Electronic Supplementary Material (ESI) for ChemComm.




## Materials and General Methods

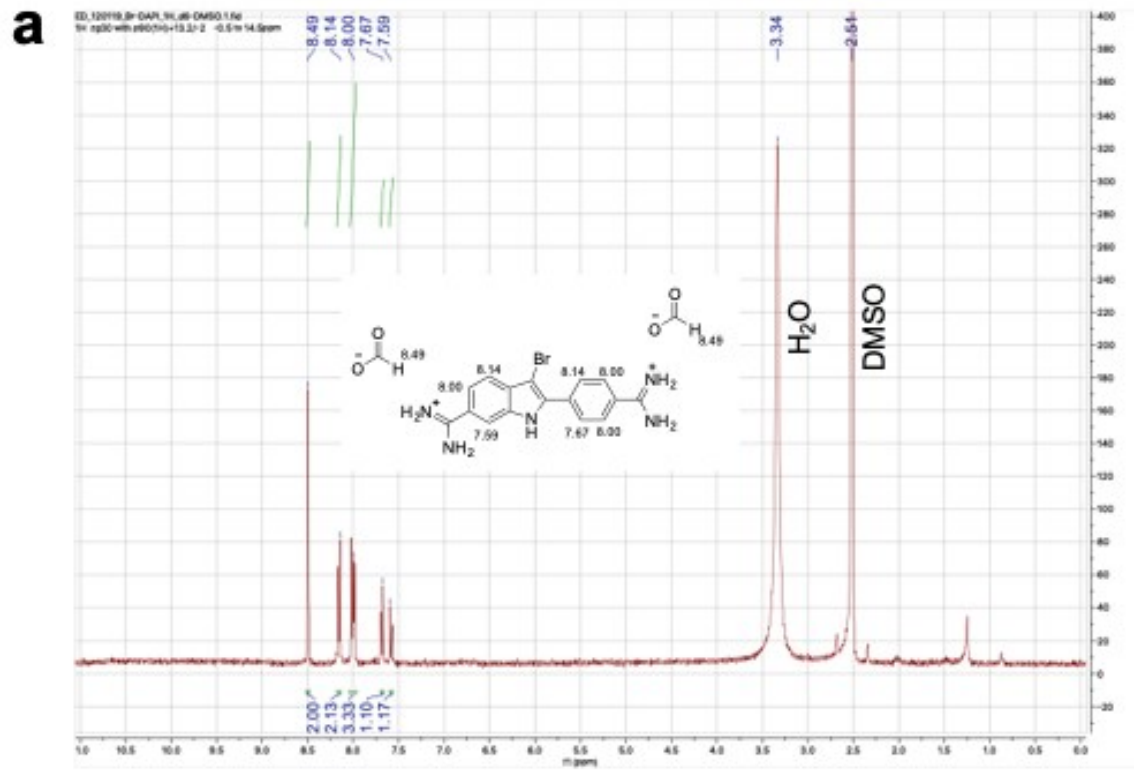
All chemicals and instruments were obtained from commercial suppliers. Stock solutions of Br-DAPI and DAPI were made in DMSO (Sigma-Aldrich). *In vitro* assays (in solution) were all performed in PBS pH 7.4 (1X) solution containing no calcium chloride or magnesium chloride (Thermo Fisher Scientific).

UV-Vis absorption spectra were recorded in a 1.0 cm path length cuvette on a Shimadzu UV-1800 UV-Vis spectrometer. The fluorescence experiments were performed with a Shimadzu RF-6000 spectrometer in a 1.0 cm path length cuvette. Irradiation experiments were performed with a mounted 365 nm LED (7.5 nm bandwidth, 360 mW LED Output Power; 8.9 $\mu$W mm$^{-2}$ maximum irradiance) purchased from ThorLabs (M365L2).

## Synthesis and Photophysical Characterization of Br-DAPI

To a 5 mL mixture of water and acetone (1:1), 50 mg of 2-(4-amidinophenyl)-6-indolecarbamidine dihydrochloride (0.1425 mmol) was added and dissolved. 31 mg of N-bromosuccinimide (0.171 mmol) was slowly added to the reaction flask and the reaction mixture was left to stir overnight at r.t. The crude reaction mixture was evaporated to dryness under reduced pressure and re-dissolved in a small quantity of water. The crude product was purified directly with RP-HPLC with a Biotage Isolera C18 column using a mixture of milli-q water, acetonitrile, and 0.5% formic acid with a flow rate of 10 mL min$^{-1}$ while monitoring the absorbance at 357 nm. The method used a gradient from 0-100% acetonitrile. The major peak with absorbance at 357 nm was lyophilized to yield 27 mg (0.06 mmol) of amino(4-(6-(amino(iminio)methyl)-3-bromo-1*H*-indol-2-yl)phenyl)methaniminium diformate in 42% yield. The reported extinction coefficient for native DAPI (27 000 M$^{-1}$ cm$^{-1}$ at 353 nm) was also used for Br-DAPI.[1]

$^{1}$H NMR (400 MHz, DMSO-$d_6$) δ 8.49 (s, 2H), 8.19-8.08 (m, 2H), 8.05-7.93 (m, 3H), 7.67 (d, $J$ = 8.4 Hz, 1H), 7.59 (dd, $J$ = 8.4, 1.6 Hz, 1H). $^{13}$C NMR (400 MHz, DMSO-$d_6$) δ 168.54, 167.10, 166.04, 137.08, 135.49, 135.28, 131.56, 129.51, 128.73, 123.95, 120.00, 119.56, 113.19, 89.60. The NMR spectra of DAPI was used as reference to confirm loss of 1H signal at C3. HRMS (ESI+ mode): calculated for $C_{16}H_{16}BrN_5^{2+}$ = 178.5289; found = 178.5281.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8.49
8.14
8.00
7.67
7.59
3.34
2.61
H2O
DMSO
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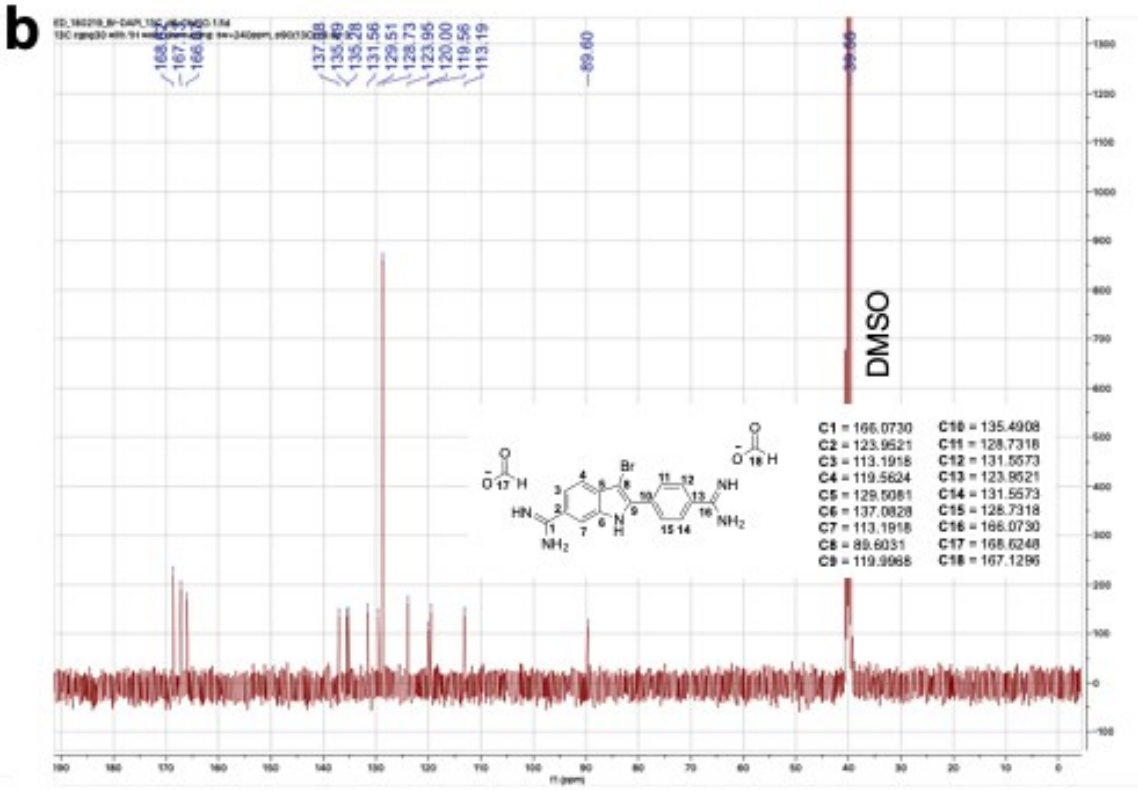
2.13
3.33
1.10
1.17


