Supplementary Material

A Ru(II) complex based COX-2 targeting type I photosensitizer evokes ferroptosis and apoptosis

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Supplementary methods

Materials and instruments. All the reagents and solvents were commercially available and used without further purification. They were purchased from Shandong Boyuan Pharmaceutical Co. Ltd., J&K, Bidepharma-Tech and Energy Chemical, and the silica gel (200-300 mesh) from Qingdao Ocean Chemical Co. LTD. The ultraviolet absorption spectrum was measured by a Perkin-Elmer lambda 35 spectrophotometer, and the phosphorescence by FluoroMax-4 spectrofluorometer. The ^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance III-400. High-resolution mass spectra (HR-MS) were performed with an Agilent 6540Q-TOF HPLC-MS spectrometer. Flow cytometry analysis was obtained using a BD LSRFortessa Cell Analyzer. Confocal imaging was realized using a Zeiss LSM 710 confocal laser scanning microscope.

UV-Vis and phosphorescence spectroscopic. Dissolve an appropriate amount of RuCXB and RuOH in DMSO to obtain a 1 mM solution as the stock solution, respectively. And they were stored at 4°C in a refrigerator. The absorption spectra and phosphorescence spectra of the different compounds were determined by ACN and PBS buffer solution diluted to 10 μM at room temperature. λ_{ex} = 450 nm and slit: 5/5.

Determination of photoinduced singlet oxygen quantum yield. The test method was consistent with that described in the literature[1]. Photoinduced singlet oxygen quantum yield (Φ_{Δ}) of Ru(II) complexes was determined in acetonitrile in the presence of 1,3-diphenylisobenzofuran (DPBF) as the $^{1}O_2$ probe, and $Ru(bpy)_3Cl_2$ as the reference (Φ_{Δ} = 0.56, in air-saturated acetonitrile). Acetonitrile solutions containing Ru(II) complexes and DPBF were used the white light irradiation. The absorbance of DPBF at 415 nm was recorded every 10 s. The singlet oxygen quantum yields of Ru(II) complexes were calculated according to the following equation:

$$\emptyset_{\Delta}(\,^{1}O_2)^{S} = \emptyset_{\Delta}(\,^{1}O_2)^{R}\frac{S^{S}F^{R}}{S^{R}F^{S}}$$

$\Phi_{\Delta}(^{1}O_2)$ represents $^{1}O_2$ quantum yields, superscript S represents the sample, superscript R represents the reference, S is the slope of a linear fit of the change in absorbance of DPBF (at 415 nm), F is the absorption correction factor which is given by $F = 1\text{-}10^{-OD}$ (OD is the optical density at the irradiation wavelength).

Reactive oxygen species (ROS) detection in the solution. DPBF (1,3-diphenylisobenzofuran), SOSG (singlet oxygen sensor green reagent) and DHR123 (dihydrorhodamine 123) were the probes to detect the production of various ROS. For DPBF as the probes to determine the production of $^{1}O_2$, please refer to *Determination of photoinduced singlet oxygen quantum yield* for details. While, for the SOSG and DHR123 of singlet oxygen ($^{1}O_2$) and superoxide anion radical ($O_2^{\cdot-}$) respectively, add Ru(II) complexes (10 μM) and the relevant probe to the fluorescence cuvette, and measure the fluorescence changes before and after irradiation (white light, 6 mW cm^{-2}, 3 min).

Cell culture. Human breast cancer cells MCF-7 were cultured in RPMI-1640 medium (with double antibody, KeyGEN) containing 10% FBS (Hyclone). Mouse breast cancer cells 4T1 and human proximaltubular epithelial cell line HK2 were cultured in DMEM medium (with double antibody, KeyGEN) containing 10% FBS (Hyclone). Human colon cancer cells HCT116 were cultured in McCoy's 5A medium (KeyGEN)

containing 10% FBS (Hyclone). The cells were cultured in an incubator at 37℃, 5% CO_2 concentration, and saturated humidity.

Cell uptake. The cell uptake experiment methods of the four cell lines were consistent, taking the MCF-7 as an example. MCF-7 cells were seeded in confocal Petri dishes with 4 wells (500 μL per well) or 6-well plates (2 mL per well). After culture for 24 h, 500 μL or 2 mL solution containing Ru(II) complexes with a concentration of 2 μM was added to each well. After the cells were incubated for 4 h, the difference in intracellular fluorescence intensity was observed by laser confocal, or the level of intracellular Ru element was detected by ICP-MS.

Cytotoxicity study (MTT assay). The test method was consistent with that described in the literature[1]. MCF-7, 4T1, HCT116 and HK2 cells were distributed in 96-well plates at a density of 5000 cells per well (100 μL), respectively. After cultured for 24 h, the cells were treated according to different concentration gradients (dark groups: 0, 4, 8, 16, 32, 64, 128, 256 μM; light groups: 0, 0.125, 0.25, 0.5, 1, 2, 4, 8 μM) at 200 μL medium per well. With the incubation of 4 h, the light groups were illuminated (white light, 6 mW cm^{-2}, 15 min). After 24 h, MTT (2.5 mg/mL) was added to the 96-well plate at the amount of 40 μL per well and the cells were continued to cultivate for 4 h. Then, the supernatant was sucked out with a syringe, and 150 μL of spectral pure DMSO was added to each well. After shaking well, the absorbance of the solution at 570 nm was detected. The experiment was repeated three times and divided into the following three groups:

1. Dark group: Ru(II) complexes with different concentration gradients were incubated in the dark for 24 h under normal oxygen conditions.
2. Light + Normoxia group: after incubation of Ru(II) complex with different concentration gradients for 4 h in the dark, the cells were exposed to white light for 15 min (6 mW cm^{-2}) and continued incubation until 24 h.
3. Light + Hypoxia group: after the cells were incubated with Ru(II) complexes of different concentration gradients in the dark for 3 h, the 96-well plates were placed in the anaerobic air bag for 1 h and then exposed to white light for 15 min (6 mW cm^{-2}). Then remove from the bag and continue to incubate until 24 h. Keep the oxygen concentration below 0.1% during irradiation.

Reactive oxygen species (ROS) detection in MCF-7 cells. DCFH-DA (2',7'-Dichlorodihydrofluorescein diacetate), SOSG and DHR123 were the probes to detect the production of ROS, $^1O_2$ and $O_2^{\cdot -}$ in cells, respectively. After cultivation for 24 h in a confocal dish with 4 wells (500 μL per well), the MCF-7 cells were incubated successively with Ru(II) complexes (2 μM) for 4 h, with the corresponding probes for 30 min and with fresh medium. Finally, the white light was given for 3 min (6 mW cm^{-2}), and the green fluorescence intensity in cells was observed by laser confocal fluorescence microscopy.

ROS detection by MTT assay. After cultivation for 24 h in 96-well plates at a density of 5000 cells per well (100 μL), MCF-7 cells were cultured with different ROS inhibitors and Ru(II) complexes (the concentration consistent with IC_{50}). After incubation for 4 h, the cells of normoxia groups were exposed to white light for 15 min (6 mW cm^{-2}), then, cultured with the fresh medium in the dark until 24 h to test the cell

survival rate. While, after incubating for 3 h, the cells of hypoxia groups were put into the anaerobic air bag for 1 h, then exposed to white light for 15 min (6 mW cm^{-2}). Finished, the cells were taken out of the bag and cultured with the fresh medium in the dark until 24 h to test the cell survival rate.

