Figure S1. ChIP-seq data and expression of *PVRL4* in breast and colorectal cancer cell lines. (A) Schematic presentation of ENCODE ChIP-seq data of H3K4Me1 and H3K27Ac in the *PVRL4* region. (B) Expression of *PVRL4* in three breast (SKBR3, T47D and MCF7) and four colorectal (DLD1, LS174T, HCT116 and RKO) cancer cell lines. Quantitative PCR analysis was performed and relative expression of *PVRL4* to *HPRT1* is shown. ARHGAP30, Rho GTPase activating protein 30; ChIP-seq, chromatin immunoprecipitation-sequencing; H3K4Me1, H3K4 mono-methylation; H3K27Ac, H3K27 acetylation; HPRT1, hypoxanthine phosphoribosyltransferase 1; HS, high sensitivity.

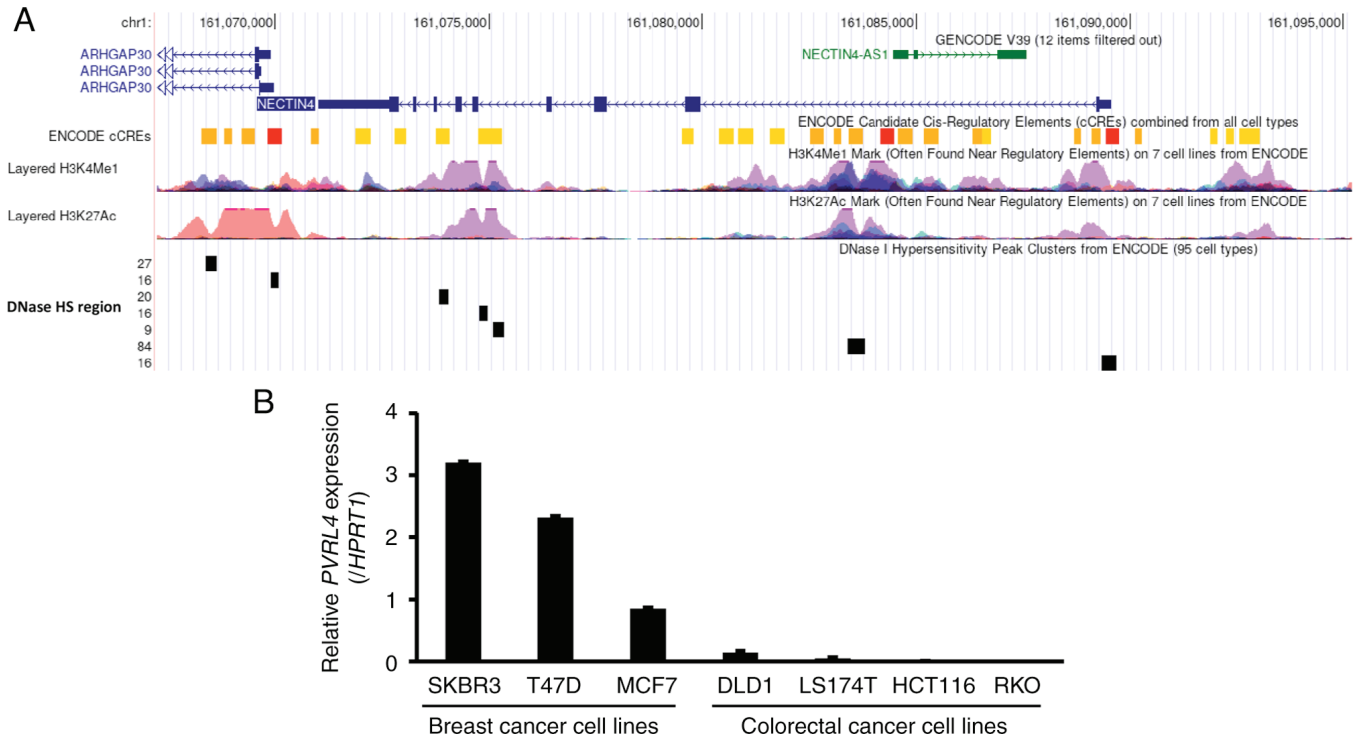

Figure S2. TADs in the *PVRL4* locus. Visualization of the TADs in the region containing *PVRL4* (chromosome 1, 160,400,000-161,450,000) using the