FIGURE LEGENDS

Supplementary Figure 1. (A) Genome-wide recruitment of H3(SMe_2)R8 in primary B-cells, Pfeiffer and SUDHL2 DLBCL cell lines. Heatmap showing PRMT5-specific epigenetic mark H3(SMe_2)R8 enrichment over the gene bodies including 2Kb upstream from TSS and 2Kb downstream from TES. (B) **Genome-wide correlation of ChIP signals**. Average coverages were computed over 10 KB bins across genome and Spearman rank correlation coefficients were calculated for each ChIP sample pair. Heatmap shows that genome-wide recruitment of H3(SMe_2)R8 is different in B cells compared to Pfeiffer and SUDHL-2 cell lines.

Supplemental Figure 2. **PRMT5 genetic knock-down and pharmacologic inhibition affect Cyclin D1 and c-Myc protein levels.** (A and B) RIPA extracts (20 µg) were prepared from control sh-GFP or sh-PRMT5 PDX and A20 cells, and analyzed by immunoblotting using the indicated antibodies. Anti-β-ACTIN antibody was included to show equal loading.

Supplementary Figure 3. Representative Venn diagram of miRs with PRMT5 load and miRs targeting c-Myc and CCND1

Supplementary Figure 4. **PRMT5 acts as a transcriptional repressor and controls transcription of CYCLIN D1 and c-MYC specific miRNAs.** (A) Expression profile of PRMT5 target miRNAs predicted to bind CYCLIN D1 3' UTR in control normal B cells (resting and activated) versus Pfeiffer and SUDHL-2 cells. Total RNA was isolated from each cell line and small RNAs were enriched using spin columns. Levels of individual miRNA were measured by real-time RT-PCR using specific primers and probes as described in materials

and methods. (B-D) Expression of CYCLIN D1 miRNAs which are PRMT5 targets were analyzed in Jeko-1, Pfeiffer, and SUDHL2 cells that were infected with either shGFP or shPRMT5 using real-time RT-PCR. (E-F) Expression of miRs33b, -96, -503, as well as PRMT5, CyclinD1 and c-Myc transcripts after PRMT5 genetic knock-down via shRNA or pharmacologic inhibition with CMP5 in PDX and A20 cells using real-time RT-PCR. Each experiment was done twice in triplicate, and the data points in each graph are represented as means ± S.D.

Supplementary Figure 5. PRMT5 and its epigenetic marks, H3(Me_2)R8 and H4(Me_2)R3, are enriched at the promoter region of miR33b, miR96, and miR503. (A,B) Cross-linked chromatin from Pfeiffer and SUDHL2 cells was immunoprecipitated using pre-immune (PI), anti-PRMT5, H3(Me_2)R8, or H4(Me_2)R3 specific antisera, and promoter sequences of miR33b, miR96 and miR503 were detected using specific primers and probes.

