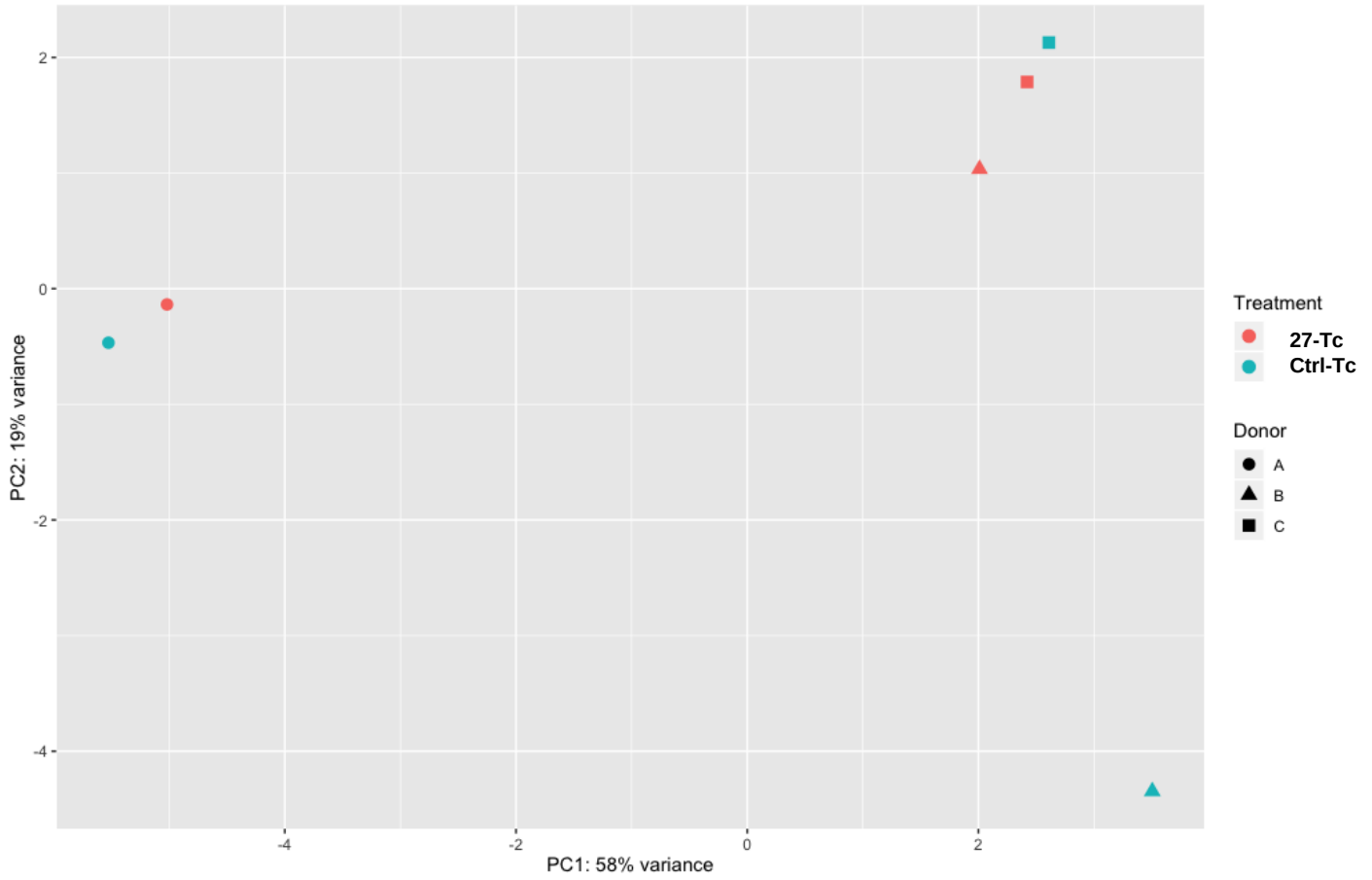
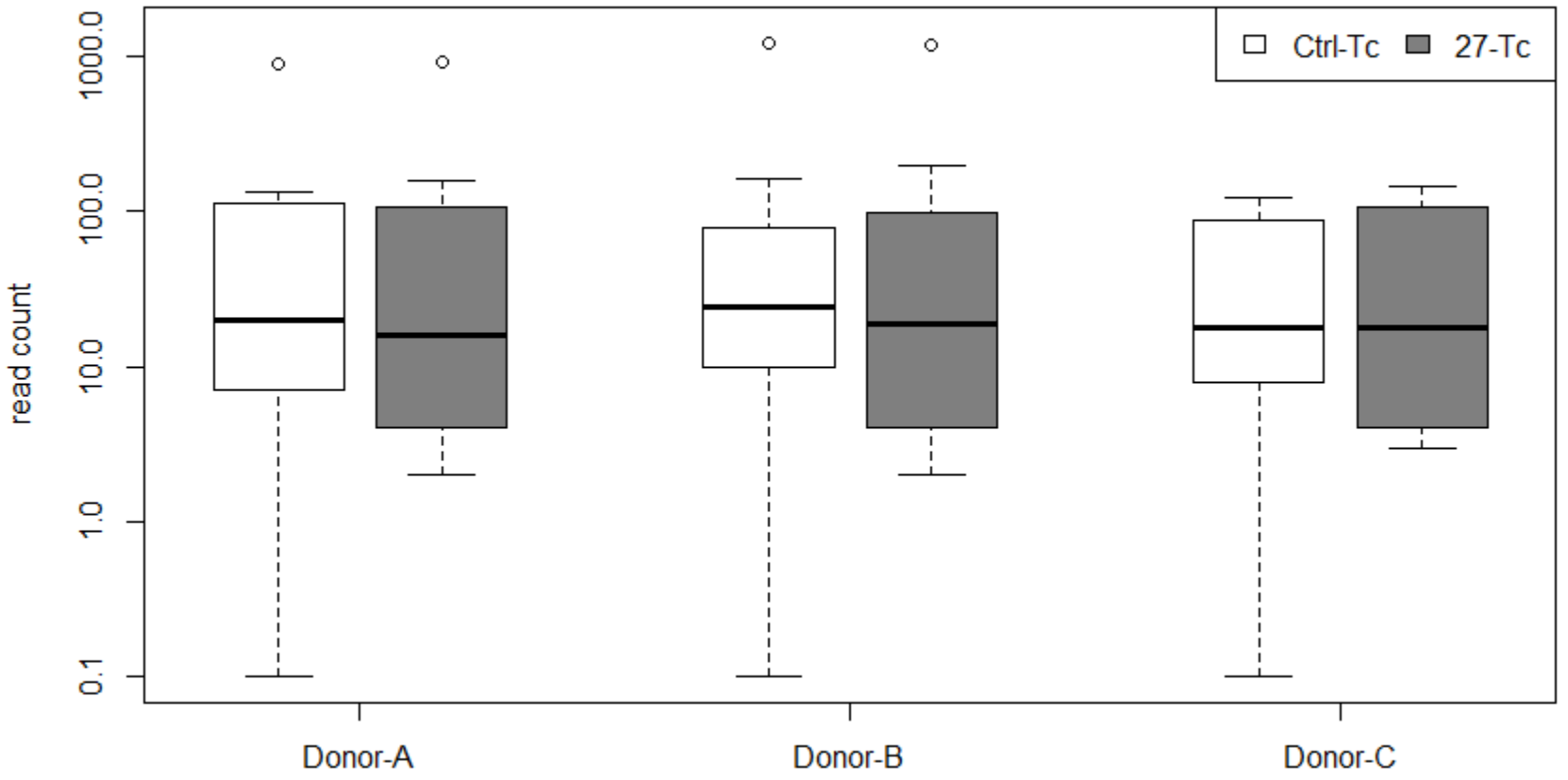
Supplemental Figure 1



