Literature Report

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Communication

Renal-Clearable Molecular Probe for Near-Infrared Fluorescence Imaging and Urinalysis of SARS-CoV-2

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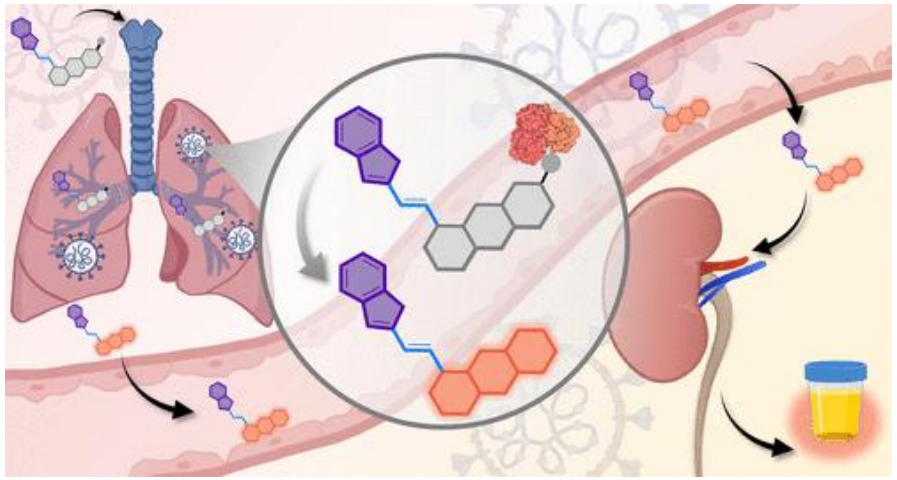

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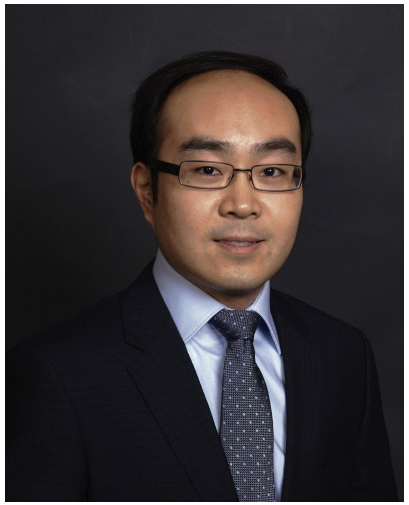
Author Information



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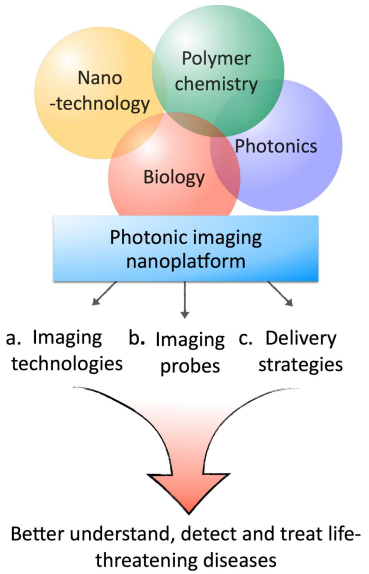
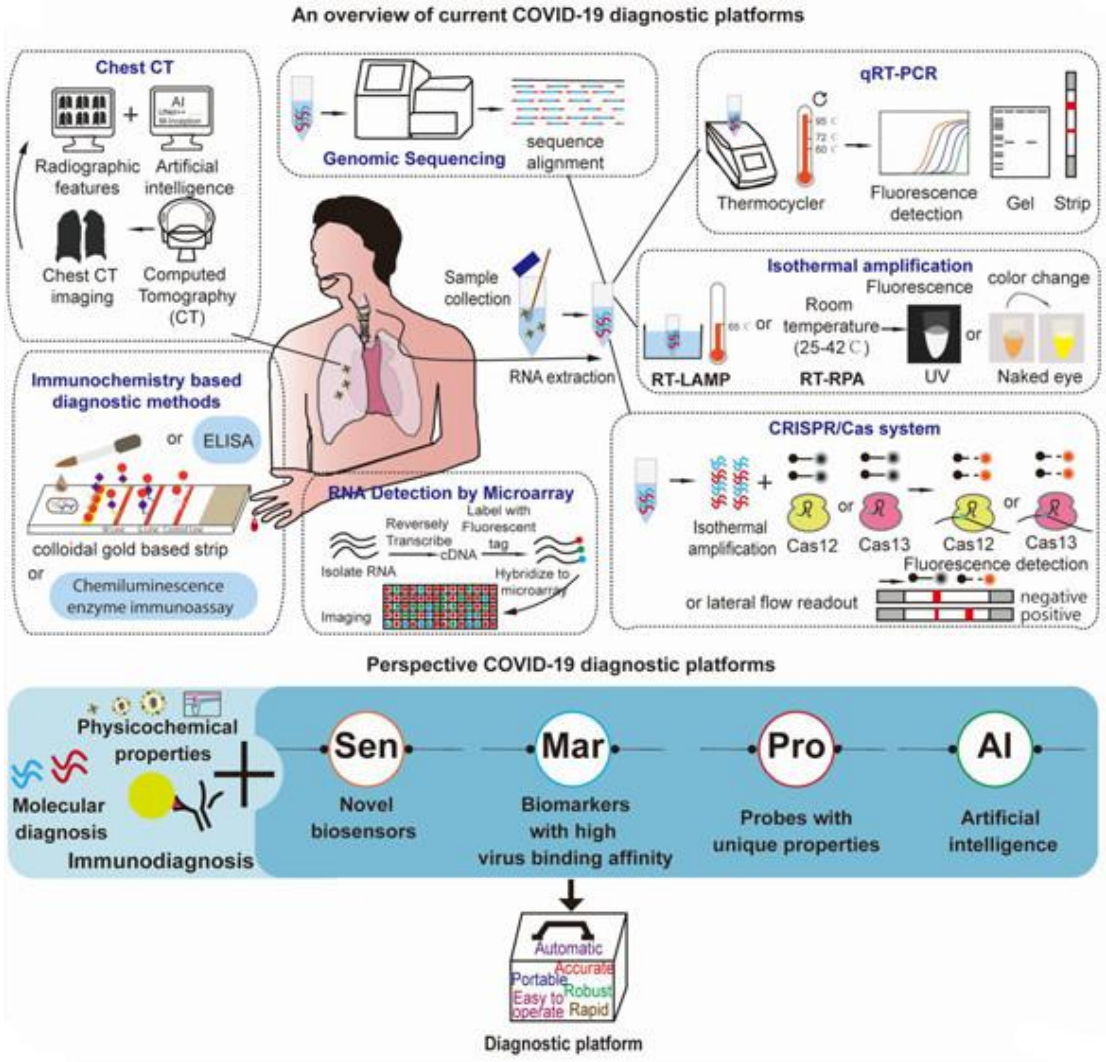


Molecular Imaging:
在分子水平上检测和监测疾病微环境中的病理过程，发展无创高通量药物筛选技术，主要是药物代谢的实时体内成像和药物诱导的毒性变化。

Nanotechnology:
开发具有最先进成像方式的有机半导体纳米材料，如光声成像、近红外荧光成像和生物发光成像，以提高成像穿透深度和空间分辨率。

Probe Design
设计和合成可激活的成像探针，揭示如活性自由基如何调节肿瘤代谢、促进转移和血管生成，并促进耐药表型等过程。

Introduction



ACS Infect. Dis. **2020**, 6, 1998−2016

现有临床诊断:

