Supplemental Information
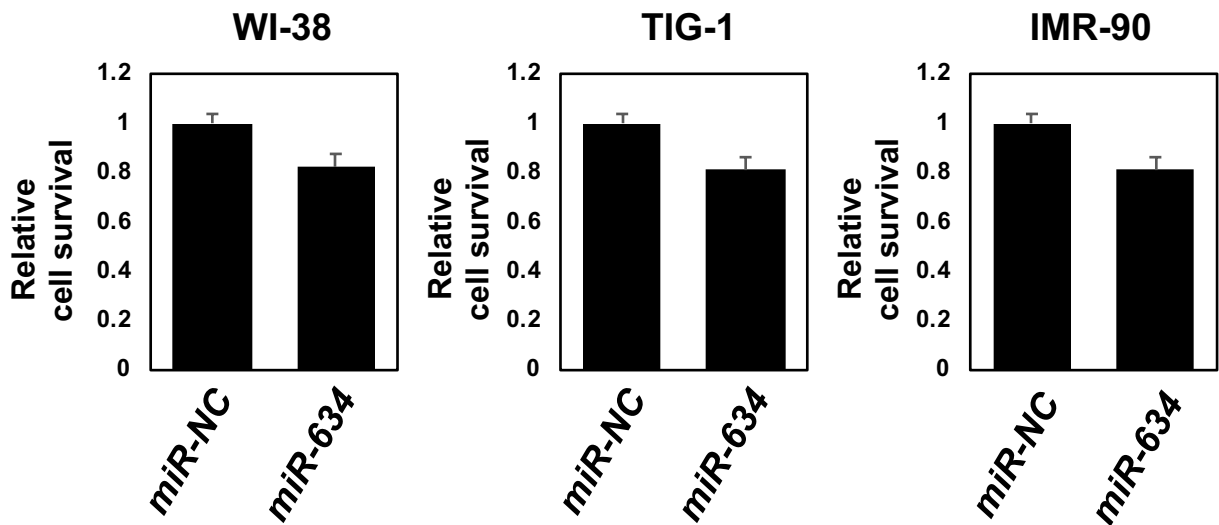
Therapeutic Potential of LNP-Mediated

**Delivery of *miR-634* for Cancer Therapy**

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Supplementary Figure 1

Supplementary Figure 1. Cell survival rate in *miR-634*-transfected fibroblasts.
Normal fibroblasts (WI-38, TIG-1, and IMR-90 cells) were transfected with 20 nmol/L *miR-NC* or *miR-634*, after 3 days cell survival rate was assessed with the CV staining assay, and the results are indicated as the relative ratio compared with *miR-NC*. Bar, SD of triplicate data.
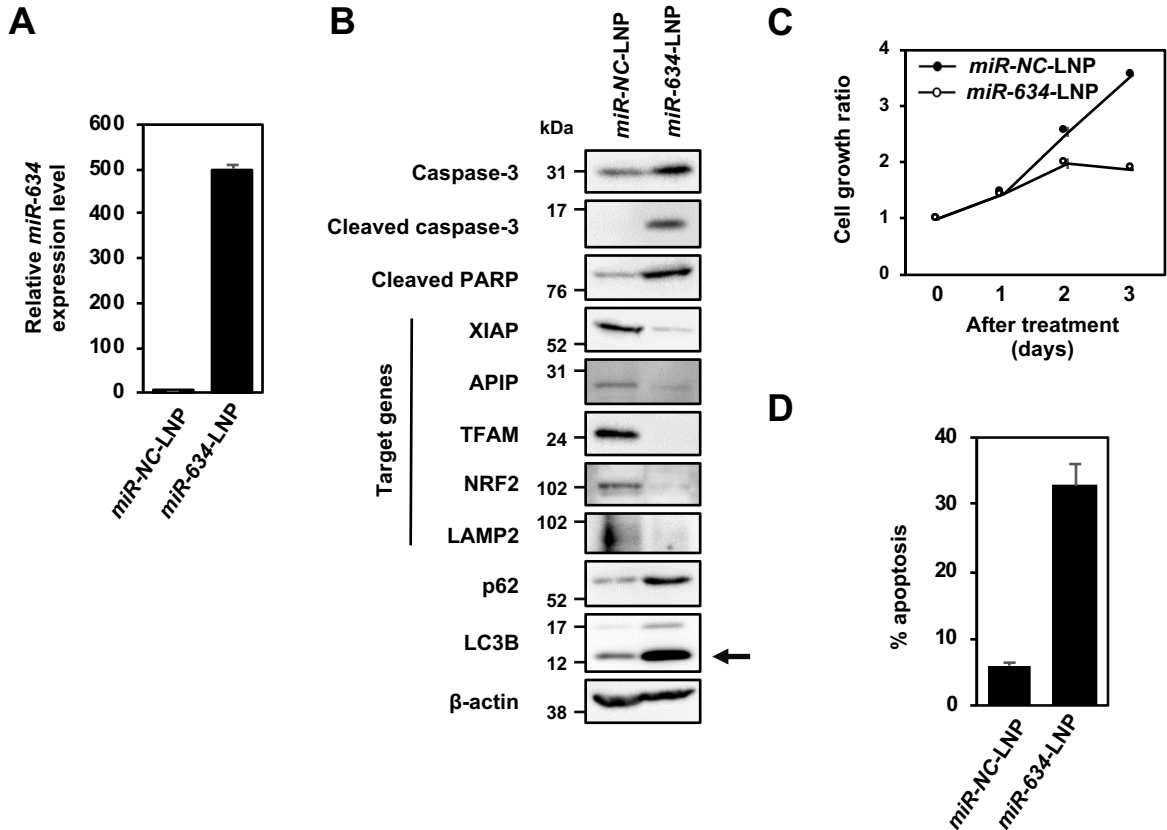
Supplementary Figure 2

