Electronic Supplementary Material (ESI) for Journal of Materials Chemistry B.

Electronic Supplementary Information

A Sequential Enzyme-activated and Light-triggered Nanosystem for Cancer Detection and Therapy

Zelin Chen[1], Bowen Li [1], Xin Xie, Fang Zeng*, Shuizhu Wu*

State Key Lab of Luminescent Materials & Devices, College of Materials Science & Engineering, South China University of Technology, Guangzhou 510640, P. R. China.

*Corresponding Author: E-mail: shzhwu@scut.edu.cn; mcfzeng@scut.edu.cn; Fax: +86 20 22236363; Tel: +86 20 22236262.

[†] These authors contributed equally to this work.

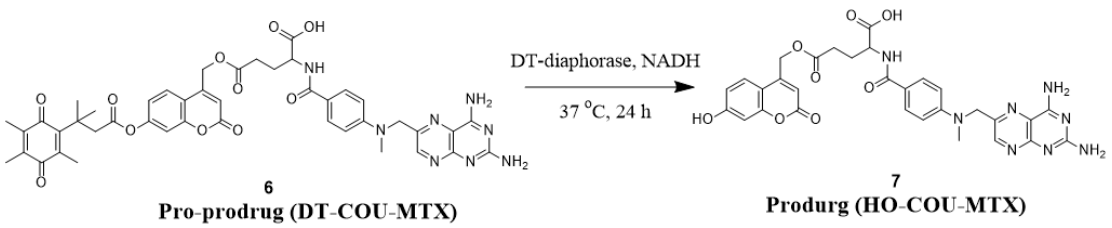

Figure S1. Synthetic route for the prodrug (HO-COU-MTX).

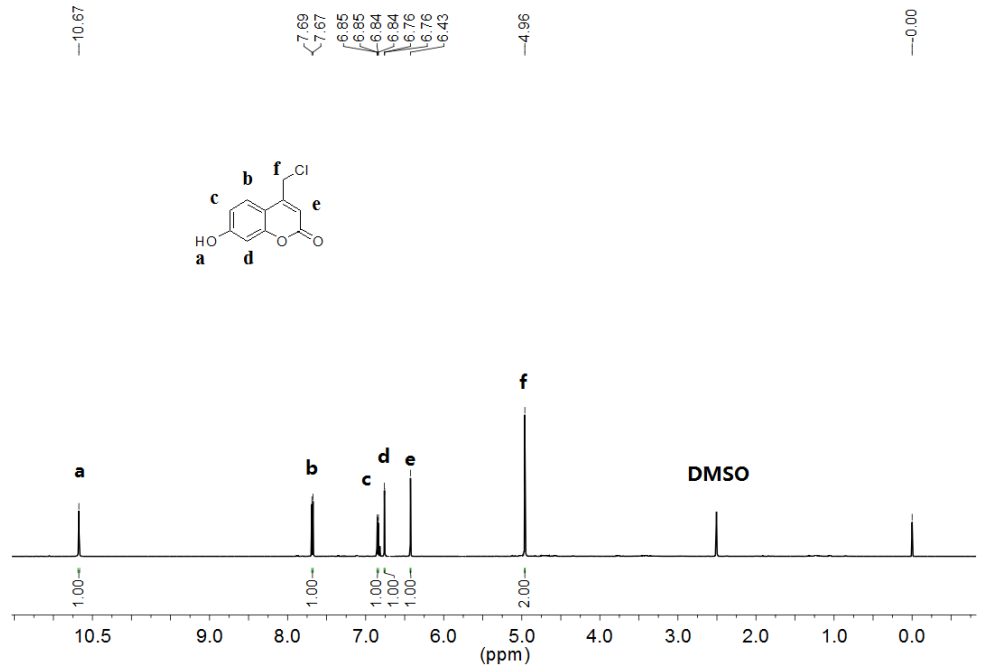

Figure S2. ^{1}H NMR spectrum of **1** (in DMSO-d_6).

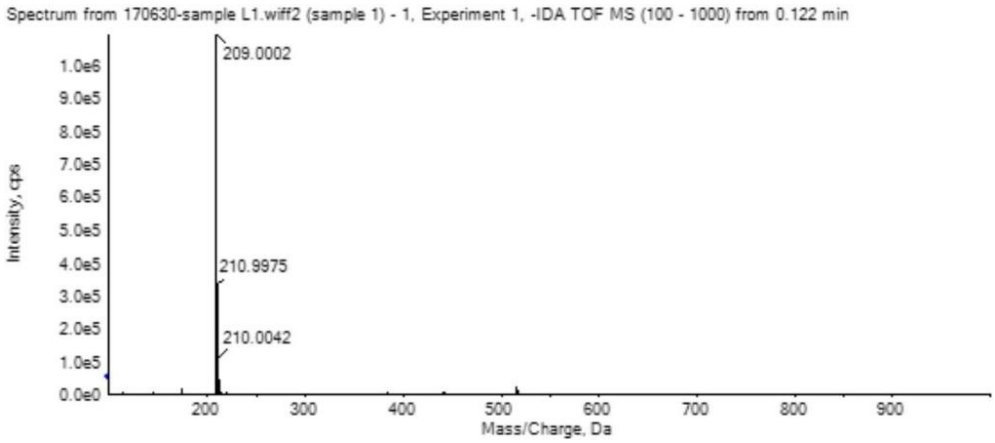

Figure S3. Mass spectrum of **1.** For **1**: HR-MS (ESI): calcd for $C_{10}H_7ClO_3$ ([M-H]$^-$) 209.0006, found: 209.0002.

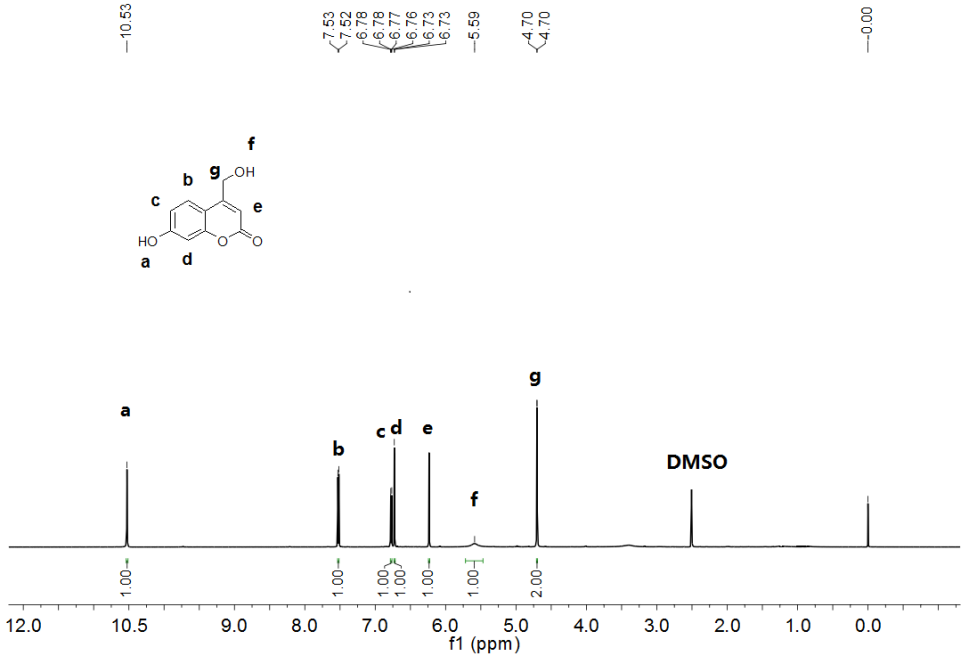

Figure S4. ^{1}H NMR spectrum of **2** (in DMSO-d_6).