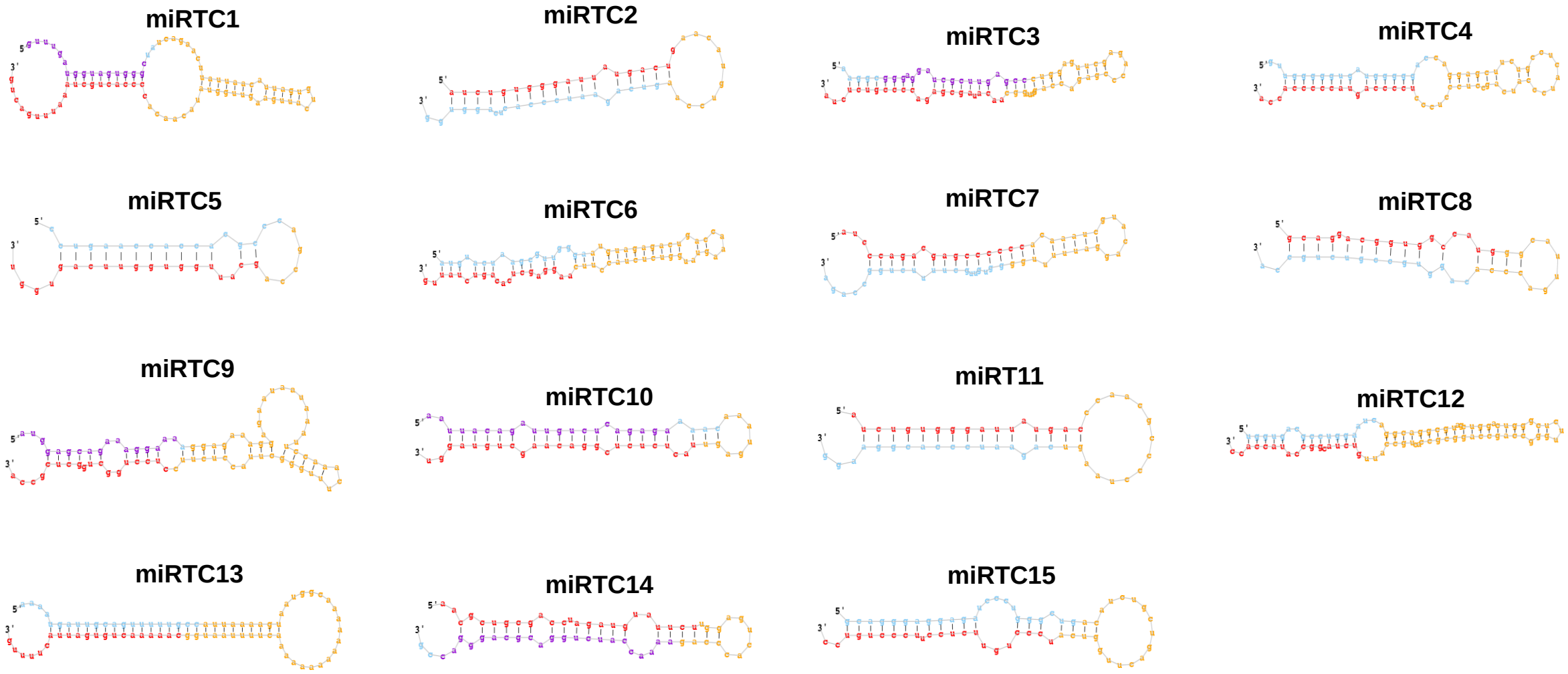
S. Figure 1: Principal component analysis (PCA) of the normalized miRNA-seq data in response to IL-27 in thee different donors. Each dot indicates untreated T cells (Ctrl-Tc; green dots) or IL-27-treated cells (27-Tc; orange dots). PCA plot demonstrated that impact of IL-27-treatment on samples' variants was smaller than donor-dependent variant in the small RNA expression.

