

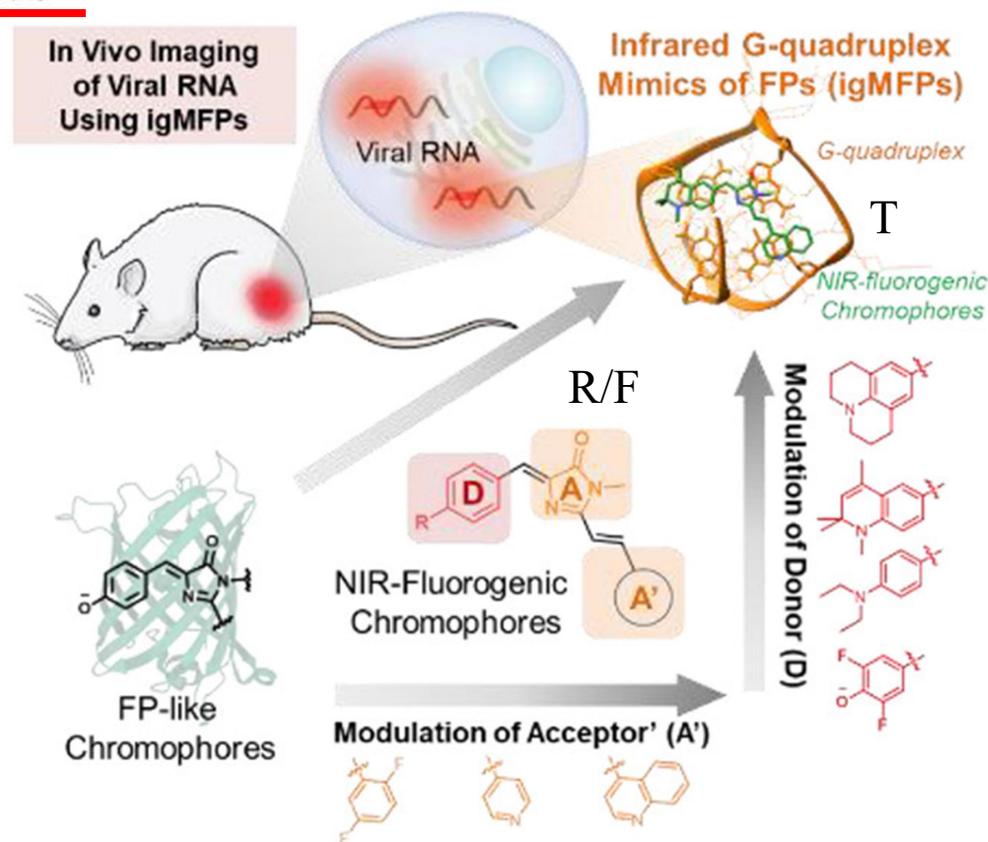
Literature Report

Reporter: Zhou Xuelian

Date: 2021-11-18

Development of Near-Infrared Nucleic Acid Mimics of Fluorescent Proteins for In Vivo Imaging of Viral RNA with Turn-On Fluorescence

Jiaheng Zhang,[⊥] Huiyi Li,[⊥] Bin Lin, Xingyu Luo, Peng Yin, Ting Yi, Binbin Xue, Xiao-Lian Zhang, Haizhen Zhu, and Zhou Nie*



T: G4

R/F: NIR-chromophores

Recognition: strong π - π stacking

Transmission: restrain TICT

Response: NIR FL emission

Corresponding author



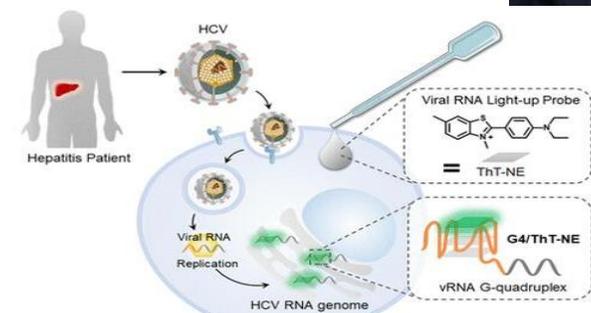
聂舟

教育及工作经历

- 1998-2002 南开大学生命科学学院 理学学士
- 2002-2007 中国科学院化学研究所 理学博士
- 2007-2008 湖南大学化学化工学院 讲师
- 2008-2010 湖南大学化学化工学院 副教授
- 2011-至今 湖南大学化学化工学院 教授 博士生导师
- 2011-2012 Purdue University(普渡大学) 博士后
- 2015-2019 湖南大学化学化工学院 副院长
- 2019-至今 湖南大学研究生院副院长兼学位办主任

研究方向

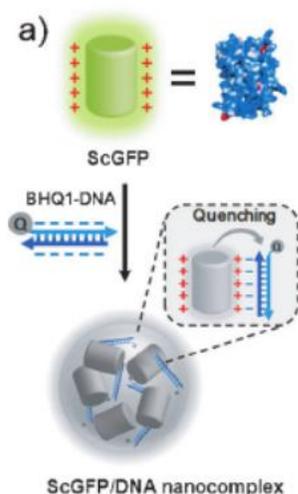
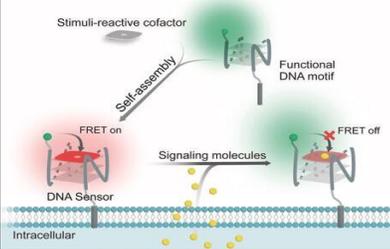
- 基于功能蛋白质和核酸的生物传感新方法；
- 化学手段调控细胞行为和命运



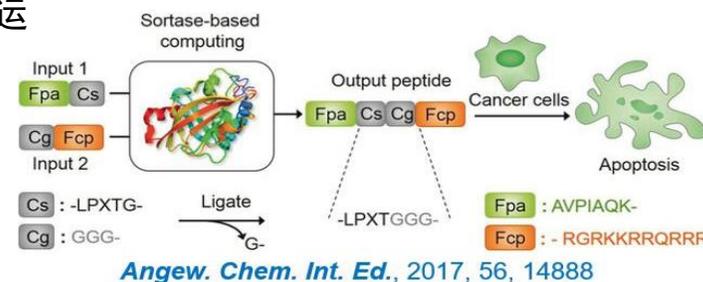
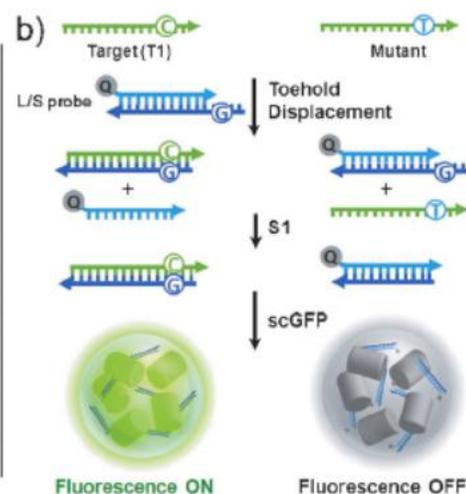
Small Molecule-based Live Cell Imaging of Viral RNA
J. Am. Chem. Soc., 2019, 141, 5182



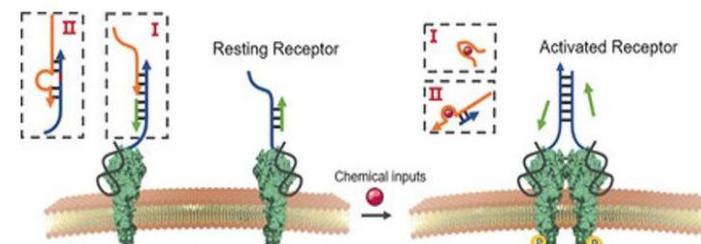
Angew. Chem. Int. Ed., 2019, 58, 6590 (VIP paper, Inside cover)



