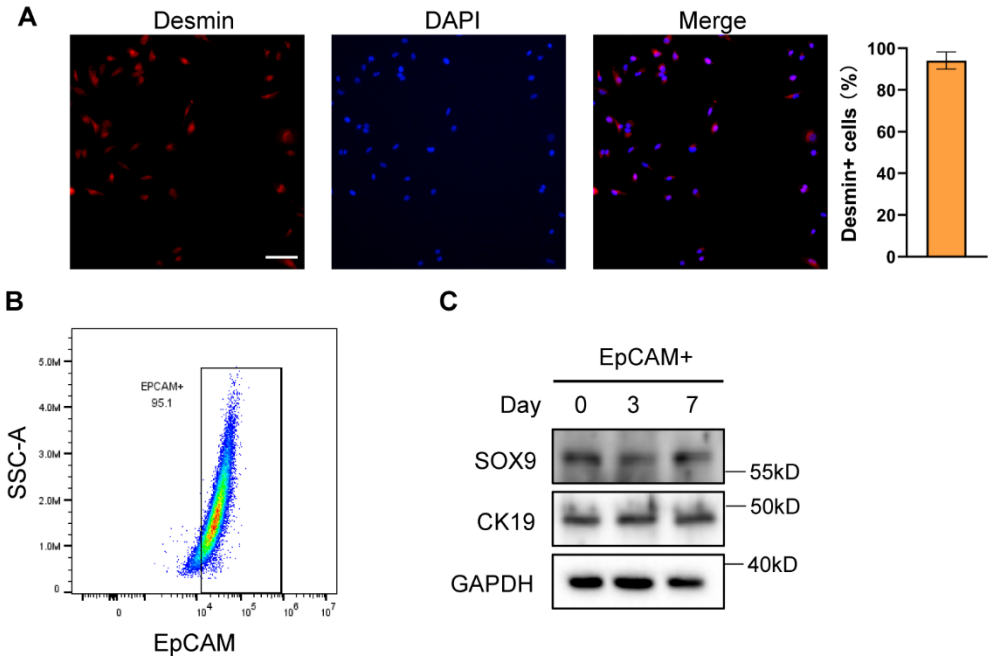
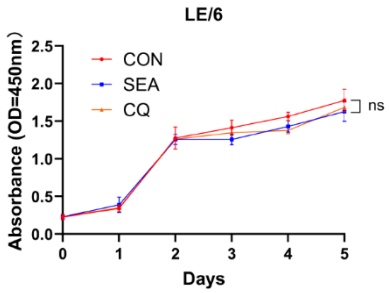
Supplementary Materials and Methods

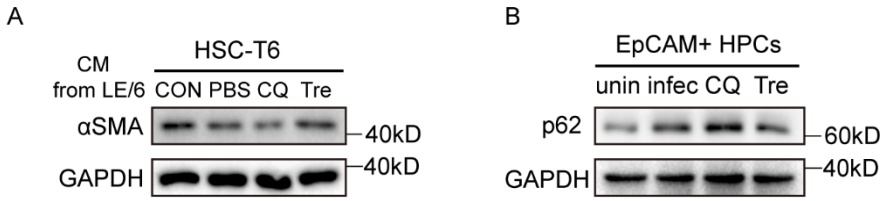


Supplementary Fig1 The purity of primary cells.

(A) The purity of primary HSCs was measured by desmin-positive cells. Desmin-positive cells were counted manually and expressed as the percentages of total cells by IF (n=3). Scale bar: 100μm. (B) The purity of EpCAM+ cells was detected through Flow cytometry. (C) Immunoblot showing CK19 and SOX9 levels in EpCAM+ cells cultured for 0, 3 and 7 days. Data were presented as mean ± SD. *$p < .05$, ** $p < .01$, *** $p < .001$; ns, not significant.

