Literature Report

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ARTICLE

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Photoactivatable metabolic warheads enable precise and safe ablation of target cells in vivo

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Edinburgh Medical School: Clinical Sciences
CENTRE FOR INFLAMMATION RESEARCH

Professor Marc Vendrell

Chair of Translational Chemistry and Biomedical Imaging

My lab works on the development of dynamic activatable fluorophores and combines expertise in peptide and organic chemistry, cell imaging, molecular biology and fluorescence spectroscopy, and we collaborate with biologists, immunologists and clinicians in a highly interdisciplinary environment.

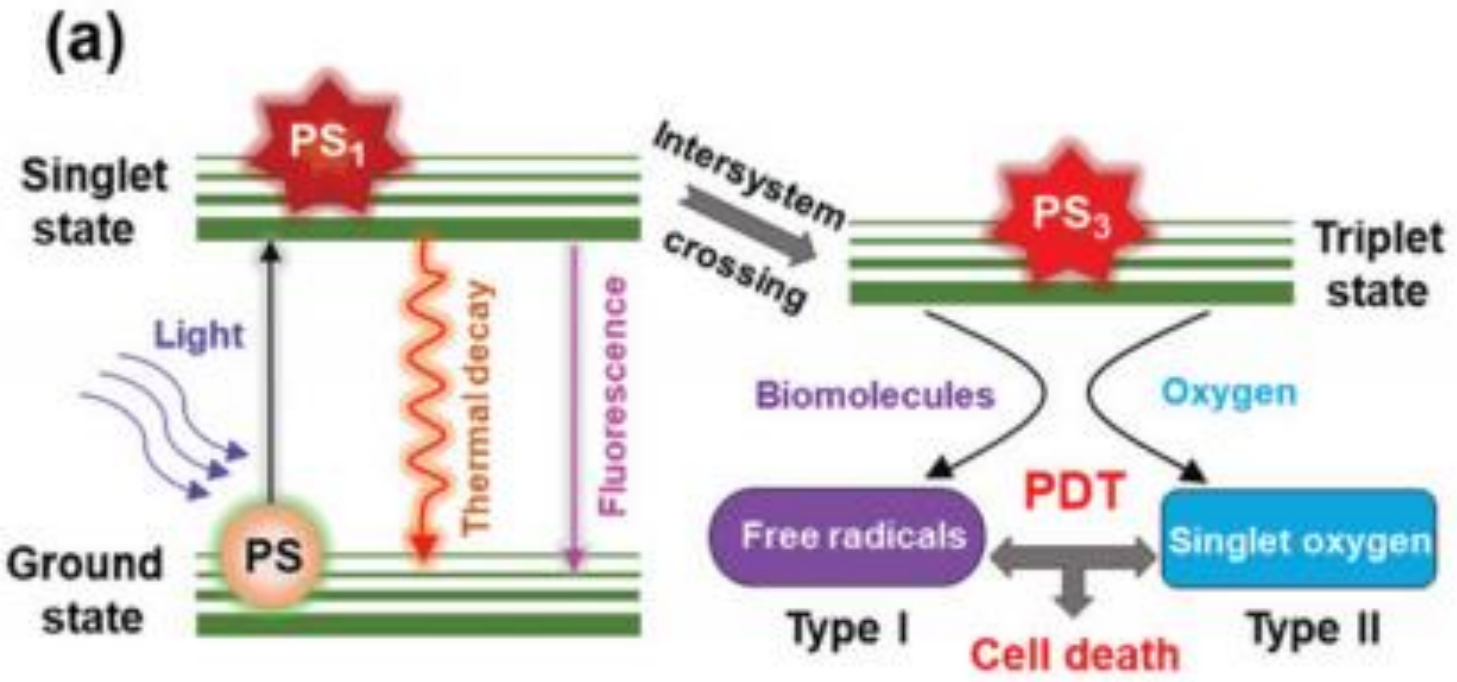
Dr Yi Feng

Reader / Wellcome Trust Sir Henry Dale Fellow

Yi Feng的小组研究了体内实时成像，重点是
斑马鱼模型中炎症对癌症进展的影响。

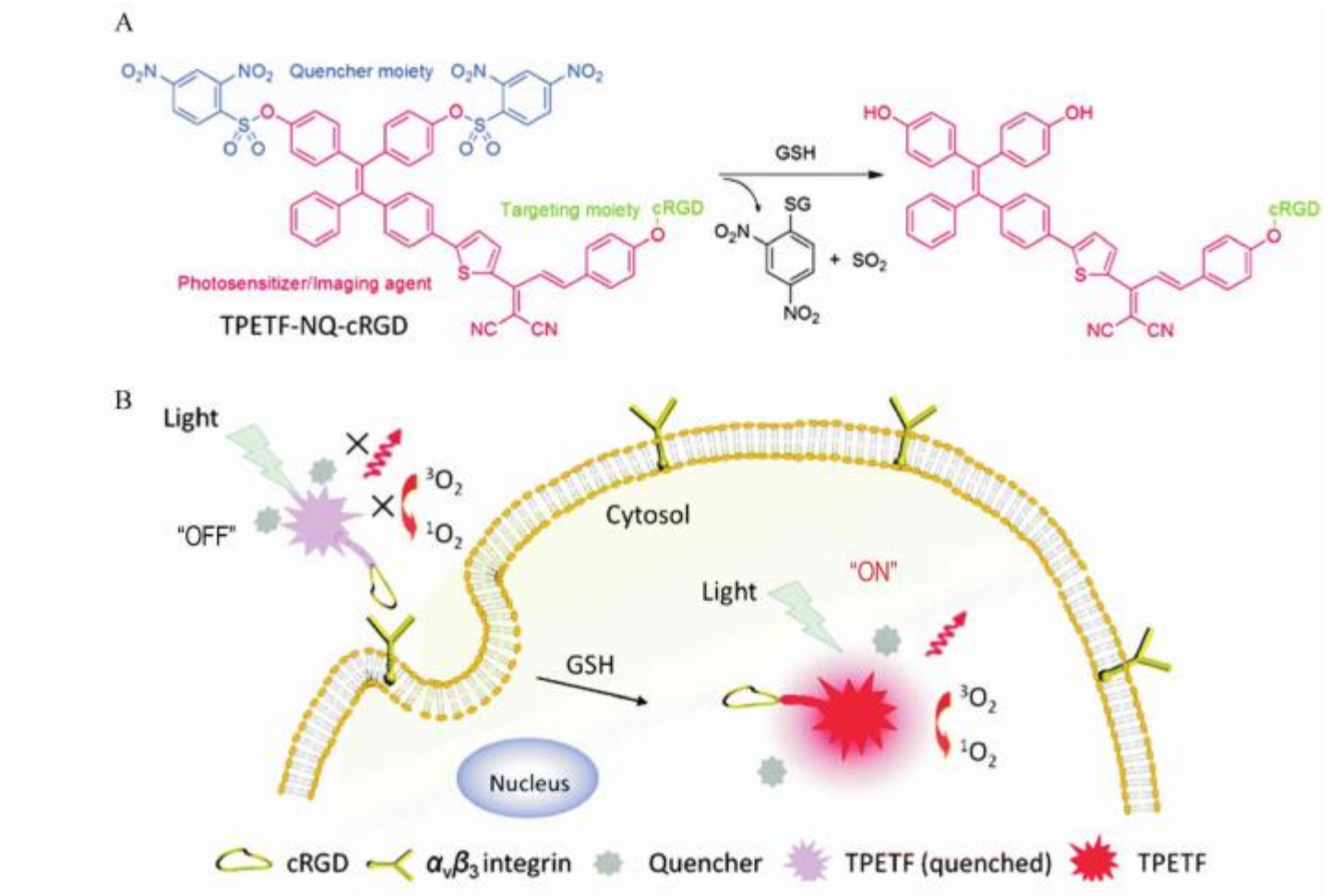
现在的惠康基金会是于1936年根据药剂师、企业家、慈善家和收藏家，亨利惠康（Henry Wellcome）爵士的遗嘱创建，是一个全球性的慈善基金会。是全球研究医学史的主要信息资源之一。
它并不是单纯的科研机构，也不是一个慈善组织，更不是一家企业。旨在“帮助伟大的想法蓬勃发展”以改善每个人的健康状况。

