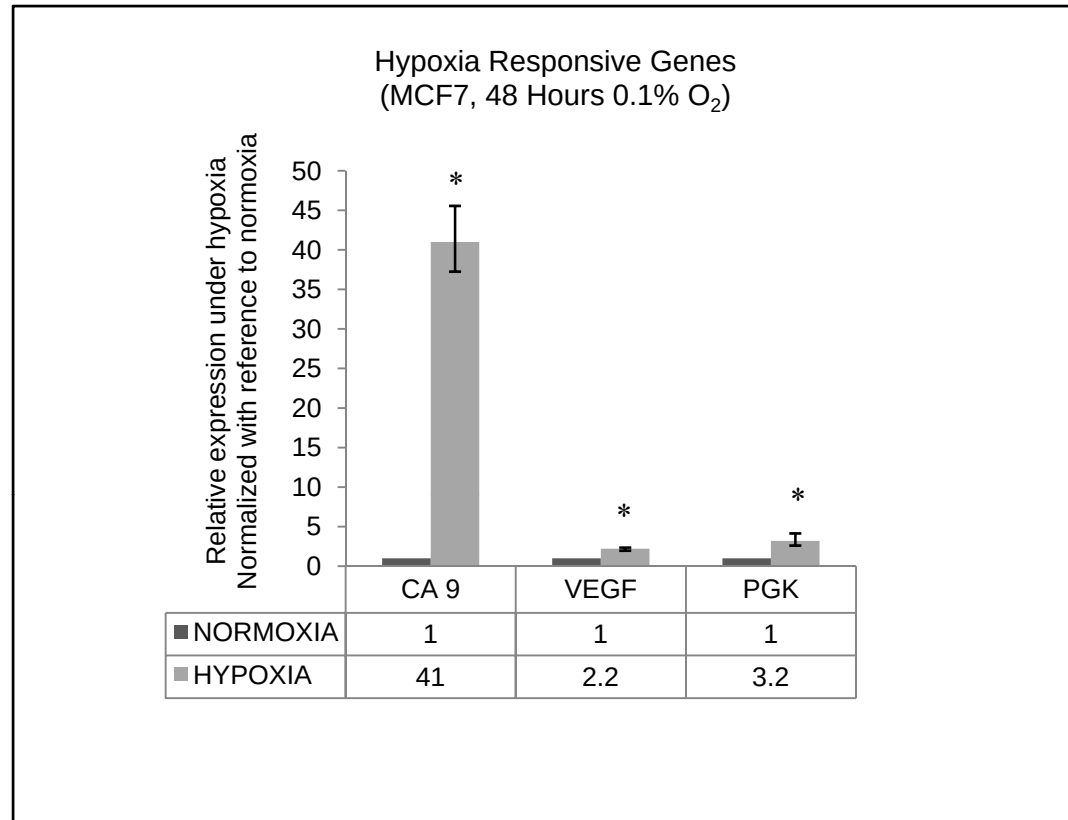
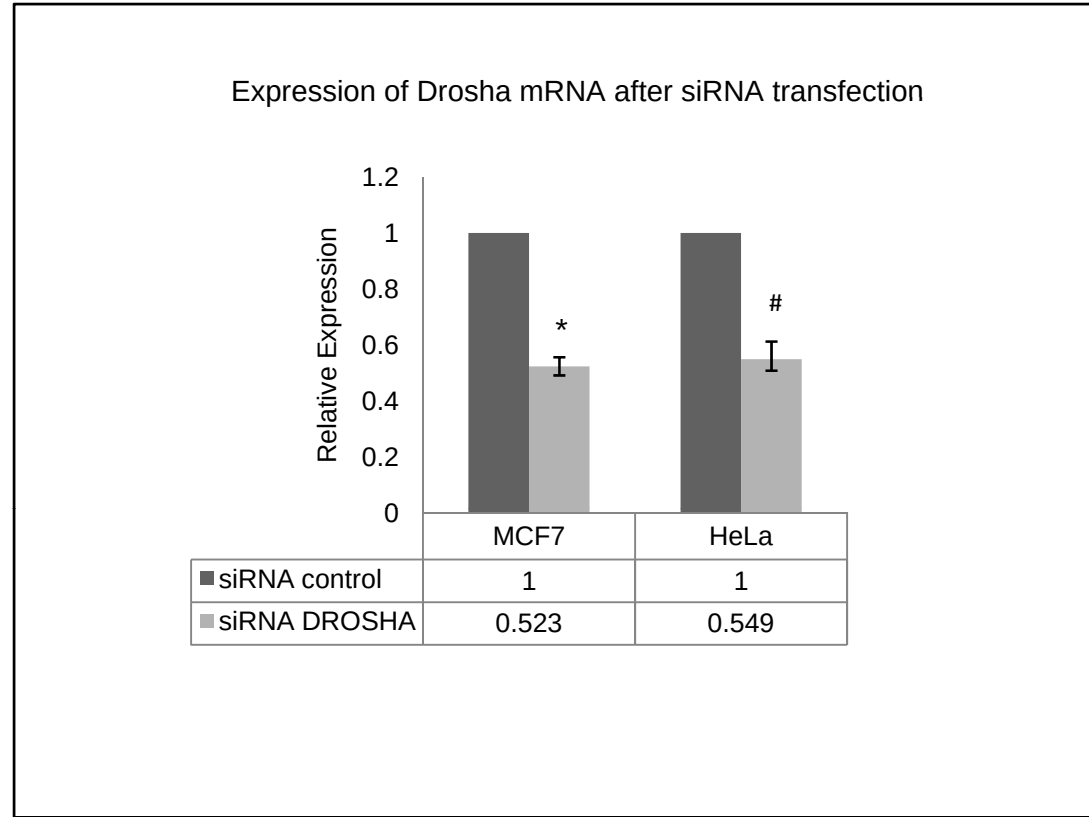




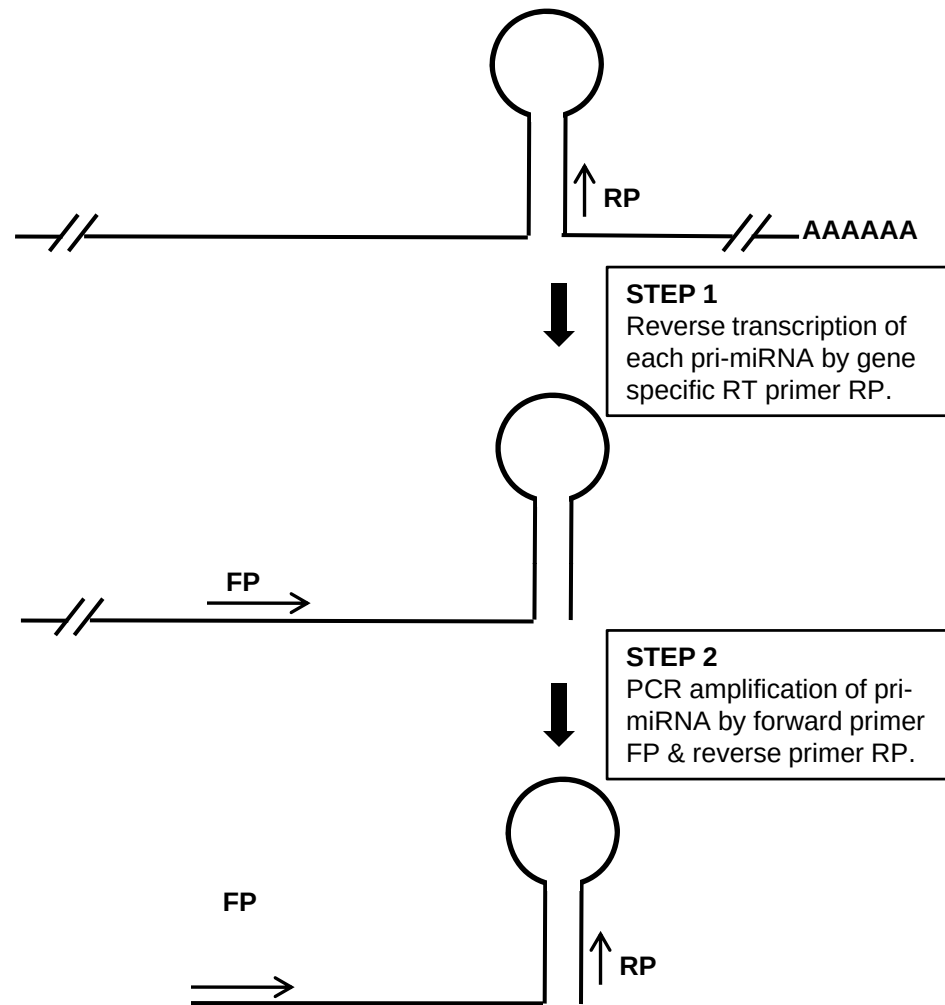
Supp. Fig.1 Confirmation of hypoxia induction in MCF7 cells.

MCF7 cells were maintained under normoxia (20% O₂) and hypoxia (0.1% O₂) for 48 hours. mRNA expression of CA9, VEGF & PGK-1 was quantified by qPCR (Methods). The fold changes represent expression under hypoxia as compared to normoxia. Expression was normalized with reference to the housekeeping genes 18s rRNA and PPIA. Error bars represent standard error of the mean (SEM). * represents $p \leq 0.05$.



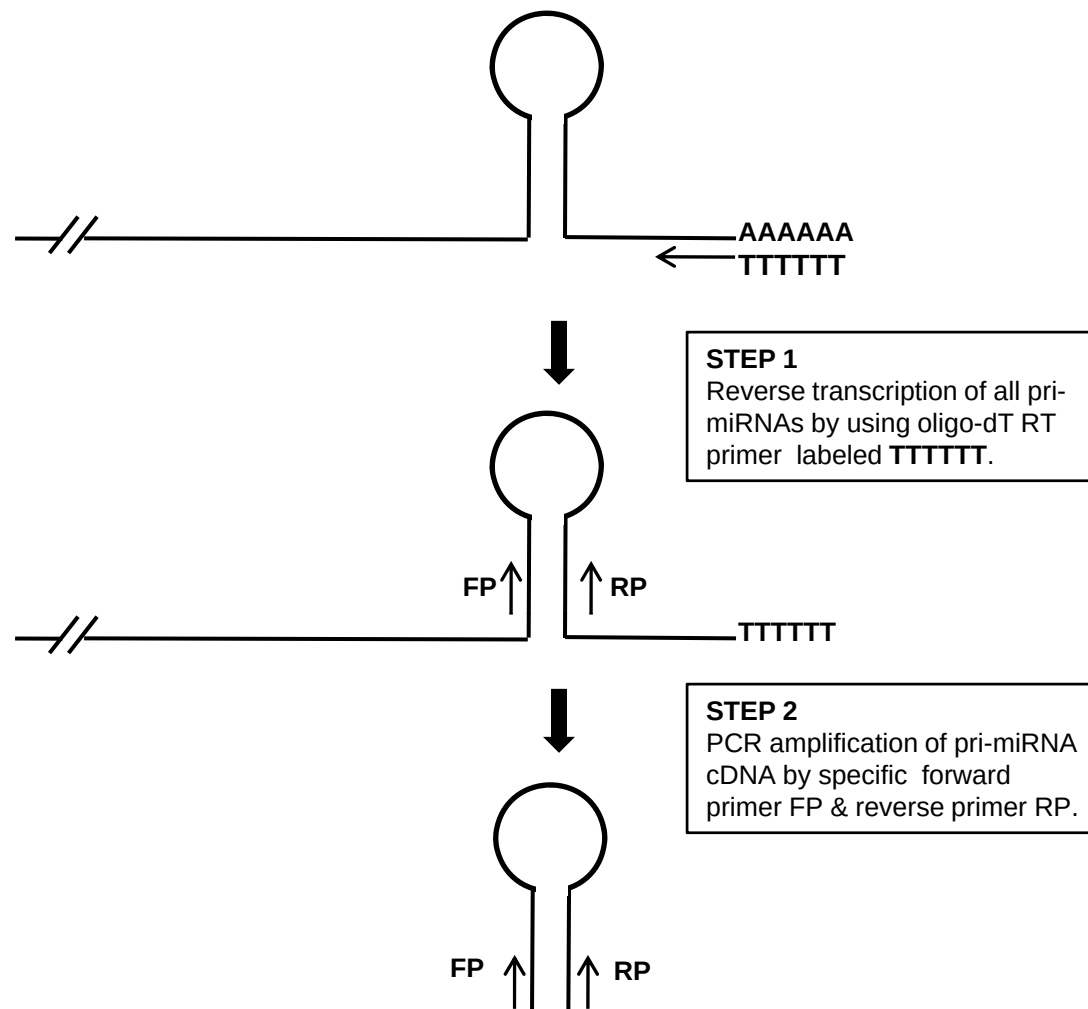
Supp. Fig.2a Confirmation of Drosha knockdown.

Expression of Drosha mRNA quantified by qPCR after Drosha knockdown in MCF7 and HeLa cells. Fold changes represent expression in Drosha siRNA transfected cells as compared to control siRNA transfected cells. Normalization was performed with reference to 18s rRNA and PPIA. * represents $p < 0.01$ and # represents $p < 0.05$



Supp. Fig.2b Schematic representation of conventional strategy of pri-miRNA quantitation by PCR.

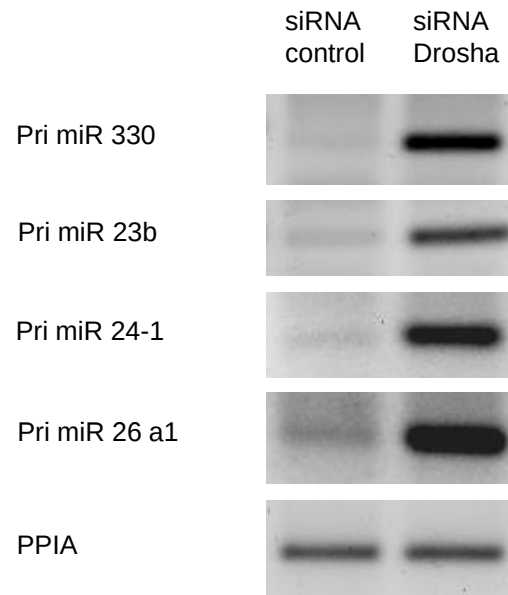
The upper panel shows the RNA sequence of any pri-miRNA. The stem-loop structure represents the precursor sequence of the corresponding miRNA and the “AAAAAA” sequence represents the poly-A tail of the pri-miRNA. RP denotes reverse primer which is used as gene specific primer during reverse transcription and as a reverse primer during subsequent PCR amplification. Middle panel represents the cDNA of a particular pri-miRNA. FP represents the binding site of the forward primer. Lower panel represents the PCR amplification of the pri-miRNA of interest.