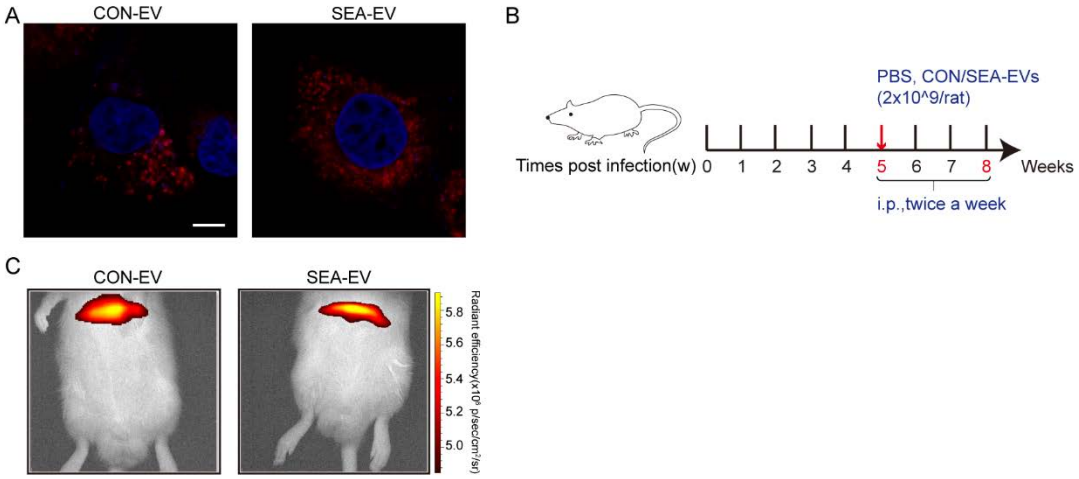


Supplementary Fig2 The effect of SEA or CQ on cell viability evaluated by CCK8 assay. (n=5)



Supplementary Fig3 Blocking autophagy ameliorates HPCs-associated fibrosis during *S. japonicum* infection

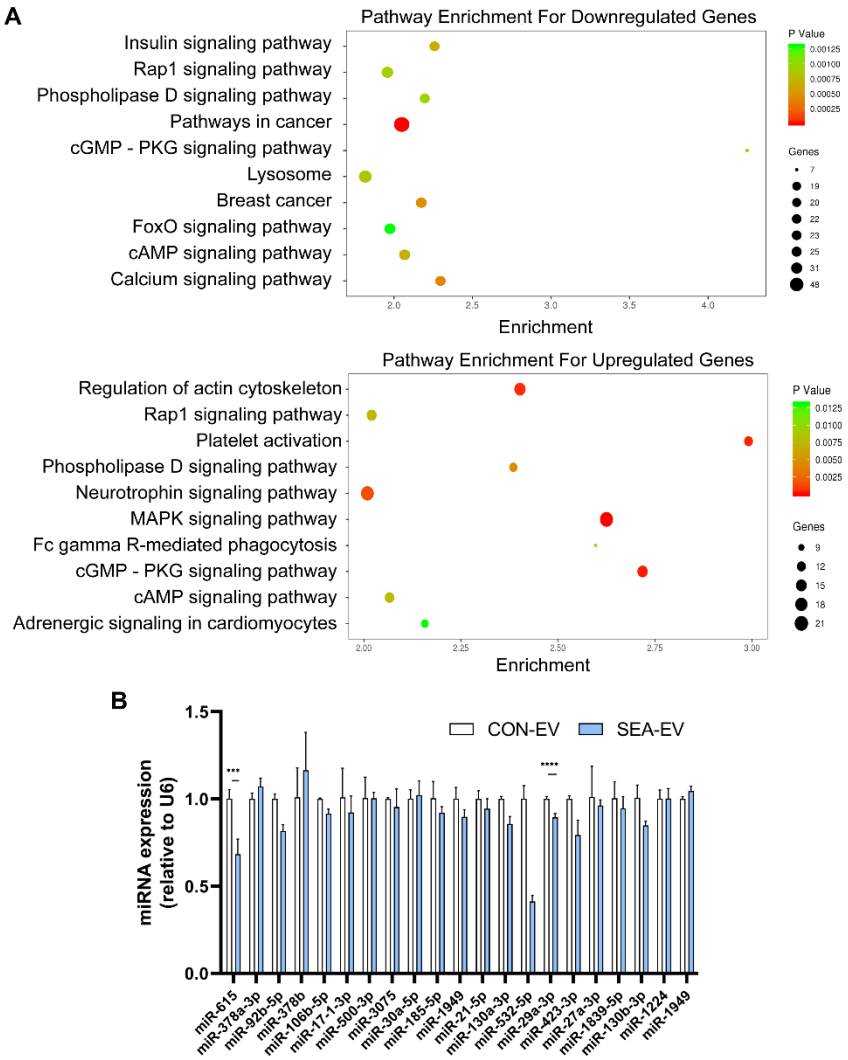
(A) αSMA was detected by WB in HSC-T6 co-cultured with conditioned medium (CM) from LE/6 stimulated with SEA, CQ, or Tre for 24h. (B) Verification of autophagy in primary HPCs by autophagy modulators. The expression of p62 was examined by WB in primary HPCs from normal or infected mice.