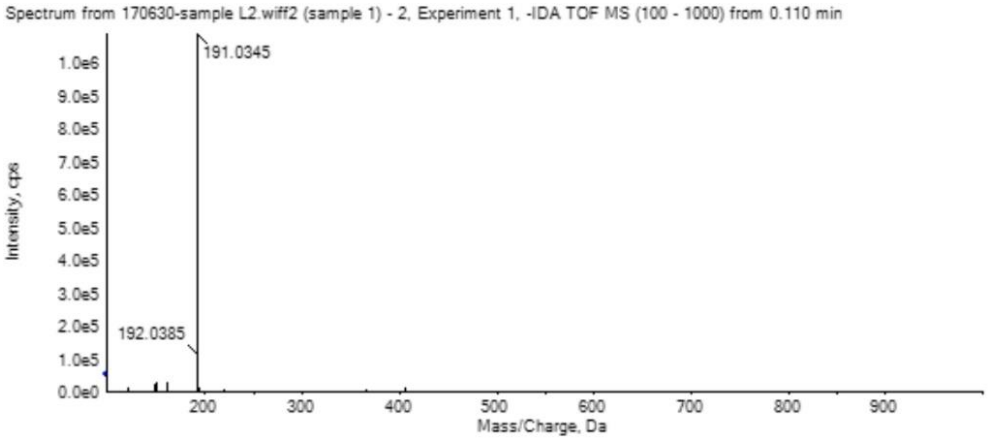

Figure S5. Mass spectrum of **2.** For **2**: HR-MS (ESI): calcd for $C_{10}H_8O_4$ ([M-H]$^-$)191.0345, found: 191.0345.

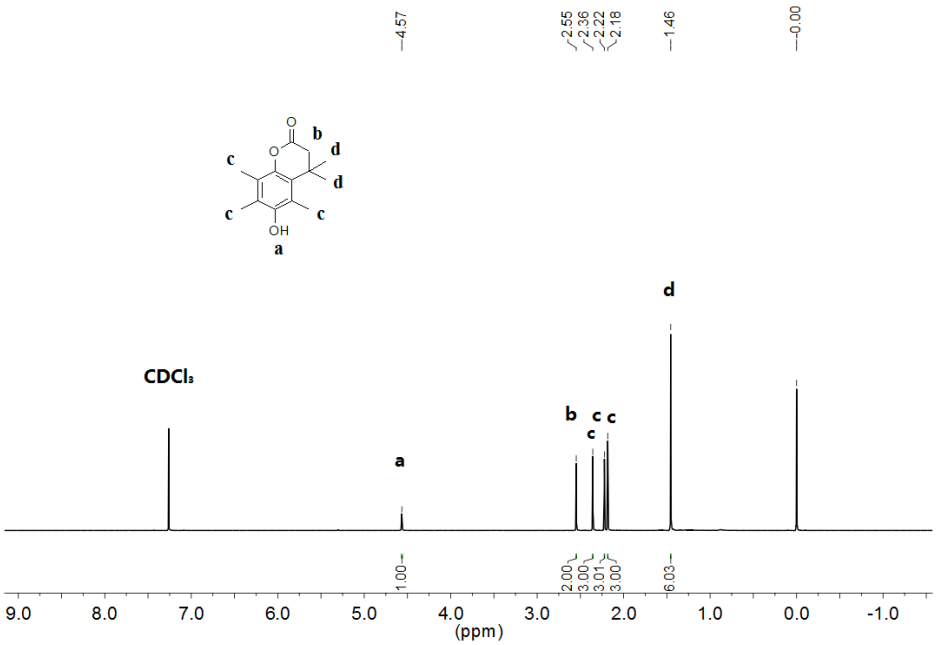

Figure S6. ^{1}H NMR spectrum of **3** (in $CDCl_3$).

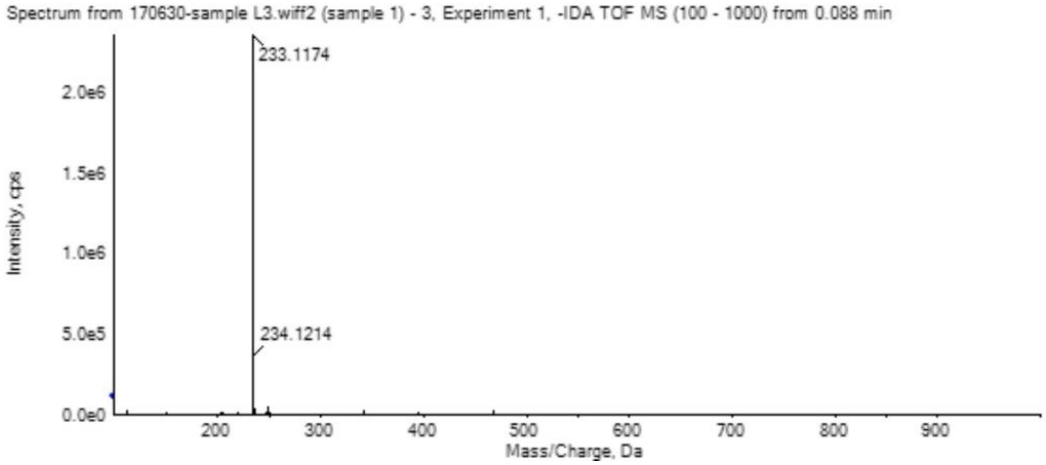

Figure S7. Mass spectrum of **3.** For **3**: HR-MS (ESI): calcd for $C_{14}H_{18}O_3$ ($[M-H]^-$) 233.1178, found: 233.1174.