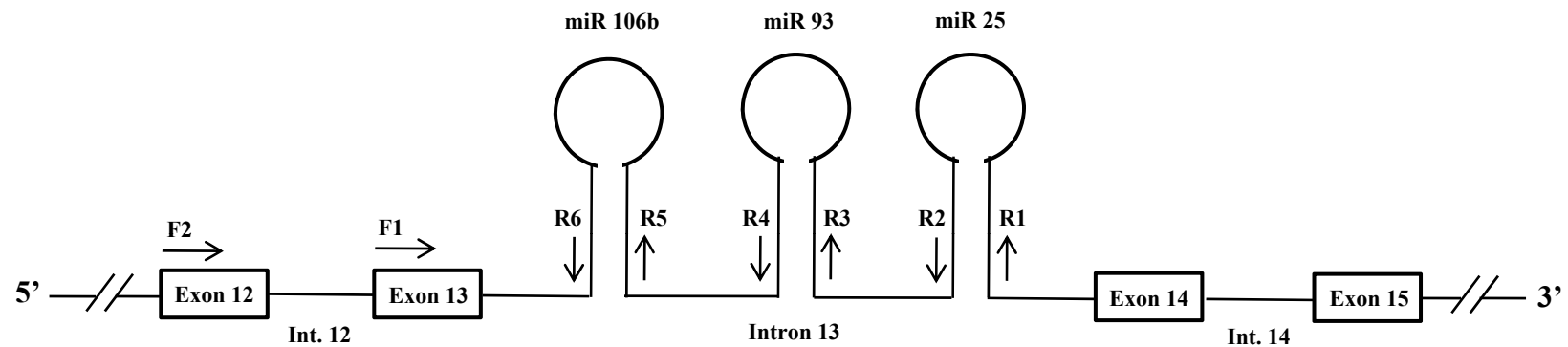
Supp. Fig.2c Schematic representation of novel strategy of pri-miRNA quantitation by RT-PCR.

The upper panel shows pri-miRNA being reverse transcribed by oligo-dT primer. Reverse transcription of precursor miRNA is precluded as they lack poly A tails. The middle panel represents the cDNA produced from a particular pri-miRNA. Arrows represent binding sites of sense (FP) and antisense (RP) primers which are specific to a particular pri-miRNA. The lower panel shows PCR amplification of the corresponding pri-miRNA. The advantages of this strategy are (a) the full length sequence of pri-miRNA need not be identified beforehand in order to design primers for pri-miRNA quantitation (b) the cDNA from a single RT reaction can be used to study multiple pri-miRNAs as well as mRNAs making normalization easier and more reliable and (c) avoids the usage of multiple gene specific RTs for each pri-miRNA reducing the bias introduced during RT step.

The same primer pair can also be used to quantify pre-miRNAs as well, if small RNA fraction (< 200 nt) is purified from total RNA . Using the small RNA fraction, the reverse primer would serve as the gene-specific RT primer for reverse transcribing the pre-miRNA of interest. Following the reverse transcription, the Forward and Reverse primers will PCR amplify the pre-miRNA of interest.

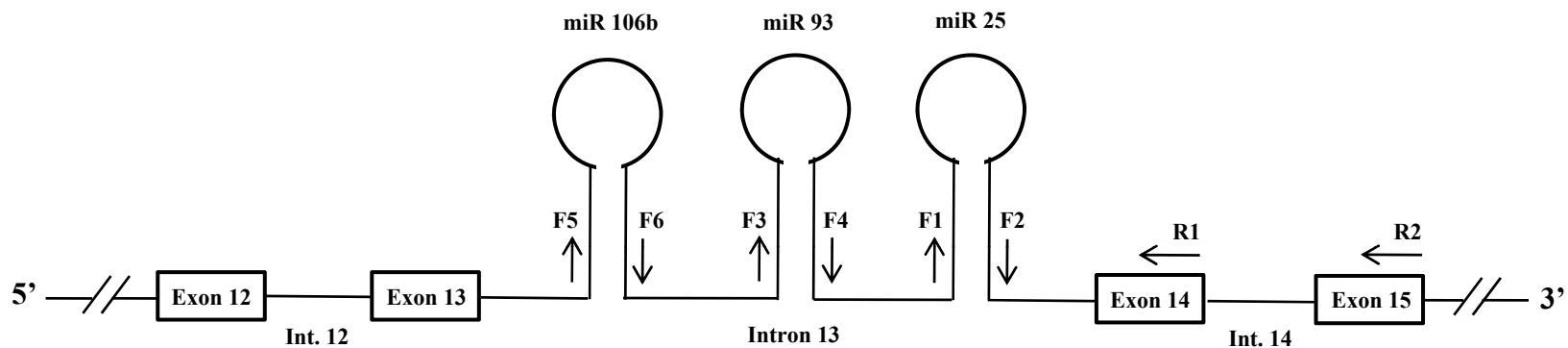


Supp. Fig. 2d Confirmation of Drosha knockdown at the functional level.
Figure shows the accumulation of pri-miRNAs of miRs 23b, 24-1, 26 a1 & 330 upon Drosha knockdown in MCF7 cells by two step RT-PCR. Expression of housekeeping gene PPIA was used as loading control.



Supp. Fig. 2e Schematic representation of primer design for 5' RACE of miRs 106b, 93 & 25.

The figure shows a schematic representation of the location of pre-miRNAs 106b, 93 & 25 (represented by stem-loop structures) with respect to the intron 13 of its host gene MCM7. Boxes represent exons and the interconnecting lines represent introns. The arrows represent the primer binding sites. The representation is not drawn according to scale. **R1** represents the primer binding site of **5-25 OUT-REV** (acronym for **5** RACE primer of miR **25**, **OUT** representing the Outer nested primer, **REV** representing Reverse (or antisense) orientation of the primer). **R2** represents the primer binding site of **5-25 IN-REV** (**IN** represents the inner nested primer). The R1 & R2 primers were designed for performing 5' RACE of miR 25. Analogously, R3 and R4 represent the nested 5' RACE primers of miR 93 and R5 & R6 for miR 106b. **F1** represents the primer binding site of MCM7 **EXON FWD** (acronym for **Forward** primer in the first 5' **Exon** flanking the miRNA harboring intron). **F2** represents the primer binding site of MCM7 **PUF** (acronym for **Primer Upstream Forward**, the forward primer situated in the second 5' Exon upstream of the miRNA harboring intron). The F1 & F2 primers were designed for assessing the efficiency of 5' RACE primers before performing RACE. The schematic representation of primer design for performing 3' RACE is shown in **Supp.Fig.2f**. Similar primers were also designed for performing 5' & 3' RACE of miRNAs 23b, 27b & 24-1 located in the 14th intron of host gene AP-O. Sequences of all the primers used are listed in **Supp.Table 1**.



Supp.Fig.2f Schematic representation of primer design for 3' RACE of miRs 106b, 93 & 25.

The figure shows a schematic representation of the location of pre-miRNAs 106b, 93 & 25 (represented by stem-loop structures) with respect to the intron 13 of its host gene MCM7. Boxes represent exons and the interconnecting lines represent introns. The arrows represent the primer binding sites. The representation is not drawn according to scale.

F1 represents the primer binding site of **3-25 OUT-FWD** [acronym for **3** RACE primer of miR **25**, **OUT** representing the Outer nested primer, **FWD** representing Forward (or sense) orientation of the primer for performing 3' RACE]. **F2** represents the corresponding nested primer **3-25-IN-FWD**. The F1 & F2 primers were designed for performing 3' RACE of miR 25. Analogously, F3 and F4 represent the nested 3' RACE primers of miR 93 and F5 & F6 for miR 106b. **R1** represents the primer binding site of MCM7 **EXON REV** (acronym for **R**everse primer in the first 3' **E**xon flanking the miRNA harboring intron). **R2** represents the primer binding site of MCM7 **PDR** (acronym for **P**rimers **D**ownstream **R**everse, the reverse primer situated in the second 3' Exon downstream of the miRNA harboring intron). The R1 & R2 primers were designed for assessing the efficiency of 3' RACE primers before performing RACE. Similar primers were also designed for performing 3' RACE of miRNAs 23b, 27b & 24-1 located in the 14th intron of host gene AP-O.

PRI 106b/93.seq (437 bp)

GTTTTGACCCTTAAAGGGGTAGCTCCTTACCGTGCTCTCATTGCCGCCTCCCCACCTCCCGCTCCAGCCCTGCCGGG
GCTAAAGTGCTGACAGTGCAGATAGTGTGTCCTCTCCGTGCTACCGCACTGTGGGTACTTGCTGCTCCAGCAGGGCAC
GCACAGCGTCCGTGGAGGGAAAGGCCTTTTCCCCACTTCTTAACCTTCACTGAGAGGGTGGTTGGGGTCTGTTTCAC
TCCATGTGTCCTAGATCCTGTGCTACAGACCTTCCTTTCTGTCTCCCGTCTTGGACCTCAGTCCTGGGGGCTCCAA
AGTGCTGTTTCGTGCAGGTAGTGTGATTACCCAACCTACTGCTGAGCTAGCACTTCCCGAGCCCCCGGGACACGTTCT
CTCTGCCAATTGTCTTCTTGGCTGAGCTCCCCAAGCTCCATCTGTCATGCTGAAAAA

TRANSEQ ORF FINDER ALGORITHM IN 3 READING FRAMES

>EMBOSS_001_1

VLTLKGVAPYRALIAASPPPAPALPGLKC*QCR*WSSPCYRTVGTCCSSRARTASVECKAFSPLLNLH*EGCWCLFH
SMCPRSCATDLPFCPPVLDLSPGGSKVLFVQVV*LPNLLS*HFPSPRDTFSLPIVFLAELPKLHLSCX

>EMBOSS_001_2

F*PLKG*LLTVLSLPPPHLPLQPCRG*SADSADSGPLRATALWVLAAPAGHAQRPWRERPFPHFLTFTERVVGVCFT
PCVLDPVLQTFLSVLPSWTSVLGAPKCCSCR*CDYPTYC*ASTSRAPGTRSLCQLSSWLSSPSSICHAX

>EMBOSS_001_3

FDP*RGSSLPCSHCRLPTSRSSPAGAKVLTQIVVLSVLPHCGYLLLQQGTHSVRGGKGLFPTS*PSLRGWLGSVSL
HVS*ILCYRPSFLSSRLGPQSWGLQSAVRAGSVITQPTAELALPEPPGHVLSANCLLG*APQAPSVML

Supp. Fig.2g Sequence of PRI 106b/93 and its ORF analysis.

The upper panel represents the full length sequence of PRI 106b/93 identified by performing 5' & 3' RLM RACE. The letters highlighted in blue & yellow represent the primer binding sites of RACE primers 3-106b OUT-FWD & 5-106b OUT-REV respectively. The red and blue letters depict the precursor miR 106b and 93 respectively the underlined letters the corresponding mature miRNA sequences. The underlined A represents the start of the poly A sequence. The lower panel depicts the translation of PRI 106b/93 in all three reading frames as predicted by EMBOSS. The stars highlighted in red represent stop codons.

Pri miR 24-1.seq (890 bp)

CCTCCAGGATCAGGATGCAGAGGTTTCGCCATCGGTGGTGTGAACTCATTGTTAAGCACAAAGTTCACGAAAGCCTACA
AAAGTCTGGAGAGGTTTCCTTCAGGAGGATCAGCCCATGGGTGCTACCTCTACGGCGAGCTGATGCTGAGTGAGGAC
GCCAGACAGCAGCAGCTCGCCCGTAGGTGCTTCGAGCGGACCAAGGAGCAGATGGATAGGTCCTCAGCCCAGGTGGT
GGCCGAAATGTTATTTTAACGAGTCCAGGCCTTCGCGTCTCCTGCGCCAGCAGACGGTGCCACGGAGCTCCCAGCT
GAGGCGCTGCTTCTCCGGGCTGTCGATTGGACCCGCCCTCCCGTGCCTACTGAGCTGATATAGTTCTCATTTTACA
CACTGGCTCAGTTCAGCAGGAACAGGAGAAAGACCACAGCAAGATTCTTTTCATTGCTCTCCTCCTAGCCTGGGGGAC
CAGGCTCGAACTGACCCTGGACATCAAAGGAGGATTATGTGGCTGCTAAAGCCATCGGCCCACAGCCCTGTTTACA
TCTTGGTGCTTCTTTTCCAGAGGCTGGTCCAGCCAGGCACACACAAAAGGAGCAGATTCTCGTAAACGCAGCCTCC
CTCCCTGGAGGCTGCCTCCTGCCCTGGATCTGGAGTGGAGCTGCTCTGAGATTTTGAGTTCTTCTGCAGAGATGATT
AAATATATCCAAGAGACATTGGAAAACCTGCTGAACATTTTACATTGGTCTGCTCAGCACATGGCTGGATGCGGATA
TTTCTATAATTCCAGAAAGTCACACAGCTCCTCTGTATGAGACCAGTGGGCGCCATTTAAAAGAACAGGATGAGAAT
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TRANSEQ ORF FINDER ALGORITHM IN 3 READING FRAMES

