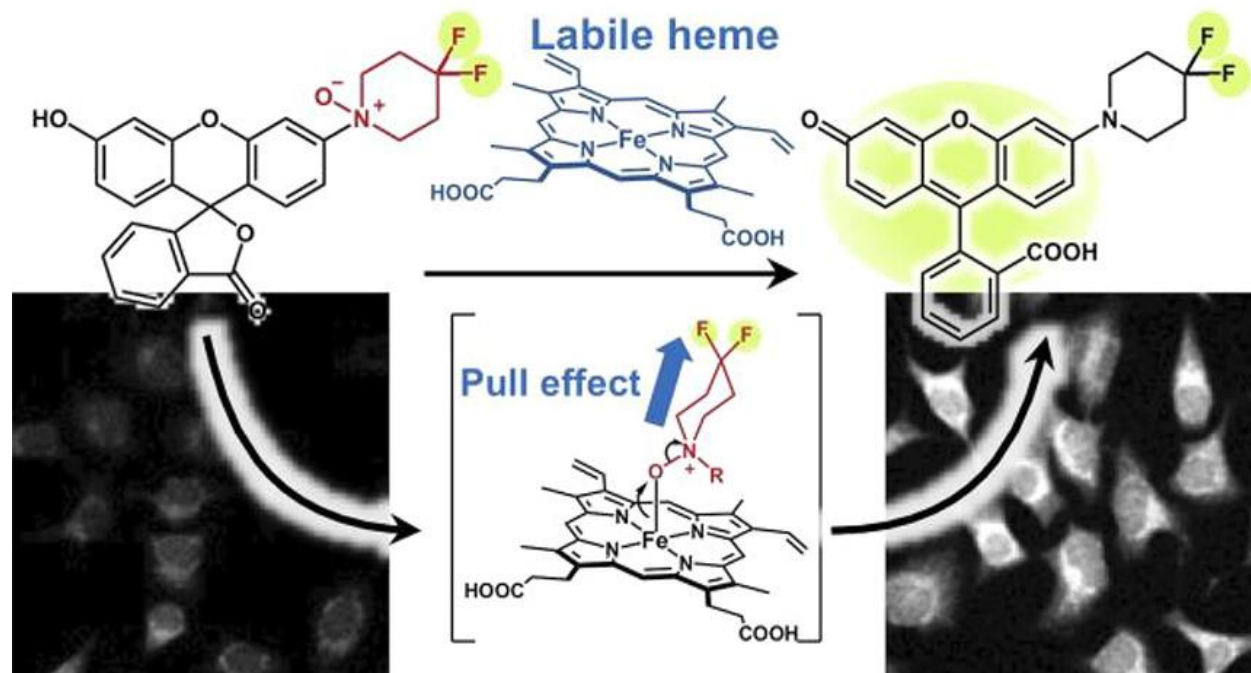


Literature Report

Reporter: 陶奕
Date: 2022-03-10

Molecular Imaging of Labile Heme in Living Cells Using a Small Molecule Fluorescent Probe

Kanta Kawai, Tasuku Hirayama,* Haruka Imai, Takanori Murakami, Masatoshi Inden, Isao Hozumi, and Hideko Nagasawa



Author Information



Tasuku Hirayama

Education:

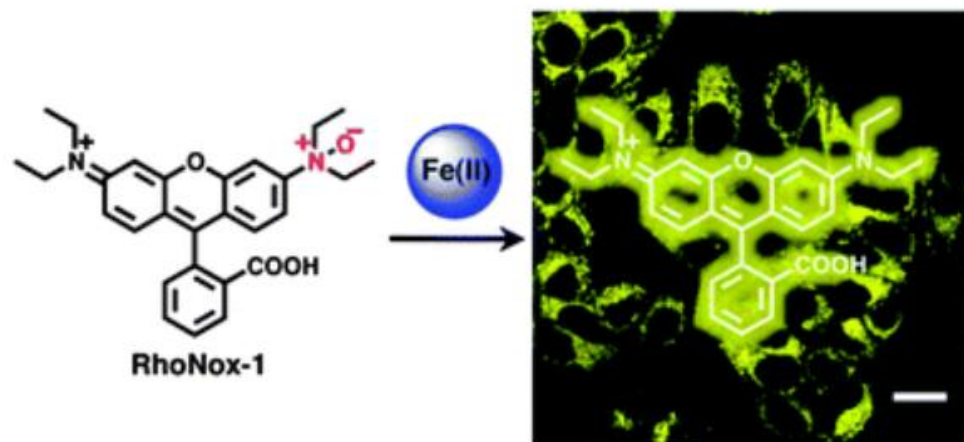
2004-2009 京都大学 硕博

2009.4-2010.9 University of California, Berkeley 博士后研究员

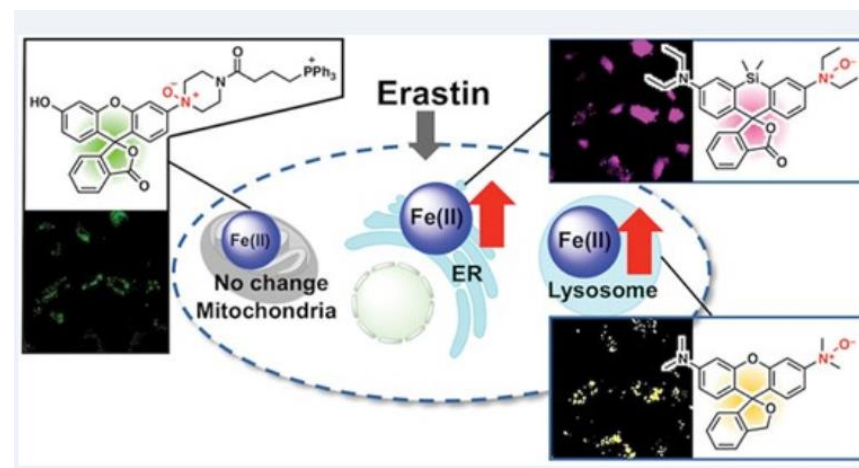
2010.10-2016.3 岐阜药科大学药化学研究室 助理教授

2016.4-现在 岐阜药科大学药化学研究室 副教授

主要研究内容：叔胺N-氧化物与Fe(II)之间会发生脱氧反应，可应用于一系列Fe²⁺选择性荧光探针。



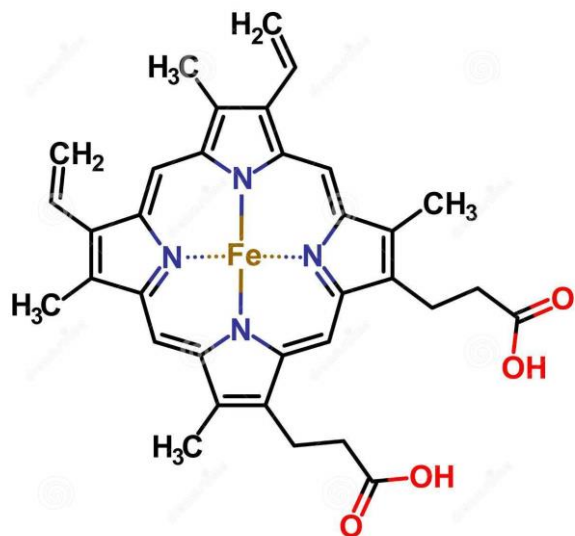
Chem. Sci., 2013,4, 1250-1256



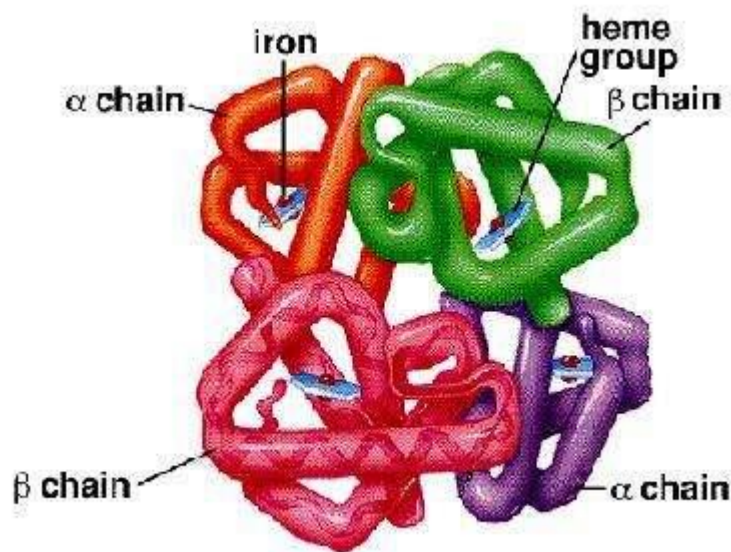
Metallomics 2019, 11 (1), 111– 117

Introduction

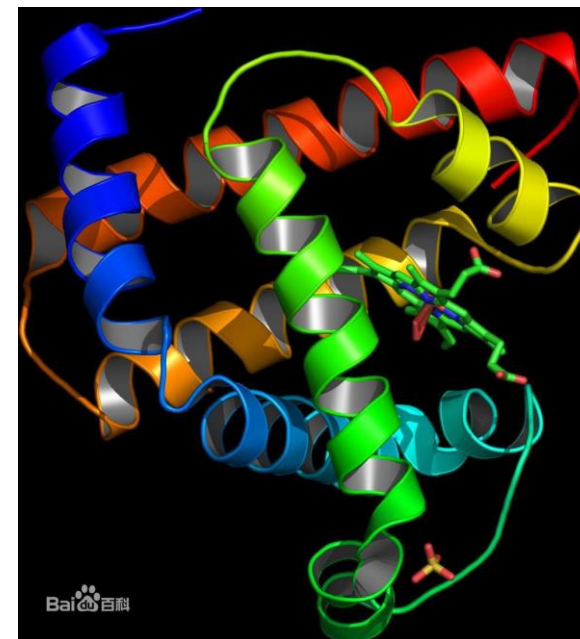
血红素 (Heme)



亚铁血红素



血红蛋白

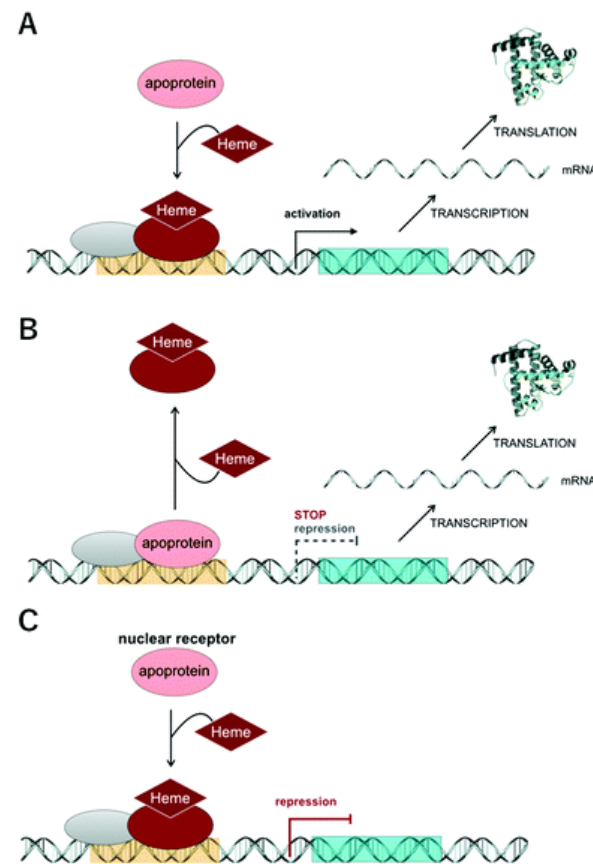
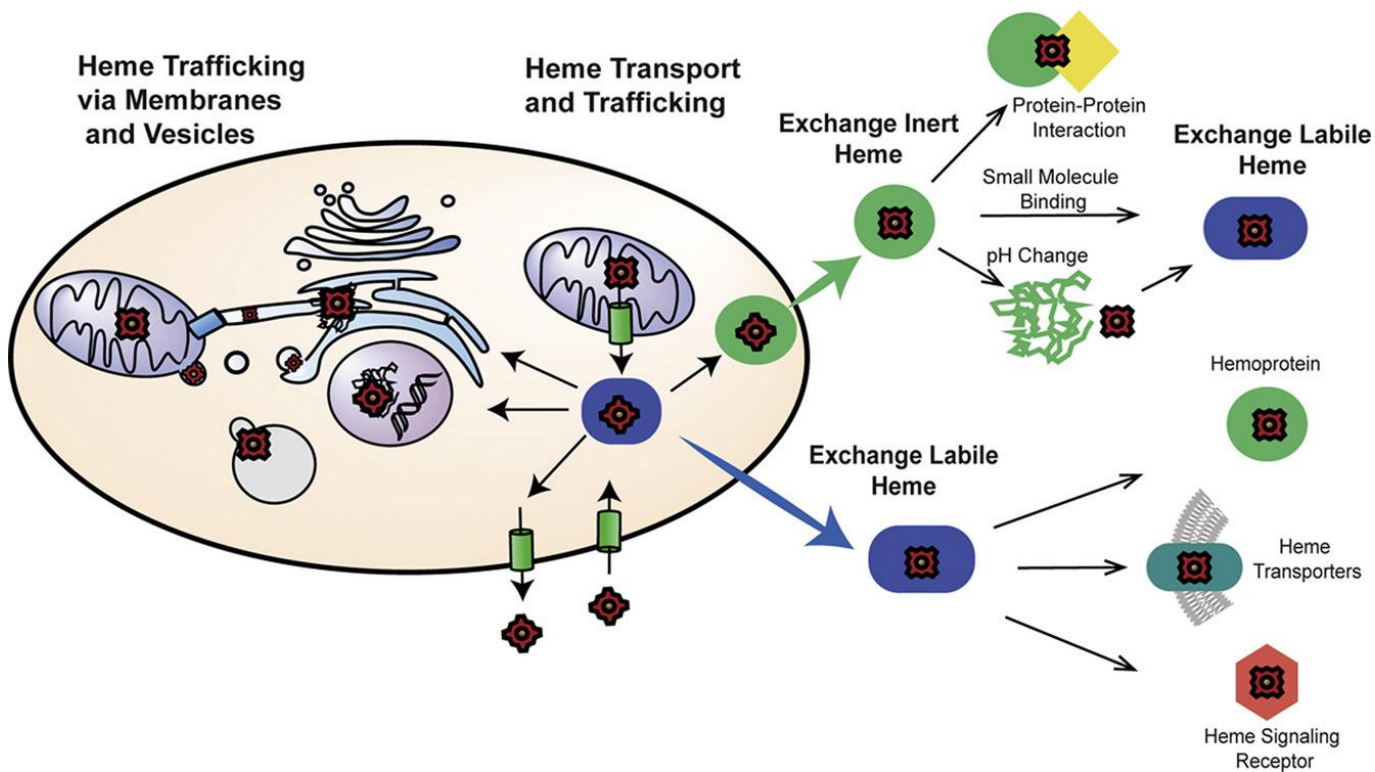