Angew. Chem. Int. Ed., 2014, 53, 8358



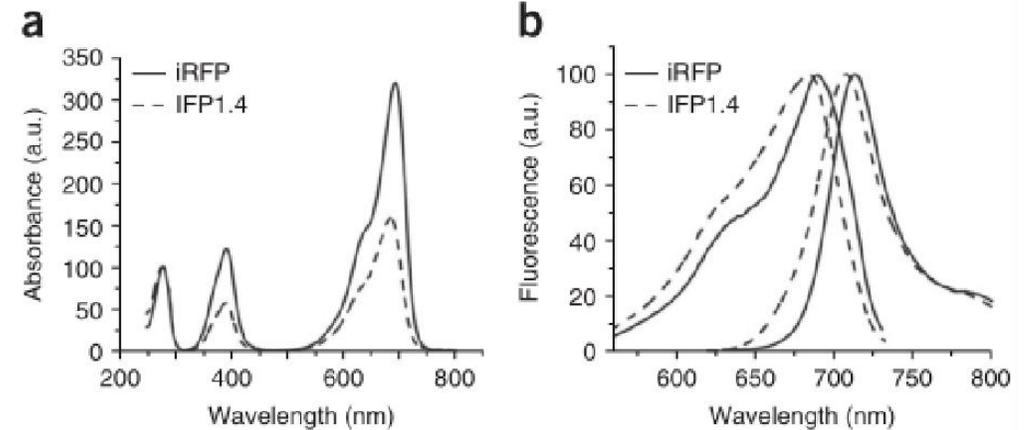
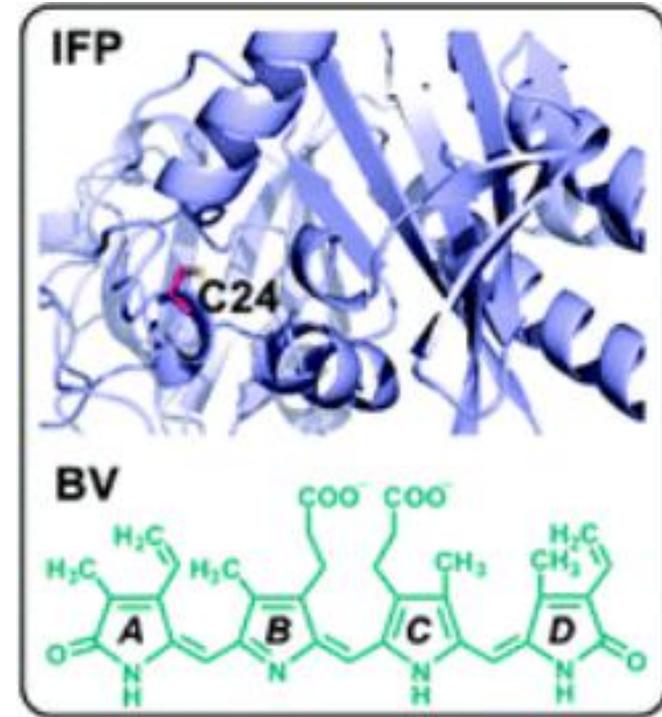
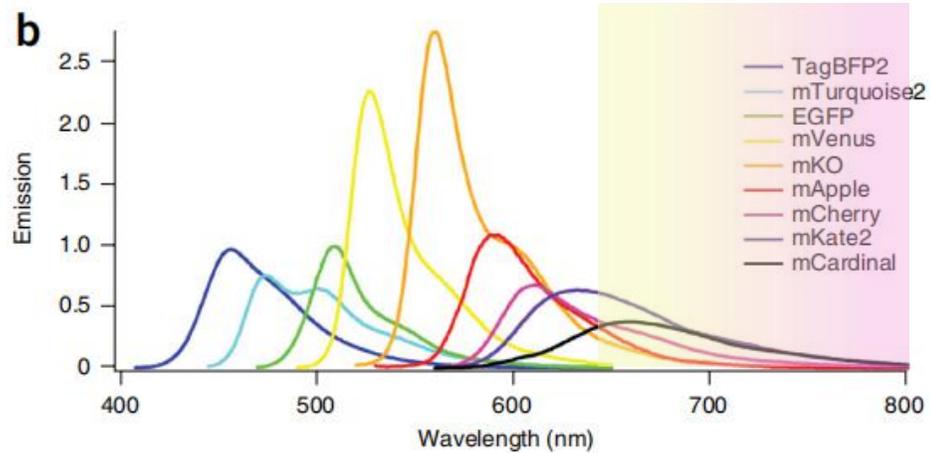
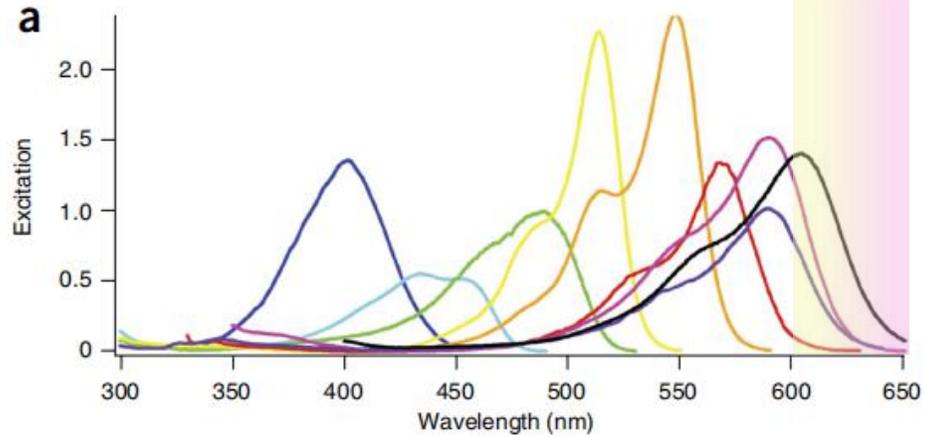
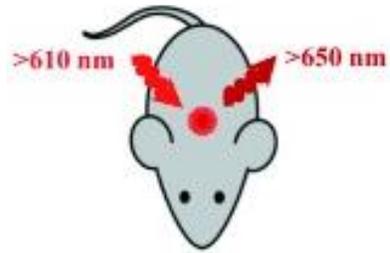
Angew. Chem. Int. Ed., 2017, 56, 14888



Angew. Chem. Int. Ed., 2018, 57, 10226 (Hot paper)

