Supporting Information for

Self-assembled Nanoscale Coordination Polymers Carrying siRNAs and Cisplatin for Effective Treatment of Resistant Ovarian Cancer

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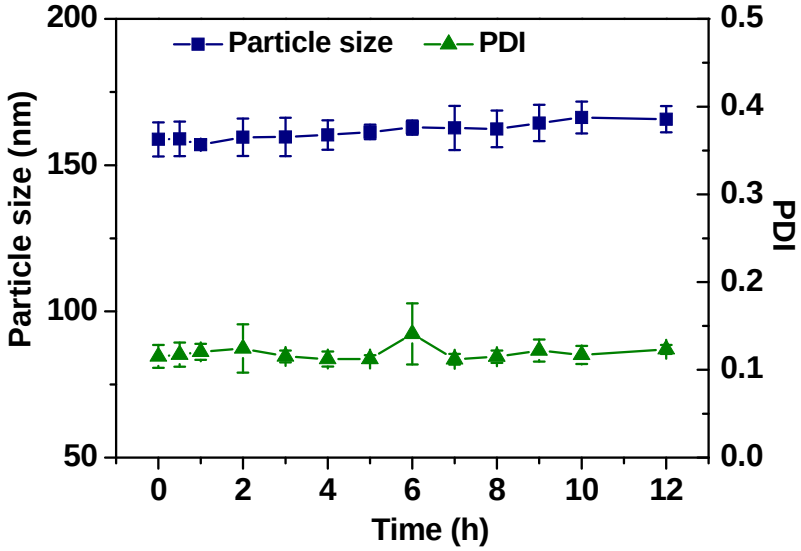

Figure S1 Stability of NCP-1/siRNAs as judged by particle sizes and PDI's in PBS containing 5 mg/mL BSA at 37 °C.

Figure S2 Gel retardation of NCP-1/siRNA (2% agarose gel, 56 V, 1 h). Lane 1-5: free siRNA, NCP-1/siRNAs, NCP-1/*sisurvivin*, NCP-1/*siBcl-2*, and NCP-1/*siP-gp*.

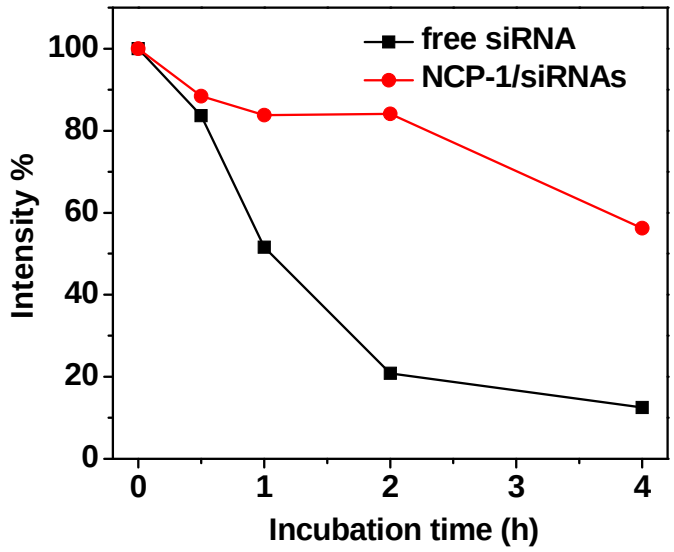

Figure S3 Degradation of siRNA in its free form and loaded into NCP-1 upon incubating with FBS for 4 hours.

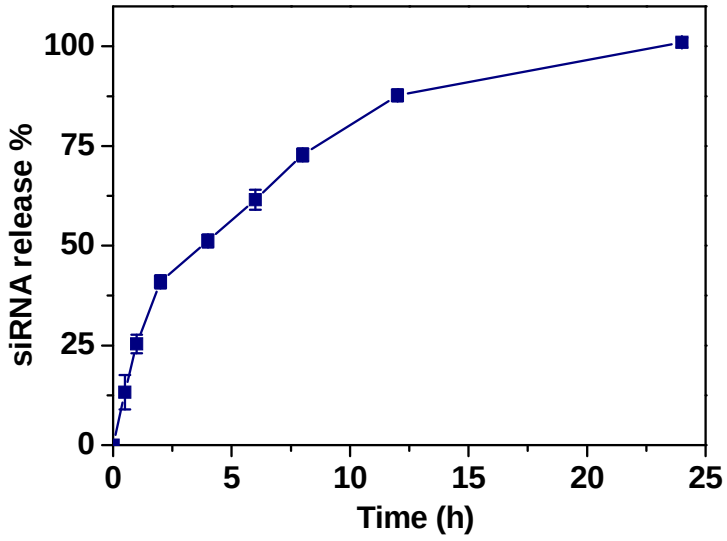

Figure S4 Cumulative release of siRNA from NCP-1/siRNAs in PBS determined by fluorimetry (n = 3).