（1）抗原检测 、IgM/IgG抗体检测、ELISA

特点:

可区分既往感染和现行感染。但是这些诊断方法是静态的，不能区分活病毒/非活病毒或反映病毒复制活性

（2）RT-PCR：检测SARS-CoV-2核糖核酸来检测病毒复制活性

特点:

高灵敏度和选择性。

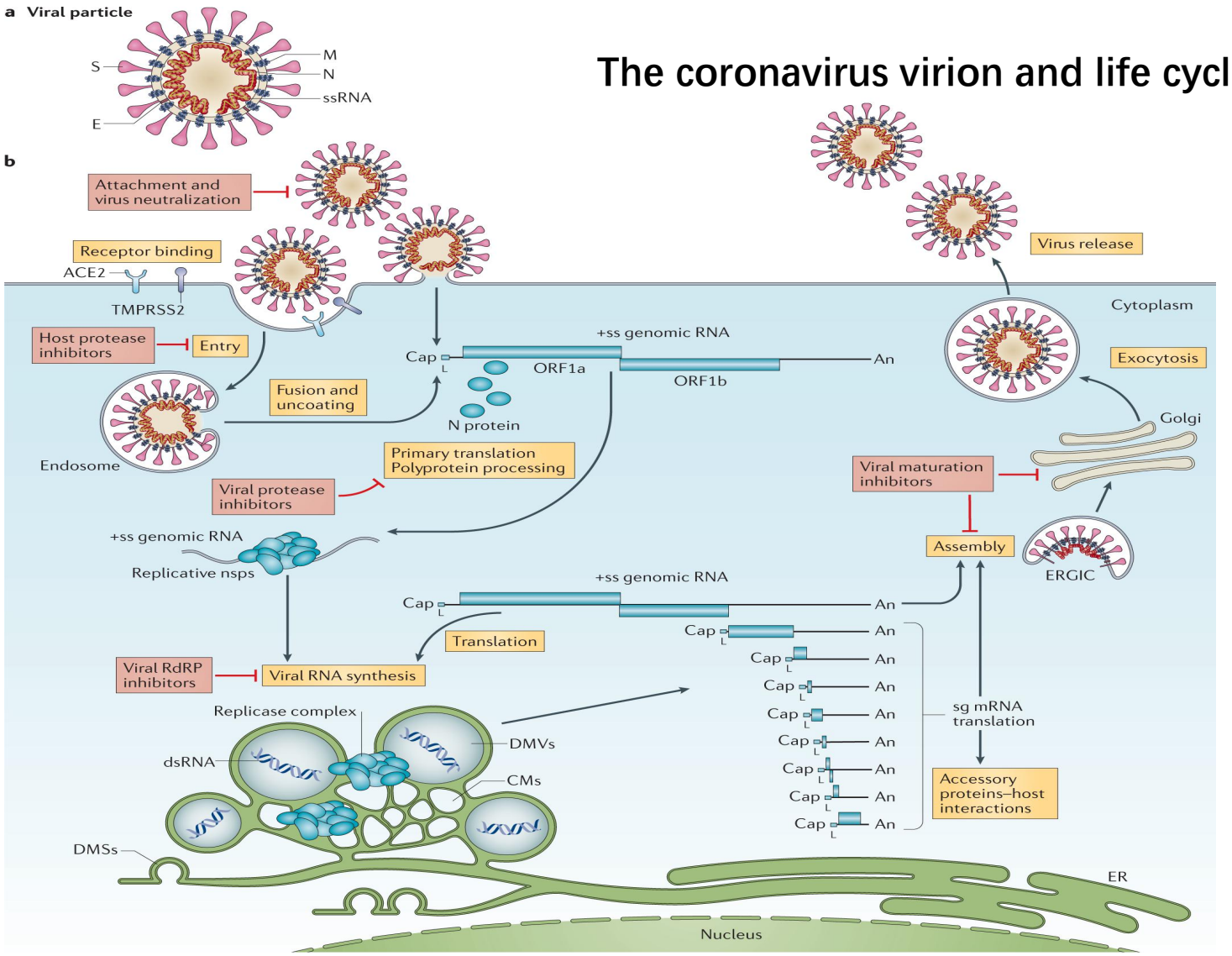
突变会增加检测的假阴性结果。

对于无症状、轻度症状，低病毒载量可能不足以进行qRT-PCR检测

新型检测技术:

（3）由生物标志物激活信号的荧光分子探针

SARS-COV-2 Mpro

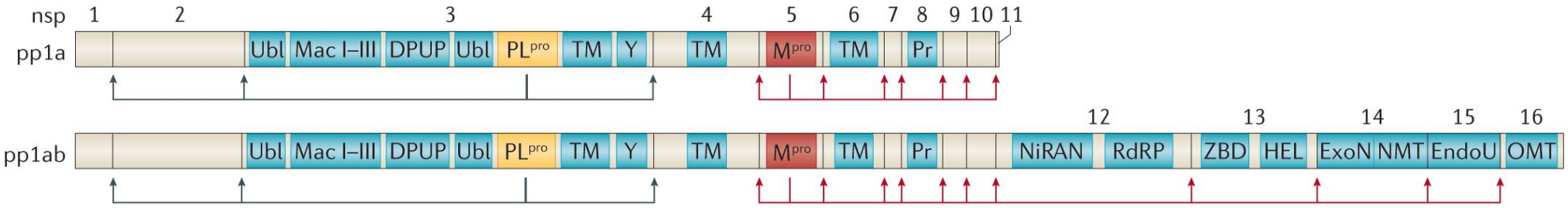


Nature reviews | *Microbiology* volume 19 | **march 2021**

SARS-COV-2 Mpro :
新冠病毒多肽复制加工过程中的主要蛋白酶Mpro,又称3CLPro

SARS-COV-2 Mpro

Coronavirus polyprotein processing and non-structural proteins



nsp1 Host mRNA degradation, translation inhibition

nsp2 Unknown

nsp3 Ubl Mac I–III DPUP Ubl PLpro TM Y — Polyprotein processing, de-ADP-ribosylation, deubiquitination, interferon antagonist, DMV formation

nsp4 TM — DMV formation

nsp5 Mpro — Polyprotein processing, inhibition of interferon signalling

nsp6 TM — DMV formation

nsp7 Cofactor for RNA-dependent RNA polymerase

nsp8 Pr — Primase or 3′-terminal adenylyltransferase, cofactor for RNA-dependent RNA polymerase