Supplementary Fig4 The uptake assay of EV

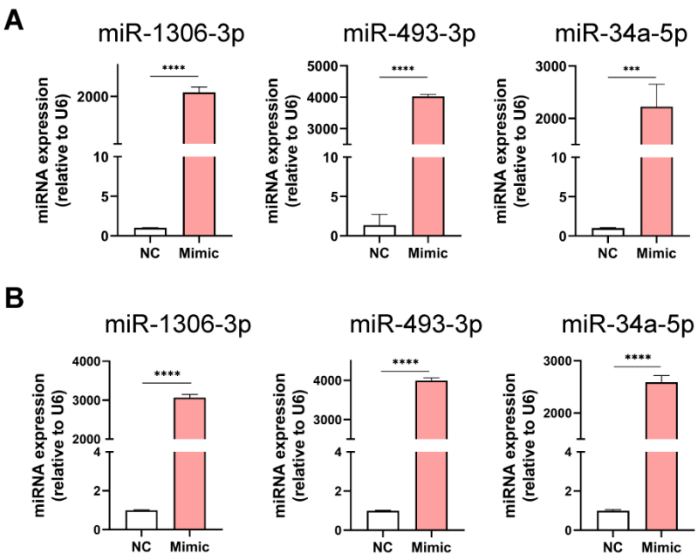
(A) Representative images indicated that PKH26 labeled EVs were taken up by HSC-T6s after 12h of incubation. Scale bar=10um. SD rats were infected percutaneously with 100 *S.japonicum* cercariae. At 5 weeks post-infection, infected rats were treated with PBS, CON-EVs or SEA-EVs (n=6) and were necropsied at 8 weeks post-infection. (B) Time schedule for parasite infection and administration of PBS, CON-EVs or SEA-EVs and sample withdrawal. (C) *In vivo* fluorescence microphotographs of

fluorescently labeled CON/SEA-EVs 24 hours after their administration intraperitoneally in rats.



Supplementary Fig5 miRNA sequencing for HPC-derived EVs

(A) Top 10 KEGG pathway enriched for upregulated and downregulated genes in EVs of miRNA sequencing data. (B) The expression of other miRNAs was examined in HSC-T6s cocultured with CON-EVs or SEA-EVs. Data were presented as mean ± SD. *$p < .05$, ** $p < .01$, *** $p < .001$; ns, not significant.



Supplementary Fig6 Verification of three miRNA mimics

(A) qPCR was performed to assess the level of miR-1306-3p, miR-493-3p, and miR-34a-5p in HSC-T6s transfected with miR-1306-3p, miR-493-3p, and miR-34a-5p mimic, respectively (n = 3). (B)qPCR was performed to assess the level of miR-1306-3p, miR-493-3p, and miR-34a-5p in LE/6s transfected with miR-1306-3p, miR-493-3p, and miR-34a-5p mimic, respectively. Data were presented as mean ± SD. *$p < .05$, ** $p < .01$, *** $p < .001$; ns, not significant.

