

Literature Report 4

Fang Xiangning

2021.05.20

Norcyanine-Carbamates Are Versatile Near-Infrared Fluorogenic Probes

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Martin J. Schnermann

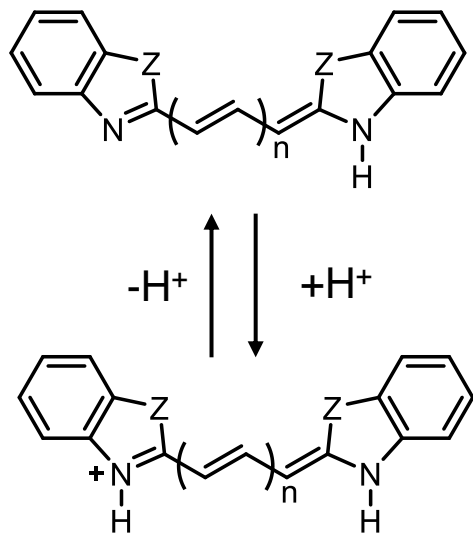
**Chemical Biology Laboratory
Center for Cancer Research, National Cancer Institute
Senior Investigator
Head, Organic Synthesis Section**

Research interests:

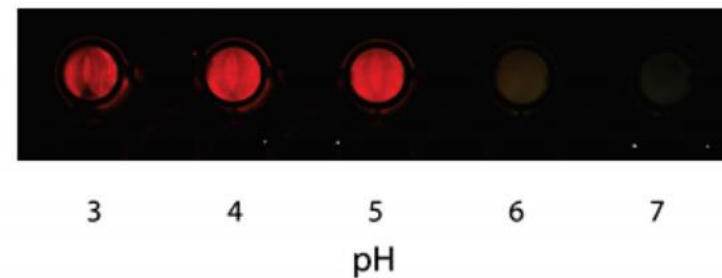
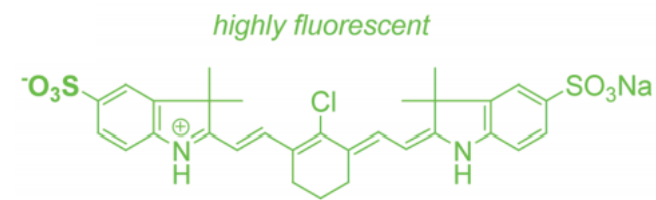
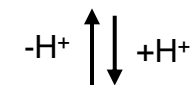
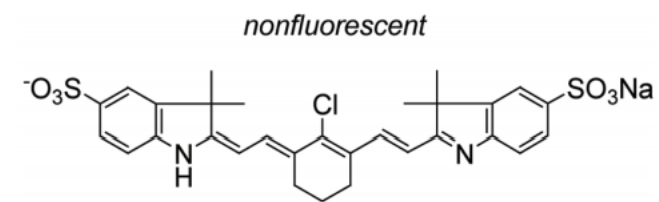
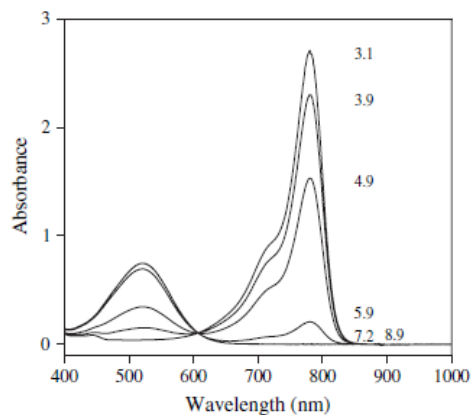
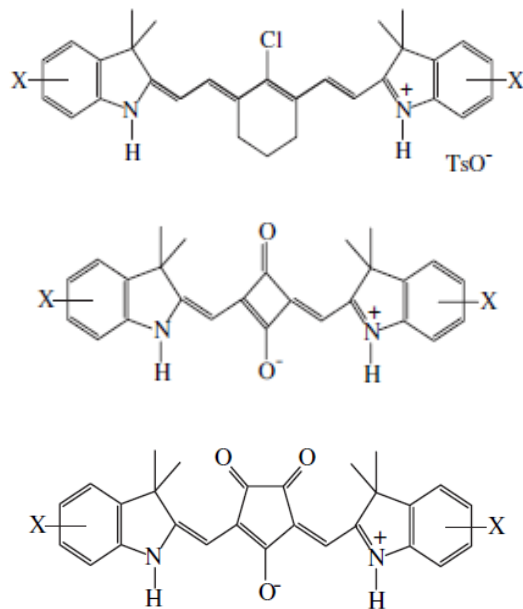
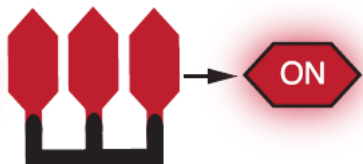
- **Fluorescent Molecules for In Vivo Imaging**
- **Novel Approaches to Drug Delivery**

