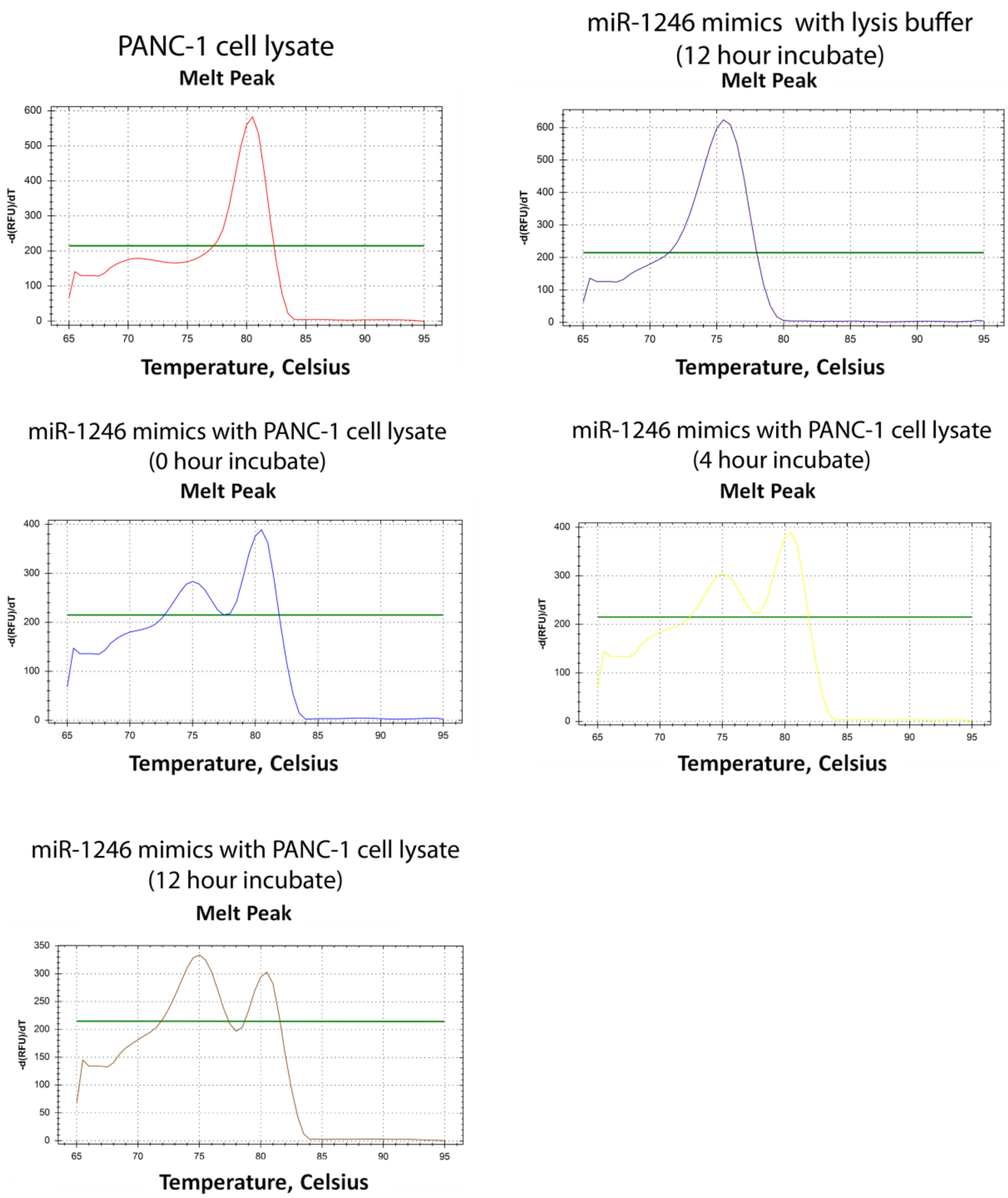
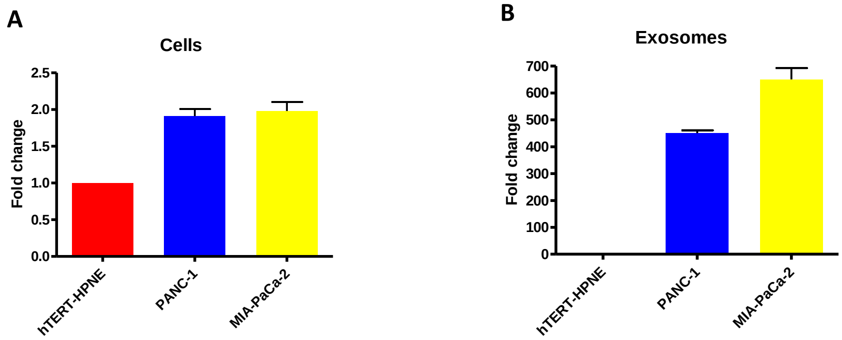
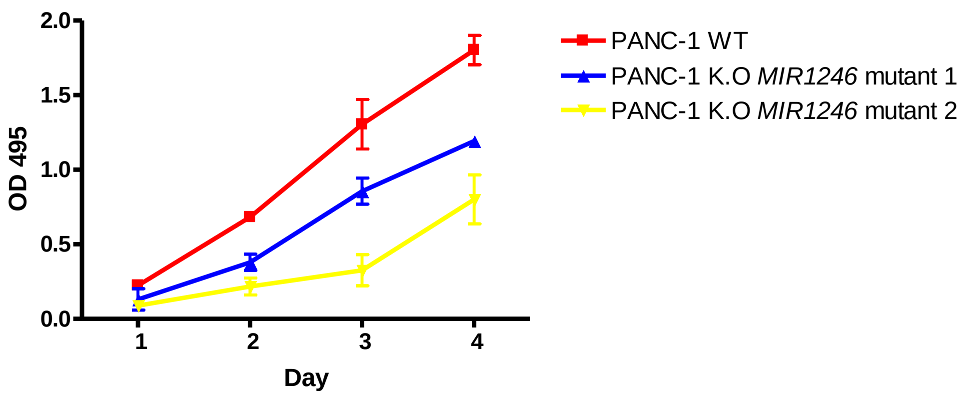
Supplement Figure 1