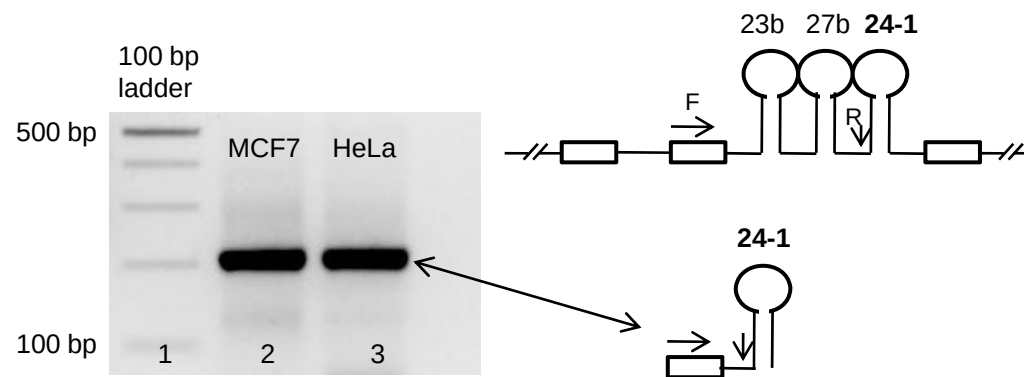
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GRNVILTSPGLRVSCASRRCPRSSQLRRCFSLSIGPALRCLLSYQFSFYTLAQFSRNRKKTARFFHSSPPSLGD
QARTDPGHQRRDYVAAKAIGPQPCSHLGASLSQRLVPARHTQKADSRKRSLLPPWRLPPALDLEWSCSEILSSSAEMI
KYIQETLENLLNLHWSAQHMAGCGFYFNSRKSHSSSVLDQWAPFKRTGESKIYYMMWIFFLX

>EMBOSS_001_2
LQDQDAEVRHRWCCELIVKHKFTKAYKSVERFLQEDQAMGVYLYGELMVSEDARQQQLARRCFERTKEQMDRSSAQVV
AEMLFQVQAFASPAPADGAHGAPSGAASPGCRLDPPSGAYADISSHFTHWLSSAGTGERPQQDSFIRLLAWGT
RLELTLDIKGGIMWLLKPSAHSVHILVLLFPRGWSQPGTHKRQILVNAASLPGGCLLPWIWGAALRFVLLQRNL
NISKRHWKCTFYIGLLSTWLDADISIIPESHATPLYETSGRHLKEQDENLRYIINKCNGFFFCX

>EMBOSS_001_3
SRIRMQRFAIGGVNSLLSTSSRKPTKVWRGSFRRIRPWVCTSTGSWVVRTPDSSSPVGASSGPRSRWIGPQPRWW
PKCYFNESRPSRLLRQQTVPTELPAEALLRAVDWTRPPVPTELISVLILHTGSVQQEQEKDHSKILSFVSSPGGP
GSNPWTSKEGLCGCSHRPTALFTSWCFSPFEAGPSQAHTKGRFSQTQPPSLEAASCPGSGVELLDFFFCRDD
IYPRDIGKPAEHFTLVCSAHGWMRIFLFQKVQTQLLCMRPVGAIKNMRMIDILLINVMDFFFV

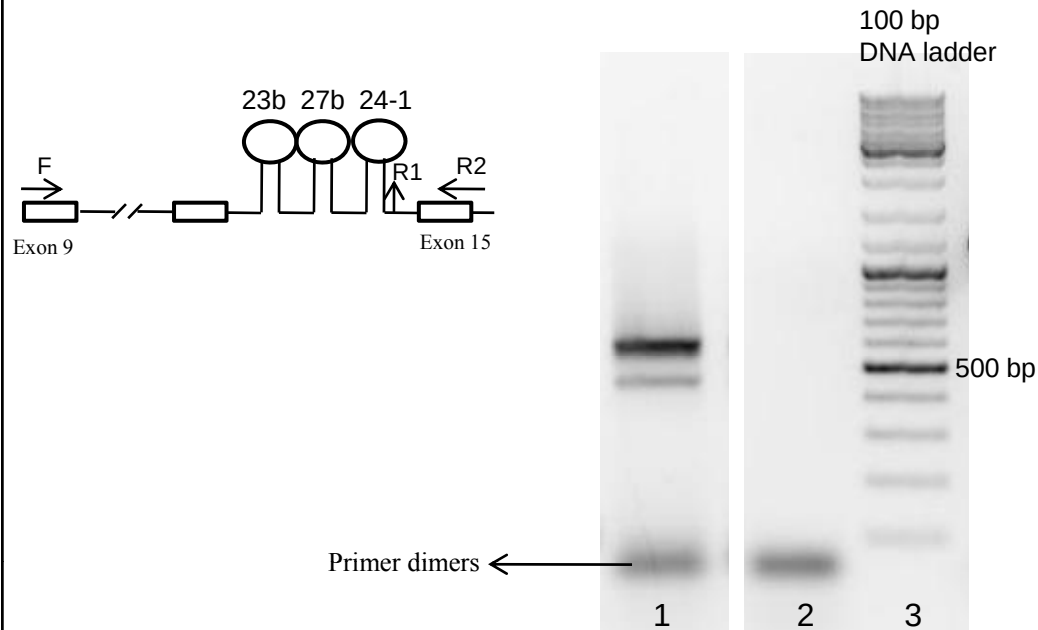
Supp. Fig.2h Sequence of PRI 24 and its ORF analysis.

The upper panel represents the full length sequence of PRI 24. The letters highlighted in green & yellow represent the primer binding sites of RACE primers 3-24 OUT-FWD & 5-24 OUT-REV respectively. The letters highlighted in pink represent exon junctions. The red letters depict the precursor miR 24 and the underlined letters the corresponding mature miR 24-1. The underlined A represents the start of the poly A sequence. The lower panel depicts the translation of Pri miR 24-1 in all three reading frames as predicted by EMBOSS. The stars highlighted in red represent stop codons.



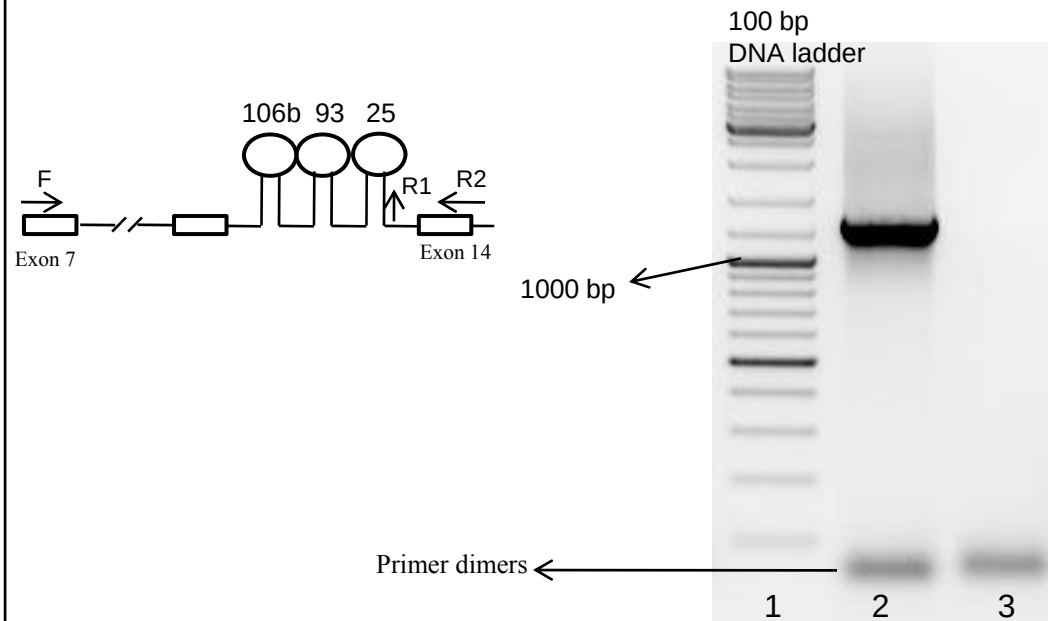
Supp. Fig. 2i Expression of PRI 24 in MCF7 & HeLa cells.

RT-PCR performed with AP-O EXON FWD as forward primer (labeled as F in the schematic representation in the RIGHT UPPER panel) and 5-24-IN REV as reverse primer (labeled as R in the schematic) with oligo dT primed cDNA. The figure shows expression of PRI 24 in both MCF7 and HeLa cells.



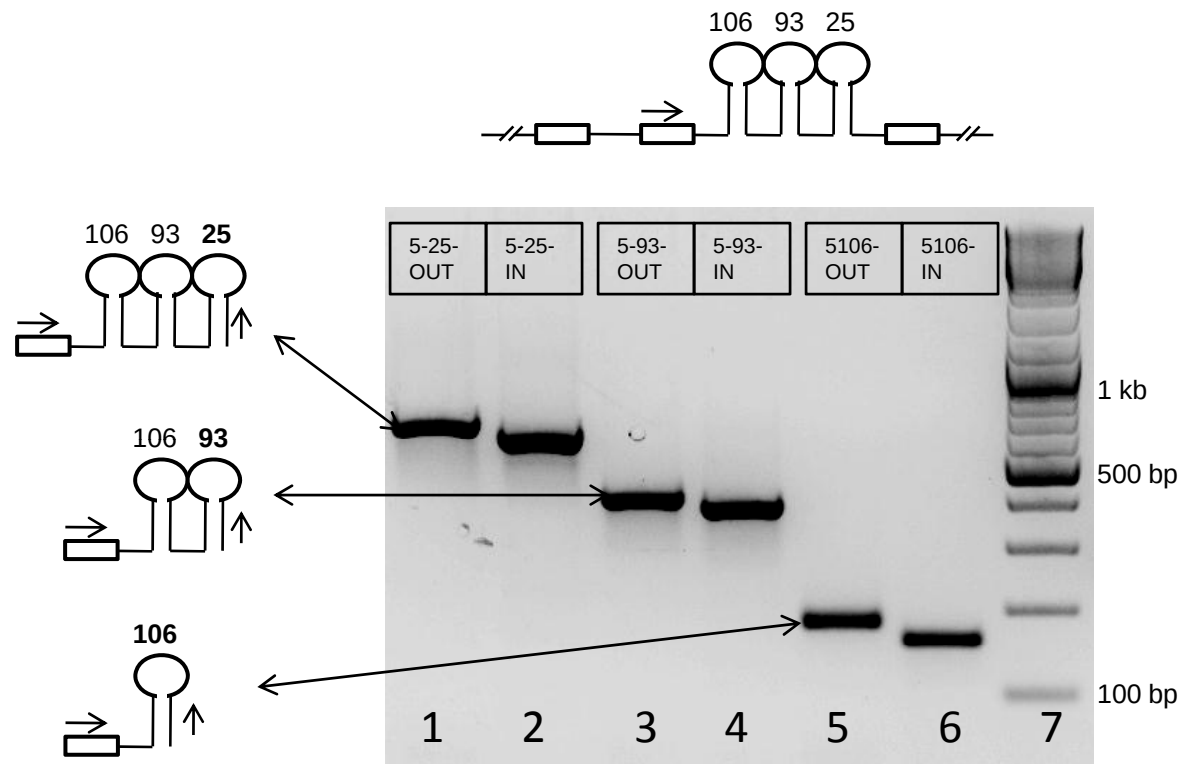
Supp. Fig. 2j Screening for alternatively spliced mRNAs of AP-O which might encode miR 24-1.

RT-PCRs performed with forward primer located in exon 9 of AP-O (labeled as F in the schematic representation in the LEFT panel). Lane 1 shows RT-PCR performed with Reverse primer R2 located in exon 15 of AP-O with oligo dT primed HeLa cDNA under Drosha knockdown conditions. The figure shows expression of the 624 bp amplicon corresponding to AP-O mRNA. Lane 2 shows RT-PCR performed with Reverse primer R1 located in pre-miR 24-1 within intron 14 of AP-O. No amplicons are observed in lane 2 which confirms that splice variants of AP-O mRNA do not harbor pre-miR 24-1. Lane 3 shows DNA molecular weight markers.



Supp. Fig. 2k Screening for alternatively spliced mRNAs of MCM7 which might encode miR 25.

RT-PCRs performed with forward primer located in exon 7 of MCM7 (labeled as F in the schematic representation in the LEFT panel). Lane 2 shows RT-PCR performed with Reverse primer R2 located in exon 14 of MCM7 with oligo dT primed HeLa cDNA under Drosha knockdown conditions. Lane 2 shows the 1169 bp PCR amplicon corresponding to MCM7 mRNA. Lane 3 shows RT-PCR performed with Reverse primer R1 located in pre-miR 25 within intron 13 of MCM7. No amplicons are observed in lane 3 which confirms that splice variants of MCM7 mRNA do not harbor pre-miR 25.



Supp. Fig.3a PCR performed with MCM EXON FWD & miRNA 5' RACE primers with DNA as template.

Agarose gel electrophoresis image of PCR products. PCR performed with MCF7 genomic DNA as template. Forward primer (MCM EXON FWD) is common to all 6 PCRs (represented by arrow in the schematic shown above the gel image). Lanes 1 represents the PCR performed with 5-25-OUT as reverse primer (schematic representation shown on left upper panel). Lane 2 represents the PCR performed with the nested primer 5-25-IN as reverse primer. Lanes 3 & 4 correspond to PCR performed with 5'RACE primers of miR 93(schematic on the left middle panel), lanes 5 & 6 correspond to miR 106b (schematic on the left lower panel). Lane 7 corresponds to 100 bp DNA ladder. Boxes inside the gel image represent the reverse primers used in the PCR.

ALT SPLICE 25.seq (294 bp)

TTTGAACCTCTGGACATGAAGCTCATGAGGCGTTACATAGCCATGTGCCGCGAGAAGCAGCCCATGGTGCCAGAGTC
TCTGGCTGACTACATCACAGCAGCATACTGAGATGAGGCGAGAGGCTTGGGCTAGTAAGGATGCCACCTATACTT
CTGCCCCGACCCTGCTGGCTATCCTGCGCCTTTCCACTGCTCTGGACAGCTGAACTCCGGGACTGGCCAGTGTTGAG
AGGCGGAGACTTGGGCAATTGCTGGACGCTGCCCTGGGCATTGCACTTGTCTCGGTCTGACAG

TRANSEQ ORF FINDER ALGORITHM IN 3 READING FRAMES

>EMBOSS_001_1

FEPLDMKLMRRYIAMCREKQPMVPESLADYITAAYVEMRREAWASKDATYTSARTLLAILRLSTALDS*TPGLASVE
RRRLGQLLDAALGIALVSV*Q

>EMBOSS_001_2

LNLWT*SS*GVT*PCARSSPWCQSLWLTTSQQHTWR*GERLGLVRMPPILLPGPCWLSCAFPLLWTAELRDWPVLR
GGDLGNCWTLPWALHLSRSDX

>EMBOSS_001_3

*TSGHEAHEALHSHVPREAAHGARVSG*LHHSSIRGDEARGLG**GCHLYFCPDPA GYPAPFHC SGQLNSGTGQC*E
AETWAIAGRCPGHCTCLGLTX

Supp. Fig.3b Sequence of ALT SPLICE 25 and its ORF analysis.

