

Recent Updates of In Vivo Fluorescent Probe

Yiyong Yan

Supervisor: Prof. Jing Zhao

Highly Selective Off–On Fluorescent Probe for Imaging Thioredoxin Reductase in Living Cells

Liangwei Zhang, Dongzhu Duan, Yaping Liu, Chunpo Ge, Xuemei Cui, Jinyu Sun, and Jianguo Fang*

State Key Laboratory of Applied Organic Chemistry and College of Chemistry and Chemical Engineering, Lanzhou University, Lanzhou, Gansu 730000, China

In Vivo and *in Situ* Tracking Cancer Chemotherapy by Highly Photostable NIR Fluorescent Theranostic Prodrug

Xumeng Wu,[†] Xuanrong Sun,[‡] Zhiqian Guo,^{*,†} Jianbin Tang,^{*,‡} Youqing Shen,[‡] Tony D. James,[⊥] He Tian,[†] and Weihong Zhu^{*,†}

[†]Key Laboratory for Advanced Materials and Institute of Fine Chemicals, Shanghai Key Laboratory of Functional Materials Chemistry, East China University of Science and Technology, Shanghai 200237, China

[‡]Key Laboratory of Biomass Chemical Engineering of Ministry of Education, Center for Bionanoengineering, and Department of Chemical and Biological Engineering, Zhejiang University, Hangzhou, Zhejiang, 310027, China

[⊥]Department of Chemistry, University of Bath, Bath BA2 7AY, United Kingdom

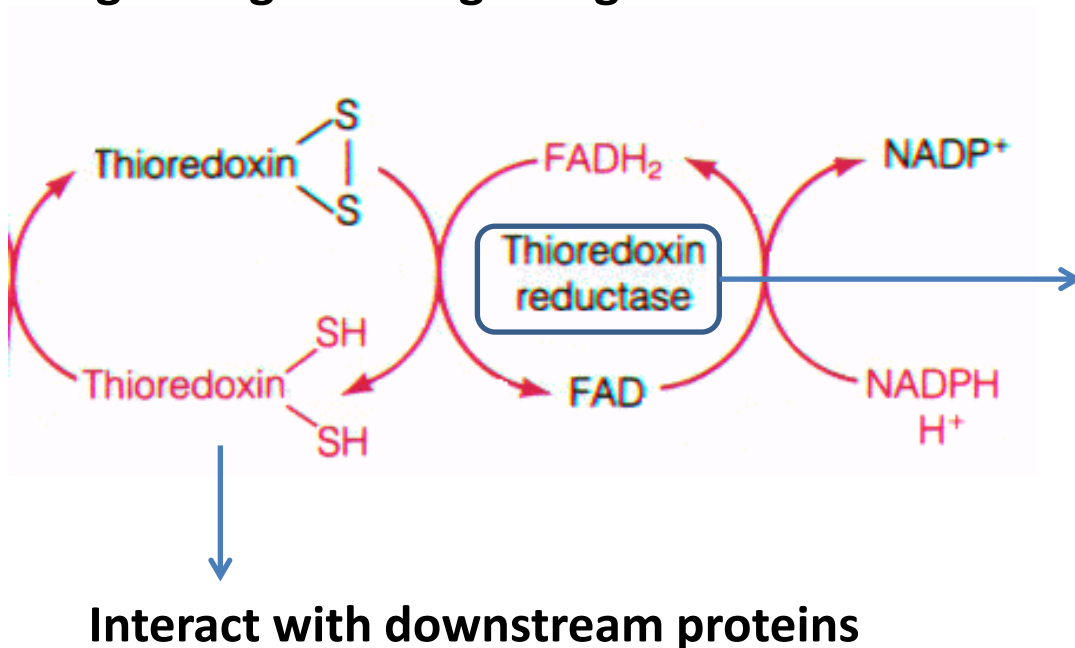
Back Ground

Thioredoxin System:

Highly conserved in all cells

Maintaining intracellular redox homeostasis

Regulating redox signaling events



TrxR

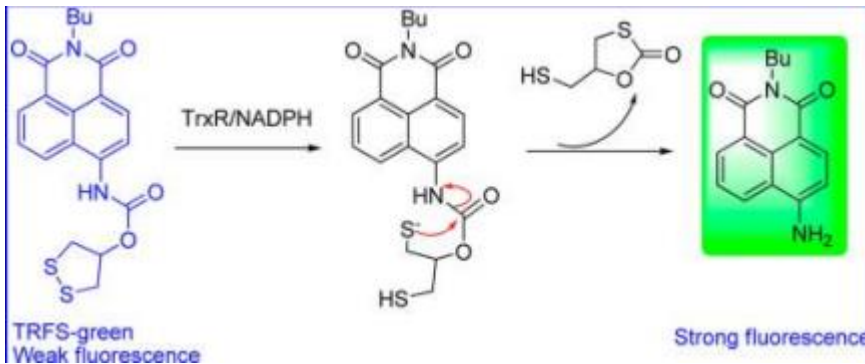
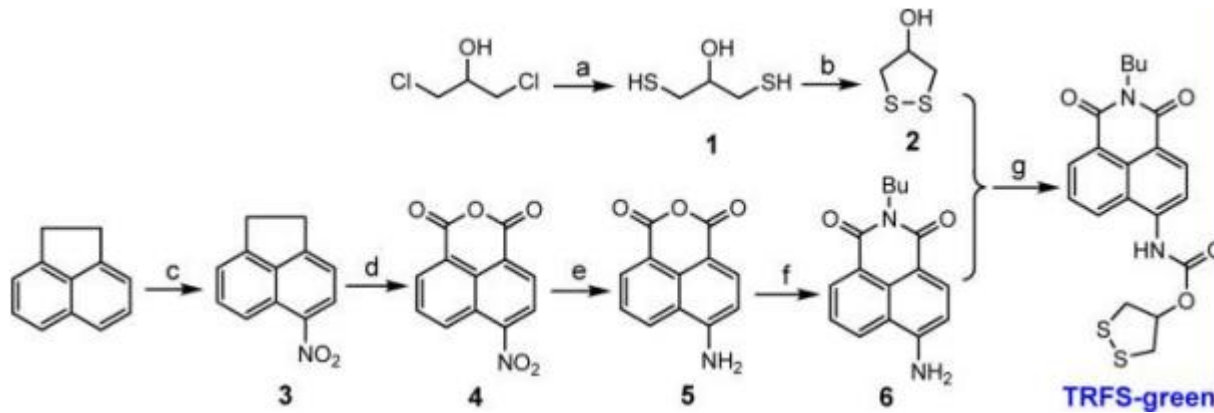
Highly expressed in cancer cells:

Drug target

Early diagnosis marker

No intracellular detection method

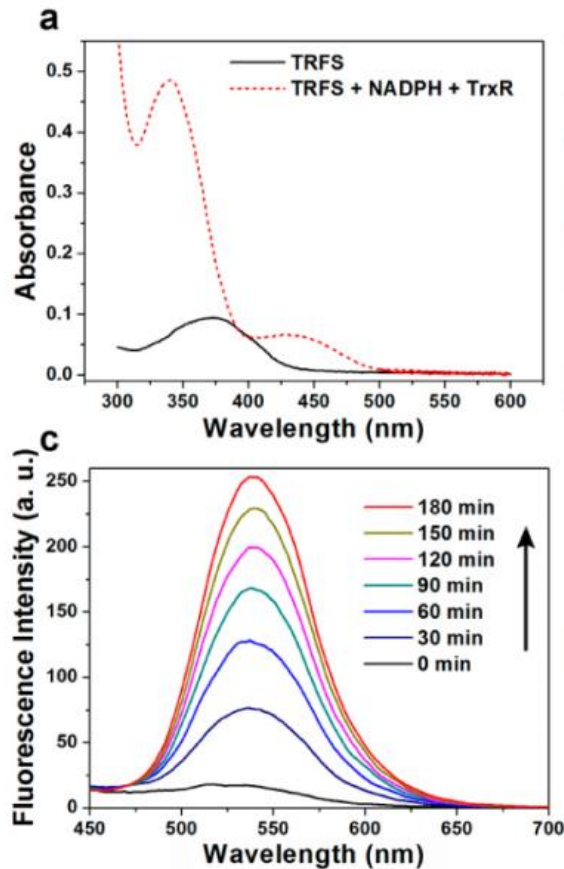
Rational Design



Linear disulfide : non selectivity
Cyclic disulfide: -320 ~ -290 mv
TrxR: -300 mv
GSH: -240 mv

