible mechanism of inhibition of IncMGC by MGC10 Gapmer



Supplementary Figure 33. Scheme depicting the potential mechanism of inhibition of nuclear lnc-MGC by MGC10. Phosphorothioated oligonucleotides can be transported into the nucleus by a protein complex (TCP1 complex)². Because MGC10 is fully phosphorothioated, it may be efficiently transported into nucleus and thereby cleave lnc-MGC RNA and also suppress the expression of miR-379 cluster (hosted within lnc-MGC).



Kidney RNA (non-coding RNAs, microRNAs, target RNAs, profibrotic genes or ER stress-related genes) Kidney protein

Kidney sections, PAS staining (glomerular hypertrophy, mesangial expansion, ER stress-related proteins)



Supplementary Figure 34. (a) **The experimental scheme for the in vivo GapmeR injection experiments in normal and diabetic mice**. Five non-diabetic mice, five diabetic mice without injection, 6 diabetic mice injected with control oligos and 6 diabetic mice injected with MGC10 were used. (b) Serum profile of mice used in this study. MGC10 injection did not have significant effects on parameters of liver or kidney toxicity. Significant increase of blood glucose was detected in all diabetic (STZ, STZ+C, STZ+MGC10) groups compared to non-diabetic group (NS). MGC10 injection did not change blood glucose levels, either. These results suggest a good safety profile for injected LNA modified GapmeRs in mice models of early DN.



Supplementary Figure 35. Cytokine profiles in sera from GapmeR injected mice. (a) Cytokine profiles in sera from GapmeR injected nondiabetic mice. No significant changes in the levels of 10 cytokines (GM-CSF, INF-g, IL-1b, IL-2, IL-4, IL-5, IL-6, IL-10, IL-12(P40/P70), TNF-a) were observed between mice injected PBS, 2mg/kg MGC10 or 5mg/kg MGC10. (b) Cytokine profiles in sera from GapmeR injected STZ-diabetic mice. No significant difference was detected in the levels of 10 cytokines (GM-CSF, INF-g, IL-1b, IL-2, IL-4, IL-5, IL-6, IL-10, IL-12,(P40/P70), TNF-a) between NS, STZ, STZ+C, STZ+MGC10 groups.



Supplementary Figure 36. Effects of MGC10 on lnc-MGC, cluster miRNAs, potential targets and profibrotic genes in kidney cortex and glomeruli from STZ diabetic mice. (a-c) Increase of lnc-MGC, lncMGC5', upstream of lnc-MGC (a), middle region lnc-MGC (b), lnc-MGC3' (mirg) (c), in kidney cortex and glomeruli from STZ diabetic mice and their inhibition by injection of MGC10. (d-f) Decrease of miR-379 cluster targets, *Tnrc6b* (d), *Cpeb4* (e), *Pumilio2* (only in glomeruli) (f) in kidney cortex and glomeruli from STZ diabetic mice and their restoration by injection of MGC10. Results are mean + SE in triplicate PCRs from each mouse. *, P<0.05.

а

С

Supplementary Figure 37

Human miR-379 upstream

AGGCACCCCTT CCCCCAT CAAT GCCACT GCCCCACATT GGAGGAGGGGTT GTTTAT GTTCACCAT GT GCCT G<mark>CTT CCAAT GCCAAAT C</mark>CAGCCT CAGAAAGCTTT C

