Literature Report

Reporter: 段承恩
Date: 2022-03-24

Reactivity Differences Enable ROS for Selective Ablation of Bacteria

Xiaofeng Wu⁺, Mengyao Yang⁺, Ji Seon Kim⁺, Rui Wang, Gyoungmi Kim, Jeongsun Ha, Heejeong Kim, Yejin Cho, Ki Taek Nam, and Juyoung Yoon**

Juyoung Yoon
Professor
Department of Chemistry and Nanoscience
Ewha Womans University, Korea

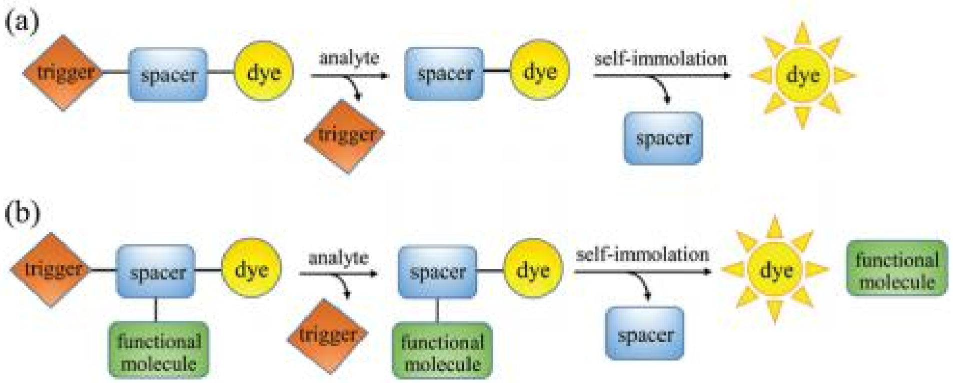
His research interests
1.fluorescent probes
2.activatable photosensitizers
3.theranostics
4.organic functional materials.

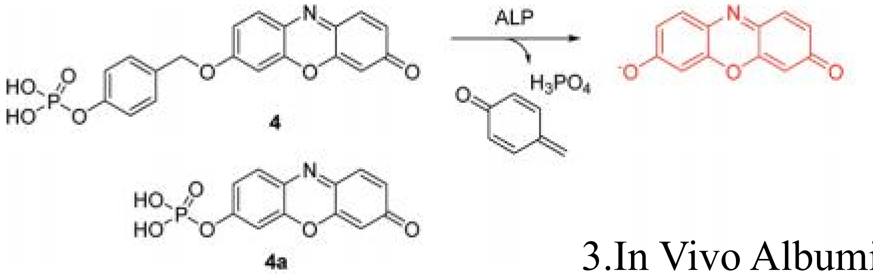
Education
1990 - 1994 Ohio State University, Columbus, Ohio, Ph. D. in Organic Chemistry
1983 - 1987 Seoul National University, Korea, B. S. in Industrial Chemistry
Professional Experience
2009 - Present Professor, Department of Chemistry Nano Science, Ewha Womans University
2002 - 2009 Assistant/Associate Professor, Department of Chemistry Nano Science,Ewha Womans University
1998 - 2002 Assistant Professor of Department of Chemistry, Silla University
1996 - 1998 Post-Doctoral Fellow, Department of Chemistry, The Scripps Research Institute, CA (Professor Kim D. Janda)
1994 - 1996 Post-Doctoral Fellow, Department of Chemistry, UCLA (Professor Doanld J. Cram)

He is a member of Korean Academy of Science and Technology, Fellow of Royal Society of Chemistry

Research Highlight

1.Self-immolative fluorescent and chemiluminescent chemosensors

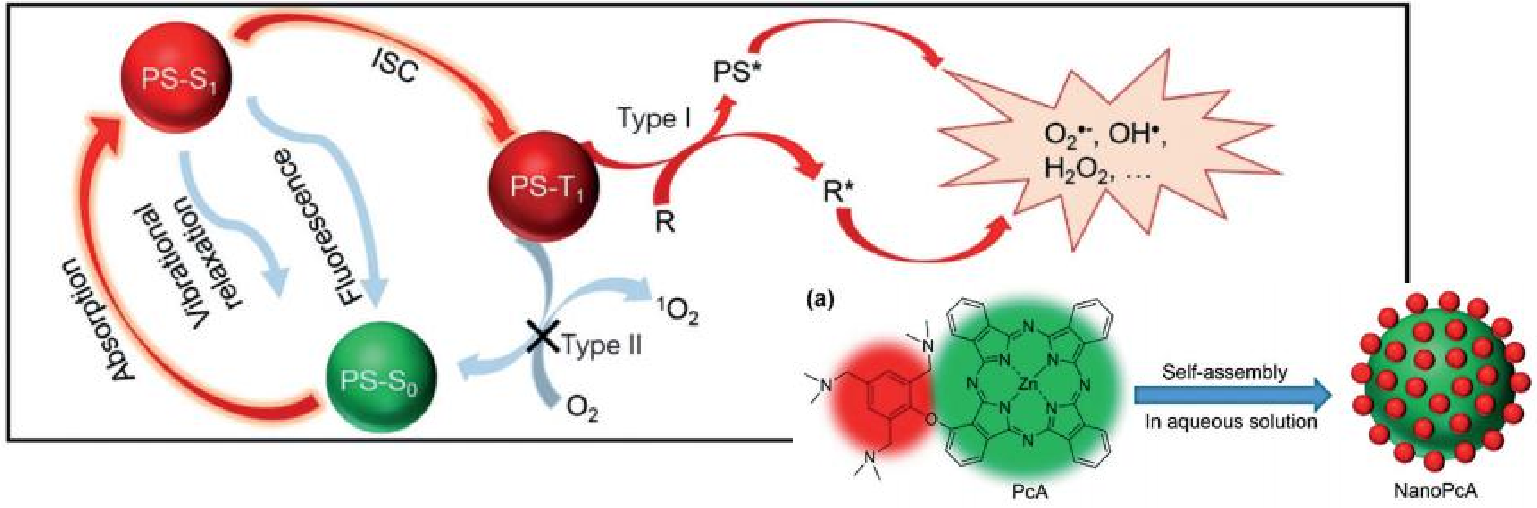


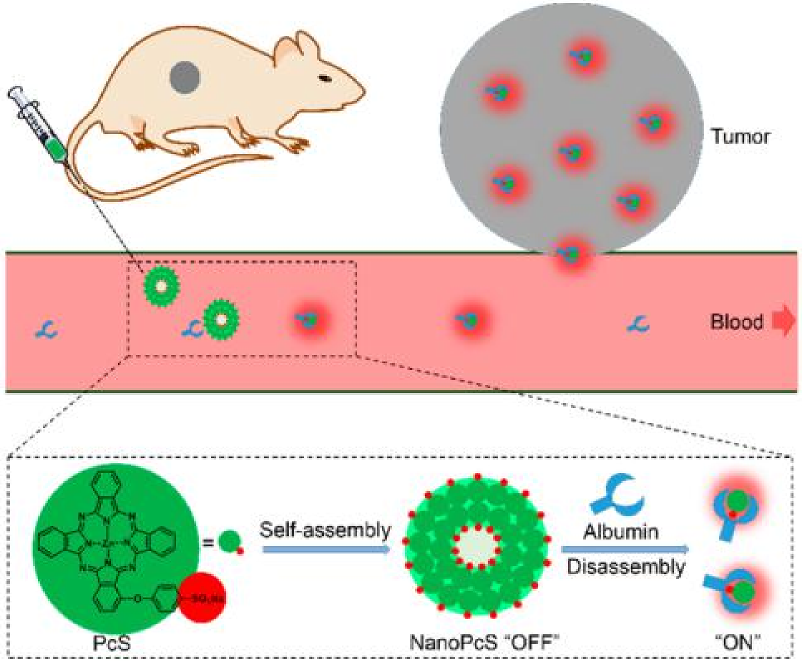


Chem. Soc. Rev. **2018**, 47(18), 6900-6916.

3.In Vivo Albumin Traps Photosensitizer Monomers from Self-Assembled Phthalocyanine Nanovesicles: A Facile and Switchable Theranostic Approach

2.The ROS generated are comprised of two groups including superoxide anion (O2-), hydrogen peroxide (H2O2) and hydroxyl radical (OH-) produced via the type I mechanism, and single oxygen (1O2) generated via the type II mechanism