Supplemental Figure 2



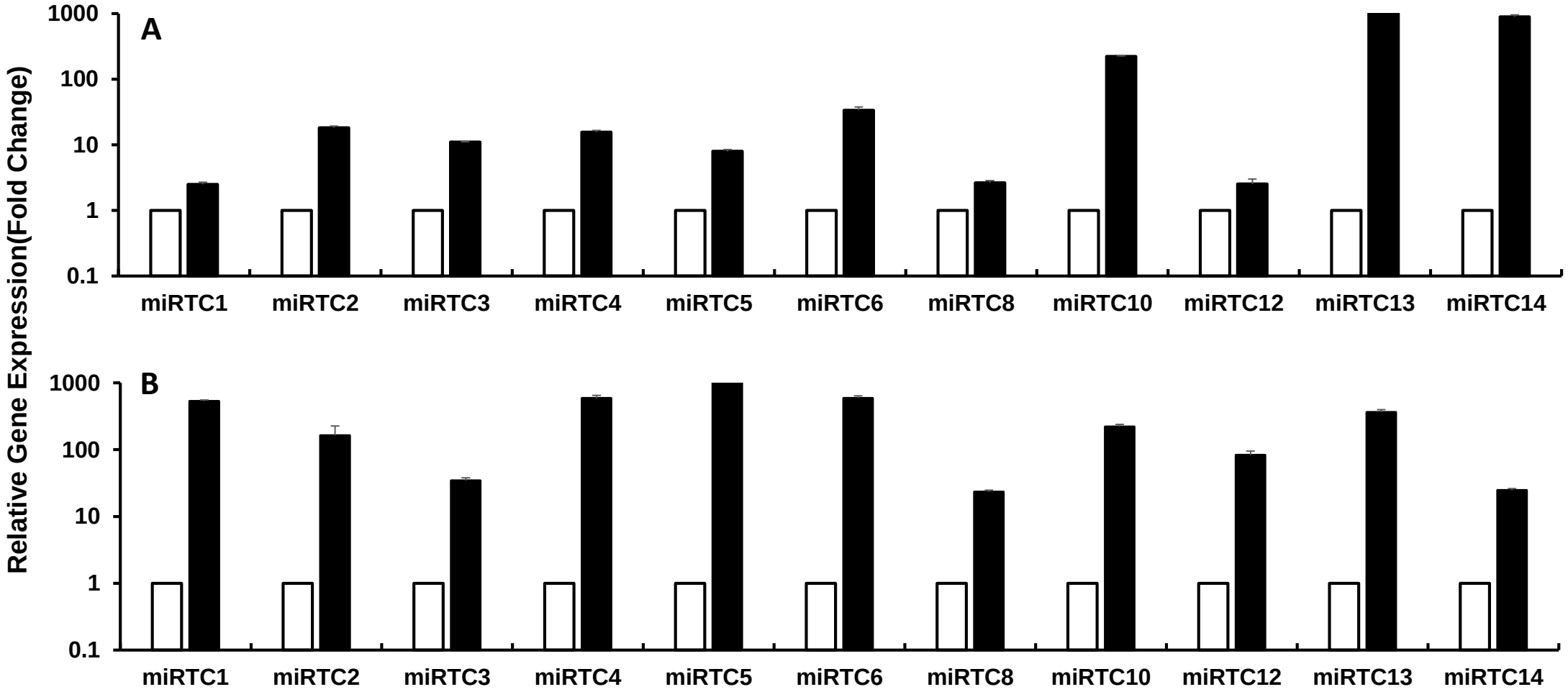
S. Figure 2: Number of reads of novel miRNAs.
The Y axis is the number of reads of each donor samples from untreated control T cells (Ctrl-Tc) and IL-27-treated T cells (27-Tc) by RNA sequencing

