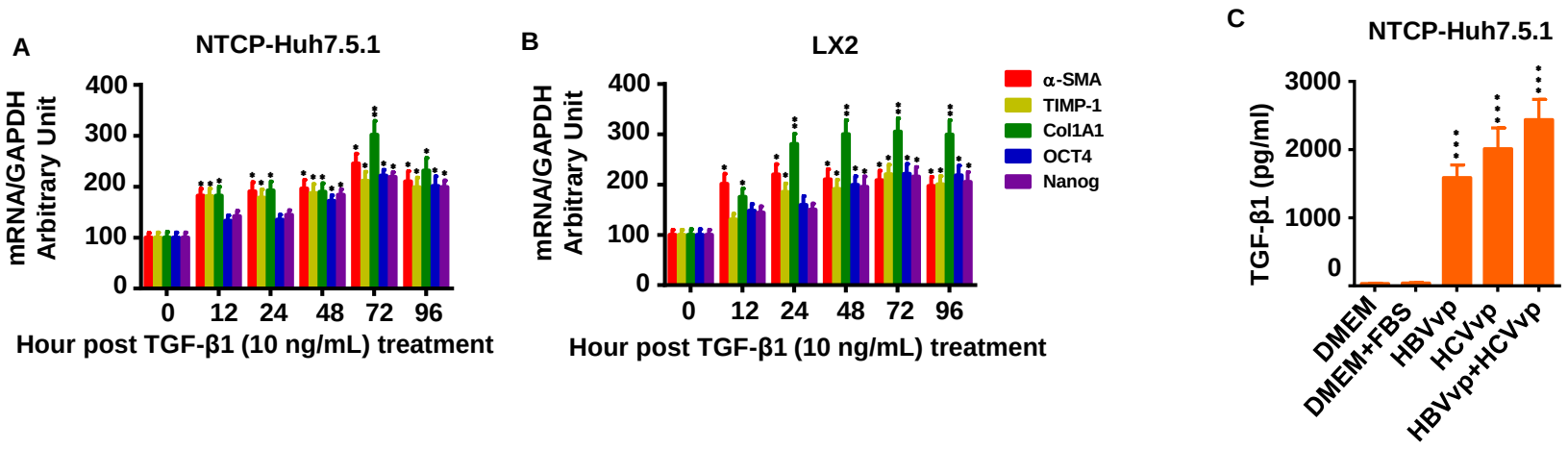
Supplemental Information

Supplemental Figure 1.



Supplemental Figure 1. TGF-β1 increases OCT4/Nanog and fibrosis-related gene expression in NTCP-Huh7.5.1 and LX2 cells. NTCP-Huh7.5.1 or LX2 cells (30,000 cell /well in 1 mL) were seeded into 24-well plates and incubated with 10 ng/mL TGF-β1 for 0-96 hours. mRNA expression of fibrosis-related genes in NTCP-Huh7.5.1 and LX2 cells were detected by qPCR and normalized to GAPDH. NTCP-Huh7.5.1 were also infected HBV/HCVvp and TGF-β1 level from supernatant was detected by ELISA Kits.