肌红蛋白

- 血红素：重要的蛋白质辅因子，生物系统利用血红素的氧结合特性和氧化还原活性，将血红素定位在高亲和力蛋白质中，以进行复杂的电子转移、氧输送和有效的酶促反应。

Introduction

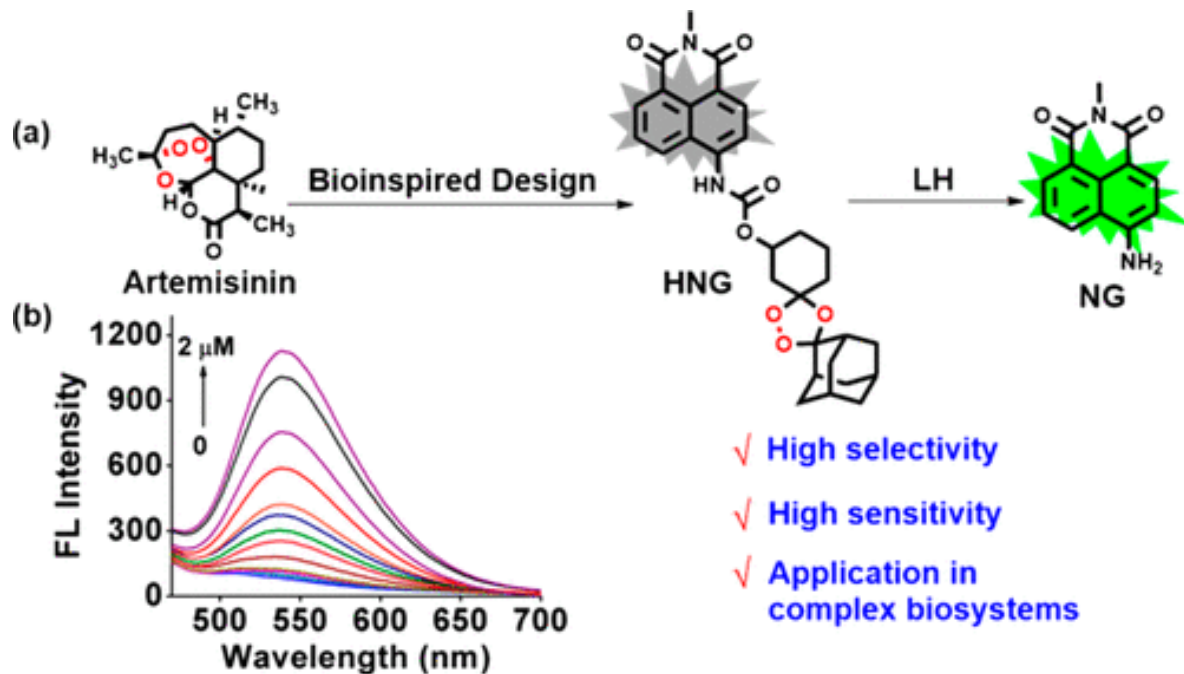
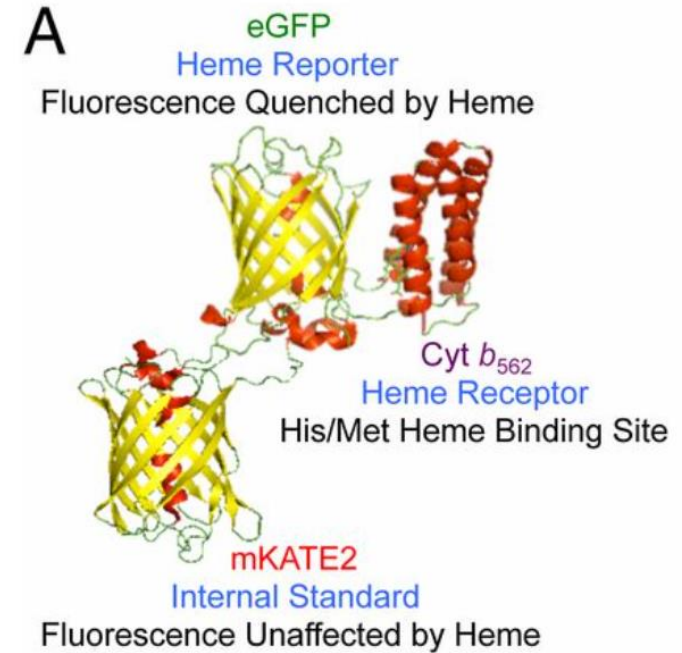
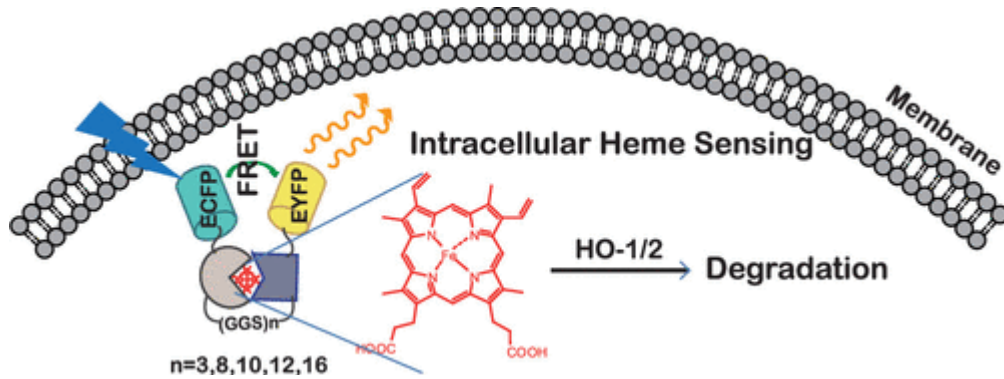
不稳定血红素 (LH)



- 惰性血红素：与蛋白质紧密结合，无法用于血红素的信号传递过程。
- 不稳定的血红素：与蛋白弱结合或以亚铁原卟啉IX复合物的形式参与各种生理过程，包括转录调节等，也会导致多种病理现象，包括血管内溶血、卟啉症等。

