Intracellular dual fluorescent light-up bioprobes for image-guided photodynamic cancer therapy

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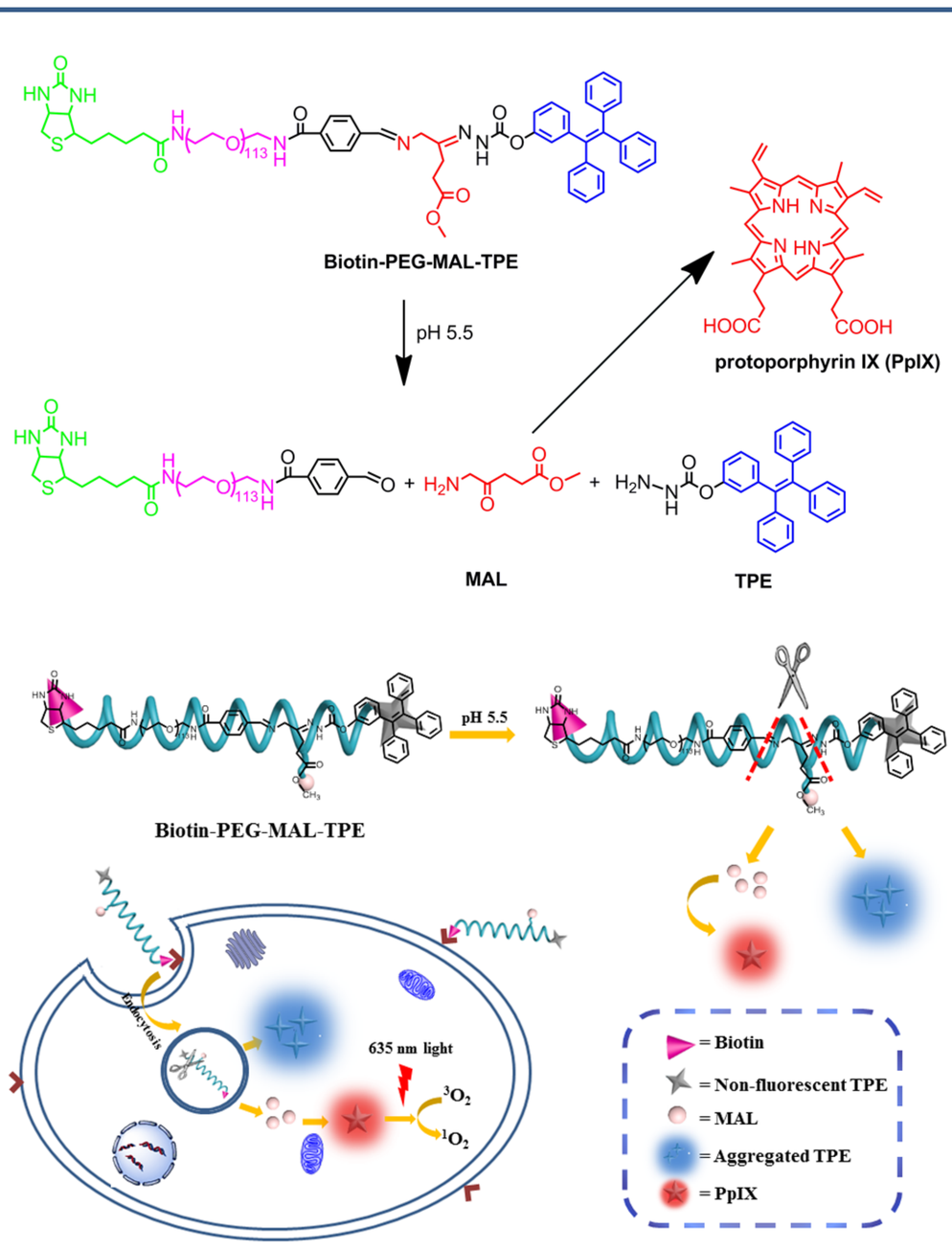
Adstract: An intracellular dual fluorescent light-up bioprobe is designed and synthesized. It can selectively light up cancer cells with blue fluorescence of tetraphenylene (TPE) and red fluorescence of PpIX. Moreover, upon endogenous generation and accumulation of PpIX in cancer cells, efficient photodynamic ablation of cancer cells after light irradiation is demonstrated with easy regulation for optimal therapeutic efficacy.



Scheme 1. Schematic illustration of the intracellular dual fluorescent light up of Biotin-PEG-MAL-TPE.