b
137.88
135.49
135.28
131.56
129.51
128.73
123.95
120.00
119.56
113.19
89.60
DMSO
C1 = 166.0730
C2 = 123.9521
C3 = 113.1918
C4 = 119.5624
C5 = 129.5081
C6 = 137.0828
C7 = 113.1918
C8 = 89.6031
C9 = 119.9968
C10 = 135.4908
C11 = 128.7318
C12 = 131.5573
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C17 = 166.6248
C18 = 167.1296

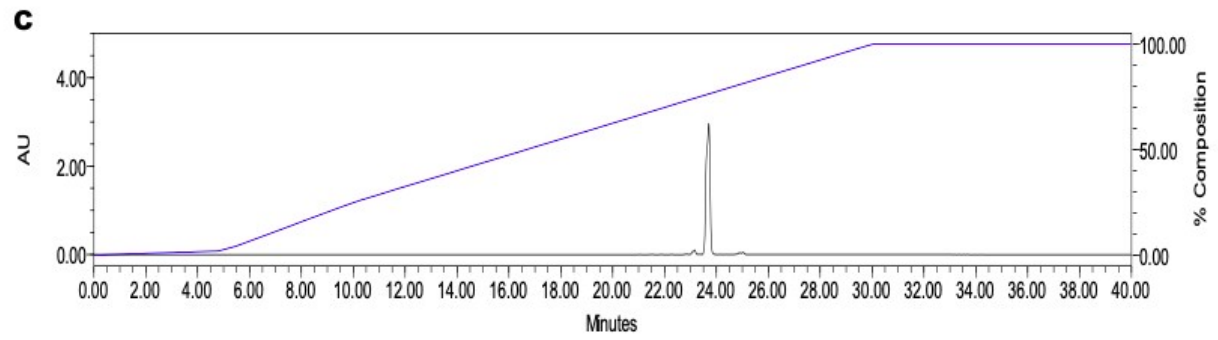


**Figure S1.** (a) $^{1}$H NMR and (b) $^{13}$C NMR spectrum of Br-DAPI in DMSO-$d_6$. (c) HPLC chromatogram for the purification of Br-DAPI in milli-q water, acetonitrile containing 0.5% formic acid.

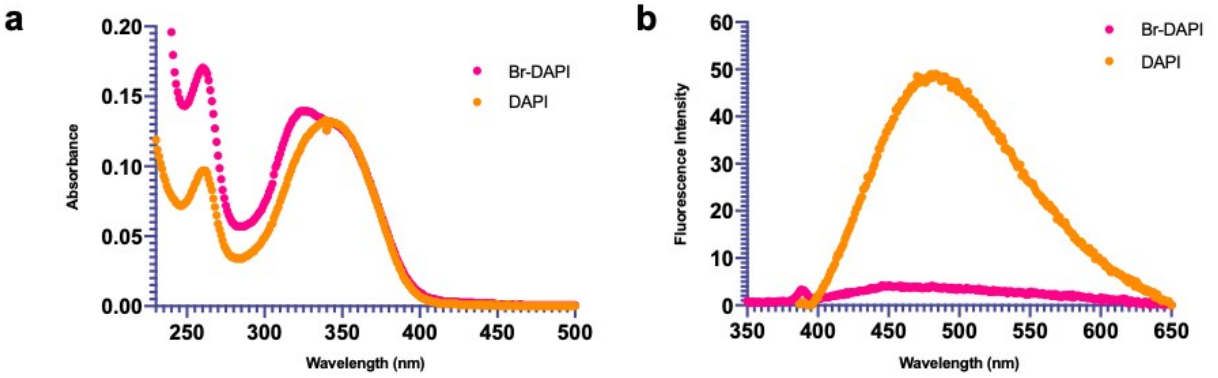


**Figure S2.** (a) Absorbance and (b) emission spectra of 5 μM DAPI and 5 μM Br-DAPI in PBS pH 7.4 (Excitation at 345 nm).

## Calf-Thymus DNA (CT-DNA) Titration with Br-DAPI and DAPI

A 60 $\mu$L solution in PBS pH 7.4 containing 20 $\mu$M of Br-DAPI or DAPI (0.4% DMSO) was prepared and an initial fluorescence spectrum measured. CT-DNA was added to the solution in increments of 10 $\mu$M until saturation of the CT-DNA was achieved – this was suggested when there were no longer any changes in the fluorescence intensity. Fluorescence measurements were carried out with the following parameters: $\lambda_{ex}$=345 nm with a 1.5 nm excitation bandwidth, $\lambda_{em}$=350-650 nm with a 3.0 nm emission bandwidth, and a scan speed of 600 nm/min with high sensitivity. The solutions were thoroughly mixed before each set of measurements and performed in triplicate. The stock solution of CT-DNA (Sigma-Aldrich) was made in 10 mM Tris buffer with 1 mM EDTA, pH 8.0.[2]

