Fig S1

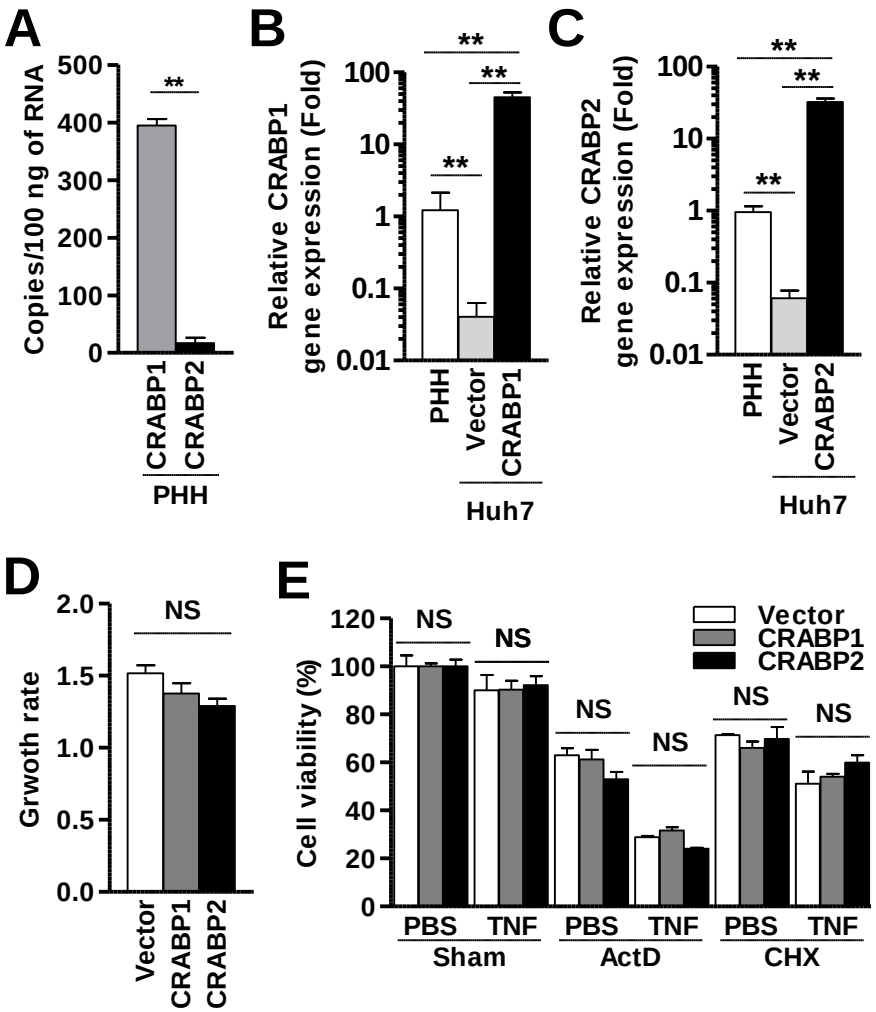

Fig S1. Expression of CRABPs on PHH and Huh7. (A) Total RNA extracted from PHH (n=3) were used for RT-qPCR analysis for the assessment of CRABP1 and 2 gene abundances. **p<0.01. **(B-C)** Total RNA extracted from PHH (n=3) and Huh7 cells stably expressing FLAG-tagged CRABPs were used for RT-qPCR analysis for the assessment of CRABP1 (B) and 2 (C) genes relative expression. **p<0.01. **(D)** Huh7 cells stably expressing FLAG-tagged CRABPs were cultured for 72 hours followed by the assessment of cellular proliferation every 24 hours. The growth rate was determined by the average cell viability. **(E)** Huh7 cells stably expressing FLAG-tagged CRABPs were treated with TNF in the absence or presence of ActD or CHX for 24 hours followed by the cell viability assessment. NS: Not Significant.