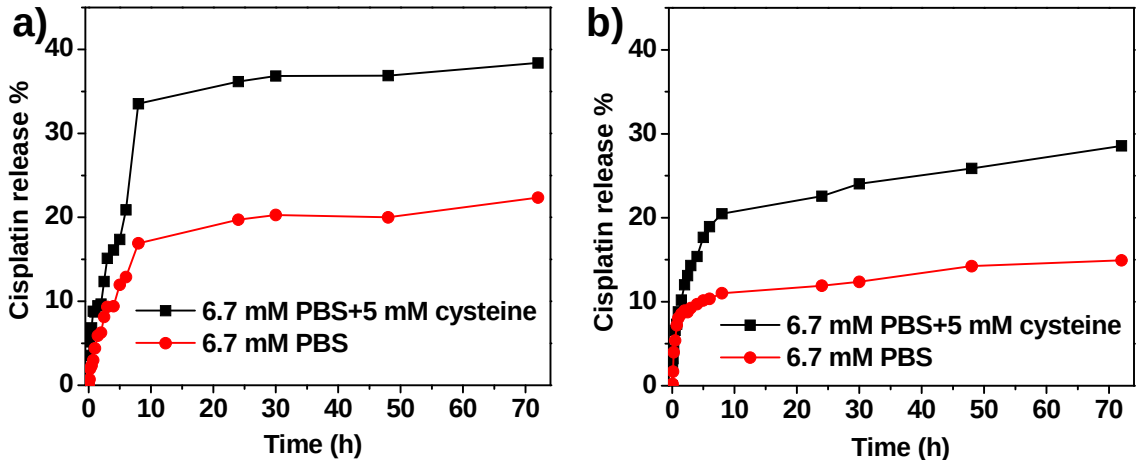

Figure S5 In vitro release of cisplatin from NCP-1 (a) and NCP-1/siRNAs (b) in 6.7 mM PBS and 6.7 mM PBS supplemented with 5 mM cysteine.

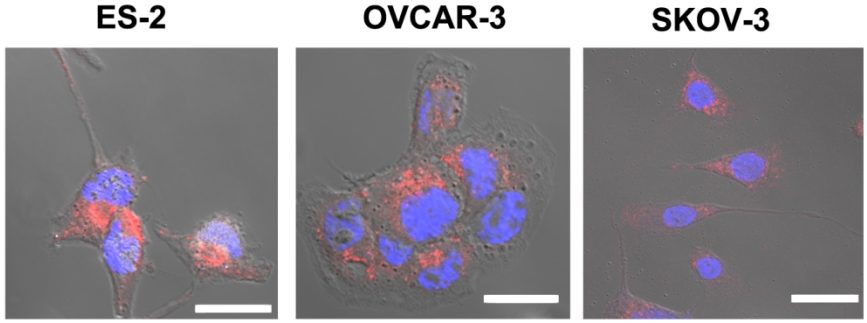

Figure S6 CLSM images showing siRNA (TAMRA-labeled, red fluorescence) could be efficiently delivered to ovarian cancer cells by NCP-1/siRNA. The nuclei were stained by DAPI. Bar represented 20 μm.

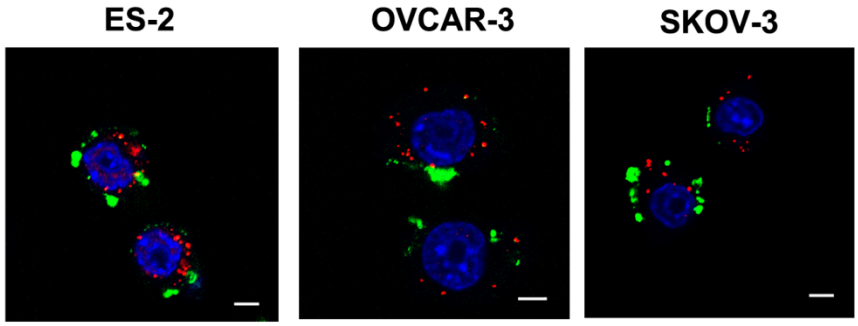

Figure S7 siRNA (TAMRA-labeled, red fluorescence) successfully escaped from endosome entrapment. Endosome/lysosome and nuclei were stained with Lysotracker Green and DAPI, respectively. Bar represented 5 μm.