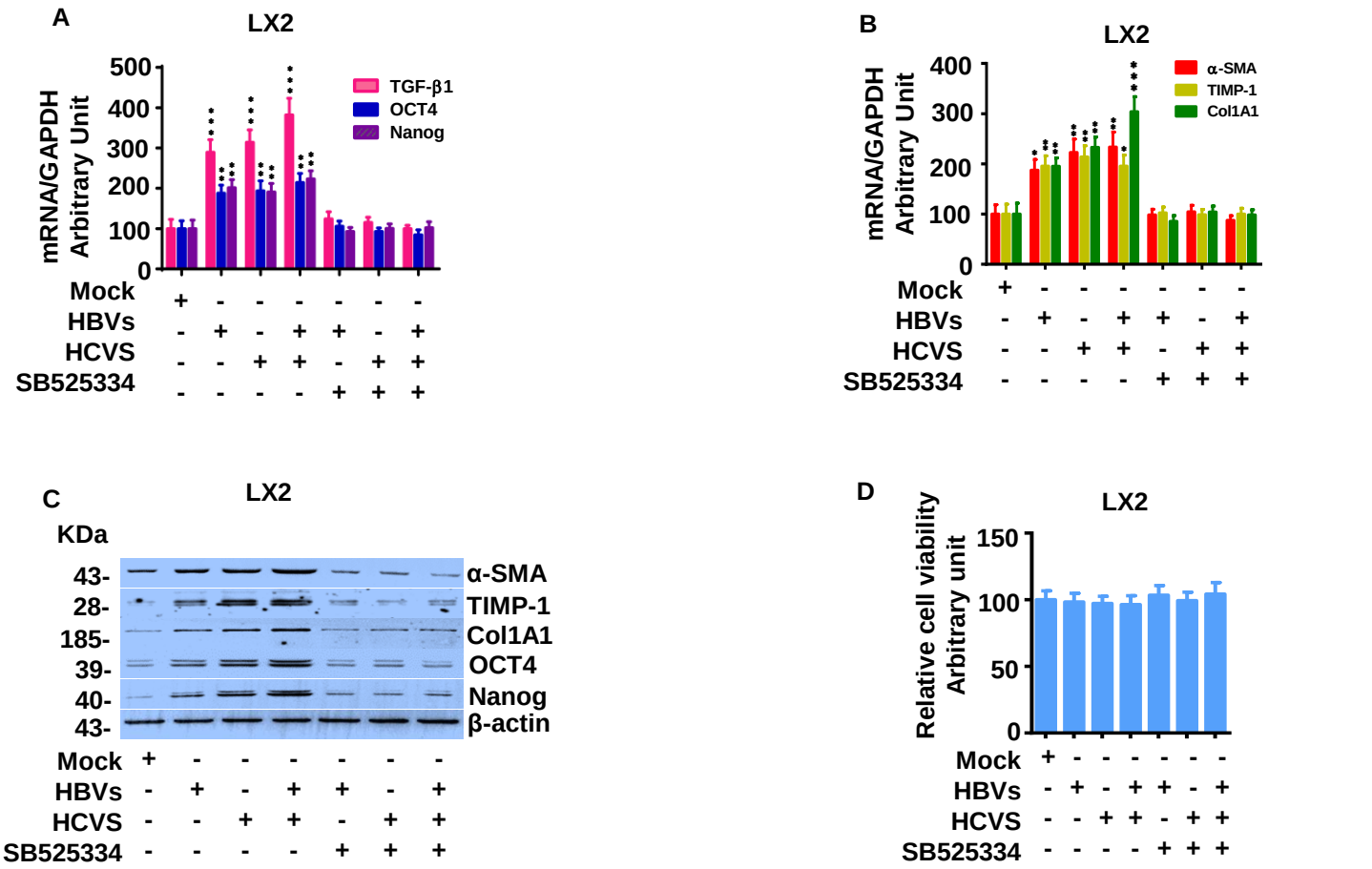
(**A**) TGF-β1 treatment enhanced α-SMA, TIMP-1,Col1A1, OCT4 and Nanog mRNA expression in NTCP-Huh7.5.1 cells.

(**B**) TGF-β1 treatment enhanced α-SMA, TIMP-1,Col1A1, OCT4 and Nanog mRNA expression in LX2 cells.

