Electronic Supporting Information

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Supporting Materials and Methods

Materials

β-cyclodextrin (β-CD) of reagent grade was recrystallized twice from H_2O and dried in vacuo for 12 h at 373 K. DMF was super dry grade and stored over a molecular sieve. Ruthenium(III) chloride hydrate (Alfa Aesar), phen (1,10-phenanthroline, Alfa Aesar), c(RGDyK)-Ad (cyclic Arg-Gly-Asp peptides (c(RGDyK) conjugated with adamantine, GL Biochem (Shanghai) Ltd.), cisplatin (Sigma Aldrich), PBS (phosphate buffered saline, Sigma Aldrich), MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide, Sigma Aldrich), **MTDR** (MitoTracker Deep Red, Life Technologies, USA), **LTDR** (LysoTracker Deep Red, Life Technologies, USA), H_2DCFDA (2',7'-dichlorodihydrofluorescein diacetate, Sigma Aldrich) and Hoechst 33342 (2'-(4-ethoxyphenyl)-5-(4-methyl-1-piperazinyl)-1H,3'H-2,5'-bibenzimidazole, Sigma Aldrich), Annexin V-FITC apoptosis detection kit was purchased from Sigma Aldrich, NAC (N-acetylcysteine, Sigma Aldrich), CCCP (carbonyl cyanide-m-chlorophenylhydrazone, Sigma Aldrich) and z-VAD-fmk (Sigma Aldrich) were used as received. Caspase-3/7 activity assay kit was purchased from Promega (USA). Magic Red MR-$(RR)_2$ was purchased from Immunochemistry Tech. Distilled water was purified by passing through a Millipore Milli-Q Biocel purification system (18.2 MΩ) with a 0.22 μm filter. Cisplatin was dissolved in saline. All the compounds tested were dissolved in distilled water just before the experiments.

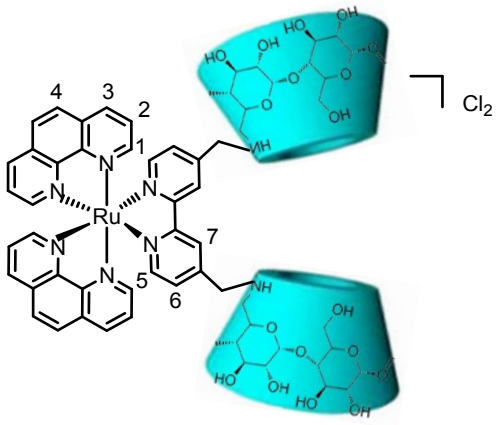
General methods

^{1}H NMR spectra were recorded on a Bruker AVANCE-400 NMR spectrometer (Germany). Elemental contents were analyzed by a Perkin-Elemer 240 elemental analyzer (Germany). ESI-MS spectra were performed on a Thremo LCQ-DECA-XP spectrometer (USA). UV-vis spectra were monitored with a Varian Cary 100 UV/vis spectrophotometer (USA). The fluorescence emission spectra were obtained on an FLS 980 combined fluorescence lifetime and steady state spectrometer (Edinburgh Instrument, UK). Ru content was measured on a Thermo X Series 2 Inductively Coupled Plasma Mass Spectrometer (Thermo Fisher Corp., USA). Morphology of the supramolecular self-assembly nanoparticles was characterized by a Bruker Multimode 8 atomic force microscope (AFM) under ScanAsyst mode (Bruker, USA). Isothermal titration calorimetry (ITC) were carried out on the MicrolCal ITC200 (Malvern, UK). Quantum yields of luminescence at room temperature were calculated according to literature procedures using $[Ru(bpy)_3]Cl_2$ as the reference.[1]

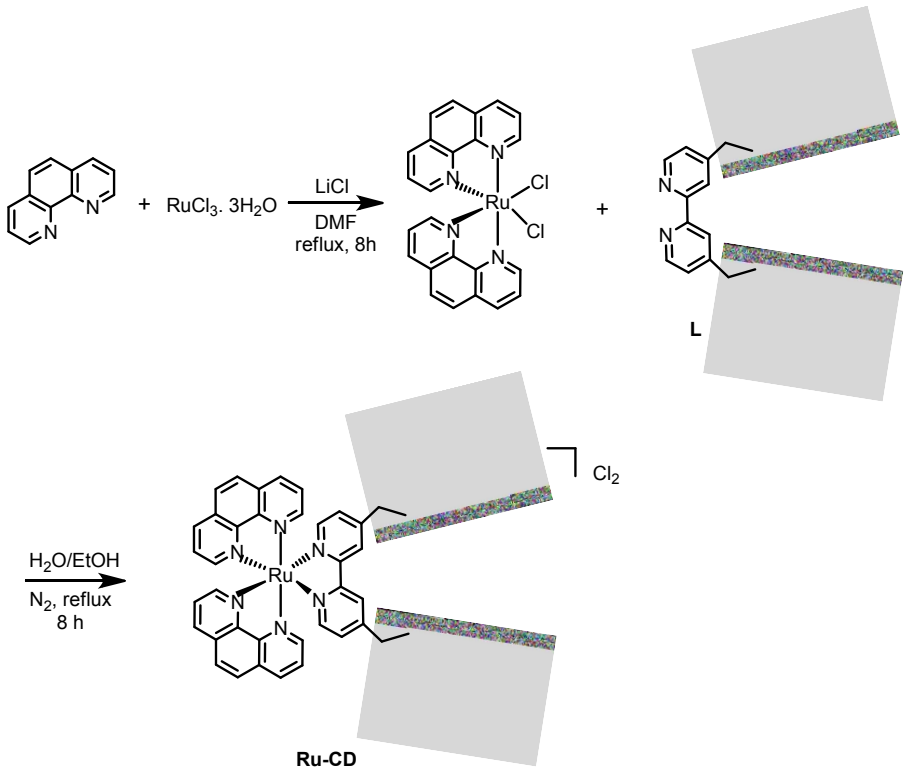
Synthetic protocols and characterizations

Cis-[Ru(phen)$_2$Cl$_2$]·2H$_2$O was synthesized using the literature method.[2] Ligand **L** (β-cyclodextrin (β-CD) dimer bridged by 4,4'-bipyridine) was synthesized according to our previously reported procedure.[3]

Synthetic procedure of Ru-CD. A mixture of *cis*-[Ru(phen)$_2$Cl$_2$]·2H$_2$O (0.24 g, 0.40 mmol) and ligand **L** (0.95 g, 0.36 mmol) was suspended in EtOH-H$_2$O (1:1, v/v) and refluxed under an inert atmosphere of nitrogen for 8 h. The mixture was then evaporated to dryness. The residue was redissolved in a small amount of water, and then poured into acetone (200 mL) to give a reddish brown precipitate. The crude product obtained was purified by Sephadex G-25 column chromatogram (mobile phase: 0.1 M NH$_3$·H$_2$O), and recrystallized from water/acetone (v/v = 3/1) giving pure compound **Ru-CD** as a reddish brown powder. Yield: 0.68 g (57%).



^{1}H NMR (400 MHz, *d*^{6}-DMSO): *δ* 8.80 (m, 6H; bpy-H-7 and phen-H-1), 8.37 (m, 4H; phen-H-3), 8.23 (d, 2H; bpy-H-5), 7.94 (d, 4H; phen-H-4), 7.70 (t, 4H; phen-H-2), 7.39 (d, 2H; bpy-H-6), 5.72-5.79 (14H, m, OH-2,3), 4.84 (7H, m, H-1), 4.44 (6H, m, OH-6), 3.93 (4H, s, bpy-CH$_2$), 3.63-3.33 (28H, m, H-3,5,6), 3.33-3.23 (14H, m, H-2,4, overlaps with H$_2$O), 2.19 (1H, s, NH). ESI-MS (H$_2$O): *m/z* 1454.3 ([M]$^{2+}$), 970.4 ([M+H]$^{3+}$). Elemental analysis: calcd (%) for C$_{120}$H$_{166}$RuN$_8$O$_{68}$Cl$_2$·23H$_2$O: C, 42.45; H, 6.29; N, 3.30; found: C, 42.77; H, 6.25; N, 3.12.