Cell death mechanism detection by MTT assay. MCF-7 cells were distributed in 96-well plates at a density of 5000 cells per well (100 μL). After 24 h, the cells were cultured with different death mode inhibitors and Ru(II) complexes (the concentration consistent with IC_{50}). After incubation for 4 h, the cells of normoxia groups were exposed to white light for 15 min (6 mW cm^{-2}), then, continued to incubate in the dark until 24 h to test the cell survival rate. While, after incubation for 3 h, the cells of hypoxia groups were put into the anaerobic air bag for 1 h, then exposed to white light for 15 min (6 mW cm^{-2}). Finished, the cells were taken out of the bag and continued to incubate in the dark until 24 h to test the cell survival rate.

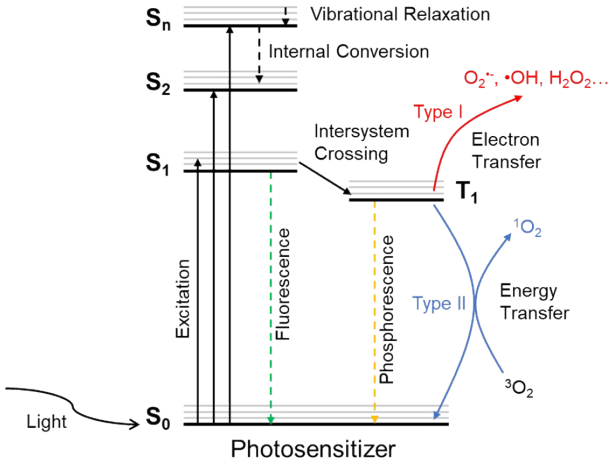
Western blot analysis for MCF-7 cells treated by Ru(II) complexes. After cultivation for 24 h in a 6-cm petri dish, MCF-7 cells were cultured in the fresh medium with or without Ru(II) complexes (the concentration consistent with IC_{50}) for 4 h. Then, the white light (6 mW cm^{-2}) was given for 15 min and the cells were continued to incubate in the dark until 24 h. Subsequently, the cells were collected and lysed with RIPA lysis buffer for 30 min, then, centrifuged at 4℃ for 15 min (12000 rpm). Taking the supernatant, the protein concentration of the supernatant was determined by the Bradford method and normalized. Subsequently, place them in a 95℃ water bath for 5 min to denature the protein. Western Blot was used to determine the expression of the target protein. Equal amounts of protein were added to each lane of SDS-PAGE gel for electrophoresis and transferred onto polyvinylidene fluoride (PVDF) membranes. After that, the membranes were shaken to block by 5% BSA for 1 h, and then specific primary antibodies were incubated at 4°C overnight. Subsequently, the primary antibody was recovered. And the membranes were washed with 1×TBST three times for 15 min, then, incubated with the secondary antibodies for 1 h at room temperature, and washed. Finally, the immunoblots were visualized by a ChemiScope series (Clinx Science Instruments Co, Ltd.) with enhanced chemiluminescence kits (Millipore Corporation, USA).

Lipid peroxidation detection in MCF-7 cells. C11-BODIPY$^{581/591}$ was used to detect the production of lipid peroxidation in cells. After cultivation for 24 h in a confocal dish with 4 wells (500 μL per well), the MCF-7 cells were incubated successively with Ru(II) complexes (2 μM) for 4 h, with C11-BODIPY$^{581/591}$ for 20 min and with fresh medium. Finally, the white light was given for 3 min (6 mW cm^{-2}), and the fluorescence intensity in cells was observed by laser confocal fluorescence microscopy.

Flow cytometric assay of apoptosis for MCF-7 cells treated by Ru(II) complexes. After cultured for 24 h in a 6-well plate, the MCF-7 cells were co-incubated with Ru(II) complexes for 4 h and illuminated (white light, 6 mW cm^{-2}, 15 min), then, continued to culture for 24 h. Subsequently, the cells were collected by trypsin and washed with PBS. After that, Binding Buffer (500 μL), Annexin V-FITC (5 μL) and Propidium Iodide (5 μL) were added in turn and mixed well. Then, the cells were incubated at room temperature for 5 min in the dark. The analysis was measured by a BD

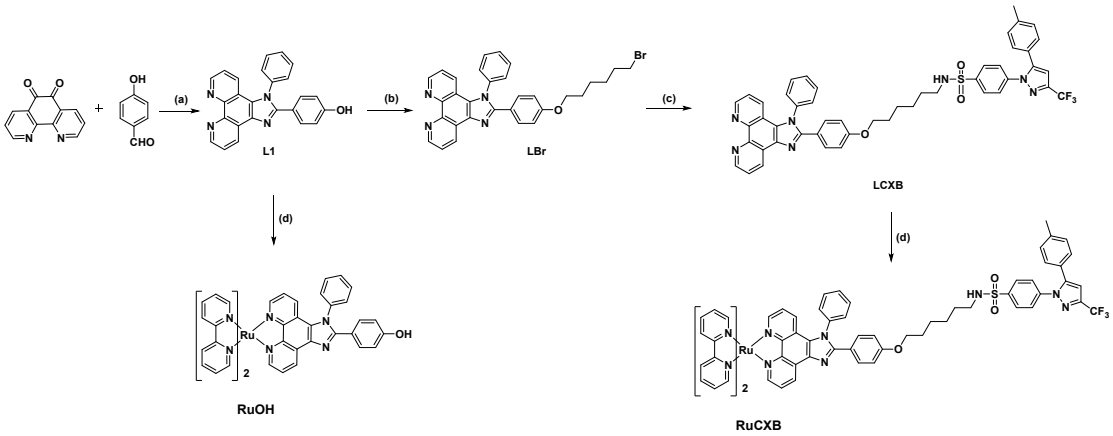
LSRFortessa Cell Analyzer within 1 h.

3D multicellular spheroids (MCSs) culture and study. MCF-7 cells were seeded in 96-well round-bottom plates with 3000 cells per well and, after 24 h, formed multicellular spheroids with a diameter of 500 μm. The spheroids were divided into four groups: control groups (dark/light) and drug groups (dark/light). The cells of the control groups were cultured in the fresh medium with nothing else and the cells of the drug groups with Ru(II) complexes (10 μM). Change the medium (control/drug groups: without/with Ru(II) complexes) every other day and after 24 h, the white light was given (6 mW cm^{-2}, 15 min) to the light groups.



Supplementary Scheme 1. A diagram of ROS generation mechanism.

Synthesis and characterization parts



a: aniline, ammonium acetale, glacid acetie acid, refluxed[2]. b: 1,6-diiodohexane, DMF, $CHCl_3$, 80°C[2]. c: celecoxib, DMF, r.t-75°C. d: dichloro (p-cymene) ruthenium(II) dimer (0.5 equiv.), 2, 2 -bipyridine (2.0 equiv.), Ethanol, H_2O, reflux, 22 h.

Supplementary Scheme 2. The synthetic routes of Ru(II) complexes.