Problem

血红素探针



- 需要基因操作和探针的过表达；
- 可能会清除LH破坏血红素体内平衡；
- 反应速率较慢。

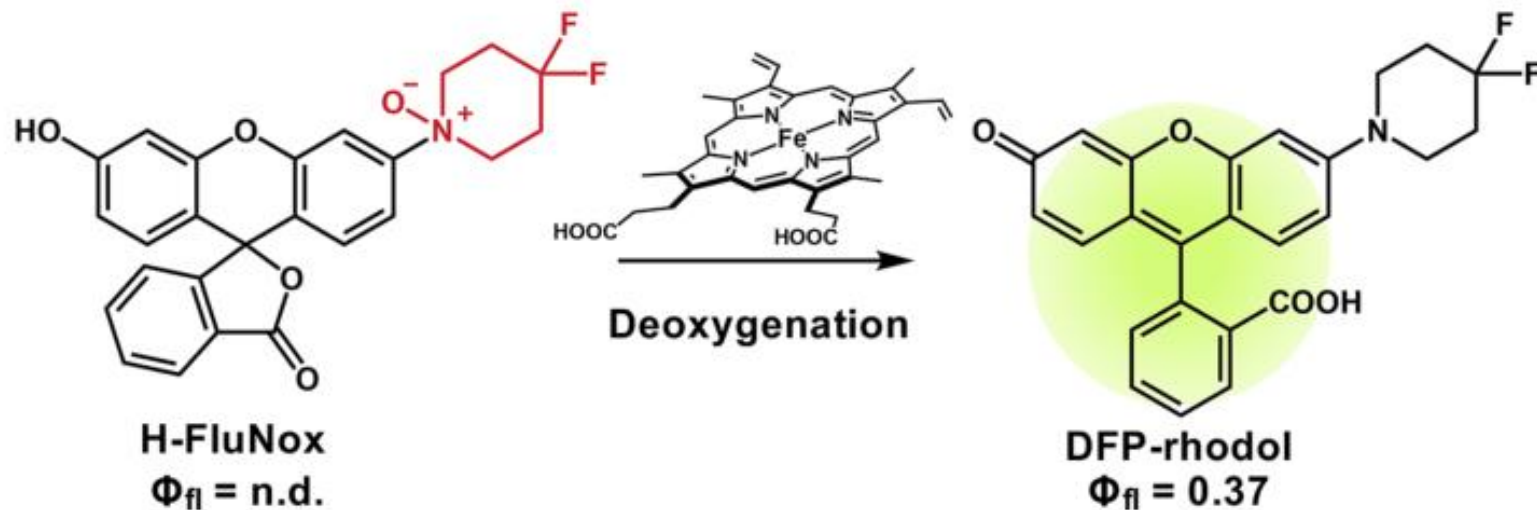
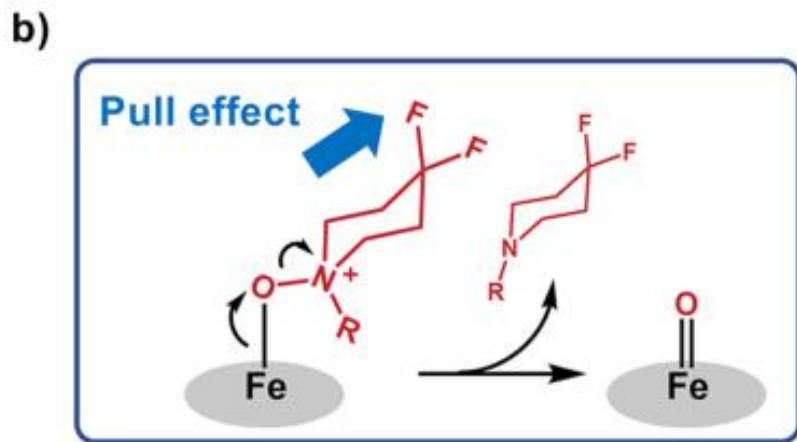
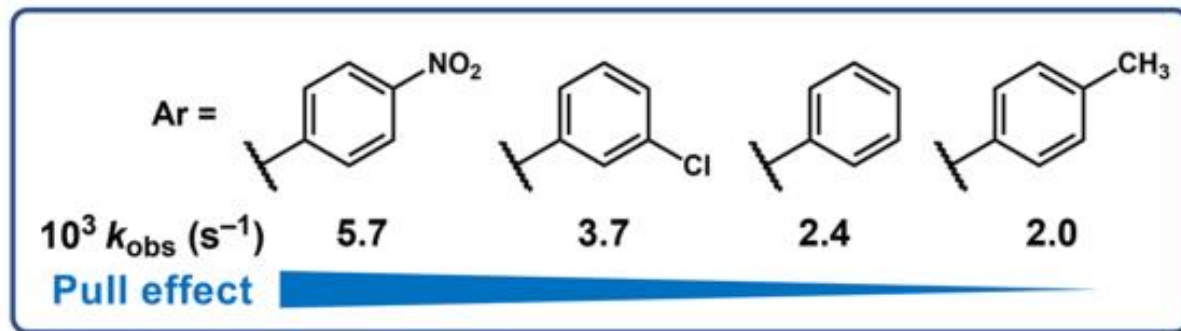
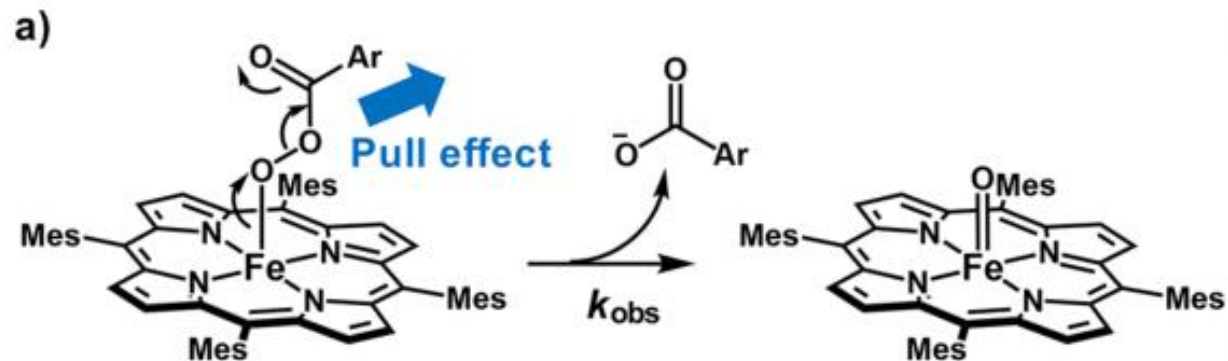
J. Am. Chem. Soc. 2020, 142, 5, 2129–2133

