

Figure S1. Classification of H3K27ac ChIP-seq peaks. (A) Seven H3K27ac peak patterns are shown. (B) All peak patterns at three time points, 24, 36 and 48 h after PRMT6 knockdown, are shown as a heatmap. The pattern one peak was upregulated in siNC and downregulated in siPRMT6#1 and #2; the pattern two peaks were upregulated in siNC and siPRMT6#1 and downregulated in siPRMT6#2; the pattern three peaks were upregulated in siNC and siPRMT6#2; the pattern four peaks were upregulated in siPRMT6#1 and downregulated in siNC and siPRMT6#2; the pattern five peaks were upregulated commonly in siPRMT6 and downregulated in siNC; the pattern six peaks were upregulated only in siPRMT6#2; the pattern seven peaks were commonly upregulated in all samples. H3K27ac, histone H3K27 acetylation; ChIP-seq, chromatin immunoprecipitation sequencing; PRMT6, protein arginine methyltransferase 6; siNC, MISSION siRNA Universal Negative Control #1.

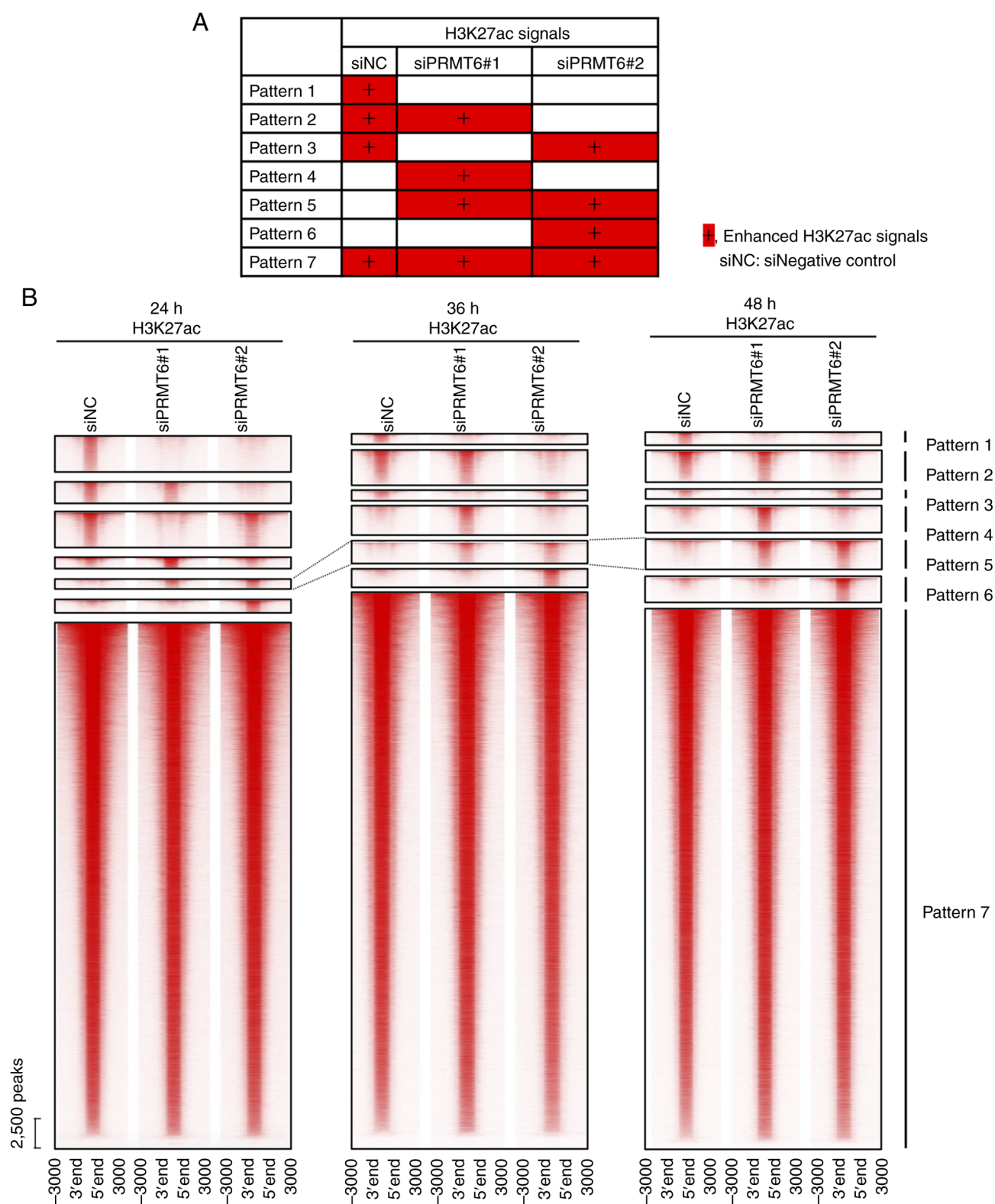