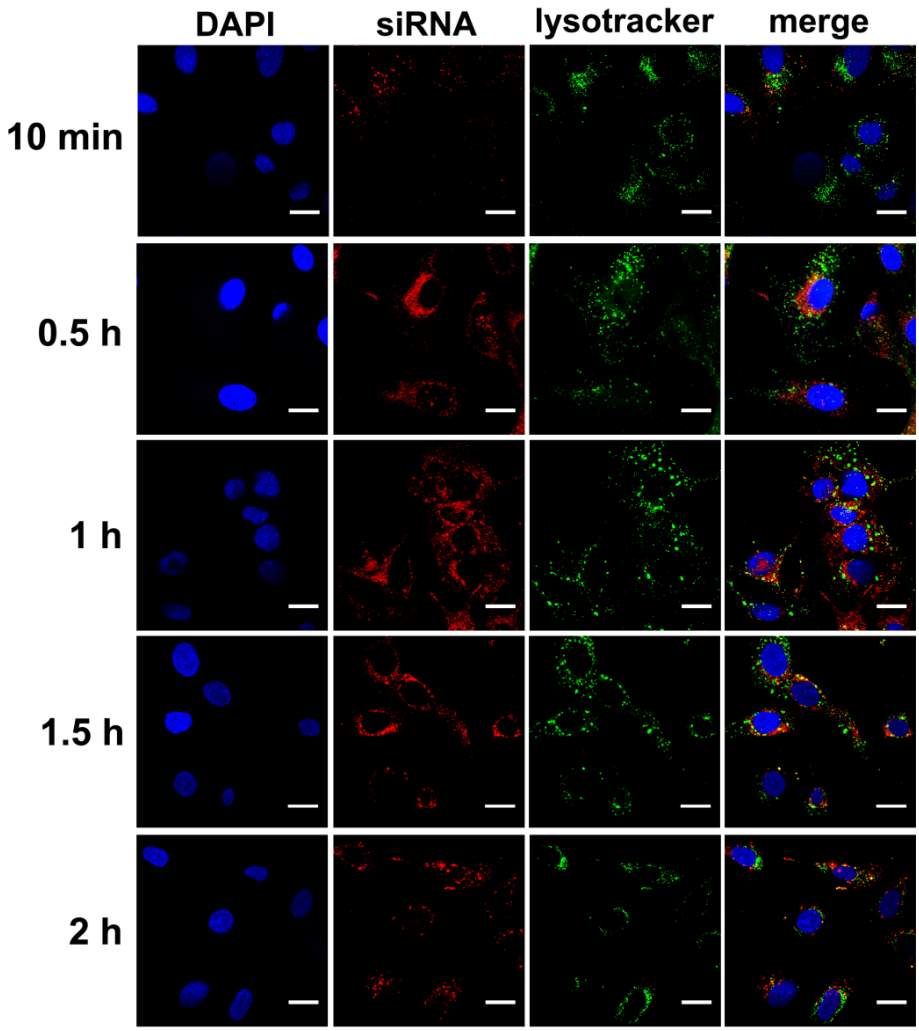

Figure S8 Time-dependent endosomal escape of siRNA loaded in NCP-1 in SKOV-3 cells. Endosome/lysosome and nuclei were stained with Lysotracker Green and DAPI, respectively. Bar represented 20 μm.

Table S1 Primer sequences of β-actin, Bcl-2, survivin, and P-gp for Real-Time PCR.

	Primer F	**Primer R**
β-actin	5’-CCACCCATGGCAAATTCCATGGCA-3’	5’-TCTAGACGGCAGGTCAGGTCCACC-3’
Bcl-2	5’-GTGGAGGAGCTCTTCAGGGA-3’	5’-AGGCACCCAGGGTGATGCAA-3’
survivin	5’-GGCATGGGTGCCCCGACGTT-3’	5’-AGAGGCCTCAATCCATGGCA-3’
P-gp	5’-AGGAAGCCAATGCCTATGACTTTA-3’	5’-CAACTGGGCCCCTCTCTCTC-3’