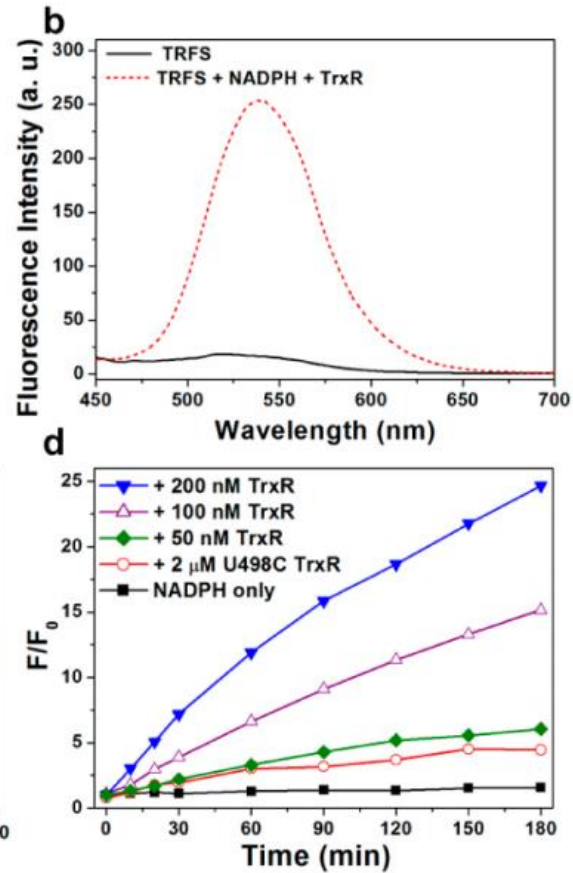
Fluorescence and Kinetics

Double signaling channel



Time dependent

Great enhancement



Concentration dependent
Great selectivity

Mechanism

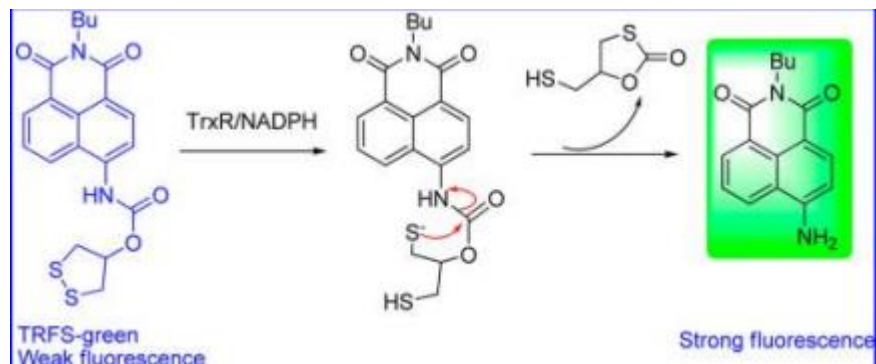
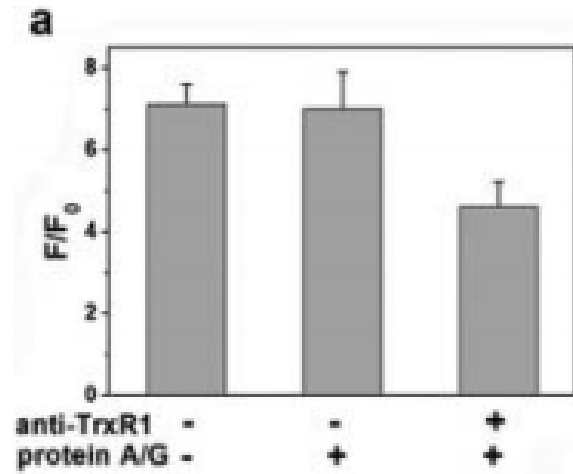
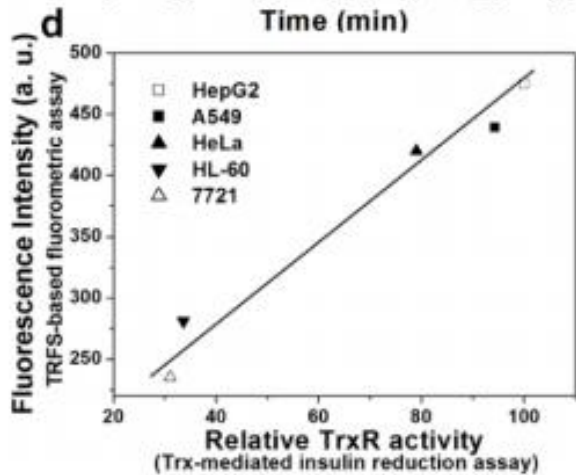
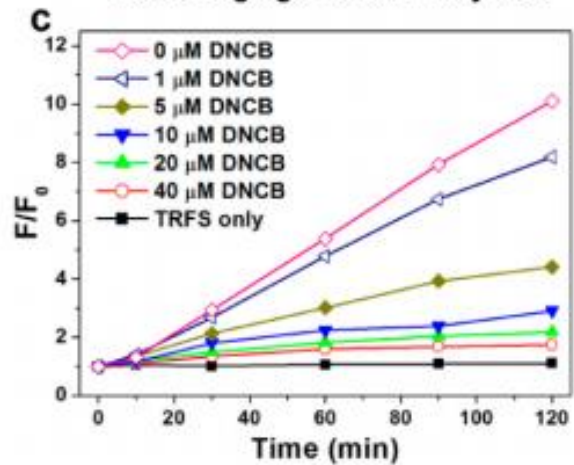
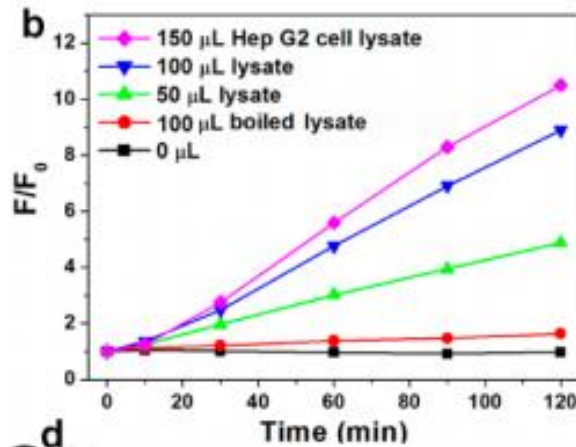
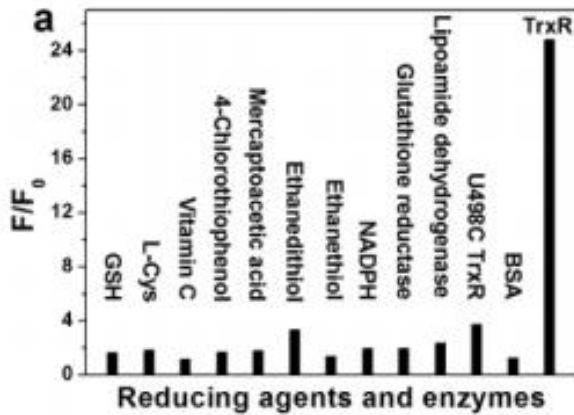