ACS Chem. Biol. 2015, 10, 7, 1610–1615

Proc. Natl. Acad. Sci. U. S. A. 2016, 113 (27), 7539–7544

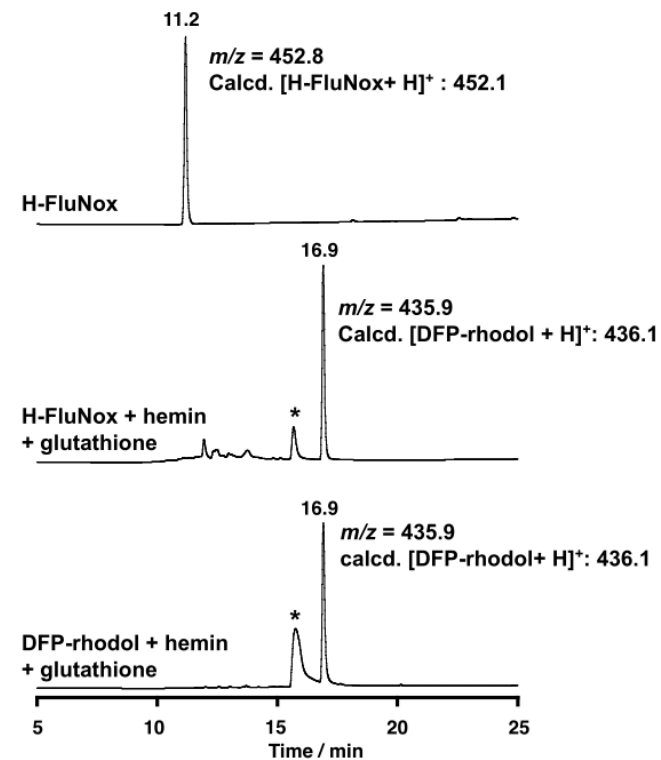
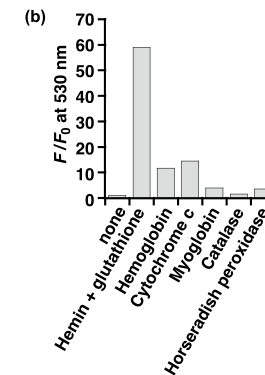
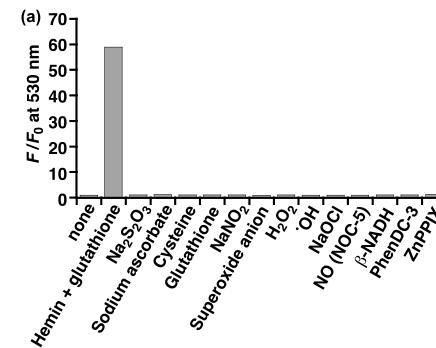
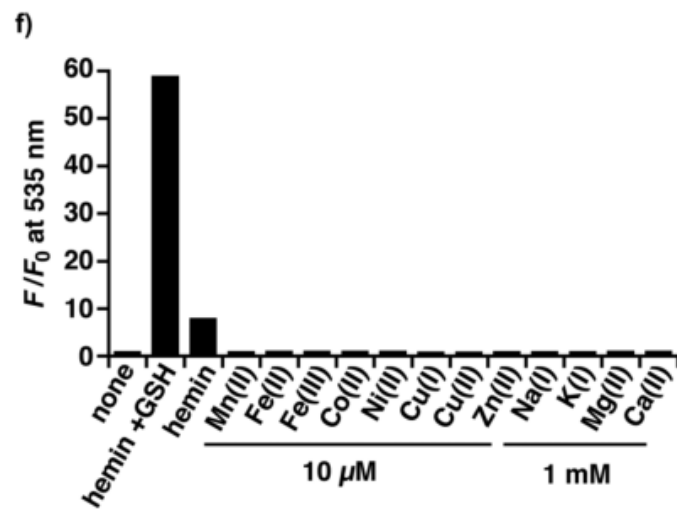
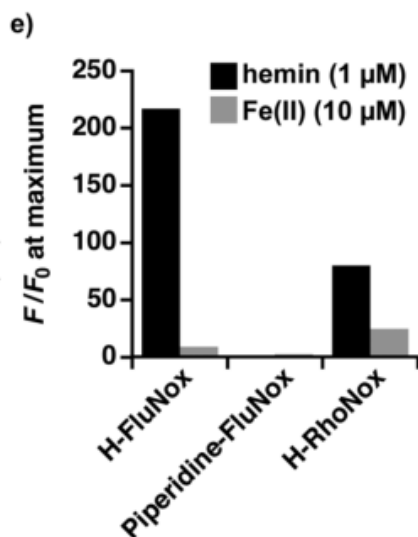
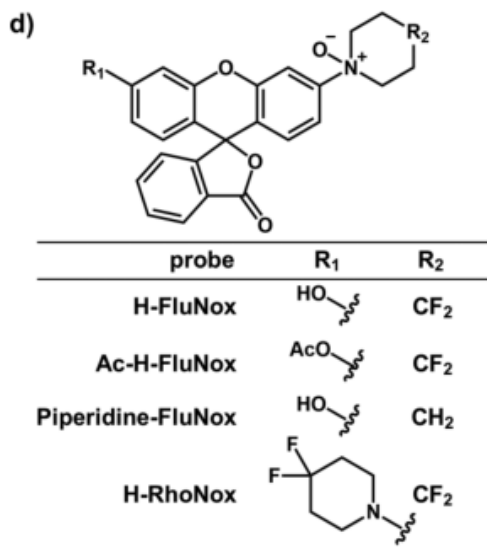
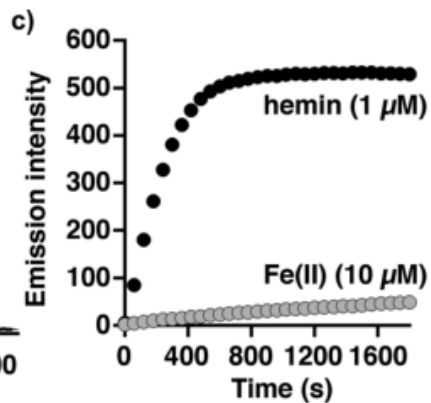
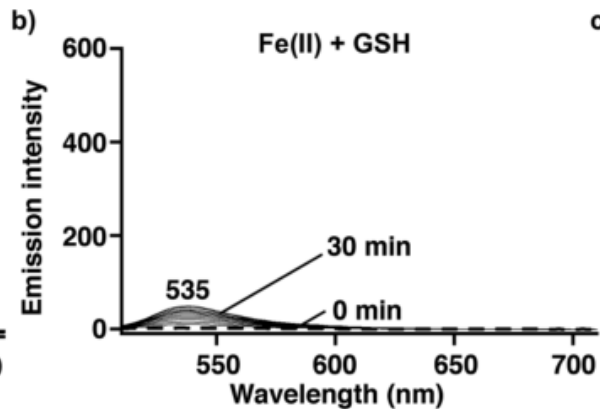
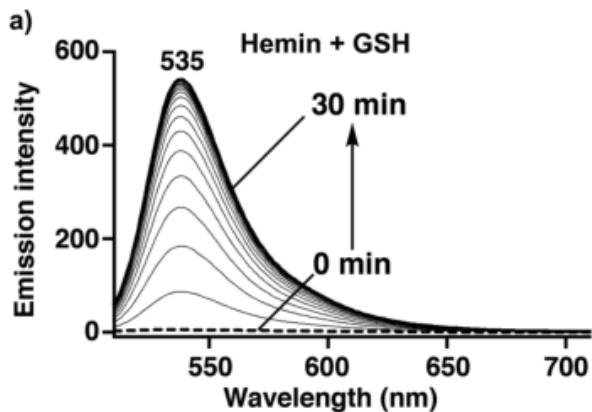
Result and Discussion