CTT CCAAT G CCAAAT C Human Mouse target CTTCCCACTGCCAAAT

HMGC10 (GATTTGGCATTGGAAG) LNA & full PS

b	nouse hunan Consensus	1 I AGTCTT , aTcTT	10 TCTGRGTT TCCRRGTT TCCaRGTT	20 RETETESCCT GACATESCCT GACATESCCT		40 INTETRCTRC GRATTACCAC	50 TGRGGGGGGGG TTRGGGTAGR TgRGGGgaGR	60 GGTGCCGCCTC GGCRCCCCTTC GGCRCCCCCTC	70 TCT-TTCRS CCCCNTCRN CCC, aTCR	80 RCCG-TGCR IGCCRCTGCC IGCCa,TGCa	90 RC-CRTTCR CCRCRTTGG CCRCRTTGG	100 IGGAGGGGTGTG IGGAGGGGGTTG IGGAGGGGgggTG		120 ICCRCRTCT ICCRTGTGCCCT ICCRCaTCT	130 6CTTCC 6CTTCC 6CTTCC	
	nouse hunan Consensus	131 CACTEC RA-TEC aA,TEC	140 CRAATCAG CRAATCCA CRAATCCA	150 GCCTCRGARA GCCTCRGARA GCCTCRGARA		170 ARGTGRCGCC ARGTGRCGCC	180 AGCTTCAGGG CARCTTCAGGG CASCTTCAGGG	190 CRAGGCCCCA SCRAGGCCCCA CRAGGCCCCA	200 GTTTCTAGG GTT-CT-GG GTT-CT-GG	210 SGTCRACACC SGTCRACACC SGTCRACACC	220 GTTCCATGGT ATTCCGTGGT ATTCCGTGGT	230 ITCCTGARGAG ITCCTGARGAG ITCCTGARGAG	240 Atgetagact Atgetagact Atgetagact	250 TATEGAACGTF TATEGAACGTF TATEGAACGTF	260 IGECETT IGECETT IGECETT	
	nouse hunan Consensus	261 ATGTTT ATGATT ATGATT	270 T-TGACCT TCTGACCT T.TGACCT	280 ATGTARCATS ATGTARCATS ATGTARCATS	290 TCCRCTRR TCCRCTRR TCCRCTRR	297 1 TCT TCT TCT										



U25 48 hour

D3348 hour

P24 48 hour





Supplementary Figure 37. Human homologue of lnc-MGC (hlnc-MGC) and its inhibition by HMGC10 in human MC. (a) Genomic sequences of human Inc-MGC. The structure of the promoter region (TATA-like elements and initiator sequence) was conserved. Human target sequence analogous to mouse MGC10 has two base mismatches and the human version of GapmeR (HMGC10) was designed based on the human sequence. Basic chemistry is the same as mouse GapmeR. HMGC10, (GATttggcattggAAG) (uppercase: LNA; lowercase: DNA, full phosphorothioate). (b) Alignment of nucleotide sequences upstream of miR-379 in mouse and human. (c) HMC were transfected with plasmids and/or small RNAs using Nucleofector (Amaxa Biosystems). Basic Nucleofector Kit for Primary Smooth Muscle Cells (Amaxa) was used. Three programs (D33, P24 and U25) were tested to examine the transfection efficiency with pmaxGFP (Amaxa). Program D33 resulted in highest transfection efficiency (-60%) and viability. Scale bar, 20um. (d) Significant inhibition of hlnc-MGC by HMGC10 in HMC compared to negative control oligo (NC). The upstream region of human miR-379 was examined by RT-PCR in HMC. Two concentrations, 20 and 40 nM of HMGC10 were tested and both significantly inhibited expression of hlnc-MGC. Results are mean + SE in triplicate PCRs of three independent culture experiments. *, P<0.05. (e-g) Significant decrease of protein levels of EDEM3 and CPEB4 was observed in HMC treated with TGF-B1 compared to serum depleted control (SD). Wider (uncropped) scans are shown in Supplementary Figure 39.







Supplementary Figure 38. Wider (uncropped) scans of blots.

Supplementary Figure 38



Supplementary Figure 39. Wider (uncropped) scans of blots.