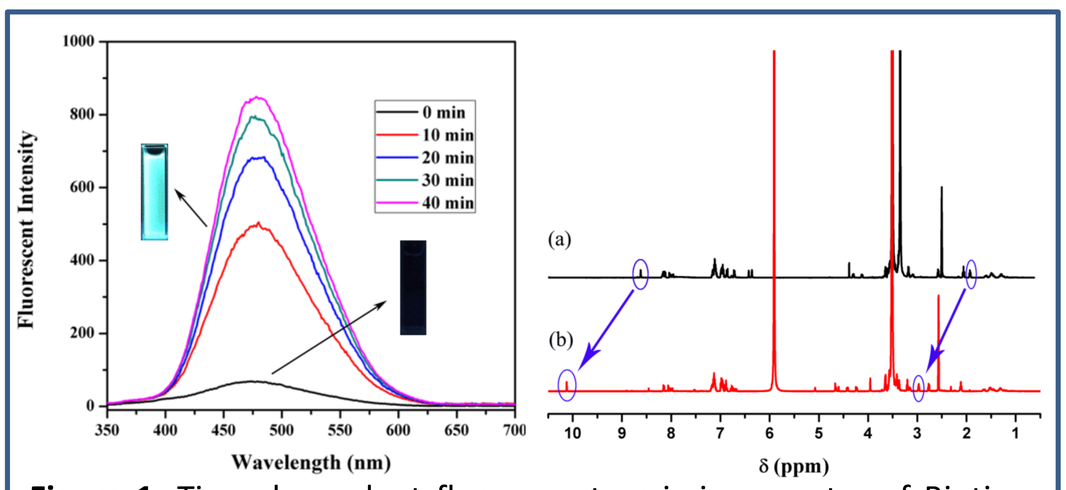


Figure 1. Time-dependent fluorescent emission spectra of Biotin-PEG-MAL-TPE bioprobe with excitation of 360 nm at pH 5.5 and ^1H NMR spectra of Biotin-PEG-MAL-TPE in (a) DMSO-d_6 and (b) DMSO-d_6 with 2% deuterium chloride for 24 h.

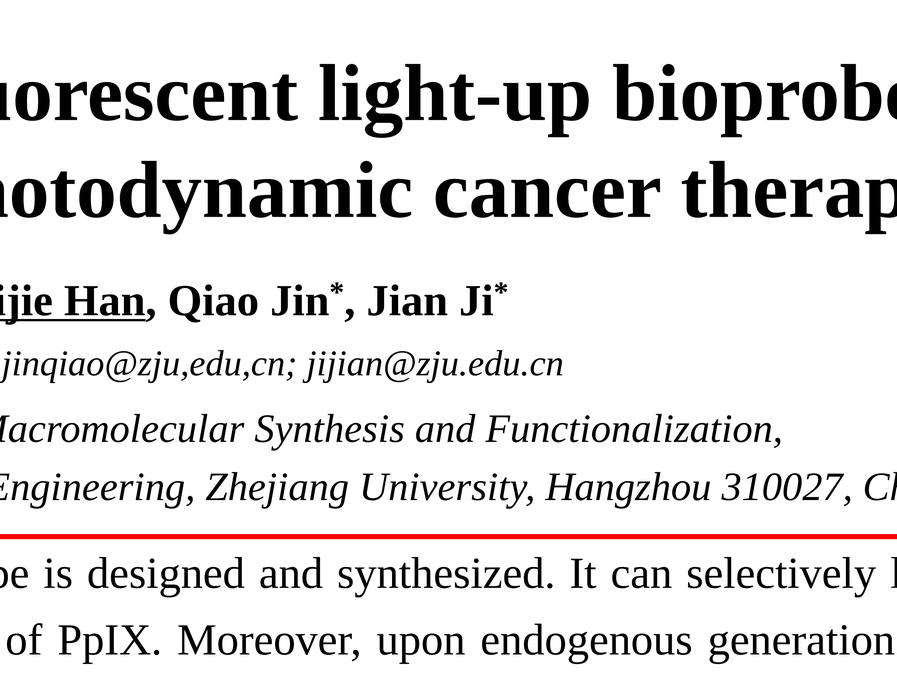


Figure 2. Fluorescence microscopy images of (a) A549 cells incubated with Biotin-PEG-MAL-TPE bioprobes, strong intracellular blue fluorescence and red fluorescence were observed; (b) HUVEC cells incubated with Biotin-PEG-MAL-TPE bioprobes, weak fluorescence was observed owing to the less receptor of biotin in HUVEC cells; (c) A549 cells incubated PEG-MAL-TPE bioprobes, very weak fluorescence was observed owing to the absence of biotin moieties.

