SUPPLEMENTARY DATA

SUPPLEMENTARY TABLE AND FIGURE LEGENDS

Table S1. TLDA Detection Summary for Prion Infected Cells

Table S2. TLDA Detection Summary for Prion Infected Exosomes

Table S3. Library quality and adapter processing

Table S4. Library mapping to genome

Table S5. Exosomes small RNA library composition

Table S6. Abundant microRNA reads differentially detected from Small RNA sequencing of Uninfected and Infected Exosomes

Table S7. Experimental validated mRNA targets of let-7b, let-7i, miR-128a, miR-21, miR-222, miR-29b, miR-342-3p and miR-424.

Figure S1. Abundant rRNA, senseRNA fragments, known ncRNAs and other ncRNAs reads in exosomes.
Sequence reads annotated to NONCODE database and mouse genome assembly NCBIM37 identified reads to classes of (**A**) ribosomal RNA, (**B**) senseRNA or mRNA fragments, (**C**) functional ncRNAs, (**D**) mRNA-like long ncRNAs (mRNAlike lncRNA), (**E**) and other ncRNAs including piwi-interacting RNAs (piRNA), long intronic ncRNAs (lincRNA) and other non-functional annotated ncRNAs. Reads were normalised in uninfected and infected exosomes to the total number of reads identified for each ncRNA class or mRNA fragments. The most abundant reads in each class is shown. Normalisation of ncRNA classes suggested that no discernable difference can be seen between uninfected and infected exosomes. Normalisation of mRNA fragments suggest that *Tmem38b* mRNA fragments < 1.3 fold decreased in prion infected exosomes while *Zfp28* and *Bmp3* mRNA fragments > 1.3 fold increased in prion infected exosomes.

Figure S2. Comparison of Prion miRNA Dysregulation
Venn Diagram of miRNA dysregulation in prion infected brain tissues from mice (17) and primates (18) compared to miRNA identified in exosomes from prion infected neuronal cells in this study. We identified miRNAs let-7b, let-7i, miR-29b, miR-222, miR-128a, miR-21, miR-342-3p, miR-424 and miR-146a to be differentially expressed in exosomes from prion infected cells in our study. let-7b, miR-128a, miR-146a and miR-342-3p was also previously identified

in end-stage prion diseased mouse brain tissue (17), while miR-128a and miR-342-3p was also identified in end-stage prion diseased mouse brain tissue and primate brain tissue (17,18). miR-128a and miR-342-3p was identified as being up-regulated in all three independent studies, while miRNAs let-7i, miR-29b, miR-222, miR-21 and miR-424 are up-regulated in prion infected exosomes identified in this study.

Figure S3. Pathway Analysis of Exosomal mediated transfer of miRNA from Prion Infected Cells to Recipient Cells may regulate expression of the PRNP Gene.
miRNAs let-7b, let-7i, miR-128a, miR-21, miR-222, miR-29b, miR-342-3p and miR-424 up-regulated in exosomes released from prion infected neuronal miR-128a, miR-21, miR-222 and miR-29b can cells can collectively target 3724 5916 predicted genes, with 385 experimental validated. Validated . 102 of these have been experimental validated miRNA targets included several genes that have known interactions with the cellular prion protein (PRNP) including AGO1/AGO2, with Ingenuity Pathway Analysis identifying BACE1, BSG1, CCND1, MCL1, SP1 and , p53. **(1)** miR-29b increases expression of the p53 protein (46), while p53 can bind to SP1 to increase its promoter binding activity (47). Interestingly, both SP1 and p53 have been shown to be required for activation of expression of the *PRNP* gene promoter (48,49). miR-29b can also target and decrease BACE expression (51). **(2)** miR-128a can target and decrease expression of AGO proteins, leading to reduction of AGO-miRNA complex formation (68). Both AGO1 and AGO2 have also been shown to bind to the PRNP protein and function in miRNA biogenesis (54,69). **(3)** let-7b/let-7i can target and decrease expression of BSG (70) and CCND1 (71). **(4)** miRNA-21, and miRNA-222, miR-424 have no known direct interactions with the PRNP, however p53 can increase expression of let-7b/let7i, miR-21, miR-222 and miR-424 (51). **(5)** miR-342-3p has no reported experimental validated targets**.** Interestingly, p53 can increase expression of our up-regulated cellular miRNAs let-7i, miR-21 and miR-23b (51).

SUPPLEMENTARY MATERIALS AND METHODS

Preparation of M1000 brain homogenate.

The M1000 prion strain was derived from the Fukuoka-1 (or FU-1) strain of mouse-adapted human prions, originally isolated from a patient with Gerstmann–Straussler Sheinker syndrome (GSS), a familial prion disease (22). This strain was originally isolated by passage in mice and is maintained by continuous passage in Balb/c wild-type mice giving reproducible incubation periods and neuropathology (72). Homogenates were prepared from the brain tissue of terminally sick Balb/c mice infected with the M1000 prion strain and subsequently used for *in vitro* infection and biochemical analysis. Homogenates were prepared in 10 % (w/v) Dulbecco's phosphate buffered saline (PBS) by passage through 18-, 21- and 26-gauge needles.

Total RNA Isolation, including miRNA.

Total RNA from exosomes/cultured cells was isolated using *mir*Vana miRNA Isolation Kit (Ambion) according to manufacturer's instructions with slight modification for organic phase separation. Briefly, cell pellets or exosome pellets were lysed in 600 µl or 300 µl lysis/binding buffer, respectively and incubated on ice for 5-min. 1/10 "lysis" volume (60 µl or 30 µl) of miRNA homogenate was then added to each lysate and incubated on ice for 10 min. Next, the Total RNA was separated from into the aqueous phase by organic extraction with TRIzol Reagent (Invitrogen). 1 "lysis" volume of TRIzol was added to each sample and incubated at room temperature for 5 min, before 200 µl of chloroform per ml of TRIzol was added to each sample. The samples were then vortexed for 30 sec, incubated for a further 2-3 min. Samples were then centrifuged at 12,000 x g for 15 min at 4°C. The upper aqueous phase was carefully removed and the volume measured. RNA was then isolated from the aqueous phase according to the *mir*Vana miRNA Isolation Kit manufacturer's instructions and eluted in a final volume of 100 µl.

miRNA profiling by Megaplex quantitative real-time PCR.

The expression of miRNA in cells and exosomes was profiled using stem–loop RT–PCR-based 384 well Taqman Low-density Array (TLDA) cards (Applied Biosystems). Briefly, total RNA (3 µl per sample, ~150 – 200 ng total RNA) was reverse transcribed using TaqMan miRNA Reverse Transcription Kit (Applied Biosystems) in combination with the stem–loop Megaplex primers pool set A in total volume of 7.5 µl. The RT cycling conditions were: 40 cycles of 16˚C for 2 min, 42˚C for 1 min and 50˚C for 1 s. Next, 2.5 µl of the Megaplex RT products was then mixed with 2.5 µl of Megaplex PreAmp Primers A and 12.5 µl TaqMan PreAmp Master Mix in a 25 µl PCR reaction and pre-amplified. The pre-amplification cycling conditions were 95˚C for 10 min, 55˚C for 2 min and 75˚C for 2 min followed by 12 cycles of 95˚C for 15 s and 60˚C for 4 min. The pre-amplified cDNA was then diluted with 0.1X TE (pH 8.0) to 100 µl. 9 µl of diluted cDNA product was used in each plate for quantitative real-time PCR (qRT-PCR) runs. qRT-PCR was performed on a 7900HT thermocycler (Applied Biosystems) using the manufacturer's recommended cycling conditions: 50˚C for 2 min, 95˚C for 10 min followed by 40 cycles of 95˚C for 15 s and 60˚C for 1 min, with data collection at the end of each cycle. Cycle threshold (Ct) values were calculated with the SDS software v2.3 using automatic baseline settings with assigned minimum Ct threshold of 0.2. Ct values > 35 were considered to be below the detection level of the assays and designated 'undetected', and excluded from data analysis. Data was analysed using the ΔΔCt method with uninfected as the reference and snoRNA135 and snoRNA202 as endogenous controls using DataAssist v3 Software (Applied Biosystems).

Small RNA Library Preparation.

Total RNA, containing the small RNA fraction, from uninfected and infected exosomes was converted to cDNA libraries using the SOLiD Small RNA Expression Kit (Applied

Biosystems), according to manufacturers instructions. Briefly, total RNA (3µl per sample, ~100 – 250 ng small RNA) that has been concentrated by Centrivap was mixed with 2 µl of Adapter Mix A, 3 µl of hybridisation solution and incubated in a thermal cycler for 65˚C for 10 min, 16˚C for 5 min. 10 µl of 2X Ligation buffer and 2 µl of Ligation Enzyme mix was then added to each sample and incubated in a thermal cycler at 16˚C overnight. Next, 20 µl of Reverse Transcription master mix containing 1 µl of ArrayScript Reverse Transcriptase was added to the Adapter-A ligated total RNA reactions, and incubated at 42˚C for 30 min to generate RNA/cDNA duplexes. 10 µl of cDNA duplexes were then digested with 1 µl of RNase H and incubated at 37˚C for 30 min to generate first-strand cDNA libraries of small RNA for each sample. 1 µl of each cDNA library was then amplified by large-scale PCR in a total volume of 100 µl (3 replicates per sample), containing 10 µl 10X PCR Buffer I, 1 µl SOLiD PCR Primers (one set per individual sample), 8 µl 2.5 mM dNTP mix and 1.2 µl AmpliTaq DNA Polymerase. Cycling conditions were as follows: denaturation for 5 min at 95°C, followed PCR cycling of 95°C for 30 sec, annealing at 62°C for 30 sec, and extension at 72°C for 30 sec for 15 cycles, and a final extension for 7 min at 72°C. Replicate PCR reactions were pooled, cleaned up and concentrated using the MinElute PCR Purification Kit (QIAGEN) in a total elution volume of 20 µl. Amplified libraries were then size selected by combining 4 µl of Gel loading solution (Ambion) to the eluted DNA and 8 µl aliquots of PCR-amplified cDNA products were run in triplicate on a 6% native TBE, polyacrylamide gel with 1 µl of 10-bp DNA ladder (Invitrogen). Gels were stained with SYBR-Gold Dye (Invitrogen) and gel fragments between 105 and 150 bp, were excised, shredded and DNA eluted from gel pieces with PAGE elution buffer. The eluted DNA was combined with the remaining gel slurry and centrifuged in filter spin columns (Ambion) for 5 min at max speed. The DNA was precipitated by addition of 1/100 volume of glycogen (Ambion) and 0.7 volume of isopropanol, incubated for 5 min and centrifuged at 13,000 x g for 20 min. The DNA pellet was then air dried and resuspended in a final volume of 20µl Nuclease-free water. The DNA in each final small RNA library was quantitated by BioSpec-nano (Shimadzu) and verified for size and quality using DNA 1000 Kit (Agilent). Equimolar amounts for each final library were pooled at a final concentration of 41 pg/µl and used in the emulsion PCR (ePCR) reaction and template bead preparation, according to the manufacturer's instructions (Applied Biosystems, SOLiD System v4 user guide). After ePCR, the templates are denatured and bead enrichment is performed. Finally, the templates on the enriched beads are 3' modified by Terminal Transferase to allow covalent bonding to a glass. Barcoded template beads from all libraries were then deposited on a single slide and sequenced using the SOLiD v4 platform (Applied Biosystems).

Bioinformatics

Analysis of the SOLiD csfasta files was performed by miR-Intess small RNA pipeline (InteRNA Genomics B.V., Netherlands). The pipeline is designed to pre-process raw reads to trim and remove adapter sequences and generate high quality reads that can be mapped to

the mouse genome assembly and miRBase (19). Only reads with a recognised 3' adapter and > 18 nucleotides in length are considered for further analysis (Table S3). Accepted reads were mapped to mouse assembly NCBIM37, UCSC database mm9, Ensembl database mus_musculus_core_59_37l, and miRBase v16 using the following parameters: Min read length: 16, Max read length: 50, Min mapped read length: 16. Reads are then aligned by either Perfect, the complete read perfectly matches the genome or Trimmed, at least 18 nucleotides match the genome with the remaining mismatched 3' bases trimmed (Table S4). Aligned reads were classified according to genomic loci annotations retrieved from Ensembl, UCSC or miRBase databases (Table S5). The classifications used were Known miRNA: previously identified isoforms of known miRNA including star strands, candidate novel miRNAs: have no bad features and at least one positive or one negative feature and 2 or more positive features described below, confident novel miRNAs: have no negative features and at least two positive features described below, non-hairpin: reads that lack a hairpin in their genomic loci, novel known miRNA: reads that represent previously undocumented processing variants of known miRNA. other RNA: RNA reads that are inconsistent with miRNA features and are not members of the following classes of RNA: ribosomal RNA (rRNA), small cytoplasmic RNA (scRNA), RNA repeats (including repetitive elements LINEs and SINEs), senseRNA (mRNA fragments), sense ncRNA, potential siRNAs, potential siRNAs derived from ncRNAs, small nuclear RNA (snRNA), small nucleolar RNA (snoRNA), or transfer RNA (tRNA). Reads that aligned to intergenic or intronic regions but not to exons, repeats, or structural RNAs, were used in the miRNA discovery and annotation part of miR-Intess to identify novel and candidate miRNAs. The miR-Intess data pipeline uses strict guidelines to identify novel miRNAs from deep sequencing data sets. In order to be considered a 'confident' novel miRNA, a sequence must have no bad features and 2 or more positive features, while to be considered a 'candidate' novel miRNA, a sequence must have no bad features and at least one positive or one negative feature and 2 or more positive features. The positive features are: the sequence is represented in multiple libraries; the sequence maps to a genomic region containing a hairpin that is consistent with Dicer and Drosha processing; and the hairpin is thermodynamically stable by Randfold. The negative features are: the sequences is inconsistent with being a Dicer product; has a high degree of 5' end variability; the hairpin sequence is too short; the sequence maps to greater than 10 locations in the genome; has high G-C content; the sequence is not in between 18– 24 nucleotides; and the sequence read overlaps the predicted hairpin sequence.

Individual miRNA assays and primers.

Individual Taqman miRNA assays (Applied Biosystems) were performed according to manufacturers instructions. Briefly, 5 µl of total RNA isolated from cells and exosomes was converted to cDNA using the microRNA reverse transcriptase Kit (Applied Biosystems) with 3 µl of specific miRNA assay RT primer in a reaction volume of 15 µl. cDNA was diluted to 45 µl and setup in quadruplicate qRT-PCR reactions in 96-well plates containing 1 µl of specific

Taqman miRNA assay, 4 µl of diluted cDNA, 10 µl of Taqman Gene Expression Mastermix in a final volume of 20 µl using the QIAGILITY liquid handing robot (QIAGEN). Plates were then run on a StepOnePlus qRT-PCR instrument (Applied Biosystems) using the manufacturer's recommended cycling conditions: 50˚C for 2 min, 95˚C for 10 min followed by 40 cycles of 95˚C for 15 s and 60˚C for 1 min, with data collection at the end of each cycle. Ct values > 35 were below detection limit and excluded. Data was analysed by the ΔΔCt method with uninfected as the reference and snoRNA135 and snoRNA202 as endogenous controls using DataAssist Software v3 (Applied Biosystems). Specific Taqman miRNAs used in this study were: hsa-let-7b ID 000378, hsa-let-7i ID 002221, hsa-mir-103 ID 000439, hsa-miR-125a-5p ID 002198, hsa-miR-125b ID 000449, hsa-miR-126-3p ID 002228, hsa-miR-128a ID 002216, hsa-miR-130a ID 000454, hsa-miR-130b ID 000456, mmu-miR-134 ID 001186, hsa-miR-142-3p ID 000464, hsa-miR-146a ID 000468, hsa-miR-16 ID 000391, mmu-miR-182 ID 002599, hsa-miR-188-5p ID 002320, mmu-miR-193b ID 002467, hsa-miR-21 ID 000397, hsa-miR-210 ID 000512, hsa-miR-222 ID 002276, hsa-miR-23a ID 000399, hsa-miR-23b ID 000400, hsa-miR-24 ID 000402, hsa-miR-296-3p ID 002101, hsa-miR-296-5p ID 000527, hsa-miR-29a ID 002112, hsa-miR-29b ID 000413, hsa-miR-29c ID 000587, hsa-miR-301a ID 000528, hsa-miR-30b ID 000602, hsa-miR-30c ID 000419, hsa-miR 342-3p ID 002260, mmu-miR-344-3p ID 001063, hsa-miR-378 ID 000567, mmu-miR-380-5p ID 002601, mmu-miR-424 ID 001076, mmu-miR-93 ID 001090, snoRNA135 ID 001230 and snoRNA202 ID 001232.