Supplementary Table 1

Abundance of miRNA read frequency (% of all mapped reads per sample) in glomeruli and tubuleinterstitial (TI) fractions of kidney biopsies of American Pima Indians.

miRNA	Glomeruli	TI	GI/TI
Other kidney-enriched r	miRNAs		
hsa-miR-21	4.67560%	9.51369%	0.5
hsa-miR-192	0.53570%	1.44438%	0.4
hsa-miR-21*	0.00987%	0.02055%	0.5
hsa-miR-192*	0.00250%	0.00740%	0.3
Cluster miRNAs			
hsa-miR-134	0.01867%	0 00725%	2.6
hsa-miR-376c	0.01104%	0.00723%	2.0
hsa-miR-409-3n	0.01033%	0.00797%	1.3
hsa-miR-381	0.00896%	0.01087%	0.8
hsa-miR-411	0.00700%	0.00721%	1
hsa-miR-323b*	0.00697%	0.00143%	4.9
hsa-miR-377	0.00576%	0.01041%	0.6
hsa-miR-379	0.00566%	0.00560%	1
hsa-miR-654	0.00476%	0.00516%	0.9
hsa-miR-382-5p	0.00348%	0.00207%	1.7
hsa-miR-487b	0.00324%	0.00414%	0.8
hsa-miR-376a-1-3p	0.00293%	0.00489%	0.6
hsa-miR-376a-2-3p	0.00293%	0.00489%	0.6
hsa-miR-485-5p	0.00227%	0.00087%	2.6
hsa-miR-409-5p	0.00200%	0.00234%	0.9
hsa-miR-495	0.00180%	0.00152%	1.2
hsa-miR-369	0.00180%	0.00331%	0.5
hsa-miR-323a	0.00164%	0.00138%	1.2
hsa-miR-494	0.00136%	0.00176%	0.8
hsa-miR-299-5p	0.00128%	0.00102%	1.3
hsa-miR-485-3p	0.00127%	0.00066%	1.9
hsa-miR-1185-1-3p	0.00110%	0.00091%	1.2
hsa-miR-410	0.00104%	0.00141%	0.7
hsa-miR-543	0.00103%	0.00076%	1.4
hsa-miR-299-3p	0.00102%	0.00130%	0.8
hsa-miR-654*	0.00101%	0.00040%	2.5
hsa-miR-369*	0.00093%	0.00084%	1.1
hsa-miR-889	0.00084%	0.00118%	0.7
hsa-miR-487a-5p	0.00076%	0.00028%	2.7

hsa-miR-376b	0.00073%	0.00124%	0.6
hsa-miR-1185-2-3p	0.00072%	0.00016%	4.6
hsa-miR-382-3p	0.00067%	0.00089%	0.8
hsa-miR-329-1	0.00062%	0.00057%	1.1
hsa-miR-329-2	0.00062%	0.00057%	1.1
hsa-miR-154-5p	0.00057%	0.00044%	1.3
hsa-miR-758	0.00056%	0.00057%	1
hsa-miR-376a-1-5p	0.00053%	0.00079%	0.7
hsa-miR-487a-3p	0.00050%	0.00054%	0.9
hsa-miR-154-3p	0.00044%	0.00059%	0.8
hsa-miR-411*	0.00041%	0.00056%	0.7
hsa-miR-656	0.00041%	0.00049%	0.8
hsa-miR-655	0.00037%	0.00058%	0.6
hsa-miR-377*	0.00036%	0.00028%	1.3
hsa-miR-376a-2-5p	0.00025%	0.00021%	1.2
hsa-miR-412-5p	0.00024%	0.00017%	1.4
hsa-miR-539	0.00022%	0.00066%	0.3
hsa-miR-1185-1-5p	0.00022%	0.00037%	0.6
hsa-miR-1185-2-5p	0.00022%	0.00037%	0.6
hsa-miR-379*	0.00021%	0.00025%	0.8
hsa-miR-380-3p	0.00020%	0.00020%	1
hsa-miR-323b	0.00016%	0.00055%	0.3
hsa-miR-376c*	0.00015%	0.00020%	0.7
hsa-miR-380-5p	0.00013%	0.00004%	3.7
hsa-miR-376b*	0.00013%	0.00017%	0.8
hsa-miR-539*	0.00010%	0.00014%	0.7
hsa-miR-668	0.00009%	0.00005%	1.7
hsa-miR-134*	0.00008%	0.00006%	1.3
hsa-miR-543*	0.00007%	0.00005%	1.4
hsa-miR-381*	0.00006%	0.00010%	0.6
hsa-miR-544-3p	0.00003%	0.00006%	0.6
hsa-miR-495*	0.00003%	0.00004%	0.6
hsa-miR-487b*	0.00003%	0.00002%	1.6
hsa-miR-544-5p	0.00003%	0.00008%	0.3
hsa-miR-1197	0.00003%	0.00006%	0.4
hsa-miR-758*	0.00002%	0.00002%	1.2
hsa-miR-1193-5p	0.00002%	0.00001%	1.8
hsa-miR-541-5p	0.00002%	0.00001%	2.8
hsa-miR-412-3p	0.00002%	0.00001%	1.5
hsa-miR-323a*	0.00002%	0.00001%	1.6
hsa-miR-496	0.00002%	0.00007%	0.2
hsa-miR-410*	0.00001%	0.00001%	1.7
hsa-miR-668*	0.00001%	0.00000%	6.6