PDT原理



- 可激活的光敏剂(PS)药物
- 具有适当波长的光源
- 周围的氧气

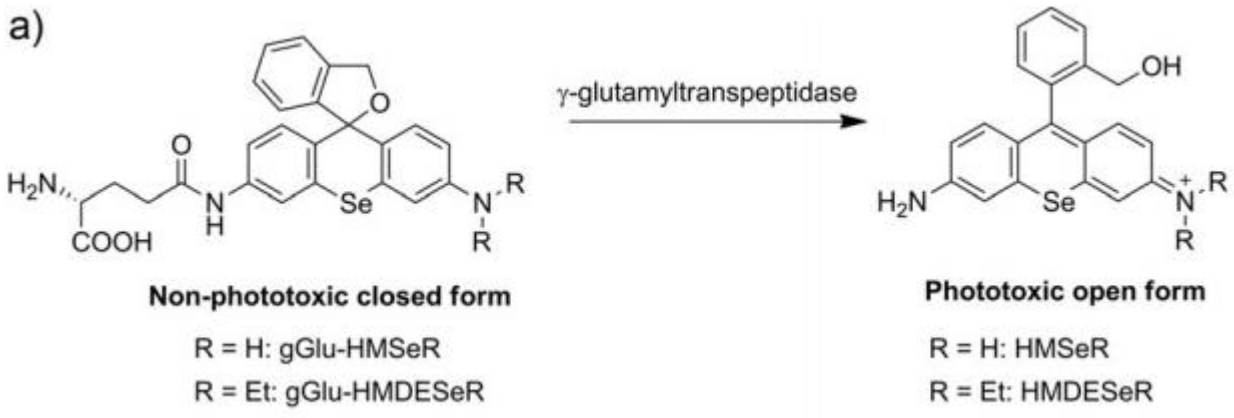
与GSH结合

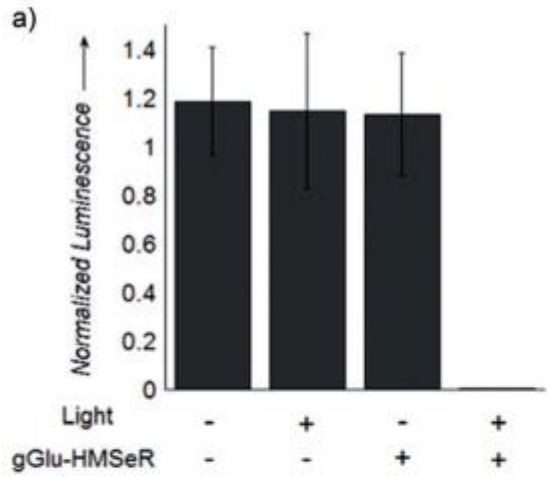


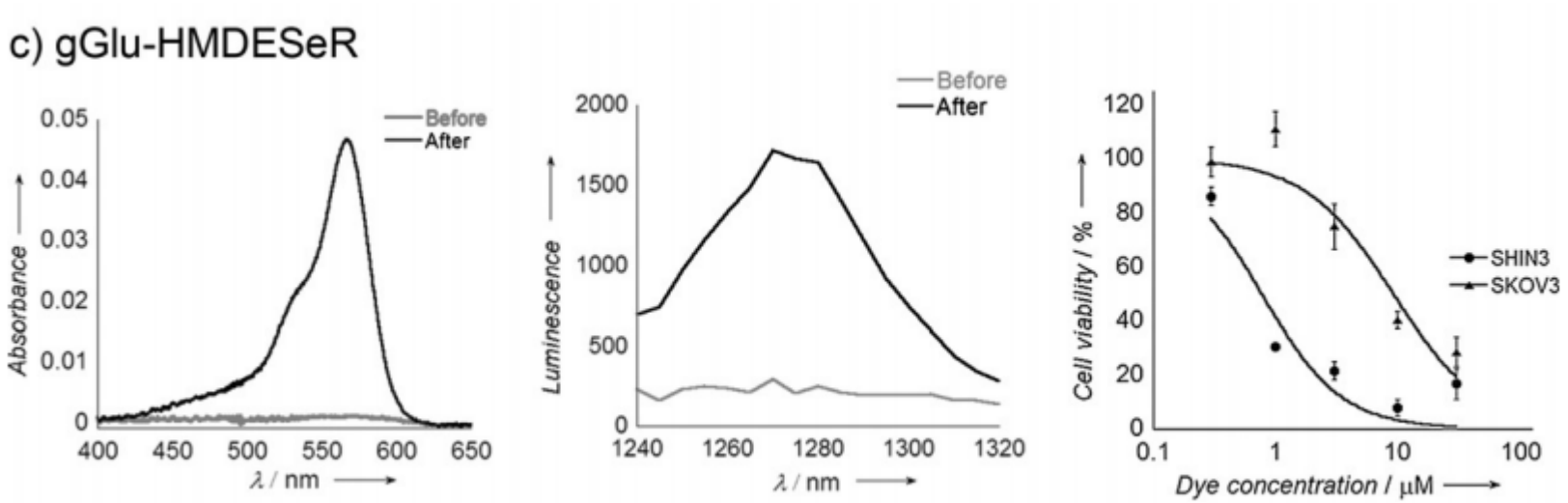
cRGD:环精氨酸-甘氨酸-天冬氨酸

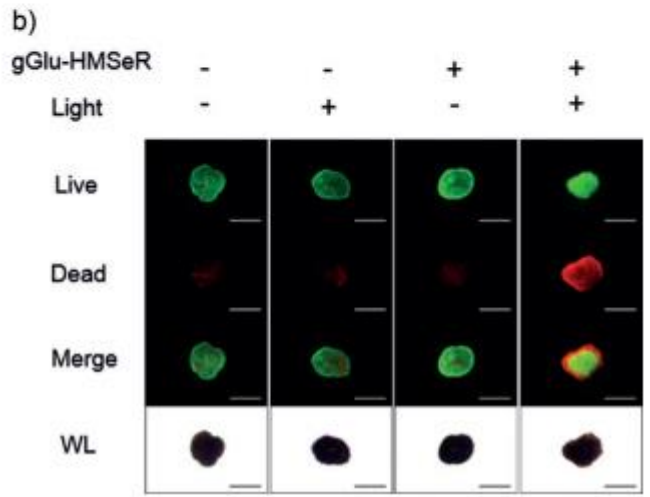
J.Mater.Chem.2016.4(1).169-176

与GGT结合



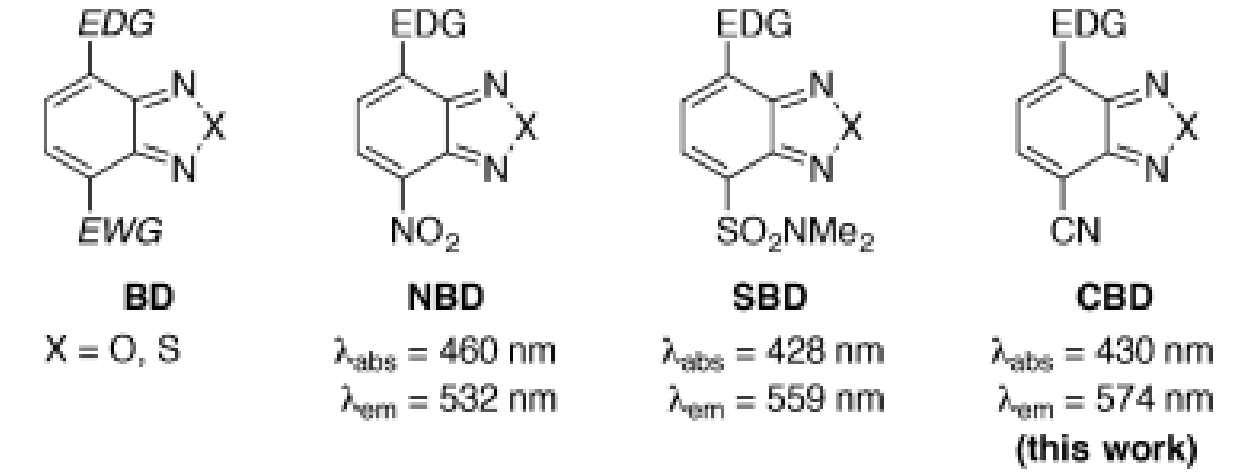




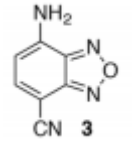


Angew. Chem. Int. Ed. 2017, 56, 10418 –10422

Photoactivatable metabolic warheads



Benzo(heteroatom)diazole



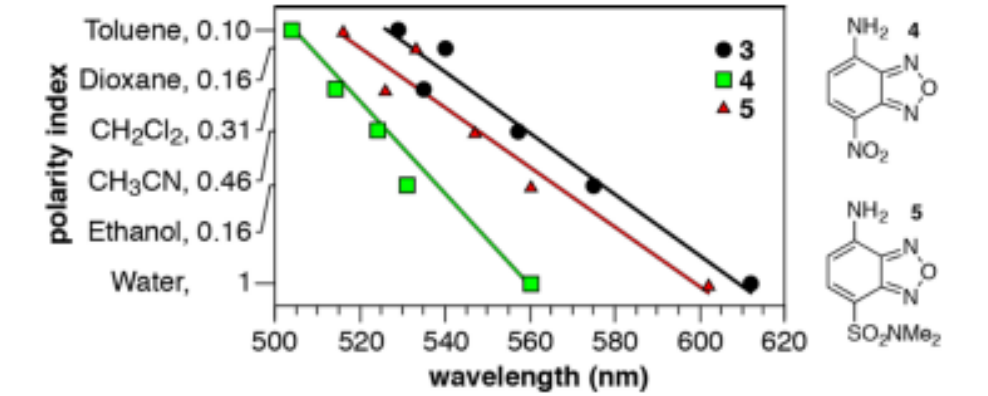


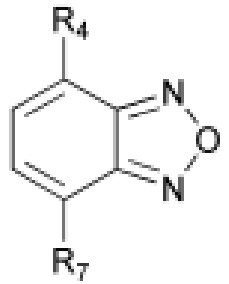
Figure 3. Comparison of polarity[22] and wavelength of emission for cyano-containing benzoxadiazole **3** previously known nitro (**4**)- and sulfonamide (**5**)-containing molecules. **4** was not soluble in hexane for analysis.

J. Org. Chem. 2017, 82, 8842−8847

Photoactivatable metabolic warheads