Fig S2

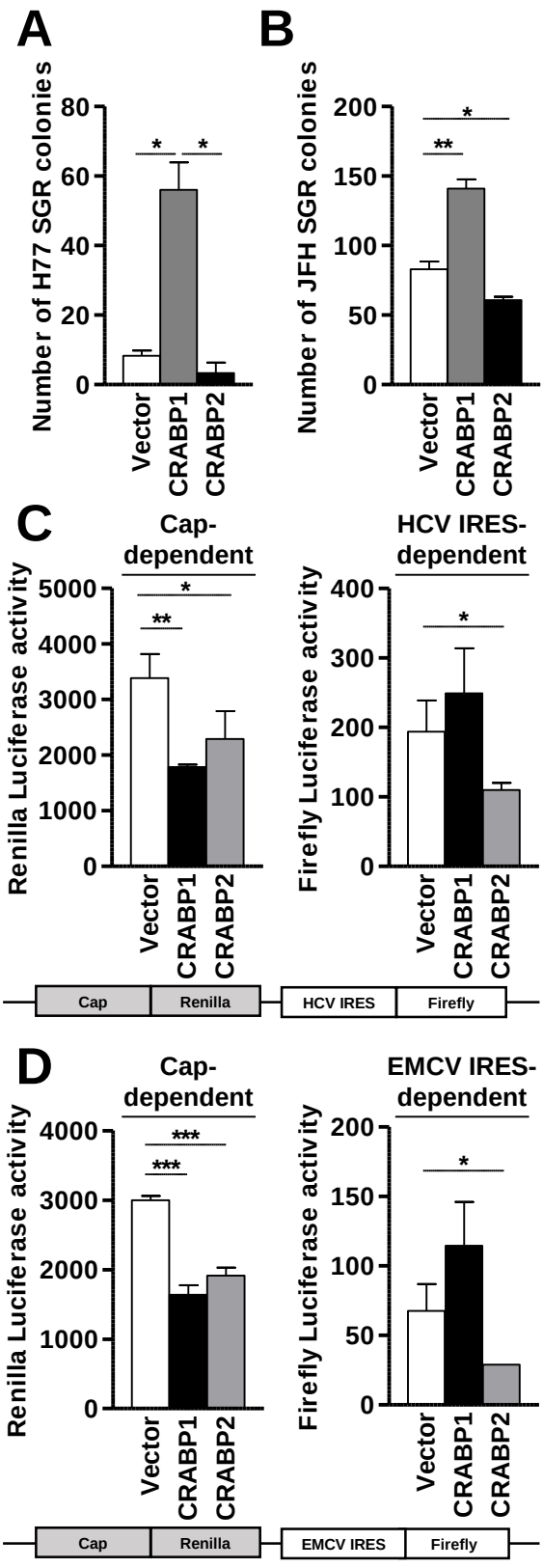

Fig S2. CRABPs regulation of IRES-dependent translation. (A-B) Huh7 cells stably expressing CRABPs were electroporated with in vitro transcribed HCV subgenomic replicon (SGR) genome (GT1a H77(A) and GT2a JFH1 (B)) followed by G418 selection for 3 weeks prior to the crystal violet staining. The graph indicates the number of SGR-containing colony numbers per 100mm tissue culture dish. *p<0.05 and **p<0.01 **(C-D)** Huh7 cells stably expressing CRABPs were transfected with the bicistronic vector encoding cap-dependent Renilla and HCV IRES-dependent firefly luciferase as indicated in the diagram under the bar graph. Cap-dependent protein translation (Left panel) or IRES-dependent protein translation (Right panel) were assessed by the Renilla or HCV IRES-dependent firefly luciferase activity, respectively (C) or by the Renilla or EMCV IRES-dependent firefly luciferase activity (D). *p<0.05, **p<0.01 and ***p<0.001

