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**Supplement Figure 1. Effects of UBE1L suppression on HBV production in HepG2.2.15 cells.** UBE1L knockdown was performed by RNAi to abrogate baseline ISGylation in HepG2.2.15 cells. **(A)** Knockdown efficiency was determined by real-time PCR showing UBE1L mRNA expression 24h after 50nM negative siRNA or 50nM UBE1L siRNA treatment. **(B)** Supernatant HBV DNA, intracellular **(C)** pgRNA and **(D)** total HBV DNA were determined by real-time PCR at 48h or 72h after UBE1L siRNA transfection. Mock, siRNA transfection reagent treatment only; 50nM negative siRNA, transfected with 50 nM negative siRNA; 50nM UBE1L siRNA, transfected with 50 nM UBE1L siRNA. The results are presented as the means  $\pm$ SD,  $n \geq 3$ , error bars indicate SD.

**Supplement Figure 2. Effects of UBE1L suppression on HBV protein expression in HepG2.2.15 cells.** UBE1L knockdown was performed by RNAi to abrogate baseline ISGylation in HepG2.2.15 cells. Culture medium was collected 48h after to detect **(A)** HBsAg and **(B)** HBeAg by ELISA, respectively. Total protein was collected at 48h or 72h after UBE1L siRNA transfection to assess **(C)** intracellular HBcAg by western blot. Mock, siRNA transfection reagent treatment only; negative siRNA, transfected with 50 nM negative siRNA; UBE1L siRNA, transfected with 50 nM UBE1L siRNA. The results are presented as the means  $\pm$ SD,  $n \geq 3$ , error bars indicate SD.

# Supplement Figure 1



