

Figure S1. M2 cells in glioblastomas tissues facilitate the migration and invasion of glioblastomas by transporting extracellular vesicles.

(A-D) The role of GW4869 on glioblastoma migration and invasion could be reversed by CD11b⁺/CD163⁺ cell-derived EVs.

(E-H) EMT markers' level in indicated groups by qRT-PCR and Western blot.

Figure S2. Characteristic of EVs isolated from M0 and M2 cells.

(A) Images of M0 and M2 derived EVs captured by transmission electron microscope.

(B-C) Size of EVs by nanoparticle tracking analysis.

(D) EVs markers detected by Western blot.

(E) EVs marked with PKH67 internalized by glioblastoma cells.

Figure S3. Characteristic of circ_0003137.

(A) Schematic illustration for the genomic loci of circ_0003137.

(B-C) Circ_0003137 RNA was resistant to RNase R.

(D) High circ_0003137 indicated poor survival of glioblastoma patients.

Figure S4. Role of circ_0003137 on glioblastoma EMT.

(A-D) The role of circ_0003137 on glioblastoma migration and invasion by Transwell assay.

(E-H) EMT markers' level in indicated groups by qRT-PCR and Western blot.

Figure S5. Role of circ_0003137 on parent gene and miRNAs.

(A-B) Role of circ_0003137 on CTNNB1 levels in glioblastoma cells by qRT-PCR and Western blot.

(C) RIP experiments were conducted using antibodies against AGO2 on extracts from glioblastoma cells.

Figure S6. Expression of 16 indicated RBPs in glioblastomas based on TCGA and CGGA.

Figure S7. Clinical features of PTBP1 in glioblastoma patients based on public databases.

(A-C) Clinical features of PTBP1 in glioblastoma patients based on TCGA.

(D-F) Clinical features of PTBP1 in glioblastoma patients based on CGGA.

Figure S8. Role of PTBP1 in glioblastoma progression.

(A-B) PTBP1 levels in glioblastoma tissues by qRT-PCR and Western blot.

(C-D) PTBP1 levels in glioblastoma cells by qRT-PCR and Western blot.

(E-F) PTBP1 levels by qRT-PCR analysis in glioblastoma cells transfected with sh-PTBP1 or corresponding negative control.

(G-J) Role of PTBP1 on glioblastoma migration and invasion by Transwell assay.

(K-L) EMT markers' level in indicated groups by qRT-PCR and Western blot.

Figure S9. Relationship between PTBP1 and COL4A1, PLOD1, VIM.

(A-D) Pearson correlation analysis showed a strong positive correlation between PTBP1 and PLOD3 based on TCGA.

(E-H) Pearson correlation analysis showed a strong positive correlation between PTBP1 and PLOD3 based on CGGA.

(I-K) RIP-qPCR analysis showed COL4A1, PLOD1, and VIM enrichment on PTBP1 in circ_0003137-overexpressed glioblastoma cells.

Figure S10. Clinical features of PLOD3 in glioblastoma patients.

(A-C) Clinical features of PLOD3 in glioblastoma patients based on TCGA.

(D-F) Clinical features of PLOD3 in glioblastoma patients based on CGGA.

Figure S11. Role of PLOD3 in glioblastoma progression.

(A-B) PLOD3 levels in glioblastoma tissues by qRT-PCR and Western blot.

(C-D) PLOD3 levels in glioblastoma cells by qRT-PCR and Western blot.

(E-F) PLOD3 expression by qRT-PCR in glioblastoma cells transfected with sh-PTBP1 or corresponding negative control.

(G-J) Role of PLOD3 on glioblastoma migration and invasion by Transwell assay.

(K-L) EMT markers' level in indicated groups by qRT-PCR and Western blot.

Figure S12. Role of PTBP1 in circ_0003137-regulated EMT progress.

(A-D) Migration and invasion ability of indicated glioblastoma cells by Transwell assay.

(E-H) EMT markers' level in indicated glioblastoma cells by qRT-PCR and Western blot.

Figure S13. Characteristics of the sh-circ_0003137-loaded nanoplatfrom system.

(A) Outline and size of the nanoplatfrom loaded with sh-NC or sh-circ_0003137 by TEM and Malvern Zetasizer NanoZS.

(B-C) Nanoplatfrom carried with sh-NC or sh-circ_0003137 can be phagocytosis by glioblastoma cells.

(D-G) Migration and invasion ability of glioblastoma cells treated with nanoplatfrom loaded with sh-NC or sh-circ_0003137 by Transwell assay.