Fig S3

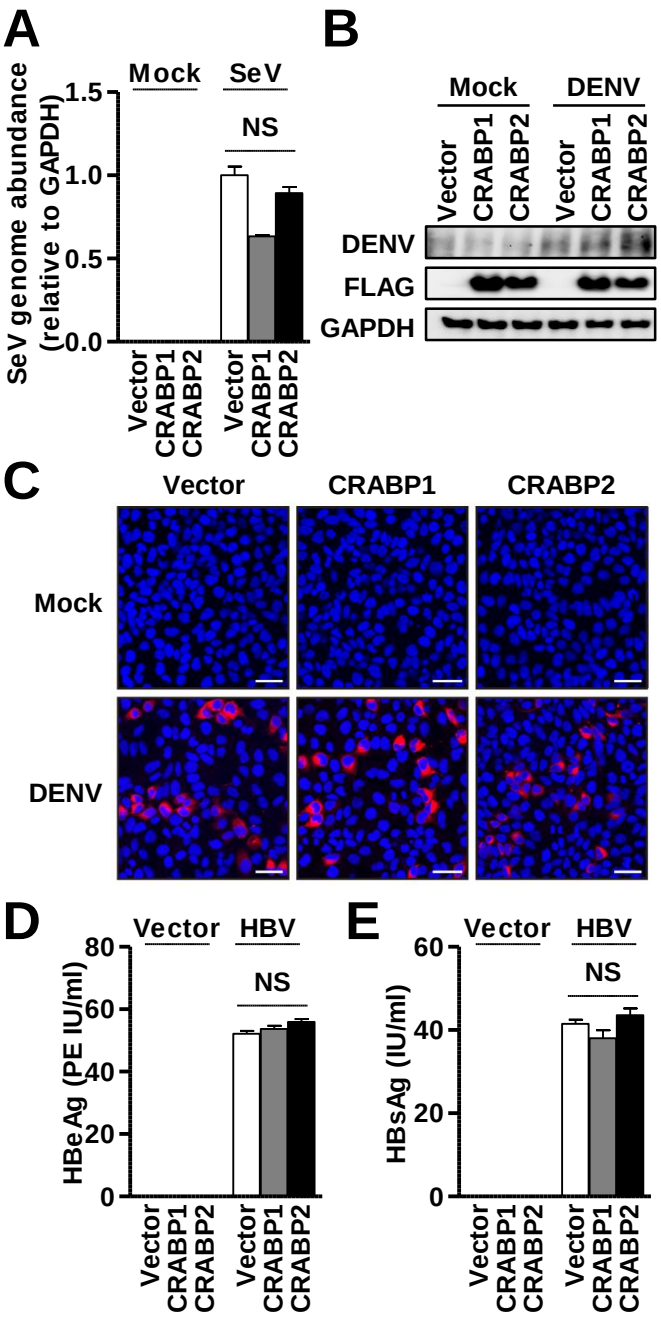

Fig S3. CRABPs regulation of viral infection. **(A)** Cell lysates from Huh7 cells stably expressing CRABPs infected with SeV at 100 HAU/ml for 24 hours were subjected to assessment of viral genome abundance via RT-qPCR. **(B-C)** Cell lysates from Huh7 cells stably expressing CRABPs infected with DENV at MOI 0.2 for 72 hours were subjected to to immunoblotting analysis for the detection of DENV (B) and the cells were stained with DENV (red), and DAPI (blue) at 48 hours after DENV infection (C). Scale bar 50μm. **(D-E)** Huh7 cells stably expressing CRABPs were transfected with p1.3x HBV DNA encoding plasmid (HBV) or control vector (Vector;pUC19) for 48 hours, followed by ELISA for the detection of HBV e-antigen (HBeAg) (D) and hepatitis B s-antigen (HBsAg) (E) in the culture supernatants. NS: Not significant.

