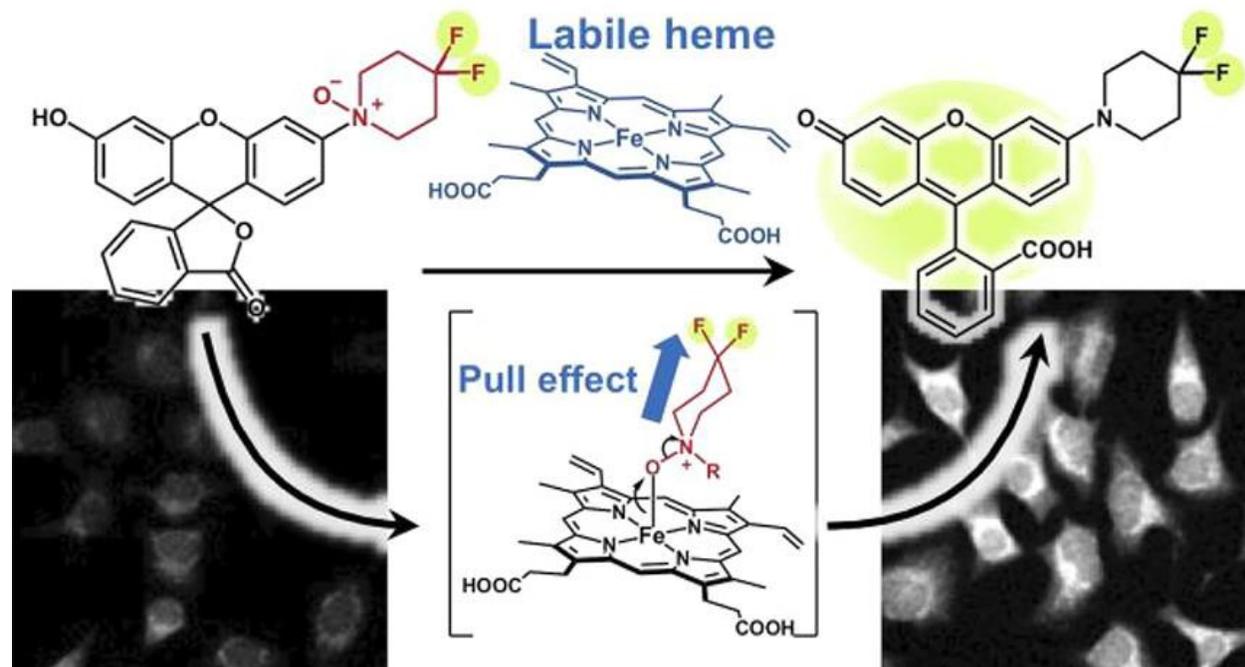


Literature Report

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



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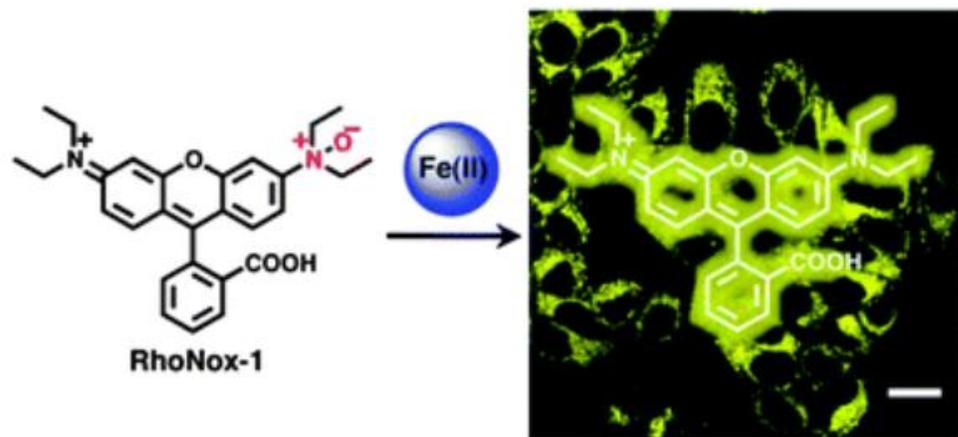
2004-2009 京都大学 硕博