Scheme S1. Synthesis of **Ru-CD**.

Synthetic procedure of Ru-CD-RGD nanoparticle. For the preparation of **Ru-CD-RGD** nanoparticles, c(RGDyK)-Ad was added into the **Ru-CD** aqueous solution with a ratio of [**Ru-CD**]:[c(RGDyK)-Ad]=1:2 under ultrasonic agitation at 4 °C for 20 min, and the mixed solution was further stirred overnight to guarantee the formation of the self-assembled nanoparticle. The mixture was stored at 4 °C before use. The final concentration of **Ru-CD-RGD** was 650 μM, which was determined based on the content of Ru(II) in solution.

UV-vis titration

Ru-CD and c(RGDyK)-Ad were dissolved in distilled water to prepare stock solutions. c(RGDyK)-Ad was titrated into **Ru-CD** (10.0 μM) in 600 μL cuvette to achieve different ratios. After each titration, the mixture solution was allowed to stabilize for 5 min before the UV-vis spectra were recorded. The absorbance changes at 262 nm (ΔA_{262}) were plotted as a function of the c(RGDyK)-Ad/**Ru-CD** ratios.

Isothermal titration calorimetry (ITC)

ITC was employed to characterize the stoichiometry value for the binding of **Ru-CD** (Host) with c(RGDyK)-Ad (Guest). The titration experiments were carried out on the MicrolCal ITC200 at 298 ±

0.1 K. The guest molecules c(RGDyK)-Ad (0.025 mM) were loaded into the 200 μL sample cell and the host molecules **Ru-CD** (0.5 mM) were loaded into the continuously rotating (750 rpm) 40 μL syringe. The titration was conducted by adding 1.5 μL aliquots of the host solution into the guest solution at an interval of 2.5 min (19 injections in total). The first 1.0 μL aliquot injection was ignored to eliminate the effect of solute diffusion across the syringe tip during the equilibration period. The titration data were fitted using a MicroCal-enabled Origin program. The value of stoichiometry N, the molar enthalpy changes (ΔH), entropic changes (Δ*S*) and the inclusion complex association constants K_a were calculated accordingly. The total heat produced during each injection was obtained by integrating heat flows over the time. The calculated total heat (μcal) was plotted against the mole ratio of the titrant (host) to the titrate (guest).

Atomic force microscopy (AFM) measurement

The aqueous solution of **Ru-CD** and c(RGDyK)-Ad was mixed together to initial the supramolecular self-assembly process ([**Ru-CD-RGD**] = 50 μM). Then the solution was dropped onto newly clipped mica and air-dried. The samples were analyzed using a Bruker Multimode 8 AFM under ScanAsyst mode in air at room temperature.

Transmission electron microscopy (TEM)

Samples were prepared by adding 5 μL of **Ru-CD-RGD** (50 μM) solution onto a carbon film supported by 300-mesh copper grid, and air-dried prior to collecting images. TEM measurements were taken with a JEOL JEM-2010HR transmission electron microscope.

Dynamic light scattering (DLS) measurements

The solution of **Ru-CD-RGD** (50 μM) was prepared as described above. The hydrodynamic size was measured using a Brookhaven EliteSizer Nanoparticle size-Zeta potential and molecular weight analyzer at a wavelength of 677 nm with a constant angle of 90° at 25 °C.

Cell lines and culture conditions

Human glioblastoma (U87MG), human breast cancer (MCF-7), human lung adenocarcinoma epithelial (A549), cisplatin-resistant A549 (A549R) and human normal liver (LO2) were obtained from Experimental Animal Center of Sun Yat-Sen University (Guangzhou, China) and cultured in a humidified incubator at 37 °C under 5% CO_2. DMEM (Dulbecco's modified Eagle's medium, Gibco BRL) or RPMI 1640 (Roswell Park Memorial Institute 1640, Gibco BRL) medium were

supplemented with 10% FBS (fetal bovine serum, Gibco BRL), 100 μg/mL streptomycin, and 100 U/mL penicillin (Gibco BRL). A549R cells were cultured in a medium containing increasing concentrations of cisplatin to maintain the resistance.

Cytotoxicity tests

The cells were plated in flat-bottomed 96-well plates and incubated at 37 °C for 24 h. The blank medium was replaced by medium containing serial concentrations of the tested agents. The plates were incubated for 44 h. At the end of the drug-exposure period, 20 μL of MTT solution was added to each well and the plates were further incubated for 4 h. The medium was removed from the wells, and the purple formazan crystals were dissolved in 150 μL of DMSO per well. The absorbance at 595 nm was measured using a microplate reader (Infinite M200 Pro, Tecan, Männedorf, Switzerland). The mean absorbance reading from the wells without drug treatment was used as the control (100% viability). IC_{50} values were determined by interpolation of the resulting curves. For the cytotoxicity assay in the presence of the inhibitors, U87MG cells were preincubated with 10 mM NAC for 1 h before the complexes were added. Percentage of cell viability was determined by MTT.

Cellular uptake studies

Confocal microscopy. U87MG or MCF-7 cells were seeded into 35 mm dishes (Corning) and incubated for 24 h and then treated with **Ru-CD-RGD** or **Ru-CD** ([Ru] = 10 μM) for 24 h. The cells were washed twice with PBS, and viewed immediately under a confocal laser-scanning microscope (LSM 710, Carl Zeiss, Göttingen, Germany) by excitation at 488 nm. Emission was collected at 620 ± 20 nm.

Flow cytometry. U87MG or MCF-7 cells were cultured in 6-well tissue culture plates for 24 h and then treated with **Ru-CD-RGD** or **Ru-CD** ([Ru] = 10 μM) for 24 h. The cells were harvested and washed twice with PBS. Data were collected by flow cytometry excited at 488 nm (FACSCalibur™, Becton Dickinson, Franklin Lakes, NJ, USA) and analyzed with the FlowJo 7.6 software (Tree Star, OR, USA). Emission was collected at 620 ± 20 nm.

ICP-MS. U87MG or MCF-7 cells were seeded in 10 cm tissue culture dishes and incubated for 24 h. The medium was removed and replaced with fresh medium containing **Ru-CD-RGD** or **Ru-CD** ([Ru] = 10 μM). After 24 h incubation, the cells were washed with PBS and harvested. The collected cells were counted and digested with HNO_3 (65%, 0.5 mL). The solution was then diluted to a final volume of 10 mL with Milli-Q water. The concentration of iridium was measured using the XSERIES 2 ICP-MS.

Colocalization assay

U87MG cells were seeded in 35 mm dishes for 24 h and then incubated with **Ru-CD-RGD** (10 μM) at 37 °C for 24 h. The cells were further co-incubated with MitoTracker Deep Red (**MTDR**) (50 nM) or LysoTracker Deep Red (**LTDR**) (50 nM) at 37 °C for 0.5 h. Cells were washed three times with PBS and visualized by a confocal microscope (LSM 710, Carl Zeiss, Göttingen, Germany) immediately. **Ru-CD-RGD** was excited at 488 nm, **MTDR** and **LTDR** were excited at 633 nm. Emission was collected at 620 ± 20 nm, 665 ± 20 nm and 668 ± 20 nm for **Ru-CD-RGD**, **MTDR** and **LTDR**, respectively.