SUPPLEMENTARY REFERENCES

17. Saba, R., Goodman, C.D., Huzarewich, R.L., Robertson, C. and Booth, S.A. (2008) A miRNA signature of prion induced neurodegeneration. *PLoS One*, **3**, e3652.
18. Montag, J., Hitt, R., Opitz, L., Schulz-Schaeffer, W.J., Hunsmann, G. and Motzkus, D. (2009) Upregulation of miRNA hsa-miR-342-3p in experimental and idiopathic prion disease. *Mol Neurodegener*, **4**, 36.
19. Kozomara, A. and Griffiths-Jones, S. (2011) miRBase: integrating microRNA annotation and deep-sequencing data. *Nucleic Acids Res*, **39**, D152-157.
22. Tateishi, J., Ohta, M., Koga, M., Sato, Y. and Kuroiwa, Y. (1979) Transmission of chronic spongiform encephalopathy with kuru plaques from humans to small rodents. *Ann Neurol*, **5**, 581-584.
46. Feng, Z., Zhang, C., Wu, R. and Hu, W. (2011) Tumor suppressor p53 meets microRNAs. *J Mol Cell Biol*, **3**, 44-50.
47. Amini, S., Saunders, M., Kelley, K., Khalili, K. and Sawaya, B.E. (2004) Interplay between HIV-1 Vpr and Sp1 modulates p21(WAF1) gene expression in human astrocytes. *J Biol Chem*, **279**, 46046-46056.
48. Bellingham, S.A., Coleman, L.A., Masters, C.L., Camakaris, J. and Hill, A.F. (2009) Regulation of prion gene expression by transcription factors SP1 and metal transcription factor-1. *J Biol Chem*, **284**, 1291-1301.
49. Vincent, B., Sunyach, C., Orzechowski, H.D., St George-Hyslop, P. and Checler, F. (2009) p53-Dependent transcriptional control of cellular prion by presenilins. *J Neurosci*, **29**, 6752-6760.
51. Tarasov, V., Jung, P., Verdoodt, B., Lodygin, D., Epanchintsev, A., Menssen, A., Meister, G. and Hermeking, H. (2007) Differential regulation of microRNAs by p53 revealed by massively parallel sequencing: miR-34a is a p53 target that induces apoptosis and G1-arrest. *Cell Cycle*, **6**, 1586-1593.

54. Gibbings, D., Leblanc, P., Jay, F., Pontier, D., Michel, F., Schwab, Y., Alais, S., Lagrange, T. and Voinnet, O. (2012) Human prion protein binds Argonaute and promotes accumulation of microRNA effector complexes. *Nat Struct Mol Biol*, **19**, 517-524.
68. Wang, W.X., Wilfred, B.R., Hu, Y., Stromberg, A.J. and Nelson, P.T. (2010) Anti-Argonaute RIP-Chip shows that miRNA transfections alter global patterns of mRNA recruitment to microribonucleoprotein complexes. *RNA*, **16**, 394-404.
69. Satoh, J., Obayashi, S., Misawa, T., Sumiyoshi, K., Oosumi, K. and Tabunoki, H. (2009) Protein microarray analysis identifies human cellular prion protein interactors. *Neuropathol Appl Neurobiol*, **35**, 16-35.
70. Fu, T.Y., Chang, C.C., Lin, C.T., Lai, C.H., Peng, S.Y., Ko, Y.J. and Tang, P.C. (2011) Let-7b-mediated suppression of basigin expression and metastasis in mouse melanoma cells. *Exp Cell Res*, **317**, 445-451.
71. Bueno, M.J., Gomez de Cedron, M., Laresgoiti, U., Fernandez-Piqueras, J., Zubiaga, A.M. and Malumbres, M. (2010) Multiple E2F-induced microRNAs prevent replicative stress in response to mitogenic signaling. *Mol Cell Biol*, **30**, 2983-2995.
72. Brazier, M.W., Lewis, V., Ciccotosto, G.D., Klug, G.M., Lawson, V.A., Cappai, R., Ironside, J.W., Masters, C.L., Hill, A.F., White, A.R. *et al.* (2006) Correlative studies support lipid peroxidation is linked to PrP(res) propagation as an early primary pathogenic event in prion disease. *Brain Res Bull*, **68**, 346-354.

Supplementary Table S1. TLDA Detection Summary for Prion Infected Cells

Taqman microRNA Assay	Uninfected Cell Rep 1 (Ct)	Infected Cell Rep 1 (Ct)	Uninfected Cell Rep 2 (Ct)	Infected Cell Rep 2 (Ct)	RQ*
ath-miR159a-4373390	undetected	undetected	undetected	undetected	n.d
MammU6-4395470	11.7949	10.6786	11.1992	11.5084	1.12 ± 0.05
mmu-let-7a-4373169	27.4229	26.6031	27.9289	28.0852	1.07 ± 0.05
mmu-let-7b-4373168	22.0358	21.9506	22.6069	22.4295	0.93 ± 0.04
mmu-let-7c-4373167	20.9586	21.0001	21.5681	21.4535	0.87 ± 0.04
mmu-let-7d-4395394	23.7139	23.2861	23.9787	23.714	1.08 ± 0.05
mmu-let-7e-4395517	23.2595	22.0558	23.4361	23.1743	1.41 ± 0.06
mmu-let-7f-4373164	26.0429	25.248	26.5396	26.1469	1.28 ± 0.06
mmu-let-7g-4395393	21.9524	20.779	22.4151	21.976	1.49 ± 0.07
mmu-let-7i-4395332	20.8302	19.6567	21.1363	21.0076	1.34 ± 0.06
mmu-miR-100-4373160	24.4497	24.3233	25.349	24.9841	1.01 ± 0.04
mmu-miR-101a-4395364	24.0653	22.8988	24.5638	24.4211	1.34 ± 0.06
mmu-miR-103-4373158	25.674	24.1458	25.4795	25.3879	1.49 ± 0.07
mmu-miR-106a-4395589	undetected	undetected	31.4746	undetected	n.d
mmu-miR-106b-4373155	21.8694	20.5555	21.8838	21.8274	1.37 ± 0.06
mmu-miR-107-4373154	29.2512	27.7429	28.4524	28.6457	1.34 ± 0.06
mmu-miR-10b-4395329	34.0889	32.0718	undetected	undetected	n.d
mmu-miR-124-4373295	30.9908	29.4954	30.9012	31.1375	1.32 ± 0.06
mmu-miR-125a-3p-4395310	27.3741	26.7387	27.1797	27.2514	1.03 ± 0.05
mmu-miR-125a-5p-4395309	19.7078	18.5759	19.1526	19.0919	1.29 ± 0.06
mmu-miR-125b-3p-4395489	27.6096	27.6411	28.225	27.9404	0.93 ± 0.04
mmu-miR-125b-5p-4373148	22.1435	21.2867	22.3987	22.0213	1.30 ± 0.06
mmu-miR-126-3p-4395339	22.7459	22.4493	22.9915	23.4738	0.80 ± 0.04
mmu-miR-126-5p-4373269	26.7372	26.8889	27.5749	27.8516	0.73 ± 0.03
mmu-miR-127-4373147	30.2238	30.2266	30.5029	32.48	0.43 ± 0.02
mmu-miR-128a-4395327	undetected	undetected	31.0852	30.5758	n.d
mmu-miR-129-3p-4373297	26.6761	25.3603	26.946	26.7831	1.42 ± 0.06
mmu-miR-129-5p-4373171	31.2715	30.2854	31.0161	29.9521	1.73 ± 0.08

mmu-miR-130a-4373145	24.9994	23.7906	25.2483	24.7707	1.53 ± 0.07
mmu-miR-130b-4373144	24.26	22.9957	24.1844	23.9413	1.43 ± 0.06
mmu-miR-132-4373143	27.488	25.2331	26.0328	25.3305	2.37 ± 0.10
mmu-miR-133a-4395357	30.5995	28.1557	29.271	28.6756	2.44 ± 0.11
mmu-miR-134-4373299	32.0926	30.5461	32.7347	29.544	4.39 ± 0.19
mmu-miR-135a-4373140	33.3672	32.8802	undetected	33.4505	n.d
mmu-miR-135b-4395372	28.6141	28.3355	28.558	28.6949	0.89 ± 0.04
mmu-miR-136-4395641	31.0669	30.3991	30.5787	31.2973	0.84 ± 0.04
mmu-miR-137-4373301	25.9156	24.5327	26.5455	25.9509	1.69 ± 0.07
mmu-miR-138-4395395	21.4261	20.3628	20.9675	20.4481	1.47 ± 0.06
mmu-miR-139-3p-4395676	undetected	undetected	undetected	undetected	n.d
mmu-miR-139-5p-4395400	22.2332	21.5755	21.5642	21.3279	1.16 ± 0.05
mmu-miR-140-4373374	21.4528	20.7171	21.7953	21.6793	1.14 ± 0.05
mmu-miR-141-4373137	32.6435	33.7185	34.4896	undetected	n.d
mmu-miR-142-3p-4373136	34.4962	31.6609	undetected	32.1579	n.d
mmu-miR-142-5p-4395359	undetected	undetected	undetected	undetected	n.d
mmu-miR-143-4395360	26.4592	25.4829	27.0028	27.0177	1.19 ± 0.05
mmu-miR-145-4395389	28.0011	26.936	27.4812	27.1731	1.37 ± 0.06
mmu-miR-146a-4373132	25.0006	27.0766	24.8399	27.942	0.14 ± 0.01
mmu-miR-146b-4373178	20.5099	19.5669	20.0027	19.9221	1.21 ± 0.05
mmu-miR-148a-4373130	undetected	undetected	undetected	undetected	n.d
mmu-miR-148b-4373129	27.4844	26.7771	27.471	27.2181	1.19 ± 0.05
mmu-miR-150-4373127	28.7831	28.0741	27.6778	28.159	0.92 ± 0.04
mmu-miR-151-3p-4373304	26.3398	25.0047	25.1514	24.7715	1.54 ± 0.07
mmu-miR-152-4395170	33.6866	33.7077	33.7471	undetected	n.d
mmu-miR-153-4373305	30.7503	30.5988	31.2348	32.1682	0.65 ± 0.03
mmu-miR-155-4395701	29.8839	27.372	28.9567	27.4422	3.43 ± 0.15
mmu-miR-15a-4373123	24.4165	23.293	24.6603	24.7602	1.21 ± 0.05
mmu-miR-15b-4373122	21.9495	21.45	22.0744	22.2983	0.94 ± 0.04
mmu-miR-16-4373121	16.0685	14.9591	15.7932	15.7422	1.27 ± 0.06
mmu-miR-17-4395419	undetected	undetected	undetected	31.0505	n.d

mmu-miR-181a-4373117	25.2257	24.3508	25.3287	25.1478	1.23 ± 0.05
mmu-miR-181c-4373115	32.574	31.435	33.0919	32.9667	1.32 ± 0.06
mmu-miR-182-4395729	28.5431	27.3329	28.8221	28.9399	1.24 ± 0.05
mmu-miR-184-4373113	29.8385	29.2297	31.0763	31.0153	1.07 ± 0.05
mmu-miR-185-4395382	25.6163	24.6346	25.4369	25.6399	1.11 ± 0.05
mmu-miR-186-4395396	21.4425	19.7274	20.1102	20.0619	1.57 ± 0.07
mmu-miR-187-4373307	26.505	25.0166	24.9705	24.8041	1.51 ± 0.07
mmu-miR-188-5p-4395431	25.5279	24.0099	24.3736	24.4345	1.41 ± 0.06
mmu-miR-190-4373110	27.9939	26.8438	28.0136	28.0226	1.26 ± 0.06
mmu-miR-191-4395410	18.3934	16.9457	17.7562	17.3125	1.64 ± 0.07
mmu-miR-192-4373108	25.6917	24.4202	25.0267	25.144	1.27 ± 0.06
mmu-miR-193-4395361	30.7408	28.6932	29.7968	29.6199	1.84 ± 0.08
mmu-miR-193b-4395597	undetected	undetected	undetected	33.7621	n.d
mmu-miR-194-4373106	26.978	25.6954	26.3705	26.4785	1.28 ± 0.06
mmu-miR-195-4373105	20.4094	19.6095	21.0386	20.8155	1.21 ± 0.05
mmu-miR-196b-4395326	33.0957	32.0745	32.7401	31.9866	1.57 ± 0.07
mmu-miR-197-4373102	29.3614	30.1515	30.2459	29.91	0.73 ± 0.03
mmu-miR-19a-4373099	undetected	undetected	undetected	undetected	n.d
mmu-miR-19b-4373098	undetected	undetected	undetected	undetected	n.d
mmu-miR-200a-4378069	30.9349	28.7591	30.0726	31.1865	1.23 ± 0.05
mmu-miR-200b-4395362	30.0199	28.1743	29.5376	29.1514	1.84 ± 0.08
mmu-miR-200c-4395411	28.3251	27.5805	27.7223	28.003	1.00 ± 0.04
mmu-miR-202-3p-4373311	29.7889	29.2079	31.3215	30.8947	1.21 ± 0.05
mmu-miR-203-4373095	28.3196	28.0016	28.8367	29.4023	0.78 ± 0.03
mmu-miR-204-4373094	23.734	22.2992	23.5707	23.248	1.56 ± 0.07
mmu-miR-205-4373093	undetected	33.2756	33.0674	33.5458	0.64 ± 0.02
mmu-miR-20a-4373286	undetected	33.0828	undetected	32.8049	n.d
mmu-miR-21-4373090	24.4924	23.0602	24.4777	24.106	1.59 ± 0.07
mmu-miR-210-4373089	30.0832	undetected	30.1849	undetected	n.d
mmu-miR-215-4373316	undetected	undetected	32.9129	undetected	n.d
mmu-miR-218-4373081	19.8666	18.5265	19.8662	19.6813	1.44 ± 0.06

mmu-miR-222-4395387	30.0609	30.0959	30.1202	31.5083	0.52 ± 0.02
mmu-miR-223-4395406	28.7649	28.1484	28.4699	28.5848	1.01 ± 0.04
mmu-miR-224-4395683	25.8604	25.5531	26.0763	26.0852	0.94 ± 0.04
mmu-miR-23b-4373073	27.6874	26.6752	27.1775	26.8533	1.35 ± 0.06
mmu-miR-24-4373072	17.7242	16.332	16.7427	16.3227	1.59 ± 0.07
mmu-miR-25-4373071	24.1617	23.6305	24.5263	24.2767	1.11 ± 0.05
mmu-miR-26a-4395166	21.5436	20.754	21.8253	21.1399	1.42 ± 0.06
mmu-miR-26b-4395167	23.0613	22.4389	23.4906	22.8429	1.32 ± 0.06
mmu-miR-27a-4373287	25.3577	24.4797	25.1598	25.54	1.01 ± 0.04
mmu-miR-27b-4373068	24.9605	23.9178	24.9498	24.5896	1.38 ± 0.06
mmu-miR-28-4373067	25.3822	24.7549	25.5741	25.8399	0.96 ± 0.04
mmu-miR-294-4373326	34.0093	undetected	34.7094	undetected	n.d
mmu-miR-295-4373327	32.0915	31.144	32.476	32.8534	1.04 ± 0.05
mmu-miR-296-3p-4395212	undetected	undetected	32.0977	30.8494	n.d
mmu-miR-296-5p-4373066	26.9338	26.2968	25.6248	25.3499	1.17 ± 0.05
mmu-miR-297c-4395610	29.1374	28.2454	27.8443	28.773	0.84 ± 0.04
mmu-miR-298-4395728	26.5608	24.2921	25.381	24.589	2.46 ± 0.11
mmu-miR-29a-4395223	19.4946	18.0362	19.5025	19.5777	1.37 ± 0.06
mmu-miR-29b-4373288	26.9323	25.8223	27.1285	27.3167	1.17 ± 0.05
mmu-miR-29c-4395171	21.6564	20.2413	22.0221	22.0833	1.36 ± 0.06
mmu-miR-301a-4373064	22.2369	21.2488	22.2966	22.2749	1.21 ± 0.05
mmu-miR-301b-4395730	21.098	20.2393	21.2837	21.1375	1.20 ± 0.05
mmu-miR-302a-4378070	undetected	34.2325	undetected	undetected	n.d
mmu-miR-302b-4378071	undetected	31.3077	undetected	33.1299	n.d
mmu-miR-302d-4373063	undetected	33.9342	undetected	undetected	n.d
mmu-miR-30a-4373061	22.4721	21.0369	21.5408	21.3656	1.49 ± 0.07
mmu-miR-30b-4373290	20.3872	19.3795	19.9786	19.8509	1.26 ± 0.06
mmu-miR-30c-4373060	19.7991	18.761	19.113	19.0798	1.23 ± 0.05
mmu-miR-30d-4373059	24.3685	23.2697	23.6637	23.4901	1.32 ± 0.06
mmu-miR-30e-4395334	23.7183	22.1906	22.6409	22.6804	1.42 ± 0.06
mmu-miR-31-4373331	29.9688	28.1696	29.1273	28.6678	1.86 ± 0.08