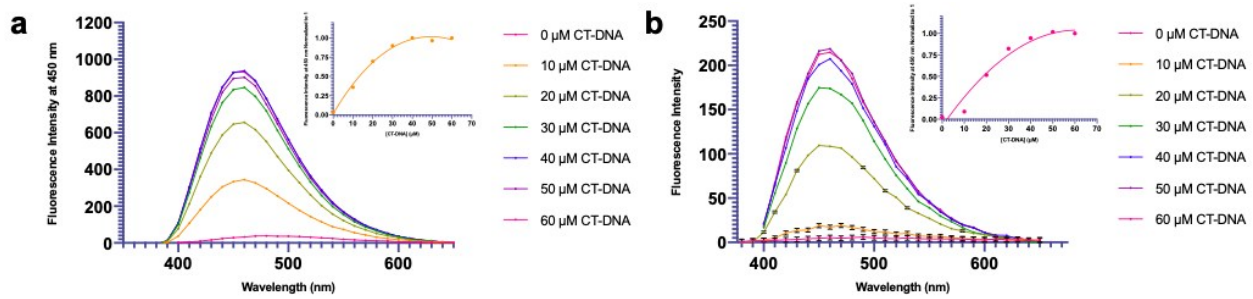


**Figure S3.** Titration of calf-thymus DNA containing (a) 20 µM DAPI or (b) 20 µM Br-DAPI in PBS pH 7.4.

## Photostability of Br-DAPI and DAPI Towards 365 nm Irradiation

A photobleaching curve was obtained to determine the photostability of Br-DAPI and DAPI towards 365 nm irradiation (4.5 J $cm^{-2}$) for a total of 5 minutes (this is the same wavelength of light and irradiation dose used for PDT). Absorbance measurements were taken every minute following irradiation of a 60 $\mu$L solution containing 4 $\mu$M Br-DAPI or DAPI (0.67% DMSO) in PBS pH 7.4. The solutions were thoroughly mixed before each set of measurements and performed in triplicate.

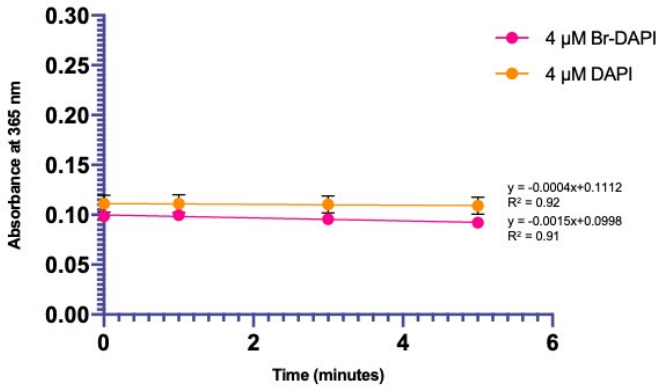


**Figure S4.** Photostability of DAPI and Br-DAPI in PBS pH 7.4 during irradiation for a total of 5 minutes with a 365 nm LED (15 mW $cm^{-2}$).

## Detection of Singlet Oxygen ($^1O_2$) produced by Br-DAPI *in vitro* (in solution)

A 60 $\mu$L solution containing 4 $\mu$M of Br-DAPI (0.67% DMSO) and either 1 $\mu$M Singlet Oxygen Sensor Green (SOSG) in PBS pH 7.4 or 10 $\mu$M 9,10-anthracenediylbis(methylene)dimalonic acid (ABDA) in PBS pH 7.4 was irradiated with a 365 nm LED (4.5 J $cm^{-2}$) for up to a total of 5 minutes with a scan taken every minute. The production of singlet oxygen was monitored by (a) an increase in the fluorescence intensity of the emission of SOSG at 530 nm or (b) the decrease in the absorbance of ABDA as the corresponding endoperoxide formed.[3–5] Fluorescence measurements for

(a) were carried out with the following parameters: $\lambda_{ex}$=505 nm (1.5 nm bandwidth), $\lambda_{em}$=510-650 nm (3.0 nm bandwidth), and a scan speed of 600 nm/min with high sensitivity. The solutions were thoroughly mixed before each set of measurements. We note that the singlet oxygen sensor 1,3-diphenylisobenzylfuran (DPBF) was also used but due to rapid photobleaching of the sensor alone upon 365 nm irradiation, we could not obtain signals over the background bleaching.

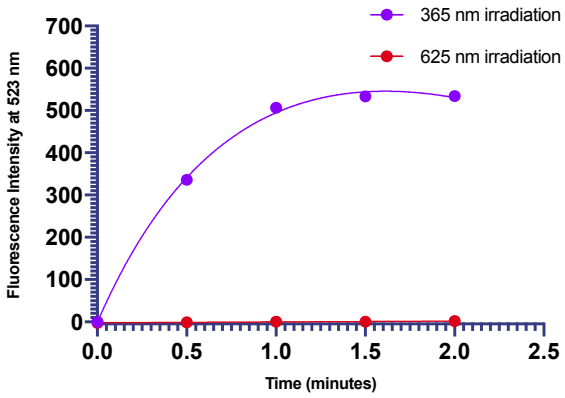


**Figure S5.** Monitoring ROS production by Br-DAPI upon irradiation with a 365 nm LED (15 mW cm$^{-2}$) or a 625 nm LED (48 mW cm$^{-2}$) using the ROS sensor, $DCFH_2$ (1 μM in PBS pH 7.4).

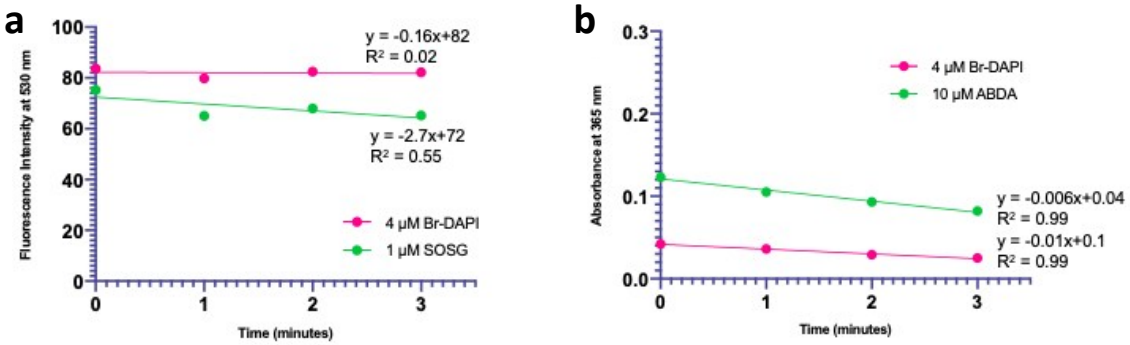


**Figure S6.** Monitoring singlet oxygen production by Br-DAPI upon irradiation with a 365 nm LED (15 mW cm$^{-2}$). Singlet oxygen production was monitored using (a) 1 μM SOSG in PBS pH 7.4, and (b) 10 μM ABDA in PBS pH 7.4. Changes in fluorescence or absorbance with irradiation time produced slopes very similar to background (i.e. singlet oxygen sensors only).