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

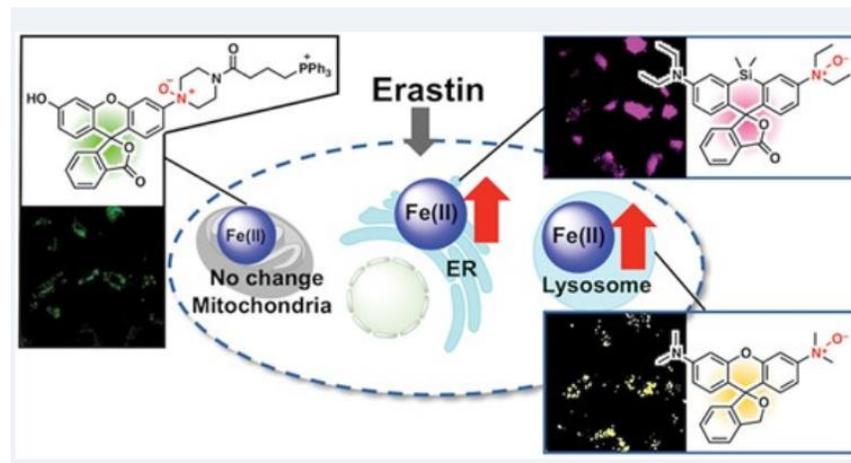
2010.10-2016.3 岐阜药科大学药化学研究室 助理教授

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。



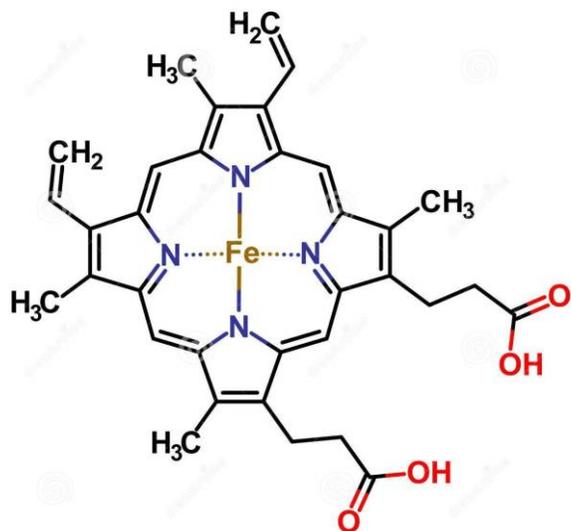
Chem. Sci., 2013,4, 1250-1256



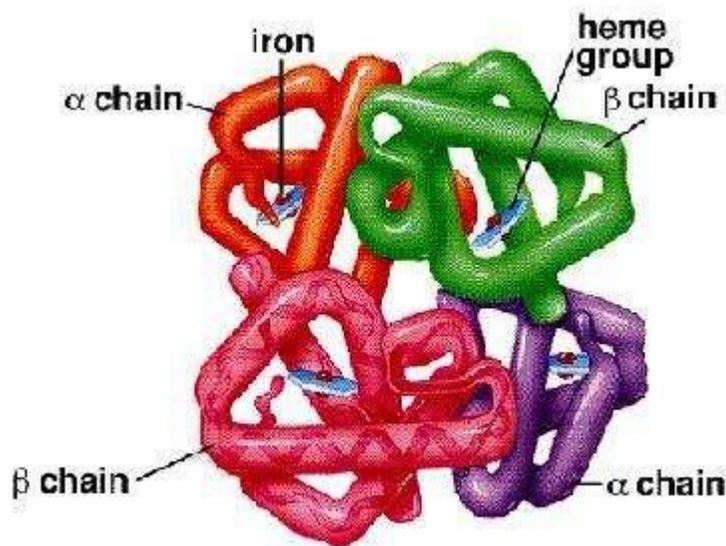
Metallomics 2019, 11 (1), 111– 117

Introduction

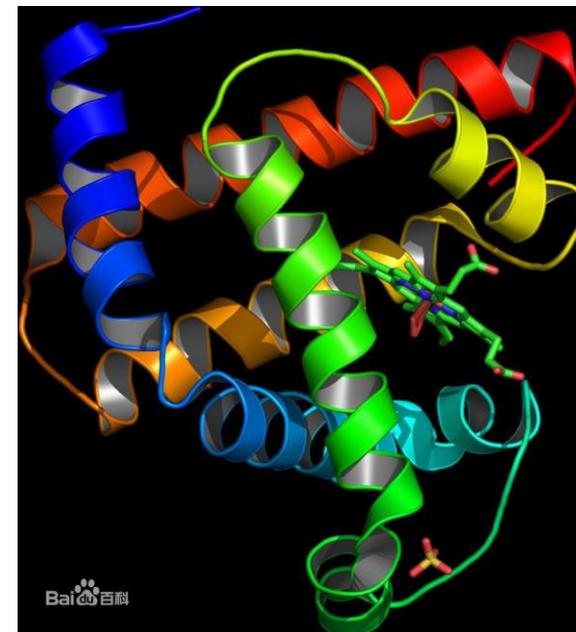
血红素 (Heme)



亚铁血红素



血红蛋白

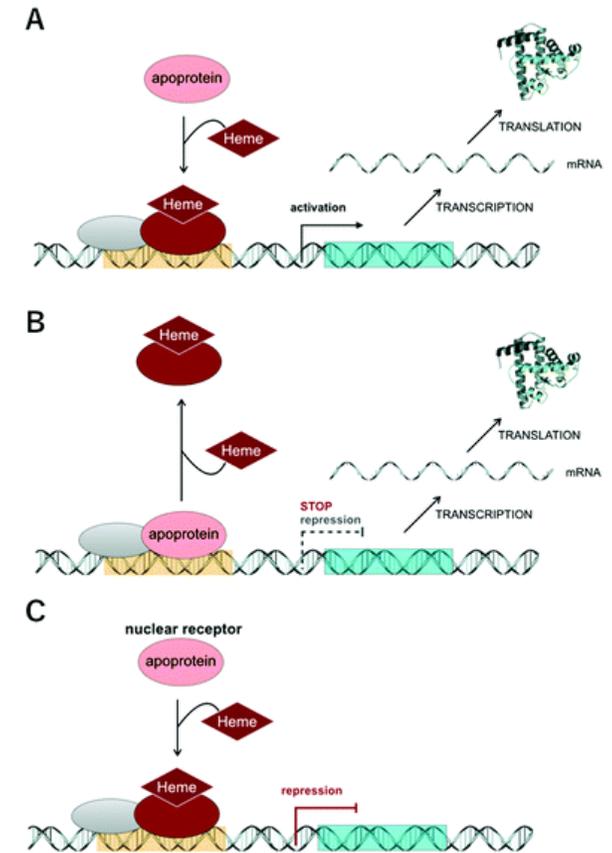
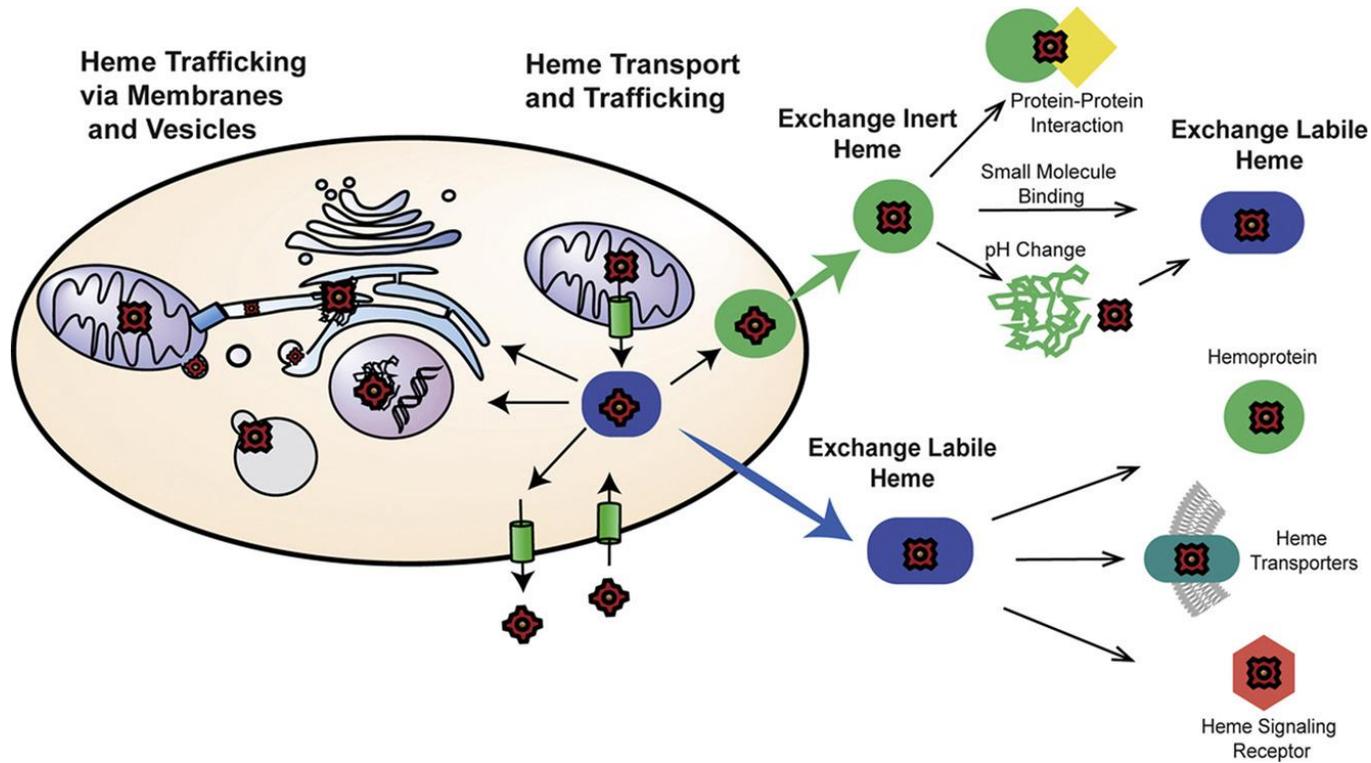