Cellular uptake with metabolic or endocytic inhibitors

U87MG cells were seeded in 35 mm dishes for 24 h and preincubated with carbonyl cyanide m-chlorophenyl hydrazone (CCCP) (30 μM) or chloroquine (CQ) (50 μM) for 1 h. The medium was removed and the cells were then incubated with **Ru-CD-RGD** (10 μM) for 24 h. The cells were washed three times with PBS and visualize by a confocal microscope (LSM 710, Carl Zeiss, Göttingen, Germany) immediately.

Hoechst staining

U87MG cells were seeded into 35 mm dishes (Corning) and incubated for 24 h and then treated with **Ru-CD-RGD** or cisplatin at the indicated concentrations for 24 h. The cells were then washed once with cold PBS and fixed with 4% paraformaldehyde at room temperature for 15 min. After washed with cold PBS, cells were labelled with Hoechst 33342 (5 μg/mL in PBS) for 5 min. The cells were analyzed immediately with a confocal laser-scanning microscope (LSM 710, Carl Zeiss, Germany).

Annexin V-FITC staining

Flow cytometry. U87MG cells were cultured in 6-well tissue culture plates for 24 h and then treated with different concentrations of **Ru-CD-RGD** for 24 h. The cells were harvested and stained using an annexin V-FITC apoptosis detection kit (Sigma Aldrich) according to the manufacturer's instructions. Data were collected by a flow cytometer (FACSCalibur^{TM}, Becton Dickinson, Franklin Lakes, NJ, USA) and analyzed with FlowJo 7.6 software (Tree Star, OR, USA).

Confocal microscopy. U87MG cells were seeded into 35 mm dishes (Corning) and incubated for 24 h and then treated with **Ru-CD-RGD** (10 μM) for 24 h. The cells were washed twice with ice-cold PBS, and stained with FITC-labelled annexin at 37 °C for 15 min in the dark, then visualized immediately by confocal microscopy (LSM 710, Carl Zeiss, Göttingen, Germany).

Detection of cathepsin B release

Cathepsin B activity was detected using the fluorogenic substrate Magic Red MR-$(RR)_2$ (Immunochemistry Tech, Bloomington, USA) according to the manufacturer's instructions. Briefly, U87MG or MCF-7 cells seeded into 35 mm dishes (Corning) were exposed to **Ru-CD-RGD** or cisplatin at the indicated concentrations for 24 h. The media was removed and the cells were washed twice with PBS and then incubated with Magic Red MR-$(RR)_2$ at 37 °C for 0.5 h. The media was removed and the cells were washed twice with PBS and visualized by confocal microscopy (LSM 710, Carl Zeiss, Göttingen, Germany). Emission was collected at 630 ± 20 nm upon excitation at 543 nm.

Measurement of intracellular reactive oxygen species (ROS)

U87MG cells were treated with **Ru-CD-RGD** at the indicated concentrations for 24 h and then incubated with 10 μM H_2DCFDA in serum-free DMEM for 15 min at 37 °C in the dark. The fluorescence intensity of the cells was measured immediately by flow cytometry (FACSCalibur™, Becton Dickinson, Franklin Lakes, NJ, USA) with excitation at 488 nm and emission at 530 nm. Green mean fluorescence intensities (MFI) were analyzed using FlowJo 7.6 software (Tree Star, OR, USA).

Caspase-3/7 activity assay

Caspase-3/7 activity was measured using the Caspase-Glo® Assay kit (Promega, Madison, WI, USA) according to the manufacturer's instructions. Briefly, cells were cultured in 48-well plates and treated with different concentration of **Ru-CD-RGD** for 24 h, and then 50 μL cell lysate was added to each well, followed by the addition of 50 μL Caspase-Glo® 3/7 reagent. The mixture was incubated at room temperature for 1 h and then the luminescence was measured using a TECAN Infinite M200 station.

Statistical analysis

All biological experiments were performed at least twice with triplicates in each experiment. The ANOVA method has been used in the biosystem statistics. Representative results were depicted in this report and data were presented as means ± standard deviations (SD).

Supporting Figures and Tables

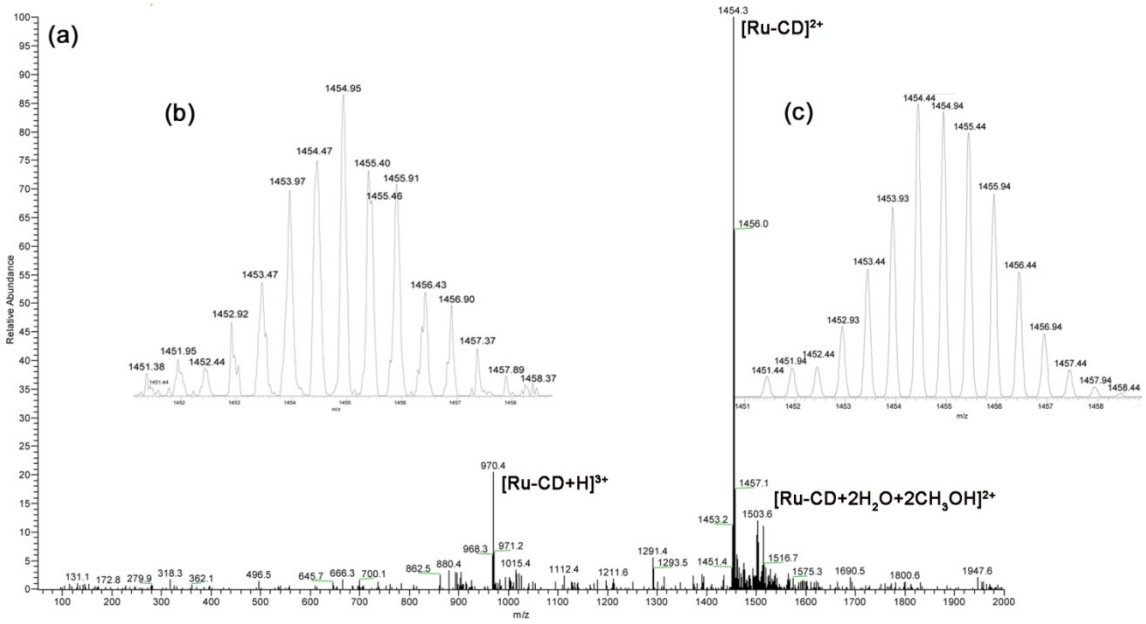


Fig. S1 ESI-MS of **Ru-CD**: a) Full range spectra; b) Bivalence ion isotopes spectra of computer simulation using formula $C_{120}H_{166}RuN_8O_{68}$, which is equivalent with [**Ru-CD**]$^{2+}$; c) Bivalence ion isotopes spectra detected.