mmu-miR-32-4395220	27.9304	27.1546	28.2914	28.2031	1.15 ± 0.05
mmu-miR-320-4395388	21.2086	20.0767	20.4821	20.2914	1.34 ± 0.06
mmu-miR-324-3p-4395639	23.6684	23.2094	24.0964	24.2249	0.95 ± 0.04
mmu-miR-324-5p-4373052	24.6861	23.2002	24.6813	24.468	1.53 ± 0.07
mmu-miR-325-4395640	30.4377	28.4332	29.9037	29.2964	2.10 ± 0.09
mmu-miR-328-4373049	24.0978	23.4495	23.4968	23.3123	1.13 ± 0.05
mmu-miR-331-3p-4373046	22.3777	21.289	22.0415	21.9811	1.27 ± 0.06
mmu-miR-331-5p-4395344	27.7857	26.7748	27.2391	26.8996	1.36 ± 0.06
mmu-miR-337-3p-4395662	undetected	34.2167	undetected	undetected	n.d
mmu-miR-337-5p-4395645	31.7488	31.3954	32.6483	32.1718	1.13 ± 0.05
mmu-miR-338-3p-4395363	28.941	27.8376	29.5956	29.6649	1.22 ± 0.05
mmu-miR-339-3p-4395663	25.2357	24.1386	24.2916	24.0979	1.33 ± 0.06
mmu-miR-339-5p-4395368	27.3635	26.7551	27.0397	27.0052	1.06 ± 0.05
mmu-miR-340-3p-4395370	24.5387	24.0138	24.9583	24.6809	1.12 ± 0.05
mmu-miR-340-5p-4395369	23.5156	22.3872	23.3709	23.2803	1.30 ± 0.06
mmu-miR-342-3p-4395371	22.4088	21.504	20.9068	21.2391	1.04 ± 0.05
mmu-miR-342-5p-4395657	29.8025	29.1055	29.7617	undetected	n.d
mmu-miR-344-4373340	21.9556	20.7211	21.7406	21.856	1.25 ± 0.06
mmu-miR-345-3p-4395659	undetected	undetected	33.9681	undetected	n.d
mmu-miR-345-5p-4395658	28.6997	27.0522	27.9694	28.6165	1.20 ± 0.05
mmu-miR-34a-4395168	29.5848	28.144	29.6887	29.5808	1.45 ± 0.06
mmu-miR-34b-3p-4395748	29.2996	27.748	27.7147	28.2348	1.22 ± 0.05
mmu-miR-34c-4373036	30.9909	28.9533	30.1271	30.1319	1.72 ± 0.08
mmu-miR-350-4395660	27.6633	26.6409	27.5418	27.2426	1.34 ± 0.06
mmu-miR-351-4373345	29.4579	27.4847	27.8679	27.7444	1.76 ± 0.08
mmu-miR-361-4373035	26.3893	25.4874	26.2945	25.9064	1.33 ± 0.06
mmu-miR-362-3p-4395746	28.2358	26.7898	28.3251	28.159	1.49 ± 0.07
mmu-miR-363-4378090	undetected	undetected	undetected	undetected	n.d
mmu-miR-365-4373194	26.0706	25.476	26.3588	26.6289	0.95 ± 0.04
mmu-miR-367-4373034	33.1845	33.464	undetected	undetected	n.d
mmu-miR-375-4373027	32.9768	31.5324	30.8353	31.2686	1.21 ± 0.05

mmu-miR-376a-4373347	32.06	30.0762	32.3503	31.7688	2.07 ± 0.09
mmu-miR-376b-4395582	28.7571	28.5082	28.5534	28.7756	0.86 ± 0.04
mmu-miR-376c-4395580	28.5207	26.966	28.8681	28.2558	1.80 ± 0.08
mmu-miR-379-4373349	28.5547	26.8215	28.6783	27.7606	2.13 ± 0.09
mmu-miR-380-5p-4395731	32.705	30.3673	31.6647	31.4558	2.06 ± 0.09
mmu-miR-381-4373020	30.1761	30.0887	30.4166	31.4104	0.62 ± 0.03
mmu-miR-383-4381093	31.7239	30.6921	32.8085	31.54	1.89 ± 0.08
mmu-miR-384-3p-4395733	28.2205	26.8509	28.2367	27.9749	1.50 ± 0.07
mmu-miR-384-5p-4395732	20.5117	18.5347	19.6996	19.0936	2.08 ± 0.09
mmu-miR-409-3p-4395443	29.1569	27.935	29.1469	28.7307	1.50 ± 0.07
mmu-miR-410-4378093	28.8171	27.8193	28.9886	28.257	1.55 ± 0.07
mmu-miR-411-4381013	27.8666	26.3857	28.1528	27.5357	1.76 ± 0.08
mmu-miR-423-5p-4395451	undetected	undetected	undetected	undetected	n.d
mmu-miR-424-4378107	26.0989	25.1013	26.458	25.965	1.43 ± 0.06
mmu-miR-425-4380926	27.2643	26.198	27.2216	26.9067	1.37 ± 0.06
mmu-miR-429-4373355	28.1294	26.6766	27.3566	27.2841	1.44 ± 0.06
mmu-miR-434-3p-4395734	30.9042	30.7621	30.9938	31.4871	0.75 ± 0.03
mmu-miR-449a-4373207	25.035	23.6979	24.6924	24.2003	1.60 ± 0.07
mmu-miR-450a-5p-4395414	31.8392	30.3125	31.0965	31.7569	1.15 ± 0.05
mmu-miR-451-4373360	undetected	32.6033	undetected	33.8565	n.d
mmu-miR-465b-5p-4395615	30.9764	30.5839	31.3593	31.0288	1.09 ± 0.05
mmu-miR-455-4395585	undetected	undetected	undetected	undetected	n.d
mmu-miR-465b-5p-4395615	undetected	undetected	undetected	undetected	n.d
mmu-miR-467c-4395647	undetected	undetected	undetected	undetected	n.d
mmu-miR-484-4381032	17.9099	16.7676	16.6725	16.7193	1.24 ± 0.05
mmu-miR-488-4381074	28.8058	27.6925	29.2916	28.9483	1.41 ± 0.06
mmu-miR-489-4378114	31.7862	30.5571	30.6722	30.9282	1.19 ± 0.05
mmu-miR-491-4381053	30.2232	28.5454	28.7459	29.1108	1.34 ± 0.06
mmu-miR-494-4395476	27.7657	27.7845	28.9231	29.9513	0.59 ± 0.03
mmu-miR-495-4381078	undetected	undetected	undetected	undetected	n.d
mmu-miR-497-4381046	23.9779	23.007	24.4142	24.4785	1.16 ± 0.05

mmu-miR-500-4395736	undetected	29.2924	30.9964	31.4249	n.d
mmu-miR-503-4395586	25.7941	23.9814	25.2908	25.5023	1.48 ± 0.07
mmu-miR-509-3p-4395651	29.2817	29.3982	30.1418	29.9758	0.86 ± 0.04
mmu-miR-532-3p-4395466	24.8845	23.6801	24.592	24.2298	1.46 ± 0.06
mmu-miR-532-5p-4380928	22.4765	21.3348	21.96	21.8508	1.31 ± 0.06
mmu-miR-542-3p-4378101	30.9792	29.671	31.0752	31.0103	1.37 ± 0.06
mmu-miR-542-5p-4395693	28.0756	27.3469	28.0588	28.3222	1.00 ± 0.04
mmu-miR-544-4395680	undetected	31.0604	32.4877	undetected	n.d
mmu-miR-547-4395694	27.7458	27.1597	27.6665	27.6514	1.05 ± 0.05
mmu-miR-551b-4380945	32.3975	30.5859	32.9808	31.6932	2.49 ± 0.11
mmu-miR-574-3p-4395460	25.7858	25.3344	24.4952	24.7777	0.90 ± 0.04
mmu-miR-582-5p-4395696	undetected	undetected	33.9637	undetected	n.d
mmu-miR-598-4395606	29.8986	28.484	29.3868	30.0745	1.09 ± 0.05
mmu-miR-652-4395463	21.5465	20.724	21.8308	21.4574	1.29 ± 0.06
mmu-miR-665-4395737	undetected	undetected	undetected	undetected	n.d
mmu-miR-667-4386769	30.5797	30.4721	undetected	31.5742	n.d
mmu-miR-671-3p-4395433	28.7177	28.4153	27.464	27.4859	0.94 ± 0.04
mmu-miR-672-4395438	21.897	21.221	22.1598	22.1237	1.09 ± 0.05
mmu-miR-674-4395193	undetected	undetected	undetected	undetected	n.d
mmu-miR-676-4386776	23.462	23.2199	24.0125	23.8656	0.97 ± 0.04
mmu-miR-677-4381075	26.9913	26.2905	27.201	28.0363	0.81 ± 0.04
mmu-miR-680-4381079	22.7125	22.4906	22.3845	22.8464	0.78 ± 0.03
mmu-miR-682-4381081	27.2642	26.2866	28.0223	28.4193	1.04 ± 0.05
mmu-miR-684-4381083	34.0519	32.2784	32.5772	undetected	n.d
mmu-miR-685-4386748	18.6503	18.0391	19.2158	19.0534	1.11 ± 0.05
mmu-miR-708-4395452	23.0801	22.0105	23.9445	23.2287	1.58 ± 0.07
mmu-miR-744-4395435	22.8316	21.7125	22.3589	22.3551	1.25 ± 0.06
mmu-miR-7a-4378130	28.3824	27.3421	28.977	28.7683	1.31 ± 0.06
mmu-miR-7b-4395685	28.2182	26.6469	28.8971	28.0604	1.96 ± 0.09
mmu-miR-872-4395375	24.2058	23.2301	24.5284	24.025	1.42 ± 0.06
mmu-miR-873-4395467	31.5353	32.0786	31.2152	31.156	0.72 ± 0.03

mmu-miR-879-4395602	33.1716	32.738	34.2005	undetected	n.d
mmu-miR-9-4373285	23.2135	22.3673	23.5206	23.1597	1.29 ± 0.06
mmu-miR-92a-4373013	26.5302	26.3655	27.4595	27.1305	1.01 ± 0.04
mmu-miR-93-4373302	20.8272	19.6757	20.5564	20.3234	1.37 ± 0.06
mmu-miR-98-4373009	26.9767	25.2671	27.2659	26.9743	1.70 ± 0.07
mmu-miR-99a-4373008	25.2166	25.1874	25.7164	25.5735	0.90 ± 0.04
mmu-miR-99b-4373007	22.3944	21.6847	22.1932	22.0503	1.14 ± 0.05
rno-miR-1-4395765	undetected	undetected	undetected	undetected	n.d
rno-miR-190b-4395749	28.5468	27.5018	29.2473	28.6864	1.48 ± 0.07
rno-miR-196c-4395750	29.3989	28.3854	28.9672	28.6038	1.37 ± 0.06
rno-miR-207-4381096	24.805	24.9196	25.0129	24.5956	0.94 ± 0.04
rno-miR-219-1-3p-4395778	undetected	undetected	undetected	undetected	n.d
rno-miR-224-4373187	26.8819	26.2025	27.0518	26.7422	1.20 ± 0.05
rno-miR-327-4381108	31.0291	30.7386	32.06	32.4724	0.82 ± 0.04
rno-miR-339-3p-4395760	27.4264	26.1585	27.127	26.7299	1.51 ± 0.07
rno-miR-343-4381123	33.6255	33.3877	32.3015	undetected	n.d
rno-miR-344-5p-4395761	33.0701	28.0343	28.2834	29.085	3.69 ± 0.16
rno-miR-345-3p-4395762	32.0176	30.389	31.4966	30.8302	1.88 ± 0.08
rno-miR-347-4381114	27.368	26.1402	26.5234	26.4267	1.35 ± 0.06
rno-miR-351-4395764	28.1602	27.1963	27.7574	27.2679	1.41 ± 0.06
rno-miR-381-4381102	undetected	undetected	undetected	undetected	n.d
rno-miR-532-5p-4395752	27.2584	25.7466	26.0551	26.378	1.28 ± 0.06
rno-miR-598-5p-4395754	undetected	32.3109	30.9522	32.0173	n.d
snoRNA135-4380912	20.4274	19.939	20.7046	20.8129	0.97 ± 0.04
snoRNA202-4380914	16.6163	16.0296	16.5936	16.6209	1.03 ± 0.05

Cycle threshold > 35 was designated 'undetected', n.d = not determined if miRNA assay is undetected in 1 or more samples.
* Relative quantitation (RQ) data represents the mean ± SEM of target miRNA normalised to sno135 and sno202 endogenous controls using the ΔΔCt method (n = 2).

Supplementary Table S2. TLDA Detection Summary for Prion Infected Exosomes

Taqman microRNA Assay	Uninfected Exosome Rep 1 (Ct)	Infected Exosome Rep 1 (Ct)	Uninfected Exosome Rep 2 (Ct)	Infected Exosome Rep 2 (Ct)	RQ*
ath-miR159a-4373390	undetected	undetected	undetected	undetected	n.d
MammU6-4395470	13.7826	14.5227	15.5376	14.3862	0.67 ± 0.15
mmu-let-7a-4373169	27.1158	26.3032	undetected	28.6202	n.d
mmu-let-7b-4373168	21.0005	21.4753	23.0731	21.5384	0.83 ± 0.19
mmu-let-7c-4373167	20.2409	19.5941	22.462	20.9594	1.22 ± 0.27
mmu-let-7d-4395394	23.6799	23.3045	25.7894	24.3205	1.09 ± 0.25
mmu-let-7e-4395517	24.5668	23.3239	26.6365	25.2144	1.45 ± 0.33
mmu-let-7f-4373164	26.2407	25.7608	28.3548	26.6667	1.22 ± 0.28
mmu-let-7g-4395393	23.1336	23.6794	26.4583	24.285	1.01 ± 0.23
mmu-let-7i-4395332	22.2208	22.0552	24.6932	22.5529	1.28 ± 0.29
mmu-miR-100-4373160	25.4694	24.9237	27.3295	26.1165	1.06 ± 0.24
mmu-miR-101a-4395364	26.7241	27.2125	30.0128	27.9574	0.99 ± 0.22
mmu-miR-103-4373158	27.388	27.3945	30.0568	27.9777	1.18 ± 0.27
mmu-miR-106a-4395589	28.6108	28.5728	30.2784	28.4552	1.10 ± 0.25
mmu-miR-106b-4373155	23.4534	23.7148	26.276	24.2061	1.08 ± 0.24
mmu-miR-107-4373154	29.9872	29.9448	31.8904	30.6399	0.90 ± 0.20
mmu-miR-10b-4395329	undetected	undetected	undetected	undetected	n.d
mmu-miR-124-4373295	33.6185	32.5394	34.819	undetected	n.d
mmu-miR-125a-3p-4395310	25.5069	25.364	26.5958	26.3148	0.67 ± 0.15
mmu-miR-125a-5p-4395309	22.366	22.7148	24.2694	23.2766	0.72 ± 0.16
mmu-miR-125b-3p-4395489	28.1303	28.3053	29.3609	28.8849	0.64 ± 0.14
mmu-miR-125b-5p-4373148	22.4203	22.5652	24.9934	23.1131	1.05 ± 0.24
mmu-miR-126-3p-4395339	24.7187	25.5976	25.5508	25.4539	0.44 ± 0.10
mmu-miR-126-5p-4373269	26.8932	27.6961	28.1292	27.5002	0.54 ± 0.12
mmu-miR-127-4373147	31.4876	30.4903	32.8601	32.0813	1.07 ± 0.24
mmu-miR-128a-4395327	undetected	undetected	undetected	undetected	n.d
mmu-miR-129-3p-4373297	27.1869	27.5254	30.2796	27.9419	1.15 ± 0.26
mmu-miR-129-5p-4373171	30.1526	29.4851	31.7902	29.5089	1.60 ± 0.36