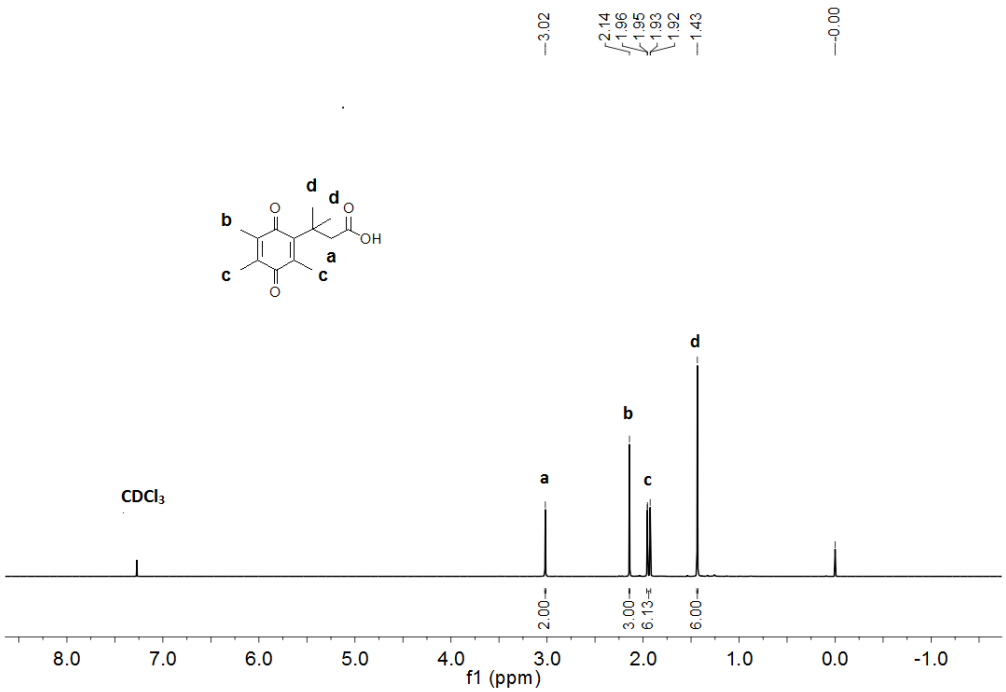

Figure S8. ^{1}H NMR spectrum of **4** (in $CDCl_3$).

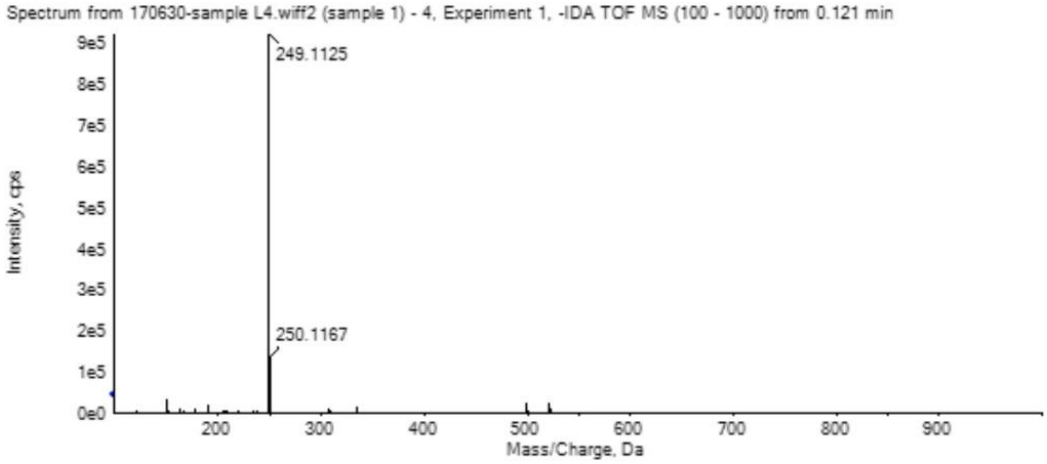

Figure S9. Mass spectrum of **4.** For **4**: HR-MS (ESI): calcd for $C_{14}H_{18}O_4$ ($[M-H]^-$) 249.1127, found: 249.1125.

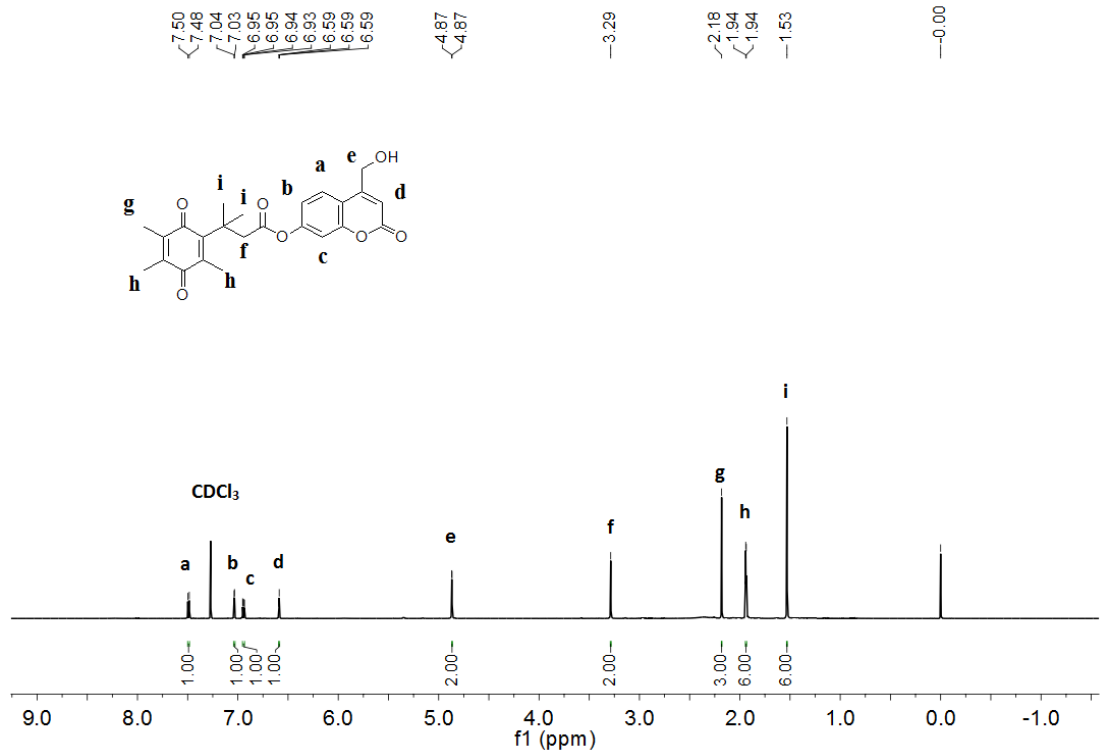

Figure S10. ^{1}H NMR spectrum of **5** (in $CDCl_3$).