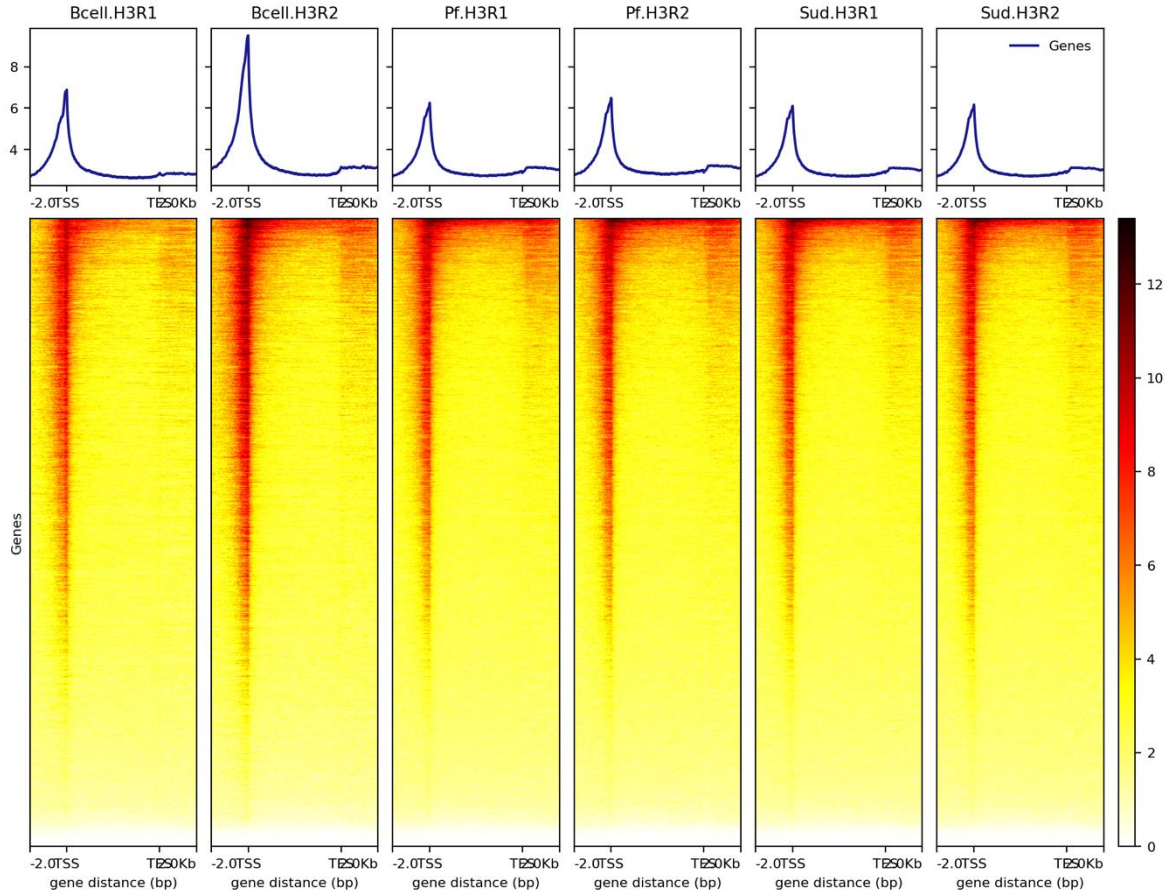
Supplementary Figure 6. PRMT5 target miRNAs regulates CYCLIN D1 and c-MYC protein expression but not RNA levels. (A, B and D) Wild-type or mutated miR33b, miR96, miR503 or control miR197 were individually electroporated as double-stranded RNA (2.5 μg) in Jeko (A), Pfeiffer (B) or SUDHL-2 (D) cells and mRNA levels of CYCLIN D1, c-MYC, or control BRG1 was measured by real-time RT-PCR using specific primers and probes. The experiment was done twice in triplicate, and the data points in each graph are represented as means ± S.D. (C and E) Wild-type or mutated miR33b, miR96 and miR503 were individually electroporated as double-stranded RNA (2.5 μg) in Pfeiffer (C) and SUDHL2 (E) cells and 20 μg of RIPA extracts were analyzed by Western blotting using indicated

antibodies. (F and G) Re-expression of miR96 and miR503 results in cellular apoptosis. Equal number (5 x 106) of Pfeiffer (F) and SUDHL2 (G) cells were electroporated with 2.5 µg of miR33b, miR96 and miR503 and cells were stained with FITC-Annexin V antibody and propidium iodide before they were analyzed by flow cytometry.