mmu-miR-130a-4373145	26.1591	26.3179	29.5108	26.9528	1.33 ± 0.30
mmu-miR-130b-4373144	24.9801	25.0697	27.4777	25.5551	1.09 ± 0.25
mmu-miR-132-4373143	26.8485	27.6575	29.5253	27.5834	0.85 ± 0.19
mmu-miR-133a-4395357	undetected	undetected	34.6393	undetected	n.d
mmu-miR-134-4373299	30.3684	30.7355	31.3937	31.5269	0.49 ± 0.11
mmu-miR-135a-4373140	undetected	34.3068	34.8203	undetected	n.d
mmu-miR-135b-4395372	31.2273	31.1717	32.7841	32.9297	0.56 ± 0.13
mmu-miR-136-4395641	undetected	34.8384	undetected	undetected	n.d
mmu-miR-137-4373301	27.0493	27.4165	30.2746	27.5899	1.29 ± 0.29
mmu-miR-138-4395395	23.9461	24.1217	25.6507	24.8884	0.71 ± 0.16
mmu-miR-139-3p-4395676	23.5044	23.5507	24.7072	24.1809	0.68 ± 0.15
mmu-miR-139-5p-4395400	22.6262	22.8796	24.3033	23.7421	0.64 ± 0.14
mmu-miR-140-4373374	24.2794	24.514	26.2604	24.9688	0.83 ± 0.19
mmu-miR-141-4373137	undetected	undetected	undetected	undetected	n.d
mmu-miR-142-3p-4373136	27.7609	28.1421	29.1962	27.5127	0.91 ± 0.20
mmu-miR-142-5p-4395359	33.7399	32.5189	33.3585	34.4223	0.61 ± 0.14
mmu-miR-143-4395360	30.3452	31.2135	32.6114	31.7294	0.58 ± 0.13
mmu-miR-145-4395389	26.6094	26.5247	28.7076	27.229	0.99 ± 0.22
mmu-miR-146a-4373132	27.7135	27.4729	29.3496	33.3421	0.16 ± 0.04
mmu-miR-146b-4373178	23.5538	24.0374	25.6865	24.6922	0.69 ± 0.16
mmu-miR-148a-4373130	undetected	undetected	34.5327	undetected	n.d
mmu-miR-148b-4373129	29.1065	29.4742	32.3755	30.2169	1.07 ± 0.24
mmu-miR-150-4373127	26.5356	26.5659	26.5552	26.0218	0.69 ± 0.15
mmu-miR-151-3p-4373304	26.676	26.8863	27.8461	27.421	0.62 ± 0.14
mmu-miR-152-4395170	33.2598	33.176	undetected	31.0539	n.d
mmu-miR-153-4373305	undetected	undetected	undetected	undetected	n.d
mmu-miR-155-4395701	31.9157	32.4291	33.1874	30.1046	1.41 ± 0.32
mmu-miR-15a-4373123	27.8278	28.298	31.2851	28.9144	1.12 ± 0.25
mmu-miR-15b-4373122	23.2847	23.4458	25.7631	24.1333	0.96 ± 0.22
mmu-miR-16-4373121	19.9216	20.211	21.5584	20.8463	0.67 ± 0.15
mmu-miR-17-4395419	28.6238	28.4339	29.3873	28.2429	0.92 ± 0.21

mmu-miR-181a-4373117	26.6035	26.7755	29.4047	27.4335	1.08 ± 0.24
mmu-miR-181c-4373115	33.5207	34.5952	undetected	34.7746	n.d
mmu-miR-182-4395729	34.528	31.5341	34.053	32.5579	2.74 ± 0.62
mmu-miR-184-4373113	31.7826	31.1101	32.49	31.9712	0.87 ± 0.20
mmu-miR-185-4395382	27.1701	28.3651	32.4091	28.7879	1.34 ± 0.30
mmu-miR-186-4395396	24.047	25.203	25.6819	25.2839	0.44 ± 0.10
mmu-miR-187-4373307	30.2558	29.8418	undetected	undetected	n.d
mmu-miR-188-5p-4395431	25.9229	26.5874	27.0084	26.6878	0.51 ± 0.12
mmu-miR-190-4373110	28.5596	28.1482	31.3778	28.9609	1.54 ± 0.35
mmu-miR-191-4395410	20.8993	21.2312	22.9003	21.9111	0.73 ± 0.16
mmu-miR-192-4373108	25.8134	25.8086	28.526	26.1807	1.30 ± 0.29
mmu-miR-193-4395361	undetected	undetected	undetected	undetected	n.d
mmu-miR-193b-4395597	29.6422	30.7735	30.4571	29.971	0.46 ± 0.10
mmu-miR-194-4373106	28.88	29.4318	31.538	30.0406	0.80 ± 0.18
mmu-miR-195-4373105	22.9343	23.2529	25.5772	23.8597	0.94 ± 0.21
mmu-miR-196b-4395326	undetected	undetected	undetected	undetected	n.d
mmu-miR-197-4373102	undetected	undetected	32.3467	undetected	n.d
mmu-miR-19a-4373099	29.9513	30.5823	31.1867	30.1667	0.66 ± 0.15
mmu-miR-19b-4373098	26.9745	27.1752	27.9403	26.815	0.80 ± 0.18
mmu-miR-200a-4378069	undetected	undetected	undetected	undetected	n.d
mmu-miR-200b-4395362	undetected	undetected	undetected	undetected	n.d
mmu-miR-200c-4395411	undetected	undetected	undetected	undetected	n.d
mmu-miR-202-3p-4373311	31.4953	33.427	undetected	31.9928	n.d
mmu-miR-203-4373095	29.0968	29.4648	34.4108	30.7555	1.80 ± 0.41
mmu-miR-204-4373094	25.1011	24.8665	27.139	25.7532	1.01 ± 0.23
mmu-miR-205-4373093	undetected	undetected	undetected	undetected	n.d
mmu-miR-20a-4373286	25.6459	25.8787	27.8075	26.2063	0.93 ± 0.21
mmu-miR-21-4373090	25.8459	26.1489	27.8713	25.9962	1.00 ± 0.22
mmu-miR-210-4373089	undetected	undetected	undetected	undetected	n.d
mmu-miR-215-4373316	undetected	undetected	undetected	undetected	n.d
mmu-miR-218-4373081	23.2249	23.6661	25.454	23.7937	0.88 ± 0.20

mmu-miR-222-4395387	29.7266	30.4407	29.4618	29.5338	0.44 ± 0.10
mmu-miR-223-4395406	26.5342	27.0136	26.9604	26.4813	0.58 ± 0.13
mmu-miR-224-4395683	26.7344	27.0332	29.1919	27.6903	0.88 ± 0.20
mmu-miR-23b-4373073	28.0218	28.5273	30.7907	28.9298	0.92 ± 0.21
mmu-miR-24-4373072	19.6936	20.0704	21.3236	20.374	0.70 ± 0.16
mmu-miR-25-4373071	25.4254	25.4055	28.0568	26.2722	1.08 ± 0.24
mmu-miR-26a-4395166	22.3924	22.3606	24.7524	23.1418	1.02 ± 0.23
mmu-miR-26b-4395167	23.3788	23.6576	25.5996	24.0955	0.88 ± 0.20
mmu-miR-27a-4373287	27.0136	27.7599	29.6662	28.1786	0.75 ± 0.17
mmu-miR-27b-4373068	25.8256	26.1028	28.7596	26.5822	1.12 ± 0.25
mmu-miR-28-4373067	26.4062	26.595	28.3424	27.3829	0.75 ± 0.17
mmu-miR-294-4373326	undetected	undetected	undetected	undetected	n.d
mmu-miR-295-4373327	undetected	undetected	undetected	undetected	n.d
mmu-miR-296-3p-4395212	27.7562	26.7395	30.4075	27.7956	2.03 ± 0.46
mmu-miR-296-5p-4373066	22.0977	21.8002	24.2195	22.3152	1.24 ± 0.28
mmu-miR-297c-4395610	undetected	undetected	undetected	undetected	n.d
mmu-miR-298-4395728	26.7184	27.8596	29.7813	27.6105	0.82 ± 0.19
mmu-miR-29a-4395223	22.9561	23.5192	25.7242	23.7649	0.94 ± 0.21
mmu-miR-29b-4373288	30.647	30.1805	33.6716	30.4458	2.08 ± 0.47
mmu-miR-29c-4395171	25.0808	25.606	28.0923	26.1572	0.94 ± 0.21
mmu-miR-301a-4373064	23.642	23.7844	26.4567	24.6347	1.03 ± 0.23
mmu-miR-301b-4395730	23.2688	23.5394	25.9116	24.2772	0.93 ± 0.21
mmu-miR-302a-4378070	undetected	undetected	undetected	undetected	n.d
mmu-miR-302b-4378071	undetected	undetected	undetected	undetected	n.d
mmu-miR-302d-4373063	undetected	undetected	undetected	undetected	n.d
mmu-miR-30a-4373061	22.8771	23.0925	25.2291	23.594	0.94 ± 0.21
mmu-miR-30b-4373290	20.8144	21.1353	23.3403	21.6397	0.93 ± 0.21
mmu-miR-30c-4373060	20.209	20.391	22.1966	20.9766	0.83 ± 0.19
mmu-miR-30d-4373059	24.5496	24.8715	26.9106	25.3372	0.89 ± 0.20
mmu-miR-30e-4395334	25.5047	25.9509	27.7556	26.4366	0.78 ± 0.18
mmu-miR-31-4373331	32.2421	30.7768	32.3048	31.5888	1.23 ± 0.28

mmu-miR-32-4395220	31.6225	33.3111	undetected	undetected	n.d
mmu-miR-320-4395388	22.5018	22.1889	23.6865	23.0321	0.81 ± 0.18
mmu-miR-324-3p-4395639	27.5631	27.6029	29.8198	28.6491	0.85 ± 0.19
mmu-miR-324-5p-4373052	25.7464	25.7211	28.4935	26.529	1.15 ± 0.26
mmu-miR-325-4395640	29.8167	30.1012	34.1877	30.9252	1.62 ± 0.36
mmu-miR-328-4373049	23.0143	23.1504	24.9475	23.6493	0.86 ± 0.19
mmu-miR-331-3p-4373046	23.678	23.9428	26.0413	24.5357	0.89 ± 0.20
mmu-miR-331-5p-4395344	28.1006	28.9268	30.3062	28.4685	0.82 ± 0.18
mmu-miR-337-3p-4395662	undetected	34.0229	undetected	undetected	n.d
mmu-miR-337-5p-4395645	33.8368	undetected	undetected	34.582	n.d
mmu-miR-338-3p-4395363	32.7444	33.766	undetected	33.5655	n.d
mmu-miR-339-3p-4395663	25.1005	25.2315	27.6391	26.0421	0.96 ± 0.22
mmu-miR-339-5p-4395368	25.4801	25.2057	28.5328	26.5712	1.25 ± 0.28
mmu-miR-340-3p-4395370	25.5834	25.5544	28.1198	26.5555	1.00 ± 0.23
mmu-miR-340-5p-4395369	25.1927	25.6067	27.9057	25.984	0.97 ± 0.22
mmu-miR-342-3p-4395371	23.4979	23.1429	25.3246	24.3541	0.91 ± 0.21
mmu-miR-342-5p-4395657	28.7813	27.6705	30.6396	28.9886	1.50 ± 0.34
mmu-miR-344-4373340	23.49	23.551	26.2953	24.3398	1.11 ± 0.25
mmu-miR-345-3p-4395659	30.6082	30.7388	32.7672	32.0996	0.70 ± 0.16
mmu-miR-345-5p-4395658	31.2698	30.9274	undetected	undetected	n.d
mmu-miR-34a-4395168	undetected	undetected	undetected	undetected	n.d
mmu-miR-34b-3p-4395748	29.2153	29.1345	31.1409	28.6562	1.40 ± 0.32
mmu-miR-34c-4373036	32.623	undetected	undetected	33.7683	n.d
mmu-miR-350-4395660	29.1289	29.2318	32.2203	29.7737	1.30 ± 0.29
mmu-miR-351-4373345	27.4203	27.6441	29.633	27.9401	0.96 ± 0.22
mmu-miR-361-4373035	26.4721	26.1886	29.5639	27.2572	1.42 ± 0.32
mmu-miR-362-3p-4395746	30.2599	30.7185	32.1431	30.4122	0.90 ± 0.20
mmu-miR-363-4378090	34.3175	undetected	undetected	34.6557	n.d
mmu-miR-365-4373194	undetected	31.2658	undetected	undetected	n.d
mmu-miR-367-4373034	34.7787	undetected	undetected	undetected	n.d
mmu-miR-375-4373027	33.3839	31.4636	undetected	32.365	n.d

mmu-miR-376a-4373347	undetected	undetected	undetected	undetected	n.d
mmu-miR-376b-4395582	32.5186	undetected	undetected	33.7577	n.d
mmu-miR-376c-4395580	31.2984	31.2011	31.9658	31.2816	0.76 ± 0.17
mmu-miR-379-4373349	30.0555	30.7902	34.0189	30.6269	1.45 ± 0.33
mmu-miR-380-5p-4395731	32.4066	33.5623	33.7924	33.3016	0.46 ± 0.10
mmu-miR-381-4373020	32.9488	33.3986	34.6836	33.3219	0.79 ± 0.18
mmu-miR-383-4381093	undetected	undetected	undetected	undetected	n.d
mmu-miR-384-3p-4395733	29.3026	29.4818	31.7423	29.8352	1.05 ± 0.24
mmu-miR-384-5p-4395732	21.9747	22.4127	24.267	22.7271	0.85 ± 0.19
mmu-miR-409-3p-4395443	31.1358	30.5368	31.306	30.7359	0.87 ± 0.19
mmu-miR-410-4378093	30.8645	30.9747	31.3818	30.6707	0.71 ± 0.16
mmu-miR-411-4381013	29.2835	29.4658	31.3669	29.5162	1.03 ± 0.23
mmu-miR-423-5p-4395451	29.4814	28.2002	32.1882	30.3373	1.71 ± 0.38
mmu-miR-424-4378107	28.9815	29.066	33.6567	29.7832	2.15 ± 0.48
mmu-miR-425-4380926	undetected	undetected	undetected	undetected	n.d
mmu-miR-429-4373355	undetected	undetected	undetected	undetected	n.d
mmu-miR-434-3p-4395734	32.7549	33.3298	undetected	undetected	n.d
mmu-miR-449a-4373207	30.6036	30.8685	31.2633	30.2672	0.74 ± 0.17
mmu-miR-450a-5p-4395414	34.222	33.6949	undetected	34.774	n.d
mmu-miR-451-4373360	29.0889	29.2295	30.2987	28.9667	0.87 ± 0.20
mmu-miR-452-4373281	undetected	undetected	undetected	30.9732	n.d
mmu-miR-455-4395585	undetected	31.394	undetected	undetected	n.d
mmu-miR-465b-5p-4395615	34.1486	34.4204	undetected	undetected	n.d
mmu-miR-467c-4395647	undetected	32.6773	undetected	undetected	n.d
mmu-miR-484-4381032	20.0397	20.4558	22.1623	21.0556	0.73 ± 0.17
mmu-miR-488-4381074	31.9172	31.3785	undetected	31.7891	n.d
mmu-miR-489-4378114	33.8821	undetected	undetected	undetected	n.d
mmu-miR-491-4381053	27.8597	27.5692	29.9165	28.3354	1.10 ± 0.25
mmu-miR-494-4395476	undetected	undetected	undetected	undetected	n.d
mmu-miR-495-4381078	undetected	34.6625	undetected	undetected	n.d
mmu-miR-497-4381046	25.8737	25.9991	28.9651	26.8048	1.17 ± 0.26

