Long-wavelength Light-triggered Drug Delivery by Upconversion-like Photolysis

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Photocleavage reaction enables spatiotemporal control of drug release/activation precisely at lesions.[1] However, the limited light wavelength hinders its biological applications.[2-4] Here, we demonstrated that a photosensitizer can directly activate boron-dipyrromethene (BODIPY)-based prodrugs by triplet-triplet energy transfer (TTET). This upconversion-like process greatly reduces the required excitation energy to initiate prodrug photolysis, allowing the usage of NIR light to activate green-light responsive BODIPYs. A wide range of BODIPY prodrugs with different bioactive molecules were activated under low-irradiance NIR light (100 mW/cm^2, 5 min) with high yields (up to 87 %). Based on the upconversion-like photolysis strategy, nanosystems have been developed for efficient light-triggered drug release for precise photoactivable therapy, which demonstrate excellent anti-cancer efficacy in tumor-bearing mouse models.

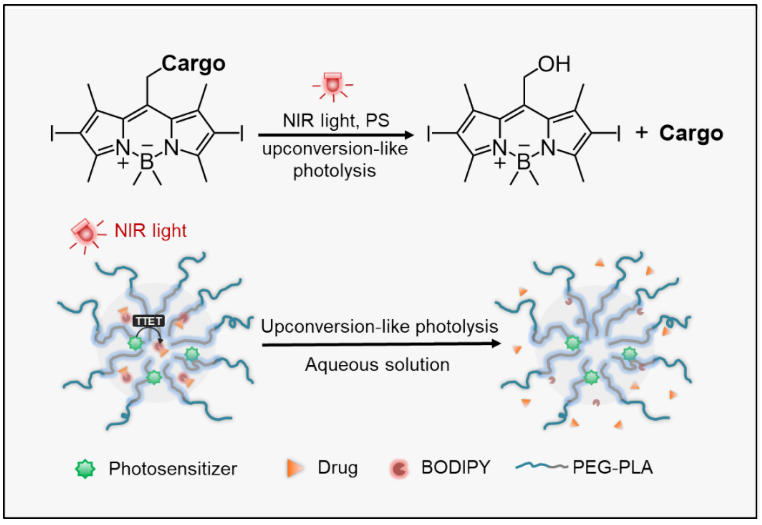

Figure 1. Schematic illustration of NIR light-triggered activation of prodrugs and prodrug-loaded nanosystem based on the upconversion-like process. (PS: photosensitizer)

References:

[1] Liu J, Kang W, Wang W. *Photochemistry and Photobiology*, **2022**, 98, 288-302.
[2] Lv W, Li Y, Li F, Lan X, Zhang Y, Du L, Zhao Q, Phillips DL, Wang W, *Journal of the American Chemical Society*, **2019**, 141, 17482-17486.
[3] Lv W, Long K, Yang Y, Chen S, Zhan C, Wang W, *Advanced Healthcare Materials*, **2020**, 9, 2001118.
[4] Long K, Han H, Kang W, Lv W, Wang L, Wang Y, Ge L, Wang W, *Journal of nanobiotechnology*, **2021**, 19, 1-4.