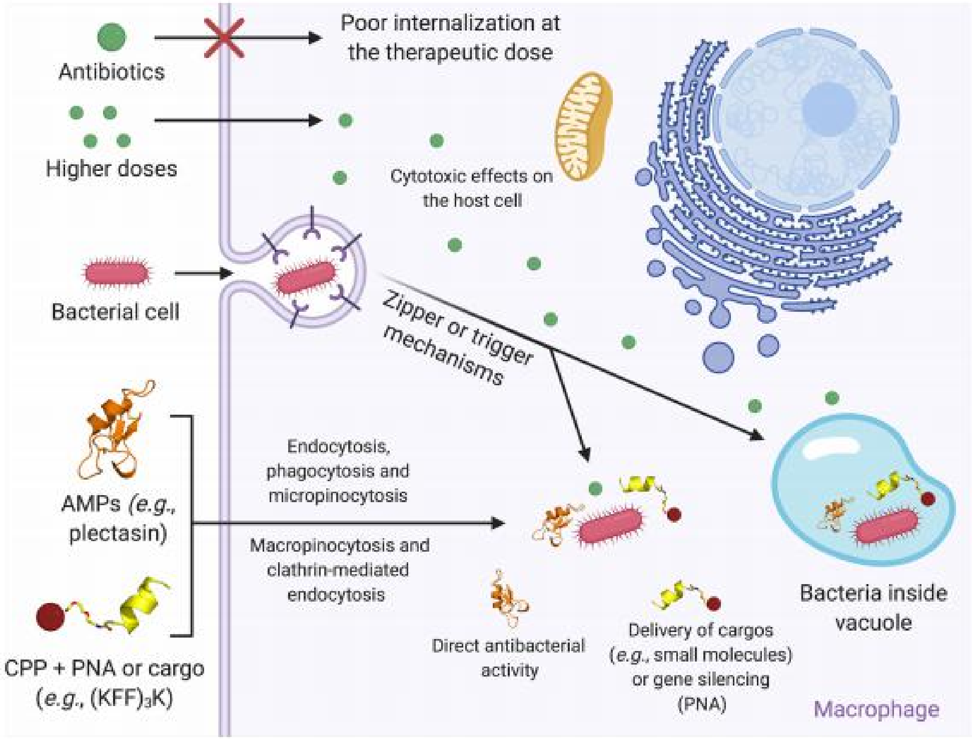




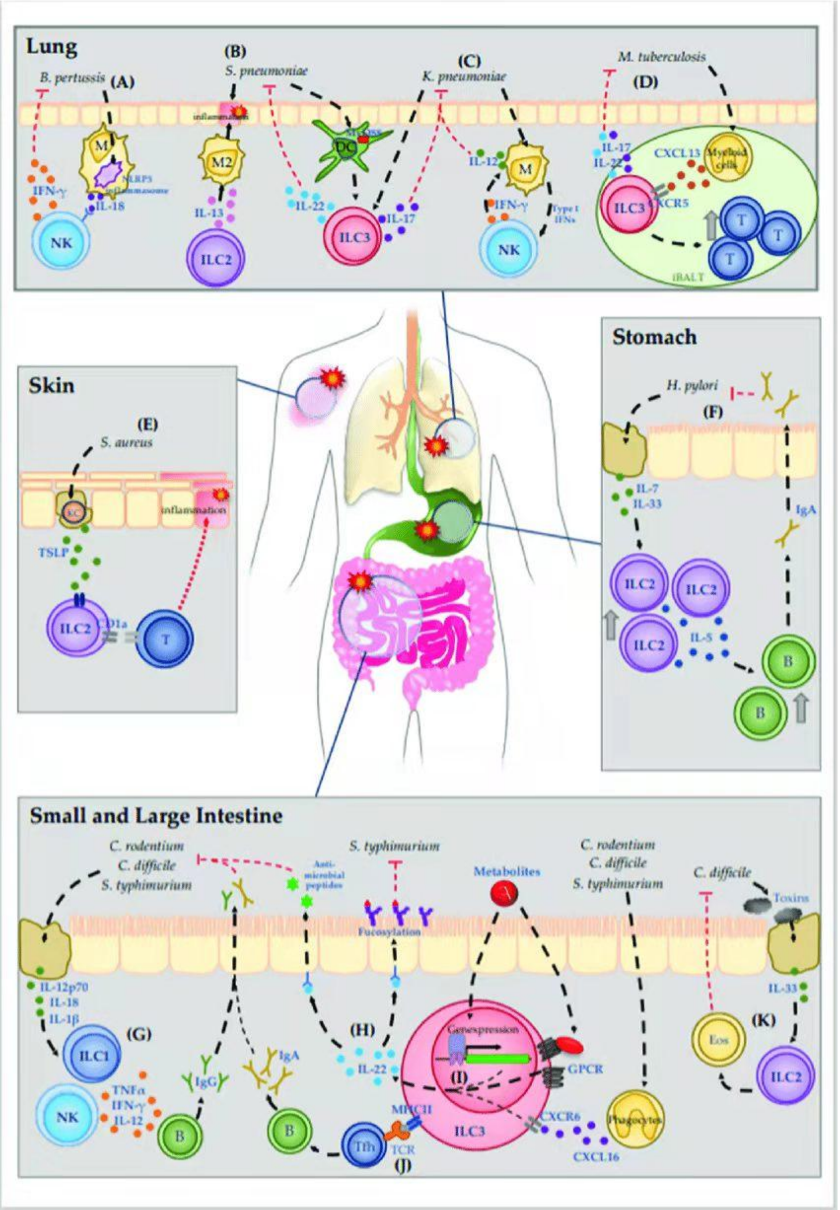
Angew. Chem. Int. Ed, **2018**, 57, 9885-9890.

J. Am. Chem. Soc. **2019**, 141(3), 1366-1372.

Background 1



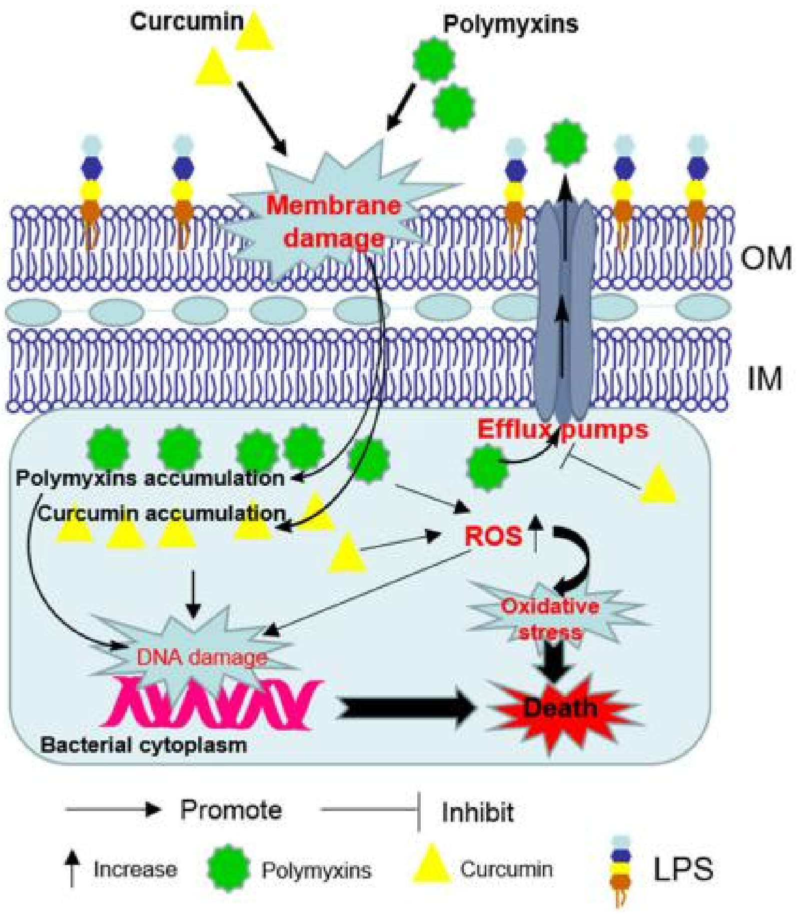
Front Cell Infect Microbiol. **2021** Feb 5;10:612931.



Microorganisms. **2020** Sep 2;8(9):1342.

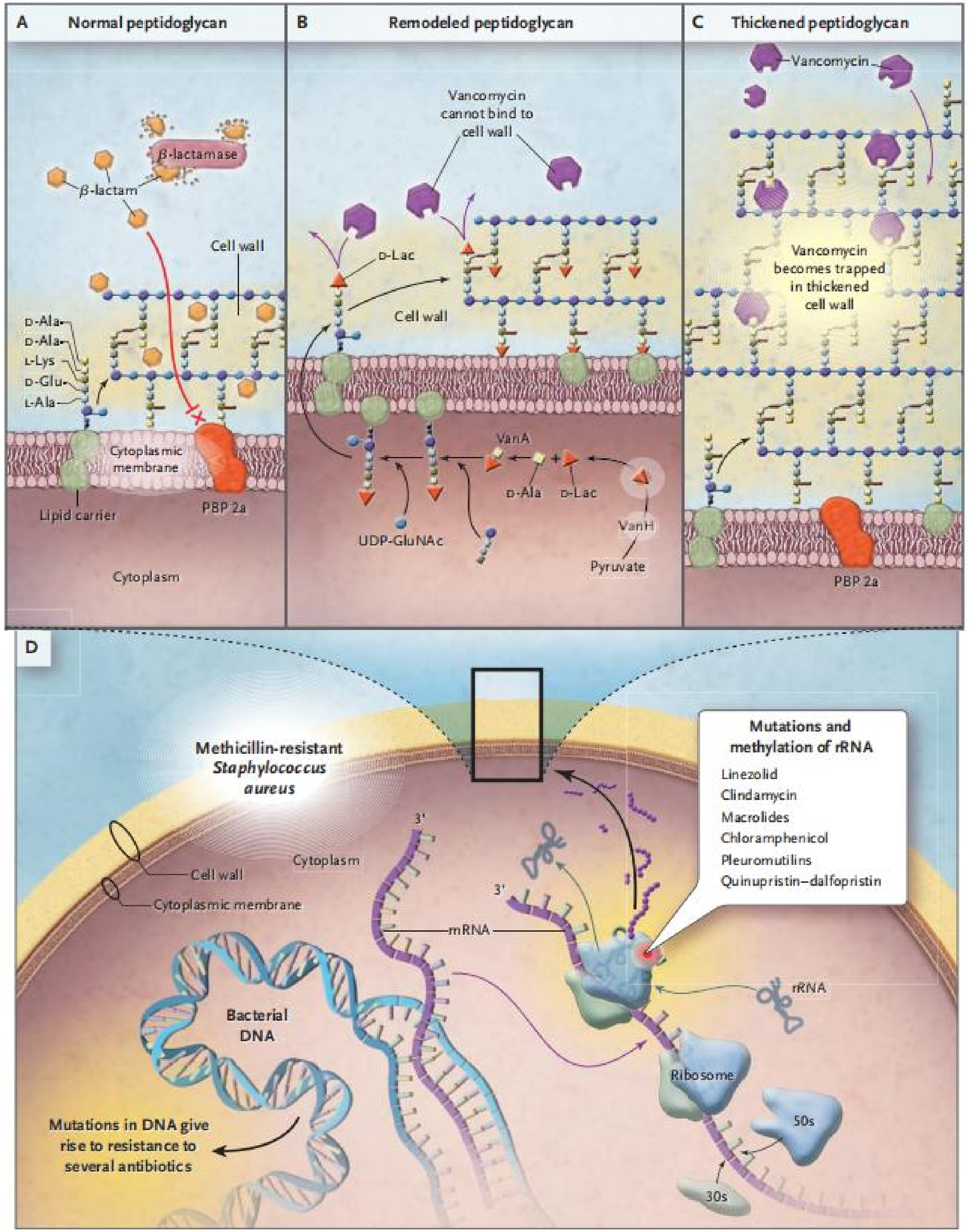
近几十年来，细菌感染仍然是世界性的挑战，主要是由于致病性的演变，外来病原体的出现和抗生素耐药性的传播，导致对人体健康构成巨大威胁。