The upper panel represents the sequence of the alternatively spliced transcript ALT SPLICE 25. The letters highlighted in blue, green & yellow represent the primer binding sites of primers MCM7 PUF, MCM7 EXON FWD & 5-25 OUT-REV respectively (see Fig. 2a for schematic). The letters highlighted in pink represent exon junctions. The red letters depict the precursor miR 25 and the underlined letters the corresponding mature miR 25. The lower panel depicts the translation of ALT SPLICE 25 in all three reading frames as predicted by EMBOSS Transeq. The stars highlighted in red represent stop codons.

ALT SPLICE 93.seq (304 bp)

TTGAACCTCTGGACATGAAGCTCATGAGGCGTTACATAGCCATGTGCCGCGAGAAGCAGCCCATGGTGCCAGAGTCT
CTGGCTGACTACATCACAGCAGCATACGTGGAGATGAGGCGAGAGGCTTGGGCTAGTAAGGATGCCACCTATACTTC
TGCCCGGACCCTGCTGGCTATCCTGCGCCTTTCCACGTCTCTGATCCTGTGCTACAGACCTTCCTTTCTGTCCTCCC
GTCTTGGACCTCAGTCCTGGGGGCTCCAAAGTGCTGTTCTGTCAGGTAGTGTGATTACCCAACCTACTGCTGA

TRANSEQ ORF FINDER ALGORITHM IN 3 READING FRAMES

>EMBOSS_001_1

LNLWTSSGVTPCAARSSPWCQSLWLTTSQQHTWRGERLGLVRMPPILLPGPCWLSCAFPLLSCATDLPFPCPP
VLDLSPGGSKVLFVQVVLPNLLX

>EMBOSS_001_2

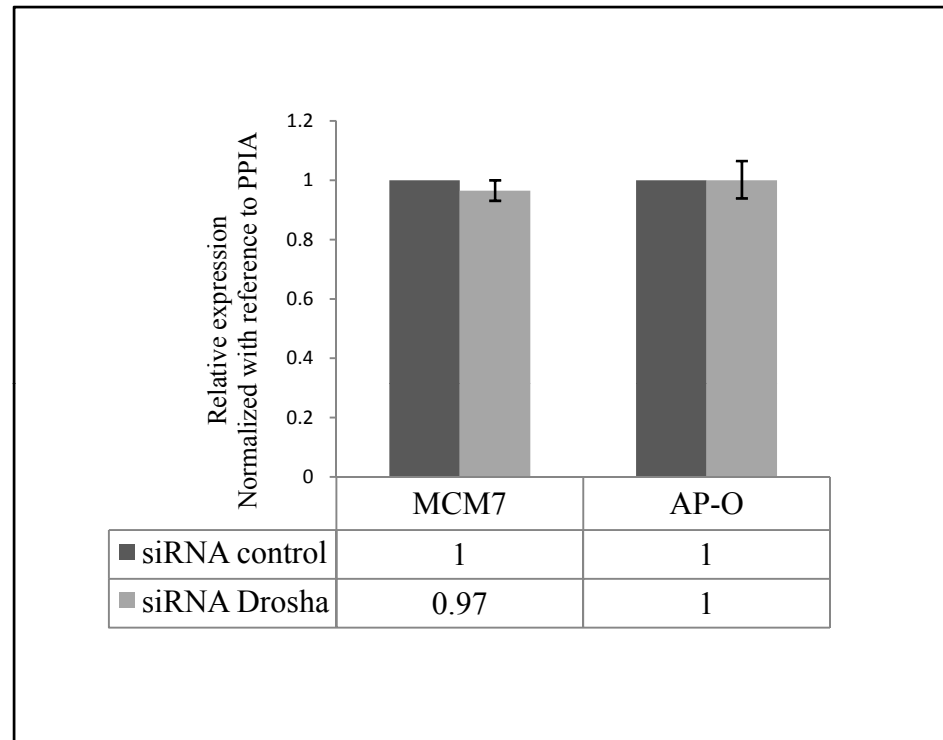
*TSGHEAHEALHSHVPREAAHGARVSG*LHHSSIRGDEARGLG**GCHLYFCPDYPAGYPAPFHCSDPVLQTFLSVLP
SWTSVLGAPKCCSCR*CDYPTYC*

>EMBOSS_001_3

EPLDMKLMRRYIAMCREKQPMVPESLADYITAAYVEMRREAWASKDATYTSARTLLAILRLSTALILCYRPSFLSSR
LGPQSWGLQSAVRAGSVITQPTAX

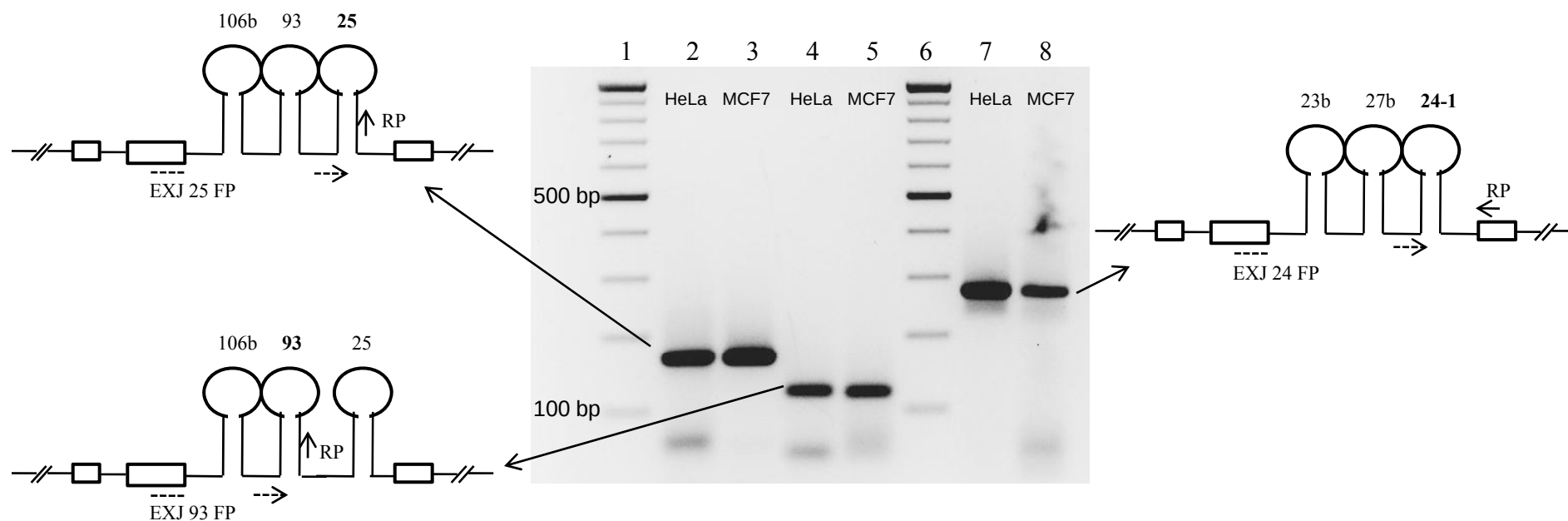
Supp. Fig.3c Sequence of ALT SPLICE 93 and its ORF analysis.

The upper panel represents the sequence of the alternatively spliced transcript ALT SPLICE 93. The letters highlighted in blue, green & yellow represent the primer binding sites of primers MCM7 PUF, MCM7 EXON FWD & 5-93 OUT-REV respectively. The letters highlighted in pink represent exon junctions. The red letters depict the precursor miR 93 and the underlined letters the corresponding mature miR 93. The lower panel depicts the translation of ALT SPLICE 93 in all three reading frames as predicted by EMBOSS. The stars highlighted in red in ORFs 1 & 2 represent stop codons. No proteins corresponding to ORF3 were identified on performing BLAST.



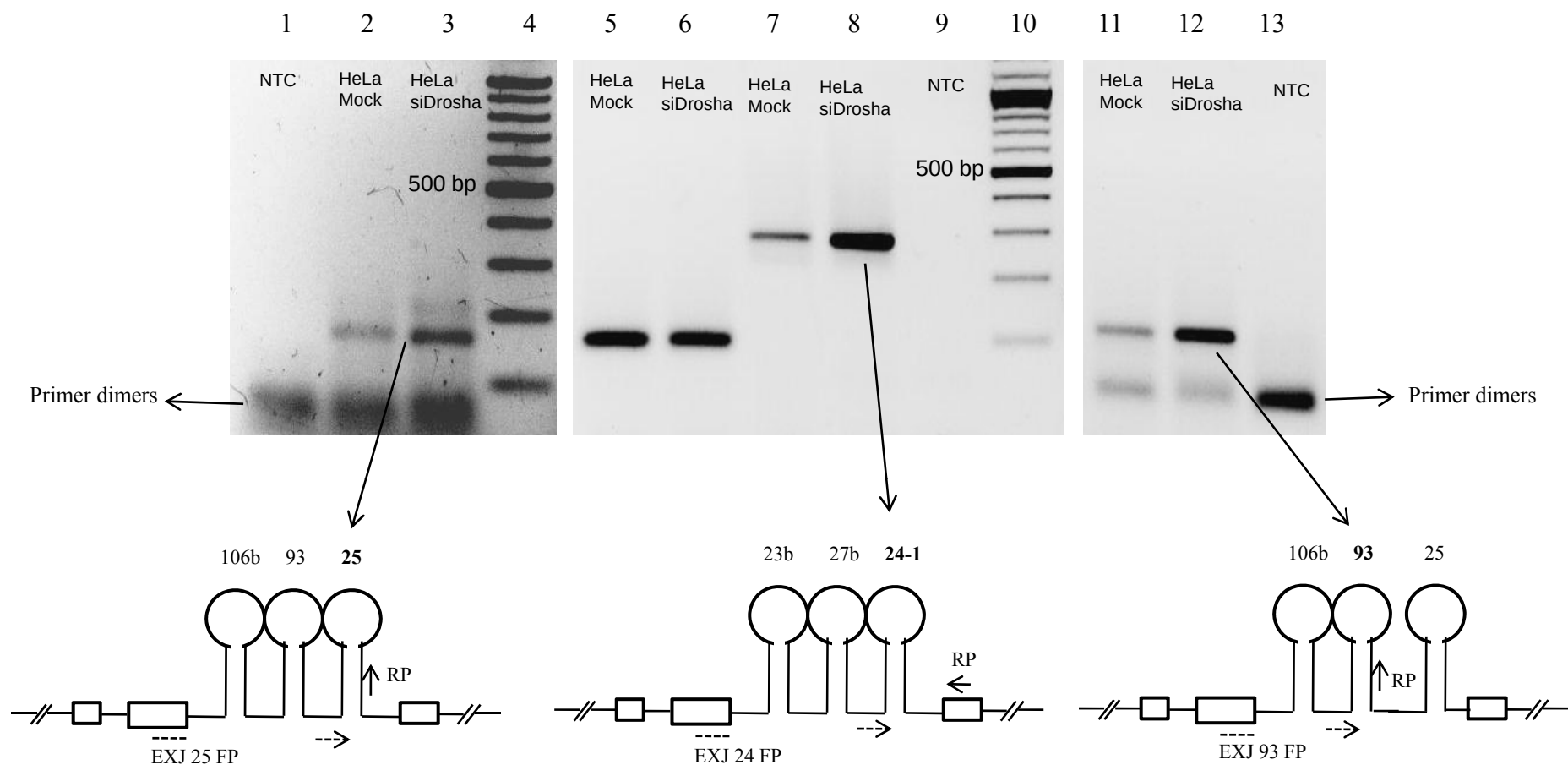
Supp. Fig.3d Expression of host genes after Drosha knockdown.

Expression of MCM7 and AP-O mRNA quantified by qPCR after Drosha knockdown in HeLa cells. Fold changes represent expression in Drosha siRNA transfected cells as compared to control siRNA transfected cells. Normalization was performed with reference to PPIA.



Supp Fig 3e. Confirmation of alternatively spliced pri-miRNAs by RT-PCR with Exon Junction Spanning primers.

EXJ 25 FP, EXJ 93 FP and EXJ 24 FP (depicted by dotted arrows in the schematics) represent the binding sites of exon junction spanning forward primers designed to bind to the region of post splicing junctions of ALT SPLICE 25, ALT SPLICE 93 and PRI 24 respectively. The RP represents the binding sites of the corresponding reverse primers. Lanes 2 and 3 represent RT-PCRs performed with exon junction spanning primers corresponding to ALT SPLICE 25 using HeLa and MCF7 Drosha knockdown cDNA. Likewise, lanes 4 & 5 show amplicons corresponding to the amplification of ALT SPLICE 93 and Lanes 7 and 8 show amplicons corresponding to PRI 24. The specificity of the amplicons were confirmed by DNA sequencing. It can be observed that the amplicons corresponding to the partly spliced host gene MCM7 (observed in Fig. 3c), are absent in Lanes 2,3,4 and 5 since the exon junction spanning primers bind exclusively to their corresponding alternatively spliced pri-miRNAs. Lanes 1 and 6 represent DNA molecular weight markers.



Supp. Fig. 3f Accumulation of ALT SPLICE 25, ALT SPLICE 93 and PRI 24 upon Drosha knockdown.

RT-PCR was performed with exon-junction spanning primers as described in Supp Fig. 3e. The agarose gel electrophoresis images show accumulation of the novel transcripts ALT SPLICE 25 (Lane 3) , PRI 24 (Lane 8) , ALT SPLICE 93 (Lane 12) upon Drosha knockdown in HeLa cells . PPIA was used as loading control (Lanes 5 and 6). Lanes 1, 9 and 13 correspond to the NTCs (No Template Controls) for ALT SPLICE 25, PRI 24 and ALT SPLICE 93 respectively. Lanes 4 and 10 represent the DNA molecular weight markers.