肌红蛋白

- 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

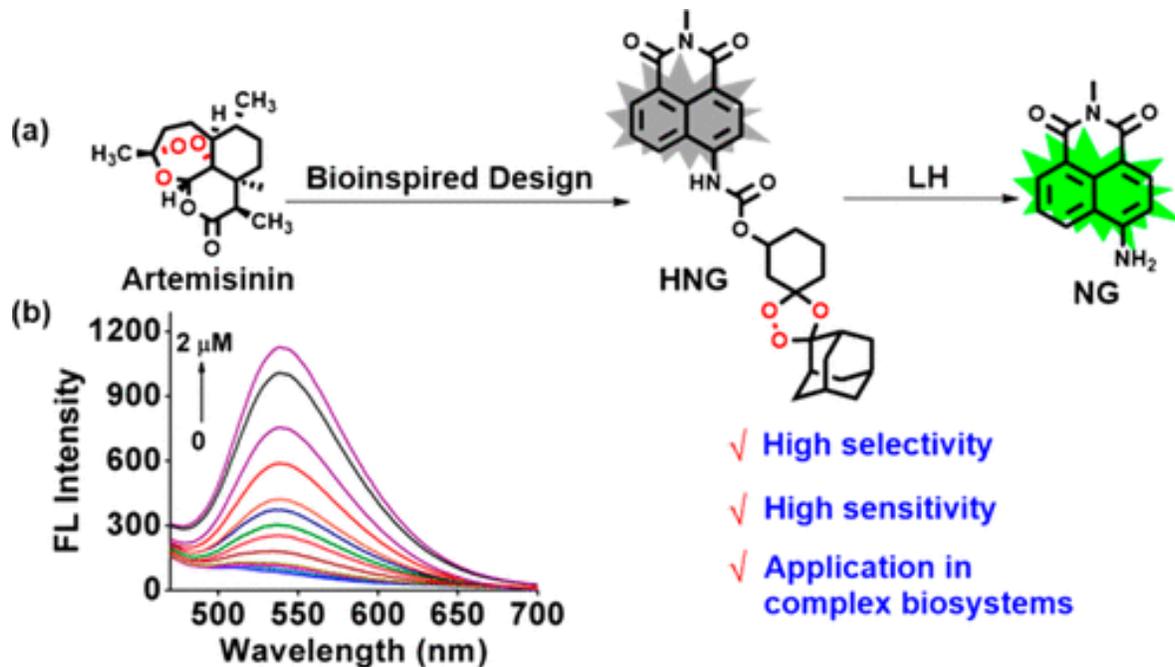
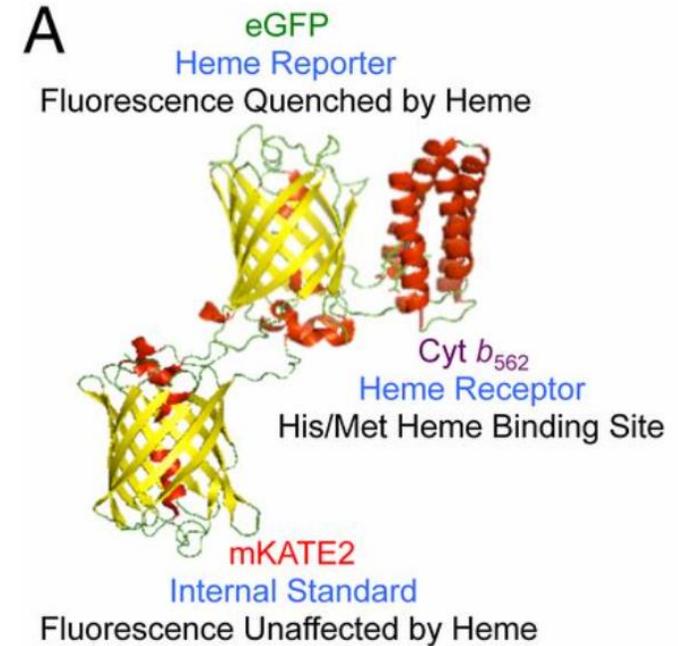
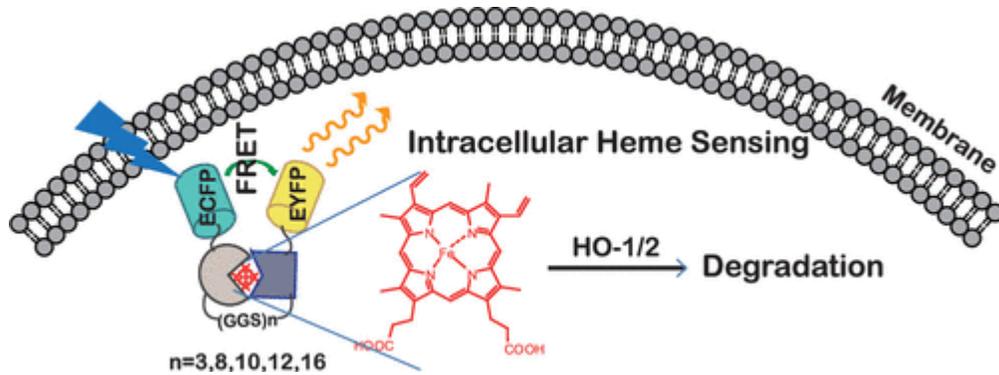
不稳定血红素 (LH)