(H-K) EMT markers' level in indicated glioblastoma cells by qRT-PCR and Western blot.

Figure S14. The sh-circ_0003137-loaded nanoplatfrom system could penetrate the BBB.

(A) Schematic illustration for the *in vitro* BBB model.

(B) Cumulative transport ratio of free FAM-sh-circ_0003137 and nanoplatfrom-carried FAM-sh-circ_0003137.

(C) Ability of glioblastoma cells to phagocytize shRNA in the BBB model by fluorescence microscopy.

(D) Images captured by fluorescence microscopy showed the distribution of FAM-shRNA in tumors formed by LN229.

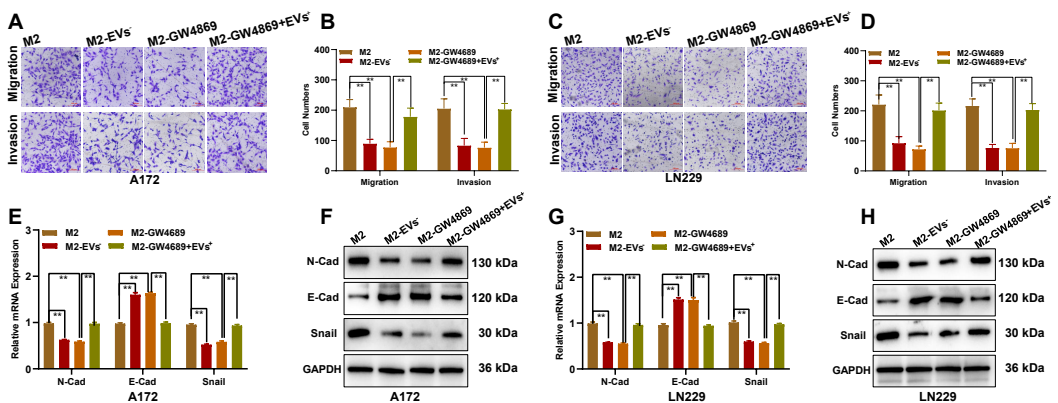
(E) H&E staining of major organs extracted from mice treated with nanoplatform, nanoplatform + sh-NC, or nanoplatform + sh-circ_0003137.

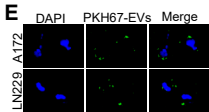
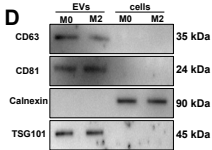
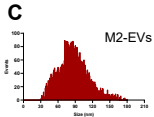
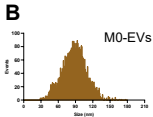
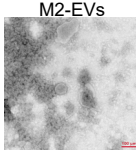
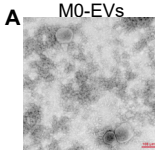
Table S1 The primers used in this study.

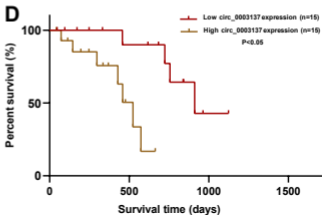
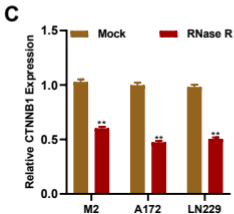
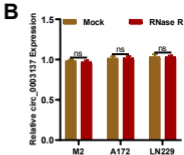
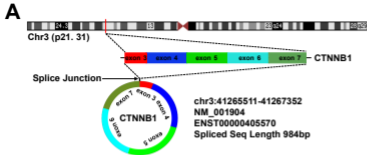
Table S2 The antibodies used in Western blot assay.

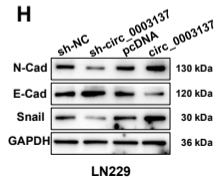
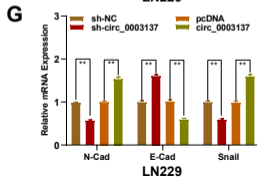
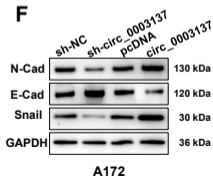
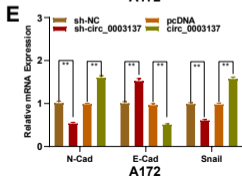
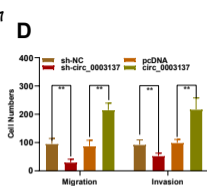
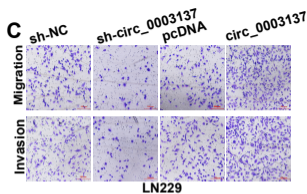
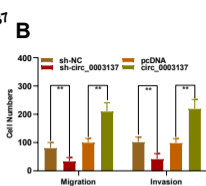
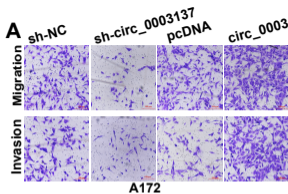
Table S3 Eepithelial-mesenchymal transition hallmark genes set.