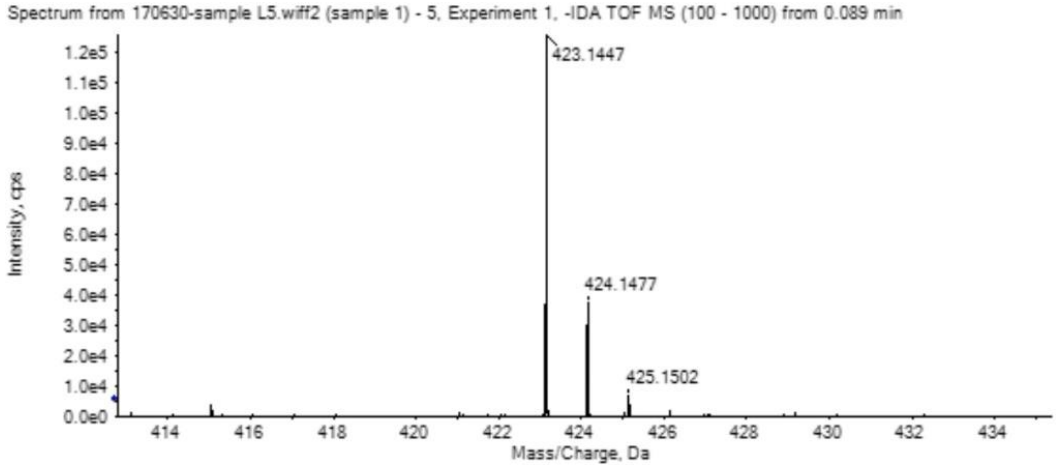

Figure S11. Mass spectrum of **5.** For **5**: HR-MS (ESI): calcd for $C_{24}H_{24}O_7$ ([M-H]$^-$) 423.1444, found:423.1447.

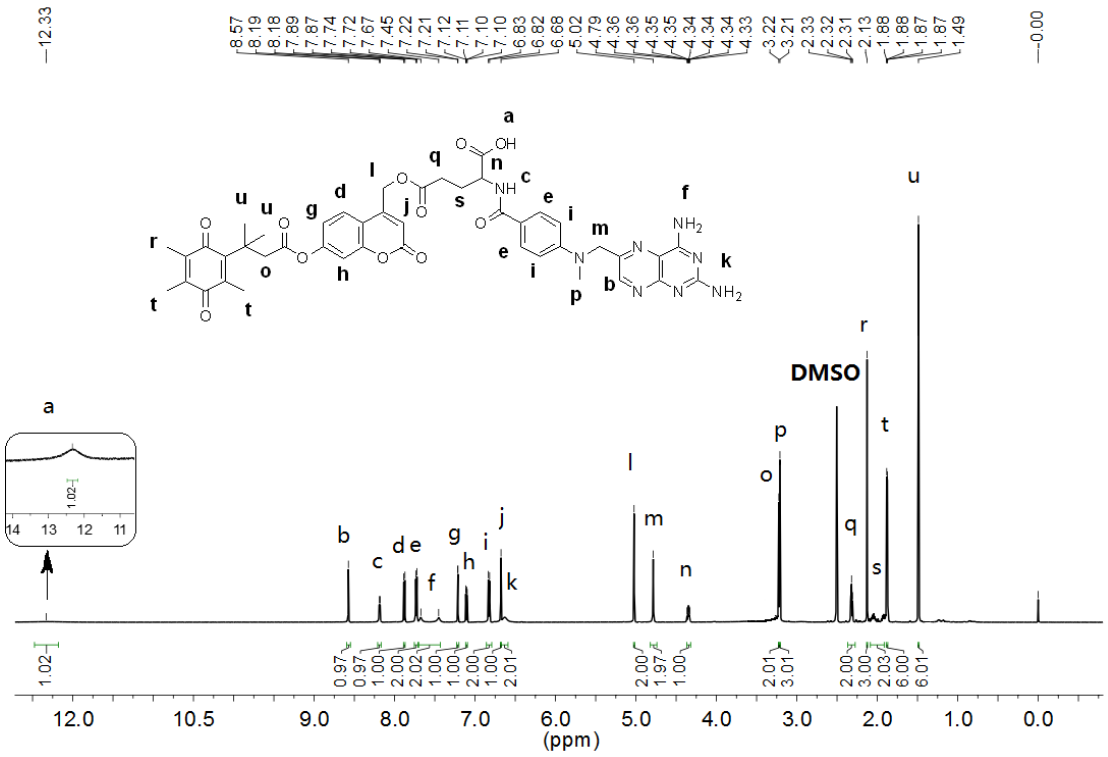

Figure S12. ^{1}H NMR spectrum of pro-prodrug (DT-COU-MTX, **6** in DMSO-d_6).

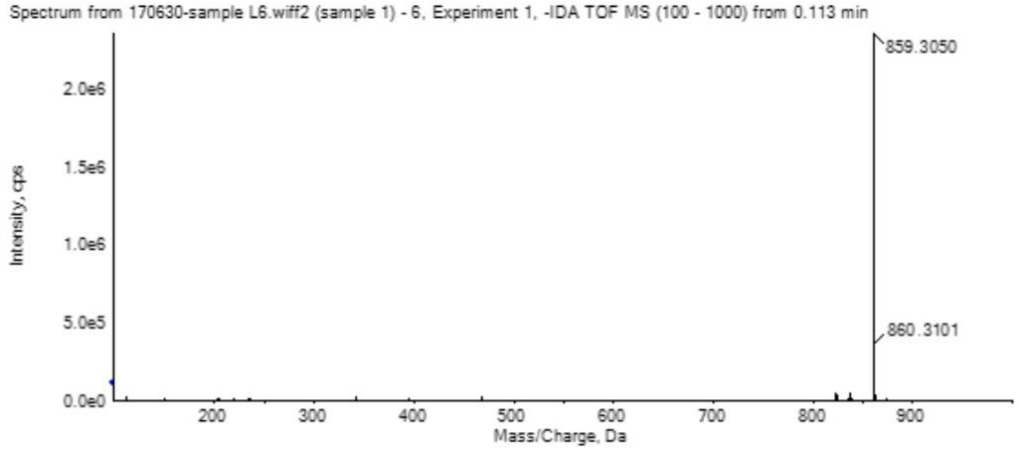

Figure S13. Mass spectrum of pro-prodrug (**6**). For **6**: HR-MS (ESI): calcd for $C_{44}H_{44}N_8O_{11}$ ([M-H]$^-$) 859.3052, found:859.3050.