Supp. Fig. 4a

HUMAN MCM7 INTRON 13 (771 bp)

GTAAGTGCCCAAATTGCTGGAGGGCCATCTGTTTTGACCCTTAAAGGGGTAGCTCCTTACCGTGCTCTCATTGCCGC
CTCCCCACCTCCCGCTCCAGCCCTGCCGGGGCTAAAGTGCTGACAGTGACAGATAGTGGTCCTCTCCGTGCTACCGCA
CTGTGGGTACTTGCTGCTCCAGCAGGGCACGCACAGCGTCCGTGGAGGGAAAGGCCCTTTCCCCACTTCTTAACCTT
CACTGAGAGGGTGGTTGGGGTCTGTTTCACTCCATGTGTCCTAGATCCTGTGCTACAGACCTTCCTTTCTGTCCTCC
CGTCTTGACCTCAGTCCTGGGGGCTCCAAAGTGCTGTTTCGTGCAGGTAGTGTGATTACCCAACCTACTGCTGAGCT
AGCACTTCCCGAGCCCCGGGACACGTTCTCTCTGCCAATTGTCTTCTTGCTGAGCTCCCCAAGCTCCATCTGTCA
TGCTGGGGAGCCAGTGGCGTTCAAAGGGTCTGGTCTCCCTCACAGGACAGCTGAACTCCGGGACTGGCCAGTGT
GAGAGGCGGAGACTTGGGCAATTGCTGGACGCTGCCCTGGGCATTGCACTTGTCTCGGTCTGACAGTGCCGGCCCAA
CACTGCGGATGCTGGGGGGAGGGGGGATTCCACTCCTGTTTTGTGAGTAGGCGACCATGGGCTGCCAGCCTTAAA
GCCAGAACAAGGTGTCCCCTGACCTCGTTCACCTGCCCTCCTCCGTTCCCATCTTCCCCCTACCTTCCCCTTA
G

Supp. Fig. 4b

MOUSE MCM7 INTRON 13 (748 bp)

GTGAGTGGTGGGTCCCTGTCAGCTGGAAAGCTGACCCCTGCCTGCCACCTCACCTAATGACCCCTCAAGCCGCCTCCT
TCCCTCCTACCAAGCCCTGCTGGGACTAAAGTGCTGACAGTGACAGATAGTGGTCCTCTCTGTGCTACCGCACTGTGGG
TACTTGCTGCTCCAGCAGGGCACGTGCAACGCCCATGGAGGGAAAGGCTGCTTGCTGCTTGAATCCATGAGGGCTAG
GACTTGAATTCCTGGTGTCTAGATATGATCTTAGAAATCTCCATTCTGTCTCCCTCCTTGGACCTTATCATGGG
GGCTCCAAAGTGCTGTTTCGTGCAGGTAGTGTAAATTACCTGACCTACTGCTGAGCTAGCACTTCCCAGCCCCAGGA
CAACACCTCTGATAGTGGCCCTAGCTGAGCGCCCCAGGCTCCATTTGTTTGATGGGGAGCCTAGTGGAGTTCAGAAG
GGTCTGGTCTCCCTCACAGGACAGCTGAACACCCACCGGGACTGGCCAGTGTGAGAGGCGGAGACTTGGGCAATTG
CTGGACGCTGCCCTGGGCATTGCACTTGTCTCGGTCTGACAGTGCCGGCCCAACACTGCAGATGTGGGGGGGCAGGG
AGGAGTCCCCATTTTGTTCATGAGTAGGCAAATGTGGCTTGCCAGGCTTGAAGCTGGAGCAAAGAAAGATCCTT
GACTTCATTCCCCTCCTCCCCTCCTATCCAATCTTTCTATGCCTTCCCCTTAG

Supp. Fig.4 Schematic representation of splice acceptor signals upstream of intronic miRNAs predicted by SplicePort .

Supp. Fig.4a Splice acceptor signals upstream of human intronic miRNAs miR 106b-93-25.

The sequence depicted represents the full length sequence of intron 13 of MCM7 gene. The sequences depicted in green, blue and black letters represent the precursor sequences of miRNAs 106b, 93 and 25 respectively. The underlined sequences represent the corresponding mature miRNA sequences. The sequences highlighted in yellow represent the splice acceptor signals predicted by SplicePort.

Supp. Fig.4b Splice acceptor signals upstream of mouse intronic miRNAs miR 106b-93-25.

Representation as in Supp. Fig. 4a. Note that the splice acceptor signals upstream of mouse miR 106b and miR 25 are almost similar in location to that of the corresponding human miRNAs.

Supp. Fig. 4c

HUMAN AP-O intron 14

```
CCTCCTGACTTGAGAGTCCCCAAAGCCTTCCCAGGGCAGCTAGAATCTGCCTGGAGAGAAGGGATCTTGTCCTCCCAAG
GGTTAGAGGCAGTAACTAATAGCAAGGACAGCTGCCTTTAGCAATTGTGTGTGTCGATGGCCGGTCCCTGCATT
TCTTC TCCCAAGCTGCACTGGCATTATATGGTCATCTCTGGAGTCCCTTTGATTCAAGAAATTATACCTCTA
GGATGCCAACTAAACGAACAACAACAGAAATCCACCTGTTTGTAGCATAAC TCCCTG AAGCGGCAGTGTGCG
CGGCGTCCCTTCGCGGAAGCCAGTGTGTGCAGACAGCAGGGGTGGCGCTGCTCTCAGGTGCTCTGGCTGCTTGGG
TTCCTGGCATGCTGATTGTGACTTAAGATTAATAATCACCATTGCCAGGGATTACCACGCAACCACGACCTTGGCTGC
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AAGCCACAGCTGAGGAAGATGCTCACCGGTACCGTCCCTTTATTTATGCCAGCGATGACCTCTCTAACAAAGGTG
CAGAGCTTAGCTGATTGGTGAACAGTATTGGTTTCCGCTTTGTTTACAGTGGCTAAGTTCTGCACCTGAAGAGAAG
GTGAGATGGGGACAGTTAAGTTGGAGCCGCTGGGGCAGAGGCCGTTGCTGACGGGCCGGCCGCTGCTGCACAGTCAG
CTTGGGTGCGGAGCGGATCCTGGAGGATGAGAGACCCTTGACCCCAAGGATGCATGTCTCCTGCTGGGAATGCT
AGCCATGTACTGAGTCCTTAAGTCTGTCCACAGAAACATGCACTAATCGGACATCTGTCTGAAAGGTCAATGTATT
GAAAGTTGCAAAATCTCTTACAAAAAATAAAACCAATGCATCACCTAAGTCGTGTGAAATCATGTGGTAGCT
CATGGCTGTGAGCGGGGGGGGGGGGGCTTTCGGAGGAGCTCCTGTTGTTCTGGGCGCGGTGAACCTCTCTTTGTA
TTGCT TCC TCCCTTCGCGTCTCCTGCGCCAGCAGAGGTGCCACGGAGCTCCAGCTGAGGCGCTGCTTCTCCG
GGCTGTGATTTGAGCCCGCCCTCCCGGTGCTACTGAGCTGATATCAGTTCTCATTTTACACACTGGCTCAGTTTCAGC
AGGAACAGGAGTCGAGCCCTTGAGCAAAAGCCTTCGTGTCTGTAAGTCCCCAGGCTCAGGAGAGCTGGGGCTCCC
```