Figure S2. PRMT6 is overexpressed in endometrial cancer. The mRNA expression of *PRMT6* was analyzed in clinical specimens of EC (n=52) and normal endometrial tissue (n=8), using reverse transcription-quantitative polymerase chain reaction. EC samples indicated with a red bar were used for the analyses presented in Figs. S5 and S10. PRMT6, protein arginine methyltransferase 6; EC, endometrial cancer.

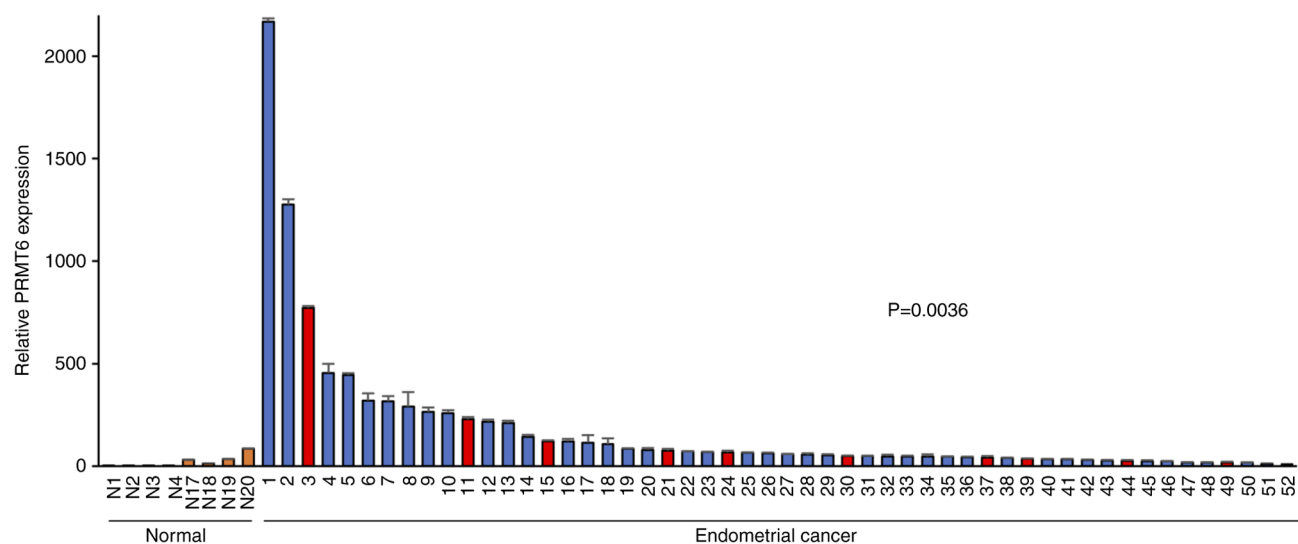


Figure S3. PRMT6 knockdown is confirmed in all EC cell lines. (A) The mRNA expression of *PRMT6* was analyzed using reverse transcription-quantitative polymerase chain reaction in PRMT6-knockdown EC cell lines (HEC265, Ishikawa, HEC151A, and HEC116). (B) The protein expression of PRMT6 evaluated using western blotting in the cell lines presented in (A). $P < 0.05$ was considered to indicate a statistically significant difference. $*P < 0.01$. PRMT6, protein arginine methyltransferase 6; EC, endometrial cancer.