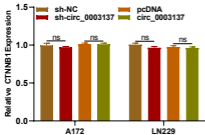
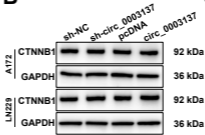
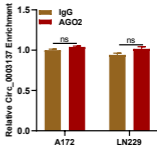
Table S4 The target genes of PTBP1 which screened according to their expression levels (based on TCGA).





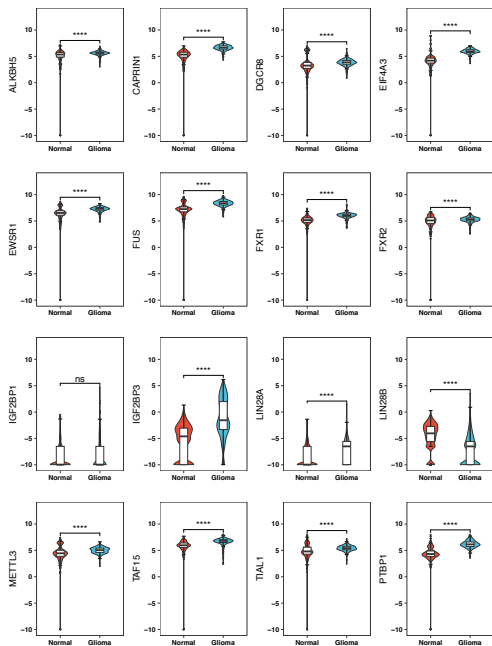




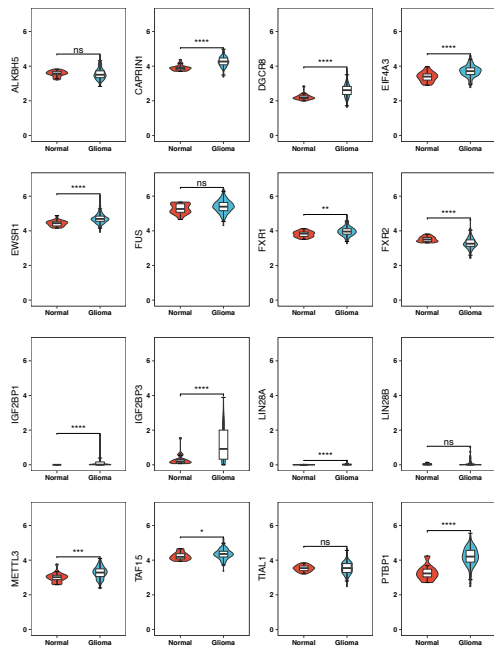
A**B****C**

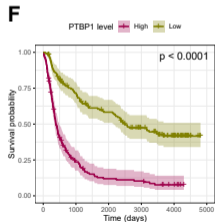
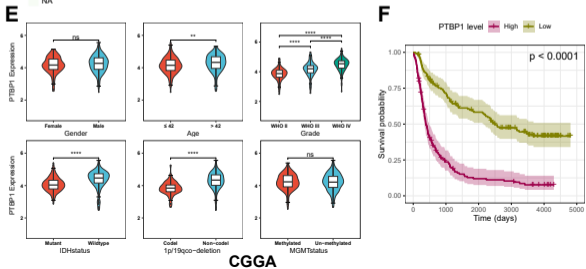
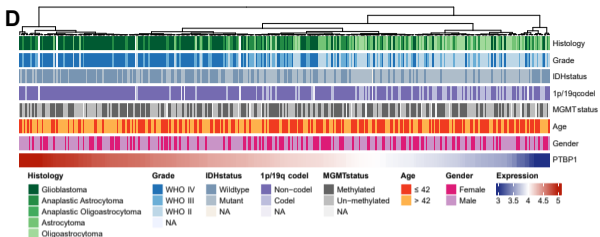
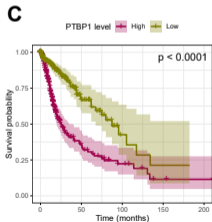
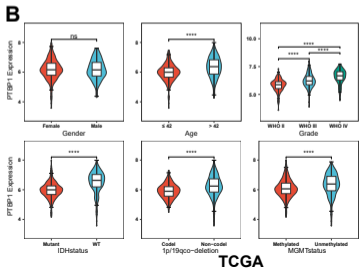
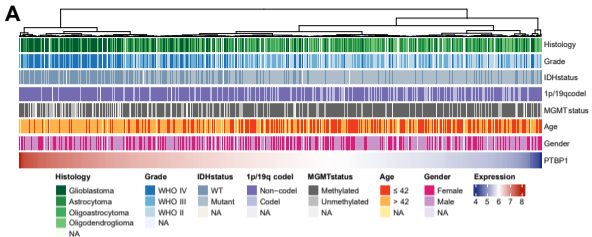
A