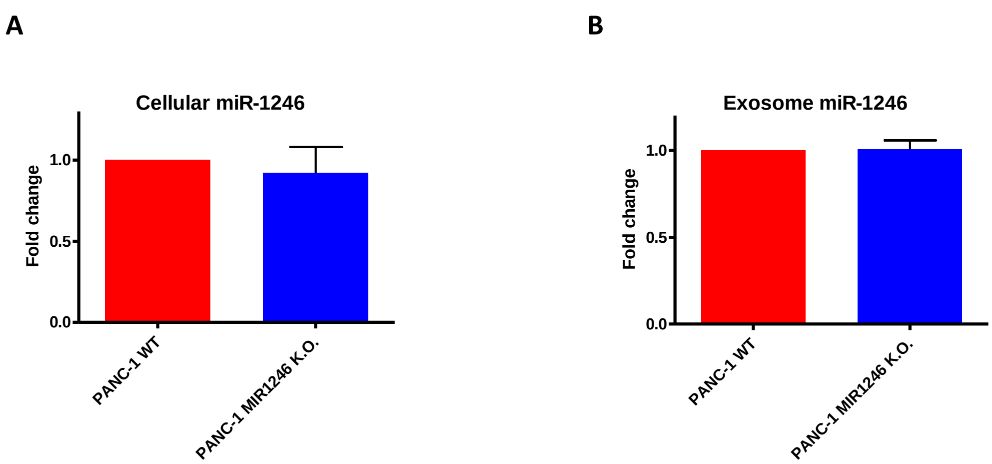
Supplement Figure 2



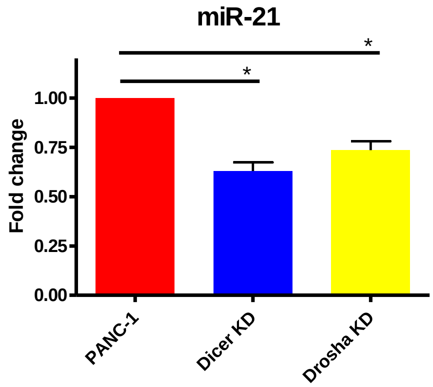
Supplement Figure 3



Supplement Figure 4



Supplement Figure 5



Supplementary Figure legend

Supplement Figure 1. Detection of miR-1246 mimics mixed with PANC-1 cell lysate. miR-1246 mimics (Dharmacon™, Cat # C-301373-00) were incubated with PANC-1 cell lysate for 4 and 12 hours. RNA was isolated and qRT-PCR was performed using the poly A tailing method to analyze miR-1246 expression.

Supplement Figure 2. Stem-loop TaqMan qRT-PCR analysis of miR-1246 expression. cDNA was made from 10 ng of total RNA using the TaqMan miRNA Reverse Transcription Kit according to the manufacturer's instructions (Life Technologies). Real-Time PCR was performed by diluting the cDNA product in 2X TaqMan Universal Master Mix II (with UNG) and 20X TaqMan miRNA Expression Assay. RNU6B was served as a miRNA expression normalization control for cellular miR-1246 expression (***A***). A synthetic *Caenorhabditis elegans* miR-54 (cel-miR-54) RNA oligonucleotide (Integrated DNA Technologies) served as a spike-in control for expression normalization of exosome miRNA detection (***B***). Real-Time PCR was performed using the TaqMan microRNA assay (ID:001361, Life Technologies) with primers for miR-1246 (primer custom assay ID: CSQJA23), RNU6B (primer custom assay ID:001093) and Cel-miR-54, as we described (30) (means ± SEM, n=3).