Supplemental Figure 3



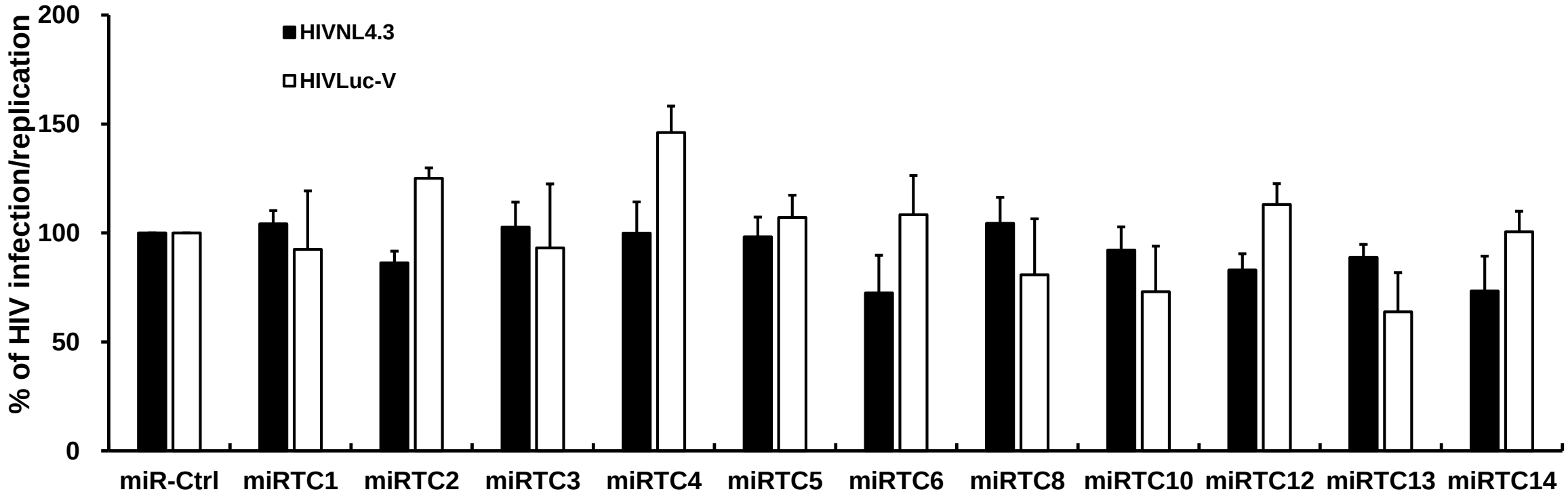
S. Figure3: Secondary structures of the novel miRNAs. All novel miRNAs were able to form stem-loop hairpin structures but each novel miRNA varied in the location, number and size of bulges. Red indicates the mature sequence; blue indicates the star sequence; yellow indicates loop structure, purple indicates star sequence.