No.	λ_{ab}/nm	ε/M^{-1}cm^{-1}	λ_{em}/nm	τ_f/ns	E_S/cm^{-1}	E_T[a]/cm^{-1}	U_{slow}/U_{total}	Φ_f	Φ_r	Φ_{isc}	Φ_{ic}
1	338	10000	ND[b]	ND	ND	17500	0.130	—	—	0.21	0.79
2	331	8000	ND	ND	ND	ND	0.248	—	0.02	0.41[c]	0.57
3	478	26300	533	0.5	17000	ND	ND	0.01	—	—	0.99
4	458	23000	524	11	18500	ND	ND	0.38	—	—	0.62
5	416	16600	ND	ND	ND	14700	0.0474	—	—	0.09	0.91
6	373	12000	ND	ND	ND	16400	0.121	—	—	0.21	0.79
7	315	4620	ND	ND	ND	ND	ND	—	0.11	—	0.89
8	385	10200	510	4.2	17700	ND	0.172	0.17	—	0.29[d]	0.54
9	425	9700	547	12	17600	ND	ND	0.06	0.09	—	0.85
10	348	6000	460	2.2	20500	ND	ND	0.10	0.05	—	0.85

[a] Measured in the mixture of methanol–ethanol (1:1) at 77 K. [b] ND: too weak to be determined. [c] Determined by assuming the E_T values to be 17500 cm^{-1} (the E_T value of **1**). [d] Determined by assuming the E_T values to be 14700 cm^{-1} (the E_T value of **5**) since the phosphorescence of **2** and **8** was not detected. But the E_T values affected little the Φ_{isc} values.

