### Table S1

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<th>Primers for RT-PCR</th>
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<tr>
<td>Cdh1 Rev primer</td>
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<td>USP37 Fwd primer</td>
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<td>USP37 Rev primer</td>
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<tr>
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<tr>
<td>B-trcp Rev primer</td>
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Fwd, forward; Rev, reverse
Figure S1

A

Serum Stv.
Time (h) 0 4 8 12 16 20 24 28
WB
α-Cyclin E
α-Cyclin A
α-p27
α-GAPDH

0 h 12 h 20 h

0 h

Asynchronous

Synchronized

B

Cyclin A

USP37
USP37-DD

0 4 8 12 16 20 24

C

OD at 560 nm

Vector HBx USP37 USP37-DD HBx-USP37 HBx-USP37-DD cMyc Vector+MMS

D

USP37
USP37 DD

*
Figure S1. Status of cell cycle regulators and cell viability under different experimental conditions. (A) IHH cells were serum starved for 72 h followed by serum stimulation and harvesting at indicated time points. Cell cycle analysis was performed by flow cytometry after staining with propidium iodide. The expression of Cyclin E, Cyclin A, p27 and GAPDH was analyzed by western blotting. (B) IHH cells were transfected with Flag-USP37 and Flag-USP37-DD and the levels of Cyclin A were measured at indicated time periods. (C) Huh7 cells were transfected with control vector; HBx; Flag-USP37; Flag-USP37-DD; HBx and Flag-USP37 and HBx and Flag-USP37-DD and cell viability was measured by MTT assay. Cells transfected with HA-Myc and vector and treated with Methyl Methane Sulphonate (97% w/v) at 0.1% v/v for 30 min were used as positive and negative control, respectively. Data (bar diagrams) are shown as mean ± SD of three independent observations. * represents statistically significant difference of p<0.005. (D) Huh7 cells transfected with Flag-USP37 and Flag-USP37-DD were analyzed for Brd-U incorporation and confocal imaging. Scale bar represents 50µm.
**Figure S2**

A. *IHH cells*

<table>
<thead>
<tr>
<th></th>
<th>Vector</th>
<th>HA-HBx</th>
<th>WB</th>
<th>α-USP37</th>
<th>α-HBx</th>
<th>α-GAPDH</th>
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B. *HEK293T*

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C. *U2OS*

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D. **Bright Field / Flourescence**

<table>
<thead>
<tr>
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<th>III</th>
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E. **Protein Blot (WB)**

<table>
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<tr>
<th></th>
<th>E2F1</th>
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<table>
<thead>
<tr>
<th></th>
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<th>α-HBx</th>
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Figure S2. Validation of HBx expression and stimulation of USP37 by HBx. IHH (A), HEK293 (B) and U2OS cells (C) were transfected with vector control or HA-HBx expression vector and the levels of USP37 and HBx were measured by western blotting. GAPDH was used for normalization of protein levels. (D) Huh7 cells were transfected with HBx-GFP along with Sc-shRNA or X-E shRNA. Bright field and fluorescence images of cells (panels I-III) showing the expression HBx-GFP fusion protein. (E) Huh7 cells were transfected with HA-HBx (along with E2F1 or E2F1-Δ1-374). And the cell lysates were western blotted with α-USP37 and α-CDC6 antibodies. GAPDH was used as a loading control.
Figure S3

A

Vector + -
HA-CDH1 - +

WB
α-USP37
1 0.25
α-HA
α-GAPDH
1 2

B

HA-CDH1 + + +
Sc-shRNA + + -

HA-HBX - + +
X-E shRNA - - +

WB
α-USP37
1 1.9 1.2
α-Cdc6
α-HA
α-HBx
α-GAPDH
1 2 3

C

Vector + - - -
HA-HBX - - + +

Flag-Emi1 - - - +

WB
α-USP37
1 1 1.8 2
α-Flag
α-HBx
α-GAPDH
1 2 3 4

D

Vector + -
Myc-β-TrCP - +

WB
α-USP37
1 0.2
α-Myc
α-GAPDH
1 2

E

Myc-β-TrCP + + +
Sc-shRNA + + -

HA-HBX - + +
X-E shRNA - - +

WB
α-USP37
1 2.1 1.3
α-β- Catenin
α-Myc
α-HBx
α-GAPDH
1 2 3

F

HA-HBX + +
Plk1i - +

WB
α-USP37
1 1.2
α-CDH1
α-HBx
α-GAPDH
1 2
Figure S3. Regulation of USP37 under HBx microenvironment. Huh7 cells were transfected with indicated recombinants and western blotted for the expression of specific antigens: (A) transfection with vector or HA-CDH1 constructs and immunoblotting for USP37; (B) transfection with HA-CDH1, HA-HBx, Sc-shRNA and/or Sc-shRNA and probing with α-USP37, α-Cdc6, α-HBx and α-HA antibodies; (C) transfection with vector, Flag-Emi1 and HA-HBx and western blotting with α-USP37, α-Flag and α-HBx antibodies; (D) transfection with vector and Myc-β-TrcP constructs and western blotting for USP37; (E) transfection with combinations of Myc-β-TrcP, HA-HBx, Sc-shRNA and X-E-shRNA as indicated and western blotted with α-USP37 and α-β-catenin antibodies; (F) transfection with HBx, treated with PLK1 inhibitor SBE13 hydrochloride (100µM) for 8h, and western blotted for USP37 and CDH1. GAPDH levels were used for normalization in the above panels.
Figure S4

**A**

<table>
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<th>X-E shRNA</th>
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<tr>
<td>Bait</td>
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<tr>
<td>Prey</td>
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**Cellular Fraction**

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</table>

**WB**

- α-USP37
- α-Histone H1
- α-GAPDH
- α-HBx

**B**

<table>
<thead>
<tr>
<th></th>
<th>Vector</th>
<th>Sc-shRNA</th>
<th>HA-HBx</th>
<th>X-E shRNA</th>
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<tbody>
<tr>
<td>Control</td>
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<tr>
<td>Bait</td>
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**WB**

- α-Flag
- α-HBx

**C**

<table>
<thead>
<tr>
<th></th>
<th>HA-HBx</th>
<th>Flag-USP37</th>
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<tbody>
<tr>
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<tr>
<td>Bait</td>
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<td>+</td>
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<tr>
<td>Prey</td>
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**WB**

- α-USP37
- α-HBx

**Input**

- α-Flag
- α-HA

**IP**

- Flag
- HA

**WB**

- 1
- 2
- 3
- 4
Figure S4. Intracellular distribution of USP37 and its interaction with HBx. (A) HEK293T cells were transfected with vector, HA-HBx, Scrambled (Sc)-shRNA and X-E shRNA constructs, and the nuclear (N) and cytoplasmic (C) fractions of cells were western blotted with USP37, Histone H1, HBx and GAPDH antibodies. (B) Amylose beads were bound with recombinant MBP (Control) or HBx-MBP fusion proteins (Prey) and incubated with cell lysates from HEK293T cells transfected with vector or Flag-USP37 (Bait). Eluted immuno-complexes were western blotted with α-Flag and α-HBx antibodies. (C) Cell lysates of Huh7 cells overexpressing HA-HBx and Flag-USP37 were immunoprecipitated using α-Flag and α-HA antibodies as indicated. Eluted immuno-complexes were western blotted with α-USP37, α-HBx, α-HA and α-Flag antibodies.