Supplemental Figure 4



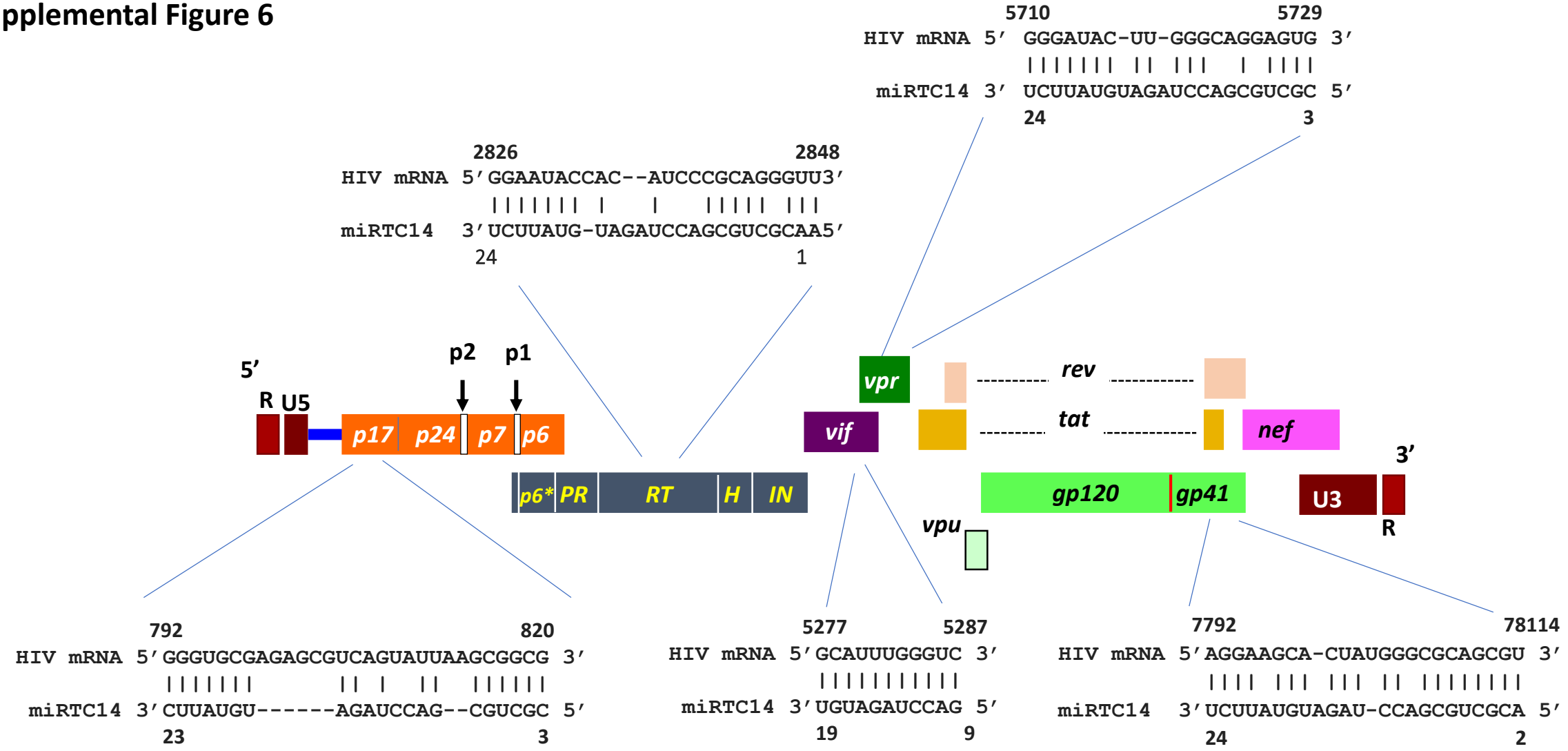
S. Figure 4: Confirmation of transfection of miRTC. T cells (A) and Mac (B) were transfected with 10 nmol of each miRNA mimic using 4D-Nucleofector system and RNaiMax, respectively. Total RNAs were extracted from the transfected cells, and then the expression of each miRTC and RNU44 (an internal control) in 10 ng RNA were quantified by real time-RT-PCR using each miRNA specific probe. miRNA level was normalized using the expression level of RNU44 in each sample. Relative fold change in each miRNA level in transfected cells (closed bars) was represent compared to the level in un-transfected cells (opened bars).