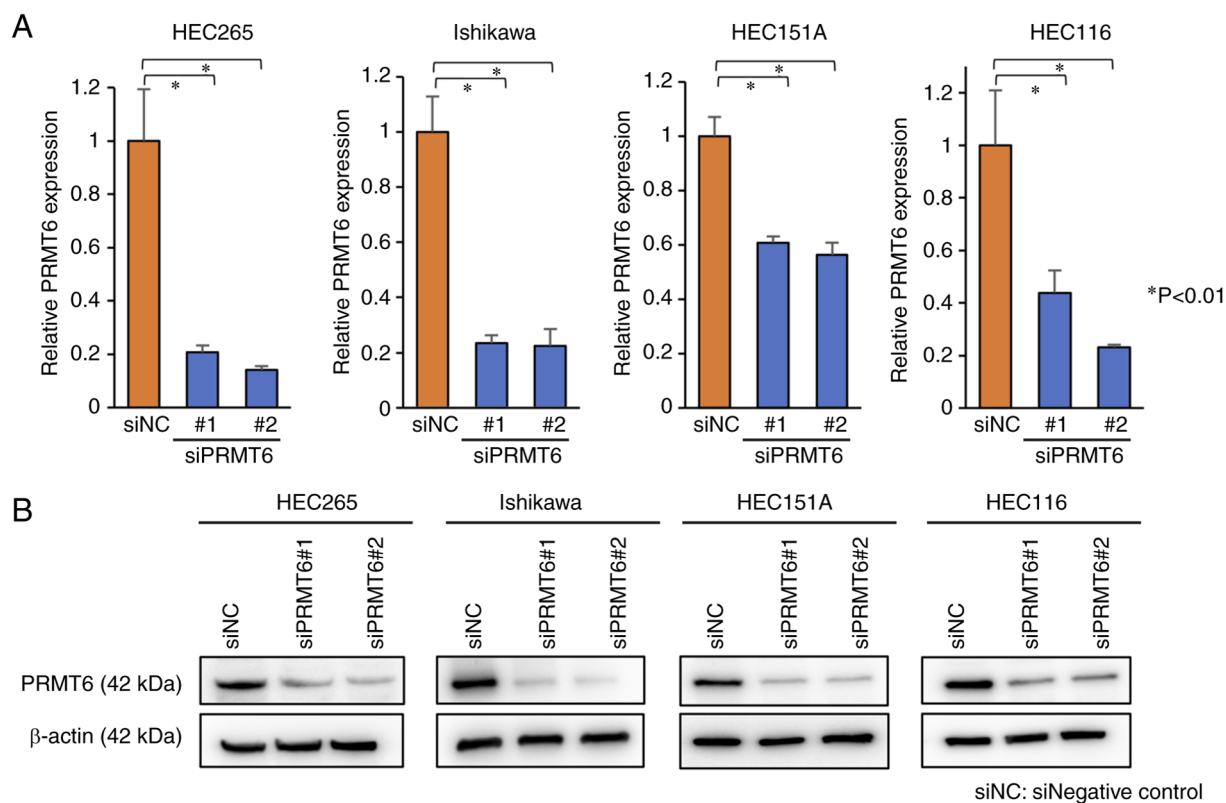


Figure S4. PRMT6 is downregulated at the protein level 24 h after siPRMT6 transfection. PRMT6, protein arginine methyltransferase 6.