Introduction

Deep-tissue imaging

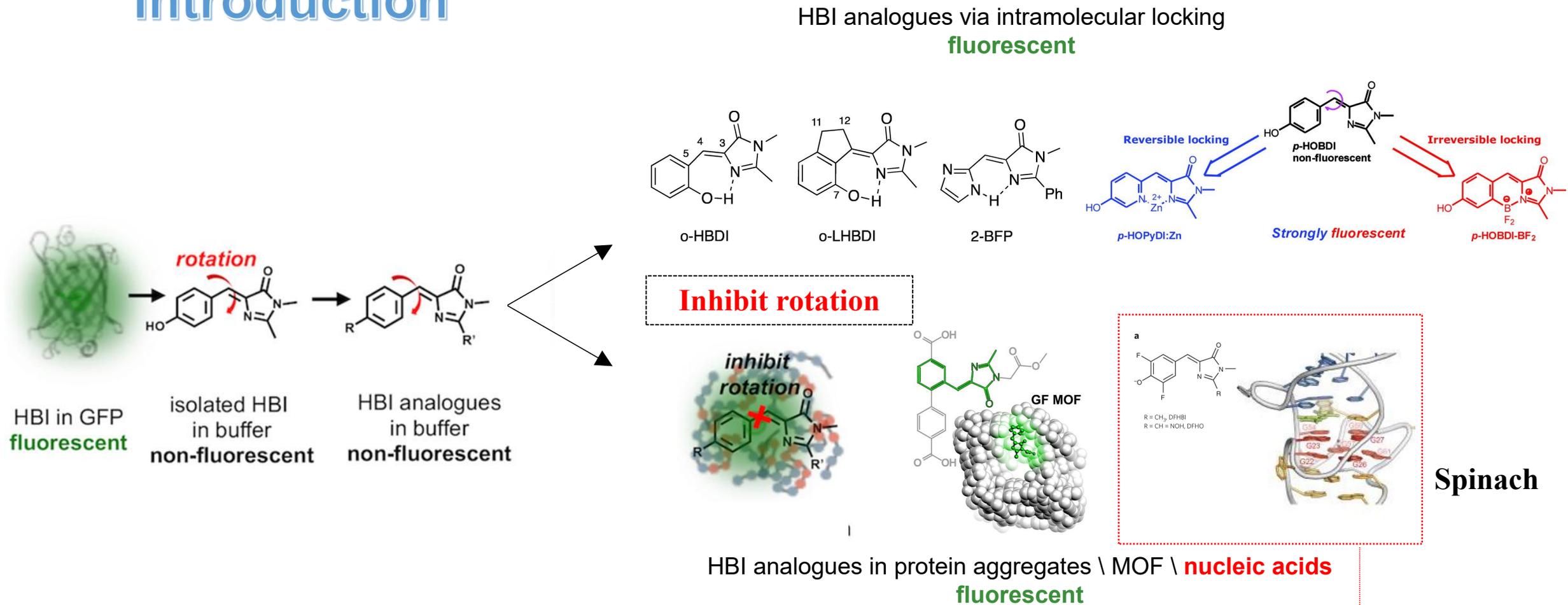


Nature Methods. 13, 557–562 (2016).

Nature. 438, 325–331(2005).

Science. 324, 5928, 804–807(2009).

Introduction



J. Am. Chem. Soc. 2020, 142, 2, 738–749

J. Am. Chem. Soc. 2012, 134, 13, 6025–6032

J. Am. Chem. Soc. 2018, 140, 24, 7381–7384

J. Am. Chem. Soc. 2015, 137, 6, 2223–2226

Nat Struct Mol Biol. 2014, 21(8): 658–663.

Introduction

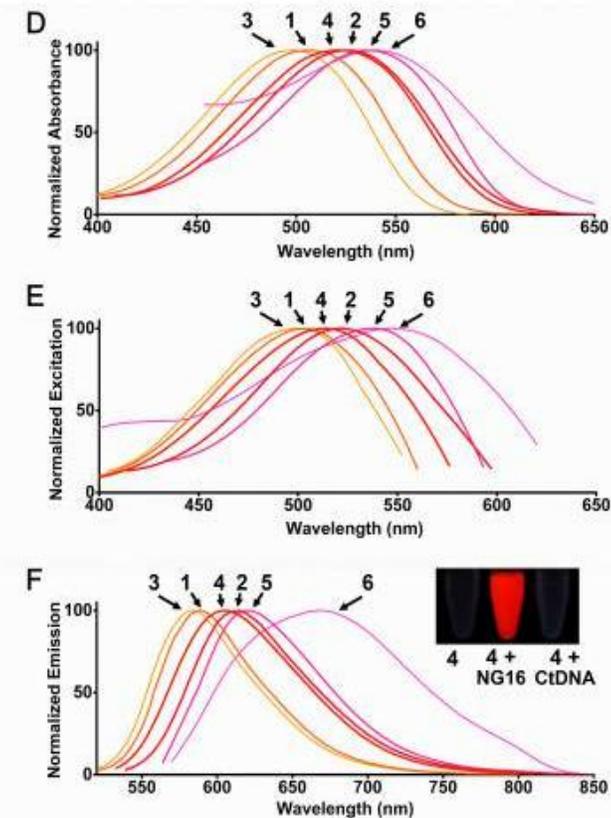
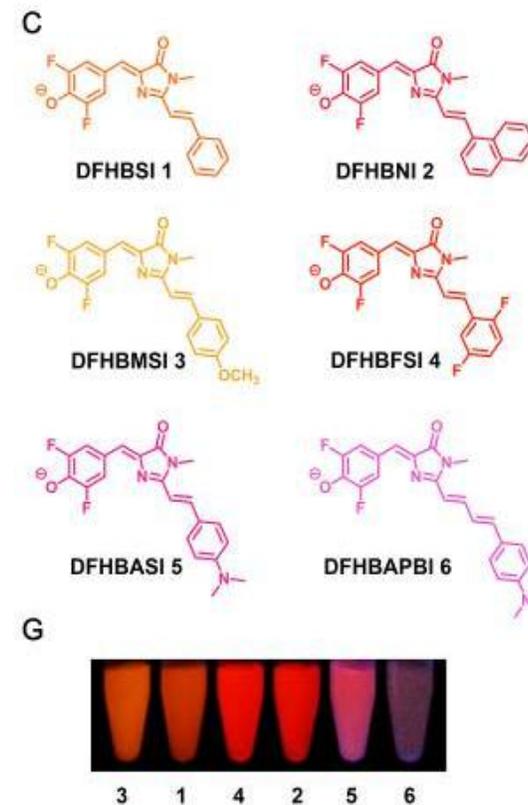
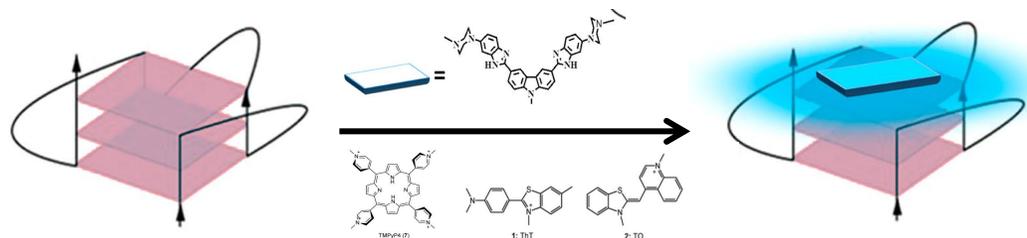
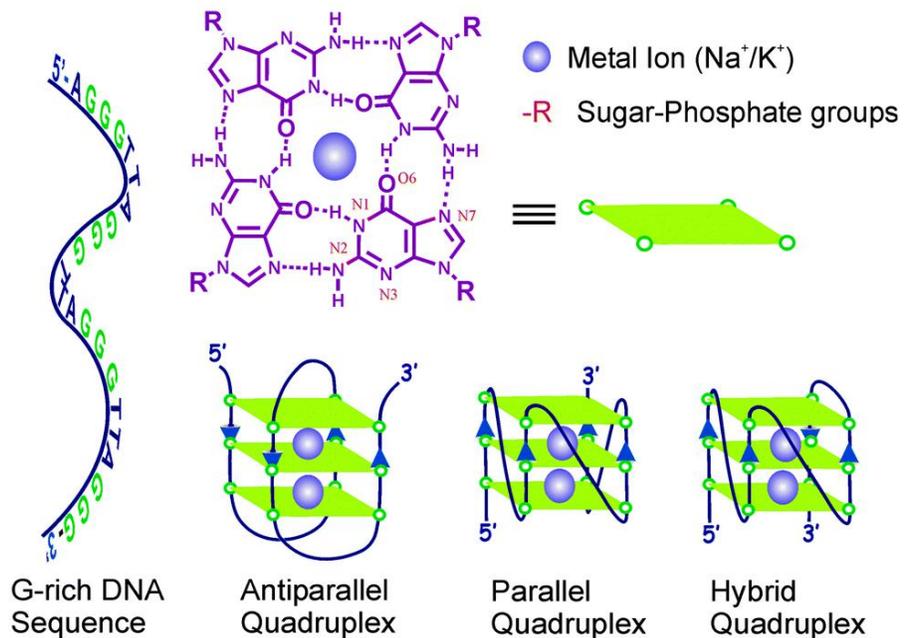