- 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。

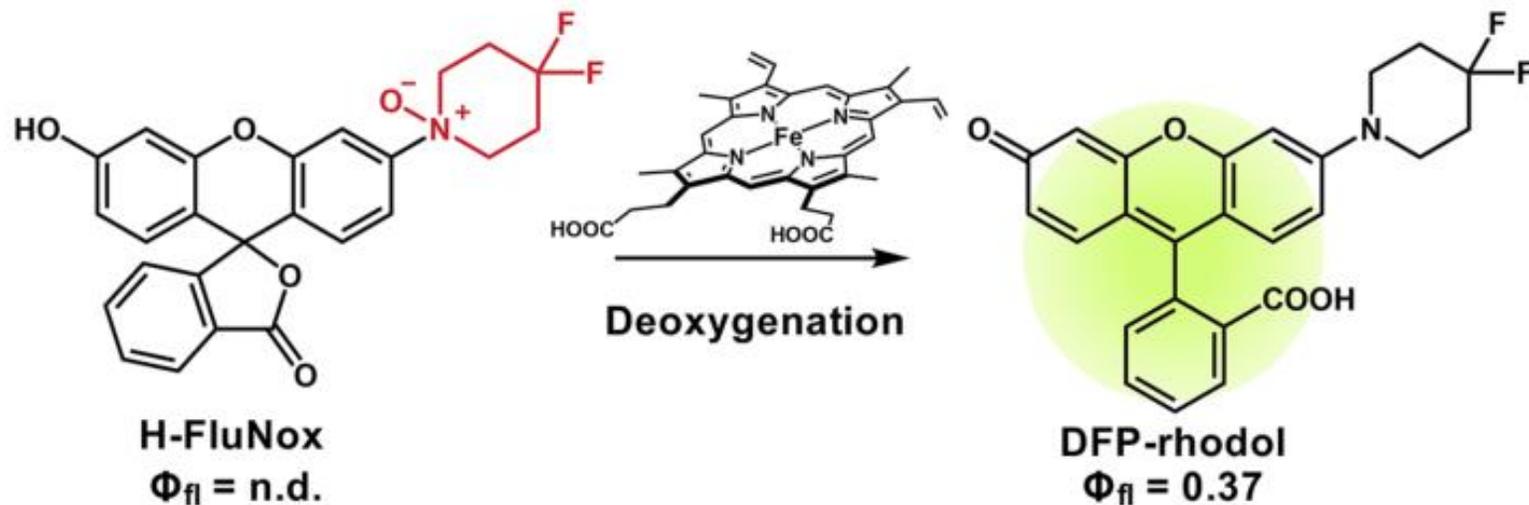
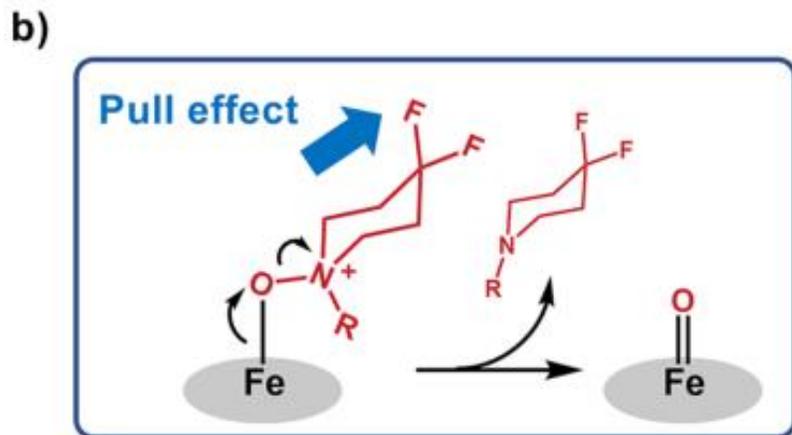
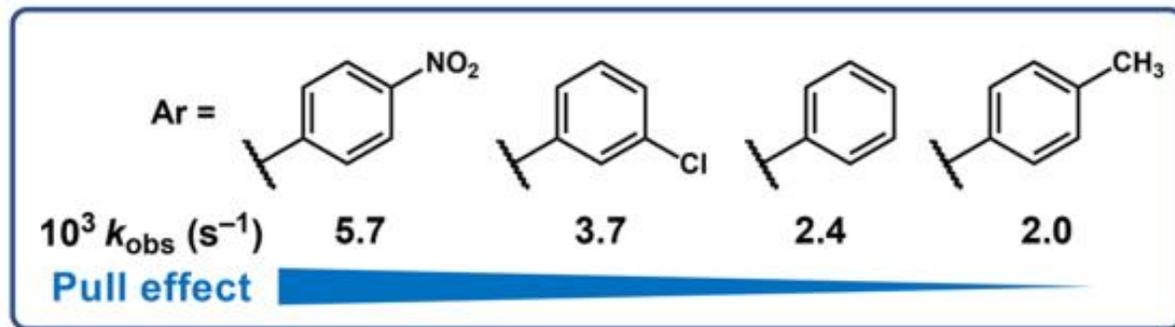
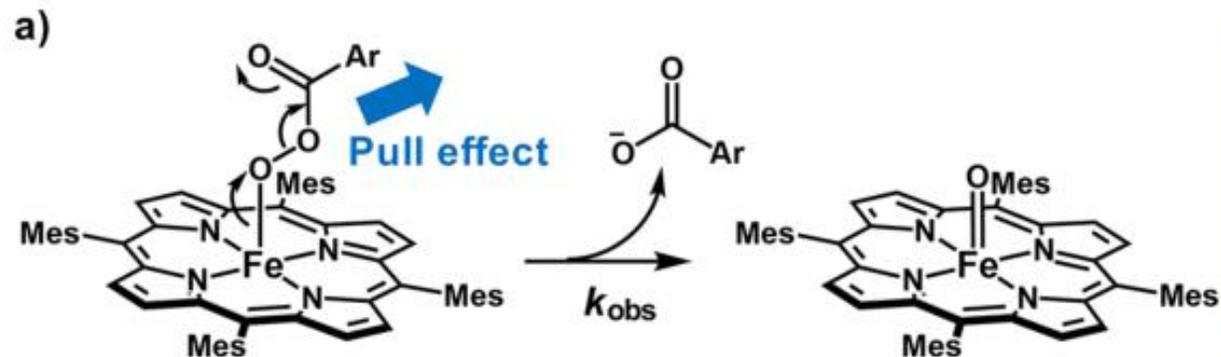
J. Am. Chem. Soc. 2020, 142, 5, 2129–2133