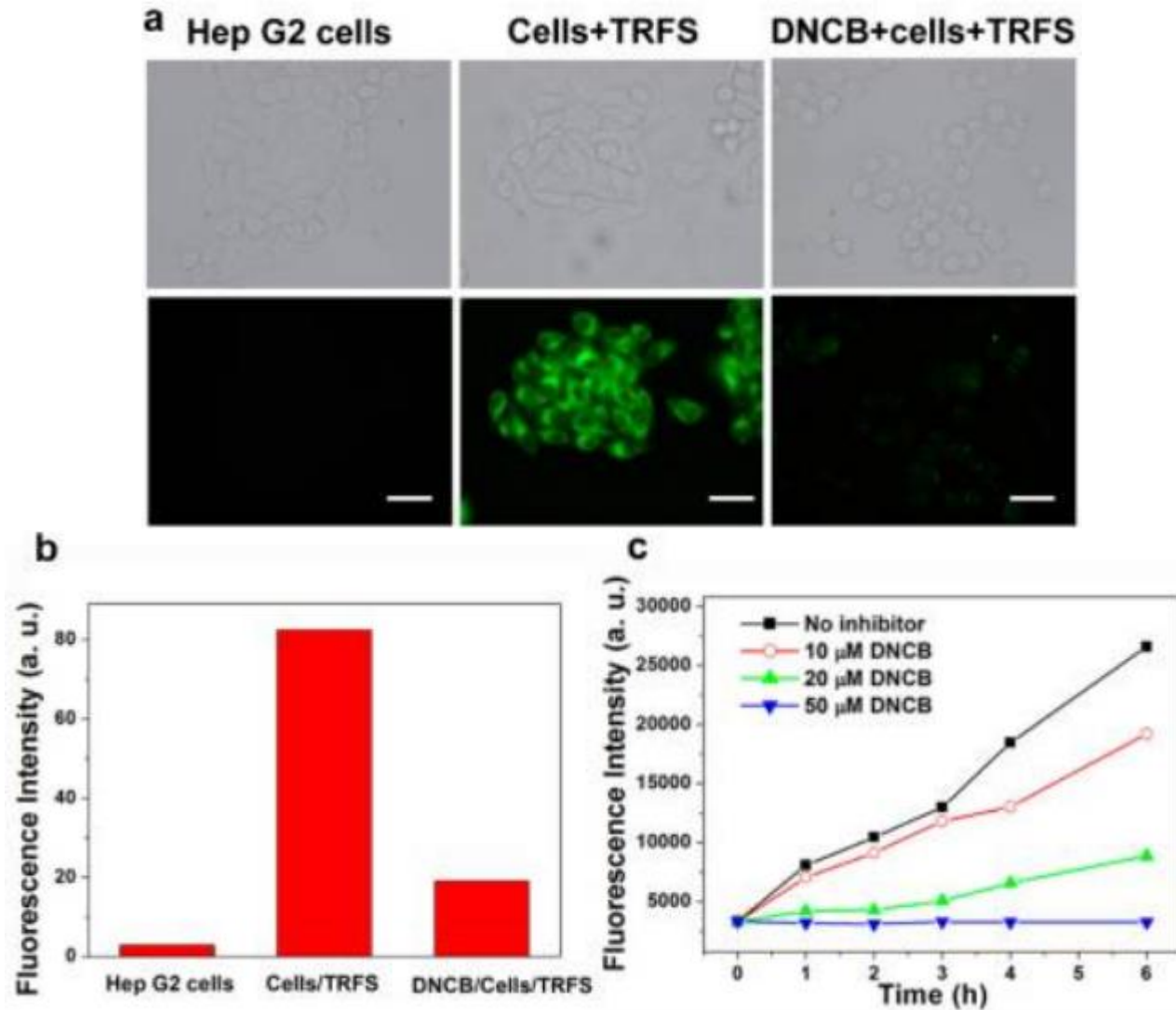
Table S1. HPLC analysis of the conversion of TRFS-green catalyzed by TrxR.

TRFS-green		Naphthalimide (6)	
Retention time: 15.92 min		Retention time: 2.82 min	
Before reaction	After 3h	Before reaction	After 3h
10 μM	6.1 μM	0 μM	4.0 μM

Selectivity and Kinetic Profile



In vivo Imaging and Detection



Summary

1. **First intracellular TrxR probe**
2. **Good selectivity for TrxR over small molecule thiol**
3. **Great signal response**
4. **Solid evidence: multiple references (inhibitor/antibody/mutated enzyme/deactivated enzyme), mechanism study**
5. **Broad application: intracellular/cell lysate/multiple cancer cells**
6. **Rational design**
7. **Disadvantage: time consuming, not good for quantification**

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Back Ground

Chemotherapy:

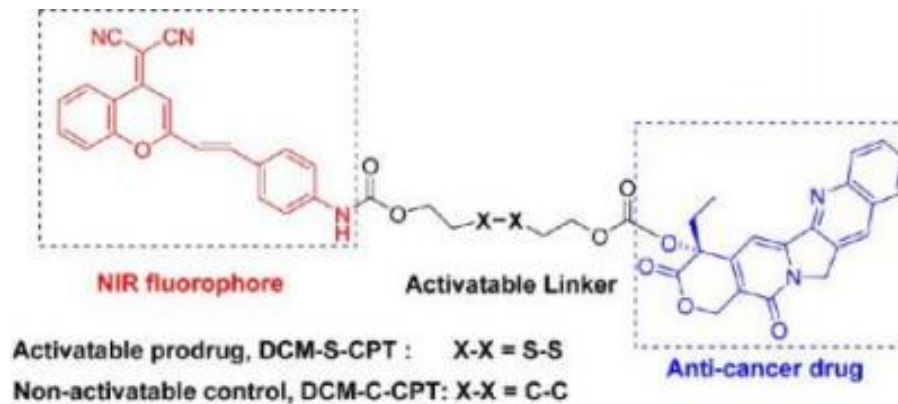
1. Selectivity

High GSH in cancer cells

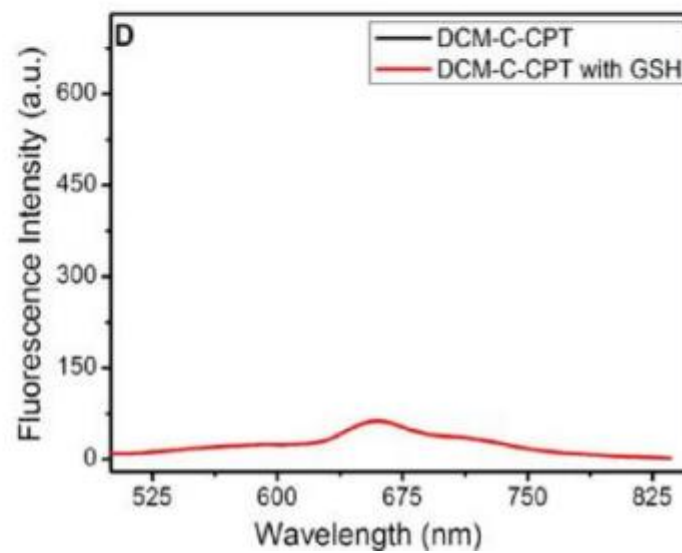
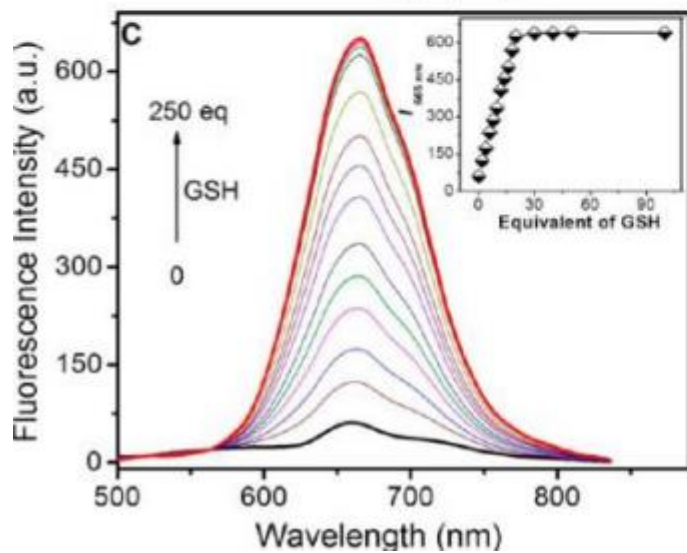
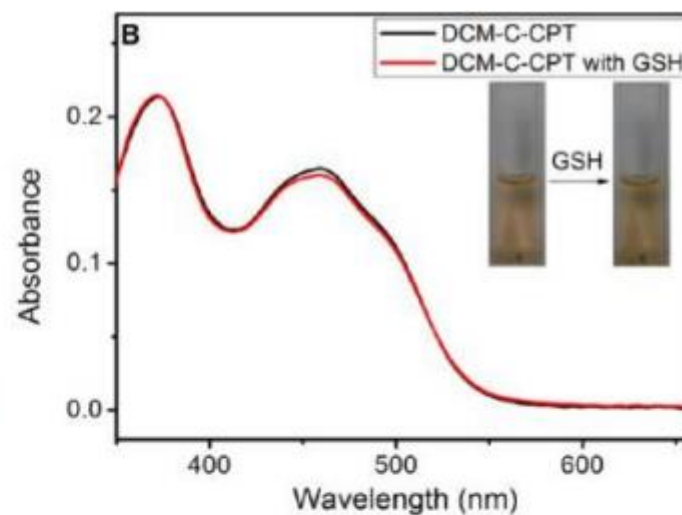
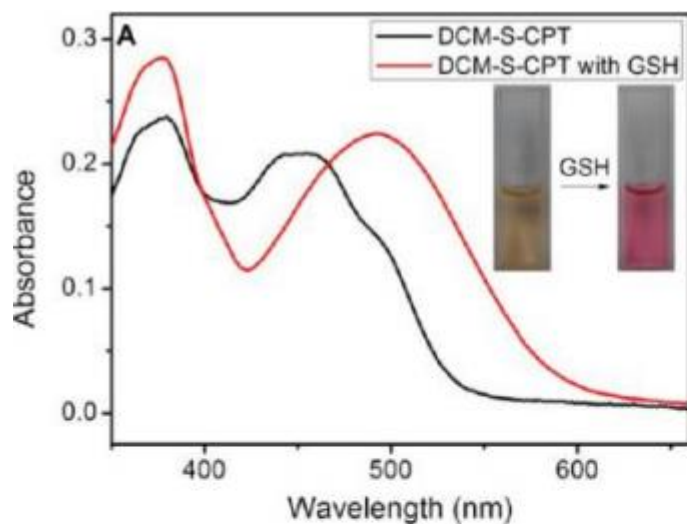
Thiol responsive drug delivery system