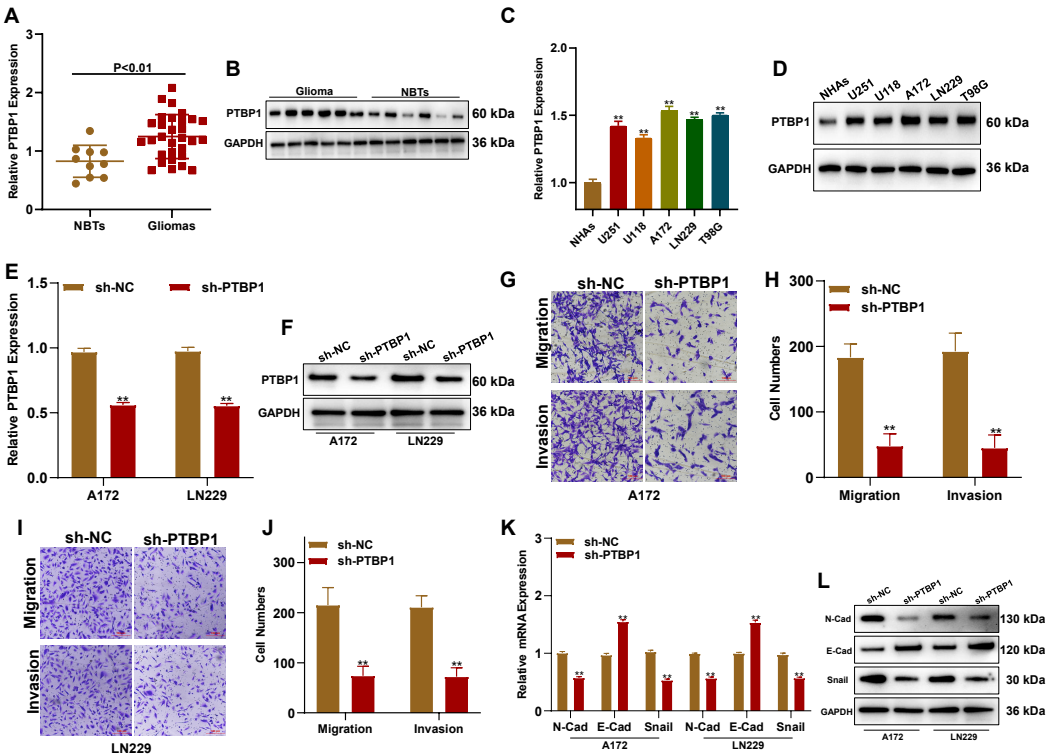
TCGA cohort

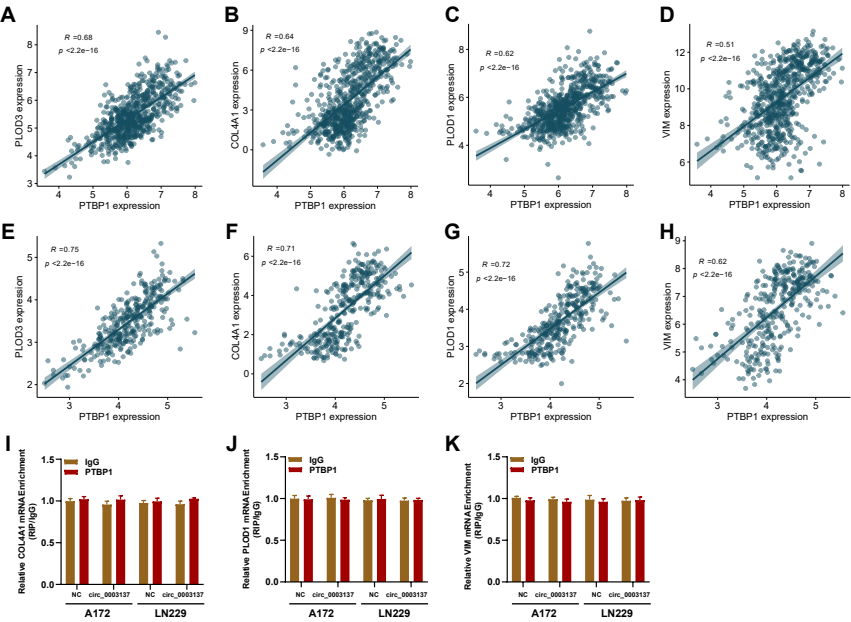
**B**

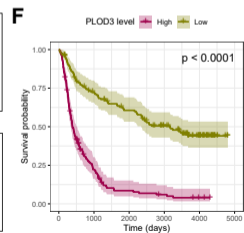