Background 1



Antioxidants **2020**, 9, 506

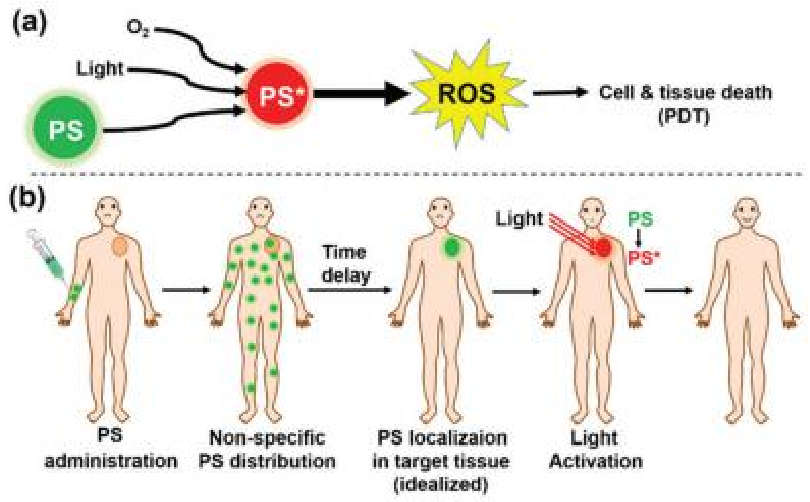
可通过抗生素治疗细菌感染带来的疾病



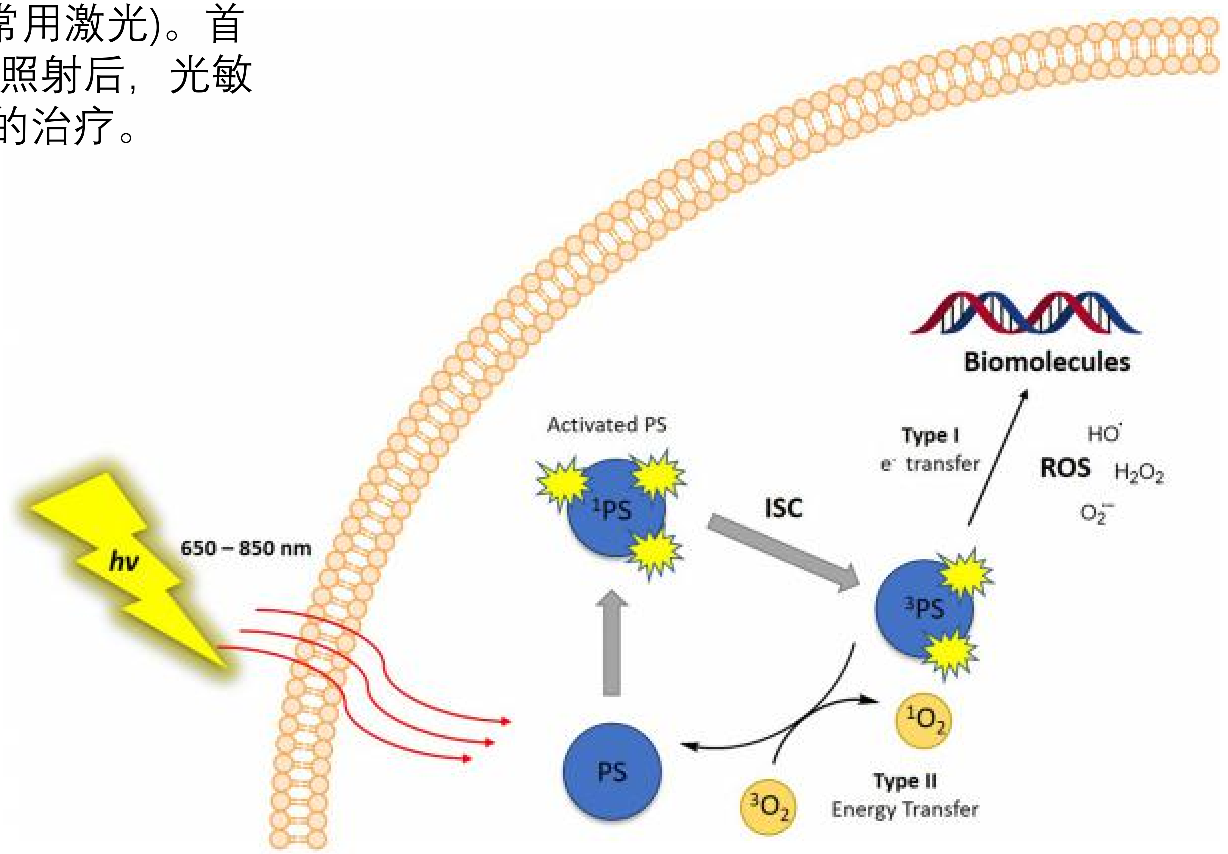
Background 2

光动力疗法（PDT）是一种治疗疾病的新型疗法，以耐药性可忽略不计、低全身毒性和副作用最小的特点实现抗菌作用和肿瘤抑制作用。

原理是光化学反应，其基本要素是氧、光敏剂和可见光(常用激光)。首先选择性摄取光敏剂，并储于其内，随后在适当波长光线局部照射后，光敏剂被激活，产生光敏效应。PDT的优势在于能够精确进行有效的治疗。