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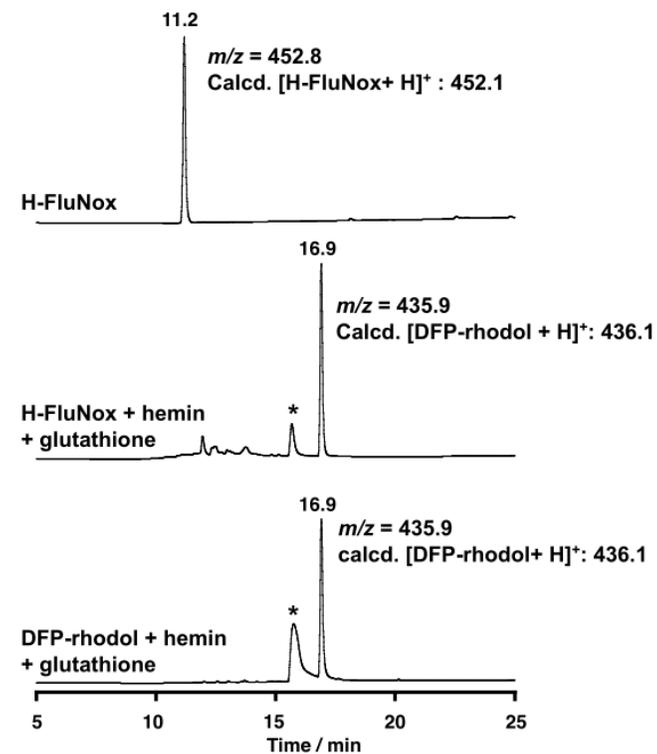
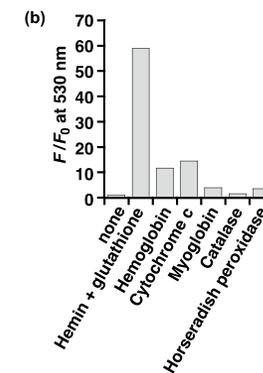
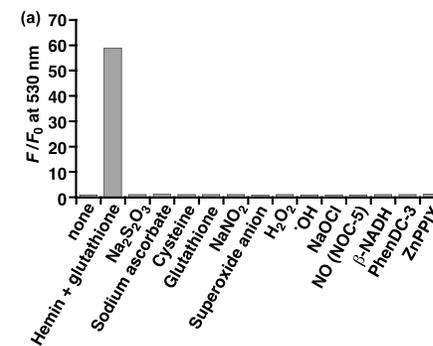
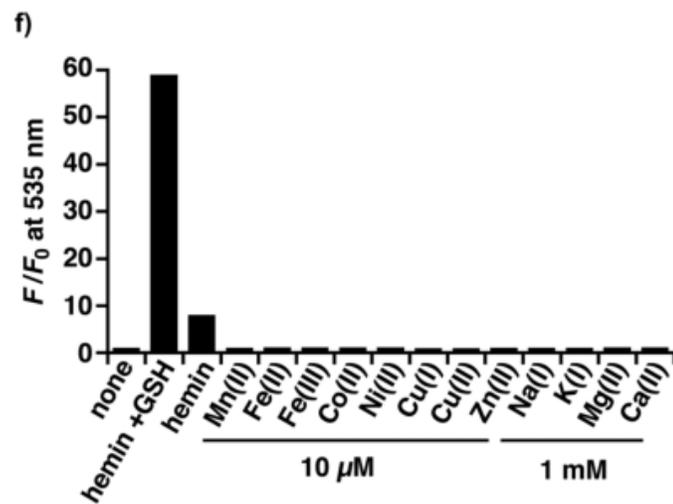
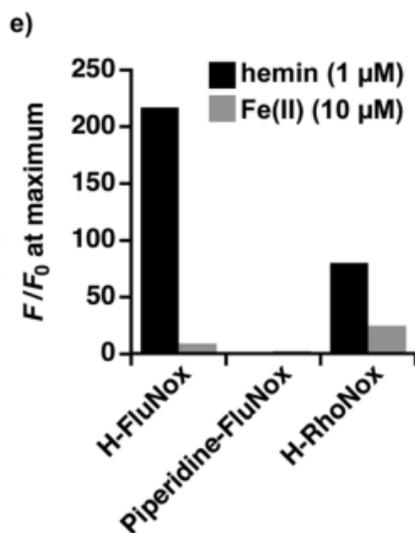
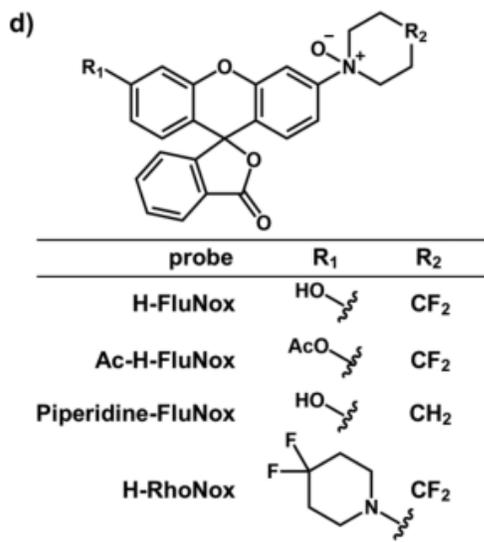
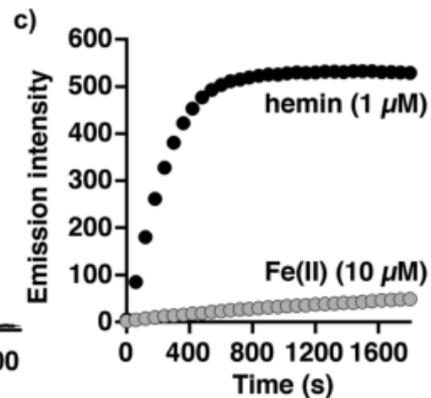
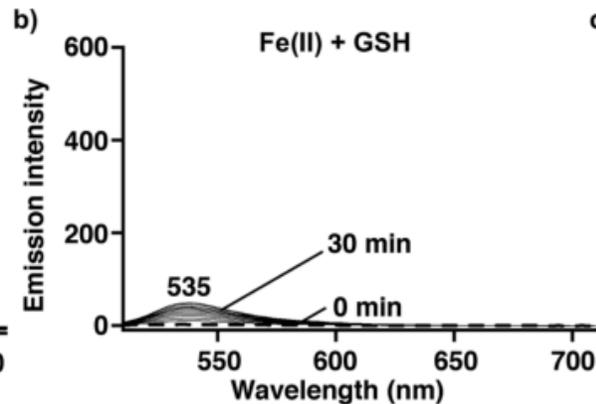
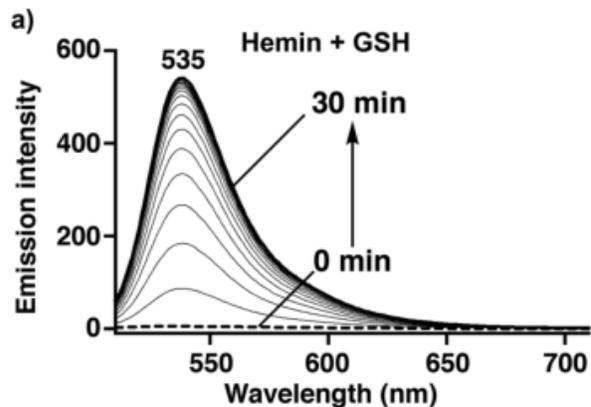
Result and Discussion