Supp. Fig. 4d

MOUSE AP-O intron 15

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CCTCAGCTTATCCAACCAATGCTTGGTCACAGGCAAGCCAGAGAGATGCTCCCTCCCTACACACCACACCTGCTGT
CTGAGGGGGCCAGAGACATCCAACCCATTTCAGTCTGCAATTGGAGAACAGGGTGTGTCCAGGGTTAAAGGCCACA
TACTCAGAGCAAGGATGTCCTTAAGGTATTGGTCTCATAGCTGATAAGTGTGTCTTTGTCTCCCT TCCCT TCCCT TATG
CTCCTCTATAC TGCAGCCAGCGCGCTGAAGGACAGCAGGCTGCATGCTAGCGTGGTGGGCTCAGAGGCGGTTTG
GAGGACACTCAGCACATGTGGATGGGAGTGGTTGGGCATGGTGTGCCCTCACCTGCTCTGGCTGCTTGGGTTCTTG
GCATGCTGATTGTGACTTGAGATTAAATCACATTGCCAGGGATTACCACGCAACCATGACCTTGGCTGCTCTTG
TGGTGAACAGTATTGGTTTCCGCTTTGTTTACAGTGGCTAAGTTCTGCACCTGAAGAGAAGGTGAGATGGGGACAG
TAACTTGCAGCTGCCAGGCAAGGCCACTGCCTGGTGGTCACTCCAGAGGAGGAGAGACCAGCTGCCTCAAGGCT
GTGTTGTCAAGAGTGCAAACAGCGTGTGACCAACCTTAAGTGTGTCTACAGAAAATACAGTTCTACTGCTAATTAG
TTCAGTGAATGTCAAGTGTATTGGGAGTCACAGAAAATAAAACCCAGGTGCATCAAGGAACTGAGCCAACTTGT
CTCAGCTGATGCCACACGTGATGGGTGGGGGTGGGTTCTTTGTCCCTGCTGGGCGTGGTGAACCTTTCTTGTA
TTC TCC TCC TCTCTCATGTCTCCACAGTCGCTGGCAAGATGATGCCAGGGCAGCCAGGAGGCACTGCCAGCTG
TGATTGGACCCGCTCCCGGTGCTACTGAGCTGATATCAGTTCTCATTTTACACACTGGCTCAGTTTCAGCAGGAAC
AGGAGTCGAGCCCTTGAGCAAAAGCCTACCATCTGTAAGTGCCTGAGGCAAGCCTCCACGGAGAAGAAGATGAA
```

Supp. Fig.4c Splice acceptor signals upstream of human intronic miRNAs miR 23b-27b-24-1.

The sequence depicted represents part of the sequence of intron 14 of human AP-O gene which harbors the intronic miRNAs. The sequences depicted in green, blue and black letters represent the precursor sequences of miRNAs 23b, 27b and 24-1 respectively. The underlined sequences represent the corresponding mature miRNA sequences. The sequences highlighted in yellow represent the splice acceptor signals predicted by SplicePort.

Supp. Fig.4d Splice acceptor signals upstream of mouse intronic miRNAs miR 23b-27b-24-1.

The sequence depicted represents part of the sequence of intron 15 of mouse AP-O gene which harbors the intronic miRNAs. Representation as in Supp. Fig. 4c. Note that the splice acceptor signals upstream of mouse miR 27b and miR 24-1 are almost similar in location to that of the corresponding human miRNAs. ESTs which support the usage of predicted splice acceptor sites upstream of mouse miR 27b and 24-1 are depicted in Supp. Figs. 6b and 6c respectively.

Supp. Fig.5a

HUMAN EGFL7 INTRON harboring miR 126

GTAAACAGCCCTGGCTGTGCCTGGCCTGGGGAGGCGGGCAGGCAGTGGACATTGCCGTGTGGCTGTTAGGCATGGTG
GGGGGCACTGGAATCTGGGCGGAAGGCGGTGGGGACTCCCTCTCCAGGGAGGGAGGATGGGGAGGGAGGATAGGTGG
GTTCCCGAGAAGTGGGGGAGGTTGCCCGGAGCCTCATATCAGCCAAAGAAGGCAGAAGTGGCCCGTCCCGGGGTCCCT
GTCTGCATCCAGCGCAGCATTCTGGAAGACGCCACGCCTCCGCTGGCGACGGGACATTATTACTTTTGGTACGCGCT
GTGACACTTCAAACTCGTACCGTGAGTAATAATGCGCCGTCCACGGCACCGCATCGAAAACGCCGCTGAGACCTCA

MOUSE EGFL7 INTRON harboring miR 126

CTGCCTGTCTAAGGAGGGGCCCTCCCGGTGGCCCCAAACCCACAGCAGGTAAACTTGCCTTTCCACCTGCTATG
ACTGACCTGGGTAGTCCTTGGGTTGTGAGCACTGTTGTGTGGCTGAGCTGAACATGGAAGACACAGGGGCAGCTAGC
CCTGGGTGGAGGCCAGCACTATGCTGTGAGGGCTGGCTCCTTGCCTGGTGGAGGGGCCACTTTACCCTGAAGAGGT
TTCTGGAAGGCATTGTGGGGCGTAAGGCATACCTGGGAGCCCCATCTCAGCCAGTTGAGTGAAGAGCCCCACACTG
GCTCTGGCCTCTGGAGACGCGCATCTTTGCCGCTGACAGCACATTATTACTTTTGGTACGCGCTGTGACACTTCA
AACTCGTACCGTGAGTAATAATGCGCGGTCAGCAGCCAGCGCCAGGAATGCATCGGACCTGGGTAAAGACCACGGC

Supp. Fig.5b

HUMAN EML2 harboring miR 330

GTGAGACCCTTTTCGAGACCACCCCCATCTCCTCTCCGCGCTCCCGGGCTTAGATCTCAGGTTTCACCCAAACCC
TGGGACCCAGACCGCGTGGGGACACGCCCTTCCCTTAAACTCTCCCGTTTCTCCCTCTGCTTGACGTTTGGTGT
GCTGGGGGAACTCGCGGTGGGGGCGCTGGGGAGCACCTTGTCTGATTAGAGGGAAGGGTCTTGGTGACTCCCTT
TTCCAGATCGCGTCCCTGCCACTTCGTGCTGTGTGATCTTTGGCGATCACTGCCCTCTCTGGGCCTGTGTCTTAGGC
TCTGCAAGATCAACCGAGCAAAGCACACGGCCTGCAGAGAGGCAGCGCTCTGCCCTTACTCGGCCCCGTTTTATC
GGAGACCTCCGGGAGCGGTGGGGTGGAGGAATGTTTCTCCCTTTTCTGAACTGAATACTAAGACCTTTTTTT

MOUSE EML2 harboring miR 330

CCCGGACCCGAAGCTCCGCCAGCAGCCGCCATGAGTAGTTTTGGAATTGGGTGAGACCCTCTTTCAGCACCCCTCCT
CCCTCCTCCTGCCCTTCTCGCCTCAGGAAGAGAAGGTGGAGACACGCCCTTCTCTGAACTTTTCATCGTCTTCTCT
GGCTGCTTGAAGTTTGGGGTGTGCTGGGTAGGGAGGGAAGGAGCGCCGGGGAGCGTTTTGTTGCTGTTGCCTAGGA
GGGAGGGTCCCTAGTGACTCCGGTTTCCAGATCGCGTGCCTGCCACATCGTGCTGTGTGACCCCTTGGCGATCTC
TGCCTCTCTGGGCCTGTGTCTTAGGCTCTTCAAGATCCAACGAGCAAAGCACAGGGCCTGCAGAGAGGTAGCGCTCT
GCTCCTTACTCGCCTGATTATTCTGTTCCAGACCTGCAGAGCCCCGGGGTTAGGGGAAGTATTCTTGTCTATCTCA
TATGCTTGCTAAACACTTATTTCTTCTCTCCCTACCCCTCTTCTCTCCCTGCATCTTTCTCTGACAGGAAA

Supp. Fig.5c

HUMAN CTDSP1 intron harboring miR 26b

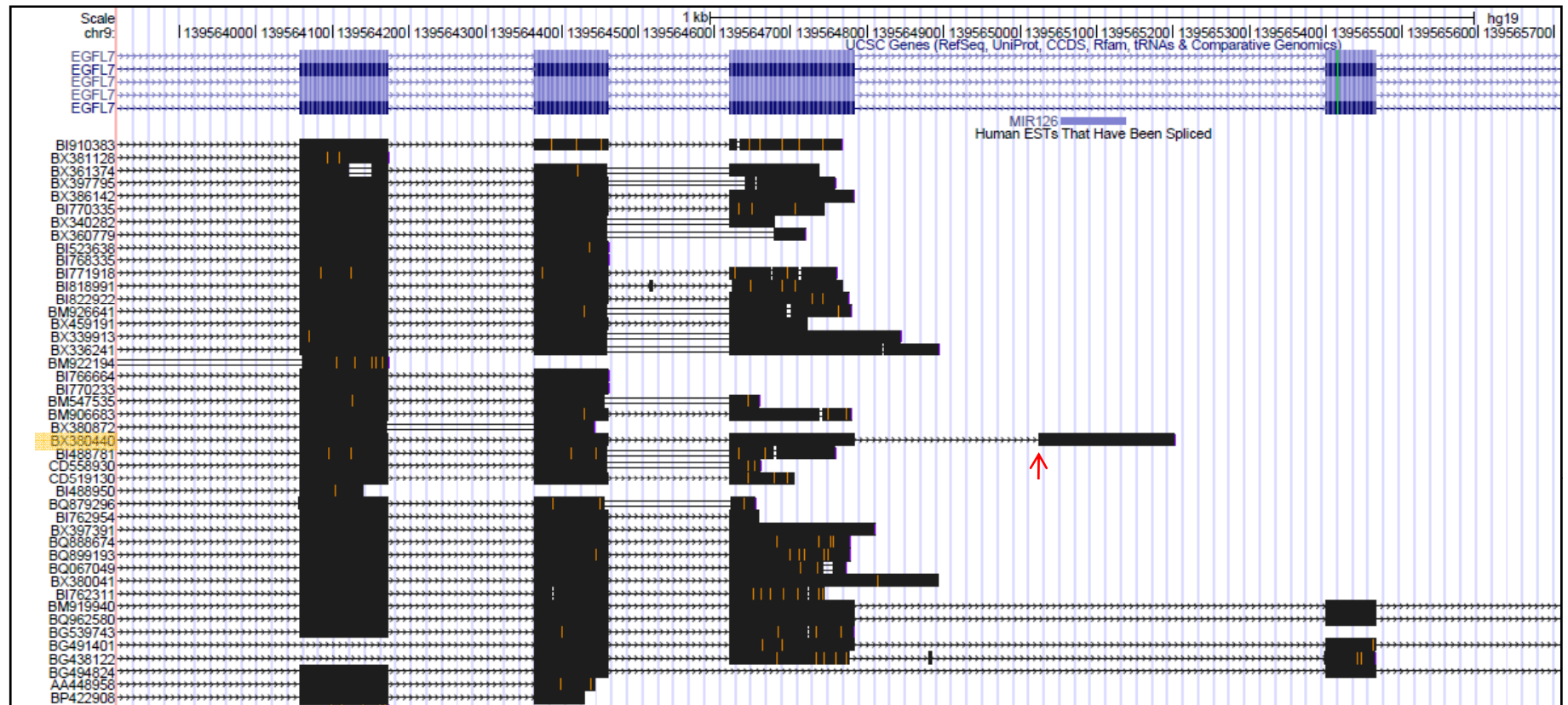
GTGAGGGCCAGGAAGAGGCAGTGGTGGGCTTGGCATCTGCCTCCAGACCCTAGGCTCTTCCCACCAATCCGGAGCGC
CTCGGATGGGAATTGGATACATGTGGAATGTCAGAGGCCAGAGAGGGTGTGAGACTTGTCCAAAGTCACACAGAA
CCTCAAGGGCTTGTGCTGACTCCAAGCTGCAGAGTGGGCTCCTCCTTAGGCTCCCCGTGCTGTGCTCCTTCGCC
CCACCTGCCCGGGACCCAGTTCAAGTAATTCAGGATAGGTTGTGTGCTGTCCAGCCTGTCTCCATTACTTGGCTC
GGGGACCGGTGCCCTGCAGCCTTGGGGTGGGGGGCTGCCCTG

MOUSE CTDSP1 intron harboring miR 26b

GTGAGGGTCAGAGGGAGGTGGGGAGCTTGGTGTCTGCACTACACCCAGTTCCTTCCCACCCCTTCTTGAGCGAGTCCC
CCATGGAACTTTAATAGATGGGGCGTGCAGAGCTCAGAAAGAGTGAGAACCAGACTACCTGGTACTCCAGAGA
TGGAGCCAGACTCCCAGACCTGCACACTGGGCTCCTTCTGGTCTGTCTTGTGACGCCCTCTTTCCCTCTTACCCC
TACTGCCCCGGGACCCAGTTCAAGTAATTCAGGATAGGTTGTGGTGTGCTGACCAGCCTGTCTCCATTACTTGGCTCGG
GGGCCGGTGCCTGCAGCCTTGGGGT

Supp. Fig.5 Splice acceptor signals predicted upstream of intronic miRNAs miR 126, 330 and 26b.

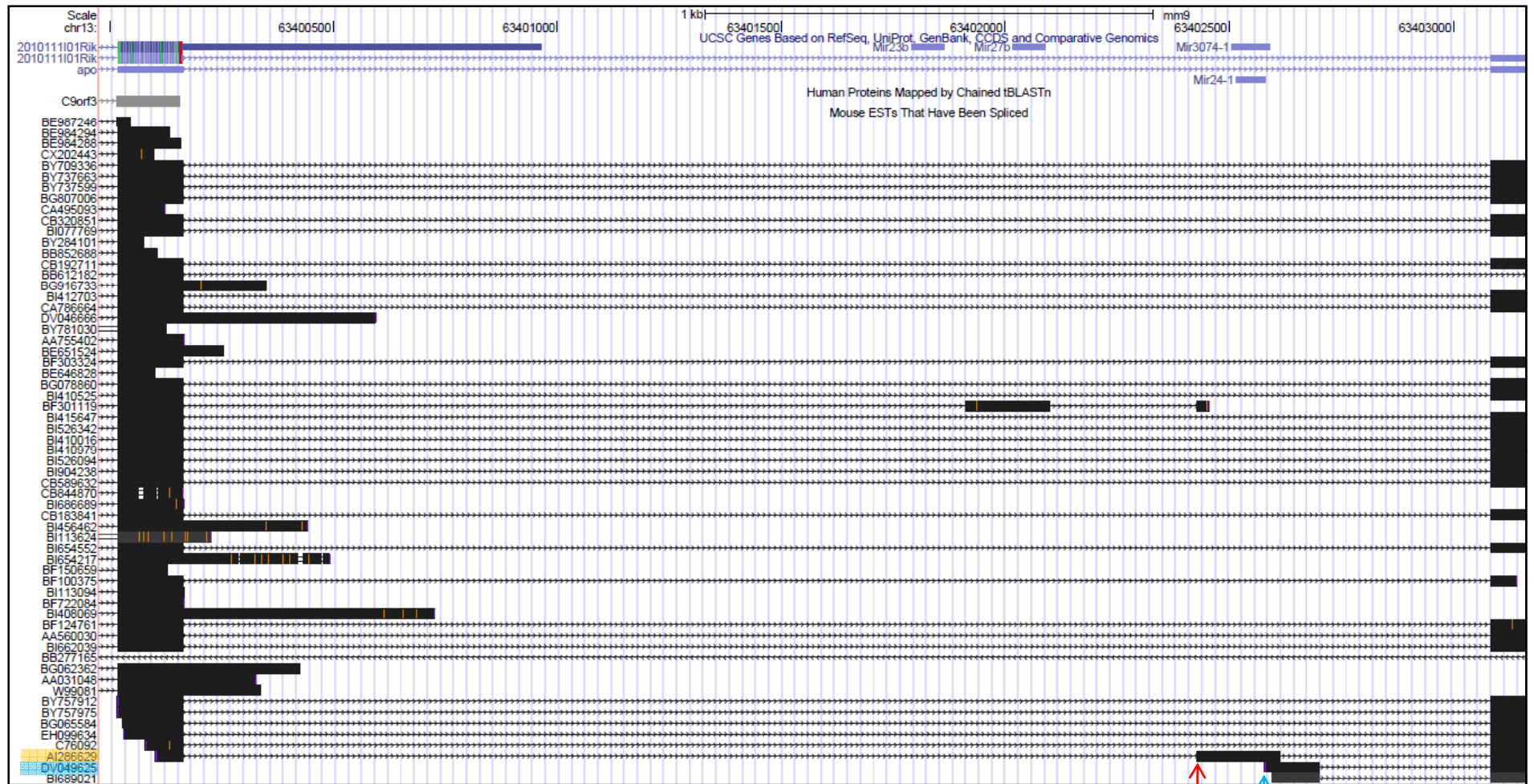
The sequences depicted in Supp. Fig. 5a, 5b & 5c represent part of the sequence of introns which harbor the human and mouse intronic miRNAs 126, 330 and 26b respectively. The sequences depicted in black letters represent the precursor miRNA sequences. The underlined sequences represent the corresponding mature miRNA sequences. The sequences highlighted in yellow represent the splice acceptor signals predicted by SplicePort. EST which supports the usage of splice acceptor site upstream of human miR 126 is shown in Supp. Fig. 6a.



Supp. Fig.6 ESTs supporting the usage of predicted splice acceptor signals upstream of intronic miRNAs.

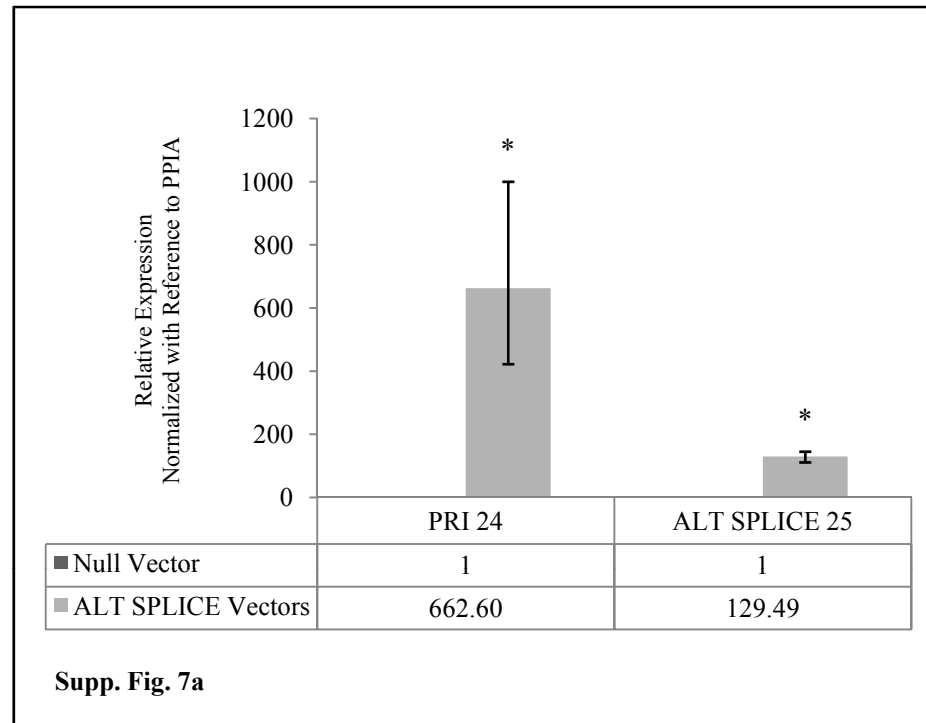
Supp. Fig.6a EST corresponding to human intronic miRNA miR 126.

The figure shows the location of precursor sequence of miR 126 in relation to its host gene EGFL7. The EST BX380440 corresponding to human miR 126 is highlighted in the left panel. The red arrow represents the location of predicted splice acceptor signal upstream of miR 126.



Supp. Fig. 6c EST corresponding to mouse intronic miRNA miR 24-1.

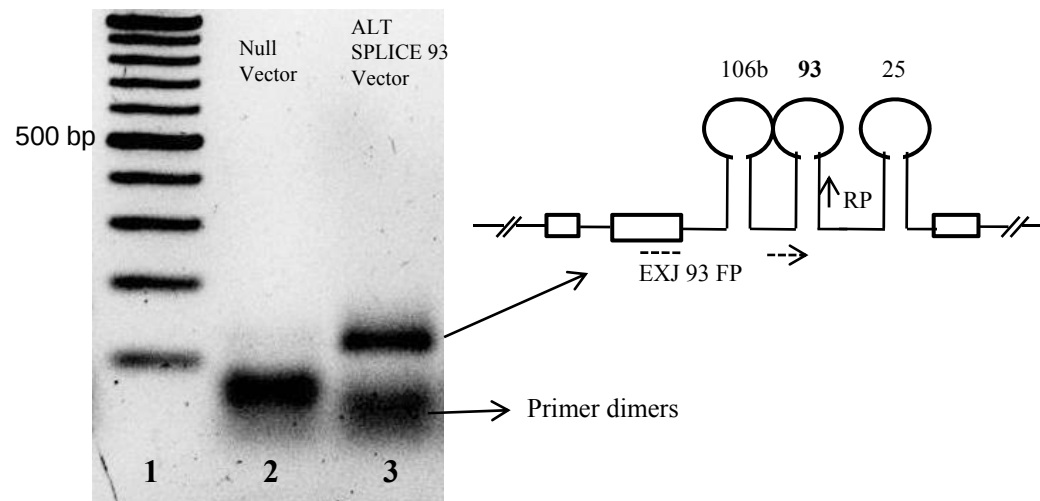
The figure shows the location of precursor sequence of mouse miR 24-1 in relation to its host gene AP-O. The EST AI286629 corresponding to mouse miR 24-1 is highlighted in orange the left panel. The red arrow represents the location of predicted splice acceptor signal upstream of miR 24-1. The blue arrow represents the location of Droscha cleavage site of pri-miR 24-1. The EST DV049625 (highlighted in blue) probably represents the Droscha cleavage product of EST AI286629 providing further evidence to suggest that EST AI286629 might represent the pri-miRNA of mouse miR 24-1.