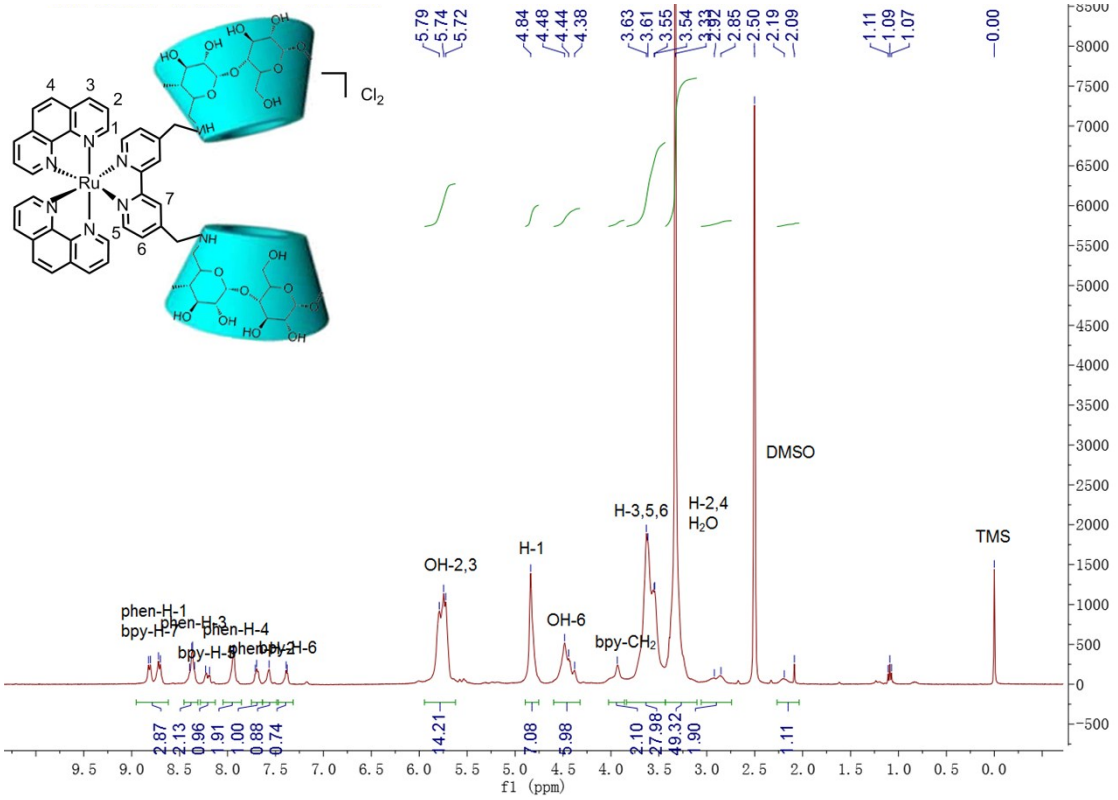


Fig. S2 ^{1}H-NMR spectrum of **Ru-CD** in d^6-DMSO.

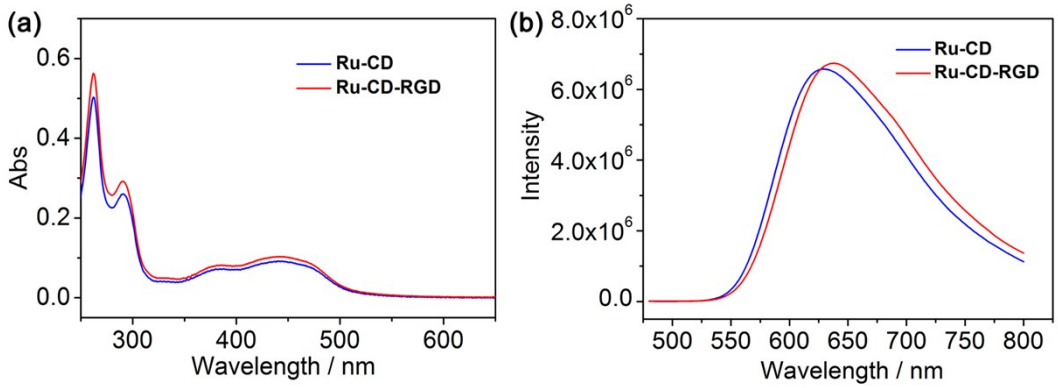


Fig. S3 (a) UV/vis spectra of **Ru-CD** and **Ru-CD-RGD** (1.0×10^{-5} M) measured in H_2O. (b) Emission spectra of **Ru-CD** and **Ru-CD-RGD** (1.0×10^{-5} M) measured in H_2O (λ_{ex} = 455 nm).

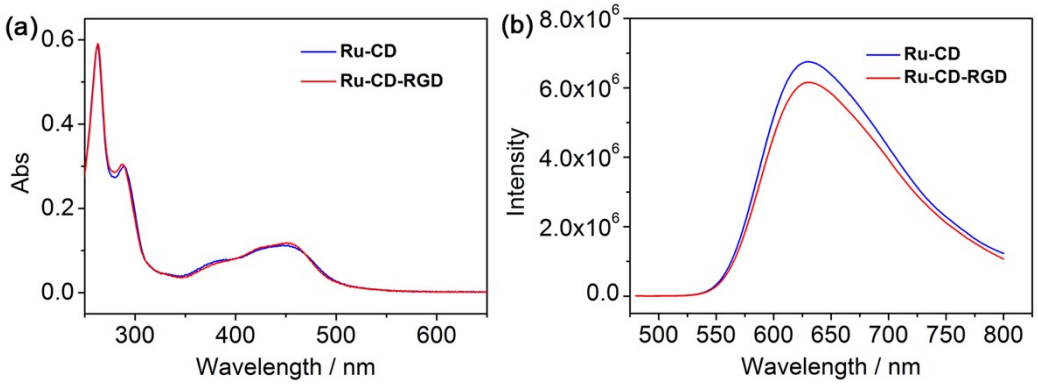


Fig. S4 (a) UV/vis spectra of **Ru-CD** and **Ru-CD-RGD** (1.0×10^{-5} M) measured in PBS. (b) Emission spectra of **Ru-CD** and **Ru-CD-RGD** (1.0×10^{-5} M) measured in PBS (λ_{ex} = 455 nm).

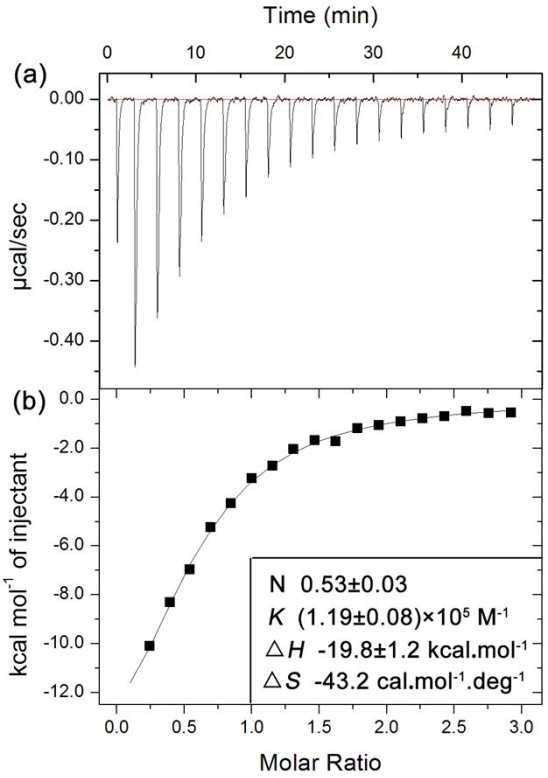


Fig. S5 (a) ITC results of the titration of c(RGDyK)-Ad with **Ru-CD** in distilled water. (b) Integration and fitted curves of the heat signals of the microcalorimetric titrations. 1.5 µL aliquots of **Ru-CD** (0.50 mM) were added into c(RGDyK)-Ad (0.025 mM) at an interval of 2.5 min (19 injections in total).

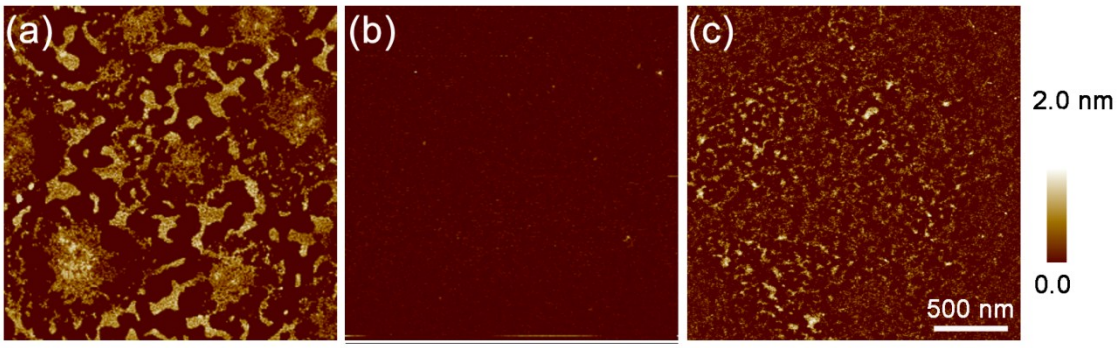


Fig. S6 Atomic force microscopy (AFM) images (2.0 ´ 2.0 µm^2) of **Ru-CD** (a), c(RGDyK)-Ad (b) and self-assembled **L** with **RGD** (c). 10 µL of sample solution was dropped onto newly clipped mica and air-dried.