LH选择性探针的设计原理



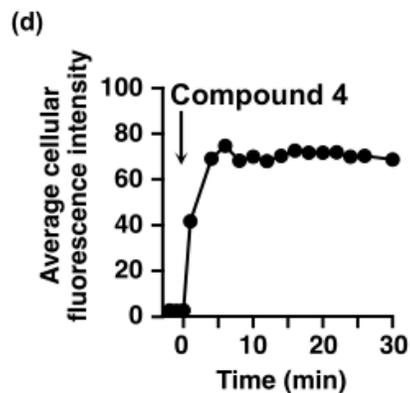
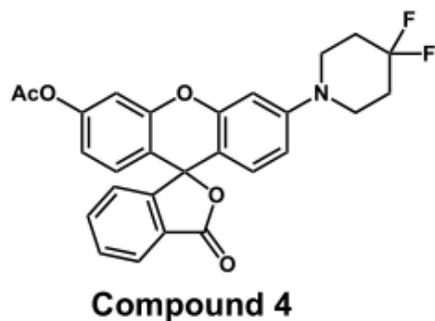
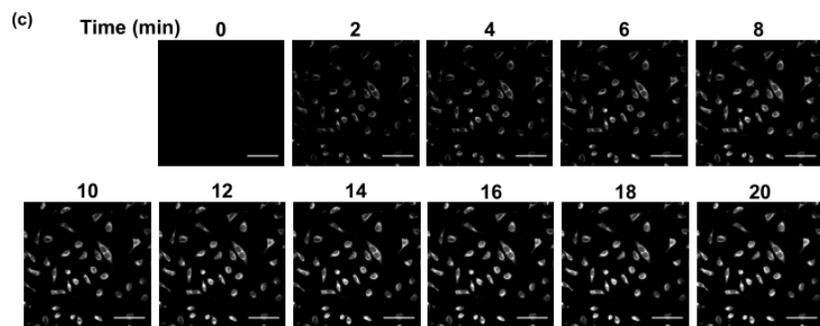
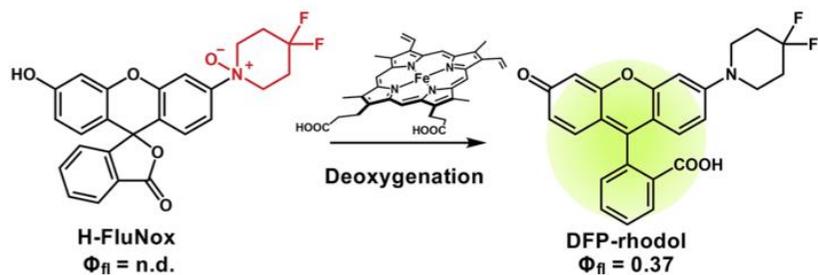
Result and Discussion

测试探针的反应性和选择性

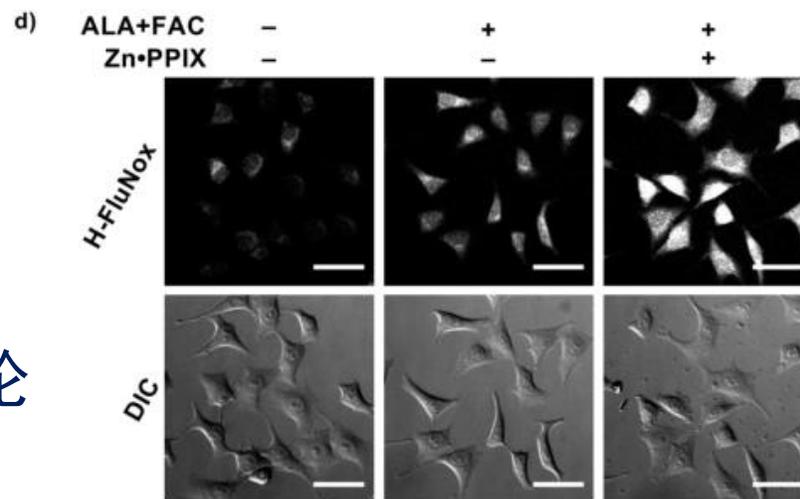
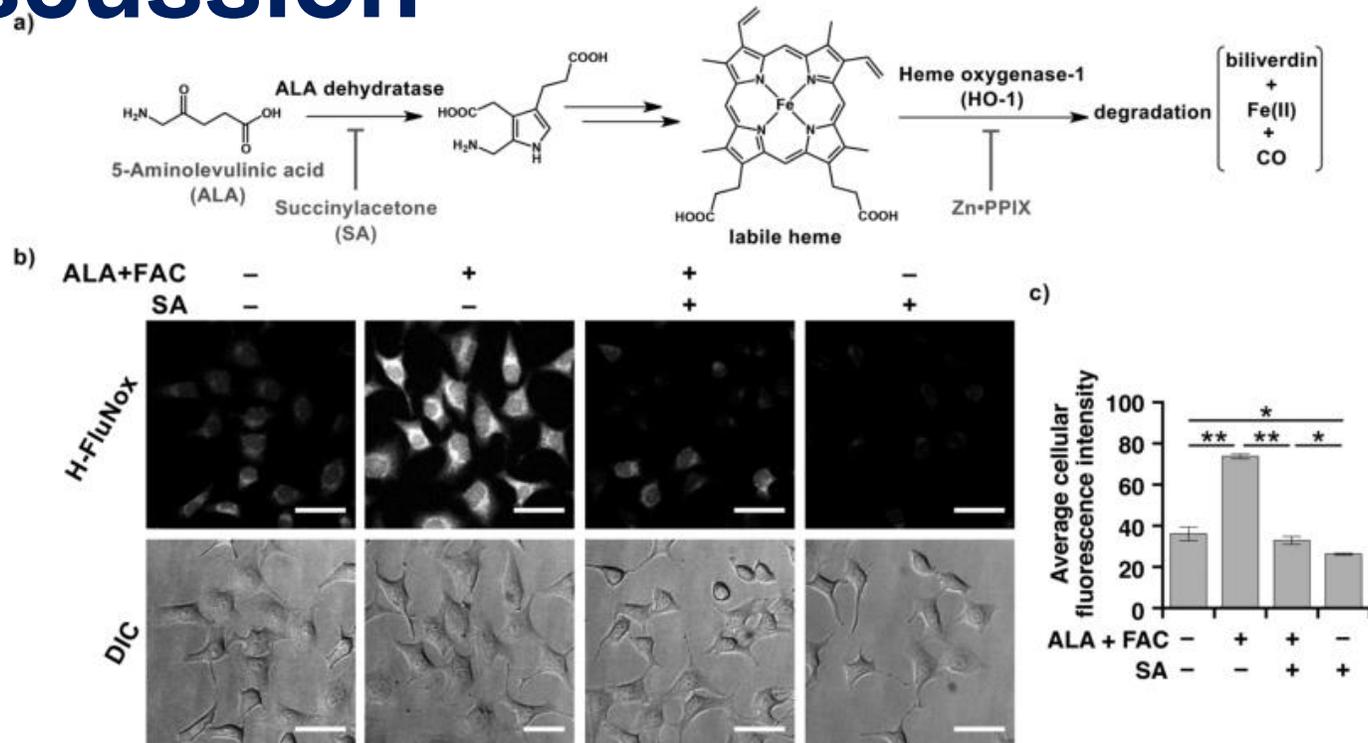