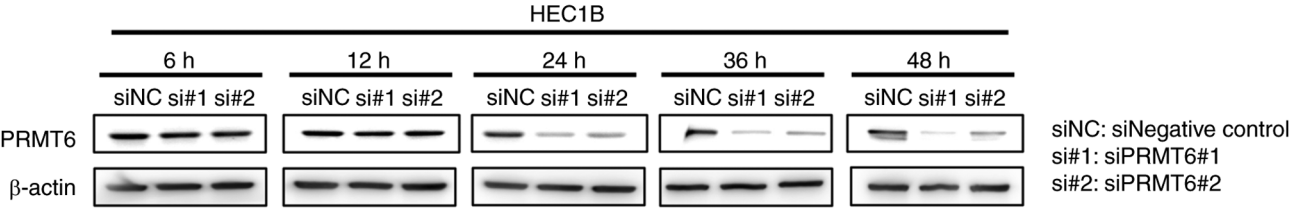


Figure S5. mRNA expression of *NKX6-1* and *PIK3R1* in EC and normal endometrial tissues. The mRNA expression of *NKX6-1* and *PIK3R1* was evaluated in clinical specimens of EC (n=10) and normal endometrial tissue (n=4) using reverse transcription-quantitative polymerase chain reaction. *NKX6-1*, NK6 homeobox 1; *PIK3R1*, phosphoinositide-3-Kinase Regulatory Subunit 1; EC, endometrial cancer.

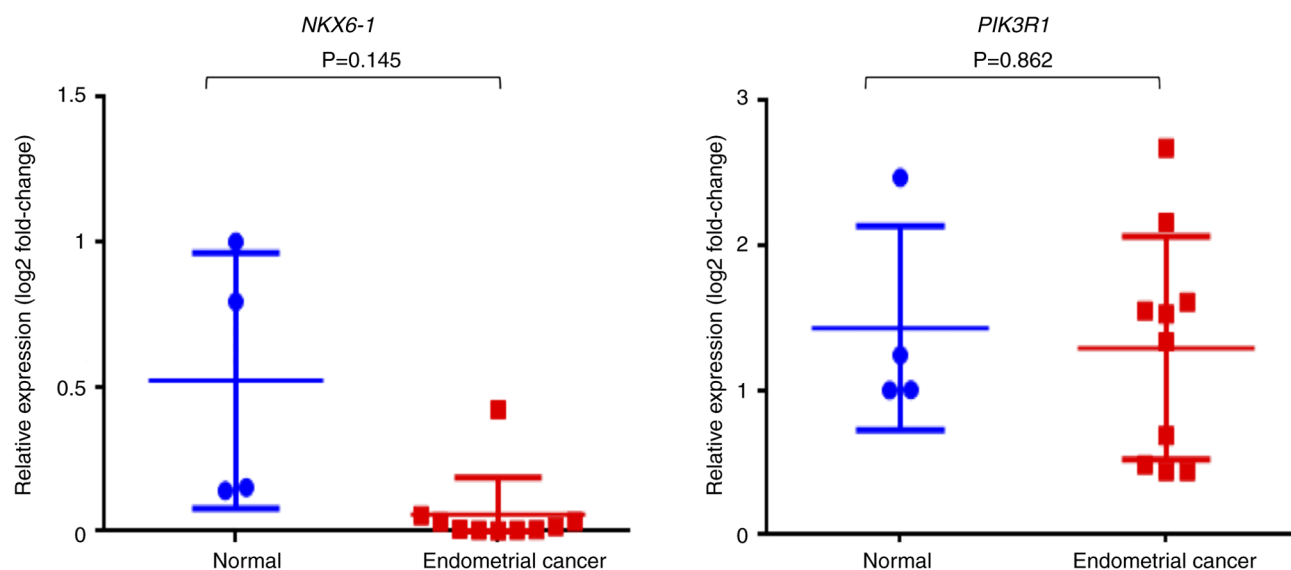


Figure S6. The integrated analysis of H3K27ac ChIP-seq and RNA-seq. In total, 423 genes upregulated due to PRMT6-KD according to the RNA-seq analysis and genes downstream of NFATC1, SMAD2 and SMAD3 are presented in the Venn diagram. H3K27ac, histone H3K27 acetylation; ChIP-seq, chromatin immunoprecipitation sequencing; RNA-seq, RNA sequencing; PRMT6, protein arginine methyltransferase 6; KD, knockdown; NFATC1, nuclear factor of activated T-cells 1.