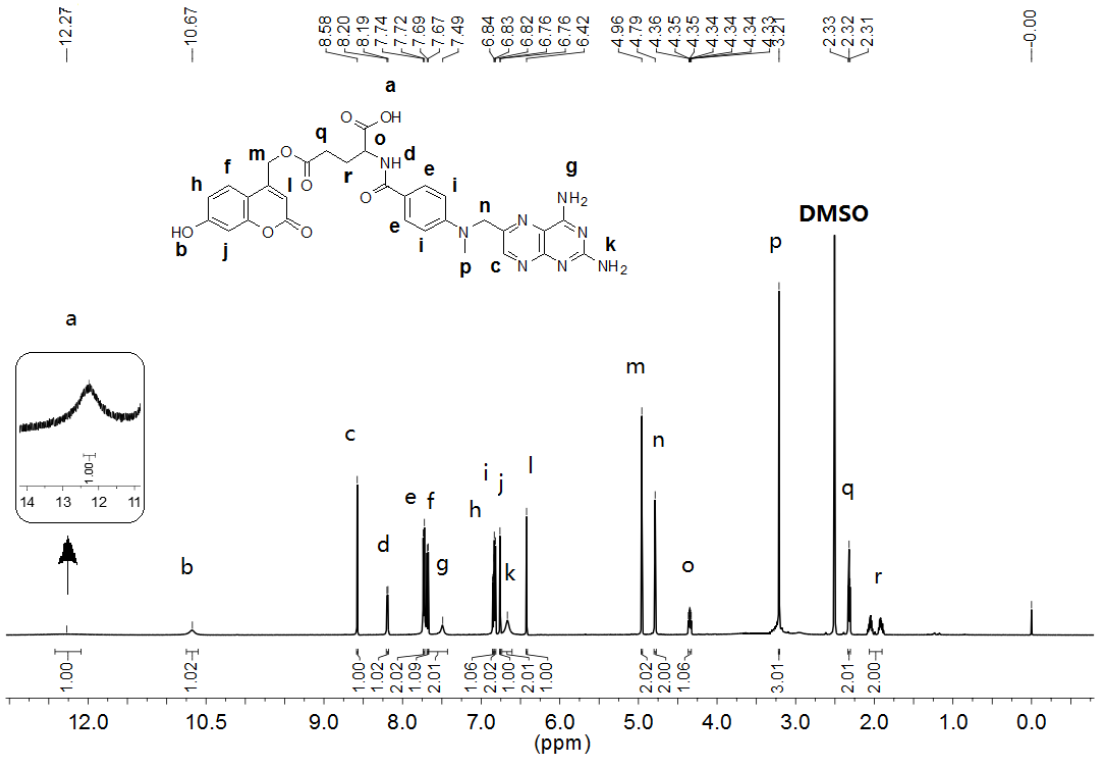

Figure S14. [1]HNMR spectrum of prodrug (**7** in DMSO-d_6).

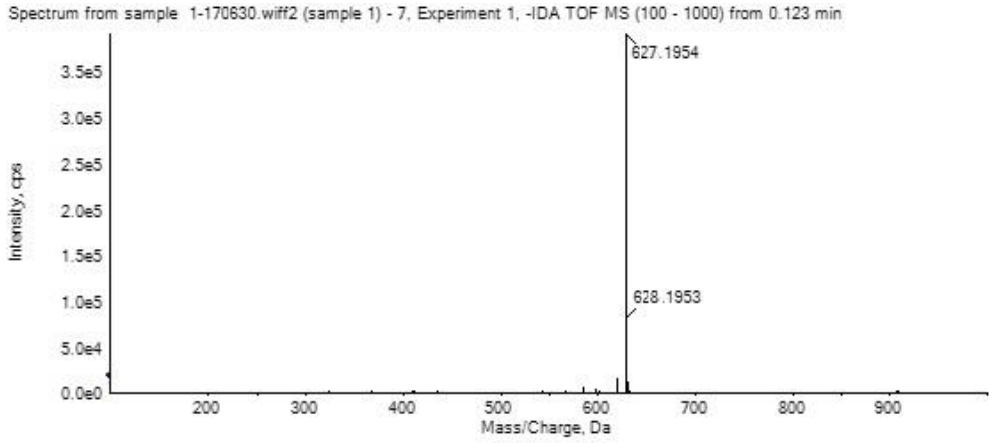

Figure S15. Mass spectrum of **7** (prodrug) for **7**: HR-MS (ESI): calcd for $C_{30}H_{38}N_8O_8$ ([M-H]$^-$) 627.1952, found:627.1954.

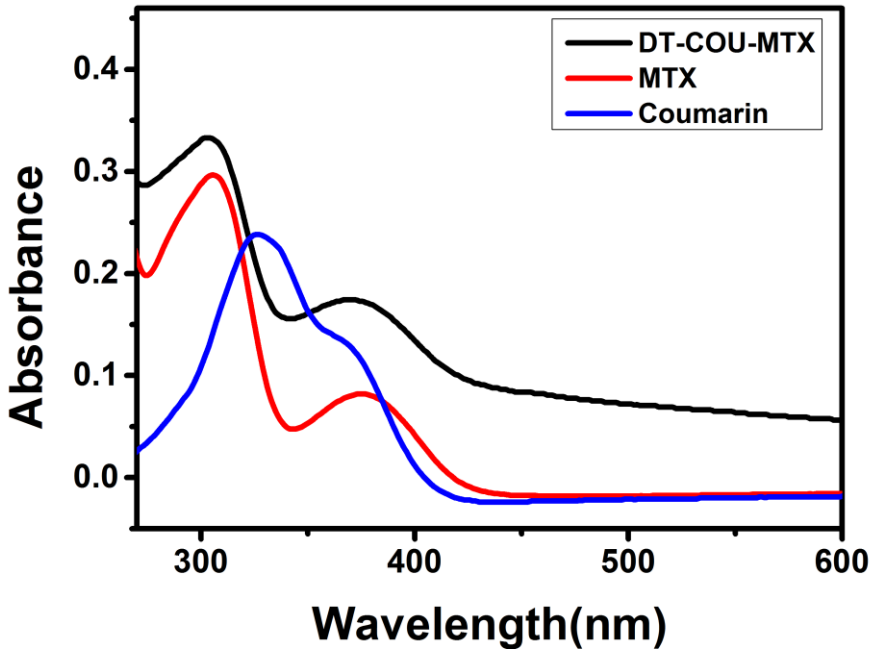

Figure S16. Absorption spectra of the DT-COU-MTX (5 μM), MTX (5 μM) and coumarin (5 μM) in pH 7.4 PBS buffered water solution (containing 1% DMSO).

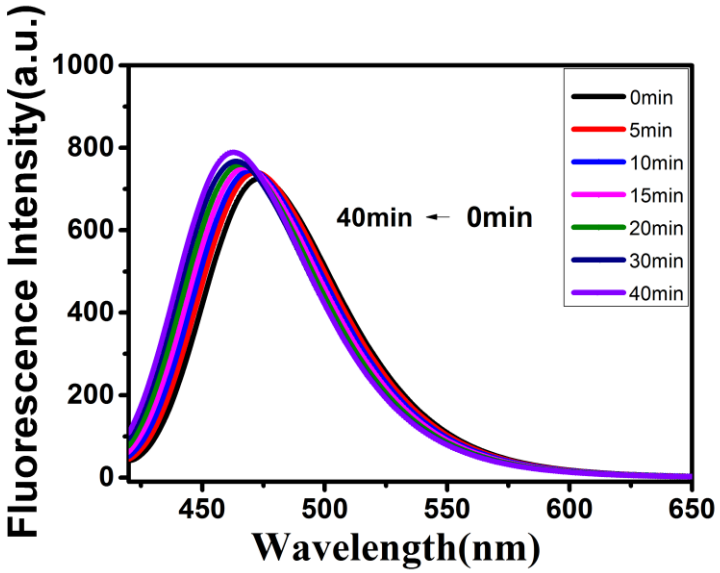

Figure S17. Photolytic processes of the unlocked prodrug (HO-COU-MTX) were monitored by fluorescence detection.