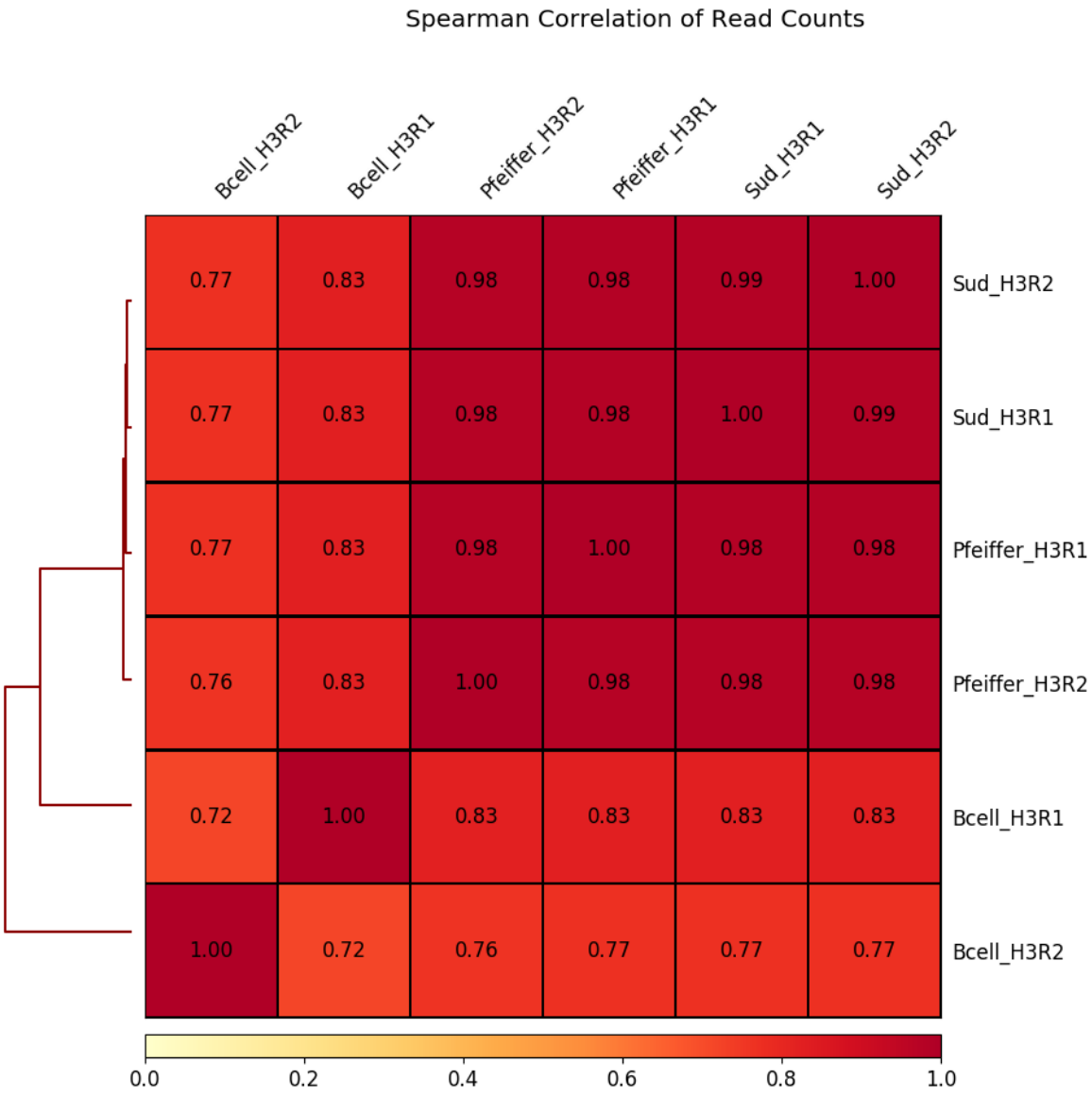
Supplementary Figure 7. PRMT5 collaborates with co-activators and co- repressors to silence expression of miR33b, miR96 and miR503. (A-F) Cross-linked chromatin from either sh-GFP or sh-PRMT5 infected Pfeiffer (A,C,E) or SUDHL2 (B,D,F) cell lines was immunoprecipitated using indicated antibodies and promoter sequences of miR96, miR33b and miR503 were detected using specific primers and probes. ChIP assays were carried out twice in triplicate. Fold enrichment with each antibody was calculated relative to the PI sample. Data in each graph are represented as mean ± SD.

Supplementary Figure 8. H3 recruitments to target miR promoters. Cross-linked chromatin from either DMSO or CMP5 treated lymphoma cell lines cells was immunoprecipitated using PI or indicated antibodies and miR96, miR33b and miR503 promoter sequences were detected using specific primers and probes. Fold enrichment with each antibody was calculated relative to the PI sample. Data in each graph are represented as mean ± SD.