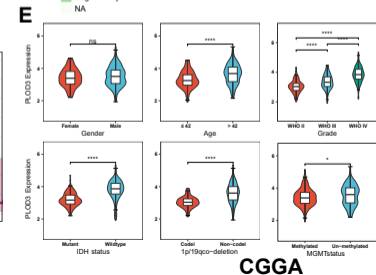
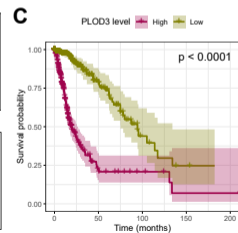
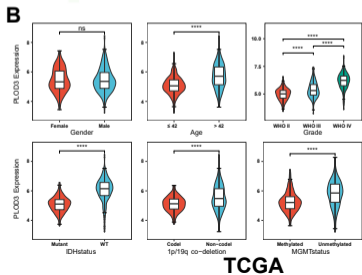
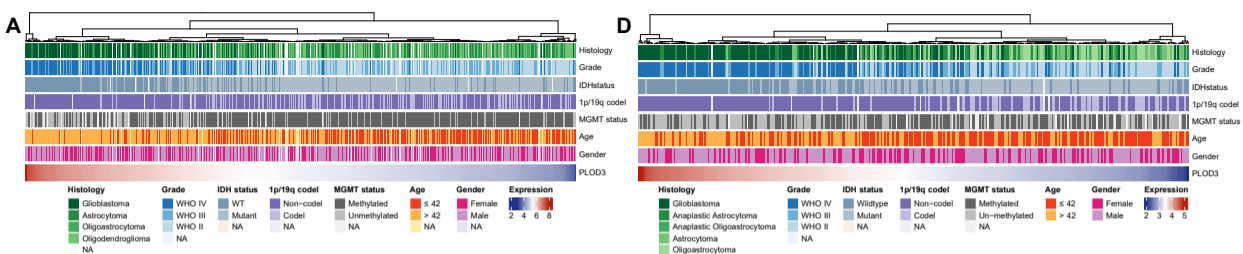
CGGA cohort