Fig S4

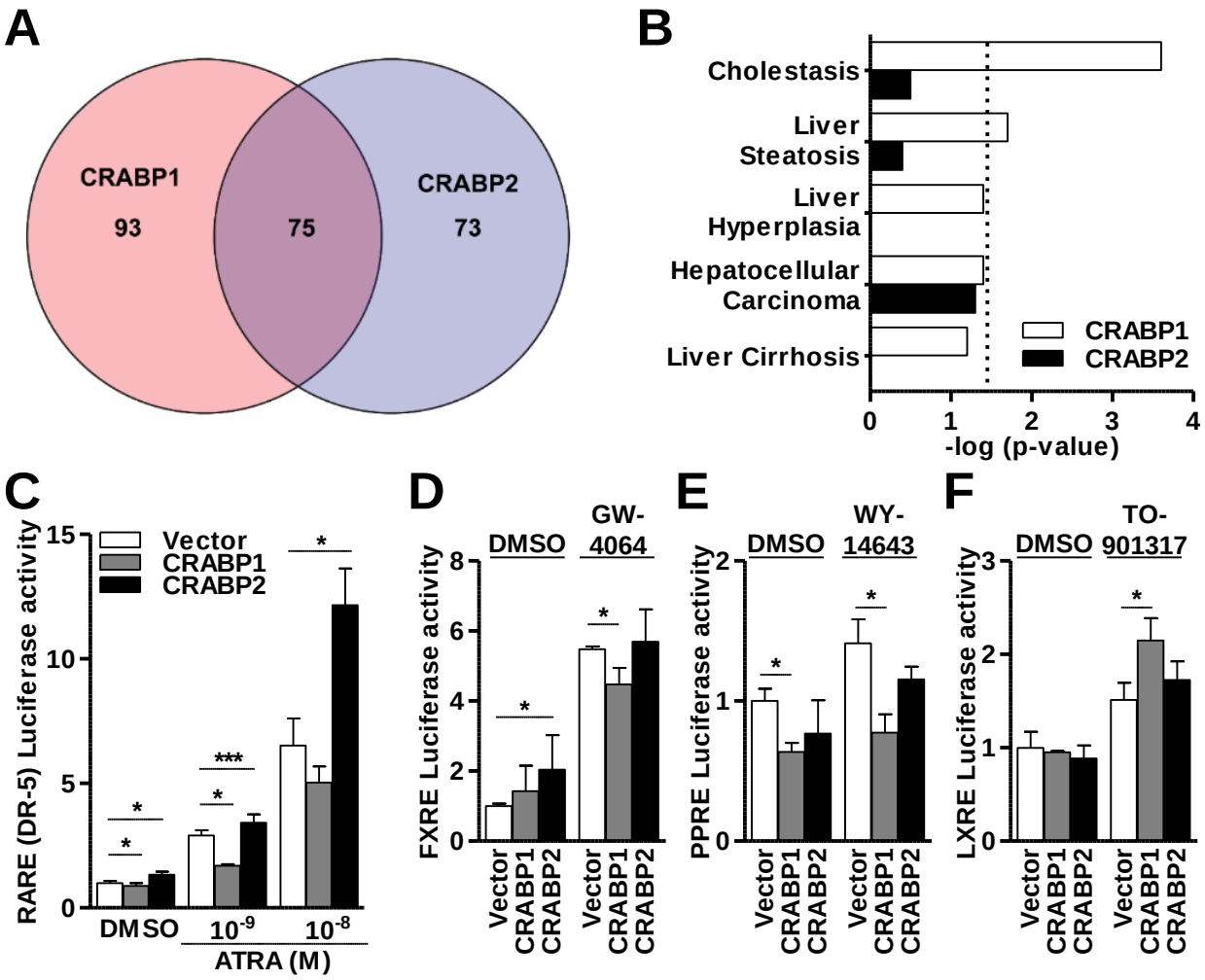

Fig S4. Cellular response to CRABPs expression. (A) Venn diagram demonstrates the number of differentially expressed genes in CRABP1 or 2-expressing Huh7 cells that were determined by the mRNA sequencing analysis shown in Fig 4A. **(B)** The uniquely and differentially expressed genes in Huh7-CRABP1 or 2 cells were analyzed for the disease association using IPA software. The dotted line indicates the statistical significance threshold. **(C-F)** Huh7 cells stably expressing CRABPs were co-transfected with firefly (FF) luciferase reporter construct that is regulated by indicated nuclear receptors along with CMV promoter regulated Renilla luciferase (RL) expression plasmid. 24 hours after the transfection, the cells were treated with the indicated agonists for 24 hours, followed by Dual Luciferase assay. RLU was calculated by the ratio of FF/RL. Agonists: ATRA (1μM) for RARE agonist (C), GW4064 (10μM) for FXRE agonist (D), WY-14643 (100μM) for PPRE agonist (E), and TO901317 (10μM) for LXRE agonist (F). *p<0.05 and ***p<0.001