nsp9 Binding of single-stranded RNA

nsp10 Cofactor for nsp14 and 16

nsp11 Unknown

nsp12 NiRAN RdRP — RNA-dependent RNA polymerase, nucleotidyltransferase

nsp13 ZBD HEL — Helicase, RNA 5′ triphosphatase

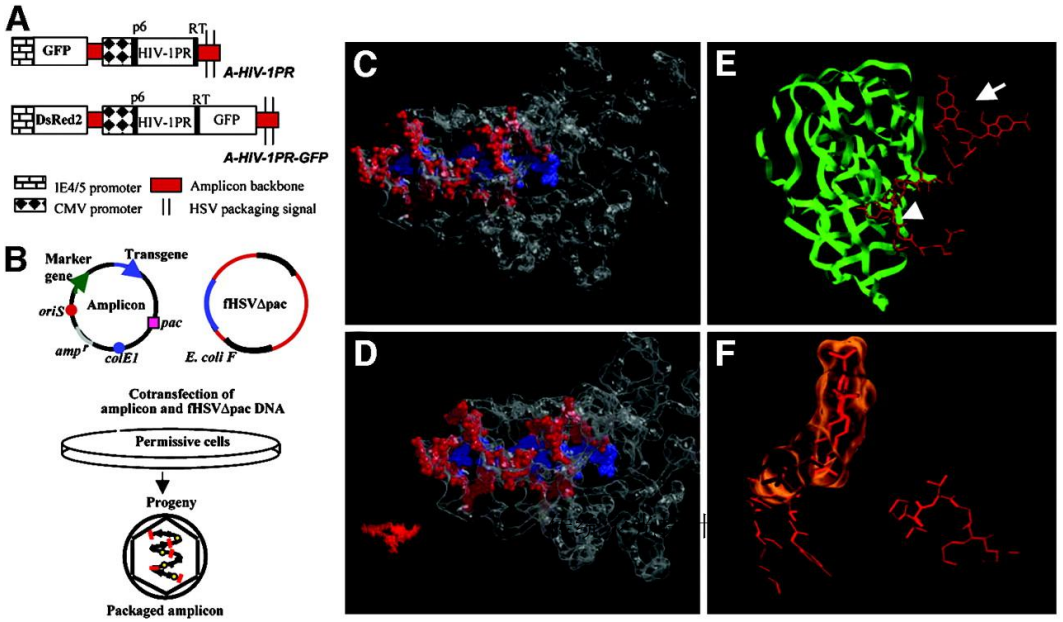
nsp14 ExoN NMT — 3′ to 5′ exoribonuclease, proofreading, RNA cap formation, guanosine *N*7-methyltransferase

nsp15 EndoU — Endoribonuclease, evasion of immune response

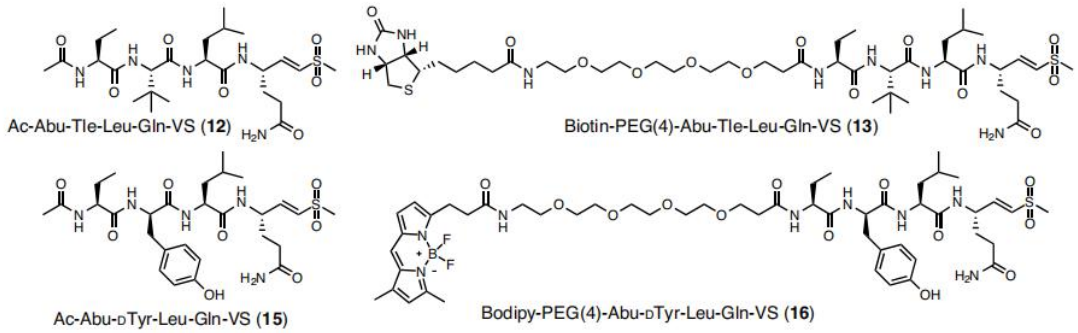
nsp16 OMT — RNA cap formation, ribose 2′-*O*-methyltransferase