Background: Norcyanine

Serguei Miltsov, Julian Alonso



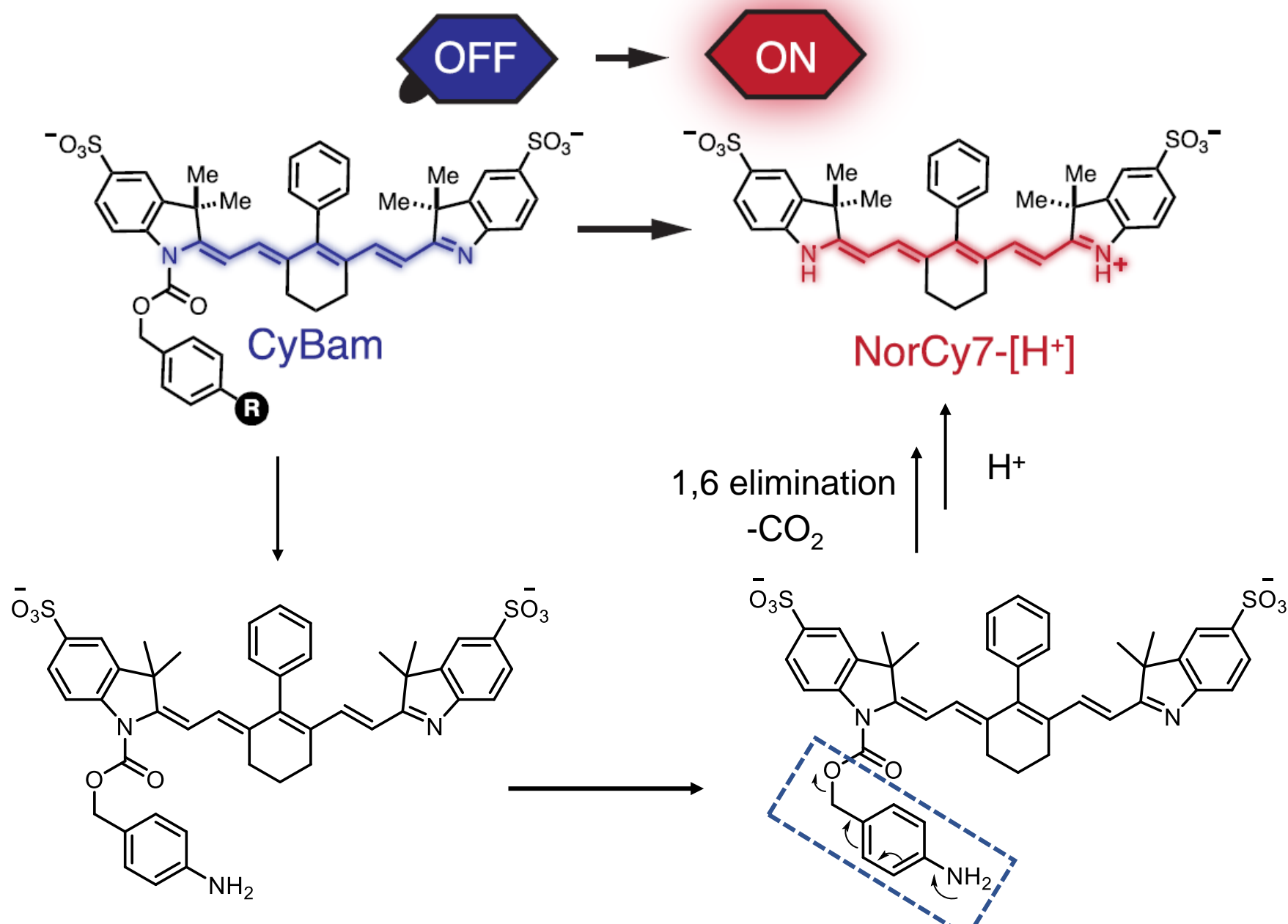
Self-Quenched



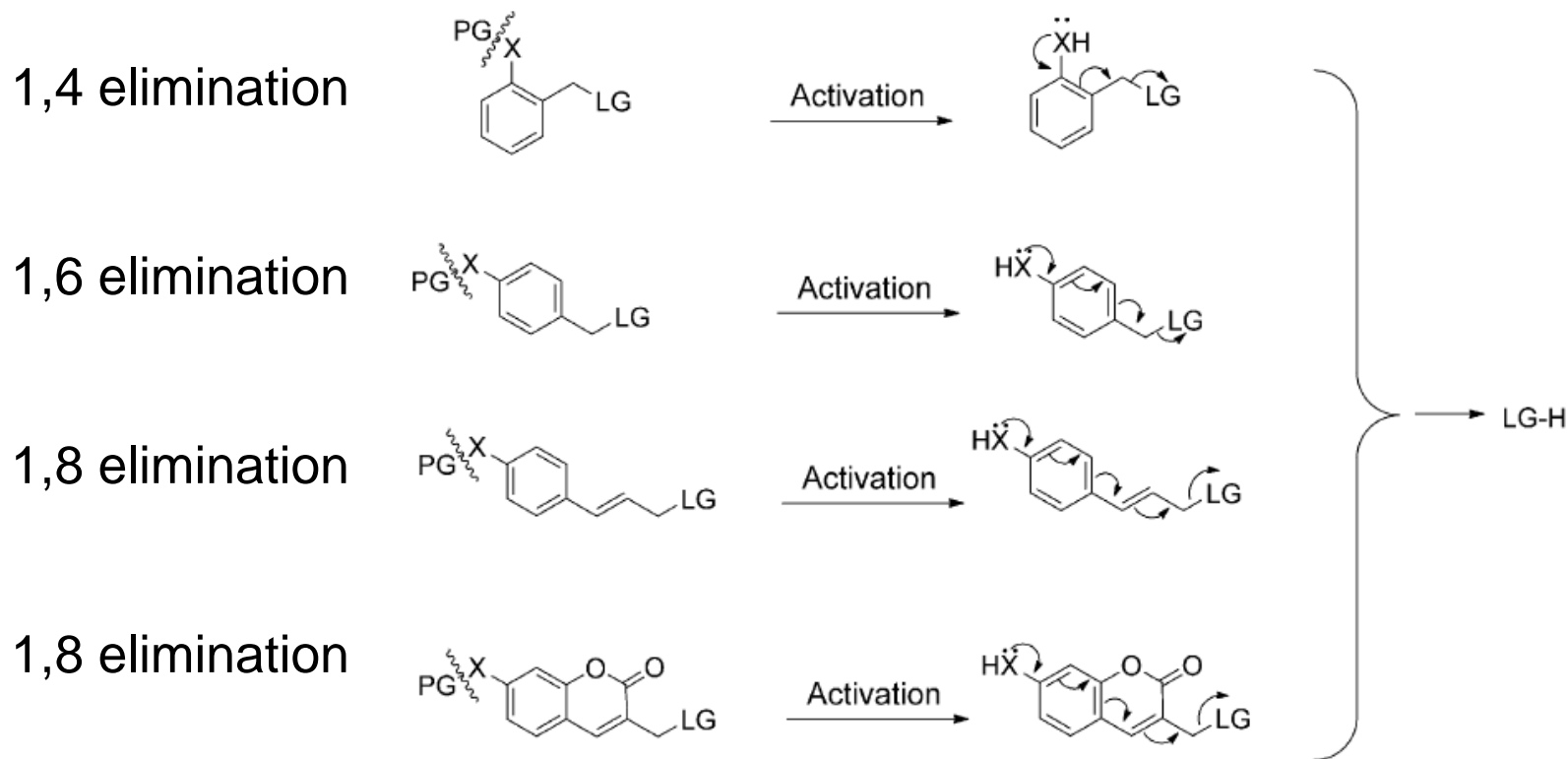
Tetrahedron Letters, 1998, 9253
Tetrahedron Letters, 1999, 4067
Dyes and Pigments, 2007, 383