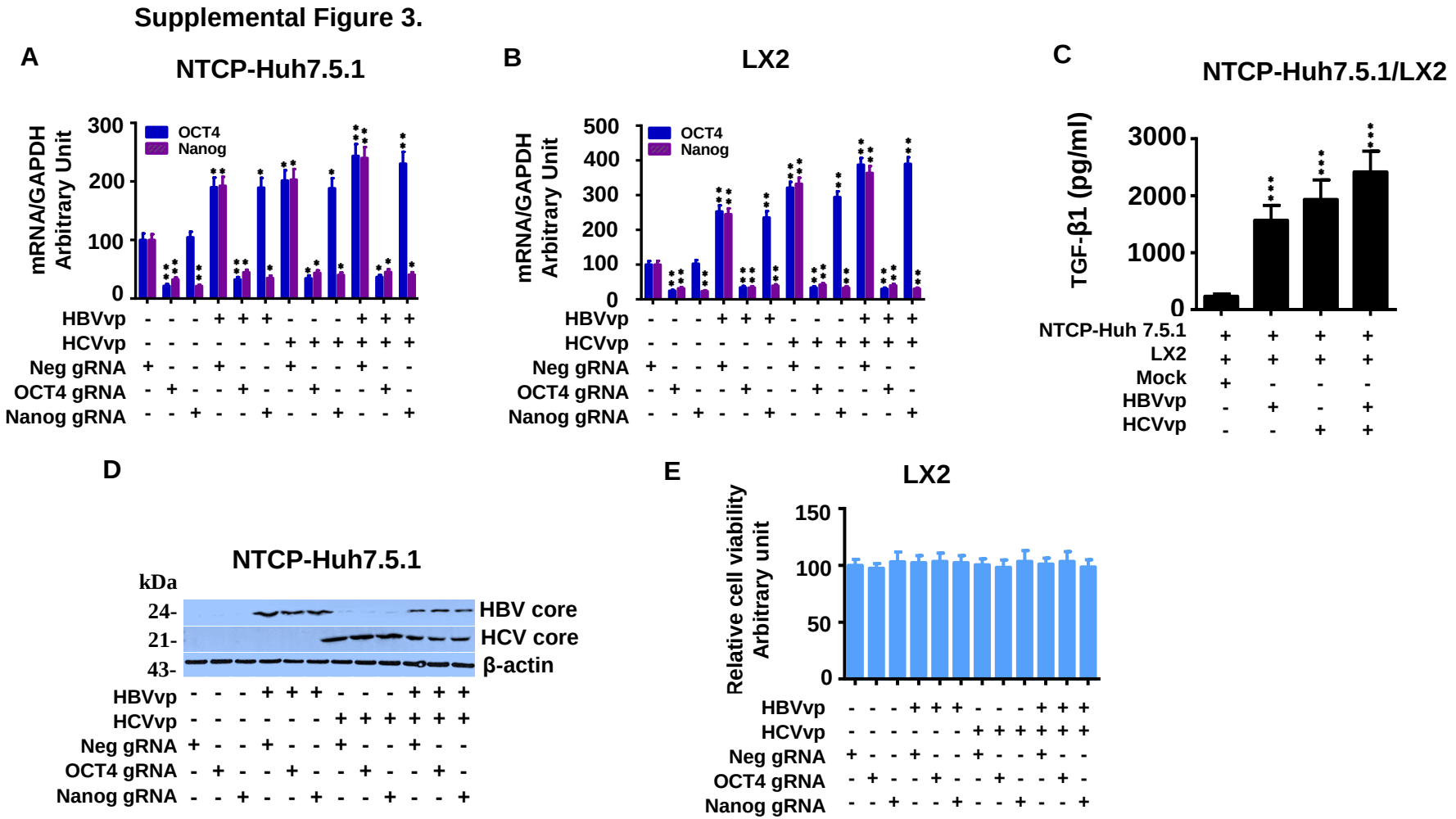
(**C**) HBVvp, HCVvp or HBVvp/HCVvp infection in NTCP-Huh7.5.1 cells significantly increased TGF-β1 levels in supernatant.

Data are representative of 3 independent experiments with similar results. Bars represent means ± SD of 3 biological repeats. *, $p < 0.05$. **, $p < 0.01$. ***, $p < 0.001$.

Supplemental Figure 2.