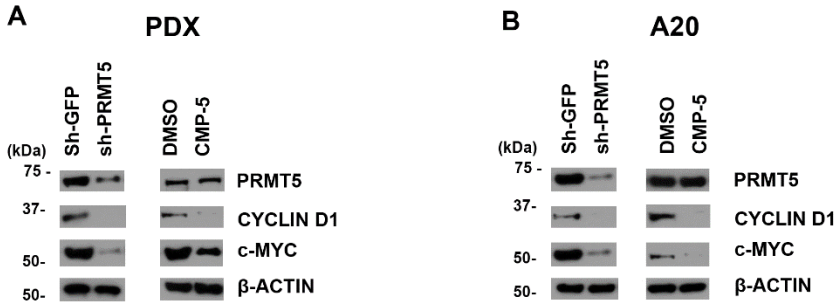
Supplementary Figure 1A



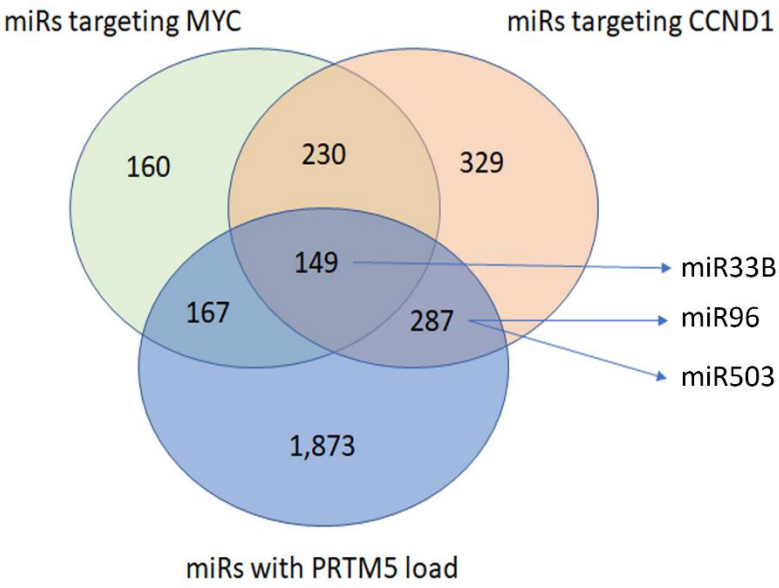
Supplementary Figure 1B



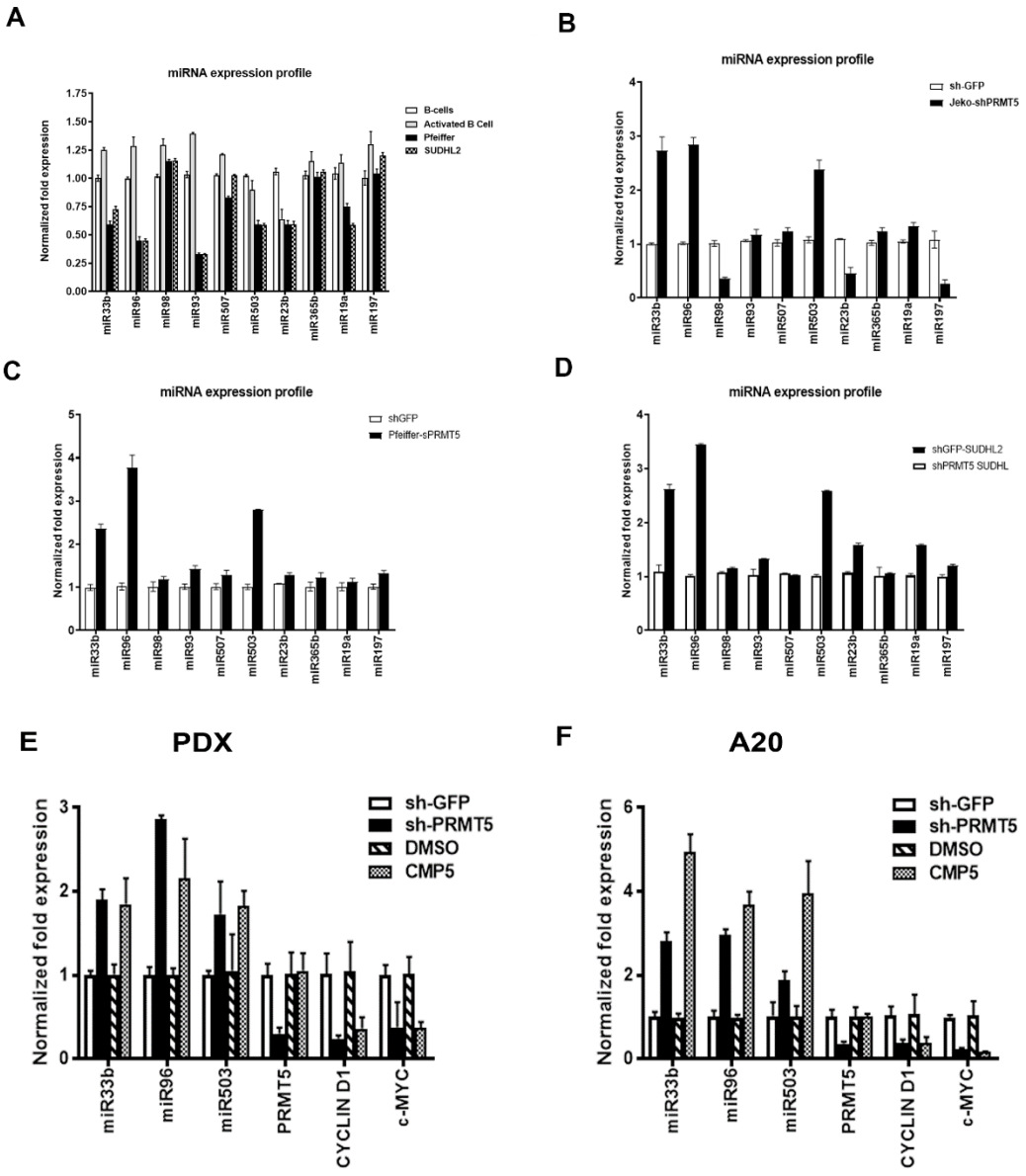
Supplementary Figure 2



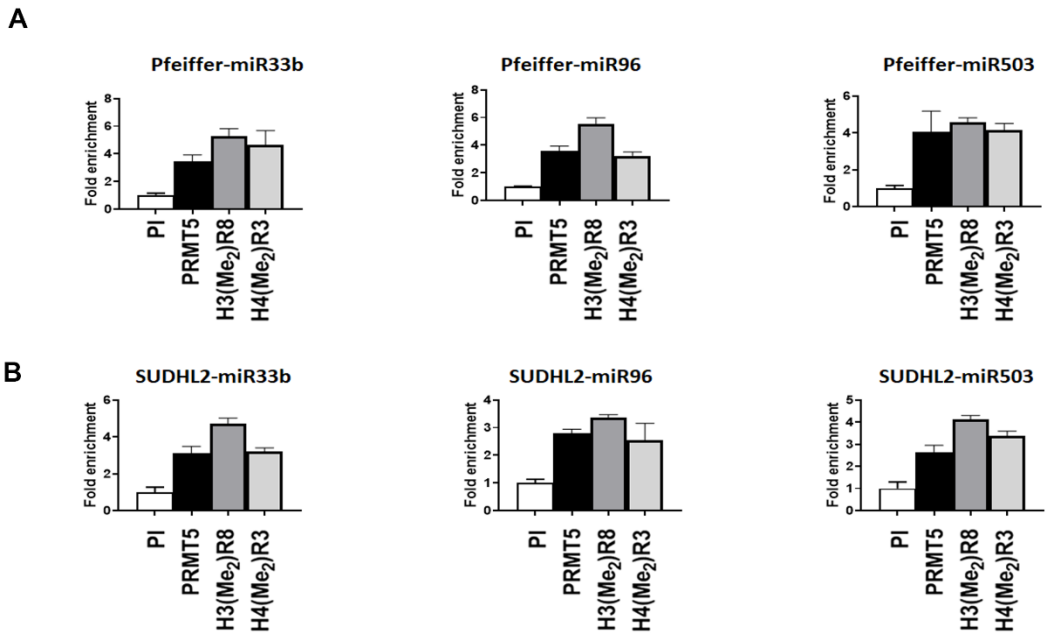
Supplementary Figure 3



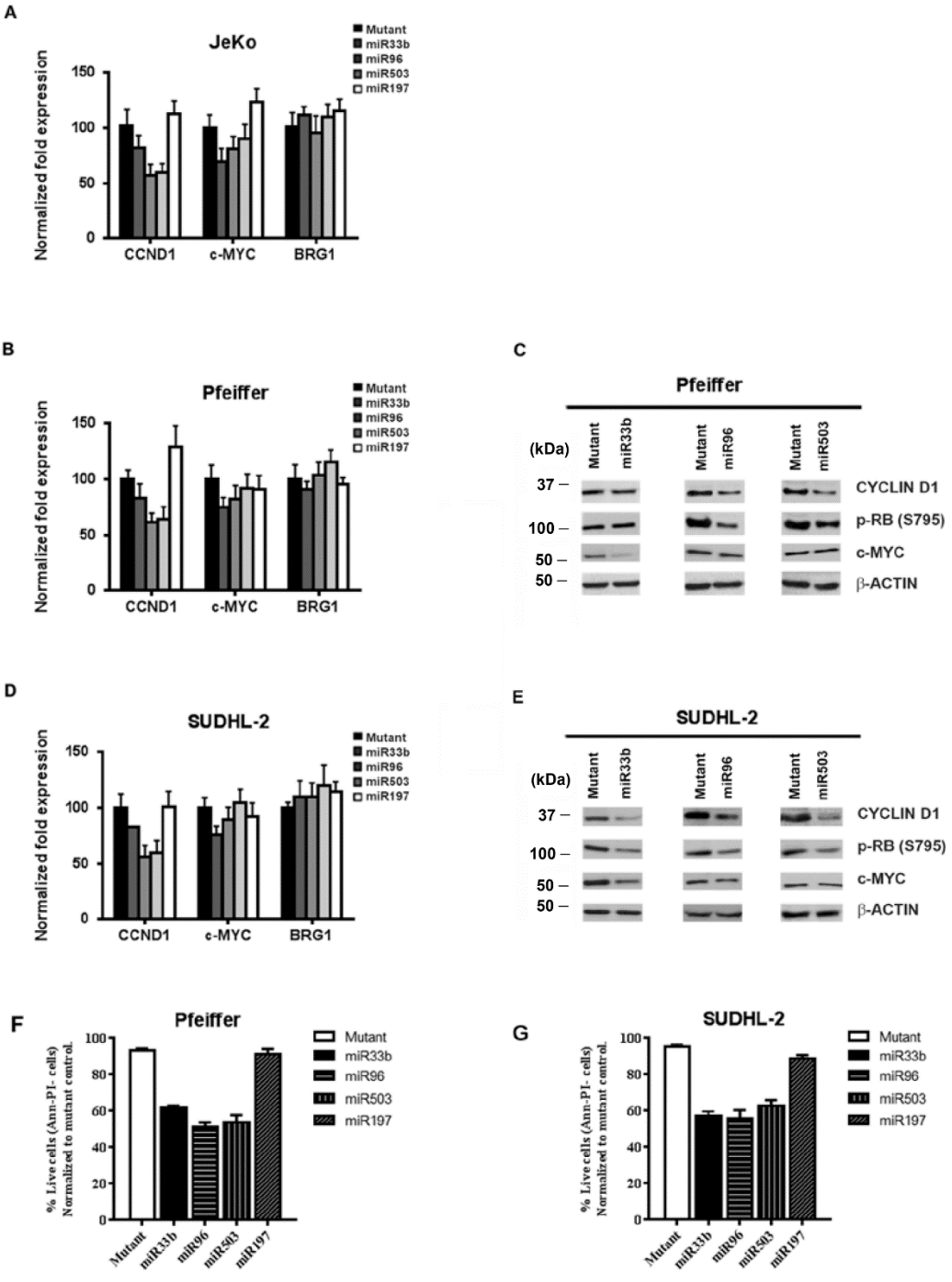
Supplementary Figure 4