mmu-miR-500-4395736	31.9969	undetected	undetected	32.7155	n.d
mmu-miR-503-4395586	31.8771	31.952	undetected	31.8378	n.d
mmu-miR-509-3p-4395651	25.8479	25.3175	27.357	25.7711	1.20 ± 0.27
mmu-miR-532-3p-4395466	25.9728	26.4024	28.0732	26.8596	0.76 ± 0.17
mmu-miR-532-5p-4380928	23.5418	23.5739	26.752	24.3707	1.30 ± 0.29
mmu-miR-542-3p-4378101	31.8723	31.8379	34.7316	32.0937	1.46 ± 0.33
mmu-miR-542-5p-4395693	31.4847	31.0961	34.9355	32.629	1.47 ± 0.33
mmu-miR-544-4395680	undetected	undetected	undetected	34.5468	n.d
mmu-miR-547-4395694	31.9481	32.7666	33.6543	32.8205	0.58 ± 0.13
mmu-miR-551b-4380945	33.6192	34.4161	undetected	33.0482	n.d
mmu-miR-574-3p-4395460	27.5522	28.2623	29.0414	28.3278	0.58 ± 0.13
mmu-miR-582-5p-4395696	32.5646	31.5933	undetected	33.4325	n.d
mmu-miR-598-4395606	29.727	29.138	32.2297	30.1494	1.46 ± 0.33
mmu-miR-652-4395463	22.9174	23.1967	26.5845	23.8645	1.35 ± 0.30
mmu-miR-665-4395737	30.6685	undetected	undetected	30.4861	n.d
mmu-miR-667-4386769	undetected	undetected	undetected	undetected	n.d
mmu-miR-671-3p-4395433	24.9756	25.3587	26.5443	25.694	0.68 ± 0.15
mmu-miR-672-4395438	22.3151	21.611	22.7925	22.1115	0.93 ± 0.21
mmu-miR-674-4395193	undetected	32.6197	undetected	undetected	n.d
mmu-miR-676-4386776	24.5904	24.1444	26.0116	25.4079	0.83 ± 0.19
mmu-miR-677-4381075	undetected	undetected	undetected	undetected	n.d
mmu-miR-680-4381079	undetected	32.7598	undetected	undetected	n.d
mmu-miR-682-4381081	29.4565	29.2823	30.4211	29.3731	0.88 ± 0.20
mmu-miR-684-4381083	undetected	undetected	undetected	undetected	n.d
mmu-miR-685-4386748	24.2055	23.751	24.7058	23.7307	0.95 ± 0.21
mmu-miR-708-4395452	26.6043	26.8308	28.5417	26.98	0.92 ± 0.21
mmu-miR-744-4395435	23.6691	23.5897	25.8944	24.2578	1.05 ± 0.24
mmu-miR-7a-4378130	28.8364	30.0198	32.2783	30.1798	0.79 ± 0.18
mmu-miR-7b-4395685	30.6	30.7992	32.5122	30.7514	0.99 ± 0.22
mmu-miR-872-4395375	25.432	25.9608	27.958	26.0224	0.94 ± 0.21
mmu-miR-873-4395467	undetected	undetected	undetected	undetected	n.d

mmu-miR-879-4395602	undetected	undetected	undetected	undetected	n.d
mmu-miR-9-4373285	25.4791	25.5953	28.2783	26.1767	1.15 ± 0.26
mmu-miR-92a-4373013	26.1154	26.0036	27.5199	26.1368	0.97 ± 0.22
mmu-miR-93-4373302	22.0304	22.5505	24.9187	23.2707	0.85 ± 0.19
mmu-miR-98-4373009	27.1035	26.391	undetected	28.3421	n.d
mmu-miR-99a-4373008	26.7697	25.4518	28.5253	27.355	1.37 ± 0.31
mmu-miR-99b-4373007	21.9581	22.0539	24.6098	22.9565	0.99 ± 0.22
rno-miR-1-4395765	undetected	undetected	33.4738	undetected	n.d
rno-miR-190b-4395749	30.8651	31.1092	33.9	31.359	1.28 ± 0.29
rno-miR-196c-4395750	32.336	32.1661	34.5432	32.8798	1.09 ± 0.25
rno-miR-207-4381096	undetected	31.6279	undetected	undetected	n.d
rno-miR-219-1-3p-4395778	27.4428	27.8441	28.536	28.4088	0.52 ± 0.12
rno-miR-224-4373187	27.5344	27.4889	29.6182	28.2533	0.94 ± 0.21
rno-miR-327-4381108	undetected	undetected	undetected	undetected	n.d
rno-miR-339-3p-4395760	31.3153	31.9615	undetected	undetected	n.d
rno-miR-343-4381123	undetected	undetected	undetected	undetected	n.d
rno-miR-344-5p-4395761	undetected	undetected	undetected	undetected	n.d
rno-miR-345-3p-4395762	30.4988	30.8257	32.7596	31.9248	0.69 ± 0.15
rno-miR-347-4381114	22.3022	22.707	24.6105	23.7539	0.68 ± 0.15
rno-miR-351-4395764	27.7282	28.5654	30.4886	28.6347	0.82 ± 0.18
rno-miR-381-4381102	25.1691	25.781	29.8534	25.6736	1.99 ± 0.45
rno-miR-532-5p-4395752	undetected	29.2709	undetected	undetected	n.d
rno-miR-598-5p-4395754	26.8619	27.4592	28.9368	27.5807	0.75 ± 0.17
snoRNA135-4380912	28.9053	28.6992	31.3605	29.4813	1.19 ± 0.27
snoRNA202-4380914	24.1674	24.3037	26.5687	25.2733	0.86 ± 0.19

Cycle threshold > 35 was designated 'undetected', n.d = not determined if miRNA assay is undetected in 1 or more samples.
* Relative quantitation (RQ) data represents the mean ± SEM of target miRNA normalised to sno135 and sno202 endogenous controls using the ΔΔCt method (n = 2).

Supplementary Table S3. Library quality and adapter processing

Library	Description	Total reads	After 3' adapter trimming	Failed 3' adapter	No 3' adapter	Short insert (<18 nt)	No insert
S1	Uninfected Exosome Rep 1	9367962	8081961 (86.27%)	1286000 (13.73%)	629103 (48.92%)	656897 (51.08%)	0 (0.00%)
S2	Infected Exosome Rep 1	8619204	7594138 (88.11%)	1025065 (11.89%)	541406 (52.82%)	483659 (47.18%)	0 (0.00%)
S3	Uninfected Exosome Rep 2	7766392	6974615 (89.81%)	791776 (10.19%)	334370 (42.23%)	457406 (57.77%)	0 (0.00%)
S4	Infected Exosome Rep 2	7240878	6206570 (85.72%)	1034307 (14.28%)	374094 (36.17%)	660213 (63.83%)	0 (0.00%)

3' adapter sequences were mapped and trimmed, allowing 2 mismatches when starting from base 20 in a read. Only reads with recognized 3' adapter and longer than 18 bases were considered in further analysis. Failed 3’ adapter reads were categorized by either no 3’ adapter or short insert

Supplementary Table S4. Library mapping to genome

Library	Description	Non-matching	Trimmed 3'	Perfect	Total mapped
S1	Uninfected Exosome Rep 1	3051052	3750172	1280737	5030909
S2	Infected Exosome Rep 1	3207370	3396836	989932	4386768
S3	Uninfected Exosome Rep 2	3215336	3038667	720612	3759279
S4	Infected Exosome Rep 2	3240287	2381194	585089	2966283

For genome mapping the following matches were accepted. Perfect: the complete read perfectly matches to the genome and Trimmed 3’ only: the best hits have at least 18 bases perfectly matching to the genome, and the remaining 3' sequence is trimmed.

Supplementary Table S5. Exosomes small RNA library composition

Library	Description	Total reads	known miRNA	Candidate miRNA	scRNA	mRNA	senseRNAnc	siRNA	siRNAnc	snRNA	snoRNA	tRNA	rRNA	repeats	other RNA	other hairpins	non-hairpin
S1	Uninfected Exosome Rep 1	5030909	9159 (0.18%)	8212 (0.16%)	30005 (0.60%)	33457 (0.66%)	20348 (0.40%)	11576 (0.23%)	8088 (0.16%)	8303 (0.17%)	848 (0.02%)	820524 (16.3%)	26514 (0.53%)	2541657 (50.5%)	318830 (6.34%)	343923 (6.84%)	849465 (16.9%)
S2	Infected Exosome Rep 1	4386768	6082 (0.12%)	8761 (0.17%)	20233 (0.40%)	28809 (0.57%)	17196 (0.34%)	12075 (0.24%)	8307 (0.17%)	7460 (0.15%)	785 (0.02%)	690100 (13.7%)	21587 (0.43%)	2158865 (42.9%)	230057 (4.57%)	338399 (6.73%)	838052 (16.7%)
S3	Uninfected Exosome Rep 2	3759279	3659 (0.07%)	12453 (0.25%)	14057 (0.30%)	25364 (0.50%)	13295 (0.26%)	10100 (0.20%)	6678 (0.13%)	5687 (0.11%)	516 (0.01%)	358316 (7.12%)	15573 (0.31%)	1981733 (39.4%)	224472 (4.46%)	328918 (6.54%)	758457 (15.1%)
S4	Infected Exosome Rep 2	2966283	2656 (0.05%)	7333 (0.15%)	18914 (0.38%)	19487 (0.39%)	10028 (0.19%)	7359 (0.15%)	4831 (0.10%)	4213 (0.08%)	371 (0.01%)	402595 (8.00%)	13756 (0.27%)	1458745 (29.0%)	169584 (3.37%)	273341 (5.43%)	573071 (11.4%)

Reads were classified as Known miRNA: previously identified isoforms of known miRNA including star strands, candidate novel miRNAs, confident novel miRNAs, non-hairpin: reads that lack a hairpin in their genomic loci, novel known miRNA: reads that represent previously undocumented processing variants of known miRNA. other RNA: RNA reads that are inconsistent with miRNA features and are not members of the following classes of RNA: ribosomal RNA (rRNA), small cytoplasmic RNA (scRNA), repeats (including repetitive elements LINEs and SINEs), senseRNA (mRNA fragments), sense ncRNA, potential siRNAs, potential siRNAs derived from ncRNAs, small nuclear RNA (snRNA), small nucleolar RNA (snoRNA), or transfer RNA (tRNA).

Supplementary Table S6. Abundant miRNA Reads Differentially detected from Small RNA sequencing of Uninfected and Infected Exosomes

miRNA	Absolute Read Count Uninfected Exosomes	Absolute Read Count Infected Exosomes	Normalised Read Count Uninfected Exosomes[1]	Normalised Read Count Infected Exosomes[2]	% Normalised Read Count Uninfected Exosomes	% Normalised Read Count Infected Exosomes	Ratio Infected/Uninfected
miR-29a	347	214	521	534	5.21	5.34	1.02
miR-125b-5p	229	130	344	324	3.44	3.24	0.94
miR-24	196	125	294	312	2.94	3.12	1.06
miR-125a	186	94	279	235	2.79	2.35	0.84
miR-301a	181	116	272	289	2.72	2.89	1.06
miR-130a	**176**	**136**	**264**	**339**	**2.64**	**3.39**	**1.30**
let-7c	150	79	225	196	2.25	1.96	0.87
let-7b	149	95	224	238	2.24	2.38	1.06
miR-93	**145**	**51**	**218**	**127**	**2.18**	**1.27**	**0.58**
miR-191	141	68	212	170	2.12	1.70	0.80
miR-296-5p	133	84	200	210	2.00	2.10	1.05
miR-99b	120	71	180	177	1.80	1.77	0.98
miR-103	119	84	178	210	1.78	2.10	1.18
miR-344-3p	**118**	**105**	**177**	**262**	**1.77**	**2.62**	**1.48**
miR-16	109	65	164	162	1.64	1.62	0.99
miR-29c	108	67	162	167	1.62	1.67	1.03
miR-342-3p	108	75	162	187	1.62	1.87	1.15
miR-23b	**106**	**43**	**159**	**107**	**1.59**	**1.07**	**0.67**
miR-21	**103**	**80**	**155**	**200**	**1.55**	**2.00**	**1.30**
miR-23a	**100**	**40**	**150**	**100**	**1.50**	**1.00**	**0.66**
miR-30c	94	61	141	152	1.41	1.52	1.08
miR-130b	89	58	134	145	1.34	1.45	1.08
miR-361	88	62	132	155	1.32	1.55	1.17
miR-378	**82**	**70**	**123**	**173**	**1.23**	**1.73**	**1.41**
miR-30b	78	37	117	92	1.17	0.92	0.79
miR-339	76	58	115	145	1.15	1.45	1.26
miR-99b	71	37	107	92	1.07	0.92	0.87
miR-107	67	35	100	87	1.00	0.87	0.87
let-7f	65	29	98	72	0.98	0.72	0.74
miR-484	64	46	96	115	0.96	1.15	1.19
miR-181a	63	34	95	85	0.95	0.85	0.90
miR-26a	62	44	93	110	0.93	1.10	1.18
let-7i	**58**	**47**	**87**	**117**	**0.87**	**1.17**	**1.35**

miR-320	56	35	84	86	0.84	0.86	1.02
miR-138	54	25	81	62	0.81	0.62	0.77
miR-342-5p	52	35	78	87	0.78	0.87	1.12
miR-872	50	24	75	60	0.75	0.60	0.80
miR-344b	50	28	75	70	0.75	0.70	0.93
miR-29b	**48**	**38**	**72**	**95**	**0.72**	**0.95**	**1.32**
miR-25	48	30	72	75	0.72	0.75	1.04
let-7a	47	25	70	62	0.70	0.62	0.89
miR-30e	44	26	66	65	0.66	0.65	0.98
miR-30a	44	25	66	62	0.66	0.62	0.94
miR-451	36	20	54	49	0.54	0.49	0.92
miR-672	31	22	46	54	0.46	0.54	1.18

Confidence threshold for miRNA abundance is 10 or more reads in 2 or more libraries. Differential Reads with a Ratio of Normalised Infected Reads/Normalised Uninfected Reads > 1.3 or < 1.3 is indicated in **bold.**

[1] Normalised to total number of reads sequenced in pooled Uninfected Exosomes libraries; N=2, 5939 total reads

[2] Normalised to total number of reads sequenced in pooled Infected Exosomes libraries; N=2, 3558 total reads

Supplementary Table S7. Experimental validated mRNA targets of let-7b/let-7i, miR-128a, miR-21, miR-222, miR-29b, miR-342-3p and miR-424

miRNA	Target Gene	Entrez Gene Name	Cellular Location	Molecular Function
let-7b/let-7i	AARSD1	alanyl-tRNA synthetase domain containing 1	unknown	enzyme
let-7b/let-7i	ACP1 (includes EG:11431)	acid phosphatase 1, soluble	Cytoplasm	phosphatase
let-7b/let-7i	AKAP8	A kinase (PRKA) anchor protein 8	Nucleus	other
let-7b/let-7i	ANAPC1/LOC100286979	anaphase promoting complex subunit 1	Nucleus	other
let-7b/let-7i	ATAD3A/ATAD3B	ATPase family, AAA domain containing 3A	Nucleus	other
let-7b/let-7i	ATP6V0A1	ATPase, H+ transporting, lysosomal V0 subunit a1	Cytoplasm	transporter
let-7b/let-7i	ATP6V1F	ATPase, H+ transporting, lysosomal 14kDa, V1 subunit F	Cytoplasm	transporter
let-7b/let-7i	AURKB	aurora kinase B	Nucleus	kinase
let-7b/let-7i	BCL2L1	BCL2-like 1	Cytoplasm	other
let-7b/let-7i	BCL2L11	BCL2-like 11 (apoptosis facilitator)	Cytoplasm	other
let-7b/let-7i	BCL7A	B-cell CLL/lymphoma 7A	unknown	other
let-7b/let-7i	BMP2K	BMP2 inducible kinase	Nucleus	kinase
let-7b/let-7i	BSG (includes EG:12215)	basigin (Ok blood group)	Plasma Membrane	transporter
let-7b/let-7i	CALCOCO2	calcium binding and coiled-coil domain 2	Nucleus	other
let-7b/let-7i	CAPG	capping protein (actin filament), gelsolin-like	Nucleus	other
let-7b/let-7i	CARHSP1	calcium regulated heat stable protein 1, 24kDa	Cytoplasm	other
let-7b/let-7i	CASP3	caspase 3, apoptosis-related cysteine peptidase	Cytoplasm	peptidase
let-7b/let-7i	CCND1	cyclin D1	Nucleus	other
let-7b/let-7i	CDC25A	cell division cycle 25 homolog A (S. pombe)	Nucleus	phosphatase
let-7b/let-7i	CDIPT	CDP-diacylglycerol--inositol 3-phosphatidyltransferase	Cytoplasm	enzyme
let-7b/let-7i	CDK6	cyclin-dependent kinase 6	Nucleus	kinase
let-7b/let-7i	CDKAL1	CDK5 regulatory subunit associated protein 1-like 1	unknown	other
let-7b/let-7i	CHMP2A	charged multivesicular body protein 2A	Cytoplasm	other
let-7b/let-7i	COIL	coilin	Nucleus	enzyme
let-7b/let-7i	COL1A2	collagen, type I, alpha 2	Extracellular Space	other
let-7b/let-7i	COMMD9	COMM domain containing 9	unknown	other
let-7b/let-7i	CSDE1	cold shock domain containing E1, RNA-binding	Cytoplasm	enzyme
let-7b/let-7i	CSNK1D	casein kinase 1, delta	Cytoplasm	kinase
let-7b/let-7i	DAD1 (includes EG:13135)	defender against cell death 1	Cytoplasm	enzyme