High-throughput chromosome conformation capture data from The Topologically Associating Domain Knowledge Base. The upper and left sides show DNase high sensitivity, H3K4Me1 and H3K27Ac peaks from the ENCODE data. TSS and candidate regions (#10, #11, #13 and #14) used for reporter assays are indicated in the same TAD. H3K4Me1, H3K4 mono-methylation; H3K27Ac, H3K27 acetylation; TAD, topologically associated domain; TSS, Transcription Start Site.

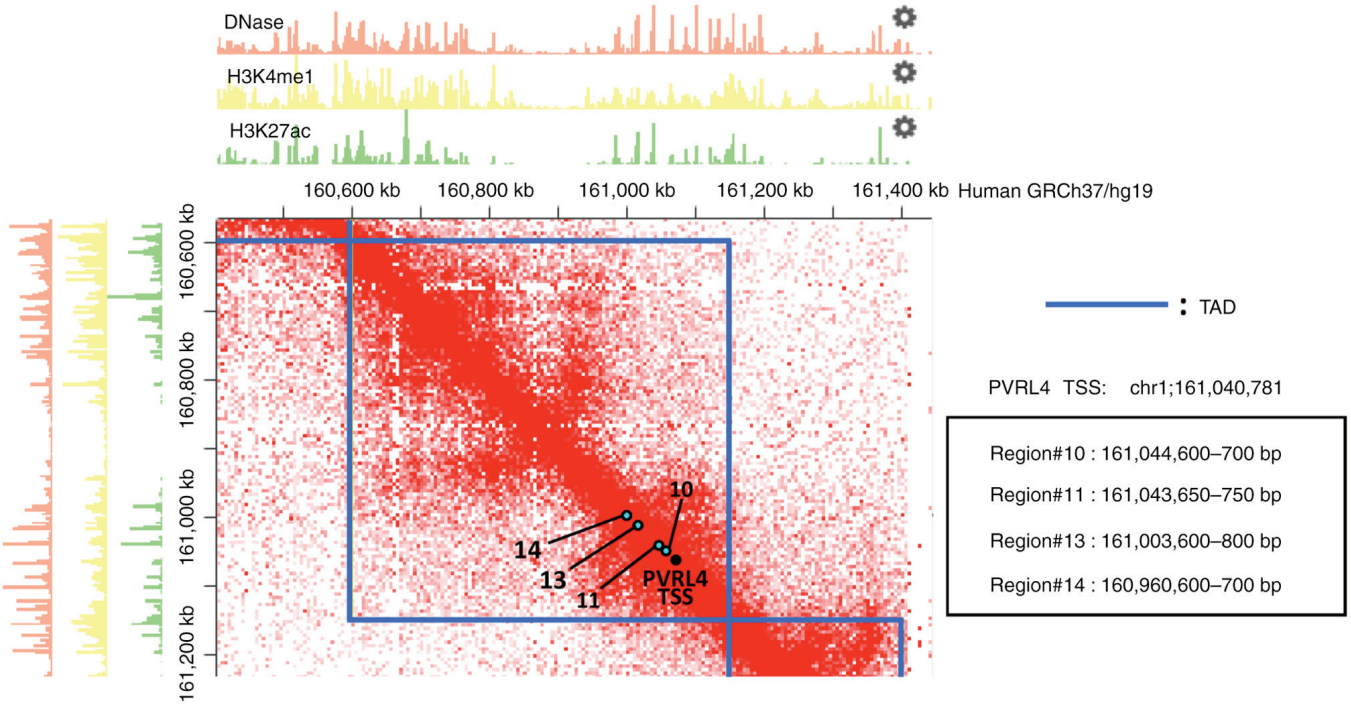

Figure S3. Identification of a transcriptional regulatory region in *PVRL4*. (A) Relative luciferase activities of plasmids containing the 14 candidate regions in T47D cells. ***P<0.005 vs. control. (B) Reporter activities of plasmids containing the wild-type region, #10, and three #10 deletion-mutant regions in T47D cells. *P<0.05, ***P<0.005 vs. #10.