Supp Fig 7a. Overexpression of alternatively spliced pri-miRNAs after transfection of CMV promoter driven miRNA mini-genes.

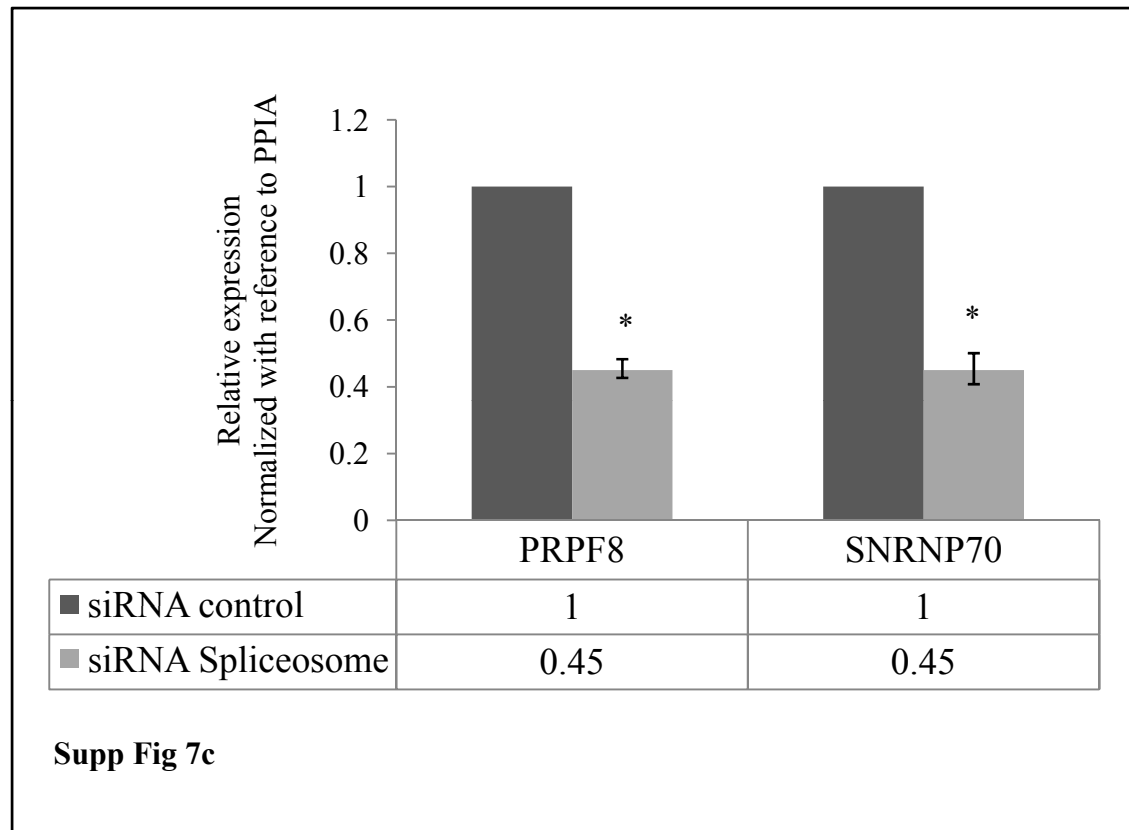
ALT SPLICE vectors refers to the pTraget Mammalian expression vectors into which the sequences corresponding to PRI 24 and ALT SPLICE 25 were cloned. Null vector refers to the pTraget vector without any insert. The vectors were transfected into HeLa cells. Column 1 depicts relative expression of PRI 24 from the Vector containing the PRI 24 insert as compared to the null vector. Column 2 depicts relative expression of ALT SPLICE 25 from the Vector containing the ALT SPLICE 25 insert as compared to the null vector. Exon junction spanning primers, as described in Supp. Fig. 3e, were used for amplifying and cloning the alternatively spliced transcripts into the vectors as well as quantifying their overexpression by RealTime PCR. Expression of PPIA was used for normalization. * denotes statistical significance and represents $p < 0.01$. Primer sequences are mentioned in Supp. Table 1.

Supp Fig 7b. Overexpression of alternatively spliced pri-miRNAs by RT-PCR.



Supp. Fig. 7b

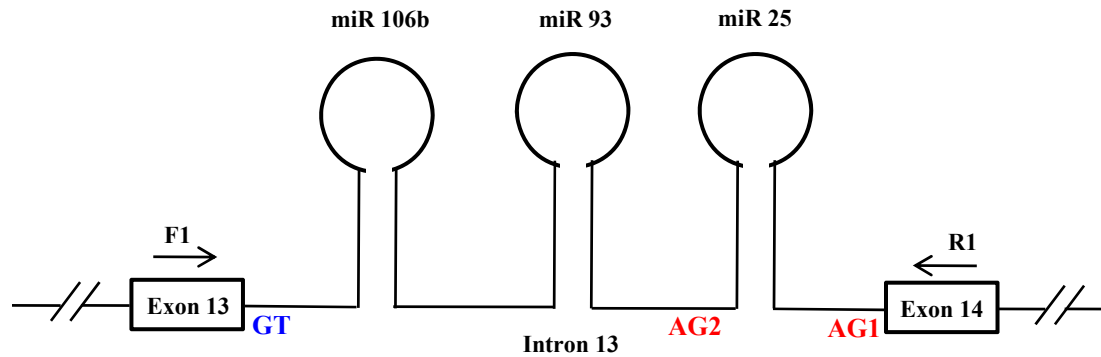
The image shows agarose gel electrophoresis of RT-PCR amplicons. ALT SPLICE 93 vector refers to the pTraget Mammalian expression vector into which the sequence corresponding to ALT SPLICE 93 was cloned. Null vector refers to the pTraget vector without any insert. The vectors were transfected into HeLa cells. Lane 3 depicts the overexpression of ALT SPLICE 93 transcript from the Vector containing the ALT SPLICE 93 insert. Lane 1 represents DNA molecular weight markers. ALT SPLICE 93 could not be quantified by RealTime PCR because of interference from its primer-dimers whose T_m was very close to the specific amplicon.



Supp. Fig.7c Confirmation of Spliceosome knockdown.

Expression of PRPF8 and SNRNP70 mRNA quantified by RealTime PCR after Spliceosome knockdown in HeLa cells. Fold changes represent expression in SNRNP70 and PRPF siRNA transfected cells as compared to control siRNA transfected cells. Normalization was performed with reference to PPIA. * denotes statistical significance and represents $p < 0.01$.

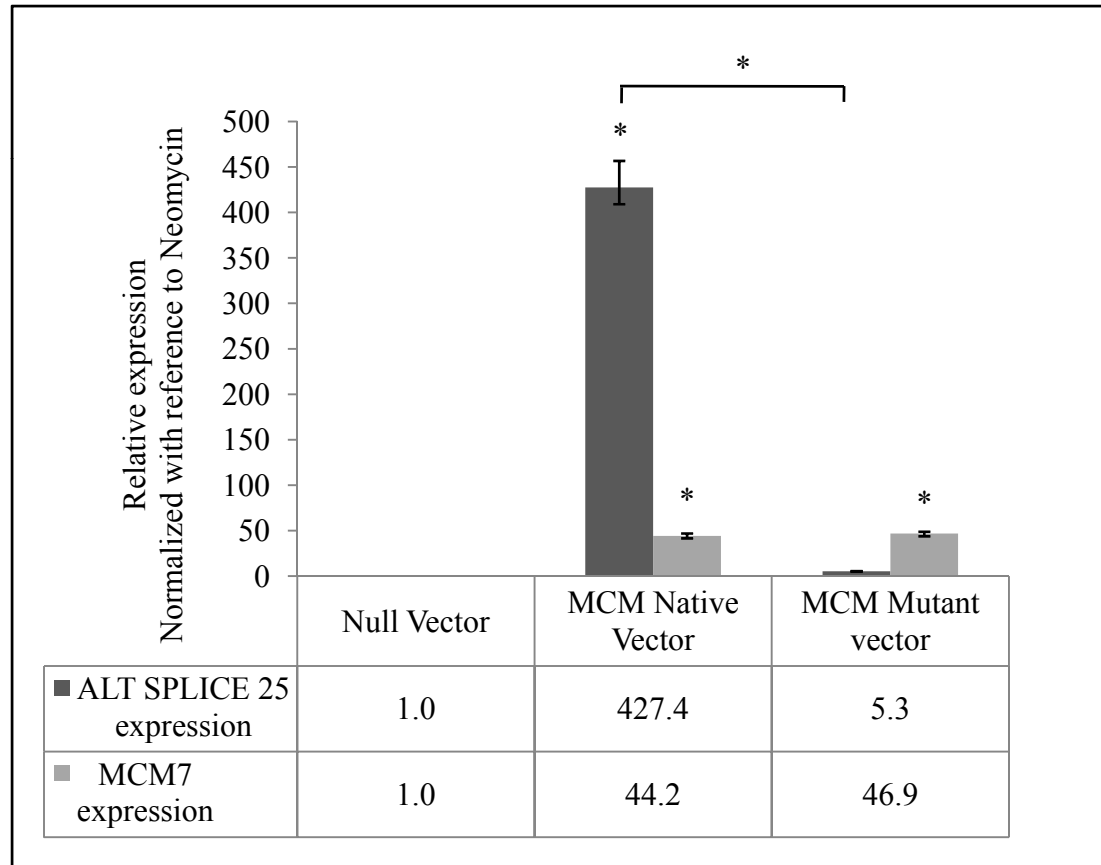
Supp Fig 7d. Site directed mutagenesis of splice acceptor signal upstream of miR 25.



The schematic on the left denotes the structure of intron 13 of MCM7 gene along with flanking exons. F1 and R1 represent the forward and reverse primers used to PCR amplify HeLa genomic DNA for construction of the MCM Native vector. The PCR amplicon generated using these primers was cloned into the pTarget Mammalian expression vector, and is denoted as MCM Native vector. GT denotes the splice donor site at the 5' end of intron 13. AG1 and AG2 denote the splice acceptor sites upstream of Exon 14 of MCM7 and ALT SPLICE 25 respectively.

Recognition of the GT-AG1 splice sites by the spliceosome results in generation of mRNA corresponding to exons 13 and 14 of MCM7. Recognition of the GT-AG2 splice sites results in the generation of the pri-miRNA of miR 25 namely ALT SPLICE 25. MCM Mutant vector was generated from the MCM Native vector by mutating the AG2 splice site using site directed mutagenesis wherein the splice acceptor site was mutated from AG to CT. Null vector represents the pTarget vector without any insert. The vectors were transfected in HeLa cells.

The graph depicted on the left denotes the expression of Spliced MCM7 mRNA (using primers F1 and R1) and ALT SPLICE 25 transcript (using exon junction spanning primers depicted in Supp. Fig. 3e) by RealTime PCR. Expression of Neomycin gene present in the vector was used for normalization of vector expression. * denotes statistical significance and represents $p < 0.01$.



AGGCCGCTGCATGTGACTTTCAAAGGACCTGCTTGTGTTGAATTTACAGCCAGCAAGTCTCCAGCATACAGAATTTGAGATTTCCCCACCCCCACCGTTTCTTCTGTTTTGT
 TCCATGTAAACAGTTCCCTGCGTAGTAACATAGACAAATATAGCAGAGAATGCTTTTCTGGAAGAAGAATGCTCCCTAAGCATTTTTTAACCATTTTTGGGAAGAATTGATCTTT
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 GCATCAGGGAGGAAGCATGCTTCATTTAGGCACAGATCCCAGAGTGATAATGGGGTAATAATAGAACTCATGCCCATGTCAATCCGTGGCTGCATTAGTCCCAAGGCTTATTCTCT
 GTCTGGGGAGCCGACAGTGACTTTCTTCGTGTGAGGCTGCAGCGCACAGCTGGGCCACGCCGGGAGGTGCCCTCCTTTGCTTTCCGAGGGGTGCAGGCAATGGGGCTTGGATG
 TTGCCATTTGCTGGTCTCTTGTACAGGCCCTGCCCTGCAAGGTCACTGATGGGACATGTCCGTGGCATTCTTCTGATGTAGGAGGTGAGCTGGCCTGTTCTGCATCATGCTAAT
 GGAAGAAATGGTGGCGGAACCTCAGT**TGCGTGGGT**GGTCTTCTGGGAGCACAGAGTGAGTGATGCCCCCGTGACAGCAGTAAGAGGCTTCTGCAAGAGTCAGGGGTTTTCTTCTAG
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 CCTATTTTGTGTAAATTTCCGAGGCAGATGCATTTTAAAAATAATGAGCTGGTCTCTGTATGGAAAAATAACCCCATCATGAATTTCTGTTTATGCAAAGGAAAGGACTTTTTG
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 TCCCCCATGAGTTAGAATAGTTACAATAAAGCCAGGTGGCCGAGGTGTTTACCAAGTGAGAGTCATTTCAAGTCTATTACAGAAGAATGGGACTCACAGAAACCTGGGAGC
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 TCTGTGTAGAGTTGCTGAGCTTTTCAAGTCTTAAAGAAAACCTAGATATACAGGTATGAATGCAGGTATTTTGTAGGTTACATATAGGTAATTGTTTGAATTTAACTGGAGCTG
 TATCTATTGGTTAAACCTAGTTGGGGTTAAGTTGAGGACCAAGCTAGTTGTCTTACTCAGGGTTTCTTTGCTCTGTGTCTCTTTAGTTTAGACCAATCCCAATGAGAGTTC
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 TGGAGCAGAAGACTCTGAGCCCCGAACCTCTGCAAAAGCCTCCAGAGGACATACCA**CCT**

Supp Fig 8a. HIF-1 α binding sites 5 kb upstream of PRI 24.

The sequence depicted above represents the 5 kb genomic region upstream of the start site of pri-miRNA of miR 24-1 namely PRI 24. The sequence **CCT** represents the start site of PRI 24. The sequences highlighted in yellow depict the predicted HIF 1- α binding sites based on its canonical binding site consensus sequence V\$HIF1_Q6 : **NRCGTGNGN**.

GACTCTGTGGGGAAGTTGGTAACTGTGCGTGGAATCGTCACTCGTGTCTCTGAAGTCAAACCCAAAGATGGTGGTGGCCACTTACACTTGTGACCAGTGTGGGGCAGAGA
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 CTCAACACCCAAAGAGAGGTCCCTGTAAATGATCTGTGTAGGGAGGAGAGAGGTGAATCAGAAAACAAATTCACGCTCCTGGAAACCCAGAGCCTCCCTTTGCGAG
 CAGGGGCTGGTCCATGGTTCTCAGGGAATGGTGGGTGGGGCTGAAATGCTGATGAGGATTTCCCGGGAAGCTTGTCCCTCTACACTGTGAGGAAGTGGCAGAGCC
 AAAGAGGACCACTAAGAGGACATGGGTGCGTAGCCCTAAGAGGGTGTCTCTTCAACCTTCTGCTCCAGGTGGGCCAGCACATCACTATGTGCACACGAC
 AGCCGGCAGCCCCCTCCAGTTGAACCTCTGGACATGAAGCTCATGAGGTAGGAGAGCTGGGTGCGGGTGGGCAACCGTTGGCGTGGGCTCTCTGAAA
 AAGTGCCTATTAGTCTTAGGGTGTGTGTTTTTACACCACCACTTCCCGCTACAGACATGTCCAGAGCCTCAGATCAGCTTTTAAGTGGAATAATCCACACTTCATATC
 ATAGGGACACAGGAATTTTGTTCCTACACTATTTATTTTTTTGAGACGAAGCTTGCTCTGTACCCAGGCTGGAGTGTAGTGATCTCAGCTCTCTGCAACCTCTG
 CCTCCAGATTCAAGCGATTCTCTGCTCAGCCTCCTGAGTAGCTGGGATTACAGGCGCAGGCCACCGCTGGTTAATTTTTTGTATTTTAGTAGAGGACAGTTTC
 ACCATGTTGGCGAGGATGCCACCTCTGCCTCCCAAAGGTGCTGGGATTACAGGCTGATGATTTCAAGCCAGCAAAATTAATCACCCTAATTTGTGTTTTCCACTTAAAA
 TTCTTGAGGGGACCATGTTAAATGGGGAGCCCTGGTACAGAAAACAACATGGGCTCATATTCACTCCCTTCCCATCTCCCTCTTCTGCTTCCCCATGAACCTTCCCC