Nature reviews | *Microbiology* volume 19 | march 2021

Probe



CANCER RESEARCH 64, 273–278, January 1, 2004



Nature Chemical Biology | VOL 17 | February 2021 | 222–228

传统荧光探针检测HIV蛋白酶：

特点

（1）方法操作简单，无创，灵敏度高，具有高时空分辨率，可以实时反应病毒复制活性

（2）缺陷在于有强自发荧光背景和活体组织中穿透能力低，显著降低了体内荧光成像的灵敏度

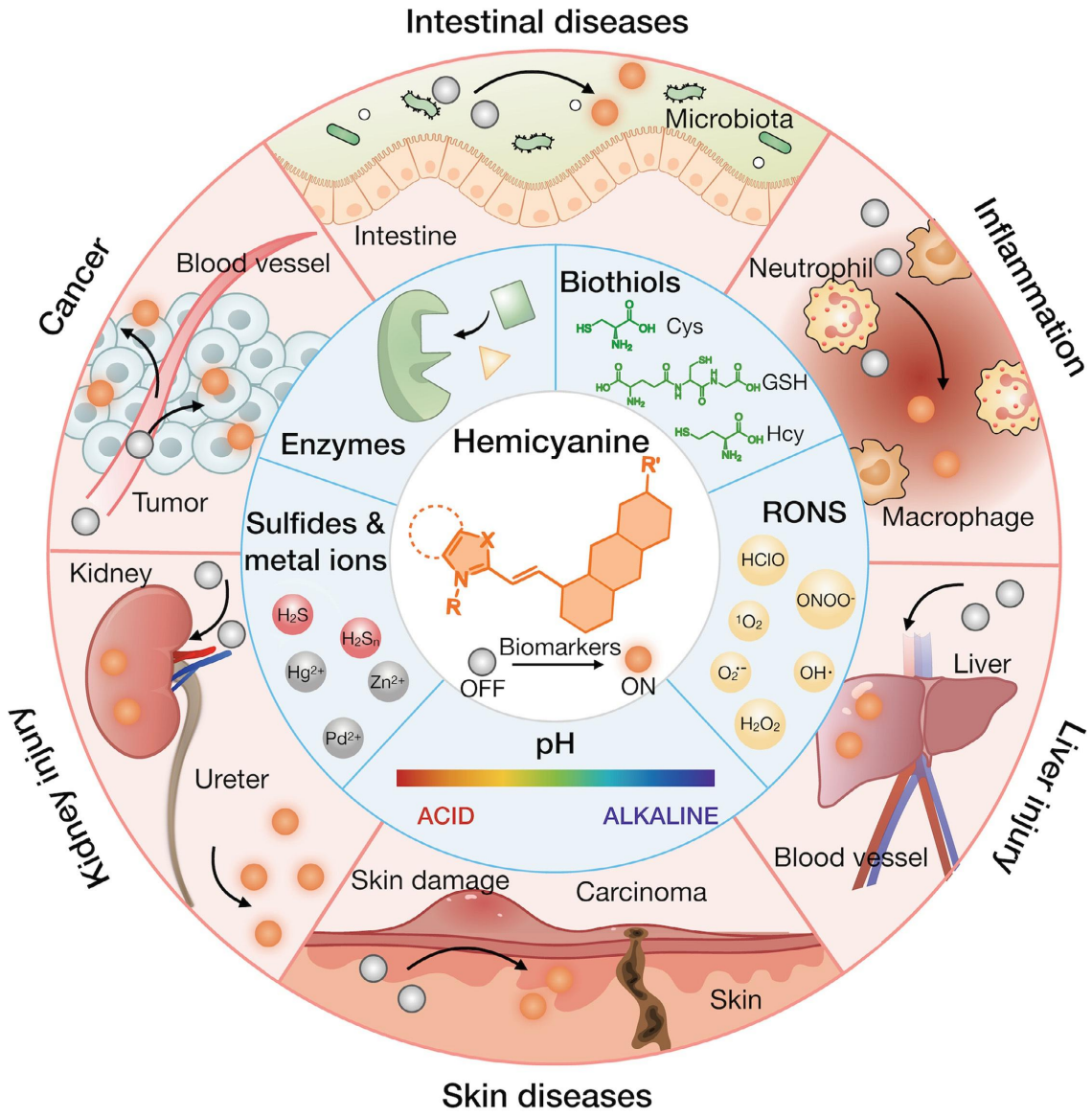
基于花菁和罗丹明支架的检测SARS-COV-2Mpro酶活性的NIR探针

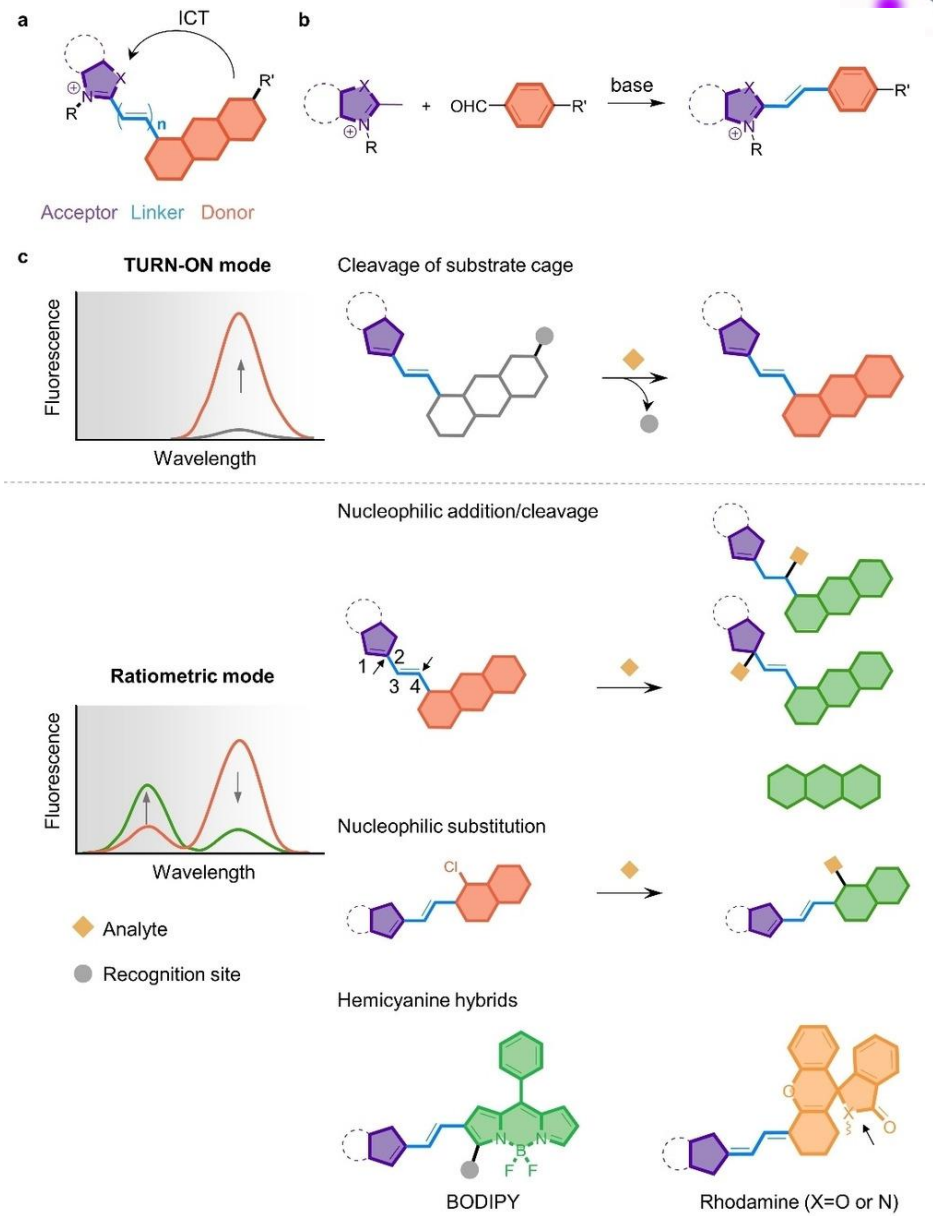
特点

（1）Stokes位移小，导致激发和发射光谱之间的严重串扰，影响检测灵敏度和准确度，

（2）同时探针在体内具有较差的靶向性，代谢和清除能力