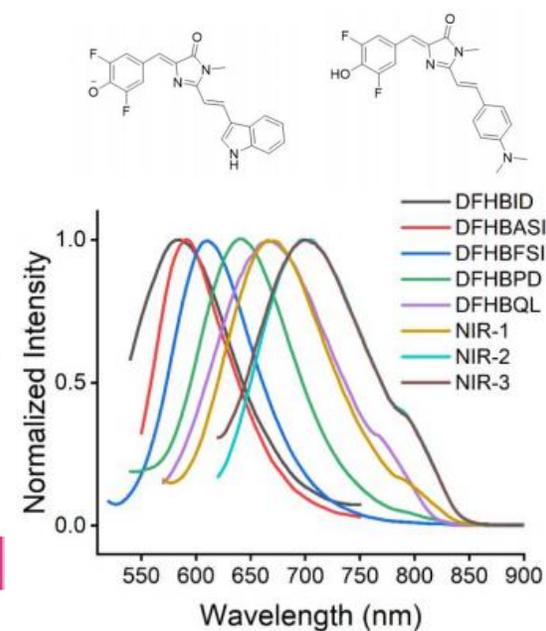
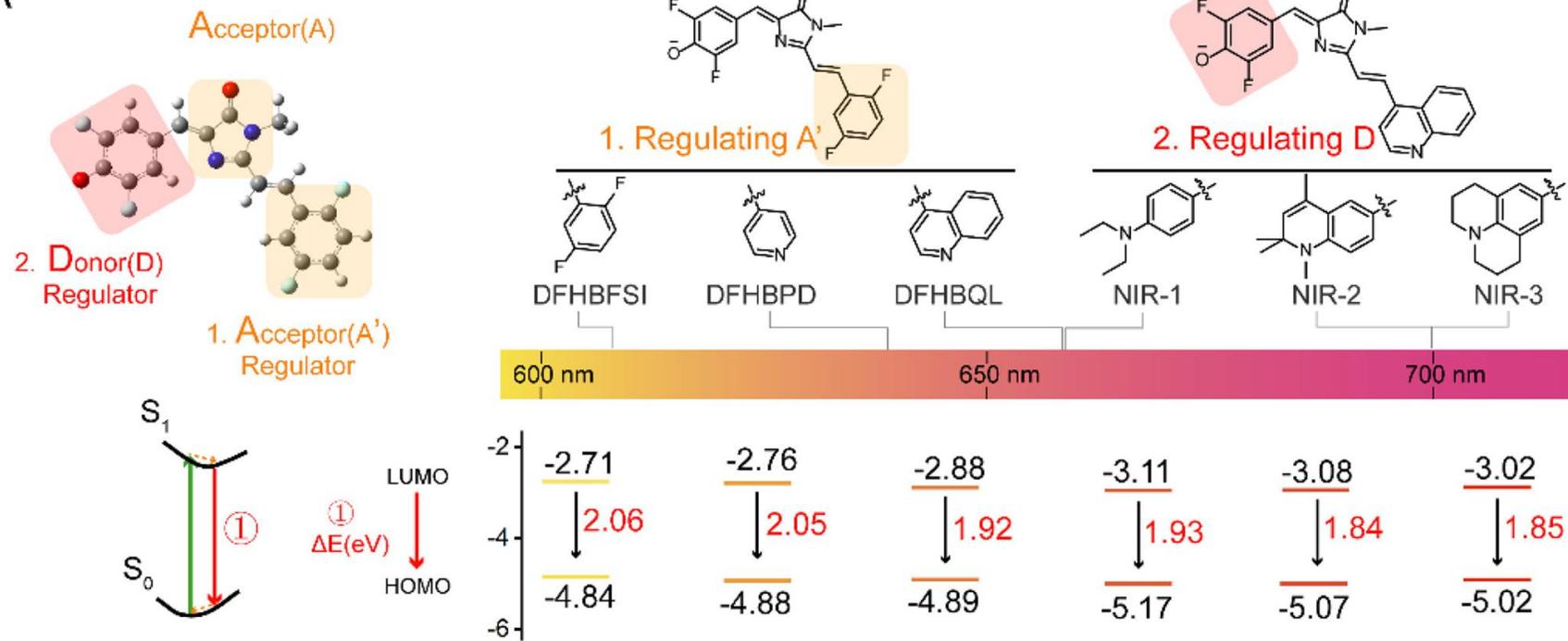
Table 1. Photophysical and binding properties of chromophores and chromophore-NG16 complexes

Chromophore	λ_{Exmax} (nm)	λ_{Emmax} (nm)	ϵ ($\text{M}^{-1} \text{cm}^{-1}$)	Stokes shift (nm)	Q.Y. ^b	K_d (μM)
DFHBMSI-NG16	499	583	16 950	84	0.37	1.56 ± 0.31
DFHBMSI	500	570	18 200	70	0.0072	N/A ^a
DFHBSI-NG16	503	590	17 350	87	0.31	1.76 ± 0.25
DFHBSI	501	576	19 210	75	0.0066	N/A
DFHBFSI-NG16	513	606	28 200	93	0.39	1.27 ± 0.11
DFHBFSI	511	594	32 000	83	0.0052	N/A
DFHBNI-NG16	521	612	37 500	91	0.30	1.37 ± 0.19
DFHBNI	517	600	38 840	83	0.0048	N/A
DFHBASI-NG16	538	620	22 800	82	0.19	2.77 ± 0.58
DFHBASI	540	614	23 890	74	0.0028	N/A
DFHBAPBI-NG16	547	668	15 500	121	0.032	24.88 ± 0.82
DFHBAPBI	548	662	16 120	114	0.0011	N/A
mCherry	587	610	72 000	23	0.22	N/A