BxPC-3	PSN-1	CFPAC-1
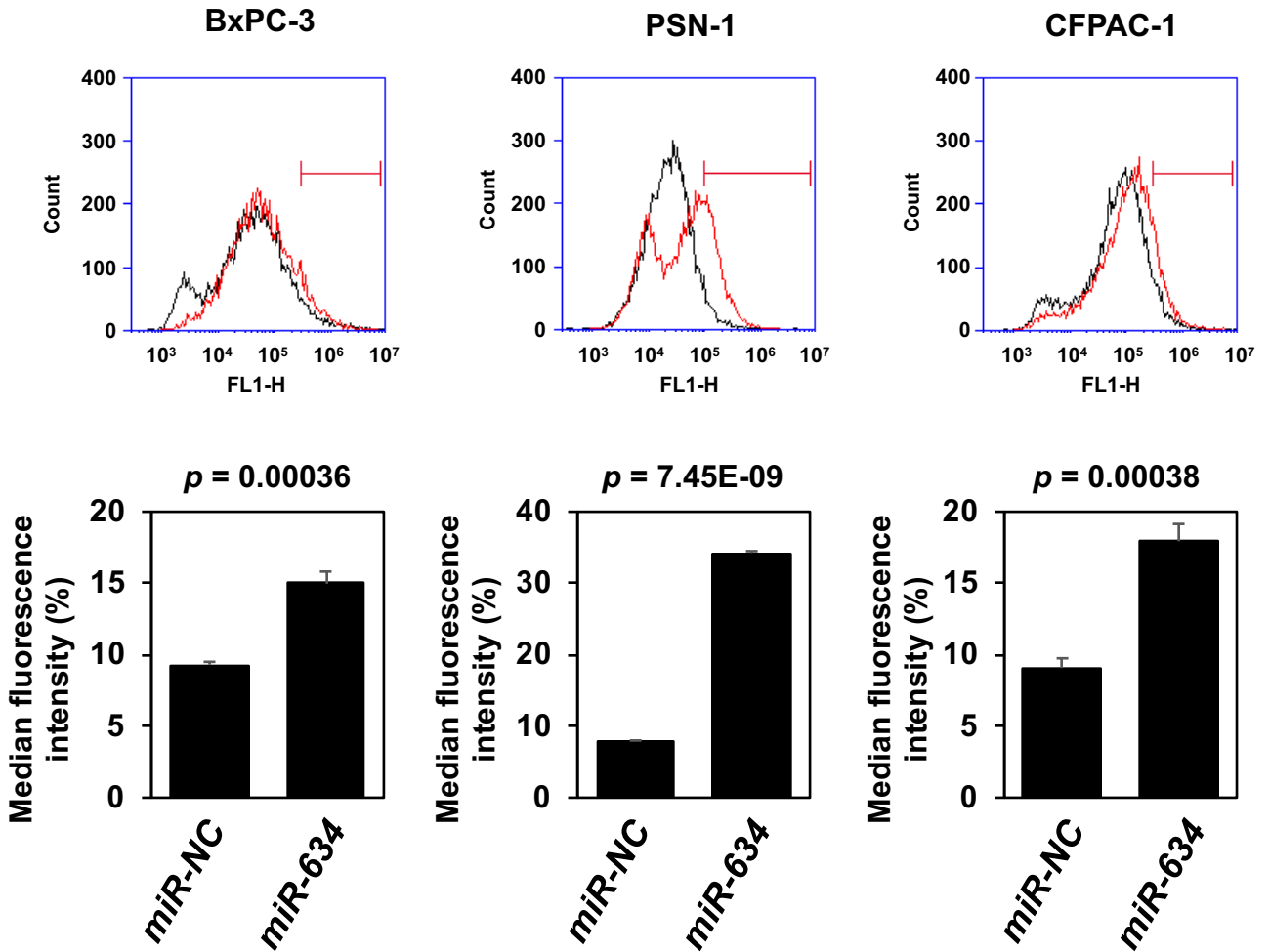
Supplementary Figure 2. Cellular ROS detection assay.
Cells were incubated with 20 µM of DCFDA for 30 minutes at 37˚C, and fluorescence intensity was measured using flow cytometry. The median fluorescence intensity is shown in the graph (lower panel). Bar; standard deviation (SD).