Supplemental Figure 2. TGF-β1 inhibitor (SB525334) blockes HBVs-/HCVs-induced activation of OCT4/Nanog and fibrosis-related genes in LX2 cells. LX2 cells (30,000 cell/well in 1 mL) were seeded into 24 well-plates. 100 µL of HBVs, HCVs, TGF-β1 inhibitor (SB525334, 1 µM final) or uninfected supernatant was added to the appropriate well for 72 hours. Cell lysates were harvested for mRNA and protein analyses or cell viability assays.
(**A**). TGF-β1 inhibitor (SB525334) blocked HBVs-, HCVs- and (HBV/HCV)s induced activation of TGF-β1, OCT4 and Nanog mRNA expression in LX2 cells.
(**B**). TGF-β1 inhibitor (SB525334) blocked HBVs-, HCVs- and (HBV/HCV)s induced activation of α-SMA, TIMP-1, and Col1A1 mRNA expression in LX2 cells.
(**C**). TGF-β1 inhibitor (SB525334) blocked HBVs-, HCVs- and (HBV/HCV)s induced activation of α-SMA, TIMP-1, Col1A1, OCT4 and Nanog in LX2 cells.
(**D**) TGF-β1 inhibitor (SB525334) did not significantly affect LX2 cell viability.
Data are representative of 3 independent experiments with similar results. Bars represent means ± SD of 3 biological repeats. *, $p < 0.05$. **, $p < 0.01$. ***, $p < 0.001$.



Supplemental Figure 3. OCT4 and Nanog gRNA reduce HBV/JFH1-HCV-induced OCT4/Nanog upregulation in NTCP-Huh7.5.1 and LX2 cells in a coculture system Methods were described in Fig 7.

(**A**). OCT4/Nanog gRNA inhibited HBV- or HCV-induced OCT4/Nanog upregulation in NTCP-Huh7.5.1 cells.

(**B**). OCT4/Nanog gRNA inhibited HBV- or HCV-induced OCT4/Nanog upregulation in LX2 cells.

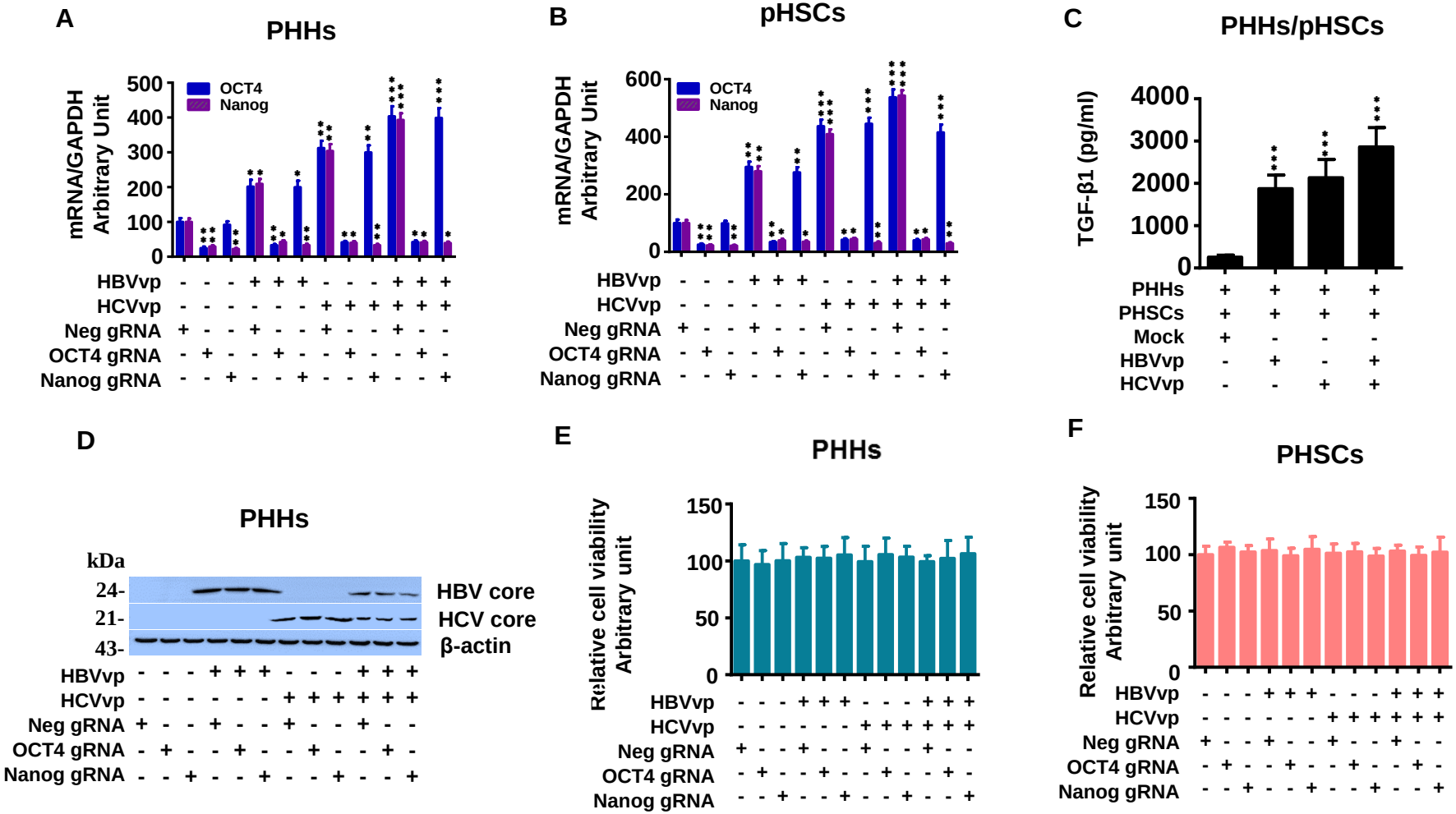
(C). HBVvp/HCVvp infection upregulated TGF-β1 levels in the supernatant of NTCP-Huh7.5.1/LX2 coculture system. TGF-β1 levels were detected by ELISA kits.