Supplementary Table 1. Detailed information of antibodies used in this study.

Regent	Code	Vendor
GW4869	HY-19363	MCE
Lyso-Tracker Red	C1046	Beyotime
Chloroquine	C6628	Sigma
Rapamycin	HY-10219	MCE
Bafilomycin A1	54645S	CST

Trehalose	HY-N1132	MCE

Western blot：

Species	**Immunogen**	**Dilution**	**Code**	**Vendor**
Rat	CK19	1:1000	10712-1-AP	Proteintech
Rat	LC3B	1:1000	2775	CST
Rat	P62	1:1000	5114	CST
Rat	CTSD	1:1000	21327-1-AP	Proteintech
Rat	CTSB	1:1000	ab214428	Abcam
Rat	TFEB	1:1000	13372-1-AP	Proteintech
Rat	LAMP1	1:1000	ab24170	Abcam
Rat	Lamin A/C	1:1000	2032s	CST
Mouse/Rat	αSMA	1:1000	19245S	CST
Mouse/Rat	GAPDH	1:5000	KC-5G4	Kang Chen Bio-tech
Rat	COL1A1	1:1000	ab260043	Abcam
Rat	CTGF	1:500	sc-14939	Santa-Cruz
Rat	FIBRONECTIN	1:1000	610077	BD Biosciences
Rat	FOXO3	1:1000	sc-48348	Santa-Cruz
Rat	CD63	1:1000	sc-5275	Santa-Cruz
Rat	ALIX	1:1000	2171	CST
Rat	TSG101	1:1000	72312	CST

Rat	Calnexin	1:1000	ab133615	Abcam

IHC and IF staining:

Species	**Immunogen**	**Dilution**	**Code**	**Vendor**
Human/Mouse	CK19	1:200	10712-1-AP	Proteintech
Mouse	EPCAM	1:200	ab71916	Abcam
Human	OV-6	1:50	MAB2020	R&D
Mouse	SOX9	1:200	AB5535	Sigma-Aldrich
Mouse	Desmin	1:200	16520-1-AP	Proteintech
Human/Rat	αSMA	1:200	19245S	CST
Rat	CD63	1:100	sc-5275	Santa-Cruz
Rat	LC3B	1:200	14600-1-AP	Proteintech
Rat	LAMP1	1:200	ab24170	Abcam
Rat	GFP	1:100	sc-9996	Santa-Cruz
Rat	P62	1:200	66184-1-Ig	Proteintech

Supplementary Table 2. Primer sequences used in this study.

Species	Gene name	Forward Sequence（5’-3’）	Reverse Sequences （5’-3’）
Rat	αSMA	TGTGCTGGACTCTGGAG	GAAGGAATAGCCACGCT

		ATG	CAG
Rat	COL1A1	ATGTTCAGCTTTGTGGA	CAGCTGACTTCAGGGATG
		CCT	T
Rat	GAPDH	GGCATTGCTCTCAATGA	ATGTAGGCCATGAGGTCC
		CAA	AC
Rat	FOXO3	CCCGTCAGCCAGTCTAT	ACCAGTGAAGTTCCCCAC
		GCAA	GTT
Rat	ATP6V0	GCTGACGCACAGAACC	ACTGCCAAAGATCTCCAC
	B	CCA	GATG
Rat	ATP6V1	TCATTCTTGCAGCATTC	GCGAGTTTCTCTTTCCGT
	H	CGTA	TG
Rat	ATP6V0	TCGTGCCCTGGTTTATC	CGCCAGAATCGCAATCAG
	E1	CCCAA	CC
Rat	ATP6V0	TTGTCGGAGATGCTGGT	TGTGGAGAGGATTAGGG
	C	GTC	CCA