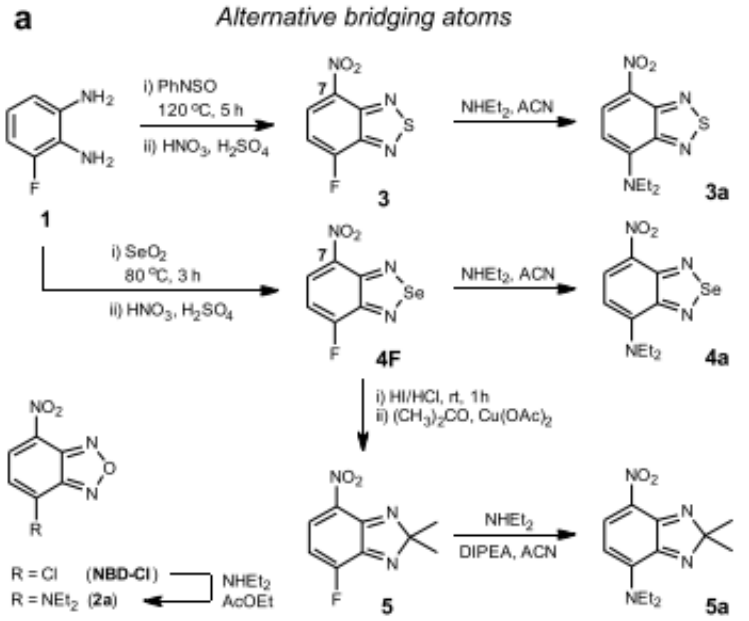


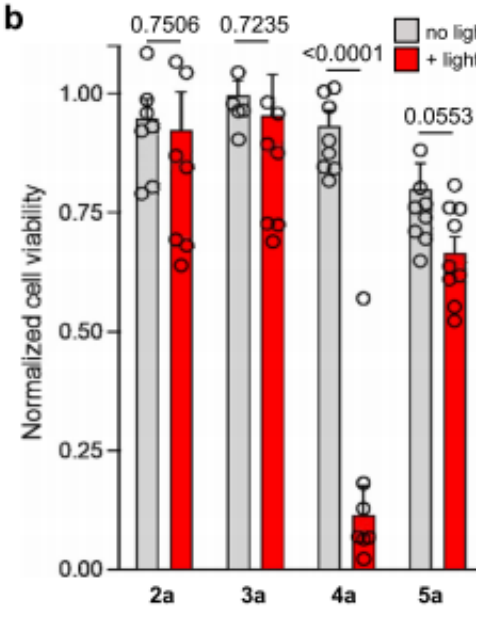
1: R_4 = Cl, R_7 = NO_2
2: R_4 = F, R_7 = NO_2
3: R_4 = NMe_2, R_7 = NO_2
4: R_4 = NHMe, R_7 = NO_2
5: R_4 = SMe, R_7 = NO_2
6: R_4 = OMe, R_7 = NO_2
7: R_4 = F, R_7 = SO_2NH_2
8: R_4 = SMe, R_7 = SO_2NH_2
9: R_4 = NHMe, R_7 = SO_2NH_2
10: R_4 = OMe, R_7 = SO_2NH_2

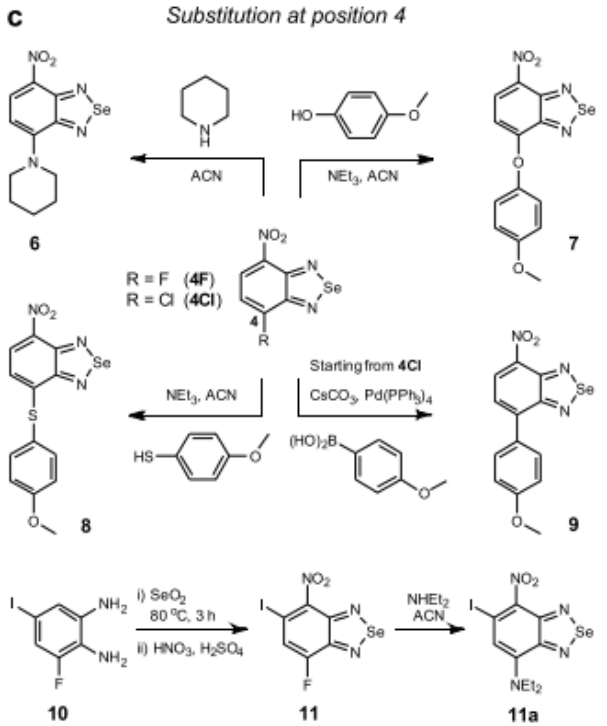
Chart 1 Chemical structures of the 4,7-disubstituted benzofurazans used in this study.

Org. Biomol. Chem. , 2003 , 1, 1067–1072

Synthetic routes for the preparation of small photosensitizers.