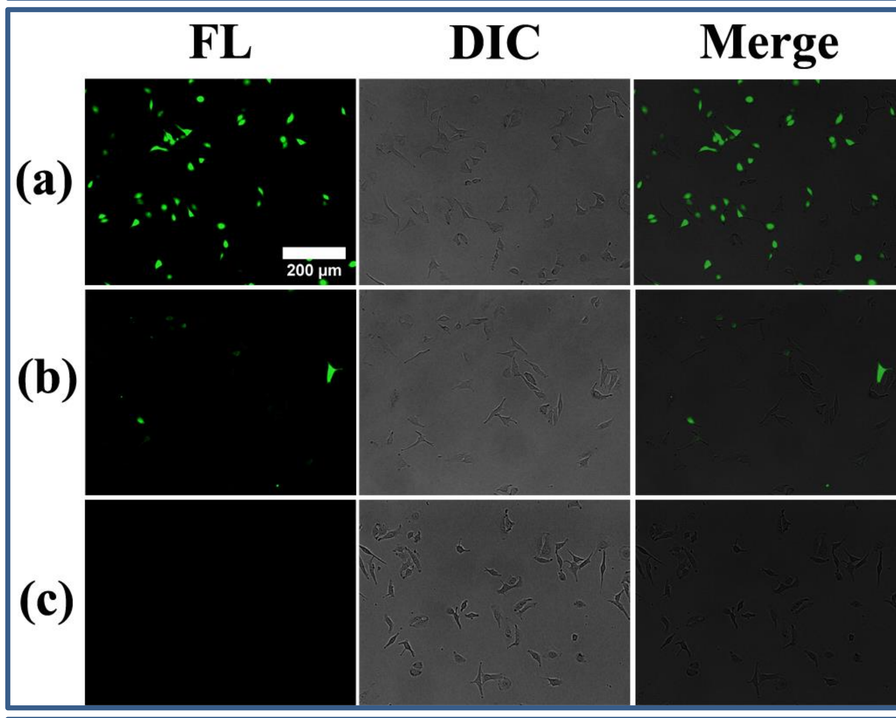


Figure 3. Reactive oxygen generation detected by fluorescence of DCFDA in A549 cells exposed to (a) Biotin-PEG-MAL-TPE prodrug after irradiated with 635 nm light at 500 mW cm^{-2} for 0.5 min, (b) PEG-MAL-TPE prodrug, after irradiated with 635 nm light at 500 mW cm^{-2} for 0.5 min and (c) control without treatment.

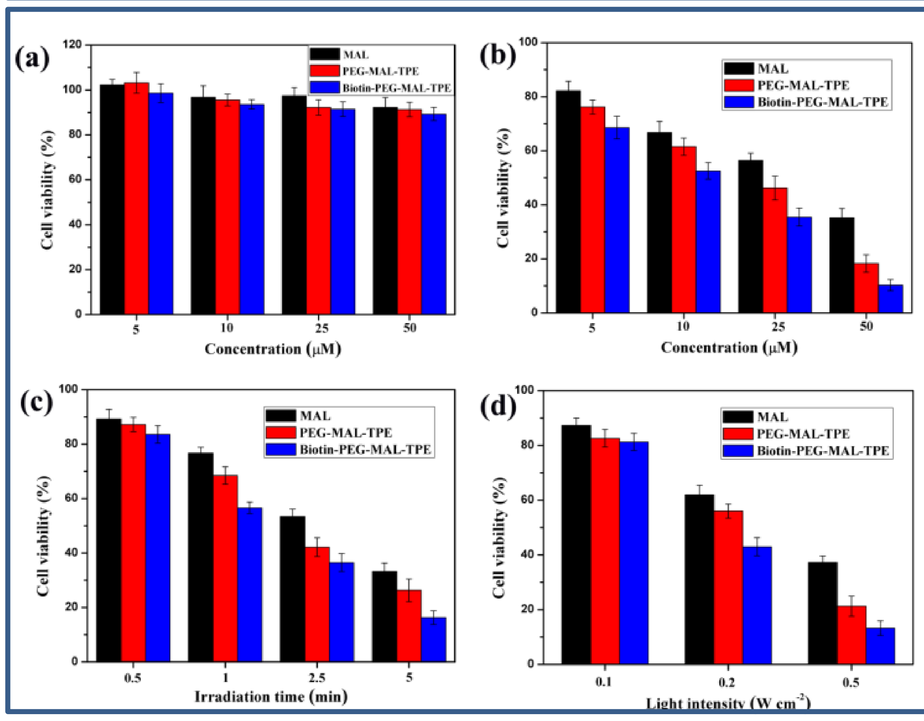


Figure 4. Cell viability of A549 cells (a) after incubation with the prodrugs at different concentrations without light irradiation; (b) upon incubation with the prodrugs at different concentrations after light irradiation; (c) upon incubation of the cells with prodrugs and irradiation with light for different time; (d) upon incubation of the cells with prodrugs and irradiation with different light intensity.

Conclusions: A pH-responsive bioprobe Biotin-PEG-MAL-TPE was successfully synthesized and utilized for intracellular dual fluorescent light-up imaging and targeted photodynamic ablation of cancer cells. After internalized into A549 cancer cells, TPE and MAL can be released in acidic lysosomal environment. Intracellular dual fluorescent light up was achieved owing to the AIE effect of TPE and heme biosynthesis of PpIX from MAL. The endogenously generated PpIX was further used as a photosensitizer for PDT. After 635 nm light irradiation, Biotin-PEG-MAL-TPE prodrugs exhibited stronger inhibition of cell viability than PEG-MAL-TPE prodrugs and free MAL. The design of endogenous dual fluorescent light-up bioporbes presents a promising potential for targeted image-guided photodynamic cancer therapy.