LH选择性探针的设计原理



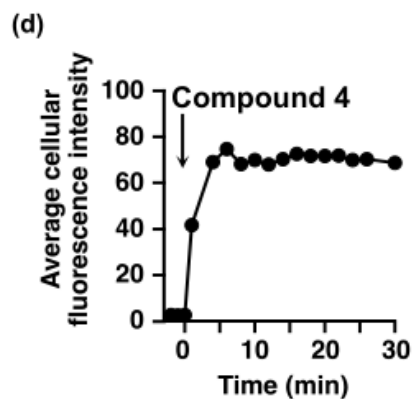
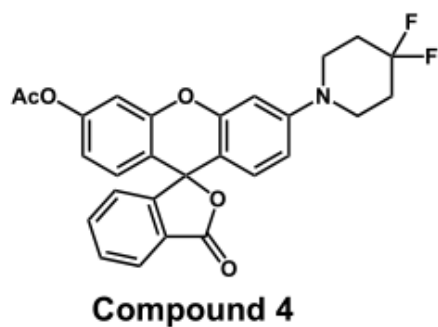
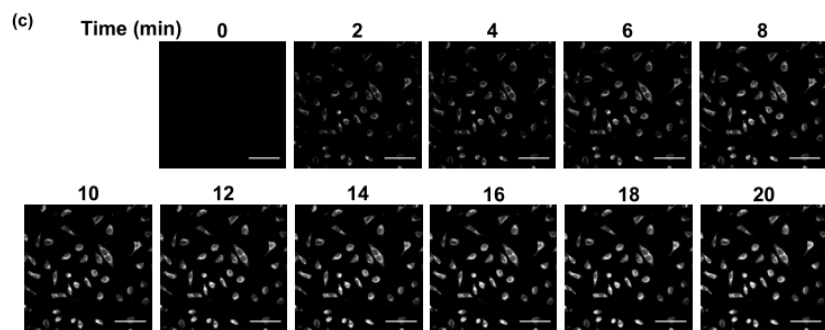
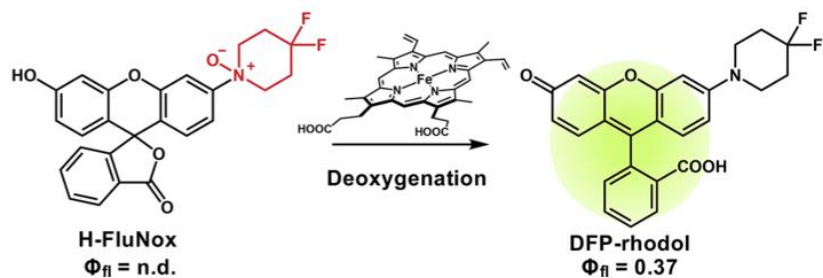
Result and Discussion

测试探针的反应性和选择性

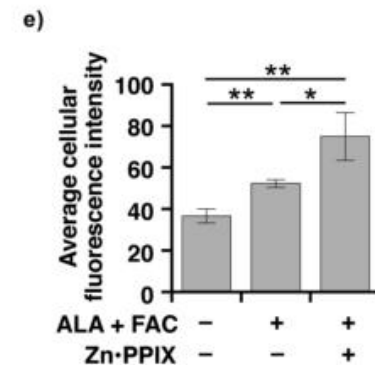
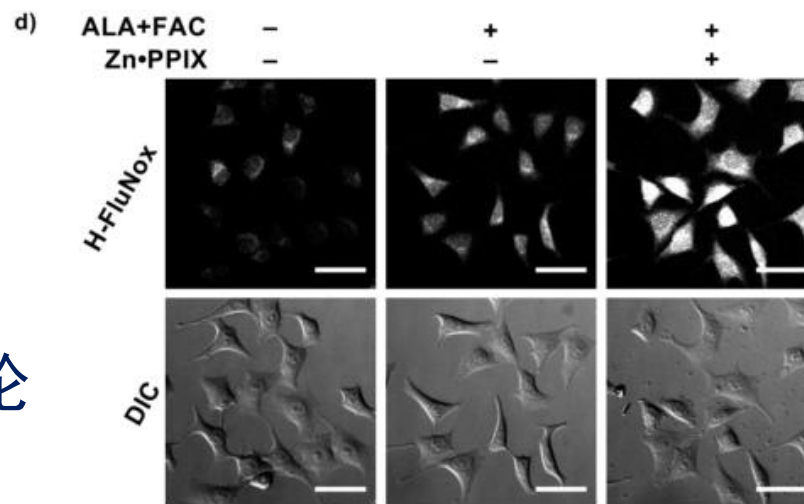
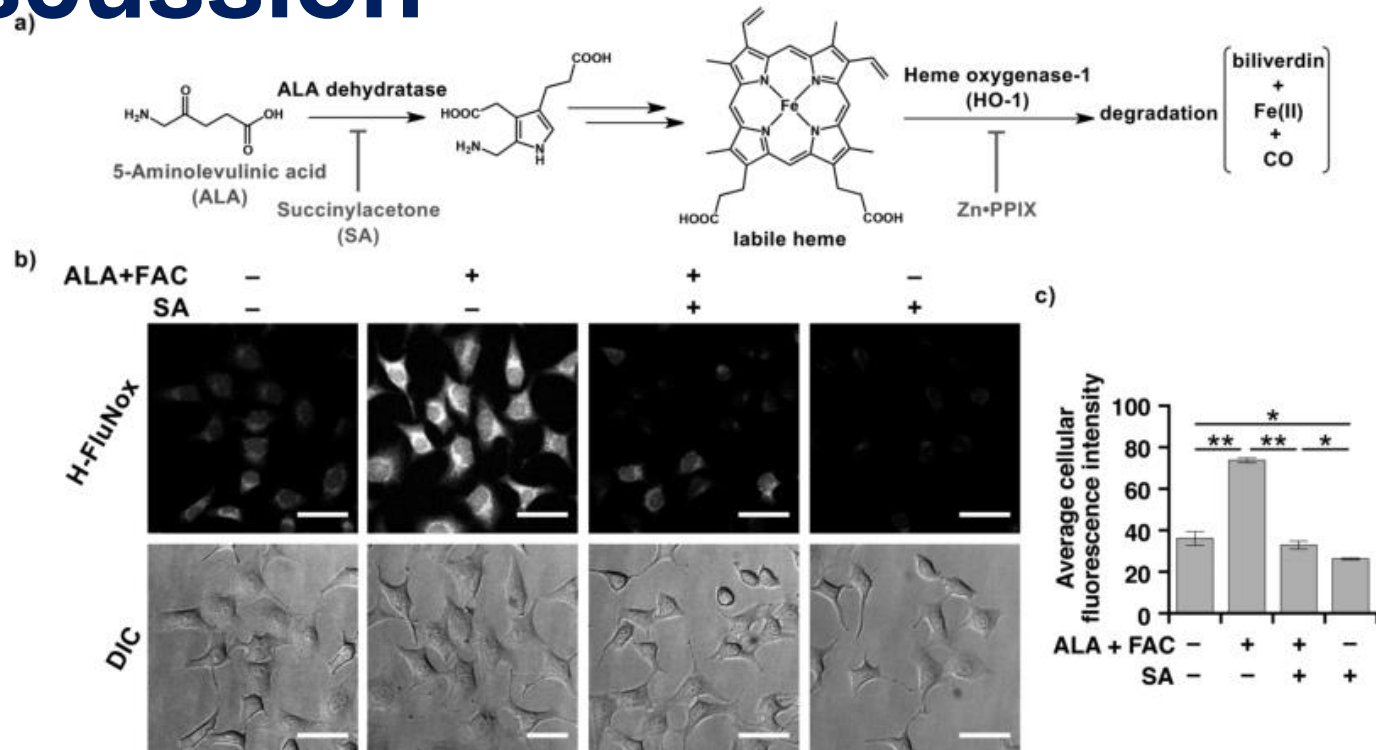