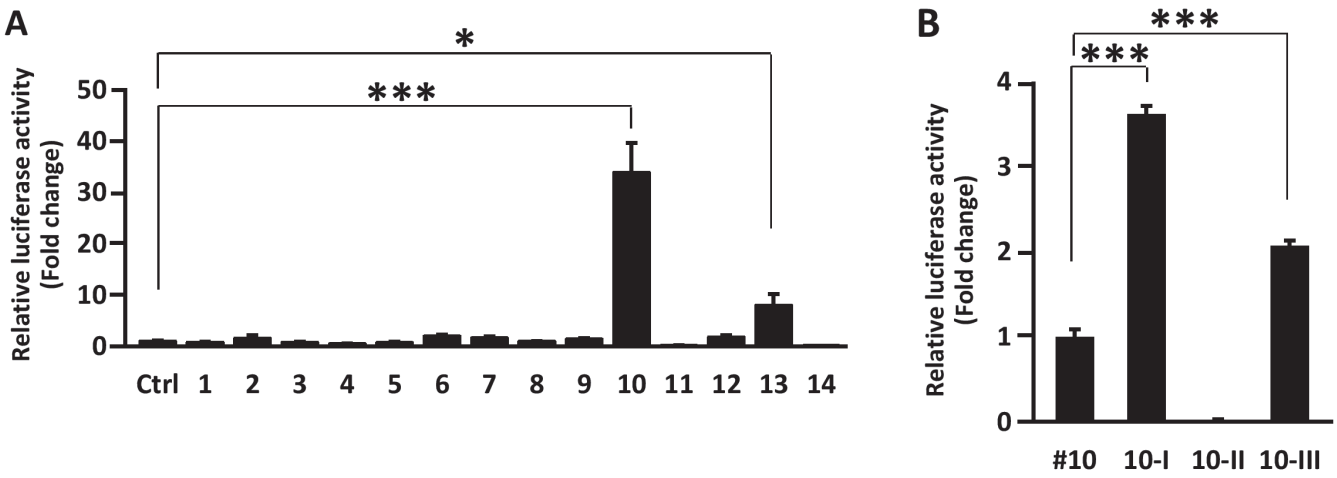

Figure S4. Effect of siRNAs on the expression of 11 candidate transcription factors. The effect of (A) ATF3, (B) ATF7, (C) CREB1, (D) CREB3L4, (E) JDP2, (F) JUN, (G) JUND, (H) JUNB and (I) FOS gene specific-siRNAs on the expression of the 11 candidate transcription factors was determined by quantitative PCR in SKBR3 cells. **P<0.01, ***P<0.005 vs. control. (J) The effect of siFOS was additionally analyzed in T47D cells ***P<0.005 vs. control. Black and gray bars show SKBR3 and T47D cells, respectively. ATF, activating transcription factor; CREB, cAMP responsive element binding protein; CTRL, control; HPRT1, hypoxanthine phosphoribosyltransferase 1; JDP2, Jun dimerization protein 2; siRNA, small interfering RNA.