Fig S5

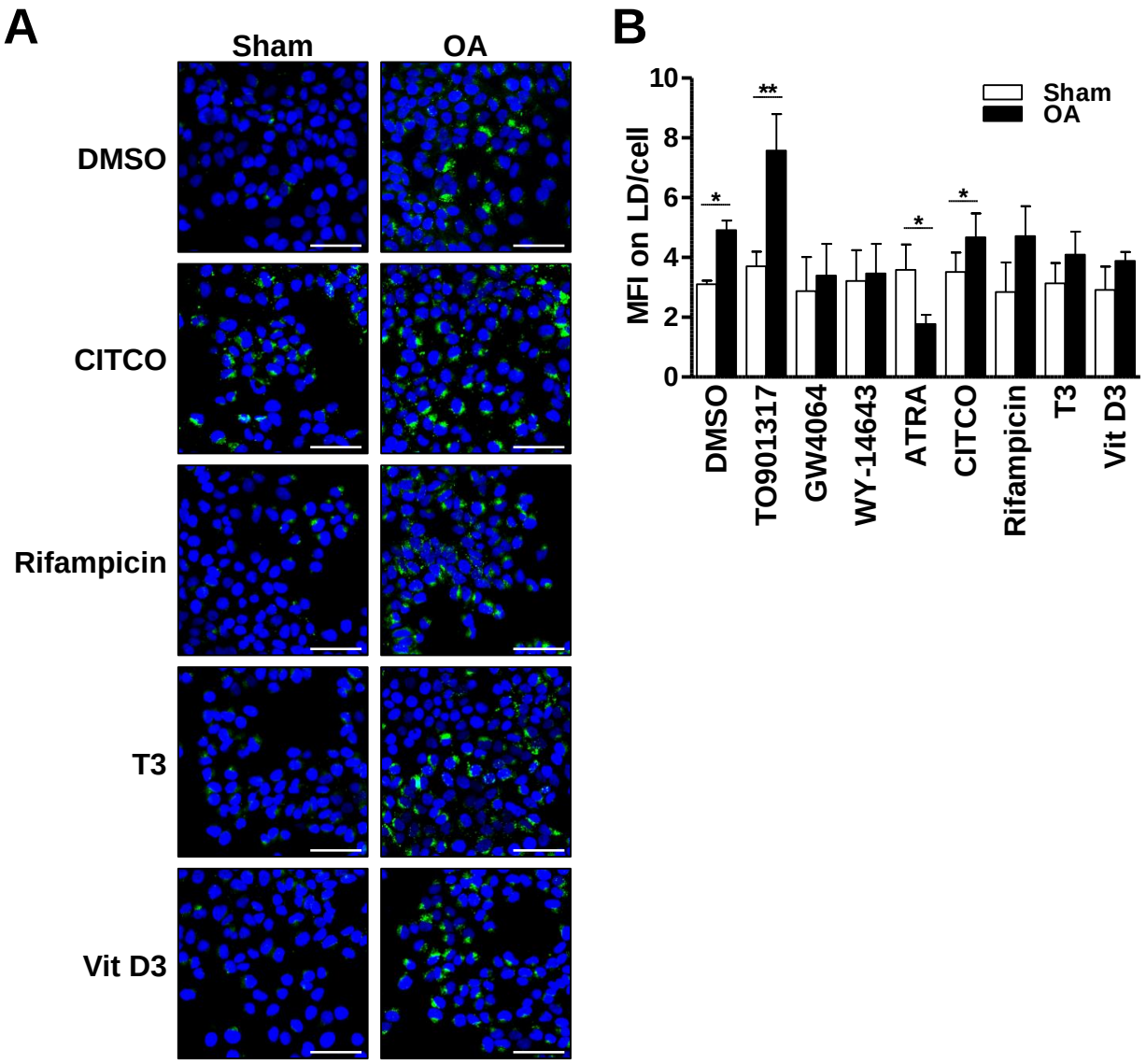

Fig S5. Nuclear receptor pathway regulation of LD abundance. (A) Huh7 cells were cultured with indicated nuclear receptor agonists (CAR: CITCO (10μM), PXR: Rifampicin (10μM), TR: T3 (1μM), VDR: Vit D3 (0.1μM)) for 72 hours in the presence of OA (50μM) followed by BODIPY (green) and DAPI staining for the fluorescence microscopic analysis. Scale bar 100μm. **(B)** The abundance of LD in the NR ligands treated cells were quantified as median fluorescence intensity (MFI) of 100 representative cells. The treatment condition for the each ligand is described in Fig 5D and S5A.