Result and Discussion

探针探测活细胞中LH的变化

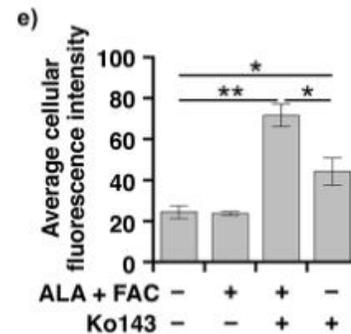
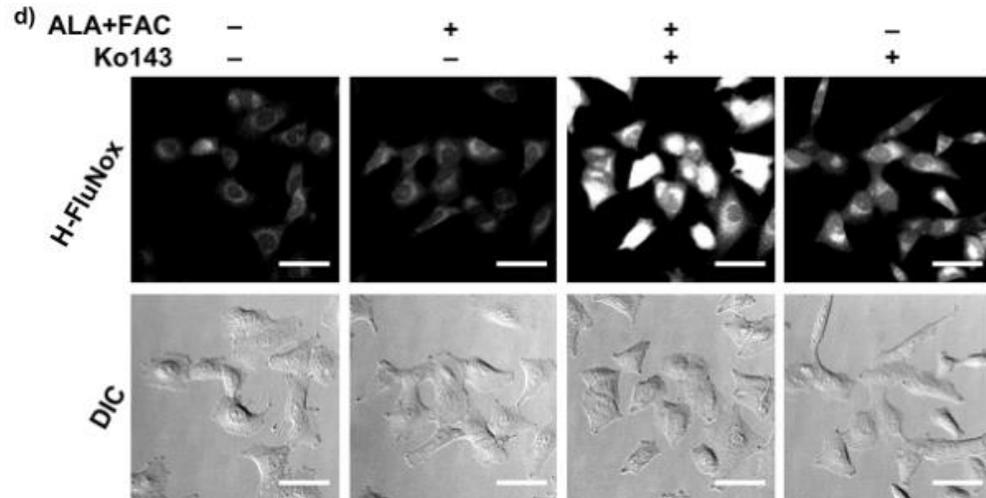
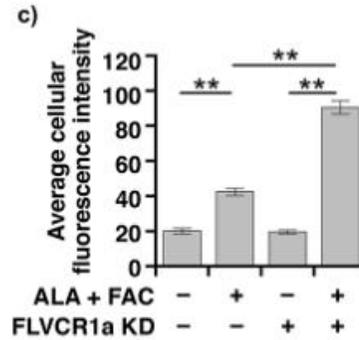
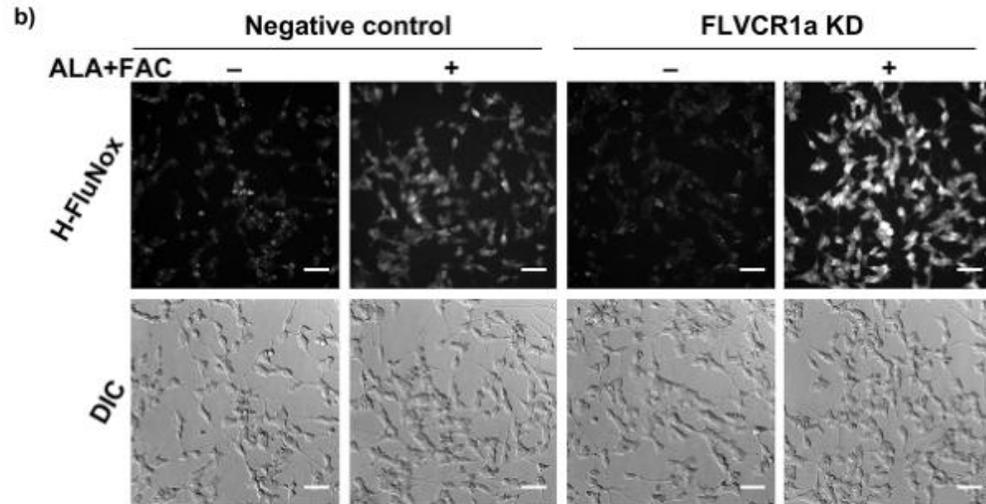
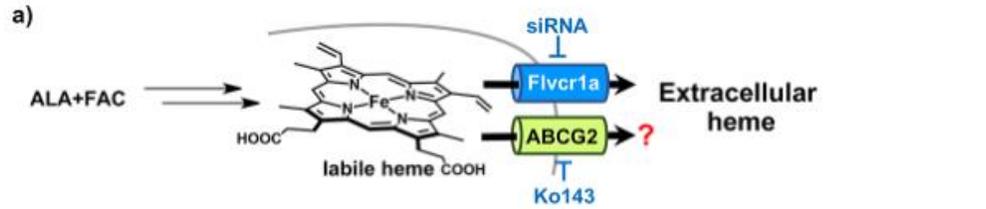