Syntheses of **LCXB.**

LBr (457 mg, 0.83 mmol), CXB (381 mg, 1.0 mmol), K_2CO_3 (230 mg, 1.66 mmol)

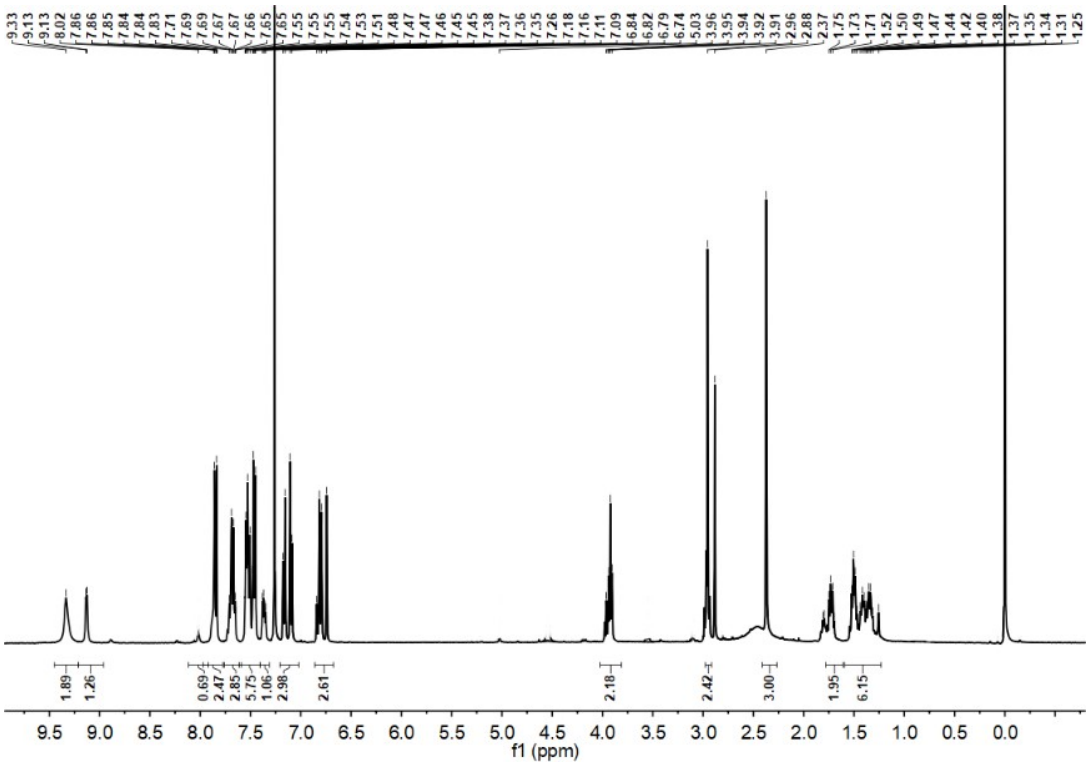
and DMF (10 mL) were added into a 50 mL flask, stirred to dissolve the mixture, and then heated to 70℃ for 10 h. After the reaction was completed, the solvent was cooled to room temperature and removed by a rotary evaporator. Then, it was extracted by DCM and dried by anhydrous $MgSO_4$. Finally, the targeted compound was purified by column chromatography using DCM and MeOH (30/1, R_f = 0.3) to obtain yellow solid (300 mg, 42%). ^{1}H NMR (400 MHz, DMSO-d_6) δ/ppm = 9.33 (s, 2H), 9.13 (d, *J* = 3.6 Hz, 1H), 8.02 (s, 1H), 7.91 - 7.75 (m, 2H), 7.76 - 7.61 (m, 3H), 7.58 - 7.43 (m, 6H), 7.36 (dd, *J* = 4.4, 4.4 Hz, 1H), 7.13 (dd, *J* = 8.0, 8.0 Hz, 3H), 6.80 (m, 3H), 3.96 - 3.91 (m, 2H), 2.96 (m, 4H), 2.37 (s, 3H), 1.75 (m, 2H), 1.61 - 1.22 (m, 6H).

Syntheses of **RuCXB** and **RuOH.**

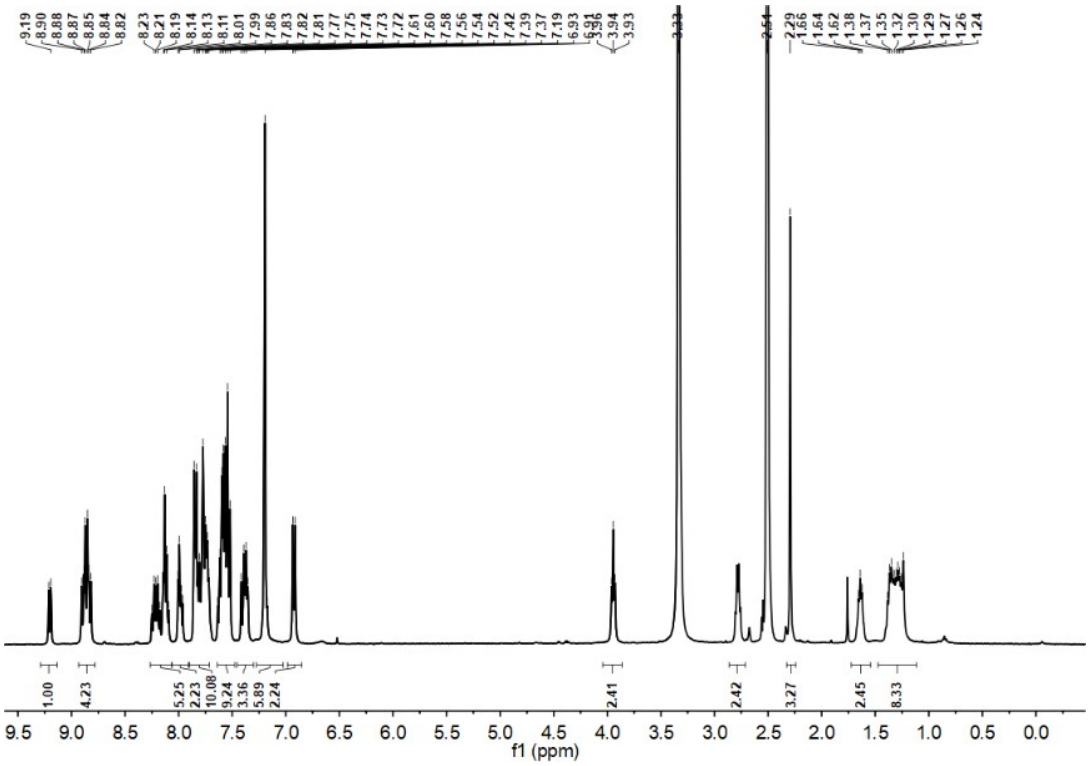
The corresponding L ligand (1.0 equiv.) and dichloro (p-cymene) ruthenium(II) dimer (0.5 equiv.) were added into a 25 mL flask under N_2 atmosphere. Then anhydrous ethanol as the solvent was added and stirred until the mixture was completely dissolved. Subsequently, the aqueous solution of 2, 2-dipyridine (2.0 equiv.) was added through the syringe and the mixture was heated to reflux. After 24 h, the reaction was completed and cooled to room temperature. The solvent was removed by rotary evaporator and the corresponding deep red solid complexes were purified by column chromatography using ACN, H_2O and 20% KNO_3 (100/9/1, R_f = 0.3).