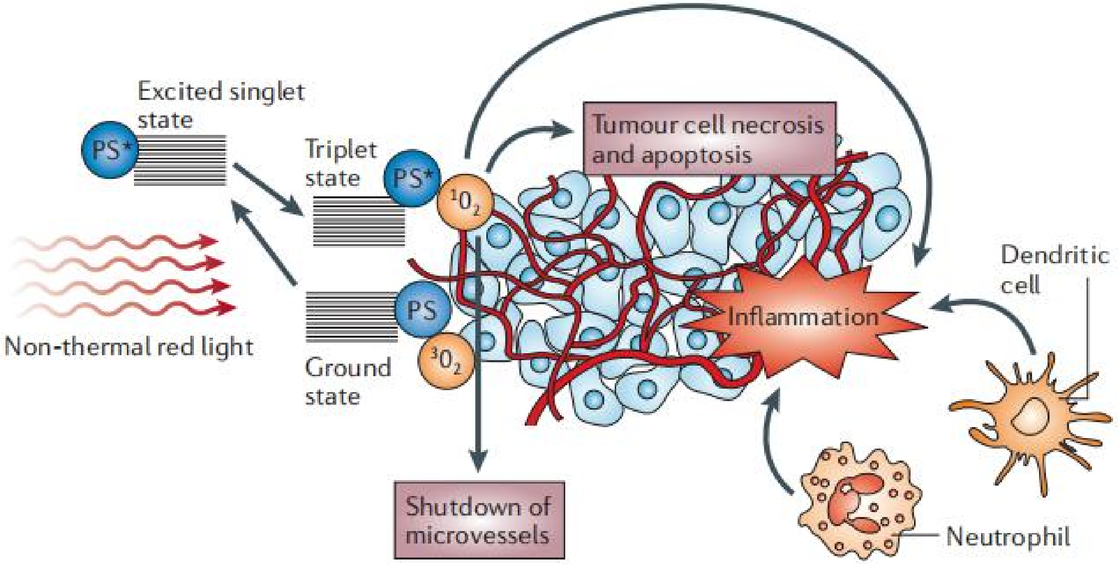


Chem. Soc. Rev., **2018**, 47, 1174--1188

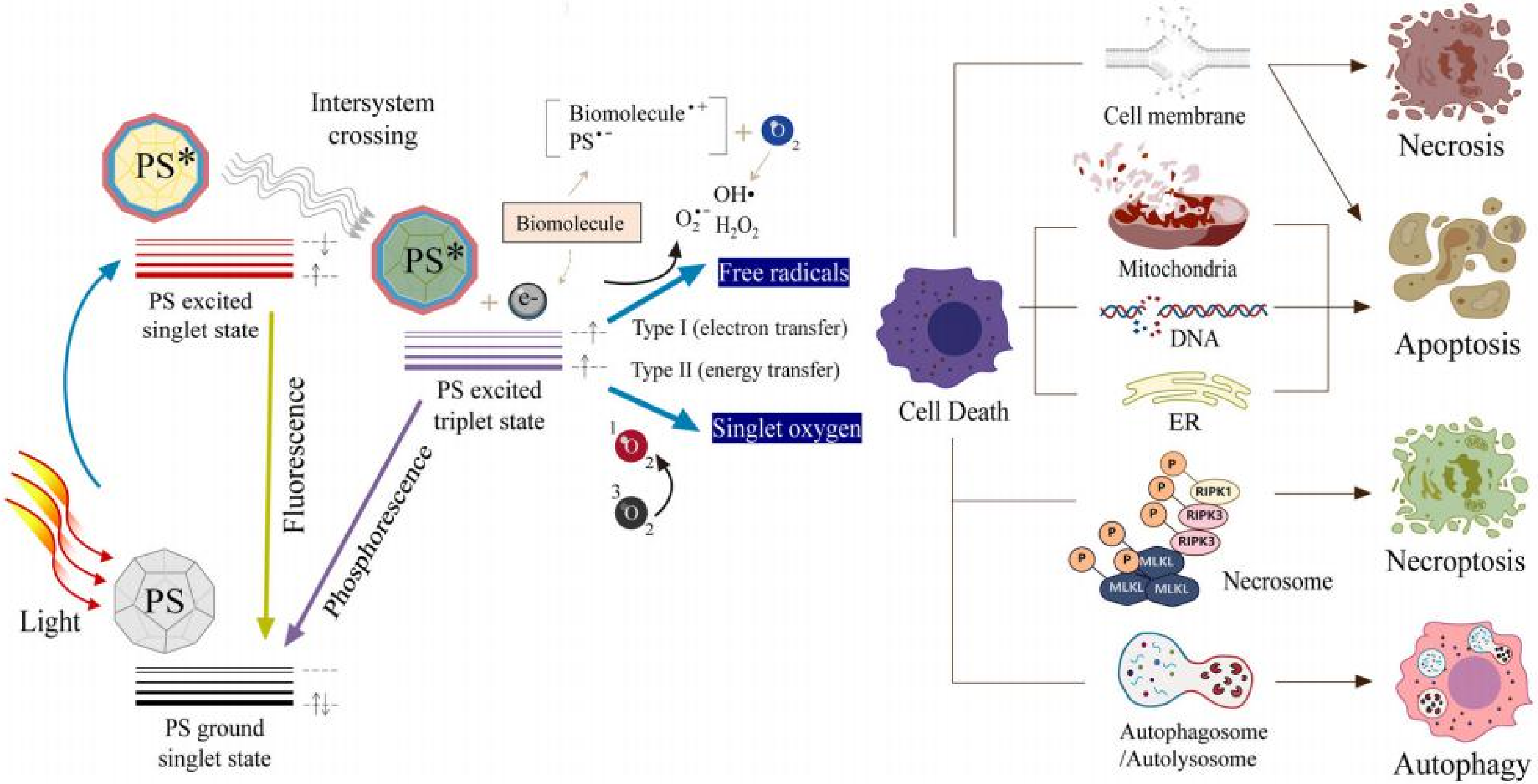


BBA - Reviews on Cancer 1872 (**2019**) 188308

Background 2

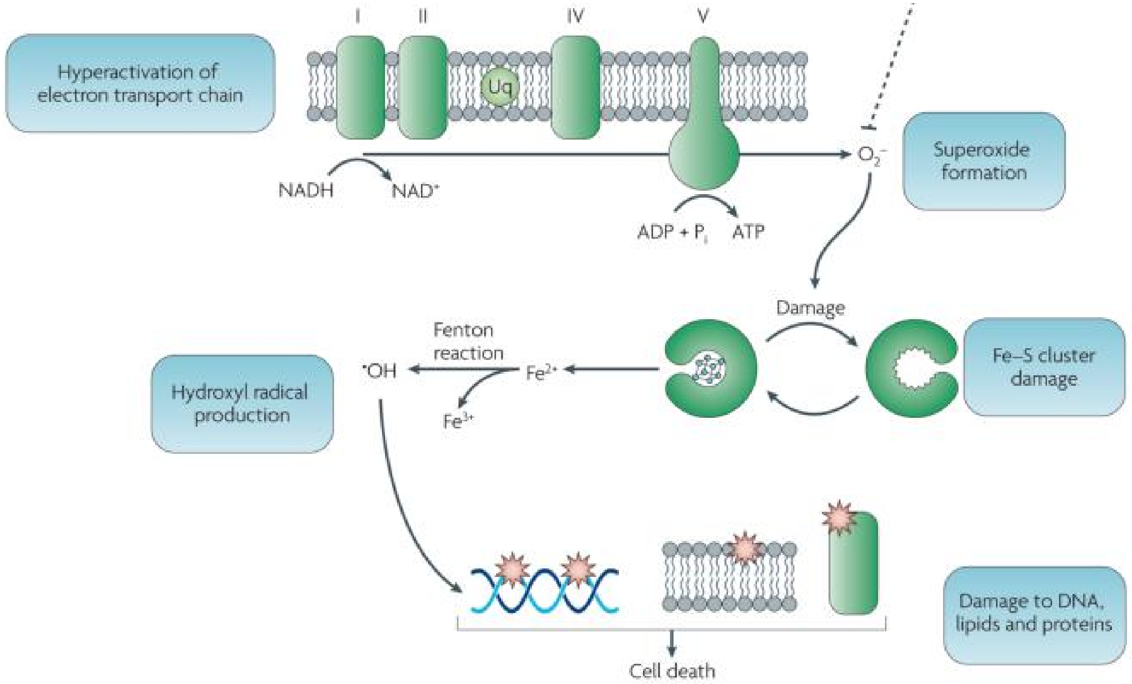


PDT肿瘤抑制作用

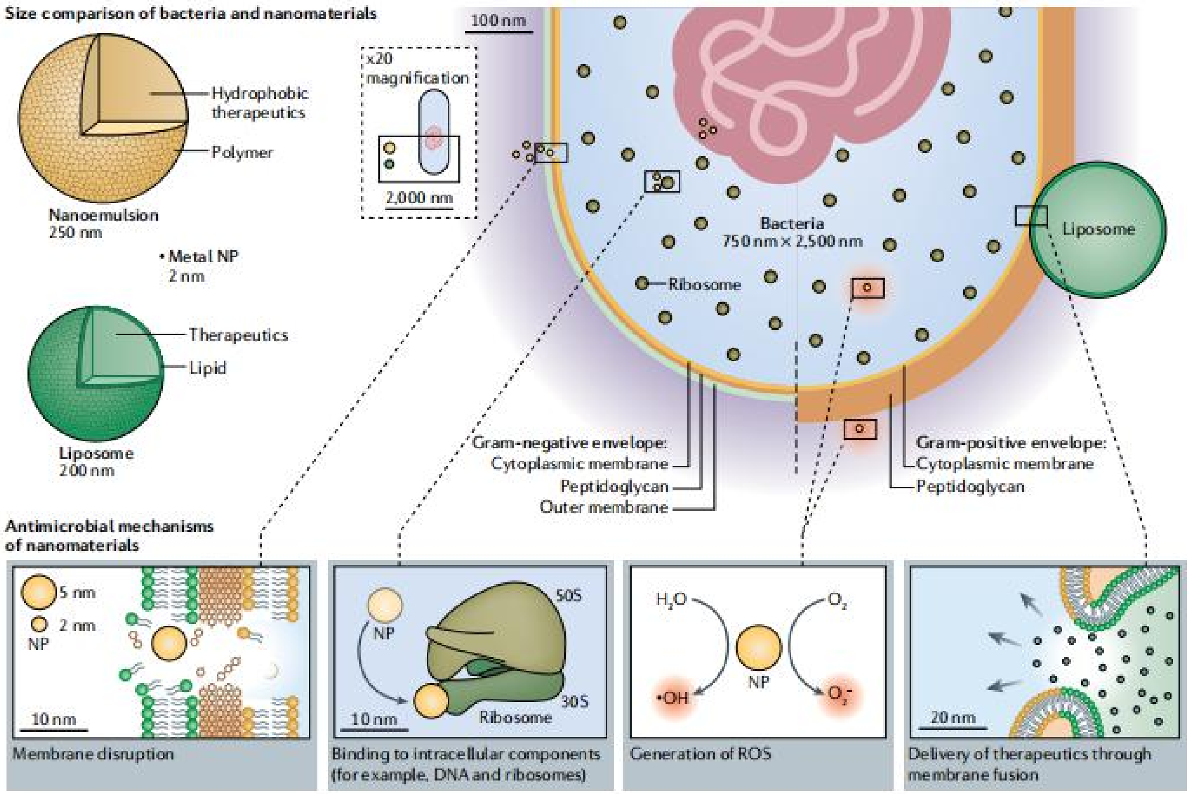


Nat Rev Cancer， JULY **2006**， 535

Background 3



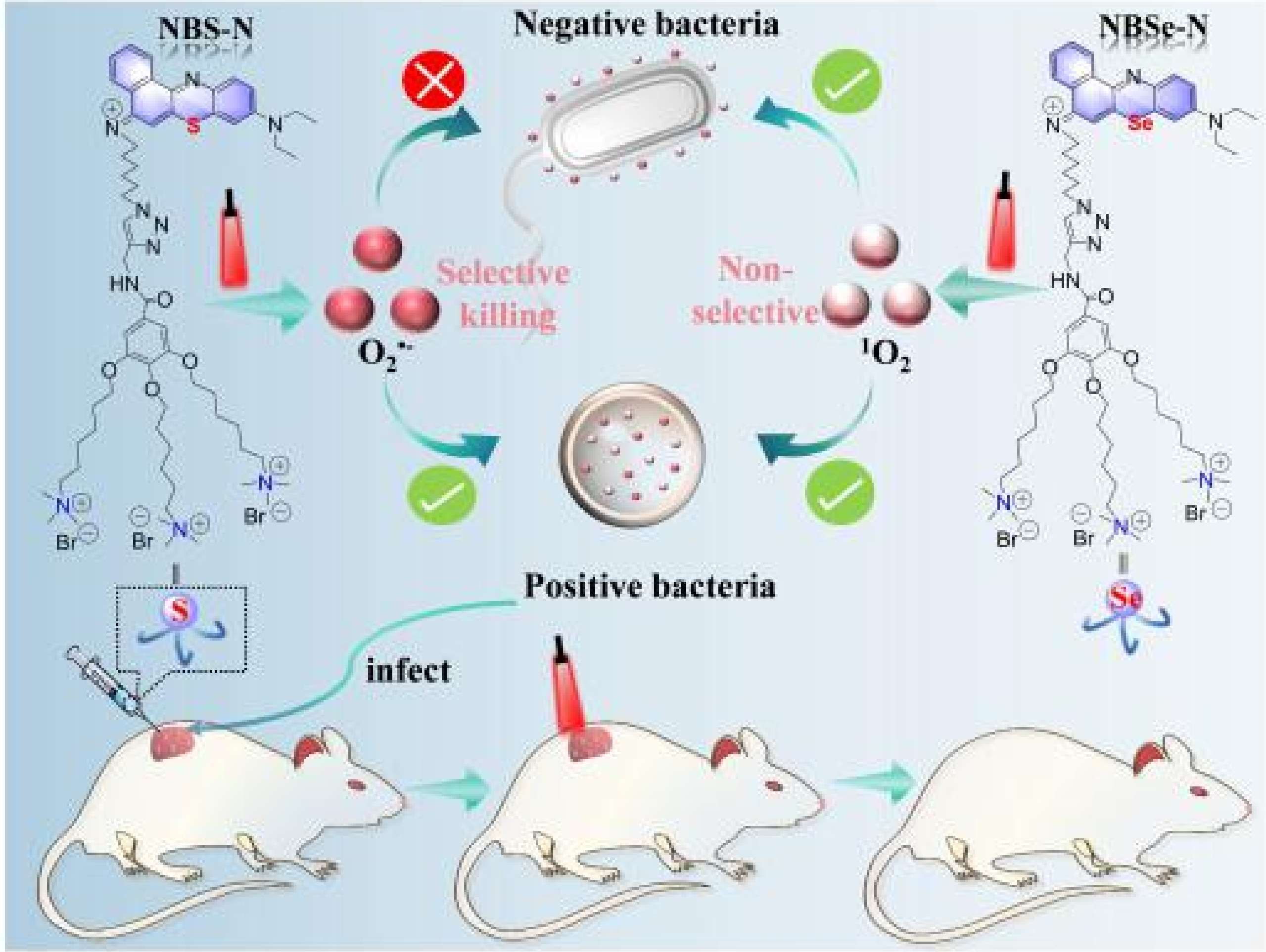
PDT抗菌作用



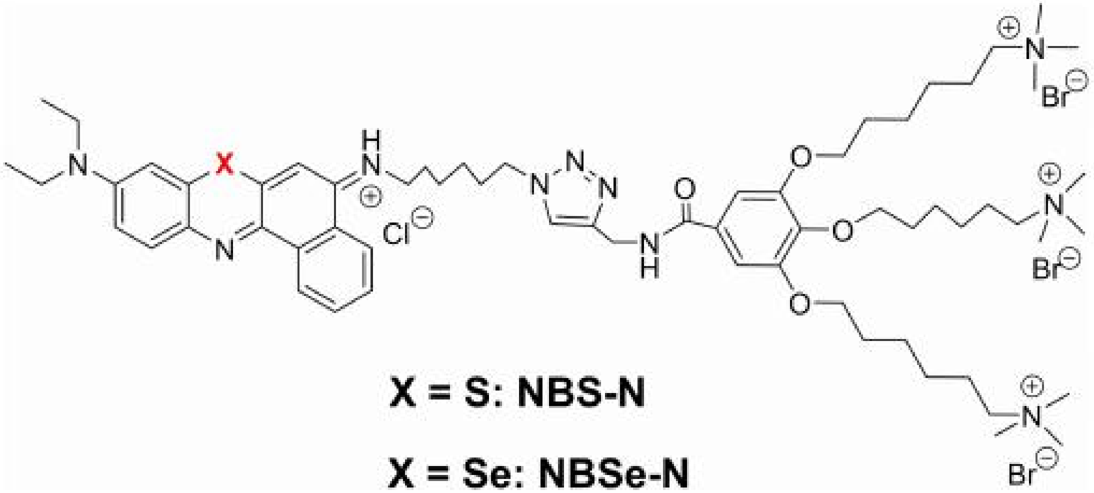
Nat Rev Microbiology; **2020**; 19

革兰氏阴性菌细菌膜比阳性菌更复杂，使得PS穿透G-比G+更困难，ROS反应活性差异启发了产生O2-的PS可能是一种选择性杀死G+的抗菌剂。

1.Design and Syntheses of NBS-N and NBSe-N

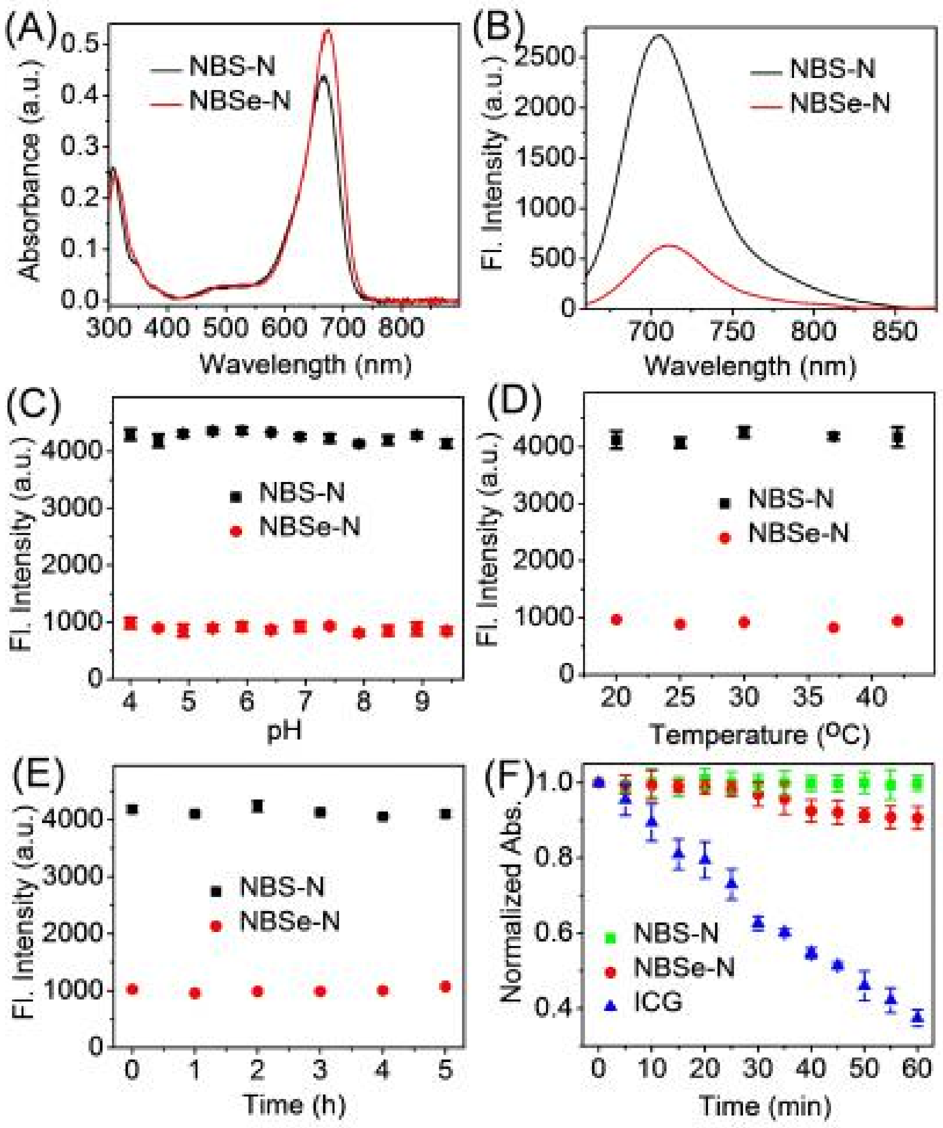


基于这些关注和启发，建立了一项概念验证研究，其中设计了两个化合物实例NBS-N和NBSe-N，以探索1o2和o2-之间的反应差异是否可以诱导根除革兰氏阳性和革兰氏阴性菌的差异。



探针设计思路：含有相同核心结构的PS，可产生不同水平的O2-和1o2

2.In vitro properties of NBS-N and NBSe-N



测试探针的有效性，研究其光谱性质

Table S1. Photophysical data of NBS-N and NBSe-N.

