SUPPLEMENTARY FIGURE LEGENDS

Fig. S1. Generation of prostate-specific p300 deletion mice. A, schematic diagram showing the gene targeting strategy for the generation of a p300 conditional allele in mice, which was adapted from the previous report (1). Exon number and relative position, selection gene cassettes, positions of Southern blot probes, PCR primer positions, LoxP sites, Frt sites, and restriction sites are indicated. B, example of PCR-based genotyping results of prostate-specific p300 heterozygous (Cre^+/p300^{L/+} or p300^{pc+/-}) and homozygous (Cre^+/p300^{L/L} or p300^{pc-/-}) mice at 4-month of age. M, 1 kb plus DNA marker. Lu, lung; Ki, Kidney; Li, Liver; H, Heart; AP, anterior prostate; DLP, dorsolateral prostate; VP, ventral prostate.

Fig. S2. Histological (hematoxylin and eosin) analysis of anterior prostate (AP) and dorsolateral prostate (DLP) of 4-month-old Pten^{pc-/-} and Pten^{pc-/-};p300^{pc-/-} mice (n = 8/genotype). Representative images were taken at 200x magnification.

Fig. S3. P300 regulates AR proteasome degradation in PCa cells. A, p300 knockdown induces AR proteasome degradation in 22Rv1 cells. Cells were transfected with control (siC) and PTEN and/or p300 specific siRNA(s). At 64 h after transfection, cells were treated with vehicle (dimethylsulfoxide, DMSO) or MG132 (20 uM) for 8 h. Cells were harvested for western blot analysis using indicated antibodies. ERK2 was a loading control. B, effect of PTEN and p300 knockdown on the protein levels of transcription factors indicated. LAPC-4 cells were transfected with control (siC) and PTEN and/or p300 specific siRNA(s) for 72 h. Cells were harvested for western blot analysis using indicated antibodies. ERK2 was a loading control. C,
D, effect of PTEN and p300 knockdown on AR stability in LAPC4 cells. Cells were transfected with siRNAs as indicated for 48 h followed by treatment with cycloheximide (50 ug/ml). At indicated time points cells were harvested for western blot analysis with indicated antibodies in (C). The density of AR protein band was first normalized by the density of the corresponding ERK2 band, and the normalized value was further normalized by the value at one-hour-treatment time point in (D). E, effect of PTEN and p300 knockdown on AR mRNA expression. LAPC-4 and 22Rv1 cells were transfected with siRNAs as in A. At 48 h after transfection, cells were harvested for RNA extraction and for real-time RT-PCR analysis of AR mRNA expression. Cells transfected with AR siRNAs were included as a positive control for AR mRNA expression.

**Fig. S4. Western blot analysis of ectopically v5-tagged cyclin B1 and CDK1 in 293T cells.**
Cells were transfected with plasmids as indicated in four different groups as in Fig. 5C. At 24 h after transfection, cells were harvested for western blot analysis with anti-V5 antibody.

**Fig. S5. Effect of p300 depletion on expression of non-AR target genes in human and mouse PCa cells.** A, RT-qPCR analysis of Pai-1 expression in the prostate tissues (combined from three individuals) of $Pten^{pc/-}$ and $Pten^{pc/-}; p300^{pc/-}$ mice at 4 months of age. Columns, mean values among three replicates. Error bars, SD. B, LAPC4 cells were transfected with control siRNAs (siC) and siRNAs for PTEN and/or p300 for 48 h and treated with or without 10 nM Mib for additional 24 h. Expression of the $p300$ gene was analyzed by RT-qPCR. Columns, mean values among three replicates. Error bars, SD. C, LAPC4 cells were transfected with control siRNAs (siC) and siRNAs for PTEN and/or p300 for 48 h. Expression of indicated genes
was analyzed by real-time RT-PCR. Columns, mean values among three replicates. Error bars, SD.

**Fig. S6. Correlation between p300 and phosphorylated AKT (AKT-p) in human PCa specimens.** A, representative images of prostate tumors exhibiting high and low expression of p300 and AKT-p, respectively. B, proportions of human prostate cancers (n = 31) that show high (SI score ≥ 3) or low (SI score < 3) expression of p300 protein and AKT-p. The correlation between p300 and AKT-p was observed as determined by Fisher’s exact test (right tail, $P = 0.027$).