Supplement Figure 3. Cell viability analysis of *MIR1246* knockout PANC-1 cells. The MTS reagent (Pormega, Madison, WI, USA) was used to evaluate cell viability of wild type and *MIR1246* knockout PANC-1 cells. Cells were plated in 96 well plate at 5,000 per well. Viability was analyzed at 1, 2, 3, and 4 days post plating by incubating cells with MTS reagent for 1 hour and recording the readings at 495 nm.

Supplement Figure 4. Stem-loop TaqMan qRT-PCR analysis of miR-1246 in *MIR1246* knockout PANC-1 cells and exosomes. qRT-PCR detection of miR-1246 using the Stem-loop TaqMan method in wild type and *MIR1246* knockout PANC-1 cells (***A***). qRT-PCR detection of miR-1246 using the Stem-loop TaqMan method in exosomes derived from wild type and *MIR1246* knockout PANC-1 cells (***B***).

Supplement Figure 5. Effects of knockdown of Drosha and Dicer on miR-21 expression in PANC-1 cells. qRT-PCR (the poly A tailing method) was performed to analyze miR-21 expression in Dicer and Drosha knockdown PANC-1 cells (means ± SEM, n=3). * p<0.05, one way ANOVA.

Supplement Table 1: RNU2-1 siRNA sequence

siRNA name	siRNA sequences
hsRi.RNU2-1 13.1	5'-CUUAUCAGUUUAAUAUCU-3'/ 5'-ACGUAUCAGAUAUUAAAC-3'
hsRi.RNU2-1 13.2	5'-GUAUCUGUUCUUAUCAGU-3' / 5'-AUAUUAAACUGAUAAGAA-3'

Alignment of Sequence_1: [inserted GFP reference sequence.xdna] with Sequence_2: [expected 3KB PCR production from miR1246 K.O mutant .xdna]

Similarity : 1006/2435 (41.31 %)

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Seq_1  1      CACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGACGCAAATG  60
                    ||||||||||||||||||||||||||||||||||||||||||||||||||||||
Seq_2  1      ------AATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGACGCAAATG  54


Seq_1  61     GGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTGGTTTAGTGAACCGTCAG  120
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Seq_2  55     GGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTGGTTTAGTGAACCGTCAG  114


Seq_1  121    ATCCGCTAGCGCTACCGGTCGCCACCATGGTGAGCAAGGGCGAGGAGCTGTTCACCGGGG  180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Seq_2  115    ATCCGCTAGCGCTACCGGTCGCCACCATGGTGAGCAAGGGCGAGGAGCTGTTCACCGGGG  174


Seq_1  181    TGGTGCCCATCCTGGTCGAGCTGGACGGCGACGTAAACGGCCACAAGTTCAGCGTGTCCG  240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Seq_2  175    TGGTGCCCATCCTGGTCGAGCTGGACGGCGACGTAAACGGCCACAAGTTCAGCGTGTCCG  234


Seq_1  241    GCGAGGGCGAGGGCGATGCCACCTACGGCAAGCTGACCCTGAAGTTCATCTGCACCACCG  300
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Seq_2  235    GCGAGGGCGAGGGCGATGCCACCTACGGCAAGCTGACCCTGAAGTTCATCTGCACCACCG  294


Seq_1  301    GCAAGCTGCCCGTGCCCTGGCCCACCCTCGTGACCACCCTGACCTACGGCGTGCAGTGCT  360
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Seq_2  295    GCAAGCTGCCCGTGCCCTGGCCCACCCTCGTGACCACCCTGACCTACGGCGTGCAGTGCT  354


Seq_1  361    TCAGCCGCTACCCCGACCACATGAAGCAGCACGACTTCTTCAAGTCCGCCATGCCCGAAG  420
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Seq_2  355    TCAGCCGCTACCCCGACCACATGAAGCAGCACGACTTCTTCAAGTCCGCCATGCCCGAAG  414


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Seq_2  415    GCTACGTCCAGGAGCGCACCATCTTCTTCAAGGACGACGGCAACTACAAGACCCGCGCCG  474


Seq_1  481    AGGTGAAGTTCGAGGGCGACACCCTGGTGAACCGCATCGAGCTGAAGGGCATCGACTTCA  540
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Seq_2  475    AGGTGAAGTTCGAGGGCGACACCCTGGTGAACCGCATCGAGCTGAAGGGCATCGACTTCA  534


Seq_1  541    AGGAGGACGGCAACATCCTGGGGCACAAGCTGGAGTACAACTACAACAGCCACAACGTCT  600
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Seq_2  715    GCCCCGTGCTGCTGCCCGACAACCACTACCTGAGCACCCAGTCCGCCCTGAGCAAAGACC  774


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Seq_2  895   CAGTCGACGGTACCGCGGGCCCGGGATCCACCGGATCTAGATAACTGATCATAATCAGCC  954

Seq_1  961   ATACCACATTTGTAGAGGTTTTACTTGCTTTAAAAAACCTCCCACACCTCCC--------  1012
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Seq_2  1135  AGCAATTAGAAAGCAGTGGTTTCCTGGGCTTGCTTCATCACCTCAAGCAAGCCTGTTAGC  1194

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