hsa-miR-329-1*	0.00001%	0.00000%	1.7
hsa-miR-329-2*	0.00001%	0.00000%	1.7
hsa-miR-889*	0.00001%	0.00001%	0.6
hsa-miR-1193-3p	0.00001%	0.00000%	1.3
hsa-miR-494*	0.00000%	0.00001%	0.4
hsa-miR-656*	0.00000%	0.00001%	0.3
hsa-miR-496*	0.00000%	0.00000%	0.5
hsa-miR-655*	0.00000%	0.00001%	0
hsa-miR-1197*	0.00000%	0.00001%	0
hsa-miR-541-3p	0.00000%	0.00001%	0

Highlighted miRNAs exhibit significant association of precursors with morphometric parameters (Supplementary Table 2). Of note, for all miRNAs that are associated with morphometric parameters -3p and -5p (or *) sequences are both detected, supporting that the sequence reads represent miRNA expression. Furthermore, several of the highlighted miRNAs have higher relative abundance in glomeruli versus TI compartment.

Supplementary Table 2

Morphometric Parameter	miRNA Precursor	r	p-value
Podocyte Density	Mir-485	-0.43	0.006
	Mir-299	-0.33	0.043
Podocyte Volume	Mir-299	0.34	0.037
GLEPP1 Volume	Mir-409	0.34	0.035
Glomerular Volume	Mir-409	0.36	0.025
	Mir-655	0.34	0.032
	Mir-654	0.32	0.045
Mesangial Index	Mir-380	0.39	0.014
	Mir-299	0.36	0.023
	Mir-889	0.34	0.032
Mesangial Volume	Mir-654	0.35	0.030
	Mir-655	0.32	0.050
Global Glomerulosclerosis	Mir-668	0.52	0.037

Association of miRNA-precursor abundance in human glomeruli with morphometric parameters

. DN in humans is associated with loss of podocytes leading to decreased podocytes density, hypertrophy of podocytes (podocytes and GLEPP1 volume), glomerular hypertrophy (glomerular volume), mesangial expansion (mesangial index and volume) and accumulation of globally sclerotic glomeruli (global glomerulosclerosis). ³⁻⁶

Reference:

Christopher L. O'Connor, Madhusudan Venkatareddy, Su Q. Wang, Laura H. Mariani, Markus Bitzer, Roger C. Wiggins, Jeffrey B. Hodgin. Morphometric Analysis of Podocyte Density and Glomerular Volume Adapted for Routine Diagnostic Biopsy Evaluation Pathology & Internal Medicine, University of Michigan, Ann Arbor, MI. SA-PO481; ASN Kidney Week 2014