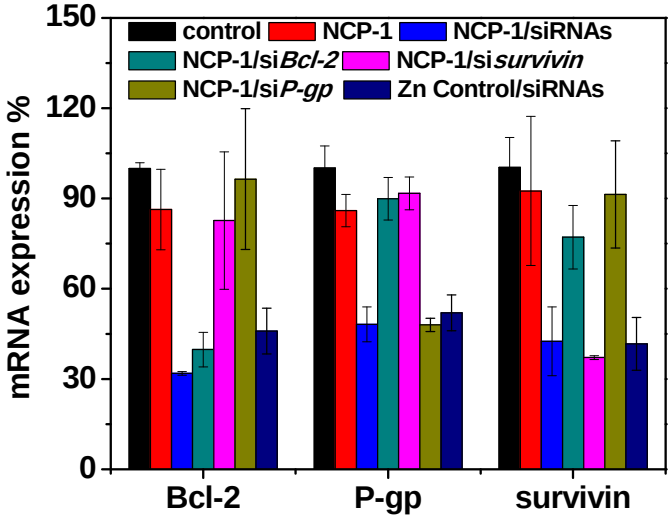

Figure S9 mRNA expression levels of Bcl-2, P-gp, and survivin in SKOV-3 cells transfected with NCP-1, NCP-1/siRNAs, NCP-1/si*survivin*, NCP-1/si*Bcl-2*, NCP-1/si*P-gp*, and Zn control/siRNAs at an siRNA concentration of 30 nM (n=3).

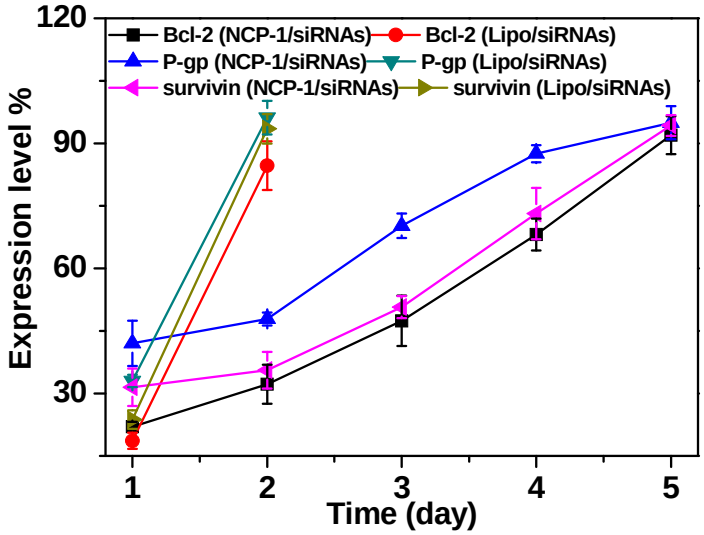

Figure S10 Time-dependent transfection efficiency mediated by NCP-1/siRNAs and Lipo/siRNAs in SKOV-3 cells (n=3).

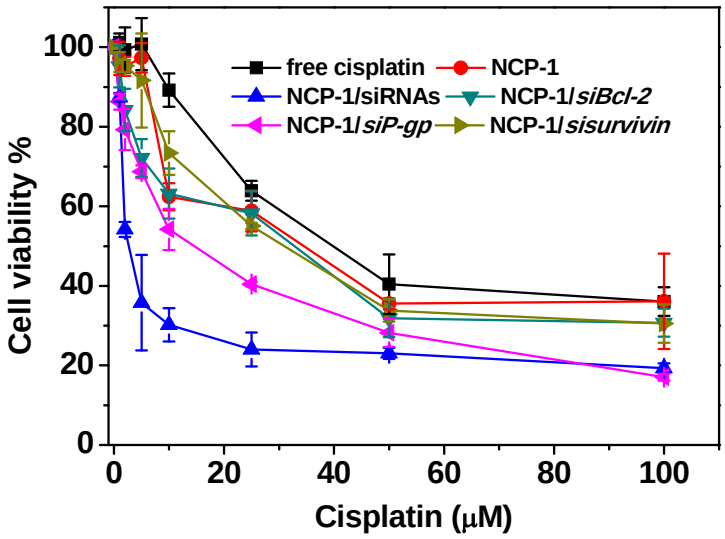

Figure S11 Cytotoxicity of NCP-1/siRNA in ES-2 cells. The cells were incubated with NCP-1/siRNA, NCP-1, or free cisplatin for 72 h followed by the MTS assay.