Fig S6

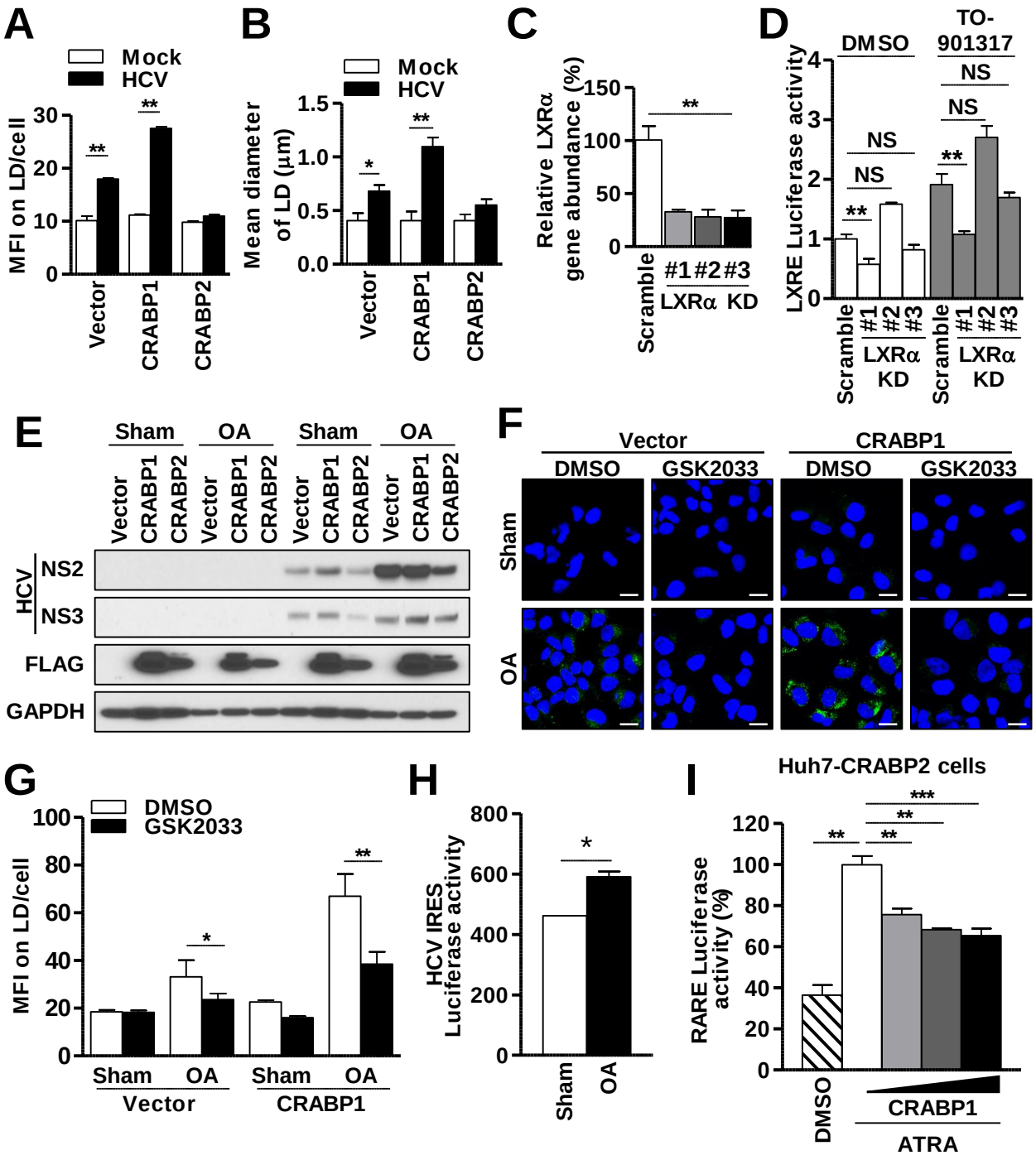
A
Mock
HCV
MFI on LD/cell
Vector
CRABP1
CRABP2
B
Mock
HCV
Mean diameter of LD (μm)
Vector
CRABP1
CRABP2
C
Relative LXRα gene abundance (%)
Scramble
#1#2#3
LXRα KD
D
DMSO
TO-901317
LXRE Luciferase activity
NS
Scramble
#1
#2
#3
LXRα KD
E
Sham
OA
Vector
CRABP1
CRABP2
HCV
NS2
NS3
FLAG
GAPDH
F
Vector
CRABP1
DMSO
GSK2033
Sham
OA
G
DMSO
GSK2033
MFI on LD/cell
Sham
OA
Vector
CRABP1
H
HCV IRES Luciferase activity
Sham
OA
I
Huh7-CRABP2 cells
RARE Luciferase activity (%)
DMSO
CRABP1
ATRA