Bioconjugate Chem., 2011, 777

Probe Design: CyBams (Cyanine-Carbamates)



Probe Design: Self-Immolation



PG=protecting group

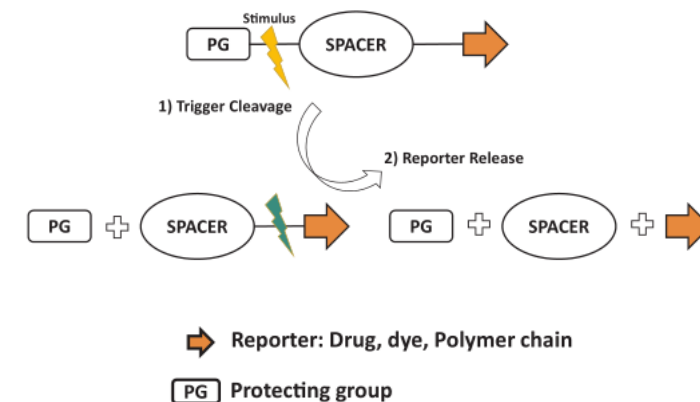
X=O, NH, S

LG=leaving group belonging to the desired compound

Angew. Chem. Int. Ed., 2015, 7492

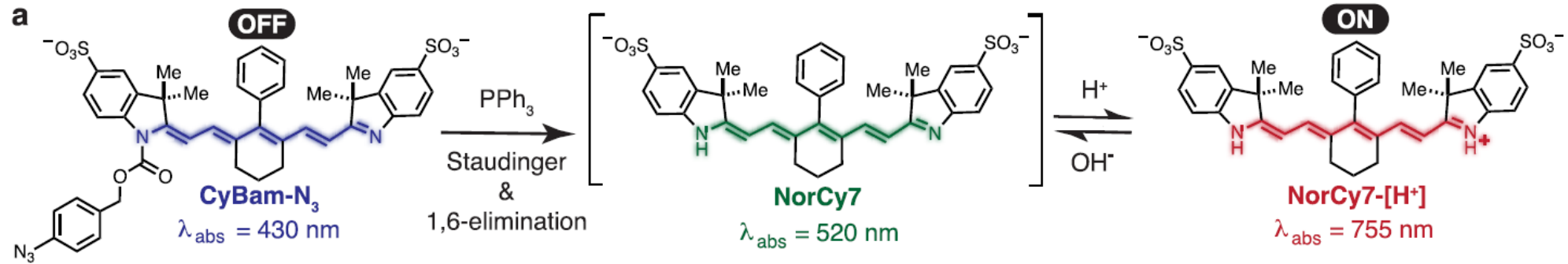
Activated switches

- Connector linkage of prodrug
- Fluorescent probes