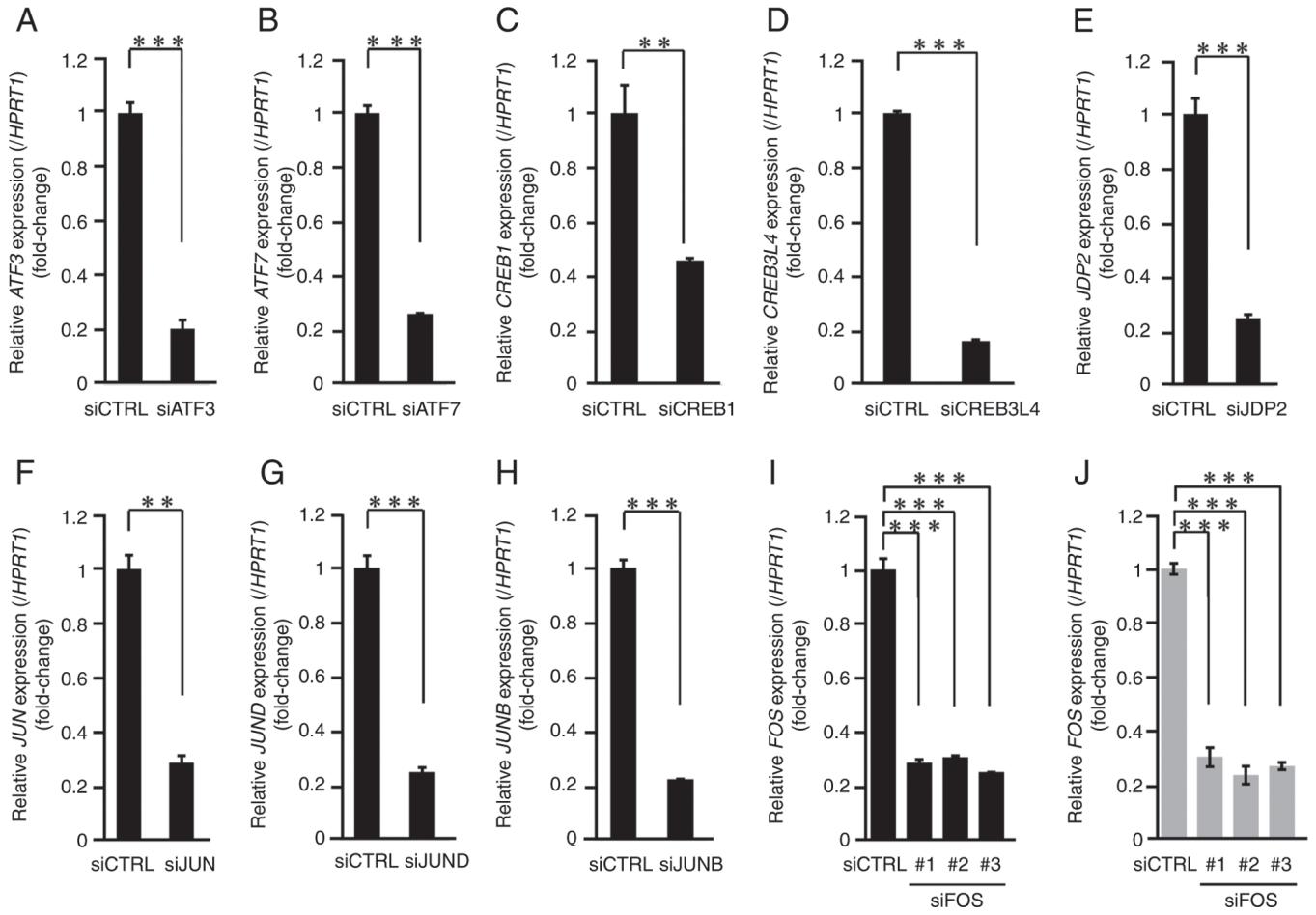

Figure S5. Effect of FOS overexpression on the enhancer activity of region #10-III. (A) Reporter activities of WT (#10-III) and the mutant plasmids (Mut1 + 2) were analyzed in T47D cells. ***P<0.005 vs. WT. (B) Overexpression of PVRL4 augmented the expression of *PVRL4* in T47D cells. *HPRT1* served as a control. ****P<0.001 vs. control. (C) Effect of exogenous FOS overexpression on the reporter activity of the WT and mutant plasmids (#10-III and Mut1 + 2, respectively) in T47D cells. **P<0.01, ***P<0.005 vs. #10-III. HPRT1, hypoxanthine phosphoribosyltransferase 1; WT, wild-type.