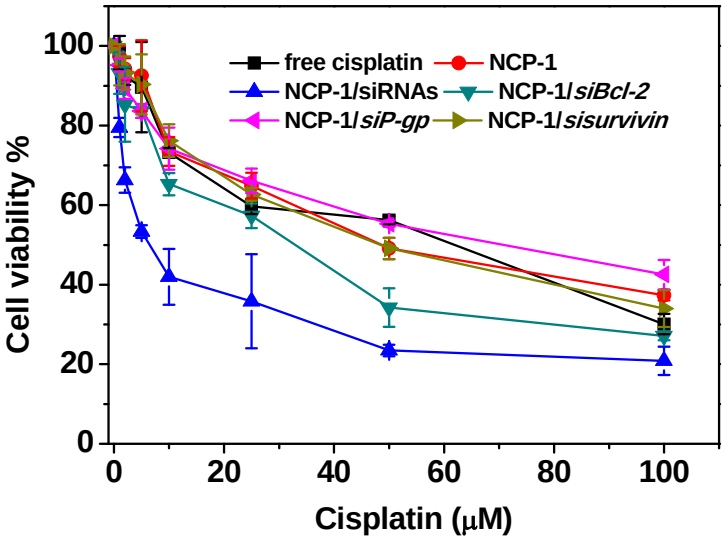

Figure S12 Cytotoxicity of NCP-1/siRNA in OVCAR-3 cells. The cells were incubated with NCP-1/siRNA, NCP-1, or free cisplatin for 72 h followed by the MTS assay.

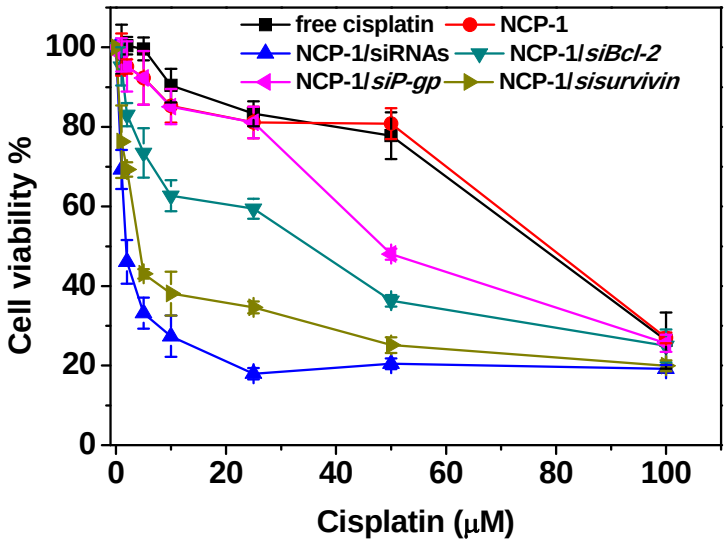

Figure S13 Cytotoxicity of NCP-1/siRNA in SKOV-3 cells. The cells were incubated with NCP-1/siRNA, NCP-1, or free cisplatin for 72 h followed by the MTS assay.

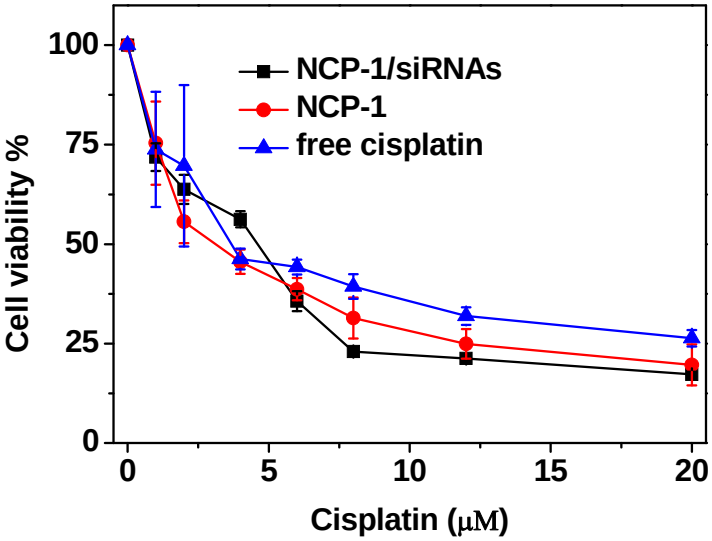

Figure S14 Cytotoxicity of NCP-1/siRNA in A2780 cells. The cells were incubated with NCP-1/pooled siRNAs, NCP-1, or free cisplatin for 72 h followed by the MTS assay.

