## **Supplementary Material**

**Supplementary Table 1. A List of RT-qPCR Primers and siRNAs.** 

Primer/siRNA	Sequence	Reference
GAPDH-F	AGAAGGCTGGGGCTCATTTG	27
GAPDH-R	CTGTGGTCATGAGTCCTTC	27
CRTC1-F	CCAACCAGTCTCCCACCTC	This work
CRTC1-R	CGCCATCTGCTGCTCATAGT	This work
CRTC2-F	TGGATTTTTAGGGGGTGAGG	This work
CRTC2-R	CAAGTTCTGGTGGTTGAAGG	This work
CRTC3-F	GAAGCCACTGCCAAAACAAC	This work
CRTC3-R	CCACCTCCAACATCACAGG	This work
pgRNA-F	GCCTTAGAGTCTCCTGAGCA	7
pgRNA-R	GAGGGAGTTCTTCTTCTAGG	7
cccDNA-F	CTCCCGTCTGTGCCTTCT	7
cccDNA-R	GCCCCAAAGCCACCCAAG	7
cccDNA-F (cell-free)	GGAAAGAAGTCAGAAGGCAA	25
cccDNA-R (cell-free)	GTGCCTTCTCATCTGCCGG	25
siNC (non-specific control)	UUCUCCGAACGUGUCACGU	29
siCRTC1-a	GAAAUCCCAGUACCUGCAA	This work
siCRTC1-b	UCGCGCUGCACAAUCAGAA	This work

**Figure S1.** Overexpression of CRTC coactivators augmented HBV transcription. (**A-**C) Effect on preS1, C and CRE promoter activity. HepG2 cells were transfected with the indicated reporter (100 ng) and pcDNA3.1-V5/His-CRTC1/2/3 (100 ng). The differences between groups 1 and 3 are statistically significant by Student's t test. The P values are 0.0081 for A (highlighted with \*\*), 0.010 for B (highlighted with \*) and 0.000000013 for C (highlighted with \*\*\*).

**Figure S2.** Interaction between CRTC1 and CREB in HepG2 cells. (**A**) Association of CRTC1 with endogenous CREB. HepG2 cells were transfected with pcDNA3.1-V5/His-CRTC1. CRTC1 was precipitated with anti-V5. The precipitates and input lysates were analyzed by Western blotting. (**B**) Association of endogenous CRTC1 with CREB in HepG2.2.15 cells. Cell were lysed and immunoprecipitated with anti-CREB or IgG. The precipitates and input lysates were analyzed by Western blotting.

**Figure S3.** Association of CRTC1 S167A mutant with HBx. HepG2 cells were transfected with pcDNA3.1-V5/His-CRTC1 S167A and pCAGEN-Flag-HA-HBx. HBx was precipitated with anti-Flag. The precipitates and the input lysates were probed with mouse anti-Flag, mouse anti-V5 and rabbit anti-CREB. α-tub: α-tubulin.

**Figure S4.** Interaction of HBx with CRTC1 and CREB in HepG2 cells. HepG2 cells were transfected with plasmids expressing the indicated combinations of CRTC1, HBx and CRTC1 proteins. HBx was precipitated with anti-HA. The precipitates and input lysates were analyzed by Western blotting.

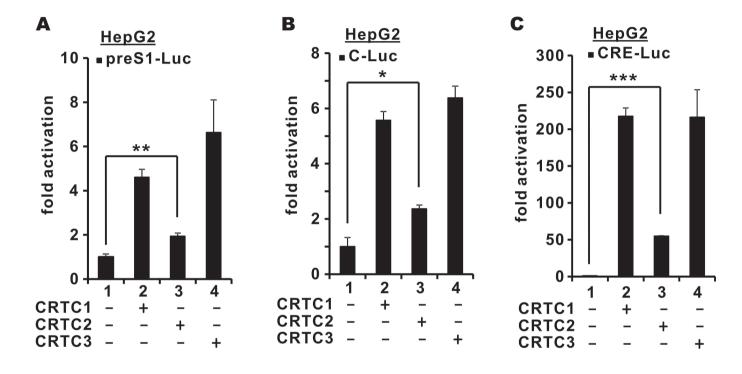


Figure S1

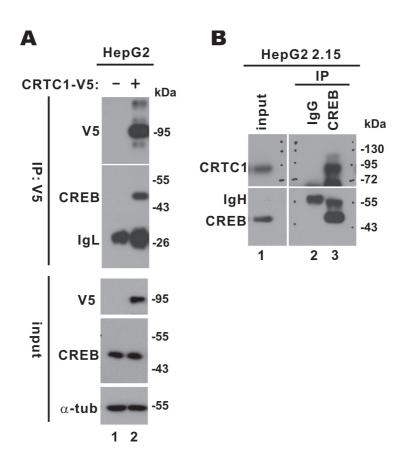


Figure S2

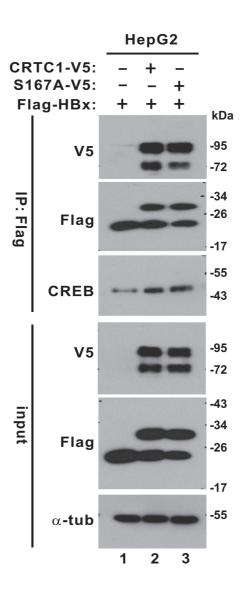


Figure S3

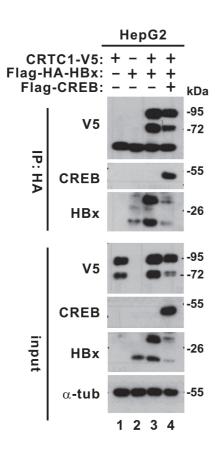


Figure S4