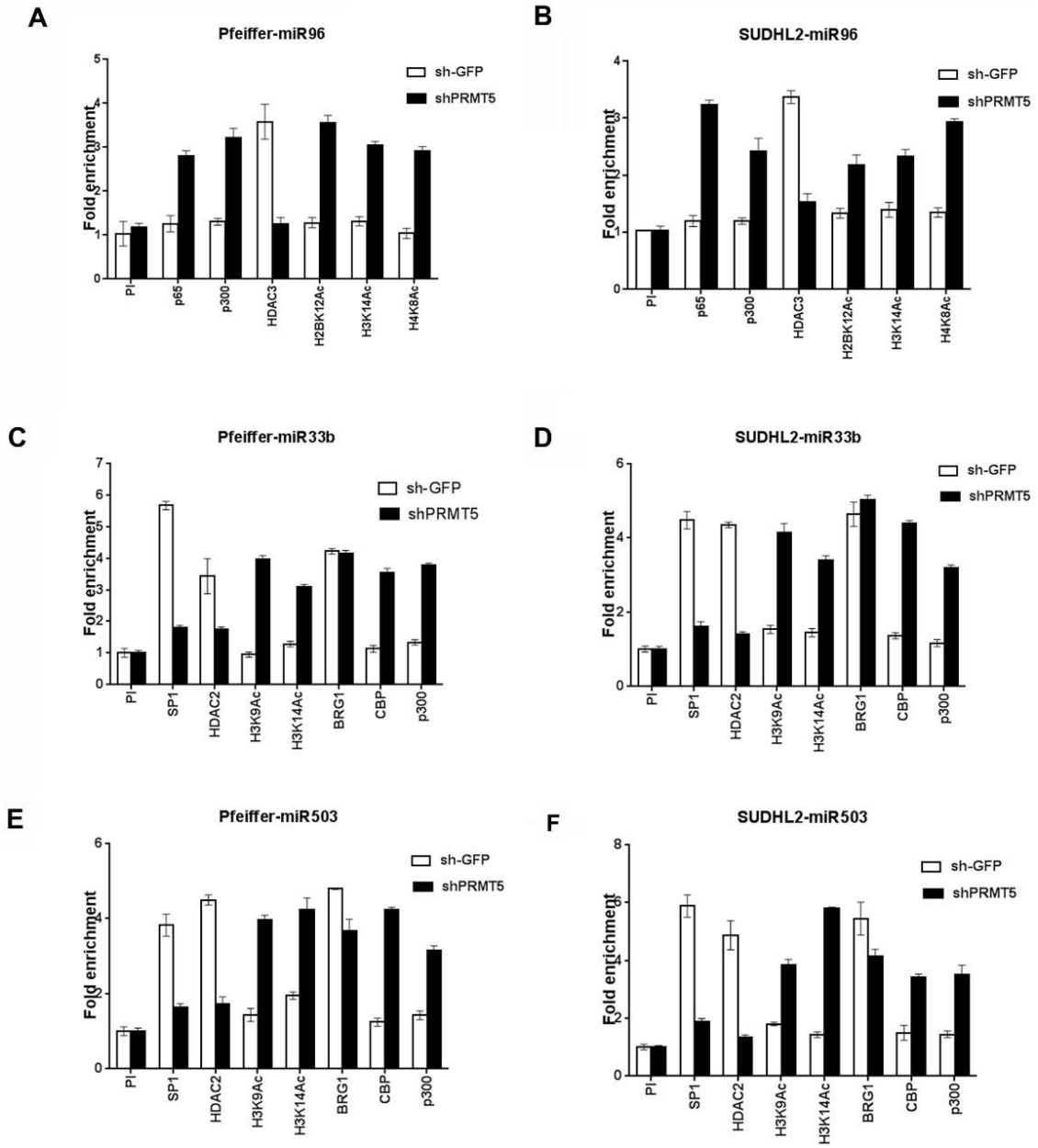
Supplementary Figure 5



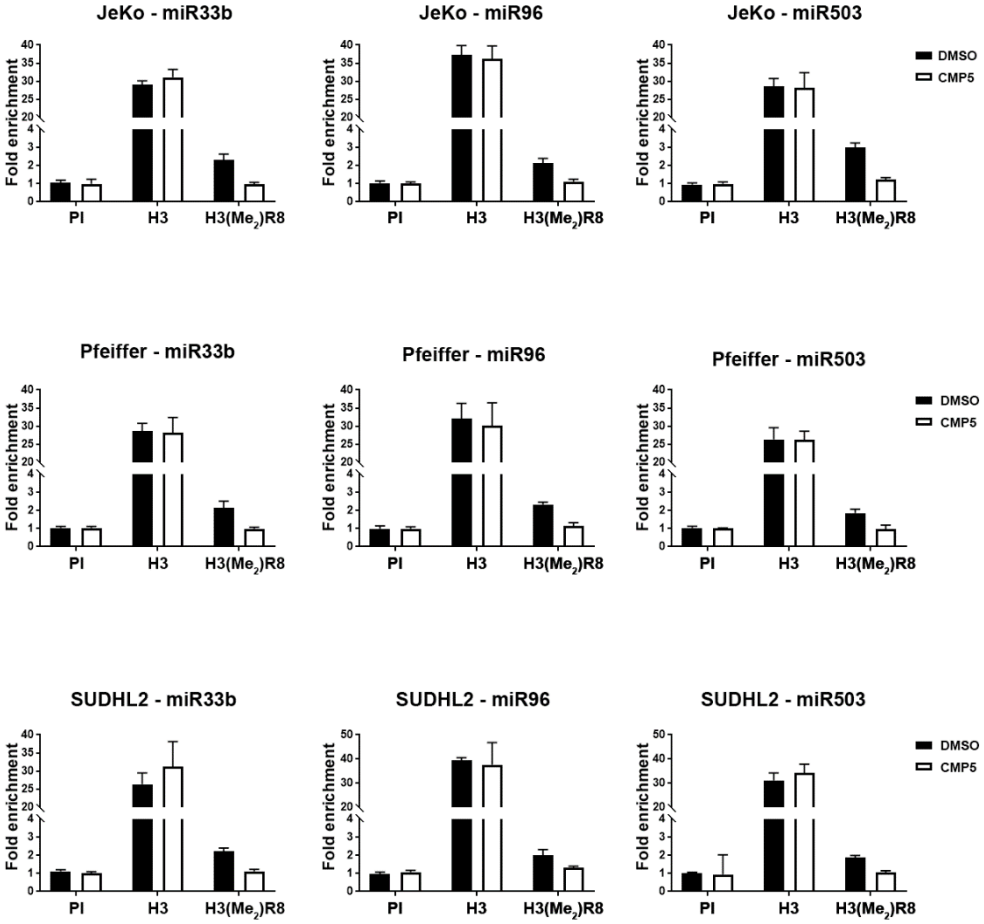
Supplementary Figure 6



Supplementary Figure 7



Supplementary Figure 8



SUPPORTING INFORMATION (Supplementary Data)

Supplementary Table 1: Included as separate excel file due to size.

Supplementary Table 2: Included as a separate excel file due to size.