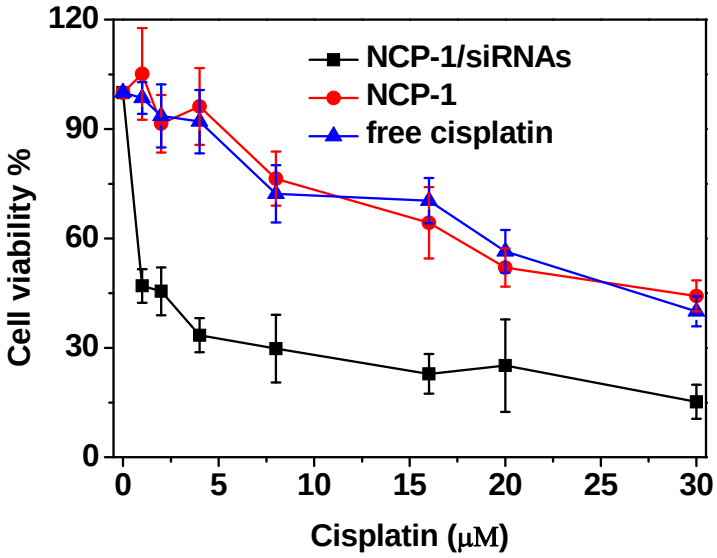

Figure S15 Cytotoxicity of NCP-1/siRNA in A2780/CDDP cells. The cells were incubated with NCP-1/pooled siRNAs, NCP-1, or free cisplatin for 72 h followed by the MTS assay.

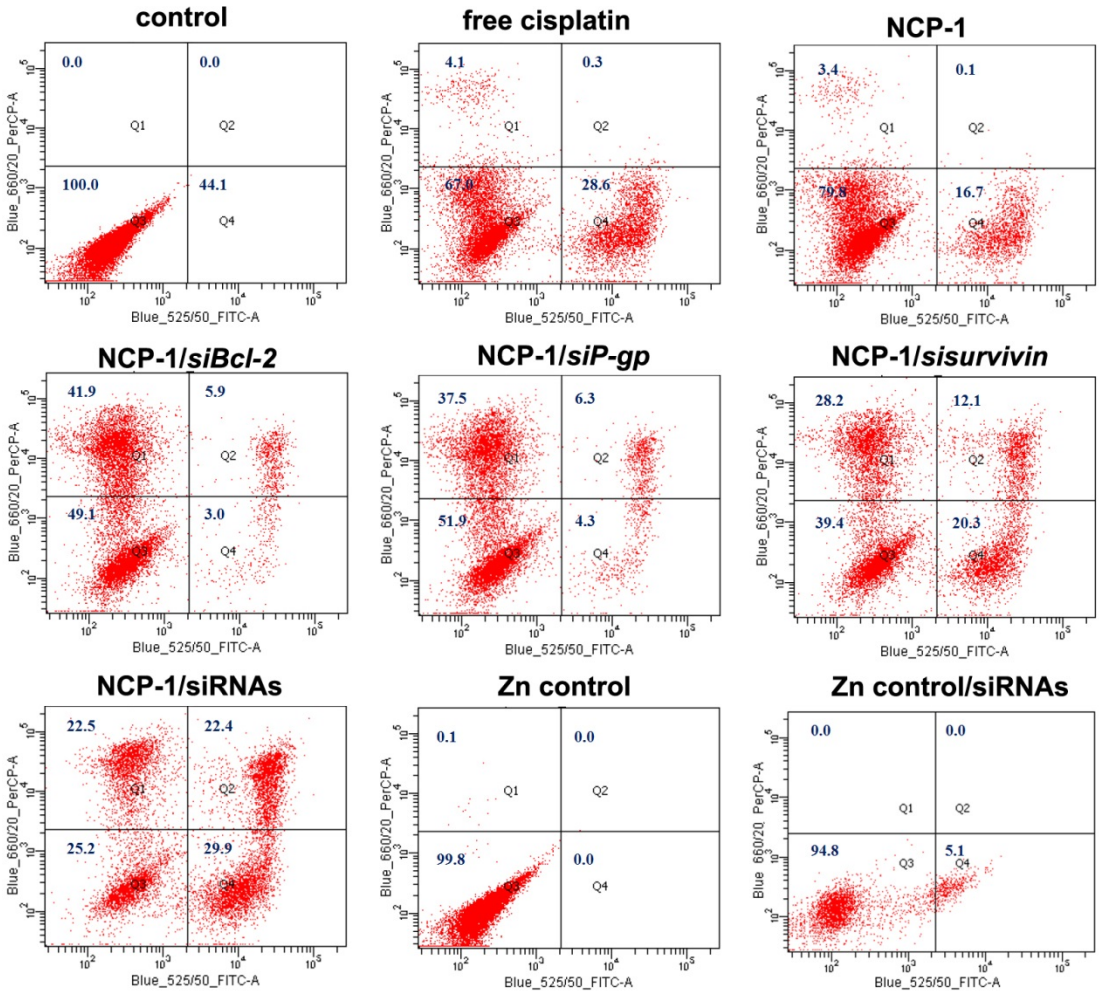

Figure S16 Annexin V/PI analysis of SKOV-3 cells after the incubation with saline (control), NCP-1, NCP-1/siRNAs, Zn control, Zn control/siRNAs, and free cisplatin for 24 h. The Q1-Q4 quadrants represent necrosis, late apoptotic, healthy, and early apoptotic cells, respectively. The percent of cells in each quadrant was shown on the graphs.