Compound	λ_{abs} (nm)[a]	ε ($\times 10^4$ M^{-1} cm^{-1})[b]	λ_{em} (nm)[c]	Φ_f[d]
NBS-N	664	4.38	706	0.22
NBSe-N	670	5.28	710	0.047

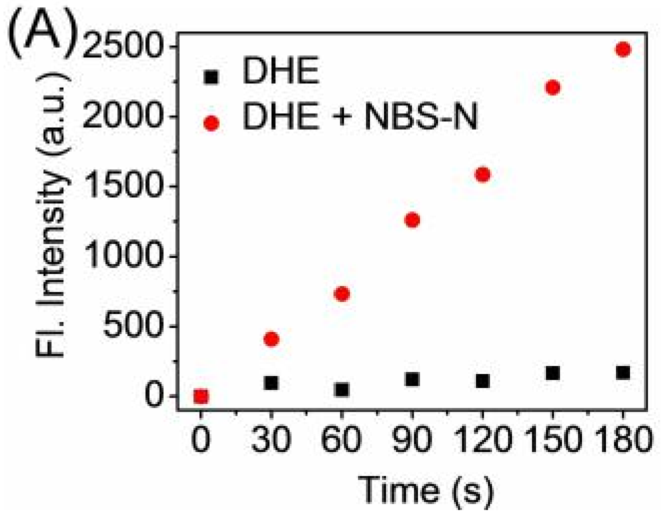
[a] Absorption peak. [b] Molar absorptivity of the corresponding absorption peak. [c] Fluorescence emission peak. [d] Fluorescence quantum yield.

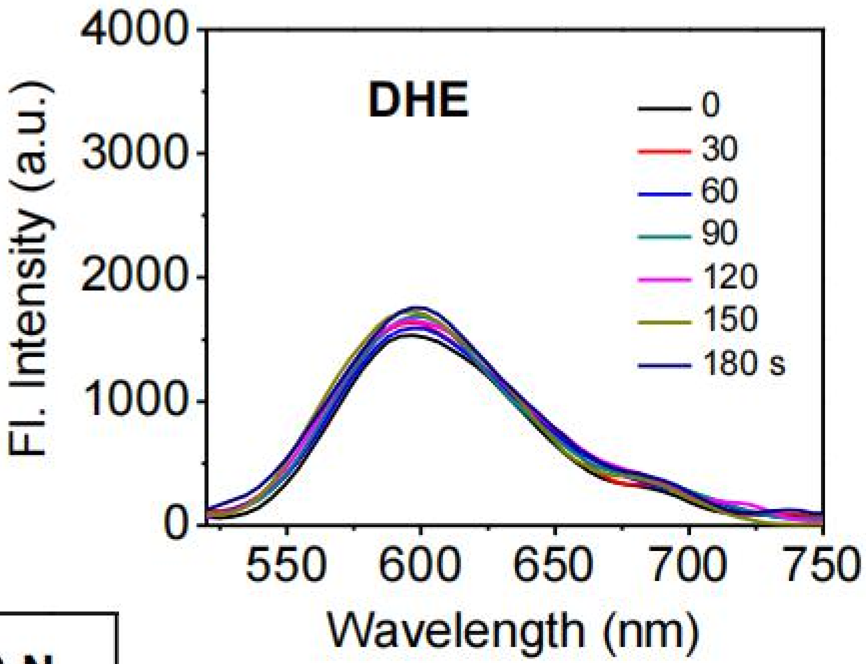
其高稳定性有利于NBS-N和NBSe-N在体内进行长期的光活性。本文测试了NBS-N和NBSe-N的（C）pH稳定性、（D）热稳定性和（E）光稳定性。

ICG 吲哚菁绿 （NIR光吸收区探针）

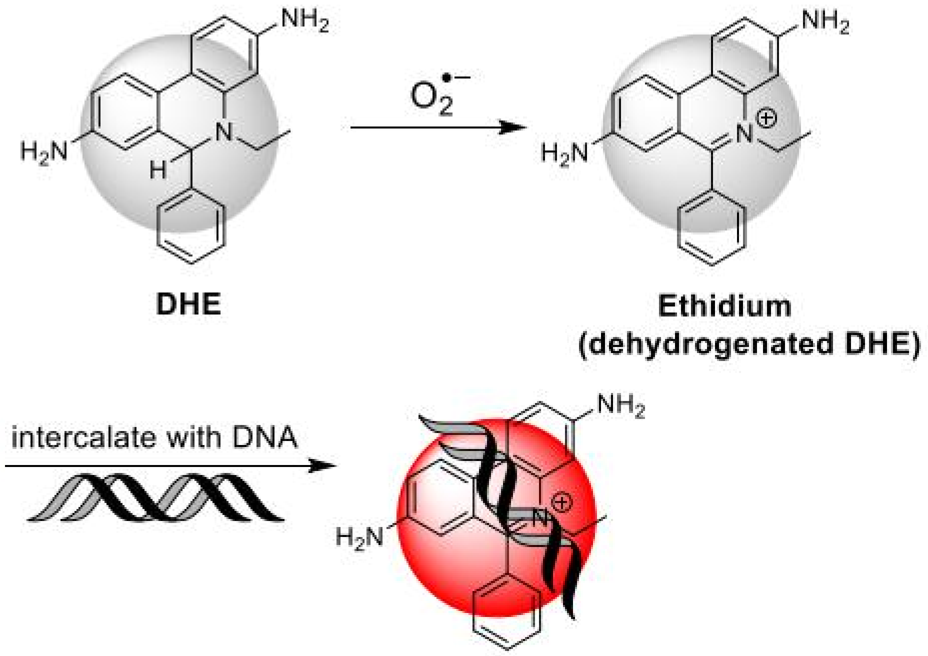
pH、高光稳定性和热稳定性对于长期照射是非常理想的，允许PSs更好地用于光疗抑制体内细菌。

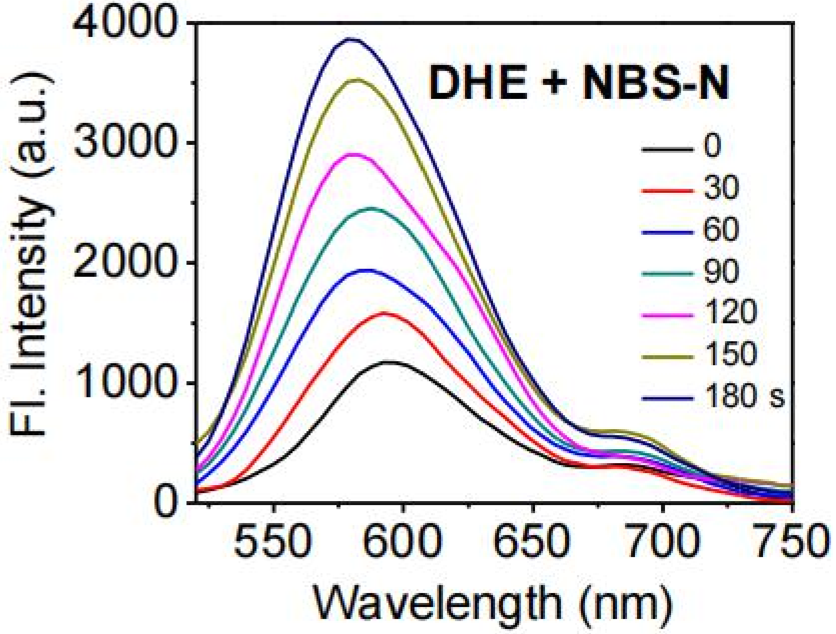
3.Photoactivities test of NBS-N and NBSe-N