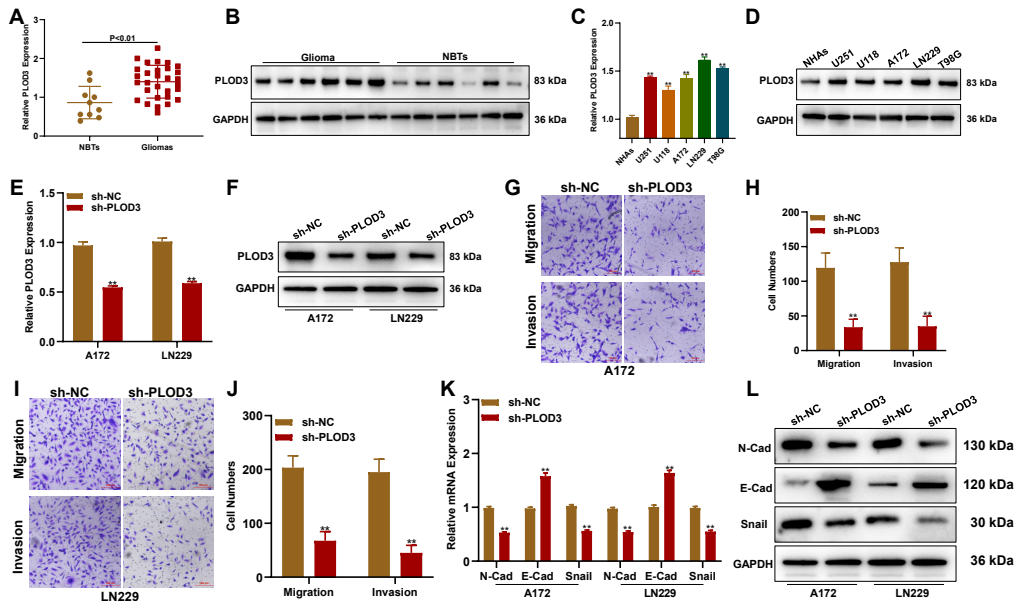


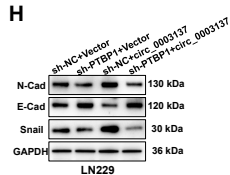
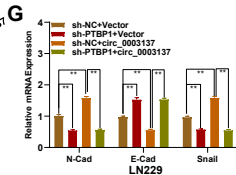
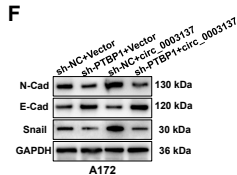
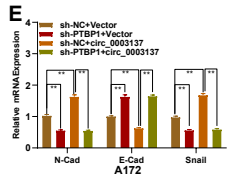
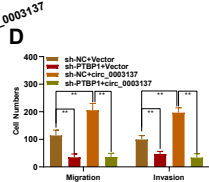
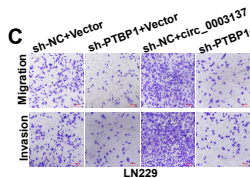
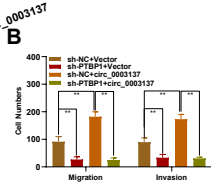
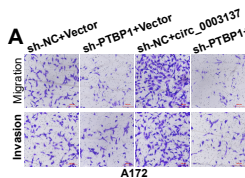