(**D**). Western blot for HBV core or HCV core confirmed the replication of HBV or HCV in NTCP-Huh7.5.1 cells in the NTCP-Huh7.5.1/LX2 coculture model.

(**E**). OCT4 gRNA and Nanog gRNA or HBVvp/HCVvp exposure did not significantly affect cell viability in LX2 cells. Cell viability was determined using the Cell Titer-Glo luminescent cell viability assay kit (Promega, Madison, WI) according to the manufacturer's instructions.

Data are representative of 3 independent experiments with similar results. Bars represent means ± SD of 3 biological repeats. *, $p < 0.05$. **, $p < 0.01$. ***, $p < 0.001$.

Supplemental Figure 4.



Supplemental Figure 4. OCT4 and Nanog gRNA inhibite activation of OCT4/Nanog in the PHHs/pHSCs coculture HBV/HCV coinfection model. Methods were described in Fig 7

(**A**). OCT4/Nanog gRNA inhibited HBV or HCV infection in NTCP-Huh7.5.1 induced mRNA enhancement of OCT4/Nanog in PHHs in the coculture.

(**B**). OCT4/Nanog gRNA inhibited HBV or HCV infection in PHHs induced mRNA enhancement of OCT4/Nanog in pHSCs in the coculture.

(**C**). HBV or HCV infection in PHHs cells increased soluble TGF-β1 levels in PHHs /pHSCs coculture.

(**D**). Western blot for HBV core or HCV core confirmed the replication of HBV or HCV in PHHs in coculture model.

(**E**). OCT4 gRNA and Nanog gRNA did not significantly affect cell viability of PHHs in PHHs /pHSCs coculture.

(**F**). OCT4 gRNA and Nanog gRNA did not significantly affect cell viability of PHSCs in PHHs/PHSCs coculture.

Data are representative of 3 independent experiments with similar results. Bars represent means ± SD of 3 biological repeats. *, $p < 0.05$. **, $p < 0.01$. ***, $p < 0.001$.