2. Where is the drug?

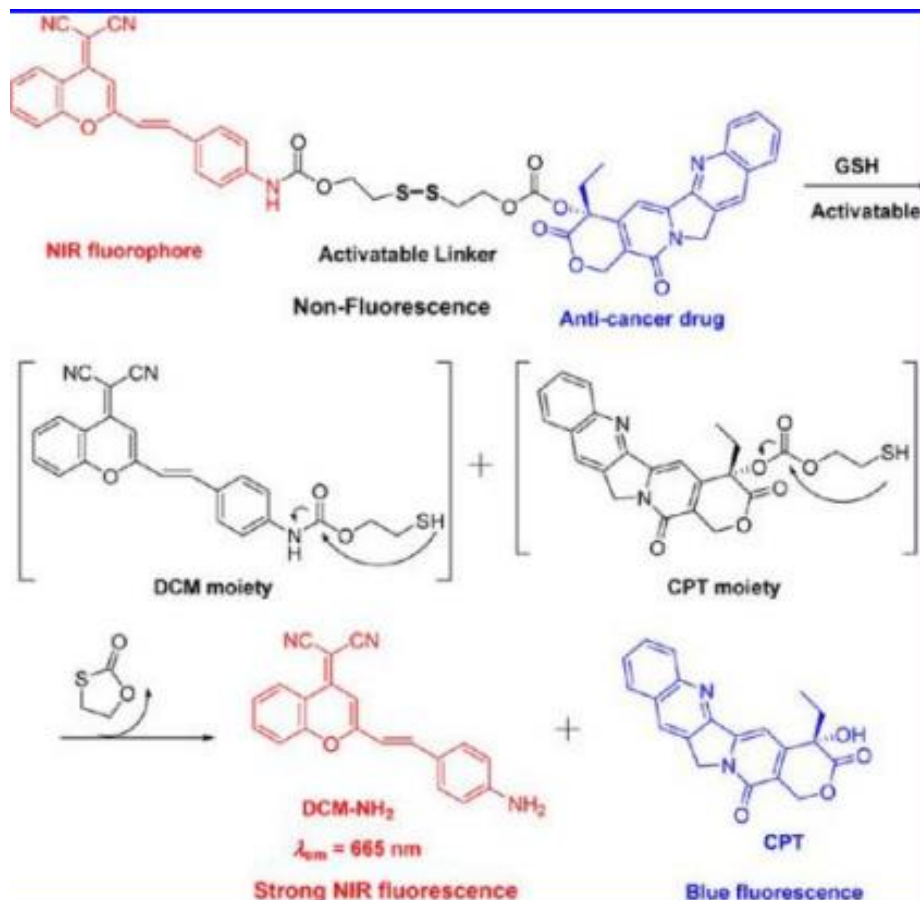
In vivo tracking probe



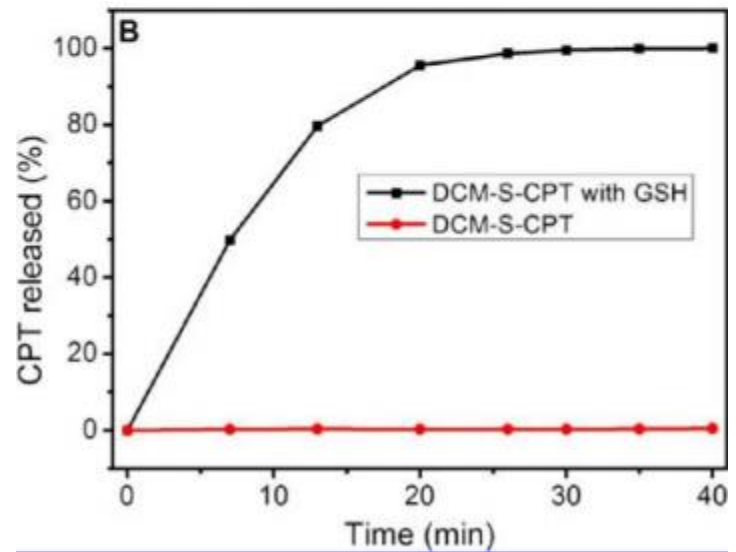
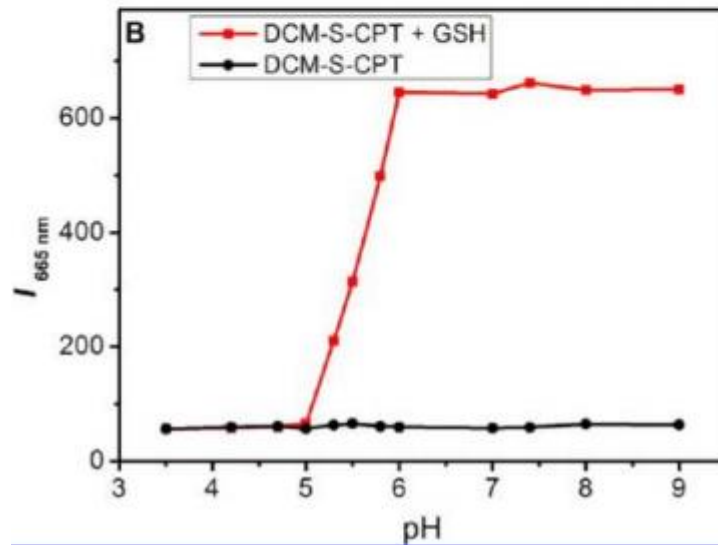
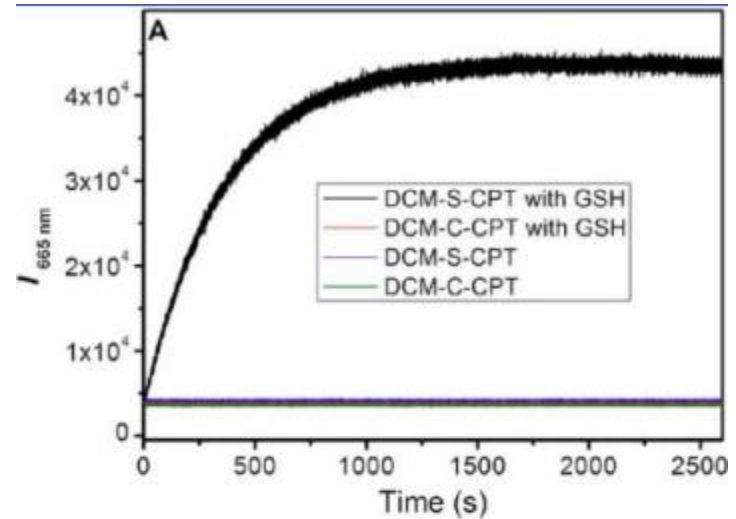
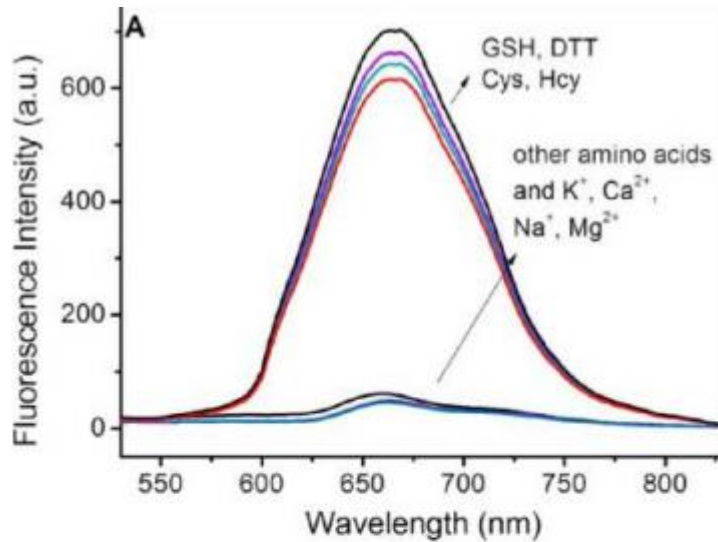
In vitro Response