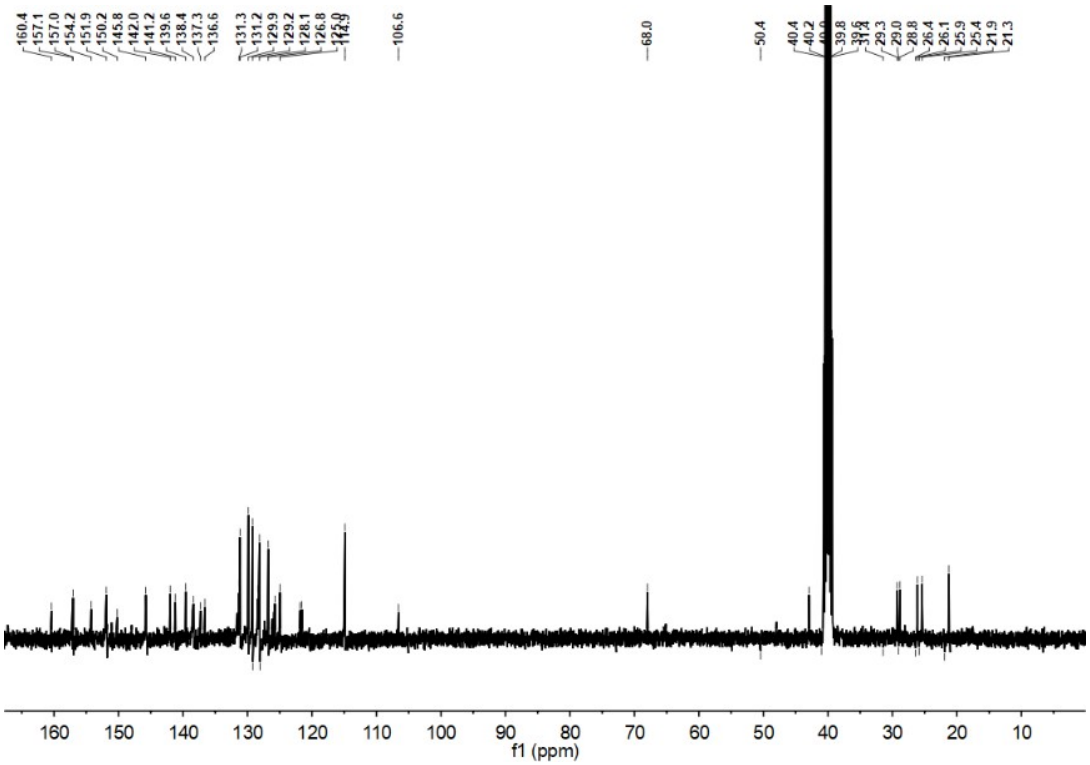
RuCXB: yield: 34%. ^{1}H NMR (400 MHz, DMSO-d_6) δ/ppm = 9.20 (d, *J* = 7.7 Hz, 8H), 8.86 (m, 4H), 8.31 - 8.07 (m, 5H), 8.03 - 7.91 (m, 2H), 7.90 - 7.69 (m, 10H), 7.65 - 7.48 (m, 9H), 7.38 (m, 3H), 7.18 (d, *J* = 8.0 Hz, 6H), 6.92 (d, *J* = 8.0 Hz, 2H), 3.94 (t, *J* = 8.0 Hz, 2H), 2.78 (dd, *J* = 4, 4 Hz, 2H), 2.29 (s, 3H), 1.68 - 1.53 (m, 2H), 1.44 - 1.12 (m, 8H). ^{13}C NMR (100 MHz, DMSO- d_6) δ/ppm = 160.4, 157.1, 157.0, 154.2, 251.9, 150.2, 145.8, 142.0, 141.2, 139.6, 138.4, 137.3, 136.6, 131.3, 131.2, 129.9, 129.2, 128.1, 126.8, 125.0, 114.9, 106.6, 68.0, 50.4, 42.9, 31.4, 29.3, 29.0, 28.8, 26.4, 26.1, 25.9, 25.4, 21.9, 21.3. HR-MS (positive mode, m/z): calcd. 632.6642, found 632.6620 for $[M\text{-}2NO_3^-]^{2+}/2$.

RuOH: yield: 35%. ^{1}H NMR (400 MHz, DMSO-d_6) δ/ppm = 10.06 (d, *J* = 4.0 Hz, 1H), 9.19 (d, *J* = 8.0 Hz, 1H), 8.87 (td, *J* = 12.0, 8.0 Hz, 4H), 8.29 - 8.16 (m, 2H), 8.16 - 8.06 (m, 3H), 8.01 - 7.92 (m, 2H), 7.87 - 7.81 (m, 2H), 7.81 - 7.70 (m, 5H), 7.65 - 7.54 (m, 5H), 7.51 - 7.29 (m, 5H), 6.77 (d, *J* = 12.0 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ/ppm = 159.6, 157.2, 157.1, 157.0, 154.7, 151.9, 151.0, 150.1, 145.6, 138.4, 137.4, 136.6, 131.5, 131.3, 131.0, 129.3, 128.2, 128.0, 127.3, 126.1, 125.9, 125.0, 121.8, 120.1, 115.8. HR-MS (positive mode, m/z): calcd. 401.0872, found 401.0859 for $[M\text{-}2NO_3^-]^{2+}/2$.