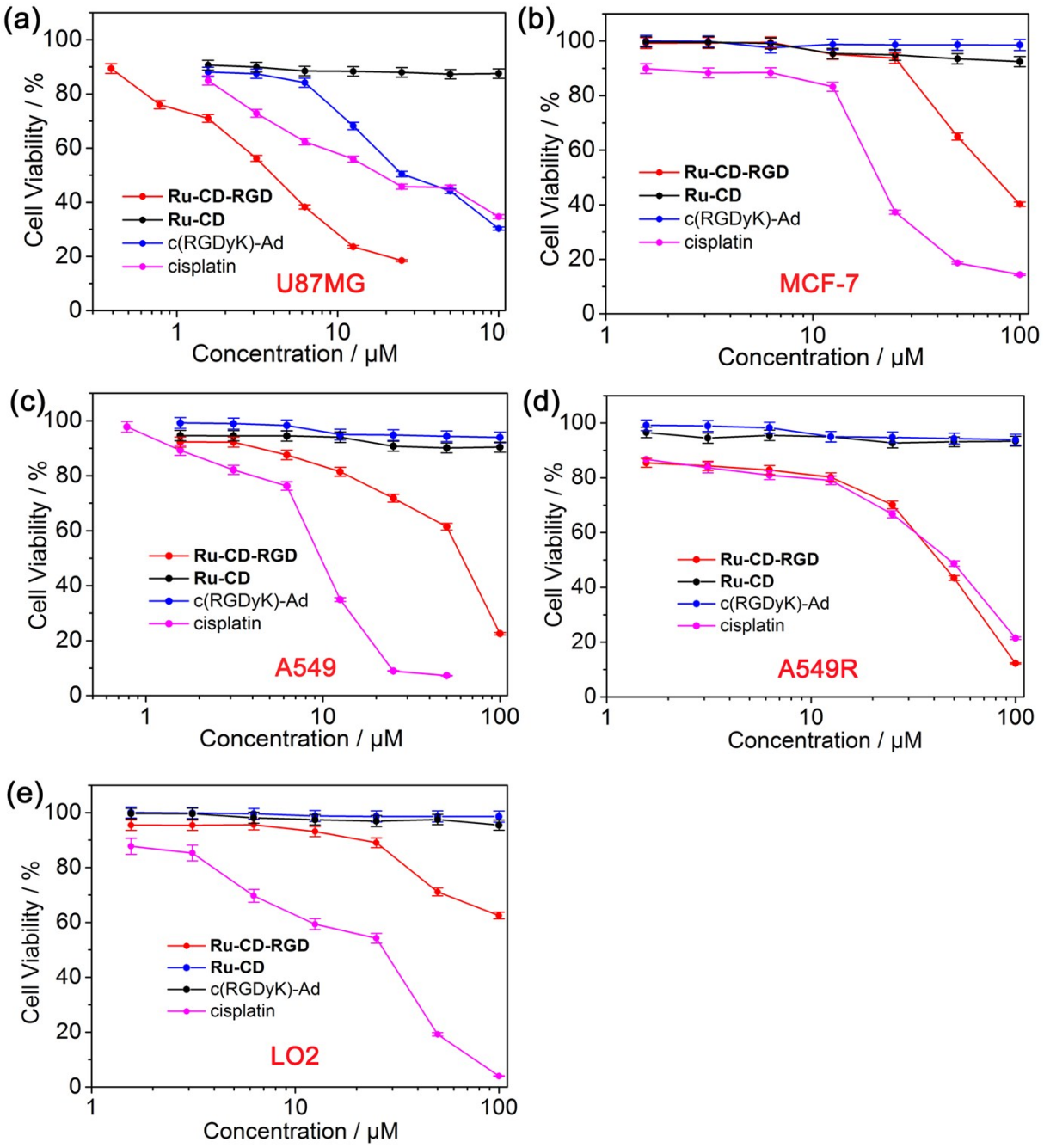


Fig. S7 In vitro cytotoxicity of **Ru-CD-RGD**, **Ru-CD**, c(RGDyK)-Ad and cisplatin against different cell lines determined by MTT assay. The cells were treated with the tested agents for 48 h and the concentration of **Ru-CD-RGD** was determined based on the content of Ru(II) in solution. Data are represented as means ± SD of three independent experiments.

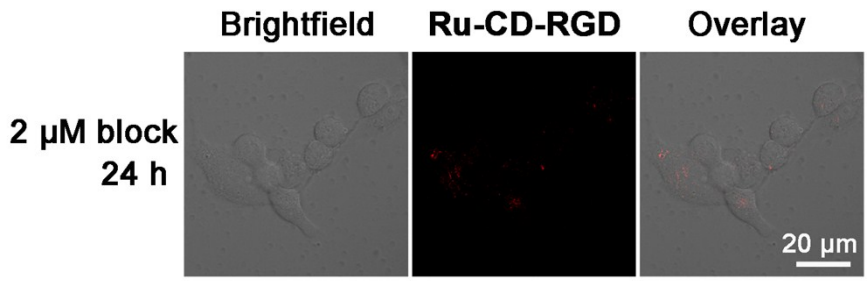


Fig. S8 Confocal microscopic images of U87MG cells after incubated with **Ru-CD-RGD** (10 μM based on the content of Ru(II) in solution) for 24 h with the blocking agent. "Blocking" denotes pre-incubation with 2 μM of c(RGDyK)-Ad for 1 h before the cells were exposed to **Ru-CD-RGD**. λ_{ex} = 488 nm, λ_{em} = 620 ± 20 nm.

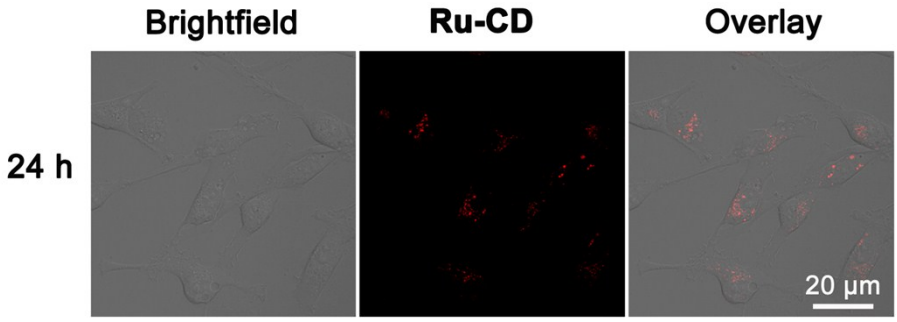


Fig. S9 Confocal microscopic images of U87MG cells after incubated with 10 μM **Ru-CD** for 24 h. λ_{ex} = 488 nm, λ_{em} = 620 ± 20 nm.