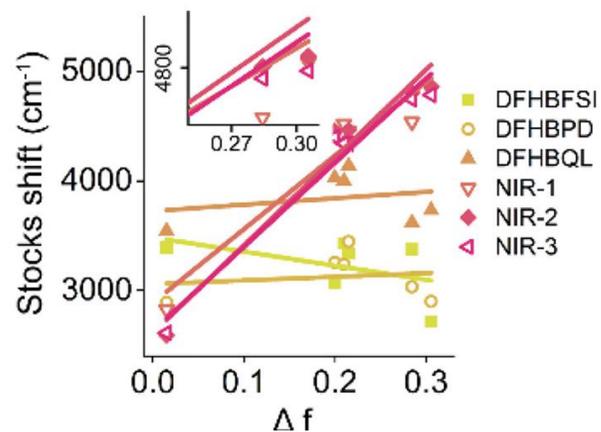


Results and discussions

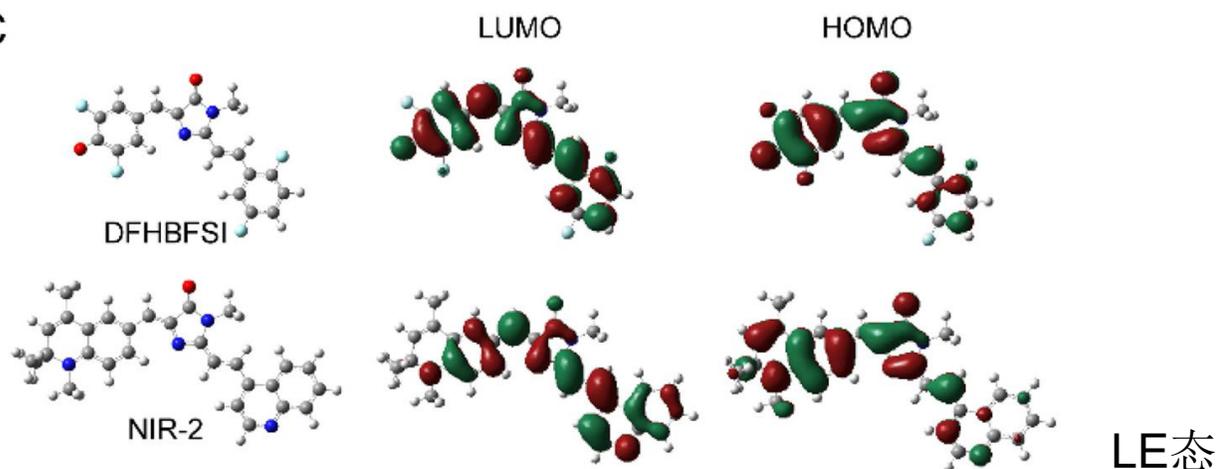
A



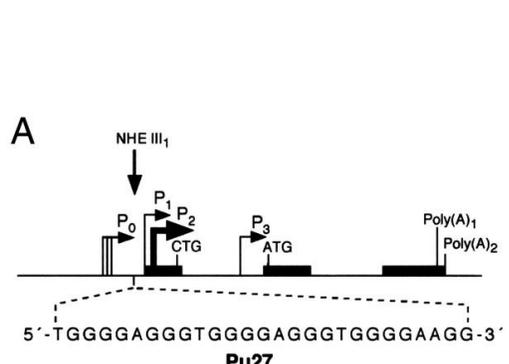
B



C

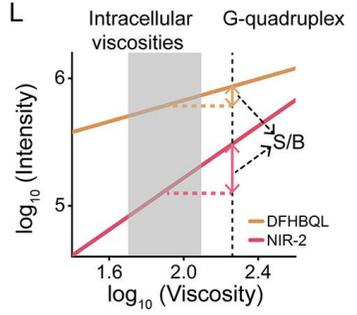
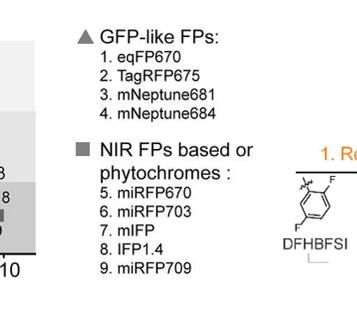
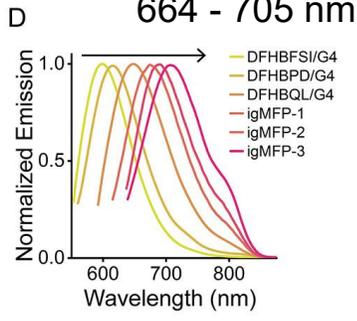
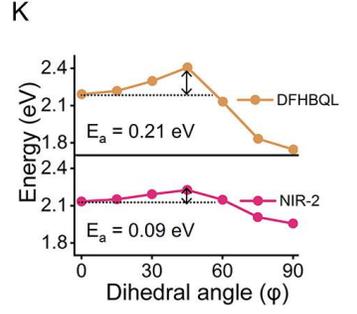
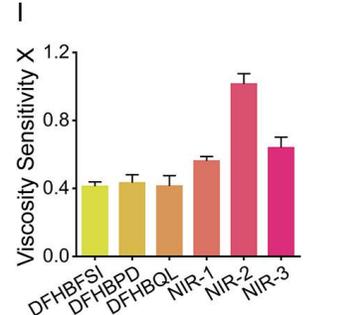
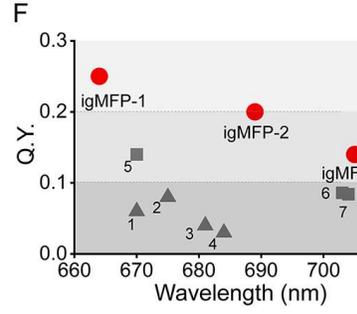
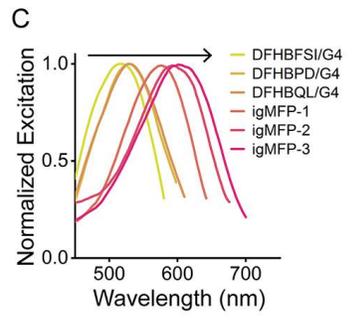
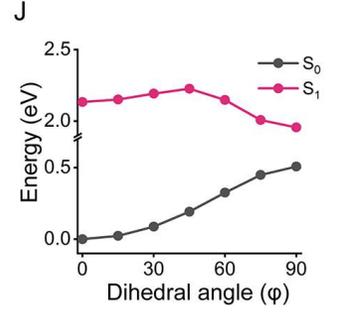
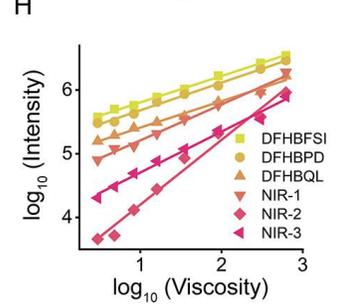
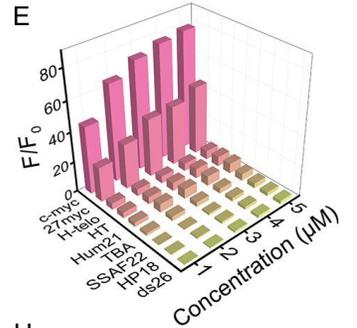
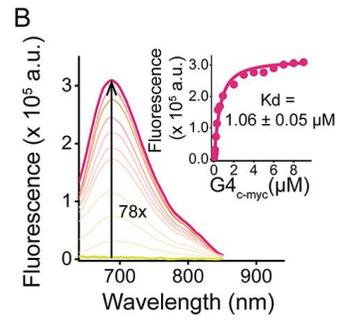
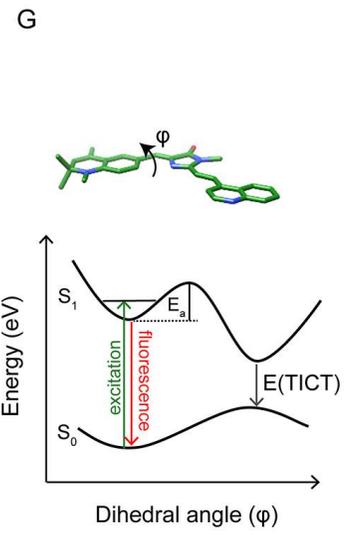
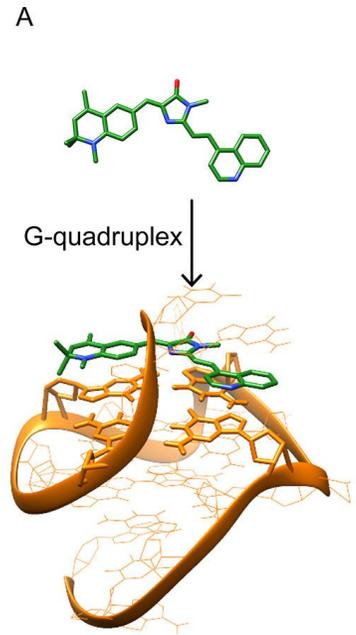


Results and discussions

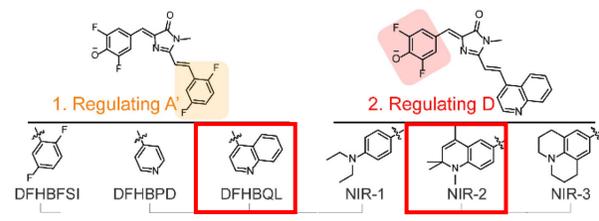


c-MYC原癌基因启动子

c-myc 和 27myc: 平行
 H-telo、HT、Hum21: 混合型
 TBA: 反平行
 G4sSSAF22: 单链
 ds26: 双链
 HP18: 发夹