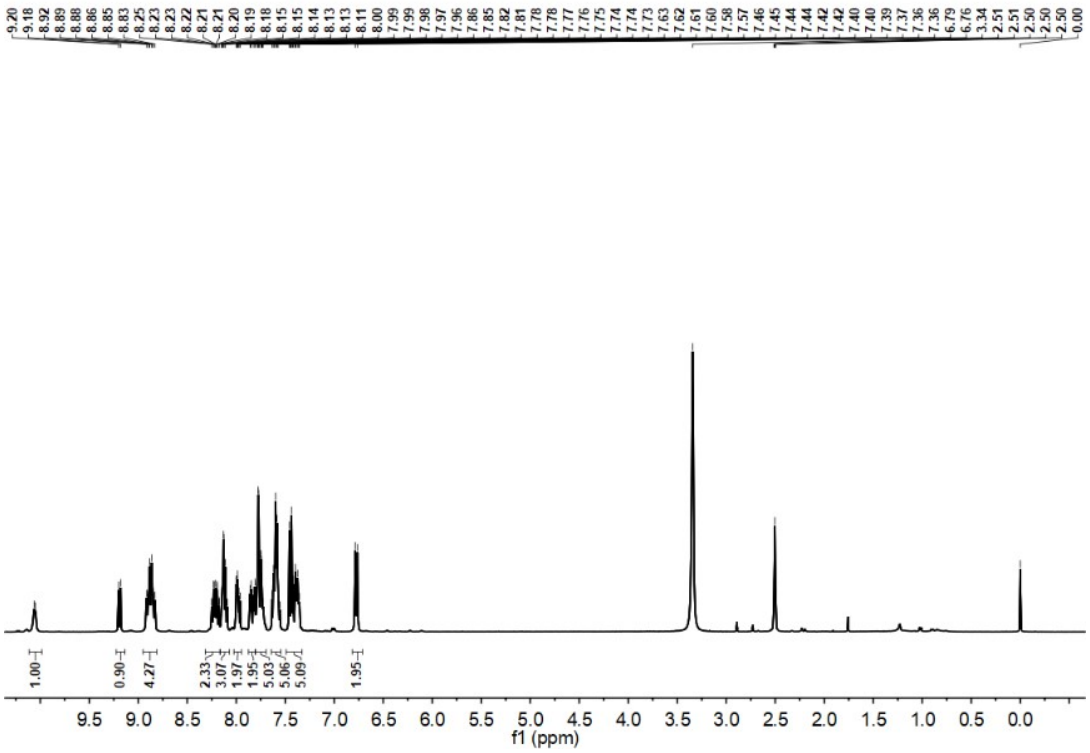


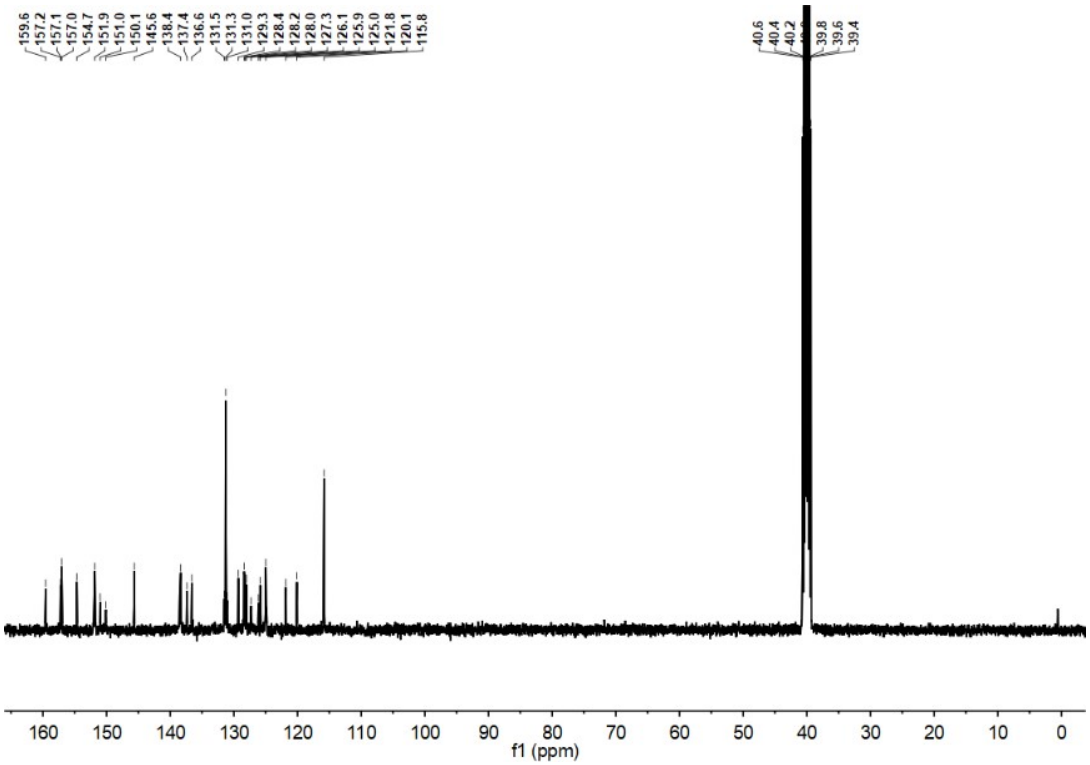
Supplementary Figure 1. ^{1}H NMR spectra of compound **LCXB**.



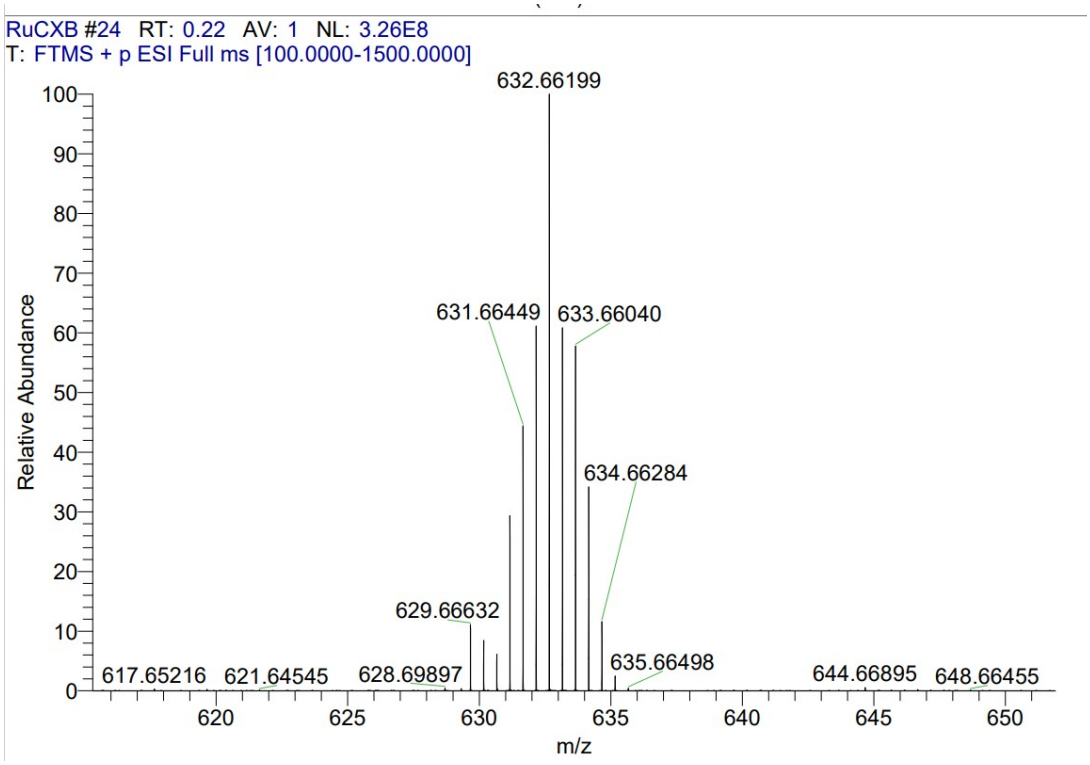


Supplementary Figure 2. ^{1}H and ^{13}C NMR spectra of compound **RuCXB**.