- Material science

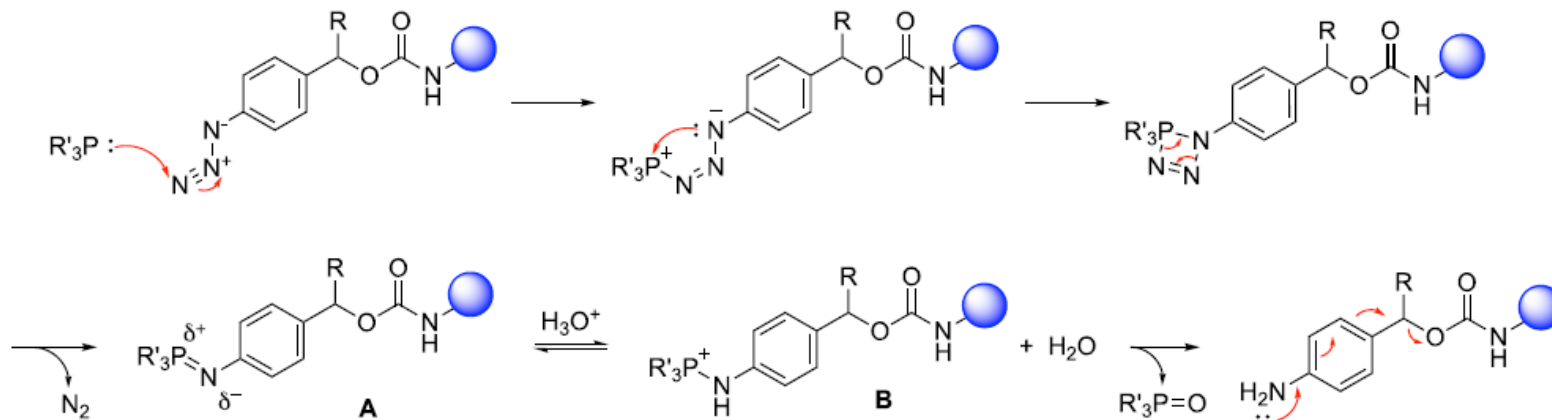


Chemical Engineering Journal, 2018, 340, 24

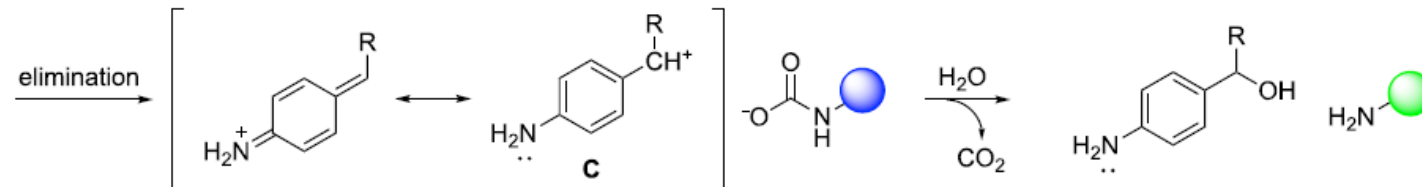
Probe Design: CyBam



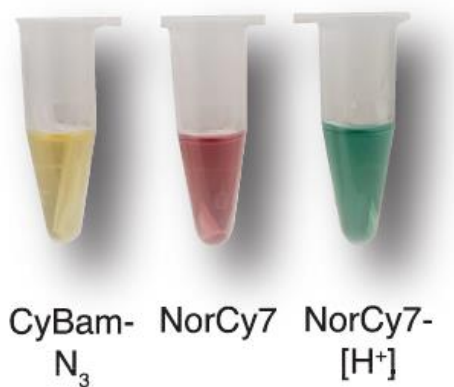
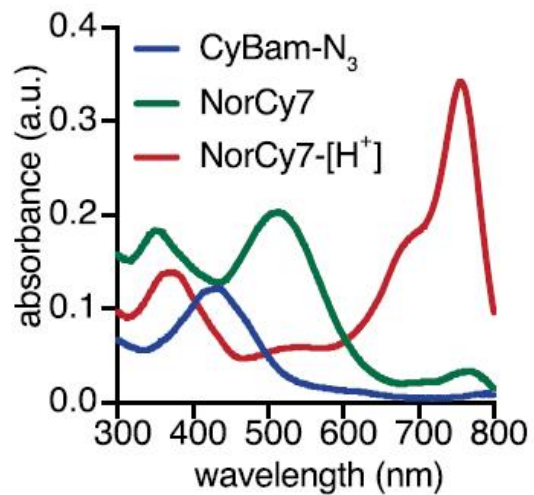
Staudinger reaction



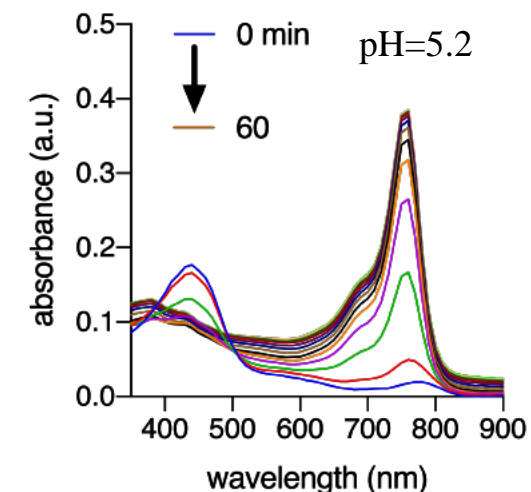
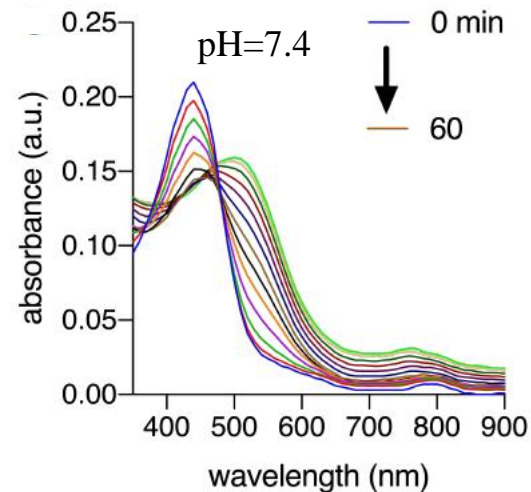
1,6-elimination