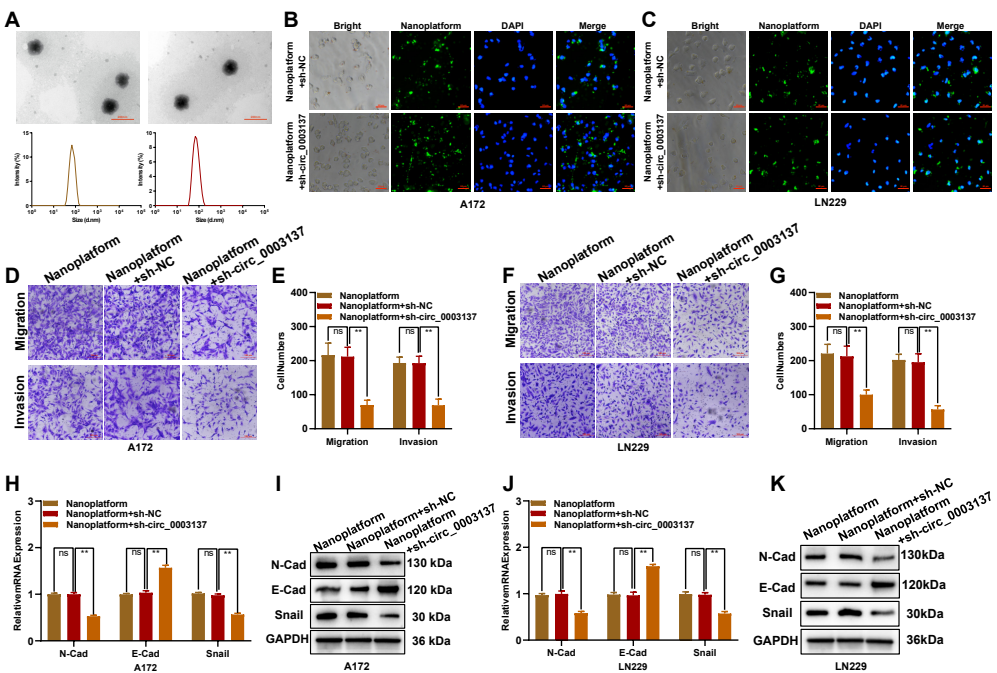


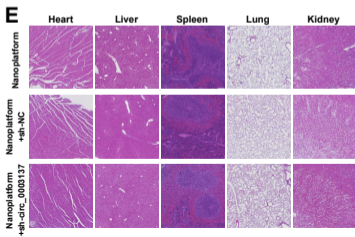
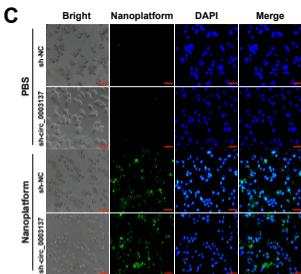
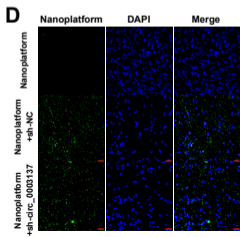
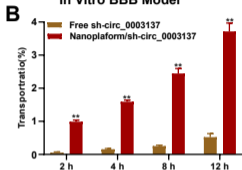
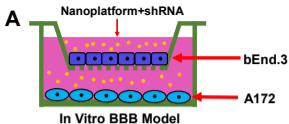












The primers used in this study.

Gene name	Forward Sequence	Reverse Sequence
GAPDH	GTCTCCTCTGACTTCAACAGCG	ACCACCCTGTTGCTGTAGCCAA
circ_0003137	CTGAGGAGCAGCTTCAGTCC	GGCCATGTCCAACATCCATCA
PTBP1	CTCCAAGTTCGGCACAGTGTTG	CAGGCGTTGTAGATGTTCTGCC
PLOD3	CGAGTGTGAGTTCTACTTCAGCC	CCAGAAGTTGGACCACAGCTTG
CTNNB1	CACAAGCAGAGTGCTGAAGGTG	GATTCCTGAGAGTCCAAAGACAG
CD68	CGAGCATCATTCTTTCACCAGCT	ATGAGAGGCAGCAAGATGGACC
CD163	CCAGAAGGAACTTGTAGCCACAG	CAGGCACCAAGCGTTTTGAGCT
CD206	AGCCAACACCAGCTCCTCAAGA	CAAAACGCTCGCGCATTGTCCA
CD86	CCATCAGCTTGTCTGTTTCATTCC	GCTGTAATCCAAGGAATGTGGTC
TNF- α	CTCTTCTGCCTGCTGCACTTTG	ATGGGCTACAGGCTTGTCACTC
HIF1 α	TATGAGCCAGAAGAACTTTTAGGC	CACCTCTTTTGGCAAGCATCCTG
COL4A1	TGTTGACGGCTTACCTGGAGAC	GGTAGACCAACTCCAGGCTCTC
PLOD1	GCCGTTTGTGTCCCTGTTCTTC	ATGCTGTGCCAGGAACCTTCC
VIM	AGGCAAAGCAGGAGTCCACTGA	ATCTGGCGTTCAGGGACTCAT
N-Cad	CCTCCAGAGTTTACTGCCATGAC	GTAGGATCTCCGCCACTGATTC
E-Cad	GCCTCCTGAAAAGAGAGTGGAAG	TGGCAGTGTCTCTCCAAATCCG
Snail	TGCCCTCAAGATGCACATCCGA	GGGACAGGAGAAGGGCTTCTC

The antibodies used in Western blot assay.

Protein name	Company	Catalogue number
CD68	Abcam	ab303565
CD163	Proteintech	16646-1-AP
CD206	Proteintech	18704-1-AP
CD86	Proteintech	13395-1-AP
TNF- α	Proteintech	60291-1-Ig
HIF1 α	Proteintech	66730-1-Ig
GAPDH	Proteintech	60004-1-Ig
PTBP1	Proteintech	67462-1-Ig
PLOD3	Proteintech	11027-1-AP
CTNNB1	Proteintech	66379-1-Ig
N-Cad	Proteintech	66219-1-Ig
E-Cad	Proteintech	20874-1-AP
Snail	Proteintech	13099-1-AP
CD63	Proteintech	25682-1-AP
CD81	Proteintech	66866-1-Ig
Calnexin	Proteintech	10427-2-AP
TSG101	Proteintech	67381-1-Ig