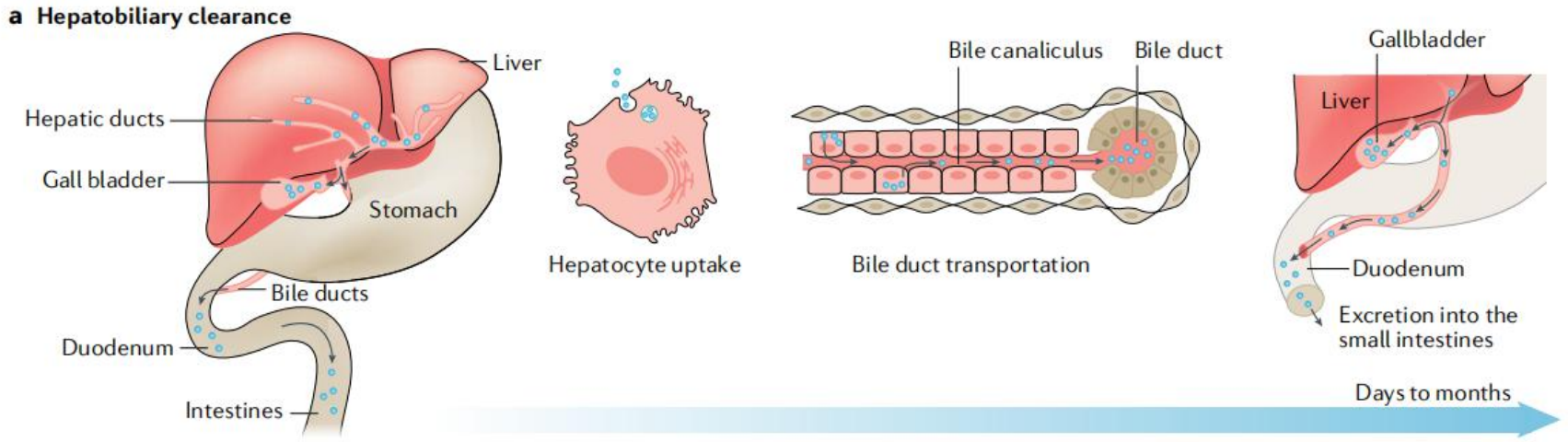
Probe design strategy

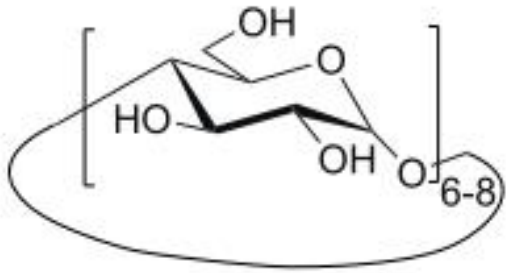




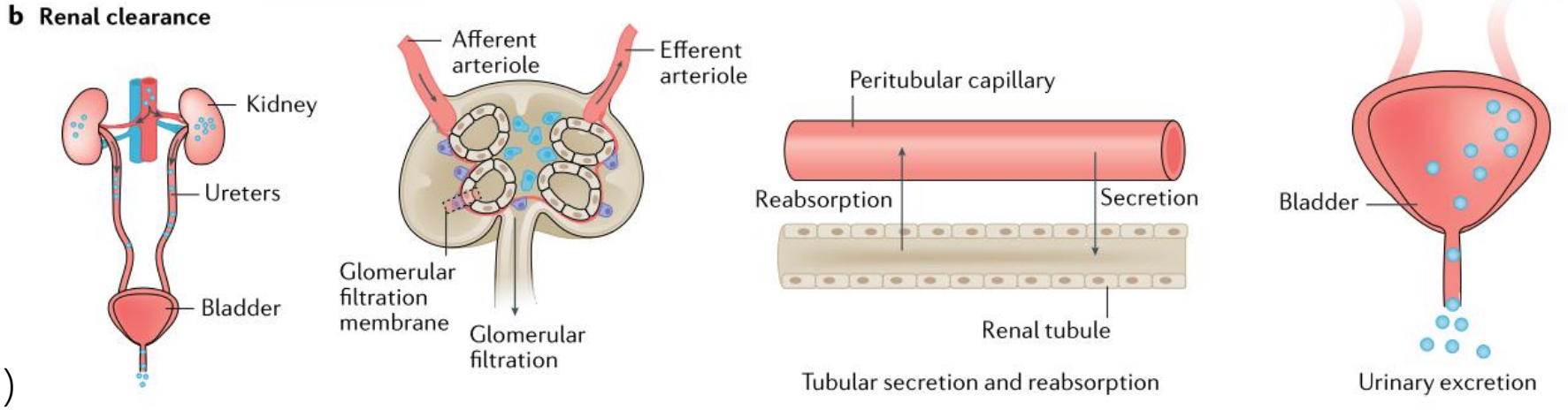
Angew. Chem. Int. Ed. **2021**, 60, 26454 – 26475

Probe design strategy



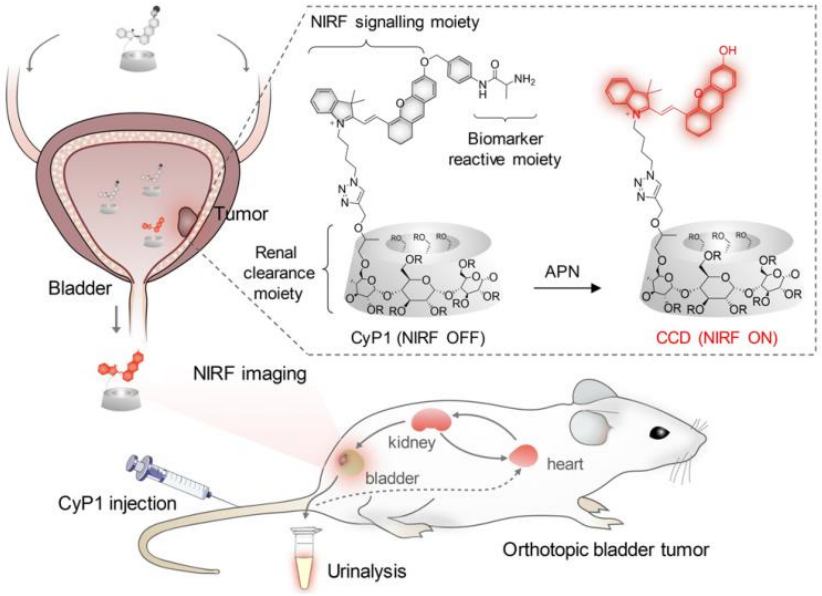


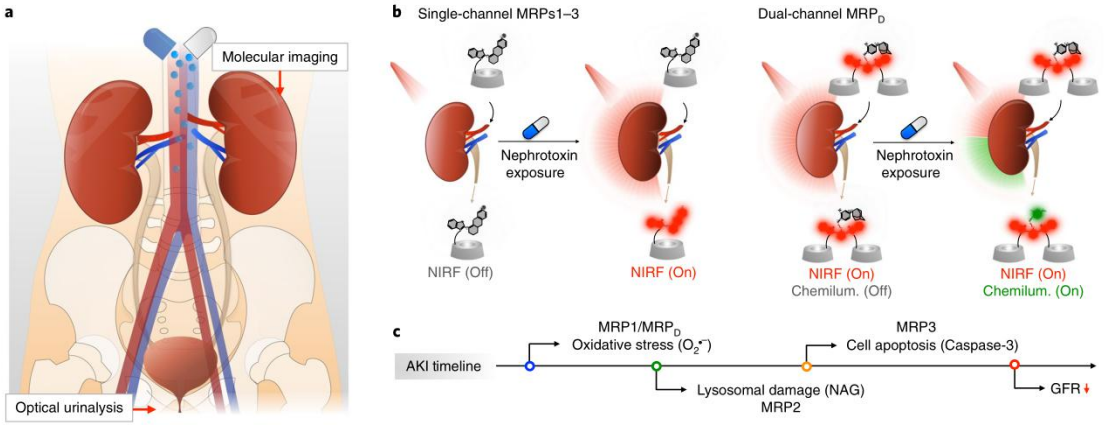
Cyclodextrin (HPβCD)



Nat. Rev. Mater. **2021** DOI: 10.1038/s41578-021-00328-6

Probe design strategy





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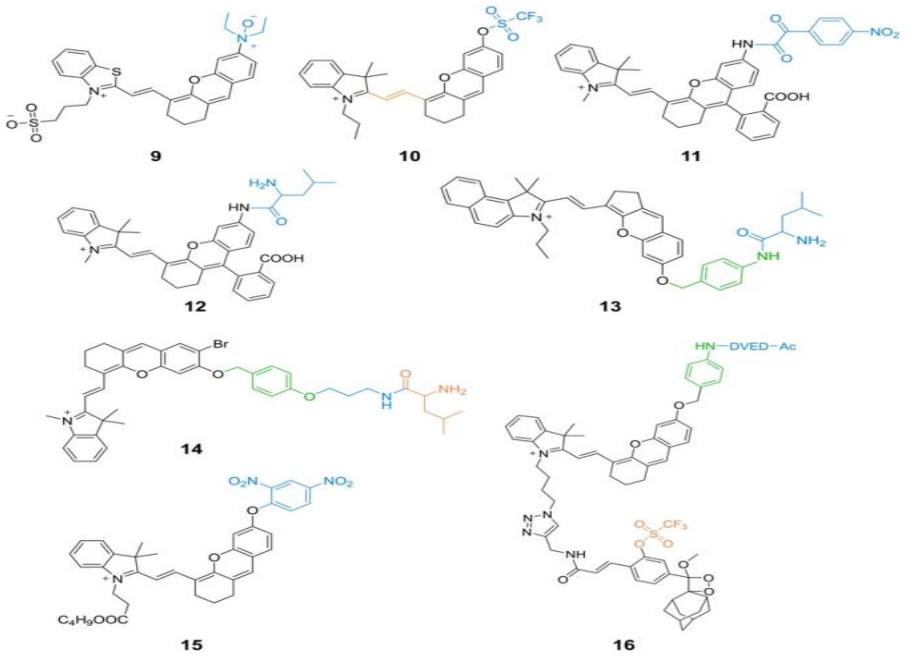