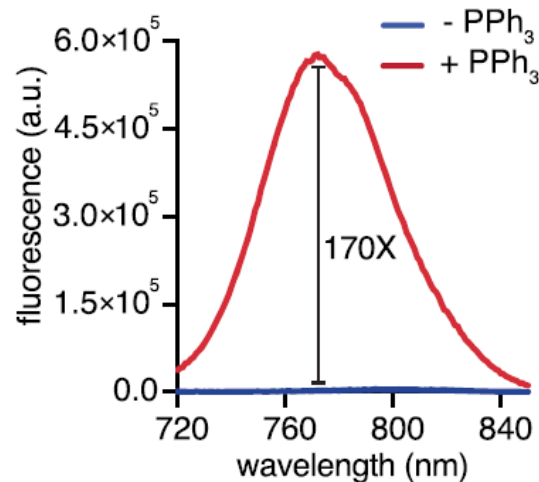
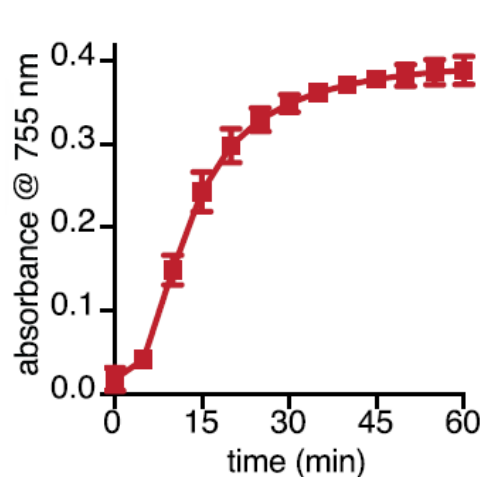
Characterization



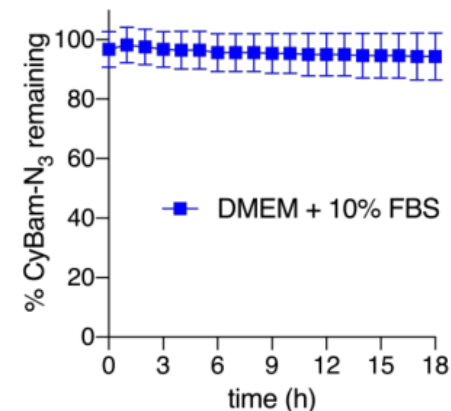
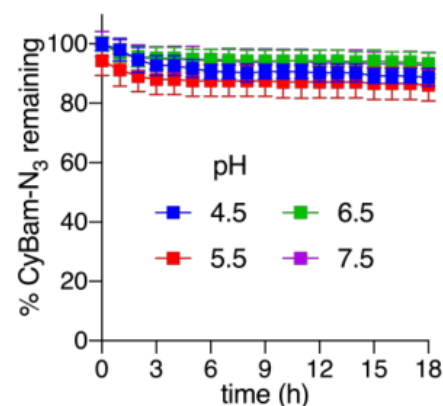
$\lambda_{\text{abs}}=430\text{nm}, 520\text{nm}, 755\text{nm}$



Staudinger release of **CyBam-N₃** (10 μM) and PPh_3 (100 μM , 10 eq) in basic (pH=7.4) and acidic (pH=5.2) conditions (MeOH:PBS; 1:1) to give **NorCy7** and **NorCy7-[H⁺]** respectively.

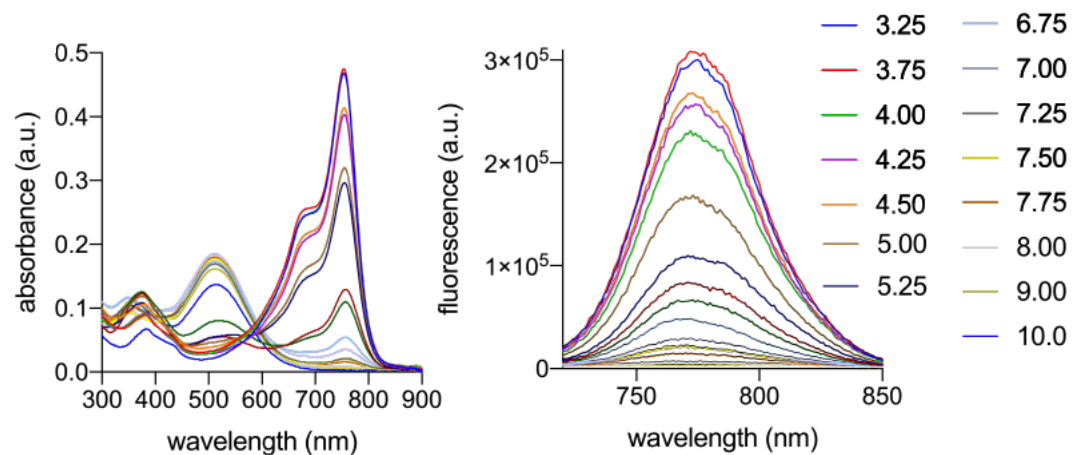


Absorbance and fluorescence spectra with 710 excitation of **CyBam-N₃** (10 μM , 1 eq) and PPh_3 (100 μM , 10 eq) in PBS:MeOH (1:1), pH=5.2.