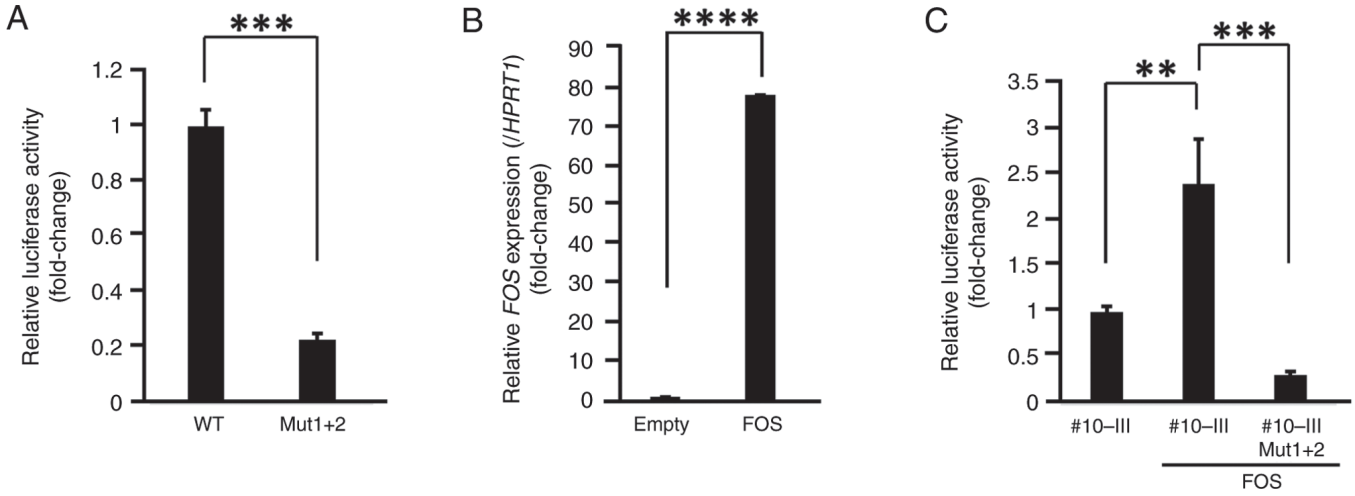

Figure S6. *PVRL4* expression was regulated by FOS. Knockdown of *FOS* by three different siRNAs reduced the expression of *PVRL4* in T47D cells. Relative expression of *PVRL4* was analyzed by quantitative PCR. **P<0.01, ***P<0.005 vs. control. CTRL, control; HPRT1, hypoxanthine phosphoribosyltransferase 1; siRNA, small interfering RNA.

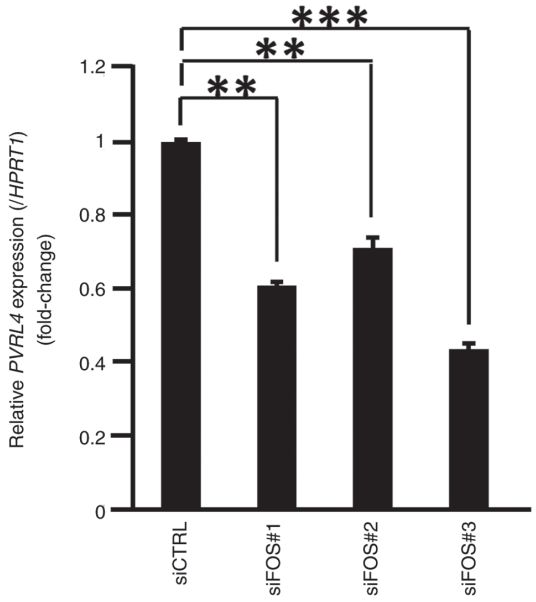

Figure S7. Effect of PVRL4 siRNA on the expression of *PVRL4*. (A) The effect of gene specific-siRNAs on the expression of *PVRL4* in SKBR3 cells was determined by quantitative PCR **P<0.01 vs. control. (B) RNA sequencing analysis of SKBR3 cells treated with PVRL4 siRNA (siPVRL4#1 and #2) and siCTRL. Up or downregulated genes were detected. CTRL, control; HPRT1, hypoxanthine phosphoribosyltransferase 1; siRNA, small interfering RNA.