Figure 5. Representative HNAPs for liver injury models. Blue moiety

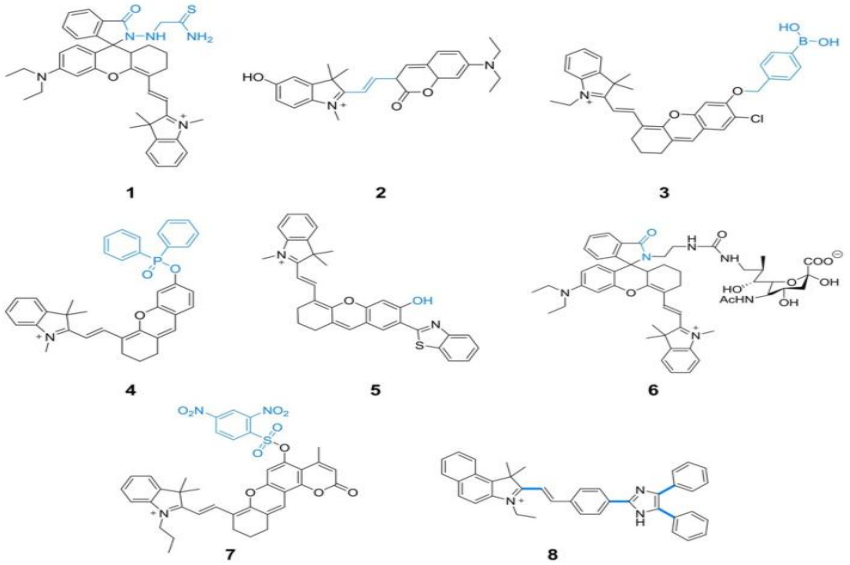
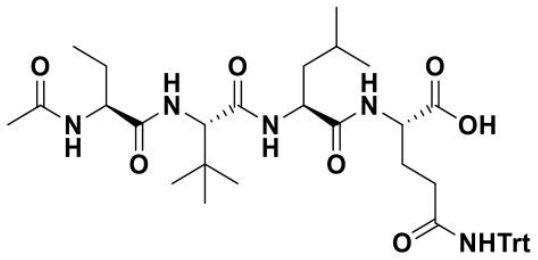


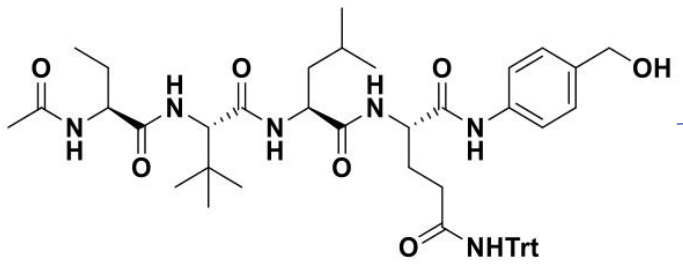
Figure 3. Representative HNAPs for inflammation models. Blue moiety represents the responsive unit.

Synthetic Procedures



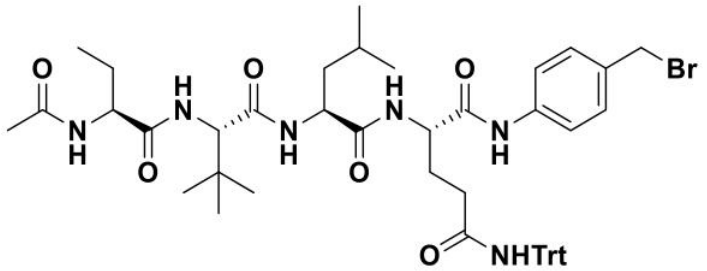
SARS(Trt)