Supplementary Figure 3

A.

B.

C.

D.

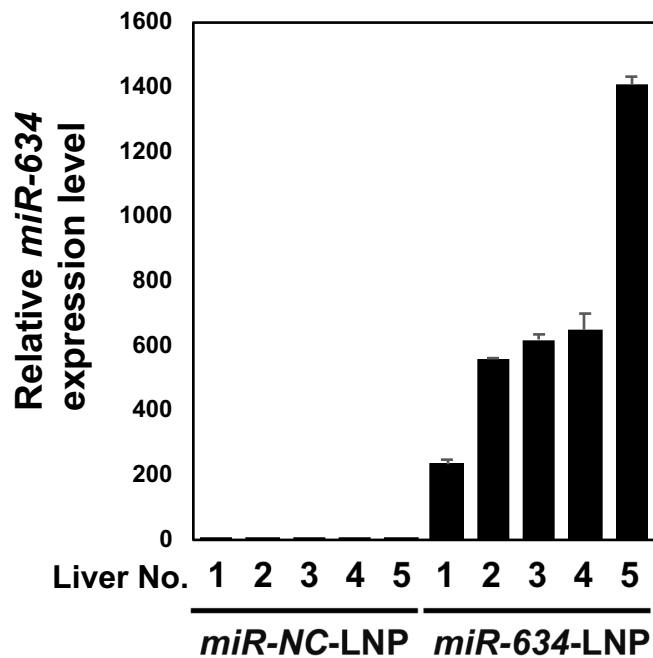**Supplementary Figure 3. Effect of *miR-634*-LNP *in vitro***
A. BxPC-3 cells were cultured in the medium including *miR-634*-LNP or *miR-NC*-LNP at the concentrations of 20 nmol/L for 3 days. The expression level of *miR-634* was measured by qRT-PCR. Bar, SD.
B. Western blotting analysis of *miR-634*-expressing cells. Cell lysates were subjected to SDS-PAGE and immunoreacted with the indicated antibodies. For the detection of LAMP2, cell lysates were prepared under nonreducing conditions (without 2-ME). Arrow indicates the band for LC3B form-II, an autophagosome marker.
C. Cell growth assay. Cell growth rate was assessed with the CV staining assay, and results are reported as the relative ratio compared with day 0 (lower panels). Bar, SD of triplicate experiments. The error bars are not visualized due to too small.
D. FACS analysis of the apoptotic cell population. FACS analysis was performed at 3 days after transfection. Cells were collected and stained with Annexin V and propidium iodide (PI). Cell population analysis was performed using an Accuri Flow Cytometer. The percentages of apoptotic cells are indicated in each graph. Bar, SD of triplicate experiments.

Supplementary Figure 4

Supplementary Figure 4. Expression analysis of *miR-634* in liver by qRT-PCR
The expression level of *miR-634* in livers from mice treated with *miR-NC*-LNPs (n=5) or *miR-634*-LNPs (n=5) was measured by qRT-PCR. Gene expression values are presented as the ratio (difference in Ct values) between *miR-634* and an internal reference, *snoRNA202*. Bar, SD.