研究探针光活性

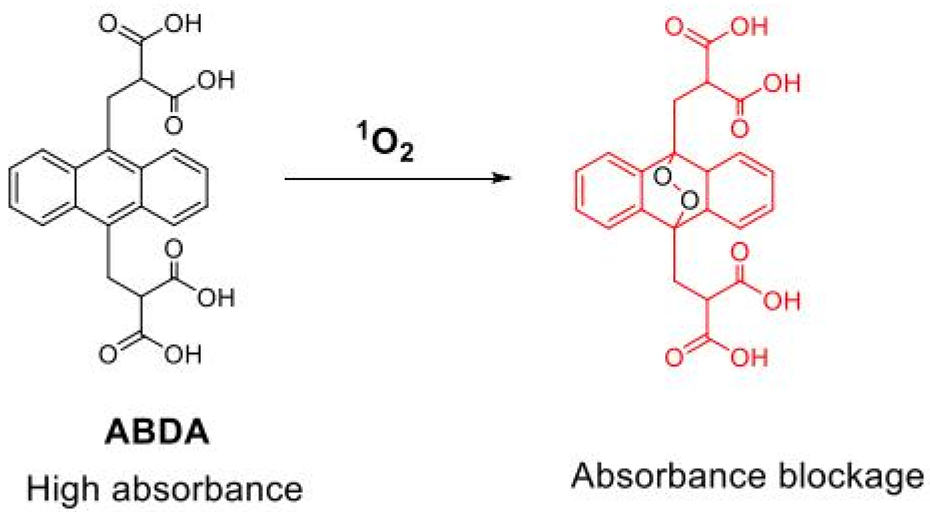


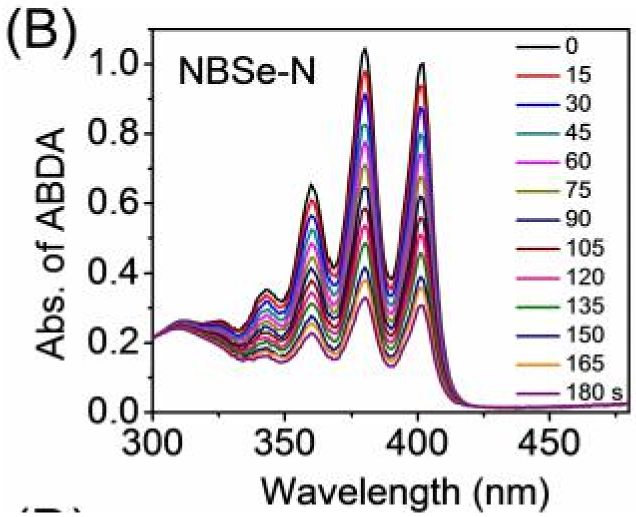


采用特异性荧光指示剂二氢乙锭(DHE)测定NBS-N的O2-的生成。脱氢的DHE本身无荧光，插入DNA后显示红色荧光

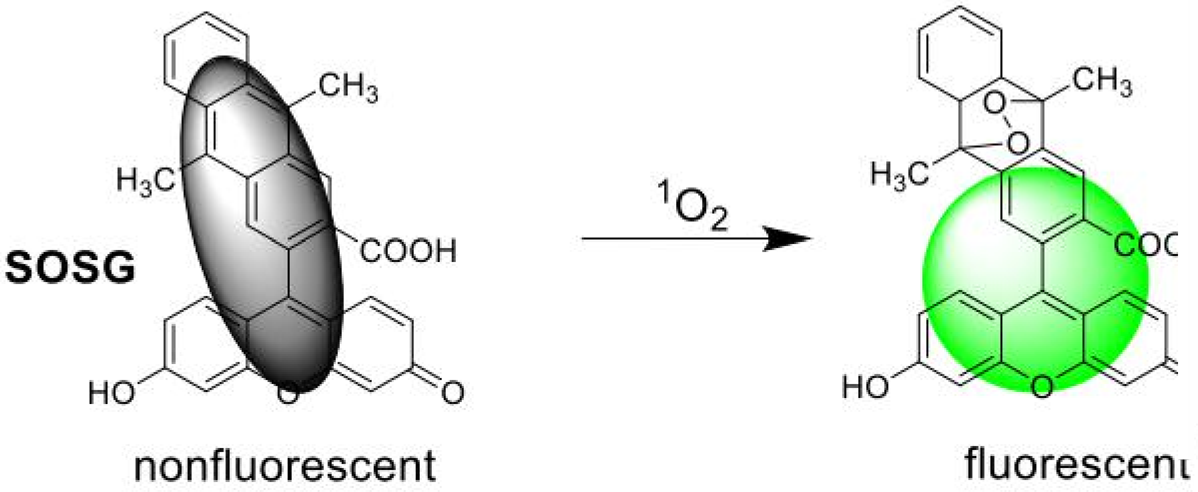
3.Photoactivities test of NBS-N and NBSe-N