对氨基
苯甲醇

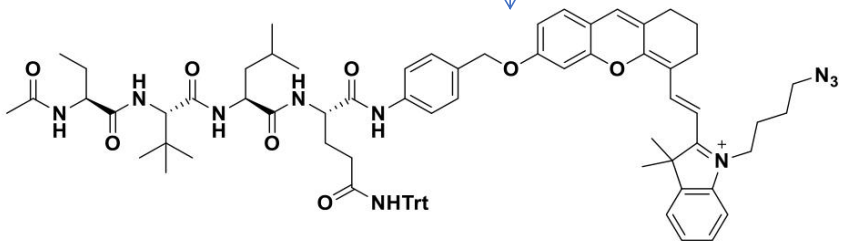


SARS(Trt)-PABA

PBr3

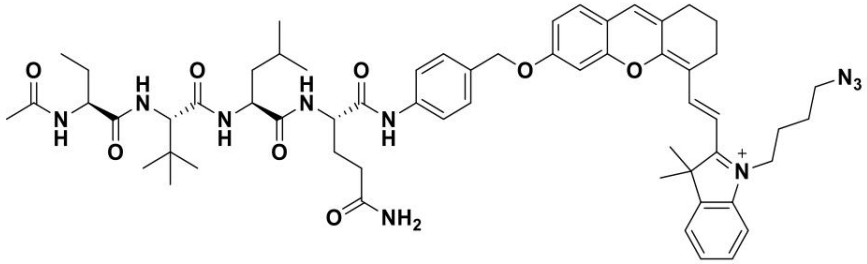


SARS(Trt)-Br

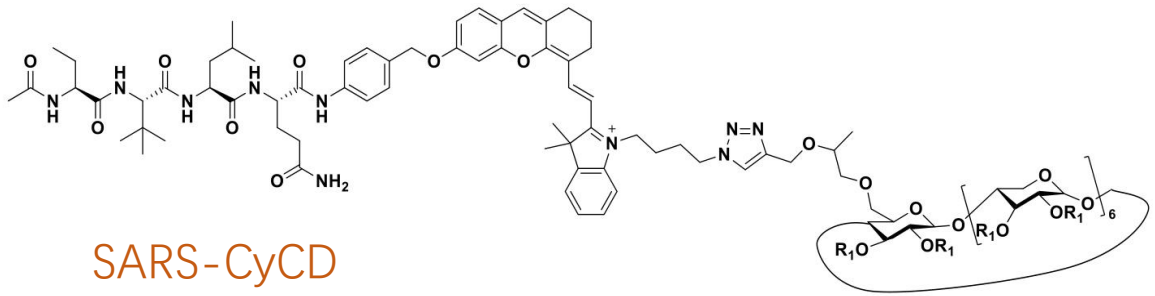


SARS(Trt)-Cy

三氟
乙酸

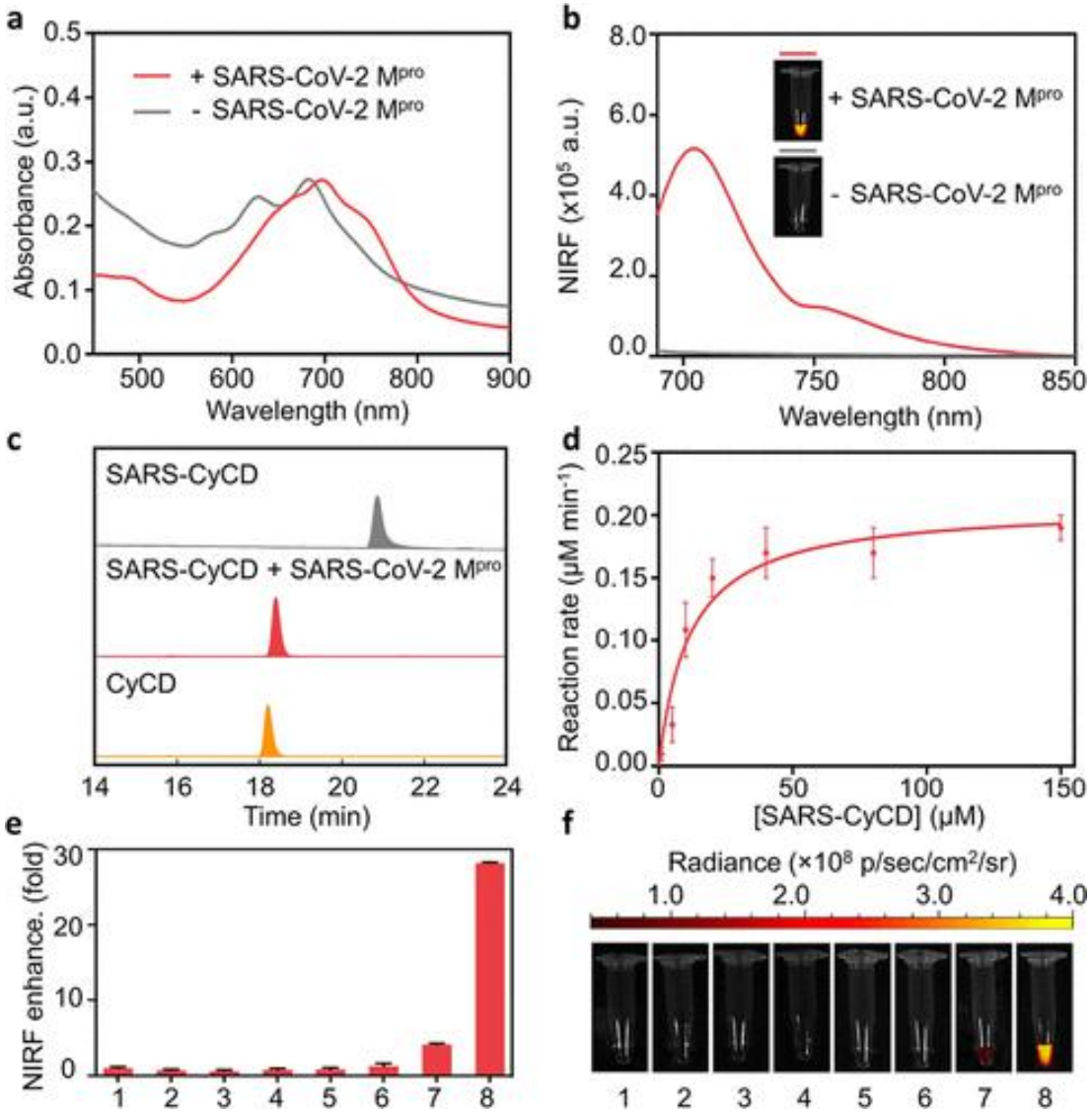


SARS-Cy



SARS-CyCD

In vitro characterization of SARS-CyCD

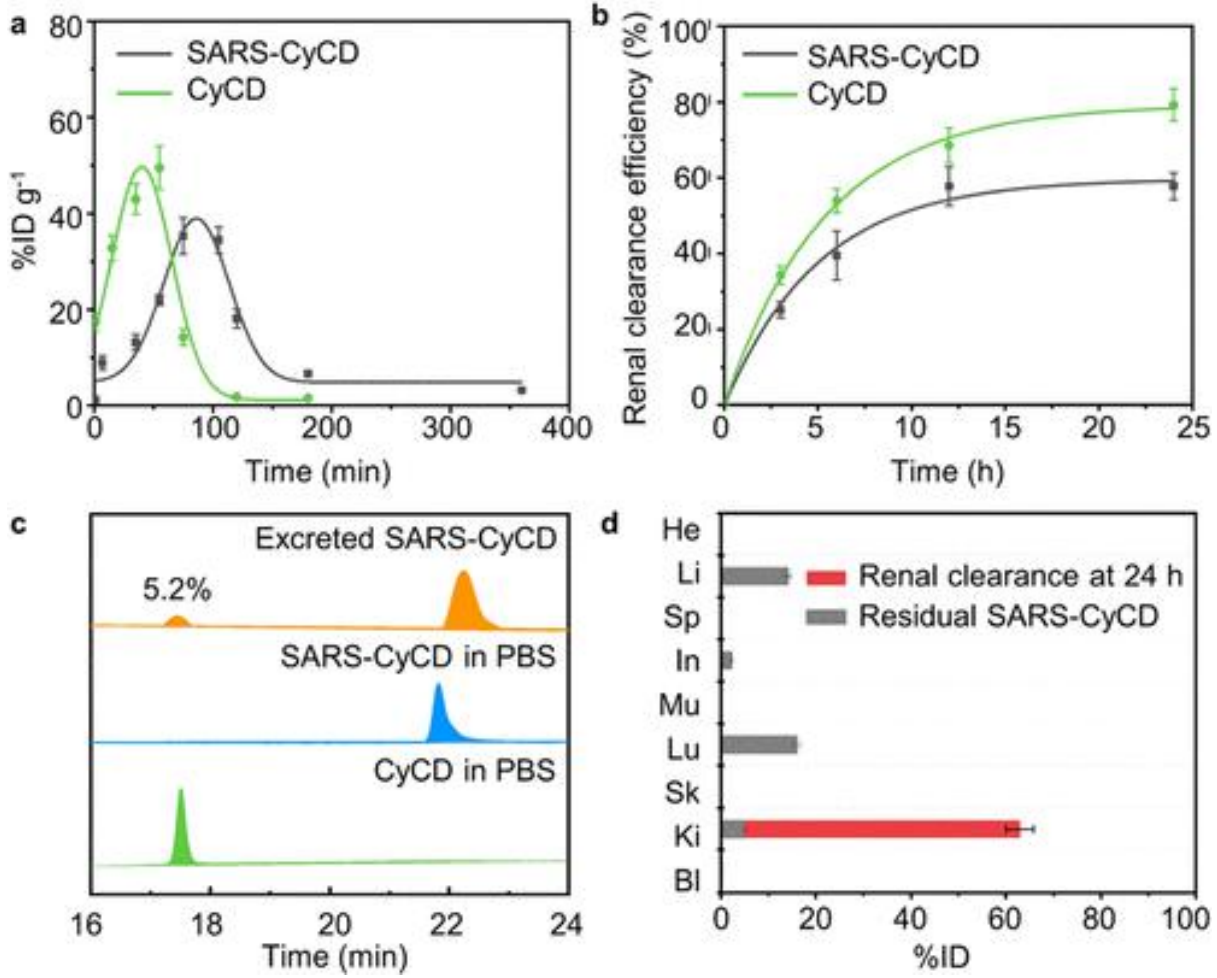


(1)体外表征其光学特性，HPLC证明SARS-CyCD成功裂解

(2)酶促反应动力学研究证明酶与底物具有较高亲和力

(3)SARS-CyCD与多种不同类型的蛋白酶反应，证明酶促反应的特异性

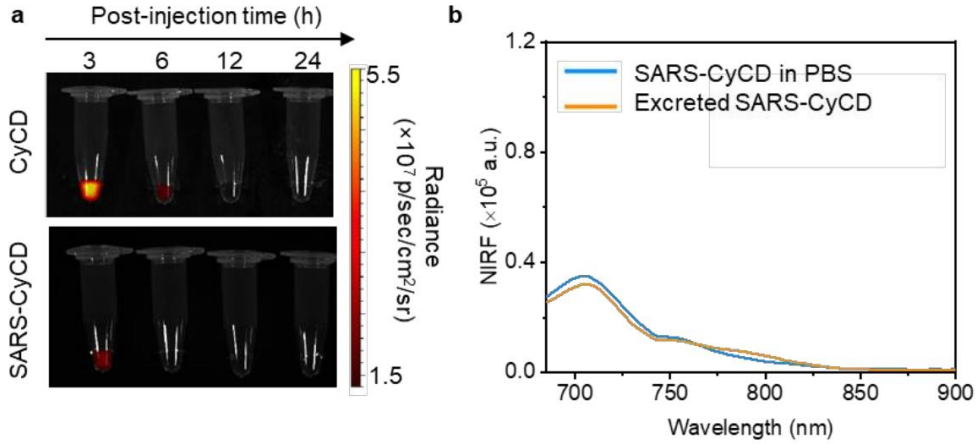
The pharmacokinetics of SARS-CyCD



结论：

（1）CyCD的消除速度和消除半衰期均快于SARS-CyCD