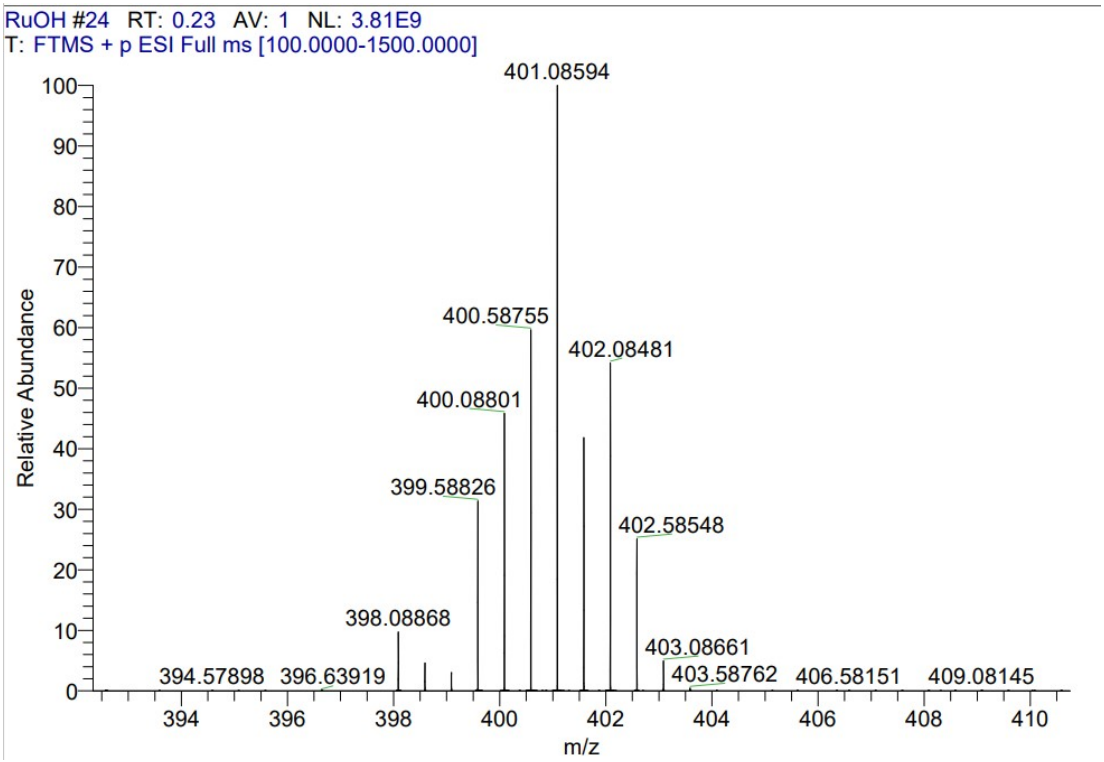




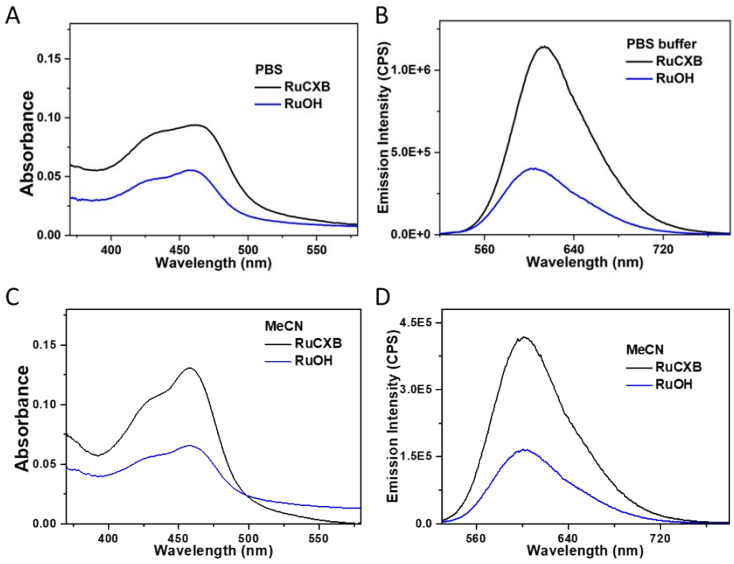
Supplementary Figure 3. ^{1}H and ^{13}C NMR spectra of compound **RuOH**.



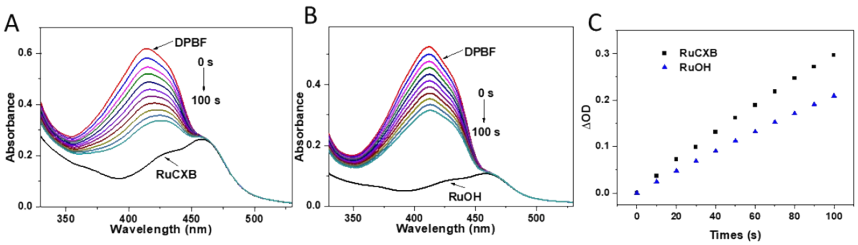
Supplementary Figure 4. HR-MS spectra for **RuCXB**.



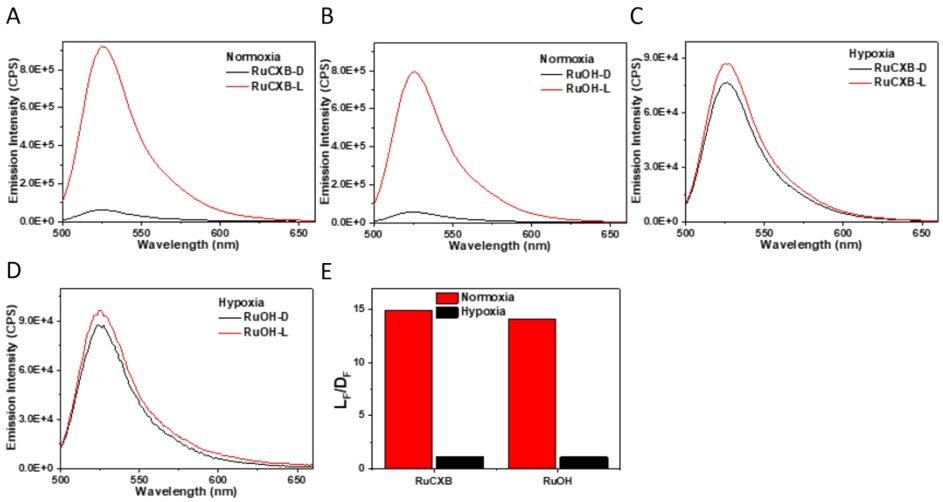
Supplementary Figure 5. HR-MS spectra for **RuOH**.



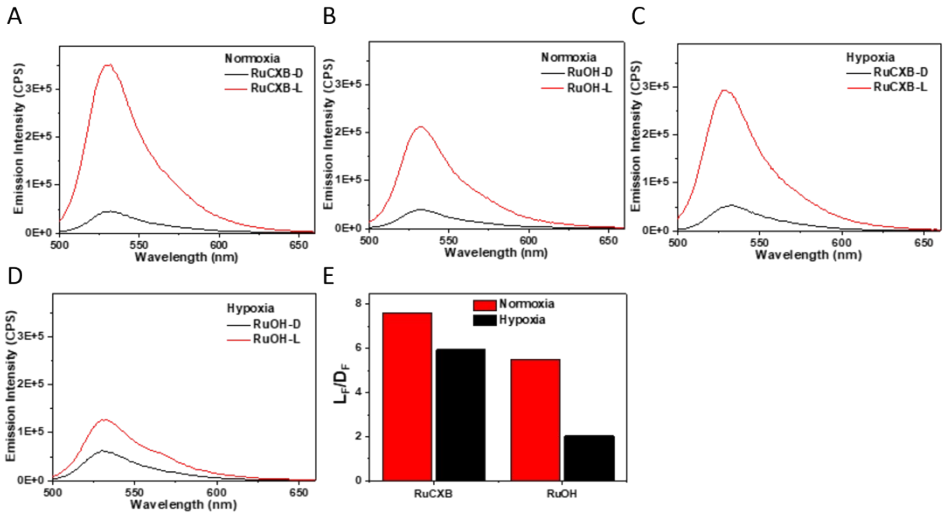
Supplementary Figure 6. The A, C) absorption and B, D) phosphorescence spectra of Ru(II) complexes (10 μM) in PBS buffer or ACN. λ_{ex} = 450 nm.