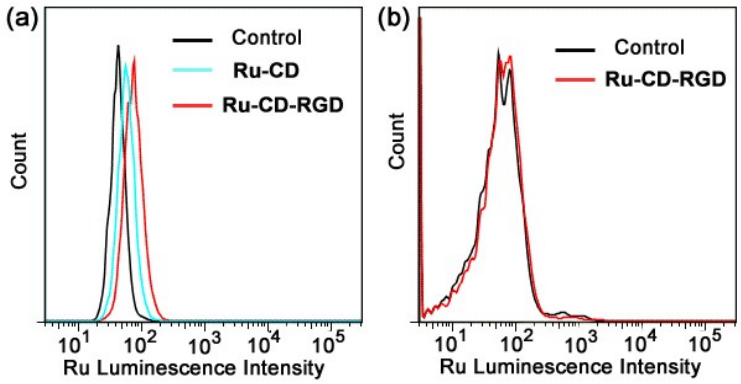


Fig. S10 Cell uptake of **Ru-CD** (10 μM) or **Ru-CD-RGD** (10 μM) in U87MG (a) and MCF-7 (b) determined by flow cytometry after 24 h incubation. The mean fluorescence intensity (MFI) of U87MG cells for control, **Ru-CD**-treated and **Ru-CD-RGD**-treated cells are 109 ± 6, 161 ± 8 and 222 ± 11, respectively. The MFI of MCF-7 cells for control and **Ru-CD-RGD**-treated cells are 83 ± 6 and 86 ± 7, respectively. Data are represented as means ± SD of three independent experiments.

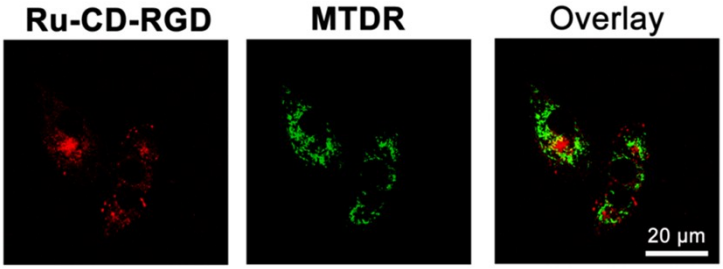


Fig. S11 Determination of colocalization of **Ru-CD-RGD** with **MTDR** by confocal microscopy. U87MG cells were incubated with **Ru-CD-RGD** (10 μM, 24 h), and then stained with **MTDR** (50 nM, 30 min) at 37 °C. **Ru-CD-RGD**: λ_{ex} = 488 nm, λ_{em} = 620 ± 20 nm; **MTDR**: λ_{ex} = 633 nm, λ_{em} = 665 ± 20 nm.

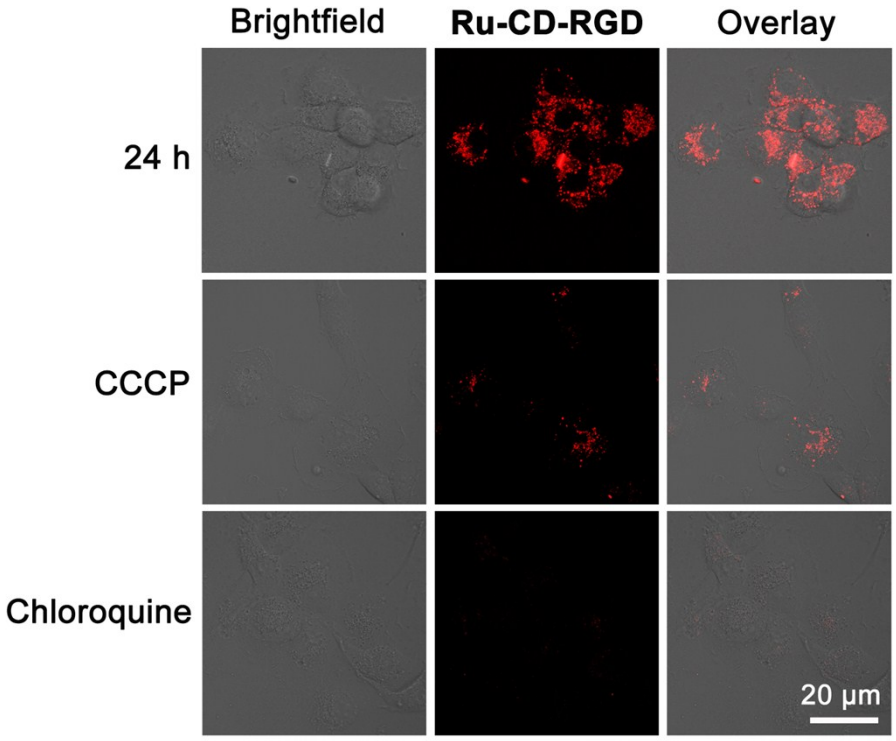


Fig. S12 Confocal images of U87MG cells incubated with **Ru-CD-RGD** (10 μM, λ_{ex} = 488 nm, λ_{em} = 620 ± 20 nm) for 24 h (the 1st line) and pretreatment with CCCP (30 μM, 1 h, the 2ed line) or CQ (50 μM, 1 h, the 3rd line) at 37 ºC.

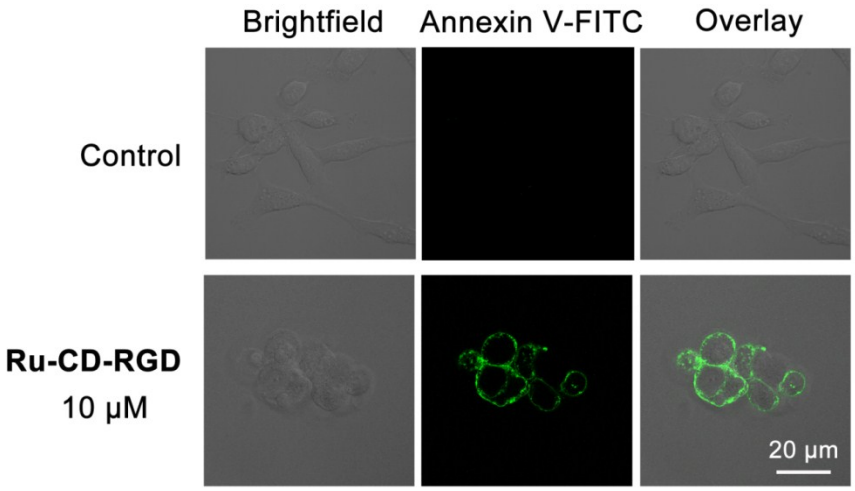


Fig. S13 Annexin V staining assay analyzed by confocal microscopy. U87MG cells were treated with **Ru-CD-RGD** (10 μM) for 24 h. λ_{ex} = 488 nm; λ_{em} = 530 ± 20 nm.