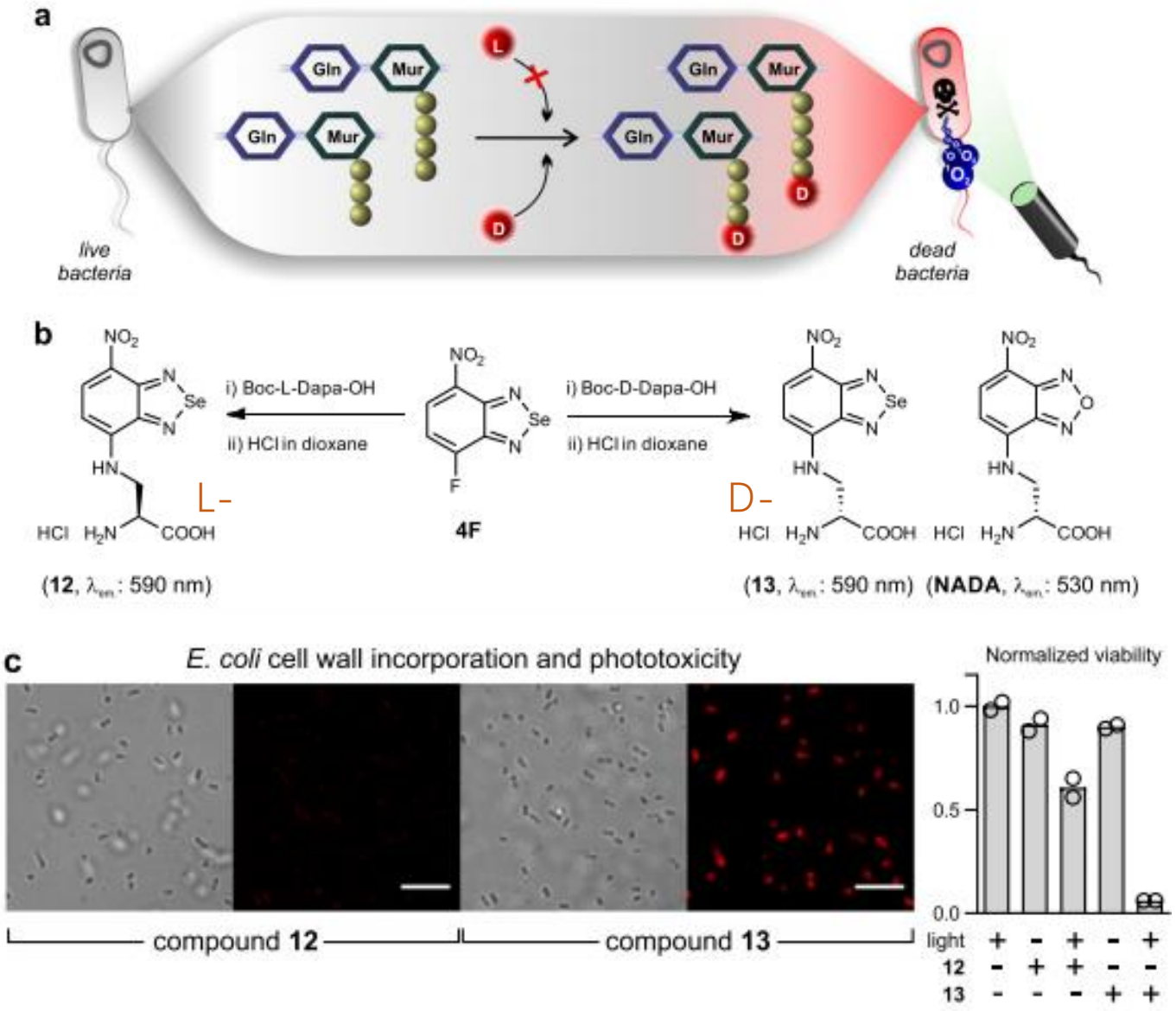




d

Code	$\lambda_{max.}$(nm)	Photoinduced toxicity
2a	490	13%
3a	480	8%
4a	510	82%
5a	565	14%
6	510	64%
7	400	2%
8	440	20%
9	425	27%
11a	500	65%
4F	442	2%

Benzoselenadiazole-conjugated retain stereo specific recognition of bacterial cells



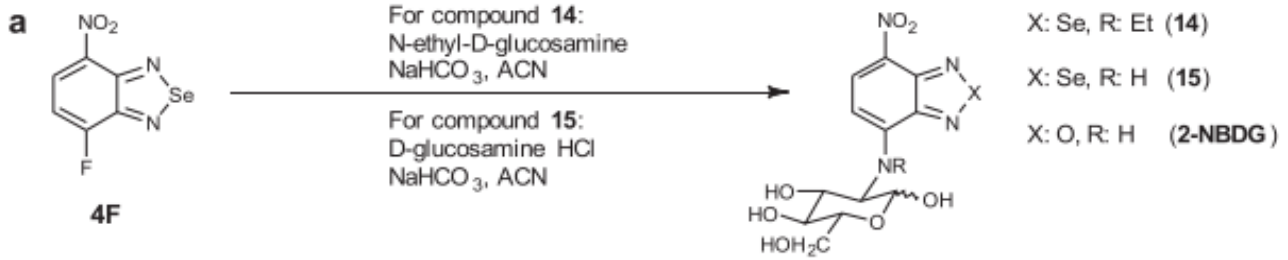
Supplementary Table 1. Chemical and spectral characterization for compounds **2a-17**.