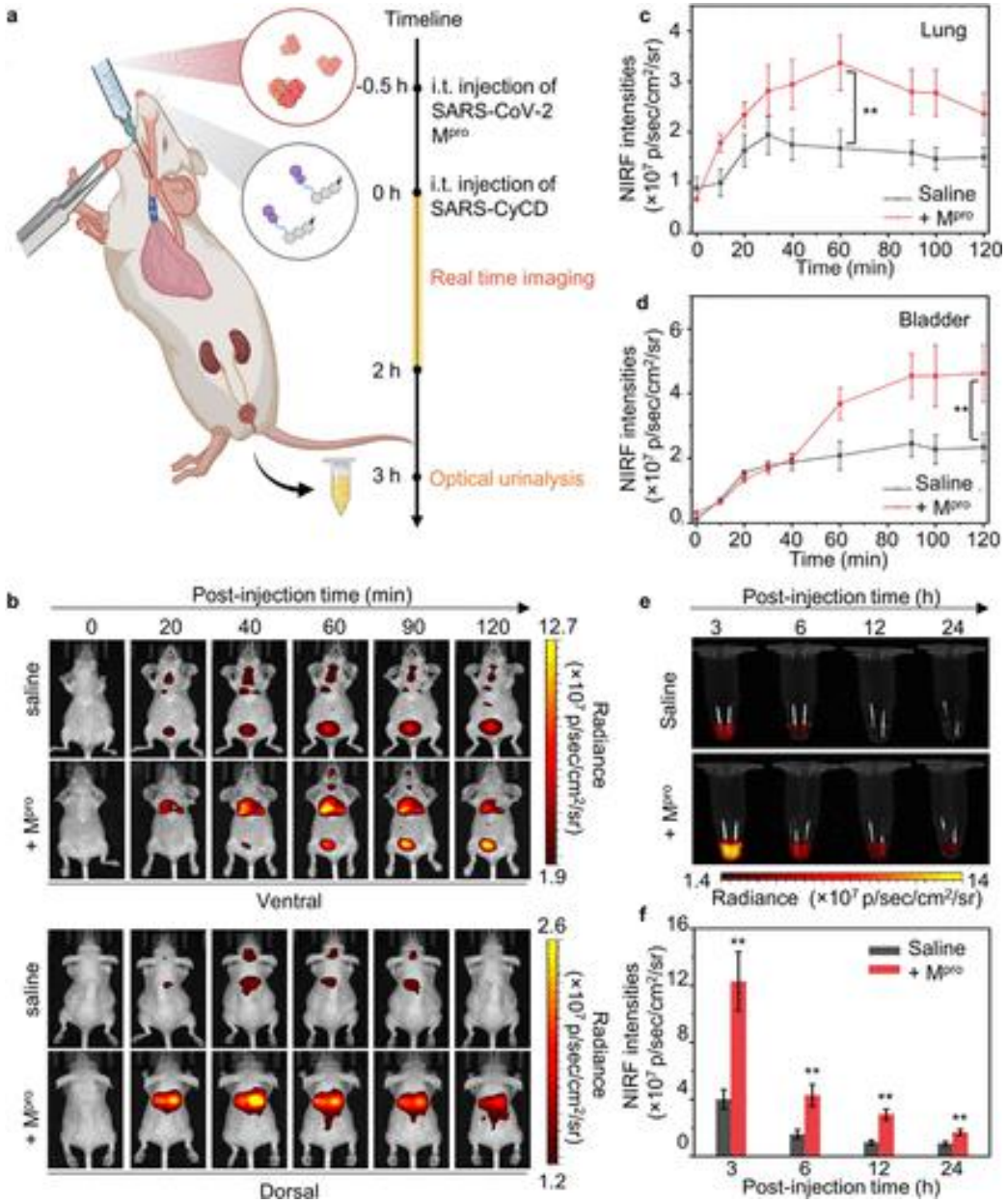
（2）CyCD的肾脏清除率高于SARS-CyCD.



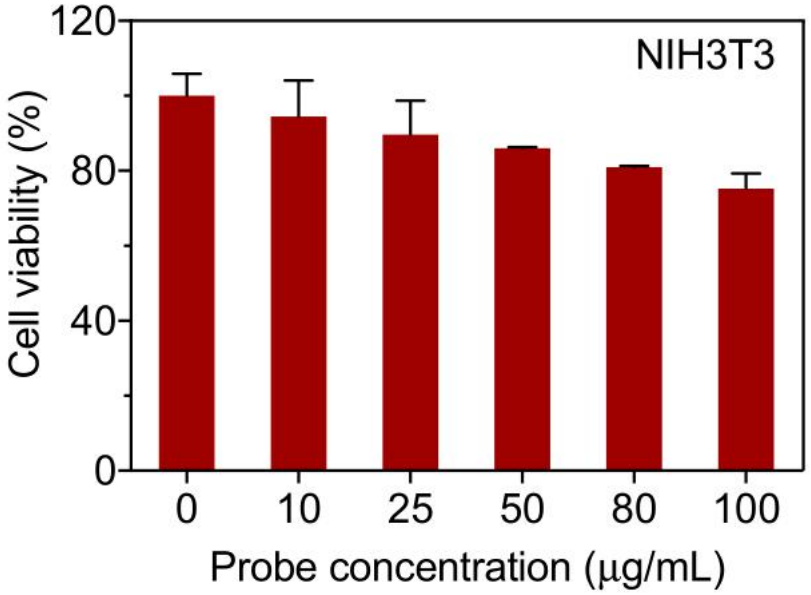
（3）尿液中排出的SARS-CyCD的荧光增强可以忽略不计，证明SARS-CyCD在活小鼠体内的代谢很少

（4）解剖小鼠发现体内少量残留的SARS-CyCD全部聚集在肺部(16%)，肝脏(14%）和肾脏(5%)，

In vivo detection of SARS-COV-2



细胞毒性检测



NIH3T3Cell

（1）证明基于SARS-CyCD的光学尿液分析特异性检测SARS-COV2感染的可行性。

（2）SARS-CyCD具有较好的生物相容性。

Summary

内容：

（1）提供了第一个能够实时、无创原位成像和尿检SARS-CoV-2感染的荧光探针

（2）由于该探针可以检测病毒蛋白酶，这种方法有可能在感染过程中直接监测病毒的复制活动，

创新：

在于体内原位成像及SARS-CyCD首次通过光学尿液分析检测SARS-COV-2感染的应用

展望：

SARS-CyCD可在呼吸机、气雾剂或便携式喷雾器的帮助下进一步发展成气雾喷剂，允许通过吸入给药。因此，SARS-CyCD可能代表了新一代基于吸入的covid-19尿液检测方法