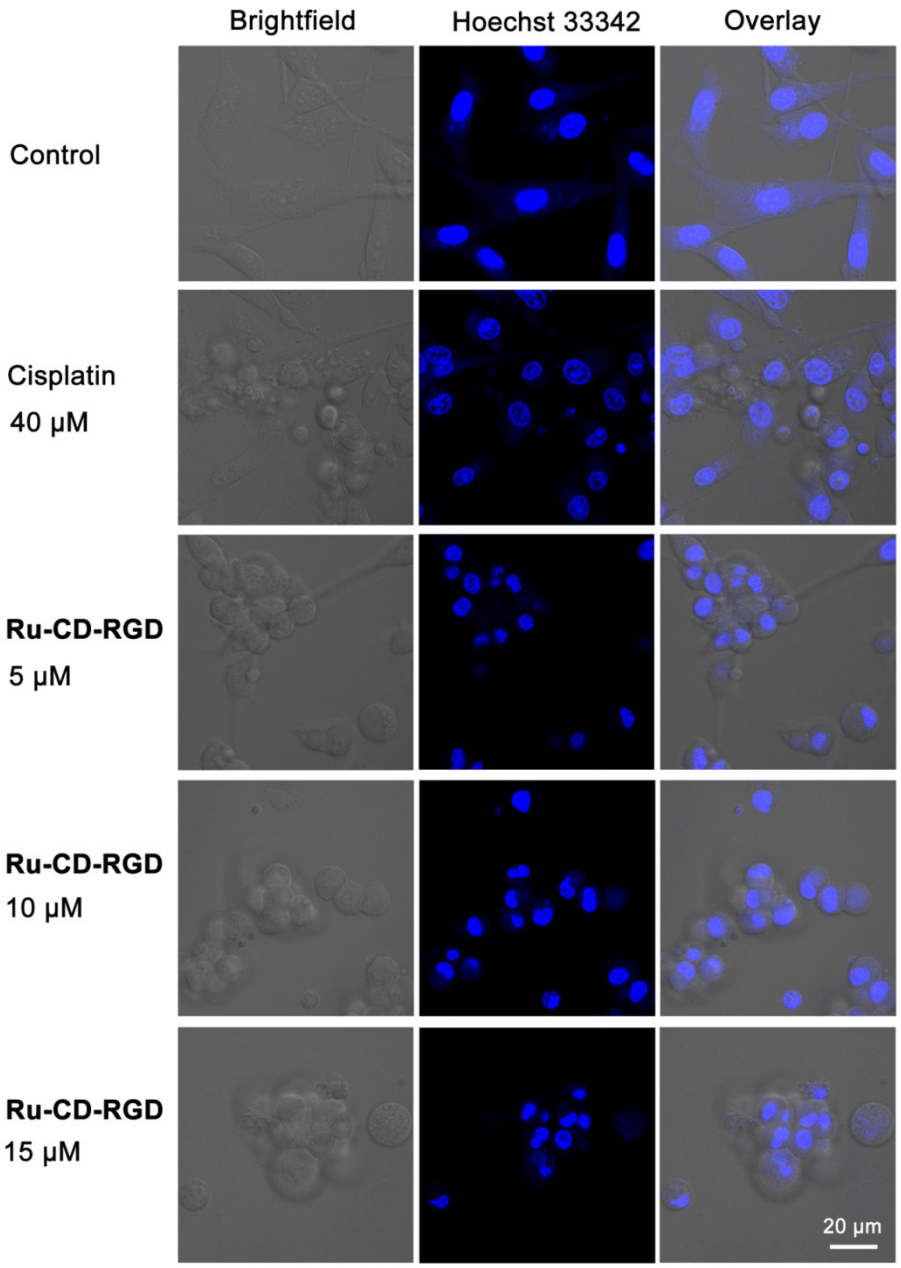


Fig. S14 Hoechst 33342 stained U87MG cells treated with **Ru-CD-RGD** or cisplatin at the indicated concentrations for 24 h. The concentration of **Ru-CD-RGD** was determined based on the content of Ru(II) in solution. λ_{ex}: 405 nm; λ_{em}: 460 ± 20 nm.

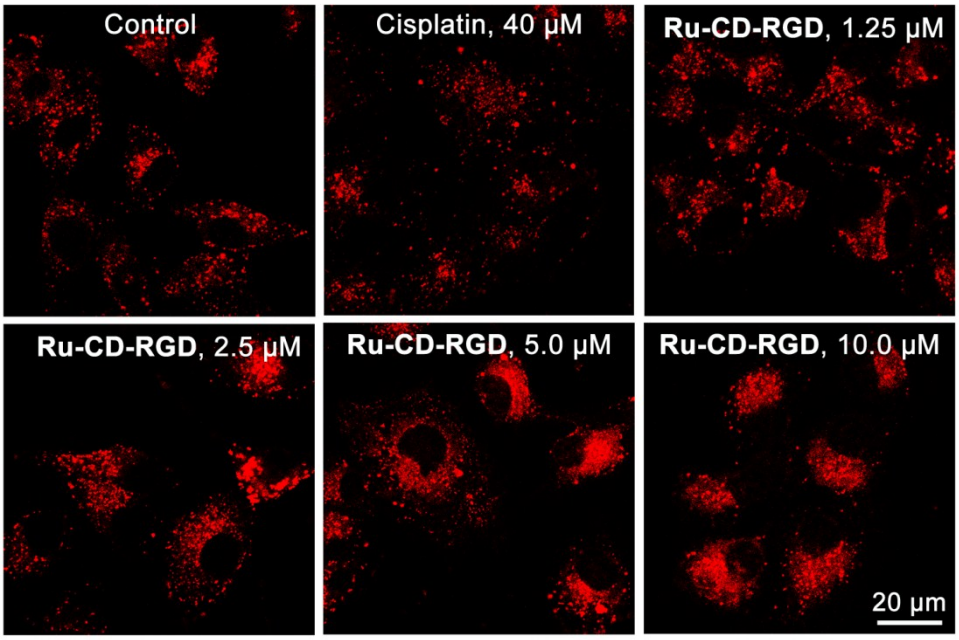


Fig. S15 Observation of cathepsin B release from lysosomes to the cytosol induced by **Ru-CD-RGD** or cisplatin at the indicated concentrations for 24 h in U87MG using the fluorogenic substrate Magic Red MR-$(RR)_2$. Emission was collected at 630 ± 20 nm upon excitation at 543 nm.

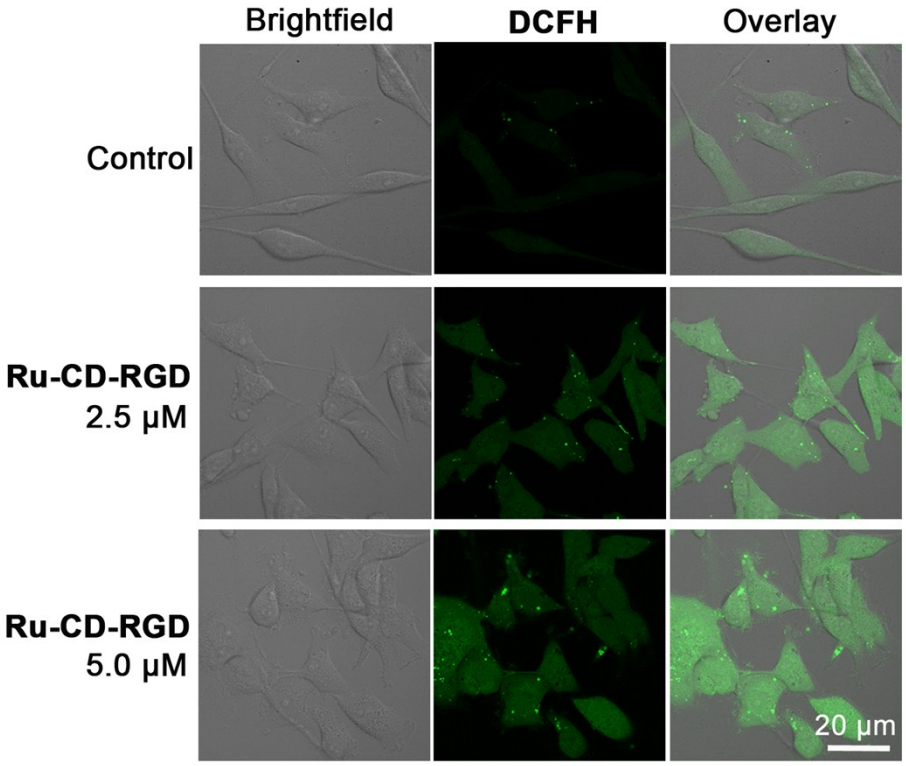


Fig. S16 Effects of **Ru-CD-RGD** on ROS generation. U87MG cells were incubated with **Ru-CD-RGD** at the indicated concentrations for 24 h, after which they were labeled with DCFH-DA and analyzed by confocal microscope (excitation at 488 nm and emission at 500–530 nm).