Supplemental Figure 5



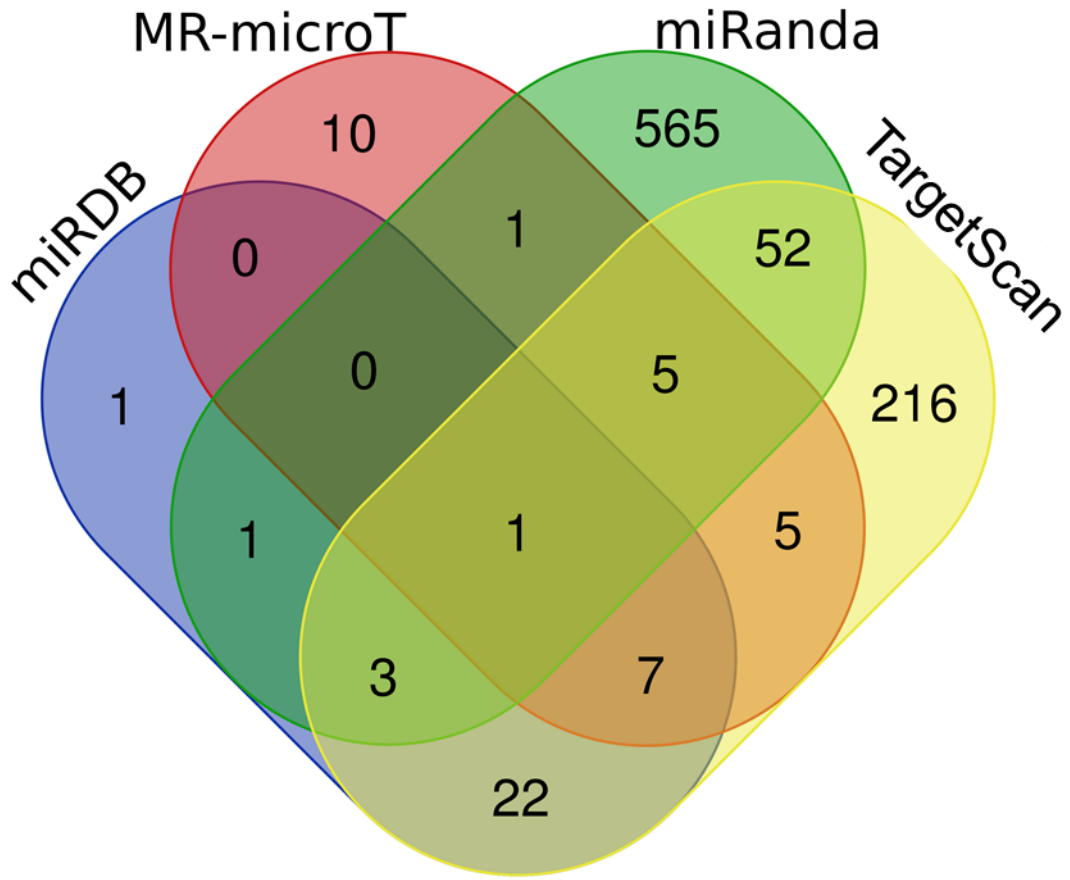
S. Figure 5: Evaluation of anti-HIV effect by miRTCs in primary T cells.
Transfection of 10 nmol of each mimic miRNA into T cells were performed using 4D-Nucleofector system according to the manufacture protocol. The cells were then infected with HIVNL4.3 or HIVLuc-V, and then cultured for 7 days and 2 days for HIVNL4.3 and HJIV-Luc-V-infected T cells, respectively. HIV Replication was monitored by HIV p24 concentrations in culture supernatants by an HIV p24 antigen capture kit, and HIV infection was monitored by luciferase activity. Three independent assays were performed and relative HIV infection/replication activity was compared to that in miR-Ctrl-transfected cells. Data shown represent mean ± SE.

Supplemental Figure 6



S. Figure 6. A diagram of location of predicted targets of miRTC14 on HIV genome.
Four prediction tools (miRanda[40], RNA22[41], IntaRNA[42] and RNAHybrid[43]) demonstrated a total of five potential miRTC14 targets on HIV mRNA. Top and bottom sequences show HIV mRNA and the corresponding miRTC14 sequences, respectively. Number on the sequences are nucleotide sequence numbers.