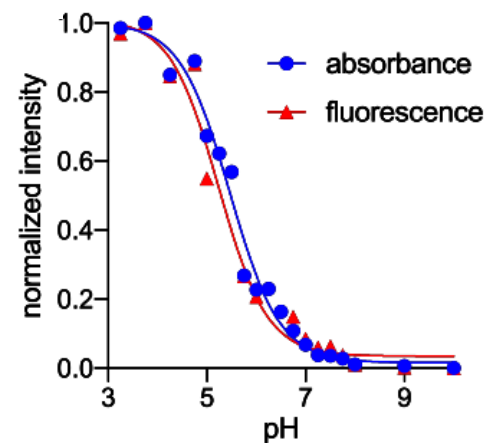


Stability of **CyBam-N₃** (20 μM) in different pH's (pH 4.5, 5.5, 6.5, and 7.5) and commonly used cell culture conditions (DMEM + 10% FBS).

Characterization



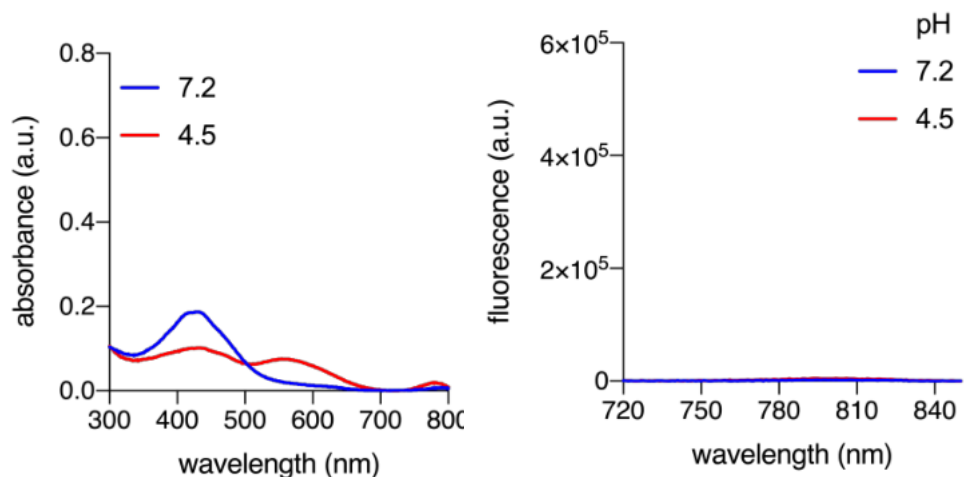
Absorbance and fluorescence spectra with 710 excitation of **NorCy7** (10 μM) at complete range of acidic and basic pH.



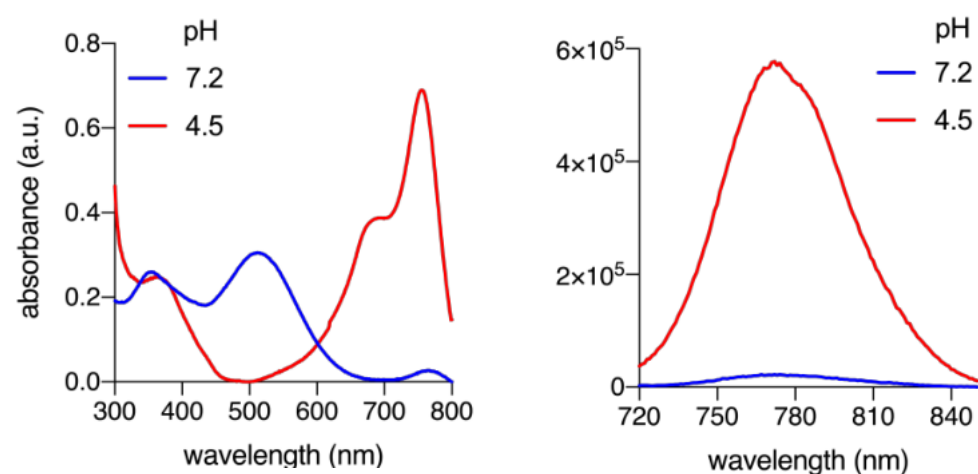
Absorbance: $pK_a = 5.4$

Fluorescence: $pK_a = 5.2$

pK_a of **NorCy7** (10 μM) was measured using increase in absorbance at 755 nm and fluorescence intensity at 775 nm over different pH.

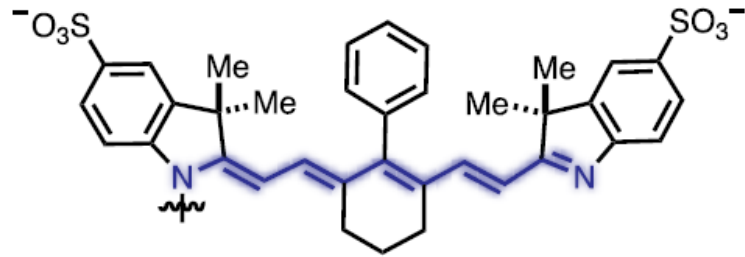


Absorbance and fluorescence spectra with 710 excitation of **CyBam-N₃** (10 μM) at pH 7.2 (PBS) and pH 4.5 (acetate buffer).



Absorbance and fluorescence spectra with 710 excitation of **NorCy7** (10 μM) at pH 7.2 (PBS) and pH 4.5 (acetate buffer).