Supplementary Table 3:

Primer Name	Sequence
Wild-type-miR33b-sense	5’- AAGTGCATTGCTGTTGCATTGCCCTGTCTC -3’
Wild-typemiR33b-anti-sense	5’-AAGCAATGCAACAGCAATGCACCCTGTCTC-3’
Wild-typemiR96-sense	5’-AATTTGGCACTAGCACATTTTTGCCCTGTCTC-3’
Wild-typemiR96-anti-sense	5-AAGCAAAAATGTGCTAGTGCCAAACCTGTCTC-3’
Wild-typemiR503-sense	5’-AATTTTGCACCTTTTGGAGTGAACCTGTCTC-3’
Wild-typemiR503-anti-sense	5’-AATTCACTCCAAAAGGTGCAAAACCTGTCTC-3’
Wild-typemiR197-sense	5’-AAGCTGGGTGGAGAAGGTGGTGAACCTGTCTC-3’
Wild-typemiR197-anti-sense	5’-AATTCAC CACCTTCTCCACCCAGCCCTGTCTC -3’
Mutant-miR33b-sense	5’-AAGTATCGTGCTGTTGCATTGCCCTGTCTC-3’
Mutant-miR33b-anti-sense	5’-AAGCAATGCAACAGCACGATACCCTGTCTC-3’
Mutant-miR96-sense	5’-AAGGCTCACATAGCACATTTTTGCCCTGTCTC-3’
Mutant-miR96-anti-sense	5’-AAGCAAAAATGTGCTATGTGAGCCCCTGTCTC-3’
Mutant-miR503-sense	5’-AATTGCTATCCTTTTGGAGTGAACCTGTCTC-3’
Mutant-miR503-anti-sense	5’-AATTCACTCCAAAAGGATAGCAACCTGTCTC-3’
Mutant-miR197-sense	5’-AAGACATTGTACGAAGGTGGTGAACCTGTCTC-3’
Mutant-miR197-anti-sense	(5’-AATTCACCACCTTCTTTCAATCTACCTGTCTC-3’