## Evidence of DNA Damage after Incubation with Br-DAPI and 365 nm Irradiation using Gel Electrophoresis

The DNA source used was pIRES2-DsRed2 – a non-viral, circular mammalian plasmid (5264 bp).[6] A 1 μg μL$^{-1}$ stock of pIRES2-DsRed2 was prepared in Ultrapure Distilled Water, DNAse and RNAse free (purchased from Invitrogen) and diluted to a 10 ng μL$^{-1}$ stock in TE buffer pH 8.5. Sample solutions for irradiation had a total volume of 10.3 μL, with all solutions containing 70 ng (2 nM) of DNA (7 μL of 10 ng μL$^{-1}$ stock). DAPI or Br-DAPI were added to solutions containing DNA to have a final concentration of 20 μM, 10

μM, or 2.5 μM (0.02% DMSO) before addition of denaturant or loading buffer. To bring the final volume of the samples for irradiation up to 10.3 μL, PBS pH 7.4 buffer or different amounts of 4.5 M $NaCl_{(aq)}$ stock were added to the sample depending on the desired conditions. The gel was composed of 1% ultrapure agarose (purchased from Invitrogen) in an alkaline buffer (50 mM Tris, 45 mM boric acid, 30 mM NaOH, 1 mM EDTA).[7] The running buffer was the same alkaline buffer used to prepare the gel. Samples selected for PDT treatment were irradiated with a 365 nm LED for varied amounts of time, with a distance of 1.5 cm between the light source and the sample (0.45-4.5 J $cm^{-2}$). All samples were denatured in a 90°C water bath for 1 minute after the addition of 1 μL of a 2 M NaOH with 0.1 M EDTA solution.[7] Denatured solutions were cooled on ice prior to loading it on the gel. 2 μL of 6X Purple Gel Loading Dye (purchased from New England Biolabs) was added to each sample for loading on the gel. The agarose gel was run on a Mini-Sub® Cell GT Cell (purchased from Bio-Rad Laboratories) at 80 V for 75 minutes. The gel was stained with 0.5 mg $mL^{-1}$ ethidium bromide and imaged in the ethidium bromide channel using BIORAD ChemiDoc™MP Imaging System.

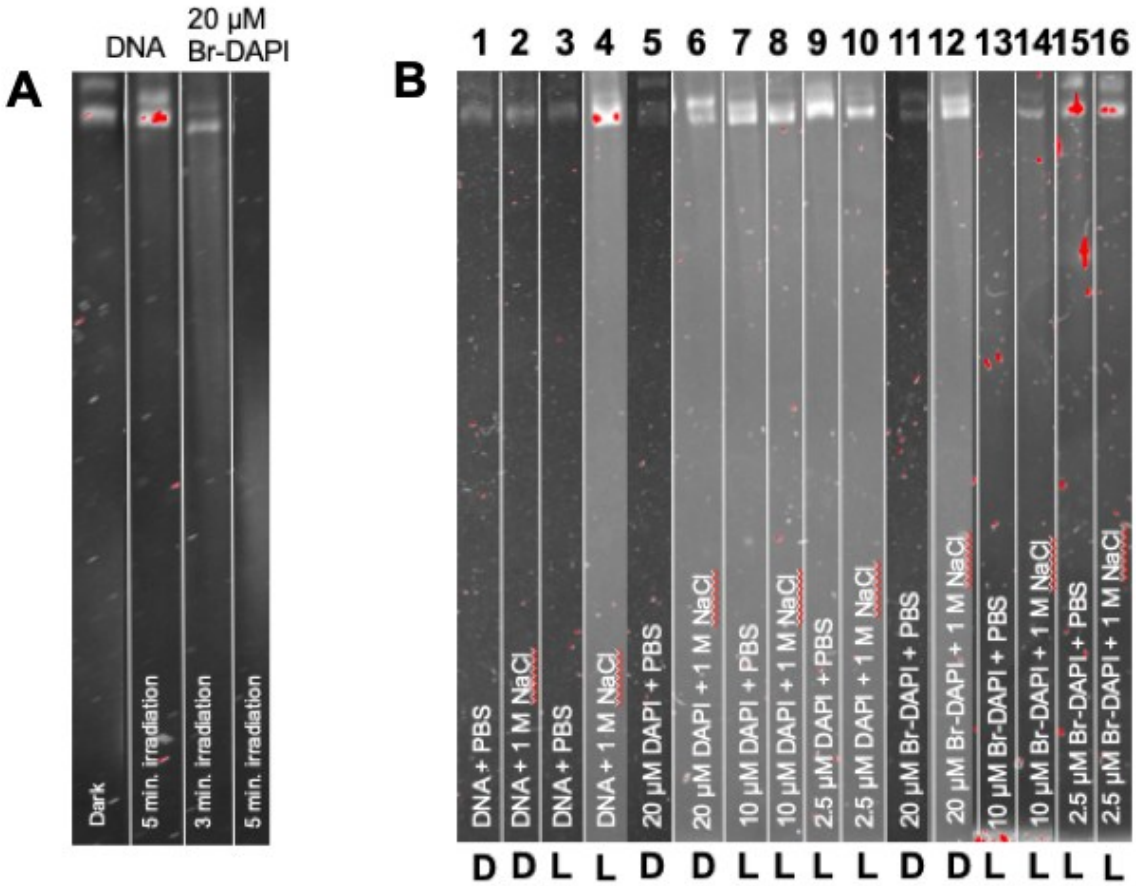


**Figure S7.** (a) Br-DAPI incubated with 2 nM plasmid DNA (pIRES2-DsRed2) and irradiated with a 365 nm LED (15 mW $cm^{-2}$) for varied times. (b) 2 nM plasmid DNA (pIRES2-DsRed2) (lanes 1-4), DAPI + DNA (lanes 5-10), and Br-DAPI + DNA (lanes 11-16). Each sample was in the dark ("D") or treated with a 365 nm LED (15 mW $cm^{-2}$) ("L") for 5 minutes of irradiation in either PBS pH 7.4 (0.135 M NaCl) or in 1 M NaCl. Gel conditions: 1% alkaline agarose gel with ethidium bromide staining.

## Fluorescence Quantum Yield ($\phi_F$) of Br-DAPI and DAPI

The fluorescence quantum yield ($\phi_F$) of the dye was determined using DAPI as a standard. After the absorbance of Br-DAPI at 345 nm was measured in a 1.0 cm glass cuvette, the cuvette containing the sample was directly transferred to the fluorometer for subsequent fluorescence measurements. Br-DAPI and DAPI measurements were done in PBS pH 7.4. Fluorescence measurements were carried out with the following parameters: $\lambda_{ex}$=345 nm with a 1.5 nm excitation bandwidth, $\lambda_{em}$=350-700 nm with a 3.0 nm emission bandwidth, and a scan speed of 60 nm/min with high sensitivity. The solutions were thoroughly mixed before each set of measurements and taken in triplicate. $\phi_F$ was calculated according to Eq.1. The fluorescence quantum yield of Br-DAPI was measured to be 0.0050 ($\pm$0.0005). The fluorescence quantum yield of Br-DAPI when bound to CT-DNA (50 $\mu$M) was measured to be 0.131 ($\pm$0.005).