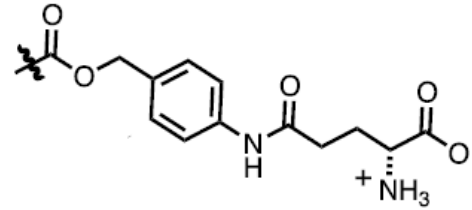
CyBams for vivo imaging



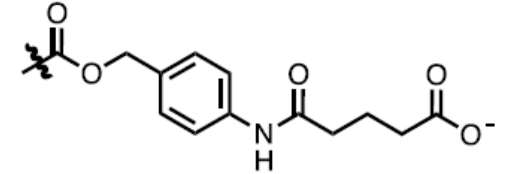
CyBam- γ -Glu

检测GGT

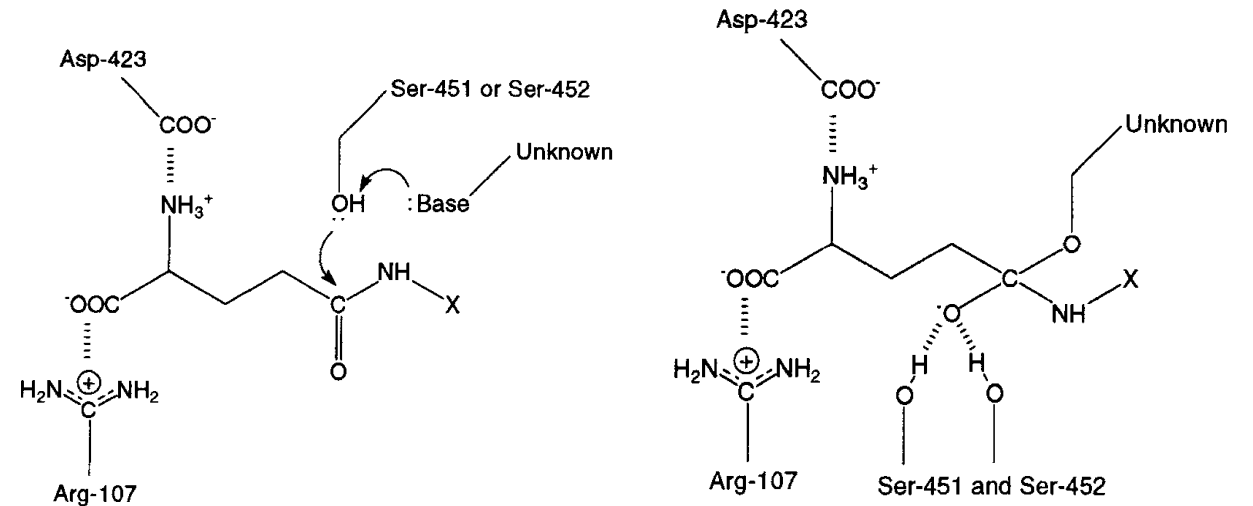
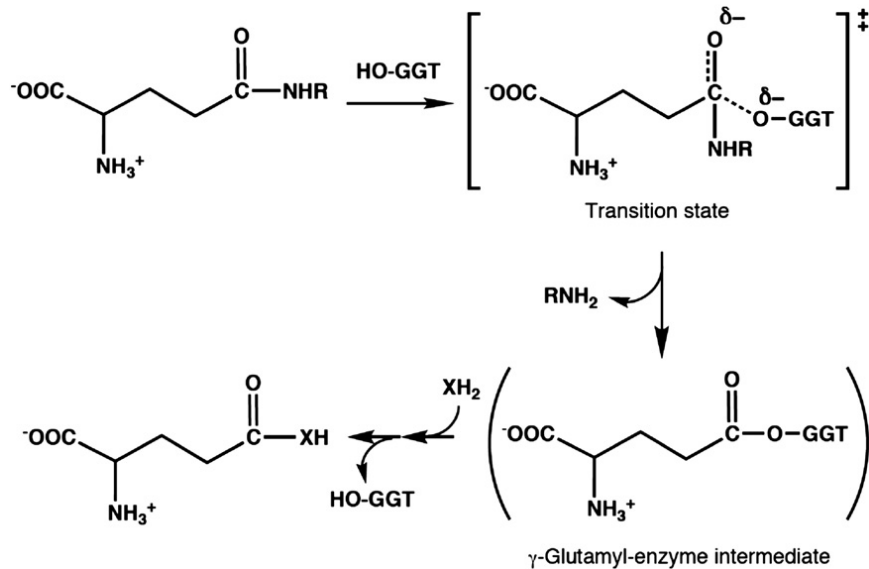
GGT: 多种肿瘤标志物, 过表达与癌细胞转移相关



CyBam-N.C.



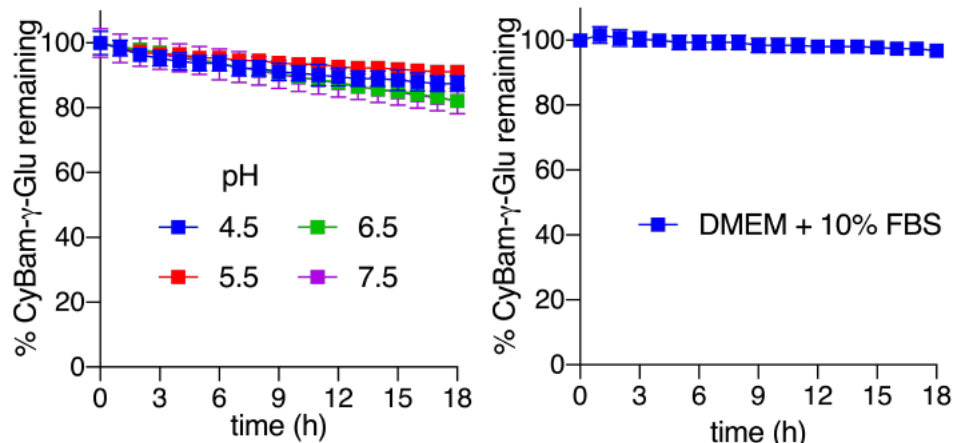
Catalytic mechanism of γ -Glutamyl transpeptidase (GGT)