Fig S6. FFA regulation of HCV infection. (A-B) Huh7 cells stably expressing CRABPs were infected with HCV for 48 hours at MOI 0.1. Then, cells were stained with BODIPY (green), and DAPI (blue) to evaluate the size and abundance of LD in both uninfected and infected cells. The fluorescent microscopic image of 20 representative cells was used for the analysis of mean fluorescent intensity (MFI) per cell (A) and the mean diameter of LD (B). *p<0.05 and **p<0.01. **(C)** Huh7 cells stably expressing shRNA scramble or LXR-α (clone #1, 2, and 3) were subjected to RT-qPCR analysis of LXR-α gene abundance. The relative abundance was normalized by GAPDH and shown in % reduction to the scramble shRNA expressing cells. **(D)** LXRE-Luc plasmid along with CMV-promoter driven renilla luciferase plasmid were transfected to Huh7 cells stably expressing shRNA scramble or LXR-α (clone #1, 2, and 3) followed by LXR-agonist (10μM) treatment for 24 hours. Then cell lysates were subjected to dual luciferase assay. **(E)** Huh7 cells stably expressing CRABPs were pretreated with OA (100μM) for 24 hours, followed by HCV infection (MOI 0.1) for 48 hours. Cell lysates were subjected to immunoblotting analysis for the detection of the indicated proteins. **(F-G)** Huh7 cells stably expressing CRABPs were pretreated with GSK2033 for 24 hours, followed by OA (50μM) treatment for 24 hours. The cells were stained with LD with BODIPY (green), and DAPI (blue) to evaluate LD formation. Scale bar 20μm (F). The abundance and size of LD in CRABP1-expressing cells were quantified as median fluorescence intensity (MFI) and diameter of LD in 20 representative cells (G). *p<0.05 and **p<0.01 **(H)** Huh7 cells transfected with bicistronic luciferase reporter plasmid (Cap-dependent Renilla- and HCV IRES-dependent firefly luciferase protein translation) for 16 hours followed by OA (100μM) treatment for an additional 48 hours. Cell lysates were subjected to dual-luciferase assay. HCV-IRES activity was determined by the normalization of Firefly luciferase activity with Renilla luciferase activity. *p<0.05. **(I)** CRABP2-expressing Huh7 cells were co-transfected with increasing amount of CRABP1 expression plasmid (0, 25, 50, 100 ng), RARE luciferase plasmid, and Renilla luciferase reporter plasmids for 8 hours followed by ATRA (0.01μM) treatment for 40 hours. The cell lysates were subjected to dual luciferase assay for the assessment of RAR-RXR activity. **p<0.01 and ***p<0.001.

Fig S7

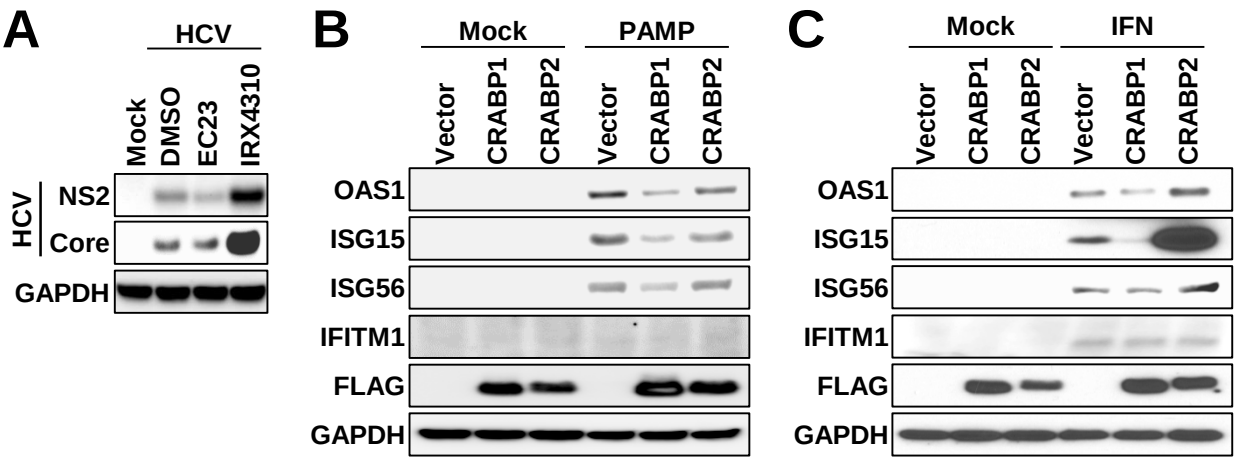

Fig S7. RAR-RXR pathway regulation of HCV. (A) Huh7 cells were treated with synthetic RAR agonist (EC23, 1μM) or RAR antagonist (IRX4310, 1μM) for 72 hours, followed by HCV infection at MOI 0.1 for 48 hours. Cell lysates were subjected to immunoblotting analysis for the abundance assessment of the indicated proteins. **(B-C)** Huh7 cells stably expressing CRABPs were either transfected with HCV PAMP (B) or treated with IFNβ (C) for 24 hours followed by immunoblotting analysis for the detection of the indicated proteins.