Table S2 Percent of healthy, apoptotic, and necrotic SKOV-3 cells after the treatment of saline (control), NCP-1, NCP-1/siRNAs, Zn control, Zn control/siRNAs, and free cisplatin for 24 h.

	Healthy (%)	Apoptosis (%)	Necrosis (%)
Control	100.0	0.0	0.0
Free cisplatin	67.0	28.9	4.1
NCP-1	79.8	16.8	3.4
NCP-1/*siBcl-2*	49.1	8.9	41.9
NCP-1/*siP-gp*	51.9	10.6	37.5
NCP-1/*sisurvivin*	39.4	32.4	28.2
NCP-1/siRNAs	25.2	52.3	22.5
Zn Control	99.8	0.0	0.1
Zn Control/siRNAs	94.8	5.1	0.0

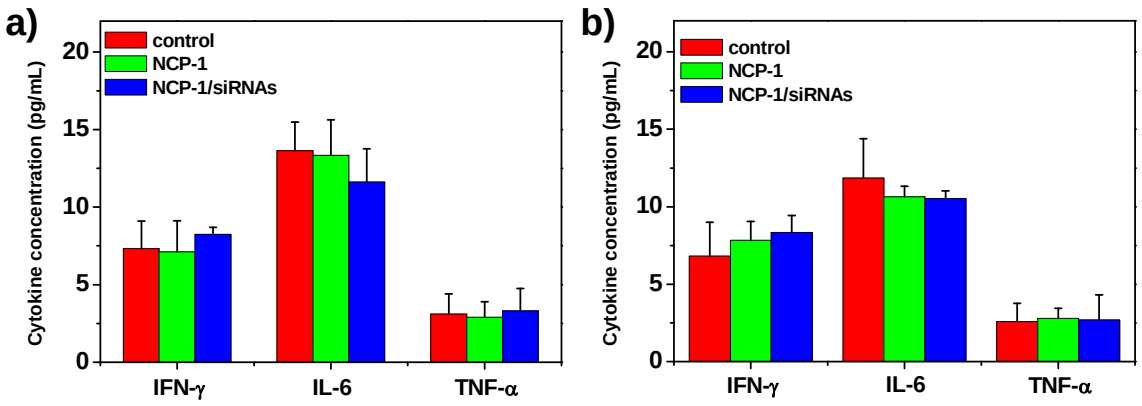

Figure S17 Immunogenic response of NCP-1 and NCP-1/pooled siRNAs in SKOV-3 (a) and Raw 264.7 (b) cells. The cells were incubated with NCP-1 or NCP-1/siRNAs for 72 h followed by the determination of TNF-α, IL-6, and IFN-γ by ELISA.

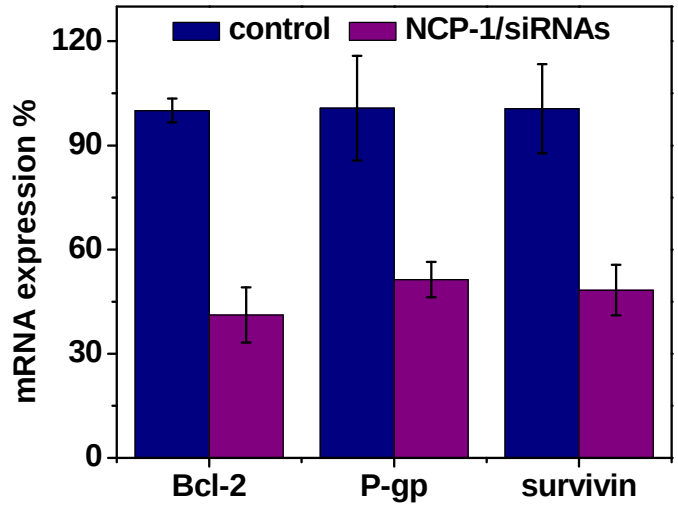

Figure S18 mRNA expression levels of Bcl-2, P-gp, and survivin in the tumors of mice receiving intratumoral injection of NCP-1/siRNAs (n=3).