let-7b/let-7i	DHX57	DEAH (Asp-Glu-Ala-Asp/His) box polypeptide 57	unknown	other
let-7b/let-7i	DICER1	dicer 1, ribonuclease type III	Cytoplasm	enzyme
let-7b/let-7i	DOCK5	dedicator of cytokinesis 5	Cytoplasm	other
let-7b/let-7i	DRD3	dopamine receptor D3	Plasma Membrane	G-protein coupled receptor
let-7b/let-7i	DSP	desmoplakin	Plasma Membrane	other
let-7b/let-7i	DUSP12	dual specificity phosphatase 12	Nucleus	phosphatase
let-7b/let-7i	DUSP23	dual specificity phosphatase 23	Cytoplasm	phosphatase
let-7b/let-7i	EIF2C4	eukaryotic translation initiation factor 2C, 4	Cytoplasm	translation regulator
let-7b/let-7i	EIF3J	eukaryotic translation initiation factor 3, subunit J	Cytoplasm	translation regulator
let-7b/let-7i	EIF4G2	eukaryotic translation initiation factor 4 gamma, 2	Cytoplasm	translation regulator
let-7b/let-7i	F2	coagulation factor II (thrombin)	Extracellular Space	peptidase
let-7b/let-7i	FADS2	fatty acid desaturase 2	Plasma Membrane	enzyme
let-7b/let-7i	FAM105A	family with sequence similarity 105, member A	unknown	other
let-7b/let-7i	FAM96A	family with sequence similarity 96, member A	Extracellular Space	other
let-7b/let-7i	FANCD2	Fanconi anemia, complementation group D2	Nucleus	other
let-7b/let-7i	FNDC3A	fibronectin type III domain containing 3A	Cytoplasm	other
let-7b/let-7i	GAK	cyclin G associated kinase	Nucleus	kinase
let-7b/let-7i	GEMIN7	gem (nuclear organelle) associated protein 7	Nucleus	other
let-7b/let-7i	GPR56	G protein-coupled receptor 56	Plasma Membrane	G-protein coupled receptor
let-7b/let-7i	GRPEL2	GrpE-like 2, mitochondrial (E. coli)	Cytoplasm	other
let-7b/let-7i	GTPBP3	GTP binding protein 3 (mitochondrial)	Cytoplasm	enzyme
let-7b/let-7i	GYS1	glycogen synthase 1 (muscle)	Cytoplasm	enzyme
let-7b/let-7i	HMGA1	high mobility group AT-hook 1	Nucleus	transcription regulator
let-7b/let-7i	HMGA2	high mobility group AT-hook 2	Nucleus	enzyme
let-7b/let-7i	HMOX1	heme oxygenase (decycling) 1	Cytoplasm	enzyme
let-7b/let-7i	HRAS	v-Ha-ras Harvey rat sarcoma viral oncogene homolog	Plasma Membrane	enzyme
let-7b/let-7i	HYOU1	hypoxia up-regulated 1	Cytoplasm	other
let-7b/let-7i	IFIT5	interferon-induced protein with tetratricopeptide repeats 5	unknown	other
let-7b/let-7i	IFRD1	interferon-related developmental regulator 1	Nucleus	other
let-7b/let-7i	IGF2BP1	insulin-like growth factor 2 mRNA binding protein 1	Cytoplasm	translation regulator
let-7b/let-7i	IPO4	importin 4	Nucleus	transporter
let-7b/let-7i	ITGB3	integrin, beta 3 (platelet glycoprotein IIIa, antigen CD61)	Plasma Membrane	transmembrane receptor

let-7b/let-7i	KCNJ16	potassium inwardly-rectifying channel, subfamily J, member 16	Plasma Membrane	ion channel
let-7b/let-7i	KLK10	kallikrein-related peptidase 10	Extracellular Space	peptidase
let-7b/let-7i	KRAS	v-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog	Cytoplasm	enzyme
let-7b/let-7i	KRT19 (human)	keratin 19	Cytoplasm	other
let-7b/let-7i	LIN28A	lin-28 homolog A (C. elegans)	Cytoplasm	other
let-7b/let-7i	MARS2	methionyl-tRNA synthetase 2, mitochondrial	Cytoplasm	enzyme
let-7b/let-7i	MED28	mediator complex subunit 28	Nucleus	other
let-7b/let-7i	MLLT1	myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila); translocated to, 1	Nucleus	transcription regulator
let-7b/let-7i	MRM1	mitochondrial rRNA methyltransferase 1 homolog (S. cerevisiae)	Cytoplasm	other
let-7b/let-7i	MRPS24	mitochondrial ribosomal protein S24	Cytoplasm	other
let-7b/let-7i	MRPS33	mitochondrial ribosomal protein S33	Cytoplasm	other
let-7b/let-7i	MTPN	myotrophin	Nucleus	transcription regulator
let-7b/let-7i	MTRR	5-methyltetrahydrofolate-homocysteine methyltransferase reductase	Cytoplasm	enzyme
let-7b/let-7i	MYC	v-myc myelocytomatosis viral oncogene homolog (avian)	Nucleus	transcription regulator
let-7b/let-7i	NEDD4	neural precursor cell expressed, developmentally down-regulated 4	Cytoplasm	enzyme
let-7b/let-7i	NF2	neurofibromin 2 (merlin)	Plasma Membrane	other
let-7b/let-7i	NRAS	neuroblastoma RAS viral (v-ras) oncogene homolog	Plasma Membrane	enzyme
let-7b/let-7i	NXN	nucleoredoxin	Nucleus	enzyme
let-7b/let-7i	PGRMC1	progesterone receptor membrane component 1	Plasma Membrane	transmembrane receptor
let-7b/let-7i	POLD2	polymerase (DNA directed), delta 2, regulatory subunit 50kDa	Nucleus	enzyme
let-7b/let-7i	POLR2C	polymerase (RNA) II (DNA directed) polypeptide C, 33kDa	Nucleus	enzyme
let-7b/let-7i	POM121/POM121C	POM121 membrane glycoprotein	Nucleus	other
let-7b/let-7i	PPP1R7	protein phosphatase 1, regulatory subunit 7	Nucleus	phosphatase
let-7b/let-7i	PRDM1	PR domain containing 1, with ZNF domain	Nucleus	transcription regulator
let-7b/let-7i	PRIM1	primase, DNA, polypeptide 1 (49kDa)	Nucleus	enzyme
let-7b/let-7i	PRRC2A	proline-rich coiled-coil 2A	Cytoplasm	other
let-7b/let-7i	PTGS2	prostaglandin-endoperoxide synthase 2	Cytoplasm	enzyme

		(prostaglandin G/H synthase and cyclooxygenase)		
let-7b/let-7i	PXDN	peroxidasin homolog (Drosophila)	Extracellular Space	enzyme
let-7b/let-7i	RABGAP1L	RAB GTPase activating protein 1-like	Cytoplasm	other
let-7b/let-7i	RBM19	RNA binding motif protein 19	Nucleus	other
let-7b/let-7i	RDH10	retinol dehydrogenase 10 (all-trans)	Nucleus	enzyme
let-7b/let-7i	RHOB	ras homolog gene family, member B	Cytoplasm	enzyme
let-7b/let-7i	RHOG	ras homolog gene family, member G (rho G)	Cytoplasm	enzyme
let-7b/let-7i	RPP38	ribonuclease P/MRP 38kDa subunit	Nucleus	enzyme
let-7b/let-7i	RRP8	ribosomal RNA processing 8, methyltransferase, homolog (yeast)	Nucleus	enzyme
let-7b/let-7i	RTCD1	RNA terminal phosphate cyclase domain 1	Nucleus	enzyme
let-7b/let-7i	SCYL1	SCY1-like 1 (S. cerevisiae)	Cytoplasm	kinase
let-7b/let-7i	SEPT3	septin 3	Cytoplasm	enzyme
let-7b/let-7i	SIGMAR1	sigma non-opioid intracellular receptor 1	Plasma Membrane	G-protein coupled receptor
let-7b/let-7i	SLC1A4	solute carrier family 1 (glutamate/neutral amino acid transporter), member 4	Plasma Membrane	transporter
let-7b/let-7i	SLC25A1	solute carrier family 25 (mitochondrial carrier; citrate transporter), member 1	Plasma Membrane	transporter
let-7b/let-7i	SLC25A13	solute carrier family 25, member 13 (citrin)	Cytoplasm	transporter
let-7b/let-7i	SLC25A24	solute carrier family 25 (mitochondrial carrier; phosphate carrier), member 24	Cytoplasm	other
let-7b/let-7i	SLC25A32	solute carrier family 25, member 32	Cytoplasm	transporter
let-7b/let-7i	SLC38A1	solute carrier family 38, member 1	Plasma Membrane	transporter
let-7b/let-7i	SMC1A	structural maintenance of chromosomes 1A	Nucleus	transporter
let-7b/let-7i	SMOX	spermine oxidase	Cytoplasm	enzyme
let-7b/let-7i	SNAP23	synaptosomal-associated protein, 23kDa	Plasma Membrane	transporter
let-7b/let-7i	SPCS3	signal peptidase complex subunit 3 homolog (S. cerevisiae)	Cytoplasm	peptidase
let-7b/let-7i	SPRYD4	SPRY domain containing 4	Cytoplasm	other
let-7b/let-7i	SYPL1	synaptophysin-like 1	Plasma Membrane	transporter
let-7b/let-7i	TAF9B	TAF9B RNA polymerase II, TATA box binding protein (TBP)-associated factor, 31kDa	Nucleus	transcription regulator
let-7b/let-7i	TAGLN	transgelin	Cytoplasm	other
let-7b/let-7i	TGFBR1	transforming growth factor, beta receptor 1	Plasma Membrane	kinase
let-7b/let-7i	THBS1	thrombospondin 1	Extracellular Space	other
let-7b/let-7i	TLR4	toll-like receptor 4	Plasma Membrane	transmembrane receptor

let-7b/let-7i	TMEM2	transmembrane protein 2	unknown	other
let-7b/let-7i	TPM2	tropomyosin 2 (beta)	Cytoplasm	other
let-7b/let-7i	TRIM71	tripartite motif containing 71	unknown	other
let-7b/let-7i	TRMT1	TRM1 tRNA methyltransferase 1 homolog (S. cerevisiae)	unknown	enzyme
let-7b/let-7i	TTC9C	tetratricopeptide repeat domain 9C	unknown	other
let-7b/let-7i	TUSC2	tumor suppressor candidate 2	Nucleus	other
let-7b/let-7i	TYMS	thymidylate synthetase	Nucleus	enzyme
let-7b/let-7i	UGT8	UDP glycosyltransferase 8	Cytoplasm	enzyme
let-7b/let-7i	UHRF1	ubiquitin-like with PHD and ring finger domains 1	Nucleus	transcription regulator
let-7b/let-7i	VIM	vimentin	Cytoplasm	other
let-7b/let-7i	VPS39	vacuolar protein sorting 39 homolog (S. cerevisiae)	Cytoplasm	transporter
let-7b/let-7i	WNT1	wingless-type MMTV integration site family, member 1	Extracellular Space	cytokine
miR-128a	ADORA2B	adenosine A2b receptor	Plasma Membrane	G-protein coupled receptor
miR-128a	AFF1	AF4/FMR2 family, member 1	Nucleus	transcription regulator
miR-128a	BMI1	BMI1 polycomb ring finger oncogene	Nucleus	transcription regulator
miR-128a	DBI	diazepam binding inhibitor (GABA receptor modulator, acyl-CoA binding protein)	Cytoplasm	other
miR-128a	DCX	doublecortin	Cytoplasm	other
miR-128a	E2F3	E2F transcription factor 3	Nucleus	transcription regulator
miR-128a	EIF2C1	eukaryotic translation initiation factor 2C, 1	Cytoplasm	translation regulator
miR-128a	LDLR	low density lipoprotein receptor	Plasma Membrane	transporter
miR-128a	MLL	myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila)	Nucleus	transcription regulator
miR-128a	NTRK3	neurotrophic tyrosine kinase, receptor, type 3	Plasma Membrane	kinase
miR-128a	RELN	reelin	Extracellular Space	peptidase
miR-128a	SNAP25	synaptosomal-associated protein, 25kDa	Plasma Membrane	transporter
miR-128a	TGFBR1	transforming growth factor, beta receptor 1	Plasma Membrane	kinase
miR-128a	TXNIP	thioredoxin interacting protein	Cytoplasm	other
miR-128a	WEE1	WEE1 homolog (S. pombe)	Nucleus	kinase
miR-21	ACTA2	actin, alpha 2, smooth muscle, aorta	Cytoplasm	other
miR-21	APAF1	apoptotic peptidase activating factor 1	Cytoplasm	other

miR-21	BMPR2	bone morphogenetic protein receptor, type II (serine/threonine kinase)	Plasma Membrane	kinase
miR-21	BTG2	BTG family, member 2	Nucleus	transcription regulator
miR-21	CDC25A	cell division cycle 25 homolog A (S. pombe)	Nucleus	phosphatase
miR-21	CDK6	cyclin-dependent kinase 6	Nucleus	kinase
miR-21	CDKN1A	cyclin-dependent kinase inhibitor 1A (p21, Cip1)	Nucleus	kinase
miR-21	CFL2	cofilin 2 (muscle)	Nucleus	other
miR-21	E2F1	E2F transcription factor 1	Nucleus	transcription regulator
miR-21	FAM3C	family with sequence similarity 3, member C	Extracellular Space	cytokine
miR-21	FAS	Fas (TNF receptor superfamily, member 6)	Plasma Membrane	transmembrane receptor
miR-21	FASLG	Fas ligand (TNF superfamily, member 6)	Extracellular Space	cytokine
miR-21	GLCCI1	glucocorticoid induced transcript 1	Cytoplasm	other
miR-21	HIPK3	homeodomain interacting protein kinase 3	Nucleus	kinase
miR-21	IL6R	interleukin 6 receptor	Plasma Membrane	transmembrane receptor
miR-21	JAG1	jagged 1	Extracellular Space	growth factor
miR-21	LRRFIP1	leucine rich repeat (in FLII) interacting protein 1	Cytoplasm	other
miR-21	MARCKS	myristoylated alanine-rich protein kinase C substrate	Plasma Membrane	other
miR-21	MTAP	methylthioadenosine phosphorylase	Nucleus	enzyme
miR-21	NFIB	nuclear factor I/B	Nucleus	transcription regulator
miR-21	PDCD4	programmed cell death 4 (neoplastic transformation inhibitor)	Nucleus	other
miR-21	PELI1	pellino homolog 1 (Drosophila)	Cytoplasm	enzyme
miR-21	PIK3R1	phosphoinositide-3-kinase, regulatory subunit 1 (alpha)	Cytoplasm	kinase
miR-21	PRRG4	proline rich Gla (G-carboxyglutamic acid) 4 (transmembrane)	Plasma Membrane	other
miR-21	PTEN	phosphatase and tensin homolog	Cytoplasm	phosphatase
miR-21	RECK	reversion-inducing-cysteine-rich protein with kazal motifs	Plasma Membrane	other
miR-21	RP2	retinitis pigmentosa 2 (X-linked recessive)	Cytoplasm	enzyme
miR-21	SERPINB5	serpin peptidase inhibitor, clade B (ovalbumin), member 5	Extracellular Space	other
miR-21	SESN1	sestrin 1	Nucleus	other
miR-21	SGK3	serum/glucocorticoid regulated kinase family, member 3	Cytoplasm	kinase
miR-21	SLC12A1	solute carrier family 12 (sodium/potassium/chloride	Plasma Membrane	transporter