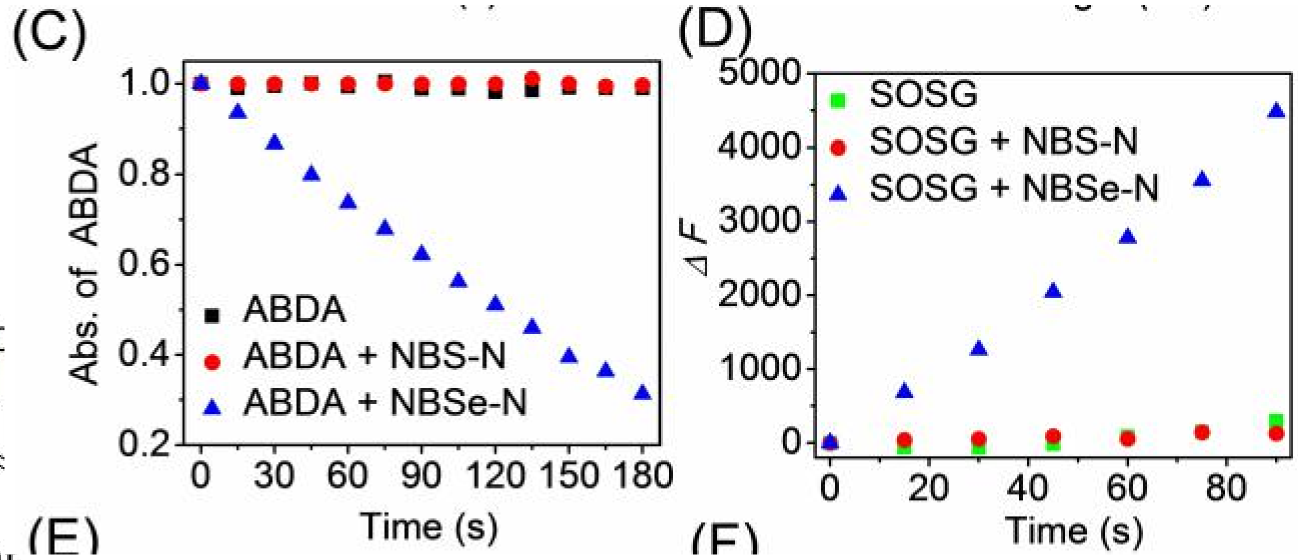
9,10-蒽二丙酸（ABDA）：单线态氧指示剂





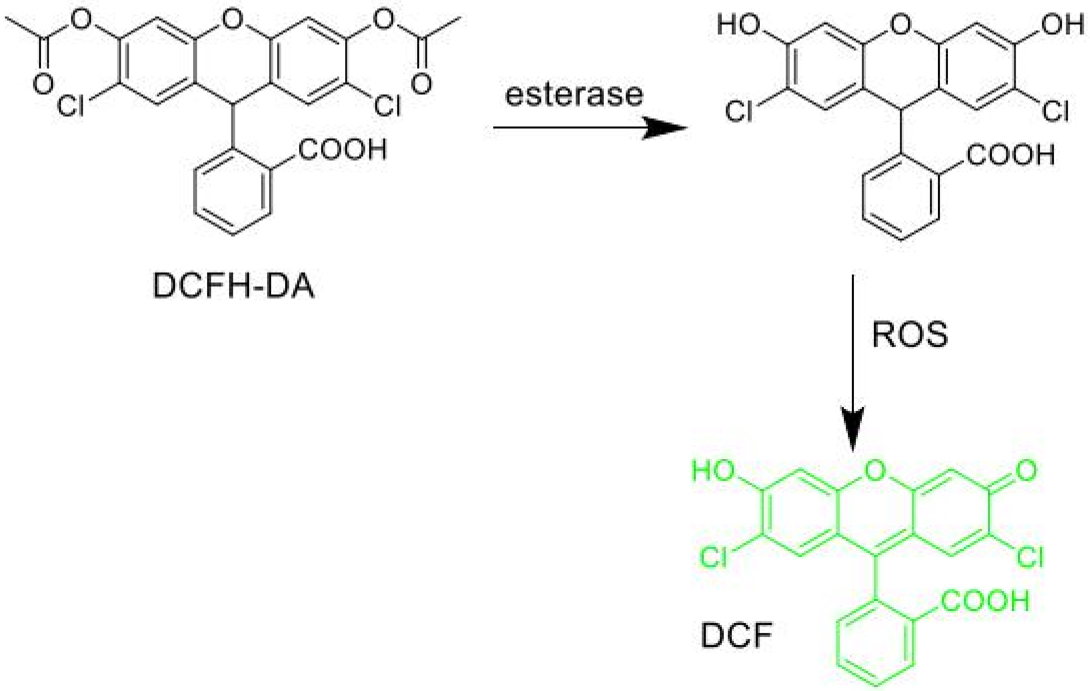
单线态氧传感器（SOSG）：绿色荧光指示剂



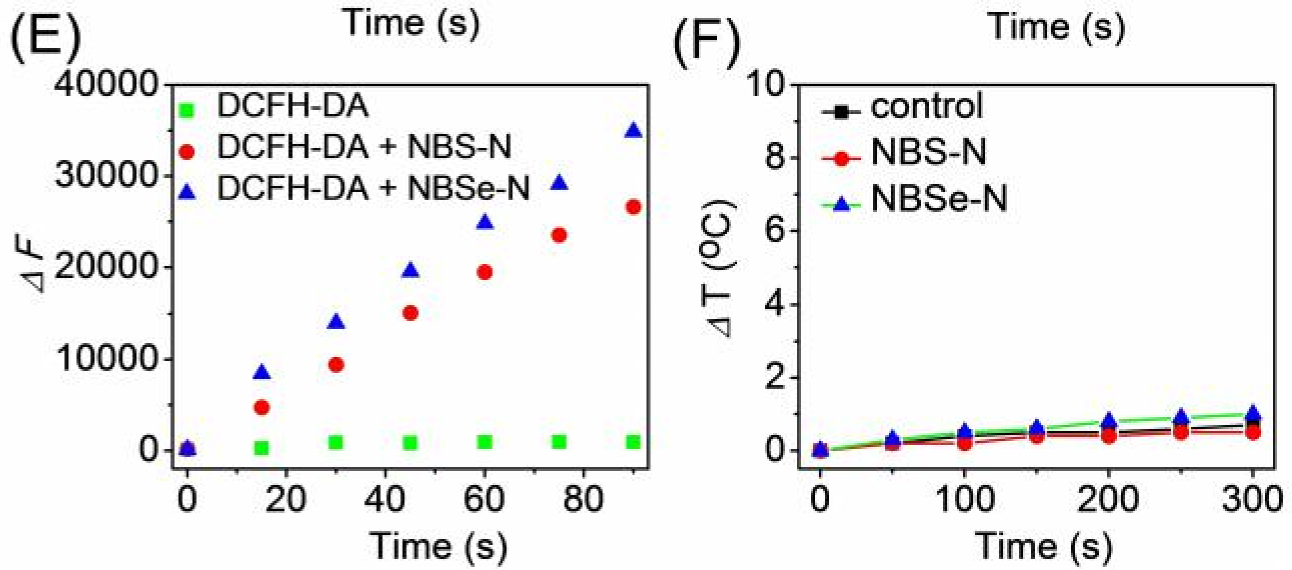


NBSe-N比NBS-N具有更强的1o2生成能力

3.Photoactivities test of NBS-N and NBSe-N



2，7-二氯荧光素（DCFH-DA）： ROS指示剂

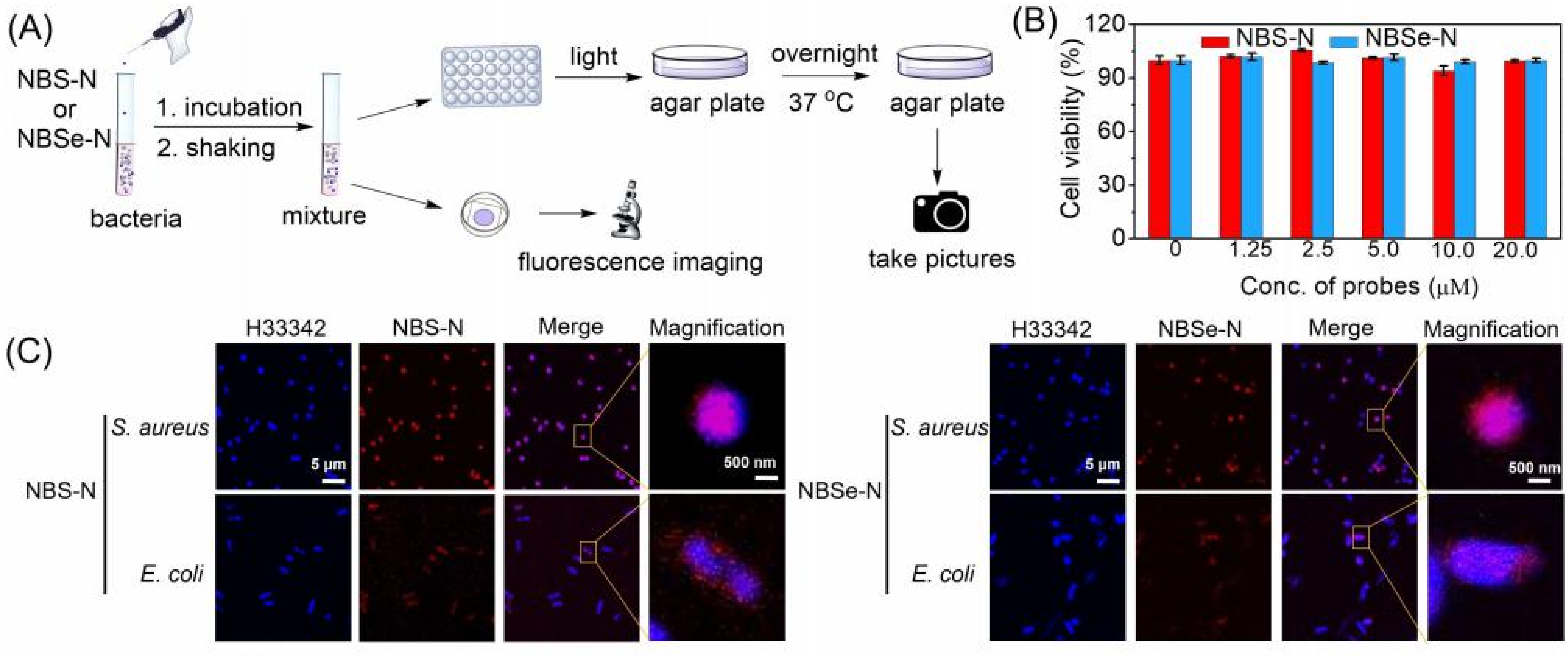


验证探针在光照射下ROS的有效生成

探针对ROS的反应性差异说明探针设计是合理有效的

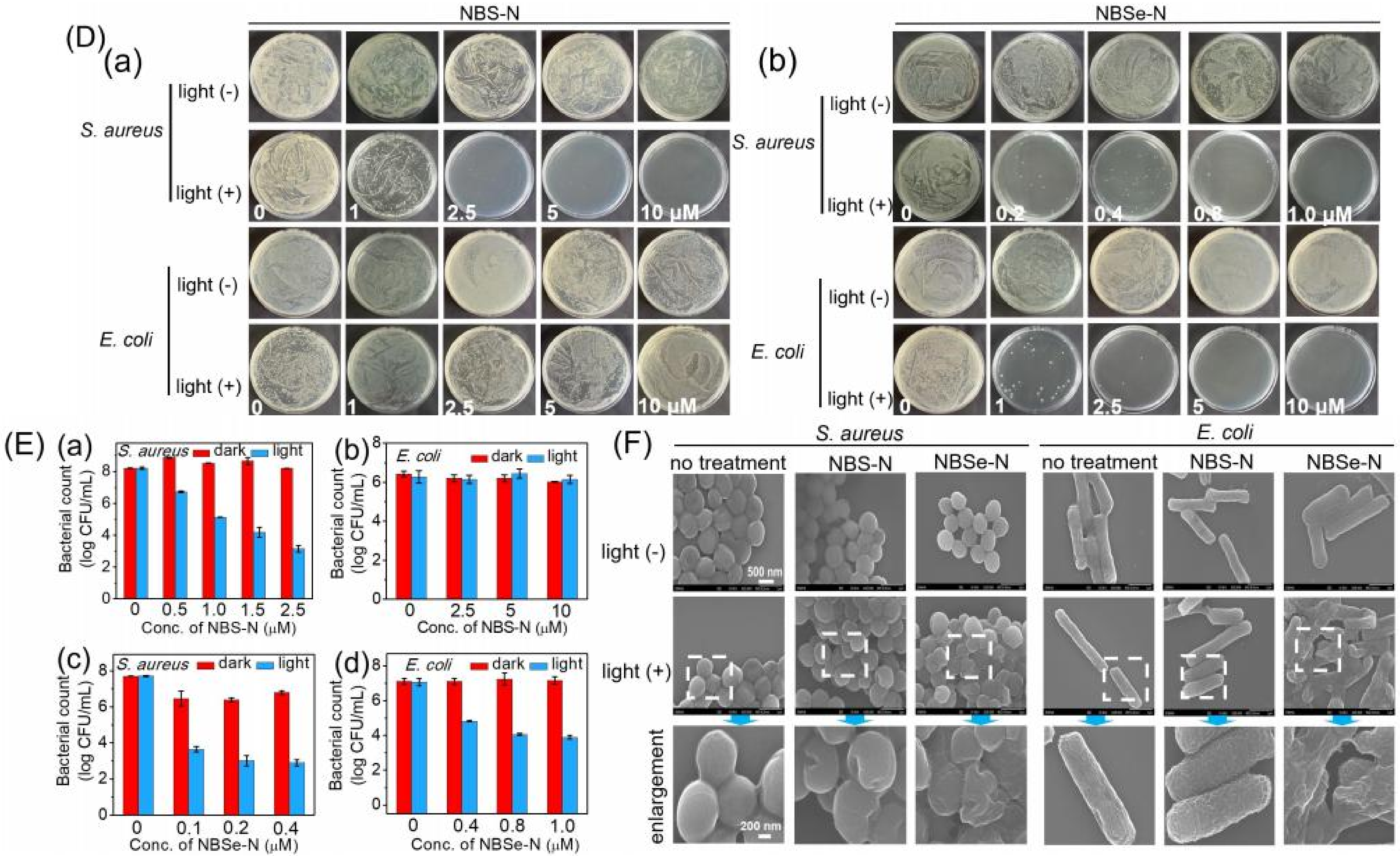
4.Fluorescence imaging and antibacterial test between probes and bacteria.

研究探针与细菌之间的荧光成像和抗菌试验



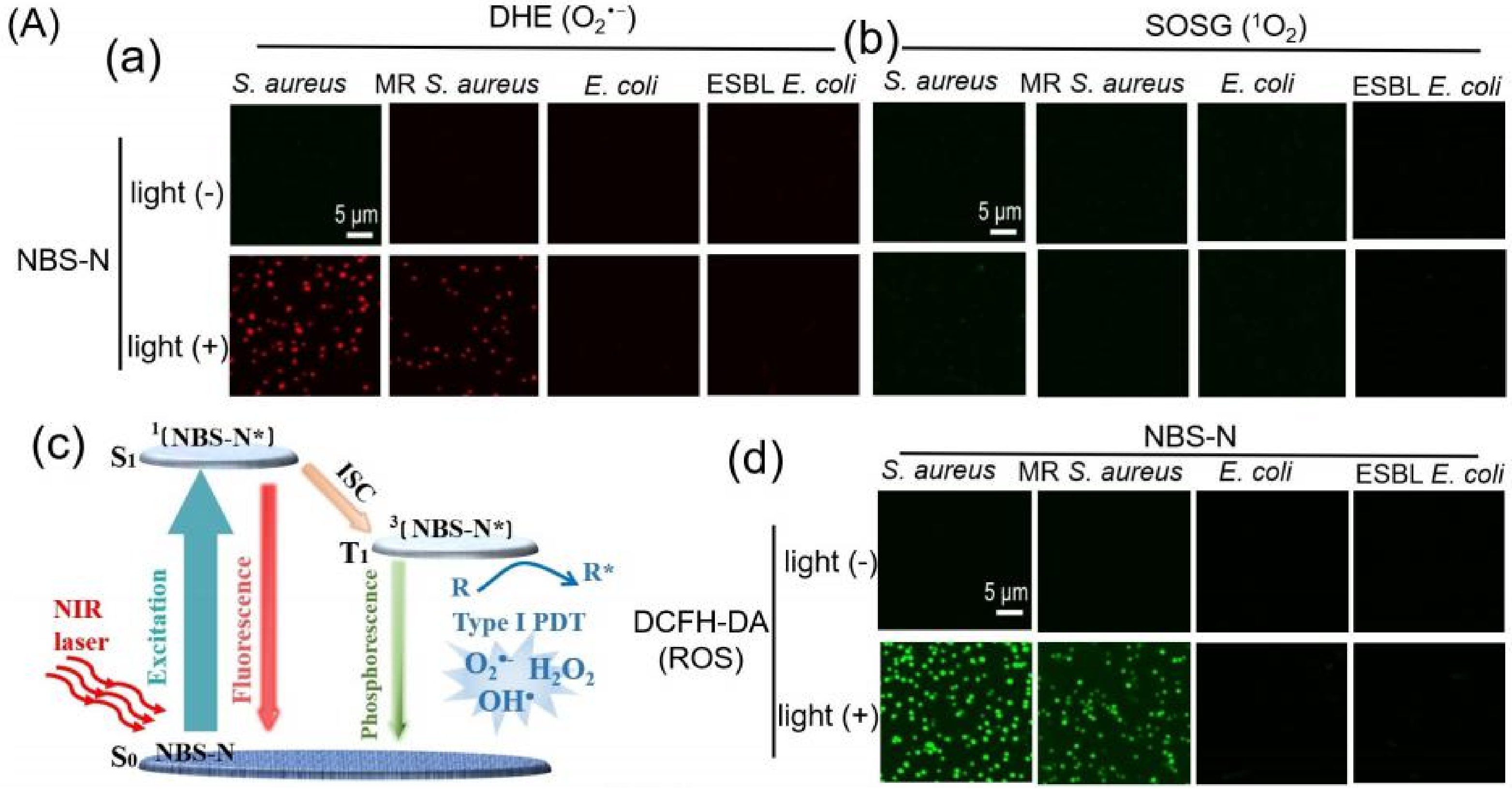
4.Fluorescence imaging and antibacterial test between probes and bacteria.