Supplemental Figure 7



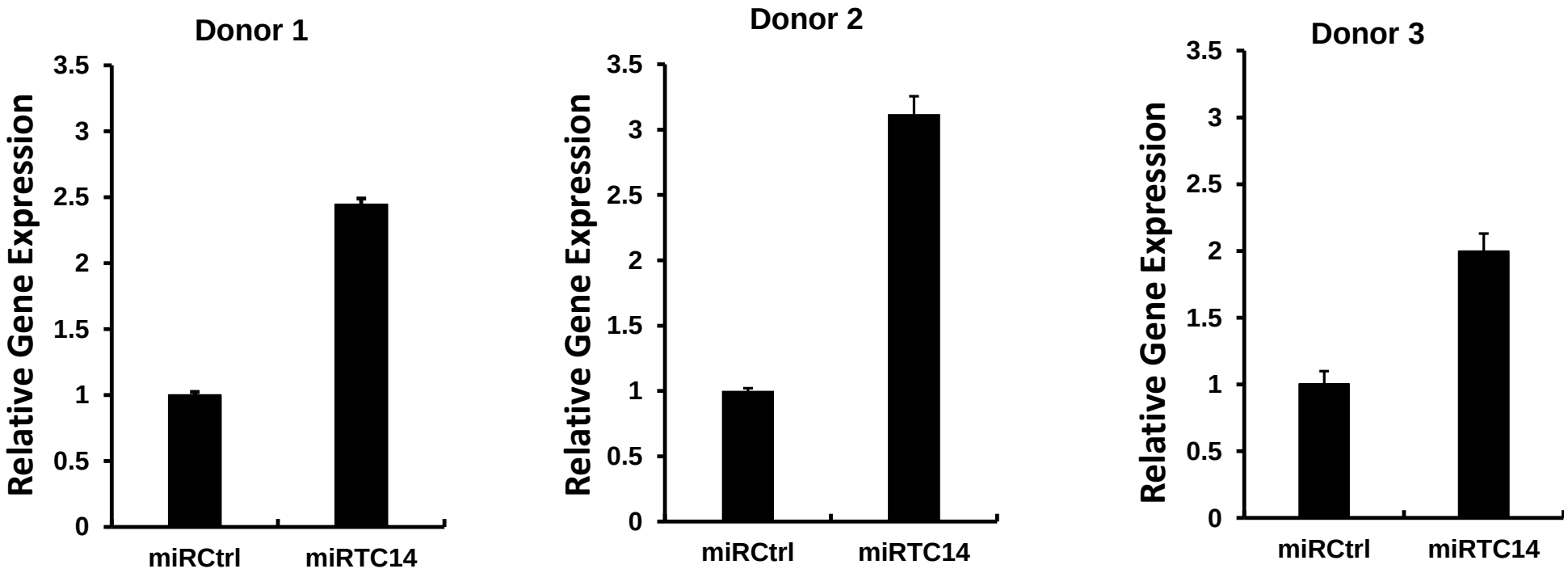
S. Figure 7. Venn diagram of the microRNA gene targets prediction.
Potential miRTC14 targets were predicted using miRanda [40] (Green), miRDB [48,49] (Blue), TargetScan [50,51] (Yellow), and MR-microT [52] (Red). To demonstrate overlapping genes among the predicted targets, Venn diagram was generated to show the number of overlapping and non-overlapping predicted targets of miRTC14. 1 gene and 15 genes overlapped in four and three of the prediction tools, respectively.

Supplemental Table 1. List of common genes in 4 prediction programs [a]

#	Gene ID	Gene_Name	Symbol
1	ENSG00000108848	LUC7 like 3 pre-mRNA splicing factor	LUC7L3

Supplemental Table 1 a: Potential miRTC14 targets were predicted using miRanda [40], miRDB[48,49], TargetScan [50, 51] and MR-microT [52]. To demonstrate overlapping genes among the predicted targets, Venn diagram analysis was performed. Data indicate the number of overlapping and non-overlapping predicted targets of miRTC14. 1 gene overlapped in the 4 prediction tools are listed.

Supplemental Figure 8



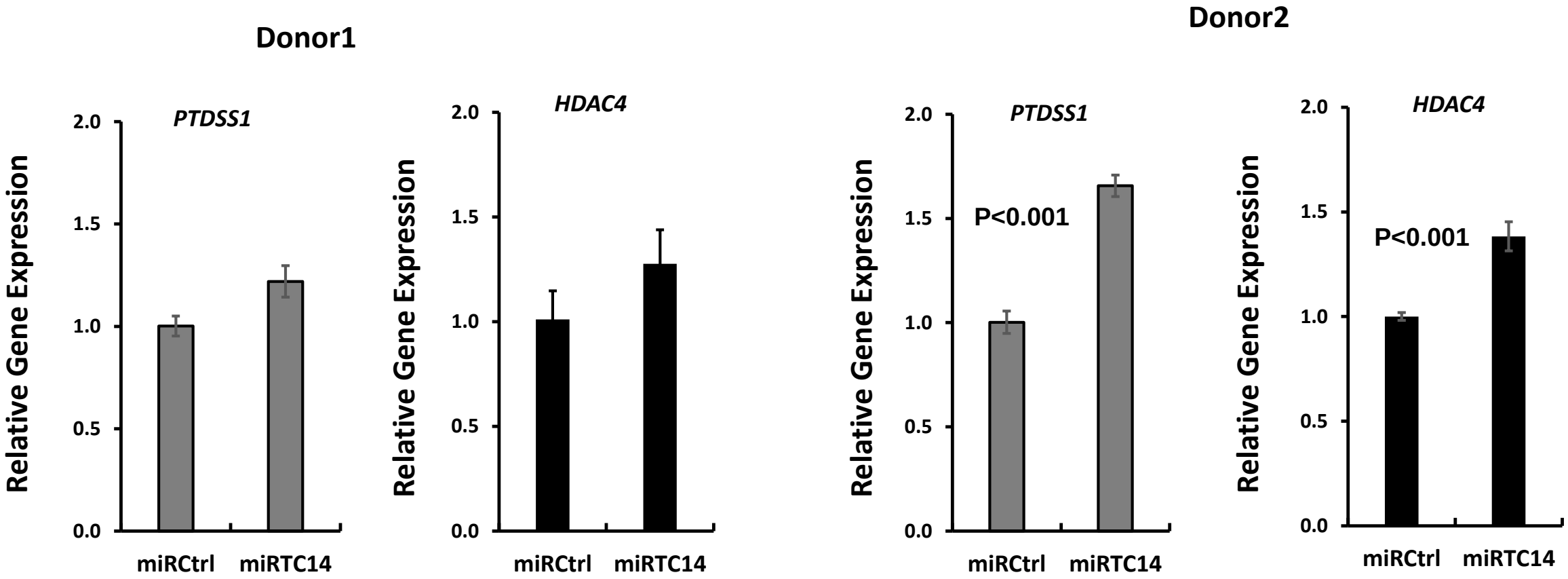
S. Figure 8. Evaluation of miRTC14 transfection on the expression of LUC7L3
MDMs from three different donors were transfected with 10nM miRCtrl or miRTC14 as described in the Materials and Methods, and then cultured for 72 hours. Total RNA was extracted and expression of LUC7L3 gene was analyzed by qRT-PCR using specific probes for LUC7L3(Supplemental Table 1). Gene expression is presented as relative expression units compared with miRCtrl transfected cells after normalization to GAPDH. Data are mean $\pm$ SD.