Supplementary Table 3

aDCD primars		
yı Cit primers		
	Forward	
	Peverse	
	Earword	
inciviou gin	Poiwaid	
1 1000	Reverse	GULAAGULAGAGAAATITGU
IncMGC mirg	Forward	
T. (1	Reverse	GIGGGAGIIGAAACAIGGGI
Tnrc6b	Forward	GGATIGCCICGGCCICIACCI
	Reverse	ACCAGCCAGTAACTAGGAcG
Cugbp2 (Celf2)	Forward	GGTCAGATAGAAGAATGCcG
	Reverse	GACAAACGCACAGCCTCGACT
Cpeb4	Forward	AAAAGGAGCTGGAAGAGTCG
	Reverse	TGGTCATCCAAGACATATGGC
Pum2(Pumilio2)	Forward	CGCAAATACACATATGGGAAGC
	Reverse	GCCCACTCTTTGAACATGGT
phf21a (BHC60)	Forward	CACTTACCTTAACAGCACAATGC
	Reverse	CCACTTTTTCTGCAAACACTGC
Edem3	Forward	CACCTTGATCCTCGAGTTTGC
	Reverse	TCGCTGTCTTTTCTCCCAGAG
Chop (Ddit, Gadd153)	Forward	GCACCTATATCTCATCCCCAG
	Reverse	TGCGTGTGACCTCTGTTG
Colla2	Forward	CAGAACATCACCTACCACTGCAA
	Reverse	TTCAACATCGTTGGAACCCTG
Col4a1	Forward	GCCTTCCGGGCTCCTCAG
	Reverse	TTATCACCAGTGGGTCCG
TGFb1	Forward	GGACTCTCCACCTGCAAGAC
	Reverse	GACTGGCGAGCCTTAGTTTG
Ctgf	Forward	GCGAAGCTGACCTGGAGGA
	Reverse	CGCACGAGTGGTGGTTCTGTGCG
Hspa5	Forward	GGAAAGAAGGTTACCCATGC
	Reverse	AGAAGAGACACATCGAAGGT
PAI1	Forward	GACGCCTTCATTTGGACGAA
	Reverse	CGGACCTTTTCCCTTCAAGAGTCCG
Fn1	Forward	CGGTGGAGTCCTGACACAATCACCG
	Reverse	GCGCCCACCAATCTGAAGT
ATF3	Forward	AACTGGCTTCCTGTGCACTT
	Reverse	TGAGGCCAGCTAGGTCATCT
CvpA (Ppia)	Forward	ATGGTCAACCCCACCGTGT
JI (F ")		

	Reverse	TTCTTGCTGTCTTTGGAACTTTGTC
ChIP primers		
Smad site	Forward	GAGAATCTACAGAGACTGAGAATCTGCACATG
	Reverse	GGTCTGAAACATCTCCATCCAGTCTGG
Chop site	Forward	GAGCTCTTGCTCTTTGCACCTGCG
	Reverse	AAGCAGGTGGAACCAGAAGTAAGCC
VDD1 onliging	Eamward	
ADP1 splicing	Forward	
	Keverse	CCATGGGAAGATGTTCTGGG
Human		
Human	Forward	
ninemice	Forward	
100002	Reverse	
neDem3	Forward	
	Reverse	GAACGIGGIIGIICAICACC
nCPEB4	Forward	
	Reverse	
nCUGBP2 (CELF2)	Forward	
	Reverse	GICCIIGCAGAGICCCGAGA
nIGF01	Forward	
1.001.1.4.2	Reverse	
hCOLIA2	Forward	
1.001.441	Reverse	
hCOL4A1	Forward	
1 53 11	Reverse	
hfni	Forward	GCCAGICCIACAACCAGIAIIC
	Reverse	CTTCTCTGTCAGCCTGTACATC
hCTGF	Forward	ACCAATGACAACGCCTCC
1 A TE2	Earword	
	Powara	
	Keverse	
псура (РРІА)	Forward	
	Reverse	GGACCCGTATGCTTTAGGATGA

Supplementary references

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