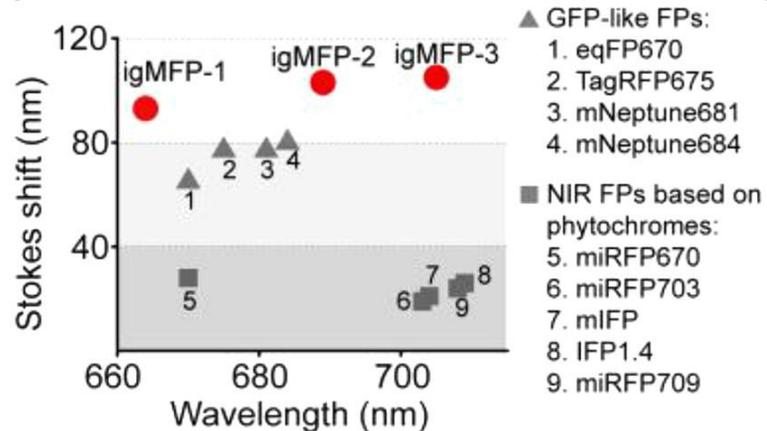
igMFP-1 = NIR-1/G4_{c-myc}
 igMFP-2 = NIR-2/G4_{c-myc}
 igMFP-3 = NIR-3/G4_{c-myc}



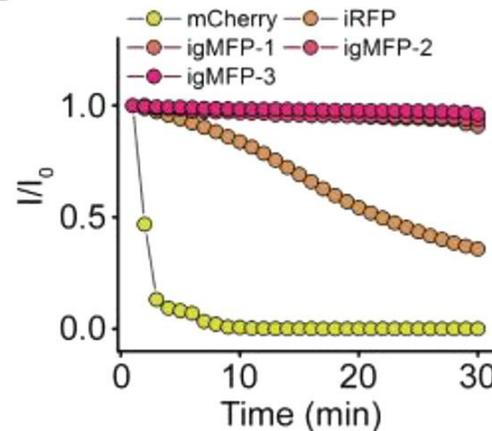
高粘度敏感的发色团能以更高敏感性和选择性识别 G4，有效减少由细胞内成分引起的背景。

Results and discussions

A 94nm 98nm 105nm

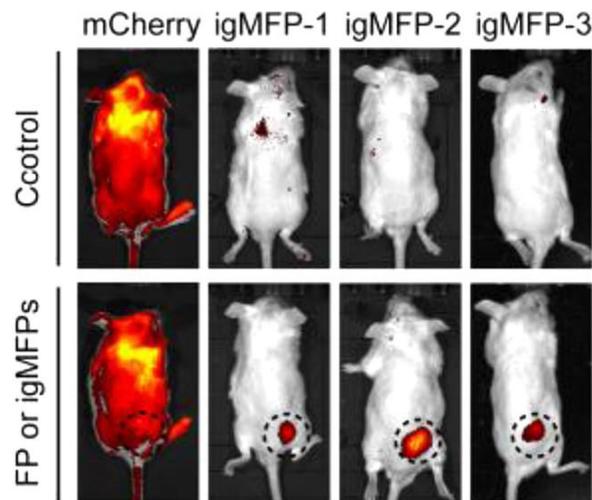


B

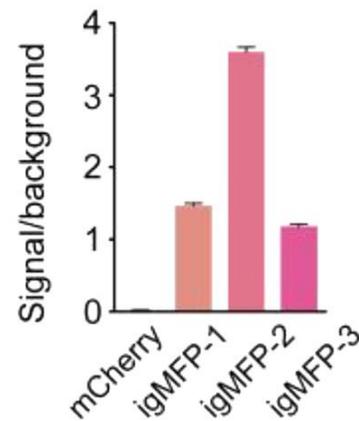


通过结合的发色团与溶液中的游离发色团的部分交换，减少了光漂白复合物的积累。

C

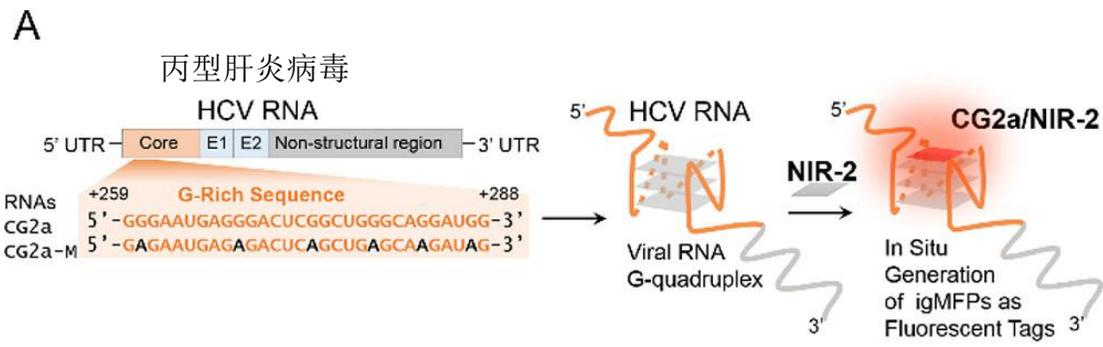


D

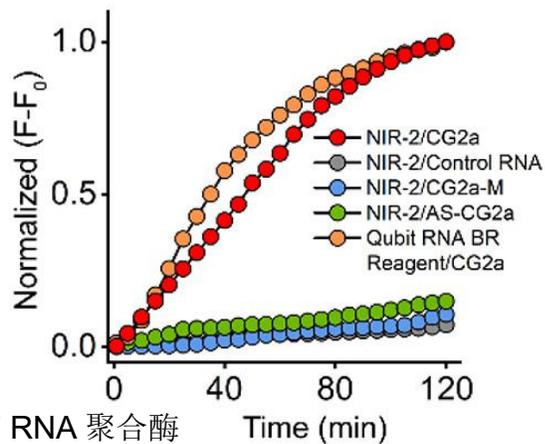


igMFP-1 = NIR-1/G4_{c-myc}
 igMFP-2 = NIR-2/G4_{c-myc}
 igMFP-3 = NIR-3/G4_{c-myc}

Results and discussions



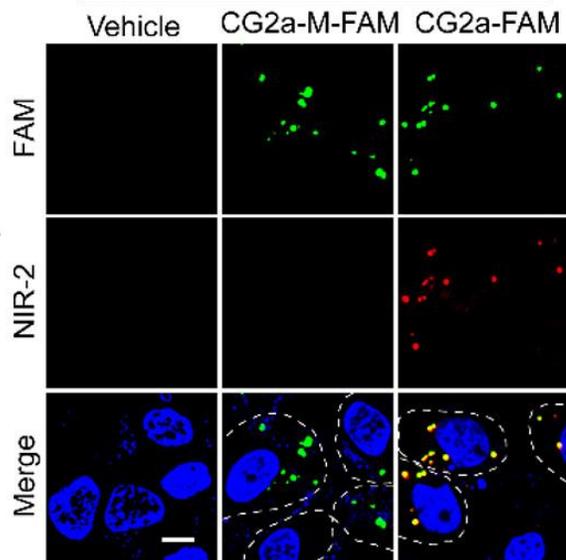
B In vitro transcription system



CG2a: T7 RNA 聚合酶
转录生成的 RNA 转录本

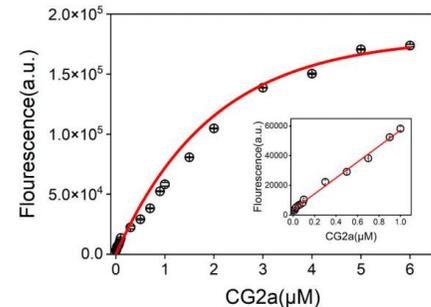
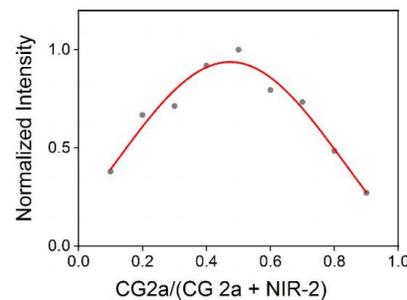
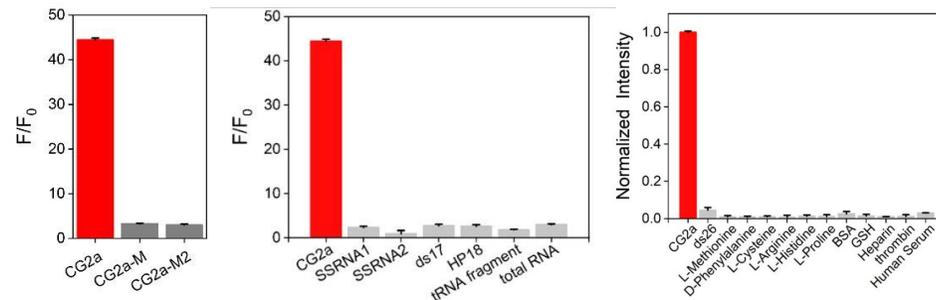
AS-CG2a: 通过杂交阻
断 G4 形成的反义链