Table S1. List of genes uniquely regulated by the expression of CRABP1

Huh7- CRABP1		
Up	**Down**	
ADAMTS12	A1BG	KYNU
ADAMTS9	ABCC3	LAMP3
AMOT	ABHD17C	LBP
B4GALNT4	AKR1B10	LGALS3BP
COL26A1	ALDH3B1	MAN2C1
COLGALT2	ALDH8A1	MICALL2
DUSP4	ALS2CL	MMP23B
FGFR1	ANKDD1A	MOGAT3
FSCN1	ANKRD23	MST1
IL1RN	ANO7	MST1L
LINGO1	ARAP3	MST1P2
LIPG	ATG16L2	NEURL1B
LPAR1	BTBD8	NGEF
LSR	CASP1	PAQR6
LYPD6B	CCDC88B	PARP11
MTCL1	CD47	PGC
NFIC	CD68	PI3
NTS	CIDEC	PLIN5
SLC25A18	CPT1B	PNPO
TNFSF4	DBH	PRKCZ
UNC5B	DZIP1	RCN3
	EFHD1	RIMKLA
	FOXG1	SHANK3
	FSIP2	SIMC1
	GABRG2	SLC2A9
	GBA3	SLC5A9
	GOLGA8IP	SPTBN5
	GOLGA8S	TENM1
	GPHN	TJP3
	GSTA1	TNFSF11
	HK1	TYMSOS
	HKDC1	WISP3
	IFT27	YJEFN3
	IL22RA1	ZNF175
	KLHL26	ZNF337

Table S2. List of genes uniquely regulated by the expression of CRABP2

Huh7- CRABP2		
Up		Down
CCDC110	PSAPL1	AK4P3
CDH17	PTN	ATP1B2
CDKN1A	RBP2	DNASE1L2
CDS1	REEP1	HHIPL1
CLDN2	RIMBP3	LDOC1
COL12A1	SEMA6D	MAB21L2
CREB3L1	SERPINE2	MT-RNR1
CYP2S1	SI	MTURN
DCHS2	SLC1A1	MYO1F
DIO1	SPARC	NOTUM
DMKN	SPDYE2	POTEJ
F2RL1	SPINT1	PPP1R3A
FMNL3	STK39	RELN
GCNT1	TAC3	SVEP1
GUCY2C	TFEC	VAMP1
HEPH	TFF2	RANBP3L
HEY1	TINAGL1	SAA1
HSPA12A	TMEM51	SAA2
ISX	TRIM2	SIAH3
KIAA1671	TRIM67	SLC23A1
LRP2	TRIM9	SLPI
MAGEA11	UNC93A	SMPD3
MALRD1	ZNF730	WWC3
MITF		ZMAT4
MUC13		
MUC3A		
MVP		
NODAL		
NOX1		
PARM1		
PLEKHB1		
PLG		
PODXL		
PPP1R14A		
PRDM1		

Table S3. List of genes commonly regulated by the expression of CRABP1 or 2

Huh7- CRABP1 or 2		
Up		Down
BCL2L10	RNF144A	ASGR1
C1orf140	RTN1	C4A
CES1	SHE	CCNY
CHRNA1	SLFN13	CDA
CMPK2	SMARCA2	DBNDD2
COL14A1	SNCAIP	EGF
COL2A1	SRSF12	F12
CTSE	TMCC3	F2RL2
DENND2A	TMEM130	FTCD
DPYSL3	TPD52L1	GC
EGLN3	TSPAN12	GFRA1
ELMO1	TSPAN5	LURAP1L
EPCAM	TUBB8P12	NEAT1
ESRRG	TUBBP5	PLIN4
FAM134B	TUSC3	RAB4B-EGLN2
FREM1	USP44	RANBP3L
FYN	ZNF511-PRAP1	SAA1
GPRIN3		SAA2
HUNK		SIAH3
INHBB		SLC23A1
IP6K3		SLPI
KCNJ8		SMPD3
KCNK2		WWC3
KIF7		ZMAT4
KRT19		
LFNG		
MRGPRF		
OSBPL10		
PBX1		
PDX1		
PITX2		
PLEKHA6		
PRNP		
PTPN22		