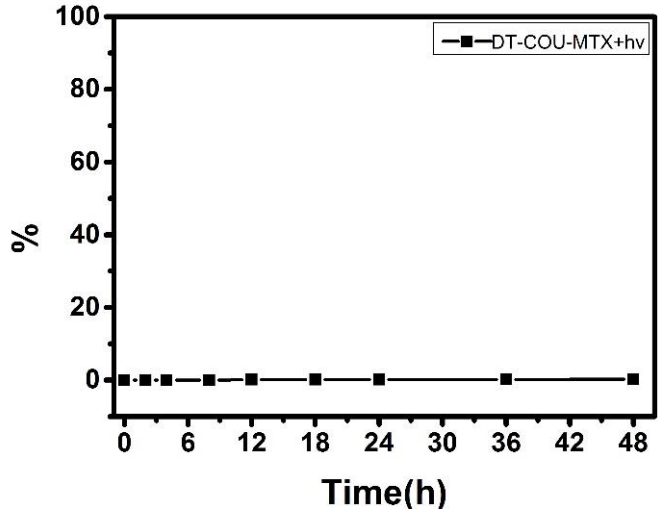

Figure S18. The MTX release rate of the DT-COU-MTX under irradiation for 48 h.

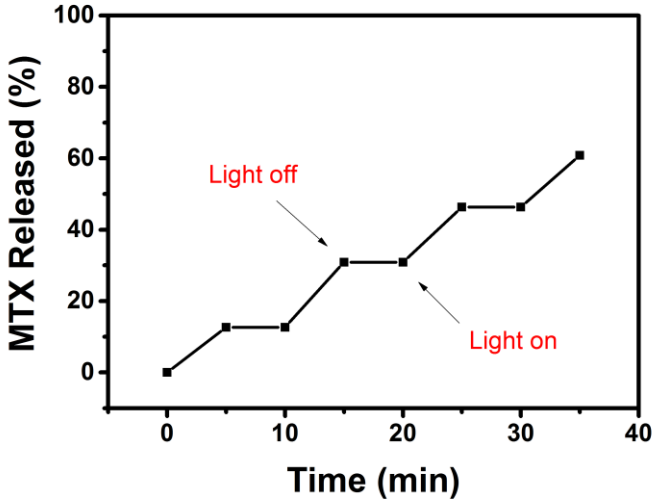

Figure S19. Relationship between MTX-release percentage (as determined by HPLC) of DT-COU-MTX after enzyme activation for various cycels of irradiation(one-photon irradiation)/dark time.

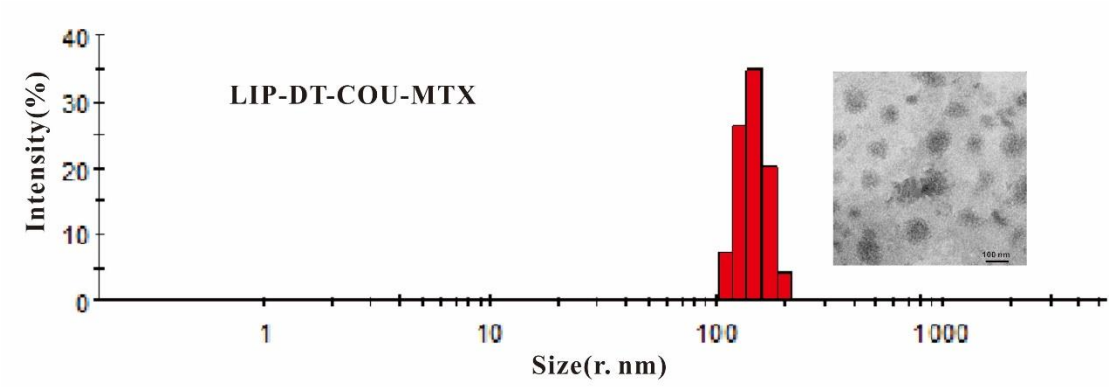

Figure S20. Particle size distribution obtained from dynamic light scattering (DLS)

and images from transmission electron microscopy (TEM) for LIP-DT-COU-MTX.

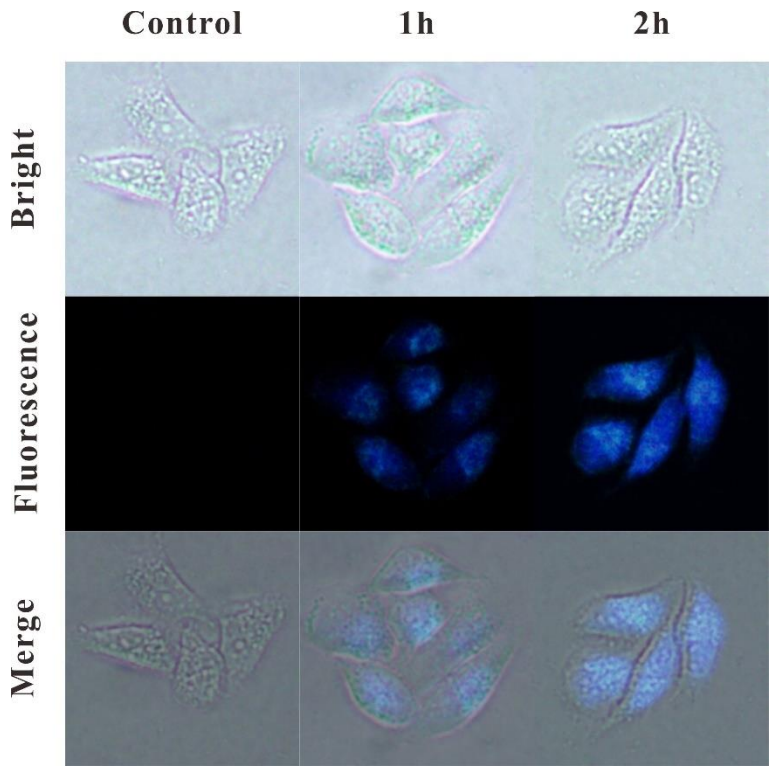

Figure S21. Fluorescent microscopic images for HeLa Cells that has been treated with LIP-DT-COU-MTX (20 μg/mL, with the incubation time of 1 h or 2 h respectively) or without a LIP-DT-COU-MTX (the control).