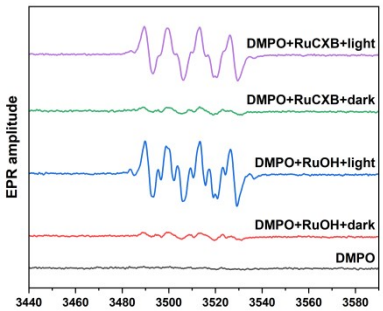
Supplementary Figure 7. Quantum yield determination for the photoinduced $^1O_2$ generation of Ru(II) complexes by measuring the absorption of 1,3-diphenylisobenzofuran (DPBF) at 413 nm in ACN, and $[Ru(bpy)_3]Cl_2$ was utilized as the reference. The solutions were irradiated with a laser of 450 nm with an interval of 10 s. A) Absorption spectrum of DPBF solution in ACN containing RuCXB; B) absorption spectrum of DPBF solution in ACN containing RuOH; C) temporal profiles and the corresponding linear-fitting lines of photoinduced DPBF absorbance change at 413 nm induced by Ru(II) complexes and $[Ru(bpy)_3]Cl_2$. ΔOD: the difference from the origin absorption intensity.



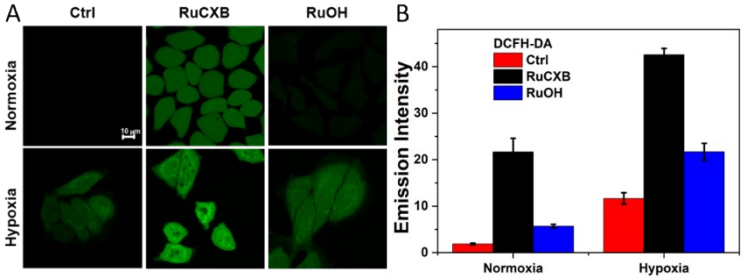
Supplementary Figure 8. Photoinduced $^1O_2$ generation ability of Ru(II) complexes determined with SOSG (5 μM) as a fluorescence probe in PBS. The fluorescence spectra were determined after photoirradiation with white light (6 mW cm^{-2}, 3 min) or not, and determined under normoxia (A and B); fluorescence spectra determined under hypoxia (C and D) (O_2＜0.1%). (E) The ratio of fluorescence emission intensity in different conditions. L_F/D_F: the ratio of fluorescence emission intensity after irradiation or not.



Supplementary Figure 9. Photoinduced $O_2^{\cdot-}$ generation ability of Ru(II) complexes determined with DHR123 (5 μM) as a fluorescence probe in PBS. The fluorescence spectra were determined after photoirradiation with white light (6 mW cm^{-2}, 3 min) or not, and determined under normoxia (A and B); fluorescence spectra determined under hypoxia (C and D) (O_2＜0.1%). (E) The ratio of fluorescence emission intensity in different conditions. L_F/D_F: the ratio of fluorescence emission intensity after irradiation or not.

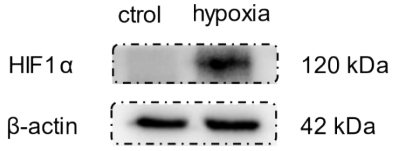


Supplementary Figure 10. EPR spectroscopy of DMPO for $O_2^{\cdot-}$ in the presence with or without Ru(II) complexes (50 μM) with or without light irradiation (200 mW cm^{-2}, 2 min).

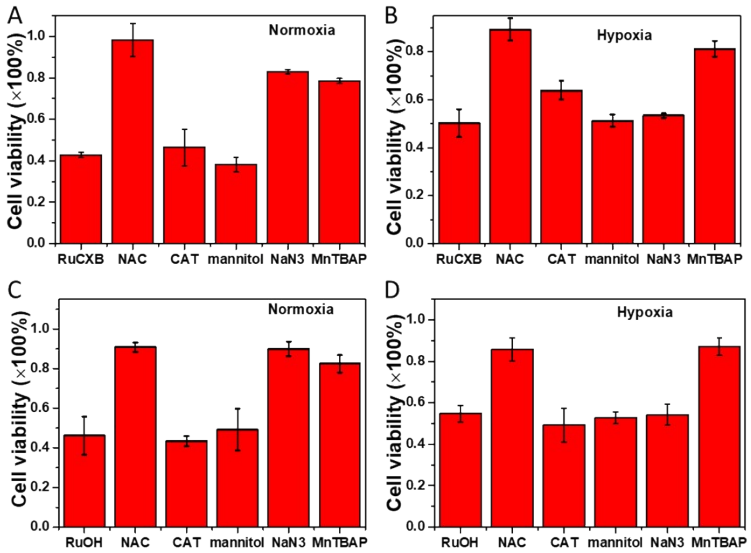


Supplementary Figure 11. A) $^1O_2$ detection in MCF-7 cells under normoxic and hypoxic conditions using DCFH-DA (5 μM, 10 min). Cells were incubated with Ru(II)

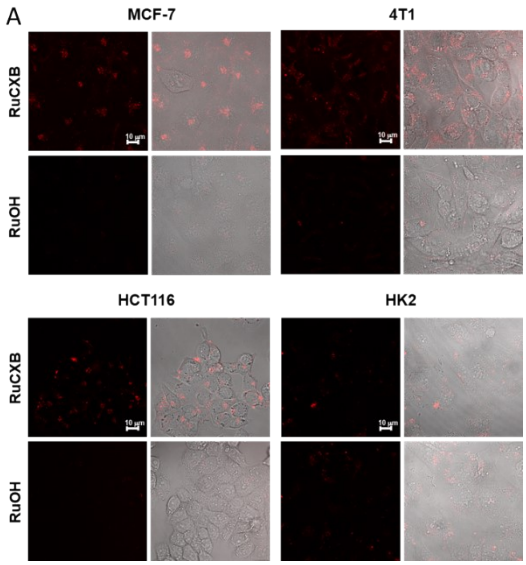
complexes (2 μM) respectively for 4 h. Irradiation was carried by white light (6 mW cm^{-2}, 3 min). Oxygen starvation was taken place in an anaerobic air bag for 1 h. Scale bar: 10 μm. λ_{ex} = 488 nm, λ_{em} = 490-590 nm. B) Different emission intensity in MCF-7 cells in A.



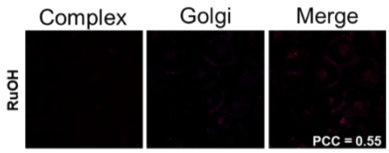
Supplementary Figure 12. The expression of HIF1α in MCF-7 cells after sealing in an anaerobic bag for 1 h.



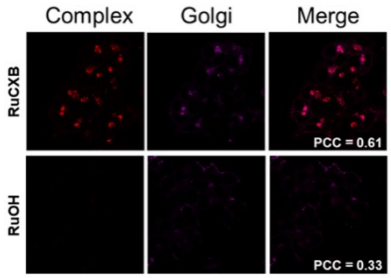
Supplementary Figure 13. The cell viability of MCF-7cells incubated with RuCXB (A, B) and RuOH (C, D) and different ROS inhibitors under normoxia or hypoxia after irradiation (white light, 6 mW cm^{-2}, 15 min) for 24 h. The concentration of Ru complexes was used with data corresponding to their respective IC_{50} values. O_2 starvation was realized by sealing the culture system in an anaerobic bag for 1 h (O_2<0.1%). NAC: N-Acetylcysteine, ROS inhibitor, 10 mM; CAT: Catalase, H_2O_2 inhibitor, 1000 U/mL; mannitol: ·OH inhibitor, 10 mM; NaN_3: $^1O_2$ inhibitor, 10 mM; MnTBAP: $O_2^{\cdot-}$ inhibitor, 100 μM.