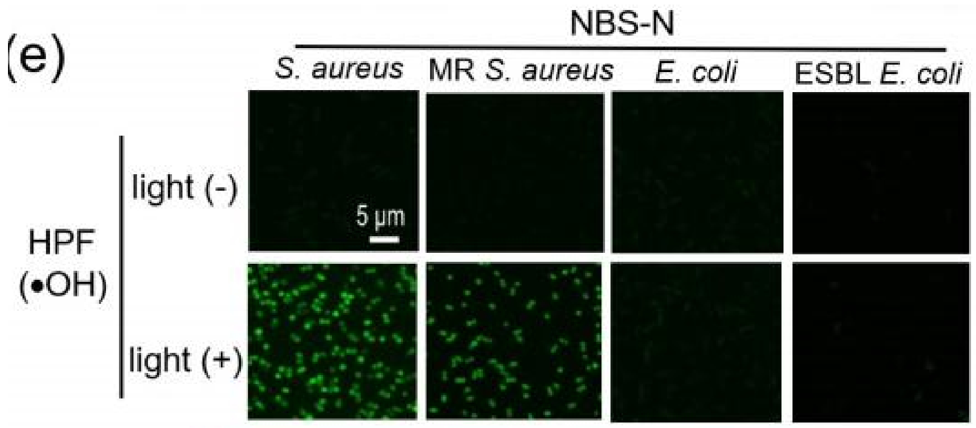
探针是否能选择性消除G+



5.Fluorescence imaging of various generated ROS in bacteria using fluorescence indicators

利用荧光指标对探针在细菌中产生的ROS成像





1. SOD-mediated disproportionated reaction

$$O_2^{\bullet-} + H^+ \xrightarrow{SOD} H_2O_2 + O_2$$

2. Fenton reaction

$$Fe^{3+} + O_2^{\bullet-} \longrightarrow Fe^{2+} + O_2^{\bullet-}$$

$$Fe^{2+} + H_2O_2 \longrightarrow Fe^{3+} + OH^- + \bullet OH$$

3. Harber-Weiss rection

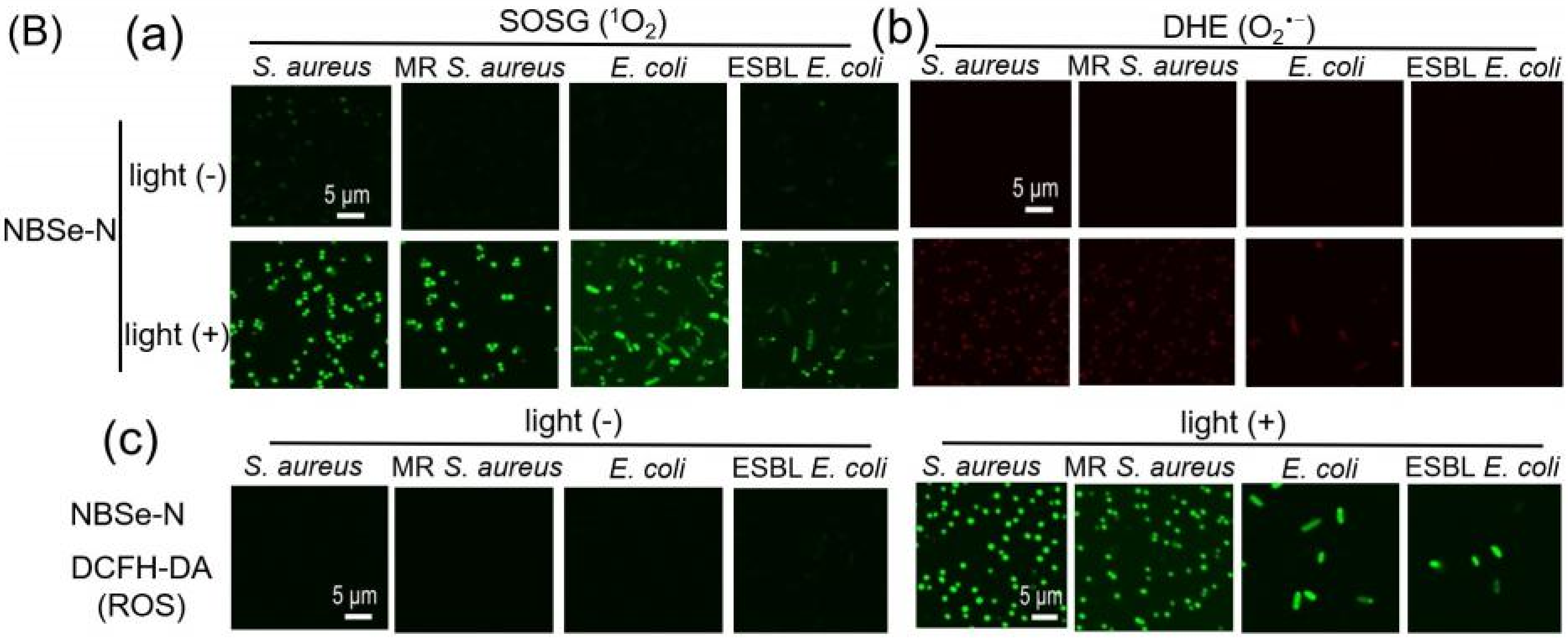
$$H_2O_2 + O_2^{\bullet-} \longrightarrow OH^- + \bullet OH + O_2$$

ISC：非辐射跃迁

表明NBS-N是设计的一个特定O2-的发生器

羟基苯基荧光素（HPF）：OH指示剂

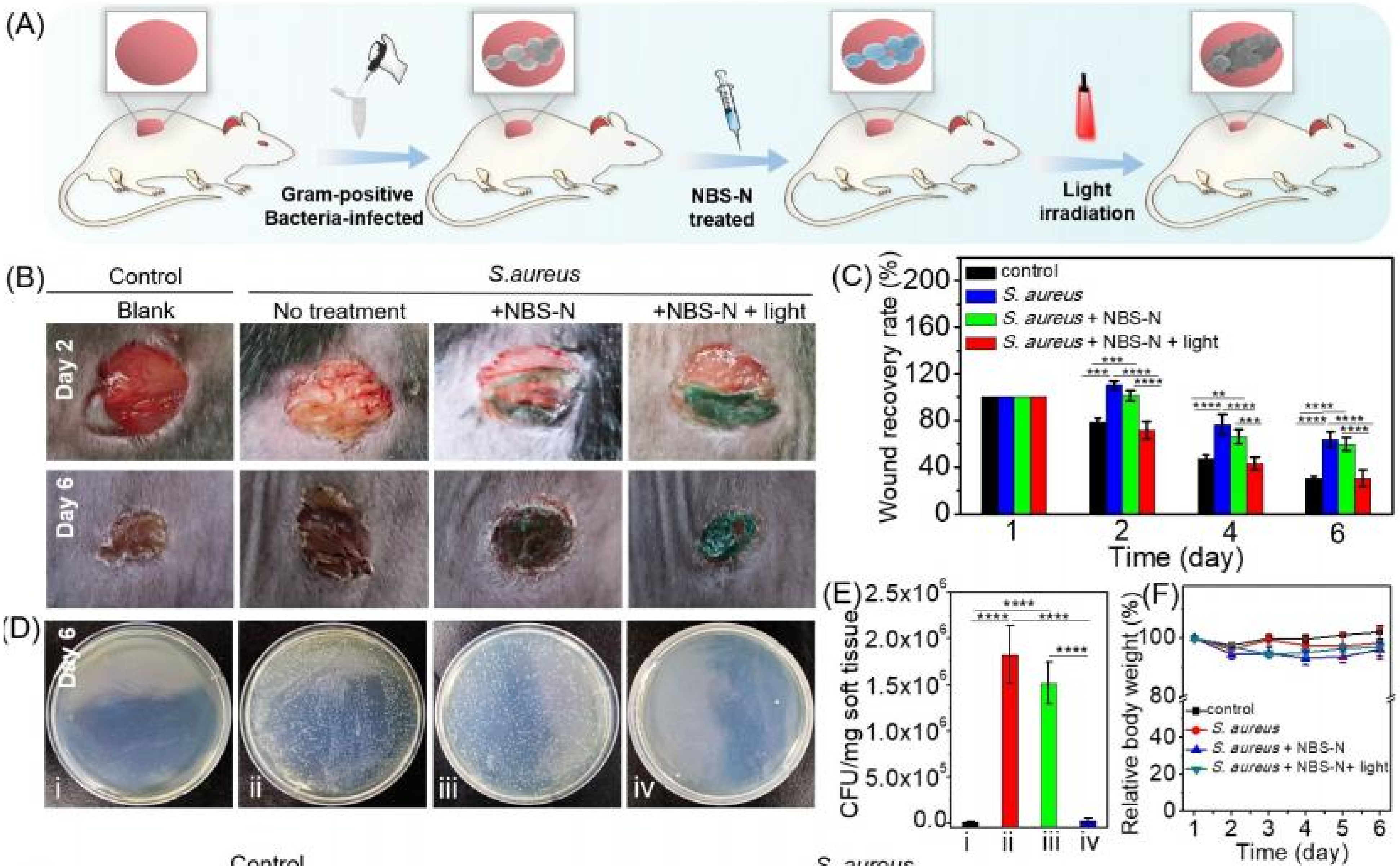
5.Fluorescence imaging of various generated ROS in bacteria using fluorescence indicators



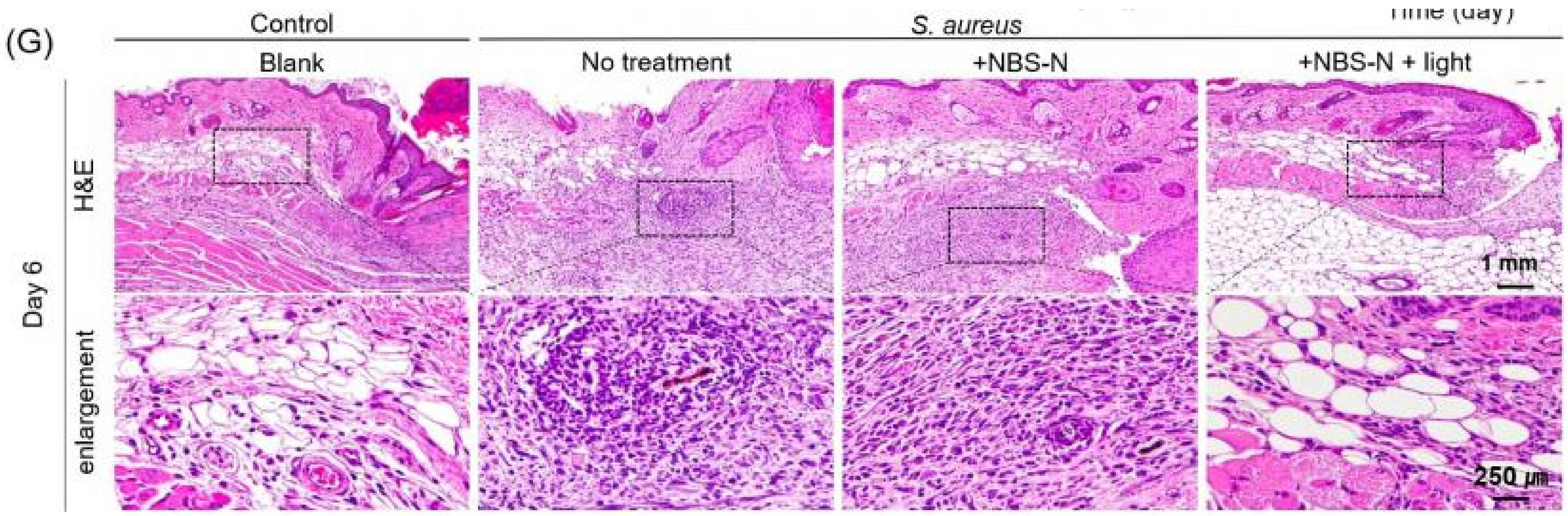
研究NBSe-N的1o2生成，强1o2的NBSe-N同时杀死G+和G-（广谱杀菌剂）

数据结果充分说明ROS反应活性差异可以导致对G+选择性消除

6.In vivo antibacterial evaluation of NBS-N on the S. aureus-infected wounds on mice.



6.In vivo antibacterial evaluation of NBS-N on the S. aureus-infected wounds on mice.



第六天感染组织的HE染色支持NBS-N对S.aureus的光诱导抗菌能力

Inspiration

本篇文章开发了两种化合物来证明ROS的反应性差异可能诱导革兰氏阳性细菌的选择性消融。（NBS-N）一种主要产生o2-，对革兰氏阳性细菌具有良好的选择性，而（NBSe-N）另一种主要产生更高一代的1o2，但对细菌没有选择性。这种差异可能为设计光动力剂选择性消融革兰氏阳性细菌开展了新的途径。

这可能是第一个基于ROS反应性的差异设计出选择性杀死细菌的光敏剂的研究，这可能为设计针对革兰氏阳性细菌及其耐药细菌的选择性抗菌剂开展了新的道路。