Table S1 Sensitivity to *miR-634* in 117 cell lines of various cancer types

Cell lines	Type	Cell survival (%)	Cell lines	Type	Cell survival (%)
YH-13	Glioblastoma	100.3	TTA-2	Thyroid	55.8
MIAPaCa-2	Pancreas	99.1	Mpanc96	Pancreas	55.5
KNS-42	Glioblastoma	97.0	PANC-1	Pancreas	54.9
KTA-2	Thyroid	96.5	KINGS-1	Glioblastoma	54.6
KP2	Pancreas	91.7	KP1NL	Pancreas	54.2
KMP8	Pancreas	90.1	CRL 1579	Melanoma	53.8
No. 10	Glioblastoma	88.1	Becker	Glioblastoma	53.4
No. 11	Glioblastoma	87.2	697 mel	Melanoma	52.8
HPC-Y25	Pancreas	87.0	MMG3	Melanoma	52.3
KNS-89	Glioblastoma	86.5	865 mel	Melanoma	51.2
KP3L	Pancreas	86.0	KTA-3	Thyroid	50.7
CAPAN-1	Pancreas	85.7	PSN-1	Pancreas	50.5
KMP2	Pancreas	85.6	U20S	Sarcoma	50.0
HPAF-II	Pancreas	85.3	CFPAC-1	Pancreas	49.8
KNS-81	Glioblastoma	84.9	U-87MG	Glioblastoma	48.5
TCO-1	Thyroid	84.8	GOTO	Neuroblastoma	48.3
G361 mel	Melanoma	83.6	HepG2	Liver	48.3
QGP-1	Pancreas	81.2	YKG-1	Glioblastoma	47.3
883 mel	Melanoma	80.0	SK MEL 2	Melanoma	47.1
HTC C3	Thyroid	80.0	A375 mel	Melanoma	45.9
U-251MG	Glioblastoma	79.9	8505c	Thyroid	45.4
KP3	Pancreas	79.6	FRO	Thyroid	44.3
PK59	Pancreas	79.5	533B mel	Melanoma	43.9
SW1990	Pancreas	79.0	624 mel	Melanoma	43.2
AsPC-1	Pancreas	78.2	1011 mel	Melanoma	42.9
NMC-G1	Glioblastoma	77.7	U-373-MG	Glioblastoma	42.1
RT4	Bladder	76.9	BxPC-3	Pancreas	41.7
KMP5	Pancreas	74.8	KMP3	Pancreas	41.6
WM115 mel	Melanoma	74.2	KMP4	Pancreas	40.3
CAPAB-2	Pancreas	74.2	MDA-MB-231	Breast	39.3
NUGC4	Gastric	74.1	537 mel	Melanoma	38.5
HPC-Y0	Pancreas	72.9	501 mel	Melanoma	38.5
KP4	Pancreas	72.6	1102 mel	Melanoma	38.3
KALS-1	Glioblastoma	72.2	KHM-5M	Thyroid	36.4
GAK	Melanoma	71.3	Huh7	Liver	35.9
Hs766T	Pancreas	71.0	HT144 mel	Melanoma	34.8
HT29	Colon	71.0	952 mel	Melanoma	34.3
ASH-3	Thyroid	70.4	RT112	Bladder	34.3
GB-1	Glioblastoma	68.6	KTA-4	Thyroid	32.7
HPC-Y3	Pancreas	68.0	729 mel	Melanoma	32.2
KTA-1	Thyroid	67.5	C32 mel	Melanoma	31.4
526 mel	Melanoma	66.8	WM266 mel	Melanoma	29.5
397 mel	Melanoma	66.4	798 mel	Melanoma	28.6
RT-BMV-C6	Neuroblastoma	65.7	HS 294T	Melanoma	28.1
TTA-3	Thyroid	65.2	A2058	Melanoma	26.0
TTA-1	Thyroid	64.6	KNS-60	Glioblastoma	25.6
PH61N	Pancreas	64.5	KM-H2	Thyroid	24.2
AGS	Gastric	63.7	HCT116	Colon	21.7
ARO	Thyroid	63.1	Marcus	Glioblastoma	21.6
A172	Glioblastoma	63.1	SK MEL 23	Melanoma	21.1
AM-38	Glioblastoma	62.4	KS-1	Glioblastoma	20.0
MMG1	Melanoma	62.2	RPMI 7951	Melanoma	19.2
T98G	Glioblastoma	61.9	8305c	Thyroid	18.8
SK MEL 28	Melanoma	61.3	SF126	Glioblastoma	15.8
KP1N	Pancreas	58.8	731 mel	Melanoma	14.2
HMV-II	Melanoma	57.9	HSC44PE	Gastric	13.4
HMV-I	Melanoma	57.4	SJ-N-CG	Neuroblastoma	6.7
SK MEL 5	Melanoma	56.3	888 mel	Melanoma	6.5
928 mel	Melanoma	56.2			

Table S2 Characterization of *miRNA* -LNPs

	miR-NC	*miR-634*
Average diameter (nm)	49	48
Polydispersity index (PDI)	0.05	0.05
Encapsulation efficiency (EE)	>90%	>90%