**Eq.1** $$\phi_{sample} = (\phi_{standard})\left(\frac{I_{sample}}{I_{standard}}\right)\left(\frac{A_{standard}}{A_{sample}}\right)\left(\frac{\eta^2{}_{sample}}{\eta^2{}_{standard}}\right)$$

## Detection of ROS produced by Br-DAPI vs. DAPI *in vitro* (in solution)

A 60 $\mu$L solution in PBS pH 7.4 containing 4 $\mu$M of either Br-DAPI or DAPI (0.67% DMSO) and 1 $\mu$M of $DCFH_2$ (2',7'-dichlorofluorescin) (in 0.1 M $NaOH_{(aq)}$) was irradiated with a 365 nm LED (4.5 J $cm^{-2}$) for a total of 2 minutes with a scan taken every 30 sec. The production of ROS was monitored by increases in the fluorescence intensity of the emission of DCF (2',7'-dichlorofluorescein) at 523 nm.[8] Fluorescence measurements were carried out with the following parameters: $\lambda_{ex}$=505 nm (1.5 nm bandwidth), $\lambda_{em}$=510-545 nm (3.0 nm bandwidth), and a scan speed of 600 nm/min with low sensitivity. The solutions were thoroughly mixed before each set of measurements and performed in triplicate.

Procedure was carried out under the same conditions with the addition of 50 $\mu$M CT-DNA. The stock solution of CT-DNA (Sigma-Aldrich) was made in 10 mM Tris buffer with 1 mM EDTA, pH 8.0.[2]

Procedure was carried out under the same conditions with 1 M $NaCl_{(aq)}$ instead of in PBS pH 7.4.

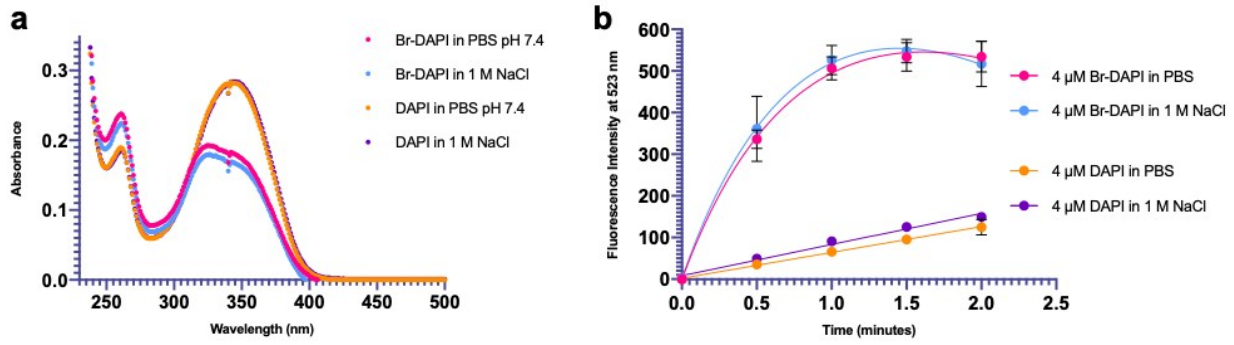


**Figure S8.** (a) Absorbance spectra of Br-DAPI and DAPI in PBS pH 7.4 (0.135 M NaCl) and 1 M NaCl. (b) ROS produced by DAPI and Br-DAPI in PBS pH 7.4 (0.135 M NaCl) and 1 M NaCl using a 365 nm LED (15 mW $cm^{-2}$).

## Cell Culture

A549 cells were cultured in Dulbecco's Modification Eagle's Medium (DMEM) with sodium pyruvate, 4.5 g/L glucose and L-glutamine (WINSET Inc.) and supplemented with 10% FBS and 1% antibiotics. Cells were cultured in 75 $cm^2$ culture flasks at 37°C under 5% $CO_2$ in a humidified incubator. For incubation of the cells with Br-DAPI (or other compounds) and to wash the cells, Dulbecco's Phosphate Buffered Saline (D-PBS) 1X without calcium and magnesium (WISENT Inc.) was used. All cell experiments were performed in Lab-Tek Chambered Coverglass w/ cvr 8-well chambers (Thermo Fisher Scientific).

## Monitoring ROS Production *in Cellulo* via Fluorescence Microscopy

A549 cells at a concentration of 50 000 cells $well^{-1}$ were cultured in 250 $\mu$L of DMEM with sodium pyruvate (full growth media) overnight at 37°C with 5% $CO_2$ in two 8-well chambers – one chamber designated for irradiation (i.e. light) and the other for no irradiation (i.e. dark). The old media was removed and replaced with 250 $\mu$L of D-PBS containing 16 $\mu$M of either Br-DAPI or DAPI (0.2% DMSO); excepting the two control wells that had 0 $\mu$M of either dye. The treated cells were incubated at 37°C on a heated microscope stage for 45 minutes. Br-DAPI and DAPI solutions were removed and cells were washed one time with D-PBS. The cells were then treated with 250 $\mu$L of a 10 $\mu$M $DCFH_2$-DA solution (0.2% DMSO) in D-PBS and incubated for 30 minutes at 37°C on a heated microscope stage. The media was removed and cells washed one time with D-PBS. 250 $\mu$L of DMEM (full growth media) was added back into each well. Each well from the light chamber was irradiated with a 365 nm LED for 5 minutes (4.5 J $cm^{-2}$). The media was removed and replaced with 250 $\mu$L of D-PBS for imaging via fluorescence microscopy. D-PBS and growth media were warmed to 37°C prior to their addition to cells.

Fluorescence microscopy images were acquired using an Olympus IX73 Inverted microscope. The cellSens software (purchased from Olympus) was used to for control of the camera and to capture and adjust the images accordingly. A Green Fluorescent Protein filter set (EGFP; $\lambda_{ex}$= 440-470 nm, $\lambda_{em}$= 525-550 nm; 100 ms camera exposure time) was used to visualize the green fluorescence emitted by DCF (which is produced upon reaction with ROS).[8] 10x images with 3% fluorescence on bright. 60x images with 3% fluorescence on dim.

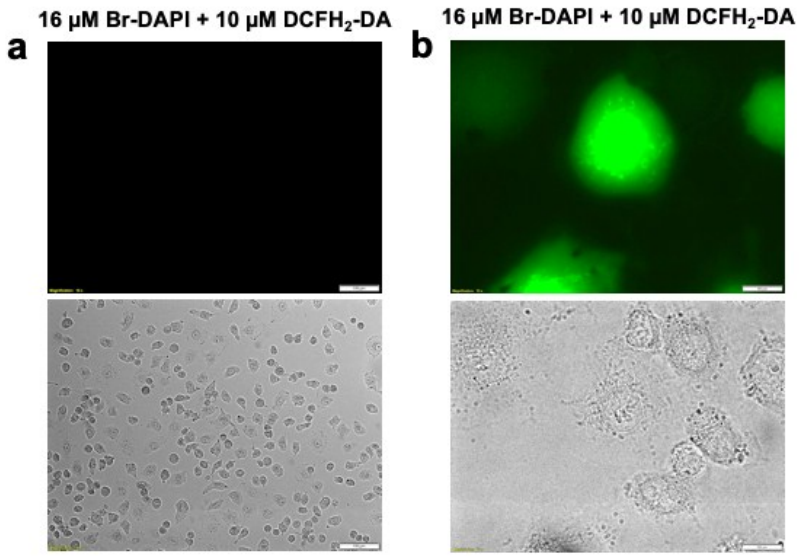


**Figure S9.** ROS production of Br-DAPI (16 μM) monitored using 10 μM $DCFH_2$-DA in A549 cells. (a) Dark (10x,100 μm scale bar). (b) After irradiation with a 365 nm LED (15 mW $cm^{-2}$) (60x,10 μm scale bar).