		transporters), member 1		
miR-21	SLC16A10	solute carrier family 16, member 10 (aromatic amino acid transporter)	Plasma Membrane	transporter
miR-21	SOCS5	suppressor of cytokine signaling 5	Extracellular Space	cytokine
miR-21	SOX5	SRY (sex determining region Y)-box 5	Nucleus	transcription regulator
miR-21	SPRY2	sprouty homolog 2 (Drosophila)	Plasma Membrane	other
miR-21	TAGLN	transgelin	Cytoplasm	other
miR-21	TCF21	transcription factor 21	Nucleus	transcription regulator
miR-21	TGFBR2	transforming growth factor, beta receptor II (70/80kDa)	Plasma Membrane	kinase
miR-21	TIMP3	TIMP metallopeptidase inhibitor 3	Extracellular Space	other
miR-21	TPM1 (includes EG:22003)	tropomyosin 1 (alpha)	Cytoplasm	other
miR-222	BBC3	BCL2 binding component 3	Cytoplasm	other
miR-222	BCL2L11	BCL2-like 11 (apoptosis facilitator)	Cytoplasm	other
miR-222	BMF	Bcl2 modifying factor	Cytoplasm	other
miR-222	BNIP3L	BCL2/adenovirus E1B 19kDa interacting protein 3-like	Cytoplasm	other
miR-222	CDKN1B	cyclin-dependent kinase inhibitor 1B (p27, Kip1)	Nucleus	kinase
miR-222	CDKN1C	cyclin-dependent kinase inhibitor 1C (p57, Kip2)	Nucleus	other
miR-222	DDIT4	DNA-damage-inducible transcript 4	Cytoplasm	other
miR-222	DIRAS3	DIRAS family, GTP-binding RAS-like 3	Plasma Membrane	enzyme
miR-222	ESR1	estrogen receptor 1	Nucleus	ligand-dependent nuclear receptor
miR-222	FOS	FBJ murine osteosarcoma viral oncogene homolog	Nucleus	transcription regulator
miR-222	FOXO3	forkhead box O3	Nucleus	transcription regulator
miR-222	ICAM1	intercellular adhesion molecule 1	Plasma Membrane	transmembrane receptor
miR-222	KIT	v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog	Plasma Membrane	kinase
miR-222	MMP1 (includes EG:300339)	matrix metallopeptidase 1 (interstitial collagenase)	Extracellular Space	peptidase
miR-222	PIK3R1	phosphoinositide-3-kinase, regulatory subunit 1 (alpha)	Cytoplasm	kinase
miR-222	PPP2R2A	protein phosphatase 2, regulatory subunit B, alpha	Cytoplasm	phosphatase
miR-222	PTEN	phosphatase and tensin homolog	Cytoplasm	phosphatase
miR-222	PTPRM	protein tyrosine phosphatase, receptor type, M	Plasma Membrane	phosphatase

miR-222	SOD2	superoxide dismutase 2, mitochondrial	Cytoplasm	enzyme
miR-222	TBK1	TANK-binding kinase 1	Cytoplasm	kinase
miR-222	TIMP3	TIMP metallopeptidase inhibitor 3	Extracellular Space	other
miR-29b	ACVR2A	activin A receptor, type IIA	Plasma Membrane	kinase
miR-29b	ARPC3	actin related protein 2/3 complex, subunit 3, 21kDa	Cytoplasm	other
miR-29b	BACE1	beta-site APP-cleaving enzyme 1	Cytoplasm	peptidase
miR-29b	CAV2	caveolin 2	Plasma Membrane	other
miR-29b	CD276	CD276 molecule	Plasma Membrane	other
miR-29b	CDC42	cell division cycle 42 (GTP binding protein, 25kDa)	Cytoplasm	enzyme
miR-29b	CDK6	cyclin-dependent kinase 6	Nucleus	kinase
miR-29b	COL15A1	collagen, type XV, alpha 1	Extracellular Space	other
miR-29b	COL1A1	collagen, type I, alpha 1	Extracellular Space	other
miR-29b	COL1A2	collagen, type I, alpha 2	Extracellular Space	other
miR-29b	COL3A1	collagen, type III, alpha 1	Extracellular Space	other
miR-29b	COL4A1	collagen, type IV, alpha 1	Extracellular Space	other
miR-29b	COL4A2	collagen, type IV, alpha 2	Extracellular Space	other
miR-29b	COL5A3	collagen, type V, alpha 3	Extracellular Space	other
miR-29b	DNMT3A	DNA (cytosine-5-)-methyltransferase 3 alpha	Nucleus	enzyme
miR-29b	DNMT3B	DNA (cytosine-5-)-methyltransferase 3 beta	Nucleus	enzyme
miR-29b	DUSP2	dual specificity phosphatase 2	Nucleus	phosphatase
miR-29b	FBN1	fibrillin 1	Extracellular Space	other
miR-29b	HDAC4	histone deacetylase 4	Nucleus	transcription regulator
miR-29b	INSIG1	insulin induced gene 1	Cytoplasm	other
miR-29b	LAMC1	laminin, gamma 1 (formerly LAMB2)	Extracellular Space	other
miR-29b	LOC100505793/SRSF10	serine/arginine-rich splicing factor 10	Nucleus	other
miR-29b	MCL1	myeloid cell leukemia sequence 1 (BCL2-related)	Cytoplasm	transporter
miR-29b	NAV3	neuron navigator 3	Nucleus	other
miR-29b	PIK3R1	phosphoinositide-3-kinase, regulatory subunit 1 (alpha)	Cytoplasm	kinase
miR-29b	PPM1D	protein phosphatase, Mg2+/Mn2+ dependent, 1D	Cytoplasm	phosphatase
miR-29b	SP1	Sp1 transcription factor	Nucleus	transcription regulator
miR-29b	SPARC	secreted protein, acidic, cysteine-rich (osteonectin)	Extracellular Space	other
miR-29b	TCL1A	T-cell leukemia/lymphoma 1A	Nucleus	other
miR-29b	TDG	thymine-DNA glycosylase	Nucleus	enzyme

miR-29b	TET1	tet methylcytosine dioxygenase 1	Nucleus	other
miR-29b	TGFB3	transforming growth factor, beta 3	Extracellular Space	growth factor
miR-29b	TP53	tumor protein 53	Nucleus	transcription regulator
miR-29b	TPM1 (includes EG:22003)	tropomyosin 1 (alpha)	Cytoplasm	other
miR-29b	YY1	YY1 transcription factor	Nucleus	transcription regulator
miR-424	ABCF2	ATP-binding cassette, sub-family F (GCN20), member 2	Cytoplasm	transporter
miR-424	ABHD10	abhydrolase domain containing 10	Cytoplasm	other
miR-424	ACP2	acid phosphatase 2, lysosomal	Cytoplasm	phosphatase
miR-424	ACTR1A	ARP1 actin-related protein 1 homolog A, centractin alpha (yeast)	Cytoplasm	other
miR-424	ADSS	adenylosuccinate synthase	Cytoplasm	enzyme
miR-424	ANAPC16	anaphase promoting complex subunit 16	Nucleus	other
miR-424	ARHGDIA	Rho GDP dissociation inhibitor (GDI) alpha	Cytoplasm	other
miR-424	ARL2	ADP-ribosylation factor-like 2	Cytoplasm	enzyme
miR-424	ASXL2	additional sex combs like 2 (Drosophila)	unknown	other
miR-424	ATG9A	ATG9 autophagy related 9 homolog A (S. cerevisiae)	Cytoplasm	other
miR-424	BCL2	B-cell CLL/lymphoma 2	Cytoplasm	transporter
miR-424	BCL2L2	BCL2-like 2	Cytoplasm	other
miR-424	BDNF	brain-derived neurotrophic factor	Extracellular Space	growth factor
miR-424	BMI1	BMI1 polycomb ring finger oncogene	Nucleus	transcription regulator
miR-424	C14orf109	chromosome 14 open reading frame 109	unknown	other
miR-424	C17orf80	chromosome 17 open reading frame 80	unknown	other
miR-424	C1orf56	chromosome 1 open reading frame 56	unknown	other
miR-424	C2orf43	chromosome 2 open reading frame 43	unknown	enzyme
miR-424	C2orf74	chromosome 2 open reading frame 74	unknown	other
miR-424	C4orf27	chromosome 4 open reading frame 27	Nucleus	other
miR-424	CA12	carbonic anhydrase XII	Plasma Membrane	enzyme
miR-424	CACNA2D1	calcium channel, voltage-dependent, alpha 2/delta subunit 1	Plasma Membrane	ion channel
miR-424	CADM1	cell adhesion molecule 1	Plasma Membrane	other
miR-424	CAPRIN1	cell cycle associated protein 1	Plasma Membrane	other
miR-424	CARD8	caspase recruitment domain family, member 8	Nucleus	other
miR-424	CCDC111	coiled-coil domain containing 111	unknown	other

miR-424	CCDC76	coiled-coil domain containing 76	unknown	other
miR-424	CCND1	cyclin D1	Nucleus	other
miR-424	CCND3	cyclin D3	Nucleus	other
miR-424	CCNE1	cyclin E1	Nucleus	transcription regulator
miR-424	CDC14B	CDC14 cell division cycle 14 homolog B (S. cerevisiae)	Nucleus	phosphatase
miR-424	CDK5RAP1	CDK5 regulatory subunit associated protein 1	Extracellular Space	other
miR-424	CDK6	cyclin-dependent kinase 6	Nucleus	kinase
miR-424	CENPJ	centromere protein J	Nucleus	transcription regulator
miR-424	CEP63	centrosomal protein 63kDa	Cytoplasm	other
miR-424	CFL2	cofilin 2 (muscle)	Nucleus	other
miR-424	CHORDC1	cysteine and histidine-rich domain (CHORD) containing 1	unknown	other
miR-424	CLDN12	claudin 12	Plasma Membrane	other
miR-424	CREBL2	cAMP responsive element binding protein-like 2	Nucleus	transcription regulator
miR-424	CRHBP	corticotropin releasing hormone binding protein	Extracellular Space	other
miR-424	CSHL1	chorionic somatomammotropin hormone-like 1	Extracellular Space	other
miR-424	DMTF1	cyclin D binding myb-like transcription factor 1	Nucleus	transcription regulator
miR-424	DNAJB4	DnaJ (Hsp40) homolog, subfamily B, member 4	Nucleus	other
miR-424	DTD1	D-tyrosyl-tRNA deacylase 1 homolog (S. cerevisiae)	Cytoplasm	enzyme
miR-424	E2F3	E2F transcription factor 3	Nucleus	transcription regulator
miR-424	ECHDC1	enoyl CoA hydratase domain containing 1	unknown	other
miR-424	EGFR	epidermal growth factor receptor	Plasma Membrane	kinase
miR-424	EIF4E	eukaryotic translation initiation factor 4E	Cytoplasm	translation regulator
miR-424	F2	coagulation factor II (thrombin)	Extracellular Space	peptidase
miR-424	FAM122C	family with sequence similarity 122C	unknown	other
miR-424	FAM69A	family with sequence similarity 69, member A	unknown	other
miR-424	FGF2	fibroblast growth factor 2 (basic)	Extracellular Space	growth factor
miR-424	FGF7	fibroblast growth factor 7	Extracellular Space	growth factor
miR-424	FGFR1	fibroblast growth factor receptor 1	Plasma Membrane	kinase
miR-424	FNDC3B	fibronectin type III domain containing 3B	Cytoplasm	other
miR-424	GALNT7	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 7 (GalNAc-T7)	Cytoplasm	enzyme
miR-424	GFM1	G elongation factor, mitochondrial 1	Cytoplasm	translation regulator
miR-424	GFPT1	glutamine--fructose-6-phosphate transaminase 1	Cytoplasm	enzyme

miR-424	GNL3L	guanine nucleotide binding protein-like 3 (nucleolar)-like	Nucleus	other
miR-424	GOLGA5	golgin A5	Cytoplasm	kinase
miR-424	GOLPH3L	golgi phosphoprotein 3-like	Cytoplasm	other
miR-424	GPAM	glycerol-3-phosphate acyltransferase, mitochondrial	Cytoplasm	enzyme
miR-424	GSTM4	glutathione S-transferase mu 4	Cytoplasm	enzyme
miR-424	GTF2H1	general transcription factor IIH, polypeptide 1, 62kDa	Nucleus	transcription regulator
miR-424	H3F3A/H3F3B	H3 histone, family 3B (H3.3B)	Nucleus	other
miR-424	HACE1	HECT domain and ankyrin repeat containing, E3 ubiquitin protein ligase 1	unknown	enzyme
miR-424	HARS	histidyl-tRNA synthetase	Cytoplasm	enzyme
miR-424	HBXIP	hepatitis B virus x interacting protein	Cytoplasm	other
miR-424	HDHD2	haloacid dehalogenase-like hydrolase domain containing 2	unknown	other
miR-424	HERC6	hect domain and RLD 6	Cytoplasm	enzyme
miR-424	HMGA1	high mobility group AT-hook 1	Nucleus	transcription regulator
miR-424	HMOX1	heme oxygenase (decycling) 1	Cytoplasm	enzyme
miR-424	HRSP12	heat-responsive protein 12	Cytoplasm	other
miR-424	HSDL2	hydroxysteroid dehydrogenase like 2	Cytoplasm	transporter
miR-424	HSP90B1	heat shock protein 90kDa beta (Grp94), member 1	Cytoplasm	other
miR-424	HSPA1A/HSPA1B	heat shock 70kDa protein 1A	Cytoplasm	other
miR-424	HYAL3	hyaluronoglucosaminidase 3	Cytoplasm	enzyme
miR-424	IFRD1	interferon-related developmental regulator 1	Nucleus	other
miR-424	IGF2R	insulin-like growth factor 2 receptor	Plasma Membrane	transmembrane receptor
miR-424	IPO4	importin 4	Nucleus	transporter
miR-424	ITGA2	integrin, alpha 2 (CD49B, alpha 2 subunit of VLA-2 receptor)	Plasma Membrane	other
miR-424	JUN	jun proto-oncogene	Nucleus	transcription regulator
miR-424	KCNN4	potassium intermediate/small conductance calcium-activated channel, subfamily N, member 4	Plasma Membrane	ion channel
miR-424	KPNA3	karyopherin alpha 3 (importin alpha 4)	Nucleus	transporter
miR-424	LAMC1	laminin, gamma 1 (formerly LAMB2)	Extracellular Space	other
miR-424	LAMTOR3	late endosomal/lysosomal adaptor, MAPK and MTOR activator 3	Cytoplasm	other
miR-424	LUZP1	leucine zipper protein 1	Nucleus	other
miR-424	LYPLA2	lysophospholipase II	Cytoplasm	enzyme

miR-424	MAP2K1	mitogen-activated protein kinase kinase 1	Cytoplasm	kinase
miR-424	MAP2K4	mitogen-activated protein kinase kinase 4	Cytoplasm	kinase
miR-424	MCL1	myeloid cell leukemia sequence 1 (BCL2-related)	Cytoplasm	transporter
miR-424	MLLT1	myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila); translocated to, 1	Nucleus	transcription regulator
miR-424	MRPL20 (includes EG:39477)	mitochondrial ribosomal protein L20	Cytoplasm	other
miR-424	MSH2	mutS homolog 2, colon cancer, nonpolyposis type 1 (E. coli)	Nucleus	enzyme
miR-424	MYB	v-myb myeloblastosis viral oncogene homolog (avian)	Nucleus	transcription regulator
miR-424	NAA15	N(alpha)-acetyltransferase 15, NatA auxiliary subunit	Nucleus	transcription regulator
miR-424	NAPG	N-ethylmaleimide-sensitive factor attachment protein, gamma	Cytoplasm	transporter
miR-424	NFIA	nuclear factor I/A	Nucleus	transcription regulator
miR-424	NIPAL2	NIPA-like domain containing 2	unknown	other
miR-424	NOTCH2	notch 2	Plasma Membrane	transcription regulator
miR-424	NPR3 (includes EG:18162)	natriuretic peptide receptor C/guanylate cyclase C (atrionatriuretic peptide receptor C)	Plasma Membrane	G-protein coupled receptor
miR-424	NT5DC1	5'-nucleotidase domain containing 1	unknown	other
miR-424	OMA1	OMA1 zinc metallopeptidase homolog (S. cerevisiae)	Cytoplasm	peptidase
miR-424	OSGEPL1	O-sialoglycoprotein endopeptidase-like 1	Cytoplasm	peptidase
miR-424	PAFAH1B2	platelet-activating factor acetylhydrolase 1b, catalytic subunit 2 (30kDa)	Cytoplasm	enzyme
miR-424	PANX1	pannexin 1	Plasma Membrane	transporter
miR-424	PDCD4	programmed cell death 4 (neoplastic transformation inhibitor)	Nucleus	other
miR-424	PDCD6IP	programmed cell death 6 interacting protein	Cytoplasm	other
miR-424	PHKB	phosphorylase kinase, beta	Cytoplasm	kinase
miR-424	PHLDB2	pleckstrin homology-like domain, family B, member 2	Cytoplasm	other
miR-424	PISD	phosphatidylserine decarboxylase	Cytoplasm	enzyme
miR-424	PLAG1	pleiomorphic adenoma gene 1	Nucleus	transcription regulator
miR-424	PLK1	polo-like kinase 1	Nucleus	kinase
miR-424	PMS1	PMS1 postmeiotic segregation increased 1 (S. cerevisiae)	Nucleus	enzyme
miR-424	PNN	pinin, desmosome associated protein	Plasma Membrane	other
miR-424	PNP	purine nucleoside phosphorylase	Nucleus	enzyme