➤ 选择性地检测细胞内LH水平，不论是升高或是降低。





Result and Discussion 抑制血红素输出物检测LH的积累

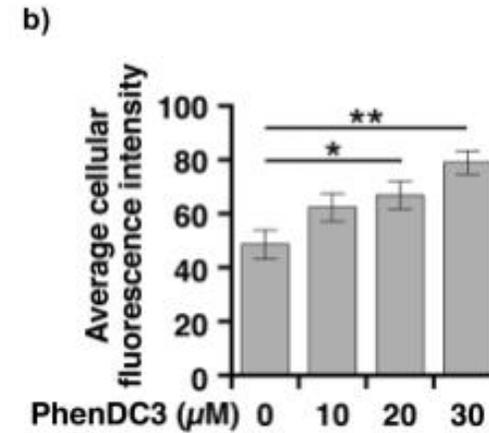
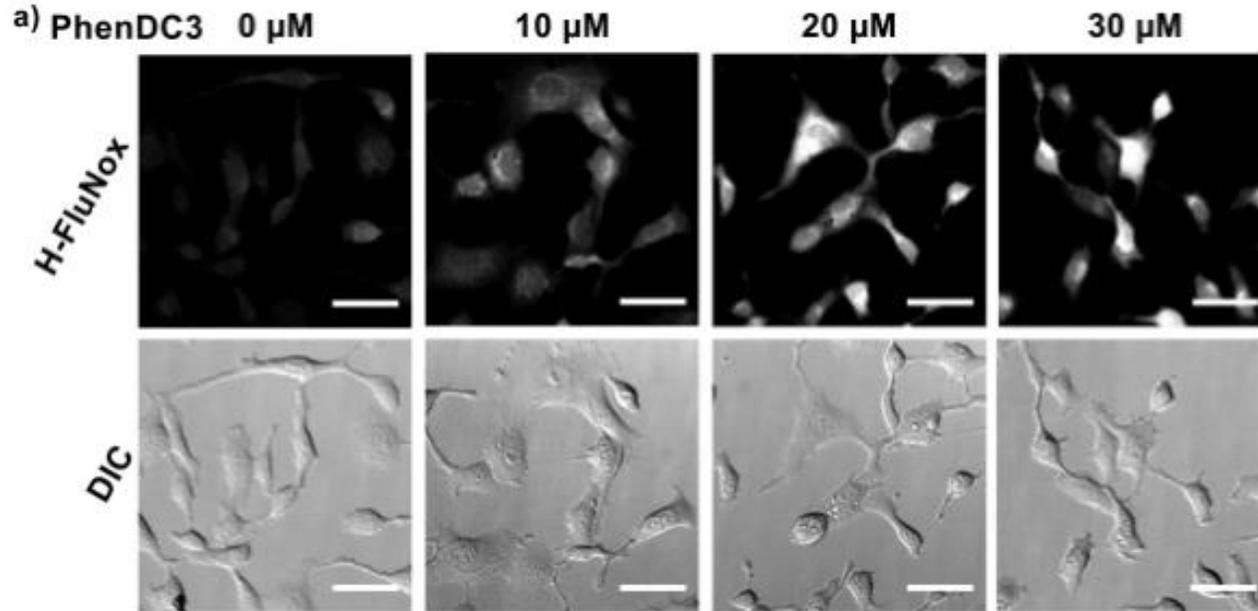


➤ ABCG2具有部分血红素输出活性，是一个局部的血红素输出者。



Result and Discussion

检测LH从G-四链体的释放

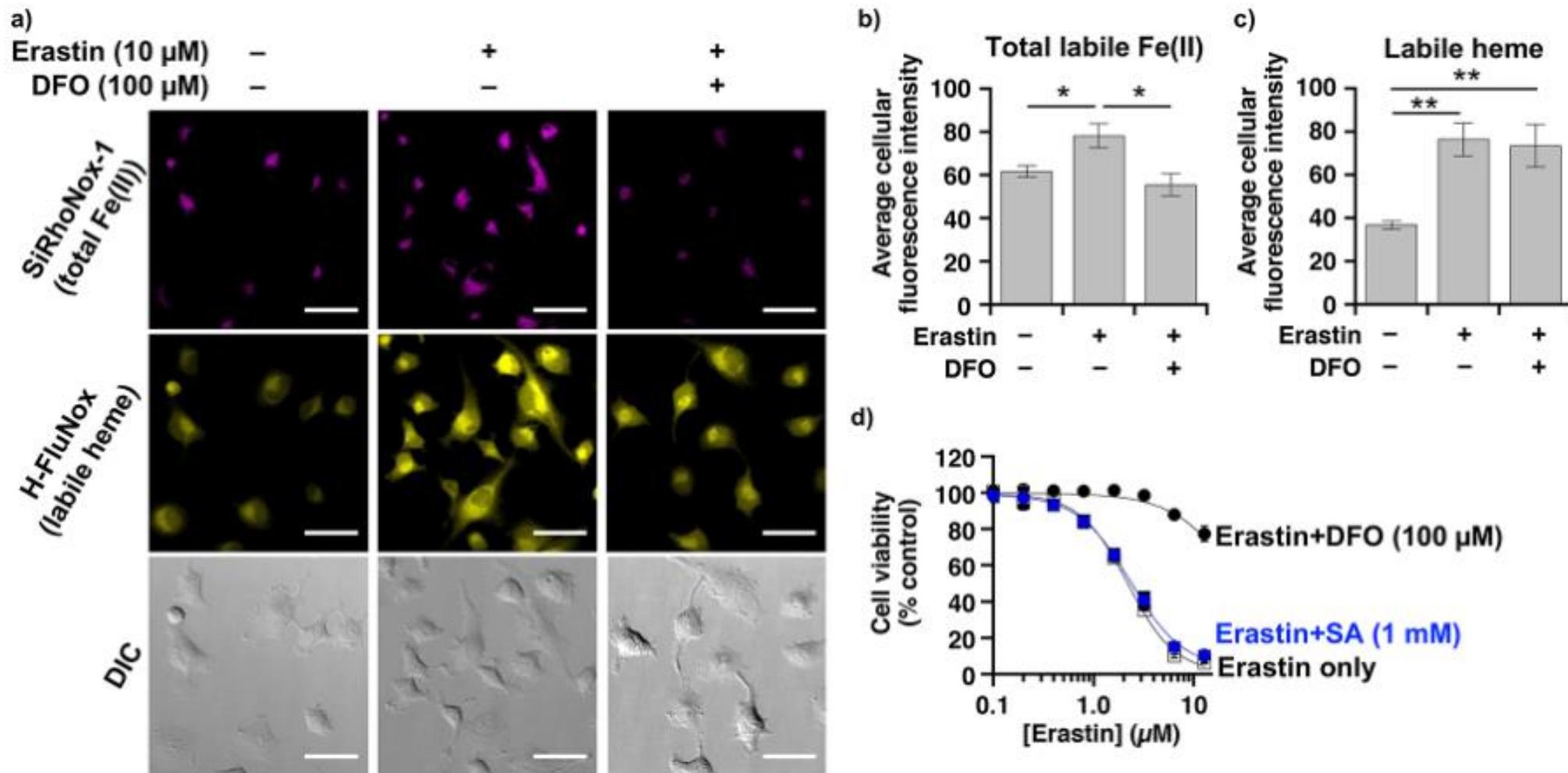


- PhenDC3促进G-四链体释放LH，从而提高细胞内LH水平。
G-四链体是细胞内LH储存池的候选物。



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。