Result and Discussion

探针探测活细胞中LH的变化

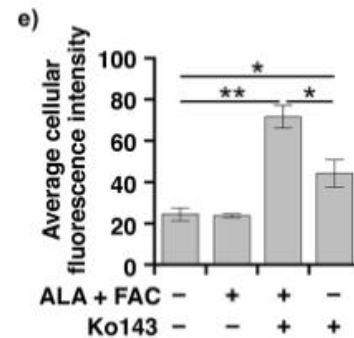
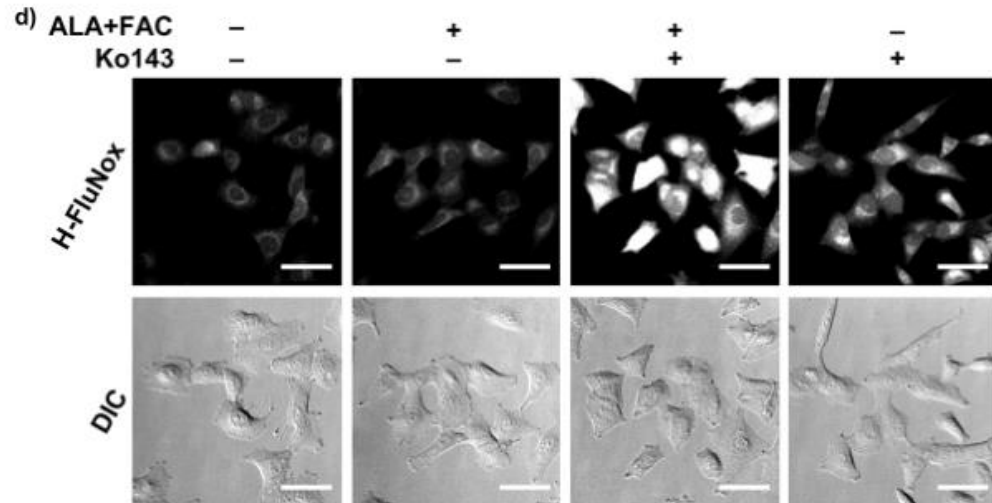
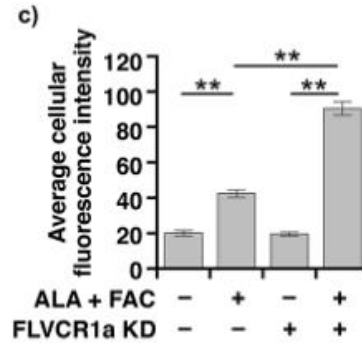
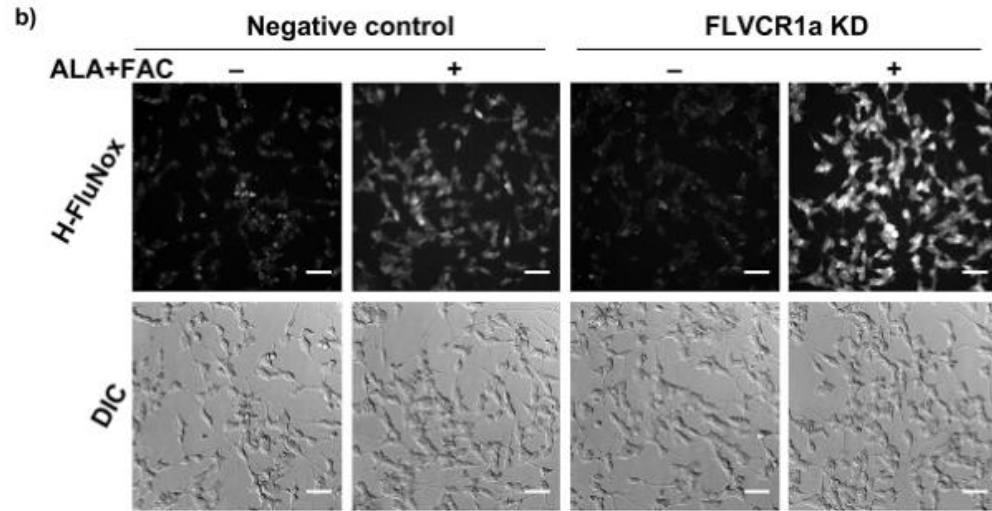
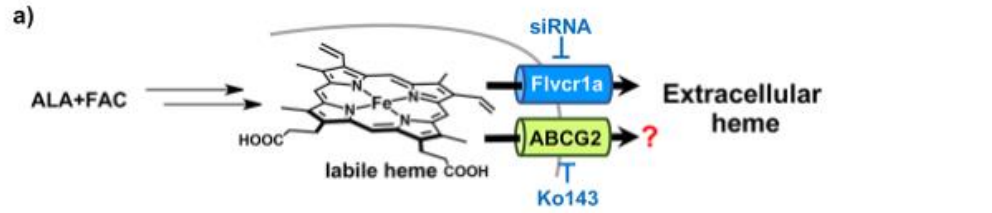