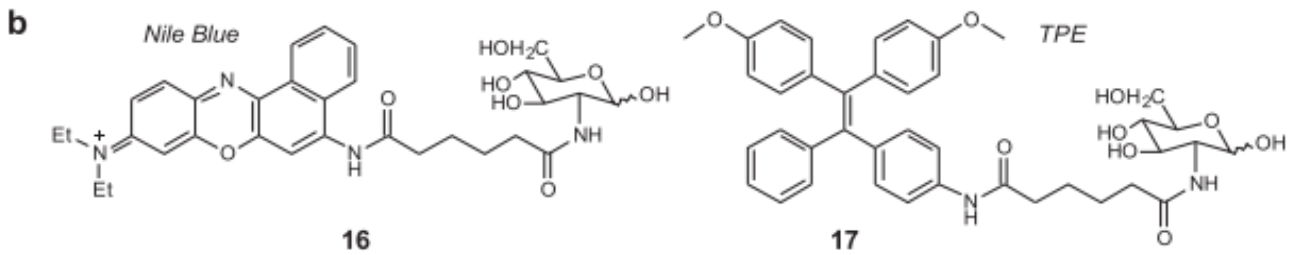
Code	HPLC purity	$M_{calc.}$	$M_{exp.}$	$\lambda_{abs.}$ (nm)¥	$\lambda_{em.}$ (nm)¥	Φ_{Δ} (%)♦
2a	99%	236.1	236.2	490	540	n.d.
3a	99%	253.1	253.2	480	545	n.d.
4a	99%	323.0	323.1	510	610	n.d.
5a	93%	263.1	263.1	565	650	n.d.
6	97%	312.2	312.4	510	620	n.d.
7	99%	352.0	352.0	400	450	n.d.
8	99%	368.0	367.9	440	630	n.d.
9	96%	355.0	355.0	425	610	n.d.
11a	93%	426.9	426.8	500	650	n.d.
12	99%	332.0	332.0	470	590	13±1
13	99%	332.0	332.0	470	590	8±1
14	96%	435.0	435.1	510	605	4.0±0.2
15	99%	407.0	407.0	495	610	24±1
16	99%	607.7	607.5	644	688	<1
17	99%	697.8	697.3	320	496	21†

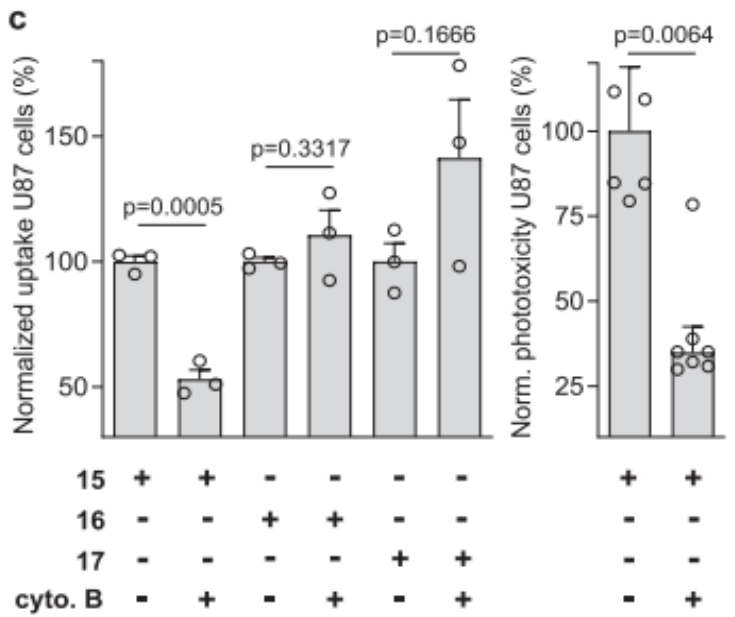
¥ Absorbance and emission wavelengths in EtOH (concentration of compounds: 100 μM).

♦ Singlet oxygen generation quantum yields were determined using DPBF in EtOH (Note: DPBF was found insoluble in water) using Rose Bengal as a reference.[2] Data presented as means±SEM (n = 3).