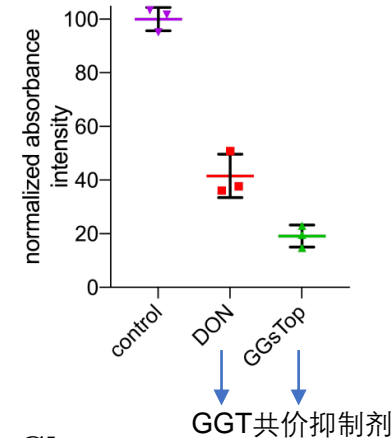
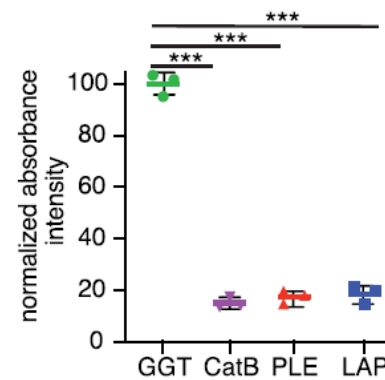
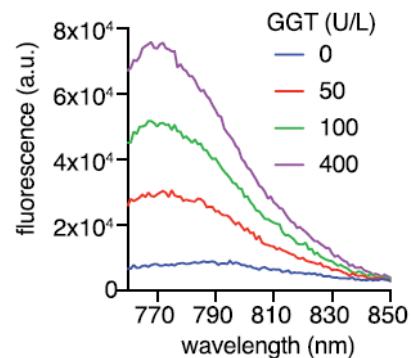
Two possible roles of Ser-451 and Ser-452 in human γ -glutamyl transpeptidase.

Adv Enzymol Relat Areas Mol Biol., 1998, 239

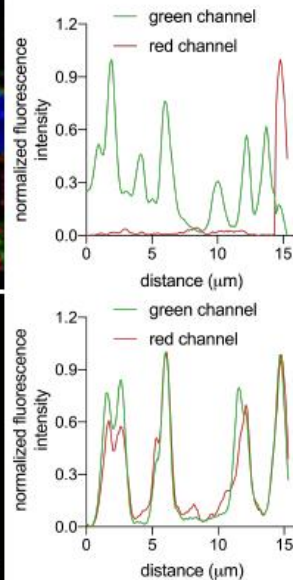
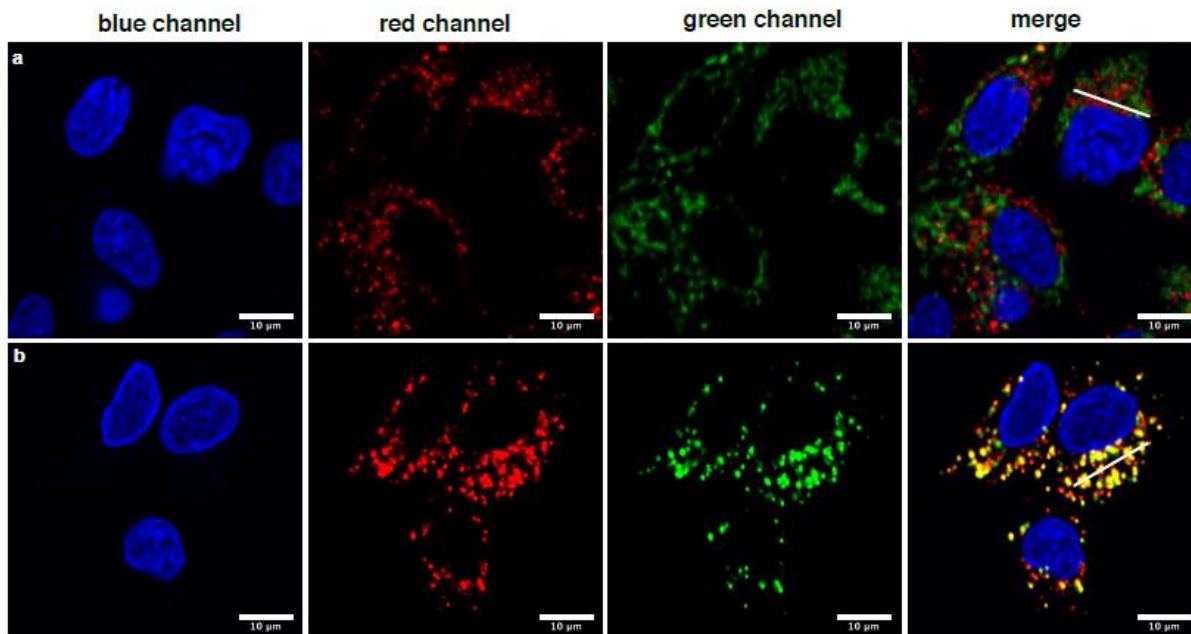
CyBams for vivo imaging



Stability of **CyBam-γ-Glu** (20 μM) in different pH's (pH=4.5, 5.5, 6.5, 7.5) and commonly used cell culture conditions (DMEM + 10% FBS).



Specificity and Selectivity of **CyBam-γ-Glu**



Red channel: **CyBam-γ-Glu**

a. Green channel: mitochondria (Mitotracker Green)

b. Green channel: lysosome (Lysotracker Green).

CyBams for vivo imaging