➤ 选择性地检测细胞内LH水平，不论是升高或是降低。





Result and Discussion 抑制血红素输出物检测LH的积累

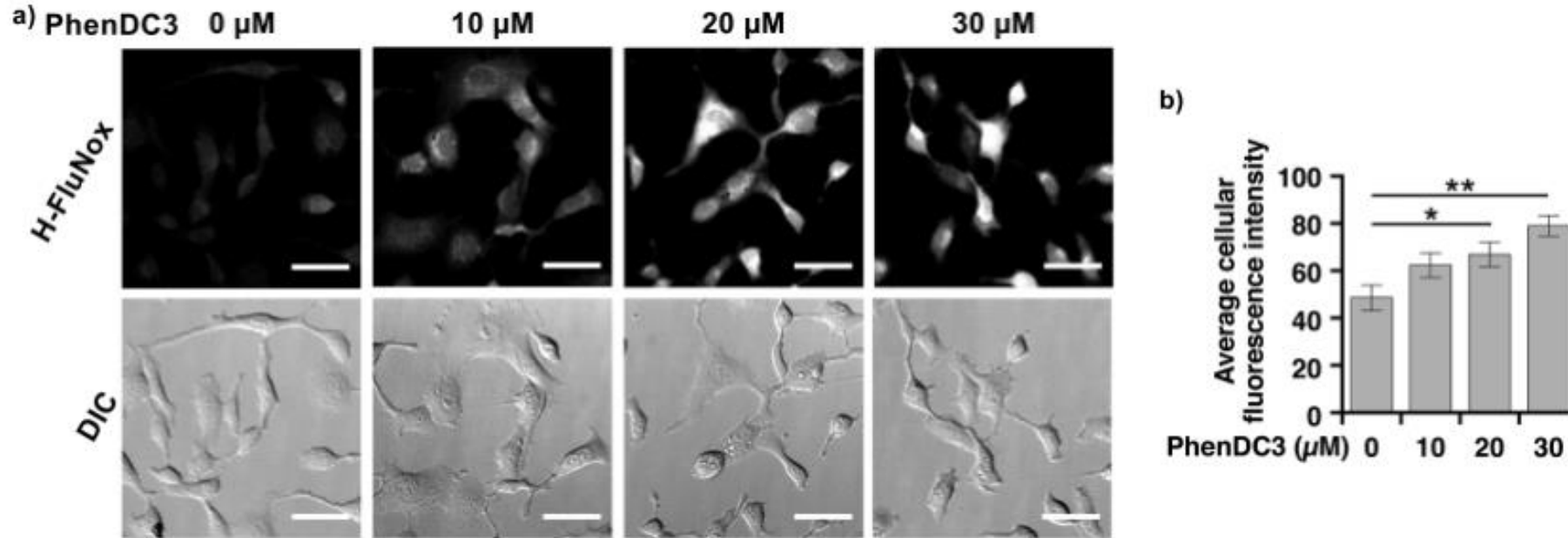


➤ ABCG2具有部分血红素输出活性，是一个局部的血红素输出者。



Result and Discussion

检测LH从G-四链体的释放

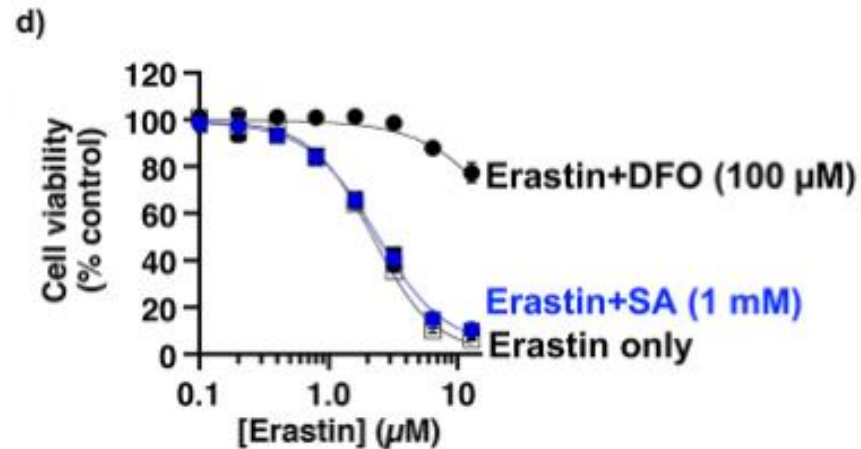
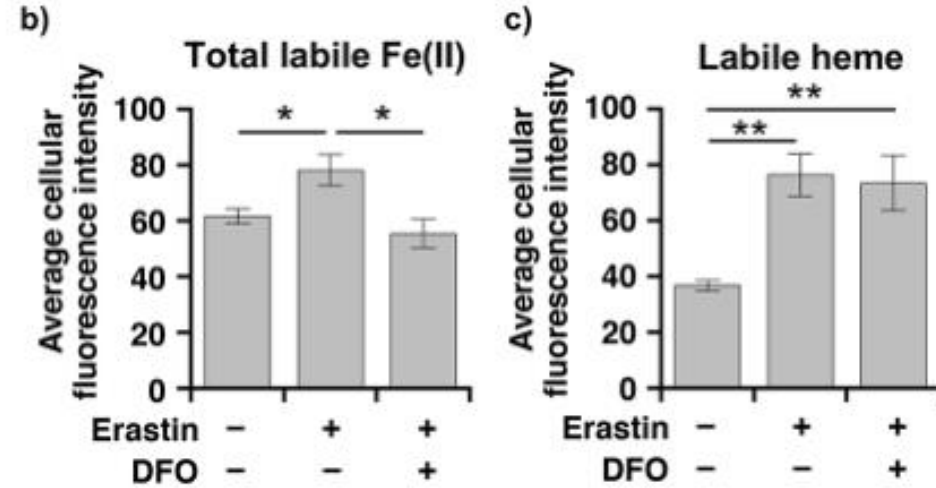
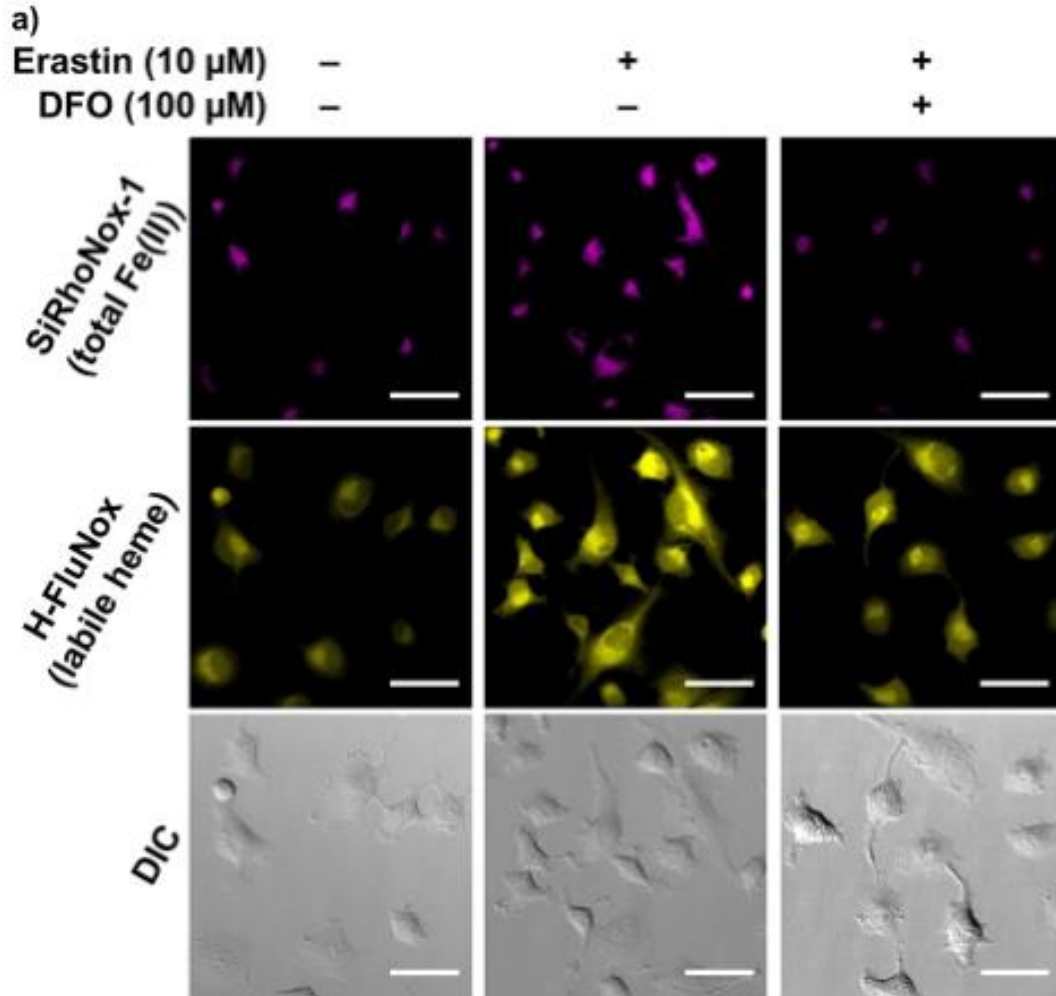


- PhenDC3促进G-四链体释放LH，从而提高细胞内LH水平。
G-四链体是细胞内LH储存池的候选物。



Result and Discussion

检测铁死亡时的LH水平



- 在铁死亡时，无论是不稳定的亚铁离子还是LH的水平都会升高，表明血红素参加了铁死亡。

Conclusion

➤ 分子设计:

血红素对氮氧化物的仿生脱氧作用，引入强吸电子基团促进脱氧作用。

➤ 应用:

揭示了血红素输出者和血红素库的两个重要方面。

- ① ABCG2作为部分血红素输出者。
- ② G-四链体是参与亚细胞LH储存池的生物分子的候选物。
- ③ 揭示了在铁死亡时LH和Fe(II)的升高，表明血红素物种参与了铁死亡。

➤ 展望:

对于探索细胞如何控制亚细胞血红素水平和分布提供了一个起点，并将潜在地有助于广泛的研究领域，包括病理学，生理学，植物生物学和生理学。