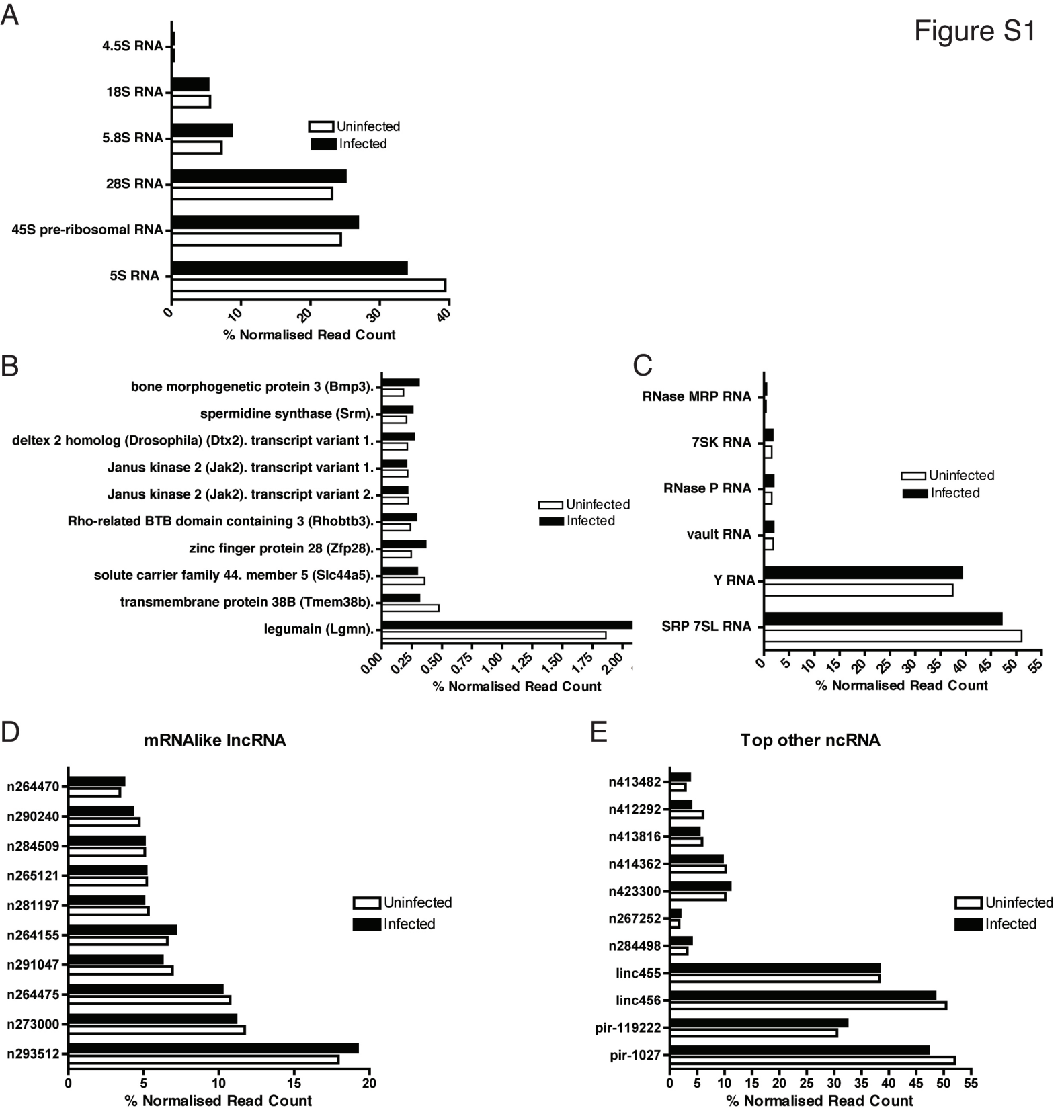
miR-424	PPIF	peptidylprolyl isomerase F	Cytoplasm	enzyme
miR-424	PPP2R5C	protein phosphatase 2, regulatory subunit B', gamma	Nucleus	peptidase
miR-424	PRIM1	primase, DNA, polypeptide 1 (49kDa)	Nucleus	enzyme
miR-424	PSAT1	phosphoserine aminotransferase 1	Cytoplasm	enzyme
miR-424	PTGS2	prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)	Cytoplasm	enzyme
miR-424	PURA	purine-rich element binding protein A	Nucleus	transcription regulator
miR-424	PWWP2A	PWWP domain containing 2A	unknown	other
miR-424	RAB21	RAB21, member RAS oncogene family	Cytoplasm	enzyme
miR-424	RAB30	RAB30, member RAS oncogene family	Cytoplasm	enzyme
miR-424	RAB9B	RAB9B, member RAS oncogene family	Plasma Membrane	enzyme
miR-424	RAD51C	RAD51 homolog C (S. cerevisiae)	Nucleus	enzyme
miR-424	RARS	arginyl-tRNA synthetase	Cytoplasm	enzyme
miR-424	RECK	reversion-inducing-cysteine-rich protein with kazal motifs	Plasma Membrane	other
miR-424	RFT1	RFT1 homolog (S. cerevisiae)	unknown	other
miR-424	RHOT1	ras homolog gene family, member T1	Cytoplasm	enzyme
miR-424	RNASEL	ribonuclease L (2',5'-oligoisoadenylate synthetase-dependent)	Cytoplasm	enzyme
miR-424	RTN4	reticulon 4	Cytoplasm	other
miR-424	SEC24A	SEC24 family, member A (S. cerevisiae)	Cytoplasm	transporter
miR-424	SERPINE2	serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 2	Extracellular Space	other
miR-424	SHOC2	soc-2 suppressor of clear homolog (C. elegans)	Cytoplasm	other
miR-424	SKAP2	src kinase associated phosphoprotein 2	Cytoplasm	other
miR-424	SLC12A2	solute carrier family 12 (sodium/potassium/chloride transporters), member 2	Plasma Membrane	transporter
miR-424	SLC16A3	solute carrier family 16, member 3 (monocarboxylic acid transporter 4)	Plasma Membrane	transporter
miR-424	SLC25A22	solute carrier family 25 (mitochondrial carrier: glutamate), member 22	Cytoplasm	transporter
miR-424	SLC35A1	solute carrier family 35 (CMP-sialic acid transporter), member A1	Cytoplasm	transporter
miR-424	SLC35B3	solute carrier family 35, member B3	Cytoplasm	other
miR-424	SLC38A1	solute carrier family 38, member 1	Plasma Membrane	transporter
miR-424	SLC38A5	solute carrier family 38, member 5	Plasma Membrane	transporter

miR-424	SLC7A1	solute carrier family 7 (cationic amino acid transporter, y+ system), member 1	Plasma Membrane	transporter
miR-424	SNX15	sorting nexin 15	Cytoplasm	transporter
miR-424	SPTLC1	serine palmitoyltransferase, long chain base subunit 1	Cytoplasm	enzyme
miR-424	SQSTM1	sequestosome 1	Cytoplasm	transcription regulator
miR-424	SRPR	signal recognition particle receptor (docking protein)	Cytoplasm	other
miR-424	SRPRB	signal recognition particle receptor, B subunit	Cytoplasm	other
miR-424	TIA1	TIA1 cytotoxic granule-associated RNA binding protein	Nucleus	other
miR-424	TMEM109	transmembrane protein 109	Cytoplasm	other
miR-424	TMEM189-UBE2V1	TMEM189-UBE2V1 readthrough	Cytoplasm	other
miR-424	TMEM43	transmembrane protein 43	Nucleus	other
miR-424	TNFSF9	tumor necrosis factor (ligand) superfamily, member 9	Extracellular Space	cytokine
miR-424	TOMM34	translocase of outer mitochondrial membrane 34	Cytoplasm	other
miR-424	TPI1	triosephosphate isomerase 1	Cytoplasm	enzyme
miR-424	TPM3	tropomyosin 3	Cytoplasm	other
miR-424	TPPP3	tubulin polymerization-promoting protein family member 3	unknown	other
miR-424	TXN2	thioredoxin 2	Cytoplasm	enzyme
miR-424	UBE2S	ubiquitin-conjugating enzyme E2S	Nucleus	enzyme
miR-424	UBE4A	ubiquitination factor E4A	Cytoplasm	enzyme
miR-424	UCP2	uncoupling protein 2 (mitochondrial, proton carrier)	Cytoplasm	transporter
miR-424	UGDH	UDP-glucose 6-dehydrogenase	Nucleus	enzyme
miR-424	UGP2	UDP-glucose pyrophosphorylase 2	Cytoplasm	enzyme
miR-424	UTP15	UTP15, U3 small nucleolar ribonucleoprotein, homolog (S. cerevisiae)	Nucleus	other
miR-424	VEGFA	vascular endothelial growth factor A	Extracellular Space	growth factor
miR-424	VPS45	vacuolar protein sorting 45 homolog (S. cerevisiae)	Cytoplasm	transporter
miR-424	VTI1B	vesicle transport through interaction with t-SNAREs homolog 1B (yeast)	Plasma Membrane	transporter
miR-424	WIPF1	WAS/WASL interacting protein family, member 1	Cytoplasm	other
miR-424	WNT3A	wingless-type MMTV integration site family, member 3A	Extracellular Space	other
miR-424	WT1	Wilms tumor 1	Nucleus	transcription regulator
miR-424	YIF1B	Yip1 interacting factor homolog B (S. cerevisiae)	unknown	other

miR-424	ZNF559	zinc finger protein 559	Nucleus	other
miR-424	ZNF622	zinc finger protein 622	Nucleus	other
miR-424	ZYX	zyxin	Plasma Membrane	other

Note: miR-342-3p has no current experimental validated mRNA targets

Figure S1


A
4.5S RNA
18S RNA
5.8S RNA
28S RNA
45S pre-ribosomal RNA
5S RNA
Uninfected
Infected
0
10
20
30
40
% Normalised Read Count
B
bone morphogenetic protein 3 (Bmp3).
spermidine synthase (Srm).
deltex 2 homolog (Drosophila) (Dtx2). transcript variant 1.
Janus kinase 2 (Jak2). transcript variant 1.
Janus kinase 2 (Jak2). transcript variant 2.
Rho-related BTB domain containing 3 (Rhobtb3).
zinc finger protein 28 (Zfp28).
solute carrier family 44. member 5 (Slc44a5).
transmembrane protein 38B (Tmem38b).
legumain (Lgmn).
Uninfected
Infected
0.00
0.25
0.50
0.75
1.00
1.25
1.50
1.75
2.00
% Normalised Read Count
C
RNase MRP RNA
7SK RNA
RNase P RNA
vault RNA
Y RNA
SRP 7SL RNA
Uninfected
Infected
0
5
10
15
20
25
30
35
40
45
50
55
% Normalised Read Count
D
mRNAlike lncRNA
n264470
n290240
n284509
n265121
n281197
n264155
n291047
n264475
n273000
n293512
Uninfected
Infected
0
5
10
15
20
% Normalised Read Count
E
Top other ncRNA
n413482
n412292
n413816
n414362
n423300
n267252
n284498
linc455
linc456
pir-119222
pir-1027
Uninfected
Infected
0
5
10
15
20
25
30
35
40
45
50
55
% Normalised Read Count

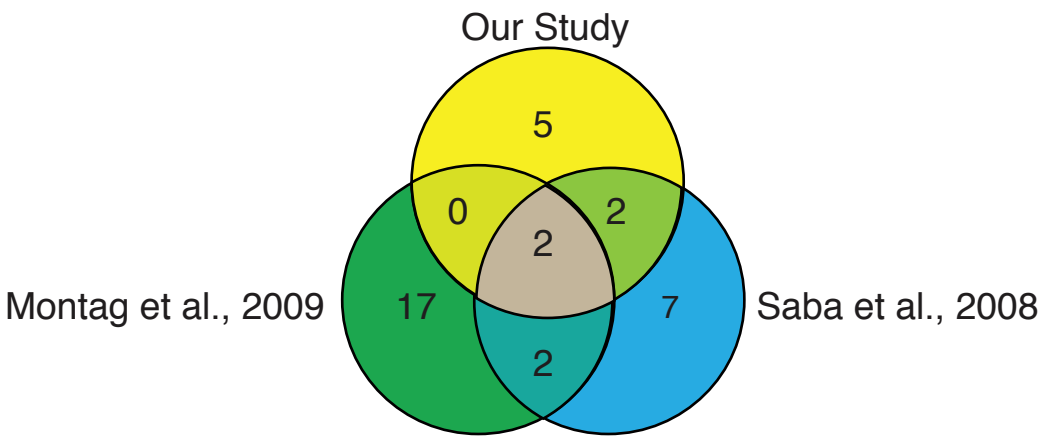


Figure S2. Comparison of Prion miRNA Dysregulation

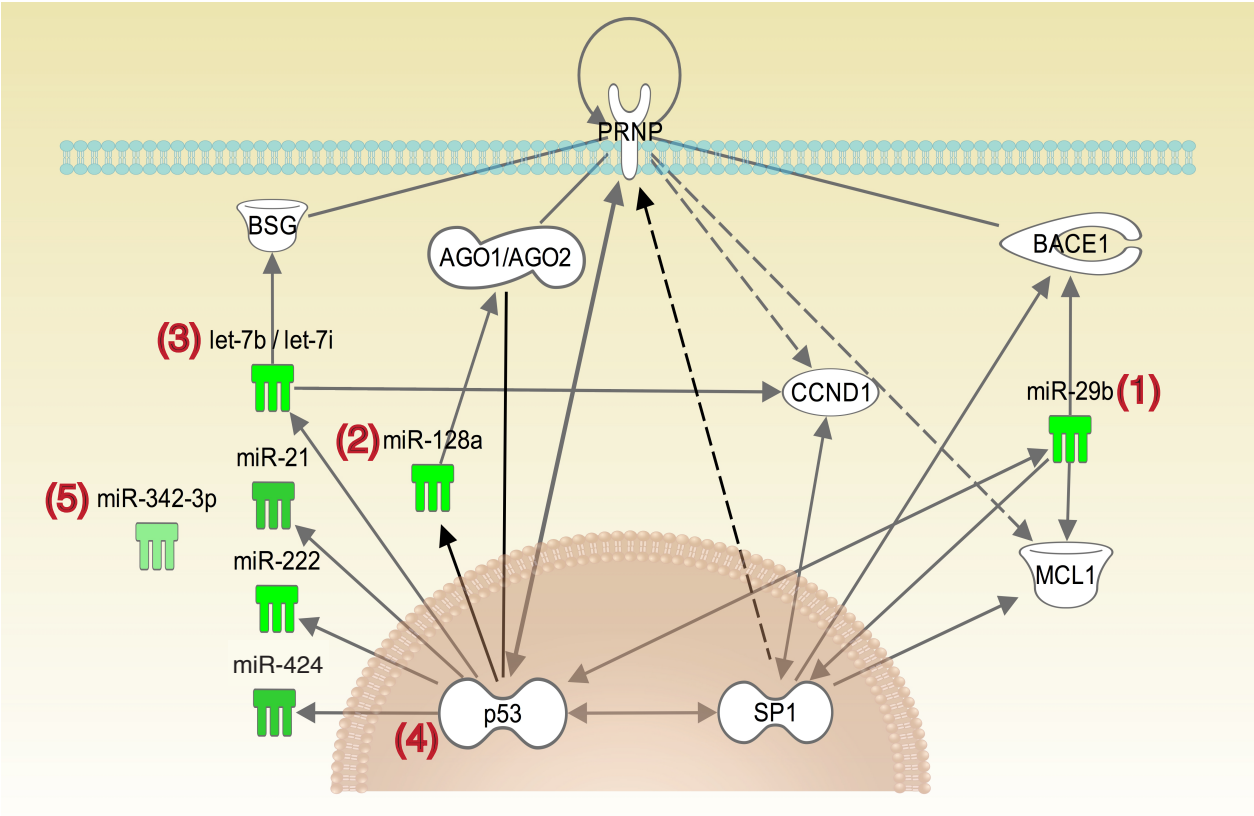


Figure S3. Pathway Analysis of Potential Exosomal mediated transfer of miRNA from Prion Infected Cells to Recipient Cells may regulate expression of the *PRNP* Gene.