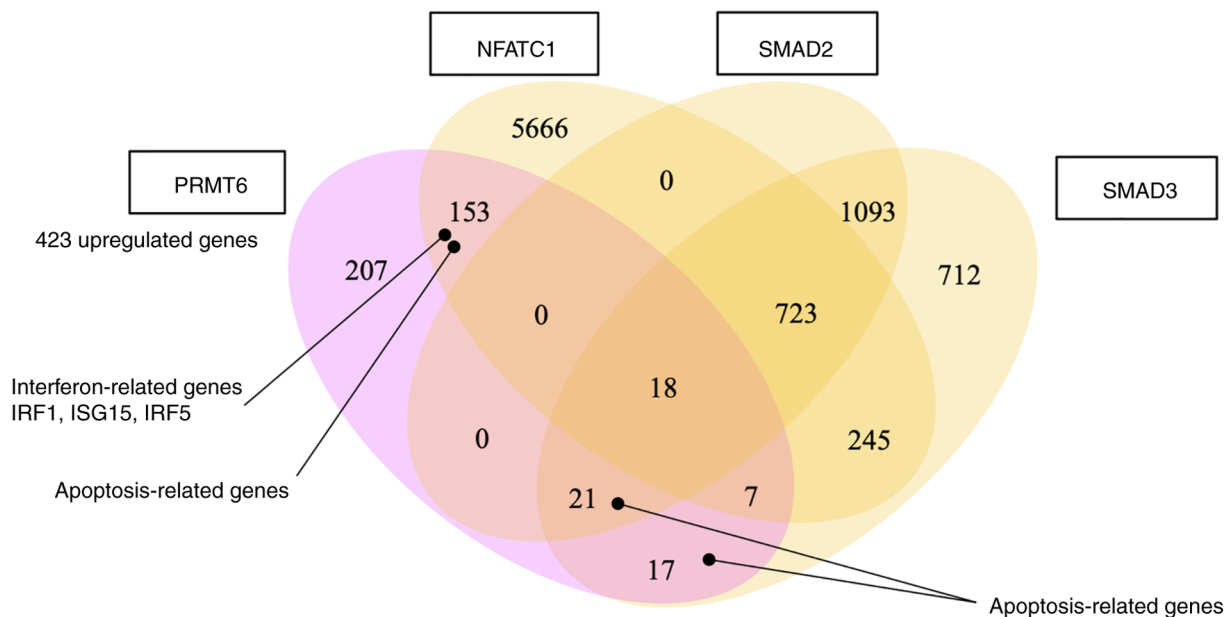


Figure S7. Biological process of GO analysis using downstream genes of NFATC1. GO analysis results, using 178 genes overlapped with genes downstream of NFATC1, a subgroup of the 423 genes upregulated by PRMT6 knockdown. GO terms satisfying the $P < 0.05$ requirement and GO terms associated with interferon and apoptosis are shown. GO, Gene Ontology; NFATC1, nuclear factor of activated T cells 1; PRMT6, protein arginine methyltransferase 6.