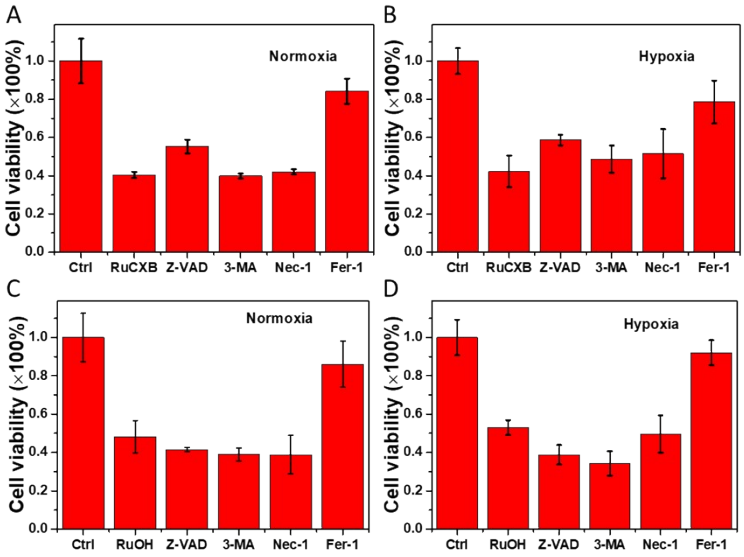
Supplementary Figure 14. Confocal imaging of different cell lines after incubation with Ru(II) complexes (2 μM) respectively for 4 h.



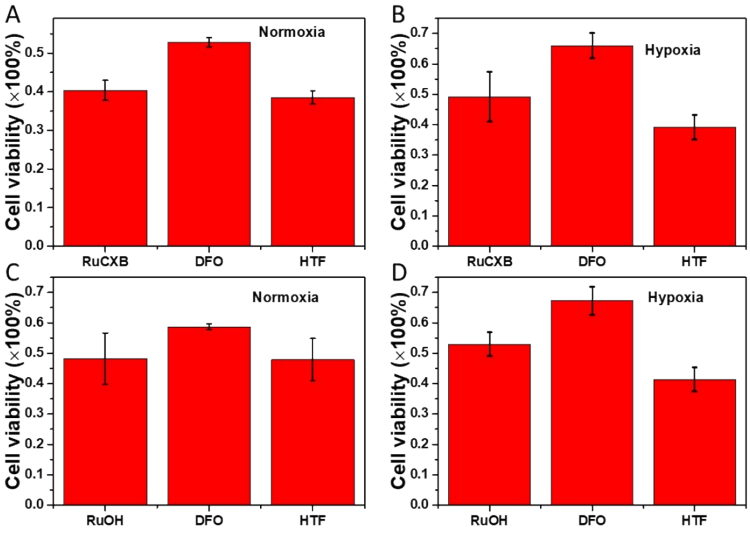
Supplementary Figure 15. Subcellular colocalization images of RuCXB (2 μM) and Golgi-Tracker Red in MCF-7 cells. Scale bar: 10 μM. RuOH: λ_{ex} = 488 nm, λ_{em} = 500-750 nm; Golgi- Tracker Red: λ_{ex}= 633 nm, λ_{em} = 650-800 nm.



Supplementary Figure 16. Subcellular colocalization images of Ru(II) compounds (2 μM) and Golgi-Tracker Red in HCT116 cells. Scale bar: 10 μM. Ru(II) compounds: λ_{ex} = 488 nm, λ_{em} = 500-750 nm; Golgi-Tracker Red: λ_{ex}= 633 nm, λ_{em} = 650-800 nm.



Supplementary Figure 17. The cell viability of MCF-7cells incubated with RuCXB (A, B) and RuOH (C, D) and different inhibitors under normoxia or hypoxia after irradiation (white light, 6 mW cm^{-2}, 15 min) for 24 h. The concentration of Ru complexes was used with data corresponding to their respective IC_{50} values. O_2 starvation was realized by sealing the culture system in an anaerobic bag for 1 h (O_2<0.1%). z-VAD: z-VAD-fmk, apoptosis inhibitor, 50 μM; 3-MA: 3-methyladenine, autophagy inhibitor, 100 μM; Nec-1: necrostatin-1, Necroptosis inhibitor, 50 μm; Fer-1: ferrostatin-1, ferroptosis inhibitor, 50 μM.



Supplementary Figure 18. The cell viability of MCF-7cells incubated with RuCXB (A, B) and RuOH (C, D) and DFO or HTF under normoxia or hypoxia after irradiation (white light, 6 mW cm^{-2}, 15 min) for 24 h. The concentration of Ru complexes was used with data corresponding to their respective IC_{50} values. O_2 starvation was realized by sealing the culture system in an anaerobic bag for 1 h (O_2<0.1%). DFO: deferoxamine mesylate, iron chelating agent, 0.1 mM; HTF: human transferrin, 20 μg/mL.

Supplementary Table 1. Optical properties of RuCXB and RuOH.

	RuCXB	RuOH
λ_{max}[a] (nm) ε (L·mol^{-1}·cm^{-1})	464 (9362)	458 (5537)
λ_{em}[a] (nm)	614	606
Φ_{em}[b](%)	3.02	1.10
Φ_{em}[c] (%)	23.14	11.44
Φ_{Δ}(%)	77	53

a: UV and PL data of Ru(II) complexes in PBS buffer, 10 μM; b: normoxia; c: hypoxia; Φ_{em}: absolute phosphorescence quantum yield; Φ_{Δ}: singlet oxygen quantum yield.

Supplementary Table 2. IC_{50} of Ru(II) complexes against various cell lines (24 h).

Compounds	Cell lines	Light [μM]		Dark [μM]
		Normaxia (PI)	Hypoxia (PI)	
RuCXB	MCF-7	0.86 ± 0.07 (42.2)	1.73 ± 0. 19 (21.0)	36.33 ± 1.26
	4T1	1.18 ± 0.19 (24.8)	1.38 ± 0.12 (21.2)	29.26 ± 2.19
	HCT116	4.75 ± 0.17 (6.4)	6.34 ± 0.33 (4.8)	30.40 ± 1.57
	HK2	3.0 ± 1.97 (23.38)	-[a]	70.15 ± 3.59
RuOH	MCF-7	4.51 ± 0.32 (-)	7.93 ± 0.85 (-)	> 128
	4T1	> 8.00 (-)	> 8.00 (-)	> 128
	HCT116	> 8.00 (-)	> 8.00 (-)	> 128
	HK2	7.59 ± 2.01 (-)	-[a]	> 128

a: HK2: Human Kidney-2, HK2 cells are normal cells and do not exist in a hypoxic environment. PI: photocytotoxicity index, the ratio of $(IC_{50})_{Dark}/(IC_{50})_{Light}$.

References

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2. M. Ouyang, L. L. Zeng, H. Y. Huang, C. Z. Jin, J. P. Liu, Y. Chen, L. N. Ji and H. Chao, *Dalton Trans.*, 2017, **46**, 6734-6744.