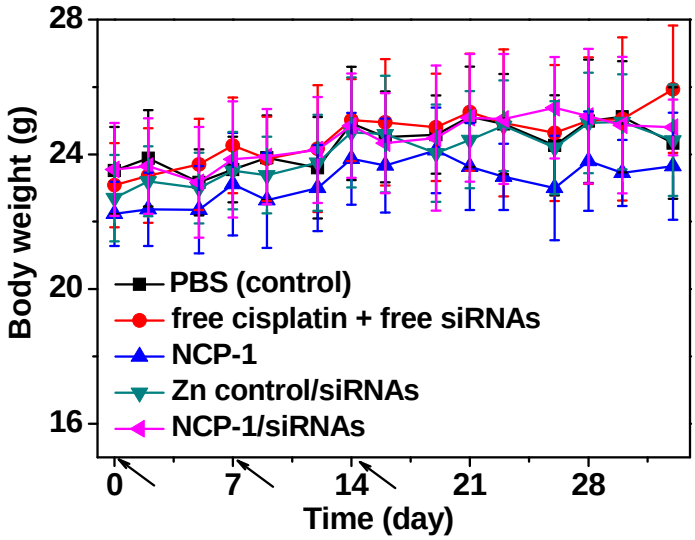

Figure S19 Body weights of SKOV-3 tumor bearing mice after the treatment with NCP-1/pooled siRNAs (n=6).

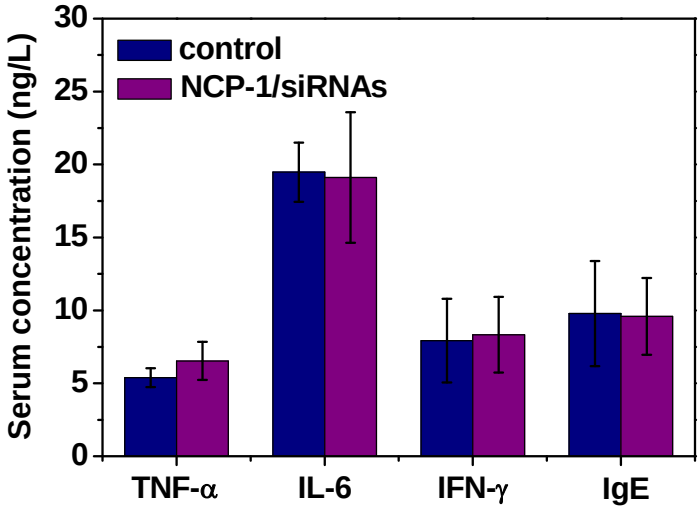

Figure S20 TNF-α, IL-6, IFN-γ, and IgE concentrations in the serum of SKOV-3 tumor bearing mice receiving intratumoral injection of NCP-1/siRNAs or PBS (control) determined by ELISA.

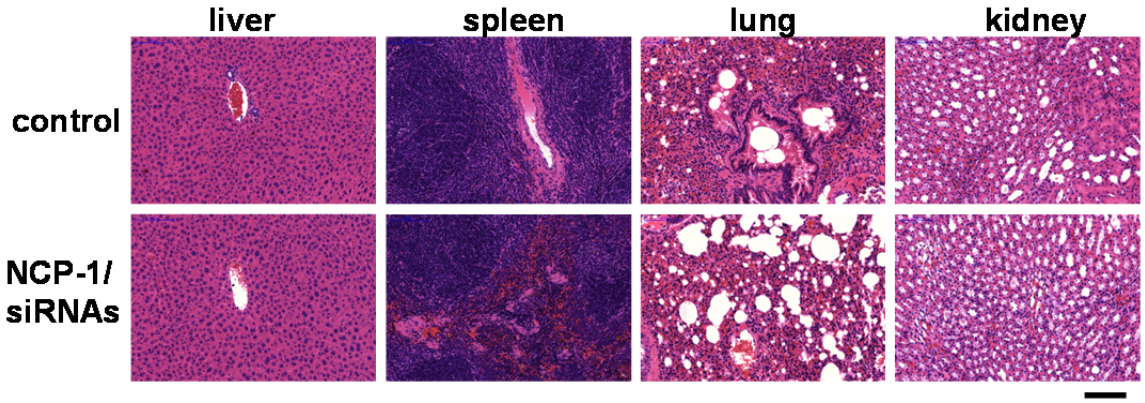

Figure S21 Histological sections of excised organs from SKOV-3 tumor bearing mice in the groups of control (PBS) and NCP-1/siRNAs. Bar: 1 mm.