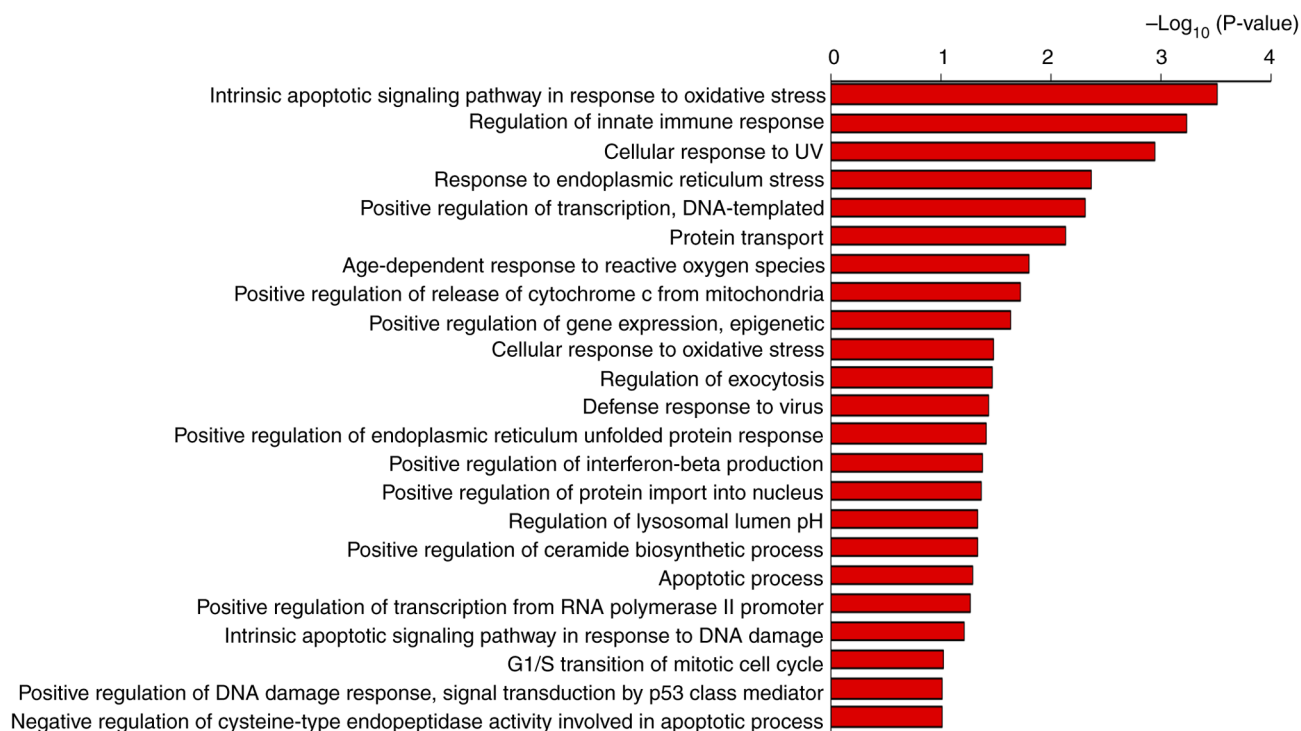


Figure S8. Biological process of Gene Ontology analysis using downstream genes of SMAD2. GO analysis results, using 39 genes overlapped with genes downstream of NFATC1, a subgroup of the 423 genes upregulated by PRMT6 knockdown. GO terms satisfying the $P < 0.05$ requirement and GO terms associated with interferon and apoptosis are presented. GO, Gene Ontology; PRMT6, protein arginine methyltransferase 6.