Epithelial-mesenchymal transition hallmark genes set

ABI3BP	ACTA2	ADAM12	ANPEP	APLP1
AREG	BASP1	BDNF	BGN	BMP1
CADM1	CALD1	CALU	CAP2	CAPG
CD44	CD59	CDH11	CDH2	CDH6
COL11A1	COL12A1	COL16A1	COL1A1	COL1A2
COL3A1	COL4A1	COL4A2	COL5A1	COL5A2
COL5A3	COL6A2	COL6A3	COL7A1	COL8A2
COMP	COPA	CRLF1	CTGF	CTHRC1
CXCL1	CXCL12	CXCL6	CYR61	DAB2
DCN	DKK1	DPYSL3	DST	ECM1
ECM2	EDIL3	EFEMP2	ELN	EMP3
ENO2	FAP	FAS	FBLN1	FBLN2
FBLN5	FBN1	FBN2	FERMT2	FGF2
FLNA	FMOD	FN1	FOXC2	FSTL1
FSTL3	FUCA1	FZD8	GADD45A	GADD45B
GAS1	GEM	GJA1	GLIPR1	GLT25D1
GPC1	GPX7	GREM1	HTRA1	ID2
IGFBP2	IGFBP3	IGFBP4	IL15	IL32
IL6	IL8	INHBA	ITGA2	ITGA5
ITGAV	ITGB1	ITGB3	ITGB5	JUN
LAMA1	LAMA2	LAMA3	LAMC1	LAMC2
LEPRE1	LGALS1	LOX	LOXL1	LOXL2
LRP1	LRRC15	LUM	MAGEE1	MATN2
MATN3	MCM7	MEST	MFAP5	MGP
MMP1	MMP14	MMP2	MMP3	MSX1
MXRA5	MYL9	MYLK	NID2	NNMT
NOTCH2	NT5E	NTM	OXTR	PCOLCE
PCOLCE2	PDGFRB	PDLIM4	PFN2	PLAUR
PLOD1	PLOD2	PLOD3	PMEPA1	PMP22
POSTN	PIIB	PRRX1	PRSS2	PTHLH
PTX3	PVR	QSOX1	RGS4	RHOB
SAT1	SCG2	SDC1	SDC4	SERPINE1
SERPINE2	SERPINH1	SFRP1	SFRP4	SGCB
SGCD	SGCG	SLC6A8	SLIT2	SLIT3
SNAI2	SNTB1	SPARC	SPOCK1	SPP1
TAGLN	TFPI2	TGFB1	TGFBI	TGFBR3
TGM2	THBS1	THBS2	THY1	TIMP1
TIMP3	TNC	TNFAIP3	TNFRSF11B	TNFRSF12A
TPM1	TPM2	TPM4	VCAM1	VCAN
VEGFA	VEGFC	VIM	WIPF1	WNT5A

Note: The data derived from <https://www.gsea-msigdb.org/gsea/msigdb/human/geneset/>

The target genes of PTBP1 which screened according to their expression levels (based on TCGA)

Gene name	HR (hazard ratio)	Pearson Correlation
SERPINH1	6	0.49
TNFRSF12A	5.6	0.43
COL5A2	5.3	0.41
COL4A1	5.1	0.55
CALU	5.1	0.5
CAPG	5	0.31
PLOD3	4.8	0.59
FN1	4.7	0.27
PLOD1	4.6	0.53
VIM	4.6	0.53
MMP14	4.6	0.48
FLNA	4.5	0.53
MEST	4.3	0.47
LAMC1	4.1	0.55
LOXL2	4	0.25
COL3A1	4	0.16
SFRP4	3.9	0.27
PMP22	3.8	0.28
CD44	3.5	0.36
MGP	3.5	0.15
TNC	3.4	0.51
PIIB	3.3	0.51
ITGB1	3.3	0.48
MMP2	3.3	0.46
PLOD2	3.1	0.41
IGFBP3	3.1	0.29
TGFBI	3.1	0.19
ECM2	2.7	0.19
GAS1	2.5	0.54
GEM	2.4	0.23
TGFB1	2.3	0.36
ITGB5	2.1	0.27
CDH11	1.9	0.49
CDH2	1.8	0.65
PCOLCE2	1.8	0.28
MCM7	1.7	0.63
MATN2	1.7	0.32
SGCB	1.7	0.11
WNT5A	1.6	0.33
NT5E	1.5	0.39
ITGAV	1.5	0.31

WIPF1	1.5	0.3
FERMT2	1.3	0.46
SNTB1	1.3	0.31
ID2	1.2	0.23
DAB2	1.2	0.17
LRP1	1.1	0.38
NOTCH2	0.98	0.32
PRRX1	0.85	0.33
HTRA1	0.73	-0.11
RHOB	0.65	-0.11
VCAN	0.57	0.19
DPYSL3	0.48	0.11
TIMP3	0.4	0.042
ABI3BP	0.4	-0.064