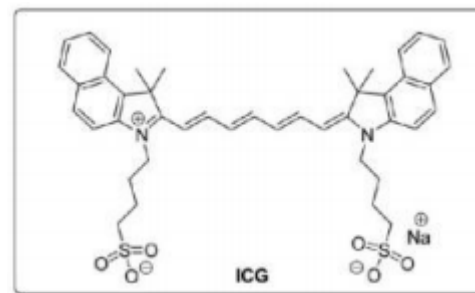
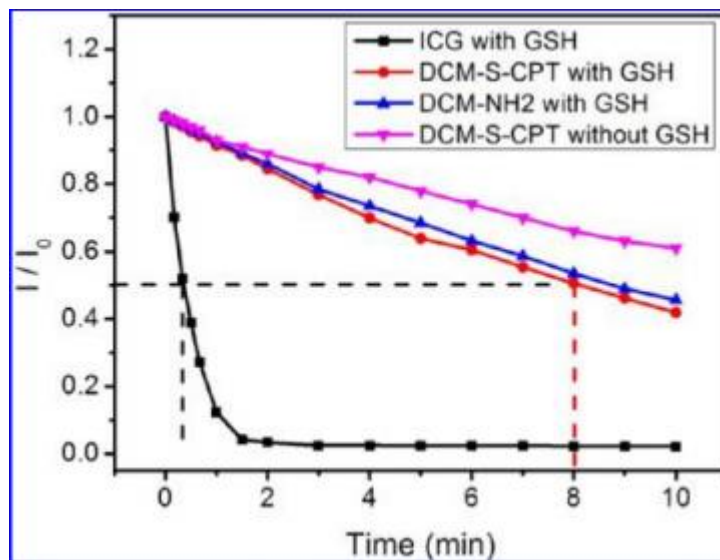
Mechanism