 CACAGCGCTTACATAGCCATGTGCCGCGAGAAGCAGCCCATGGTGCCAGAGTCTCTGGCTGACTACATCAGCAGCATACGTGGAGATGAGGCGAGAGGCTTGGGCTA
 GTAAGGATGCCACCTATACTTCTGCCCGGACCTGCTGGCTATCTGCGCCTTCCACTGCTCTGGTAAGTGCCCAAATTGCTGGAGGGCCATCTGTT

Supp Fig 8b. HIF-1 α binding sites 5 kb upstream of PRI 106b/93.

The sequence depicted above represents the 5 kb genomic region upstream of the start site of pri-miRNA PRI 106b/93. The sequence **GTT** represents the start site of PRI 106b/93. The sequences highlighted in yellow depict the predicted HIF 1- α binding sites based on its canonical binding site consensus sequence V\$HIF1_Q6 : **NRCGTGNGN**.

S.No.	miRNA	miRNA Classification	Pri-miRNA classification	Technique employed to characterize the Pri-miRNA	Reference
1	miR 23a	intergenic	Unspliced	Primer Extension	Lee 2004
2	miR 155	intergenic	Spliced	RACE	Eis et al 2005
3	miR 146a	intergenic	Spliced	RACE	Taganov et al 2006
4	miR 146b	intergenic	Unspliced	RACE	Taganov et al 2006
5	miR 127	intergenic	Unspliced	RACE	Saito et al 2006
6	miR 34a	intergenic	Spliced	RACE	Chang 2007
7	miR 223	intergenic	Spliced	RACE	Fukao et al 2007
8	miR 17	intergenic	Unspliced *	RACE	Woods et al 2007
9	miR 1-2	intergenic	Unspliced *	Primer Extension	Fujita et al 2008
10	miR 133a1	intergenic	Unspliced *	Primer Extension	Fujita et al 2008
11	miR 199a2	intergenic	Unspliced	Primer Extension	Fujita et al 2008
12	miR 122	intergenic	Spliced	RACE	Chien et al 2011
13	mir 24-1	intronic	Spliced	RACE	This study
14	miR 106b-93	intronic	Unspliced	RACE	This study

Supp Fig 8c. List of full length pri-miRNAs corresponding to human miRNAs identified till date.

The above table lists the human miRNAs for which their full length pri-miRNAs have been characterized. The pri-miRNA classification is based on whether their sequences include multiple exons (spliced pri-miRNAs) or single exons (unspliced pri-miRNAs). * represents miRNAs for which spliced ESTs which encode these miRNAs in one of their exons have been identified. ENST00000581072 is a transcript which encodes miR 1-2 and miR 133 a1 in its third exon. ENST00000581816 is a transcript which encodes miR 17 in its third exon. It must be noted that primer extension studies cannot predict exon-intron structures because they assume lack of introns between the primer binding sites and Transcription termination site.

Supp. Table 1. List of primer sequences.

RACE primers		
S.No.	Primer ID	Sequence (5' to 3')
1	5-106b OUT-REV	AGTGCGGTAGCACGGAGAGGAC
2	5-106b IN-REV	ACTATCTGCACTGTCAGCACTTTAGC
3	5-93 OUT-REV	TCAGCAGTAGGTTGGGTAATCACA
4	5-93 IN-REV	CTACCTGCACGAACAGCACTTTG
5	5-25 OUT-REV	CTGTCAGACCGAGACAAGTGCAATG
6	5-25 IN-REV	AGCGTCCAGCAATTGCCCAAGTC
7	3-106b OUT-FWD	GCTAAAGTGCTGACAGTGCAGATAG
8	3-106b IN-FWD	CCGCACTGTGGGTACTTGCTG
9	3-93 OUT-FWD	CAAAGTGCTGTTCGTGCAGGTAG
10	3-93 IN-FWD	TGTGATTACCCAACCTACTGCTGA
11	3-25 OUT-FWD	GAGACTTGGGCAATTGCTGGAC
12	3-25 IN-FWD	GCATTGCACTTGTCTCGGTCTG
13	MCM7 PUF	TTGAACCTCTGGACATGAAGCTC
14	MCM7 PDR	TATCACATCTGCTGGTCTCTGAGTC
15	MCM7 EXON FWD	CTATCCTGCGCCTTTCCAC
16	MCM7 EXON REV	AGCCTGATGGCTTCATTCAC
17	5-24-1 OUT-REV	TCCTGTTCTGCTGAACTGAGCCAG
18	5-24-1 IN-REV	TGATATCAGCTCAGTAGGCACCG
19	3-24-1 OUT-FWD	CTCCGGTGCCTACTGAGCTGATATC
20	3-24-1 IN-FWD	CACACTGGCTCAGTTCAGCAGGAAC
21	AP-O EXON FWD	TGAGGACGCCAGACAGCAGCAG
22	AP-O EXON REV	TGATGTCCAGGGTCAGTTCGAGCC

**Supp. Table 1.
Contd..**

Housekeeping genes, host genes and Drosha primers		
S.No.	Primer ID	Sequence (5' to 3')
1	18s rRNA FWD	GTAACCCGTTGAACCCCAT
2	18s rRNA REV	CCATCCAATCGGTAGTAGCG
3	B2M FWD	TAGCTGTGCTCGCGCTACT
4	B2M REV	TCTCTGCTGGATGACGTGAG
5	TUBB FWD	TAACCATGAGGGAAATCGTG
6	TUBB REV	TCGATGCCATGTTCACTACT
7	PPIA FWD	CACCGTGTTCTTCGACATTG
8	PPIA REV	TTCTGCTGTCTTTGGGACCT
9	POLR2A FWD	CATCAAGAGAGTCCAGTTCGG
10	POLR2A REV	CCCTCAGTCGTCTCTGGGTA
11	ACTIN FWD	TCATGAAGTGTGACGTTGACATCCGT
12	ACTIN REV	CCTAGAAGCATTGCGGTGCACGATG
13	GAPDH FWD	CCAAGGTCATCCATGACAACTTTGGT
14	GAPDH REV	TGTTGAAGTCAGAGGAGACCACCTG
15	CA9 FWD	CTTTGAATGGGCGAGTGATT
16	CA9 REV	CTTCTGTGCTGCCTTCTCATCT
17	PGK FWD	CCGAGCCAGCCAAAATAGA
18	PGK REV	GCTGGATCTTGTCTGCAACTTTAG
19	VEGF FWD	ACCATGAACCTTCTGCTGTCTTG
20	VEGF REV	ATGGCTTGAAGATGTACTCGATCTC
21	MCM7 FWD	GGAAATATCCCTCGTAGTATCAC
22	MCM7 REV	CTGAGAGTAAACCCTGTACCA
23	AP-O FWD	CTTCTGAGGCCAACTTCAGG
24	AP-O REV	AAAGACCCGATGAGGAATGA
25	DROSHA FWD	CATGCCCGAACCTACACTG
26	DROSHA REV	TTCAAGCGCATCCATTGC

**Supp. Table 1.
Contd..**

Primers for pri-miRNA quantitation		
	Primer ID	Sequence (5' to 3')
1	Pri-miR 23b FWD	GGCTGCTTGGGTTCCTGGCATGCTG
2	Pri-miR 23b REV	GGTTGCGTGGTAATCCCTGGCAATG
3	Pri-miR 24-1 FWD	CTCCGGTGCCTACTGAGCTGATATC
4	Pri-miR 24-1 REV	TCCTGTTTCCTGCTGAACTGAGCCAG
5	Pri-miR 26a1 FWD	TGGCCTCGTTCAAGTAATCCAGGATAGG
6	Pri-miR 26a1 REV	GCGTCCCCGTGCAAGTAACCAAG
7	Pri-miR 330 FWD	CTTTGGCGATCACTGCCTCTCTGG
8	Pri-miR 330 REV	TGCCTCTCTGCAGGCCGTGTG

Exon Junction spanning primers to validate spliced pri-miRNAs		
S.No.	Primer ID	Sequence 5' to 3'
1. Primers for validating PRI 24	EXJ MIR24 FWD	TTTAACGAGTCCAGGCCTTCGC
	AP-O REV	TGATGTCCAGGGTCAGTTCGAGCC
2. Primers for ALT SPLICE 25	EXJ MIR25 FWD	CACTGCTCTGGACAGCTGAACTC
	MCM PUR	ACTCACAAAACAGGAGTGGAATCC
3. Primers for ALT SPLICE 93	EXJ MIR93 FWD	TCCACTGCTCTGATCCTGTGC
	5-93 OUT-REV	TCAGCAGTAGGTTGGGTAATCACA

Primers for cloning spliced pri-miRNAs into expression vectors		
S.No.	Primer ID	Sequence 5' to 3'
1. Primers for PRI 24	EXJ MIR24 FWD	TTTAACGAGTCCAGGCCTTCGC
	AP-O REV	TGATGTCCAGGGTCAGTTCGAGCC
2. Primers for ALT SPLICE 25	EXJ MIR25 FWD	CACTGCTCTGGACAGCTGAACTC
	MCM PUR	ACTCACAAAACAGGAGTGGAATCC
3. Primers for ALT SPLICE 93	EXJ MIR93 FWD	TCCACTGCTCTGATCCTGTGC
	NEW 93 REV	GCTCCCCAGCATGACAGATG

Supp. Table 1.
Contd..

Primers for cloning MCM7 mini-gene into expression vector		
S.No.	Primer ID	Sequence 5' to 3'
1. Primers for MCM Native Vector	MCM EXON FWD	CTATCCTGCGCCTTTCCAC
	MCM EXON REV	AGCCTGATGGCTTCATTAC

5' Phosphorylated Primers for site directed mutagenesis		
S.No.	Primer ID	Sequence 5' to 3'
1	miR 25 AG MUT FWD	GGTCTCCCTCACCTGACAGCTGAACTCC
	miR 25 AG MUT REV	AGACCCTTTTGAACGCCACTGGGC

Primers for quantifying spliceosome knockdown and other miscellaneous primers		
S.No.	Primer ID	Sequence 5' to 3'
1	PRPF8 FWD	CAACTTCATGGGTGTTCCGGC
2	PRPF8 REV	CATACAGGTCCTCCCGATCC
3	SNRNP70 FWD	CGAGACATGCACTCCGCTTAC
4	SNRNP70 REV	GCCTGAATGCCGGATGTTC
5	NEOMYCIN FWD	CTTGCTCCTGCCGAGAAAGT
6	NEOMYCIN REV	TTCGCTTGGTGGTCGAATG
7	APO EXON 9 FWD	CCAAGACTGGCTTGAGAGTTCCGG
8	APO EXON 15 REV	TGATGTCCAGGGTCAGTTCGAGCC
9	MCM7 EXON 7 FWD	GGAAATATCCCTCGTAGTATCAC
10	MCM7 EXON 14 REV	AGCCTGATGGCTTCATTAC
11	T7 PROMOTER FWD	CACTATAGGGCGAATTCGGATC
12	pTarget REV	CGCCAAGTTATTTAGGTGACACG

Supp. Table 2. List of siRNA sequences

S.No.	siRNA ID	siRNA Sequence (5' to 3')
1	Drosha sense	CGAGUAGGCUUCGUGACUU
2	Drosha antisense	AAGUCACGAAGCCUACUCG
3	PRP8 sense	CCCUACAUGUGAACAACGA
4	PRP8 antisense	UCGUUGUUCACAUGUAGGG
5	SNRNP70 sense	GGUCUACAGUAAGCGGUCA
6	SNRNP70 antisense	UGACCGCUUACUGUAGACC