C HCV RNA mimicking system

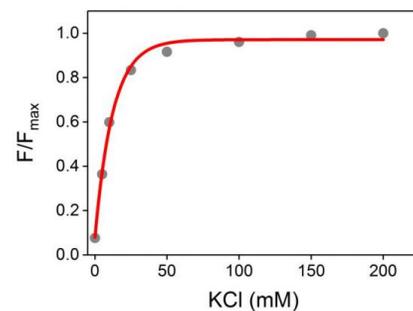


Huh7
肝癌细胞

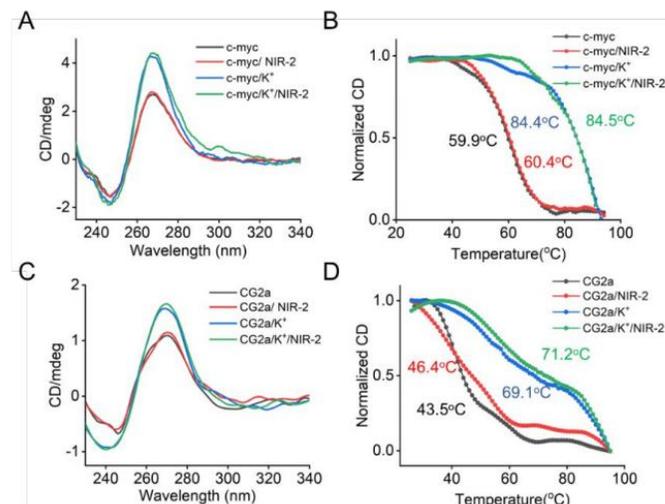
OLC = 0.91



$K_d = 1.58 \pm 0.18 \mu\text{M}$
检测限: $0.015 \mu\text{M}$

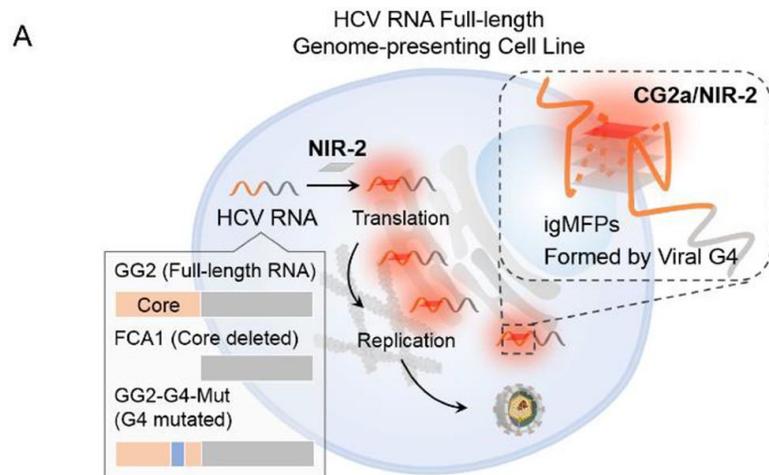


K⁺生理浓度: 100 mM



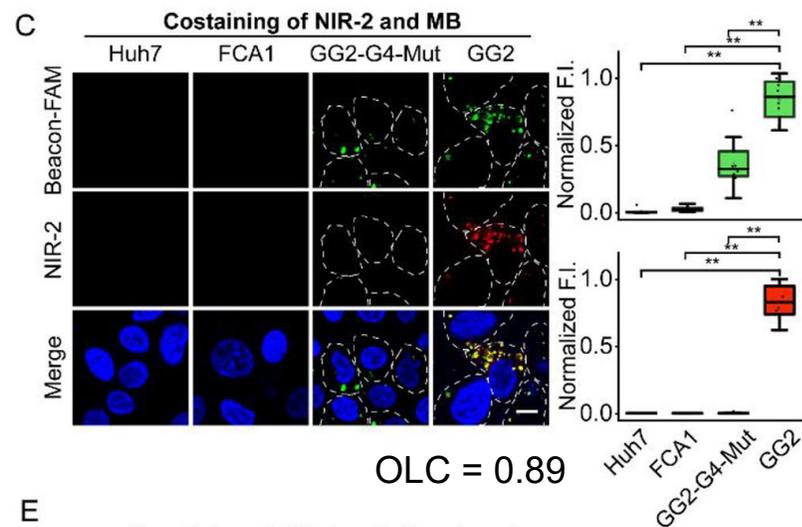
Results and discussions

GG2细胞：能够复制/翻译全长 HCV 2a 基因组并随后产生和分泌病毒颗粒。

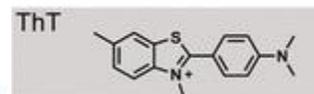
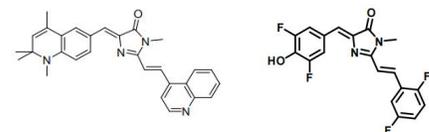
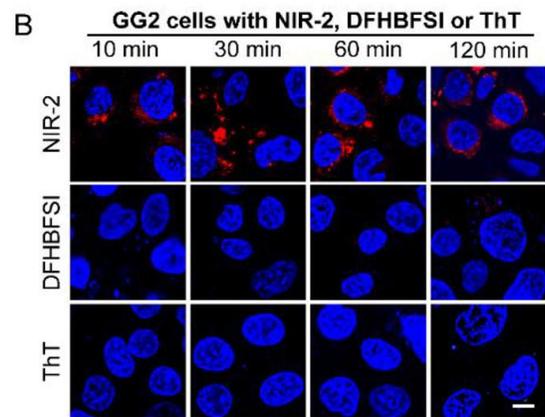
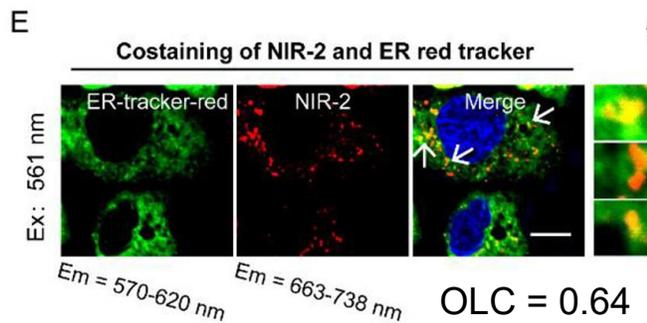