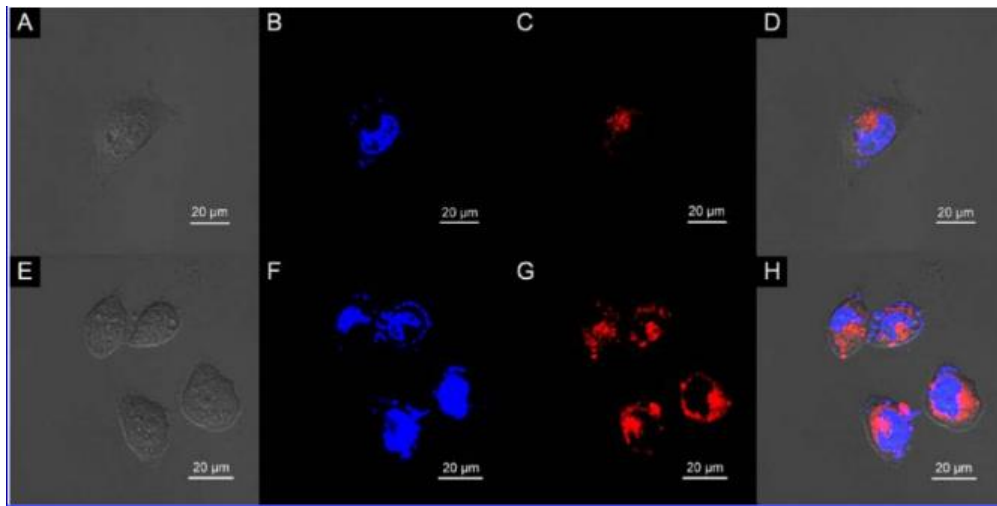
Selectivity and Kinetic Profile



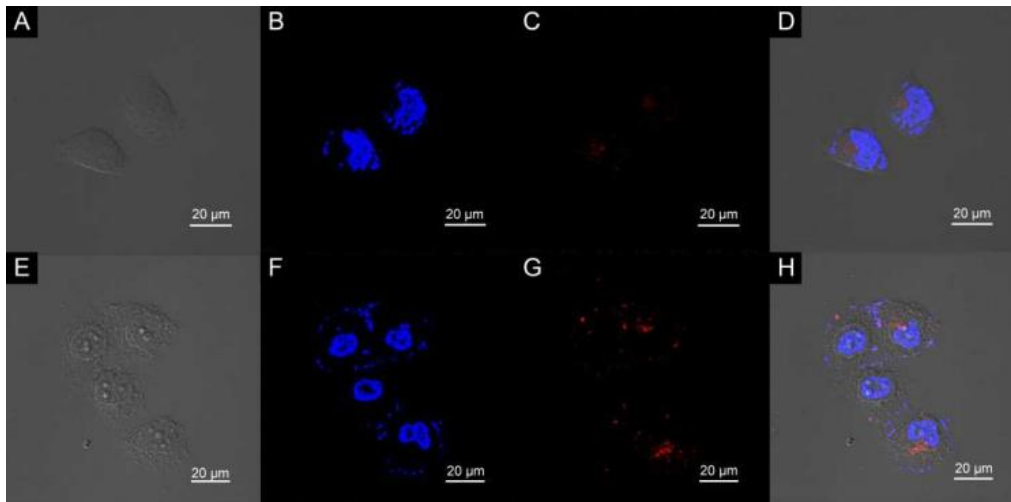
Photostability



In vivo Tracking

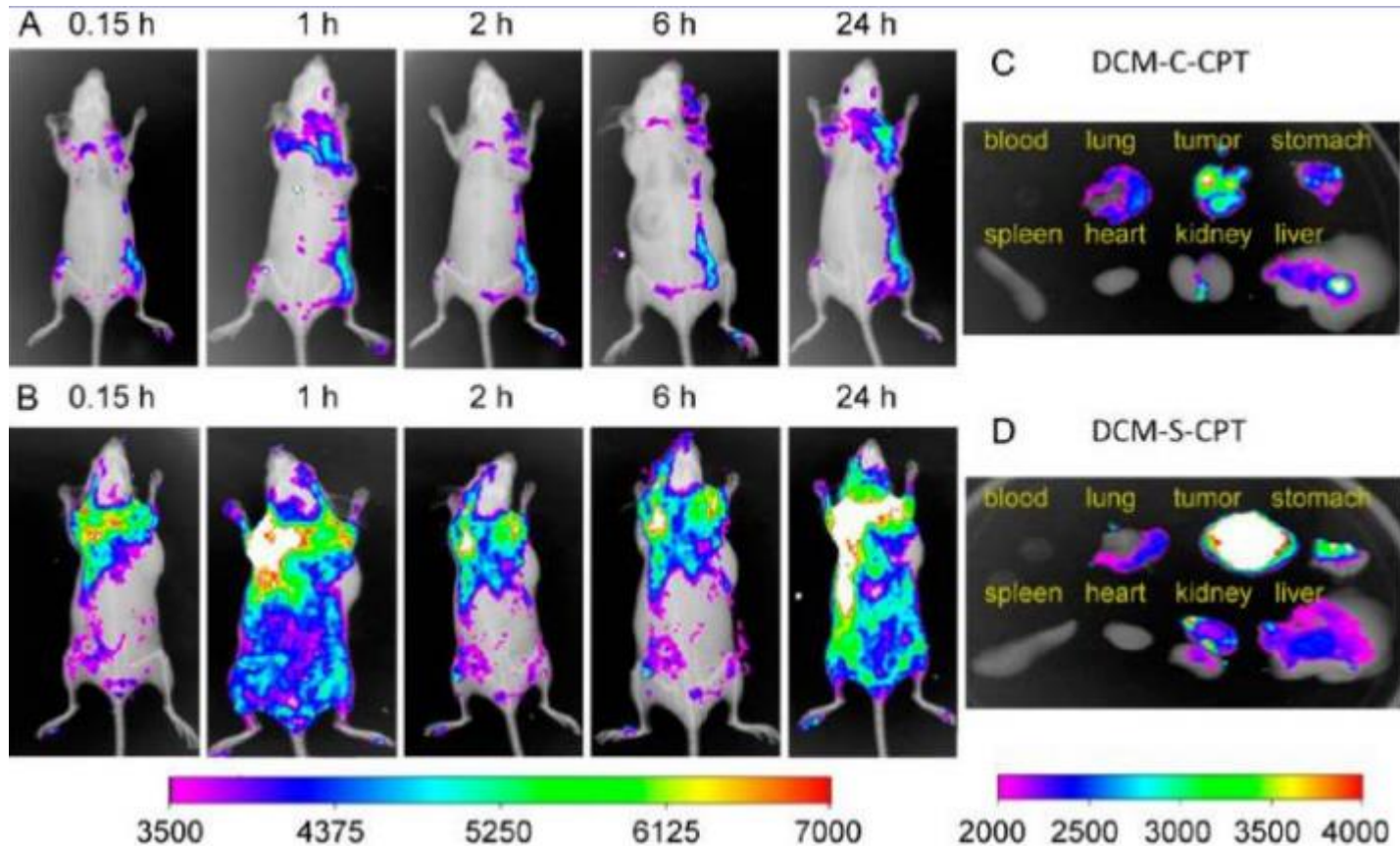


S-S



C-C

In vivo Tracking



Summary

- 1. Tumor targeting specificity in mice**
- 2. Near infrared fluorescence**
- 3. Photostability**
- 4. Fast responsive**
- 5. Disadvantage: no localization of the anticancer drug in vivo**

Thanks