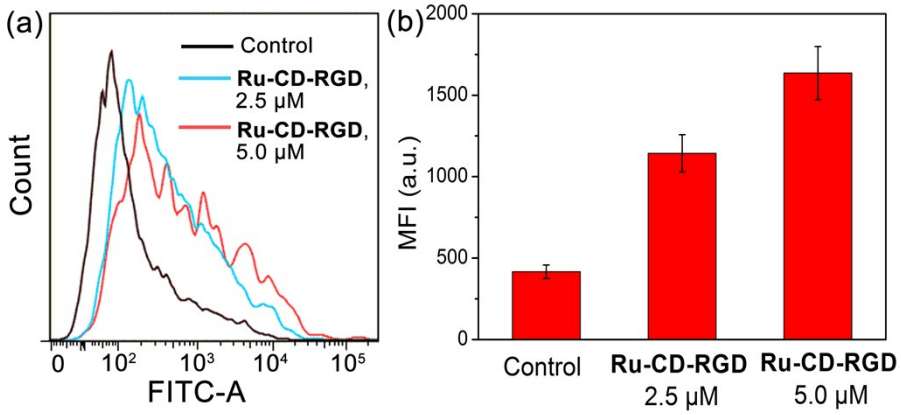


Fig. S17 Effects of **Ru-CD-RGD** on ROS generation. (a) U87MG cells were incubated with **Ru-CD-RGD** at the indicated concentrations for 24 h, after which they were labeled with DCFH-DA and analyzed by flow cytometry (excitation at 488 nm and emission at 500–530 nm). (b) The MFI of DCF fluorescence intensity in U87MG cells after treatment with **Ru-CD-RGD** at the indicated concentrations. Data are represented as means ± SD of three independent experiments.

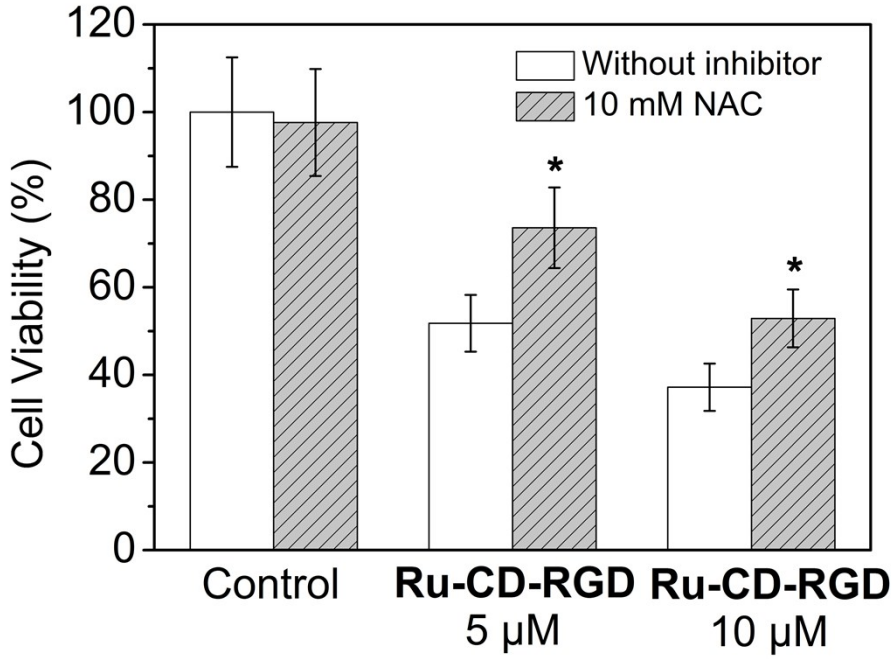


Fig. S18 The impact of NAC on the cytotoxicity of **Ru-CD-RGD**. U87MG cells were treated with **Ru-CD-RGD** for 48 h at the indicated concentrations in the absence or presence of NAC. Cell viability was measured by MTT assay. Data are represented as means ± SD of three independent experiments. *$p < 0.05$, **$p < 0.01$.

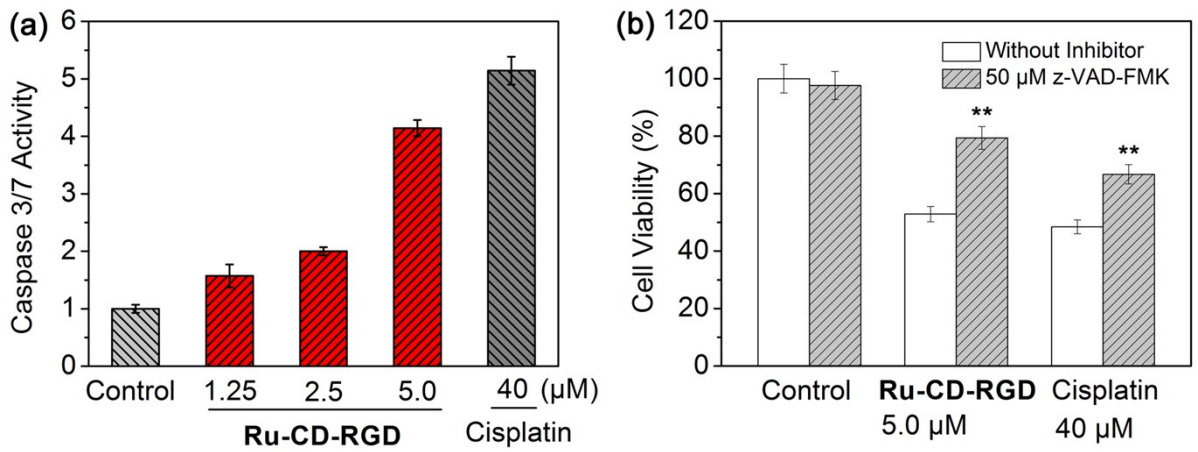


Fig. S19 Apoptosis induced by **Ru-CD-RGD** is caspase-dependent. (a) Detection of caspase-3/7 activity in U87MG cells after **Ru-CD-RGD** or cisplatin treatment for 24 h at the indicated concentrations. (b) The impact of z-VAD-FMK on the cytotoxicity of **Ru-CD-RGD**. U87MG cells were treated with **Ru-CD-RGD** or cisplatin for 48 h at the indicated concentrations in the absence or presence of z-VAD-FMK. Cell viability was measured by MTT assay. Data are represented as means ± SD of three independent experiments. *$p < 0.05$, **$p < 0.01$.

Table S1. Photophysical data for **Ru-CD** and **Ru-CD-RGD**[a]

Compounds	Medium	$\lambda_{abs,max}$ (nm)	$\lambda_{em,max}$ (nm)	Φ_{em}[b]	τ_{av} / ns[c]
Ru-CD	H_2O	445	627	0.058	507.4979
	PBS	452	629	0.080	494.1338
Ru-CD-RGD	H_2O	442	632	0.063	501.9282
	PBS	452	628	0.070	519.3832
$[Ru(bpy)_3]Cl_2$	H_2O	453	627	0.042	357.4476
	PBS	453	627	0.042	348.0846

[a]All emission decays were obtained on freshly prepared samples placed in quartz cuvettes. Samples were 1.0×10^{-5} M in concentration. [b]Solutions of $[Ru(bpy)_3]Cl_2$ were used as the standard, H_2O and PBS are both degassed (Φ_{em} = 0.042)[1]. [c]Decay curves of compounds were recorded by an Edinburgh FLS 980 Spectrometer. All curves were fitted into a two exponential formula $F(t) = A + B_1 \exp(-t/\tau_1) + B_2 \exp(-t/\tau_2) + B_3 \exp(-t/\tau_3)$; $\tau_{ay} = \frac{B_1\tau_1^2 + B_2\tau_2^2 + B_3\tau_3^2}{B_1\tau_1 + B_2\tau_2 + B_3\tau_3}$

Table S2. Cell uptake of **Ru-CD-RGD** (10 μM) or **Ru-CD** (10 μM) in U87MG and MCF-7 determined by ICP-MS after 24 h incubation. Data are represented as means ± SD of three independent experiments.

	U87MG (ng/10^6 cells)	MCF-7 (ng/10^6 cells)
Ru-CD-RGD	12.7 ± 0.6	3.9 ± 0.3
Ru-CD	2.6 ± 0.2	undetermined

Supporting References

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