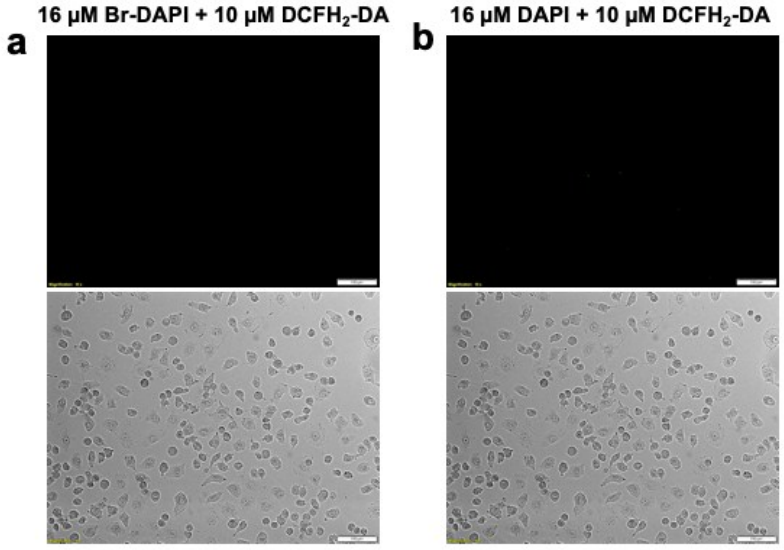


**Figure S10.** ROS production in A549 cells incubated in the dark with 10 μM $DCFH_2$-DA and (a) Br-DAPI (16 μM) or (b) DAPI (16 μM). 10x magnification,100 μm scale bar.

## Identification of the Optimal Time to Irradiate Cells to Maximize PDT Cytotoxicity and Minimize Br-DAPI Dark Toxicity

A549 cells at a concentration of 50 000 cells $well^{-1}$ were cultured in 250 μL of DMEM (full growth media) overnight at 37 °C with 5% $CO_2$ in an 8-well chamber – 7 wells were designated for irradiation (i.e. light) and 1 well as a dark control (i.e. no irradiation). The old media was removed and replaced with 250 μL solutions containing 16 μM Br-DAPI

(0.2% DMSO) in D-PBS; excepting the 0 μM control well. The cells were incubated with the dye for 45 minutes at 37°C on a heated microscope stage. After a wash with D-PBS, 250 μL of DMEM (full growth media) was added back into each well. The wells containing Br-DAPI were irradiated with a 365 nm LED (0.45-4.5 J $cm^{-2}$). Irradiation time varied within a range of 0.5-5 minutes. The cells were left to incubate overnight at 37°C with 5% $CO_2$. The old media was removed and replaced with 250 μL of a 5 mg $mL^{-1}$ solution of thiazolyl blue tetrazolium bromide in DMEM (full growth media). The cells were incubated for 2 hours at 37°C with 5% $CO_2$. The media was removed and 150 μL of DMSO was added to each well and the cells were resuspended. The absorbance of these solutions were evaluated with UV Vis Spectrometry and the percentage of viable cells were quantified (MTT assay).[9] Cell viability was performed in triplicate. D-PBS and growth media were warmed to 37°C prior to their addition to cells.

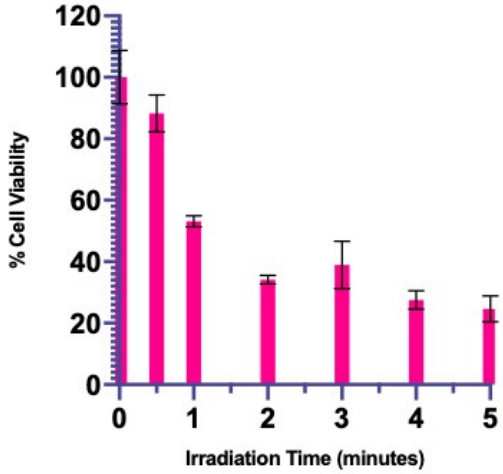


**Figure S11.** A549 cell viability after pre-incubated with 16 μM Br-DAPI followed by irradiation with a 365 nm LED (15 mW $cm^{-2}$) at varying times.

## Cell Viability after PDT

A549 cells at a concentration of 50 000 cells $well^{-1}$ were cultured in 250 μL of DMEM (full growth media) overnight at 37°C with 5% $CO_2$ in two 8-well chambers – one chamber designated for irradiation (i.e. light) and the other for no irradiation (i.e. dark). The old media was removed and replaced with 250 μL solutions containing Br-DAPI (0-64 μM) in D-PBS (all solutions contained <0.64% DMSO). The cells were incubated with the dye for 45 minutes on a heated microscope stage at 37°C. After incubation, the cells were washed once with D-PBS and 250 μL of DMEM (full growth media) was added back into each well. Each well from the light chamber was irradiated with a 365 nm LED for 5 minutes (4.5 J $cm^{-2}$). The cells in both the light and dark chambers were incubated overnight at 37°C with 5% $CO_2$. The old media was removed and replaced with 250 μL of DMEM (full growth media) containing 0.5 mg $mL^{-1}$ of thiazolyl blue tetrazolium bromide (Alfa Aesar). The cells were incubated at 37°C with 5% $CO_2$ for 2 hours. The media was removed and 150 μL of DMSO was added to each well to resuspend the cells into solution. The absorbance of these solutions were evaluated with UV-Vis spectrophotometry to

quantify the percentage of viable cells in each well (MTT assay).[9] Cell viability for dark and light chambers were performed in triplicate. D-PBS and growth media were warmed to 37°C prior to their addition to cells.

Dark toxicity was quantified using the absorbance for the 0 μM control well in the dark chamber as reference for dark chamber wells preincubated with Br-DAPI. To quantify the percentage of viable cells after PDT, the dark concentration cell viabilities were each normalized to 100%, while the cell viability for light wells were calculated relative to the absorbance of its corresponding dark well containing the same concentration of Br-DAPI.

Cell viability with DAPI after PDT was also tested in A549 cells with the same procedure outlined above.