Compound 15 shows high potency and selectivity





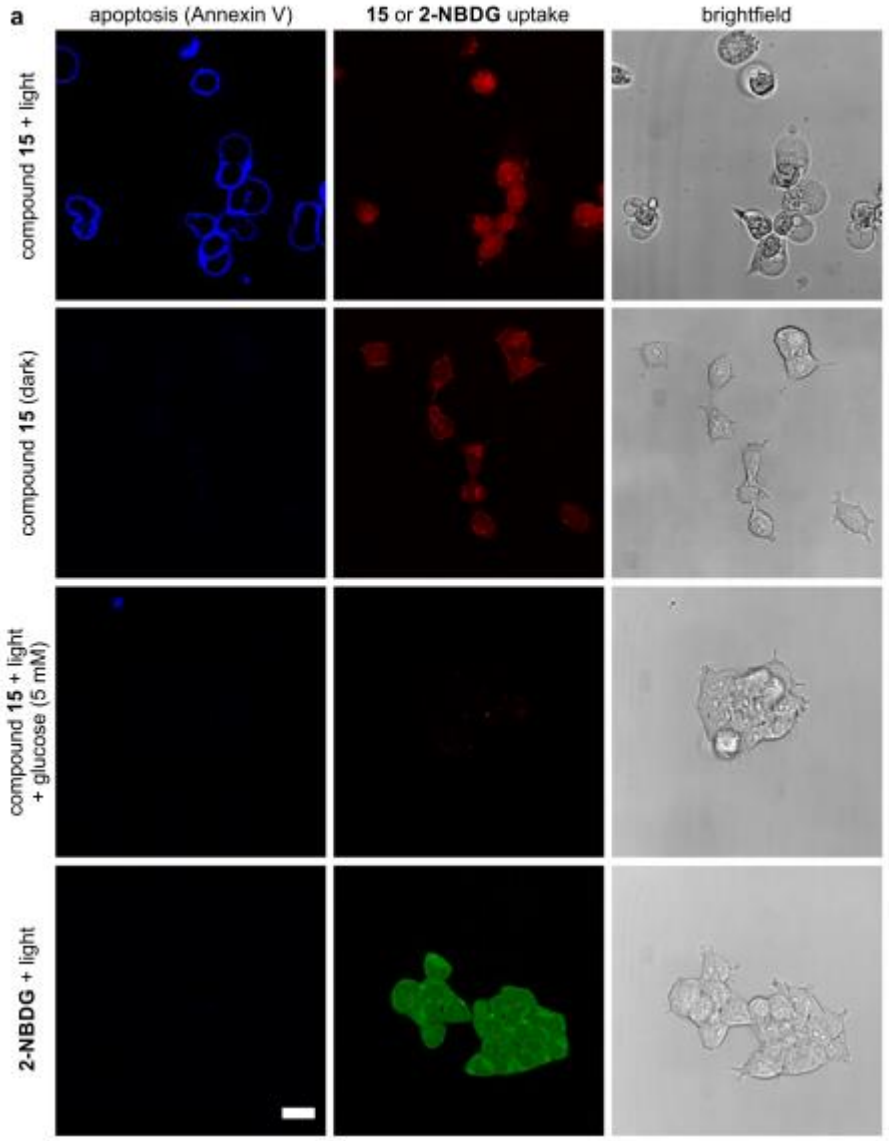


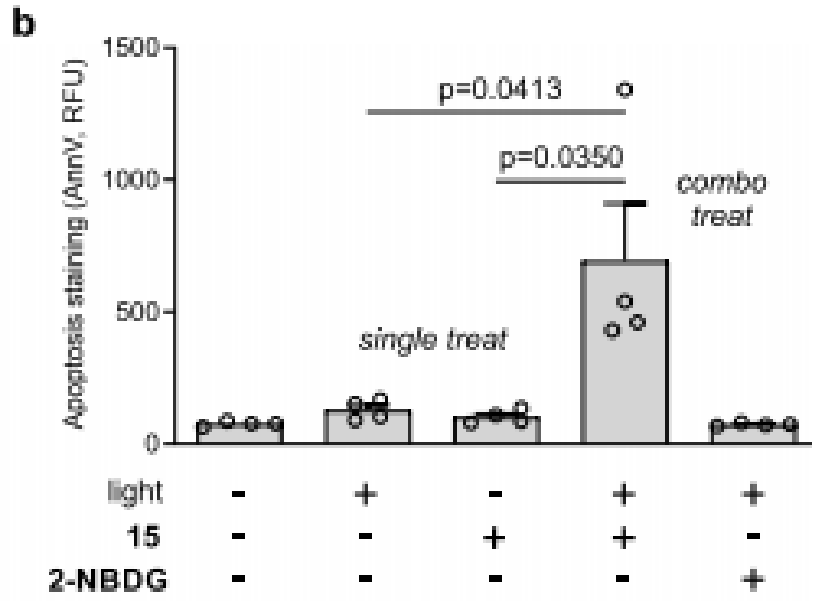
d

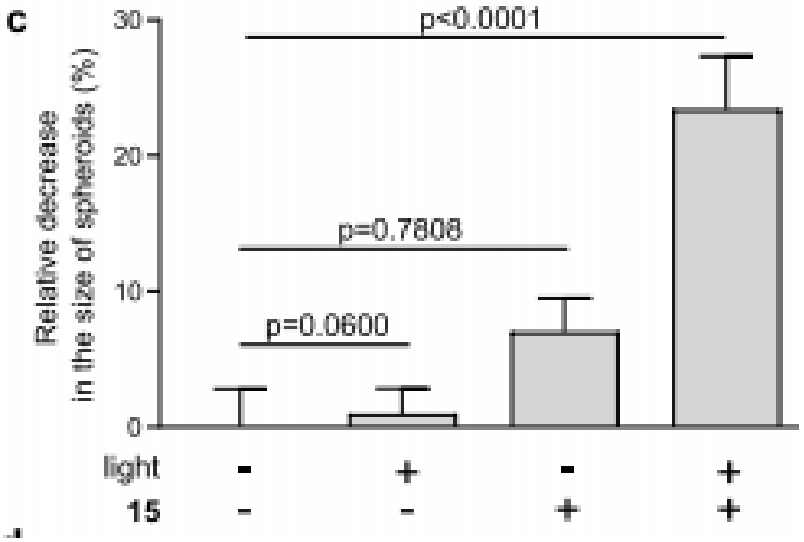
Compound	Exc. light (nm)	Φ_Δ
4F	520	< 1%
14	520	4%
15	520, 970*	24%
16	640	< 1%
17	white light	21%†
5-ALA¥	405, 640	54%
2-NBDG	520	< 1%

葡萄糖抑制剂

Compound 15 kills metabolically-active human glioblastoma cells in vitro







Compound 15 enables safe removal of microtumors in vivo