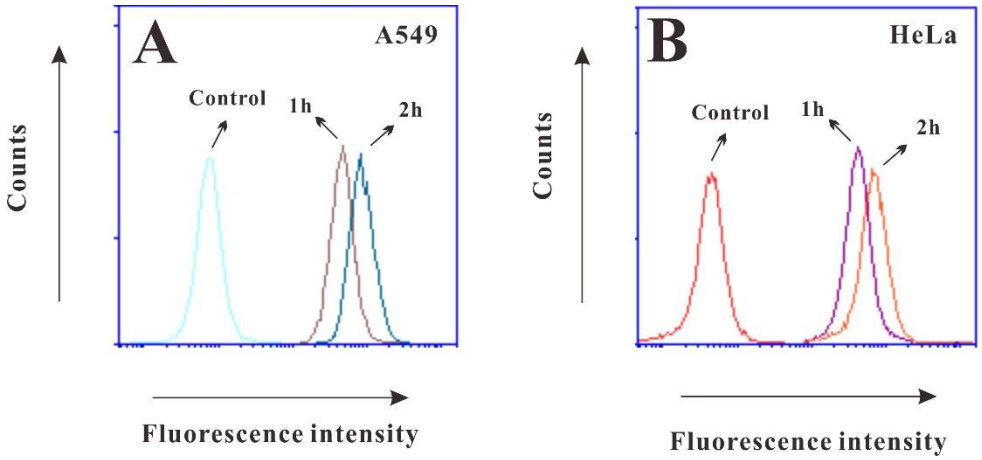

Figure S22. Flow cytometry profiles for (A) A549 cells and (B) HeLa cells in the absence (the control) and presence of the LIP-DT-COU-MTX (20 μg/mL) for 1 or 2 h.

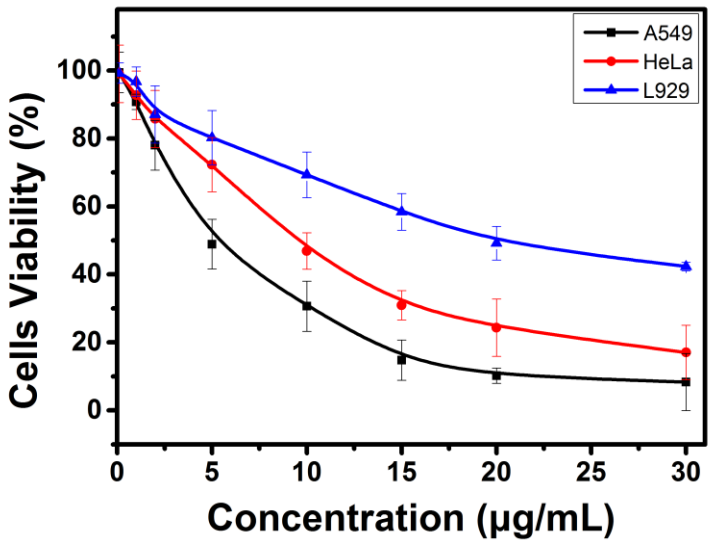

Figure S23. Cell viabilities of A549, HeLa and L929 cells treated with different concentrations of MTX (0.1μg/mL to 30μg/mL) for 48h.

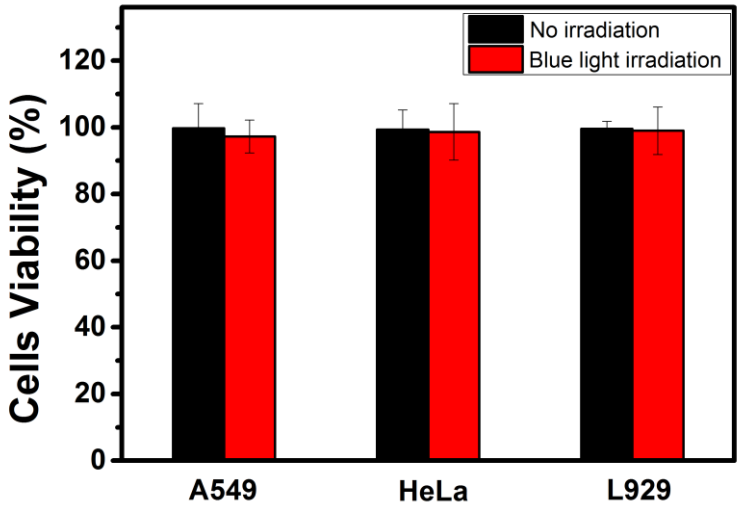

Figure S24. Cell viability of the two cell lines upon exposure to blue light irradiation (or with no irradiation) but not treated with the LIP-DT-COU-MTX.

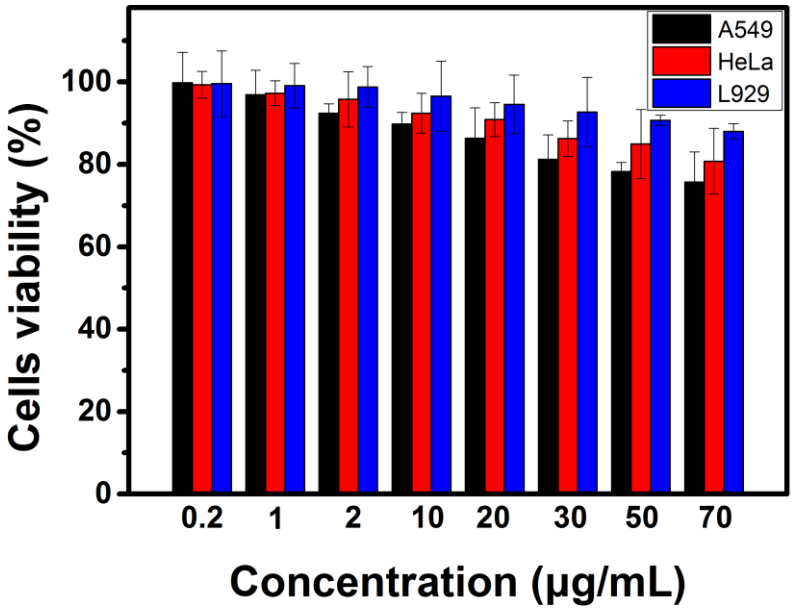

Figure S25. Cell viability of three groups of cells treated with LIP-DT-COU-MTX without irradiation.