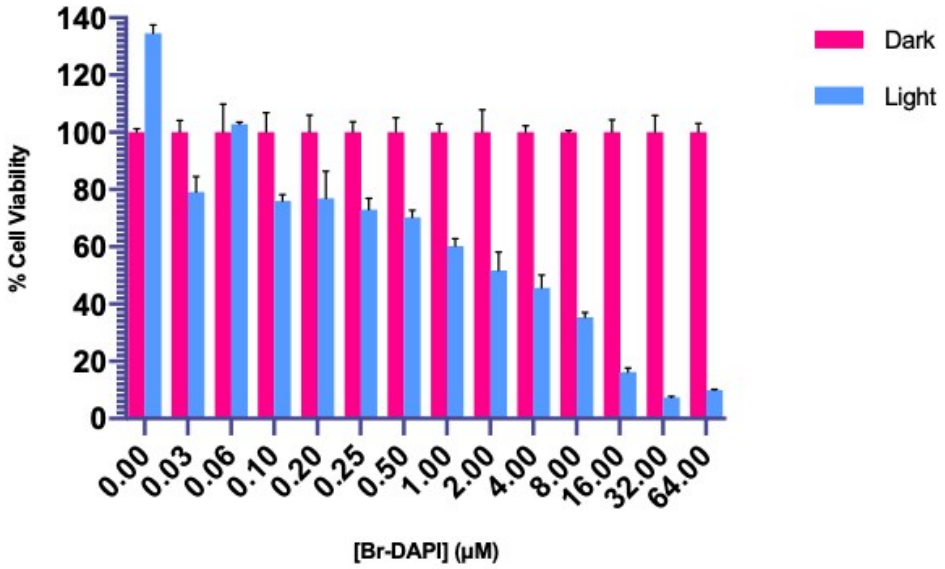


**Figure S12.** A549 cell viability after incubation with Br-DAPI in the dark compared to A549 cells pre-incubated with Br-DAPI followed by 5 minutes of irradiation with a 365 nm LED (15 mW $cm^{-2}$). At 0 μM Br-DAPI, cells are viable after treatment with light.

## Annexin V-FITC and Propidium iodide Staining to Illustrate Br-DAPI-induced Cell Apoptosis/Necrosis after PDT

A549 cells at a concentration of 50 000 cells $well^{-1}$ were cultured in 250 μL of DMEM (full growth media) overnight at 37°C with 5% $CO_2$ in an 8-well chamber. The old media was removed and replaced with 250 μL solutions containing 16 μM Br-DAPI or 16 μM DAPI (0.2% DMSO) in D-PBS, with two wells containing neither dye as controls. The cells were incubated with the dyes for 45 minutes on a heated microscope stage at 37°C. After incubation, the cells were washed once with D-PBS and 250 μL of DMEM (full growth media) was added back into each well. Each well was irradiated with a 365 nm LED for 5 minutes (4.5 J $cm^{-2}$). The cells were incubated for (a) 20 min, (b) 1 h or (c) 4 h at 37°C with 5% $CO_2$. At each time point, the media was removed in the appropriate wells and

replaced with a 200 $\mu$L solution containing 5 $\mu$L of annexin V-FITC in 1X annexin V binding buffer (purchased from Invitrogen). The cells were incubated for 10 minutes with annexin V-FITC on a heated microscope stage at 37°C. After incubation, the cells were washed once with D-PBS. A 200 $\mu$L solution containing 5 $\mu$L of propidium iodide in 1X annexin V binding buffer (purchased from Invitrogen) was then added to the wells. The cells were incubated for 10 minutes with propidium iodide on a heated microscope stage at 37°C. After incubation, the cells were washed once with D-PBS and 250 $\mu$L of 1X annexin V binding buffer was added to each well for imaging via fluorescence microscopy. D-PBS and growth media were warmed to 37°C prior to their addition to cells.

Fluorescence microscopy images were acquired using an Olympus IX73 Inverted microscope. The cellSens software (purchased from Olympus) was used to for control of the camera and to capture and adjust the images accordingly. A Green Fluorescent Protein filter set (EGFP; $\lambda_{ex}$= 440-470 nm, $\lambda_{em}$= 525-550 nm; 1 s camera exposure time) was used to visualize the green fluorescence emitted by annexin V-FITC when it binds to phosphatidylserine on the exterior of the plasma membrane of apoptotic cells.[10] A customized filter set (AP; $\lambda_{ex}$= 530-555 nm, $\lambda_{em}$= 650-700 nm; 1 s camera exposure time) was used to visualize the red fluorescence emitted when PI binds to the nuclei of cells undergoing necrosis.[10] 20x images with 3% fluorescence on bright.

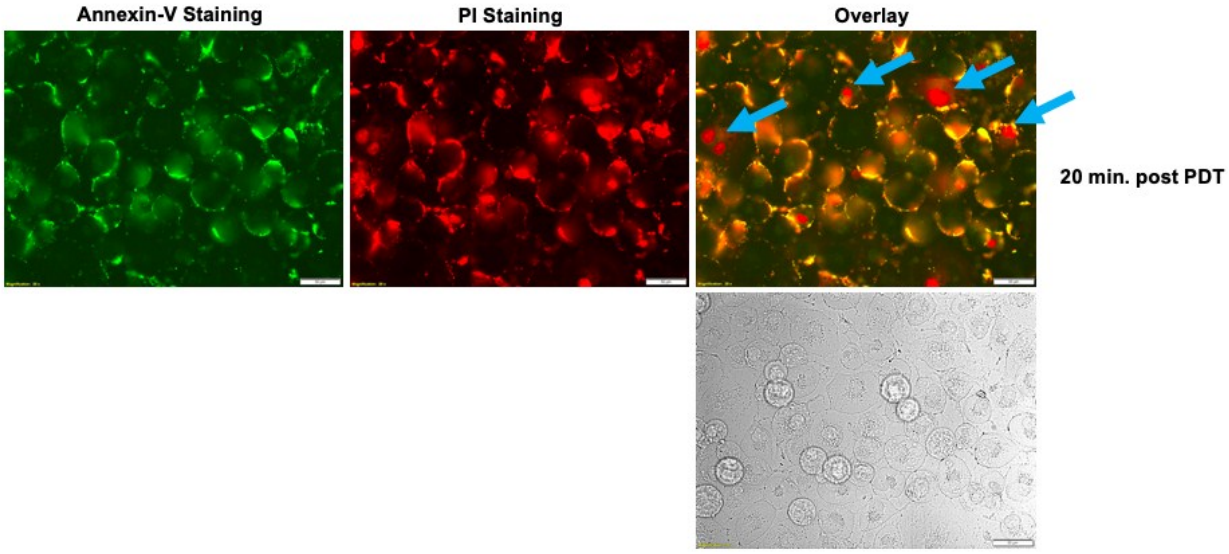


**Figure S13.** A459 cells incubated with 16 μM Br-DAPI and irradiated with a 365 nm LED (15 mW cm$^{-2}$) for 5 minutes. Cells were stained with Annexin V-FITC and PI 20 minutes post PDT. Arrows in overlay indicate PI staining of the nuclei, indicative of some pore formation in the membranes. 20x magnification, 50 μm scale bar.