Supplemental Table 2. List of common genes in 3 programs [a]

#	Gene ID	Gene_Name	Symbol
1	ENSG00000204764	RAN binding protein 17	RANBP17
2	ENSG00000151240	disco interacting protein 2 homolog C	DIP2C
3	ENSG00000141424	solute carrier family 39 member 6	SLC39A6
4	ENSG00000174136	repulsive guidance molecule BMP co-receptor b	RGMB
5	ENSG00000092148	HECT domain E3 ubiquitin protein ligase 1	HECTD1
6	ENSG00000165501	leucine rich repeat protein 1	LRR1
7	ENSG00000183963	smoothelin	SMTN
8	ENSG00000114857	natural killer cell triggering receptor	NKTR
9	ENSG00000152503	tripartite motif containing 36	TRIM36
10	ENSG00000198843	selenoprotein T	SELENOT
11	ENSG00000141562	nuclear prelamin A recognition factor	NARF
12	ENSG00000170100	zinc finger protein 778	ZNF778
13	ENSG00000157933	SKI proto-oncogene	SKI
14	ENSG00000176407	potassium channel modulatory factor 1	KCMF1
15	ENSG00000167037	small G protein signaling modulator 1	SGSM1

a: Potential miRTC14 targets were predicted using miRanda [40], miRDB[48,49], TargetScan[50, 51] and MR-microT[52]. To demonstrate overlapping genes among the predicted targets, Venn diagram analysis was performed. Data indicate the number of overlapping and non-overlapping predicted targets of miRTC14. 11 genes overlapped in three of the 4 prediction tools are listed.

Supplemental Figure 9



S. Figure 9. Evaluation of miRTC14 transfection on the expression of PTDSS1 and HDAC4

MDMs from two different donors were transfected with 10nM miRCtrl or miRTC14 as described in the Materials and Methods, and then cultured for 72 hours. Total RNA was extracted and expression of PTDSS1 and HDAC4 gene was analyzed by qRT-PCR using specific probes for PTDSS1 and HDAC4 (Supplemental Table 1). Gene expression is presented as relative expression units compared with miRCtrl transfected cells after normalization to GAPDH. Data are mean $\pm$ SD.

Supplemental Table 3. List of probes for real-time RT-qPCR [a]

Gene name	Probe ID
IFNA1	Hs04189288_g1
IFNA2	Hs00265051_s1
IFNA4	Hs03406429_gH
IFNA6	Hs00819627_s1
IFNA7	Hs01652729_s1
IFNA8	Hs00266883_s1
IFNA13	Hs04190680_gH
IFNA14	Hs00353663_s1
IFNA16	Hs03005057_sH
IFNA17	Hs00819693_sH
IFNB1	Hs00277188_s1
IFNL1	Hs00601677_g1
IFNL2	Hs00820125_g1
IFNL2/3	Hs04193049_gH
IFNL4	Hs04400217_g1
PTDSS1	Hs00207371_m1
HDAC4	Hs01041648_m1
LUC7L3	Hs00895240_m1
GAPDH	Hs02786624_g1
RNU44	PN4440887

a: All probes were obtained from Thermo Fisher.

Supplemental Figure 10