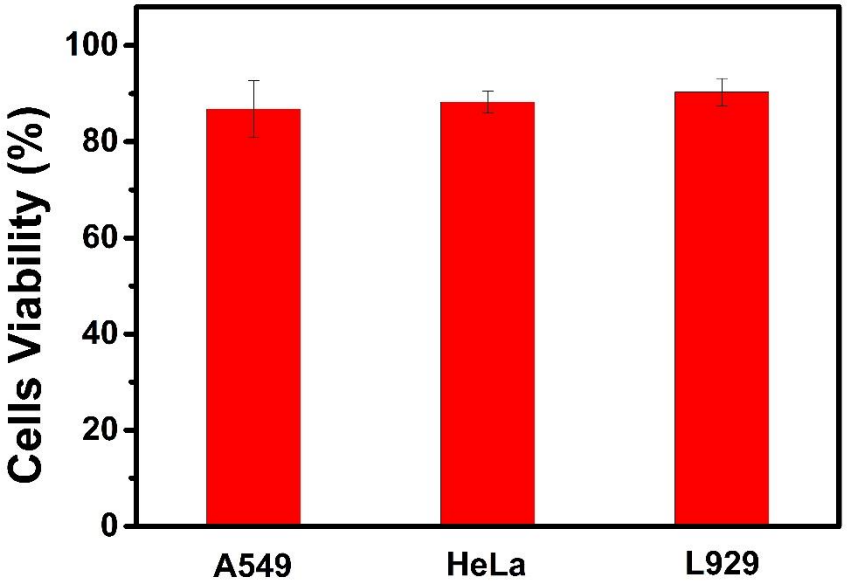

Figure S26. Cell viabilities for A549, HeLa and L929 cell lines treated with the 20 μM dicoumarol (DIC) for 48 h.

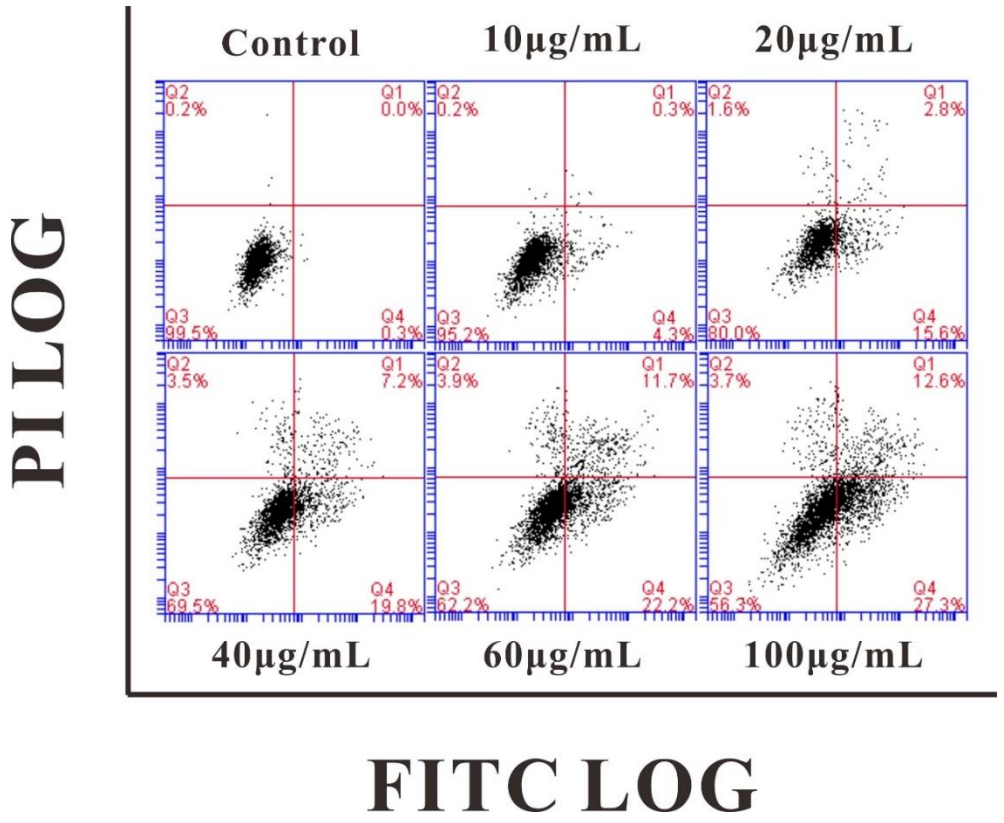

Figure S27. Flow cytometry diagram of HeLa cells respectively treated with the LIP-DT-COU-MTX of varied concentrations (10 μg/mL to 100 μg/mL) and under light irradiation.

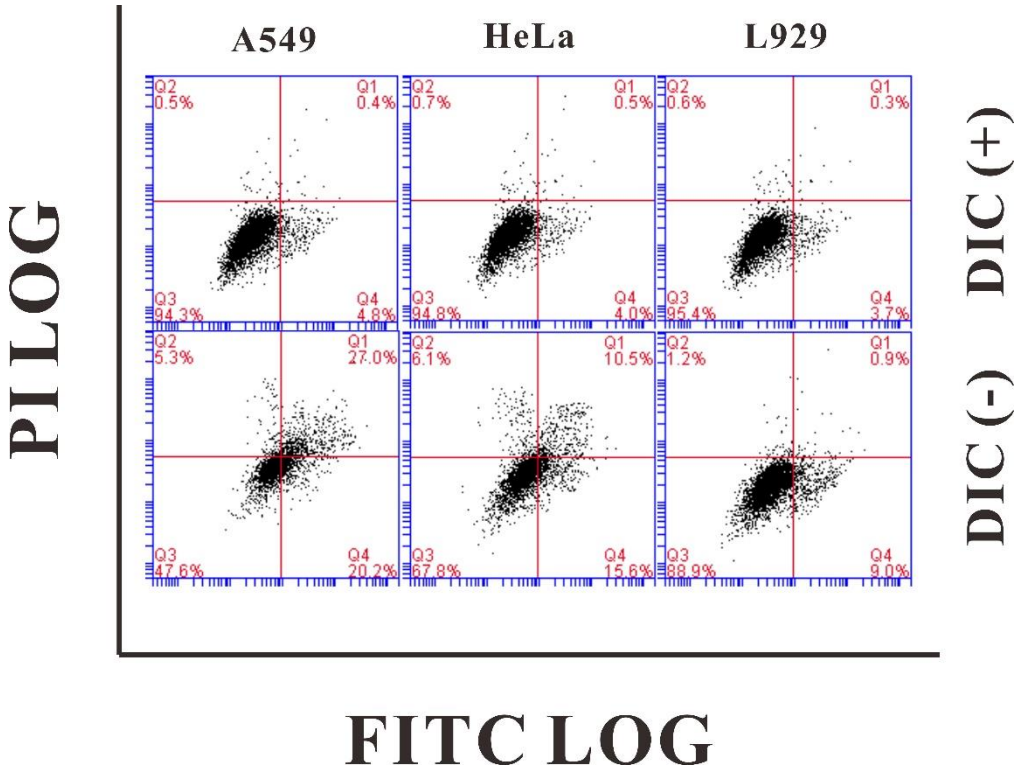

Figure S28. Flow cytometry diagram of A549, HeLa and L929 cell lines upon being

pre-treated with 20 μM dicoumarol (DIC) or not for 4 h and then treated with the LIP-DT-COU-MTX (70 μg/mL) (light-irradiation conditions are the same as those for Figure 5B).