FCA1 细胞：一种核心基因缺失的对照细胞系，表达没有核心基因区域的 HCV RNA 亚基因组

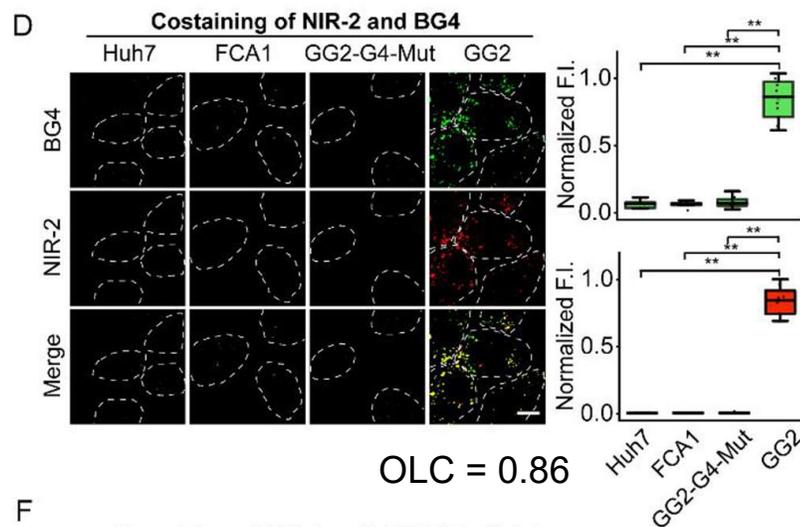
MB: 具有 FAM/BHQ1 (荧光团/淬灭剂) 对的靶向 HCV RNA 核心基因的特异分子信标探针



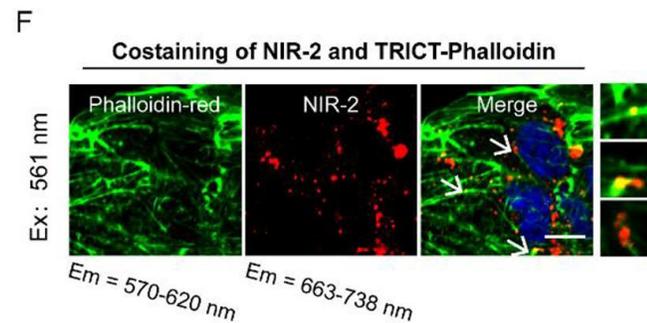
HCV RNA 基因组的复制及其在病毒颗粒中的包装主要发生在 ER 相关膜



NIR-2 ($\log P = 4.85$) 比 DFHBFSI (3.64) 和 ThT (4.29) 更具疏水性，并且 NIR-2 是电中性，DFHBFSI 和 ThT 带电，促进 NIR-2 细胞膜渗透



BG4: 识别 G4 的特异性抗体

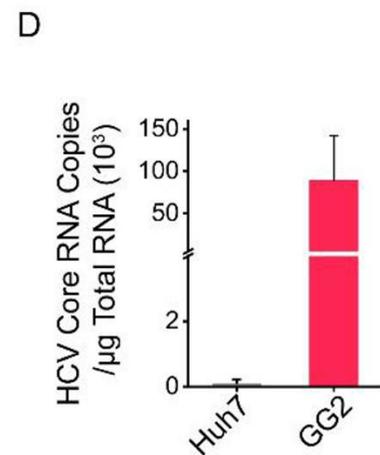
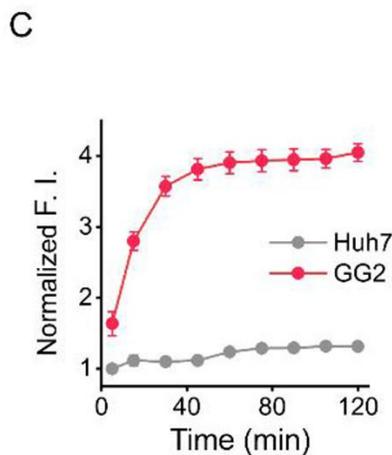
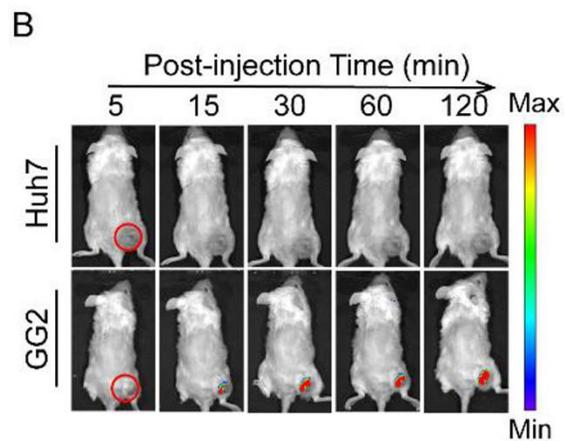
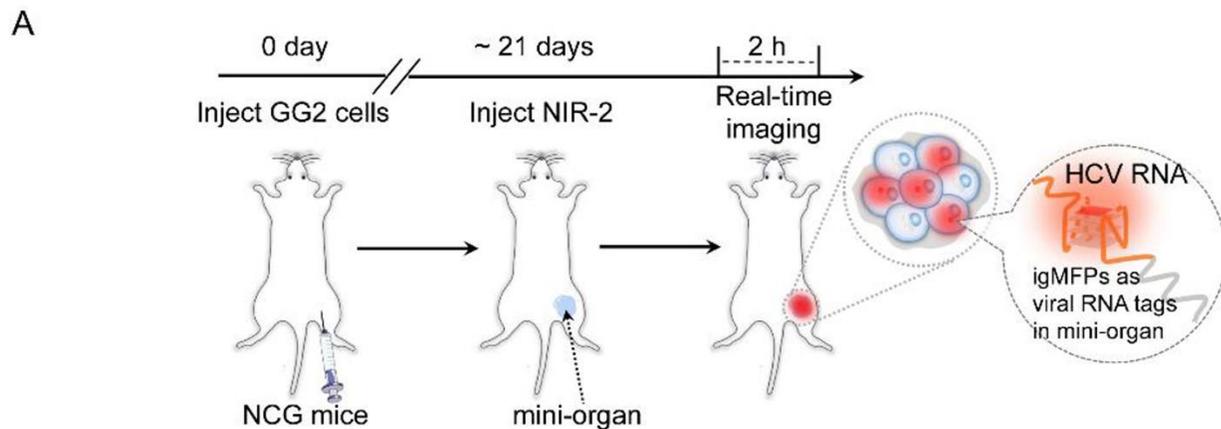


EX 561
Collected 570-620 nm / 663-738 nm

肌动蛋白丝是 HCV RNA 复制复合体运动的轨道

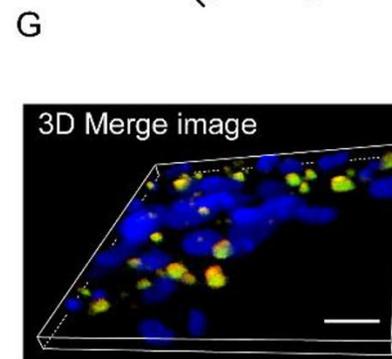
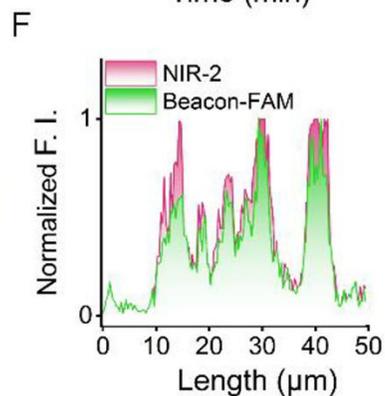
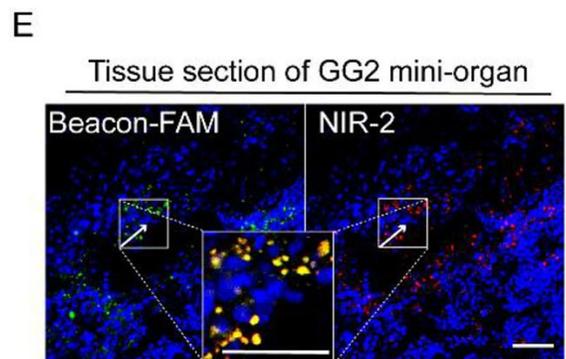
Results and discussions

NCG 小鼠：广泛用于人类细胞移植的严重免疫缺陷的人源化小鼠模型



HCV 病毒核心基因的高复制水平

RT-qPCR



igMFP 可用于在活体小鼠中的精确 HCV RNA 成像

OLC = 0.88

THANKS!