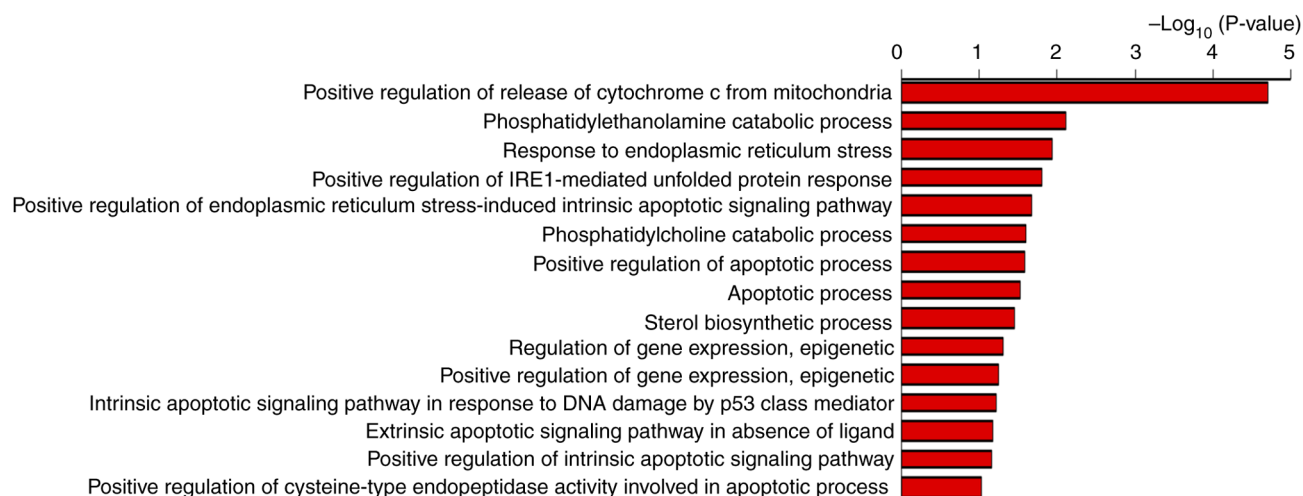


Figure S9. Biological processes of GO analysis using downstream genes of SMAD3. GO analysis results, using 63 genes overlapped with downstream genes of NFATC1, a subgroup of the 423 genes upregulated by PRMT6 knockdown. GO terms satisfying the $P < 0.05$ requirement and GO terms associated with interferon and apoptosis are presented. GO, Gene Ontology; PRMT6, protein arginine methyltransferase 6.

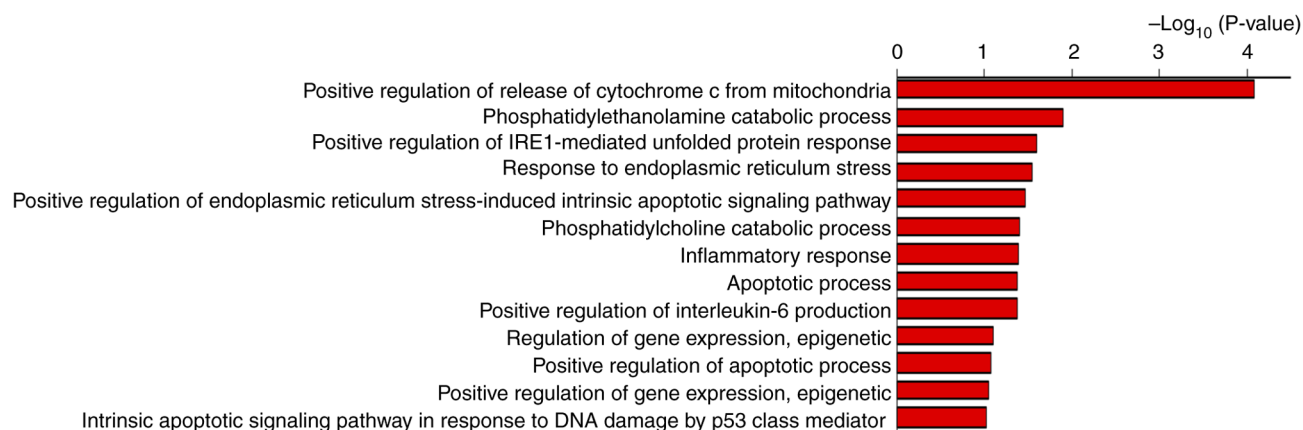


Figure S10. mRNA expression of ERV genes in EC and normal endometrial tissues. The mRNA expression of ERV genes was evaluated in clinical specimens of EC (n=10) and normal endometrial tissue (n=4), using reverse transcription-quantitative polymerase chain reaction. ERV, endogenous retrovirus; EC, endometrial cancer.