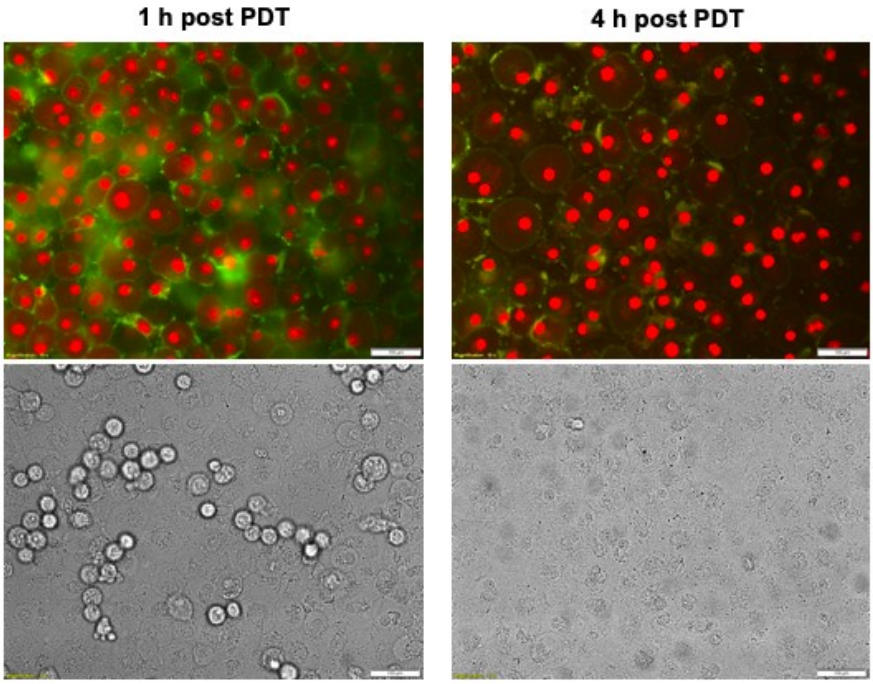


**Figure S14.** A459 cells incubated with 16 μM Br-DAPI and irradiated with a 365 nm LED (15 mW $cm^{-2}$) for 5 minutes. Cells were stained with Annexin V-FITC and PI 1 hour and 4 hours post PDT. 20x magnification, 50 μm scale bar.

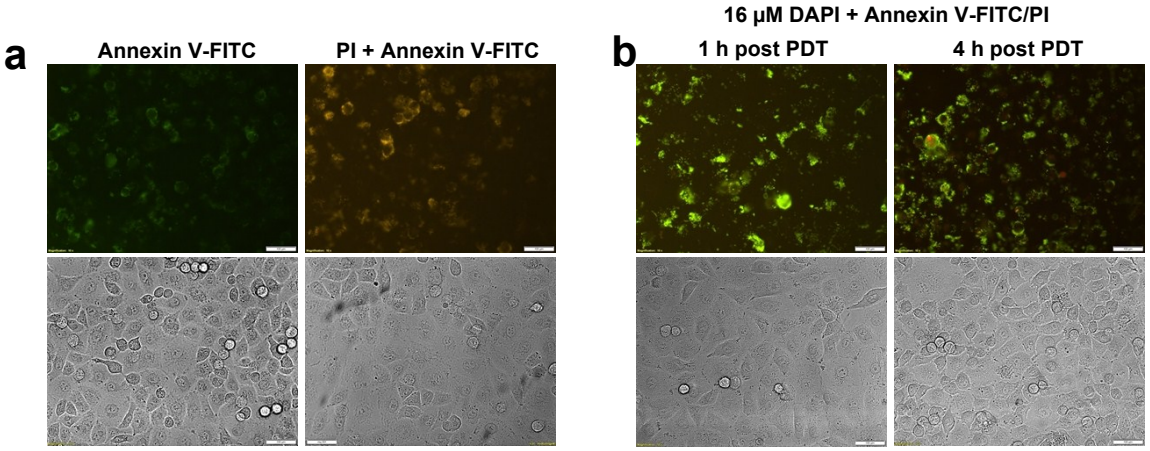


**Figure S15.** (a) A549 cells were irradiated with a 365 nm LED (15 mW $cm^{-2}$) for 5 minutes, stained with PI or Annexin V-FITC and PI, then imaged after 1 hour. (b) A459 cells pre-incubated with 16 μM DAPI and irradiated with a 365 nm LED (15 mW $cm^{-2}$) for 5 minutes. Cells were then stained with Annexin V-FITC and PI 1 hour and 4 hours post PDT. 20x magnification, 50 μm scale bar.

**Phase-contrast/ Fluorescence Microscopy of Br-DAPI before and after PDT**

A549 cells at a concentration of 50 000 cells well$^{-1}$ were cultured in 250 $\mu$L of DMEM (full growth media) overnight at 37$^{o}$C with 5% $CO_2$ in an 8-well chamber. The old media was removed and replaced with a 250 $\mu$L solution containing 16 $\mu$M Br-DAPI (0.2% DMSO) in D-PBS. The cells were incubated with the dye for 45 minutes on a heated microscope stage at 37$^{o}$C. After incubation, the cells were washed once with D-PBS and 250 $\mu$L of D-PBS was added back into the well for imaging prior to PDT via fluorescence microscopy. After imaging, 250 $\mu$L of DMEM (full growth media) was added back into the well. The cells were then irradiated with a 365 nm LED for 5 minutes (4.5 J cm$^{-2}$). 250 $\mu$L of D-PBS was added back into the well for imaging post-PDT via fluorescence microscopy. D-PBS and growth media were warmed to 37$^{o}$C prior to their addition to cells.

Phase contrast/ fluorescence microscopy images were acquired an Olympus IX73 Inverted microscope. The cellSens software was used to for control of the camera and to capture and adjust the images accordingly. was used to for control of the camera and to capture and adjust the images accordingly. Differential interference contrast components (1 s camera exposure time) were used to capture the phase-contrast images. A DAPI filter set (DAPI; $\lambda_{ex}$= 350-377 nm, $\lambda_{em}$= 409-425 nm; 1 s camera exposure time) was used to visualize the blue fluorescence emitted by DAPI. 60x images with 3% fluorescence on bright.

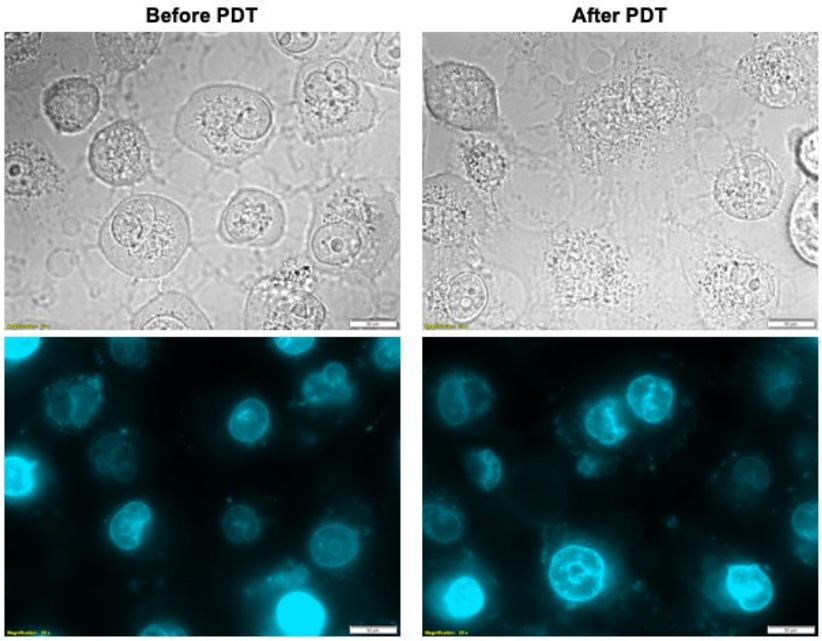


**Figure S16.** A549 cells incubated with 16 µM Br-DAPI before and after irradiation with a 365 nm LED (15 mW cm$^{-2}$) for 5 minutes. 60x magnification, 10µM scale bar.

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